

## **Modest effects of dietary supplements during the COVID-19 pandemic: insights from 445,850 users of the COVID Symptom Study app**

Panayiotis Louca (0000-0001-5956-1433), PhD Student<sup>1\*</sup>, Benjamin Murray (0000-0002-8198-8131), Senior Research Associate<sup>2\*</sup>, Kerstin Klaser (0000-0002-5230-6939), Research Associate<sup>2\*</sup>, Mark S Graham (0000-0002-4170-1095), Research Fellow<sup>2</sup>, Mohsen Mazidi (0000-0003-3059-229X), Research Associate<sup>1</sup>, Emily R Leeming (0000-0002-0531-4901), PhD Student<sup>1</sup>, Ellen Thompson (0000-0003-2118-821X), Research Associate<sup>1</sup>, Ruth Bowyer (0000-0002-6941-8160), Research Associate<sup>1</sup>, David A Drew (0000-0002-8813-0816), Instructor<sup>3</sup>, Long H Nguyen (0000-0002-5436-4219)<sup>3</sup>, Instructor, Jordi Merino (0000-0001-8312-1438), Instructor<sup>3</sup>, Maria Gomez (0000-0001-6210-3142), Professor<sup>4</sup>, Olatz Mompeo (0000-0002-1754-6136), PhD Student<sup>1</sup>, Ricardo Costeira, (0000-0002-8316-5219), Research Associate<sup>1</sup>, Carole H Sudre (0000-0001-5753-428X), Lecturer<sup>5</sup>, Rachel Gibson (0000-0002-5823-6468) Lecturer<sup>7</sup>, Claire J Steves (0000-0002-4910-0489), Clinical Senior Lecturer<sup>1</sup>, Jonathan Wolf (0000-0002-0530-2257), CEO<sup>6</sup>, Paul W Franks (0000-0002-0520-7604), Professor<sup>4</sup>, Sebastien Ourselin (0000-0002-5694-5340), Professor<sup>2</sup>, Andrew T Chan (0000-0001-7284-6767), Professor<sup>3</sup>, Sarah E Berry (0000-0002-5819-5109), Senior Lecturer<sup>7</sup>, Ana M Valdes (0000-0003-1141-4471), Professor<sup>1,8</sup>, Philip C Calder (0000-0002-6038-710X) Professor<sup>9</sup>, Tim D Spector (0000-0002-9795-0365), Professor<sup>1\*</sup>, Cristina Menni (0000-0001-9790-0571), Lecturer<sup>1\*</sup>

<sup>1</sup> Department of Twin Research and Genetic Epidemiology, King's College London, London SE1 7EH, UK

<sup>2</sup> School of Biomedical Engineering & Imaging Sciences, King's College London, London SE1 7EU, UK

<sup>3</sup> Clinical & Translational Epidemiology Unit, Massachusetts General Hospital and Harvard Medical School, 100 Cambridge Street, Boston, MA, USA

<sup>4</sup> Department of Clinical Sciences, Lund University, Diabetes Centre Lund University, Malmö, Sweden

<sup>5</sup> MRC Unit for Lifelong Health and Ageing at UCL, University College London, 1-19 Torrington Place, WC1E 7HB London UK

<sup>6</sup> Zoe Global Limited, London SE1 7RW, UK

<sup>7</sup> Department of Nutritional Sciences, King's College London, London SE1 9NH, UK

<sup>8</sup> Division of Rheumatology, Orthopaedics and Dermatology, School of Medicine, University of Nottingham, Nottingham NG5 1PB, UK

<sup>9</sup> Faculty of Medicine, University of Southampton, Southampton SO16 6YD, UK

\*Denotes equal contribution

**Correspondence to:**

Cristina Menni, PhD

Department of Twin Research, King's College London, St Thomas' Hospital Campus, 3<sup>rd</sup> Floor South Wing Block D, Westminster Bridge Road, London SE1 7EH, UK

Phone: +44 (0) 207 188 7188 (ext. 52594); email: [cristina.menni@kcl.ac.uk](mailto:cristina.menni@kcl.ac.uk)

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## **Abstract**

**Objectives:** Dietary supplements may ameliorate SARS-CoV-2 infection, although scientific evidence to support such a role is lacking. We investigated whether users of the COVID Symptom Study App who regularly took dietary supplements were less likely to test positive for SARS-CoV-2 infection.

**Design:** App-based community survey.

**Setting:** 445,850 subscribers of an app that was launched to enable self-reported information related to SARS-CoV-2 infection for use in the general population in the UK (n=372,720), US (n=45,757) and Sweden (n=27,373).

**Main Exposure:** Self-reported regular dietary supplement usage (constant use during previous 3 months) in the first waves of the pandemic up to 31<sup>st</sup> July 2020.

**Main Outcome Measures:** SARS-CoV-2 infection confirmed by viral RNA polymerase chain reaction test (RT-PCR) or serology test before 31<sup>st</sup> July 2020

**Results:** In 372,720 UK participants (175,652 supplement users and 197,068 non users), those taking probiotics, omega-3 fatty acids, multivitamins or vitamin D had a lower risk of SARS-CoV-2 infection by 14% (95%CI: [8%,19%]), 12%(95%CI: [8%,16%]), 13%(95%CI: [10%,16%]) and 9%(95%CI: [6%,12%]), respectively, after adjusting for potential confounders. No effect was observed for those taking vitamin C, zinc or garlic supplements. Upon stratification by sex, age and body mass index (BMI), the protective associations in individuals taking probiotics, omega-3 fatty acids, multivitamins and vitamin D were observed in females across all ages and BMI groups, but were not seen in men. The same overall pattern of association was observed in both the US and Swedish cohorts.

**Conclusion:** In women, we observed a modest but significant association between use of probiotics, omega-3 fatty acid, multivitamin or vitamin D supplements and lower risk of testing positive for SARS-CoV-2. We found no clear benefits for men nor any effect of vitamin C, garlic or zinc. Randomised controlled trials are required to confirm these observational findings before any therapeutic recommendations can be made.

## **INTRODUCTION**

A number of micronutrients, including vitamins C and D and zinc, have been shown to play key roles in supporting immune function [1,2] and in reducing risk of respiratory infection [2,3]. These nutrients can be obtained from the diet but are also available as dietary supplements either alone or as part of multivitamin or multinutrient mixtures. There are many other dietary supplements available including, omega-3 fatty acids (“fish oil”), probiotics and plant isolates like garlic [4]. The use of specific dietary supplements in both prevention and acute treatment of infection with SARS-CoV-2 has been promoted by prominent medical entertainment personalities on television and social media since the beginning of the current coronavirus pandemic [5]. The UK supplement market increased by 19.5% in the period leading up to the national “lockdown” in early March 2020 [6], with a 110% rise in sales of vitamin C and a 93% rise in sales of multivitamin supplements [6]. Likewise, zinc supplement sales increased by 415% over the 7-day period ending 8<sup>th</sup> March, at the height of COVID-19 concern in the US [5].

A biologically plausible role exists for certain vitamins and minerals in immune pathways [1]. For example, vitamin D has been suggested to reduce SARS-CoV-2 transmission by enhancing antiviral immunity and to reduce mortality by mitigating the cytokine storm linked with severe COVID-19 [7,8]. Moreover, zinc also supports the function of the immune system [9] and may have specific antiviral effects [10]. However, robust evidence to support a role for vitamins and minerals in preventing infection with SARS-CoV-2 is not available [11]. Any such evidence would need to take into account factors such as socioeconomic status, ethnicity, and occupational exposure to the virus as well as the requirement of a large sample size and a clear confirmation of infection.

By using data from the COVID Symptom Study App [12], we tested the hypothesis that individuals taking dietary supplements, were at lower risk of testing positive for SARS-CoV-2, during the first wave of the pandemic. We initially examined whether supplement use was associated with SARS-CoV-2 infection among 327,720 UK participants who reported having been tested for SARS-CoV-2 using a reverse transcriptase polymerase chain reaction (RT-PCR) or serology-based test. Next, we used data from 45,757 US and 27,373 Swedish users of the app who also reported tests for SARS-CoV-2 infection to replicate UK findings.

## **METHODS**

### **Study setting and participants**

The COVID Symptom Study app was developed by health data company Zoe Global Ltd with input from King's College London, the Massachusetts General Hospital, Lund University, Sweden and Uppsala University, Sweden. In the UK it was launched in English on Tuesday the 24<sup>th</sup> March 2020; in the US in English and Spanish on Sunday the 29<sup>th</sup> March 2020; and in Sweden it was launched in Swedish on the 29<sup>th</sup> April 2020 as previously described [12,13]. Anyone over 18 years is able to sign up without any restriction. Individuals are also permitted to record information for dependencies under the age of 18. Here we included individuals above 16 years of age (**Figure S1**). The app enabled self-reported information related to SARS-CoV-2 infection to be captured. On first use, the app recorded self-reported location, age, and core health risk factors. With continued use, participants provided daily updates on symptoms, health care visits, SARS-CoV-2 test results, and if they were self-quarantining or seeking health care, including the level of intervention and related outcomes. Individuals without apparent symptoms were also encouraged to use the app. Through direct updates, new or modified questions were added in real-time to capture data to test emerging hypotheses about COVID-19 symptoms and treatments. Here we analysed data from the 31st July 2020 data dump.

### **Assessment of Exposure**

Starting on the 2<sup>nd</sup> June 2020, in the three countries, via the app, users were retrospectively asked if they had been taking supplements regularly (defined as: more than 3 times a week for at least three months) (**Figure S1**). Each user was able to fill in the supplements questionnaire only once (See **Table S1** for list of questions). The questionnaire included use of probiotics, garlic, omega-3 fatty acids ("fish oils"), multivitamins, vitamin D, vitamin C or zinc or no intake of any supplement. Supplement use was recorded as yes/no. For all the analyses, the control group consisted of individuals not taking any supplement.

### **Ascertainment of outcomes**

Participants were asked if they had been tested for COVID-19 using a RT-PCR or serology-based test and the results (none, negative, pending, or positive). Our primary outcome was a report of a positive COVID-19 test between the time when they first reported on the COVID Symptom Study app and the 31st July 2020. Participants without a positive or negative test result were excluded (**Figure S1**).

### **Ascertainment of covariates**

Covariates including age, sex, BMI, smoking, ethnicity, healthcare worker status, and presence of comorbidities (i.e., cancer, diabetes, eczema, heart disease, lung disease, kidney disease and hay fever) were self-reported via the app. The app also facilitated the index of

multiple deprivation (IMD) to be generated from the relevant government websites UK [14], Scotland [15], Wales [16], with the most recent IMD available at the time of analysis used. The IMD was then categorised into quintiles within-population, where 1 is the least deprived and 5 is the most deprived. A subset of the UK app users (n = 234,271) also completed a second retrospective questionnaire investigating diet quality at two time points. Here we included data from the “peri-pandemic” time point described as the previous month (from user access). The questionnaire included the validated Leeds Short Form food frequency questionnaire (FFQ) developed by Cleghorn and collaborators and listed in the Nutritools ([www.nutritools.org](http://www.nutritools.org)) library [17,18]. We computed the validated Diet Quality Score, as previously described [18]. Briefly, the Diet Quality Score was composed of fruit, vegetable, oily fish, fat and non-milk extrinsic sugar (NMES) intakes reflecting five dietary components recognized as indicators of a healthy diet. Standard portion sizes were assigned to each food item on the FFQ [18].

## **Ethics**

Ethical approval for use of the app for research purposes in the UK was obtained from King’s College London Ethics Committee (review reference LRS-19/20-18210) and all users provided consent for non-commercial use. The US protocol was approved by the Partners Human Research Committee (protocol 2020P000909) [19]. The Swedish protocol was approved by the Swedish Ethical Review Authority (protocol 2020-01803).

## **Data sharing**

Anonymised research data are shared with third parties via the centre for Health Data Research UK ([HDRUK.ac.uk](http://HDRUK.ac.uk)). US investigators are encouraged to coordinate data requests through the COPE Consortium ([www.monganinstitute.org/cope-consortium](http://www.monganinstitute.org/cope-consortium)). Data updates can be found on <https://covid.joinzoe.com>.

## **Statistical analysis**

We studied 372,720 UK app users (aged 16-90 years) who self-reported information regarding regular dietary supplement usage and outcome of a COVID-19 test. Of these, 23,521 individuals tested positive for SARS-CoV-2 and 349,199 tested negative. Multivariate logistic regression adjusting for age, sex, body mass index (BMI) and health status at sign-up was applied to investigate the association between supplement use and testing positive for SARS-CoV-2. We then repeated the analyses (i) adjusting for age, sex, BMI, comorbidities (including type-2 diabetes, cancer, asthma, heart disease, eczema, hay fever, kidney disease and lung

disease), index of multiple deprivation, smoking, ethnicity, health worker/carer status and diet quality and (ii) stratifying by sex, age group (< 40, 40-60, > 60 years) and BMI categories (normal weight, overweight, obese/morbidly obese).

Replication was conducted in two independent datasets including 45,757 US and 27,373 Swedish (SE) app users (**Figure 2**).

All P values presented were two-sided, with statistical significance determined by the Bonferroni corrected threshold of significance ( $P = 0.05/7 = 0.007$ ). Statistical analysis was performed using Stata v12 and ExeTera, a Python library developed at KCL to clean and process the raw dataset [20].

### **Patient and public involvement**

No patients were directly involved in designing the research question or in conducting the research. No patients were asked for advice on interpretation or writing up the results. There are no plans to involve patients or relevant patient community in dissemination at this moment.

### **RESULTS**

The demographic characteristics of the study population are presented in **Table 1**. Briefly, our discovery cohort included 372,720 UK app users who reported having had an RT-PCR-based or serology test for SARS-CoV-2 and who completed the app-based dietary supplement questionnaire. The study sample was predominantly female (66.8%) and more than 50% were overweight (BMI(SD) = 26.8(5.6) kg/m<sup>2</sup>).

As shown in **Table 1**, out of the 372,720 UK app users, 175,652 (47%) self-reported using supplements regularly since the beginning of the pandemic, while 197,068 self-reported they were not taking any supplement. This is in line with the UK general population supplement usage as reported in the National Diet and Nutrition Survey [4,21].

In the UK cohort, users regularly supplementing their diet (i) with multivitamins had a lower risk of testing positive for SARS-CoV-2 by 13% (OR[95%CI]= 0.87[0.84,0.90],  $P=1.62 \times 10^{-14}$ ), (ii) with vitamin D had a lower risk by 9% (OR[95%CI]= 0.91[0.88,0.94],  $P=2.07 \times 10^{-8}$ ); (iii) with probiotics had a lower risk by 14% OR[95%CI]=0.86[0.81,0.92],  $P=1.99 \times 10^{-6}$ ); and (iv) with omega-3 fatty acids had a lower risk by 12% (OR[95%CI]= 0.88[0.84,0.92],  $P=5.8 \times 10^{-8}$ ), after adjusting for age, sex, BMI, sign-up health status and multiple testing (**Figure 1**). There were no significant associations in those supplementing with zinc, vitamin C or garlic (**Figure 1**). Crude results are presented in **Table S2**. To account for a potential healthy user bias, we did a sensitivity analysis further adjusting for ethnicity, comorbidities, smoking, index of multiple deprivation and health worker/carer status, results remained were consistent with the previous

analysis (**Figure 1**), though the effect of probiotics appeared weaker. We also adjusted for the diet quality score. In line with the literature [22], we found diet quality and supplements usage to be positively correlated ( $r=0.07$ ,  $p<0.0001$ ), supporting that people whose diet are closer to the recommended one are more likely to take supplements compared to those whose diet is far from the recommendation. However, when we adjust for diet quality, results remain consistent, suggesting that the effect of supplement use is independent from the effect of diet quality (**Figure 1**).

Next, we ran the analyses stratifying by sex, age group and BMI categories and we detected sexual dimorphism in the association between supplement use and testing positive for SARS-CoV-2 (**Figure 1**). Females taking probiotics, omega-3 fatty acids, multivitamins and vitamin D had a lower risk of infection across all age groups and BMI categories (OR[95%CI] ranging from 0.73[0.63,0.85] for probiotics in women < 40 years of age to 0.91[0.86,0.96] for vitamin D in women aged between 40-60 years). No protective association was observed in males overall. However, in post-hoc subgroup analyses, men aged < 40 years or normal weight and taking multivitamins and men aged 40-60 years and taking omega-3 fatty acids were less likely to be infected (**Figure 1**). In contrast, there was a positive association in men aged > 60 years taking zinc (1.4[1.16,1.69],  $P=4.92 \times 10^{-4}$ ) or vitamin C supplements (1.22[1.05,1.41],  $P=8.1 \times 10^{-3}$ ) (**Figure 1**) for testing positive for SARS-CoV-2.

To replicate significant findings from the UK cohort we next used data from the 45,757 US and 27,373 Swedish app users. Cohorts were similar, in that they were also predominantly female (US: 67.8%, SE: 68.6%) and a greater proportion were overweight (BMI(SD), US: 27.3(5.9) kg/m<sup>2</sup>, SE: 26(4.7) kg/m<sup>2</sup>). Overall UK findings were mirrored in both cohorts (**Figure 2**). However, findings by gender varied different in different cohorts (**Figure 2**).

Associations in females were replicated in the US cohort, but omega-3 supplement use was not associated with testing positive in Swedish females (**Figure 2**). US males using probiotics or vitamin D had a decreased risk of a positive test for SARS-CoV-2 (**Figure 2**), while Swedish men taking probiotics, omega-3 fatty acids, multivitamins or vitamin D had a decreased risk of infection (**Figure 2**).

## DISCUSSION

In the largest observational study on SARS-CoV-2 infection and dietary supplement use to date on over 400,000 app users from three different countries, we show a significant association between users of omega-3 fatty acid, probiotic, multivitamin or vitamin D supplements and lower risk of testing positive for infection with SARS-CoV-2. However, our stratified analysis in the tested group shows a strong sexual dimorphism with the consistent protective effect present only in females, at least in the UK, and for some supplements in the



US and SE. This association has several potential explanations including (i) Biological explanations include discordant immune systems between sexes that could respond differently to supplements [23]. Indeed, a sexual dimorphism in nutrient metabolism has been previously reported, with females having a more robust immune response than men [24]. Moreover, females typically possess a more resilient immune system than males with higher numbers of circulating B cells when matched for age, BMI and clinical parameters [25], as well as a slower age related decline in circulating T- and B-cells [25]. It is therefore plausible that supplements could better support the immune system of females than males, although the lack of consistency between countries is problematic; (ii) differences in body weight and body composition between males and females meaning that supplement dosing on a per body weight basis may be higher in females [26], (iii) residual confounding due to sex differences in health-related behaviours, including COVID-19 [27]. Polling reveals that a greater percentage of females versus males are anxious for the health of themselves or their family and therefore are more precautionary, cancelling plans and staying home more often [27]. Females who purchase vitamins may also be more health conscious than males, such as having greater use of wearing face masks and hand-washing [28–30]. Indeed, in our data, we found that women tended to wear masks more often than males (44% of women report wearing a mask at least some of the time when outside, compared to 36% of men,  $P < 0.001$ ).

**Vitamin D:** A potential antimicrobial role of vitamin D in infections dates back almost a century [31], with several mechanistic study supporting a positive physiological role [3]. Immune cells express the vitamin D receptor and some can synthesise the active form of vitamin D. Vitamin D influences the function of antigen-presenting cells, T-cells and B-cells [32]. It also promotes production of cathelicidin, a microbicidal component of the innate immune system [33]. The overlap between risk factors for vitamin D deficiency and risk of severe COVID-19, such as obesity, age, and ethnicity, gives some plausibility to a protective role of vitamin D [31]. A meta-analysis of 39 randomised controlled trials reported that vitamin D reduces the risk of respiratory infections by around 11% but there was considerable heterogeneity [34]. However, a Mendelian Randomisation study, suggests that genetic levels of vitamin D are not associated to COVID-19 susceptibility [35], in line with recent results from the UKBiobank [36].

In our data, we find a modest protective effect for infection, with a 9% reduction in risk of testing positive for SARS-CoV-2 in the overall UK cohort, 24% in the US cohort and 19% in the SE group.

**Multivitamins:** Multivitamin supplements typically include not just multiple vitamins, but also multiple minerals including trace elements [37]; many of these have antioxidant properties and roles in supporting the immune system [1,2]. Specific micronutrient deficiencies, including

zinc, selenium, vitamin A, vitamin D and vitamin E, have been shown to be detrimental during viral infections [38–40]. Although some randomised controlled trials have shown that multivitamin supplements reduce the risk of respiratory infections [41], a recent review argues that this evidence is weak and unclear [42]. Here, we provide evidence to support a modest protective effect in those taking multivitamin supplements similar to vitamin D with a 13% reduction in risk of testing positive for SARS-CoV-2 in the overall UK cohort, 12% in the US cohort and 22% in the SE cohort.

**Omega-3 fatty acids:** Omega-3 fatty acids can influence antigen presenting cell, T-cell and B-cell function, although their effects on these cell types in humans is not consistently reported. However, they are clearly demonstrated to be anti-inflammatory [43] and to be converted to specialised pro-resolving mediators such as resolvins, protectins and maresins [44]. Whether this is a mechanism by which they reduce risk of testing positive for SARS-CoV-2 is not clear. Nevertheless, here we provide evidence to support a protective effect in omega-3 fatty acid supplements users with a 12% reduction in risk of testing positive for SARS-CoV-2 in the overall UK cohort, 21% in the US cohort and 16% in the SE cohort. Although, in the UK, stratified analysis shows this effect is largely driven by females, and only significant in one male stratum.

**Probiotics:** Probiotics modify the host's gut microbiota and may generate anti-viral metabolites, and they interact with the host's gut associated immune system [45]. This can result in improved immunity, including enhanced responses to the seasonal influenza vaccine [46]. Mechanistic studies support a gut-lung axis [47], whereby immune effects of microbiota at the gut level can be transferred to the lung, most likely through movement of immune cells. This could explain why some probiotic organisms reduce risk [48–50] and severity [51] of respiratory tract infections. Here we provide evidence to suggest that people taking probiotics supplements are modestly protected with a 14% reduction in risk of testing positive for SARS-CoV-2 in the overall UK cohort, 18% in the US cohort and 37% in the SE cohort. However, effects of probiotics are strain and species specific and we have no information of which probiotics or their quality were being used by participants in this study. Moreover, when we adjusted for other covariates including diet, the effect of probiotics was weaker suggesting that probiotic use may be confounded by a healthy diet.

**Zinc, Vitamin C and garlic:** We saw no protective effects of zinc, garlic or vitamin C. Both zinc and vitamin C have been previously suggested to support the immune system and to prevent respiratory infections [1,2,52]. Although, their efficacy and evidence base has been questioned and a meta-analysis of vitamin C showed no preventive benefit and a modest reduction in symptom duration by less than a day [53,54].

Strengths of our study include its large sample size, the confirmation of SARS-CoV-2 through a RT-PCR- or serology-based test, and the replication of the key findings from the UK cohort in two other cohorts, one in the US and the other in SE. Furthermore, we had information on diet quality. Indeed, consistent with the literature [22], in our data we found a positive correlation between diet quality and supplements usage suggesting that people with a healthier diet were more likely to take supplements. However, we were able to adjust for diet quality and showed that the effect of supplements is independent from the effect of diet quality.

Our study also has a number of limitations. First, we used self-reported data which can introduce information bias, including misclassification, or effect bias exposure if participants started taking supplements after developing symptoms. There is also a possibility of participants having COVID-19 symptoms (and likely having COVID-19) but not having had any test because of low testing capacity [55] and then started taking supplements. We believe this is possible-although would have reduced any real effect. To help mitigate potential spurious associations we adjusted for self-reported health status at sign-up. Second, participants using the app were a self-selected group and may not be fully representative of the general population. Indeed, our study population is predominantly female, though supplement usage and BMI are in line with data for the UK general population [4,21]. This may cause collider bias that is, both use of supplements and having COVID-19 might influence the probability of an individual participating in the COVID Symptom Study, and this selection effect could introduce an apparent association between supplement use and COVID-19 status [56]. Third, the SARS-CoV-2 infection diagnosis was mainly based on the RT-PCR test that has less than 100% sensitivity (true positive rate) [57,58]. Fourth, participants might have been taking supplements in addition to the seven we asked them about, and we were not able to account for multiple sources of vitamins/minerals. Fifth, malnutrition is a significant risk factor for a severe form of COVID-19 infection [59], however though we had information on diet we were unable to infer vitamin/mineral deficiencies. Sixth, we do not know the exact intakes of the ingredients within the supplements used by the participants, nor we had any information regarding dosage and hence we were not able to link supplements dosage or intakes from multiple sources with disease outcome. Furthermore, within the useful timeframe, the app has not captured information on behaviours such as washing hands, use of disinfectants or social distancing and only a proportion of participants replied to the questions on use of masks. We also were only able to adjust for a crude, area-based, measure of deprivation rather than individually based measures of socioeconomic background, such as educational attainment, occupation and income; thus, residual confounding by socioeconomic status is possible. Finally, this is observational data captured during a specific timeframe, and our study design does not allow an inference of causality.

In conclusion, our data shows that women taking multivitamins, omega-3 fatty acids, vitamin D or probiotics have a slightly lower risk of SARS-CoV-2 infection in the UK, US and SE, but no effect in those taking zinc, vitamin C or garlic. Given the interest in supplements during the pandemic, large randomised controlled trials of selected supplements testing their protective effects, and also possible adverse effects, on disease severity are required before any evidence-based recommendations can be made. We eagerly await the result of ongoing trials, including of vitamin D, omega-3 fatty acids and probiotics and COVID-19 risk [60].

#### **Section 1: What is already known on this topic**

- Dietary supplements have been shown to play key roles in supporting immune function, but the extent to which specific supplements are associated with reduced risk of SARS-CoV-2 infection is not known.

#### **Section 2: What this study adds**

- Individuals taking multivitamins, omega-3 fatty acids, probiotics or vitamin D were less likely to be tested positive for SARS-CoV-2 in three large independent cohorts of app users.
- There was a significant protective association for vitamin D, omega-3 fatty acids, probiotics and multivitamins in female users across all ages and BMI categories within the largest (UK) cohort. Yet, there was no association in male users of this cohort.
- Vitamin C, zinc and garlic supplements had no association with risk for SARS-CoV-2.
- There is a need for randomised controlled trials of selected supplements.

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CM and TDS are responsible for the overall content as guarantors. The guarantors accept full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. The manuscript's guarantors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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## Figure legends:

**Figure 1.** Associations between testing positive for SARS-CoV-2 and self-reported use of supplements in UK app users. Each cell of the matrix displays the odds ratio of the association between use of a type of supplement and testing positive with the corresponding P value in parentheses. The table is colour coded according to the odds ratio, with blue denoting a reduced risk and red denoting an increased risk of testing positive. Bold entries are statistically significant after accounting for multiple testing using Bonferroni correction. Dem = adjusted for age, sex, BMI and health status at sign up; All = adjusted for Dem, index of multiple deprivation, ethnicity, comorbidities (type-2 diabetes, cancer, asthma, heart disease, eczema, hay fever, kidney disease and lung disease), smoking, diet quality; stratified analyses are adjusted for age, (BMI) and health status at sign up as appropriate.

**Figure 2.** Odds ratios and 95% confidence intervals for the associations between testing positive for SARS-CoV-2 and self-reported use of supplements in three cohorts (n = 372,720 UK, n = 45,575 US and n = 27,373 SE). Overall sample analyses are adjusted for age, sex, BMI, and health status at sign up. Analyses according to sex are adjusted for age, BMI and health status at sign up.

## Supplementary material

**Figure S1.** Flow chart of the study design

**Table S1.** List of questions on supplements usage

**Table S2.** Associations between testing positive for SARS-CoV-2 and self-reported use of supplements in UK, US and SE app users. Crude OR[95%CI] are reported.

**Table 1. Demographic Characteristics of the Study Population**

	UK (n=372,720)		US (n=45,757)		SE (n=27,373)	
	Supplement users		Supplement users		Supplement users	
	YES	NO	YES	NO	YES	NO
<b>N (%)</b>	175,652 (47.1%)	197,068 (52.9%)	32,314 (70.6%)	13,443 (29.4%)	13,422 (49%)	13,951 (51%)
<b>SARS-CoV-2 positive, N (%)</b>	10,508 (6%)	13,013 (6.6%)	2,002 (6.2%)	1,211 (9%)	1,806 (13.5%)	2,206 (15.8%)
<b>Females, N(%)</b>	123,462 (70.3%)	125,651 (63.8%)	22,817 (70.6%)	8,210 (61.1%)	9,694 (72.2%)	9,088 (65.1%)
<b>White, N(%)</b>	163,479 (93.1%)	188,030 (95.4%)	28,143 (87.1%)	11,757 (87.5%)	13,411 (99.9%)	13,943 (99.9%)
<b>Current smoker N(%)</b>	6,004 (3.4%)	10,773 (5.5%)	1,252 (3.9%)	924 (6.9%)	735 (5.5%)	795 (5.7%)
	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>	<i>Mean (SD)</i>
<b>Age, yrs</b>	49.57 (14.2)	46.26 (14.4)	56.24 (15.2)	47.8 (16.0)	49.0 (13.0)	46.63 (12.9)
<b>BMI, kg/m<sup>2</sup></b>	26.59 (5.6)	27.04 (5.7)	27.27 (5.9)	27.21 (6)	26.1 (4.8)	26 (4.7)

<b>IMD, median (IQR)</b>	7 (5)	6 (5)	-	-	-	-
<b>DQI, median (IQR)</b>	11 (3)	11 (3)	-	-	-	-
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
<b>Omega-3</b>	39,263 (22.4%)	-	8,663 (26.8%)	-	3,039 (22.6%)	-
<b>Probiotics</b>	20,449 (11.6%)	-	7,268 (22.5%)	-	1,715 (12.8%)	-
<b>Garlic</b>	7,235 (4.1%)	-	1,137 (3.5%)	-	941 (7%)	-
<b>Multivitamins</b>	77,034 (43.9%)	-	18,843 (58.3%)	-	5,496 (41%)	-
<b>Vitamin D</b>	86,190 (49.1%)	-	19,444 (60.2%)	-	6,722 (50.1%)	-
<b>Vitamin C</b>	46,755 (26.6%)	-	10,136 (31.4%)	-	4,045 (30.1%)	-
<b>Zinc</b>	21,776 (12.4%)	-	4,330 (13.4%)	-	2,394 (17.8%)	-

<b>Type-2 diabetes</b>	5,047 (2.9%)	4,842 (2.5%)	1,787 (5.5%)	437 (3.3%)	331 (2.5%%)	251 (1.8%%)
<b>Cancer</b>	2,178 (1.2%)	1,902 (1%)	977 (3%)	217 (1.6%)	157 (1.2%)	130 (0.9%)
<b>Asthma</b>	27,146 (15.5%)	26,020 (13.2%)	5,015 (15.5%)	1,788 (13.3%)	2,039 (15.2%)	1,673 (12%)
<b>Heart disease</b>	5,708 (3.3%)	5,278 (2.7%)	2,388 (7.4%)	590 (4.4%)	654 (4.9%)	592 (4.2%)
<b>Eczema</b>	22,896 (13%)	23,454 (11.9%)	3,423 (10.6%)	1,346 (10%)	1,768 (13.2%)	1,779 (12.8%)
<b>Hay fever</b>	79,024 (45%)	80,114 (40.7%)	17,000 (52.6%)	6,256 (46.5%)	5,497 (41%)	5,256 (37.7%)
<b>Kidney disease</b>	1,702 (1%)	1,542 (0.8%)	630 (2%)	143 (1.1%)	117 (0.9%)	102 (0.7%)
<b>Lung disease</b>	24,651 (14%)	22,924 (11.6%)	4,331 (13.4%)	1,329 (9.9%)	1,894 (14.1%)	1,488 (10.1%)

IMD, index of multiple deprivation; BMI, body mass index; DQI, Diet Quality Score; IQR, Inter-quartile range; SE, Sweden. Self-reported comorbidities were not asked at sign-up and therefore not reported by all subjects