

The association of smoking status with SARS-CoV-2 infection, hospitalization and mortality from COVID-19: a living rapid evidence review with Bayesian meta-analyses (version 7)

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ABSTRACT

Aims To estimate the association of smoking status with rates of (i) infection, (ii) hospitalization, (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, hospitalization, disease severity and mortality stratified by smoking status. Study quality was assessed (i.e. 'good', 'fair' and 'poor'). **Findings** Version 7 (searches up to 25 August 2020) included 233 studies with 32 'good' and 'fair' quality studies included in meta-analyses. Fifty-seven studies (24.5%) reported current, former and never smoking status. 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 [relative risk (RR) = 0.74, 95% credible interval (CrI) = 0.58–0.93, $\tau = 0.41$]. Data for former smokers were inconclusive (RR = 1.05, 95% CrI = 0.95–1.17, $\tau = 0.17$), but favoured there being no important association (21% probability of $RR \geq 1.1$). Former compared with never smokers were at somewhat increased risk of hospitalization (RR = 1.20, CrI = 1.03–1.44, $\tau = 0.17$), greater disease severity (RR = 1.52, CrI = 1.13–2.07, $\tau = 0.29$) and mortality (RR = 1.39, 95% CrI = 1.09–1.87, $\tau = 0.27$). Data for current smokers were inconclusive (RR = 1.06, CrI = 0.82–1.35, $\tau = 0.27$; RR = 1.25, CrI = 0.85–1.93, $\tau = 0.34$; RR = 1.22, 95% CrI = 0.78–1.94, $\tau = 0.49$, respectively), but favoured there being no important associations with hospitalization and mortality (35% and 70% probability of $RR \geq 1.1$, respectively) and a small but important association with disease severity (79% 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 hospitalization, increased disease severity and mortality from COVID-19. However, it is uncertain whether these associations are causal.

Keywords COVID-19, e-cigarettes, hospitalization, infection, living review, mortality, nicotine replacement therapy, SARS-CoV-2, smoking, tobacco.

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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 [1]; however, these differences are currently unexplained. SARS-CoV-2 enters epithelial cells

through the angiotensin-converting enzyme 2 (ACE-2) receptor [2]. Some evidence suggests that gene expression and subsequent receptor levels are elevated in the airway and oral epithelium of current smokers [3,4], thus putting smokers at higher risk of contracting SARS-CoV-2. Other studies, however, suggest that nicotine down-regulates the ACE-2 receptor [5]. These uncertainties

notwithstanding, both former and current smoking is known to increase the risk of respiratory viral [6,7] and bacterial [8,9] 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 [10]. 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 hospitalization or mortality [11]. It has also been hypothesized that nicotine might protect against a hyperinflammatory response to SARS-CoV-2 infection, which may lead to adverse outcomes in patients with COVID-19 disease [12].

There are several reviews that fall within the scope of smoking and COVID-19 [11,13–18]. We aimed to produce a rapid synthesis of available evidence pertaining to the rates of infection, hospitalization, 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 [19]. 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 [20]. This study was not pre-registered, but evolved from a report written for a UK medical society [21]. The most recent (and all future) version(s) of this living review is <https://www.qeios.com/read/latest-UJR2AW>. A completed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist is included in Supporting information, Fig. S1.

Eligibility criteria

Studies were included if they:

1. Were primary research studies using experimental (e.g. randomized 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) hospitalization with COVID-19, (iv) severity of COVID-19 disease in those hospitalized 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 or nicotine replacement therapy (NRT) use;
5. Were available in English; and
6. Were published in a peer-reviewed journal, as a pre-print or a public health report by reputable agents (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); (x) use of alternative nicotine products; (xi) SARS-CoV-2 testing; (xii) SARS-CoV-2 infection; (xiii) diagnosis of COVID-19; (xiv) hospitalization with COVID-19; (xv) disease severity in those hospitalized with COVID-19; and (xvi) mortality.

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 version 3.6.3 [22]. 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 against 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* [23] 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 (μ) and the between-study heterogeneity (τ), with μ 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 [24], and τ 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 (20000 burn-ins followed by 80000 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 (RR) 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 the 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 regard 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 CrIs 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 μ was specified as a normal distribution with a mean of 0 and standard deviation of 1 and τ as described above. Second, an informative prior as described above for μ was used with τ 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 visualization of smoking prevalence in the included studies, 95% bootstrap percentile confidence intervals (CIs) were calculated for each study. We performed 1000 bootstrap replications, with the 2.5th and 97.5th percentiles of the empirical distribution forming the 95% bootstrap percentile CIs [25]. It should be noted that prevalence estimates in the included studies were not adjusted for age, sex, socio-economic position or region within countries.

DATA AVAILABILITY

All data contributing to the current and future review versions are <https://doi.org/10.6084/m9.figshare.12756020>. All code required to reproduce the current and future analyses are <https://doi.org/10.5281/zenodo.4002046>.

RESULTS

In the current review (version 7) with searches up to 25 August 2020, a total of 347 new records were identified, with 233 studies included in a narrative synthesis and 32 studies included in meta-analyses (see Fig. 1).

Study characteristics

Characteristics of included studies are presented in Table 1. Studies were conducted across 33 countries. Sixty-two studies were conducted in the United States, 53 in China, 26 in the United Kingdom, 13 in Spain, 12 in Mexico, 11 in France, seven in Italy, six across multiple international sites, four in Brazil and Iran, three in Israel and Turkey, two in Bangladesh, Chile, Denmark, Finland, India, Japan and Qatar and one from 15 further countries (see

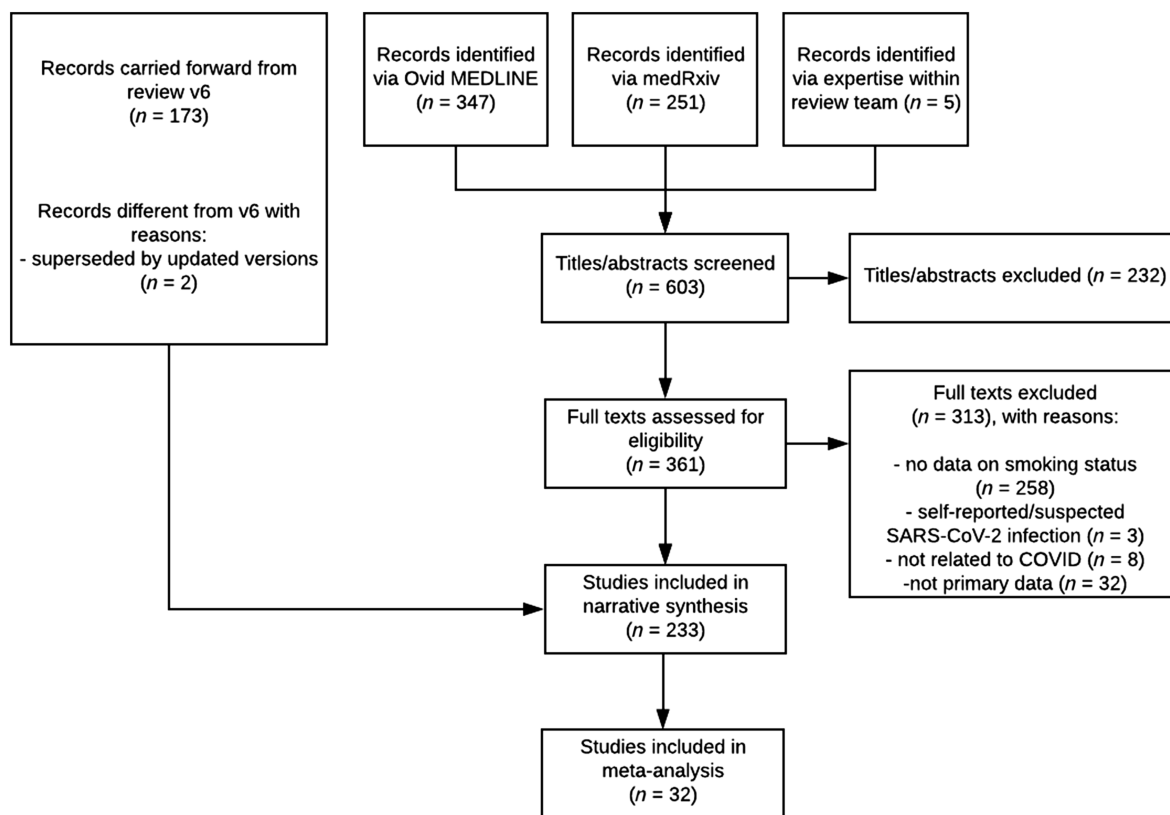


FIGURE I Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of included studies.

Supporting information, Fig. S1). The majority of studies used observational designs (see Supporting information, Table S1). One hundred and fifty-five studies were conducted in hospital settings, 62 studies included a community component in addition to hospitalized patients, 14 studies were conducted exclusively in the community, one study was conducted in a quarantine centre and one did not state the study setting. Studies had a median of 404 (interquartile range = 115–1631) participants. The majority of studies (93.5%) used reverse transcriptase–polymerase chain reaction (RT–PCR) for confirmation of SARS-CoV-2 infection, 2.6% used an antibody test to confirm prior infection and 3.9% further studies relied on a combination of RT–PCR and clinical diagnosis (see Supporting information, Table S1).

Smoking status

Categorization of smoking status was heterogeneous (see Table 1). One hundred and forty-five studies collected data on smoking status through routine electronic health records (EHRs), 59 studies used a bespoke case report form for COVID-19 and 29 studies did not state the source for information on smoking status. None of the studies verified smoking status biochemically. Notably, only 57 (24.4%) studies reported current, former and never smoking status (see Supporting information, Table S2a), with a further 17

studies reporting ever and never smoking status (see Supporting information, Table S2b). The remaining 159 studies reported current, current/former or current and former smoking status but did not explicitly state whether remaining participants were never smokers or if data were missing on smoking status (see Supporting information, Table S2c). Seventy-eight studies explicitly reported the proportion with missing data on smoking status, which ranged from 0.08 to 96.4%.

Use of alternative nicotine products

Five studies recorded the use of alternative nicotine products in current and/or former smokers but did not report COVID-19 outcomes stratified by nicotine use [26–30].

Quality appraisal

One study was performed in a random, representative population sample and was rated as ‘good’ quality. Forty-six studies were rated as ‘fair’ quality. The remaining 186 studies were rated as ‘poor’ quality (see Table 1).

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 Fig. 2a,b. Lower

TABLE 1 Characteristics of included studies.

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|------|-------------|----------------|---------|-------------|---------------|-------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [1] | Guan, Ni | 2020-02-28 | China | 1099 | Hospital | 47 (35-58) | 41.9 | 12.5 | 1.9 | - | 84.3 | - | 1.27 | Fair |
| [50] | Guan, Liang | 2020-03-26 | China | 1590 | Hospital | 49 (33-64) | 42.7 | - | - | 7.0 | 93.0 | - | 0.00 | Poor |
| [51] | Lian | 2020-03-25 | China | 788 | Hospital | NA | 38.5 | 6.9 | - | - | - | - | 93.15 | Poor |
| [52] | Jin | 2020-03-24 | China | 651 | Hospital | 46 (32-60) | 49.2 | 6.3 | - | - | - | - | 93.70 | Poor |
| [53] | Chen | 2020-03-26 | China | 548 | Hospital | 62 (44-70) | 37.6 | 4.4 | 2.6 | - | - | - | 93.07 | Poor |
| [54] | Zhou, Yu | 2020-03-11 | China | 191 | Hospital | 56 (46-67) | 38.0 | 5.8 | - | - | - | - | 94.24 | Poor |
| [55] | Mo | 2020-03-16 | China | 155 | Hospital | 54 (53-66) | 44.5 | 3.9 | - | - | - | - | 96.13 | Poor |
| [56] | Zhang, Dong | 2020-02-19 | China | 140 | Hospital | 57 [†] (25-87) | 46.3 | 1.4 | 5.0 | - | - | - | 93.57 | Poor |
| [57] | Wan | 2020-03-21 | China | 135 | Hospital | 47 (36-55) | 46.7 | 6.7 | - | - | - | - | 93.33 | Poor |
| [58] | Liu, Tao | 2020-02-28 | China | 78 | Hospital | 38 (33-57) | 50.0 | - | - | 6.4 | - | - | 93.59 | Poor |
| [59] | Huang, Wang | 2020-01-24 | China | 41 | Hospital | 49 (41-58) | 27.0 | 7.3 | - | - | - | - | 92.68 | Poor |
| [60] | Zhang, Cai | 2020-03-20 | China | 645 | Hospital | NA | 49.1 | 6.4 | - | - | - | - | 93.64 | Poor |
| [61] | Guo | 2020-03-27 | China | 187 | Hospital | 59 (45-73) | 51.3 | 9.6 | - | - | - | - | 90.37 | Poor |
| [62] | Liu, Ming | 2020-03-12 | China | 41 | Hospital | 39 (30-48) | 58.5 | 9.8 | - | - | - | - | 90.24 | Poor |
| [63] | Huang, Yang | 2020-03-05 | China | 36 | Hospital | 69 (60-78) | 30.6 | - | - | 11.1 | - | - | 88.89 | Poor |
| [64] | Xu | 2020-03-08 | China | 53 | Hospital | NA | 47.2 | 11.3 | - | - | - | - | 88.68 | Poor |
| [65] | Li | 2020-02-12 | China | 17 | Hospital | 45 (33-57) | 47.1 | 17.6 | - | - | - | - | 82.35 | Poor |

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Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|------|---------------|----------------|-------------|-------------|------------------------|-------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [31] | Rentsch | 2020-04-14 | USA | 3528 | Community and Hospital | 66 (60-70) | 4.6 | 27.2 | 30.6 | - | 36.9 | - | 5.30 | Fair |
| [66] | Hu | 2020-03-25 | China | 323 | Hospital | 61 [†] (23-91) | 48.6 | - | - | 11.8 | - | - | 88.24 | Poor |
| [67] | Wang, Pan | 2020-03-24 | China | 125 | Hospital | 41 (26-66) | 43.2 | - | - | 12.8 | - | - | 87.20 | Poor |
| [68] | Chow (US CDC) | 2020-03-31 | USA | 7162 | Community and Hospital | NA | - | 1.3 | 2.3 | - | - | - | 96.36 | Poor |
| [69] | Dong, Cao | 2020-03-20 | China | 9 | Hospital | 44 (30-46) | 66.7 | 11.1 | - | - | - | - | 88.89 | Poor |
| [70] | Kim | 2020-04-01 | South Korea | 28 | Hospital | 43 (30-56) | 46.4 | 17.9 | - | - | - | - | 82.14 | Poor |
| [71] | Shi, Yu | 2020-03-18 | China | 487 | Hospital | 46 (27-65) | 46.8 | - | - | 8.2 | - | - | 91.79 | Poor |
| [72] | Yang, Yu | 2020-02-24 | China | 52 | Hospital | 60 (47-73) | 37.0 | 3.8 | - | - | - | - | 96.15 | Poor |
| [73] | Argenziano | 2020-05-29 | USA | 1000 | Hospital | 63 (50-75) | 40.4 | 4.9 | 17.9 | - | 77.2 | - | 0.00 | Fair |
| [74] | Solis | 2020-04-25 | Mexico | 650 | Hospital | 46 (NA) | 42.1 | 9.4 | - | - | - | - | 90.62 | Poor |
| [75] | Richardson | 2020-04-22 | USA | 5700 | Hospital | 63 (52-75) | 39.7 | - | - | 9.8 | 52.8 | - | 37.42 | Poor |
| [76] | Fontanet | 2020-04-23 | France | 661 | Community and Hospital | 37 (16-47) | 62.0 | 10.4 | - | - | - | 89.6 | 0.00 | Poor |
| [77] | Zheng, Gao | 2020-04-19 | China | 66 | Hospital | 47 [†] (NA) | 25.8 | 12.1 | - | - | - | - | 87.88 | Poor |
| [78] | Liao, Feng | 2020-04-24 | China | 1848 | Hospital | 55 (48-61) | 54.7 | - | - | 0.4 | - | - | 99.57 | Poor |
| [79] | Gi-Agudo | 2020-04-24 | Spain | 7 | Hospital | 68 (34-75) | 28.6 | - | - | 42.9 | 57.1 | - | 0.00 | Poor |
| [80] | Shi, Ren | 2020-04-23 | China | 134 | Hospital | 46 (34-58) | 51.5 | - | - | 10.4 | - | - | 89.55 | Poor |

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Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|------|------------------------------|----------------|---------|--------------|------------------------|-------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [81] | Hadjadj | 2020-04-23 | France | 50 | Hospital | 55 (50-63) | 22.0 | 2.0 | 18.0 | - | 80.0 | - | 0.00 | Fair |
| [82] | Gold (US CDC) | 2020-04-20 | USA | 305 | Hospital | NA | 50.5 | 5.2 | - | - | - | - | 94.75 | Poor |
| [83] | Yu, Cai | 2020-04-27 | China | 95 | Hospital | NA | 44.2 | 8.4 | - | - | - | - | 91.58 | Poor |
| [84] | Zheng, Xiong | 2020-04-30 | China | 73 | Hospital | 43 [†] (NA) | 45.2 | - | - | 11.0 | 89.0 | - | 0.00 | Poor |
| [85] | de la Rica | 2020-05-11 | Spain | 48 | Hospital | 66 [‡] (33-88) | 33.0 | - | - | 20.8 | - | - | 79.17 | Poor |
| [86] | Yin, Yang | 2020-05-10 | China | 106 | Hospital | 73 (61-85) | 39.6 | - | - | 17.0 | - | - | 83.02 | Poor |
| [87] | Shi, Zuo | 2020-05-17 | USA | 172 | Hospital | 63 [†] (44-82) | 44.0 | - | - | 26.2 | - | - | 73.84 | Poor |
| [88] | Cho | 2020-05-11 | UK | 322 341 | Community and Hospital | NA | 49.2 | 14.2 | 21.4 | - | 64.4 | - | 0.00 | Fair |
| [89] | Allenbach | 2020-05-08 | France | 152 | Hospital | 77 (60-83) | 31.1 | - | - | 6.6 | - | - | 93.42 | Poor |
| [90] | Robilotti | 2020-05-08 | USA | 423 | Hospital | NA | 50.0 | 2.1 | 37.6 | - | 58.6 | - | 1.65 | Fair |
| [91] | The OpenSAFELY Collaborative | 2020-07-01 | UK | 17278 392 | Community and Hospital | NA | 50.1 | 17.0 | 32.9 | - | 45.9 | - | 4.17 | Fair |
| [92] | Borobia | 2020-05-06 | Spain | 2226 | Hospital | 61 (46-78) | 52.0 | 7.1 | - | - | - | - | 92.95 | Poor |
| [93] | Giacomelli | 2020-05-06 | Italy | 233 | Hospital | 61 (50-72) | 31.9 | - | - | 30.0 | 70.0 | - | 0.00 | Poor |
| [94] | Shah | 2020-05-06 | USA | 316 | Hospital | 63 (43-72) | 48.1 | 16.5 | 17.7 | - | 42.1 | - | 23.73 | Poor |
| [95] | Kolin | 2020-05-05 | UK | 502 536 | Community and Hospital | 56.5 (48-64) | 54.4 | 10.5 | 34.4 | - | 54.4 | - | 0.59 | Fair |
| [96] | Lubetzky | 2020-05-08 | USA | 54 | Hospital | 57 (29-83) | 62.0 | - | - | 22.2 | - | - | 77.78 | Poor |

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Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|--------------|----------------|-------------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [97] | Goyal | 2020-04-17 | USA | 393 | Hospital | 62.2 (49-74) | 39.3 | 5.1 | - | - | - | - | 94.91 | Poor |
| [98] | Feng | 2020-04-10 | China | 476 | Hospital | 53 (40-64) | 43.1 | 9.2 | - | - | - | - | 90.76 | Poor |
| [99] | Yao | 2020-04-24 | China | 108 | Hospital | 52 (37-58) | 60.2 | 3.7 | - | - | - | - | 96.30 | Poor |
| [100] | Sami | 2020-05-19 | Iran | 490 | Hospital | 56.6 (41-71) | 39.0 | 14.1 | - | - | - | 85.9 | 0.00 | Poor |
| [101] | Almazeedi | 2020-05-15 | Kuwait | 1096 | Hospital | 41 (25-57) | 19.0 | 4.0 | - | - | - | 96.0 | 0.00 | Poor |
| [102] | Carillo-Vega | 2020-05-14 | Mexico | 10544 | Community and Hospital | 46.5 [†] (30-62) | 42.3 | 8.9 | - | - | - | - | 91.12 | Poor |
| [103] | Yanover | 2020-05-13 | Israel | 4353 | Community and Hospital | 35 (22-54) | 44.5 | 11.8 | 3.0 | - | 85.2 | - | 0.00 | Fair |
| [104] | Hamer | 2020-05-13 | UK | 387 | Hospital | 56.2 (48-64) | 55.1 | 9.7 | 34.8 | - | 55.5 | - | 0.00 | Fair |
| [105] | Regina | 2020-05-14 | Switzerland | 200 | Hospital | 70 (55-81) | 40.0 | 4.5 | - | - | - | - | 95.50 | Poor |
| [39] | de Lusignan | 2020-05-15 | UK | 3802 | Community and Hospital | 58 (34-73) | 57.6 | 10.9 | 46.1 | - | 29.6 | - | 13.44 | Fair |
| [106] | Targher | 2020-05-13 | China | 339 | Hospital | 48.4 [†] (NA) | 52.8 | 8.3 | - | - | - | - | 91.74 | Poor |
| [107] | Valenti | 2020-05-18 | Italy | 789 | Community | 40.7 [†] (NA) | 35.0 | 25.9 | - | - | - | - | 74.14 | Poor |
| [108] | Feuth | 2020-05-18 | Finland | 28 | Hospital | 56 (47-72) | 46.0 | 10.7 | 28.6 | - | 60.7 | - | 0.00 | Fair |
| [109] | Ge | 2020-05-18 | China | 51 | Hospital | 70 (58-79) | 27.5 | 13.7 | - | - | - | - | 86.27 | Poor |
| [110] | Parrotta | 2020-05-18 | USA | 76 | Community and Hospital | 44.9 (13-71) | 61.8 | 2.6 | 26.3 | - | 68.4 | - | 2.63 | Fair |
| [111] | Shekhar | 2020-05-18 | USA | 50 | Hospital | 55.5 (20-85) | 54.0 | 48.0 | - | - | - | - | 52.00 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-----------------|----------------|--------------|-------------|-------------------|----------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [112] | Mejia-Vilet | 2020-05-16 | Mexico | 329 | Hospital | 49 (41-60) | 36.0 | - | - | 7.0 | - | - | 93.01 | Poor |
| [113] | Chen, Jiang | 2020-05-16 | China | 135 | Hospital | NA | 42.2 | - | - | 9.6 | - | - | 90.37 | Poor |
| [114] | Li, Chen | 2020-05-16 | China | 1008 | Hospital | 55 (44-65) | 43.6 | 5.7 | - | - | - | - | 94.35 | Poor |
| [27] | Rimland | 2020-05-19 | USA | 11 | Hospital | 59 (48-65) | 18.2 | 9.1 | - | - | - | - | 81.82 | Poor |
| [115] | Palaodimos | 2020-05-15 | USA | 200 | Hospital | 64 (50-73.5) | 51.0 | - | - | 32.5 | 67.5 | - | 0.00 | Poor |
| [116] | Ip | 2020-05-25 | USA | 2512 | Hospital | 64 (52-76) | 37.6 | 3.1 | 17.8 | - | 64.5 | - | 14.61 | Fair |
| [117] | Heili-Frades | 2020-05-25 | Spain | 4712 | Hospital | 62 (47-77) | 50.5 | 4.9 | 17.4 | - | - | 66.5 | 11.16 | Poor |
| [118] | Vaquero-Roncero | 2020-05-24 | Spain | 146 | Hospital | 66 [†] (59-72) | 32.2 | - | - | 6.8 | - | - | 93.15 | Poor |
| [119] | Kim, Garg | 2020-05-22 | USA | 2491 | Hospital | 62 (50-75) | 46.8 | 6.0 | 25.8 | - | - | 68.1 | 0.08 | Poor |
| [120] | Wu | 2020-05-21 | Italy | 174 | Hospital | 61.2 [†] (50-71) | 30.5 | - | - | 33.3 | - | - | 66.67 | Poor |
| [121] | Shi, Zhao | 2020-05-20 | China | 101 | Hospital | 71 (59-80) | 40.6 | - | - | 5.0 | - | - | 95.05 | Poor |
| [122] | Al-Hindawi | 2020-05-20 | UK | 31 | Hospital | 61 (NA) | 12.9 | 3.2 | 71.0 | - | 25.8 | - | 0.00 | Fair |
| [123] | Basse | 2020-05-19 | France | 141 | Hospital | 62 (52-72) | 72.0 | 17.7 | - | - | - | - | 82.27 | Poor |
| [124] | Freites | 2020-05-19 | Spain | 123 | Hospital | 59.88 [†] (44-74) | 69.9 | 3.3 | - | - | - | - | 96.75 | Poor |
| [125] | Alshami | 2020-05-19 | Saudi Arabia | 128 | Quarantine Centre | 39.6 [†] (24-55) | 53.9 | 15.6 | 2.3 | - | - | - | 82.03 | Poor |
| [126] | Berumen | 2020-05-26 | Mexico | 102 875 | Hospital | NA | 49.1 | - | - | 9.6 | - | 90.4 | 0.00 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|---------------|----------------|----------|-------------|------------------------|----------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [127] | Gianfrancesco | 2020-05-29 | Multiple | 600 | Community and Hospital | 56 (45-67) | 71.0 | - | - | 21.5 | 64.8 | - | 13.67 | Poor |
| [128] | Li, Long | 2020-05-28 | China | 145 | Not Stated | 49 [†] (13-80) | 61.0 | - | - | 5.5 | - | - | 94.48 | Poor |
| [129] | Batty | 2020-06-17 | UK | 908 | Hospital | 57.27 [†] (48-66) | 44.3 | 11.2 | - | - | - | - | 88.77 | Poor |
| [130] | Israel | 2020-06-01 | Israel | 24906 | Community and Hospital | 40 (27-59) | 48.7 | 16.8 | 12.7 | - | 70.5 | - | 0.00 | Fair |
| [131] | del Valle | 2020-05-30 | USA | 1484 | Hospital | 62 (52-72) | 40.6 | 5.5 | 23.3 | - | - | - | 71.16 | Poor |
| [132] | Chaudhry | 2020-05-29 | USA | 40 | Community and Hospital | 52 (45.5-61) | 60.0 | - | - | 15.0 | - | - | 85.00 | Poor |
| [133] | Louis | 2020-05-28 | USA | 22 | Hospital | 66.5 [†] (55-77) | 36.4 | - | - | 45.5 | - | - | 54.55 | Poor |
| [134] | Soto-Mota | 2020-06-05 | Mexico | 400 | Hospital | NA | 30.0 | - | - | 12.0 | - | - | 88.00 | Poor |
| [135] | Garibaldi | 2020-05-26 | USA | 832 | Hospital | 63 (49-75) | 47.0 | 5.5 | 22.6 | - | - | - | 71.88 | Poor |
| [136] | Docherty | 2020-05-22 | Multiple | 20133 | Hospital | 72.9 (58-82) | 40.0 | 4.2 | 21.7 | - | 44.5 | - | 29.55 | Poor |
| [137] | Boulware | 2020-06-03 | Multiple | 821 | Community | 40 (33-50) | 51.6 | 3.3 | - | - | - | - | 96.71 | Poor |
| [138] | Kuderer | 2020-05-28 | Multiple | 928 | Community and Hospital | 66 (57-76) | 50.0 | 4.6 | 35.1 | - | 50.5 | - | 9.70 | Fair |
| [139] | Romao | 2020-06-08 | Portugal | 34 | Community | 41 [†] (26-66) | 67.7 | - | - | 26.5 | - | - | 73.53 | Poor |
| [140] | Giannouchos | 2020-06-07 | Mexico | 236 | Community and Hospital | 42.5 [†] (25-59) | 49.1 | 9.1 | - | - | - | 90.9 | 0.00 | Poor |
| [141] | Ramlall | 2020-06-06 | USA | 11116 | Community and Hospital | 52 (34.7-69.5) | 55.2 | - | - | 26.8 | 73.2 | - | 0.00 | Poor |
| [142] | Wang, Oekelen | 2020-06-05 | USA | 58 | Community and Hospital | 67 (NA) | 48.0 | - | - | 36.2 | - | - | 63.79 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-------------------|----------------|---------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [143] | Perrone | 2020-06-05 | Italy | 1189 | Hospital | NA | 21.2 | - | - | 21.9 | - | - | 78.13 | Poor |
| [144] | Sharma | 2020-06-05 | India | 501 | Hospital | 35.1 [†] (18-51) | 36.0 | - | - | 4.2 | - | - | 95.81 | Poor |
| [145] | Eugen-Olsen | 2020-06-02 | Denmark | 407 | Hospital | 64 (47-77) | 57.7 | 20.6 | 36.9 | - | 39.6 | - | 2.95 | Fair |
| [146] | Martinez-Portilla | 2020-06-02 | Mexico | 224 | Community and Hospital | 29 (26-33) | 100.0 | - | - | 3.1 | - | - | 96.88 | Poor |
| [147] | Raisi-Estabragh | 2020-06-02 | UK | 4510 | Hospital | NA | 48.8 | - | - | 51.8 | - | - | 48.20 | Poor |
| [148] | Luo | 2020-06-02 | China | 625 | Hospital | 46 (NA) | 47.7 | 3.0 | - | - | - | - | 96.96 | Poor |
| [149] | Houlihan | 2020-06-09 | UK | 200 | Community | 34 (29-44) | 61.0 | 11.0 | 16.5 | - | 66.5 | - | 6.00 | Fair |
| [150] | Cen | 2020-06-08 | China | 1007 | Hospital | 61 (49-68) | 51.0 | - | - | 8.7 | - | - | 91.26 | Poor |
| [151] | Klang | 2020-05-23 | USA | 3406 | Hospital | NA | 61.8 | - | - | 23.3 | - | - | 76.72 | Poor |
| [152] | Maraschini | 2020-06-12 | Italy | 146 | Hospital | 32.5 [†] (27-38) | 100.0 | - | 9.6 | - | 80.8 | - | 9.59 | Poor |
| [153] | Wang, Zhong | 2020-06-12 | USA | 7592 | Community and Hospital | NA | 45.1 | 3.6 | 17.1 | - | 51.9 | - | 27.42 | Poor |
| [154] | McQueenie | 2020-06-12 | UK | 428 | Community and Hospital | NA | 54.9 | - | - | 44.4 | 55.0 | - | 0.59 | Poor |
| [26] | Miyara | 2020-06-12 | France | 479 | Community and Hospital | NA | 44.7 | 6.7 | 31.6 | - | 59.5 | - | 1.87 | Fair |
| [155] | Apea | 2020-06-12 | UK | 1737 | Hospital | 63.4 [†] (NA) | 30.4 | - | - | 10.0 | - | - | 90.04 | Poor |
| [156] | Woolford | 2020-06-11 | UK | 4510 | Community and Hospital | 70.5 (NA) | 51.2 | 13.0 | 38.1 | - | 48.1 | - | 0.80 | Fair |
| [157] | Hultcrantz | 2020-06-11 | USA | 127 | Community and Hospital | 68 (41-91) | 46.0 | - | - | 26.8 | 72.4 | - | 0.79 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-------------------|----------------|----------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [158] | Rajter | 2020-06-10 | USA | 280 | Hospital | 59.6 [†] (41-77) | 45.5 | 5.7 | 10.7 | - | 74.6 | - | 8.93 | Fair |
| [159] | Lan | 2020-06-09 | USA | 104 | Community | 49 [†] (34-63) | 47.1 | - | - | 24.0 | - | - | 75.96 | Poor |
| [160] | Zeng | 2020-06-16 | China | 1031 | Hospital | 60.3 [†] (46-74) | 47.8 | - | - | 10.2 | - | - | 89.82 | Poor |
| [161] | Suleyman | 2020-06-16 | USA | 463 | Hospital | 57.5 [†] (40-74) | 55.9 | - | - | 34.6 | - | - | 65.44 | Poor |
| [162] | Chen, Yu | 2020-06-16 | China | 1859 | Hospital | 59 (45-68) | 50.0 | 2.4 | 3.6 | - | 94.0 | - | 0.00 | Fair |
| [163] | Garassino | 2020-06-12 | Multiple | 200 | Community and Hospital | 68 (61.8-75) | 30.0 | 24.0 | 55.5 | - | 18.5 | - | 2.00 | Fair |
| [164] | Hernandez-Garduno | 2020-06-11 | Mexico | 32583 | Community and Hospital | 45 (34-56) | 48.7 | - | - | 11.0 | - | 88.8 | 0.15 | Poor |
| [165] | Govind | 2020-06-20 | UK | 6309 | Community and Hospital | 46.5 [†] (31-61) | 38.3 | 66.3 | 26.8 | - | 5.5 | - | 1.49 | Fair |
| [166] | Siso-Almirall | 2020-06-20 | Spain | 322 | Community and Hospital | 56.7 [†] (38-74) | 50.0 | - | - | 25.2 | - | - | 74.84 | Poor |
| [167] | Gu | 2020-06-18 | USA | 5698 | Community and Hospital | 47 [†] (26-67) | 62.0 | 7.0 | 24.7 | - | 50.8 | - | 17.53 | Fair |
| [168] | Kibler | 2020-06-16 | France | 702 | Community and Hospital | 82 [†] (75-88) | 56.0 | 3.7 | - | - | - | - | 96.30 | Poor |
| [169] | Ikitimur | 2020-06-03 | Turkey | 81 | Hospital | 55 [†] (38-72) | 44.0 | - | - | 28.4 | - | - | 71.60 | Poor |
| [170] | Sierpinski | 2020-06-03 | Poland | 1942 | Community | 50 (NA) | 60.0 | 6.3 | - | - | - | 49.7 | 44.03 | Poor |
| [171] | Zhou, He | 2020-06-10 | China | 238 | Hospital | 55.5 (35-67) | 57.0 | 2.9 | - | - | - | - | 97.06 | Poor |
| [172] | Crovetto | 2020-06-19 | Spain | 874 | Community and Hospital | 33.7 [†] (28-38) | 100.0 | 1.1 | - | - | - | 13.2 | 85.70 | Poor |
| [173] | Veras | 2020-06-09 | Brazil | 32 | Hospital | 58.9 [†] (40-77) | 47.0 | - | - | 25.0 | - | - | 75.00 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-----------------|----------------|---------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [174] | Sterlin | 2020-06-11 | France | 135 | Hospital | 61 (50-72) | 41.0 | 3.7 | 38.5 | - | 57.8 | - | 0.00 | Fair |
| [175] | Rossi | 2020-06-09 | France | 246 | Hospital | 68 [†] (53-83) | 39.0 | - | - | 25.2 | - | - | 74.80 | Poor |
| [176] | Duan | 2020-06-22 | China | 616 | Hospital | 64 (53-70) | 57.5 | 3.7 | - | - | - | - | 96.27 | Poor |
| [177] | Martin-Jimenez | 2020-06-09 | Spain | 339 | Hospital | 81.6 (72-87) | 39.5 | - | - | 30.7 | - | - | 69.32 | Poor |
| [178] | Elezkurtaj | 2020-06-17 | Germany | 26 | Hospital | 70 (61.8-78.3) | 34.6 | - | - | 19.2 | - | - | 80.77 | Poor |
| [179] | Lenka | 2020-06-22 | USA | 32 | Hospital | 62.2 [†] (51-73) | 37.5 | - | - | 50.0 | - | - | 50.00 | Poor |
| [180] | Olivares | 2020-06-16 | Chile | 21 | Hospital | 61 [†] (26-85) | 76.2 | - | - | 9.5 | - | - | 90.48 | Poor |
| [181] | Salton | 2020-06-20 | Italy | 173 | Hospital | 64.4 [†] (NA) | 34.9 | - | - | 29.5 | - | - | 70.52 | Poor |
| [182] | Wei | 2020-06-18 | USA | 147 | Hospital | 52 [†] (34-70) | 41.0 | 14.3 | - | - | - | - | 85.71 | Poor |
| [183] | Zuo, Estes | 2020-06-17 | China | 172 | Hospital | 61 [†] (25-95) | 44.0 | - | - | 26.2 | - | - | 73.84 | Poor |
| [184] | Killerby | 2020-06-17 | USA | 531 | Community and Hospital | 51.6 (38-62) | 57.1 | - | - | 17.1 | 71.4 | - | 11.49 | Poor |
| [185] | Petrilli | 2020-05-22 | USA | 5279 | Community and Hospital | 54 (38-66) | 51.5 | 5.5 | 17.1 | - | 61.9 | - | 15.55 | Fair |
| [186] | Magagnoli | 2020-06-05 | USA | 807 | Hospital | 70 (60-75) | 4.3 | - | - | 15.9 | - | - | 84.14 | Poor |
| [33] | Niedzwiedz | 2020-05-29 | UK | 392 | Community and Hospital | NA | 54.9 | 9.8 | 34.8 | - | 55.4 | - | 0.00 | Fair |
| [187] | Bello-Chavolla | 2020-05-31 | Mexico | 177 | Community and Hospital | 42.6 (26-59) | 48.9 | - | - | 9.3 | - | - | 90.72 | Poor |
| [188] | Zuo, Yalavarthi | 2020-04-24 | USA | 50 | Hospital | 61 (46-76) | 34.0 | - | - | 36.0 | - | - | 64.00 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-------------------------------|----------------|----------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [189] | Sigel | 2020-06-28 | USA | 493 | Hospital | 60 (55-67) | 24.1 | - | - | 28.6 | - | - | 71.40 | Poor |
| [190] | Nguyen | 2020-06-29 | USA | 689 | Community and Hospital | 55 (40-68) | 57.0 | - | - | 24.8 | - | - | 75.18 | Poor |
| [191] | de Melo | 2020-06-29 | Brazil | 181 | Hospital | 55.3 [‡] (34-76) | 60.8 | 9.9 | 12.2 | - | 38.1 | - | 39.78 | Poor |
| [192] | Auvinen | 2020-06-29 | Finland | 61 | Hospital | 53 (41-67) | 36.0 | 18.0 | 27.9 | - | 54.1 | - | 0.00 | Fair |
| [193] | Souza | 2020-06-28 | Brazil | 8443 | Hospital | NA | 53.0 | - | - | 1.7 | - | 96.3 | 2.01 | Poor |
| [194] | Mendy | 2020-06-27 | USA | 689 | Community and Hospital | 49.5 (35.2-67.5) | 47.0 | - | - | 24.7 | - | - | 75.33 | Poor |
| [195] | Pongpirul | 2020-06-26 | Thailand | 193 | Hospital | 37 (29-53) | 41.5 | - | - | 15.0 | 66.3 | - | 18.65 | Poor |
| [196] | Jin, Gu | 2020-06-25 | China | 6 | Hospital | 60.5 [‡] (51-75) | 33.3 | 33.3 | - | - | - | - | 66.67 | Poor |
| [197] | Favara | 2020-05-23 | UK | 70 | Community and Hospital | 41 (23-64) | 87.1 | 10.0 | - | - | - | - | 90.00 | Poor |
| [198] | Fisman | 2020-06-23 | Canada | 21922 | Community and Hospital | NA | 57.0 | - | - | 2.3 | - | - | 97.65 | Poor |
| [199] | Madariaga | 2020-06-23 | USA | 103 | Community and Hospital | 41.8 [‡] (27-55) | 48.5 | - | - | 25.2 | 74.8 | - | 0.00 | Poor |
| [200] | Senkal | 2020-07-07 | Turkey | 611 | Hospital | 57 [‡] (18-98) | 40.6 | 11.3 | - | - | - | - | 88.71 | Poor |
| [201] | Mohamud | 2020-07-02 | USA | 6 | Hospital | 65.8 [‡] (55-78) | 16.7 | - | - | 16.7 | - | - | 83.33 | Poor |
| [202] | Magleby | 2020-06-30 | USA | 678 | Hospital | 68 (50-81) | 38.9 | - | - | 28.6 | - | - | 71.39 | Poor |
| [203] | Kimmig | 2020-07-06 | USA | 111 | Hospital | 63 [‡] (48-78) | 44.1 | 7.2 | 36.0 | - | 56.8 | - | 0.00 | Fair |
| [204] | Bello-Chavolla, Antonio-Villa | 2020-07-04 | Mexico | 60121 | Community and Hospital | 45.5 [‡] (29-61) | 47.0 | - | - | 10.5 | - | - | 89.52 | Poor |
| [205] | Zacharioudakis | 2020-07-04 | USA | 314 | Hospital | 64 (54-72) | 34.7 | - | - | 22.8 | - | - | 77.22 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-------------------|----------------|-----------|-------------|------------------------|-----------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [206] | Antonio-Villa | 2020-07-04 | Mexico | 34263 | Community and Hospital | 40 [†] (29-50) | 62.9 | 9.7 | - | - | - | - | 90.32 | Poor |
| [207] | Patel | 2020-07-03 | USA | 129 | Hospital | 60.8 [†] (47-74) | 45.0 | 37.2 | - | - | - | 55.8 | 6.98 | Poor |
| [208] | Merzon | 2020-07-03 | Israel | 7807 | Community and Hospital | 46.2 [†] (NA) | 58.6 | - | - | 16.2 | - | - | 83.82 | Poor |
| [34] | Trubiano | 2020-07-02 | Australia | 2935 | Community and Hospital | 39 (29-53) | 63.5 | - | - | 8.8 | - | - | 91.18 | Poor |
| [209] | Fan | 2020-07-11 | UK | 1425 | Community and Hospital | NA | 46.7 | 12.2 | 40.1 | - | 46.9 | - | 0.84 | Fair |
| [210] | Shi, Resurreccion | 2020-07-11 | UK | 1521 | Community and Hospital | 61.5 [†] (57-66.8) | 45.9 | - | - | 54.9 | - | - | 45.10 | Poor |
| [211] | Maucourant | 2020-07-10 | Sweden | 27 | Hospital | 57 (18-78) | 22.2 | 11.1 | 25.9 | - | 40.7 | - | 22.22 | Poor |
| [212] | Elmunzer | 2020-07-09 | Multiple | 1992 | Hospital | 60 [†] (43-76) | 43.0 | 6.3 | 28.6 | - | 59.0 | - | 6.12 | Fair |
| [213] | Alizadehsani | 2020-07-09 | Iran | 319 | Hospital | 45.48 [†] (26-63) | 55.5 | - | - | 0.3 | - | - | 99.69 | Poor |
| [214] | Xie | 2020-07-07 | China | 619 | Hospital | NA | 52.0 | - | - | 8.2 | - | - | 91.76 | Poor |
| [36] | Merkely | 2020-07-17 | Hungary | 10474 | Community | 48.7 [†] (30-66) | 53.6 | 28.0 | 20.5 | - | 51.4 | - | 0.16 | good |
| [215] | Fox | 2020-07-17 | UK | 55 | Community and Hospital | 63 (23-88) | 31.0 | 1.8 | 10.9 | - | 56.4 | - | 30.91 | Poor |
| [56] | Zhang, Cao | 2020-07-14 | China | 289 | Hospital | 57 (22-88) | 46.6 | 3.5 | 6.2 | - | - | - | 90.31 | Poor |
| [216] | Martinez-Resendez | 2020-07-20 | Mexico | 8 | Hospital | 57 (48-69) | 25.0 | - | - | 12.5 | - | - | 87.50 | Poor |
| [217] | Hoertel | 2020-07-20 | France | 12612 | Hospital | 58.7 [†] (39-77) | 49.6 | - | - | 9.3 | - | - | 90.72 | Poor |
| [218] | McCrail | 2020-07-19 | USA | 209 | Hospital | 62.5 (NA) | 38.8 | - | - | 18.7 | - | - | 81.34 | Poor |
| [219] | Pandolfi | 2020-07-17 | Italy | 33 | Hospital | 62 (52-65) | 21.1 | 3.0 | 24.2 | - | 72.7 | - | 0.00 | Fair |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-----------------------|----------------|---------|-------------|------------------------|----------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [28] | Girardeau | 2020-07-17 | France | 10 | Community | 30 (29-33) | 50.0 | 40.0 | 10.0 | - | - | - | 40.00 | Poor |
| [220] | Kurashima | 2020-07-17 | Japan | 53 | Hospital | 62.9 [†] (49-76) | 35.8 | - | - | 50.9 | - | - | 49.06 | Poor |
| [221] | Zhan | 2020-07-16 | China | 75 | Hospital | 57 (25-75) | 48.0 | - | - | 12.0 | - | - | 88.00 | Poor |
| [222] | Omrani | 2020-07-16 | Qatar | 1409 | Community and Hospital | 39 (30-50) | 17.2 | - | - | 9.2 | - | - | 90.77 | Poor |
| [223] | Gupta | 2020-07-16 | USA | 496 | Hospital | 70 (60-78) | 46.0 | - | - | 7.3 | - | 31.7 | 61.09 | Poor |
| [87] | Shi, Zuo | 2020-07-15 | USA | 172 | Hospital | 61.48 [†] (25-96) | 44.0 | - | - | 26.2 | - | - | 73.84 | Poor |
| [224] | Hussein | 2020-07-15 | USA | 502 | Hospital | 60.9 [†] (45-76) | 52.0 | 9.0 | 22.1 | - | - | 68.9 | 0.00 | Poor |
| [225] | Bian | 2020-07-15 | China | 28 | Hospital | 56 [†] (42-67) | 42.9 | 7.1 | - | - | - | - | 92.86 | Poor |
| [226] | Eiros | 2020-07-14 | Spain | 139 | Community and Hospital | 52 (41-57) | 72.0 | 4.3 | 50.4 | - | - | - | 45.32 | Poor |
| [227] | Marcos | 2020-07-14 | Spain | 918 | Hospital | 72.8 [†] (58-87) | 42.2 | 6.1 | - | 15.3 | - | - | 78.65 | Poor |
| [228] | Hoertel, Sanchez-Rico | 2020-07-14 | France | 7345 | Hospital | NA | 49.3 | 8.5 | - | - | - | - | 91.52 | Poor |
| [229] | Soares | 2020-07-16 | Brazil | 10713 | Community and Hospital | NA | 55.0 | 2.0 | - | - | - | 98.0 | 0.00 | Poor |
| [230] | Zobairy | 2020-07-28 | Iran | 203 | Community and Hospital | 49.2 [†] (32-65) | 44.8 | 5.9 | - | - | - | 94.1 | 0.00 | Poor |
| [231] | Altamimi | 2020-07-27 | Qatar | 68 | Hospital | 49 [†] (40-58) | 2.0 | 16.4 | - | - | - | 83.6 | 0.00 | Poor |
| [232] | Thompson | 2020-07-27 | UK | 470 | Hospital | 71 (57-82) | 46.0 | 14.0 | 27.2 | - | 58.7 | - | 0.00 | Fair |
| [233] | Reiter | 2020-07-26 | Austria | 235 | Community | 44.2 [†] (32-55) | 70.0 | 22.6 | 22.6 | - | 54.7 | - | 0.00 | Fair |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|--------------|----------------|-------------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [234] | Motta | 2020-07-26 | USA | 374 | Hospital | 64.7 [†] (46-82) | 41.4 | - | - | 33.2 | 66.8 | - | 0.00 | Poor |
| [235] | Santos | 2020-07-25 | USA | 43 | Community and Hospital | 50 (34-73) | 63.0 | - | - | 4.7 | - | - | 95.35 | Poor |
| [236] | Schneeweiss | 2020-07-22 | USA | 24313 | Community and Hospital | 67 [†] (53-80) | 53.0 | - | - | 2.9 | - | - | 97.12 | Poor |
| [237] | Concha-Mejia | 2020-07-24 | Colombia | 72 | Community and Hospital | 46 (28-64) | 47.0 | 8.3 | 11.1 | - | - | - | 80.56 | Poor |
| [238] | Izquierdo | 2020-07-24 | Spain | 71192 | Community and Hospital | 42 [†] (18-66) | 59.0 | 10.0 | - | - | - | 90.0 | 0.00 | Poor |
| [239] | Bernaola | 2020-07-21 | Spain | 1645 | Hospital | NA | 38.5 | 2.5 | 10.9 | - | 86.6 | - | 0.00 | Fair |
| [30] | Islam | 2020-08-18 | Bangladesh | 1016 | Community and Hospital | 37 (28-49) | 35.9 | 18.2 | - | - | - | - | 77.85 | Poor |
| [240] | Qi | 2020-03-03 | China | 267 | Hospital | 48 (35-65) | 45.2 | 19.9 | - | - | - | 80.1 | 0.00 | Poor |
| [241] | Peters | 2020-08-15 | Netherlands | 1893 | Hospital | 66.8 [†] (52-81) | 39.4 | 4.9 | - | - | - | - | 95.14 | Poor |
| [242] | Ouyang | 2020-08-14 | China | 217 | Hospital | 46.5 [†] (30-62) | 53.5 | 16.6 | - | - | - | - | 83.41 | Poor |
| [47] | Ward | 2020-08-21 | UK | 99908 | Community | NA | 56.1 | 10.6 | - | - | - | 88.4 | 0.98 | Poor* |
| [243] | Valenzuela | 2020-08-14 | Chile | 29 | Hospital | 56.9 [†] (43-70) | 6.9 | 17.2 | - | - | - | 82.8 | 0.00 | Poor |
| [244] | Monteiro | 2020-08-14 | USA | 112 | Hospital | 61 (45-74) | 34.0 | 6.2 | 17.9 | - | 68.8 | - | 7.14 | Fair |
| [245] | Phillipose | 2020-08-14 | UK | 466 | Hospital | 67 (6-97) | 41.8 | 6.0 | 73.2 | - | 16.5 | - | 4.29 | Fair |
| [246] | Weerahandi | 2020-08-14 | USA | 394 | Community | 63 (55-70) | 37.0 | 5.3 | 25.9 | - | 55.8 | - | 12.94 | Fair |
| [29] | Ebinger | 2020-08-04 | USA | 6062 | Community | 41.5 [†] (29-53) | 67.8 | 1.7 | - | - | - | - | 96.88 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|---------------|----------------|------------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [247] | Altibi | 2020-08-11 | USA | 706 | Hospital | 66.7 [†] (51-81) | 43.0 | 4.0 | 37.3 | - | 58.8 | - | 0.00 | Fair |
| [248] | Izzi-Engbeaya | 2020-08-11 | UK | 889 | Hospital | 65.8 [†] (48-83) | 40.0 | - | - | 21.3 | 33.2 | - | 45.6 | Poor |
| [249] | Rizzo | 2020-08-11 | USA | 76819 | Hospital | 54 (38-67) | 55.2 | 6.7 | 20.8 | - | 50.4 | - | 22.05 | Poor |
| [250] | Dashti | 2020-08-04 | USA | 4140 | Community and Hospital | 52 (36-65) | 55.0 | - | - | 28.4 | 51.6 | - | 19.95 | Poor |
| [251] | Morshed | 2020-08-02 | Bangladesh | 103 | Community | 37 (31-53) | 28.2 | 31.1 | - | - | - | 68.9 | 0.00 | Poor |
| [252] | Jun | 2020-08-01 | USA | 3086 | Hospital | 66 (56-77) | 40.9 | 3.7 | 21.3 | - | 52.8 | - | 22.23 | Poor |
| [253] | Higuchi | 2020-07-30 | Japan | 57 | Hospital | 52 (35-70) | 43.9 | 12.3 | 29.8 | - | 57.9 | - | 0.00 | Fair |
| [254] | Zhou, Sun | 2020-07-29 | China | 144 | Hospital | 47 (38-56) | 46.5 | 9.0 | - | - | - | 91.0 | 0.00 | Poor |
| [255] | Salerno | 2020-08-22 | USA | 15920 | Hospital | 49 (30-65) | 57.0 | - | - | 36.8 | 55.9 | - | 7.29 | Poor |
| [256] | Kumar | 2020-07-29 | India | 91 | Hospital | 47 [†] (41-52) | 21.0 | 44.0 | - | - | - | - | 56.04 | Poor |
| [257] | Hao | 2020-06-01 | China | 788 | Hospital | 46 (35-56) | 48.4 | 6.9 | - | - | - | - | 93.15 | Poor |
| [258] | Iversen | 2020-08-03 | Denmark | 28792 | Community and Hospital | 44.4 [†] (31-57) | 78.9 | 16.0 | 6.5 | - | 76.8 | - | 0.67 | Fair |
| [259] | Hippisley-Cox | 2020-07-13 | UK | 8275 949 | Community and Hospital | 48.5 [†] (30-66) | 50.3 | 17.2 | 21.4 | - | 57.3 | - | 4.04 | Fair |
| [260] | Fillmore | 2020-08-24 | USA | 22914 | Community and Hospital | NA | - | 37.5 | 40.7 | - | 15.5 | - | 6.38 | Fair |
| [261] | Rashid | 2020-08-22 | UK | 517 | Hospital | 72.8 [†] (59-86) | 31.9 | 9.9 | 29.0 | - | 29.4 | - | 31.72 | Poor |
| [262] | Pan | 2020-08-22 | USA | 12084 | Community and Hospital | 45.5 [†] (27-63) | 54.3 | - | - | 17.5 | - | - | 82.49 | Poor |

(Continues)

Table 1. (Continued)

| Ref. | Lead author | Date published | Country | Sample size | Study setting | Median (IQR) | Female % | Current smoker % | Former smokers % | Current/former smokers % | Never smokers % | Never/unknown smokers % | Missing % | Study quality |
|-------|-------------|----------------|---------|-------------|------------------------|---------------------------|----------|------------------|------------------|--------------------------|-----------------|-------------------------|-----------|---------------|
| [263] | Alkurt | 2020-08-20 | Turkey | 932 | Community and Hospital | 34.8 [†] (25-44) | 64.4 | 24.5 | - | - | - | - | 75.54 | Poor |
| [264] | Zhao, Chen | 2020-07-30 | USA | 641 | Hospital | 60 (NA) | 40.1 | 21.7 | - | - | - | - | 78.32 | Poor |
| [265] | Holman | 2020-08-13 | UK | 10989 | Community and Hospital | NA | 38.8 | 5.5 | 42.6 | - | 49.0 | - | 2.82 | Fair |
| [266] | Qu | 2020-07-29 | China | 246 | Hospital | 53.6 [†] (38-68) | 53.3 | 42.3 | - | - | - | - | 57.72 | Poor |
| [267] | Chand | 2020-08-19 | USA | 300 | Hospital | 58.2 [†] (45-70) | 39.3 | 22.3 | - | - | - | - | 77.67 | Poor |

NA Age not provided for total sample. - Not reported for total sample. [†]Denotes mean ± standard deviation. 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.

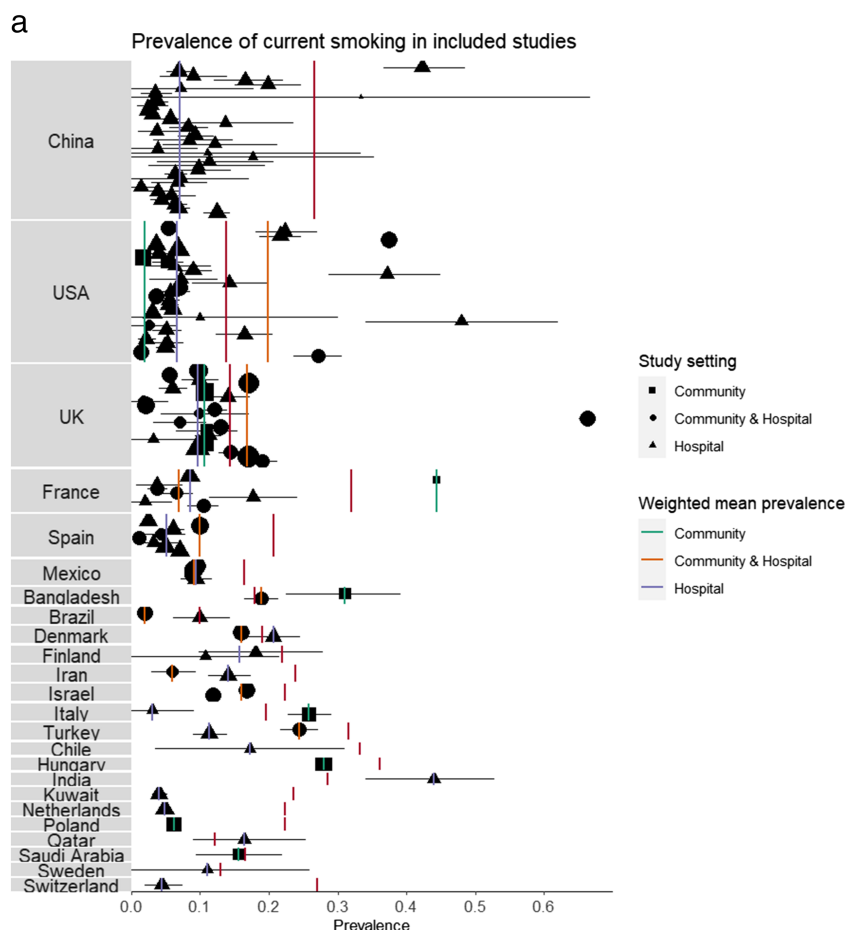


FIGURE 2 (a) Weighted mean prevalence of current smoking in included studies with 95% bootstrap confidence intervals (CIs) compared with national current smoking prevalence (solid red lines), split by country. Shape corresponds to study setting (community, community and hospital, hospital) and shape size corresponds to relative study sample size. (b) Weighted mean prevalence of former smoking in included studies (where this was reported) with 95% bootstrap CIs compared with national former smoking prevalence (solid red lines), split by country. Shape corresponds to study setting (community, community and hospital, hospital) and shape size corresponds to relative study sample size. [Colour figure can be viewed at wileyonlinelibrary.com]

than expected current smoking prevalence was generally observed. Former smoking prevalence was more similar to expected prevalence when reported. National smoking prevalence estimates used for comparison are presented in Supporting information, Table S3.

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 years [31], current smokers were more likely to receive a test: 42.3% (1603 of 3789) of the sample were current smokers compared with 23.8% of all veterans aged 50+ years using any tobacco product between 2010 and 2015 [32]. In the UK Biobank cohort [33], former (RR = 1.29, 95% CI = 1.14–1.45, $P < 0.001$) and current (RR = 1.44, 95% CI = 1.20–1.71, $P < 0.001$) compared

with never smokers were more likely to receive a test in a multivariable analysis. In an Australian rapid assessment screening clinic for COVID-19 [34], 9.4% (397 of 4226) of the self-referred sample (subsequently assessed by a health-care professional to decide on testing) were current smokers. 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

Forty-five 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 one 'good' and 16 'fair' quality studies (see Figs 3 and 4). Current smokers were at reduced risk of testing positive for SARS-CoV-2 compared with never smokers (RR = 0.74, 95% CrI = 0.58–0.93, $\tau = 0.41$, 95% CI = 0.24–0.64). The

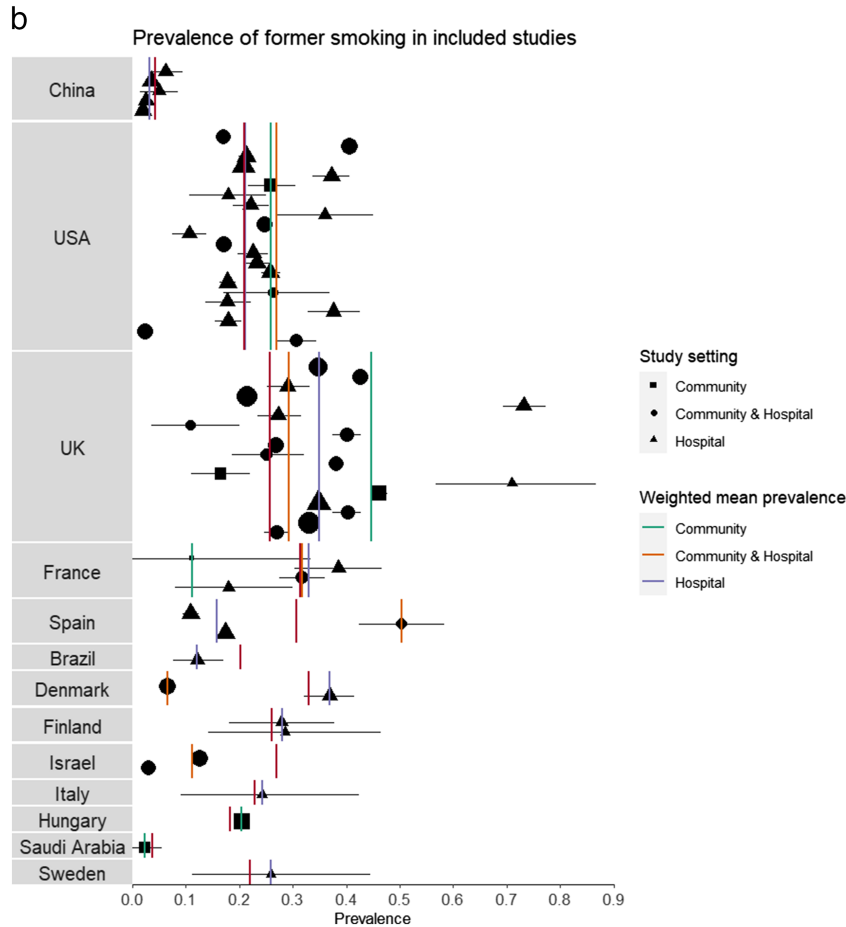


FIGURE 2 Continued.

probability of current smokers being at reduced risk of infection compared with never smokers ($RR \leq 0.9$) was 95%. Former compared with never smokers were at increased risk of testing positive, but data were inconclusive ($RR = 1.05$, 95% CrI = 0.95–1.17, $\tau = 0.17$, 95% CI = 0.10–0.26) 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 21%. Results were materially unchanged in the two sensitivity analyses (see Supporting information, Fig. S2).

Hospitalization for COVID-19 by smoking status

Twenty-nine studies examined hospitalization for COVID-19 disease stratified by smoking status (see Table 3). Meta-analyses were performed for eight ‘fair’ quality studies (see Figs 5 and 6). Current ($RR = 1.06$, CrI = 0.82–1.35, $\tau = 0.27$, 95% CI = 0.08–0.55) and former ($RR = 1.20$, CrI = 1.03–1.44, $\tau = 0.17$, 95% CI = 0.06–0.37) compared with never smokers were at increased risk of hospitalization with COVID-19, but 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 hospitalization compared with never smokers was 35 and 89%, respectively. Results were materially unchanged in two sensitivity analyses (see Supporting information, Fig. S3).

Disease severity by smoking status

Sixty studies reported disease severity in hospitalized 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 Figs 7 and 8). Current ($RR = 1.25$, CrI = 0.85–1.93, $\tau = 0.34$, 95% CI = 0.01–0.86) and former ($RR = 1.52$, CrI = 1.13–2.07, $\tau = 0.29$, 95% CI = 0.47–0.66) 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 compared with never smokers was 79 and 98%, respectively. Results were materially unchanged in two sensitivity analyses (see Supporting information, Fig. S4).

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 (%) | Never smoker (%) | Not stated (%) |
| Rentsch | 3528 | 2974 (84.30%) | 1444 (48.55%) | 704 (23.67%) | - | 826 (27.77%) | - | 554 (15.70%) | 159 (28.70%) | 179 (32.31%) | - | 216 (38.99%) | - |
| Fontanet | 661 | 490 (74.13%) | 64 (13.06%) | - | - | 426 (86.94%) | - | 171 (25.87%) | 5 (2.92%) | - | - | 166 (97.08%) | - |
| Cho | 1331 | 793 (59.58%) | 142 (17.91%) | 214 (26.99%) | - | 437 (55.11%) | - | 538 (40.42%) | 111 (20.63%) | 145 (26.95%) | - | 282 (52.42%) | - |
| Shah | 243 | 212 (87.24%) | 52 (24.53%) | 47 (22.17%) | - | 113 (53.30%) | - | 29 (11.93%) | 0 (0.00%) | 9 (31.03%) | - | 20 (68.97%) | - |
| 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%) | - | 303 (45.29%) | 9 (1.35%) |
| de Lusignan | 3291 | 2740 (83.26%) | 366 (13.36%) | 1450 (52.92%) | - | 924 (33.72%) | - | 551 (16.74%) | 47 (8.53%) | 303 (54.99%) | - | 201 (36.48%) | - |
| Valenti | 789 | 689 (87.33%) | 197 (28.59%) | - | - | - | 492 (71.41%) | 40 (5.07%) | 7 (17.50%) | - | - | - | 33 (82.50%) |
| 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%) | - | 25 (67.57%) | 1 (2.70%) |
| Berumen | 102875 | 71353 (69.36%) | - | - | 7173 (10.05%) | 64180 (89.95%) | - | 31522 (30.64%) | - | - | 2748 (8.72%) | 28774 (91.28%) | - |
| Israel | 24906 | 20755 (83.33%) | 3783 (18.23%) | 2671 (12.87%) | - | 14301 (68.90%) | - | 41151 (165.23%) | 406 (0.99%) | 483 (1.17%) | - | 3262 (7.93%) | - |
| del Valle | 1108 | 143 (12.91%) | 27 (18.88%) | 53 (37.06%) | - | - | 63 (44.06%) | 965 (87.09%) | 55 (5.70%) | 293 (30.36%) | - | - | 617 (63.94%) |
| Romao | 34 | 20 (58.82%) | - | - | 5 (25.00%) | - | 15 (75.00%) | 14 (41.18%) | - | - | 4 (28.57%) | - | 10 (71.43%) |
| Ramlall | 11116 | 4723 (42.49%) | - | - | - | - | - | 6393 (57.51%) | - | - | 1643.001 (25.70%) | 4749.999 (74.30%) | - |
| Sharma | 501 | 267 (53.29%) | - | - | 1 (0.37%) | - | 266 (99.63%) | 234 (46.71%) | - | - | 20 (8.55%) | - | 214 (91.45%) |
| Eugen-Olsen | 407 | 290 (71.25%) | 76 (26.21%) | 104 (35.86%) | - | 102 (35.17%) | - | 117 (28.75%) | 8 (6.84%) | 46 (39.32%) | - | 59 (50.43%) | - |

(Continues)

Table 2. (Continued)

| 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 (%) | Never smoker (%) | Not stated (%) |
| Raisi-Estabragh | 4510 | 3184 (70.60%) | - | - | 1653 (51.92%) | - | 1531 (48.08%) | 1326 (29.40%) | - | - | 683 (51.51%) | - | 643 (48.49%) |
| Houlihan | 177 | 97 (54.80%) | 14 (14.43%) | 14 (14.43%) | - | 69 (71.13%) | 80 (45.20%) | 7 (8.75%) | 19 (23.75%) | 19 (23.75%) | 54 (67.50%) | - | |
| McQueenie | 428199 | 424355 (99.10%) | - | - | 189299 (44.61%) | 235056 (55.39%) | 1311 (0.31%) | - | - | 669 (51.03%) | 642 (48.97%) | - | |
| Woolford | 4474 | 3161 (70.65%) | 441 (13.95%) | 1194 (37.77%) | - | 1526 (48.28%) | 1313 (29.35%) | 145 (11.04%) | 525 (39.98%) | 525 (39.98%) | 643 (48.97%) | - | |
| Lan | 104 | 83 (79.81%) | - | - | 24 (28.92%) | - | 21 (71.08%) | 21 (20.19%) | - | 1 (4.76%) | - | 20 (95.24%) | |
| Hernandez-Garduno | 32583 | 20279 (62.24%) | - | - | 2399 (11.83%) | 17861 (88.08%) | 12304 (37.76%) | - | - | 1191 (9.68%) | 11083 (90.08%) | - | |
| Govind | 6215 | 6207 (99.87%) | 4104 (66.12%) | 1669 (26.89%) | - | 342 (5.51%) | 102 (1.64%) | 78 (76.47%) | 20 (19.61%) | - | 2 (1.96%) | - | |
| Gu | 4699 | 3815 (81.19%) | 360 (9.44%) | 1142 (29.93%) | - | 2313 (60.63%) | 884 (18.81%) | 40 (4.52%) | 264 (29.86%) | - | 580 (65.61%) | - | |
| Kibler | 702 | 680 (96.87%) | 25 (3.68%) | - | - | - | 22 (3.13%) | 1 (4.55%) | - | - | - | 21 (95.45%) | |
| Petrilli | 10620 | 5341 (50.29%) | 3454 (64.67%) | 816 (15.28%) | - | 541 (10.13%) | 5279 (49.71%) | 3268 (61.91%) | 902 (17.09%) | - | 288 (5.46%) | 821 (15.55%) | |
| Bello-Chavolla | 150200 | 98567 (65.62%) | - | - | 9624 (9.76%) | - | 51633 (34.38%) | - | - | 4366 (8.46%) | - | 47267 (91.54%) | |
| Auvinen | 61 | 33 (54.10%) | 10 (30.30%) | 8 (24.24%) | - | 15 (45.45%) | 28 (45.90%) | 1 (3.57%) | 9 (32.14%) | - | 18 (64.29%) | - | |
| Favara | 70 | 55 (78.57%) | 5 (9.09%) | - | - | - | 15 (50.91%) | 2 (13.33%) | - | - | - | 13 (86.67%) | |
| Antonio-Villa | 34263 | 23338 (68.11%) | 2293 (9.83%) | - | - | - | 21045 (31.89%) | 1023 (9.36%) | - | - | - | 9902 (90.64%) | |
| Merzouk | 7807 | 7025 (89.98%) | - | - | 1136 (16.17%) | - | 5889 (83.83%) | 782 (10.02%) | - | 127 (16.24%) | - | 655 (83.76%) | |

(Continues)

Table 2. (Continued)

| 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 (%) | Never smoker (%) | Not stated (%) | | | | | | | | |
| Trubiano | 2935 | 2827 (96.66%) | - | - | 256 (9.06%) | - | 2586 (91.48%) | 108 (3.68%) | - | - | 3 (2.78%) | - | 105 (97.22%) | | | | | | | | |
| Shi, Resurreccion | 1521 | 1265 (83.17%) | - | - | 681 (53.83%) | - | 584 (46.17%) | 256 (16.83%) | - | - | 154 (60.16%) | - | 102 (39.84%) | | | | | | | | |
| Riley | 120620 | 120461 (99.87%) | 2594 (2.15%) | - | - | 19914 (16.53%) | 97953 (81.32%) | 159 (0.13%) | 3 (1.89%) | - | - | 17 (10.69%) | 139 (87.42%) | | | | | | | | |
| Alizadehsani | 319 | 196 (61.44%) | - | - | - | 196 (100.00%) | 123 (38.56%) | 1 (0.81%) | - | - | - | - | 122 (99.19%) | | | | | | | | |
| Merkely | 10474 | 10336 (98.68%) | 2904 (28.10%) | 2107 (20.39%) | - | 5310 (51.37%) | 15 (0.15%) | 16 (22.86%) | 15 (21.43%) | - | - | 38 (54.29%) | 1 (1.43%) | | | | | | | | |
| McGrail | 209 | 118 (56.46%) | - | - | 31 (26.27%) | - | 87 (73.73%) | 91 (43.54%) | - | 8 (8.79%) | - | - | 83 (91.21%) | | | | | | | | |
| Izquierdo | 71192 | NA | - | - | - | - | - | 1006 (1.41%) | - | - | - | - | 895 (88.97%) | | | | | | | | |
| Ward | 99908 | 94416 (94.50%) | 10202 (10.81%) | - | - | 84214 (89.19%) | 5492 (5.50%) | 433 (7.88%) | - | - | - | - | 5059 (92.12%) | | | | | | | | |
| Ebinger | 6062 | 5850 (96.50%) | 99 (1.69%) | - | - | 5668 (96.89%) | 212 (3.50%) | 3 (1.42%) | - | - | - | - | 205 (96.70%) | | | | | | | | |
| Salerno | 15920 | 14753 (92.67%) | - | - | 5517 (37.40%) | 8278 (56.11%) | 958 (6.49%) | 1167 (7.33%) | - | 339 (29.05%) | 626 (53.64%) | 202 (17.31%) | | | | | | | | | |
| Iversen | 28792 | 27629 (95.96%) | 4430 (16.03%) | 1799 (6.51%) | - | 21217 (76.79%) | 246 (0.89%) | 1163 (4.04%) | 78 (6.71%) | - | 898 (77.21%) | 10 (0.86%) | | | | | | | | | |
| Hippisley-Cox | 8275949 | NA | - | - | - | - | - | 19486 (0.24%) | 5715 (29.33%) | - | 12036 (61.77%) | 381 (1.96%) | | | | | | | | | |
| Fillmore | 22914 | 21120 (92.17%) | 8137 (38.53%) | 8416 (39.85%) | - | 3227 (15.28%) | 1340 (6.34%) | 1794 (7.83%) | 899 (50.11%) | - | 322 (17.95%) | 121 (6.74%) | | | | | | | | | |
| Alkurt | 119 | NA | - | - | - | - | - | 119 (100.00%) | - | - | - | 105 (88.24%) | | | | | | | | | |

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

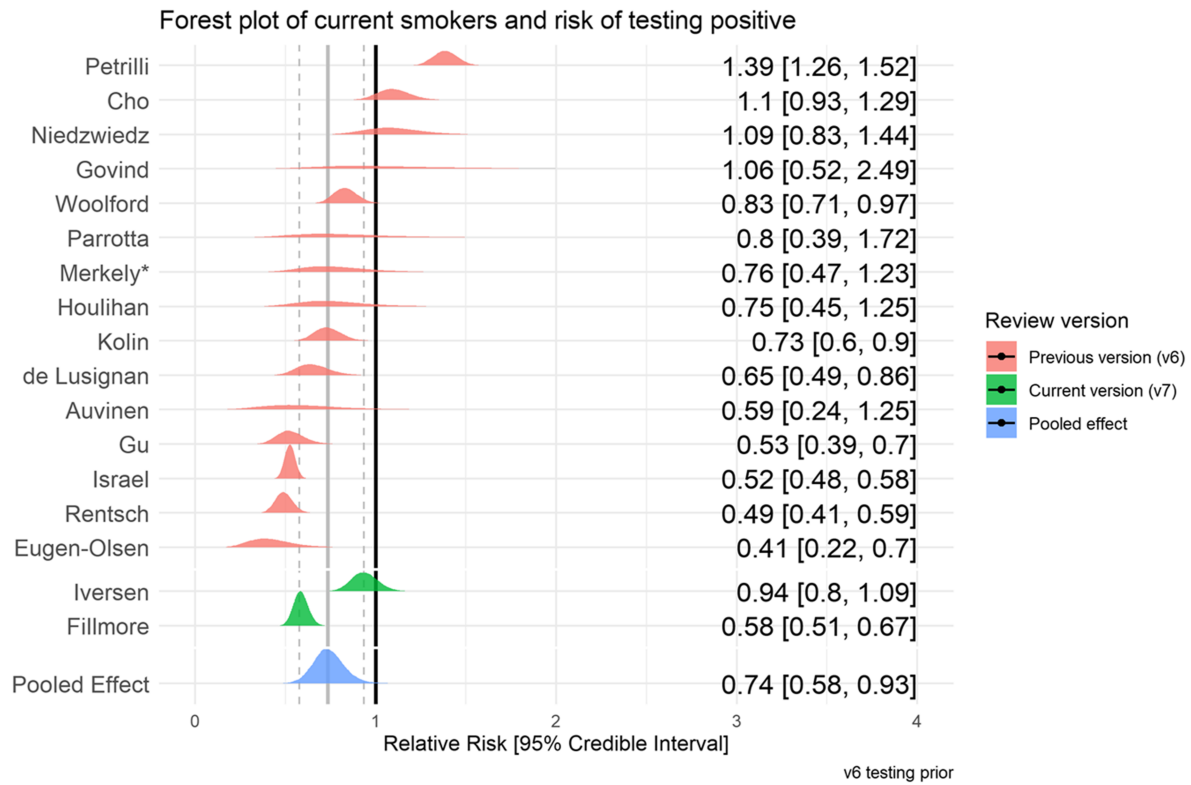


FIGURE 3 Forest plot for risk of testing positive for SARS-CoV-2 in current versus never smokers. *This was a ‘good’ quality study. [Colour figure can be viewed at wileyonlinelibrary.com]

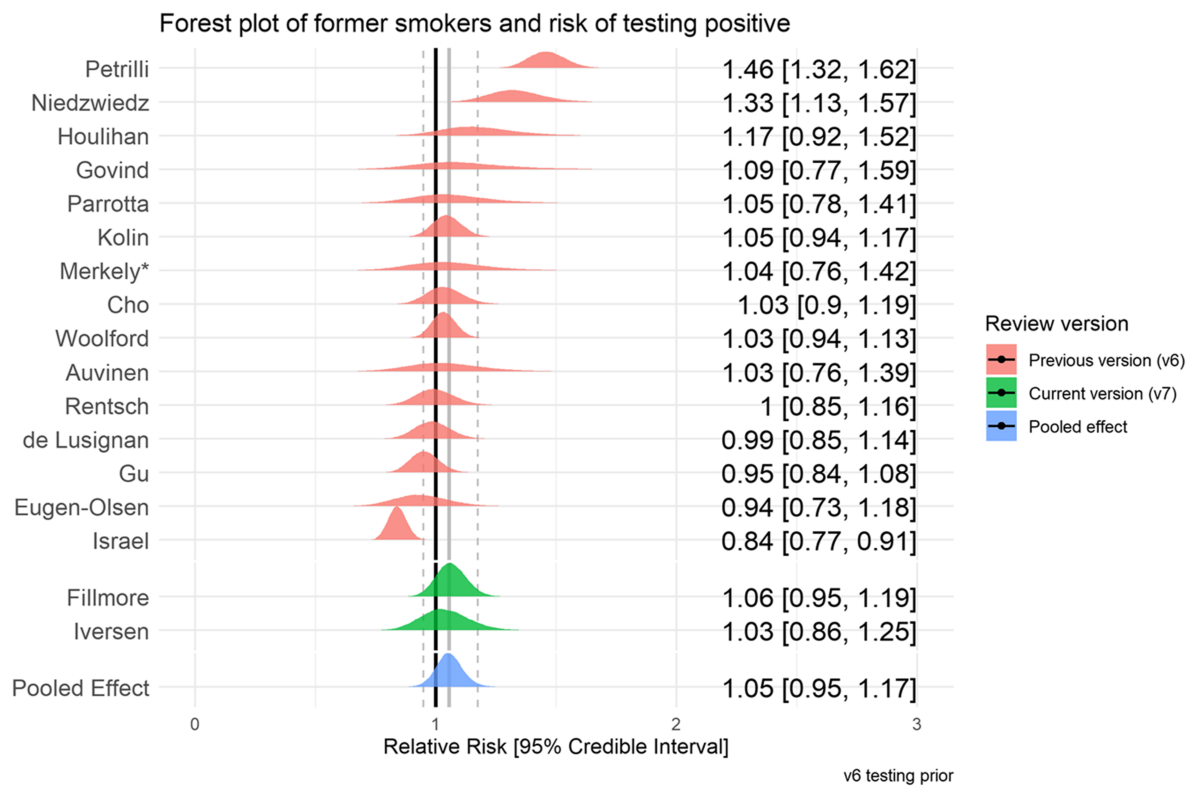


FIGURE 4 Forest plot for risk of testing positive for SARS-CoV-2 in former versus never smokers. *This was a ‘good’ quality study. [Colour figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Hospitalization with COVID-19 by smoking status.

| Author | Population with outcome | Community | | | | | | | | | | Hospitalized | | | | | | | | | | | | | |
|---------------|-------------------------|----------------|---------------|-----------------|--------------|-----------------------|-----------------|--------------|---------------|----------------------|---------------|--------------|--------------|----------------|--------------|---------------|-----|-----------------------|-----|--------------|-----|----------------------|----------------|---------------|-----|
| | | Current smoker | | Former smoker | | Current/former smoker | | Never smoker | | Never/unknown smoker | | Not stated | | Current smoker | | Former smoker | | Current/former smoker | | Never smoker | | Never/unknown smoker | | Not stated | |
| | | n (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) | (%) |
| Rentsch | 554 | 269 (48%) | 69 (25.65%) | 90 (33.46%) | - | - | 110 (40.89%) | - | - | - | - | 285 (51%) | 90 (31.58%) | 89 (31.23%) | 106 (37.19%) | - | - | - | - | - | - | - | - | - | - |
| Chow (US CDC) | 6637 | 5143 (77%) | 61 (1.19%) | 80 (1.56%) | - | - | - | - | - | - | 5002 (97.26%) | 1494 (22%) | 27 (1.81%) | 78 (5.22%) | - | - | - | - | - | - | - | - | - | 1389 (92.97%) | |
| Argenziano | 1000 | 151 (15%) | 14 (9.27%) | 18 (11.92%) | - | - | 119 (78.81%) | - | - | - | - | 849 (84%) | 35 (4.12%) | 161 (18.96%) | 653 (76.91%) | - | - | - | - | - | - | - | - | - | |
| Lubetzky | 54 | 15 (27%) | - | - | 4 (26.67%) | - | - | - | - | - | 11 (73.33%) | 39 (72%) | - | - | 8 (20.51%) | - | - | - | - | - | - | - | 31 (79.49%) | | |
| Carillo-Vega | 9946 | 3922 (39%) | 408 (10.40%) | - | - | - | - | - | - | 3514 (89.60%) | 6024 (60%) | 486 (8.07%) | - | - | - | - | - | - | - | - | - | - | 5538 (91.93%) | | |
| Yanover | 4353 | 4180 (96%) | 484 (11.58%) | 118 (2.82%) | - | - | 3578 (85.60%) | - | - | - | 173 (3%) | 30 (17.34%) | 11 (6.36%) | 132 (76.30%) | - | - | - | - | - | - | - | - | - | | |
| Hamer | 387109 | 386 (99%) | 37333 (9.66%) | 134542 (34.82%) | - | - | 214474 (55.51%) | - | - | - | 760 (0%) | 93 (12.24%) | 313 (41.18%) | 354 (46.58%) | - | - | - | - | - | - | - | - | - | | |
| 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%) | - | - | 2029 (74.08%) | - | - | - | - | - | - | - | - | |
| Freites | 123 | 69 (56%) | 1 (1.45%) | - | - | - | - | - | 68 (98.55%) | 68 (98.55%) | 54 (43%) | 3 (5.56%) | - | - | - | - | - | - | - | - | - | - | 51 (94.44%) | | |
| Berumen | 102875 | 18832 (18%) | - | - | 1546 (8.21%) | - | - | - | - | - | 12 (12%) | 690 (12%) | - | - | 1202 (9.47%) | - | - | - | - | - | - | - | 11488 (90.53%) | | |
| Gianfrancesco | 600 | 323 (53%) | - | - | 61 (18.89%) | - | - | - | 262 (81.11%) | 262 (81.11%) | 277 (46%) | - | - | 68 (24.55%) | - | - | - | - | - | - | - | - | 209 (75.45%) | | |
| Chaudhry | 40 | 19 (47%) | - | - | 0 (0.00%) | - | - | - | 19 (100.00%) | 19 (100.00%) | 21 (52%) | - | - | 6 (28.57%) | - | - | - | - | - | - | - | - | 15 (71.43%) | | |
| Giannouchos | 89756 | 58485 (65%) | 4679 (8.00%) | - | - | - | 53806 (92.00%) | - | - | - | 31 (34%) | 2721 (8.70%) | - | - | - | - | - | - | - | - | - | - | 28550 (91.30%) | | |
| Wang, Oekelen | 57 | 22 (38%) | - | - | 6 (27.27%) | - | - | - | 16 (72.73%) | 16 (72.73%) | 36 (63%) | - | - | 15 (41.67%) | - | - | - | - | - | - | - | - | 20 (55.56%) | | |

(Continues)

Table 3. (Continued)

| Author | Population with outcome | Community | | | | | | Hospitalized | | | | | | |
|---------------|-------------------------|-------------|--------------------|-------------------|---------------------------|------------------|--------------------------|----------------|--------------|--------------------|-------------------|---------------------------|------------------|--------------------------|
| | | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) |
| Miyara | 470 | 132 (28%) | 14 (10.61%) | 41 (31.06%) | - | 77 (58.33%) | - | 338 (71%) | 18 (5.33%) | 111 (32.84%) | - | 209 (61.83%) | - | - |
| Suleyman | 463 | 108 (23%) | - | - | 23 (21.30%) | - | 85 (78.70%) | 355 (76%) | - | 137 (38.59%) | - | - | - | 218 (61.41%) |
| Garassino | 196 | 48 (24%) | 10 (20.83%) | 27 (56.25%) | - | 11 (22.92%) | - | 152 (77%) | 38 (25.00%) | 84 (55.26%) | - | 26 (17.11%) | - | - |
| Siso-Almirall | 260 | 119 (45%) | - | - | 31 (26.05%) | - | 88 (73.95%) | 141 (54%) | - | - | 50 (35.46%) | - | - | 91 (64.54%) |
| Gu | 884 | 511 (57%) | 30 (5.87%) | 126 (24.66%) | - | 355 (69.47%) | - | 373 (42%) | 10 (2.68%) | 138 (37.00%) | - | 225 (60.32%) | - | - |
| Killerby | 531 | 311 (58%) | - | - | 37 (11.90%) | 222 (71.38%) | 52 (16.72%) | 220 (41%) | - | - | 54 (24.55%) | 157 (71.36%) | - | 9 (4.09%) |
| Petrilli | 5279 | 2538 (48%) | 147 (5.79%) | 337 (13.28%) | - | 1678 (66.12%) | 376 (14.81%) | 2741 (51%) | 141 (5.14%) | 565 (20.61%) | - | 1590 (58.01%) | - | 445 (16.23%) |
| Nguyen | 689 | 333 (48%) | - | - | 57 (17.12%) | - | 276 (82.88%) | 356 (51%) | - | - | 114 (32.02%) | - | - | 242 (67.98%) |
| Mendy | 689 | 473 (68%) | - | - | 84 (17.76%) | - | 389 (82.24%) | 216 (31%) | - | - | 86 (39.81%) | - | - | 130 (60.19%) |
| Soares | 10713 | 9561 (89%) | 132 (1.38%) | - | - | 9429 (98.62%) | - | 1152 (10%) | 77 (6.68%) | - | - | - | 1075 (93.32%) | - |
| Zobairy | 203 | 65 (32%) | 1 (1.54%) | - | - | 64 (98.46%) | - | 138 (67%) | 11 (7.97%) | - | - | - | 127 (92.03%) | - |
| Izquierdo | 1006 | 743 (73%) | 52 (7.00%) | - | - | 691 (93.00%) | - | 263 (26%) | 16 (6.08%) | - | - | - | 247 (93.92%) | - |
| Rizzo | 76819 | 60039 (78%) | 3931 (6.55%) | 11379 (18.95%) | - | 30042 (50.04%) | 14687 (24.46%) | 16 (7.47%) | 1254 (7.47%) | 4585 (27.32%) | - | 8693 (51.81%) | - | 2248 (13.40%) |
| Dashti | 4140 | 2759 (66%) | - | - | 600 (21.75%) | 1541 (55.85%) | 618 (22.40%) | 1381 (33%) | - | - | 577 (41.78%) | - | 596 (43.16%) | 208 (15.06%) |
| Pan | 12084 | 8548 (70%) | - | - | 1263 (14.78%) | - | 7285 (85.22%) | 3536 (29%) | - | - | 874 (24.72%) | - | - | 2662 (75.28%) |

NA = not available; CDC = Centers for Disease Control

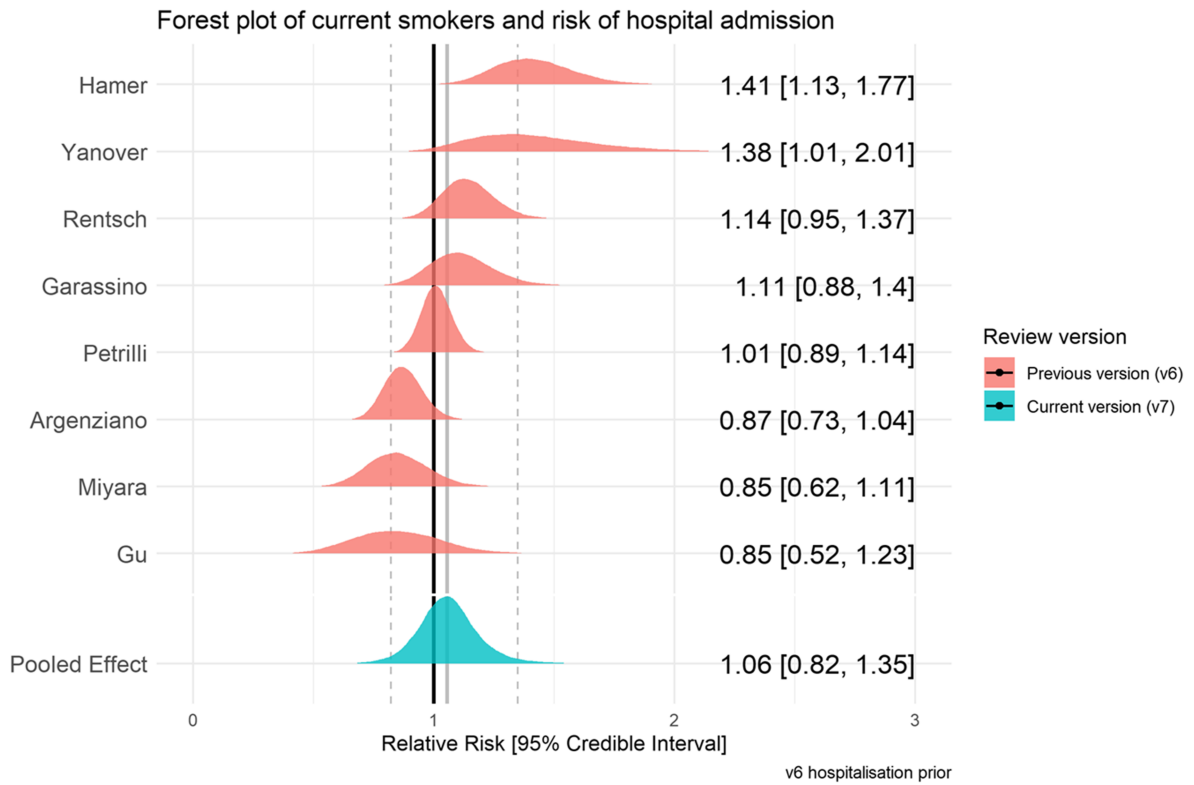


FIGURE 5 Forest plot for risk of hospitalization in current versus never smokers. [Colour figure can be viewed at wileyonlinelibrary.com]

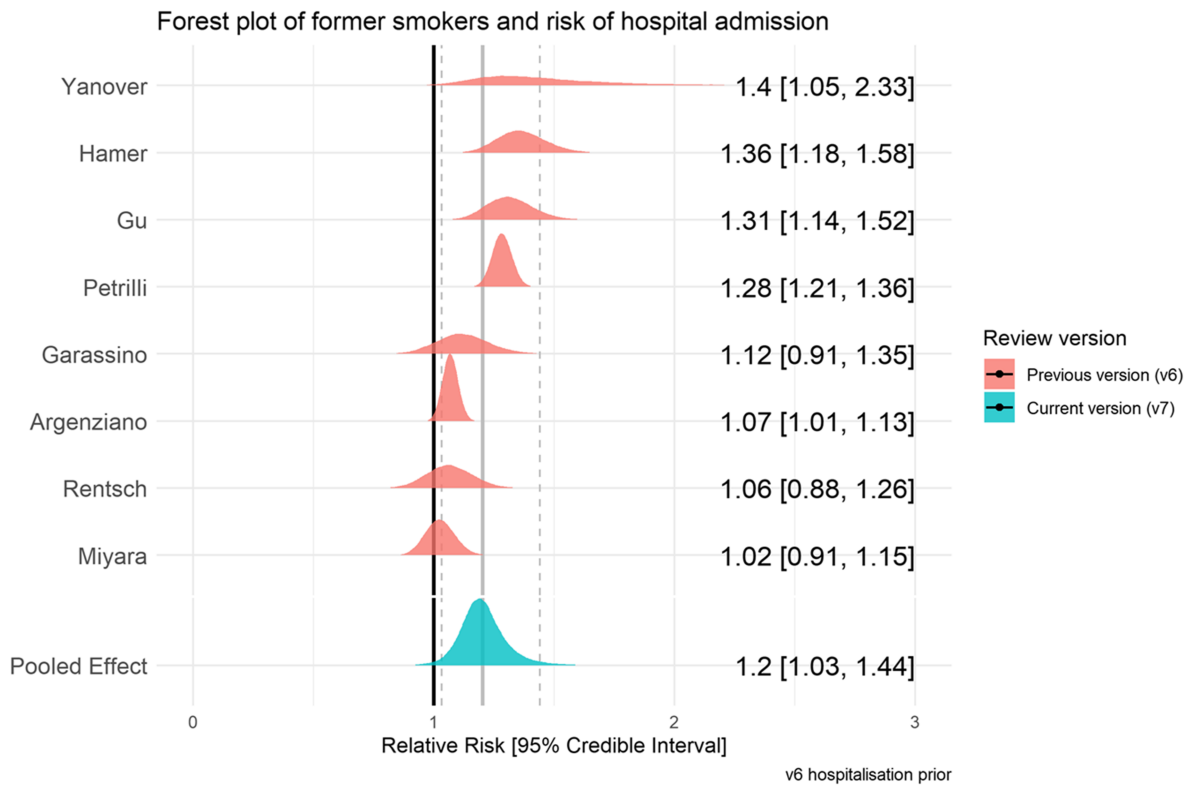


FIGURE 6 Forest plot for risk of hospitalization in former versus never smokers. [Colour figure can be viewed at wileyonlinelibrary.com]

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 (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) | | | | | | |
| Guan, Ni | 1085 | 913 (84%) | 108 (11.83%) | 12 (1.31%) | - | 793 (86.86%) | - | 172 (15%) | 29 (16.86%) | 9 (5.23%) | - | 134 (77.91%) | - | - | | | | | | | |
| Zhang, Dong | 9 | 3 (33%) | 0 (0.00%) | 3 (100.00%) | - | 0 (0.00%) | - | 6 (66%) | 2 (33.33%) | 4 (66.67%) | - | 0 (0.00%) | - | - | | | | | | | |
| Wan | 9 | 8 (88%) | 8 (100.00%) | 0 (0.00%) | - | 0 (0.00%) | - | 1 (11%) | 1 (100.00%) | 0 (0.00%) | - | 0 (0.00%) | - | - | | | | | | | |
| Huang, Wang | 3 | 3 (100%) | 3 (100.00%) | 0 (0.00%) | - | 0 (0.00%) | - | 0 (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%) | - | 38 (32.48%) | - | - | | | | | | | |
| Hu | 323 | 151 (46%) | - | - | 12 (7.95%) | - | 139 (92.05%) | 172 (53%) | - | - | 26 (15.12%) | 146 (84.88%) | - | - | | | | | | | |
| Wang, Pan | 125 | 100 (80%) | - | - | 9 (9.00%) | - | 91 (91.00%) | 25 (20%) | - | - | 7 (28.00%) | 18 (72.00%) | - | - | | | | | | | |
| Kim | 27 | 21 (77%) | 3 (14.29%) | - | - | - | 18 (85.71%) | 6 (22%) | 2 (33.33%) | 0 (0.00%) | - | 4 (66.67%) | - | - | | | | | | | |
| Shi, Yu | 474 | 425 (89%) | - | - | 34 (8.00%) | - | 391 (92.00%) | 49 (10%) | - | - | 6 (12.24%) | 43 (87.76%) | - | - | | | | | | | |
| Liao, Feng | 148 | 92 (62%) | - | - | 5 (5.43%) | - | - | 56 (37%) | 3 (5.36%) | - | - | - | 53 (94.64%) | - | | | | | | | |
| Shi, Ren | 134 | 88 (65%) | - | - | 8 (9.09%) | - | - | 46 (34%) | - | - | 6 (13.04%) | - | 40 (86.96%) | - | | | | | | | |
| Hadjadj | 50 | 15 (30%) | 1 (6.67%) | 2 (13.33%) | - | 12 (80.00%) | - | 35 (70%) | 0 (0.00%) | 7 (20.00%) | - | 28 (80.00%) | - | - | | | | | | | |
| Zheng, Xiong | 73 | 43 (58%) | - | - | 6 (13.95%) | 37 (86.05%) | - | 30 (41%) | - | - | 2 (6.67%) | 28 (93.33%) | - | - | | | | | | | |
| de la Rica | 48 | 26 (54%) | - | - | 6 (23.08%) | - | - | 20 (41%) | - | - | 4 (20.00%) | - | 16 (80.00%) | - | | | | | | | |
| Yin, Yang | 106 | 47 (44%) | - | - | 6 (12.77%) | - | - | 41 (55%) | - | - | 12 (20.34%) | - | 47 (79.66%) | - | | | | | | | |
| Allenbach | 147 | 100 (68%) | - | - | 9 (9.00%) | - | - | 47 (31%) | - | - | 0 (0.00%) | - | 47 (100.00%) | - | | | | | | | |

(Continues)

Table 4. (Continued)

| Author | Population with severity | Non-severe disease | | | | | | | | | | Severe disease | | | | | | | | | | | |
|-----------------|--------------------------|---------------------------|--------------------|-------------------|---------------------------|--------------------------|--------------------------|--------------------|-------------------|---------------------------|--------------------------|---------------------------|--------------------|-------------------|---------------------------|--------------------------|--------------------------|--------------------|-------------------|---------------------------|--------------------------|----------------|--|
| | | Current/former smoker (%) | | | | | Never/unknown smoker (%) | | | | | Current/former smoker (%) | | | | | Never/unknown smoker (%) | | | | | | |
| | | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never/unknown smoker (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never/unknown smoker (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never/unknown smoker (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never/unknown smoker (%) | Not stated (%) | |
| Goyal | 393 | 263 (66%) | 14 (5.32%) | - | - | - | 249 (94.68%) | - | - | - | 130 (33%) | 6 (4.62%) | - | - | - | 124 (95.38%) | | | | | | | |
| Feng | 454 | 333 (73%) | 27 (8.11%) | - | - | - | 306 (91.89%) | - | - | - | 121 (26%) | 17 (14.05%) | - | - | - | 104 (85.95%) | | | | | | | |
| Yao | 108 | 83 (76%) | 1 (1.20%) | - | - | - | 82 (98.80%) | - | - | - | 25 (23%) | 3 (12.00%) | - | - | - | 22 (88.00%) | | | | | | | |
| Sami | 490 | 400 (81%) | 53 (13.25%) | - | - | - | 347 (86.75%) | - | - | - | 90 (18%) | 16 (17.78%) | - | - | - | 74 (82.22%) | | | | | | | |
| Regina | 200 | 163 (81%) | 9 (5.52%) | - | - | - | 154 (94.48%) | - | - | - | 37 (18%) | 0 (0.00%) | - | - | - | 37 (100.00%) | | | | | | | |
| Feuth | 28 | 21 (75%) | 1 (4.76%) | 7 (33.33%) | 13 (61.90%) | - | - | - | - | 7 (25%) | 2 (28.57%) | 1 (14.29%) | 4 (57.14%) | - | - | - | | | | | | | |
| Mejia-Vilet | 329 | 214 (65%) | - | - | - | 201 (93.93%) | - | - | - | 115 (34%) | - | - | 10 (8.70%) | - | - | 105 (91.30%) | | | | | | | |
| Chen, Jiang | 135 | 54 (40%) | - | - | 4 (7.41%) | 50 (92.59%) | - | - | - | 81 (60%) | - | - | 9 (11.11%) | - | - | 72 (88.89%) | | | | | | | |
| Vaquero-Roncero | 146 | 75 (51%) | - | - | 4 (5.33%) | 71 (94.67%) | - | - | - | 71 (48%) | - | - | 6 (8.45%) | - | - | 65 (91.55%) | | | | | | | |
| Kim, Garg | 2490 | 1692 (67%) | 112 (6.62%) | 395 (23.35%) | - | 1185 (70.04%) | - | - | - | 798 (32%) | 38 (4.76%) | 247 (30.95%) | - | - | 512 (64.16%) | | | | | | | | |
| Wu | 174 | 92 (52%) | - | - | 47 (51.09%) | 45 (48.91%) | - | - | - | 82 (47%) | 11 (13.41%) | - | - | 71 (86.59%) | | | | | | | | | |
| Chaudhry | 40 | 34 (85%) | - | - | 5 (14.71%) | 29 (85.29%) | - | - | - | 6 (15%) | - | - | 1 (16.67%) | - | - | 5 (83.33%) | | | | | | | |
| Garibaldi | 832 | 532 (63%) | 25 (4.70%) | 107 (20.11%) | - | 400 (75.19%) | - | - | - | 300 (36%) | 21 (7.00%) | 81 (27.00%) | - | - | 198 (66.00%) | | | | | | | | |
| Kuderer | 928 | 686 (73%) | 35 (5.10%) | 210 (30.61%) | 370 (53.94%) | 29 (4.23%) | - | - | - | 242 (26%) | 8 (3.31%) | 116 (47.93%) | 99 (40.91%) | - | - | 4 (1.65%) | | | | | | | |
| Romao | 14 | 14 (100%) | - | - | 4 (28.57%) | 10 (71.43%) | - | - | - | 0 (0%) | - | - | - | - | - | - | | | | | | | |

(Continues)

Table 4. (Continued)

| 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 (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) |
| Giannouchos | 89756 | 78050 (86%) | 6322 (8.10%) | - | - | - | - | 11706 (13%) | 1089 (9.30%) | - | - | - | - | 10617 (90.70%) | - |
| Cen | 1007 | 720 (71%) | - | - | 70 (9.72%) | - | 650 (90.28%) | 287 (28%) | - | 18 (6.27%) | - | - | - | - | 269 (93.73%) |
| Maraschini | 132 | 89 (67%) | - | 11 (12.36%) | - | 78 (87.64%) | - | 43 (32%) | - | 3 (6.98%) | 40 (93.02%) | - | - | - | - |
| Siso-Almirall | 260 | 212 (81%) | - | - | 60 (28.30%) | - | 152 (71.70%) | 48 (18%) | - | 21 (43.75%) | - | - | - | - | 27 (56.25%) |
| Gu | 884 | 511 (57%) | 30 (5.87%) | 126 (24.66%) | - | 355 (69.47%) | - | 134 (15%) | 3 (2.24%) | 61 (45.52%) | 70 (52.24%) | - | - | - | - |
| Petrilli | 2729 | 1739 (63%) | 97 (5.58%) | 325 (18.69%) | - | 1067 (61.36%) | 250 (14.38%) | 990 (36%) | 44 (4.44%) | 236 (23.84%) | 517 (52.22%) | - | - | - | 193 (19.49%) |
| Mendy | 689 | 598 (86%) | - | - | 133 (22.24%) | - | 465 (77.76%) | 91 (13%) | - | 37 (40.66%) | - | - | - | - | 54 (59.34%) |
| Pongpirul | 193 | 161 (83%) | - | - | 25 (15.53%) | 106 (65.84%) | 30 (18.63%) | 32 (16%) | - | 4 (12.50%) | 21 (65.62%) | - | - | - | 7 (21.88%) |
| Jin, Gu | 6 | 2 (33%) | - | - | 0 (0.00%) | - | 4 (200.00%) | 4 (66%) | - | 2 (50.00%) | - | - | - | - | 2 (50.00%) |
| Senkal | 611 | 446 (73%) | 48 (10.76%) | - | - | - | 398 (89.24%) | 165 (27%) | 21 (12.73%) | - | - | - | - | - | 144 (87.27%) |
| Patel | 129 | 89 (68%) | 26 (29.21%) | - | - | 58 (65.17%) | 5 (5.62%) | 40 (31%) | 22 (55.00%) | - | - | - | 14 (35.00%) | - | 4 (10.00%) |
| Maucourant | 27 | 10 (37%) | 1 (10.00%) | 2 (20.00%) | - | 2 (20.00%) | 5 (50.00%) | 17 (62%) | 2 (11.76%) | 5 (29.41%) | 9 (52.94%) | - | - | - | 1 (5.88%) |
| Xie | 619 | 469 (75%) | - | - | 32 (6.82%) | - | 437 (93.18%) | 150 (24%) | - | 19 (12.67%) | - | - | - | - | 131 (87.33%) |
| Fox | 55 | 30 (54%) | 1 (3.33%) | 4 (13.33%) | - | 17 (56.67%) | 8 (26.67%) | 25 (45%) | 0 (0.00%) | 2 (8.00%) | 14 (56.00%) | - | - | - | 9 (36.00%) |
| Zhang, Cao | 240 | 162 (67%) | 2 (1.23%) | 6 (3.70%) | - | - | 154 (95.06%) | 78 (32%) | 4 (5.13%) | 4 (5.13%) | - | - | - | - | 70 (89.74%) |

(Continues)

Table 4. (Continued)

| Author | Population with severity | Non-severe disease | | | | | | Severe disease | | | | | | |
|-----------------------|--------------------------|--------------------|--------------------|-------------------|---------------------------|------------------|--------------------------|----------------|--------------------|-------------------|---------------------------|------------------|--------------------------|----------------|
| | | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) |
| Kurashima | 53 | 10 (18%) | - | - | 3 (30.00%) | - | - | 7 (70.00%) | 43 (81%) | - | 24 (55.81%) | - | - | 19 (44.19%) |
| Zhan | 75 | NA | - | - | - | - | - | 75 (100%) | 75 (100%) | - | 9 (12.00%) | - | - | 66 (88.00%) |
| Omrani | 858 | 806 (93%) | - | - | 121 (15.01%) | - | 685 (84.99%) | 52 (6%) | 52 (6%) | - | 9 (17.31%) | - | - | 43 (82.69%) |
| Marcos | 918 | 555 (60%) | 38 (6.85%) | - | 69 (12.43%) | - | 448 (80.72%) | 363 (39%) | 363 (39%) | 18 (4.96%) | 71 (19.56%) | - | - | 292 (80.44%) |
| Hoertel, Sanchez-Rico | 7345 | 6014 (81%) | 433 (7.20%) | - | - | - | 5581 (92.80%) | 1331 (18%) | 1331 (18%) | 190 (14.27%) | - | - | - | 1141 (85.73%) |
| Qi | 267 | 217 (81%) | 22 (10.14%) | - | - | - | - | 50 (18%) | 50 (18%) | 31 (62.00%) | - | - | 19 (38.00%) | - |
| Monteiro | 112 | 84 (75%) | 3 (3.57%) | 14 (16.67%) | - | 63 (75.00%) | 4 (4.76%) | 28 (25%) | 28 (25%) | 4 (14.29%) | 6 (21.43%) | 14 (50.00%) | - | 4 (14.29%) |
| Dashti | 1381 | 619 (44%) | - | - | 239 (38.61%) | 292 (47.17%) | 88 (14.22%) | 762 (55%) | 762 (55%) | - | 338 (44.36%) | - | - | 120 (15.75%) |
| Morshed | 103 | 87 (84%) | 28 (32.18%) | - | - | 59 (67.82%) | - | 16 (15%) | 16 (15%) | 4 (25.00%) | - | - | 12 (75.00%) | - |
| Zhou, Sun | 144 | 108 (75%) | 11 (10.19%) | - | - | - | 97 (89.81%) | 36 (25%) | 36 (25%) | 2 (5.56%) | - | - | - | 34 (94.44%) |
| Hippisley-Cox | - | NA | - | - | - | - | - | 1286 (25%) | 1286 (25%) | 56 (4.35%) | 427 (33.20%) | 791 (61.51%) | - | 12 (0.93%) |
| Zhao, Chen | 641 | 398 (62%) | 87 (21.86%) | - | - | - | 311 (78.14%) | 195 (30%) | 195 (30%) | 52 (26.67%) | - | - | - | 143 (73.33%) |
| Qu | 246 | 226 (91%) | 90 (39.82%) | - | - | - | 136 (60.18%) | 20 (8%) | 20 (8%) | 14 (70.00%) | - | - | - | 6 (30.00%) |

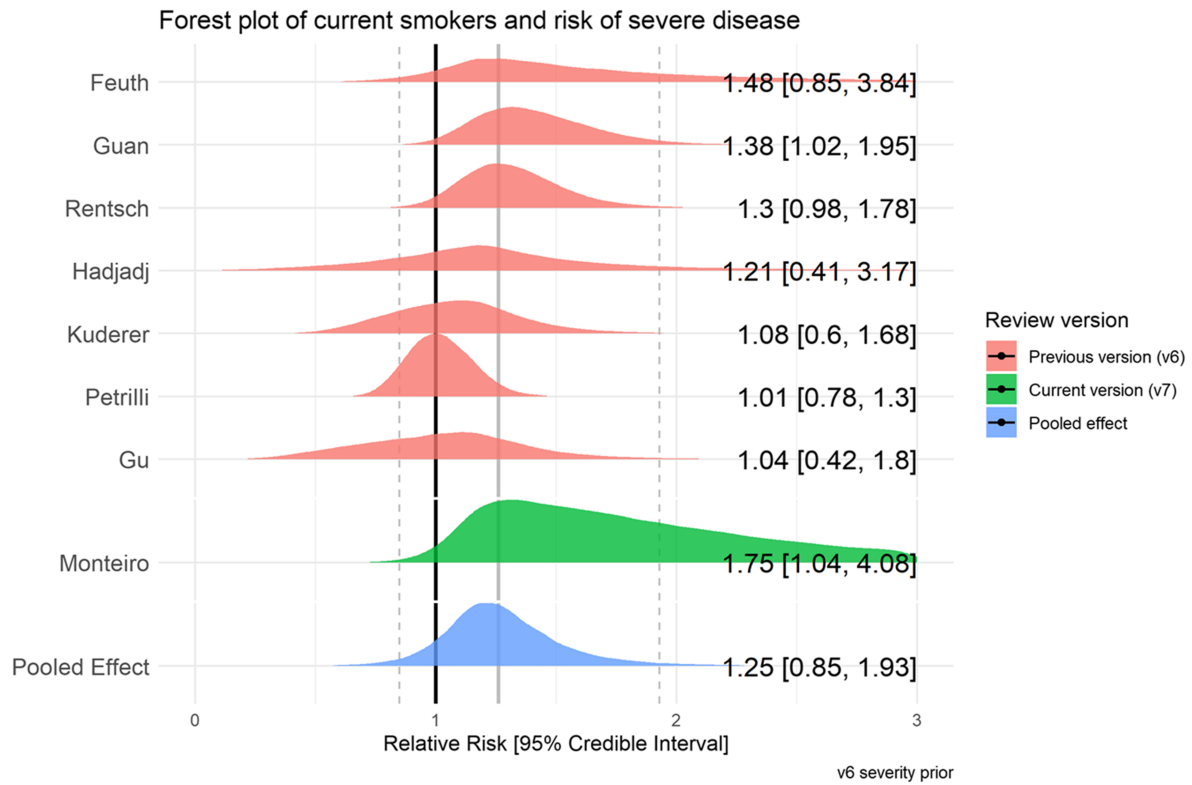


FIGURE 7 Forest plot for the risk of severe disease in current versus never smokers. [Colour figure can be viewed at wileyonlinelibrary.com]

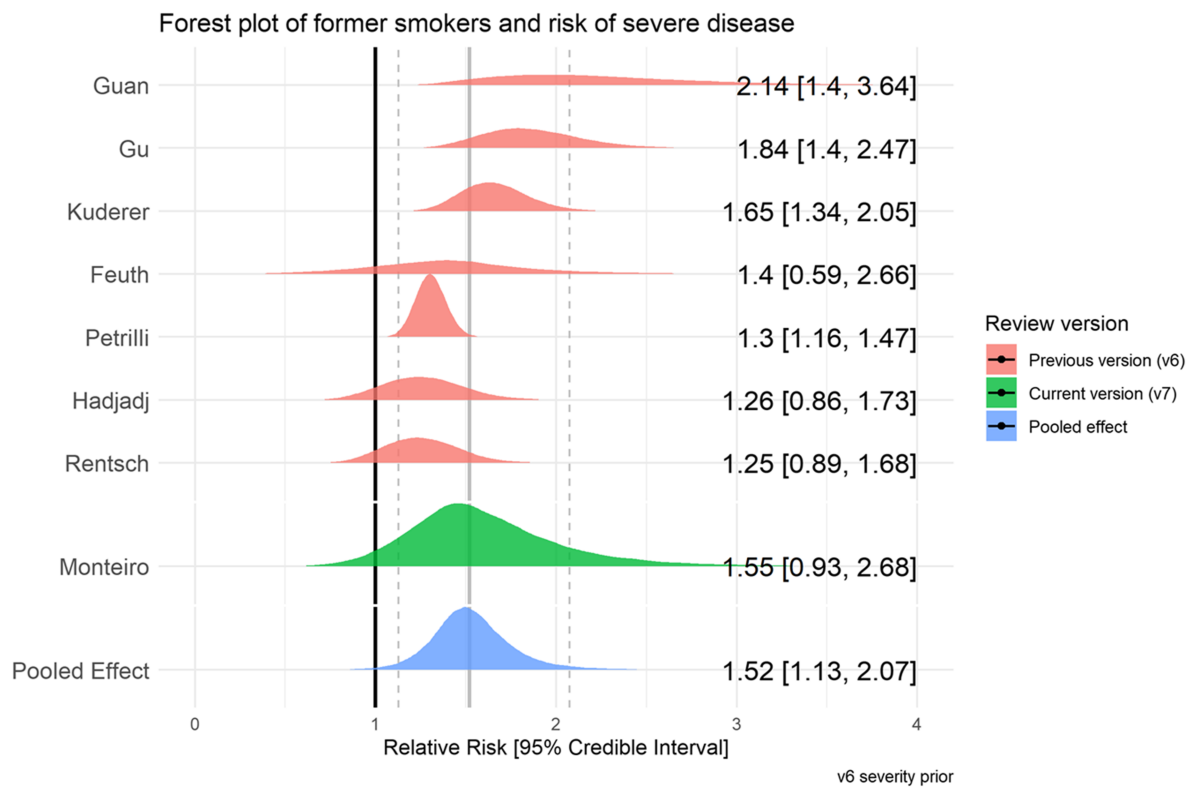


FIGURE 8 Forest plot for the risk of severe disease in former versus never smokers. [Colour figure can be viewed at wileyonlinelibrary.com]

Mortality by smoking status

Fifty studies reported mortality from COVID-19 by smoking status (see Table 5), with nine 'fair' quality studies included in meta-analyses (see Figs 9 and 10). Current (RR = 1.22, 95% CrI = 0.78–1.94, τ = 0.49, 95% CI = 0.16–0.99) and former (RR = 1.39, 95% CrI = 1.09–1.87, τ = 0.27, 95% CI = 0.05–0.58) compared with never smokers were at increased risk of in-hospital mortality from COVID-19. Data for current smokers were inconclusive, but favoured there being no important association. The probability of current and former smokers being at greater risk of in-hospital mortality compared with never smokers was 70 and 97%, respectively. Results were materially unchanged in two sensitivity analyses (see Supporting information, Fig. S5).

DISCUSSION

This living rapid review found uncertainty in the majority of 233 studies arising from the recording of smoking status. Notwithstanding these uncertainties, compared with overall adult national prevalence estimates, recorded current smoking rates in most countries were lower than expected. In a subset of better of quality studies ($n = 17$), current smokers had a reduced risk of testing positive for SARS-CoV-2 but appeared more likely to present for testing and/or receive a test. Data for current smokers on the risk of hospitalization, disease severity and mortality were inconclusive, but favoured there being no important associations with hospitalization and mortality and a small but important increase in the risk of severe disease. Former smokers were at increased risk of hospitalization, 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 Fig. 11):

1. Exposure to SARS-CoV-2 is heterogeneous, with different subgroups at heightened risk of infection at different stages of the pandemic. This will likely introduce bias in studies assessing the rate of infection by smoking status conducted early on.
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 [35]. 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 will be more informative than currently available data. We identified one population study conducted in Hungary reporting on seroprevalence and smoking status [36]; however, the response rate was fairly low, at 58.8%, and the current smoking rate was 10 percentage points below national prevalence estimates, thus questioning the representativeness of the final sample. Smoking status is being collected in at least two large representative infection and antibody surveys in the United Kingdom [37,38].

3. Testing for acute infection requires swabbing of the mucosal epithelium, which may be disrupted in current smokers, potentially altering the sensitivity of assays [39].
4. Diagnostic criteria for SARS-CoV-2 infection and COVID-19 have changed during the course of the pandemic [40]. It was not possible to extract details on the specific RT-PCR technique or platforms used across the included studies due to reporting gaps. Different platforms have varying sensitivity and specificity to detect SARS-CoV-2 infection.
5. Most included studies relied on EHRs as the source of information on smoking status. Research shows large discrepancies between EHRs and actual behaviour [41]. Known failings of EHRs include implausible longitudinal changes, such as former smokers being recorded as never smokers at subsequent hospital visits [41]. Misreporting on the part of the patient (perhaps due to perceived stigmatization) has also been observed, with biochemical measures showing higher rates of smoking compared with self-report in hospitalized patients in the United States [42]. It is hence possible that under-reporting of current and former smoking status in hospitals occurred across the included studies.
6. 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).
7. 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.
8. If there is a protective effect of nicotine on COVID-19 disease outcomes, abrupt nicotine withdrawal upon hospitalization may lead to worse outcomes [12].
9. 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.

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 (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) |
| Chen | 274 | 161 (58%) | 5 (3.11%) | 5 (3.11%) | - | - | 151 (93.79%) | 7 (6.19%) | 2 (1.77%) | - | - | - | - | 104 (92.04%) |
| Zhou, Yu | 191 | 137 (71%) | 6 (4.38%) | - | - | 131 (95.62%) | 54 (28%) | 5 (9.26%) | - | - | - | - | - | 49 (90.74%) |
| Yang, Yu | 52 | 20 (38%) | 2 (10.00%) | - | - | 18 (90.00%) | 32 (61%) | - | - | - | - | 32 (100.00%) | - | - |
| Borobia | 2226 | 1766 (79%) | 113 (6.40%) | - | - | 1653 (93.60%) | 460 (20%) | 44 (9.57%) | - | - | - | - | - | 416 (90.43%) |
| Giacomelli | 233 | 185 (79%) | - | 53 (28.65%) | 132 (71.35%) | - | 48 (20%) | - | - | 17 (35.42%) | 31 (64.58%) | - | - | 0 (0.00%) |
| Yao | 108 | 96 (88%) | 1 (1.04%) | - | - | 95 (98.96%) | 12 (11%) | 3 (25.00%) | - | - | - | - | - | 9 (75.00%) |
| Carillo-Vega | 9946 | 8983 (90%) | 795 (8.85%) | - | - | 8188 (91.15%) | 963 (9%) | 99 (10.28%) | - | - | - | - | - | 864 (89.72%) |
| Heng | 51 | 39 (76%) | 6 (15.38%) | - | - | 33 (84.62%) | 12 (23%) | 1 (8.33%) | - | - | - | - | - | 11 (91.67%) |
| Chen, Jiang | 135 | NA | - | - | - | - | 31 (22%) | - | - | 4 (12.90%) | - | - | - | 27 (87.10%) |
| Helli-Frades | 4712 | 4086 (86%) | 210 (5.14%) | 659 (16.13%) | - | 3217 (78.73%) | 626 (13%) | 23 (3.67%) | 161 (25.72%) | - | - | 442 (70.61%) | - | |
| Kim, Garg | 2490 | 2070 (83%) | 128 (6.18%) | 481 (23.24%) | - | 1461 (70.58%) | 420 (16%) | 22 (5.24%) | 161 (38.33%) | - | - | 236 (56.19%) | - | |
| Al-Hindawi | 31 | 15 (48%) | 0 (0.00%) | 10 (66.67%) | 5 (33.33%) | - | 16 (51%) | 1 (6.25%) | 12 (75.00%) | - | 3 (18.75%) | - | - | |
| Louis | 22 | 16 (72%) | - | 7 (43.75%) | - | 9 (56.25%) | 6 (27%) | - | - | 3 (50.00%) | - | - | 3 (50.00%) | |
| Soto-Mota | 400 | 200 (50%) | - | 23 (11.50%) | - | 177 (88.50%) | 200 (50%) | - | - | 25 (12.50%) | - | - | - | 175 (87.50%) |
| Garibaldi | 747 | 634 (84%) | 36 (5.68%) | 129 (20.35%) | - | 469 (73.97%) | 113 (15%) | 6 (5.31%) | 36 (31.86%) | - | - | - | 71 (62.83%) | |

(Continues)

Table 5. (Continued)

| 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 (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) | | | | | | |
| Doeherty | 13 364 | 8199 (61%) | 370 (4.51%) | 1832 (22.34%) | - | 4179 (50.97%) | - | 1818 (22.17%) | 5165 (38%) | 214 (4.14%) | 1350 (26.14%) | - | 2105 (40.76%) | - | 1496 (28.96%) | | | | | | |
| Kuderer | 928 | 807 (86%) | 38 (4.71%) | 262 (32.47%) | - | 425 (52.66%) | - | 31 (3.84%) | 121 (13%) | 5 (4.13%) | 64 (52.89%) | - | 44 (36.36%) | - | 2 (1.65%) | | | | | | |
| Ramlall | 11116 | 10498 (94%) | - | - | 2771 (26.40%) | 7727 (73.60%) | - | - | 618 (5%) | - | - | 208 (33.66%) | 410 (66.34%) | - | - | | | | | | |
| Wang, Oekelen | 57 | 43 (75%) | - | - | 14 (32.56%) | - | 29 (67.44%) | 14 (24%) | - | - | - | 7 (50.00%) | - | 7 (50.00%) | | | | | | | |
| Martinez-Portilla | 224 | 217 (96%) | - | - | 7 (3.23%) | - | 210 (96.77%) | 7 (3%) | - | - | - | 0 (0.00%) | - | 7 (100.00%) | | | | | | | |
| Cen | 1007 | 964 (95%) | - | - | 87 (9.02%) | - | 877 (90.98%) | 43 (4%) | - | - | - | 1 (2.33%) | - | 42 (97.67%) | | | | | | | |
| Klang | 3406 | 2270 (66%) | - | - | 492 (21.67%) | - | 1778 (78.33%) | 1136 (33%) | - | - | 301 (26.50%) | - | - | 835 (73.50%) | | | | | | | |
| Wang, Zhong | 5510 | 4874 (88%) | 247 (5.07%) | 1083 (22.22%) | - | 3544 (72.71%) | - | - | 636 (11%) | 28 (4.40%) | 214 (33.65%) | - | 394 (61.95%) | - | | | | | | | |
| Miyara | 338 | 211 (62%) | 13 (6.16%) | 58 (27.49%) | - | 141 (66.82%) | - | - | 46 (13%) | 1 (2.17%) | 23 (50.00%) | - | 21 (45.65%) | - | | | | | | | |
| Rajter | 255 | 209 (81%) | - | - | 28 (13.40%) | 181 (86.60%) | - | - | 53 (20%) | - | - | 18 (33.96%) | 28 (52.83%) | - | | | | | | | |
| Zeng | 1031 | 866 (84%) | - | - | 69 (7.97%) | - | 797 (92.03%) | 165 (16%) | - | - | - | 36 (21.82%) | - | 129 (78.18%) | | | | | | | |
| Chen, Yu | 1859 | 1651 (88%) | 32 (1.94%) | 54 (3.27%) | - | 1565 (94.79%) | - | - | 208 (11%) | 13 (6.25%) | 12 (5.77%) | - | 183 (87.98%) | - | | | | | | | |
| Garassino | 190 | 124 (65%) | - | - | 92 (74.19%) | 32 (25.81%) | - | - | 66 (34%) | - | 61 (92.42%) | - | 5 (7.58%) | - | | | | | | | |
| Gu | 884 | 864 (97%) | 40 (4.63%) | 250 (28.94%) | - | 219 (25.35%) | - | - | 20 (2%) | 0 (0.00%) | 14 (70.00%) | - | 6 (30.00%) | - | | | | | | | |
| Sigel | 88 | 70 (79%) | - | - | 37 (52.86%) | - | 33 (47.14%) | 18 (20%) | - | - | - | 11 (61.11%) | - | 7 (38.89%) | | | | | | | |

(Continues)

Table 5. (Continued)

| 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 (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) | |
| Nguyen | 356 | 308 (86%) | - | - | 91 (29.55%) | - | - | 217 (70.45%) | 45 (12%) | - | 23 (51.11%) | - | - | 22 (48.89%) | | |
| de Souza | 8443 | 7826 (92%) | - | - | 95 (1.21%) | - | 160 (2.04%) | 617 (7%) | 617 (7%) | - | 47 (7.62%) | - | 560 (90.76%) | 10 (1.62%) | | |
| Mendy | 532 | 663 (124%) | - | - | 160 (24.13%) | - | 502 (75.72%) | 26 (4%) | 26 (4%) | - | 10 (38.46%) | - | - | 16 (61.54%) | | |
| Shi, Resurreccion | 256 | 210 (82%) | - | - | 128 (60.95%) | - | 82 (39.05%) | 46 (17%) | 46 (17%) | - | 26 (56.52%) | - | - | 20 (43.48%) | | |
| Xie | 619 | 591 (95%) | - | - | 43 (7.28%) | - | 548 (92.72%) | 28 (4%) | 28 (4%) | - | 8 (28.57%) | - | - | 20 (71.43%) | | |
| Fox | 54 | 35 (64%) | 4 (11.43%) | 18 (51.43%) | - | 12 (34.29%) | 19 (55%) | 0 (0.00%) | 19 (55%) | 2 (10.53%) | - | 12 (63.16%) | - | 5 (26.32%) | | |
| Zhang, Cao | 289 | 240 (83%) | 6 (2.50%) | - | - | 224 (93.33%) | 49 (16%) | 4 (8.16%) | 49 (16%) | 8 (16.33%) | - | - | - | 37 (75.51%) | | |
| Gupta | 496 | 255 (51%) | - | - | 15 (5.88%) | - | 160 (62.75%) | 241 (48%) | 241 (48%) | - | 21 (8.71%) | 77 (31.95%) | - | 143 (59.34%) | | |
| Soares | 1075 | 696 (64%) | 38 (5.46%) | - | - | 658 (94.54%) | - | 39 (8.55%) | 39 (8.55%) | - | - | - | 417 (91.45%) | - | | |
| Thompson | 470 | 301 (64%) | 39 (12.96%) | 79 (26.25%) | - | 183 (60.80%) | 169 (35%) | 27 (15.98%) | 169 (35%) | 49 (28.99%) | - | 93 (55.03%) | - | - | | |
| Bernaola | 1645 | 1382 (84%) | 35 (2.53%) | 146 (10.56%) | - | 1201 (86.90%) | 263 (15%) | 6 (2.28%) | 263 (15%) | 33 (12.55%) | - | 218 (82.89%) | - | - | | |
| Islam | 654 | 631 (96%) | 103 (16.32%) | - | - | 507 (80.35%) | 23 (3%) | 3 (13.04%) | 23 (3%) | - | - | - | - | - | | |
| Philipose | 466 | 267 (57%) | 19 (7.12%) | 204 (76.40%) | - | 44 (16.48%) | 199 (42%) | 9 (4.52%) | 199 (42%) | 137 (68.84%) | - | 33 (16.58%) | - | 20 (10.05%) | | |
| Dashti | 4140 | 3953 (95%) | - | - | 1068 (27.02%) | - | 804 (20.34%) | 187 (4%) | 187 (4%) | - | 109 (58.29%) | 56 (29.95%) | - | 22 (11.76%) | | |
| Fillmore | 1794 | 1566 (87%) | 408 (26.05%) | 758 (48.40%) | - | 279 (17.82%) | 98 (6.26%) | 44 (19.30%) | 228 (12%) | 141 (61.84%) | - | 43 (18.86%) | - | 23 (10.09%) | | |

(Continues)

Table 5. (Continued)

| Author | Population with mortality | Recovered | | | | | | Died | | | | | | |
|------------|---------------------------|------------|--------------------|-------------------|---------------------------|------------------|--------------------------|--------------|--------------------|-------------------|---------------------------|------------------|--------------------------|----------------|
| | | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | n (%) | Current smoker (%) | Former smoker (%) | Current/former smoker (%) | Never smoker (%) | Never/unknown smoker (%) | Not stated (%) |
| Pan | 3536 | 3302 (93%) | - | - | 862 (26.11%) | - | - | 234 (6%) | - | - | 82 (35.04%) | - | - | 152 (64.96%) |
| Zhao, Chen | 474 | 398 (83%) | 87 (21.86%) | - | - | - | 311 (78.14%) | 82 (17%) | 36 (43.90%) | - | - | - | 46 (56.10%) | |
| Holman | 10989 | NA | - | - | - | - | - | 10989 (100%) | 609 (5.54%) | 4684 (42.62%) | - | 5386 (49.01%) | 310 (2.82%) | |
| Chand | 300 | 143 (47%) | 23 (16.08%) | - | - | - | 120 (83.92%) | 157 (52%) | 44 (28.03%) | - | - | - | 113 (71.97%) | |

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.

- Given the 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.
- Reasons for hospitalization vary by country and time in the pandemic. For example, early cases may have been hospitalized for isolation and quarantine reasons and not due to medical necessity. It is plausible that 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 [43], where conditioning on a collider (e.g. testing or hospitalization) by design or analysis may introduce a spurious association between current or former smoking (a potential cause of testing or hospitalization) and SARS-CoV-2 infection/adverse outcomes from COVID-19 (potentially exacerbated by smoking) [44].

Limitations

This living rapid evidence review was limited by having a single reviewer extracting data with a second independently verifying the data extracted to minimize 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 upon self-reported suspected or confirmed SARS-CoV-2 infection (which means they do not meet our eligibility criteria) [35,45,46]. We also did not include a large, UK-based, representative seroprevalence study [47] in our meta-analyses, as the odds of testing positive in former smokers was not reported. However, the odds of infection for current smokers (odds ratio = 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 [17].

Implications for research, policy and practice

Further scientific research is needed to resolve the mixed findings summarized in our review. First, clinical trials of

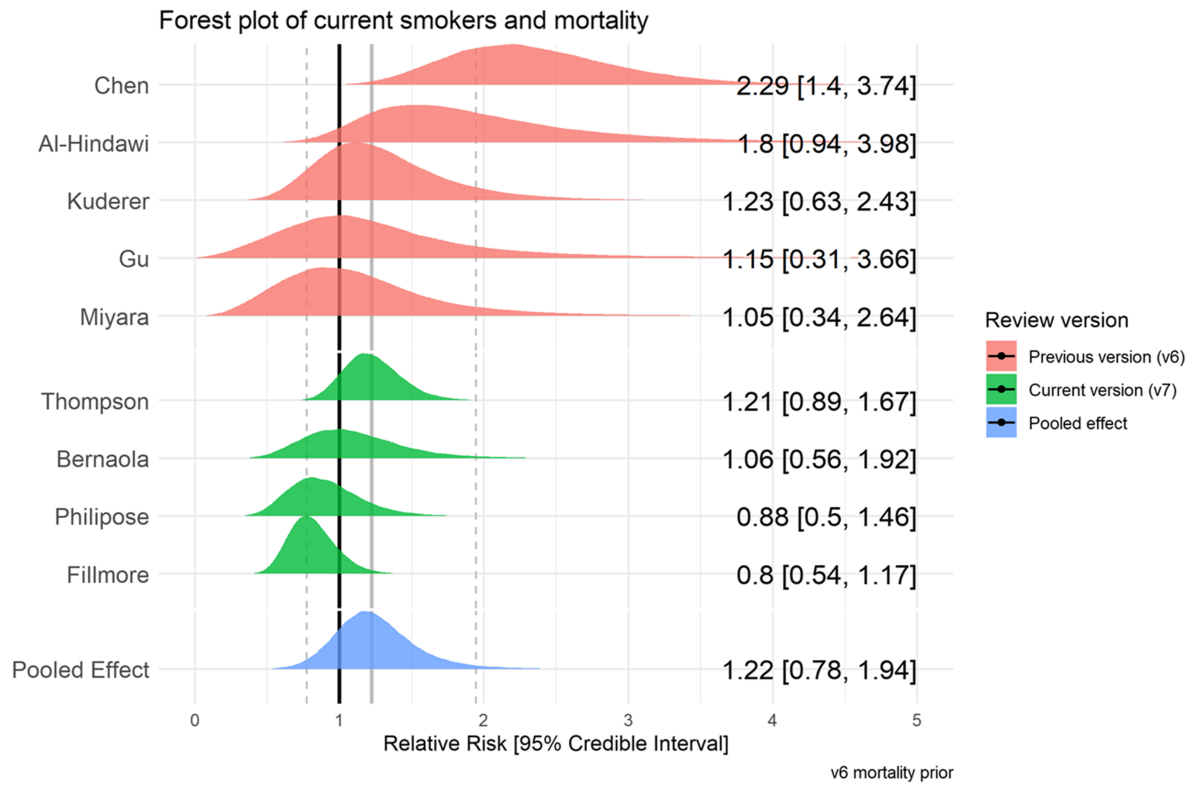


FIGURE 9 Forest plot for the risk of mortality in current versus never smokers. [Colour figure can be viewed at wileyonlinelibrary.com]

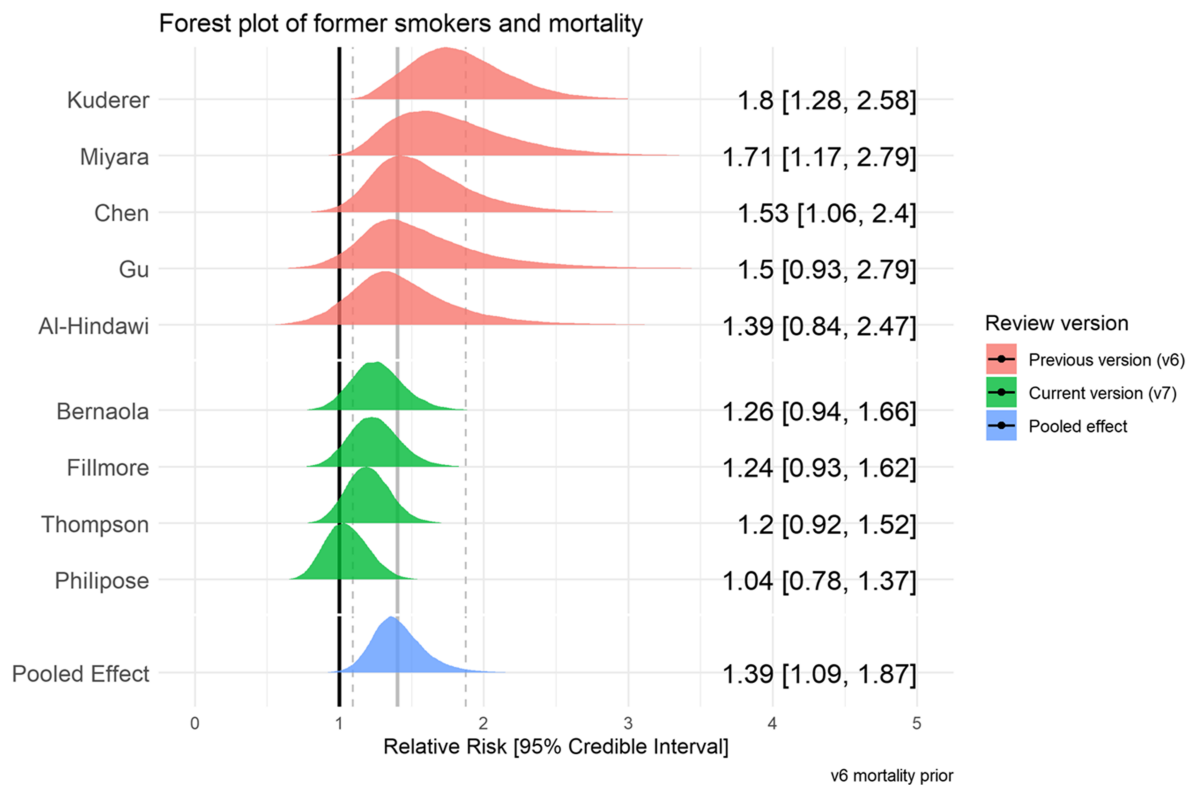


FIGURE 10 Forest plot for the risk of mortality in former versus never smokers. [Colour figure can be viewed at wileyonlinelibrary.com]

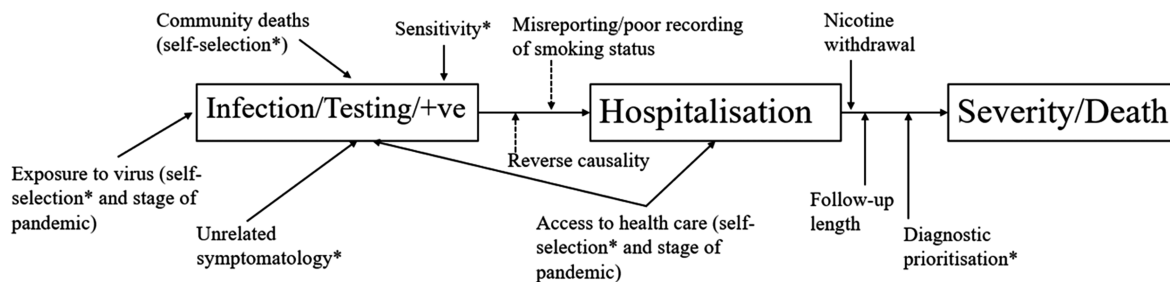


FIGURE 11 A schematic of some of the interpretation issues for the association of smoking and SARS-CoV-2/COVID-19. *Indicates potential confounding with smoking status.

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 upon 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 versus ingested), as this can affect pharmacokinetics [48] 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 emphasize 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 health-care system [49]. GPs and other health-care providers can play a crucial role—brief, high-quality and free on-line training is available at National Centre for Smoking Cessation and Training.

CONCLUSION

Across 233 studies, recorded 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 hospitalization, disease severity and mortality compared with never smokers.

Declaration of interests

D.S. and O.P. have no conflicts of interest to declare. L.S. has received a research grant and honoraria for a talk and travel expenses from manufacturers of smoking cessation medications (Pfizer and Johnson & Johnson). J.B. 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.

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Author contributions

David Simons: Conceptualization; data curation; formal analysis; methodology; writing-original draft; writing-review & editing. **Lion Shahab:** Conceptualization; data curation; formal analysis; methodology; writing-original draft; writing-review & editing. **Jamie Brown:** Conceptualization; data curation; formal analysis; methodology; writing-original draft; writing-review & editing. **Olga Perski:** Conceptualization; data curation; formal analysis; methodology; writing-original draft; writing-review & editing.

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>

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

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1 Map of countries where included studies were conducted. Six studies were performed in multiple countries and are not included here.

Table S1 Study design, use of clinical diagnosis and stratification of smoking status by sex, age or socio-economic position.

Table S2a Studies reporting complete smoking status

Table S2b Studies reporting partially complete smoking status

Table S2c Studies reporting incomplete smoking status

Table S3 Smoking prevalence in countries with included studies

Figure S2 Supporting Information

Figure S3 Supporting Information

Figure S4 Supporting Information

Figure S5 Supporting Information