

Does a physically active lifestyle attenuate the association between alcohol consumption and mortality risk? Findings from the UK biobank

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Abstract

Alcohol consumption is common across Western culture, despite its associations with adverse health outcomes, including cancer and cardiovascular disease (CVD). Physical activity (PA) has beneficial effects on many alcohol related outcomes, with data suggesting PA may offset the association between alcohol consumption and mortality. This study examined the joint associations of PA and alcohol on all-cause, CVD and cancer mortality. Participants were recruited between 2006 and 2010 in the United Kingdom. Alcohol consumption was categorised based on current UK guidelines (14 units/week). PA was categorised based on the Metabolic Task Equivalent of PA as low, moderate and high. Data were analysed using Cox proportional-hazard models. The final analysis, conducted in 2019, included 297 988 adults aged ≥ 40 . Over an average follow-up of 6.9 years, 6079 deaths were recorded, including 1219 CVD deaths and 3112 cancer deaths. We observed greater point estimates for risk of all-cause mortality among low PA individuals who consumed alcohol at the same level as active individuals. For example, low PA participants who reported alcohol consumption \geq double guidelines had a greater HR (1.55, 95% CI 1.25, 1.93) than active individuals (moderate PA HR 1.21, 95% CI 0.95, 1.54; high PA HR 1.21, 95% CI 1.00, 1.46). Considering CVD, we observed a similar trend with lower point estimates of risk of mortality among active individuals. We found some evidence that PA modified the associations of alcohol and all-cause and CVD mortality in this large population sample of British adults.

Key words

Physical activity; mortality; alcohol; effect modification; epidemiology

Introduction

Alcohol consumption is associated with an increased risk of cancer (1), cardiovascular disease (CVD) (2) and mortality (3), with recent data suggesting the safest level of consumption is abstinence (4). Alcohol consumption is also linked with societal consequences including an increased risk of violence and road traffic accidents (5). Yet, alcohol use is deeply embedded in Western culture. Over 80% of adults in Australia and the United Kingdom are considered current drinkers, with only minimal changes in the number of individuals who regularly consume alcohol over recent decades (4). In addition to systemic measures to reduce consumption, such as the restriction of alcohol advertising and sales hours, strategies are needed to minimise the health risks associated with drinking alcohol.

Although not empirically established, physical inactivity and alcohol may influence the development of chronic disease through shared pathways (6). However, the relationship between alcohol consumption and physical activity appears complex, with some research suggesting physically active individuals also consume greater amounts of alcohol (7). Small to medium sized observational studies ($n=17\ 410$ to $n=36\ 370$) indicate physical activity (PA) and cardiorespiratory fitness (6, 8, 9) can attenuate the association between alcohol consumption and all-cause mortality. For example, among individuals who are active at the lower World Health Organisation (WHO) PA guideline (equivalent to 150 mins/week of moderate PA (MPA)) (10), the risk of alcohol-related all-cause mortality was reduced up to a hazardous level of alcohol consumption (14-35 UK units of alcohol/week for women, 21-49 units/week for men). In the same study, PA essentially eliminated the risk of alcohol-related cancer mortality among individuals who were active at the upper WHO PA guideline(6) (equivalent to 300 mins MPA (10)). However, the current evidence base is limited by an extremely small number of studies. The three published studies (6, 8, 9) also used baseline measurements ranging from 1973 to 2006. It is likely that alcohol drinking patterns in addition to the type of beverage consumed have changed over time, which may not be reflected in this data.

The aim of this study was to investigate the possible joint effects of PA and alcohol consumption on all-cause, CVD and cancer mortality in a large sample of adults residing in the United Kingdom.

Methods

This research has been conducted using the UK Biobank Resource under Application Number 25813. The UK Biobank is a prospective cohort study including 502 547 participants aged 40-69 years. Participants were recruited from 22 centres across the UK between 2006 and 2010. Full details of the study methods have been published elsewhere (11). All participants provided consent for the use of their de-identified data and access to their health-related records (11).

Participants who suffered from a major cardiovascular event ($n=18\ 851$) or had been diagnosed with cancer ($n=41\ 787$) prior to baseline were excluded from analyses. We also excluded participants with missing data in PA ($n=34\ 886$), alcohol ($n=91\ 570$), or other covariates included in the analyses ($n=17\ 426$) or implausible values of sedentary behaviour (>23 hours/day) ($n=39$).

Outcomes

Date of death was obtained through linkage with national datasets from the National Health Service (NHS) Information Centre (England and Wales) and the NHS Central Register Scotland (Scotland).

Participants were followed until January 2016. Primary cause of death was recorded based on the International Classification of Diseases 10th revision (ICD10). CVD deaths included codes I01.0 to I199. Cancer deaths included codes C00.0 to D48.9.

Alcohol consumption

Participants were classified based on their self-reported alcohol drinking status. The level of consumption was quantified as the number of UK units of alcohol consumed per week, computed by

summing the average weekly intake of red wine; champagne and white wine; beer and cider; spirits; fortified wine; and other alcoholic drinks. In the UK, one unit is equal to 8 grams of alcohol (12). We separated participants that consumed alcohol above the recommended levels into two groups due to previous research that has shown the risk of all-cause mortality spikes between 200g alcohol/week and 400g alcohol/week (13). Participants were, therefore, grouped into five categories based on the current UK alcohol guidelines (12): 1) never drinker; 2) previous-drinkers, 3) within guidelines (<14 UK units of alcohol/week); 4) above guidelines (≥ 14 UK units of alcohol/week and <28 UK units of alcohol/week); and 5) double the guidelines or more (≥ 28 UK units of alcohol/week).

Physical activity (PA)

PA was quantified using the short-form International Physical Activity Questionnaire (IPAQ)(14). IPAQ assesses PA across leisure time, domestic activities, occupational activity and transport-related activity (15). Physical activity was quantified using the Metabolic Equivalent Task (MET)-mins of PA/week, calculated by multiplying the MET value of activity by the number of mins/week. We classified participants' physical activity as low (0-599 MET-mins PA/week), moderate (600-1199 MET-mins/week) and high (≥ 1200 MET-mins week).

Covariates

In line with previous research (6, 8, 9), we included age, sex, diet, socioeconomic status, BMI, PA (using the aforementioned categorisations of MET-mins PA/week), smoking status, sedentary behaviour, and baseline hypertension and diabetes as covariates in the model. We calculated body mass index (BMI) from the participant's measured weight (kg)/height (m^2). To classify diet, we calculated average daily fruit and vegetable consumption as the sum of servings of cooked vegetables, salad and raw vegetables, fresh fruit and dried fruit consumed per day. We used the Townsend deprivation index as an indicator of socioeconomic status, which assigns each participant a score relative to the output area (the smallest UK

census area) in which their postcode was located. Higher scores indicate greater socioeconomic deprivation (16). We calculated a proxy measure of sedentary behaviour by summing the total time spent watching television, using a computer screen or driving.

Statistical analyses

The statistical analyses were conducted in 2019 using Cox proportional-hazard models. Firstly, we examined the associations between alcohol consumption and all-cause, CVD and cancer mortality, using never-drinkers as the referent group. To examine the joint associations of PA and alcohol consumption on all-cause, CVD and cancer mortality, we derived a combined variable with 15 groups (17). The combined variable with the highest PA and the lowest alcohol consumption (never drinkers) served as the referent group. We used SPSS Version 22.0 (IBM, Chicago, IL, USA) for the statistical analyses.

Results

Table 1 shows baseline characteristics of the sample ($n=297\ 988$). 6079 deaths, 1219 CVD deaths and 3112 cancer deaths occurred over an average follow-up length of 6.9 years (SD 0.9).

The risk of all-cause, CVD and cancer mortality by alcohol consumption categories are presented in Supplementary Table 1. The highest risk of all-cause mortality was observed in previous drinkers (hazard ratio (HR) of model 2 (fully-adjusted) 1.41, 95% CI 1.21, 1.63), followed by \geq double guidelines (HR 1.22, 95% CI 1.06, 1.40). For CVD, alcohol consumption within guidelines was associated with reduced risk of mortality (HR 0.73, 95% CI 0.56, 0.95). For cancer, we observed a greater risk of cancer mortality among previous drinkers (HR 1.43, 95% CI 1.16, 1.78) and \geq double guidelines (HR 1.26, 95% CI 1.02, 1.54).

Joint associations of physical activity and alcohol on mortality

The joint associations of PA and alcohol with all-cause mortality are presented in Figure 1 and Supplementary Table 2. We observed greater point estimates for risk of all-cause mortality among low PA individuals who consumed alcohol at the same level as active individuals. For example, low PA participants who reported alcohol consumption \geq double guidelines had a greater HR (1.55, 95% CI 1.25, 1.93) than active individuals (moderate PA HR 1.21, 95% CI 0.95, 1.54; high PA HR 1.21, 95% CI 1.00, 1.46).

Considering CVD, we observed a similar trend. For instance, alcohol consumption within guidelines was associated with a lower risk of mortality among highly active individuals (HR 0.65, 95% CI 0.46, 0.93), than moderately active or low PA individuals (moderate PA HR 0.76, 95% CI 0.52, 1.12; low PA HR 0.84, 95% CI 0.58, 1.23; Supplementary Figure 1). We did not find clear evidence that PA moderated the association between alcohol consumption and cancer mortality (Supplementary Figure 2).

Discussion

In this large prospective cohort study, we found some evidence that PA moderates the association between alcohol consumption and the risk of all-cause and CVD mortality. Among participants who reported previous consumption and consumption at double the guidelines or more, we found a positive association between alcohol and risk of all-cause mortality. In the joint analysis of PA and alcohol, this association was attenuated by higher levels of activity. Our findings are consistent with two large-scale pooled British studies that found PA attenuated the association between alcohol consumption and all-cause mortality (6, 9). For instance, in an analysis of eight population-based cohorts (6), effect modification was clear for both the lower (>7.5 MET-hour/week) and upper PA recommendations (>15 MET-hour/week). There are several possible explanations for our findings. Alcohol and physical activity may influence the development of chronic disease through opposing actions on shared pathways. For

example, heavy alcohol consumption is suggested to promote carcinogenesis whilst physical activity may inhibit it through similar biological processes (6, 9). Social factors may also contribute to the interaction effects of physical activity and alcohol consumption on mortality as both activities can be considered social in nature and may be linked, particularly in regard to sport. In their literature review, Piazza-Gardner and Barry (7) highlighted a unique relationship between alcohol and physical activity, finding moderate drinkers performed more physical activity than lifelong alcohol abstainers. Of the studies included in the review, some reported a linear relationship between alcohol consumption and physical activity whereas, other studies reported a curvilinear relationship in which physical activity increased with moderate alcohol consumption but decreased with heavy consumption. It is also possible that physically active drinkers are less likely to binge drink, meaning their alcohol consumption patterns are potentially less harmful. Further research is needed to establish why drinkers tend to exercise more than non-drinkers.

We also found evidence that PA attenuated the risk of CVD mortality. Among highly active individuals, we found a slightly protective effect of alcohol consumption at levels within the current UK guidelines. Our findings are convergent with prior research that has found a reduced risk of CVD mortality among active individuals who reported occasional alcohol consumption (6). Conversely, we did not find evidence of a joint association between PA and alcohol on cancer mortality risk.

Study limitations and strengths

To our knowledge, the present study is the largest to date to examine PA and alcohol-related mortality, incorporating a study population of 297 988 individuals. We adjusted for a broad range of confounders, such as socioeconomic deprivation and dietary intake, which were not always considered in previous studies (6, 9). Our findings are limited by the use of self-reported measures of PA and alcohol consumption. The possibility of misclassification between alcohol consumption groups also remains as

social desirability bias is common across alcohol literature and may have produced under-reporting of true alcohol consumption levels (18). Despite its size, our sample may not be representative of the broader population, as research has suggested the Biobank cohort differs from the UK population in some health behaviours, including alcohol consumption (19). Select groups of the population, however, tend to reveal the same risk factor-disease associations as the general population (20). Therefore, while the prevalence of selected characteristics will differ in the UK Biobank, risk factor–health outcome associations should not.

Conclusions

In conclusion, we found evidence that PA modified the association between alcohol and all-cause and CVD mortality in this large population sample of British adults. Future investigations could include objective measures of PA to further our understanding of the possible protective effects of PA on alcohol-related mortality.

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Conflicts of interest

None

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References

1. Nelson DE, Jarman DW, Rehm J, Greenfield TK, Rey G, Kerr WC, et al. Alcohol-attributable cancer deaths and years of potential life lost in the United States. *American Journal of Public Health*. 2013;103(4):641-8.
2. Mostofsky E, Chahal HS, Mukamal KJ, Rimm EB, Mittleman MA. Alcohol and immediate risk of cardiovascular events: a systematic review and dose-response meta-analysis. *Circulation*. 2016:CIRCULATIONAHA. 115.019743.
3. Di Castelnuovo A, Costanzo S, Bagnardi V, Donati MB, Iacoviello L, De Gaetano G. Alcohol dosing and total mortality in men and women: an updated meta-analysis of 34 prospective studies. *Archives of internal medicine*. 2006;166(22):2437-45.
4. Griswold MG, Fullman N, Hawley C, Arian N, Zimsen SR, Tymeson HD, et al. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *The Lancet*. 2018;392(10152):1015-35.
5. Wagenaar AC, Murray DM, Toomey TL. Communities Mobilizing for Change on Alcohol (CMCA): Effects of a randomized trial on arrests and traffic crashes. *Addiction*. 2000;95(2):209-17.
6. Perreault K, Bauman A, Johnson N, Britton A, Rangul V, Stamatakis E. Does physical activity moderate the association between alcohol drinking and all-cause, cancer and cardiovascular diseases mortality? A pooled analysis of eight British population cohorts. *Br J Sports Med*. 2017;51(8):651-7.
7. Piazza-Gardner AK, Barry AE. Examining physical activity levels and alcohol consumption: are people who drink more active? *American Journal of Health Promotion*. 2012;26(3):e95-e104.
8. Shuval K, Barlow CE, Chartier KG, Gabriel KP. Cardiorespiratory fitness, alcohol, and mortality in men: the Cooper Center Longitudinal Study. *American journal of preventive medicine*. 2012;42(5):460-7.
9. Soedamah-Muthu SS, De Neve M, Shelton NJ, Tielemans SM, Stamatakis E. Joint associations of alcohol consumption and physical activity with all-cause and cardiovascular mortality. *The American journal of cardiology*. 2013;112(3):380-6.

10. World Health Organization. Global recommendations on physical activity for health 2010.
11. Sudlow C, Gallacher J, Allen N, Beral V, Burton P, Danesh J, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS medicine*. 2015;12(3):e1001779.
12. Department of Health. Alcohol Guidelines Review—Report from the Guidelines development group to the UK Chief Medical Officers. Department of Health London; 2016.
13. Wood AM, Kaptoge S, Butterworth AS, Willeit P, Warnakula S, Bolton T, et al. Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies. *The Lancet*. 2018;391(10129):1513-23.
14. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. *Medicine & science in sports & exercise*. 2003;35(8):1381-95.
15. IPAQ Research Committee. Guidelines for data processing and analysis of the International Physical Activity Questionnaire (IPAQ)-short and long forms. <http://www.ipaq.kise/scoringpdf>. 2005.
16. Townsend P, Phillimore P, Beattie A. Health and deprivation: inequality and the North: Routledge; 1988.
17. Stamatakis E, Gale J, Bauman A, Ekelund U, Hamer M, Ding D. Sitting time, physical activity, and risk of mortality in adults. *Journal of the American College of Cardiology*. 2019;73(16):2062-72.
18. Klatsky AL, Udaltsova N. Alcohol Drinking and Total Mortality Risk. *Annals of Epidemiology*. 2007;17(5, Supplement):S63-S7.
19. Fry A, Littlejohns TJ, Sudlow C, Doherty N, Adamska L, Sprosen T, et al. Comparison of sociodemographic and health-related characteristics of UK Biobank participants with those of the general population. *American journal of epidemiology*. 2017;186(9):1026-34.
20. Batty GD, Shipley M, Tabák A, Singh-Manoux A, Brunner E, Britton A, et al. Generalizability of occupational cohort study findings. *Epidemiology*. 2014;25(6):932-3.

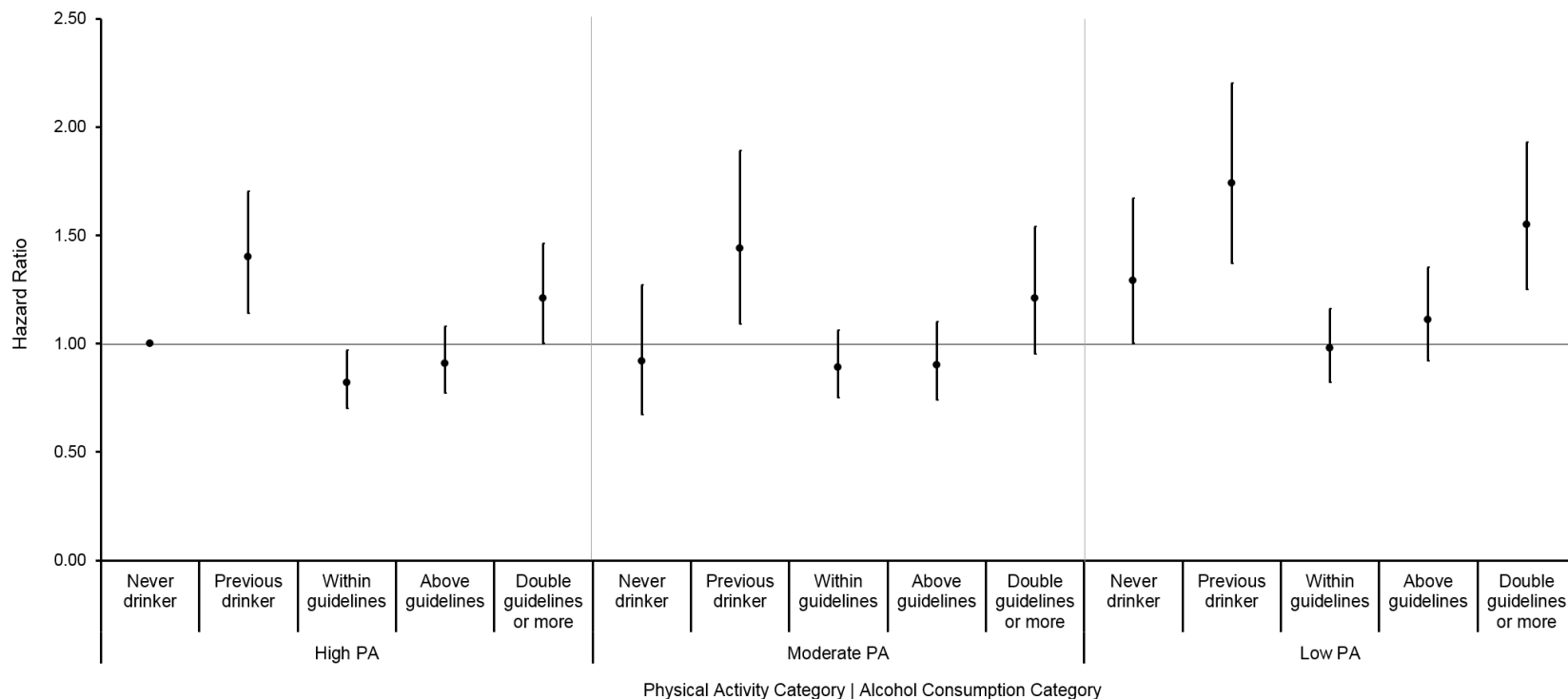


Figure 1. Multivariate adjusted Cox proportional hazard ratios describing the joint associations of physical activity (PA) and baseline alcohol consumption (units per week) and all-cause mortality events in the UK Biobank (n=297 988). PA was quantified using the Metabolic Equivalent Task (MET)-mins of PA/week by multiplying the MET value of activity by the number of minutes/week. We classified participants as low PA (0-599 MET-mins/week), moderate PA (600-1199 MET-mins/week) and high PA (≥ 1200 MET-mins/week). Alcohol consumption categories are based on the average weekly intake of standard drinks relative to UK guidelines. In the UK, one standard drink equals to 8 grams of pure alcohol. Within guidelines: <14 units/week; above guidelines: ≥ 14 units/week and <28 units/week; double the guidelines or more: ≥ 28 units/week. The model was adjusted for diet, socioeconomic status, body mass index, smoking status, sedentary behaviour, baseline hypertension and diabetes. The interaction term for PA (MET-mins/week)*alcohol consumption was $p=0.76$.