Lifestyle Risk Factors, Inflammatory Mechanisms, and COVID-19 Hospitalization: A Community-Based Cohort Study of 387,109 Adults in UK

Mark Hamer,a Mika Kivimäki,b Catharine R. Gale,c,d G. David Batty,b

a Division of Surgery and Interventional Sciences, Faculty Medical Sciences, University College London, London, UK
b Department of Epidemiology and Public Health, University College London, UK
c MRC Lifecourse Epidemiology Unit, University of Southampton, UK
d Lothian Birth Cohorts, Department of Psychology, University of Edinburgh, UK

Correspondence: Professor Mark Hamer, Division of Surgery and Interventional Sciences, Faculty Medical Sciences, University College London, 43–45 Foley Street, London, W1W 7TS, U.K. E. m.hamer@ucl.ac.uk

Manuscript statistics: 2,809 words, 24 references, 3 tables

Running head: Lifestyle and COVID-19

Disclosures: None of the authors have any competing interests to declare.
Abstract

We conducted the first large-scale general population study on lifestyle risk factors (smoking, physical inactivity, obesity, and excessive alcohol intake) for COVID-19 using prospective cohort data with national registry linkage to hospitalisation. Participants were 387,109 men and women (56.4 ±8.8 yr; 55.1% women) residing in England from UK Biobank study. Physical activity, smoking, and alcohol intake, were assessed by questionnaire at baseline (2006-2010). Body mass index, from measured height and weight, was used as an indicator of overall obesity. Outcome was cases of COVID-19 serious enough to warrant a hospital admission from 16-March-2020 to 26-April-2020. There were 760 COVID-19 cases. After adjustment for age, sex and mutually for each lifestyle factor, physical inactivity (Relative risk, 1.32, 95% confidence interval, 1.10, 1.58), smoking (1.42;1.12, 1.79) and obesity (2.05 ;1.68, 2.49) but not heavy alcohol consumption (1.12; 0.93, 1.35) were all related to COVID-19. We also found a dose-dependent increase in risk of COVID-19 with less favourable lifestyle scores, such that participants in the most adverse category had 4-fold higher risk (4.41; 2.52 – 7.71) compared to people with the most optimal lifestyle. C-reactive protein levels were associated with elevated risk of COVID-19 in a dose-dependent manner, and partly (10 – 16%) explained associations between adverse lifestyle and COVID-19. Based on UK risk factor prevalence estimates, unhealthy behaviours in combination accounted for up to 51% of the population attributable fraction of severe COVID-19. Our findings suggest that an unhealthy lifestyle synonymous with an elevated risk of non-communicable disease is also a risk factor for COVID-19 hospital admission, which might be partly explained by low grade inflammation. Adopting simple lifestyle changes could lower the risk of severe infection.

KEY WORDS: Physical activity, smoking, obesity, infection, coronavirus, C-reactive protein, population cohort
1. Introduction

For non-communicable disease outcomes, lifestyle risk factors have been consistently associated with morbidity, mortality and loss of disease-free years of life.\textsuperscript{1-4} There are also population cohort data on possible adverse effects of poor lifestyle on serious respiratory infections. For example, physical inactivity and smoking appear to be independently associated with higher risk of community-acquired pneumonia and pneumonia mortality.\textsuperscript{5-9} Evidence for alcohol intake and diet on risk of respiratory infection are less clear.\textsuperscript{8,9}

A better understanding of the links between lifestyle risk factors and COVID-19 has obvious implications for prevention of severe outcomes and also in identifying characteristics of those people most at risk. We are, however, unaware of any existing data on the relation of lifestyle risk factors with COVID-19. Accordingly, we examined the association of lifestyle risk factors with new cases of COVID-19-hospitalisations in a general population-based cohort study.

2. Methods

2.1 Study Population

We used data from UK Biobank, a prospective cohort study, the sampling and procedures of which have been well described.\textsuperscript{10} Baseline data collection took place between 2006 and 2010 across twenty-two research assessment centres in the UK giving rise to a sample of 502,655 people aged 40 to 69 years (response rate 5.5\%).\textsuperscript{10} Ethical approval was received from the North-West Multi-centre Research Ethics Committee, and the research was carried out in accordance with the Declaration of Helsinki of the World Medical Association, and participants gave informed consent. No specific ethical approval was required for the present analyses of anonymised data.

2.2 Lifestyle Measures
Physical activity, smoking, and alcohol consumption were assessed by questionnaire at baseline. These characteristics have demonstrated face validity in the UK Biobank sample through their associations with mortality and cardiovascular disease. Participants were categorised into never, previous, and current smokers. From information on the weekly intake of beer and cider (1 pint = 2 units), wines (1 standard glass = 2 units) and spirits (1 shot = 1 unit), we aggregated units of alcohol intake per week. Heavy alcohol intake was defined as ≥14 units in women and ≥21 units in men. Physical activity was assessed using the International Physical Activity Questionnaire (IPAQ) short form that measures duration and frequency of moderate-to-vigorous physical activity (MVPA) from all domains in the last week. Meeting activity guidelines was defined as ≥150 min/week MVPA or ≥75 min/week vigorous PA. Body weight was measured using Tanita BC418MA scales and standing height using a Seca height measure. Body mass index (BMI) was calculated [weight (kilograms)/height$^2$ (meters$^2$) squared] and categorised into standard groups: healthy weight < 25; overweight 25 - < 30; obese ≥ 30 kg/m$^2$.

2.3 Covariates
During the clinic visit, data were collected via self-report for ethnicity (White, South Asian, Black, Chinese, other), educational attainment (college/degree; A-level; O-level; CSEs or equivalent; National vocational Qualifications/ Higher National Diploma or equivalent; other professional qualification; none), and self-reported physician diagnosed cardiovascular diseases (heart attack, angina, stroke) and diabetes. Hypertension was defined as elevated measured blood pressure (≥140/90 mmHg) and /or use of anti-hypertensive medication.

2.4 Ascertainment of Hospitalisation for COVID-19
Provided by Public Health England, data on COVID-19 status covered the period from 16th March 2020, after which testing was restricted to those with symptoms in hospital (http://biobank.ndph.ox.ac.uk/showcase/field.cgi?id=40100). For the present analyses COVID-19 testing results up to 26th April 2020 were included. These data can be regarded as a proxy for hospitalisations for severe cases of the disease for England only; study members from Scotland and Wales were therefore omitted from our analytical sample. COVID-19 disease tests were performed on
samples from combined nose/throat swabs, using real time polymerase chain reaction (RT-PCR) in accredited laboratories.\textsuperscript{13}

2.5 Statistical Analyses
Analyses were performed using SPSS Version 26. We assigned points to different levels of each lifestyle behaviour: smoking history (0=never; 1=past; 2=current), physical activity (0=meeting guidelines; 1= active but below guideline; 2=inactive), alcohol (0= moderate intake within guidelines; 1= never or very occasional; 2= heavy intake exceeding guidelines), obesity (0=healthy weight; 1=overweight; 2 = obese). Thus, scores ranged from 0 (optimal) to 8 (worst). We fitted regression models to estimate relative risk (RR) and 95% confidence intervals for associations between lifestyle scores and COVID-19. Relative risks were first adjusted for age and sex, followed by education, ethnicity, diabetes, hypertension, and cardiovascular diseases. We calculated Population Attributable Fraction (PAF) using our mutually-adjusted effect estimates on lifestyle factors and COVID-19 and lifestyle factor prevalence from Health Survey for England\textsuperscript{14,15} (a representative, population-based survey of adults aged 16 and over living in private households in England) to evaluate the proportion of severe COVID-19 cases that could be avoided if high-risk people adopted a healthier lifestyle:

\[
P_{AF \ in \ group \ j} = P_j \left( RR_j - 1 \right) / \left[ 1 + \sum_{i=1}^{K} P_i \left( RR_i - 1 \right) \right]
\]

\[
P_{AF} = \sum_{j=1}^{K} P_{AF \ j}
\]

where \( P_i \) = proportion of the population in group \( i \); \( RR_i \) = rate ratio in group \( i \); \( K \) = number of non-reference risk groups

3. Results
The analytical sample comprised 387,109 participants (56.2±8.0 years; 55.1% women) who were alive up to 5\textsuperscript{th} March 2020, and had available data on lifestyle exposures and covariates. Participants were largely white British (94.5%). Of the lifestyle factors, 33.5% exceeded alcohol intake guidelines, 23.5% were obese, 9.7% smokers, 17.8% physically inactive, and 4.9% had a diabetes diagnosis, 56.1%
hypertension, and 5.2% cardiovascular disease. Around 0.2% (N=760) of the sample were hospitalized with a COVID-19 infection during the follow-up period, and their risk profile was characterized as being male, older age, smokers, physically inactive, less highly educated, non-white ethnicity, and higher prevalence of cardiometabolic comorbidity (Table 1).

3.1 Lifestyle and COVID-19

There was a dose-dependent association between the risk of COVID-19 with worsening lifestyle scores, such that participants in the most unfavourable category had 4-fold higher risk (RR=4.41; 95% CI, 2.52, 7.71) (Table 2). These associations were little attenuated after adjustment for covariates. Risk ratios adjusted for age, sex and mutually for each lifestyle factor were raised for physical inactivity (1.32; 1.10, 1.58), smoking (1.42;1.12, 1.79), obesity (2.05 ;1.68, 2.49) but not for heavy alcohol consumption (1.12; 0.93, 1.35) in relation to COVID-19 compared to optimal reference categories.

3.2 Population attributable fraction

Using the Health Survey for England prevalence estimates (17% for current smoking, 25% for ex-smoking, 27% for physical inactivity, 35% for overweight and 28% for obesity), the PAF for the three unhealthy lifestyle factors in combination was 51.4% (13.3% for smoking, 8.6% for physical inactivity, and 29.5% for overweight and obesity).

3.3 Inflammatory mechanisms

We further explored potential mechanisms, specifically if low grade inflammation might partly explain associations between adverse lifestyle and risk of COVID-19. Data on high sensitivity C-reactive protein (hsCRP), measured at baseline at least 10 years before possible infection, were available in a sub-sample of participants (n=363,263). We observed an association between adverse lifestyle score and higher hsCRP levels (B= 0.10, 95% CI, 0.09, 0.11) after adjustment for age, sex, education, ethnicity, diabetes, hypertension, cardiovascular disease. hsCRP levels were associated with elevated risk of COVID-19 in a dose-dependent manner (Table 3). When the association between lifestyle score and COVID-19 was adjusted for hsCRP, the effect estimates were attenuated by 10 – 16 % suggesting a possible mediating effect (Table 3).
4. Discussion

The present study demonstrates associations between adverse lifestyle and higher risk of COVID-19 in a large community-dwelling cohort. The associations were not explained by taking into account covariates such as education, ethnicity and self-reported cardiometabolic diseases, although further adjustment for hsCRP did partially attenuate the association. Based on UK risk factor prevalence estimates, unhealthy behaviors in combination accounted for up to 51% of the population attributable fraction of severe COVID-19.

Physical activity has been previously shown to protect against serious community acquired infections in population cohort studies.\(^5,9\) Other studies\(^17\text{-}20\) in athletic populations have described a “J” shaped association between exercise volume and infection with optimal protection at moderate levels of activity. In the present study, protective associations of physical activity on COVID-19 were observed even at relatively low levels of activity below the current guidelines (i.e., < 150 min moderate to vigorous activity) and no dose-response effect was observed for higher levels. There are plausible biological mechanisms explaining the immunological benefits of exercise,\(^17\) for example, anti-inflammatory effects and beneficial effects on adaptive immune responses.\(^21\)

The existing evidence on obesity and infection have been mixed. Some data suggested BMI above 25 kg.m\(^{-2}\) was protective against pneumonia mortality\(^7,8\) whilst others have suggested that overweight and obesity was associated with higher risk of respiratory and skin infections whilst protective against viral and fungal infections.\(^22\) In a large Norwegian cohort, overweight and obesity were associated with higher 30 day mortality risk after detection of blood borne bacterial infection.\(^9\) Our results suggested both overweight and obesity were risk factors for severe COVID-19 infection, consistent with emerging data in small clinical studies.\(^23\) The potential mechanisms have been linked to immune hyper-reactivity, impaired metabolic responses, and the adverse effects of obesity on lung function, diminishing forced expiratory volume and forced vital capacity.\(^23\)
We found only weak evidence for a link between excessive alcohol intake and COVID-19, which was attenuated to the null in models mutually adjusted for other behavioral risk factors. This is largely consistent with our previous work on alcohol and infectious disease mortality. Interestingly, ‘none drinkers’ were at greater risk of COVID-19, which is likely non-causal as this group have often stopped drinking due to prescribed medication and underlying health conditions.

The role of low-grade inflammation in susceptibility to severe COVID-19 infection remains poorly understood. Our data suggests low grade inflammation was a risk factor for severe COVID-19, and partially explained links between lifestyle behaviors and infection. C-reactive protein is known to play an important role in immune function thus the findings are plausible.

There are several caveats to our work. Some cases of COVID-19 could have been captured in patients originally hospitalized for reasons other than the infection. We did not capture COVID-19 infections treated outside hospital settings; rather, our outcome was people with the infection of sufficient severity to warrant in-patient care. The response rate to the original baseline survey in UK Biobank was 5.5%. As such, this is a select group: relative to the general population, the study sample is healthier and better educated. While this means that estimates of the occurrence of disease, including COVID-19, have little utility, because exposures range is wide and the study sample is large, risk factors associations are not affected. PAF reflects the prevalence of the risk factor in the population and the strength of its association with the outcome being considered; the core assumption is that the risk factor has a causal link to the outcome. As our results are based on observational data rather than an intervention, the present PAF-findings may overestimate of the proportion of COVID-19 hospitalisation that could be been prevented by lifestyle change.

In conclusion, these data suggest that adopting simple lifestyle changes could lower the risk of severe COVID-19 infection.
Acknowledgements

Funding: GDB is supported by the UK Medical Research Council (MR/P023444/1) and the US National Institute on Aging (1R56AG052519-01; 1R01AG052519-01A1); MK by the UK Medical Research Council (MR/R024227), US National Institute on Aging (NIH), US (R01AG056477), NordForsk (75021), and Academy of Finland (311492); There was no direct financial or material support for the work reported in the manuscript.

Acknowledgement: We thank the UK Biobank study member for their generosity in participating.

Access to data: This research has been conducted using the UK Biobank Resource under Application 10279. (http://www.ukbiobank.ac.uk/)

Conflict of interest: None

Contributions: MH and GDB generated the idea for the present paper, and with MK formulated an analytical plan; CRG prepared the data set; MH carried out all the data analyses and wrote the manuscript; All authors commented on an earlier version of the manuscript. MH will act as guarantors for this work. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Role of the funding source: The funders of the studies had no role in study design, data collection, data analysis, data interpretation, or report preparation. CRG/MH had full access to UK Biobank data. MH takes responsibility for the decision to submit the manuscript for publication.
References

1. Colpani V, Baena CP, Jaspers L, van Dijk GM, Farajzadegan Z, Dhana K, Tielemans MJ, Voortman T, Freak-Poli R, Veloso GGV, Chowdhury R, Kavousi M, Muka T, Franco OH. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. Eur J Epidemiol. 2018 Sep;33(9):831-845.

2. Schlesinger S, Neuenschwander M, Ballon A, Nöthlings U, Barbaresko J. Adherence to healthy lifestyles and incidence of diabetes and mortality among individuals with diabetes: a systematic review and meta-analysis of prospective studies. J Epidemiol Community Health. 2020 May;74(5):481-487.

3. Nyberg ST, Singh-Manoux A, Pentti J, Madsen IEH, Sabia S, Alfredsson L, Bjorner JB, Borritz M, Burr H, Goldberg M, Heikkilä K, Jokela M, Knutsson A, Lallukka T, Lindbohm JV, Nielsen ML, Nordin M, Oksanen T, Peijersen JH, Rahkonen O, Rugulies R, Shipley MJ, Spiliä PN, Stenholm S, Suominen S, Vahtera J, Virtanen M, Westerlund H, Zins M, Hamer M, Batty GD, Kivimäki M. Association of Healthy Lifestyle With Years Lived Without Major Chronic Diseases. JAMA Intern Med. 2020 Apr 6. doi: 10.1001/jamainternmed.2020.0618. [Epub ahead of print]

4. Li Y, Schoufour J, Wang DD, Dhana K, Pan A, Liu X, Song M, Liu G, Shin HJ, Sun Q, Al-Shaar L, Wang M, Rimm EB, Hertzmark E, Stampfer MJ, Willett WC, Franco OH, Hu FB. Healthy lifestyle and life expectancy free of cancer, cardiovascular disease, and type 2 diabetes: prospective cohort study. BMJ. 2020 Jan 8;368:l6669. doi: 10.1136/bmj.l6669.

5. Wang HE, Baddley J, Griffin RL, et al. Physical inactivity and long-term rates of community-acquired sepsis. Prev Med 2014; 65: 58-64.

6. Baik I, Curhan GC, Rimm EB, Bendich A, Willett WC, Fawzi WW. A prospective study of age and lifestyle factors in relation to community-acquired pneumonia in US men and women. Arch Intern Med 2000; 160(20): 3082-8.

7. Inoue Y, Koizumi A, Wada Y, et al. Risk and protective factors related to mortality from pneumonia among middle aged and elderly community residents: the JACC Study. J Epidemiol 2007; 17(6): 194-202.

8. Hamer M, O'Donovan G, Stamatakis E. Lifestyle risk factors, obesity and infectious disease mortality in the general population: Linkage study of 97,844 adults from England and Scotland. Prev Med. 2019;123:65-70.

9. Paulsen J, Askim A, Mohus RM, et al. Associations of obesity and lifestyle with the risk and mortality of bloodstream infection in a general population: a 15-year follow-up of 64 027 individuals in the HUNT Study. Int J Epidemiol 2017; 46(5): 1573-81.

10. Sudlow C, Gallacher J, Allen N, 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 Med 2015; 12(3): e1001779.

11. Said MA, Verweij N, van der Harst P. Associations of Combined Genetic and Lifestyle Risks With Incident Cardiovascular Disease and Diabetes in the UK Biobank Study. JAMA Cardiol. 2018 Aug 1;3(8):693-702.

12. Craig CL, Marshall AL, Sjorstrom M, Bauman AE, Booth ML, Ainsworth BE, Pratt M, Ekelund UL, Yngve A, Sallis JF, Oja P. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sport Exerc. 2003 Aug;35(8):1381-95.

13. NHS England and NHS Improvement. COVID-19 virus testing in NHS laboratories. Accessed 5/3/20 https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/03/guidance-and-sop-covid-19-virus-testing-in-nhs-laboratories-v1.pdf

14. NHS Digital. Health Survey for England 2018 Overweight and obesity in adults and children. Accessed 5/5/20 https://files.digital.nhs.uk/52/FD7E18/HSE18-Adult-Child-Obesity-rep.pdf
15. NHS Digital. Health Survey for England 2018 Adult’s health-related behaviours. Accessed 5/5/20 https://files.digital.nhs.uk/B5/771AC5/HSE18-Adult-Health-Related-Behaviours-rep-v3.pdf
16. Fry D, Almond R, Moffat S, Gordon M, Singh P. UK Biobank Biomarker Project: Companion document to accompany serum biomarker data Accessed 5/5/20 https://biobank.ndph.ox.ac.uk/showcase/showcase/docs/serum_biochemistry.pdf
17. Schwellnus M, Soligard T, Alonso JM, et al. How much is too much? (Part 2) International Olympic Committee consensus statement on load in sport and risk of illness. Br J Sports Med 2016; 50(17): 1043-52.
18. Spence L, Brown WJ, Pyne DB, et al. Incidence, etiology, and symptomatology of upper respiratory illness in elite athletes. Med Sci Sports Exerc 2007; 39(4): 577-86.
19. Matthews CE, Ockene IS, Freedson PS, Rosal MC, Merriam PA, Hebert JR. Moderate to vigorous physical activity and risk of upper-respiratory tract infection. Med Sci Sports Exerc 2002; 34(8): 1242-8.
20. Nieman DC, Henson DA, Austin MD, Sha W. Upper respiratory tract infection is reduced in physically fit and active adults. Br J Sports Med 2011; 45(12): 987-92.
21. Pascoe AR, Fiatarone Singh MA, Edwards KM. The effects of exercise on vaccination responses: a review of chronic and acute exercise interventions in humans. Brain Behav Immun 2014; 39: 33-41.
22. Harpsøe MC, Nielsen NM, Friis-Moller N, et al. Body Mass Index and Risk of Infections Among Women in the Danish National Birth Cohort. Am J Epidemiol 2016; 183(11): 1008-17.
23. Sattar N, McInnes IB, McMurray JJV. Obesity a Risk Factor for Severe COVID-19 Infection: Multiple Potential Mechanisms. Circulation. 2020 Apr 22. doi: 10.1161/CIRCULATIONAHA.120.047659. [Epub ahead of print]
24. Del Giudice M, Gangestad SW. Rethinking IL-6 and CRP: Why they are more than inflammatory biomarkers, and why it matters. Brain Behav Immun. 2018 May;70:61-75.
25. Batty GD, Gale CR, Kivimäki M, Deary IJ, Bell S. Comparison of risk factor associations in UK Biobank against representative, general population based studies with conventional response rates: prospective cohort study and individual participant meta-analysis. BMJ. 2020;368:m131. Published 2020 Feb 12. doi:10.1136/bmj.m131
Table 1. Baseline characteristics of sample in relation to COVID-19

|                                | COVID-19 hospitalisation |
|--------------------------------|--------------------------|
|                                | No           | Yes          |
| Age (yrs)                      | 56.4 ± 8.0  | 57.1 ± 9.0  |
| Sex (% men)                    | 44.8         | 55.3         |
| Smokers                        | 9.8          | 11.9         |
| Physical inactivity            | 17.8         | 25.0         |
| Moderate alcohol intake        | 36.2         | 28.6         |
| Degree educated                | 32.8         | 26.7         |
| White ethnicity                | 94.5         | 86.7         |
| Diabetes                       | 4.8          | 9.5          |
| Hypertension                   | 56.1         | 63.9         |
| Cardiovascular disease         | 5.2          | 9.4          |
| Body mass index (kg/m²)        | 27.3 ± 4.7   | 29.0 ± 5.4  |
| Waist-Hip ratio                | 0.87 ±0.1    | 0.91 ± 0.1  |
| Total cholesterol (mmol/l)     | 5.7±1.1      | 5.4±1.2     |
| HDL cholesterol (mmol/l)       | 1.5±0.4      | 1.3±0.3     |
| Glycated haemoglobin (mmol/mol)| 35.9±6.5     | 38.0±8.8    |
| C-reactive protein (log units) | 0.98±0.64    | 1.12±0.68   |

Results are expressed as percentage or mean ± SD.
Table 2. Combined and individual lifestyle behavioral risk factors in relation to COVID-19 hospitalisation (N=387,109)

| Total lifestyle score | CASES/N     | Relative Risk (95% CI) | Model 1 | Model 2 |
|-----------------------|-------------|------------------------|---------|---------|
|                       |             |                        |         |         |
| 0 (optimal)           | 13 / 19,776 | 1.0 (ref)              | 1.0 (ref) |         |
| 1                     | 55 / 52,053 | 1.58 (0.86, 2.59)      | 1.48 (0.81, 2.71) |     |
| 2                     | 142 / 77,861| 2.73 (1.55, 4.81)     | 2.43 (1.38, 4.29) |     |
| 3                     | 163 / 87,998| 2.76 (1.57, 4.85)     | 2.41 (1.37, 4.25) |     |
| 4                     | 160 / 75,123| 3.12 (1.77, 5.49)     | 2.70 (1.53, 4.75) |     |
| ≥5 (worst)            | 227 / 74,298| 4.41 (2.52, 7.71)     | 3.73 (2.12, 6.54) |     |
|                       |              | p-trend                | <0.001  | <0.001  |

**Individual behaviours**

| Smoking              |              |          |         |         |
|----------------------|-------------|---------|---------|---------|
| Never                | 354 / 214,828| 1.0 (ref) | 1.0 (ref) |         |
| Past                 | 313 / 134,855| 1.34 (1.15, 1.56) | 1.36 (1.15, 1.59) |     |
| Current              | 93 / 37,426  | 1.45 (1.16, 1.83) | 1.36 (1.08, 1.71) |     |
| Physical activity    |              |          |         |         |
| Sufficient           | 382 / 209,489| 1.0 (ref) | 1.0 (ref) |         |
| Insufficient         | 192 / 108,707| 0.98 (0.83, 1.17) | 0.99 (0.84, 1.18) |     |
| None                 | 186 / 68,913 | 1.51 (1.27, 1.81) | 1.38 (1.15, 1.64) |     |
| Alcohol consumption  |              |          |         |         |
| Below guideline      | 216 / 140,908| 1.0 (ref) | 1.0 (ref) |         |
| Rarely/never         | 304 / 116,389| 1.88 (1.55, 2.24) | 1.57 (1.31, 1.88) |     |
| Above guideline      | 240 / 129,812| 1.23 (1.00, 1.45) | 1.24 (1.03, 1.50) |     |
| Body mass index      |              |          |         |         |
| Healthy weight       | 166 / 131,162| 1.0 (ref) | 1.0 (ref) |         |
| Overweight           | 317 / 165,052| 1.41 (1.16, 1.70) | 1.32 (1.09, 1.60) |     |
| Obesity              | 277 / 90,895 | 2.28 (1.88, 2.77) | 1.97 (1.61, 2.42) |     |

Model 1 adjusted for age and sex

Model 2 adjusted for age, sex, education, ethnicity, diabetes, hypertension, cardiovascular disease (heart attack, angina, or stroke)
Table 3. Lifestyle risk factors, C-reactive protein, and Hospital Admission for COVID-19 in A Sub-sample with Available Biomarkers (N=363,263)

| Lifestyle score | Relative Risk (95% confidence interval) | Model 1 * | Model 2 † |
|----------------|----------------------------------------|-----------|-----------|
| 0 (optimal)    | 1.0 (ref)                              | 1.0 (ref) |           |
| 1              | 1.46 (0.78, 2.74)                      | 1.41 (0.75, 2.65) |       |
| 2              | 2.44 (1.35, 4.40)                      | 2.30 (1.27, 4.16) |       |
| 3              | 2.44 (1.39, 4.39)                      | 2.26 (1.25, 4.08) |       |
| 4              | 2.77 (1.54, 5.00)                      | 2.52 (1.39, 4.55) |       |
| ≥5 (worst)     | 3.74 (2.09, 6.72)                      | 3.30 (1.83, 5.95) |       |

C-reactive protein quintile

| C-reactive protein quintile | Relative Risk (95% confidence interval) | Model 1 * | Model 2 † |
|---------------------------|----------------------------------------|-----------|-----------|
| ≤0.55 mg/L                | -                                      | 1.0 (Ref) |           |
| 0.56 – 1.02 mg/L          | -                                      | 1.18 (0.90, 1.54) |       |
| 1.03 – 1.75 mg/L          | -                                      | 1.32 (1.01, 1.71) |       |
| 1.76 – 3.33 mg/L          | -                                      | 1.48 (1.15, 1.92) |       |
| > 3.33 mg/L               | -                                      | 1.47 (1.13, 1.91) |       |

* Adjusted for age, sex, education, ethnicity, diabetes, hypertension, cardiovascular diseases.
† Additionally adjusted for high-sensitivity C-reactive protein.