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1 Diet quality and risk and severity of COVID-19: a prospective cohort study

- 2
- Jordi Merino, Ph.D.;^{1,2,3#} Amit D. Joshi, MBBS, Ph.D.;^{4,5#} Long H. Nguyen, M.D., M.S.;^{4,5,6#}
- 4 Emily R. Leeming MSc.;⁷ Mohsen Mazidi, Ph.D.;⁷ David A Drew, Ph.D.;^{4,5} Rachel Gibson
- 5 Ph.D.;⁸ Mark S. Graham Ph.D.;⁹ Chun-Han Lo M.D., M.P.H.;^{4,5} Joan Capdevila, Ph.D.;¹⁰
- 6 Benjamin Murray, Ph.D.;⁹ Christina Hu, BA.;¹⁰ Somesh Selvachandran, MEng.;¹⁰ Sohee Kwon,
- 7 Ph.D.;^{4,5} Wenjie Ma, Ph.D.;^{4,5} Cristina Menni, M.D.;⁷ Alexander Hammers, M.D., Ph.D.;^{9,11}
- 8 Shilpa N. Bhupathiraju, Ph.D.;^{3,12} Shreela V. Sharma, Ph.D.;¹⁴ Carole Sudre Ph.D.;⁹ Christina M.
- 9 Astley, M.D., Sc.D.;^{2,13} Walter C. Willet, M.D., Dr.P.H.;^{12,15,16} Jorge E. Chavarro, M.D.,
- 10 Sc.D.;^{12,15,16}, Sebastien Ourselin, Ph.D.;⁹ Claire J. Steves, MBBS, M.D.;⁷ Jonathan Wolf, MA.;¹⁰
- 11 Paul W. Franks, Ph.D.;^{12,17} Tim D. Spector, MBBS, M.D.;^{8*} Sarah E. Berry, Ph.D.;^{8*} Andrew T.
- 12 Chan, M.D., M.P.H.;^{4,5*}
- 13
- 14
- Diabetes Unit and Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA,
 USA.
- 17 2. Program in Medical and Population Genetics, Broad Institute, Cambridge, MA, USA.
- 18 3. Department of Medicine, Harvard Medical School, Boston, MA, USA.
- 19 4. Clinical and Translational Epidemiology Unit, Massachusetts General Hospital and Harvard
- 20 Medical School, Boston, MA, USA.
- Division of Gastroenterology, Massachusetts General Hospital and Harvard Medical School,
 Boston, MA, USA.
- 23 6. Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA.
- 24 7. Department of Twin Research, King's College London, London UK
- 25 8. Department of Nutritional Sciences, King's College London, London UK
- 26 9. School of Biomedical Engineering & Imaging Sciences, King's College London, London, UK
- 27 10. Zoe Global Limited, London, UK
- 28 11. King's College London & Guy's and St Thomas' PET Centre, King's College London, London,
- 29 UK
- 30 12. Department of Nutrition, Harvard TH Chan School of Public Health, Boston, MA, USA

- 31 13. Division of Endocrinology & Computational Epidemiology, Boston Children's Hospital,
- 32 Harvard Medical School, Boston, M
- 33 14. Department of Epidemiology, Human Genetics, and Environmental Sciences, UTHealth, School
- 34 of Public Health, Houston, TX, USA
- 35 15. Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA
- 36 16. Channing Division of Network Medicine, Department of Medicine, Brigham and Women's
- 37 Hospital and Harvard Medical School, Boston, MA, USA
- 38 17. Department of Clinical Sciences, Lund University, Malmö, Sweden
- 3940 # Authors share co-first authorship
 - 41 * Authors share co-last authorship
 - 42
 - 43
 - 44

45 **Correspondence:**

- 46 Andrew T. Chan, M.D., M.P.H. Clinical and Translational Epidemiology Unit, Massachusetts
- 47 General Hospital, 100 Cambridge Street Boston, MA 02114; Phone: 617-726-7802; Fax: 617-
- 48 643-0195; Email: <u>achan@mgh.harvard.edu</u>
- 49
- 50

52 Abstract

53 Objective: Poor metabolic health and certain lifestyle factors have been associated with risk and 54 severity of coronavirus disease 2019 (COVID-19), but data for diet are lacking. We aimed to 55 investigate the association of diet quality with risk and severity of COVID-19 and its intersection 56 with socioeconomic deprivation.

57 **Design:** We used data from 592,571 participants of the smartphone-based COVID Symptom 58 Study. Diet quality was assessed using a healthful plant-based diet score, which emphasizes 59 healthy plant foods such as fruits or vegetables. Multivariable Cox models were fitted to 60 calculate hazard ratios (HR) and 95% confidence intervals (95% CI) for COVID-19 risk and 61 severity defined using a validated symptom-based algorithm or hospitalization with oxygen 62 support, respectively.

63 **Results:** Over 3,886,274 person-months of follow-up, 31,815 COVID-19 cases were

64 documented. Compared with individuals in the lowest quartile of the diet score, high diet quality

65 was associated with lower risk of COVID-19 (HR, 0.91; 95% CI, 0.88-0.94) and severe COVID-

66 19 (HR, 0.59; 95% CI, 0.47-0.74). The joint association of low diet quality and increased

67 deprivation on COVID-19 risk was higher than the sum of the risk associated with each factor

alone ($P_{interaction}=0.005$). The corresponding absolute excess rate for lowest vs highest quartile of

69 diet score was 22.5 (95% CI, 18.8-26.3) and 40.8 (95% CI, 31.7-49.8; 10,000 person-months)

among persons living in areas with low and high deprivation, respectively.

71 Conclusions: A dietary pattern characterized by healthy plant-based foods was associated with

12 lower risk and severity of COVID-19. These association may be particularly evident among

73 individuals living in areas with higher socioeconomic deprivation.

74 Introduction

Poor metabolic health^{1,2} has been associated with increased risk and severity of coronavirus 75 76 disease 2019 (COVID-19), and excess adiposity or preexisting liver disease might be causally associated with increased risk of death from COVID-19.^{3,4} Underlying these conditions is the 77 78 contribution of a diet, which may be independently associated with COVID-19 risk and severity. 79 On the basis of prior scientific evidence, diet quality scores have been developed to evaluate the healthfulness of dietary patterns.^{5–7} Dietary patterns capture the complexity of food intakes better 80 81 than any one individual food item and offer the advantage of describing usual consumption of 82 foods in typical diets.⁸ One such diet score is the healthful plant-based diet index (hPDI), which 83 emphasizes intake of healthy plant foods, such as fruits, vegetables, and whole grains, and has been associated with lower risk of metabolic diseases.^{5,9,10} 84 85 Adherence to healthful dietary patterns may also be a proximal manifestation of distal social determinants of health.¹¹⁻¹³ Addressing adverse social determinants of health, such as poor 86 nutrition, has been shown to reduce the burden of certain infectious diseases in the past,¹⁴ 87 88 supporting calls for prioritizing social determinants of health in the public health response to 89 COVID-19. However, evidence on the association between diet quality and the risk and severity 90 of COVID-19 is lacking, especially in the context of upstream social determinants of health. To 91 address this evidence gap, we analyzed data for 592,571 United Kingdom (UK) and United States (US) participants from the smartphone-based COVID Symptom Study,¹⁵ to prospectively 92 93 investigate the association of diet quality with risk and severity of COVID-19 and its intersection 94 with socioeconomic deprivation.

95 Materials and Methods

96 Study design and participants

97 The COVID Symptom Study is a smartphone-based study conducted in the UK and US. Study design and sampling procedures have been published elsewhere.¹⁵ This analysis included 98 99 participants recruited from March 24, 2020 and followed until December 2, 2020. Participants 100 who reported any symptoms related to COVID-19 prior to start of follow-up, or reported 101 symptoms that classified them as having predicted COVID-19 within 24 hours of first entry, or 102 who tested positive for COVID-19 at any time prior to start of follow-up or 24 hours after first 103 entry were excluded. We also excluded participants younger than 18 years old, pregnant, and 104 participants who logged only one daily assessment during follow-up. At enrollment, we obtained 105 informed consent to the use of volunteered information for research purposes and shared relevant 106 privacy policies and terms of use agreements. The study protocol was approved by the Mass 107 General Brigham Human Research Committee (protocol 2020P000909) and King's College 108 London Ethics Committee (REMAS ID 18210, LRS-19/20-18210).

109 **Data collection procedures**

110 Information on demographic factors was collected through standardized questionnaires at

111 baseline,¹⁵ including self-reported COVID-19 or any COVID-19 related symptoms and personal

112 medical history including lung disease, diabetes, cardiovascular disease, cancer, kidney disease,

- and use of medications. During follow-up, daily prompts queried for updates on interim
- symptoms, health care visits, and COVID-19 testing results. Through software updates, a survey
- 115 to examine self-reported diet and lifestyle habits during the pre/early-pandemic period was

launched between August and September 2020. Details about this survey are available in the
Supplementary Methods and published elsewhere.¹⁶

118 Assessment of diet quality

Diet quality was assessed using information obtained from an amended version of the Leeds Short Form Food Frequency Questionnaire¹⁷ that included 27 food items (online supplementary methods). Participants were asked how often on average they had consumed one portion of each item in a typical week. The responses had eight frequency categories ranging from "rarely or never" to "five or more times per day".

Diet quality was quantified using the validated hPDI score.⁵ To compute the hPDI, the 27 food 124 125 items were combined into 14 food groups (online supplementary table 1). The original hPDI 126 score included 18 food groups but nuts, vegetable oils, tea or coffee, and animal fat were not 127 specifically queried. Food groups were ranked into quintiles and given positive (healthy plant 128 food groups) or reverse scores (less healthy plant and animal food groups). With positive scores, 129 participants within the highest quintile of a food group received a score of 5, following on 130 through to participants within the lowest quintile who received a score of 1. With reverse scores, 131 this pattern of scoring was inverted. All component scores were summed to obtain a total score 132 ranging from 14 (lowest diet quality) to 70 (highest) points. Criteria for generation of the hPDI 133 are provided in online supplemental table 2. As an additional method to quantify diet quality 134 based on available diet information, we used the Diet Quality Score (DQS).¹⁷ The DQS is a score 135 for adherence to UK dietary guidelines and was computed from five broad categories including 136 fruits, vegetables, total fat, oily fish, and non-milk extrinsic sugars. Each component was scored 137 from 1 (unhealthiest) to 3 (healthiest) points, with intermediate values scored proportionally

(online supplementary table 3). All component scores were summed to obtain a total scoreranging from 5 (lowest diet quality) to 15 (highest) points (online supplementary table 4).

140 Assessment of COVID-19 risk and severity

141 The primary outcome of this analysis was COVID-19 risk defined using a validated symptombased algorithm,¹⁸ which provides similar estimates of COVID-19 prevalence and incidence as 142 those reported from the Office for National Statistics Community Infection Survey.¹⁹ Details on 143 144 the symptoms included in the predictive algorithm and corresponding weights are provided in the 145 online supplementary methods. In brief, the symptom-based approach uses an algorithm to 146 predict whether a participant has been infected with SARS-CoV-2 on the basis of their reported 147 symptoms, age, and sex. The rationale for symptom-based classifier as a primary outcome was due to widespread difficulties obtaining testing during the early stages of the pandemic.²⁰ 148 149 Secondary outcomes were confirmed COVID-19 based on a self-report of a reverse transcription 150 polymerase chain reaction (RT-PCR) positive test and COVID-19 severity. COVID-19 severity 151 was ascertained based on a report of the need for a hospital visit which required 1) non-invasive 152 breathing support, 2) invasive breathing support, and 3) administration of antibiotics combined 153 with oxygen support (online supplementary methods).

154 Statistical analysis

We summarized continuous measurements by using medians and interquartile ranges, and present categorical observations as frequency and percentages. Based on zip code (US) or post code (UK) of residence, participants were assigned to country-specific community-level socioeconomic measures including socioeconomic deprivation and population density (online supplementary methods). The methods for classifying socioeconomic deprivation, population density, and other *a priori* selected covariates are provided in online supplementary methods.

Multiple imputations by chained equations with five imputations were used to impute missing
values. All covariates in the primary analysis were included in the multiple imputation
procedure, and estimates generated from each imputed dataset were combined using Rubin's
rules.²¹

165 Follow-up time for each participant started 24 hours after first log-in to the time of predicted 166 COVID-19 (or to time of secondary outcomes) or date of last entry prior to December 2, 2020, 167 whichever occurred first. We modeled the diet quality score as a continuous variable and 168 generated categories of the score based on quartiles of the distribution (quartile 1, low diet 169 quality; quartiles 2-3, intermediate diet quality; quartile 4, high diet quality). Cox regression 170 models stratified by calendar date at study entry, country of origin, and 10-year age group were 171 used to calculate hazard ratio (HR) and 95% confidence intervals (95% CI) for COVID-19 risk 172 and severity (age-adjusted model 1). Model 2 was further adjusted for sex, race/ethnicity, index 173 of multiple deprivation, population density, presence of diabetes, cardiovascular disease, lung 174 disease, cancer, kidney disease, and healthcare worker status. Model 3 was further adjusted for 175 body mass index, smoking status, and physical activity. We verified the proportional hazards assumption of the Cox model by using the Schoenfeld residuals technique.²² Absolute risk was 176 177 calculated as the percentage of COVID-19 cases occurring per 10,000 person-months in a given 178 group. We used restricted cubic splines with four knots (at the 2.5th, 25th, 75th, and 97.5th) 179 percentiles) to assess for non-linear associations between diet quality and COVID-19 risk. 180 In secondary analyses, we used a self-report of a positive test to define COVID-19 risk. For these 181 analyses, we used inverse probability-weighted Cox models to account for predictors of 182 obtaining country-specific testing. Inverse probability-weighted analyses included presence of 183 COVID-19-related symptoms, interaction with a person with COVID-19, occupation as a

184 healthcare worker, age group, and race. Inverse probability-weighted Cox models were stratified 185 by 10-year age group and date with additional adjustment for the covariates used in previous 186 models. For severe COVID-19 analyses, we adjusted for the same covariates used in previous 187 models. As an additional method to quantify diet quality we used the DQS and tested for 188 associations between diet quality and COVID-19 risk and severity. In addition, we censored our 189 analyses to cases that occurred after completing the diet survey to investigate potential bias due 190 to time-varying confounding. 191 In subgroup analyses, we assessed the association between diet quality and COVID-19 risk 192 according to comorbidities, demographic, and lifestyle characteristics. We also classified 193 participants according to categories of the diet quality score and socioeconomic deprivation (nine 194 categories based on thirds of diet quality score and deprivation index) and conducted joint 195 analyses for COVID-19 risk. We tested for additive interactions by assessing the relative excess 196 risk due to interaction, and further examined the COVID-19 risk proportions attributable to diet, 197 deprivation, and to their interaction (online supplementary methods).²³ 198 We conducted sensitivity analyses to account for regional differences in the effective 199 reproductive number (R_t) or other risk mitigating behaviors such as mask wearing. Details on 200 how we obtained and classified individuals for these analyses are provided in online 201 supplementary methods. Two-sided p-values of <0.05 were considered statistically significant 202 for main analyses. All statistical analyses were performed using R software, version 4.0.3 (R 203 Foundation).

205 **Results**

206 Self-reported diet quality was evaluated in 647,137 survey responders, of which 54,566 were 207 excluded due to prevalent COVID (n=1,555), presence of any symptoms at baseline (n=47,594), 208 logged only once (n=1,201), pregnancy (n=1,129), or age under 18 year (n=3,087); online 209 supplementary figure 1). Baseline characteristics of the 592,571 participants included in this 210 study according to categories of the hPDI score are shown in table 1. Participants in the highest 211 quartile of the diet score (reflecting a healthier diet) were more likely than participants in the 212 lowest quartile to be older, female, healthcare workers, of lower BMI, engage in physical 213 activities \geq 5 days/week, and less likely to reside in areas with higher socioeconomic deprivation. 214 The hPDI score was normally distributed (online supplementary figure 2). 215 Over 3,886,274 person-months of follow-up, 31,815 COVID-19 cases were documented. Crude 216 COVID-19 rates per 10,000 person-months were 72.0 (95% CI, 70.4-73.7) for participants in the 217 highest quartile of the diet score and 104.1 (95% CI, 101.9-106.2) for those in the lowest 218 quartile. The corresponding age-adjusted HR for COVID-19 risk was 0.80 (95% CI, 0.78-0.83, 219 table 2). Differences in the risk of COVID-19 persisted after adjustment for potential 220 confounders. In fully adjusted models, the multivariable-adjusted HR for COVID-19 risk was 221 0.91 (95% CI, 0.88-0.94) when we compared participants with high diet quality to those with 222 low diet quality. We observed non-linear decreasing trends in the risk of COVID-19 with higher 223 diet quality (P < 0.001 for non-linearity), in which COVID-19 risk plateau among individuals 224 with a diet quality score > 50 (online supplementary figure 3). The association between diet 225 quality and COVID-19 risk was consistent but attenuated in secondary analyses using the DQS 226 score (HR, 0.92; 95% CI, 0.89-0.95; online supplementary table 5), and became non-significant 227 in fully adjusted models (HR, 1.00; 95% CI, 0.97-1.03). We also investigated whether our

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- completion of the diet survey. These analyses showed that high diet quality, compared to low
- diet quality, was associated with lower COVID-19 risk (multivariable-adjusted HR 0.88; 95%
- 231 CI, 0.83-0.93; online supplementary table 6).
- 232 In secondary analyses for COVID-19 risk based on a positive test, we showed that crude
- 233 COVID-19 incidence rates per 10,000 person-months were 12.9 (95% CI 12.2-13.6) for
- individuals with high diet quality and 16.4 (95% CI 15.5-17.2) for individuals with low diet
- 235 quality. The corresponding multivariable-adjusted HR for risk of COVID-19 was 0.82 (95% CI,
- 236 0.78-0.86; table 2). For risk of severe COVID-19, crude incidence rates were lower for
- individuals reporting high diet quality compared to those with low diet quality (1.6 (95% CI, 1.3-
- 1.8) vs. 2.1 (95% CI, 1.9-2.5; per 10,000 person-months) table 2). In the fully adjusted model,
- high diet quality, as compared to low diet quality, was associated lower risk of severe COVID-19
- 240 with an a HR of 0.59 (95% CI, 0.47-0.74; table 2).

241 In stratified analyses, the inverse association between diet quality and COVID-19 risk was more 242 evident in participants living in areas of high socioeconomic deprivation and those reporting low 243 physical activity levels (P < 0.05; table 3). We found no significant effect modification for other 244 characteristics such age, BMI, race/ethnicity or population density. When diet quality and 245 socioeconomic deprivation were combined, there was a risk gradient with low diet quality and 246 high socioeconomic deprivation. Compared with individuals living in areas with low 247 socioeconomic deprivation and high diet quality, the multivariable-adjusted HR for risk of 248 COVID-19 for low diet quality was 1.08 (95% CI, 1.03-1.14) among those living in areas with

- low socioeconomic deprivation, 1.23 (95% CI, 1.17-1.29) for those living in areas with
- intermediate socioeconomic deprivation, and 1.47 (95% CI, 1.38-1.52) for those living in areas

051	with high any interpreting (figure 1). The init appreciations of distance liter and
251	with high socioeconomic deprivation (figure 1). The joint associations of diet quality and
252	socioeconomic deprivation was higher than the sum of the risk associated with each factor alone
253	(relative excess risk due to interaction (RERI) = 0.05 (95% CI 0.02-0.08); $P_{interaction}$ =0.005;
254	online supplementary table 7). The proportion of contribution to excess COVID-19 risk was
255	estimated to be 31.9% (95% CI, 18.2-45.6) to diet quality, 38.4% (95% CI, 26.5-50.3) to
256	socioeconomic deprivation, and 29.7% (95% CI, 2.1-57.3) to their interaction. The absolute
257	excess rate of COVID-19 per 10,000 person-months for lowest vs highest quartile of the diet
258	score was 22.5 (95% CI, 18.8-26.3) among individuals living in areas with low socioeconomic
259	deprivation and 40.8 (95% CI, 31.7-49.8) among individuals living in areas with high
260	deprivation (online supplementary figure 4)
261	We conducted a series of sensitivity analyses to further account for variation in R_t or mask
262	wearing. For peak R_t censored analyses, crude COVID-19 rates per 10,000 person-months were
263	148.1 (95% CI, 139.9-156.8) among participants with low diet quality and 92.9 (95% CI, 86.6-
264	99.5) for participants with high diet quality. The corresponding multivariable-adjusted HR was
265	0.84 (95% CI, 0.76-0.92, figure 2). The same trend was observed for nadir R_t censored analyses,
266	in which crude COVID-19 rates per 10,000 person-months were 67.1 (95% CI, 61.7-73.0)
267	among participants with low diet quality and 45.8 (95% CI, 41.3-50.5) for participants with high
268	diet quality (multivariable-adjusted HR, 0.89; 95% CI, 0.80-1.00, figure 2). We further adjusted
269	our models for mask wearing. This analysis showed that high diet quality, as compared to low
270	diet quality, was associated with lower risk of COVID-19 with an adjusted HR of 0.88 (95% CI,
271	0.83-0.94; online supplementary table 8).
272	

274 Discussion

281

deprivation.

In this large survey among UK and US participants prospectively assessing risk and severity of COVID-19 infection, we found that a dietary patterns characterized by healthy plant foods was associated with lower risk and severity of COVID-19. We observed a risk gradient of poor diet quality and increased socioeconomic deprivation that departed from the additivity of the risks attributable to each factor separately, suggesting that the beneficial association of diet with COVID-19 may be particularly evident among individuals with higher socioeconomic

282 Our findings are aligned with preliminary evidence showing that improving nutrition could help reduce the burden of infectious diseases.^{12,14,24} Early studies have shown that the administration 283 284 of arachidonic or linoleic acid partially suppresses SARS-CoV-1 and coronavirus 229E viral 285 replication,²⁵ and that specific nutrients or dietary supplements associate with modest reductions in COVID-19 risk.²⁶ Results from this observational study could expand previous single nutrient 286 287 observations and highlight the beneficial association of healthy dietary patterns, which was most 288 pronounced for risk of severe COVID-19. Our findings also concur with a comparative risk 289 assessment study suggesting that a 10% reduction in the prevalence of diet-related conditions 290 such as obesity and type 2 diabetes would have prevented ~11% of the COVID-19 hospitalizations that have occurred among US adults since November 2020.²⁷ 291 292 The association of healthy diet with lower COVID-19 risk appears particularly evident among 293 individuals living in areas of higher socioeconomic deprivation. Our models estimate that nearly 294 a third of COVID-19 cases would have been prevented if one of two exposures (diet and 295 deprivation) were not present. Although these estimated attributable risks should be interpreted

in the context of the population-specific prevalence, and are likely to change over time with the

297 prevailing SARS-CoV-2 infection rate, our observations are consistent with data from ecological 298 studies showing that people living in regions with greater social inequalities are likely to have higher rates of COVID-19 incidence and deaths.²⁸ By generating a granular deprivation index 299 300 based on zip code information our study adds to previous country-level ecological studies. In 301 addition, recent studies on the impact of socioeconomic status on COVID-19 have shown that 302 community-level deprivation indices are strongly associated with COVID-19 risk and mortality.^{29,30} However, it is still possible that differences in deprivation exists within 303 304 communities. Further studies including information about household characteristics, built 305 environment, or access to healthy foods are needed to expand these initial associations. 306 Our study adds to knowledge by formally investigating how diet quality, in the context of distal 307 social determinants of health, associates with risk and severity of COVID-19. While our study 308 supports the beneficial association of diet quality with COVID-19 risk and severity, particularly 309 among individuals with higher deprivation, we cannot completely rule out the potential for 310 residual confounding. Individuals who eat healthier diets are likely to share other features that 311 might be associated with lower risk of infection such as the adoption of other risk mitigation 312 behaviors, better household conditions and hygiene, or access to care. However, it is reassuring 313 that our findings were consistent despite controlling for additional surrogate markers of SARS-314 CoV-2 infection such as mask wearing or community transmission rate, two of the most relevant factors associated with virus transmission and COVID-19 risk.³¹ These findings suggest that 315 316 efforts to address disparities in COVID-19 risk and severity should consider specific attention to 317 access to healthy foods as a social determinants of health.

318 We acknowledge several limitations. First, as an observational study, we are unable to confirm a 319 direct causal association between diet and COVID-risk or infer specific mechanisms. Second,

320 our study population was not a random sampling of the population. Although this limitation is 321 inherent to any study requiring voluntary provision of information, we recognize our participants 322 are mainly white participants and less likely to live in low deprived areas and are less ethnically diverse than the general population.¹⁹ Thus, generalizability of our finding even to the wider 323 324 British and American population is uncertain. Third, our results could be biased due to the time lapse between the dietary recalls, administered a few months after the relevant period of 325 326 exposure (pre-pandemic). However, our sensitivity analyses in which we censored cases that had 327 occurred before the administration of the diet survey showed consistent results. Fourth, the self-328 reported nature of the diet questionnaire is prone to measurement error and bias, and the use of a 329 short food frequency survey could have further reduced the resolution of dietary data collected. 330 More accurate dietary intake assessment methods such as the use of dietary intake biomarkers would be valuable in future studies.³² but also difficult to implement in large-scale and time-331 332 sensitive investigations. Fifth, we defined risk of severe COVID-19 according to reports of 333 hospitalization with oxygen support, which may not have captured more severe or fatal cases.

334 Conclusions

335 In conclusion, our data provide evidence that a healthy diet was associated with lower risk of 336 COVID-19 and severe COVID-19 even after accounting for other healthy behaviors, social 337 determinants of health, and virus transmission measures. The joint association of diet quality 338 with socioeconomic deprivation was greater than the addition of the risks associated with each 339 individual factor, suggesting that diet quality may play a direct influence in COVID-19 340 susceptibility and progression. Our findings suggest that public health interventions to improve 341 nutrition and poor metabolic health and address social determinants of health may be important 342 for reducing the burden of the pandemic.

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351	library.
352	
353	Conflict of Interest:
354	JW, CH, SS, and JC are employees of Zoe Global Ltd. TDS, ERL, SEB, area consultant to Zoe
355	Global Ltd. DAD, JM, and ATC previously served as investigators on a clinical trial of diet and
356	lifestyle using a separate mobile application that was supported by Zoe Global Ltd. Other authors
357	have no conflict of interest to declare.
358	
359	Contributions:
360	JM, ADJ, LHN, ERL, TDS, SEB, and ATC conceived the study design. JM, ADJ, ERL, MSG,
361	JC, BM, SS contributed to the statistical analysis. All authors were involved in acquisition,
362	analysis, or interpretation of data. JM, LHN, and DAD wrote the first draft of the manuscript.
363	DAD, WCW, SO, CJS, JW, PWF, TDS, SEB, ATC obtained funding. JM, ADJ, LHN provided
364	administrative, technical, or material support. TDS, SEB, ATC jointly supervised this work. All
365	authors contributed to the critical revision of the manuscript for important intellectual content

366	and approved the final version of the manuscript. The corresponding authors attest that all listed
367	authors meet authorship criteria and that no others meeting the criteria have been omitted.
368	
369	
370	Data availability statement:
371	Zoe Platform data used in this study is available to researchers through UK Health Data
372	Research using the following link:
373	https://web.www.healthdatagateway.org/dataset/fddcb382-3051-4394-8436-b92295f14259. The
374	diet quality data used for this study are held by the department of Twin Research at Kings'
375	College London. The data can be released to bona fide researchers using our normal procedures
376	overseen by the Wellcome Trust and its guidelines as part of our core funding. We receive
377	around 100 requests per year for our datasets and have a meeting three times a month with
378	independent members to assess proposals. Application is via https://twinsuk.ac.uk/resources-for-
379	researchers/access-our-data/. This means that the data needs to be anonymized and conform to
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477 Figure legends

- 478 **Figure 1.**
- 479 **Title:** Risk of COVID-19 according to diet quality and socioeconomic deprivation.
- 480 Figure legend: Shown are adjusted hazard ratios and 95% confidence interval of the estimate for
- 481 predicted COVID-19 according to categories of diet quality and socioeconomic deprivation. Cox
- 482 model stratified by calendar date at study entry, country of origin, and 10-year age group, and
- 483 adjusted for sex, race/ethnicity, index of multiple deprivation, population density, presence of
- 484 diabetes, cardiovascular disease, lung disease, cancer, kidney disease, healthcare worker status,
- 485 body mass index, smoking status, and physical activity. In these comparisons, participants with
- 486 high-quality diet and low socioeconomic deprivation served as the reference group.

487

488 **Figure 2.**

489 **Title:** Risk of COVID-19 according to community transmission rate and diet quality

490 **Figure legend:** COVID-19 incidence rate per 10,000 person-month and 95% confidence interval

491 of the estimate based on different community transmission rate and diet quality categories. Peak

- 492 R_t and nadir R_t were defined using (methods). Adjusted hazard ratios and 95% confidence
- 493 interval of the estimate for risk of COVID-19 were obtained from fully adjusted Cox models.
- 494
- 495

496 **TABLES and FIGURES**

497 **Table 1.** Baseline characteristics of study participants according to categories of the diet quality

498 score

	All participants (n=592,571)	Low hPDI (Q1; n=148,143)	Intermediate hPDI (Q2-Q3; n=296,286)	High hPDI (Q4; n=148,142)
hPDI score, median [IQR]	50 (47 to 54)	45 (43-47)	51 (49-52)	56 (55-58)
Demographic characteristics				
Age, years	56 (44-65)	52 (41-62)	57 (45-66)	57 (45-65)
≥18-24	14,397 (2.4)	5,146 (3.4)	5,846 (2.0)	3,405 (2.3)
25-34	52,922 (8.9)	16,535 (11.2)	23,150 (7.8)	13,237 (8.9)
35-44	86,251 (14.6)	26,907 (18.2)	40,145 (13.5)	19,199 (13.0)
45-54	125,802 (21.2)	34,890 (23.6)	62,491 (21.1)	28,421 (19.2)
55-64	158,637 (26.8)	34,279 (23.1)	81,837 (27.6)	42,521 (28.7)
≥65	153,810 (26.0)	30,215 (20.4)	82,413 (27.8)	41,182 (27.8)
Missing	752 (0.1)	171 (0.1)	404 (0.1)	177 (0.1)
Sex, No. (%)				
Male	187,450 (31.6)	58,199 (39.3)	93,162 (31.4)	36,089 (24.4)
Female	404,126 (68.2)	89,706 (60.5)	202,605 (68.4)	111,815 (75.5)
Prefer not to say	995 (0.2)	238 (0.2)	519 (0.2)	238 (0.2)
Race ^{ε} , No. (%),				
White	568,770 (96.0)	141,365 (95.4)	284,804 (96.1)	142,601 (96.3)
Black	4,328 (0.7)	1,466 (1.0)	2,053 (0.7)	809 (0.5)
Asian	10,435 (1.8)	2,954 (1.9)	5,043 (1.7)	2,438 (1.6)
Other	7,228 (1.2)	1,925 (1.3)	3,463 (1.2)	1,840 (1.2)
Missing	1,810 (0.3)	433 (0.3)	923 (0.3)	454 (0.3)
Country, No. (%)				
UK	543,984 (91.8)	135,360 (91.4)	272,494 (92.0)	136,130 (91.9)
US	48,587 (8.2)	12,783 (8.6)	23,792 (8.0)	12,012 (8.1)
Index of deprivation, No. $(\%)^{\P}$				
Most deprived, decile 1	1,3416 (2.3)	4,696 (3.1)	6,163 (2.1)	2,557 (1.7)
Least deprived, decile 10	103,608 (17.5)	23,122 (15.6)	53,652 (18.1)	26,834 (18.1)
Missing	40,759 (6.9)	10,489 (7.1)	20,249 (6.8)	10,021 (6.8)
Population density, km ² , No. (%) [¶]				
<500	119,782 (20.2)	28,139 (19.0)	61,230 (20.7)	30,413 (20.5)
500-1,999	90,541 (15.3)	23,631 (16.0)	45,902 (15.5)	21,008 (14.2)
2,000 4,999	94,345 (15.9)	24,813 (16.7)	47,233 (15.9)	22,299 (15.1)
≥5,000	244,295 (41.2)	60,156 (40.6)	120,319 (40.6)	63,820 (43.1)
Missing	43,608 (7.4)	11,404 (7.7)	21,602 (7.3)	10,602 (7.2)
Healthcare worker, yes, No. (%)	41,141 (6.9)	10,633 (2.3)	20,183 (6.8)	10,325 (7.0)

Smoking status, No (%)				
Never	475,347 (81.9)	113,165 (79.0)	238,192 (81.9)	123,990 (84.6)
Former	87,901 (15.1)	22,683 (15.8)	44,771 (15.4)	20,447 (13.9)
Current	17,401 (3.0)	7,402 (5.2)	7,837 (2.6)	2,162 (1.5)
Physical activity				
< 1 day/week	106,294 (17.9)	37,258 (25.2)	50,713 (17.1)	18,323 (12.4)
1-2 days/week	224,606 (37.9)	59,325 (40.0)	113,749 (38.4)	51,532 (34.8)
3-4 days/week	143,548 (24.2)	30,009 (20.3)	73,601 (24.8)	39,938 (27.0)
\geq 5 days/week	117,007 (19.7)	21,164 (14.3)	57,701 (19.5)	38,142 (25.7)
Missing	1,116 (0.2)	387 (0.3)	522 (0.2)	207 (0.1)
Body mass index, Kg/m ²	25.1 (22.6-28.7)	26.6 (23.6-30.7)	25.2 (22.7-28.5	24.0 (21.8-26.9
<18.5	12,004 (2.0)	2,680 (1.8)	5,540 (1.9)	3,784 (2.6)
18.5-24.9	277,536 (46.8)	52,109 (35.2)	138,503 (46.7)	86,924 (58.7)
25-29.9	189,197 (31.9)	51,517 (34.8)	97,919 (33.0)	39,761 (26.8)
≥30	113,056 (19.1)	41,655 (28.1)	53,909 (18.2)	17,492 (11.8)
Missing	778 (0.1)	182 (0.1)	415 (0.1)	181 (0.1)
Mask wearing, No $(\%)^{\dagger}$				
Most of the time / always	437,782 (73.9)	113,202 (76.4)	218,402 (73.7)	106,178 (71.6)
Never / sometimes	152,551 (25.7)	34,240 (23.1)	76,809 (25.9)	41,502 (28.0)
Missing	2,238 (0.4)	701 (0.5)	1,075 (0.4)	462 (0.3)
Clinical history, yes, No. (%)				
Diabetes	20,058 (3.4)	6,079 (4.1)	10,158 (3.4)	3,821 (2.6)
Heart disease	20,376 (3.4)	5,200 (3.5)	10,660 (3.6)	4,516 (3.0)
Cancer	6,559 (1.9)	1,643 (1.8)	3,348 (1.9)	1,568 (1.8)
Lung disease	62,999 (10.6)	17,534 (11.8)	31,227 (10.5)	14,238 (9.6)
Kidney disease	5,134 (0.9)	1,492 (1.0)	2,594 (0.9)	1,048 (0.7)

499

500 **Table Legend:** Values are median (IQR) for continuous variables; numbers and (percentages) for categorical

501 variables.

502 ^εRace was self-reported by the participants.

503 [¶]Index of deprivation and population density were generated using zipcode or postcode information linked with 504 census track data. Country-specific deprivation indices were generated (supplement).

[†]Mask wearing information was collapsed into two categories: participants who wore masks 'none of the time or sometimes', and those who reported wearing masks 'most of time/ always'.

^{*}hPDI ranges from 0 to 70, with higher scores indicating higher adherence to a healthy plant-based diet.

508

509

Table 2. Adjusted hazard ratios of COVID-19 risk and severity according to healthful plant-based dietary index scores.

	Low hPDI (Q1; n=148,143)	Intermediate hPDI (Q2-Q3; n=296,286)	High hPDI (Q4; n=148,142)	P for trend
hPDI score, median (IQR)	45 (43-47)	51 (49-52)	56 (55-58)	
COVID-19 risk				
No. of events/person-months	8,739 / 839,747	15,733 / 2,026,824	7,359 / 1,022,078	_
Incidence rate (10,000 person-months; 95% CI)	104.1 (101.9-106.2)	77.6 (76.4-78.8)	72.0 (70.4-73.7)	—
Age-adjusted model	1.00 (Ref)	0.85 (0.82-0.87)	0.80 (0.78-0.83)	< 0.001
Multivariable model 2	1.00 (Ref)	0.85 (0.83-0.87)	0.81 (0.78-0.83)	< 0.001
Multivariable model 3	1.00 (Ref)	0.91 (0.89-0.93)	0.91 (0.88-0.94)	< 0.001
COVID-19 risk (positive test)				
No. of events/person-months	1,423 / 869,664	2,829 / 2,081,970	1,350 / 1,046,887	_
Incidence rate (10,000 person-months; 95% CI)	16.4 (15.5-17.2)	13.6 (13.1-14.1)	12.9 (12.2-13.6)	_
Age-adjusted model ^{\$}	1.00 (Ref)	0.86 (0.83-0.90)	0.79 (0.75-0.83)	< 0.001
Multivariable model 2 ⁸	1.00 (Ref)	0.87 (0.84-0.91)	0.80 (0.76-0.84)	< 0.001
Multivariable model 3 ⁸	1.00 (Ref)	0.88 (0.85-0.92)	0.82 (0.78-0.86)	< 0.001
Severe COVID-19				
No. of events/person-months	187 / 871,995	390 / 2,086,790	163 / 1,049,476	_
Incidence rate (10,000 person-months; 95% CI)	2.1 (1.9-2.5)	1.9 (1.7-2.1)	1.6 (1.3-1.8)	_
Age-adjusted model	1.00 (Ref)	0.66 (0.56-0.77)	0.45 (0.36-0.57)	< 0.001
Multivariable model 2	1.00 (Ref)	0.66 (0.57-0.78)	0.45 (0.36-0.57)	< 0.001
Multivariable model 3	1.00 (Ref)	0.77 (0.66-0.91)	0.59 (0.47-0.74)	< 0.001

Table Legend: Hazards ratios and 95% CI for COVID-19 risk and severity. COVID-19 risk defined using a validated symptom-based model. COVID-19 or a RT-PCR positive test report. COVID-19 severity was defined based on hospitalization with requirement of oxygen support (methods, supplement).

Cox proportional hazards models were stratified by calendar date at study entry, country of origin, and 10-year age group (Age-adjusted model).

Multivariable model 2 was further adjusted for sex (male, female), race/ethnicity (White, Black, Asian, Other), index of multiple deprivation (most deprived <3, intermediate deprived 3 to 7, less deprived >7), population density (<500 individuals/km², 500 to 1,999 individuals/km², 2,000 to 4,999 individuals/km², and \geq 5,000 individuals/km²), and healthcare worker status (yes with interaction with COVID-19 patients, yes without interaction with COVID-19 patients, no).

Model 3 was further adjusted for presence of comorbidities [diabetes (yes, no), cardiovascular disease (yes, no), lung disease (yes, no), cancer (yes, no), kidney disease (yes, no)], body mass index (<18.5 kg/m2, 18.5 to 24.9 kg/m2, 25.0 to 29.9 kg/m2, and \geq 30 kg/m2), smoking status (yes, no), and physical activity (<1 day/week, 1 to 2 days/week, 3 to 4 days/week).

^{\$} Inverse probability-weighted analyses were conducted to account for predictors of obtaining RT-PCR testing (presence of COVID-19-related symptoms, interaction with a COVID-19 case, healthcare worker, age group, and race). inverse probability-weighted Cox proportional hazards models were stratified by 10-year age group and date with additional adjustment for the covariates used in previous models.

1 **Table 3.** Adjusted hazard ratios of COVID risk according to healthful plant-based dietary index

2 scores stratified by sociodemographic and clinical characteristics.

3

Factor	No. of events/ person- months [#]	HR per 1-SD increase in diet quality score	P value
Age,			
<60	25,329 / 2,285,329	0.94 (0.93-0.95)	
≥60	6,486 / 1,600,945	0.94 (0.92-0.97)	0.63
Sex,			
Male	9,338 / 1,232,656	0.95 (0.93-0.97)	
Female	22,428 / 2,647,254	0.96 (0.95-0.98)	0.21
Race,			
White	30,335 / 3,736,972	0.96 (0.95-0.97)	
Non-white	1,480 / 149,303	0.96 (0.91-1.01)	0.95
Socioeconomic deprivation*			
High	5,244 / 45,6271	0.94 (0.91-0.96)	
Intermediate	13,172 / 1,567,516	0.96 (0.94-0.98)	
Low	13,399 / 1,862,489	0.97 (0.95-0.99)	0.04
Population density, km ² , No.			
<2000	10,581 / 1,490,084	0.96 (0.94-0.98)	
≥2,000	21,234 / 2,396,190	0.96 (0.94-0.97)	0.74
Healthcare worker			
Yes	2,908 / 140,087	0.95 (0.92-0.99)	
No	28,907 / 3,638,588	0.96 (0.95-0.97)	0.78
Body mass index, Kg/m ²			
<25	13,989 / 1,905,517	0.96 (0.94-0.97)	
25-30	9,854 / 1,252,222	0.96 (0.94-0.98)	
≥30	7,972 / 728,536	0.96 (0.94-0.98)	0.73
Physical activity			
< 1 day/week	6,751 / 683,562	0.94 (0.91-0.96)	
1-4 day/week	19,476 / 2,425,198	0.96 (0.94-0.97)	
\geq 5 day/week	5,588 / 777,515	0.99 (0.96-1.01)	0.01

⁴

5 **Table Legend:** Association between predicted COVID-19 and diet quality according to sociodemographic and

6 clinical characteristics. *Socioeconomic deprivation categories were based on deciles of the deprivation index
 7 (methods). Cox models were adjusted for the same covariates as previous model 3. P-values obtained using the Q

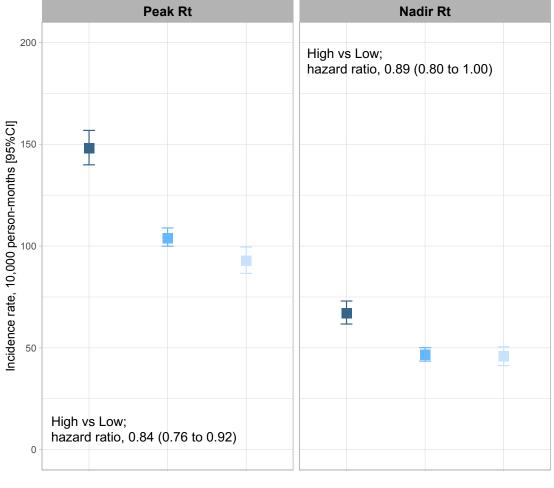
7 (methods). Cox models were adjusted for the same covariates as previous model 3. P-values obtained using the Q8 test for heterogeneity

9 # Number of observations varies among imputations.

Figure 1

Total No. of COVID-19 cases Adjusted HR P Value Subgroup participants Person-Month [95% CI] Low Socioeconomic Deprivation High hPDI 66,714 2,916 / 446,623 1.00 [Reference] Intermediate hPDI 133,557 6,139 / 892,602 1.02 [0.97-1.06] 0.481 Low hPDI 60,759 3,499 / 398,407 1.08 [1.03-1.14] 0.002 _ Intermediate Socioeconomic Deprivation High hPDI 56,354 2,905 / 372,964 1.12 [1.06-1.18]<0.001 Intermediate hPDI 110,890 5,660 / 731,895 1.09 [1.04-1.15] < 0.001 3,810 / 359,896 1.23 [1.17-1.29] <0.001 Low hPDI 56,143 High Socioeconomic Deprivation High hPDI 15,053 979 / 97,708 1.28 [1.18-1.37] < 0.001 Intermediate hPDI 31,590 2,152 / 202,751 1.33 [1.25-1.40] <0.001 Low hPDI 20,752 1,787 / 126,752 1.47 [1.38-1.56] < 0.001 Г 0.8 1.2 1.4 1.6 1 Estimated COVID risk, HR (95%CI)

Figure 2



Healthful plant-based dietary index scores 🖶 Low 🚽 Intermediate 🚽 High