Wine, Liquor, Beer, and Mortality

Arthur L. Klatsky1,2, Gary D. Friedman2, Mary Anne Armstrong2, and Harald Kipp2

1 Division of Cardiology, Department of Medicine, Kaiser Permanente Medical Center, Oakland, CA.
2 Division of Research, Kaiser Permanente Medical Care Program, Oakland, CA.

Received for publication July 11, 2002; accepted for publication March 25, 2003.

A substantially increased risk for heavy drinkers and a slightly reduced risk for lighter drinkers results in the J-shaped alcohol-mortality curve. Limited data suggest a more favorable mortality experience for drinkers of wine than for drinkers of liquor or beer. To examine these relations, the authors performed a cohort study of participants in a large Northern California prepaid health care program. Demographic and history data were collected from 128,934 adults undergoing health evaluations in 1978–1985, with subsequent death ascertained by an automated linkage system. Cox proportional hazards models with eight covariates were used to determine relative risk estimates according to total alcohol intake and days per week of drinking wine, wine types, beer, or liquor. The J-shaped alcohol-mortality relation was stable for 20 years. Independently, frequency of wine drinking was associated with lower mortality risk (p < 0.001) largely because of lower coronary disease risk. Similar risk reductions were associated with red wine, white wine, other types of wine, and combinations of wine types. Much of the lower risk associated with light drinking was related to wine drinking. The authors conclude that drinkers of any type of wine have a lower mortality risk than do beer or liquor drinkers, but it remains unclear whether this reduced risk is due to nonalcoholic wine ingredients, drinking pattern, or associated traits.

alcohol drinking; alcoholic beverages; beer; mortality; risk; wine

Abbreviations: CI, confidence interval; ICD-9, International Classification of Diseases, Ninth Revision.

A balanced view of alcohol drinking and health should consider harmful and beneficial effects, amount of alcohol, beverage choice, and drinking patterns. Mortality has been studied as one specific global measure. Heavy drinking, defined as usual daily intake of three or more standard-sized drinks, carries excess mortality from cardiovascular and noncardiovascular causes (1–13), presumably due to both physiologic effects of alcohol and behavioral traits of heavy drinkers. It is unclear whether choice of wine, liquor, or beer plays a role in the adverse effects of heavy alcohol drinking, and relatively few studies have examined this aspect.

Lighter drinking carries lower total mortality risk (1–16), largely because of lower coronary disease risk. Behavioral traits of light drinkers compared with those of abstainers probably also play some role in the lower risk for light drinkers. However, demonstration of plausible protective mechanisms of alcohol against coronary disease, including an effect via high density lipoprotein cholesterol and anti-thrombotic actions (17–24), has resulted in widespread acceptance of a protective hypothesis (25–30).

Interest in possible additional benefits of wine developed when international comparisons (31, 32) showed that persons in wine-drinking countries had a lower coronary disease mortality risk than persons in countries where the preponderant beverages were beer or liquor. Further support came from demonstration of potentially protective non-alcohol antioxidant and anti-thrombotic compounds in wine, especially red wine (25, 33–35). Prospective population studies have provided no consensus that wine is more protective than liquor or beer against coronary disease (36–41).

Limited data exist about beverage choice and total mortality. Danish studies show that wine drinkers, compared with beer or liquor drinkers, have lower risks of total mortality (42, 43), cancer (44), and stroke (45), and a French report indicates lower total and cardiovascular disease mortality (46). Attention to behavioral and other user trait
differences (36–50) has generally found more favorable health traits among wine drinkers.

A Kaiser Permanente (Oakland, California) report of 4,501 deaths in 1978–1988 among 128,934 persons (8) compared subsets (29 percent of deaths) of those who drank preponderantly wine, beer, or liquor (“preferrers”). Wine and beer preferrers had a nonsignificantly lower total mortality risk; the relative risk versus liquor preferrers was 0.9 for each type (p > 0.05). Wine preferrers had a lower cardiovascular mortality risk (relative risk vs. liquor = 0.7, p = 0.01), but beer drinkers did not (relative risk vs. liquor = 0.9, p = 0.2). With more data needed, here we present findings involving 10 additional follow-up years with a total of 16,431 deaths. A more comprehensive analysis of the role of beverage choice is the major focus.

MATERIALS AND METHODS

Subjects and data

The Institutional Review Board of the Kaiser Permanente Medical Care Program approved the study protocols. Baseline data were derived from 1978–1985 health examinations of 128,934 adults in San Francisco and Oakland, California. Voluntarily taken as a health appraisal, the examination included health measurements and queries about sociodemographic status, habits, and medical history (51). Usable data about alcohol were supplied by 79.8 percent of examinees. Persons not supplying data consisted largely of those taking the examination in the absence of the special alcohol questionnaire research clerk and those who declined (largely persons who were not fluent in English).

Lifelong abstainers (n = 15,498) were defined as persons who reported no alcohol drinking during the past year and “never or almost never” drinking. Ex-drinkers (n = 4,194) were nondrinkers during the previous year who indicated prior drinking. Current drinkers reported usual amount as less than once per month (“special occasions only”), more than once per month but less than one drink per day, or daily number of drinks: one or two, three to five, six to eight, and nine or more. Size of “drinks” was not specified in this query. Drinkers received separate questions (47) about the number of days per week that they drank wine, liquor, or beer. Wine drinkers were asked to write in “type(s) of wine you usually drink,” leading to classification as red table wine only (n = 3,128), white table wine only (n = 10,762), both red and white table wine (n = 15,461), and “other specified” wine (fortified, champagne, rose, combinations) (n = 4,619) as well as wine drinkers who did not respond to the “type of wine” query (n = 33,388). Table 1 presents selected further details about the study population.

Mortality ascertainment

We followed subjects through December 1998 or known death by using an automated matching system (52) to ascertain death in California. We accepted primary International Classification of Diseases, Ninth Revision (ICD-9) death certificate codes, converting from International Classification of Diseases, Eighth Revision codes when necessary. We studied deaths from all causes, cardiovascular causes (ICD-9 codes 390–459), noncardiovascular causes (all except ICD-9 codes 390–459), cancer (ICD-9 codes 140–209), coronary disease (ICD-9 codes 410–414), respiratory conditions (ICD-9 codes 460–519), liver disease/cirrhosis (ICD-9 code 571), and unnatural causes (ICD-9 codes 800–999). Presumption of complete follow-up yielded a calculated 2,211,000 person-years, but estimates (52) suggest a sensitivity of 89 percent for the method used.

Analytical methods

We used Cox proportional hazards models determined by the PHREG procedure of Statistical Analysis System software, release 6.12 (SAS Institute, Inc., Cary, North Carolina). Covariates in multivariate models included age, sex, race, education (no college, some college, college graduate), marital status (now married, never married, formerly married), body mass index (weight (kg)/height (m)^2), cigarette smoking (never, ex-smoker, <1 pack/day, ≥1 pack/day), and a composite of affirmative responses (any “yes”) to 12 coronary disease risk or symptom items (47, 53). An indicator of drinking variability (47), constructed from queries about drinking on weekends versus weekdays, during the past day or week versus usual, and during the past year versus the past 10 years, was a covariate in some models.

We studied total alcohol drinking categorically, with lifelong abstainers used as the referent for ex-drinkers and five drinking categories. Some models included four drinking categories, up to three or more drinks per day. Analyses of beverage choice excluded lifelong abstainers, ex-drinkers, and drinkers reporting drinking less than once per month. All analyses of beverage choice presented here were controlled for total alcohol intake by using as the referent for total alcohol persons reporting alcohol drinking more than monthly but less than one drink per day. In most models, choice of wine, liquor, and beer was a continuous variable derived from days per week for each type, with the following assigned values: never or almost never, 0.0; once per week or less, 0.5; 2–3 days per week, 2.5; 4–5 days per week, 4.5; and daily or almost daily, 6.5. The models for type of wine were identical except that wine days per week was categorized into subgroups. The beverage types and wine types in these analyses were modeled simultaneously. The number of days per week for the beverage types showed good correlation with the number of drinks per week of the types in a 1984–1985 subset (47).

For drinkers who drank more than once per month, we defined beverage preference as drinking one beverage type exclusively or on more days per week than either of the other two types (47). Drinkers without a preference reported two or three types with equal frequency. We studied total alcohol intake in these groups and for all persons who reported drinking wine, beer, or liquor 2 or more days per week. We also compared those who preferred wine, liquor, or beer with nonpreferrers. To further compare drinkers of the beverage types, we studied those who exclusively reported each type (i.e., drank none of the other two types).

In this paper, we present results as relative risks with 95 percent confidence intervals and associated p values.
RESULTS

Relations of total alcohol intake to mortality

The mean baseline age of the study population was 40.6 years; of the 16,431 persons who later died, it was 60.8 years (mean age at death, 69.5 years). Multivariate data showed that heavy and ex-drinkers had an increased relative risk of total mortality (table 2), consistent in subgroups of race, age brackets, smoking, and interval to death (data not shown). Lighter drinkers had a lower relative risk of total mortality, which was more evident for women (p > 0.05 for men); this finding was otherwise fairly consistent in subgroups (data not shown).

Of all 16,431 deaths, 62 percent (n = 10,150) were attributed to noncardiovascular causes, the three largest subsets being cancer (n = 4,878), respiratory conditions (n = 1,412), and unnatural causes (n = 949). Of 6,281 (38 percent of the total) deaths attributed to cardiovascular causes, about half (n = 3,049) were due to coronary disease. An increased relative risk for heavy drinkers came substantially from cancer, liver cirrhosis, respiratory conditions, and unnatural causes, with a slight contribution from cardiovascular causes. The increased relative risk for ex-drinkers was largely attributable to cancer, cirrhosis, respiratory conditions, and cardiovascular causes. Women who reported light drinking had a lower relative risk of death from coronary and respiratory disease. Male light drinkers had less of a reduction than women in the relative risk of coronary disease death, but the p value was 0.003 for one or two drinks per day, with consistency in race groups (data not shown). Male light drinkers had no reduced relative risk of respiratory death.

Mortality from all causes in beverage choice groups

For heavy drinkers, the increased total mortality risk was lower for those drinking beer 2 or more days per week than for those drinking either wine or liquor 2 or more days per week (table 3). Light drinkers who reported drinking either beer or wine 2 or more days per week, but not liquor, had a lower total mortality risk. The increased risk for heavy...
drinking was lower in preponderant (“preferrers”) and exclusive wine drinkers than in corresponding liquor and beer subsets. Only two deaths occurred in heavy, exclusive wine drinkers, limiting data interpretation.

**Frequency of beverage choice and risk of death**

Independent of total alcohol intake, wine drinking frequency was associated with lower risk of total mortality and several other endpoints, most notably coronary disease and respiratory deaths (table 4). Respiratory death results were similar for influenza/pneumonia (ICD-9 codes 480–487, n = 664) and chronic respiratory conditions (ICD-9 codes 490–496, n = 532) (data not shown). Only a slightly lower risk of cancer was associated with wine drinking frequency, and deaths from cirrhosis and unnatural causes were not inversely related to wine drinking frequency. Frequency of liquor drinking was independently related to higher cirrhosis risk, and beer drinking frequency was weakly related to increased noncardiovascular risk among women.

The relative risks shown in this paper represent risks per days per week. We also performed analyses with beverage types entered as categories of days per week. When the analyses were conducted in this way, the relative risks of coronary disease mortality for categories of wine drinking frequency were 0.94 (p = 0.3) for less than once per week, 0.84 (p = 0.04) for 2–3 days per week, 0.77 (p = 0.04) for 4–5 days per week, and 0.67 (p < 0.001) for daily or almost daily. For coronary disease mortality in men, the relative risk for drinking wine daily or almost daily was 0.78 (p = 0.02); for women, it was 0.48 (p < 0.001). For all persons, the relative risk of coronary disease mortality for daily or almost daily drinking of liquor was 0.99 (p = 0.9); for beer, it was 0.92 (p = 0.4).

The variability index was independently related to risk of death (data not shown). However, its introduction into the model had little effect on the relations of beverage type to risk of death (data not shown).

The lower risk of death for wine drinkers was consistent in subsets of age, smoking, education, and death date. This paper presents details for smoking and death date subsets. For total mortality, the relative risks for wine drinking per day per week were 0.97 (95 percent confidence interval (CI): 0.95, 0.99) for never smokers, 0.96 (95 percent CI: 0.94, 0.98) for ex-smokers, and 0.96 (95 percent CI: 0.95, 0.98) for

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**Table 2. Adjusted risk of death† through 1998 for all persons from all causes and various diagnoses according to total alcohol intake compared with abstinence, Northern California**

<table>
<thead>
<tr>
<th>Relative risk for each drinking category†</th>
<th>Deaths (no.)</th>
<th>Ex-dinker</th>
<th>&lt;1 drink/month</th>
<th>&gt;1 drink/month:</th>
<th>1–2 drinks/day</th>
<th>3–5 drinks/day</th>
<th>≥6 drinks/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>16,431</td>
<td>1.2**</td>
<td>1.0</td>
<td>0.9**</td>
<td>0.9**</td>
<td>1.1</td>
<td>1.4**</td>
</tr>
<tr>
<td>Men</td>
<td>9,102</td>
<td>1.3**</td>
<td>1.1</td>
<td>0.9</td>
<td>0.9</td>
<td>1.1</td>
<td>1.5**</td>
</tr>
<tr>
<td>Women</td>
<td>7,329</td>
<td>1.2**</td>
<td>0.9†</td>
<td>0.8**</td>
<td>0.9**</td>
<td>1.1</td>
<td>1.6**</td>
</tr>
<tr>
<td>Noncardiovascular causes</td>
<td>10,150</td>
<td>1.3**</td>
<td>1.0</td>
<td>0.9</td>
<td>1.0</td>
<td>1.2**</td>
<td>1.6**</td>
</tr>
<tr>
<td>Men</td>
<td>5,651</td>
<td>1.3*</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1*</td>
<td>1.5**</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>4,499</td>
<td>1.3**</td>
<td>1.0</td>
<td>0.9</td>
<td>1.0</td>
<td>1.2†</td>
<td>1.9**</td>
</tr>
<tr>
<td>Cardiovascular causes</td>
<td>6,281</td>
<td>1.1†</td>
<td>1.0</td>
<td>0.8**</td>
<td>0.8**</td>
<td>0.9†</td>
<td>1.1</td>
</tr>
<tr>
<td>Men</td>
<td>3,451</td>
<td>1.3*</td>
<td>1.2†</td>
<td>1.0</td>
<td>0.9</td>
<td>0.9</td>
<td>1.3†</td>
</tr>
<tr>
<td>Women</td>
<td>2,830</td>
<td>1.0</td>
<td>0.9</td>
<td>0.7**</td>
<td>0.8**</td>
<td>0.9</td>
<td>1.1</td>
</tr>
<tr>
<td>Coronary disease</td>
<td>3,054</td>
<td>1.2</td>
<td>1.0</td>
<td>0.8**</td>
<td>0.7**</td>
<td>0.8*</td>
<td>1.0</td>
</tr>
<tr>
<td>Men</td>
<td>1,855</td>
<td>1.3†</td>
<td>1.1</td>
<td>0.9</td>
<td>0.8*</td>
<td>0.8</td>
<td>1.1</td>
</tr>
<tr>
<td>Women</td>
<td>1,199</td>
<td>1.1</td>
<td>0.9</td>
<td>0.6**</td>
<td>0.6**</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Cancer</td>
<td>4,878</td>
<td>1.4**</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.3**</td>
<td>1.4**</td>
</tr>
<tr>
<td>Men</td>
<td>2,536</td>
<td>1.4*</td>
<td>1.2†</td>
<td>1.1</td>
<td>1.1</td>
<td>1.3*</td>
<td>1.4*</td>
</tr>
<tr>
<td>Women</td>
<td>2,342</td>
<td>1.4*</td>
<td>1.0</td>
<td>1.0</td>
<td>1.1</td>
<td>1.3*</td>
<td>1.7*</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>232</td>
<td>3.4*</td>
<td>0.9</td>
<td>1.2</td>
<td>2.7*</td>
<td>6.9**</td>
<td>14.9**</td>
</tr>
<tr>
<td>Men</td>
<td>146</td>
<td>1.7</td>
<td>0.7</td>
<td>0.5</td>
<td>1.3</td>
<td>3.3*</td>
<td>8.3**</td>
</tr>
<tr>
<td>Women</td>
<td>86</td>
<td>6.5*</td>
<td>1.2</td>
<td>2.5</td>
<td>4.7*</td>
<td>14.2**</td>
<td>15.2**</td>
</tr>
<tr>
<td>Respiratory conditions</td>
<td>1,412</td>
<td>1.4†</td>
<td>0.9</td>
<td>0.8†</td>
<td>0.9</td>
<td>1.3†</td>
<td>1.7*</td>
</tr>
<tr>
<td>Men</td>
<td>754</td>
<td>1.8**</td>
<td>1.1</td>
<td>0.9</td>
<td>1.0</td>
<td>1.7*</td>
<td>2.2**</td>
</tr>
<tr>
<td>Women</td>
<td>658</td>
<td>0.9</td>
<td>0.8</td>
<td>0.7†</td>
<td>0.8</td>
<td>1.0</td>
<td>0.9</td>
</tr>
<tr>
<td>Unnatural causes</td>
<td>949</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.1</td>
<td>1.4†</td>
<td>2.2**</td>
</tr>
<tr>
<td>Men</td>
<td>625</td>
<td>1.0</td>
<td>0.9</td>
<td>1.0</td>
<td>1.0</td>
<td>1.3</td>
<td>1.8†</td>
</tr>
<tr>
<td>Women</td>
<td>324</td>
<td>1.3</td>
<td>1.3</td>
<td>1.2</td>
<td>1.4</td>
<td>1.2</td>
<td>5.0**</td>
</tr>
</tbody>
</table>

* p < 0.01; ** p < 0.001.
† Computed by using Cox proportional hazards models controlled for age, sex, race, body mass index, education, marital status, smoking, and a coronary disease risk/symptoms variable; referent, lifelong abstainers.
Wine, Liquor, Beer, and Mortality

There were 693 deaths among persons reporting drinking any wine but no liquor or beer, and 414 deaths among those reporting drinking any beer but no wine or liquor. Comparing these groups for total mortality risk in multivariate analyses showed the following relative risks: wine versus liquor, 0.82 (95 percent CI: 0.73, 0.92; p < 0.001); wine versus beer, 0.83 (95 percent CI: 0.73, 0.97; p = 0.02); and beer versus liquor, 0.98 (95 percent CI: 0.97, 1.11). This apparent lower risk for wine drinkers was due primarily to the data on women; for example, comparing the wine drinkers with the liquor and beer drinkers combined yielded the following relative risks for wine versus liquor/beer: men, 0.93 (95 percent CI: 0.81, 1.08); women, 0.74 (95 percent CI: 0.64, 0.86; p < 0.001).

Type of wine

Almost identical reductions in risk were associated with drinking either red or white table wine exclusively, both red and white table wine, or “other” wine (table 5). Of the wine groups, men constituted 61 percent of the red only, 41 percent of the white only, 52 percent of the red and white, 58 percent of the other specified, and 49 percent of the unspecified.

Covariate relations

As an indication of comparability with established predictors of coronary disease, a few examples of the relative risks for total mortality follow: male versus female, 1.6 (95 percent CI: 1.6, 1.7); African-American versus White, 1.2 (95 percent CI: 1.1, 1.2); Asian-American versus White, 0.8 (95 percent CI: 0.7, 0.9); college graduate versus no college, 0.8 (95 percent CI: 0.7, 0.8); smoking one or more packs of cigarettes per day versus having never smoked, 2.3 (95 percent CI: 2.2, 2.4); not married versus married, 1.1 (95 percent CI: 1.0, 1.2); and married versus never married, 1.2 (95 percent CI: 1.1, 1.3).

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**TABLE 3. Adjusted risk of death† through 1998 from all causes in various beverage choice groups according to total alcohol intake compared with abstinence, Northern California**

<table>
<thead>
<tr>
<th>Group‡</th>
<th>Deaths (no.)</th>
<th>Relative risk for each drinking category‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;1 drink/day</td>
</tr>
<tr>
<td>Drink wine ≥2 days/week</td>
<td>3,096</td>
<td>0.8***</td>
</tr>
<tr>
<td>Drink liquor ≥2 days/week</td>
<td>4,043</td>
<td>0.9</td>
</tr>
<tr>
<td>Drink beer ≥2 days/week</td>
<td>2,326</td>
<td>0.7**</td>
</tr>
<tr>
<td>Prefer wine</td>
<td>1,575</td>
<td>0.8***</td>
</tr>
<tr>
<td>Prefer liquor</td>
<td>2,207</td>
<td>0.9*</td>
</tr>
<tr>
<td>Prefer beer</td>
<td>1,121</td>
<td>0.9*</td>
</tr>
<tr>
<td>Have no preference</td>
<td>4,653</td>
<td>0.9***</td>
</tr>
<tr>
<td>Drink wine exclusively</td>
<td>378</td>
<td>0.8*</td>
</tr>
<tr>
<td>Drink liquor exclusively</td>
<td>591</td>
<td>0.9</td>
</tr>
<tr>
<td>Drink beer exclusively</td>
<td>252</td>
<td>0.9</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01; *** p < 0.001.
† For persons drinking more than once per month; computed by using Cox proportional hazards models controlled for age, sex, race, body mass index, education, marital status, smoking, and a coronary disease risk/symptoms variable; referent, lifelong abstainers.
‡ Refer to the Materials and Methods section of the text and the footnotes to table 1 for definitions. Each row represents a separate analysis, with lifelong abstainers as the referent for the total drinking amounts.

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Current smokers (p < 0.001 for all three subsets). For death date subsets, the relative risks were 0.95 (95 percent CI: 0.93, 0.96) for deaths in 1978–1988, 0.96 (95 percent CI: 0.94, 0.98) for deaths in 1989–1993, and 0.96 (95 percent CI: 0.94, 0.98) for deaths in 1993–1998 (p < 0.001 for all three subsets). A lower risk related to wine was not observed for African Americans and Asian Americans (data not shown), who drank wine less often than Whites did. Among Whites, African Americans, and Asian Americans, the proportions reporting wine drinking at least 2 days per week were 23.4 percent, 10.1 percent, and 8.9 percent, respectively. In contrast, in 38 total mortality subset analyses for liquor or beer frequency, only one subset (ex-smokers) showed a borderline decreased risk (data not shown).

On the basis of the responses of 12,600 subjects in 1974–1975 to a supplemental query about the number of drinks they consumed per day of each beverage type (47), we estimated that beverage preferers consumed, on average, 80–90 percent of their drinks as the preferred beverage. Data showed less risk for wine preferers, especially of cardiovascular deaths, and a higher risk of noncardiovascular death for liquor preferers. When nonpreferers were used as the referent and we controlled for total alcohol intake, the relative risks of noncardiovascular death for preferers were 0.89 (95 percent CI: 0.82, 0.95) for wine (p < 0.001), 1.08 (95 percent CI: 1.01, 1.16) for liquor (p = 0.02), and 1.05 (95 percent CI: 0.97, 1.14) for beer. For cardiovascular death, the corresponding relative risks were 0.78 (95 percent CI: 0.70, 0.86) for wine (p < 0.001), 1.02 (95 percent CI: 0.93, 1.12) for liquor, and 1.02 (95 percent CI: 0.90, 1.16) for beer. For coronary disease deaths, the relative risks were 0.72 for wine preferers (p < 0.001), 0.79 for men (p = 0.007), and 0.62 for women (p < 0.001).

There were 693 deaths among persons reporting drinking any wine but no liquor or beer, and 601 deaths among those who reported drinking any liquor but no beer or wine, and 414 deaths among those reporting drinking any beer but no wine or liquor. Comparing these groups for total mortality risk in multivariate analyses showed the following relative risks: wine versus liquor, 0.82 (95 percent CI: 0.73, 0.92; p < 0.001); wine versus beer, 0.83 (95 percent CI: 0.73, 0.97; p = 0.02); and beer versus liquor, 0.98 (95 percent CI: 0.97, 1.11). This apparent lower risk for wine drinkers was due primarily to the data on women; for example, comparing the wine drinkers with the liquor and beer drinkers combined yielded the following relative risks for wine versus liquor/beer: men, 0.93 (95 percent CI: 0.81, 1.08); women, 0.74 (95 percent CI: 0.64, 0.86; p < 0.001).
 Baptiste et al.  

**DISCUSSION**

**Wine drinking and risk**

The major finding in these data was the independent relation of wine drinking frequency to lower total mortality risk. This interpretation was buttressed by consistency in most population subsets. Perhaps most convincing was the lower risk associated with wine drinking frequency at each of three total drinking levels (less than one, one or two, and three or more drinks per day). The reduction in wine-related risk was clearest for deaths attributed to coronary disease and respiratory causes.

**Problems of interpretation and confounding**

Since any independent effect of wine on mortality is likely to be additional to the role of alcohol, interpretive problems are substantial. Although data from populations that drink preponderantly wine (e.g., Mediterranean countries) show a lower risk of coronary disease death than do data from other countries (31, 32), these studies lacked information about individuals and thus were inadequately controlled for major confounders. International differences in coding criteria may also play a role, since the Mediterranean countries do not enjoy greater overall longevity than other developed countries (32). Prospective cohort studies using data about individuals have shown statistically significant inverse relations of light drinking to coronary disease for beer (2, 8, 37), liquor (16, 37), and wine (36, 37, 42, 43, 46) and tend to show inverse, nonsignificant relations for all beverage types (38, 39).

Persons in Northern California who drink preponderantly wine are more often women, college graduates, nonsmokers,
and temperate drinkers, characteristics even more pronounced in persons drinking wine exclusively (47). In Denmark, wine drinking is associated with better perceptions of overall health (49), higher socioeconomic status and intelligence quotients (50), and intake of a "healthy" diet (high in fruits, vegetables, fish, salads, and olive oil) (48). Higher socioeconomic status is associated with good health, and healthy habits tend to be clustered in the same person (54–56). A report on University of North Carolina alumni (57) showed that wine drinkers had healthier lifestyle habits than did consumers of other beverage types. Since drinking pattern probably has a role in health effects (38, 43, 58–60), the usual pattern of ingesting wine slowly with food may be important. In this context, a recent report that beer drinkers are more likely than wine drinkers to progress to heavier drinking is both interesting and potentially important (61). In a comprehensive review of possible benefits of wine additional to those of alcohol (62), the conclusion was reached that confounding is a likely factor. We agree that uncontrolled traits in our analyses (e.g., dietary, exercise) were

### Table 5. Adjusted risk of death† through 1998 for selected diagnoses per day per week of intake of wine types, Northern California

<table>
<thead>
<tr>
<th>Wine type (no. of deaths)</th>
<th>Red only (n = 355)</th>
<th>White only (n = 808)</th>
<th>Red and white (n = 1,635)</th>
<th>Other specified (n = 572)</th>
<th>Unspecified (n = 3,556)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All causes</td>
<td>0.97**</td>
<td>0.96***</td>
<td>0.97***</td>
<td>0.98*</td>
<td>0.97***</td>
</tr>
<tr>
<td>Men</td>
<td>0.97**</td>
<td>0.99</td>
<td>0.97**</td>
<td>0.99</td>
<td>0.97***</td>
</tr>
<tr>
<td>Women</td>
<td>0.98*</td>
<td>0.94***</td>
<td>0.96***</td>
<td>0.96*</td>
<td>0.96*</td>
</tr>
<tr>
<td>All cardiovascular causes</td>
<td>0.94**</td>
<td>0.95**</td>
<td>0.96**</td>
<td>0.98</td>
<td>0.96***</td>
</tr>
<tr>
<td>Men</td>
<td>0.94*</td>
<td>0.95*</td>
<td>0.98</td>
<td>0.99</td>
<td>0.96**</td>
</tr>
<tr>
<td>Women</td>
<td>0.97</td>
<td>0.93*</td>
<td>0.92***</td>
<td>0.95</td>
<td>0.95*</td>
</tr>
<tr>
<td>All noncardiovascular causes</td>
<td>0.98</td>
<td>0.97</td>
<td>0.97***</td>
<td>0.98</td>
<td>0.97**</td>
</tr>
<tr>
<td>Men</td>
<td>0.99</td>
<td>1.00</td>
<td>0.97**</td>
<td>0.99</td>
<td>0.98*</td>
</tr>
<tr>
<td>Women</td>
<td>0.98</td>
<td>0.94**</td>
<td>0.96*</td>
<td>0.96</td>
<td>0.97*</td>
</tr>
<tr>
<td>Coronary disease</td>
<td>0.94*</td>
<td>0.95*</td>
<td>0.98</td>
<td>0.94*</td>
<td>0.93***</td>
</tr>
<tr>
<td>Men</td>
<td>0.95</td>
<td>0.98</td>
<td>1.00</td>
<td>0.95</td>
<td>0.94**</td>
</tr>
<tr>
<td>Women</td>
<td>0.93</td>
<td>0.89*</td>
<td>0.92*</td>
<td>0.91</td>
<td>0.92*</td>
</tr>
</tbody>
</table>

* p < 0.05 but ≥ 0.01; ** p < 0.01 but ≥ 0.001; *** p < 0.001.
† For persons drinking more than once per month; controlled for age, sex, race, education, marital status, smoking, body mass index, total alcohol intake, and days/week of liquor and beer drinking. Refer to the Materials and Methods section of the text for definitions of wine types.

### Table 6. Adjusted risk of death† through 1998 from coronary disease in beverage choice groups according to total alcohol intake compared with abstainers, Northern California

<table>
<thead>
<tr>
<th>Group (no. of coronary disease deaths)‡</th>
<th>Relative risk for each drinking category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;1 drink/month; 1–2 drinks/day 3–5 drinks/day ≥6 drinks/day</td>
</tr>
<tr>
<td>Drink wine ≥2 days/week (n = 480)</td>
<td>0.7*** 0.6*** 0.6*** 0.8</td>
</tr>
<tr>
<td>Drink liquor ≥2 days/week (n = 686)</td>
<td>0.8*   0.8*   0.8               1.0</td>
</tr>
<tr>
<td>Drink beer ≥2 days/week (n = 329)</td>
<td>0.7*   0.7*** 0.7* 0.9</td>
</tr>
<tr>
<td>Prefer wine (n = 235)</td>
<td>0.6*** 0.5*** 0.6** 1.1</td>
</tr>
<tr>
<td>Prefer liquor (n = 383)</td>
<td>0.7**  0.8*   0.9               1.0</td>
</tr>
<tr>
<td>Prefer beer (n = 140)</td>
<td>0.6**  0.6*** 0.8               1.0</td>
</tr>
<tr>
<td>Have no preference (n = 831)</td>
<td>0.7    0.6**  1.0               1.1</td>
</tr>
<tr>
<td>Drink wine exclusively (n = 109)</td>
<td>0.5**  0.4*** 0.9               0.7</td>
</tr>
<tr>
<td>Drink liquor exclusively (n = 186)</td>
<td>0.5*   1.0               1.6</td>
</tr>
<tr>
<td>Drink beer exclusively (n = 62)</td>
<td>0.3*   0.7               0.8</td>
</tr>
</tbody>
</table>

* p < 0.05; ** p < 0.01; *** p < 0.001.
† Computed by using Cox proportional hazards models controlled for age, sex, race, body mass index, education, marital status, smoking, and coronary disease risk/symptoms variable; referent, lifelong abstainers.
‡ Refer to the Materials and Methods section of the text and the footnotes to table 1 for definitions.
probably more favorable to wine drinkers, making some of the apparent additional benefit of wine due to residual confounding.

Protective wine ingredients

Antioxidant and antithrombotic substances, mostly in red wine and potentially beneficial against atherothrombosis, have been extensively detailed in reviews (35, 38, 41). The hypothesis that these substances protect against coronary disease is appealing, since oxidative modification of low density lipoprotein cholesterol is involved in the development of atherosclerotic plaques. Antioxidant compounds may well be antiatherogenic, yet prospective clinical trials of antioxidant supplements are inconclusive (63–65). Since, in our data, all wine types seemed equally protective, nonalcoholic factors responsible for the lower risk among wine drinkers would have to be present in both red and white wine.

Heavy drinking and beverage choice

Some aspects of these data suggest attenuation of increased risk for heavier wine drinkers compared with heavier liquor or beer drinkers. For example, wine drinking frequency showed less relation to cirrhosis risk than liquor or beer drinking did. Attenuation of increased risk in heavy drinkers preferring or exclusively drinking wine must be interpreted in light of the probability that confounding by “healthy” traits becomes progressively more likely in these groups (47). Of 71,600 persons drinking any beverage type 2 or more days per week, 52 percent were preferers, but only 10 percent were exclusive drinkers of one beverage type. Liquor drinkers are most likely and wine drinkers least likely to consume larger-than-standard drinks (47), another factor probably important in the risk for chronic heavy drinkers.

The risk of alcoholic liver cirrhosis is related primarily to lifetime alcohol intake (66). In countries with preponderant wine drinking, most heavy drinkers drink the prevalent beverage, resulting in reports of other wine-induced disorders, including hypertension (67), cardiomyopathy (68, 69), and peripheral neuropathy (70). It is thus clear that heavy chronic wine drinking carries substantial risks.

The relation of heavy drinking to coronary disease is incompletely resolved (27, 39). Studies of coronary disease mortality have generally shown a U-curve relation to total alcohol intake (27), with heavy drinkers at higher risk than lighter drinkers and, in some studies, abstainers. Some studies of nonfatal coronary disease fail to show an upturn in risk with heavy drinking. Questions arise about misattribution of some deaths to coronary disease (27). Beverage choice for heavy drinkers, via drinking pattern, size of drinks, or risk trait differences, could play a selective role in apparent coronary disease mortality. In particular, a binge pattern among some beer drinkers, with associated deaths from cardiac rhythm disturbances, might account for the disparity between this report of coronary disease mortality and our report (36) that both wine and beer drinking carried a lower risk of nonfatal coronary events.

Total alcohol intake and mortality

The J-shaped alcohol-mortality relation was stable for 20 years in this cohort. With longer follow-up, there was more apparent protection for women regarding coronary disease and total mortality. Thus, the magnitude of the sex disparity among light drinkers increased. This finding is not readily explained by known sex differences in potential mechanisms for alcohol’s benefit, such as increased high density lipoprotein cholesterol levels, antithrombotic effects, endothelial effects, or decreased insulin resistance (23–25, 41). Equivalent alcohol doses do result in higher average blood alcohol levels in women than in men because of women’s smaller size, larger body fat proportion, and reduced gastric metabolism of ethanol (27, 41). More benefit from lighter drinking and more harm from heavy drinking might ensue. Drinking pattern is another probable factor, since men, on average, binge drink more than women (27, 41, 69). If wine is associated with extra benefit, the fact that women in this study were more likely to drink preponderantly wine may also be a factor.

We previously attributed apparent protection from lighter drinking against deaths from respiratory conditions to probable less-overt or -occult coronary disease (8). It is also possible that light drinking and wine drinking in particular are directly protective against death from pneumonia and chronic respiratory conditions, but mechanisms were not evident to us.

Is lower risk due entirely to wine?

In some respects, our findings are in general agreement with those from Danish and French studies that suggest a benefit primarily from wine (42–46). However, our study shows that each beverage type apparently protects against coronary disease mortality (table 6). Previous studies and evidence that protective mechanisms are related to ethyl alcohol mitigate against the hypothesis that only wine offers coronary disease protection (27, 37, 38). Epidemiologic data from beer-drinking populations (2, 11) are especially convincing. Yet, the unexpected strength and consistency in our data showing an apparent additional benefit from wine raises the likelihood of a causal association.

Limitations

Determination of habits only at baseline is a limitation, but drinking amount and beverage preference were relatively stable in this population (37, 71). Additionally, relations of beverage choice to mortality risk were as strong in the last 5 years as for those who died earlier. It is possible that wine drinkers might be more likely than liquor or beer drinkers to persist with their drinking as they become older. A second limitation is our lack of data about wine type for more than 50 percent of wine drinkers and about the proportions of red and white wine consumed by persons reporting both types. However, persons in “red only” and “white only” categories represent clearly defined groups that showed quite similar mortality risks. A third limitation is the already mentioned inability to control for some traits with probable relations to beverage choice and/or mortality risk. There was also prob-
able residual confounding for controlled variables; for example, control for packs per day of cigarette smoking does not fully measure the effective dose of harmful components.

A fourth limitation is ascertainment of deaths only in California. However, while previous pilot studies indicate that 7–17 percent of current or former health care plan members die outside of California (52), we do not believe that these findings are likely to reflect bias related to alcohol drinking or beverage choice. Excluding the known dead, we examined proportions of persons remaining in the health plan in 1998 as a plausible marker for continued residence in California, with the following results: entire cohort, 56.1 percent; drinkers of wine 2 or more days per week, 55.7 percent; and preferers of wine; 56.6 percent. A fifth limitation was our lack of control for drink size, known in this population to be, on average, largest for liquor drinkers and smallest for wine drinkers (47). Thus, “moderate” liquor drinkers might include a larger proportion of heavier drinkers than exists among “moderate” wine drinkers. Finally, like all reported studies of alcoholic beverage choice and mortality, this study was observational. Only a controlled clinical trial can account completely for all confounders.

Conclusions

Frequency of wine drinking but not of liquor or beer drinking was independently related to lower mortality risk, especially for coronary disease and respiratory deaths. Red, white, and other types of wine had similar relations to lower risk. Associated traits and/or drinking patterns among wine drinkers and/or a specific benefit from wine may be involved.

ACKNOWLEDGMENTS

This work was supported by grants from the Alcoholic Beverage Medical Research Foundation of Baltimore, Maryland; the National Institute of Alcoholism and Alcohol Abuse (1 RO1 AA 10830-01); and the Wine Institute of San Francisco, California.

The authors thank Cynthia Landy for assistance with data collection and Sally McBride Allen and Teresa Klask for technical assistance.

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