Short communication

Alcohol intake and mortality risk of COVID-19, pneumonia, and other infectious diseases: An analysis of 437191 UK biobank participants

Bo-Huei Huang [a], Elif Inan-Eroglu [b], Ramon Z. Shaban [c], Mark Hamer [d], Annie Britton [e], Emmanuel Stamatakis [a],*,[1]

[a] Charles Perkins Centre, School of Health Sciences, the University of Sydney, New South Wales, Australia
[b] the Boden Collaboration for Obesity, Nutrition, Exercise & Eating Disorders, Charles Perkins Centre, Faculty of Medicine and Health, the University of Sydney, New South Wales, Australia
[c] Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney and Western Sydney Local Health District, New South Wales Ministry of Health, New South Wales, Australia
[d] Institute Sport Exercise & Health, Division of Surgery & Interventional Science, University College London, London, UK
[e] Institute of Epidemiology & Health Care, University College London, London, UK

ARTICLE INFO

ABSTRACT

This study aims to investigate the association between alcohol consumption and COVID-19, infectious diseases, and pneumonia mortality. This is a prospective analysis of 437,191 UK Biobank participants (age 56.3 years, 54% female). The main exposure was self-reported alcohol consumption. In addition to never and previous drinkers, we applied quartiles-based and UK guidelines-based criteria to divide current drinkers by weekly consumption into four groups. Outcomes included COVID-19, infectious diseases, and pneumonia mortality, obtained from the national death registries until May 2020. After an 11-year follow-up, compared to never drinkers, previous drinkers had higher mortality risks of infectious diseases and pneumonia (adjusted HR: 1.29 [95% CI 1.06–1.57] and 1.35 [1.07–1.70], respectively), but not COVID-19. There was a curvilinear association of alcohol consumption with infectious diseases and pneumonia mortality. Drinking within-guidelines (<14 UK units/wk) and amounts up to double the recommendation (14 to < 28 UK units/wk) was associated with the lowest mortality risks of infectious diseases (0.70 [0.59–0.83] and 0.70 [0.59–0.83], respectively) and pneumonia (0.71 [0.58–0.87] and 0.72 [0.58–0.88], respectively). Alcohol consumption was associated with lower risks of COVID-19 mortality (e.g., drinking within-guidelines: 0.53 [0.33–0.86]). Drinkers reporting multiples of the recommended alcohol drinking amounts did not have higher mortality risks of COVID-19 and other infectious diseases than never drinkers. Despite the well-established unfavorable effects on general health, we found no deleterious associations between alcohol consumption and the risk of infectious diseases, including COVID-19. Future research with other study designs is needed to confirm the causality.

1. Introduction

SARS-CoV-2 causes COVID-19, which was declared by the World Health Organization as a global pandemic in March 2020 (Coronavirus Disease (COVID-19) – World Health Organization, 2020). Preliminary epidemiological reports have shown that, amid pandemics, both alcohol sales and alcohol consumption surge enormously (Anne et al., 2020; Chick, 2020; Colbert et al., 2020; Lechner et al., 2020), potentially due to psychological distress and the use of alcohol as a coping mechanism

(Aghababaeian et al., 2020; Chick, 2020; Lechner et al., 2020). However, different alcohol consumption patterns mediate innate and adaptive immune systems in distinctive ways (Bailey et al., 2021; Barr et al., 2016; Chick, 2020; Szabo & Saha, 2015).

Although adverse effects of alcohol abuse on the risk of infectious diseases have been discussed (Bailey et al., 2021; Barr et al., 2016; Szabo & Saha, 2015), the role of drinking habits in determining the risk of the most severe consequences of infections, including COVID-19, are still largely unknown. Recent prospective studies have reported potentially

---

favorable effects of moderate alcohol consumption on COVID-19 hospitalization as well as vulnerabilities to upper respiratory infectious illness (Cohen, 2020; Hamer et al., 2020), but these studies either did not include heavy drinkers or did not distinguish previous drinkers from never drinkers.

We examined the effects of alcohol consumption with extended categorization on risks of COVID-19, overall infectious diseases, and pneumonia death in a large population sample of adults residing in the UK.

2. Methods

The UK Biobank is a prospective cohort including 502,616 participants aged 37–73 years recruited across the UK between 2006 and 2010, approved by the National Research Ethics Service (Ref 11/NW/0382), with details described elsewhere (Sudlow et al., 2015). Participants completed baseline questionnaires/physical measurements and provided consent for the use of de-identified data and health-related records. We stepwise excluded those with missing/unusable covariates (n = 64,016) or exposures (n = 1,409), yielding a total of 437,191 participants in the present study.

A self-administered questionnaire collected alcohol consumption. Participants were firstly classified based on their drinking status (never, previous, or current). Then, weekly alcohol consumption of current drinkers was computed as the number of UK units of alcohol (1 unit = 10 mL = 8 g alcohol). We applied quartiles-based and UK guidelines-based (14 UK units/wk) criteria to further divide current drinkers by their weekly consumption into four groups each. Table A.1 describes this categorization in detail.

The date of death was accessed via linkage with the national datasets from the National Health Service Information Centre (England and Wales) and the NHS Central Register Scotland (Scotland) up to May 2020. For the COVID-19 mortality-specific analyses, participants with death events earlier than the onset of the pandemic (January 2020) were further excluded, ending up with a 414,398 sub-sample. Outcomes included both the ICD-10-based primary and contributory cause of death. Codes for COVID-19 were U07.1 and U07.2; for infectious diseases included A.00 to B.99 and J.09 to J.18; for pneumonia were J.12 to J.18.

We selected covariates that have been linked to infectious diseases risk (Bodilsen et al., 2018; Cabanas-Sánchez et al., 2018; Schmitt et al., 2019; Simou et al., 2018): age, sex, socioeconomic status, body mass index (BMI), smoking, major illness (cardiovascular diseases, diabetes mellitus, cancer, chronic respiratory diseases, hepatic diseases, human immunodeficiency virus disease), diet, physical activity, sedentary behavior and sleep duration (Table A.2). In the analyses of COVID-19 mortality, models were further adjusted for country of residence to reflect the different lockdown/social distancing policies.

All the models were performed using SAS 9.4 software. Cox-proportional hazard models examined the association of alcohol drinking (categorical) with disease mortality; "never drinkers" served as the reference. We found no noticeable violations against the proportional hazard assumption. Initial models included minimal adjustment (only sex and age as covariates) (Model 1), and additionally adjusted for all the covariates mentioned above (Model 2).

In the sensitivity analysis, we extended the UK guidelines-based categorization to distinguish heavy drinkers further to increase the granularity of the exposure. The temporal consistency of alcohol consumption was tested with a sub-sample with repeated measurement of exposure between 2012 and 2018 (n = 40,293).

3. Results

Among the 437,191 participants (56.3 years, 54% female, 11.0 ± 1.5 follow-up years), there were 318 COVID-19 deaths and 3,545 infectious diseases deaths (including 2,614 pneumonia deaths). 34% of the participants were within-guidelines drinkers (8.2 ± 3.3 UK units/wk), while 4% were never drinkers. The sample characteristics are shown in Table 1.

In the fully adjusted model (Model 2), previous drinkers had higher risks of both infectious diseases and pneumonia mortality (Hazard Ratios (HR): 1.29 [95% CI, 1.06 to 1.57] and 1.35 [95% CI, 1.07 to 1.70], respectively) compared to never drinkers (Table A.3; Fig. 1a, b). There was a curvilinear (U-shape) association of alcohol consumption with both conditions. Current drinkers within the second (3.2 to < 10.5 UK units/wk) and third quartile (10.5 to < 21.5 UK units/wk) had the lowest mortality risks (e.g., HR for infectious diseases mortality, 0.71 [95% CI, 0.60 to 0.85] and 0.68 [95% CI, 0.57 to 0.81], respectively). Models with UK guidelines-based categorization were in close agreement with the results above (Fig. 2a, b).

Previous drinkers did not have a higher risk of COVID-19 mortality as observed in infectious diseases and pneumonia (Table A.3; Figs. 1c, 2c). Alcohol consumption was associated with a lower risk of COVID-19 mortality compared to never drinkers (e.g., HR of drinkers with at least double the recommended amounts (≥28 UK units/wk): 0.48 [0.28–0.81]).

The favorable associations of alcohol consumption with infectious diseases and pneumonia mortality diminished when the drinking amount surpassed at least quadruple the recommended amounts (56 UK units/wk) (Table A.4). Regarding the temporal consistency of alcohol consumption, only 23% of the repeated-measured sub-sample decreased their alcohol consumption over the follow-up period (Table A.5).

4. Discussion

To our knowledge, this is the first prospective study extensively investigating the association of alcohol consumption with COVID-19 and infectious diseases mortality. Our findings suggest a curvilinear association with infectious diseases and pneumonia mortality risk. Compared to never drinkers, alcohol consumption at amounts ranging from within-guidelines to at least double the recommendation did not show detrimental associations with infectious diseases death. Previous drinkers had a higher risk of infectious disease mortality but not for COVID-19.

Reviews have shown that alcohol abuse increases both infection susceptibility and severity as a result of the immunosuppressive effects of alcohol (Bailey et al., 2021; Barr et al., 2016; Szabo & Saha, 2015), while moderate consumption (~12 to 25 UK units/wk) potentially enhances immune responses (Barr et al., 2016). Our results further suggested that this favorable threshold might be higher as consumption of up to 42 UK units/wk (336 g/wk of alcohol) (Table A.4). Similar to our results, another recent prospective analysis of the UK Biobank also suggested that moderate drinkers had the lowest risk of COVID-19 hospitalization (Hamer et al., 2020). However, it is well established that high levels of alcohol consumption are linked to severe increases in risks of cancer (Feng et al., 2020), cardiovascular disease (Perreault et al., 2017), as well as societal consequences, e.g., domestic violence (Colbert et al., 2020). One recent *meta*-analysis reported a dose–response relationship between alcohol consumption and community-acquired pneumonia (mostly bacterial), as each 1.25 to 2.5 UK units/d was associated with 8% higher risks (Simou et al., 2018). Since our finding suggested that only previous drinkers had higher mortality risks of infectious diseases and pneumonia, future studies are warranted.

5. Limitations

We cannot confirm the causality of the associations we reported due to the observational design. Especially, a recent Mendelian randomization study of cardiovascular disease highlighted that the protective effects of moderate alcohol consumption could be caused by reverse causation and residual confounding (Millwood et al., 2019). Although the UK Biobank was not population-representative and thereby its

Table 1

Characteristics of study sample by level of alcohol consumption [a] (n = 437,191).

Characteristics	Total	Never Drinkers	Previous Drinkers	Occasional Drinkers	Within Guidelines Drinkers	Above Guidelines, but Less than Double the Recommended Amounts	At Least Double the Recommended Amounts
No. (%)	437,191 (100)	16,837 (4)	14,614 (3)	95,949 (22)	147,115 (34)	96,649 (22)	66,027 (15)
Wkly alcohol units (mean (S.D.))	15.5 (16.7)	NaN (NA)	NaN (NA)	1.7 (1.2)	8.2 (3.3)	20.0 (4.0)	45.1 (19.0)
Male (No. (%))	201,801 (46)	4,817 (29)	6,589 (45)	31,542 (33)	53,361 (36)	54,732 (57)	50,760 (77)
Age (years) (mean (S.D.))	56.3 (8.1)	57.0 (8.6)	56.9 (8.0)	55.9 (8.3)	56.6 (8.0)	56.3 (8.0)	56.3 (7.8)
Follow-up (month) (mean (S.D.))	132.2 (17.8)	131.4 (18.2)	129.1 (22.9)	131.9 (17.82)	132.7 (16.5)	132.8 (17.2)	131.7 (19.7)
Townsend Deprivation Index (mean (S.D.))	−1.4 (3.0)	−0.5 (3.4)	−0.2 (3.5)	−1.0 (3.2)	−1.8 (2.8)	−1.7 (2.9)	−1.3 (3.1)
BMI (kg/m^2) (mean (S.D.))	27.3 (4.7)	27.9 (5.6)	28.1 (5.6)	28.1 (5.4)	26.6 (4.4)	27.0 (4.2)	27.8 (4.2)
Vegetable and fruit consumption (servings/day) (mean (S.D.))	4.4 (3.0)	4.9 (3.6)	4.8 (3.6)	4.6 (3.2)	4.5 (2.8)	4.4 (2.8)	4.0 (2.9)
Sitting time (hours) (mean (S.D.))	4.8 (2.4)	4.6 (2.7)	5.1 (2.8)	4.9 (2.6)	4.6 (2.2)	4.8 (2.3)	5.1 (2.5)
Country of residence (No. (%))							
England	387,480 (89)	14,988 (89)	12,897 (88)	84,911 (89)	130,589 (89)	85,382 (88)	58,713 (89)
Scotland	31,586 (7)	1,186 (7)	1,084 (7)	6,937 (7)	10,538 (7)	7,270 (8)	4,571 (7)
Wales	18,125 (4)	663 (4)	633 (4)	4,101 (4)	5,988 (4)	3,997 (4)	2,743 (4)
Smoking Status (No. (%))							
Never	240,617 (55)	13,863 (82.3)	6,578 (45.0)	58,789 (61.3)	91,219 (62.0)	47,026 (48.7)	23,142 (35.0)
Previous	152,832 (35)	2,018 (12.0)	5,905 (40.4)	26,865 (28.0)	46,627 (31.7)	40,149 (41.5)	31,268 (47.4)
Current	43,742 (10)	956 (5.7)	2,131 (14.6)	10,295 (10.7)	9,269 (6.3)	9,474 (9.8)	11,617 (17.6)
Physical activity (No. (%))							
<10 MET hs/wk	97,819 (22)	4,467 (27)	3,864 (26)	24,278 (25)	32,231 (22)	19,342 (20)	13,637 (21)
10-<20 MET hs/wk	76,770 (18)	2,969 (18)	2,340 (16)	16,530 (17)	26,838 (18)	17,074 (18)	11,019 (17)
>=20 MET hs/wk	262,602 (60)	9,401 (56)	8,410 (58)	55,141 (58)	88,046 (60)	60,233 (62)	41,371 (63)
Sleep Duration (No. (%))							
<7h/d	23,756 (5)	947 (6)	1,143 (8)	5,998 (6)	6,298 (4)	4,712 (5)	4,658 (7)
7–9 h/d	265,659 (61)	9,786 (58)	8,853 (61)	57,899 (60)	86,506 (59)	59,216 (61)	43,399 (66)
>9h/d	147,776 (34)	6,104 (36)	4,618 (32)	32,052 (33)	54,311 (37)	32,721 (34)	17,970 (27)
Infectious Diseases Death (No. (%))	3545 (0.8)	162 (1.0)	269 (1.8)	843 (0.9)	884 (0.6)	675 (0.7)	712 (1.1)
Pneumonia Death (No. (%))	2614 (0.6)	113 (0.7)	202 (1.4)	587 (0.6)	648 (0.4)	507 (0.5)	557 (0.8)
Coronavirus Death (No. (%))	318 (0.1)	19 (0.1)	22 (0.2)	72 (0.1)	74 (0.1)	84 (0.1)	47 (0.1)

[a] The level of alcohol consumption was based on the UK guideline. Occasional Drinkers were those who reported drinking on special occasions or one to three times a month. Participants reported drinking at least once per week were further categorized based on their weekly drinking unit as: within guidelines (<14 UK units/wk); above guidelines (14 to < 28 UK units/wk); double guidelines and over (≥28 UK units/wk).

generalizability was limited, the distribution of alcohol consumption in the present sample was aligned with the result of the national health survey (Health Survey for England 2018, 2019). The self-reported measure of alcohol may be prone to systematic under-reporting (Stockwell et al., 2016). All the exposures and covariates were assumed to be constant throughout the follow-up in the statistical modelling, and we were not able to assess change in the alcohol consumption associated with the COVID-19 pandemic. The present study focused on the fatal events; the association of alcohol consumption with non-fatal outcomes might be different. Lastly, we did not distinguish different kinds of pneumonia, as most pneumonia death events in our sample were not organism-specific.

6. Conclusions

Alcohol consumption was not associated with increased risks of COVID-19 and other infectious diseases death in this study. However, future research with a study design less susceptible to confounding and

reverse causation (e.g., Mendelian randomization) is needed to confirm causality.

CRediT authorship contribution statement

Bo-Huei Huang: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Elif Inan-Eroglu:** Writing – original draft. **Ramon Z. Shaban:** Methodology, Validation, Writing – review & editing. **Mark Hamer:** Conceptualization, Methodology, Writing – review & editing. **Annie Britton:** Methodology, Validation, Writing – review & editing. **Emmanuel Stamatakis:** Conceptualization, Methodology, Resources, Writing – review & editing, Supervision, Project administration.

Declaration of Competing Interest

Bo-Huei Huang is a PhD student supported by the Taiwanese Ministry of Education and the University of Sydney The authors declare that
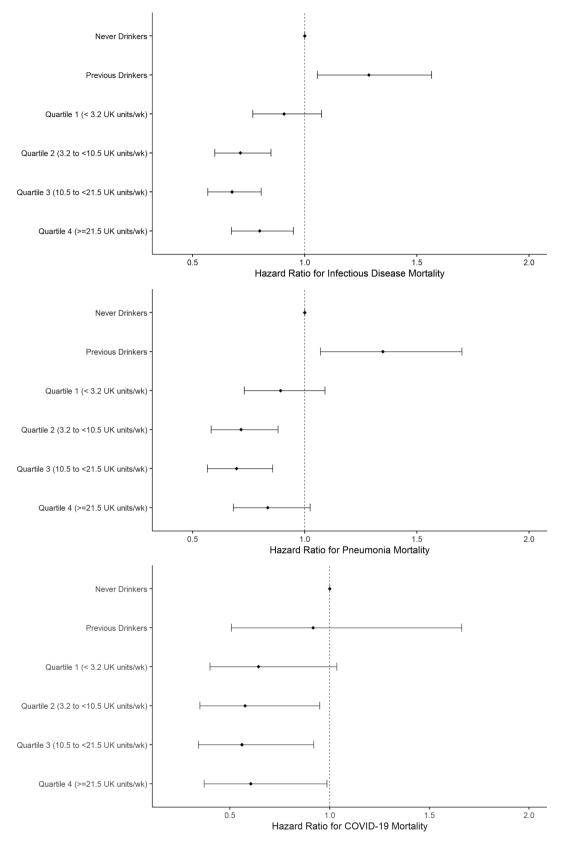
Fig. 1. Hazard Ratios for (a) Infectious Diseases, (b) Pneumonia, and (c) COVID-19 Mortality Between Quartiles-Based Alcohol Consumption. Models were adjusted for age, sex, socioeconomic status (Townsend deprivation index), BMI, smoking status, major illness (cardiovascular diseases, diabetes mellitus, cancer, chronic respiratory diseases, hepatic diseases, human immunodeficiency virus disease), diet (vegetable and fruit consumption), physical activity, sedentary behavior, and sleep duration. In analyses of COVID-19, models were further adjusted for country of residence.
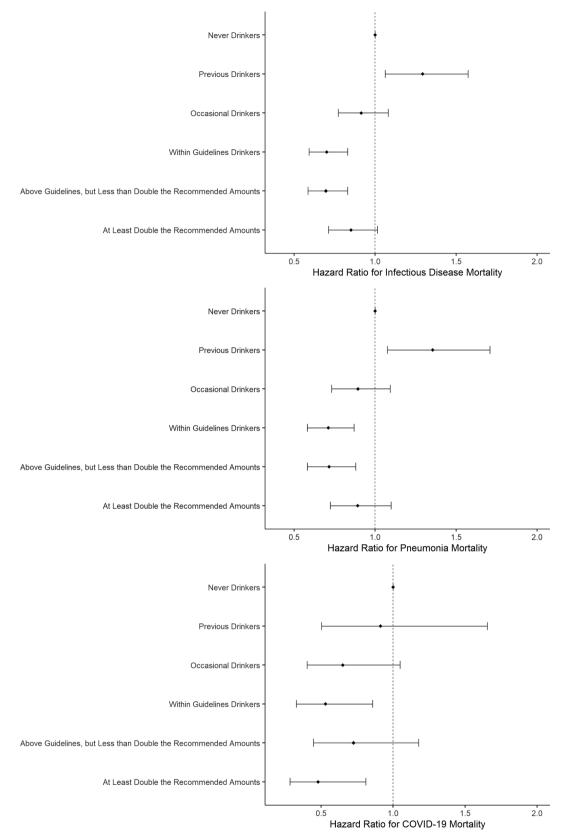
Fig. 2. Hazard Ratios for (a) Infectious Diseases, (b) Pneumonia, and (c) COVID-19 Mortality Between UK Guidelines-Based Alcohol Consumption. Models were adjusted for age, sex, socioeconomic status (Townsend deprivation index), BMI, smoking status, major illness (cardiovascular diseases, diabetes mellitus, cancer, chronic respiratory diseases, hepatic diseases, human immunodeficiency virus disease), diet (vegetable and fruit consumption), physical activity, sedentary behavior, and sleep duration. In analyses of COVID-19, models were further adjusted for country of residence.

they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.pmedr.2022.101751.

References

Aghababaeian, H., Hamdanieh, L., Ostadtaghizadeh, A., 2020. Alcohol intake in an attempt to fight COVID-19: a medical myth in Iran. Alcohol 88, 29–32 https://doi.org/10/gg5knx.

Anne, K., Ekaterini, G., Falk, K., Thomas, H., 2020. Did the general population in germany drink more alcohol during the COVID-19 pandemic lockdown? Alcohol Alcohol. 55 (6), 698–699 https://doi.org/10/gg8wnf.

Bailey, K.L., Samuelson, D.R., Wyatt, T.A., 2021. Alcohol use disorder: a pre-existing condition for COVID-19? Alcohol 90, 11–17 https://doi.org/10/ghkdfr.

Barr, T., Helms, C., Grant, K., Messaoudi, I., 2016. Opposing effects of alcohol on the immune system. Progr. Neuro-Psychopharmacol. Biol. Psychiatry 65, 242–251 https://doi.org/10/gg8wnj.

Bodilsen, J., Storgaard, M., Larsen, L., Wiese, L., Helweg-Larsen, J., Lebech, A.-M., Brandt, C., Østergaard, C., Nielsen, H., 2018. Infectious meningitis and encephalitis in adults in Denmark: a prospective nationwide observational cohort study (DASGIB). Clin. Microbiol. Infect. 24 (10), 1102.e1–1102.e5 https://doi.org/10/gg8wng.

Cabanas-Sánchez, V., Guallar-Castillón, P., Higueras-Fresnillo, S., García-Esquinas, E., Rodríguez-Artalejo, F., Martinez-Gomez, D., 2018. Physical activity, sitting time, and mortality from inflammatory diseases in older adults. Front. Physiol. 9, 898 https://doi.org/10/gdx4qq.

Chick, J., 2020. Alcohol and COVID-19. Alcohol. Alcohol. (Oxford, Oxfordshire) 55 (4), 341–342 https://doi.org/10/gg5q86.

Cohen, S., 2020. Psychosocial vulnerabilities to upper respiratory infectious illness: implications for susceptibility to coronavirus disease 2019 (COVID-19). Perspect. Psychol. Sci. 16 (1) https://doi.org/10/gg4hzn.

Colbert, S., Wilkinson, C., Thornton, L., Richmond, R., 2020. COVID-19 and alcohol in Australia: Industry changes and public health impacts. Drug Alcohol. Rev. 39 (5), 435–440 https://doi.org/10/gg8wnc.

Coronavirus disease (COVID-19) – World Health Organization. (2020). https://www.who.int/emergencies/diseases/novel-coronavirus-2019.

Y. Feng L. Powell A.J. Vassallo M. Hamer E. Stamatakis Does adequate physical activity attenuate the associations of alcohol and alcohol-related cancer mortality? A pooled study of 54 686 British adults International Journal of Cancer ijc.33052 2020 10/gg8wnd.

Hamer, M., Kivimäki, M., Gale, C.R., Batty, G.D., 2020. Lifestyle risk factors, inflammatory mechanisms, and COVID-19 hospitalization: A community-based cohort study of 387,109 adults in UK. Brain, Behavior, and Immunity 87, 184–187 https://doi.org/10/ggw3cg.

Health Survey for England 2018. (2019). NHS Digital. https://digital.nhs.uk/data-and-information/publications/statistical/health-survey-for-england/2018.

Lechner, W.V., Laurene, K.R., Patel, S., Anderson, M., Grega, C., Kenne, D.R., 2020. Changes in alcohol use as a function of psychological distress and social support following COVID-19 related University closings. Addict. Behav. 110 https://doi.org/10/gg6p2d.

Millwood, I.Y., Walters, R.G., Mei, X.W., Guo, Y., Yang, L., Bian, Z., Bennett, D.A., Chen, Y., Dong, C., Hu, R., Zhou, G., Yu, B., Jia, W., Parish, S., Clarke, R., Davey Smith, G., Collins, R., Holmes, M.V., Li, L., Chen, Z., 2019. Conventional and genetic evidence on alcohol and vascular disease aetiology: as prospective study of 500 000 men and women in China. Lancet 393 (10183), 1831–1842 https://doi.org/10/ggb348.

Perreault, K., Bauman, A., Johnson, N., Britton, A., Rangul, V., Stamatakis, E., 2017. 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. 51 (8), 651–657.

Schmitt, S., MacIntyre, A.T., Bleasdale, S.C., Ritter, J.T., Nelson, S.B., Berbari, E.F., Burdette, S.D., Hewlett, A., Miles, M., Robinson, P.A., Siddiqui, J., Trotman, R., Martinelli, L., Zeitlin, G., Rodriguez, A., Smith, M.W., McQuillen, D.P., 2019. Early infectious diseases specialty intervention is associated with shorter hospital stays and lower readmission rates: a retrospective cohort study. Clin. Infect. Dis. 68 (2), 239–246 https://doi.org/10/gg8wnh.

Simou, E., Britton, J., Leonardi-Bee, J., 2018. Alcohol and the risk of pneumonia: a systematic review and meta-analysis. BMJ Open 8 (8) https://doi.org/10/gd4cwm.

Stockwell, T., Zhao, J., Greenfield, T., Li, J., Livingston, M., Meng, Y., 2016. Estimating under- and over-reporting of drinking in national surveys of alcohol consumption: Identification of consistent biases across four English-speaking countries. Addiction 111 (7), 1203–1213 https://doi.org/10/bfmz.

Sudlow, C., Gallacher, J., Allen, N., Beral, V., Burton, P., Danesh, J., Downey, P., Elliott, P., Green, J., Landray, M., Liu, B., Matthews, P., Ong, G., Pell, J., Silman, A., Young, A., Sprosen, T., Peakman, T., Collins, R., 2015. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. PLoS Med. 12 (3), e1001779. https://doi.org/10.1371/journal.pmed.1001779.

Szabo, G., Saha, B., 2015. Alcohol's effect on host defense. Alcohol. Res. Curr. Rev. 37 (2), 159–170. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4590613/.