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# The association of smoking status with SARS-CoV-2 infection, hospitalisation and mortality from COVID-19: A living rapid evidence review with Bayesian meta-analyses (version 10)

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**Funding:** The author(s) received no specific funding for this work.

**Potential competing interests:** The author(s) declared that no potential competing interests exist.

## Abstract

**Aims:** To estimate the association of smoking status with rates of i) infection, ii) hospitalisation, iii) disease severity, and iv) mortality from SARS-CoV-2/COVID-19 disease.

**Design:** Living rapid review of observational and experimental studies with random-effects hierarchical Bayesian meta-analyses. Published articles and pre-prints were identified via MEDLINE and medRxiv.

**Setting:** Community or hospital. No restrictions on location.

**Participants:** Adults who received a SARS-CoV-2 test or a COVID-19 diagnosis.

**Measurements:** Outcomes were SARS-CoV-2 infection, hospitalisation, disease severity and mortality stratified by smoking status. Study quality was assessed (i.e. 'good', 'fair' and 'poor').

**Findings:** Version 10 (searches up to 15 December 2020) included 345 studies with 52 'good' and 'fair' quality studies included in unadjusted meta-analyses. One-hundred-and-one studies (29.3%) reported current, former and never smoking status with the remainder using broader categories. Recorded smoking prevalence among people with COVID-19 was generally lower than national prevalence. Current compared with never smokers were at reduced risk of SARS-CoV-2 infection (RR = 0.69, 95% Credible Interval (CrI) = 0.58-0.82,  $\tau = 0.36$ ). Data for former smokers were inconclusive (RR = 1.03, 95% CrI = 0.94-1.13,  $\tau = 0.18$ ) but favoured there being no important association (8% probability of RR  $\geq 1.1$ ). Former compared with never smokers were at increased risk of hospitalisation (RR = 1.18, CrI = 1.07-1.31,  $\tau = 0.14$ ), greater disease severity (RR = 1.52, CrI = 1.12-2.06,  $\tau = 0.29$ ) and mortality (RR = 1.40, 95% CrI = 1.20-1.64,  $\tau = 0.19$ ). Data for current smokers on hospitalisation, disease severity and mortality were inconclusive (RR =

1.08, CrI = 0.95-1.23,  $\tau$  = 0.18; RR = 1.26, CrI = 0.85-1.93,  $\tau$  = 0.34; RR = 1.05, 95% CrI = 0.77-1.41,  $\tau$  = 0.39, respectively) but favoured there being no important associations with hospitalisation and mortality (31% and 38% probability of RR  $\geq 1.1$ , respectively) and a small but important association with disease severity (80% probability of RR  $\geq 1.1$ ).

**Conclusions:** Compared with never smokers, current smokers appear to be at reduced risk of SARS-CoV-2 infection while former smokers appear to be at increased risk of hospitalisation, greater disease severity and mortality from COVID-19. However, it is uncertain whether these associations are causal.

v7 of this living review article has been published in *Addiction* and is available here <https://doi-org.libproxy.ucl.ac.uk/10.1111/add.15276>

## Definitions

### Angiotensin-Converting Enzyme

Defined by National Cancer Institute

### SARS Coronavirus

Defined by National Cancer Institute

### Cigarette Smoker

Defined by National Cancer Institute

### Nicotine

Defined by National Cancer Institute

### Inflammation

Defined by National Cancer Institute

### Fibrosis

Defined by National Cancer Institute

### Living Systematic Review

Defined by Julian H. Elliott et al.

### Randomized controlled trials

Defined by David F Marks

### Meta-analysis

Defined by Arindam Basu

### Bayesian Approach

Defined by National Cancer Institute

## Introduction

COVID-19 is a respiratory disease caused by the [SARS-CoV-2](#) virus. Large age and gender differences in case severity and mortality have been observed in the ongoing COVID-19 pandemic<sup>1</sup>; however, these differences are currently

unexplained. SARS-CoV-2 enters epithelial cells through the [angiotensin-converting enzyme 2 \(ACE-2\)](#) receptor<sup>2</sup>. Some evidence suggests that gene expression and subsequent receptor levels are elevated in the airway and oral epithelium of current [smokers](#)<sup>3,4</sup>, which could put smokers at higher risk of contracting SARS-CoV-2. Other studies, however, suggest that [nicotine](#) downregulates the ACE-2 receptor<sup>5</sup>. These uncertainties notwithstanding, both former and current smoking is known to increase the risk of respiratory viral<sup>6,7</sup> and bacterial<sup>8,9</sup> infections and is associated with worse outcomes once infected. Cigarette smoke reduces the respiratory immune defence through peri-bronchiolar [inflammation](#) and [fibrosis](#), impaired mucociliary clearance and disruption of the respiratory epithelium<sup>10</sup>. There is also reason to believe that behavioural factors (e.g. regular hand-to-mouth movements) involved in smoking may increase SARS-CoV-2 infection and transmission in current smokers. However, early data from the COVID-19 pandemic have not provided clear evidence for a negative impact of current or former smoking on SARS-CoV-2 infection or COVID-19 disease outcomes, such as hospitalisation or mortality<sup>11</sup>. It has also been hypothesised that nicotine might protect against a hyper-inflammatory response to SARS-CoV-2 infection, which may lead to adverse outcomes in patients with COVID-19 disease<sup>12</sup>.

There are several reviews that fall within the scope of smoking and COVID-19<sup>11,13–18</sup>. We aimed to produce a rapid synthesis of available evidence pertaining to the rates of infection, hospitalisation, disease severity and mortality from SARS-CoV-2/COVID-19 stratified by smoking status. Given the increasing availability of data on this topic, this is a living review with regular updates. As evidence accumulates, the review will be expanded to include studies reporting COVID-19 outcomes by alternative nicotine use (e.g., nicotine replacement therapy or e-cigarettes).

## Methods

### *Study design*

This is a [living evidence review](#) which is updated as new evidence becomes available<sup>19</sup>. We adopted recommended best practice for rapid evidence reviews, which involved limiting the search to main databases and having one reviewer extract the data and another verify<sup>20</sup>. This study was not pre-registered but evolved from a report written for a UK medical society<sup>21</sup>. The most recent (and all future) version(s) of this living review is available here (<https://www.qeios.com/read/latest-UJR2AW>). Version 7 of this living review has been published in a peer-reviewed journal<sup>22</sup>. A completed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist is included in Supplementary file 1.

### *Eligibility criteria*

Studies were included if they:

1. Were primary research studies using experimental (e.g. [randomised controlled trial](#)), quasi-experimental (e.g. pre- and post-test) or observational (e.g. case-control, retrospective cohort, prospective cohort) study designs;

2. Included adults aged 16+ years;
3. Recorded as outcome i) results of a SARS-CoV-2 diagnostic test (including antibody assays), ii) clinical diagnosis of COVID-19, iii) hospitalisation with COVID-19, iv) severity of COVID-19 disease in those hospitalised or v) mortality from COVID-19;
4. Reported any of the outcomes of interest by self-reported or biochemically verified smoking status (e.g. current smoker, former smoker, never smoker) or current vaping and nicotine replacement therapy (NRT) use;
5. Were available in English;
6. Were published in a peer-reviewed journal, as a pre-print or a public health report by reputable bodies (e.g. governments, scientific societies).

### ***Search strategy***

The following terms were searched for in Ovid MEDLINE (2019-search date) as free text or Medical Subject Headings:

1. Tobacco Smoking/ or Smoking Cessation/ or Water Pipe Smoking/ or Smoking/ or Smoking Pipes/ or Cigar Smoking/ or Smoking Prevention/ or Cigarette Smoking/ or smoking.mp. or Pipe Smoking/ or Smoking, Non-Tobacco Products/ or Smoking Water Pipes/
2. Nicotine/ or nicotine.mp. or Electronic Nicotine Delivery Systems/ or Nicotine Chewing Gum/
3. vaping.mp. or Vaping/
4. 1 or 2 or 3
5. Coronavirus/ or Severe Acute Respiratory Syndrome/ or Coronavirus Infections/ or covid.mp.
6. 4 and 5

The following terms were searched for in titles, abstracts and full texts in [medRxiv](#) (no time limitations):

1. covid (this term captures both covid and SARS-CoV-2) AND smoking
2. covid AND nicotine
3. covid AND vaping

Additional articles/reports of interest were identified through mailing lists, Twitter, the International Severe Acute Respiratory and Emerging Infection Consortium ([ISARIC](#)) and the US Centers for Disease Control and Prevention ([CDC](#)). Where updated versions of pre-prints or public health reports were available, old versions were superseded.

### ***Selection of studies***

One reviewer screened titles, abstracts and full texts against the inclusion criteria.

### **Data extraction**

Data were extracted by one reviewer and verified (i.e. independently checked against pre-prints and published reports) by another on i) author (year); ii) date published; iii) country; iv) study design; v) study setting; vi) sample size; vii) sex; viii) age; ix) smoking status (e.g. current, former, never, not stated, missing) and whether it was biochemically verified; x) use of alternative nicotine products; xi) SARS-CoV-2 testing; xii) SARS-CoV-2 infection; xiii) diagnosis of COVID-19; xiv) hospitalisation with COVID-19; xv) disease severity in those hospitalised with COVID-19; xvi) mortality; xvii) adjustment of smoking specific risk estimates for relevant covariates (e.g. age, sex); and xviii) whether a representative or random sampling method was used.

### **Quality appraisal**

The quality of included studies was assessed to determine suitability for inclusion in [meta-analyses](#). Studies were judged as 'good' quality if they: i) had <20% missing data on smoking status and used a reliable self-report measure that distinguished between current, former and never smoking status; AND ii) used biochemical verification of smoking status and reported results from adjusted analyses; OR reported data from a representative/random sample. Studies were rated as 'fair' if they fulfilled only criterion i) and were otherwise rated as 'poor'. The quality appraisal was conducted by one reviewer and verified by a second.

### **Evidence synthesis**

A narrative synthesis was conducted. Data from 'good' and 'fair' quality studies were pooled in R v.3.6.3<sup>23</sup>. In a living review where new data are regularly added to the analyses, it may be more appropriate to use a [Bayesian](#) (as opposed to frequentist) approach where prior knowledge is used in combination with new data to estimate a posterior risk distribution. A Bayesian approach mitigates the issue of performing multiple statistical tests, which can inflate family-wise error. A series of random-effects hierarchical Bayesian meta-analyses were performed with the *brms*<sup>24</sup> package to estimate the relative risk for each comparison with accompanying 95% credible intervals (Cris). We first defined prior distributions for the true pooled effect size ( $\mu$ ) and the between-study heterogeneity ( $\tau$ ), with  $\mu$  specified as a normal distribution with a mean equal to the derived point estimate from each comparison of interest in the immediately preceding version of this living review<sup>25</sup>, and  $\tau$  specified as a half-Cauchy distribution with a mean of 0 and standard deviation of 1. The half-Cauchy distribution was selected to reflect prior knowledge that high levels of between-study heterogeneity are more likely than lower levels. Markov Chain Monte Carlo methods (20,000 burn-ins followed by 80,000 iterations) were then used to generate a risk distribution for each study, in addition to a pooled effect for the posterior risk distribution. We report forest plots with the pooled effect for the posterior risk distribution displayed as the median relative risk with an accompanying 95% Cris. We used the empirical cumulative distribution function (ECDF) to estimate the probability of there being a 10% reduction or 10% increase in relative risk (RR) (i.e.  $RR \geq 1.1$  or  $RR \leq 0.9$ ). Due to a lack of indication as to what constitutes a clinically or epidemiologically meaningful effect (e.g. with regards to onward disease transmission or requirements for

intensive care beds), we deemed a 10% change in risk as small but important. Where data were inconclusive (as indicated by CIs crossing  $RR = 1.0$ ), to disambiguate whether data favoured no effect or there being a small but important association, we estimated whether there was  $\geq 75\%$  probability of  $RR \geq 1.1$  or  $RR \leq 0.9$ .

Two sensitivity analyses were performed. First, a minimally informative prior for  $\mu$  was specified as a normal distribution with a mean of 0 and standard deviation of 1 and  $\tau$  as described above. Second, an informative prior as described above for  $\mu$  was used with  $\tau$  specified as a half-Cauchy distribution with a mean of 0.3 and standard deviation of 1 to reflect greater between-study heterogeneity.

To aid in the visualisation of smoking prevalence in the included studies, the weighted mean prevalence of current and former smoking was calculated for countries with  $\geq 3$  studies and plotted for comparison with national prevalence estimates. It should be noted that prevalence estimates in the included studies were not adjusted for age, sex, socioeconomic position, or geographic region within countries.

## Results

In the current review version (v10) with searches up to 15 December 2020, a total of 874 records were identified, with 345 studies included in a narrative synthesis and 52 studies included in meta-analyses (see Figure 1).

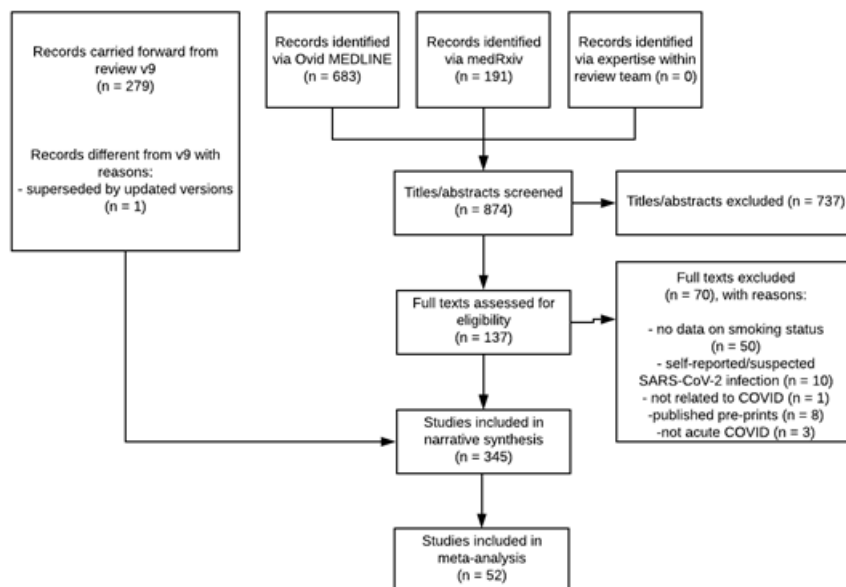


Figure 1. PRISMA flow diagram of included studies.

## Study characteristics

Characteristics of included studies are presented in Table 1. Studies were conducted across 39 countries. Ninety-three



Ref.	Lead author	Date published	Country	Sample size	Study setting	Median (IQR)	Female %	smoker %	smokers %	Current/former smokers %	smokers %	Never/unk smokers %
1	Guan, Ni	2020-02-28	China	1,099	Hospital	47 (35-58)	41.9	12.5	1.9	-	84.3	-
59	Guan, Liang	2020-03-26	China	1,590	Hospital	49 (33-64)	42.7	-	-	7.0	93.0	-
60	Lian	2020-03-25	China	788	Hospital	NA	38.5	6.9	-	-	-	-
61	Jin	2020-03-24	China	651	Hospital	46 (32-60)	49.2	6.3	-	-	-	-
62	Chen	2020-03-26	China	548	Hospital	62 (44-70)	37.6	4.4	2.6	-	-	-
63	Zhou, Yu	2020-03-11	China	191	Hospital	56 (46-67)	38.0	5.8	-	-	-	-
64	Mo	2020-03-16	China	155	Hospital	54 (53-66)	44.5	3.9	-	-	-	-
65	Zhang, Dong	2020-02-19	China	140	Hospital	57^ (25-87)	46.3	1.4	5.0	-	-	-
66	Wan	2020-03-21	China	135	Hospital	47 (36-55)	46.7	6.7	-	-	-	-
67	Liu, Tao	2020-02-28	China	78	Hospital	38 (33-57)	50.0	-	-	6.4	-	-
68	Huang, Wang	2020-01-24	China	41	Hospital	49 (41-58)	27.0	7.3	-	-	-	-
69	Zhang, Cai	2020-03-20	China	645	Hospital	NA	49.1	6.4	-	-	-	-
70	Guo	2020-03-27	China	187	Hospital	59 (45-73)	51.3	9.6	-	-	-	-
71	Liu, Ming	2020-03-12	China	41	Hospital	39 (30-48)	58.5	9.8	-	-	-	-
72	Huang, Yang	2020-03-05	China	36	Hospital	69 (60-78)	30.6	-	-	11.1	-	-
73	Xu	2020-03-08	China	53	Hospital	NA	47.2	11.3	-	-	-	-
74	Li	2020-02-12	China	17	Hospital	45 (33-57)	47.1	17.6	-	-	-	-
32	Rentsch	2020-04-14	USA	3,528	Community and Hospital	66 (60-70)	4.6	27.2	30.6	-	36.9	-
75	Hu	2020-03-25	China	323	Hospital	61^ (23-91)	48.6	-	-	11.8	-	-
76	Wang, Pan	2020-03-24	China	125	Hospital	41 (26-66)	43.2	-	-	12.8	-	-
77	Chow (US CDC)	2020-03-31	USA	7,162	Community and Hospital	NA	-	1.3	2.3	-	-	-
78	Dong, Cao	2020-03-20	China	9	Hospital	44 (30-46)	66.7	11.1	-	-	-	-
79	Kim	2020-04-01	South Korea	28	Hospital	43 (30-56)	46.4	17.9	-	-	-	-
80	Shi, Yu	2020-03-	China	487	Hospital	46	46.8	-	-	8.2	-	-



	Study ID	Date	Country	N	Setting	ICU	ICU	ICU	ICU	ICU	ICU	ICU
		18			Hospital	(27-65)						
81	Yang, Yu	2020-02-24	China	52	Hospital	60 (47-73)	37.0	3.8	-	-	-	-
82	Argenziano	2020-05-29	USA	1,000	Hospital	63 (50-75)	40.4	4.9	17.9	-	77.2	-
83	Solis	2020-04-25	Mexico	650	Hospital	46 (NA)	42.1	9.4	-	-	-	-
84	Richardson	2020-04-22	USA	5,700	Hospital	63 (52-75)	39.7	-	-	9.8	52.8	-
85	Fontanet	2020-04-23	France	661	Community and Hospital	37 (16-47)	62.0	10.4	-	-	-	89.6
86	Zheng, Gao	2020-04-19	China	66	Hospital	47^ (NA)	25.8	12.1	-	-	-	-
87	Liao, Feng	2020-04-24	China	1,848	Hospital	55 (48-61)	54.7	-	-	0.4	-	-
88	Gil-Agudo	2020-04-24	Spain	7	Hospital	68 (34-75)	28.6	-	-	42.9	57.1	-
89	Shi, Ren	2020-04-23	China	134	Hospital	46 (34-58)	51.5	-	-	10.4	-	-
90	Hadjadj	2020-04-23	France	50	Hospital	55 (50-63)	22.0	2.0	18.0	-	80.0	-
91	Gold (US CDC)	2020-04-20	USA	305	Hospital	NA	50.5	5.2	-	-	-	-
92	Yu, Cai	2020-04-27	China	95	Hospital	NA	44.2	8.4	-	-	-	-
93	Zheng, Xiong	2020-04-30	China	73	Hospital	43^ (NA)	45.2	-	-	11.0	89.0	-
94	de la Rica	2020-05-11	Spain	48	Hospital	66^ (33-88)	33.0	-	-	20.8	-	-
95	Yin, Yang	2020-05-10	China	106	Hospital	73 (61-85)	39.6	-	-	17.0	-	-
96	Shi, Zuo	2020-05-17	USA	172	Hospital	63^ (44-82)	44.0	-	-	26.2	-	-
97	Cho	2020-05-11	UK	322,341	Community and Hospital	NA	49.2	14.2	21.4	-	64.4	-
98	Allenbach	2020-05-08	France	152	Hospital	77 (60-83)	31.1	-	-	6.6	-	-
99	Robilotti	2020-05-08	USA	423	Hospital	NA	50.0	2.1	37.6	-	58.6	-
100	The Opensafely Collaborative	2020-07-01	UK	17,278,392	Community and Hospital	NA	50.1	17.0	32.9	-	45.9	-
101	Borobia	2020-05-06	Spain	2,226	Hospital	61 (46-78)	52.0	7.1	-	-	-	-
102	Giacomelli	2020-05-06	Italy	233	Hospital	61 (50-72)	31.9	-	-	30.0	70.0	-
103	Shah	2020-05-06	USA	316	Hospital	63 (43-72)	48.1	16.5	17.7	-	42.1	-

104	Kolin	2020-05-05	UK	502,536	Community and Hospital	56.5 (48-64)	54.4	10.5	34.4	-	54.4	-
105	Lubetzky	2020-05-08	USA	54	Hospital	57 (29-83)	62.0	-	-	22.2	-	-
106	Goyal	2020-04-17	USA	393	Hospital	62.2 (49-74)	39.3	5.1	-	-	-	-
107	Feng	2020-04-10	China	476	Hospital	53 (40-64)	43.1	9.2	-	-	-	-
108	Yao	2020-04-24	China	108	Hospital	52 (37-58)	60.2	3.7	-	-	-	-
109	Sami	2020-05-19	Iran	490	Hospital	56.6 (41-71)	39.0	14.1	-	-	-	85.9
110	Almazeedi	2020-05-15	Kuwait	1,096	Hospital	41 (25-57)	19.0	4.0	-	-	-	96.0
111	Carillo-Vega	2020-05-14	Mexico	10,544	Community and Hospital	46.5^ (30-62)	42.3	8.9	-	-	-	-
112	Yanover	2020-05-13	Israel	4,353	Community and Hospital	35 (22-54)	44.5	11.8	3.0	-	85.2	-
113	Hamer	2020-05-13	UK	387,109	Hospital	56.2 (48-64)	55.1	9.7	34.8	-	55.5	-
114	Regina	2020-05-14	Switzerland	200	Hospital	70 (55-81)	40.0	4.5	-	-	-	-
115	de Lusignan	2020-05-15	UK	3,802	Community and Hospital	58 (34-73)	57.6	10.9	46.1	-	29.6	-
116	Targher	2020-05-13	China	339	Hospital	48.4^ (NA)	52.8	8.3	-	-	-	-
117	Valenti	2020-05-18	Italy	789	Community	40.7^ (NA)	35.0	25.9	-	-	-	-
118	Feuth	2020-05-18	Finland	28	Hospital	56 (47-72)	46.0	10.7	28.6	-	60.7	-
119	Ge	2020-05-18	China	51	Hospital	70 (58-79)	27.5	13.7	-	-	-	-
120	Parrotta	2020-05-18	USA	76	Community and Hospital	44.9 (13-71)	61.8	2.6	26.3	-	68.4	-
121	Shekhar	2020-05-18	USA	50	Hospital	55.5 (20-85)	54.0	48.0	-	-	-	-
122	Mejia-Vilet	2020-05-16	Mexico	329	Hospital	49 (41-60)	36.0	-	-	7.0	-	-
123	Chen, Jiang	2020-05-16	China	135	Hospital	NA	42.2	-	-	9.6	-	-
124	Li, Chen	2020-05-16	China	1,008	Hospital	55 (44-65)	43.6	5.7	-	-	-	-
27	Rimland	2020-05-19	USA	11	Hospital	59 (48-65)	18.2	9.1	-	-	-	-
		2020-05				64						

125	Palaiodimos	2020-05-15	USA	200	Hospital	(50-73.5)	51.0	-	-	32.5	67.5	-
126	Ip	2020-05-25	USA	2,512	Hospital	64 (52-76)	37.6	3.1	17.8	-	64.5	-
127	Heili-Frades	2020-05-25	Spain	4,712	Hospital	62 (47-77)	50.5	4.9	17.4	-	-	66.5
128	Vaquero-Roncero	2020-05-24	Spain	146	Hospital	66^ (59-72)	32.2	-	-	6.8	-	-
129	Kim, Garg	2020-05-22	USA	2,491	Hospital	62 (50-75)	46.8	6.0	25.8	-	-	68.1
130	Wu	2020-05-21	Italy	174	Hospital	61.2^ (50-71)	30.5	-	-	33.3	-	-
131	Shi, Zhao	2020-05-20	China	101	Hospital	71 (59-80)	40.6	-	-	5.0	-	-
132	Al-Hindawi	2020-05-20	UK	31	Hospital	61 (NA)	12.9	3.2	71.0	-	25.8	-
133	Basse	2020-05-19	France	141	Hospital	62 (52-72)	72.0	17.7	-	-	-	-
134	Freites	2020-05-19	Spain	123	Hospital	59.88^ (44-74)	69.9	3.3	-	-	-	-
135	Alshami	2020-05-19	Saudi Arabia	128	Quarantine Centre	39.6^ (24-55)	53.9	15.6	2.3	-	-	-
136	Berumen	2020-05-26	Mexico	102,875	Hospital	NA	49.1	-	-	9.6	-	90.4
137	Gianfrancesco	2020-05-29	Multiple	600	Community and Hospital	56 (45-67)	71.0	-	-	21.5	64.8	-
138	Li, Long	2020-05-28	China	145	Not Stated	49^ (13-80)	61.0	-	-	5.5	-	-
139	Batty	2020-06-17	UK	908	Hospital	57.27^ (48-66)	44.3	11.2	-	-	-	-
140	Israel	2020-06-01	Israel	24,906	Community and Hospital	40 (27-59)	48.7	16.8	12.7	-	70.5	-
141	del Valle	2020-05-30	USA	1,484	Hospital	62 (52-72)	40.6	5.5	23.3	-	-	-
142	Chaudhry	2020-05-29	USA	40	Community and Hospital	52 (45.5-61)	60.0	-	-	15.0	-	-
143	Louis	2020-05-28	USA	22	Hospital	66.5^ (55-77)	36.4	-	-	45.5	-	-
144	Soto-Mota	2020-06-05	Mexico	400	Hospital	NA	30.0	-	-	12.0	-	-
145	Garibaldi	2020-05-26	USA	832	Hospital	63 (49-75)	47.0	5.5	22.6	-	-	-
146	Docherty	2020-05-22	Multiple	20,133	Hospital	72.9 (58-82)	40.0	4.2	21.7	-	44.5	-
147	Boulware	2020-06-03	Multiple	821	Community	40 (33-50)	51.6	3.3	-	-	-	-
		2020-05			Community	66						

148	Kuderer	2020-05-28	Multiple	928	and Hospital	50 (57-76)	50.0	4.6	35.1	-	50.5	-
149	Romao	2020-06-08	Portugal	34	Community	41^ (26-66)	67.7	-	-	26.5	-	-
150	Giannouchos	2020-06-07	Mexico	236,439	Community and Hospital	42.5^ (25-59)	49.1	9.1	-	-	-	90.9
151	Ramlall	2020-06-06	USA	11,116	Community and Hospital	52 (34.7-69.5)	55.2	-	-	26.8	73.2	-
152	Wang, Oekelen	2020-06-05	USA	58	Community and Hospital	67 (NA)	48.0	-	-	36.2	-	-
153	Perrone	2020-06-05	Italy	1,189	Hospital	NA	21.2	-	-	21.9	-	-
154	Sharma	2020-06-05	India	501	Hospital	35.1^ (18-51)	36.0	-	-	4.2	-	-
155	Eugen-Olsen	2020-06-02	Denmark	407	Hospital	64 (47-77)	57.7	20.6	36.9	-	39.6	-
156	Martinez-Portilla	2020-06-02	Mexico	224	Community and Hospital	29 (26-33)	100.0	-	-	3.1	-	-
157	Raisi-Estabragh	2020-06-02	UK	4,510	Hospital	NA	48.8	-	-	51.8	-	-
158	Luo	2020-06-02	China	625	Hospital	46 (NA)	47.7	3.0	-	-	-	-
159	Houlihan	2020-06-09	UK	200	Community	34 (29-44)	61.0	11.0	16.5	-	66.5	-
160	Cen	2020-06-08	China	1,007	Hospital	61 (49-68)	51.0	-	-	8.7	-	-
161	Klang	2020-05-23	USA	3,406	Hospital	NA	61.8	-	-	23.3	-	-
162	Maraschini	2020-06-12	Italy	146	Hospital	32.5^ (27-38)	100.0	-	9.6	-	80.8	-
163	Wang, Zhong	2020-06-12	USA	7,592	Community and Hospital	NA	45.1	3.6	17.1	-	51.9	-
164	McQueenie	2020-06-12	UK	428,199	Community and Hospital	NA	54.9	-	-	44.4	55.0	-
26	Miyara	2020-06-12	France	479	Community and Hospital	NA	44.7	6.7	31.6	-	59.5	-
165	Apea	2020-06-12	UK	1,737	Hospital	63.4^ (NA)	30.4	-	-	10.0	-	-
166	Woolford	2020-06-11	UK	4,510	Community and Hospital	70.5 (NA)	51.2	13.0	38.1	-	48.1	-
167	Hultcrantz	2020-06-11	USA	127	Community and Hospital	68 (41-91)	46.0	-	-	26.8	72.4	-
168	Raiter	2020-06-	USA	280	Hospital	59.6^	45.5	5.7	10.7	-	74.6	-

	Author	Date	Country	Count	Location	Age (years)	ICU	ICU	ICU	ICU	ICU	ICU
169	Lan	2020-06-09	USA	104	Community	49 <sup>^</sup> (34-63)	47.1	-	-	24.0	-	-
170	Zeng	2020-06-16	China	1,031	Hospital	60.3 <sup>^</sup> (46-74)	47.8	-	-	10.2	-	-
171	Suleyman	2020-06-16	USA	463	Hospital	57.5 <sup>^</sup> (40-74)	55.9	-	-	34.6	-	-
172	Chen, Yu	2020-06-16	China	1,859	Hospital	59 (45-68)	50.0	2.4	3.6	-	94.0	-
173	Garassino	2020-06-12	Multiple	200	Community and Hospital	68 (61.8-75)	30.0	24.0	55.5	-	18.5	-
174	Hernandez-Garduno	2020-06-11	Mexico	32,583	Community and Hospital	45 (34-56)	48.7	-	-	11.0	-	88.8
175	Govind	2020-06-20	UK	6,309	Community and Hospital	46.5 <sup>^</sup> (31-61)	38.3	66.3	26.8	-	5.5	-
176	Siso-Almirall	2020-06-20	Spain	322	Community and Hospital	56.7 <sup>^</sup> (38-74)	50.0	-	-	25.2	-	-
177	Gu	2020-06-18	USA	5,698	Community and Hospital	47 <sup>^</sup> (26-67)	62.0	7.0	24.7	-	50.8	-
178	Kibler	2020-06-16	France	702	Community and Hospital	82 <sup>^</sup> (75-88)	56.0	3.7	-	-	-	-
179	Ikitimur	2020-06-03	Turkey	81	Hospital	55 <sup>^</sup> (38-72)	44.0	-	-	28.4	-	-
180	Sierpinski	2020-06-03	Poland	1,942	Community	50 (NA)	60.0	6.3	-	-	-	49.7
181	Zhou, He	2020-06-10	China	238	Hospital	55.5 (35-67)	57.0	2.9	-	-	-	-
182	Crovetto	2020-06-19	Spain	874	Community and Hospital	33.7 <sup>^</sup> (28-38)	100.0	1.1	-	-	-	13.2
183	Veras	2020-06-09	Brazil	32	Hospital	58.9 <sup>^</sup> (40-77)	47.0	-	-	25.0	-	-
184	Sterlin	2020-06-11	France	135	Hospital	61 (50-72)	41.0	3.7	38.5	-	57.8	-
185	Rossi	2020-06-09	France	246	Hospital	68 <sup>^</sup> (53-83)	39.0	-	-	25.2	-	-
186	Duan	2020-06-22	China	616	Hospital	64 (53-70)	57.5	3.7	-	-	-	-
187	Martin-Jimenez	2020-06-09	Spain	339	Hospital	81.6 (72-87)	39.5	-	-	30.7	-	-
188	Elezkurtaj	2020-06-17	Germany	26	Hospital	70 (61.8-78.3)	34.6	-	-	19.2	-	-
189	Lenka	2020-06-22	USA	32	Hospital	62.2 <sup>^</sup> (51-73)	37.5	-	-	50.0	-	-
190	Olivares	2020-06-16	Chile	21	Hospital	61 <sup>^</sup> (26-85)	76.2	-	-	9.5	-	-

191	Salton	2020-06-20	Italy	173	Hospital	64.4 <sup>^</sup> (NA)	34.9	-	-	29.5	-	-
192	Wei	2020-06-18	USA	147	Hospital	52 <sup>^</sup> (34-70)	41.0	14.3	-	-	-	-
193	Zuo, Estes	2020-06-17	China	172	Hospital	61 <sup>^</sup> (25-95)	44.0	-	-	26.2	-	-
194	Killerby	2020-06-17	USA	531	Community and Hospital	51.6 (38-62)	57.1	-	-	17.1	71.4	-
195	Petrilli	2020-05-22	USA	5,279	Community and Hospital	54 (38-66)	51.5	5.5	17.1	-	61.9	-
196	Magagnoli	2020-06-05	USA	807	Hospital	70 (60-75)	4.3	-	-	15.9	-	-
34	Niedzwiedz	2020-05-29	UK	392,116	Community and Hospital	NA	54.9	9.8	34.8	-	55.4	-
197	Bello-Chavolla	2020-05-31	Mexico	177,133	Community and Hospital	42.6 (26-59)	48.9	-	-	9.3	-	-
198	Zuo, Yalavarthi	2020-04-24	USA	50	Hospital	61 (46-76)	34.0	-	-	36.0	-	-
199	Sigel	2020-06-28	USA	493	Hospital	60 (55-67)	24.1	-	-	28.6	-	-
200	Nguyen	2020-06-29	USA	689	Community and Hospital	55 (40-68)	57.0	-	-	24.8	-	-
201	de Melo	2020-06-29	Brazil	181	Hospital	55.3 <sup>^</sup> (34-76)	60.8	9.9	12.2	-	38.1	-
202	Auvinen	2020-06-29	Finland	61	Hospital	53 (41-67)	36.0	18.0	27.9	-	54.1	-
203	Souza	2020-06-28	Brazil	8,443	Hospital	NA	53.0	-	-	1.7	-	96.3
204	Mendy	2020-06-27	USA	689	Community and Hospital	49.5 (35.2-67.5)	47.0	-	-	24.7	-	-
205	Pongpirul	2020-06-26	Thailand	193	Hospital	37 (29-53)	41.5	-	-	15.0	66.3	-
206	Jin, Gu	2020-06-25	China	6	Hospital	60.5 <sup>^</sup> (51-75)	33.3	33.3	-	-	-	-
207	Fisman	2020-06-23	Canada	21,922	Community and Hospital	NA	57.0	-	-	2.3	-	-
208	Madariaga	2020-06-23	USA	103	Community and Hospital	41.8 <sup>^</sup> (27-55)	48.5	-	-	25.2	74.8	-
209	Senkal	2020-07-07	Turkey	611	Hospital	57 <sup>^</sup> (18-98)	40.6	11.3	-	-	-	-
210	Mohamud	2020-07-02	USA	6	Hospital	65.8 <sup>^</sup> (55-78)	16.7	-	-	16.7	-	-
211	Maclebv	2020-06-	USA	678	Hospital	68	38.9	-	-	28.6	-	-

		30				(50-81)						
212	Kimmig	2020-07-06	USA	111	Hospital	63 <sup>^</sup> (48-78)	44.1	7.2	36.0	-	56.8	-
213	Bello-Chavolla, Antonio-Villa	2020-07-04	Mexico	60,121	Community and Hospital	45.5 <sup>^</sup> (29-61)	47.0	-	-	10.5	-	-
214	Zacharioudakis	2020-07-04	USA	314	Hospital	64 (54-72)	34.7	-	-	22.8	-	-
215	Antonio-Villa	2020-07-04	Mexico	34,263	Community and Hospital	40 <sup>^</sup> (29-50)	62.9	9.7	-	-	-	-
216	Patel	2020-07-03	USA	129	Hospital	60.8 <sup>^</sup> (47-74)	45.0	37.2	-	-	-	55.8
217	Merzon	2020-07-03	Israel	7,807	Community and Hospital	46.2 <sup>^</sup> (NA)	58.6	-	-	16.2	-	-
35	Trubiano	2020-07-02	Australia	2,935	Community and Hospital	39 (29-53)	63.5	-	-	8.8	-	-
218	Fan	2020-07-11	UK	1,425	Community and Hospital	NA	46.7	12.2	40.1	-	46.9	-
219	Shi, Resurreccion	2020-07-11	UK	1,521	Community and Hospital	61.5 <sup>^</sup> (57-66.8)	45.9	-	-	54.9	-	-
220	Maucourant	2020-07-10	Sweden	27	Hospital	57 (18-78)	22.2	11.1	25.9	-	40.7	-
221	Elmunzer	2020-07-09	Multiple	1,992	Hospital	60 <sup>^</sup> (43-76)	43.0	6.3	28.6	-	59.0	-
222	Alizadehsani	2020-07-09	Iran	319	Hospital	45.48 <sup>^</sup> (26-63)	55.5	-	-	0.3	-	-
223	Xie	2020-07-07	China	619	Hospital	NA	52.0	-	-	8.2	-	-
43	Merkely	2020-07-17	Hungary	10,474	Community	48.7 <sup>^</sup> (30-66)	53.6	28.0	20.5	-	51.4	-
224	Fox	2020-07-17	UK	55	Community and Hospital	63 (23-88)	31.0	1.8	10.9	-	56.4	-
65	Zhang, Cao	2020-07-14	China	289	Hospital	57 (22-88)	46.6	3.5	6.2	-	-	-
225	Martinez--Resendez	2020-07-20	Mexico	8	Hospital	57 (48-69)	25.0	-	-	12.5	-	-
226	Hoertel	2020-07-20	France	12,612	Hospital	58.7 <sup>^</sup> (39-77)	49.6	-	-	9.3	-	-
227	Mcgrail	2020-07-19	USA	209	Hospital	62.5 (NA)	38.8	-	-	18.7	-	-
228	Pandolfi	2020-07-17	Italy	33	Hospital	62 (52-65)	21.1	3.0	24.2	-	72.7	-
28	Girardeau	2020-07-17	France	10	Community	30 (29-33)	50.0	40.0	10.0	-	-	-
229		2020-07-				62.9 <sup>^</sup>						

230	Kurashima	17	Japan	53	Hospital	(49-76)	35.8	-	-	50.9	-	-
231	Zhan	2020-07-16	China	75	Hospital	57 (25-75)	48.0	-	-	12.0	-	-
232	Omrani	2020-07-16	Qatar	1,409	Community and Hospital	39 (30-50)	17.2	-	-	9.2	-	-
96	Gupta	2020-07-16	USA	496	Hospital	70 (60-78)	46.0	-	-	7.3	-	31.7
233	Shi, Zuo	2020-07-15	USA	172	Hospital	61.48^ (25-96)	44.0	-	-	26.2	-	-
234	Hussein	2020-07-15	USA	502	Hospital	60.9^ (45-76)	52.0	9.0	22.1	-	-	68.9
235	Bian	2020-07-15	China	28	Hospital	56^ (42-67)	42.9	7.1	-	-	-	-
236	Eiros	2020-07-14	Spain	139	Community and Hospital	52 (41-57)	72.0	4.3	50.4	-	-	-
237	Marcos	2020-07-14	Spain	918	Hospital	72.8^ (58-87)	42.2	6.1	-	15.3	-	-
238	Hoertel, Sanchez-Rico	2020-07-14	France	7,345	Hospital	NA	49.3	8.5	-	-	-	-
239	Soares	2020-07-16	Brazil	10,713	Community and Hospital	NA	55.0	2.0	-	-	-	98.0
240	Zobairy	2020-07-28	Iran	203	Community and Hospital	49.2^ (32-65)	44.8	5.9	-	-	-	94.1
241	Altamimi	2020-07-27	Qatar	68	Hospital	49^ (40-58)	2.0	16.4	-	-	-	83.6
242	Thompson	2020-07-27	UK	470	Hospital	71 (57-82)	46.0	14.0	27.2	-	58.7	-
243	Reiter	2020-07-26	Austria	235	Community	44.2^ (32-55)	70.0	22.6	22.6	-	54.7	-
244	Motta	2020-07-26	USA	374	Hospital	64.7^ (46-82)	41.4	-	-	33.2	66.8	-
245	Santos	2020-07-25	USA	43	Community and Hospital	50 (34-73)	63.0	-	-	4.7	-	-
246	Schneeweiss	2020-07-22	USA	24,313	Community and Hospital	67^ (53-80)	53.0	-	-	2.9	-	-
247	Concha-Mejia	2020-07-24	Colombia	72	Community and Hospital	46 (28-64)	47.0	8.3	11.1	-	-	-
248	Izquierdo	2020-07-24	Spain	71,192	Community and Hospital	42^ (18-66)	59.0	10.0	-	-	-	90.0
30	Bernaola	2020-07-21	Spain	1,645	Hospital	NA	38.5	2.5	10.9	-	86.6	-
30	Islam	2020-08-18	Bangladesh	1,016	Community and Hospital	37 (28-49)	35.9	18.2	-	-	-	-



249	Qi	2020-03-03	China	267	Hospital	48 (35-65)	45.2	19.9	-	-	-	80.1
250	Peters	2020-08-15	Netherlands	1,893	Hospital	66.8 <sup>^</sup> (52-81)	39.4	4.9	-	-	-	-
251	Ouyang	2020-08-14	China	217	Hospital	46.5 <sup>^</sup> (30-62)	53.5	16.6	-	-	-	-
56	Ward	2020-08-21	UK	99,908	Community	NA	56.1	10.6	-	-	-	88.4
252	Valenzuela	2020-08-14	Chile	29	Hospital	56.9 <sup>^</sup> (43-70)	6.9	17.2	-	-	-	82.8
253	Monteiro	2020-08-14	USA	112	Hospital	61 (45-74)	34.0	6.2	17.9	-	68.8	-
254	Philipose	2020-08-14	UK	466	Hospital	67 (6-97)	41.8	6.0	73.2	-	16.5	-
255	Weerahandi	2020-08-14	USA	394	Community	63 (55-70)	37.0	5.3	25.9	-	55.8	-
29	Ebinger	2020-08-04	USA	6,062	Community	41.5 <sup>^</sup> (29-53)	67.8	1.7	-	-	-	-
256	Altibi	2020-08-11	USA	706	Hospital	66.7 <sup>^</sup> (51-81)	43.0	4.0	37.3	-	58.8	-
257	Izzi-Engbeaya	2020-08-11	UK	889	Hospital	65.8 <sup>^</sup> (48-83)	40.0	-	-	21.3	33.2	-
258	Rizzo	2020-08-11	USA	76,819	Hospital	54 (38-67)	55.2	6.7	20.8	-	50.4	-
259	Dashti	2020-08-04	USA	4,140	Community and Hospital	52 (36-65)	55.0	-	-	28.4	51.6	-
260	Morshed	2020-08-02	Bangladesh	103	Community	37 (31-53)	28.2	31.1	-	-	-	68.9
261	Jun	2020-08-01	USA	3,086	Hospital	66 (56-77)	40.9	3.7	21.3	-	52.8	-
262	Higuchi	2020-07-30	Japan	57	Hospital	52 (35-70)	43.9	12.3	29.8	-	57.9	-
263	Zhou, Sun	2020-07-29	China	144	Hospital	47 (38-56)	46.5	9.0	-	-	-	91.0
264	Salerno	2020-08-22	USA	15,920	Hospital	49 (30-65)	57.0	-	-	36.8	55.9	-
265	Kumar	2020-07-29	India	91	Hospital	47 <sup>^</sup> (41-52)	21.0	44.0	-	-	-	-
266	Hao	2020-06-01	China	788	Hospital	46 (35-56)	48.4	6.9	-	-	-	-
267	Iversen	2020-08-03	Denmark	28,792	Community and Hospital	44.4 <sup>^</sup> (31-57)	78.9	16.0	6.5	-	76.8	-
268	Hippisley-Cox	2020-07-13	UK	8,275,949	Community and Hospital	48.5 <sup>^</sup> (30-66)	50.3	17.2	21.4	-	57.3	-
269	Fillmore	2020-08-24	USA	22,914	Community and Hospital	NA	-	37.5	40.7	-	15.5	-
270	Rashid	2020-08-	UK	517	Hospital	72.8 <sup>^</sup>	31.9	9.9	29.0	-	29.4	-

		22				(59-86)						
271	Pan	2020-08-22	USA	12,084	Community and Hospital	45.5 <sup>^</sup> (27-63)	54.3	-	-	17.5	-	-
272	Alkurt	2020-08-20	Turkey	932	Community and Hospital	34.8 <sup>^</sup> (25-44)	64.4	24.5	-	-	-	-
273	Zhao, Chen	2020-07-30	USA	641	Hospital	<sup>60</sup> (NA)	40.1	21.7	-	-	-	-
274	Holman	2020-08-13	UK	10,989	Community and Hospital	NA	38.8	5.5	42.6	-	49.0	-
275	Qu	2020-07-29	China	246	Hospital	53.6 <sup>^</sup> (38-68)	53.3	42.3	-	-	-	-
276	Chand	2020-08-19	USA	300	Hospital	58.2 <sup>^</sup> (45-70)	39.3	22.3	-	-	-	-
277	Oliveira	2020-08-31	USA	131	Hospital	61 (49.5-71.5)	64.9	-	-	17.6	26.7	-
278	Hussein, Galal	2020-09-01	Egypt	444	Community	33.1 <sup>^</sup> (21-45)	56.8	13.1	9.0	-	77.9	-
279	Vilar-Garcia	2020-09-01	Spain	7,699,568	Community and Hospital	43 (24-59)	50.9	17.1	-	-	-	-
280	Ibarra, Nava	2020-09-01	Mexico	416,546	Community and Hospital	NA	46.9	7.4	-	-	-	-
281	Ibrahim	2020-08-27	USA	38	Hospital	63 <sup>^</sup> (51-75)	47.0	10.5	-	-	-	-
282	Rubio-Rivas	2020-09-01	Spain	186	Hospital	64.3 <sup>^</sup> (51-77)	30.6	4.3	20.4	-	75.3	-
283	Mamtani	2020-09-02	USA	403	Hospital	55 <sup>^</sup> (41-68)	32.3	9.7	12.7	-	68.5	-
284	Ren	2020-09-02	China	432	Hospital	NA	57.9	10.0	-	-	90.0	-
285	Yoo	2020-08-31	USA	4,840	Hospital	66.4 (54.9-77.8)	43.5	4.4	21.4	-	53.3	-
286	Mutambudzi	2020-09-03	UK	120,075	Community and Hospital	NA	54.2	11.7	26.4	-	61.9	-
287	Yan	2020-09-07	China	578	Hospital	49.2 <sup>^</sup> (35-63)	49.3	9.2	-	-	-	-
288	Mancilla-Galindo	2020-09-08	Mexico	183,779	Community and Hospital	45 <sup>^</sup> (28-61)	46.0	7.6	-	-	-	-
289	Ullah	2020-09-08	UK	212	Community and Hospital	66.7 (54.2-80.5)	44.8	11.3	48.1	-	37.7	-
259	Dashti	2020-09-13	USA	12,347	Community and Hospital	47 (32-62)	53.3	4.6	15.9	-	57.1	-
290	Nicholson	2020-09-17	USA	1,042	Hospital	64 (50-75)	43.2	8.3	22.2	-	37.1	-

		17				(53-75)						
291	Ariza	2020-09-18	Colombia	351	Community and Hospital	30.5 (NA)	54.0	6.8	-	-	-	93.2
44	Carrat	2020-09-18	France	14,628	Community	NA	60.3	12.0	40.8	-	45.6	-
292	Zhu	2020-09-21	China	432	Community and Hospital	49 (35-60)	47.9	14.4	-	-	-	-
293	Sun	2020-08-16	USA	323	Community and Hospital	NA	57.6	-	-	39.3	-	60.7
294	Kalan	2020-05-01	Iran	193	Hospital	52.6^ (37-67)	36.3	7.3	-	-	85.0	-
295	Burrell	2020-09-16	Australia	204	Hospital	63.5 (53-72)	31.4	-	-	13.2	-	82.8
296	Meini	2020-09-23	Italy	461	Hospital	NA	51.2	10.4	25.8	-	63.8	-
297	Favara	2020-09-20	UK	434	Community	40 (19-66)	82.0	8.5	-	-	-	91.5
298	da Silva Neto	2020-09-23	Brazil	91	Community and Hospital	49^ (29-68)	49.4	-	-	19.8	-	80.2
299	Li, Cai	2020-09-28	China	98	Hospital	68.5 (63-75)	58.2	-	-	11.2	-	88.8
300	Wang	2020-09-29	USA	1,078	Hospital	NA	38.2	3.7	24.9	-	49.0	-
301	Lopez-Medrano	2020-09-30	Spain	261	Hospital	NA	43.7	-	-	37.2	-	62.8
302	Incerti	2020-10-02	USA	13,658	Hospital	62 (49-75)	48.1	6.3	22.6	-	45.4	-
303	Collard	2020-10-01	Netherlands	1,604	Hospital	65.7^ (50-80)	39.5	4.9	-	-	-	-
304	Robinson	2020-10-05	USA	3,248	Hospital	51^ (34-68)	72.0	4.0	17.6	-	61.8	-
305	Erber	2020-10-06	Germany	4,554	Community	38.5^ (NA)	70.4	-	-	18.0	-	82.0
306	Chaudhary	2020-10-06	Nepal	220	Hospital	31.5 (25-37)	17.7	11.4	7.7	-	80.0	-
307	Roederer	2020-10-09	France	818	Community	NA	20.4	36.9	8.8	-	53.9	-
308	Savarraj	2020-10-18	USA	48	Hospital	50^ (33-67)	48.0	10.4	-	-	-	-
309	Israel, Schaffer	2020-10-18	Israel	26,959	Hospital	NA	50.6	6.8	15.2	-	77.0	-
310	El-Solh	2020-10-20	USA	7,816	Hospital	69 (60-74)	5.5	-	-	45.3	-	54.7
311	Chudasama	2020-10-23	UK	1,706	Community and Hospital	68 (48-85)	42.5	13.8	41.0	-	45.3	-
312	Salama	2020-10-23	Multiple	377	Hospital	55.9^ (41-70)	40.8	5.8	17.0	-	77.2	-

		23				(41-70)						
313	Makaronidis	2020-10-01	UK	567	Community	39.4 <sup>^</sup> (27-51)	69.1	9.3	-	-	-	90.7
314	Ramachandran	2020-10-12	USA	188	Hospital	NA	-	18.6	-	-	-	-
315	Hadi	2020-08-05	USA	370	Community and Hospital	48.2 <sup>^</sup> (34-62)	29.5	-	-	15.1	84.9	-
316	Luo, Rizvi	2020-10-03	USA	102	Hospital	68 (61-75)	52.0	-	-	26.5	-	73.5
317	Ioannou	2020-09-23	USA	88,747	Community and Hospital	NA	9.0	20.6	37.5	-	29.3	-
318	ISARIC	2020-10-04	Multiple	88,463	Hospital	72 (NA)	43.0	-	-	5.2	-	37.6
319	Perico	2020-10-22	Italy	423	Community	44.3 <sup>^</sup> (34-54)	36.4	21.7	18.0	-	60.3	-
320	Lamure	2020-10-12	France	89	Hospital	67 (19-92)	34.0	5.6	32.6	-	48.3	-
321	Yadaw	2020-10-01	USA	5,051	Community and Hospital	NA	-	3.6	15.9	-	51.4	-
322	Zinellu	2020-10-11	Italy	105	Hospital	72 (59.5-80)	33.3	30.5	10.5	-	59.0	-
323	Ziehr	2020-04-29	USA	66	Hospital	58 (23-87)	35.0	-	-	33.3	63.6	-
324	Zhou, He, Yang	2020-10-27	China	1,087	Hospital	NA	51.7	-	-	85.0	15.0	-
325	Zhou, Song	2020-10-22	China	124	Hospital	67 (30-86)	48.0	19.1	-	-	-	-
326	Zhou, Qin	2020-08-25	China	51	Hospital	57.37 <sup>^</sup> (42-72)	29.4	-	-	78.4	21.6	-
327	Zhang, Li	2020-12-06	UK	1,746	Community and Hospital	68.8 <sup>^</sup> (59-78)	47.1	10.1	35.1	-	44.2	-
328	Zhan, Liu	2020-08-31	China	405	Hospital	56 <sup>^</sup> (17-95)	54.1	-	-	11.4	88.6	-
329	Wang, Shu	2020-07-20	China	59	Hospital	67.4 <sup>^</sup> (56-78)	35.6	-	-	15.3	-	-
330	Wang, Zheutlin	2020-10-26	USA	3,273	Hospital	65 (53-77)	42.7	3.5	20.7	-	53.2	-
331	Vila-Corcoles	2020-12-10	Spain	79,083	Community	NA	52.4	-	-	16.1	-	-
332	Torres-Macho	2020-09-23	Spain	1,968	Hospital	NA	44.0	-	-	23.4	-	-
333	Tao	2020-08-06	China	70	Hospital	33.24 <sup>^</sup> (12-53)	48.6	-	-	15.7	-	-
334	Talavera	2020-10-01	Spain	576	Hospital	67.2 <sup>^</sup> (52-81)	43.4	-	-	20.5	-	-
335	Serling-Boyd	2020-11-30	USA	831	Hospital	NA	76.0	3.0	23.2	-	50.1	-

336	Raines	2020-10-07	USA	453	Community and Hospital	60.8 <sup>^</sup> (46-74)	10.7	-	-	53.0	41.9	-
337	Parra-Bracamonte	2020-08-14	Mexico	331,298	Community and Hospital	44 (33-56)	46.2	-	-	7.4	-	-
338	O'Reilly	2020-09-21	Australia	1,334	Hospital	NA	-	-	-	28.5	-	-
339	Martini	2020-12-04	Italy	146	Hospital	NA	49.0	-	-	46.6	53.4	-
340	Li, Long, Zhang	2020-12-03	China	954	Hospital	NA	-	-	-	5.9	94.1	-
341	Lassale	2020-06-01	UK	900	Hospital	57.2 <sup>^</sup> (48-66)	44.4	11.4	41.9	-	46.7	-
342	Klang, Soffer	2020-08-09	USA	1,320	Hospital	NA	41.5	-	-	24.7	-	-
343	Kim, Han	2020-11-09	South Korea	4,787	Hospital	55 (38-68)	60.1	5.5	2.8	-	91.7	-
344	Jehi	2020-08-11	USA	4,536	Community and Hospital	NA	-	7.3	28.5	-	49.9	-
345	Jakob	2020-10-01	Multiple	2,155	Community and Hospital	NA	40.3	6.6	7.3	-	34.3	-
346	Invernizzi	2020-09-20	Italy	54	Hospital	49.9 <sup>^</sup> (34-65)	29.7	-	-	24.1	-	-
347	Ilic	2020-11-19	Serbia	107	Community and Hospital	39.1 <sup>^</sup> (27-50)	-	29.9	-	-	-	-
348	Hamadah	2020-09-10	Kuwait	1,123	Hospital	40 (1-93)	18.7	3.9	-	-	-	96.1
349	Gianfrancesco, Leykina	2020-11-03	USA	1,324	Community and Hospital	NA	75.9	-	-	26.7	68.2	-
350	Ghinai	2020-10-12	USA	1,435	Homeless Shelters	NA	27.6	36.6	17.5	-	33.2	-
351	Fond	2020-07-30	France	1,092	Hospital	62.5 (51-76)	45.7	11.4	-	-	-	88.6
352	Best	2020-10-12	USA	3,471	Hospital	63.5 <sup>^</sup> (47-79)	51.2	-	-	28.6	-	71.4
353	Bellan	2020-11-26	Italy	1,697	Hospital	71 (58-80)	41.0	3.2	-	-	-	15.2
354	Alharthy	2020-10-03	Saudi Arabia	352	Hospital	50.6 <sup>^</sup> (37-63)	12.8	49.4	-	-	-	50.6
355	Alguwaihes	2020-12-05	Saudi Arabia	439	Hospital	55 (19-101)	31.7	2.1	-	-	-	97.9
356	Aksu	2020-08-19	Turkey	123	Community and Hospital	49.7 <sup>^</sup> (36-63)	33.3	11.4	-	-	-	88.6
357	Adrish	2020-10-05	USA	1,173	Hospital	NA	38.6	14.0	14.7	-	71.4	-
358	Hoertel,	2020-10-	-	-	-	-	-	-	-	-	-	-

358	Sanchez, Vernet	27	France	12,210	Hospital	NA	50.1	9.0	-	-	-	-
359	Arleo	2020-10-27	USA	70	Community and Hospital	56.6 <sup>^</sup> (48-65)	80.0	1.4	28.6	-	70.0	-
360	Bermejo, Martin	2020-10-27	Spain	250	Community and Hospital	NA	64.0	6.0	-	-	-	-
361	Joubert	2020-10-29	France	74	Community and Hospital	NA	-	5.4	-	-	-	-
362	Kortela	2020-11-01	Finland	3,008	Community and Hospital	51 (36-69)	59.6	11.0	14.0	-	29.2	-
363	Sourij	2020-11-16	Austria	238	Hospital	71.1 <sup>^</sup> (58-83)	36.1	1.7	16.0	-	82.4	-
364	Galal	2020-11-12	Egypt	430	Community	37.4 <sup>^</sup> (24-50)	63.7	6.0	7.7	-	86.3	-
365	Clavario	2020-11-16	Italy	110	Community	61.7 (53.5-69.2)	40.9	40.9	-	-	-	-
366	Saeed	2020-11-16	United Arab Emirates	173	Hospital	NA	34.1	6.4	-	-	-	-
367	Cadegiani	2020-11-18	Brazil	130	Community	42 <sup>^</sup> (NA)	0.0	7.7	-	-	-	-
368	Benaim	2020-11-19	Israel	693	Hospital	59.8 (NA)	47.9	-	-	5.1	-	-
369	Singh	2020-11-20	UK	930	Hospital	71.4 <sup>^</sup> (54-87)	44.8	-	-	19.0	-	81.0
370	ISARIC	2020-11-23	Multiple	95,966	Hospital	72 (NA)	43.0	5.2	-	-	-	37.5
371	Marquez-Salinas	2020-11-24	Mexico	1,068	Hospital	53 (44-63)	36.8	-	-	15.0	-	-
372	Diez-Manglano	2020-11-24	Spain	4,393	Hospital	53 <sup>^</sup> (NA)	40.8	6.6	-	-	-	-
373	Woolcott	2020-11-26	Mexico	1,636,050	Community and Hospital	42 (34-54)	51.9	-	-	8.8	-	-
374	Simons	2020-11-30	UK	446	Hospital	64.9 (52.4-76.2)	35.9	9.4	38.6	-	52.0	-
375	Dupraz	2020-11-30	Switzerland	219	Community	NA	54.8	11.0	-	-	-	-
376	Chen, Varathraja	2020-11-29	USA	10,123	Community and Hospital	40 (28-54)	53.6	4.4	9.7	-	45.9	-
377	Martinez, Laczada	2020-12-01	Spain	10,433	Hospital	65.8 <sup>^</sup> (49-82)	42.8	5.2	23.8	-	66.0	-
378	Barasa	2020-11-30	USA	394	Hospital	NA	47.7	14.7	36.0	-	41.6	-
379		2020-11-										

379	Ren, Guo	30	China	481	Hospital	NA	45.7	7.7	0.6	-	91.7	-
380	O'Gallagher	2020-12-04	UK	1,721	Hospital	71 (56-83)	43.4	6.6	18.5	-	74.9	-
381	Modrak	2020-12-22	Czechia	213	Hospital	69 (58-80)	51.0	-	-	13.1	-	-
382	Zuo, Warnock	2020-12-05	USA	118	Hospital	61^ (44-78)	46.0	-	-	23.7	-	-
383	Bisso	2020-12-11	Argentina	168	Hospital	67 (58-75)	34.0	10.7	-	-	-	-
384	Rentsch, Beckman	2020-12-11	USA	4,297	Hospital	68 (58-75)	6.6	36.8	39.3	-	1.9	-
385	Thiabaud	2020-12-11	Switzerland	3,582	Hospital	68 (54-79)	40.5	-	-	6.6	-	50.5
386	Iftime	2020-12-14	Spain	468	Hospital	NA	44.9	-	-	7.9	-	-
387	Vila, Corcoles, Statue, Gracia	2020-12-11	Spain	282	Community and Hospital	65.9^ (53-78)	50.3	8.9	-	-	-	-
388	Levy	2020-12-12	France	61	Hospital	60 (50-69)	20.0	8.2	-	-	-	-

*Note.* – Age not provided for total sample; ^ Denotes mean (SD). \* This study was rated as ‘poor’ quality as the manuscript only presents data for current (but not former) smokers despite having obtained complete smoking status, thus resulting in >20% missing data on smoking status.

### ***Smoking prevalence by country***

Unadjusted smoking prevalence compared with overall estimates for national adult smoking prevalence split by country and study setting is presented in Figure 2a and 2b. Lower than expected current smoking prevalence was generally observed, especially in studies with hospitalised samples. Former smoking prevalence was typically higher than expected prevalence when reported. National smoking prevalence estimates used for comparison are presented in Supplementary table 3.

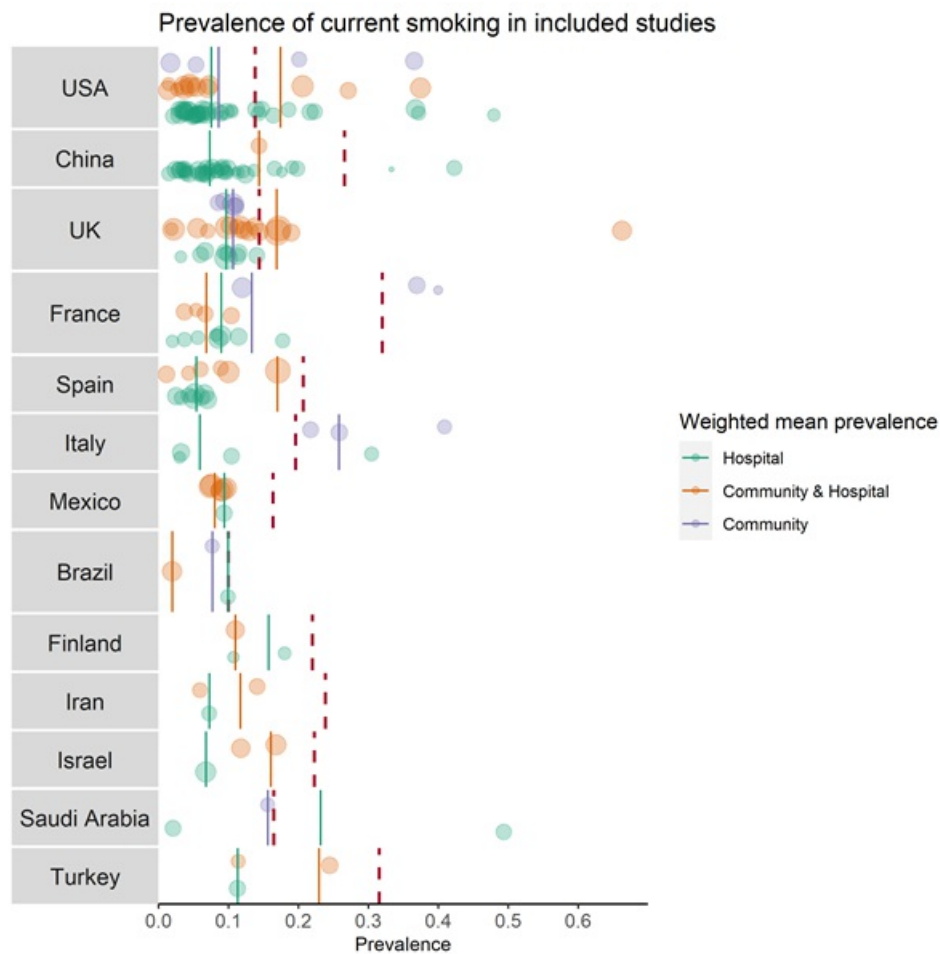
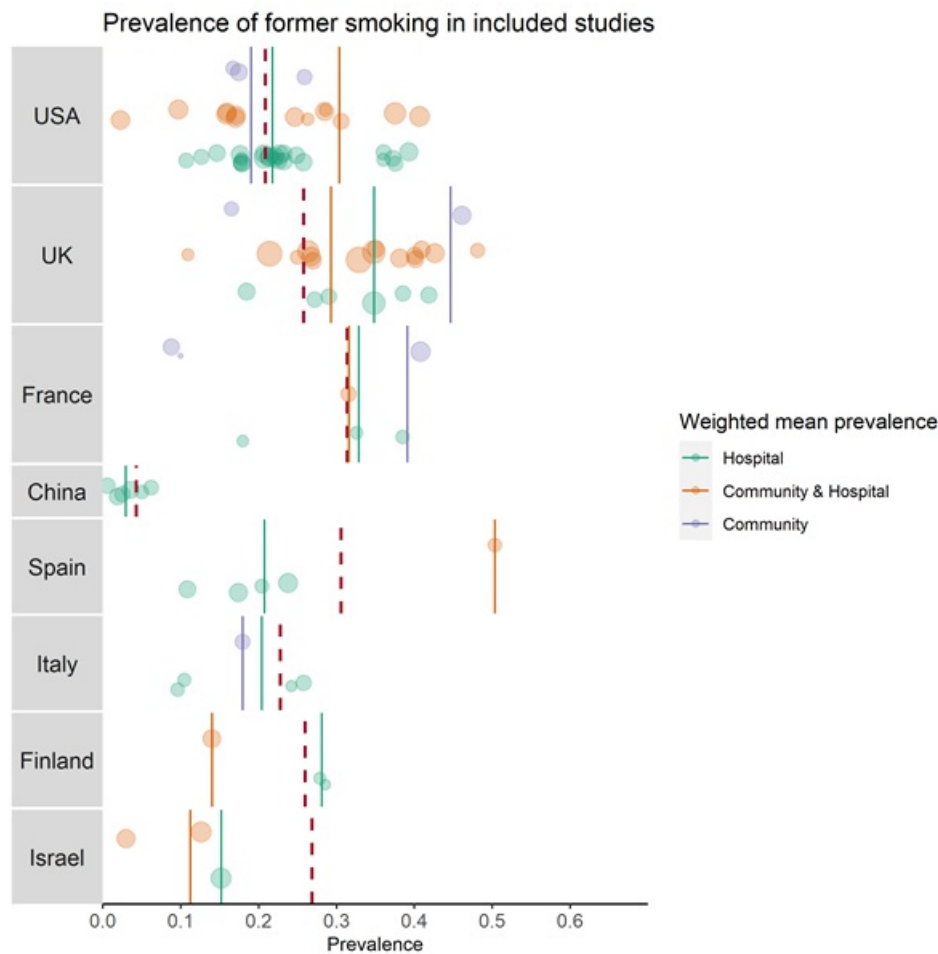


Figure 2a. Weighted mean prevalence of current smoking in included studies, split by country (solid lines). The circles represent individual studies, with colour corresponding to study setting (i.e. community, community and hospital, hospital) and size corresponding to relative study sample size. For comparison, national current smoking prevalence is shown by the dashed red lines. Countries with three or more eligible studies are shown.





*Figure 2b.* Prevalence of former smoking in included studies, split by country (solid lines). The circles represent individual studies, with colour corresponding to study setting (i.e. community, community and hospital, hospital) and size corresponding to relative study sample size. For comparison, national former smoking prevalence is shown by dashed red lines. Countries with three or more eligible studies are shown.

### **SARS-CoV-2 testing by smoking status**

Three studies provided data on access to SARS-CoV-2 diagnostic testing for those meeting local testing criteria by smoking status. In a cohort study of US military veterans aged 54-75<sup>32</sup>, current smokers were more likely to receive a test: 42.3% (1,603/3,789) of the sample were current smokers compared with 23.8% of all veterans aged 50+ years using any tobacco product between 2010-2015<sup>33</sup>. In the UK Biobank cohort<sup>34</sup>, a multivariable analysis showed former (RR = 1.29, 95% CI = 1.14-1.45,  $p < .001$ ) and current (RR = 1.44, 95% CI = 1.20-1.71,  $p < .001$ ) compared with never smokers to be more likely to receive a test. In an Australian rapid assessment screening clinic for COVID-19<sup>35</sup>, 9.4% (397/4,226) of the self-referred sample (subsequently assessed by a healthcare professional to decide on testing) were current smokers. Of these self-referrals, healthcare professionals decided that current compared with former or never smokers were less likely to require a test (RR = 0.93, 95% CI = 0.86-1.0,  $p = 0.045$ ).

## SARS-CoV-2 infection by smoking status

Sixty-three studies provided data on SARS-CoV-2 infection for people meeting local testing criteria by smoking status (see Table 2). Meta-analyses were performed for two ‘good’ and 23 ‘fair’ quality studies (see Figure 3 and 4). Current smokers were at reduced risk of testing positive for SARS-CoV-2 compared with never smokers (RR = 0.69, 95% Credible Interval (CrI) = 0.58-0.82,  $\tau = 0.36$ ). The probability of current smokers being at reduced risk of infection compared with never smokers (RR  $\leq 0.9$ ) was 99.8%. Former compared with never smokers were at increased risk of testing positive, but data were inconclusive (RR = 1.03, 95% CrI = 0.94-1.13,  $\tau = 0.18$ ) and favoured there being no important association. The probability of former smokers being at increased risk of infection (RR  $\geq 1.1$ ) compared with never smokers was 7.8%. Results were materially unchanged in the two sensitivity analyses.

Table 2. SARS-CoV-2 infection by smoking status.

Author	Total population tested	SARS-CoV-2 negative						SARS-CoV-2 positive			
		N (%)	Current smoker (%)	Former smoker (%)	Current/former smoker (%)	Never smoker (%)	Not stated (%)	N (%)	Current smoker (%)	Former smoker (%)	Current/former smoker (%)
Rentsch	3528	2974 (84.30%)	1444 (48.55%)	704 (23.67%)	-	826 (27.77%)	-	554 (15.70%)	159 (28.70%)	179 (32.31%)	-
Fontanet	661	490 (74.13%)	64 (13.06%)	-	-	426 (86.94%)	-	171 (25.87%)	5 (2.92%)	-	-
Cho	1331	793 (59.58%)	142 (17.91%)	214 (26.99%)	-	437 (55.11%)	-	538 (40.42%)	111 (20.63%)	145 (26.95%)	-
Shah	243	212 (87.24%)	52 (24.53%)	47 (22.17%)	-	113 (53.30%)	-	29 (11.93%)	0 (0.00%)	9 (31.03%)	-
Kolin	1474	805 (54.61%)	141 (17.52%)	307 (38.14%)	-	354 (43.98%)	3 (0.37%)	669 (45.39%)	72 (10.76%)	285 (42.60%)	-
de Lusignan	3291	2740 (83.26%)	366 (13.36%)	1450 (52.92%)	-	924 (33.72%)	-	551 (16.74%)	47 (8.53%)	303 (54.99%)	-
Valenti	789	689 (87.33%)	197 (28.59%)	-	-	-	492 (71.41%)	40 (5.07%)	7 (17.50%)	-	-
Parrotta	76	39 (51.32%)	1 (2.56%)	10 (25.64%)	-	27 (69.23%)	1 (2.56%)	37 (48.68%)	1 (2.70%)	10 (27.03%)	-
Berumen	102875	71353 (69.36%)	-	-	7173 (10.05%)	64180 (89.95%)	-	31522 (30.64%)	-	-	2748 (8.72%)
Israel	24906	20755 (83.33%)	3783 (18.23%)	2671 (12.87%)	-	14301 (68.90%)	-	41151 (165.23%)	406 (0.99%)	483 (1.17%)	-
del Valle	1108	143 (12.91%)	27 (18.88%)	53 (37.06%)	-	-	63 (44.06%)	965 (87.09%)	55 (5.70%)	293 (30.36%)	-
Romao	34	20 (58.82%)	-	-	5 (25.00%)	-	15 (75.00%)	14 (41.18%)	-	-	4 (28.57%)
Ramlall	11116	4723 (42.49%)	-	-	-	-	-	6393 (57.51%)	-	-	1643.001 (25.70%)
Sharma	501	267 (53.29%)	-	-	1 (0.37%)	-	266 (99.63%)	234 (46.71%)	-	-	20 (8.55%)
Eugen-Olsen	407	290 (71.25%)	76 (26.21%)	104 (35.86%)	-	102 (35.17%)	-	117 (28.75%)	8 (6.84%)	46 (39.32%)	-

		(100.0%)	(0.00%)	(0.00%)		(0.00%)		(0.00%)	(0.00%)	(0.00%)	
Raisi-Estabragh	4510	3184 (70.60%)	-	-	1653 (51.92%)	-	1531 (48.08%)	1326 (29.40%)	-	-	683 (51.51%)
Houlihan	177	97 (54.80%)	14 (14.43%)	14 (14.43%)	-	69 (71.13%)	-	80 (45.20%)	7 (8.75%)	19 (23.75%)	-
McQueenie	428199	424355 (99.10%)	-	-	189299 (44.61%)	235056 (55.39%)	-	1311 (0.31%)	-	-	669 (51.03%)
Woolford	4474	3161 (70.65%)	441 (13.95%)	1194 (37.77%)	-	1526 (48.28%)	-	1313 (29.35%)	145 (11.04%)	525 (39.98%)	-
Lan	104	83 (79.81%)	-	-	24 (28.92%)	-	59 (71.08%)	21 (20.19%)	-	-	1 (4.76%)
Hernandez-Garduno	32583	20279 (62.24%)	-	-	2399 (11.83%)	17861 (88.08%)	-	12304 (37.76%)	-	-	1191 (9.68%)
Govind	6215	6207 (99.87%)	4104 (66.12%)	1669 (26.89%)	-	342 (5.51%)	-	102 (1.64%)	78 (76.47%)	20 (19.61%)	-
Gu	4699	3815 (81.19%)	360 (9.44%)	1142 (29.93%)	-	2313 (60.63%)	-	884 (18.81%)	40 (4.52%)	264 (29.86%)	-
Kibler	702	680 (96.87%)	25 (3.68%)	-	-	-	655 (96.32%)	22 (3.13%)	1 (4.55%)	-	-
Petrilli	10620	5341 (50.29%)	3454 (64.67%)	816 (15.28%)	-	541 (10.13%)	530 (9.92%)	5279 (49.71%)	3268 (61.91%)	902 (17.09%)	-
Bello-Chavolla	150200	98567 (65.62%)	-	-	9624 (9.76%)	-	88943 (90.24%)	51633 (34.38%)	-	-	4366 (8.46%)
Auvinen	61	33 (54.10%)	10 (30.30%)	8 (24.24%)	-	15 (45.45%)	-	28 (45.90%)	1 (3.57%)	9 (32.14%)	-
Favara	70	55 (78.57%)	5 (9.09%)	-	-	-	50 (90.91%)	15 (21.43%)	2 (13.33%)	-	-
Antonio-Villa	34263	23338 (68.11%)	2293 (9.83%)	-	-	-	21045 (90.17%)	10925 (31.89%)	1023 (9.36%)	-	-
Merzon	7807	7025 (89.98%)	-	-	1136 (16.17%)	-	5889 (83.83%)	782 (10.02%)	-	-	127 (16.24%)
Trubiano	2676	2827 (105.64%)	-	-	256 (9.06%)	-	2586 (91.48%)	108 (4.04%)	-	-	3 (2.78%)
Shi, Resurreccion	1521	1265 (83.17%)	-	-	681 (53.83%)	-	584 (46.17%)	256 (16.83%)	-	-	154 (60.16%)
Riley	120620	120461 (99.87%)	2594 (2.15%)	-	-	19914 (16.53%)	97953 (81.32%)	159 (0.13%)	3 (1.89%)	-	-
Alizadehsani	319	196 (61.44%)	-	-	-	-	196 (100.00%)	123 (38.56%)	-	-	1 (0.81%)
Merkely	10474	10336 (98.68%)	2904 (28.10%)	2107 (20.39%)	-	5310 (51.37%)	15 (0.15%)	70 (0.67%)	16 (22.86%)	15 (21.43%)	-
Mcgrail	209	118 (56.46%)	-	-	31 (26.27%)	-	87 (73.73%)	91 (43.54%)	-	-	8 (8.79%)
Izquierdo	71192	NA (NA%)	-	-	-	-	-	1006 (1.41%)	111 (11.03%)	-	-
Ward	99908	94416 (94.50%)	10202 (10.81%)	-	-	-	84214 (89.19%)	5492 (5.50%)	433 (7.88%)	-	-
Ebinger	6062	5850 (96.50%)	99 (1.69%)	-	-	-	5668 (96.89%)	212 (3.50%)	3 (1.42%)	-	-
Salerno	15920	14753 (92.67%)	-	-	5517 (37.40%)	8278 (56.11%)	958 (6.49%)	1167 (7.33%)	-	-	339 (29.05%)

Iversen	28792	27629 (95.96%)	4430 (16.03%)	1799 (6.51%)	-	21217 (76.79%)	246 (0.89%)	1163 (4.04%)	177 (15.22%)	78 (6.71%)	-
Hippisley-Cox	8275949	NA (NA%)	-	-	-	-	-	19486 (0.24%)	1354 (6.95%)	5715 (29.33%)	-
Fillmore	22914	21120 (92.17%)	8137 (38.53%)	8416 (39.85%)	-	3227 (15.28%)	1340 (6.34%)	1794 (7.83%)	452 (25.20%)	899 (50.11%)	-
Alkurt	119	NA (NA%)	-	-	-	-	-	119 (100.00%)	14 (11.76%)	-	-
Ariza	351	322 (91.74%)	21 (6.52%)	-	-	-	301 (93.48%)	29 (8.26%)	3 (10.34%)	-	-
Carrat	14393	13426 (93.28%)	1652 (12.30%)	5620 (41.86%)	-	6154 (45.84%)	-	967 (6.72%)	98 (10.13%)	353 (36.50%)	-
Meini	461	243 (52.71%)	39 (16.05%)	66 (27.16%)	-	138 (56.79%)	-	218 (47.29%)	9 (4.13%)	53 (24.31%)	-
Favara	434	354 (81.57%)	28 (7.91%)	-	-	-	326 (92.09%)	80 (18.43%)	9 (11.25%)	-	-
Erber	4554	4446 (97.63%)	-	-	806 (18.13%)	-	3640 (81.87%)	108 (2.37%)	-	-	11 (10.19%)
Roederer	815	390 (47.85%)	175 (44.87%)	32 (8.21%)	-	183 (46.92%)	-	425 (52.15%)	127 (29.88%)	40 (9.41%)	-
Makaronidis	567	127 (22.40%)	16 (12.60%)	-	-	-	111 (87.40%)	440 (77.60%)	37 (8.41%)	-	-
Ioannou	88747	78616 (88.58%)	17138 (21.80%)	29245 (37.20%)	-	22327 (28.40%)	9906 (12.60%)	10131 (11.42%)	1135 (11.20%)	4073 (40.20%)	-
Perico	423	260 (61.47%)	69 (26.54%)	35 (13.46%)	-	156 (60.00%)	-	163 (38.53%)	23 (14.11%)	41 (25.15%)	-
Vila-Corcoles	2,324	1944 (83.65%)	-	-	-	-	-	380 (16.35%)	-	-	27 (7.11%)
O'Reilly	1,334	1284 (96.25%)	-	-	376 (29.28%)	-	908 (70.72%)	50 (3.75%)	-	-	4 (8.00%)
Martini	146	108 (73.97%)	-	-	56 (51.85%)	52 (48.15%)	-	38 (26.03%)	-	-	12 (31.58%)
Ghinai	1,435	1004 (69.97%)	412 (41.04%)	155 (15.44%)	-	341 (33.96%)	96 (9.56%)	431 (30.03%)	113 (26.22%)	96 (22.27%)	-
Kortela	2,993	2419 (80.82%)	300 (12.40%)	340 (14.06%)	-	636 (26.29%)	1143 (47.25%)	574 (19.18%)	26 (4.53%)	80 (13.94%)	-
Gallichotte	239	190 (79.50%)	40 (21.05%)	28 (14.74%)	-	110 (57.89%)	-	49 (20.50%)	8 (16.33%)	12 (24.49%)	-
Saeed	173	69 (39.88%)	2 (2.90%)	-	-	-	67 (97.10%)	104 (60.12%)	9 (8.65%)	-	-
Woolcott	1,636,050	878840 (53.72%)	-	-	85816 (9.76%)	-	793024 (90.24%)	757210 (46.28%)	-	-	57451 (7.59%)
Barasa	394	277 (70.30%)	49 (17.69%)	105 (37.91%)	-	110 (39.71%)	13 (4.69%)	117 (29.70%)	9 (7.69%)	37 (31.62%)	-

*Note.* Niedzwiedz et al. reported on SARS-CoV-2 infection by smoking status in multivariable analyses but did not present raw data.

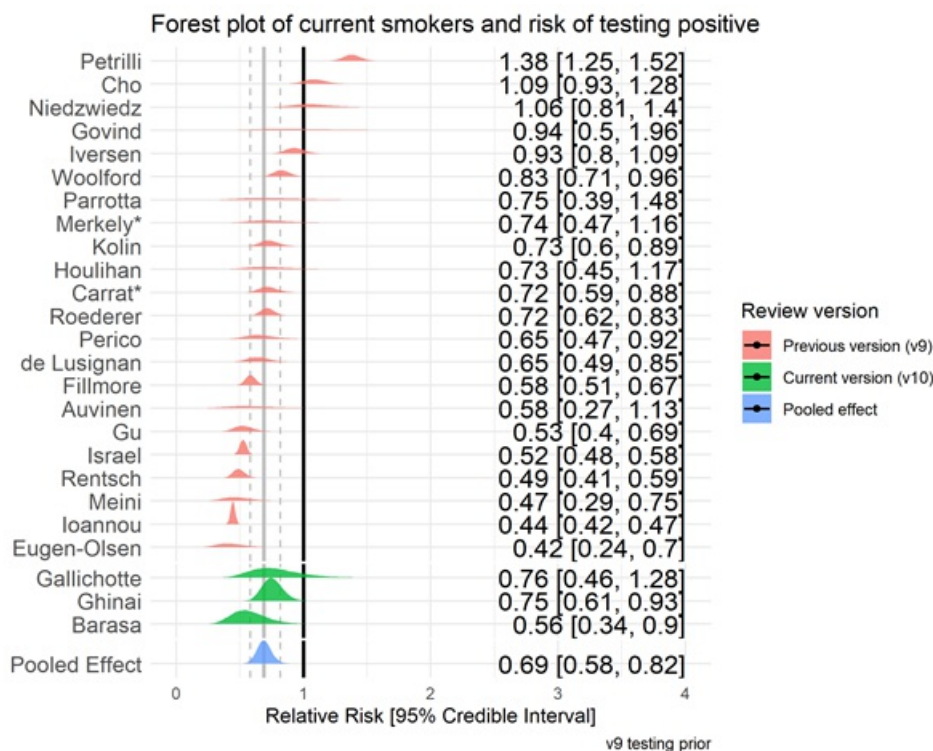


Figure 3. Forest plot for risk of testing positive for SARS-CoV-2 in current vs. never smokers. \* Indicates 'good' quality studies. The prior from the previous review version (v9) was RR = 0.69.

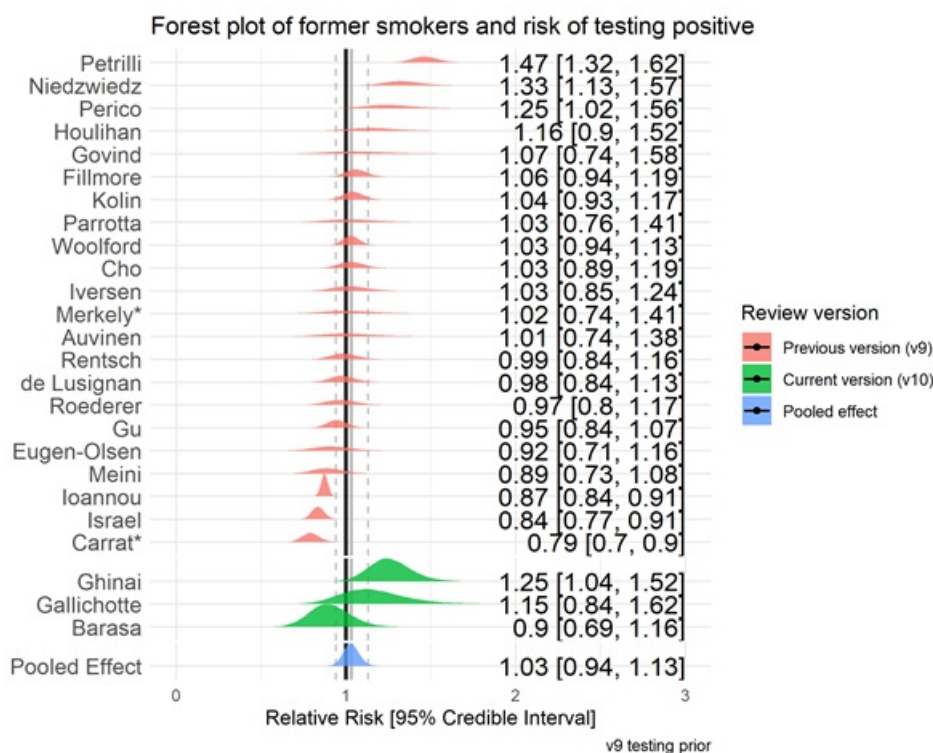


Figure 4. Forest plot for risk of testing positive for SARS-CoV-2 in former vs. never smokers. \* Indicates 'good' quality studies. The prior from the previous review version (v9) was RR = 1.02.

### Hospitalisation for COVID-19 by smoking status

Forty-one studies examined hospitalisation for COVID-19 disease, stratified by smoking status (see Table 3). Meta-analyses were performed for 13 ‘fair’ quality studies (see Figure 5 and 6). Current (RR = 1.08, CrI = 0.95-1.23,  $\tau = 0.18$ ) and former (RR = 1.18, CrI = 1.07-1.31,  $\tau = 0.14$ ) compared with never smokers were at increased risk of hospitalisation with COVID-19. However, data for current smokers were inconclusive and favoured there being no important association. The probability of current and former smokers being at increased risk of hospitalisation (RR  $\geq 1.1$ ) compared with never smokers was 31% and 89%, respectively. Results were materially unchanged in two sensitivity analyses.

Table 3. Hospitalisation with COVID-19 by smoking status.

Author	Population with outcome	Community							Hospitalised			
		N (%)	Current smoker (%)	Former smoker (%)	Current/former smoker (%)	Never smoker (%)	Never/unknown smoker (%)	Not stated (%)	N (%)	Current smoker (%)	Former smoker (%)	Current/former smoker (%)
Rentsch	554	269 (48%)	69 (25.65%)	90 (33.46%)	-	110 (40.89%)	-	-	285 (51%)	90 (31.58%)	89 (31.23%)	-
Chow (US CDC)	6637	5143 (77%)	61 (1.19%)	80 (1.56%)	-	-	-	5002 (97.26%)	1494 (22%)	27 (1.81%)	78 (5.22%)	-
Argenziano	1000	151 (15%)	14 (9.27%)	18 (11.92%)	-	119 (78.81%)	-	-	849 (84%)	35 (4.12%)	161 (18.96%)	-
Lubetzky	54	15 (27%)	-	-	4 (26.67%)	-	-	11 (73.33%)	39 (72%)	-	-	8 (20%)
Carillo-Vega	9946	3922 (39%)	408 (10.40%)	-	-	-	-	3514 (89.60%)	6024 (60%)	486 (8.07%)	-	-
Yanover	4353	4180 (96%)	484 (11.58%)	118 (2.82%)	-	3578 (85.60%)	-	-	173 (3%)	30 (17.34%)	11 (6.36%)	-
Hamer	387109	386349 (99%)	37333 (9.66%)	134542 (34.82%)	-	214474 (55.51%)	-	-	760 (0%)	93 (12.24%)	313 (41.18%)	-
Heili-Frades	4712	1973 (41%)	121 (6.13%)	222 (11.25%)	-	-	1630 (82.62%)	1630 (82.62%)	2739 (58%)	112 (4.09%)	598 (21.83%)	-
Freites	123	69 (56%)	1 (1.45%)	-	-	-	-	68 (98.55%)	54 (43%)	3 (5.56%)	-	-
Berumen	102875	18832 (18%)	-	-	1546 (8.21%)	-	17286 (91.79%)	-	12690 (12%)	-	-	120 (1%)
Gianfrancesco	600	323 (53%)	-	-	61 (18.89%)	-	-	262 (81.11%)	277 (46%)	-	-	68 (24%)
Chaudhry	40	19 (47%)	-	-	0 (0.00%)	-	-	19 (100.00%)	21 (52%)	-	-	6 (28%)
Giannouchos	89756	58485 (65%)	4679 (8.00%)	-	-	-	53806 (92.00%)	-	31271 (34%)	2721 (8.70%)	-	-
Wang, Oekelen	57	22 (38%)	-	-	6 (27.27%)	-	-	16 (72.73%)	36 (63%)	-	-	15 (41%)
Miyara	470	132 (28%)	14 (10.61%)	41 (31.06%)	-	77 (58.33%)	-	-	338 (71%)	18 (5.33%)	111 (32.84%)	-
Suleyman	463	108 (23%)	-	-	23 (21.30%)	-	-	85 (78.70%)	355 (76%)	-	-	137 (38%)
Garassino	196	48 (24%)	10 (20.83%)	27 (56.25%)	-	11 (22.92%)	-	-	152 (77%)	38 (25.00%)	84 (55.26%)	-

Siso-Almirall	260	119 (45%)	-	-	31 (26.05%)	-	-	88 (73.95%)	141 (54%)	-	-	50 (
Gu	884	511 (57%)	30 (5.87%)	126 (24.66%)	-	355 (69.47%)	-	-	373 (42%)	10 (2.68%)	138 (37.00%)	-
Killerby	531	311 (58%)	-	-	37 (11.90%)	222 (71.38%)	-	52 (16.72%)	220 (41%)	-	-	54 (
Petrilli	5279	2538 (48%)	147 (5.79%)	337 (13.28%)	-	1678 (66.12%)	-	376 (14.81%)	2741 (51%)	141 (5.14%)	565 (20.61%)	-
Nguyen	689	333 (48%)	-	-	57 (17.12%)	-	-	276 (82.88%)	356 (51%)	-	-	114
Mendy	689	473 (68%)	-	-	84 (17.76%)	-	-	389 (82.24%)	216 (31%)	-	-	86 (
Soares	10713	9561 (89%)	132 (1.38%)	-	-	-	9429 (98.62%)	-	1152 (10%)	77 (6.68%)	-	-
Zobairy	203	65 (32%)	1 (1.54%)	-	-	-	64 (98.46%)	-	138 (67%)	11 (7.97%)	-	-
Izquierdo	1006	743 (73%)	52 (7.00%)	-	-	-	691 (93.00%)	-	263 (26%)	16 (6.08%)	-	-
Rizzo	76819	60039 (78%)	3931 (6.55%)	11379 (18.95%)	-	30042 (50.04%)	-	14687 (24.46%)	16780 (21%)	1254 (7.47%)	4585 (27.32%)	-
Dashti	4140	2759 (66%)	-	-	600 (21.75%)	1541 (55.85%)	-	618 (22.40%)	1381 (33%)	-	-	577
Pan	12084	8548 (70%)	-	-	1263 (14.78%)	-	-	7285 (85.22%)	3536 (29%)	-	-	874
Vilar-Garcia	328892	291254 (88%)	64792 (22.25%)	-	-	-	-	226462 (77.75%)	37638 (11%)	9526 (25.31%)	-	-
Ibarra-Nava	416546	302693 (72%)	26773 (8.84%)	-	-	-	-	275920 (91.16%)	113853 (27%)	8875 (7.80%)	-	-
Dashti	12347	8946 (72%)	353 (3.95%)	1099 (12.28%)	-	5133 (57.38%)	-	2361 (26.39%)	3401 (27%)	210 (6.17%)	860 (25.29%)	-
Da Silva Neto	91	44 (48%)	-	-	4 (9.09%)	-	40 (90.91%)	-	47 (51%)	-	-	14 (
Israel, Schaffer	26676	13706 (51%)	944 (6.89%)	2166 (15.80%)	-	10596 (77.31%)	-	-	12970 (48%)	880 (6.78%)	1936 (14.93%)	-
Ioannou	10131	6624 (65%)	716 (10.81%)	2484 (37.50%)	-	2542 (38.38%)	-	882 (13.32%)	3507 (34%)	419 (11.95%)	1593 (45.42%)	-
Zhang, Li	1,596	576 (36%)	63 (10.94%)	190 (32.99%)	-	318 (55.21%)	-	5 (0.87%)	1020 (63%)	116 (11.37%)	429 (42.06%)	-
Parra-Bracamonte	331,298	235840 (71%)	-	-	16676 (7.07%)	-	-	219164 (92.93%)	95458 (28%)	-	-	751
Jehi	4,536	3578 (78%)	247 (6.90%)	943 (26.36%)	-	1795 (50.17%)	-	593 (16.57%)	958 (21%)	82 (8.56%)	349 (36.43%)	-
Ilic	107	69 (64%)	21 (30.43%)	-	-	-	-	48 (69.57%)	38 (35%)	11 (28.95%)	-	-
Arleo	70	36 (51%)	1 (2.78%)	10 (27.78%)	-	25 (69.44%)	-	-	34 (48%)	0 (0.00%)	10 (29.41%)	-
Kortela	604	246 (40%)	12 (4.88%)	14 (5.69%)	-	55 (22.36%)	-	165 (67.07%)	328 (54%)	14 (4.27%)	66 (20.12%)	-



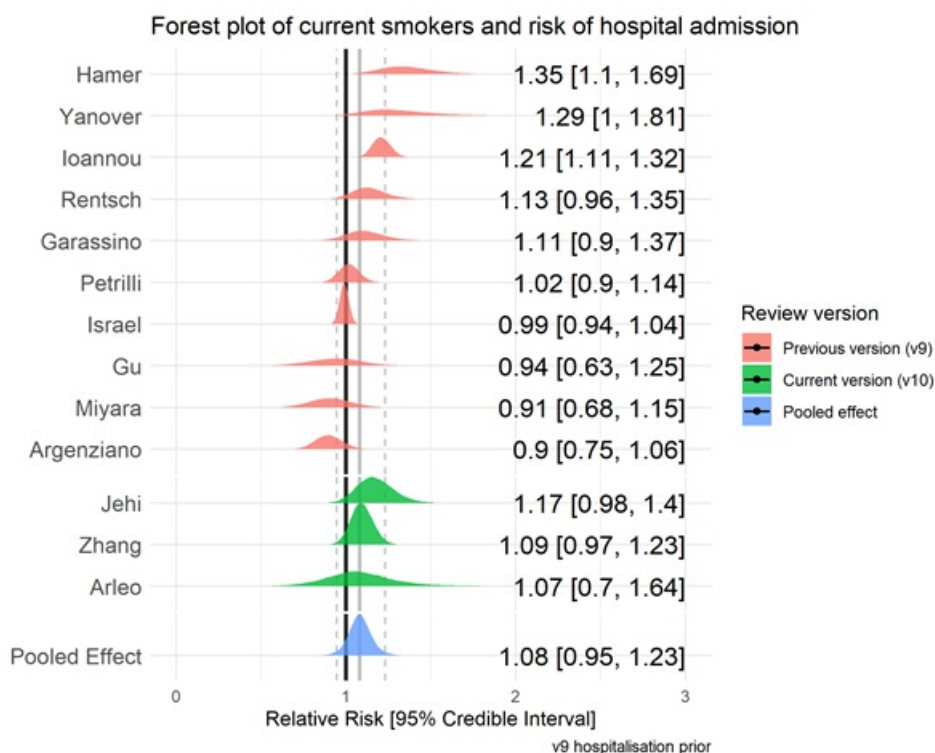


Figure 5. Forest plot for risk of hospitalisation in current vs. never smokers. The prior from the previous review version (v9) was RR = 1.06.

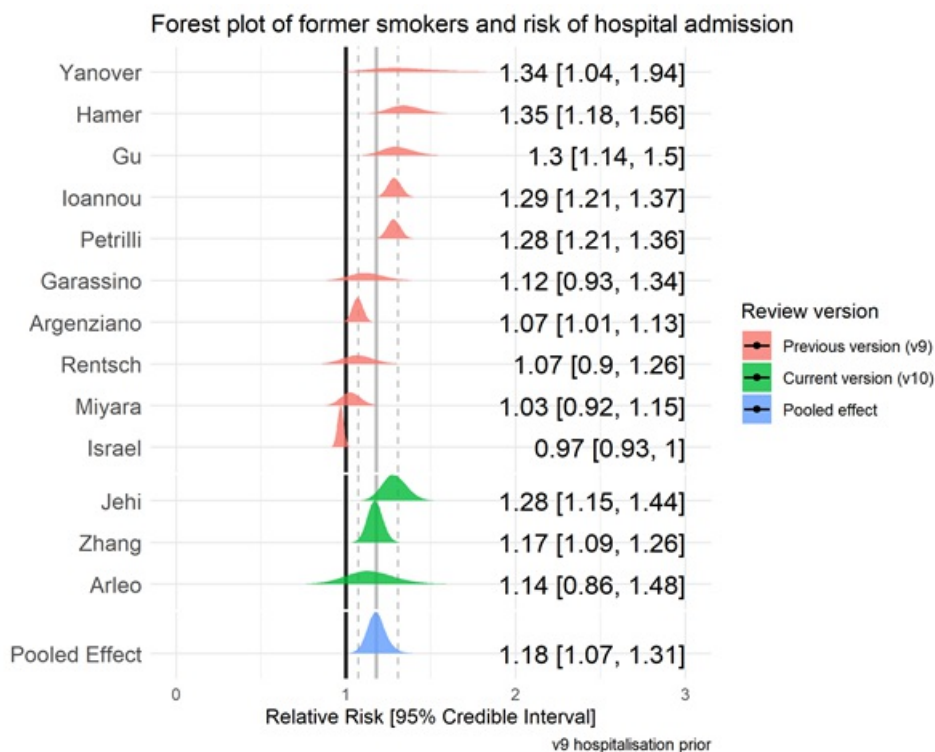


Figure 6. Forest plot for risk of hospitalisation in former vs. never smokers. The prior from the previous version (v9) was RR = 1.17.



### Disease severity by smoking status

Sixty-five studies reported disease severity in hospitalised patients stratified by smoking status (see Table 4). Severe (as opposed to non-severe) disease was broadly defined as requiring intensive treatment unit (ITU) admission, requiring oxygen as a hospital inpatient or in-hospital death. Meta-analyses were performed for eight 'fair' quality studies (see Figure 7 and 8). Current (RR = 1.26, CrI = 0.86-1.94,  $\tau$  = 0.34, 95% CI = 0.01-0.86) and former (RR = 1.52, CrI = 1.12-2.06,  $\tau$  = 0.29, 95% CI = 0.05-0.65) compared with never smokers were at increased risk of greater disease severity; data for current smokers were inconclusive but favoured there being a small but important association. The probability of current and former smokers having increased risk of greater disease severity (RR  $\geq$  1.1) compared with never smokers was 80% and 98%, respectively. Results were materially unchanged in two sensitivity analyses.

Table 4. Disease severity by smoking status.

Author	Population with severity	Non severe disease							Severe disease			
		N (%)	Current smoker (%)	Former smoker (%)	Current/former smoker (%)	Never smoker (%)	Never/unknown smoker (%)	Not stated (%)	N (%)	Current smoker (%)	Former smoker (%)	CrI
Guan, Ni	1085	913 (84%)	108 (11.83%)	12 (1.31%)	-	793 (86.86%)	-	-	172 (15%)	29 (16.86%)	9 (5.23%)	-
Zhang, Dong	9	3 (33%)	0 (0.00%)	3 (100.00%)	-	0 (0.00%)	-	-	6 (66%)	2 (33.33%)	4 (66.67%)	-
Wan	9	8 (88%)	8 (100.00%)	0 (0.00%)	-	0 (0.00%)	-	-	1 (11%)	1 (100.00%)	0 (0.00%)	-
Huang, Wang	3	3 (100%)	3 (100.00%)	0 (0.00%)	-	0 (0.00%)	-	-	0 (0%)	0 (-%)	0 (-%)	-
Rentsch	285	168 (58%)	47 (27.98%)	53 (31.55%)	-	68 (40.48%)	-	-	117 (41%)	43 (36.75%)	36 (30.77%)	-
Hu	323	151 (46%)	-	-	12 (7.95%)	-	139 (92.05%)	-	172 (53%)	-	-	26
Wang, Pan	125	100 (80%)	-	-	9 (9.00%)	-	91 (91.00%)	-	25 (20%)	-	-	7
Kim	27	21 (77%)	3 (14.29%)	-	-	-	18 (85.71%)	-	6 (22%)	2 (33.33%)	0 (0.00%)	-
Shi, Yu	474	425 (89%)	-	-	34 (8.00%)	-	391 (92.00%)	-	49 (10%)	-	-	6
Liao, Feng	148	92 (62%)	-	-	5 (5.43%)	-	-	87 (94.57%)	56 (37%)	3 (5.36%)	-	-
Shi, Ren	134	88 (65%)	-	-	8 (9.09%)	-	-	80 (90.91%)	46 (34%)	-	-	6
Hadjadj	50	15 (30%)	1 (6.67%)	2 (13.33%)	-	12 (80.00%)	-	-	35 (70%)	0 (0.00%)	7 (20.00%)	-
Zheng, Xiong	73	43 (58%)	-	-	6 (13.95%)	37 (86.05%)	-	-	30 (41%)	-	-	2
de la Rica	48	26 (54%)	-	-	6 (23.08%)	-	-	20 (76.92%)	20 (41%)	-	-	4

Yin, Yang	106	47 (44%)	-	-	6 (12.77%)	-	-	41 (87.23%)	59 (55%)	-	-	12
Allenbach	147	100 (68%)	-	-	9 (9.00%)	-	-	91 (91.00%)	47 (31%)	-	-	0
Goyal	393	263 (66%)	14 (5.32%)	-	-	-	-	249 (94.68%)	130 (33%)	6 (4.62%)	-	-
Feng	454	333 (73%)	27 (8.11%)	-	-	-	-	306 (91.89%)	121 (26%)	17 (14.05%)	-	-
Yao	108	83 (76%)	1 (1.20%)	-	-	-	-	82 (98.80%)	25 (23%)	3 (12.00%)	-	-
Sami	490	400 (81%)	53 (13.25%)	-	-	-	-	347 (86.75%)	90 (18%)	16 (17.78%)	-	-
Regina	200	163 (81%)	9 (5.52%)	-	-	-	-	154 (94.48%)	37 (18%)	0 (0.00%)	-	-
Feuth	28	21 (75%)	1 (4.76%)	7 (33.33%)	-	13 (61.90%)	-	-	7 (25%)	2 (28.57%)	1 (14.29%)	-
Mejia-Vilet	329	214 (65%)	-	-	13 (6.07%)	-	-	201 (93.93%)	115 (34%)	-	-	10
Chen, Jiang	135	54 (40%)	-	-	4 (7.41%)	-	-	50 (92.59%)	81 (60%)	-	-	9
Vaquero-Roncero	146	75 (51%)	-	-	4 (5.33%)	-	-	71 (94.67%)	71 (48%)	-	-	6
Kim, Garg	2490	1692 (67%)	112 (6.62%)	395 (23.35%)	-	-	1185 (70.04%)	-	798 (32%)	38 (4.76%)	247 (30.95%)	-
Wu	174	92 (52%)	-	-	47 (51.09%)	-	45 (48.91%)	-	82 (47%)	11 (13.41%)	-	-
Chaudhry	40	34 (85%)	-	-	5 (14.71%)	-	-	29 (85.29%)	6 (15%)	-	-	1
Garibaldi	832	532 (63%)	25 (4.70%)	107 (20.11%)	-	-	-	400 (75.19%)	300 (36%)	21 (7.00%)	81 (27.00%)	-
Kuderer	928	686 (73%)	35 (5.10%)	210 (30.61%)	-	370 (53.94%)	-	29 (4.23%)	242 (26%)	8 (3.31%)	116 (47.93%)	-
Romao	14	14 (100%)	-	-	4 (28.57%)	-	-	10 (71.43%)	0 (0%)	-	-	-
Giannouchos	89756	78050 (86%)	6322 (8.10%)	-	-	-	71728 (91.90%)	-	11706 (13%)	1089 (9.30%)	-	-
Cen	1007	720 (71%)	-	-	70 (9.72%)	-	-	650 (90.28%)	287 (28%)	-	-	18
Maraschini	132	89 (67%)	-	11 (12.36%)	-	78 (87.64%)	-	-	43 (32%)	-	3 (6.98%)	-
Siso-Almirall	260	212 (81%)	-	-	60 (28.30%)	-	-	152 (71.70%)	48 (18%)	-	-	21
Gu	884	511 (57%)	30 (5.87%)	126 (24.66%)	-	355 (69.47%)	-	-	134 (15%)	3 (2.24%)	61 (45.52%)	-
Petrilli	2729	1739 (63%)	97 (5.58%)	325 (18.69%)	-	1067 (61.36%)	-	250 (14.38%)	990 (36%)	44 (4.44%)	236 (23.84%)	-
Mendy	689	598 (86%)	-	-	133 (22.24%)	-	-	465 (77.76%)	91 (13%)	-	-	37
Pongpirul	193	161 (83%)	-	-	25 (15.53%)	106 (65.84%)	-	30 (18.63%)	32 (16%)	-	-	4
		2						4	4			

Jin, Gu	6	- (33%)	-	-	0 (0.00%)	-	-	-	(200.00%)	(66%)	-	-	2
Senkal	611	446 (73%)	48 (10.76%)	-	-	-	-	-	398 (89.24%)	165 (27%)	21 (12.73%)	-	-
Patel	129	89 (68%)	26 (29.21%)	-	-	-	58 (65.17%)	-	5 (5.62%)	40 (31%)	22 (55.00%)	-	-
Maucourant	27	10 (37%)	1 (10.00%)	2 (20.00%)	-	2 (20.00%)	-	-	5 (50.00%)	17 (62%)	2 (11.76%)	5 (29.41%)	-
Xie	619	469 (75%)	-	-	32 (6.82%)	-	-	-	437 (93.18%)	150 (24%)	-	-	19
Fox	55	30 (54%)	1 (3.33%)	4 (13.33%)	-	17 (56.67%)	-	-	8 (26.67%)	25 (45%)	0 (0.00%)	2 (8.00%)	-
Zhang, Cao	240	162 (67%)	2 (1.23%)	6 (3.70%)	-	-	-	-	154 (95.06%)	78 (32%)	4 (5.13%)	4 (5.13%)	-
Kurashima	53	10 (18%)	-	-	3 (30.00%)	-	-	-	7 (70.00%)	43 (81%)	-	-	24
Zhan	75	NA (NA%)	-	-	-	-	-	-	-	75 (100%)	-	-	9
Omrani	858	806 (93%)	-	-	121 (15.01%)	-	-	-	685 (84.99%)	52 (6%)	-	-	9
Marcos	918	555 (60%)	38 (6.85%)	-	69 (12.43%)	-	-	-	448 (80.72%)	363 (39%)	18 (4.96%)	-	71
Hoertel, Sanchez- Rico	7345	6014 (81%)	433 (7.20%)	-	-	-	-	-	5581 (92.80%)	1331 (18%)	190 (14.27%)	-	-
Qi	267	217 (81%)	22 (10.14%)	-	-	-	195 (89.86%)	-	-	50 (18%)	31 (62.00%)	-	-
Monteiro	112	84 (75%)	3 (3.57%)	14 (16.67%)	-	63 (75.00%)	-	-	4 (4.76%)	28 (25%)	4 (14.29%)	6 (21.43%)	-
Dashti	1381	619 (44%)	-	-	239 (38.61%)	292 (47.17%)	-	-	88 (14.22%)	762 (55%)	-	-	39
Morshed	103	87 (84%)	28 (32.18%)	-	-	-	59 (67.82%)	-	-	16 (15%)	4 (25.00%)	-	-
Zhou, Sun	144	108 (75%)	11 (10.19%)	-	-	-	-	-	97 (89.81%)	36 (25%)	2 (5.56%)	-	-
Hippisley- Cox	-	NA	-	-	-	-	-	-	-	1286	56 (4.35%)	427 (33.20%)	-
Zhao, Chen	641	398 (62%)	87 (21.86%)	-	-	-	-	-	311 (78.14%)	195 (30%)	52 (26.67%)	-	-
Qu	246	226 (91%)	90 (39.82%)	-	-	-	-	-	136 (60.18%)	20 (8%)	14 (70.00%)	-	-
Ren	432	314 (72%)	26 (8.28%)	-	-	288 (91.72%)	-	-	-	118 (27%)	17 (14.41%)	-	-
Yan	578	450 (77%)	31 (6.89%)	-	-	-	-	-	419 (93.11%)	128 (22%)	20 (15.62%)	-	-
Nicholson	1042	550 (52%)	37 (6.73%)	106 (19.27%)	-	211 (38.36%)	-	-	196 (35.64%)	401 (38%)	41 (10.22%)	92 (22.94%)	-
Zhu	432	285 (65%)	46 (16.14%)	-	-	-	-	-	239 (83.86%)	147 (34%)	16 (10.88%)	-	-
Kalan	193	122 (63%)	9 (7.38%)	-	-	102 (83.61%)	-	-	11 (9.02%)	71 (36%)	5 (7.04%)	-	-

Burrell	204	85 (41%)	-	-	7 (8.24%)	-	75 (88.24%)	3 (3.53%)	119 (58%)	-	-	20
Chudasama	1706	NA (NA%)	-	-	-	-	-	-	1706 (100%)	235 (13.77%)	699 (40.97%)	-
Lamure	89	NA (NA%)	-	-	-	-	-	-	25 (28%)	1 (4.00%)	5 (20.00%)	-
Zhou, He, Yang	1,087	990 (91%)	-	-	849 (85.76%)	141 (14.24%)	-	-	97 (8%)	-	-	75
Zhou, Qin	51	NA (NA%)	-	-	-	-	-	-	51 (100%)	-	-	40
Zhan, Liu	405	257 (63%)	-	-	21 (8.17%)	236 (91.83%)	-	-	148 (36%)	-	-	25
Li, Long, Zhang	954	838 (87%)	-	-	34 (4.06%)	804 (95.94%)	-	-	116 (12%)	-	-	22
Jakob	2,155	1400 (64%)	-	-	92 (6.57%)	99 (7.07%)	-	669 (47.79%)	755 (35%)	51 (6.75%)	58 (7.68%)	-
Aksu	123	34 (27%)	3 (8.82%)	-	-	-	31 (91.18%)	-	89 (72%)	11 (12.36%)	-	-
Adrish	1,173	162 (13%)	-	-	36 (22.22%)	-	126 (77.78%)	-	1011 (86%)	-	-	30
Hoertel, Sanchez, Vernet	12,210	11018 (90%)	921 (8.36%)	-	-	-	-	10097 (91.64%)	1192 (9%)	181 (15.18%)	-	-
Vila-Corcoles, Statue-Gracia	282	218 (77%)	-	-	21 (9.63%)	-	-	197 (90.37%)	64 (22%)	-	-	4

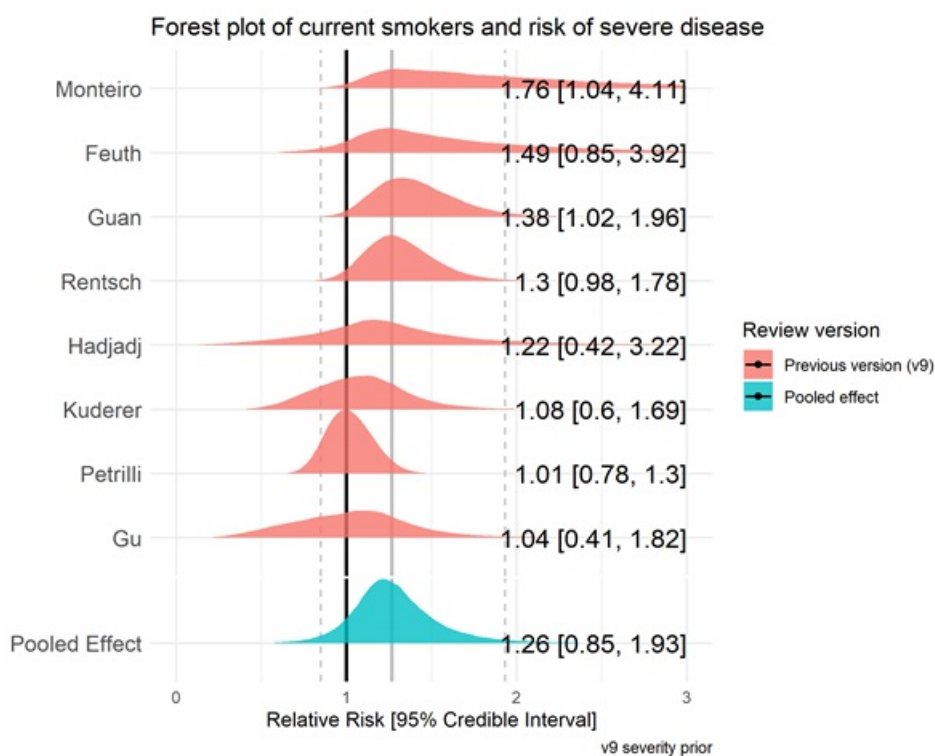


Figure 7. Forest plot for the risk of severe disease in current vs. never smokers. The prior from the

previous review version (v9) was RR = 1.26.

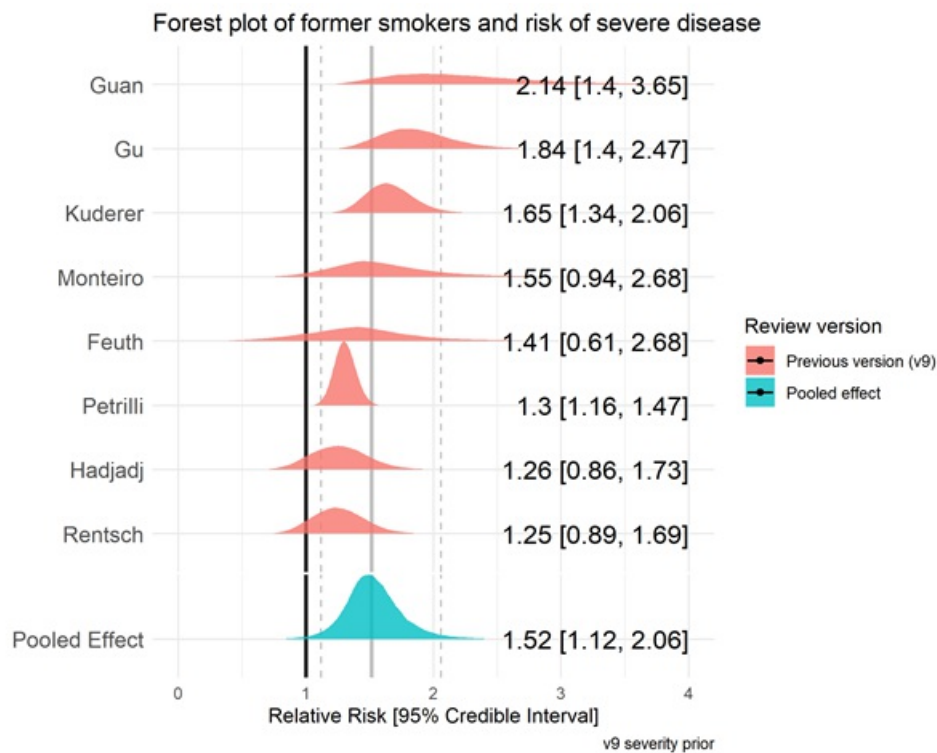


Figure 8. Forest plot for the risk of severe disease in former vs. never smokers. The prior from the previous review version (v9) was RR = 1.52.

### Mortality by smoking status

Seventy-seven studies reported mortality from COVID-19 by smoking status (see Table 5), with 16 ‘fair’ quality studies included in meta-analyses (see Figure 9 and 10). Current (RR = 1.05, 95% CrI = 0.77-1.41,  $\tau$  = 0.39) and former (RR = 1.40, 95% CrI = 1.2-1.64,  $\tau$  = 0.19) compared with never smokers were at increased risk of in-hospital mortality from COVID-19. However, data for current smokers were inconclusive and favoured there being no important association. The probability of current and former smokers being at greater risk of in-hospital mortality (RR  $\geq$  1.1) compared with never smokers was 38% and 99.8%, respectively. Results were materially unchanged in two sensitivity analyses.

Table 5. Mortality by smoking status.

Author	Population with mortality	Recovered							Died			
		N (%)	Current smoker (%)	Former smoker (%)	Current/former smoker (%)	Never smoker (%)	Never/unknown smoker (%)	Not stated (%)	N (%)	Current smoker (%)	Former smoker (%)	Curr smo
Chen	274	161 (58%)	5 (3.11%)	5 (3.11%)	-	-	-	151 (93.79%)	113 (41%)	7 (6.19%)	2 (1.77%)	-

Zhou, Yu	191	137 (71%)	6 (4.38%)	-	-	-	-	131 (95.62%)	54 (28%)	5 (9.26%)	-	-
Yang, Yu	52	20 (38%)	2 (10.00%)	-	-	-	18 (90.00%)	-	32 (61%)	-	-	-
Borobia	2226	1766 (79%)	113 (6.40%)	-	-	-	-	1653 (93.60%)	460 (20%)	44 (9.57%)	-	-
Giacomelli	233	185 (79%)	-	-	53 (28.65%)	132 (71.35%)	-	-	48 (20%)	-	-	17 (3)
Yao	108	96 (88%)	1 (1.04%)	-	-	-	-	95 (98.96%)	12 (11%)	3 (25.00%)	-	-
Carillo-Vega	9946	8983 (90%)	795 (8.85%)	-	-	-	-	8188 (91.15%)	963 (9%)	99 (10.28%)	-	-
Heng	51	39 (76%)	6 (15.38%)	-	-	-	-	33 (84.62%)	12 (23%)	1 (8.33%)	-	-
Chen, Jiang	135	NA (NA%)	-	-	-	-	-	-	31 (22%)	-	-	4 (12)
Heili-Frades	4712	4086 (86%)	210 (5.14%)	659 (16.13%)	-	-	3217 (78.73%)	-	626 (13%)	23 (3.67%)	161 (25.72%)	-
Kim, Garg	2490	2070 (83%)	128 (6.18%)	481 (23.24%)	-	-	1461 (70.58%)	-	420 (16%)	22 (5.24%)	161 (38.33%)	-
Al-Hindawi	31	15 (48%)	0 (0.00%)	10 (66.67%)	-	5 (33.33%)	-	-	16 (51%)	1 (6.25%)	12 (75.00%)	-
Louis	22	16 (72%)	-	-	7 (43.75%)	-	-	9 (56.25%)	6 (27%)	-	-	3 (50)
Soto-Mota	400	200 (50%)	-	-	23 (11.50%)	-	-	177 (88.50%)	200 (50%)	-	-	25 (1)
Garibaldi	747	634 (84%)	36 (5.68%)	129 (20.35%)	-	-	-	469 (73.97%)	113 (15%)	6 (5.31%)	36 (31.86%)	-
Docherty	13364	8199 (61%)	370 (4.51%)	1832 (22.34%)	-	4179 (50.97%)	-	1818 (22.17%)	5165 (38%)	214 (4.14%)	1350 (26.14%)	-
Kuderer	928	807 (86%)	38 (4.71%)	262 (32.47%)	-	425 (52.66%)	-	31 (3.84%)	121 (13%)	5 (4.13%)	64 (52.89%)	-
Ramlall	11116	10498 (94%)	-	-	2771 (26.40%)	7727 (73.60%)	-	-	618 (5%)	-	-	208 (
Wang, Oekelen	57	43 (75%)	-	-	14 (32.56%)	-	-	29 (67.44%)	14 (24%)	-	-	7 (50)
Martinez-Portilla	224	217 (96%)	-	-	7 (3.23%)	-	-	210 (96.77%)	7 (3%)	-	-	0 (0.0)
Cen	1007	964 (95%)	-	-	87 (9.02%)	-	-	877 (90.98%)	43 (4%)	-	-	1 (2.5)
Klang	3406	2270 (66%)	-	-	492 (21.67%)	-	-	1778 (78.33%)	1136 (33%)	-	-	301 (
Wang, Zhong	5510	4874 (88%)	247 (5.07%)	1083 (22.22%)	-	3544 (72.71%)	-	-	636 (11%)	28 (4.40%)	214 (33.65%)	-
Miyara	338	211 (62%)	13 (6.16%)	58 (27.49%)	-	141 (66.82%)	-	-	46 (13%)	1 (2.17%)	23 (50.00%)	-
Rajter	255	209 (81%)	-	-	28 (13.40%)	181 (86.60%)	-	-	53 (20%)	-	-	18 (3)
Zeng	1031	866 (84%)	-	-	69 (7.97%)	-	-	797 (92.03%)	165 (16%)	-	-	36 (2)

Chen, Yu	1859	1651 (88%)	32 (1.94%)	54 (3.27%)	-	1565 (94.79%)	-	-	208 (11%)	13 (6.25%)	12 (5.77%)	-
Garassino	190	124 (65%)	-	-	92 (74.19%)	32 (25.81%)	-	-	66 (34%)	-	61 (92.42%)	-
Gu	884	864 (97%)	40 (4.63%)	250 (28.94%)	-	219 (25.35%)	-	-	20 (2%)	0 (0.00%)	14 (70.00%)	-
Sigel	88	70 (79%)	-	-	37 (52.86%)	-	-	33 (47.14%)	18 (20%)	-	-	11 (6
Nguyen	356	308 (86%)	-	-	91 (29.55%)	-	-	217 (70.45%)	45 (12%)	-	-	23 (5
de Souza	8443	7826 (92%)	-	-	95 (1.21%)	-	7571 (96.74%)	160 (2.04%)	617 (7%)	-	-	47 (7
Mendy	532	663 (124%)	-	-	160 (24.13%)	-	-	502 (75.72%)	26 (4%)	-	-	10 (3
Shi, Resurreccion	256	210 (82%)	-	-	128 (60.95%)	-	-	82 (39.05%)	46 (17%)	-	-	26 (5
Xie	619	591 (95%)	-	-	43 (7.28%)	-	-	548 (92.72%)	28 (4%)	-	-	8 (28
Fox	54	35 (64%)	1 (2.86%)	4 (11.43%)	-	18 (51.43%)	-	12 (34.29%)	19 (35%)	0 (0.00%)	2 (10.53%)	-
Zhang, Cao	289	240 (83%)	10 (4.17%)	6 (2.50%)	-	-	-	224 (93.33%)	49 (16%)	4 (8.16%)	8 (16.33%)	-
Gupta	496	255 (51%)	-	-	15 (5.88%)	-	80 (31.37%)	160 (62.75%)	241 (48%)	-	-	21 (8
Soares	1075	696 (64%)	38 (5.46%)	-	-	-	658 (94.54%)	-	456 (42%)	39 (8.55%)	-	-
Thompson	470	301 (64%)	39 (12.96%)	79 (26.25%)	-	183 (60.80%)	-	-	169 (35%)	27 (15.98%)	49 (28.99%)	-
Bernaola	1645	1382 (84%)	35 (2.53%)	146 (10.56%)	-	1201 (86.90%)	-	-	263 (15%)	6 (2.28%)	33 (12.55%)	-
Islam	654	631 (96%)	103 (16.32%)	-	-	-	-	507 (80.35%)	23 (3%)	3 (13.04%)	-	-
Philipose	466	267 (57%)	19 (7.12%)	204 (76.40%)	-	44 (16.48%)	-	-	199 (42%)	9 (4.52%)	137 (68.84%)	-
Dashti	4140	3953 (95%)	-	-	1068 (27.02%)	2078 (52.57%)	-	804 (20.34%)	187 (4%)	-	-	109 (
Fillmore	1794	1566 (87%)	408 (26.05%)	758 (48.40%)	-	279 (17.82%)	-	98 (6.26%)	228 (12%)	44 (19.30%)	141 (61.84%)	-
Pan	3536	3302 (93%)	-	-	862 (26.11%)	-	-	2440 (73.89%)	234 (6%)	-	-	82 (3
Zhao, Chen	474	398 (83%)	87 (21.86%)	-	-	-	-	311 (78.14%)	82 (17%)	36 (43.90%)	-	-
Holman	10989	NA (NA%)	-	-	-	-	-	-	10989 (100%)	609 (5.54%)	4684 (42.62%)	-
Chand	300	143 (47%)	23 (16.08%)	-	-	-	-	120 (83.92%)	157 (52%)	44 (28.03%)	-	-
Oliveira	131	105 (80%)	-	-	16 (15.24%)	-	83 (79.05%)	6 (5.71%)	26 (19%)	-	-	7 (26
Vilar-Garcia	328892	316605 (96%)	71215 (22.49%)	-	-	-	-	245390 (77.51%)	12287 (3%)	3103 (25.25%)	-	-
Ibarrondo	416516	370038	27001					343037	46508	3817		

Ullah-Rivava	410050	(88%)	(7.30%)	-	-	-	-	(92.70%)	(11%)	(8.21%)	-	-
Rubio-Rivas	186	147 (79%)	7 (4.76%)	32 (21.77%)	-	-	108 (73.47%)	-	39 (20%)	1 (2.56%)	6 (15.38%)	-
Ren	432	289 (66%)	25 (8.65%)	-	-	-	264 (91.35%)	-	143 (33%)	18 (12.59%)	-	125 (
Ullah	212	158 (74%)	22 (13.92%)	67 (42.41%)	-	-	63 (39.87%)	-	6 (3.80%)	54 (25%)	2 (3.70%)	35 (64.81%)
Dashti	3401	2892 (85%)	190 (6.57%)	689 (23.82%)	-	-	1756 (60.72%)	-	257 (8.89%)	509 (14%)	20 (3.93%)	171 (33.60%)
Nicholson	1040	829 (79%)	70 (8.44%)	163 (19.66%)	-	-	320 (38.60%)	-	276 (33.29%)	211 (20%)	16 (7.58%)	68 (32.23%)
Kalan	193	188 (97%)	14 (7.45%)	-	-	-	162 (86.17%)	-	12 (6.38%)	5 (2%)	0 (0.00%)	-
Incerti	13658	11495 (84%)	785 (6.83%)	2450 (21.31%)	-	-	5450 (47.41%)	2810 (24.45%)	-	2163 (15%)	81 (3.74%)	642 (29.68%)
Ioannou	10131	9033 (89%)	1054 (11.67%)	3549 (39.29%)	-	-	3339 (36.96%)	-	1091 (12.08%)	1098 (10%)	81 (7.38%)	528 (48.09%)
Lamure	89	59 (66%)	4 (6.78%)	16 (27.12%)	-	-	31 (52.54%)	-	8 (13.56%)	30 (33%)	1 (3.33%)	13 (43.33%)
Yadaw	5051	4635 (91%)	162 (3.50%)	709 (15.30%)	-	-	2394 (51.65%)	-	1370 (29.56%)	416 (8%)	17 (4.09%)	105 (25.24%)
Zinellu	105	77 (73%)	24 (31.17%)	8 (10.39%)	-	-	45 (58.44%)	-	-	28 (26%)	8 (28.57%)	3 (10.71%)
Zhang, Li	399	NA (NA%)	-	-	-	-	-	-	-	399 (100%)	60 (15.04%)	186 (46.62%)
Wang, Shu	59	18 (30%)	-	-	0 (0.00%)	-	-	-	18 (100.00%)	41 (69%)	-	-
Wang, Zheutlin	2,448	1706 (69%)	57 (3.34%)	315 (18.46%)	-	-	954 (55.92%)	-	380 (22.27%)	742 (30%)	25 (3.37%)	197 (26.55%)
Torres-Macho	1,968	1643 (83%)	-	-	335 (20.39%)	-	-	-	1308 (79.61%)	325 (16%)	-	-
Raines	440	408 (92%)	-	-	222 (54.41%)	-	186 (45.59%)	-	-	32 (7%)	-	-
Parra-Bracamonte	331,298	292988 (88%)	-	-	21269 (7.26%)	-	-	-	271719 (92.74%)	38310 (11%)	-	-
Li, Long, Zhang	954	876 (91%)	-	-	48 (5.48%)	-	828 (94.52%)	-	-	78 (8%)	-	-
Bellan	407	285 (70%)	30 (10.53%)	-	-	-	-	191 (67.02%)	64 (22.46%)	122 (29%)	24 (19.67%)	-
Alharthy	352	239 (67%)	109 (45.61%)	-	-	-	-	130 (54.39%)	-	113 (32%)	65 (57.52%)	-
Adrish	1,173	783 (66%)	-	-	205 (26.18%)	-	578 (73.82%)	-	-	390 (33%)	-	-
Hoertel, Sanchez, Vernet	12,210	12210 (100%)	898 (7.35%)	-	-	-	-	-	9904 (81.11%)	1408 (11%)	204 (14.49%)	-
Sourij	238	180 (75%)	4 (2.22%)	26 (14.44%)	-	-	150 (83.33%)	-	-	58 (24%)	0 (0.00%)	12 (20.69%)
Simons	446	318 (71%)	30 (9.43%)	109 (34.28%)	-	-	179 (56.29%)	-	-	128 (28%)	12 (9.38%)	63 (49.22%)
		122	13						109	46	5	



Bisso	168	(72%)	(10.66%)	-	-	-	-	(89.34%)	(27%)	(10.87%)	-	-
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Note. Solis et al. and the OpenSAFELY Collaborative reported on mortality by smoking status in a multivariable analysis but did not present raw data for both the exposure and outcome variables.

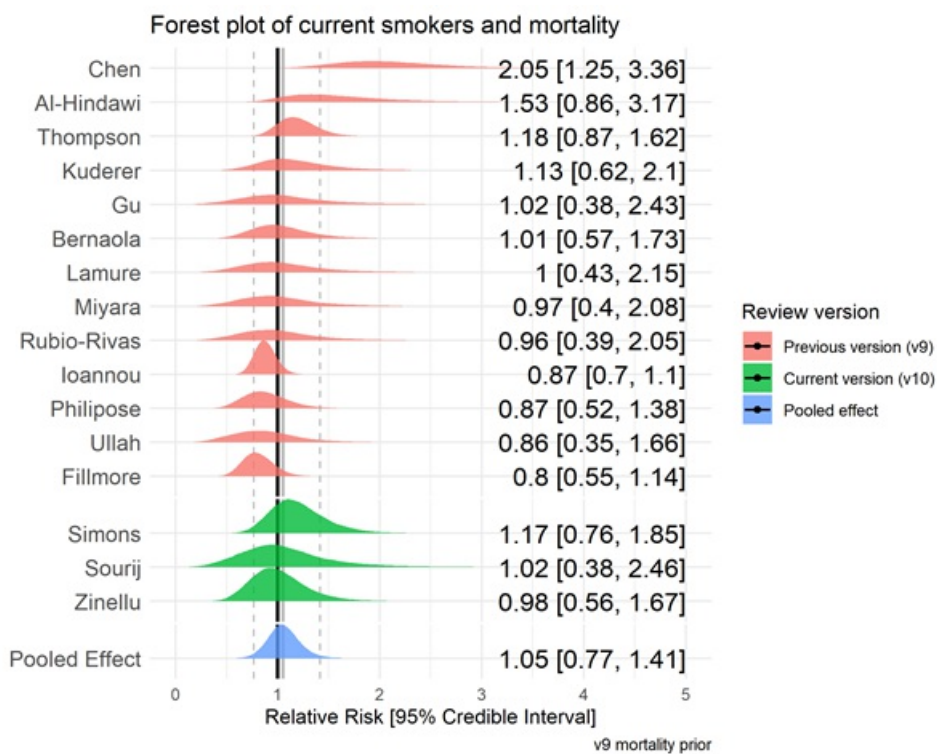


Figure 9. Forest plot for the risk of mortality in current vs. never smokers. The prior from the previous review version (v9) was RR = 1.05.

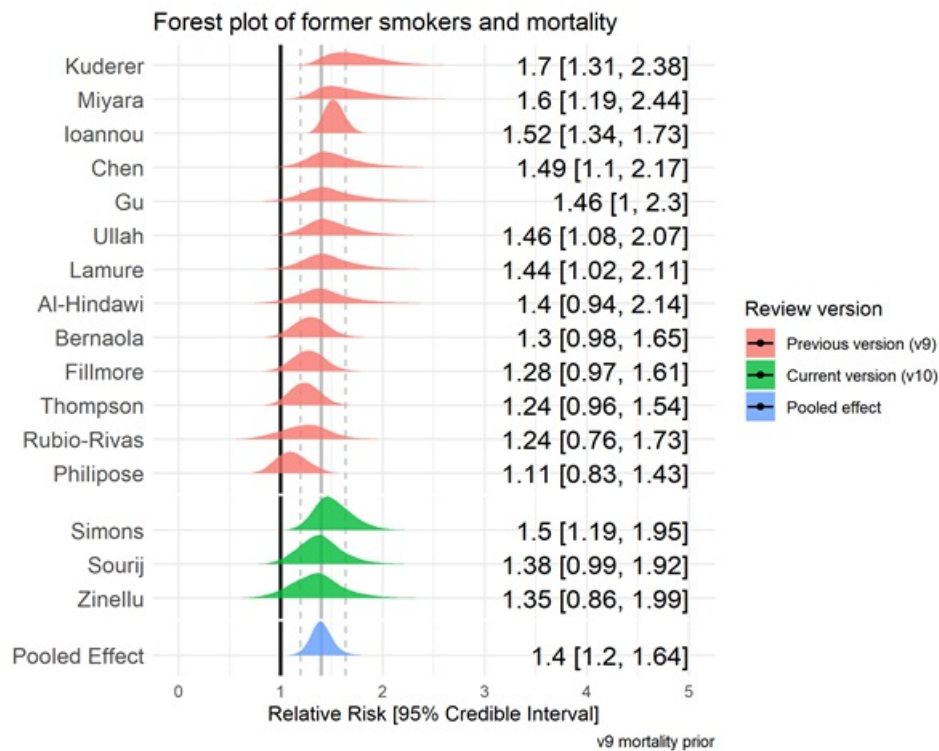


Figure 10. Forest plot for the risk of mortality in former smokers vs. never smokers. The prior from the previous version (v9) was RR = 1.39.

## Discussion

This living rapid review found uncertainty in the majority of 345 studies arising from the recording of smoking status. Notwithstanding these uncertainties, compared with overall adult national prevalence estimates, recorded current smoking rates in most studies were lower than expected. In a subset of better-quality studies ( $n = 25$ ), current but not former smokers had a reduced risk of testing positive for SARS-CoV-2 but current smokers appeared somewhat more likely to present for testing and/or receive a test. Data for current smokers on the risk of hospitalisation, disease severity and mortality were inconclusive, and favoured there being no important associations with hospitalisation and mortality and a small but important increase in the risk of severe disease. Former smokers were at increased risk of hospitalisation, disease severity and mortality compared with never smokers.

### Issues complicating interpretation

Interpretation of results from studies conducted during the first phase of the SARS-CoV-2 pandemic is complicated by several factors (see Figure 11):

#### 1) Exposure to SARS-CoV-2

1. Exposure to the SARS-CoV-2 virus is heterogeneous with different subgroups at heightened risk of infection at different stages of the pandemic, at least partly due to differential contact matrices by age, sex and socioeconomic position<sup>36</sup>, which are associated with smoking status.
2. The probability of viral exposure depends largely on local prevalence, which varies over time. This likely introduces bias in studies assessing the rate of infection by smoking status conducted in the early phase of the pandemic.

## 2) Infection with SARS-CoV-2

1. Infection following viral exposure depends on individual differences in, for example, genetic susceptibility or immunocompetence, which are poorly understood at present. For example, the household secondary attack rate for COVID-19 is estimated at 17%<sup>37</sup>.
2. Heated and humidified air may act to disrupt the ability of the virus to persist in the airway mucosa of smokers. There is some evidence that transient localised hyperthermia can inhibit replication of rhinoviruses, a non-enveloped virus that causes the common cold<sup>38</sup>. However, as SARS-CoV-2 is an enveloped virus<sup>39</sup>, it is unclear whether a similar protective effect against viral replication or invasion by heated and humidified air may occur.

## 3) Symptomatic COVID-19

1. An estimated 20% (95% CI = 17-25%) of COVID-19 cases are asymptomatic<sup>40</sup>, with some evidence suggesting younger people are more likely to be asymptomatic<sup>41</sup>. Testing is hence likely limited in some subgroups, with the potential for these groups to include an overrepresentation of current smokers.
2. Current and former smokers may be more likely to meet local criteria for community testing due to increased prevalence of symptoms consistent with SARS-CoV-2 infection, such as cough, increased sputum production or altered sense of smell or taste<sup>42</sup>. Evidence from a small number of studies indicates that current smokers may be more likely to present for testing, hence increasing the denominator in comparisons with never smokers and potentially inflating the rate of negative tests in current smokers. Infection positivity rates estimated among random samples are more informative. We identified one population study conducted in Hungary reporting on seroprevalence and smoking status<sup>43</sup>; however, the response rate was only 58.8% and the current smoking rate was 10 percentage points below national prevalence estimates, which raises some doubt about representativeness of the final sample. Similarly, a second representative population survey with results from three regions in France<sup>44</sup> reported a current smoking rate of more than 10 percentage points below national prevalence (12% vs. 25% daily smoking prevalence)<sup>45</sup>.

## 4) Testing positive for SARS-CoV-2

1. Smokers with COVID-19 may be less likely to receive a SARS-CoV-2 test or present to hospital due to lack of access to healthcare and may be more likely to die in the community from sudden complications (i.e. self-selection bias) and thus

not be recorded<sup>46</sup>.

2. Diagnostic criteria for SARS-CoV-2 infection and COVID-19 have changed during the course of the pandemic<sup>47</sup>. It was not possible to extract details on the specific RT-PCR or antibody-based techniques or platforms used across the included studies due to reporting gaps. Different platforms have varying sensitivity and specificity to detect SARS-CoV-2 infection. In addition, testing for acute infection requires swabbing of the mucosal epithelium, which may be disrupted in current smokers, potentially altering the sensitivity of assays<sup>48</sup>.

### 5) Hospitalisation with COVID-19

1. Reasons for hospitalisation vary by country and time in the pandemic. For example, early cases may have been hospitalised for isolation and quarantine reasons and not due to medical necessity. It is plausible this may have skewed early data towards less severe cases. In addition, the observed association between former smoking and greater disease severity may be explained by collider bias<sup>49</sup>, where conditioning on a collider (e.g. testing or hospitalisation) by design or analysis may introduce a spurious association between current or former smoking (a potential cause of testing or hospitalisation) and SARS-CoV-2 infection/adverse outcomes from COVID-19 (potentially exacerbated by smoking)<sup>50</sup>.
2. The majority of included studies relied on EHRs as the source of information on smoking status. Research shows large discrepancies between EHRs and actual behaviour<sup>51</sup>. Known failings of EHRs include implausible longitudinal changes, such as former smokers being recorded as never smokers at subsequent hospital visits<sup>51</sup>. Misreporting on the part of the patient (perhaps due to perceived stigma) has also been observed, with biochemical measures showing higher rates of smoking compared with self-report in hospitalised patients in the US<sup>52</sup>. It is hence possible that under-reporting of current and former smoking status in hospitals occurred across the included studies.
3. The majority of included studies were conducted in hospital settings. It is plausible that a non-trivial proportion of patients were infected with SARS-CoV-2 while being an inpatient for a different medical reason. If so, this may have biased the hospitalised populations towards older and more frail groups, who are less likely to be smokers<sup>53</sup>.
4. Individuals with severe COVID-19 symptoms may have stopped smoking immediately before admission to hospital and may therefore not have been recorded as current smokers (i.e. reverse causality).

### 6) COVID-19 disease severity and death

1. Given lack of knowledge of the disease progression and long-term outcomes of COVID-19, it is unclear whether studies conducted thus far in the pandemic have monitored patients for a sufficient time period to report complete survival outcomes or whether they are subject to early censoring. Adding to this, COVID-19 related mortality has been differentially defined across countries and epidemic phases. For example, in some UK reporting, death within 28 days of a COVID-19 diagnosis is required for attributing the cause of death to the virus. However, according to the UK Office for National Statistics, COVID-19 deaths are recorded only if this was stated on the death certificate.
2. If there is a protective effect of nicotine on COVID-19 disease outcomes, abrupt nicotine withdrawal upon

hospitalisation may lead to worse disease outcomes including death<sup>12</sup>.

3. During periods of heightened demand of limited healthcare resources, current and former smokers with extensive comorbidities may have reduced priority for intensive care admission, thus leading to higher in-hospital mortality.

COVID-19 outcomes are currently limited to in-hospital death or survival to discharge. This binary outcome does not capture potential long-term morbidity attributed to COVID-19, such as stroke, amputation or acute cardiac events, which may be moderated by smoking status.

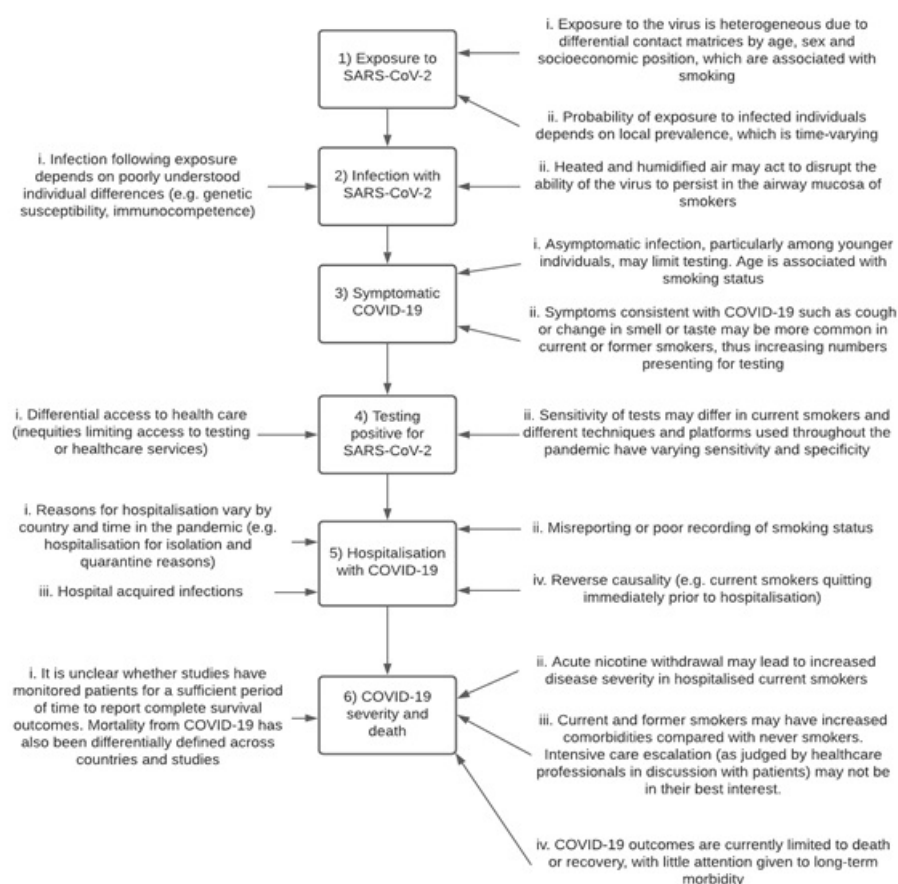


Figure 11. A schematic of some of the interpretation issues for the association of smoking status and COVID-19 infection, hospitalisation, disease severity and mortality. Numbers refer to the issues listed in the above section. Issues on the right-hand side relate explicitly to smoking status.

In addition, the emergence of new variants and strains of the SARS-CoV-2 virus may also change associations with risk factors, including smoking status.

## Limitations

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This living rapid evidence review was limited by having a single reviewer extracting data with a second independently verifying the data extracted to minimise errors, restricting the search to one electronic database and one pre-print server and by not including at least three large population surveys due to their reliance on self-reported suspected or confirmed SARS-CoV-2 infection (which means they do not meet our eligibility criteria)<sup>42,54,55</sup>. We also did not include a large, UK-based, representative seroprevalence study<sup>56</sup> in our meta-analyses as the odds of testing positive in former smokers was not reported. However, the odds of infection for current smokers (OR = 0.64, 95% CI = 0.58-0.71) was in concordance with the pooled estimate in our meta-analysis. Population surveys – particularly with linked data on confirmed infection or antibodies – will be included in future review versions to help mitigate some of the limitations of healthcare based observational studies. The comparisons of current and former smoking prevalence in the included studies with national prevalence estimates did not adjust observed prevalence for the demographic profile of those tested/admitted to hospital. Other reviews focused on this comparison have applied adjustments for sex and age, and continue to find lower than expected prevalence – notwithstanding the issues complicating interpretation described above<sup>17</sup>.

### ***Implications for research, policy and practice***

Further scientific research is needed to resolve the mixed findings summarised in our review. First, clinical trials of the posited therapeutic effect of nicotine could have important implications both for smokers and for improved understanding of how the SARS-CoV-2 virus causes disease in humans. Such trials should focus on medicinal nicotine (as smoked tobacco is a dirty delivery mechanism that could mask beneficial effects) and potentially differentiate between different modes of delivery (i.e. inhaled vs. ingested) since this can affect pharmacokinetics<sup>57</sup> and potential therapeutic effects. A second research priority would be a large, representative (randomly sampled) population survey with a validated assessment of smoking status which distinguishes between recent and long-term ex-smokers – ideally biochemically verified – and assesses seroprevalence and links to health records.

In the meantime, public-facing messages about the possible protective effect of smoking or nicotine are premature. In our view, until there is further research, the quality of the evidence does not justify the huge risk associated with a message likely to reach millions of people that a lethal activity, such as smoking, may protect against COVID-19. It continues to be appropriate to recommend smoking cessation and emphasise the role of alternative nicotine products to support smokers to stop as part of public health efforts during COVID-19. At the very least, smoking cessation reduces acute risks from cardiovascular disease and could reduce demands on the healthcare system<sup>58</sup>. GPs and other healthcare providers can play a crucial role – brief, high-quality and free online training is available at [National Centre for Smoking Cessation and Training](#).

### ***Conclusion***

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Across 345 studies, recorded current but not past smoking prevalence was generally lower than national prevalence

estimates. Current smokers were at reduced risk of testing positive for SARS-CoV-2 and former smokers were at increased risk of hospitalisation, disease severity and mortality compared with never smokers.

### ***Acknowledgements***

An original short review for the Royal College of Physicians was converted to an extended living review after a request by Martin Dockrell, Tobacco Control Lead, Public Health England. All scientific decisions were made by the authors independently of funders and external organisations. The authors would like to thank Rosemary Koper for her assistance in running the electronic searches and data extraction up until v7, and all authors who responded to requests for additional data.

### ***Declaration of conflicts of interest***

DS and OP have no conflicts of interest to declare. LS has received a research grant and honoraria for a talk and travel expenses from manufacturers of smoking cessation medications (Pfizer and Johnson & Johnson). JB has received unrestricted research funding to study smoking cessation from companies who manufacture smoking cessation medications. All authors declare no financial links with tobacco companies or e-cigarette manufacturers or their representatives.

### ***Funding statement***

DS is supported by a PhD studentship from the UK Biotechnology and Biological Sciences Research Council [BB/M009513/1]. OP receives salary support from Cancer Research UK (C1417/A22962). JB, LS, & OP are members of SPECTRUM, a UK Prevention Research Partnership Consortium (MR/S037519/1). UKPRP is an initiative funded by the UK Research and Innovation Councils, the Department of Health and Social Care (England) and the UK devolved administrations, and leading health research charities.

### ***Future review versions***

<https://www.qeios.com/read/latest-UJR2AW>

### ***Previous review versions***

**Version 1:** <https://doi.org/10.32388/UJR2AW>

**Version 2:** <https://doi.org/10.32388/UJR2AW.3>

**Version 3:** <https://doi.org/10.32388/UJR2AW.4>

**Version 4:** <https://doi.org/10.32388/UJR2AW.5>

**Version 5:** <https://doi.org/10.32388/UJR2AW.6>

**Version 6:** <https://doi.org/10.32388/UJR2AW.7>



**Version 7:** <https://doi.org/10.1111/add.15276>

**Version 8:** <https://doi.org/10.32388/UJR2AW.9>

**Version 9:** <https://doi.org/10.32388/UJR2AW.10>

### **Data availability**

All data contributing to the current and future review versions are available

here: <https://doi.org/10.6084/m9.figshare.12756020>

All code required to reproduce the current and future analyses are available here:

<https://doi.org/10.5281/zenodo.4002046>

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