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Supplementary appendix

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Supplementary Appendix

Supplement to
"Risk of COVID-19 among frontline healthcare workers and the general community: a prospective cohort study"

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Supplementary Methods

Symptom-based classifier

Since reporting a positive COVID-19 test is conditional upon receiving a test and to potentially capture the spectrum of disease that may not necessarily present for diagnostic evaluation and treatment, we used the COVID Symptom Study to generate a symptom-based classifier among a subset of 7,104 COVID-19-positive cases compared to 11,297 COVID-19-negative controls to generate a linear model for likelihood of COVID-19 infection described in Menni *et al*. Selected factors were retained on the basis of a stepwise linear regression.

Predicted COVID-19 infection = -(0·01 x age) + (0·44 x male sex) + (1·75 x loss of smell/taste) + (0·31 x significant/severe persistent cough) + (0·49 x severe fatigue) + (0·39 x skipped meals) + intercept

This model achieved a sensitivity of 0·65 (95% CI: 0·62 to 0·67) and specificity of 0·78 (95% CI: 0·76 to 0·80) with an area under the receiver operating curve (AUROC) of 0.75.

Inverse probability weighting

To explore if the risk of a positive COVID-19 test was explained by differences in testing access and criteria, we calculated the probability of receiving a COVID-19 test as a function of demographic factors, including age, contact with a known or suspected person with COVID-19 in the community, and having symptoms at baseline (**Suppl. Table 4**) within both the U.S. and the U.K. This procedure was performed separately among the U.S.-based and U.K.-based participants to account for the possibility that predictors for obtaining a COVID-19 test differed by country of enrollment. We then performed inverse probability weighted (IPW) Cox proportional hazards modeling stratified by 5-year age group and calendar date at study entry and additionally adjusted for sex, history of diabetes, heart disease, lung disease, kidney disease, and smoker status (each yes/no), and body mass index (17-19·9, 20-24·9, 25-29·9, and $\geq$30 kg/m^2). Country-specific estimates were then meta-analyzed using the *metaphor* package in R.

Supplementary Tables

Supplementary Table 1. Partnering cohorts within the COPE Consortium and the number of participants from each.

Cohort Name	COPE Consortium contact	Participants using the COVID Symptom Tracker to date[a]
ACS Cancer Prevention Study 3	Alpa V. Patel, Anusila Deka	6,714
The Agricultural Health Study	Laura Beane-Freeman/ Dale P Sandler	50
ASPREE-XT	Michael E. Ernst, Brenda Kirpach, Anne M. Murray	25
Black Women's Health Study	Julie R. Palmer, Lynn Rosenberg	550
Growing Up to Today Study	Jaime E. Hart, Jorge E. Chavarro	1,170
The GuLF Study	Dale P. Sandler	199
Health Professionals Follow-up Study	Lorelei A. Mucci, Walter C. Willett	1,044
Multiethnic Cohort Study	Loic Le Marchand, Lynne R. Wilkens	3,112
Nurses' Health Study I, II and 3	Meir Stampfer, Walter C. Willett, Heather A. Eliassen, Jaime E. Hart, Jorge E. Chavarro	15,718
PREDICT 2	Andrew T. Chan, Tim D. Spector	251
The Sister Study	Dale P. Sandler	2,036
Stanford Nutrition Studies	Christopher D. Gardner	362
UCSD/COH California Teachers Study	Maria Elena Martinez, James V. Lacey	928
Twins U.K.	Tim D. Spector	4,367

[a]Only including users who both confirmed being a member of a participating study and agreed to data linkage. Cohorts invited participants beginning on different dates and over different time periods.

Supplementary Table 2. COVID Symptom Tracker smartphone application questions as of April 24, 2020.

Baseline Questions	
About your work	
Are you a health care worker (including hospital, elderly care or in the community)?	- Yes, currently treat patients - Yes, do not currently treat patients - No
Do you care for multiple people in the community, with direct contact with your patients?	- Yes/No
Since the COVID-19 epidemic began, have you physically worked in?	- Hospital inpatient - Hospital outpatient - Clinic outside a hospital - Nursing home/elderly care or group care facility - Home health - School clinic - Other health care facility
Have you EVER interacted (in person) with patients with documented or presumed COVID-19 infection?	- Yes, documented COVID-19 cases only - Yes, suspected COVID-19 case only - Yes, both documented & suspected COVID-19 cases - Not that I know of
Since the COVID-19 epidemic began, have you used personal protective equipment (PPE) at work? *Depending on your specific work requirements, PPE might include gloves, masks, face shields, etc.	- Always - Sometimes - Never
If always:	- I have had all the PPE I need for work - I had to reuse PPE because of shortage
If sometimes:	- I haven't always needed to use PPE, but have had enough when I did - I would have used PPE all the time, but I haven't had enough - I've had to reuse PPE because of shortage
If never:	- I haven't needed PPE - I needed PPE, but it wasn't available
About you	
What year were you born?	Please enter your year of birth
What sex were you assigned at birth?	- Male - Female - Intesex - Prefer not to say

Baseline Questions	
Which of the following best describes your ethnicity? (Asked in the UK only, as a supplemental baseline question starting on April 18, 2020 of existing and at baseline for all new app users going forward)	- Asian/Asian British (e.g. Indian, Pakistani, Bangladeshi, other) - Black/Black British (e.g. Caribbean, African, other) - Mixed race- White and Black/Black British - Mixed race - other - White - British, Irish, other - Chinese/Chinese British - Middle Eastern/Middle Eastern British (e.g. Arab, Turkish, other) - Other ethnic group - Prefer not to say
What is your race (check all that apply): (Asked in the US only, as a supplemental baseline question starting on April 18, 2020 of existing and at baseline for all new app users going forward)	- American Indian or Alaska Native - Asian - Black or African-American - Native Hawaiian or other Pacific Islander - White - Other, please specify - Prefer not to say
What is your ethnicity: (Asked in the US only, as a supplemental baseline question starting on April 18, 2020 of existing and at baseline for all new app users going forward)	- Hispanic or Latino or Spanish origin - Not Hispanic or Latino, or Spanish origin - Prefer not to say
Your height?	Please enter your height in feet & inches/centimetres
Your weight?	Please enter your weight in pounds/kilograms
In general, do you have any health problems that require you to stay at home?	- Yes/No
Have you EVER been exposed to someone with documented or presumed COVID-19 infection (such as co-workers, family members, or others)? Please check all that apply.	- Yes, documented COVID-19 cases - Yes, both documented & suspected COVID-19 cases - Yes, presumed COVID-19 cases - Not that I know of
About your health	
Are you pregnant?	- Yes/No
Do you have heart disease?	- Yes/No
Do you have diabetes?	- Yes/No
Do you have lung disease or asthma?	- Yes/No
Do you smoke?	- Yes/No

Baseline Questions	
Do you have kidney disease?	- Yes/No
Are you living with cancer?	- Yes/No
Are you on chemotherapy or immunotherapy for cancer?	- Yes/No
Do you regularly take immunosuppressant medications (including steroids, methotrexate, biologics)?	- Yes/No
Do you regularly take aspirin (baby aspirin or standard dose)? +	- Yes/No
Do you regularly take "NSAIDs" like ibuprofen, nurofen, diclofenac, naproxen?	- Yes/No
Are you regularly taking blood pressure medications ending in -pril, such as enalapril, lisinopril, captopril, ramipril) ?	- Yes/No

Follow-Up Questions (Asked Daily)	
COVID-19 Test	
Have you had a test for COVID-19?	- Yes/No
Did you test positive for COVID-19?	- Yes/No
How You Feel	
How do you feel right now?	- I feel as healthy as normal - I'm not feeling quite right
Describe Symptoms	
Do you have a fever?	- Yes/No
If you are able to measure it, what is your temperature?	Please enter your temperature
Do you have a persistent cough (coughing a lot for more than an hour, or 3 or more coughing episodes in 24 hours)?	- Yes/No
Are you experiencing unusual fatigue?	- No - Mild fatigue - Severe fatigue

Follow-Up Questions (Asked Daily)	
	- I struggle to get out of bed
Are you experiencing unusual shortness of breath?	- No - Yes. Mild symptoms - slight shortness of breath during ordinary activity - Yes. Significant symptoms - breathing is comfortable only at rest - Yes. Severe symptoms - breathing is difficult even at rest
Do you have a loss of smell/taste?	- Yes/No
Do you have an unusually hoarse voice?	- Yes/No
Are you feeling an unusual chest pain or tightness in your chest?	- Yes/No
Do you have an unusual abdominal pain?	- Yes/No
Are you experiencing diarrhoea?	- Yes/No
Do you have any of the following symptoms: confusion, disorientation or drowsiness?	- Yes/No
Have you been skipping meals?	- Yes/No
Do you have a headache?	- Yes/No
Do you have a sore throat?	- Yes/No
Do you have unusual strong muscle pains?	- Yes/No
Are there other important symptoms you want to share with us?	- Yes/No
Healthcare Worker Exposure	
In the last day, did you treat patients in person with documented or presumed COVID-19 infection?	- Yes, documented COVID-19 cases - Yes, both documented & suspected COVID-19 cases - Yes, presumed COVID-19 cases - Not that I know of
In the last day, did you use personal protective equipment (PPE) at work? *Depending on your specific work requirements, PPE might include gloves, masks, face shields, etc.	- Always - Sometimes - Never

Follow-Up Questions (Asked Daily)	
If always:	- I have had all the PPE I need for work - I had to reuse PPE because of shortage
If sometimes:	- I haven’t always needed to use PPE, but have had enough when I did - I would have used PPE all the time, but I haven’t had enough - I’ve had to reuse PPE because of shortage
If never:	- I haven’t needed PPE - I needed PPE, but it wasn't available

Supplementary Table 3. Baseline characteristics of frontline healthcare workers compared to the general community by country.

	United States (U.S.) (*n*=139,536)		United Kingdom (U.K). (*n*=1,995,654)	
	Frontline HCWs (*n*=14,531)	**General population (*n*=125,005)**	**Frontline HCWs (*n*=85,264)**	**General population (*n*=1,910,390)**
Age (years)	50 [38, 61]	57 [41, 68]	41 [32, 51]	43 [32, 56]
<25	1.9	2.2	4.9	4.9
25-34	15.0	9.7	26.1	19.9
35-44	21.8	14.6	25.8	22.0
45-54	18.9	14.8	24.4	19.9
55-64	27.5	19.6	15.8	16.0
≥65	14.4	34.7	2.0	11.6
Missing	0.6	4.3	1.1	5.8
Male sex (%)	15·0	33·0	18·0	37·0
Race (%)				
Non-Hispanic white	82.6	84.4	89.6	93.5
Hispanic/Latinx	4.9	4.0	0.1	0.1
Black	2.1	2.4	1.0	0.4
Asian	3.7	3.7	4.6	2.0
More than one /other	2.4	3.1	2.4	2.9
Missing / Prefer not to say	4.3	2.4	2.3	1.1
BMI (kg/m^2)	25.8 [22.9, 30.6]	25.8 [22.8, 30.0]	25.8 [22.8, 30.1]	25.3 [22.5, 29.1]
17-19·9	5.8	8.0	5.8	8.2
20-24·9	36.6	34.8	38.1	39.2
25-29·9	29.9	31.8	30.0	31.3
≥30	27.0	24.6	25.6	20.7
Missing	0.6	0.7	0.5	0.5
Comorbidities (%)				
Diabetes	4.5	6.1	2.2	2.9
Heart Disease	3.7	6.1	1.3	2.2
Lung Disease	14.7	12.9	12.8	12.1

	United States (U.S.) (*n*=139,536)		United Kingdom (U.K). (*n*=1,995,654)	
	Frontline HCWs (*n*=14,531)	**General population (*n*=125,005)**	**Frontline HCWs (*n*=85,264)**	**General population (*n*=1,910,390)**
Kidney Disease	1.0	1.5	0.5	0.6
Cancer				
Yes	1.1	2.3	0.3	1.2
Missing	0.0	0.1	0.4	0.4
Pregnant (% of females)	1·1	0·7	0·9	1·1
Medication usage (%)				
NSAIDs	18.0	15.4	6.5	5.5
Immunosuppressants	3.5	3.8	2.3	3.1
Chemotherapy/Immunotherapy	0.2	0.5	0.1	0.2
ACE inhibitor				
Yes	6.6	9.9	4.1	4.3
Missing	28.7	14.0	6.9	3.6
Current smoking (%)				
Yes	5.1	5.3	11.0	8.7
Missing	0.3	0.3	0.2	0.2

Abbreviations: ACE (angiotensin converting enzyme), BMI (body mass index), m (meter), kg (kilogram), Non-steroidal anti-inflammatory drugs (NSAIDs)
Median [IQR] is presented for continuous variables.
Frequencies and proportions are calculated based on the total number of participants with available data.
History of cancer, ACE inhibitor use, and smoking status have been queried since launch in the U.S. and since 3/29/2020 in the U.K. Race was queried as of 4/17/2020.
Definitions for race/ethnicity: Non-hispanic White (U.K. White, U.S. White, no designation of other race or ethnicity), Hispanic/Latinx (designated as Hispanic/Latino), Black (U.K. Black/Black British, U.S. Black or African-American), White (U.K. White, U.S. White), Asian (U.K. Asian/Asian British, U.K. Chinese/Chinese British, U.S. Asian, U.S. Native Hawaiian or other Pacific Islander), and More than One/Other (U.K. Mixed Race-White and Black/Black British U.K., Mixed Race Other, U.K. Middle Eastern/Middle Eastern British, U.S. American Indian or Alaska Native, Other, or denoted more than one race).

Supplementary Table 4. Symptoms reported by frontline healthcare workers compared to the general community at study entry and at the time of positive COVID-19 testing.

	Study entry (*n*=2,135,190)		Positive COVID-19 testing[a] (*n*=5,545)	
	Frontline HCWs (*n*=99,795)	General population† (*n*=2,035,395)	Frontline HCWs (*n*=1,922)	General population† (*n*=3,623)
Fever	2·8	1·6	48·7	43·7
Persistent cough	7·0	4·9	63·5	57·5
Fatigue	13·8	9·5	86·5	78·0
Shortness of breath	6·1	4·9	45·8	47·8
Loss of smell/taste	4·6	2·0	58·4	51·2
Hoarse voice	4·3	1·9	37·5	32·9
Chest pain	6·9	3·2	43·2	43·7
Abdominal pain	2·9	1·3	24·7	23·9
Diarrhea	3·5	2·7	29·2	31·2
Delirium	1·8	2·2	14·8	23·4
Skipped meals/anorexia	4·6	2·9	43·7	43·1
Headache	12·3	6·2	74·3	57·2
Sore throat	10·1	5·4	55·1	37·9
Myalgias	3·1	1·1	32·6	21·0
No symptom	79·8	85·6	3·3	11·7

Presented as %.
[a]Symptoms reported at the time of positive testing.
Proportions are calculated based on the total number of participants with available data.

Supplementary Table 5. Risk of reporting a positive test for COVID-19 or predicted COVID-19 infection among HCWs compared with the general community by country

	No. with Event/Person-days	Incidence (30-day)	Hazard Ratio (95% CI)		
			Age-adjusted	Multivariate-adjusted	IP Weighted
United Kingdom					
Overall					
General community	3,450/31,839,670	0·33%	1·0 (ref.)	1·0 (ref.)	1·0 (ref.)
Frontline healthcare worker	1,851/1,309,285	4·24%	12·52 (11·77 to 13·31)	12·52 (11·77 to 13·31)[a]	3·43 (3·18 to 3·69)[a]
United States					
Overall					
General community	173/1,140,901	0·45%	1·0 (ref.)	1·0 (ref.)	1·0 (ref.)
Frontline healthcare worker	71/145,416	1·46%	2·87 (2·14 to 3·85)	2·80 (2·09 to 3·75)[a]	1·97 (1·36 to 2·85)[a]

Abbreviations: CI (confidence interval), IP (inverse probability)
All models were stratified by 5-year age group and calendar date at study entry.
Multivariate risk factor models were adjusted for sex, history of diabetes, heart disease, lung disease, kidney disease, and current smoking (each yes/no), and body mass index (17-19·9, 20-24·9, 25-29·9, and ≥30 kg/m^2).
[a]$p_{\text{difference}}$<0·0001

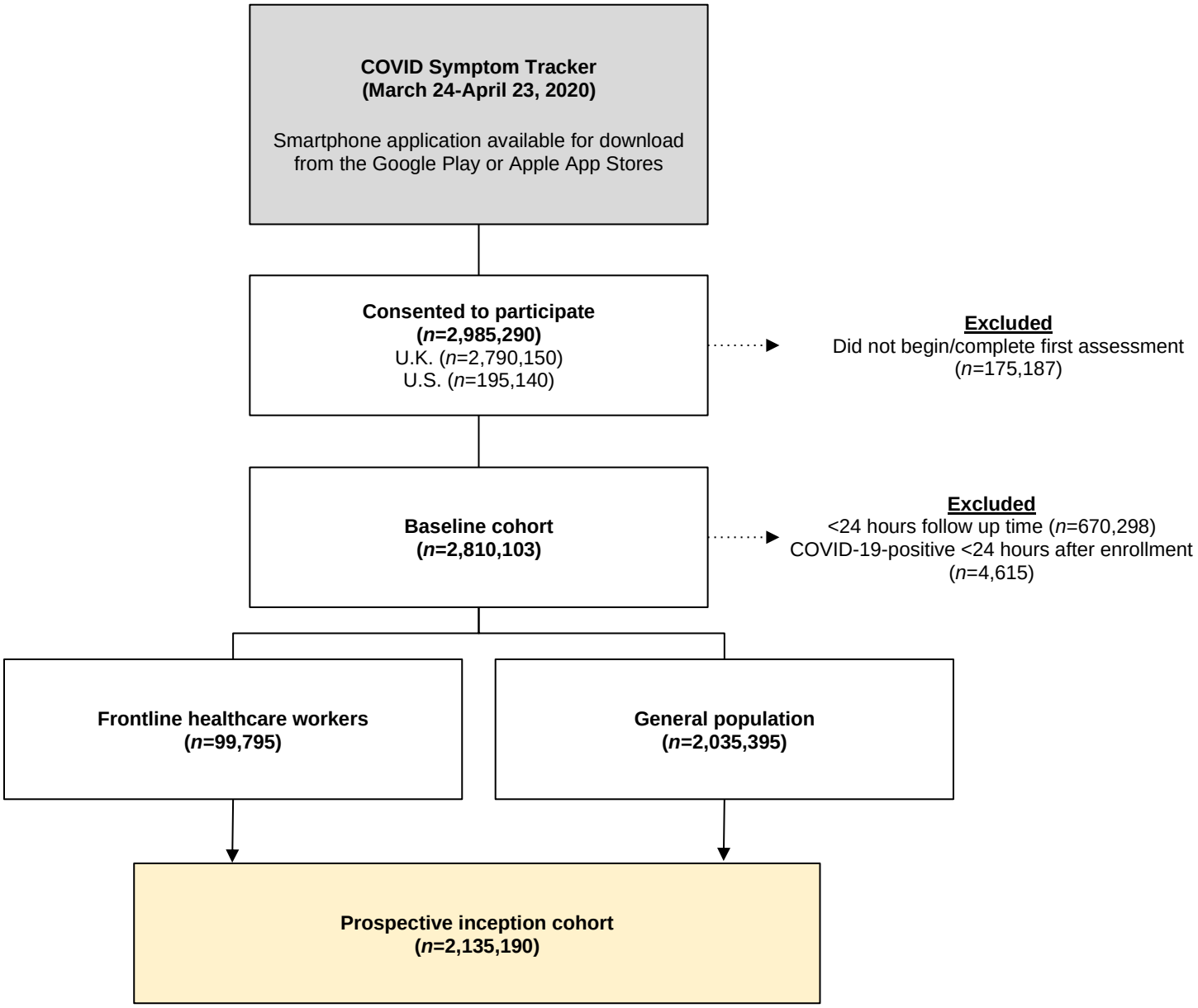
Supplementary Table 6. Risk of working in high-risk clinical settings or caring for patients with suspected or documented COVID-19 according to race/ethnicity.

	Odds Ratio (95% CI)
	Multivariate-adjusted
Overall	
Working in inpatient settings or nursing homes	
Non-Hispanic white frontline healthcare worker	1·0 (ref.)
BAME frontline healthcare worker	1·13 (1·03 to 1·23)
Caring for suspected or documented COVID-19 patients	
Non-Hispanic white frontline healthcare worker	1·0 (ref.)
BAME frontline healthcare worker	1·20 (1·09 to 1·30)
According to racial/ethnic group	
Working in inpatient settings or nursing homes	
Non-Hispanic white frontline healthcare worker	1·0 (ref.)
Hispanic/Latinx frontline healthcare worker	1·09 (0·82 to 1·43)
Black frontline healthcare worker	1·42 (1·12 to 1·79)
Asian frontline healthcare worker	1·08 (0·95 to 1·79)
More than one race/other race frontline healthcare worker	1·15 (0·97 to 1·36)
Caring for suspected or documented COVID-19 patients	
Non-Hispanic white frontline healthcare worker	1·0 (ref.)
Hispanic/Latinx frontline healthcare worker	1·00 (0·76 to 1·32)
Black frontline healthcare worker	1·30 (1·04 to 1·64)
Asian frontline healthcare worker	1·17 (1·03 to 1·34)
More than one race/other race frontline healthcare worker	1·30 (1·11 to 1·53)

Abbreviations: BAME (Black, Asian, and Minority Ethnic), CI (confidence interval), IP (inverse probability)
Multivariate risk factor models were adjusted for 5-year age group and sex.
BAME was defined among individuals who either did not have missing racial information and did not identify as non-Hispanic white.

Supplementary Figures

Supplementary Figure 1. Study Diagram



Supplementary Figure 2. Incidence of COVID-19 infection in frontline healthcare workers compared to the general community.

Survival distributions compared using the log-rank test. Data from March 24-April 23, 2020 shown with the number remaining at risk for each timepoint.