#### ALCOHOL AND CARDIOVASCULAR DISEASE

https://www.hsph.harvard.edu/nutritionsource/alcohol-full-story/

#### DYNAMED:

## Association of alcohol consumption and cardiovascular disease

- "benefit" of moderate alcohol consumption might be due to misclassification error in published studies
  - o based on systematic review of observational trials
  - systematic review of 54 prospective studies evaluating all-cause mortality and 35 prospective studies of coronary mortality based on classification of alcohol use patterns
  - subjects who reduced or quit drinking (perhaps due to ill health) often classified as abstainers, possibly making abstainers seem less healthy than continued light drinkers and never-drinkers
  - o former drinker misclassification error defined as failure to separate former drinkers (no drink in past year) from complete abstainers
  - occasional drinker misclassification error defined as failure to separate occasional drinkers (drinking once per month or less) from complete abstainers
  - o differences in all-cause mortality compared to complete abstainers
    - analysis of all 54 studies found significant increase in former drinkers and heavy drinkers, and significant decreases in occasional and light drinkers
    - analysis of 26 studies with both errors similar to overall analysis
    - analysis of 21 studies with former drinker misclassification error found significant decrease in light drinkers
    - analysis of 7 studies with neither error found no significant differences, though trends consistent with overall analysis
  - o differences in coronary mortality compared to complete abstainers
    - analysis of all 35 studies found significant increase in former drinkers, and significant decreases in light, moderate and heavy drinkers
    - analysis of 25 studies with both errors similar to overall analysis
    - analysis of 8 studies found no significant differences, though trends consistent with overall analysis
    - analysis of 2 studies with neither error found no significant differences, though trends toward increases in moderate and heavy drinkers
  - Reference <u>Addiction Research and Theory 2006 Apr;14(2):101</u>, discussion by meta-analysis authors can be found in <u>Ann Epidemiol 2007 May;17(5 Suppl):S16</u>
  - apparent benefit of moderate alcohol consumption may be related to increased risk among ex-drinkers in control groups
    - based on study of 22,836 men aged 40-64 years, with 818 deaths
    - moderate alcohol drinkers and never drinkers had similar mortality risks
    - ex-drinkers had 2 times mortality risk
    - Reference JAMA 2001 Sep 12;286(10):1177

- light-to-moderate alcohol consumption associated with decreased all-cause mortality and coronary heart disease mortality
  - o based on 4 systematic reviews of observational studies
  - light-to-moderate alcohol consumption associated with decreased mortality and risk of adverse cardiovascular outcomes
    - based on systematic review of observational studies with heterogeneity
    - systematic review of 84 prospective cohort studies with > 1 million adults evaluating relationship between alcohol consumption and cardiovascular outcomes
    - mean follow-up 11 years
    - compared to nondrinkers (all results limited by significant heterogeneity)
      - alcohol drinking associated with decreased risk of
        - mortality due to cardiovascular disease (relative risk [RR]
          0.75, 95% CI 0.7-0.8) in analysis of 21 studies
        - coronary heart disease (RR 0.71, 95% CI 0.66-0.77) in analysis of 29 studies
        - mortality due to coronary heart disease (RR 0.75, 95% 0.68-0.81) in analysis of 31 studies
        - all-cause mortality (RR 0.87, 95% CI 0.83-0.92) in analysis of 31 studies
      - risk lowest for above outcomes with alcohol intake 2.5-14.9 g/day
        (≤ 1 drink/day)
      - > 60 g/day ( $\ge 5 \text{ drinks/day}$ ) associated with increased risk of
        - all-cause mortality (RR 1.3, 95% CI 1.22-1.38) in analysis of 8 studies
        - stroke (RR 1.62, 95% CI 1.3-1.98) in analysis of 4 studies
    - Reference <u>BMJ 2011 Feb 22;342:d671 full-text</u>, commentary can be found in <u>BMJ 2012 Mar 27;344:e2276</u>
  - o moderate alcohol consumption (up to 4 drinks/day in men or 2 drinks/day in women) associated with lower all-cause mortality
    - based on systematic review of observational studies
    - systematic review of 34 prospective studies evaluating association between alcohol consumption and mortality in 1,015,835 men and women
    - 94,533 deaths occurred
    - alcohol consumption inversely associated with total mortality for up to 4 drinks/day in men and up to 2 drinks/day in women
    - higher amounts of alcohol consumption associated with increased mortality
    - Reference <u>Arch Intern Med 2006 Dec 11;166(22):2437</u>, commentary can be found in <u>ACP J Club 2007 Mar-Apr;146(2):48</u>
  - consumption of 1-3 drinks/day of alcohol may be associated with reduced ischemic heart disease mortality compared to never use
    - based on systematic review of observational studies
    - systematic review of 44 case-control and cohort studies reporting association between alcohol consumption and ischemic heart disease in

- 957,684 adults
- consumption of 2.5-35.99 g/day (1-3 drinks/day) of alcohol associated with reduced ischemic heart disease mortality compared to lifetime abstinence
  - in men
    - relative risk (RR) 0.81 (95% CI 0.74-0.9) for 2.5-11.99 g in analysis of 34 studies, results limited by significant heterogeneity
    - RR 0.74 (95% CI 0.66-0.84) for 12-23.99 g in analysis of 26 studies, results limited by significant heterogeneity
    - RR 0.74 (95% CI 0.63-0.86) for 24-35.99 g in analysis of 20 studies, results limited by significant heterogeneity
  - in women
    - RR 0.77 (95% CI 0.7-0.84) for 2.5-11.99 g in analysis of 18 studies, results limited by significant heterogeneity
    - RR 0.74 (95% CI 0.6-0.9) for 12-23.99 g in analysis of 15 studies, results limited by significant heterogeneity
    - RR 0.67 (95% CI 0.56-0.8) for 24-35.99 g in analysis of 10 studies
- Reference <u>Addiction 2012 Jul;107(7):1246 full-text</u>, editorial can be found in <u>Addiction 2012 Jul;107(7):1261</u>, commentary can be found in <u>Addiction 2013 Feb;108(2):429</u>
- low-to-moderate daily alcohol consumption associated with decreased allcause mortality and risk of cardiovascular disease in patients with hypertension
  - based on systematic review of observational studies
  - systematic review of 9 prospective cohort studies evaluating association between alcohol consumption and risk of all-cause death or cardiovascular disease in 394,840 patients with hypertension
  - alcohol consumption was stratified into 4 categories by grams of alcohol per day, assuming alcohol content 10-12 g per 1 drink
  - compared to abstainers/occasional drinkers (median alcohol consumption 0 g/day)
    - decreased risk of all-cause mortality associated with median alcohol consumption of
      - 10 g/day (relative risk [RR] 0.83, 95% CI 0.77-0.9) in analysis of 4 studies
      - 20 g/day (RR 0.8, 95% CI 0.68-0.95) in analysis of 4 studies, results limited by significant heterogeneity
    - no significant difference in all-cause mortality comparing abstainers/ occasional drinkers to patients with highest (median 30 g/day) alcohol consumption in analysis of 3 studies
    - decreased risk of cardiovascular disease associated with median alcohol consumption of
      - 10 g/day (RR 0.72, 95% CI 0.68-0.77) in analysis of 8

- studies
- 20 g/day (RR 0.81, 95% CI 0.71-0.93) in analysis of 4 studies
- 30 g/day (RR 0.6, 95% CI 0.54-0.67) in analysis of 8 studies
- Reference Mayo Clin Proc 2014 Sep;89(9):1201, commentary can be found in Mayo Clin Proc 2015 Jan;90(1):160
- low-to-moderate alcohol consumption without heavy episodic drinking associated with decreased risk of ischemic heart disease
  - o based on systematic review of observational studies
  - o systematic review of 7 observational studies evaluating alcohol consumption patterns and risk of ischemic heart disease in 225,132 adults
    - low-to-moderate alcohol consumption defined as mean alcohol intake < 30 g/day
    - heavy alcohol consumption defined as mean alcohol intake  $\geq 60$  g/day
  - o compared to lifetime abstainers
    - low-to-moderate alcohol consumption without heavy episodic drinking associated with decreased risk of ischemic heart disease (relative risk 0.64, 95% CI 0.53-0.71) in analysis of all studies
    - no significant difference in risk of ischemic heart disease with low-to-moderate alcohol consumption and heavy episodic drinking (relative risk 1.12, 95% CI 0.91-1.37) in analysis of 5 studies
  - Reference <u>BMC Med 2014 Oct 21;12(1):182 full-text</u>
- moderate alcohol consumption associated with reduced risk for myocardial infarction in healthy men
  - based on 3 cohort studies not included in systematic review noted above
  - o 22,071 male physicians aged 40-84 years followed for 10-13 years
    - 690 developed myocardial infarction and 1,368 had new-onset angina
    - 1 drink/day associated with reduced risk for myocardial infarction (relative risk 0.65, 95% CI 0.52-0.81) and angina (relative risk 0.69, 95% CI 0.59-0.81)
    - ≥ 2 drinks/day associated with reduced risk for myocardial infarction (relative risk 0.53, 95% CI 0.32-0.85) and angina (relative risk 0.44, 95% CI 0.29-0.66)
    - Reference Ann Intern Med 1997 Mar 1;126(5):372
  - o 9,778 men aged 50-59 years without ischemic heart disease followed for 10 years
    - 80% reported regular drinking ( $\ge 1$  day/week and < 50 g on  $\ge 1$  occasion)
    - 2.6% reported binge drinking (> 50 g on ≥ 1 day/week)
    - 3.3% had hard coronary events (myocardial infarction, coronary death)
    - compared to regular drinking, increased risk of developing hard coronary events associated with
      - never drinking (hazard ratio [HR] 2.03, 95% CI 1.41-2.94)
      - binge drinking (HR 1.97, 95% CI 1.21-3.22)
      - former drinking (HR 1.57, 95% CI 1.11-2.21)

- no significant difference in risk of hard coronary events comparing never drinking to binge drinking
- wine drinking associated with decreased risk of hard coronary events compared to non-wine drinking (HR 0.57, 95% CI 0.38-0.85)
- Reference <u>BMJ 2010 Nov 23;341:c6077 full-text</u>
- o 16-year follow-up of 8,867 men free of major illness
  - moderate alcohol consumption (5-29.9 g/day) associated with lower risk for myocardial infarction, even in men with favorable lifestyle behaviors
  - Reference Arch Intern Med 2006 Oct 23;166(19):2145, commentary can be found in Arch Intern Med 2007 May 14;167(9):970
- in men with hypertension, moderate alcohol consumption associated with decreased risk for mortality and myocardial infarction
  - based on 2 cohort studies
  - moderate alcohol consumption associated with decreased risk for mortality and myocardial infarction in men with hypertension
    - based on cohort study
    - 14,125 men with hypertension were followed for 75,710 person-years
    - light-to-moderate alcohol consumption associated with lower mortality in patients with hypertension
    - Reference Arch Intern Med 2004 Mar 22;164(6):623
  - moderate alcohol consumption (> 10 g/day) associated with reduced risk of myocardial infarction but nonsignificant increase in risk of stroke in men with hypertension
    - based on prospective cohort study
    - 11,711 men with hypertension from Health Professionals Follow-Up study were evaluated
    - increasing alcohol consumption associated with decreasing risk of myocardial infarction, fatal coronary heart disease, and nonfatal myocardial infarction compared to alcohol abstinence (p for trend ≤ 0.018 for each)
    - alcohol consumption not significantly associated with risk of all-cause mortality or cardiovascular-related mortality compared to alcohol abstinence
    - moderate alcohol consumption (10-29.9 g/day) associated with nonsignificantly increased risk of total stroke (hazard ratio 1.4, 95% CI 0.93-2.12) and ischemic stroke (hazard ratio 1.55, 95% CI 0.9-2.68) compared to alcohol abstinence
    - Reference <u>Ann Intern Med 2007 Jan 2;146(1):10</u>, editorial can be found in <u>Ann Intern Med 2007 Jan 2;146(1):65</u>
- light-to-moderate alcohol consumption (2.5-24 g/day) associated with lower cardiovascular and all-cause mortality in patients with cardiovascular disease
  - o based on systematic review of observational studies
  - systematic review of 8 studies reporting alcohol consumption and cardiovascular and total mortality in 16,351 patients with history of cardiovascular events
  - alcohol consumption associated with
    - 22% reduction in all-cause mortality for 2.5-8 g/day (95% CI 2-39%) in

- analysis of 7 studies with 16,398 patients
- 26% reduction in cardiovascular mortality for 8-24 g/day (95% CI 13-37%) in analysis of 7 studies with 12,819 patients
- Reference J Am Coll Cardiol 2010 Mar 30;55(13):1339
- moderate alcohol use associated with improved cardiovascular biomarkers (<u>level 3</u> [<u>lacking direct</u>] <u>evidence</u>)
  - o based on systematic review without clinical outcomes
  - systematic review of 32 randomized trials and 31 observational studies evaluating effects of moderate alcohol use on biological markers of coronary heart disease in 1,686 adults without known cardiovascular disease
  - moderate alcohol use defined as ≤ 1 drink/day for women and ≤ 2 drinks/day for men
  - o moderate alcohol use significantly associated with increased high density lipoproteins, apolipoprotein A1, and adiponectin and decreased fibrinogen
  - O Reference BMJ 2011 Feb 22;342:d636 full-text

### Type of alcohol and cardiovascular disease

- association between moderate alcohol drinking (< 60 g alcohol/day) and decreased all-cause mortality may be limited to wine drinking)
  - based on prospective cohort study in France
  - 36,583 healthy middle-aged men with normal results on electrocardiogram and not taking drugs for cardiovascular disease risk factors (that is, excluding men who were at higher risk for cardiovascular disease) were followed for 13-21 years
  - reference group (abstinence from alcohol) had significantly lower mean corpuscular volumes, gamma glutamyl transferase activity, blood pressure, concentrations of serum cholesterol and glucose, and percentage of smokers compared to other groups at baseline
  - o compared to abstinence, moderate wine drinking (consuming < 60 g alcohol/day and no beer) associated with decreased risk of all-cause mortality (statistically significant in 3 of 4 analyses by quartiles of systolic blood pressure)
  - o consuming ≥ 60 g alcohol/day or consuming beer and wine were not associated with decreased risk of all-cause mortality
  - Reference Am J Clin Nutr 2004 Sep;80(3):621 full-text
  - earlier report of this cohort can be found in <u>Arch Intern Med 1999 Sep 13;159(16)</u>:
    1865
- wine consumption may be associated with healthier lifestyle compared with beer consumption
  - based on cohort study
  - 5,000 randomly selected military personnel from Belgium were given questionnaires on food and drink intake, physical activity, and health-related and lifestyle characteristics
    - dietary pattern evaluated using Healthy Eating Index 2010, Mediterranean diet score, and healthy dietary pattern (principal component analysis)
    - activity evaluated using International Physical Activity Questionnaire

(IPAQ)

- 0 1,699 persons (34%) responded to questionnaires and were evaluated
- compared with daily wine consumption, daily beer consumption associated with less healthy dietary pattern, less physical activity, and higher prevalence of smoking
- Reference Mil Med Res 2015 Dec 14;2:33 full text
- review of wine, beer, alcohol, and polyphenols on cardiovascular disease can be found in Nutrients 2012 Jul;4(7):759
- review of red wine consumption and cardiovascular risk reduction can be found in <u>J Am</u> Coll Surg 2005 Mar;200(3):428

# Changing alcohol consumption and cardiovascular disease

- transition from nondrinking or occasional drinking (< 1 drink/week) to moderate alcohol consumption might reduce risk for cardiovascular disease
  - o based on 4 cohort studies with borderline statistical significance
  - beginning moderate alcohol consumption in middle age associated with reduced risk for cardiovascular disease
    - based on cohort study
    - 7,697 adults aged 45-64 years who were nondrinkers at baseline were evaluated
    - patients followed up to 10 years
    - 6% began moderate drinking within 6 years (≤ 2 drinks/day for men, ≤ 1 drink/day for women)
    - new moderate drinking associated with decreased risk of cardiovascular disease compared to persistent nondrinking after 4 years (adjusted odds ratio 0.62, 95% CI 0.4-0.95)
    - new moderate drinking not associated with risk of all-cause mortality compared to persistent drinking after 4 years
    - Reference Am J Med 2008 Mar;121(3):201
  - moderate increase in alcohol consumption might reduce risk of cardiovascular disease in men initially consuming ≤ 1 drink/week)
    - based on prospective cohort study
    - 18,455 men aged 40-84 years in Physician's Health Study without history of cardiovascular disease or cancer at baseline were evaluated
    - 1,091 developed cardiovascular disease (myocardial infarction, angina pectoris, revascularization, stroke, cardiovascular disease-related death) during median follow-up 5.8 years
    - among 7,360 men initially consuming ≤ 1 drink/week, moderate increases in alcohol intake (> 1 to < 6 drinks/week) associated with nonsignificant decrease in risk of cardiovascular disease compared to no change in alcohol intake (adjusted relative risk 0.71, 95% CI 0.5-1)
    - among 6,612 men initially consuming > 1 to 6 drinks/week, moderate increases in alcohol intake not associated with risk of cardiovascular disease compared to no change in alcohol intake
    - among 4,483 men initially consuming  $\ge 1$  drink/day, large increases in

- alcohol intake (≥ 6 drinks/week) associated with increased risk of cardiovascular disease compared to no change in alcohol intake (adjusted relative risk 1.63, 95% CI 1.1-2.4)
- Reference <u>Arch Intern Med 2000 Sep 25;160(17):2605</u>
- new regular drinking might decrease risk of major coronary heart disease events but increase risk of noncardiovascular mortality among men with occasional drinking
  - based on prospective cohort study
  - 6,503 British men aged 40-59 years without history of coronary heart disease at baseline were evaluated
  - 874 major coronary events and 1,613 deaths occurred during follow-up of mean 17 years
  - stable occasional drinking defined as < 2 drinks/month</li>
  - regular drinking included categories of light drinking (1-15 drinks/week), moderate drinking (15-42 drinks/week), and heavy drinking (> 42 drinks/week)
  - compared to stable occasional drinking, new regular drinking
    - associated with nonsignificant decrease in risk of major coronary heart disease events (adjusted relative risk [RR] 0.7, 95% CI 0.48-1.03)
    - associated with nonsignificant increase in risk of noncardiovascular mortality (adjusted RR 1.4, 95% CI 0.99-1.97)
    - not associated with risk of cardiovascular mortality
  - compared to stable occasional drinking, continued regular drinking associated with
    - decreased risk of major coronary heart disease events (adjusted RR 0.77, 95% CI 0.64-0.92)
    - decreased risk of overall cardiovascular mortality (adjusted RR 0.75, 95% CI 0.61-0.91)
    - nonsignificant increase in risk of noncardiovascular mortality (adjusted RR 1.18, 95% CI 0.97-1.44)
  - Reference Heart 2002 Jan;87(1):32 full-text
- increasing alcohol intake by 7-14 drinks/week over 5 years associated with decreased risk of coronary heart disease compared to stable intake in postmenopausal women
  - based on prospective cohort study
  - 21,523 postmenopausal women in Denmark were assessed for alcohol intake between 1993 and 2003
  - 8.1% developed coronary heart disease during 11-year follow-up
  - 1 drink defined as 12 g of pure alcohol
  - baseline median 5 drinks/week
  - compared to stable alcohol intake over 5-year period
    - decreased risk of coronary heart disease associated with increasing alcohol intake by

- 7 drinks/week (adjusted hazard ratio 0.89, 95% CI 0.81-0.97)
- 14 drinks/week (adjusted hazard ratio 0.78, 95% CI 0.64-0.95)
- no significant difference in risk of coronary heart disease with decreasing alcohol intake
- consistent findings in analysis excluding 188 women with any cardiovascular disease prior to study entry
- Reference <u>BMJ 2016 May 11;353:i2314 full-text</u>