The neurology and neuropsychiatry of COVID-19: a systematic review and meta-analysis of the early literature reveals frequent CNS manifestations and key emerging narratives

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ABSTRACT

Objectives

There is accumulating evidence of the neurological and neuropsychiatric features of infection with SARS-CoV-2. In this systematic review and meta-analysis, we aimed to describe the characteristics of the early literature and estimate point prevalences for neurological and neuropsychiatric manifestations.

Methods

We searched MEDLINE, Embase, PsycInfo and CINAHL up to 18 July 2020 for randomised controlled trials, cohort studies, case-control studies, cross-sectional studies and case series. Studies reporting prevalences of neurological or neuropsychiatric symptoms were synthesised into meta-analyses to estimate pooled prevalence.

Results

13,292 records were screened by at least two authors to identify 215 included studies, of which there were 37 cohort studies, 15 case-control studies, 80 cross-sectional studies and 83 case series from 30 countries. 147 studies were included in the meta-analysis. The symptoms with the highest prevalence were anosmia (43.1% [35.2—51.3], *n*=15,975, 63 studies), weakness (40.0% [27.9—53.5], *n*=221, 3 studies), fatigue (37.8% [31.6—44.4], *n*=21,101, 67 studies), dysgeusia (37.2% [30.0—45.3], *n*=13,686, 52 studies), myalgia (25.1% [19.8—31.3], *n*=66.268, 76 studies), depression (23.0 % [11.8—40.2], *n*=43,128, 10 studies), headache (20.7% [95% CI 16.1—26.1], *n*=64,613, 84 studies), anxiety (15.9% [5.6—37.7], *n*=42,566, 9 studies) and altered mental status (8.2% [4.4—14.8], *n*=49,326, 19 studies). Heterogeneity for most clinical manifestations was high.

Conclusions

Neurological and neuropsychiatric symptoms of COVID-19 in the pandemic's early phase are varied and common. The neurological and psychiatric academic communities should develop systems to facilitate high-quality methodologies, including more rapid examination of the longitudinal course of neuropsychiatric complications of newly emerging diseases and their relationship to neuroimaging and inflammatory biomarkers.

INTRODUCTION

COVID-19 stimulated a global academic response to examine the clinical sequelae and biology of the SARS-CoV-2 virus, including its neurological and neuropsychiatric impact. [1,2] Although the earliest reports naturally highlighted respiratory symptoms, [1] it was quickly recognised that SARS-CoV-2, like other coronaviruses, [2] can affect the central and peripheral nervous system. [3,4]

Many of the very earliest studies of the neurological and neuropsychiatric complications of SARS-CoV-2 infection were small retrospective case reports or series. [7,8] These initial studies were feasible to deliver quickly in the context of a new and poorly understood disease. Case reports [5,6] were superseded by case series [7,8], then case-control [9] and cohort studies [10,11], which suggested significant morbidity and mortality from neurological or neuropsychiatric complications. [12] Currently, large multi-centre prospective studies are underway [13] and already reporting. [14] We anticipate that the quality of evidence, and our knowledge, will improve considerably as these data continue to emerge rapidly.

In response to these signals, we aimed to develop a novel, sustainable platform to evaluate emerging knowledge of the neurology and neuropsychiatry of COVID-19. This also served to assist colleagues in keeping up to date with the literature relevant to their specialty, given the extraordinary volume and pace with which research is being published. In May 2020 we started logging literature on relevant symptoms, clinical associations, and putative underlying mechanisms in our blog, "The neurology and neuropsychiatry of COVID-19", published weekly on the *Journal of Neurology, Neurosurgery and Psychiatry* website. [15] This catalogue of observational studies, reviews, editorials, and mechanistic studies has had over 27,000 global views, but it is essentially a library in which studies are narratively summarised and filed. We recognised the potential value of extending this platform to enable analytic summaries by synthesising evidence in the form of a systematic review and meta-analysis, which we termed **S**ystematically **A**nalyse and **R**eview **S**tudies of **COV**ID-19 **Neuro**logy and neuropsychiatry (**SARS-COV-Neuro**).

In the current report we aimed to answer two questions:

1. What were the key methodological characteristics of the early evolving literature on the neurological and neuropsychiatric consequences of COVID-19?
2. What was the prevalence of neurological and neuropsychiatric complications in COVID-19 patients in observational or interventional studies during this early period of evolving knowledge?

This review is the most comprehensive attempt yet to synthesise the data on the neurological and neuropsychiatric consequences of COVID-19. Other previous works are less up-to-date, incorporate fewer clinical parameters or have limited scope for meta-analysis. [2,16–19]

METHODS

We conducted a systematic review and meta-analysis, based on a registered protocol (PROSPERO ID CRD42020200768) and reported according to PRISMA guidelines [20] (see Supplementary Table 1 for completed PRISMA checklist).

The overall strategy was to combine synonyms for COVID-19 infection with synonyms for neurological and neuropsychiatric syndromes. We searched Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, EMBASE (via Ovid), APA PsycInfo (via OVID) and CINAHL (via EBSCO) from 1st January 2020 to 18th July 2020. Reference lists of other systematic reviews were examined and cross-checked against our database and eligibility criteria. The full search strategy is presented in Supplementary methods 1.

We included any controlled trials, cross-sectional, case-control, cohort studies or case series reporting neuropsychiatric or neurological manifestations in confirmed or clinically suspected COVID-19 patients. We excluded non-English language reports. We excluded studies reporting on fewer than 10 infected patients to avoid the reporting biases common in small studies. Meta-analysis was conducted where a clinical manifestation was reported by three or more eligible studies. Studies were included in the meta-analysis only where they provided representative samples of patients with COVID-19 in whom the point prevalence of neurological or neuropsychiatric features could be estimated; studies where patient inclusion was based on neurological or

neuropsychiatric complications (e.g. only those referred for clinical neuroimaging) were therefore excluded from the meta-analysis.

Screening of titles, abstracts and full texts for each article was conducted by two of the authors (CW, JS, AGR, BC, MB, DH, JB, ER), each blinded to the other's ratings. Where there was disagreement about study inclusion, a third author who was a senior member of the team (AGR, MB, JS or JPR) arbitrated. Zotero was used for reference management and Rayyan QCRI was used for eligibility screening.

Data extraction was performed on structured forms by two authors: one of the authors (ER, DH, BC, CW, HM, JB) entered the data, then a second author (AGR, MB, CH, AS, JB, JS, BC, ER, HM, DA, SR or MFL) ensured the accuracy of each data item by cross-checking against the original source. We recorded the methodological characteristics of studies and the frequency of neurological and neuropsychiatric manifestations reported by each study (see full list of variables extracted in Supplementary table 2). Where data were available for an outcome at follow-up rather than during the acute illness, prevalences at follow-up were presented separately. Where studies reported asthenia as a manifestation, this was coded as fatigue; where a paper reported both asthenia and fatigue, only the figures for fatigue were used.

Levels of evidence were assessed by use of the Oxford Centre for Evidence-based Medicine Levels of Evidence. [21] Quality of studies and risk of bias were assessed using the Newcastle-Ottawa Scale, including its adaptation for cross-sectional studies. [22,23] Quality was assessed by two authors in parallel with arbitration by a third author in cases of disagreement.

For the systematic review, we descriptively reported methodological characteristics of the evolving literature with analytic statistical tests where appropriate. All eligible studies were listed in a table with their study design, demographics and main findings.

For the meta-analysis, the primary outcome was point prevalence of neurological and neuropsychiatric manifestations with 95% confidence intervals. Given the potential for estimation errors with a double-arcsine

transformation of proportion, [24] we used the *metafor* package in *R* version 4.0.2 to calculate generalised linear mixed models (GLMMs) for each outcome, [25,26] before then using the double arcsine transformation as a comparative sensitivity analysis. [27,28] Outcome proportions were transformed using a logit transformation. Between-study heterogeneity was calculated using the I^2 statistic. We planned *a priori* to analyse the following subgroups: retrospective or prospective design, method of SARS-CoV-2 diagnosis, severity of COVID-19, and time-point in relation to infection. Ultimately, we only conducted subgroup analysis for retrospective or prospective design and severity of COVID-19 because of lack of consistently presented data for the other subgroups. In addition, due to high heterogeneity, we conducted an additional exploratory subgroup analysis examining country of origin. Subgroup analyses were conducted on the five clinical manifestations most commonly studied: anosmia, dysgeusia, fatigue, myalgia, and headache. Significance testing was performed to assess differences in reported frequencies by sub-group.

RESULTS

De-duplicated searches returned a total of 13,292 titles. Abstract and full text screening generated a final list of 215 eligible studies (Figure 1). A complete list of all included studies is presented in Supplementary Table 3.

Methodological characteristics of the literature

Methodological characteristics of the studies are summarised in Table 1. The most common study type was a case series (83 studies, 38.6%). To explore whether designs evolved in the first half of 2020, we considered studies that started data collection in December 2019 to February 2020 to be earlier and those between March and July 2020 to be later. Among the earlier studies, 37 out of 65 (57%) were case series, whereas this proportion fell to 40 out of 115 (34.8%) among the subsequent studies, p=0.004. Change in study design is illustrated in Figure 2. Overall, therefore, there was at least a two-month lag period from the first official report of the outbreak in Wuhan by the Chinese authorities (31st Dec 2019) to the first group of cohort studies.

Studies were written by a primary author affiliated with an institution from a total of 30 countries globally (Figure 3). The most frequent contributors were China *(*n=50 studies), USA (n=32 studies), Italy (n=28 studies), and France *(*n=23 studies). All but three studies starting recruitment in Jan 2020 were located in China. Globally, most studies

(138, 64.2%) were single-centre without a significant shift towards multi-centre studies as the pandemic accelerated: where collection date was clear, 44/65 (67.7%) of earlier studies were single-centre, compared to 72/115 (62.6%) of later studies (p=0.49).

Studies were predominantly in hospitalised patients (118 studies, 54.9%) and during the acute illness (144, 67.0%). There were a total of 105,638 subjects. Number of subjects in each study varied between 10 and 40,469 (median 101, IQR 196). There were 18 studies with 1000 or more subjects.

There was evidence for ethical approval and informed consent in most studies, but this was waived in a minority, frequently because of the particular circumstances of the pandemic.

Quality assessment found only 23 (10.7%) studies to be of high quality, 98 (45.6%) were of moderate quality and 94 (43.7%) were of low quality.

Table 1: Methodological characteristics of included studies

Study characteristic	**Number of studies (n=215)**	**%**
Study design		
- Case series	83	38.6
- Cross-sectional	80	37.2
- Case-control	15	7.0
- Cohort	37	17.2
Time-point relative to outcomes		
- Prospective	91	42.3
- Retrospective	119	55.3
- Unclear	5	2.3
OCEBM Level of Evidence		
- Random sampled study (Level 1)	2	0.9
- Local, non random sample (Level 3)	150	69.8
- Case series (Level 4)	63	29.3
Number of centres		
- Single-centre	138	64.2
- Multicentre	77	35.8
Setting		
- Hospital inpatients	118	54.9

- Outpatients	46	21.4
- Emergency department attendances	3	1.4
- Mixed treatment settings	39	18.1
- Not stated	9	4.2
Diagnostic method		
- PCR	157	73.0
- Other laboratory technique	18	8.4
- Radiology	2	0.9
- Clinical opinion	6	2.8
- Mixed method	9	4.2
- Not stated	22	10.2
Disease stage		
- Acute illness	144	67.0
- After hospital discharge or recovery	11	5.1
- Deceased	1	0.5
- Mixed	6	2.8
- Not stated	53	24.7
Ethical approval		
- Granted	156	72.6
- Exempt	12	5.6
- Not stated	47	21.9
Informed consent		
- Required	57	26.5
- Waived	40	18.6
- Not stated	118	54.9
NOS quality assessment		
- High	23	10.7
- Moderate	98	45.6
- Low	94	43.7

Prevalence of neuropsychiatric and neurological manifestations

Twenty neurological or neuropsychiatric manifestations were estimated by at least 3 studies, such that we included 147 studies (reporting on 99,905 infected patients) in the meta-analysis. Overall prevalences are shown in Table 2 with forest plots available in Figure 4 and Supplementary Figures 1-20. The most *often-studied* symptoms were headache (examined in 84 studies, *n*=64,613), myalgia (76 studies, *n*=66,268), fatigue (67 studies, n=21,101), anosmia (63 studies, 15,975) and dysgeusia (52 studies, *n*=13,686). The most *prevalent* symptoms were anosmia (43.1% [35.2-51.3], *n*=15,975 in 63 studies), weakness (40.0% [27.9-53.5], *n*=221 in 3 studies), fatigue (37.8% [31.6-44.4], *n*=21,101 in 67 studies) dysgeusia (37.2% [29.8-45.3], *n*=13,686 in 52 studies) and myalgia (25.1% [19.8-31.3], *n*=66,268 in 76 studies). Sleep disorder was a broad term that was used in a number of studies; of the 8 studies

reporting a sleep problem, 2 specified insomnia, 1 sleep impairment and the remainder an unspecified sleep disorder.

Between-study heterogeneity was mostly high with I^2≥90% for 13 manifestations, ≥50% and <90% for 2 manifestations and <50% for 5 manifestations. Most symptoms were recorded merely as 'present' or 'absent' by study authors. The robustness of the main analyses was assessed by repeating the analyses on headache, myalgia, anosmia, fatigue and dysgeusia using the standard random-effects model for meta-analysis with the Freeman-Tukey double arcsine transformation. The results were in line with the main analysis (see Supplementary table 4).

Table 2: Overall meta-analytic estimates of point prevalence of neurological or neuropsychiatric symptoms

Symptom/Syndrome	Studies	*n*	Point prevalence (%)	95% CI	I^2
Headache	84	64,613	20.7	16.1 - 26.1	99.0%
Myalgia	76	66,268	25.1	19.8-31.3	99.1%
Fatigue	67	21,101	37.8	31.6 – 44.4	98.7%
Anosmia	63	15,975	43.1	35.2 – 51.3	98.8%
Dysgeusia	52	13,686	37.2	29.8 – 45.3	98.6%
Dizziness/vertigo	26	47,619	6.4	4.0 - 10.0	97.1%
Altered mental status	19	49,326	8.2	4.4 - 14.8	99.0%
Anosmia at follow-up	11	3,182	11.8	5.5 – 23.5	98.5%
Depression	10	43,128	23.0	11.8 - 40.2	99.3%
Anxiety	9	42,566	15.9	5.6 - 37.7	99.5%
Sleep disorder	8	42,221	23.5	12.0 - 40.9	98.9%
Ischaemic stroke	8	5,258	1.9	1.3 – 2.8	61.7%
Other CVD	6	43,701	1.6	0.3 – 7.9	98.7%
Dysgeusia at follow-up	6	2,065	11.7	5.1– 25.0	96.7%
Seizure	5	41,929	0.06	0.06 – 0.07	0.0%

Haemorrhagic stroke	5	3,074	0.4	0.3 - 0.7	0.0%
Visual defect	5	678	3.0	1.9 - 4.5	0.0%
Hearing impairment	4	557	2.0	1.1 – 3.5	0.0%
Tinnitus	4	455	3.5	1.7 – 7.4	51.8%
Weakness	3	221	40.0	27.9 – 53.5	45.4%

Subgroup analyses:

Subgroup analysis was conducted by study design (prospective and retrospective; Table 3), case severity (outpatient, mixed non-severe, non-severe inpatients, severe but not admitted to ITU and admitted to ITU; Table 4) and country of origin (Supplementary Table 5). For headache, myalgia, anosmia and dysgeusia, there were significantly higher reported rates in prospective studies than in retrospective studies. In the severity subgroup analysis, compared to the ITU group, headache was more common in mixed non-severe and outpatient populations (p<0.001); myalgia was more common in mixed non-severe and outpatient populations (p=0.04 and <0.001 respectively); anosmia was more common in mixed non-severe and outpatient populations (p=0.05 and 0.04, respectively), and dysgeusia was more common in mixed non-severe populations (p=0.02); there were no significant differences between groups for fatigue.

Table 3: Subgroup analysis by study design for 5 most commonly studied clinical manifestations

Manifestation	**Retrospective**			**Prospective**			***p***
	Studies	**Prevalence (95% CI)**	***I*²**	**Studies**	**Prevalence (95% CI)**	***I*²**	
Headache	46	11.1 (8.0-15.3)	98.3	34	37.5 (29.3-46.5)	98.2	<0.001
Myalgia	42	16.8 (11.8-23.1)	99.1	30	38.6 (29.6-48.5)	98.5	<0.001
Anosmia	16	22.3 (11.4-39.0)	98.0	44	50.8 (42.5-59.1)	98.6	<0.005
Dysgeusia	13	22.3 (11.0-40.2)	97.8	36	42.4 (34.4-50.9)	98.5	0.04
Fatigue	41	33.5 (26.1-41.8)	98.8	24	43.3 (33.2-54.1)	98.5	0.14

Table 4: Subgroup analysis by case severity for 5 most commonly studied clinical manifestations

Manifestation	Outpatients			Mixed non-severe			Non-severe inpatients			Severe non-ITU			Includes ITU		
	Studies	Prevalence (95% CI)	I^2	Studies	Prevalence (95% CI)	I^2	Studies	Prevalence (95% CI)	I^2	Studies	Prevalence (95% CI)	I^2	Studies	Prevalence (95% CI)	I^2
Headache	14	44.0 (32.8-55.8)	96.7	20	41.9 (30.9-53.7)	99.1	12	8.9 (3.5-20.8)	97.9	16	12.1 (7.9-17.9)	94.3	19	10.8 (7.1-16.2)	96.7
Myalgia	14	46.7 (36.8-56.8)	95.7	19	40.9 (28.2-55.0)	99.3	9	9.9 (3.6-24.4)	98.6	13	11.3 (6.2-19.5)	97.0	19	20.4 (14.7-27.6)	97.9
Anosmia	17	51.7 (42.2-61.1)	97.1	22	51.2 (40.8-61.4)	98.2	8	24.1 (8.2-53.1)	98.0	8	35.9 (10.4-73.0)	99.0	6	22.3 (11.0-40.1)	95.2
Dysgeusia	17	45.2 (34.1-56.8)	98.0	14	50.2 (37.9-62.4)	98.3	6	21.6 (10.6-39.2)	95.3	7	25.3(10.5-49.5)	97.9	6	17.3 (7.8-33.8)	94.8
Fatigue	10	55.1 (43.3-66.3)	97.8	13	42.2 (29.3-56.3)	98.1	10	30.7(16.7-49.4)	98.0	16	24.0 (15.9-34.4)	97.3	15	44.3 (31.5-58.0)	99.1

DISCUSSION

To our knowledge, this is the largest and most comprehensive systematic review of the neurological and neuropsychiatric manifestations of COVID-19. We identified 215 studies, published between January and July 2020, with a total population of 105,638, containing a large variation in the size of studies. We uncovered some general findings about the methodological characteristics of early-evolving literature in response to a novel pathogen. Studies varied substantially in design, geographical location, treatment setting, illness stage, sample size, diagnostic method and clinical manifestations studied. More studies were retrospective than prospective and case series comprised a significant minority of the early literature. In terms of country of origin, after the first few

weeks of the pandemic in which the literature was dominated by studies from China, a wide range of research was produced from 30 countries, among which less economically developed countries were mostly absent. Most studies confirmed formal ethical review and most required informed consent, but these requirements were waived in a subset of cases.

In our review we summarise point prevalence of 20 neurological and neuropsychiatric complications of COVID-19. The most frequently *studied* symptoms were heavily weighted towards non-specific features of systemic illness, such as headache, myalgia, fatigue, anosmia and dysgeusia, which are unlikely to be 'primary' neurological symptoms. It was predominantly these more non-specific symptoms that were found to have the highest prevalences, ranging from 20.7% [16.1-26.1] to 43.1% [35.2-51.3] (headache and anosmia, respectively). Of note, more specific neurological and neuropsychiatric symptoms such as altered mental status, depression, anxiety, sleep disorder, stroke and seizures were less frequently studied. However, the core psychiatric disorders of depression (23.0% [11.8-40.2]) and anxiety (15.9% [5.6-37.7]) appeared to be highly prevalent. The reported prevalence of major neurological disorders such as ischaemic stroke (1.9% [1.3-2.8]), haemorrhagic stroke (0.4% [0.3-0.7%]) and seizure (0.06% [0.06-0.07]) were substantially lower. Subgroup analyses suggested that study design (prospective versus retrospective), severity of illness and country of origin of a study affected the prevalence figures obtained. Importantly, for myalgia, fatigue, anosmia and dysgeusia, prevalence rates were substantially higher in prospective studies compared to retrospective studies.

There are several limitations to our study, relating both to the quality of the underlying evidence and to the data synthesis. Major limitations in the study design were the frequent absence of comparison groups, limiting conclusions about the specificity of symptoms to COVID-19; retrospective study designs, which meant that only those symptoms that happened to be enquired about were included; and small sample sizes, which risk reporting bias. In terms of populations, the frequent use of hospital inpatients is unrepresentative of the majority of patients with COVID-19, who are not admitted to hospital. Regarding clinical manifestations, the main limitations were reliance on self-report measures, which risks recall biases; lack of baseline assessment, which prevents estimation of incidence; and a focus on non-specific neuropsychiatric symptoms rather than on major neurological and neuropsychiatric disorders. In addition, some of the most commonly studied symptoms (such as weakness and

fatigue) have some conceptual overlap, [29] so it is possible that the prevalences found in this review may be underestimated. Terminology connoting altered mental status varied, with terms such as delirium and encephalopathy chosen in different studies, despite existing recommendation on standardisation of the nomenclature. [30] The finding that only 14.4% of the studies were of high quality limits the strength of any conclusions that can be drawn. In terms of the data synthesis, we were limited by excluding studies not published in English, which may particularly have reduced the number of important studies included from China, and the generalisability of our results may be limited by the geographical scope of the studies. The rapidly evolving literature means that any review on this subject risks becoming out of date. Furthermore, the high heterogeneity between studies, even after subgroup analyses, suggests that variation in populations, outcomes and measurement techniques might account for much of the differences between studies. Finally, the cross-sectional nature and the focus on acute presentations of most studies reported to-date limit our ability to draw conclusions about the long-term impact of neuropsychiatric post-COVID-19 symptom burden. Future well-designed prospective cohorts, such as the UK-based Post-hospitalisation COVID-19 study (https://www.phosp.org/), may be able to address this gap in the knowledge.

There are several implications of this review for future research. Firstly, while retrospective studies are important in identifying associations in large patient populations, they are likely to underestimate the prevalence of important symptoms. This may particularly be the case with some neuropsychiatric disorders such as depression and delirium, which are known to be generally under-recognised. [31,32] Therefore, even in the context of a pandemic, there is a need to improve the speed with which the academic community can produce prospectively designed studies, which are based on registered protocols and use validated and objective measures. Standardised case definitions and record forms for common neurological manifestations of viral infections were produced by the Brain Infections Global Network from early in the pandemic [33] and made freely available. These have been modified by other international groups, [34] and are being incorporated into the WHO case report forms. [35] More studies are required of those not admitted to hospital and the timing of neurological and neuropsychiatric symptoms relative to diagnosis must be specified. In terms of the clinical manifestations, many of the common and debilitating neurological symptoms (such as headache, myalgia and anosmia) were assessed systematically by a large number of studies, allowing for meaningful prevalence estimates and subgroup analyses. However, some

severe neurological and neuropsychiatric disorders, such as depression, stroke and seizures, received comparatively scant attention and would benefit from similar study. Finally, the occasional waivers of ethical review and the more frequent waivers of informed consent in these studies illustrates that some aspects of study review may be overly burdensome - and therefore potentially neglected - during a pandemic. Whilst we acknowledge the need for proper ethical and institutional oversight, COVID-19 may be an opportunity for this process to be streamlined across the field, especially for non-interventional studies, where the risks to participants are minimal, so that studies during a pandemic (and beyond) can start quickly and inform urgent policy needs.

There are several clinical implications of our study. Firstly, practitioners should be aware that neurological and neuropsychiatric symptoms are very common with four (anosmia, weakness, dysgeusia and fatigue) estimated to occur in more than 30% of patients. Secondly, these non-specific neurological and neuropsychiatric symptoms appear to be the most common. Neuropsychiatric disorders such as anxiety and depression occupy an intermediate space with prevalence of between 15.9% [5.6-37.7] and 23.0% [11.8-40.2]), while major neurological disorders such as stroke and seizures are much rarer. However, because of the very high number of individuals infected with SARS-CoV-2 worldwide, even less frequent symptoms may still result in a substantial increase in the burden of disease. This means that services for those with common mental illnesses and neurological rehabilitation should be resourced and equipped for an increase in case numbers. Many of these disorders can become chronic, so the neurological and psychiatric impact of the pandemic may substantially outlast the current phase. Thirdly, given the multitude of symptoms reported, neurological and neuropsychiatric comorbidity is likely to be the norm rather than the exception in COVID-19, so there must be accessible advice and input from these specialties for patients who are acutely unwell. Finally, although there is a relative lack of data on non-hospitalised patients, the data available suggest that several symptoms, such as anosmia, dysgeusia, fatigue, headache and myalgia, are common even among those with milder illness. Although long-term evidence from this earliest literature was sparse, it gives some initial indication that the symptoms described in 'long COVID' may be a continuation of some of those experienced in the acute phase of the illness. [36] Long COVID is, however, likely to be a heterogeneous entity with a multifactorial aetiology, including viral persistence, inflammatory changes, physical deconditioning and psychological factors. Our finding that the most frequently reported neurological symptoms actually occurred more frequently in those with less severe COVID-19 suggests that neurological symptoms are not necessarily

correlated with systemic or respiratory symptoms, implying that different mechanisms or timing of mechanisms may be involved.

In conclusion, COVID-19 is accompanied by a wide range of neurological and neuropsychiatric symptoms from the common, such as fatigue and anosmia, to the more infrequent but severe, such as stroke and seizure. There is substantial psychiatric morbidity, but a lack of control groups limits to what extent causality can be attributed.

Author Contributions

TRN and AGR conceived the study. AGR and JPR led and coordinated the study. JPR wrote the manuscript. MB compared the work to other systematic reviews. CW. BC, MB, JS, DH, ERR, LT, AGR and JB screened studies for eligibility. AGR, JPR, JS and MB consulted on study inclusion. CW, BC, DH, HM, ERR, LT, SR, RDS and JB extracted data. JB, MB, JS, DH, HM, ERR, LT, SR, AS, RDS, CKH, MFL, DA, AGR and BC checked data extraction AGR conducted OCEBM ratings. JPR calculated descriptive statistics. CW and KJ conducted the meta-analysis, supported by HH. CW and DH created figures. JPR, BC, MB, JS, DH, HM, LT, SR, AS, RDS, CKH, MFL, VS, ZH, SC, EB, DW, TAP, ME, IK, TRN, AGR and JB conducted quality assessment. JPR and AS supervised and arbitrated quality assessment. JB made the PRISMA flowchart. JPR, MB and JB sorted references. JB checked adherence to PRISMA guidelines. AGR, JPR, JB, ERR, VS and MB drafted the manuscript. JPR, MB, JS and JB checked the completed manuscript. ERR and ZH created tables. MFL sorted funding statements. JPR and EB formatted the manuscript. DW, ME, IK, TS, BDM, TRN, AGR and TAP provided senior review of the manuscript. JPR and AGR are responsible for the overall content of the study.

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Competing Interests

Jonathan Rogers has received payment by the Alberta Psychiatric Association for a lecture and has held one unpaid advisory meeting with representatives from Promentis Pharmaceuticals Inc regarding drug development. Lucretia Thomas is in receipt of a bursary as part of the Royal College of Psychiatrists PsychStar scheme. By winning a prize from the Royal College of Psychiatrists, she has received prize money and free attendance at a meeting. She is President of the University of Birmingham Psychiatry Society. All other authors declare no competing interests. Ivan Koychev has been supported by the Medical Research Council through Dementias Platform UK and by the National Institute for Health Research through the Oxford Health Biomedical Research Centre. He has been a medical advisor to Mantrah Ltd and Sharp Therapeutics Ltd, digital technology start-ups. He holds stock options in Sharp Therapeutics Ltd. Tom Solomon is supported by the National Institute for Health Research (NIHR) Health Protection Research Unit in Emerging and Zoonotic Infections (Grant Nos. IS-HPU-1112-10117 and NIHR200907), NIHR Programme Grant for Applied Research (No. RP-PG-0108-10,048), NIHR Global Health Research Group on Brain Infections (No. 17/63/110), and the European Union's Horizon 2020 research and innovation program ZikaPLAN (Preparedness Latin America Network), grant agreement No. 734584. He receives royalties from Oxford University Press, Elsevier, Liverpool University Press and Cambridge University Press. He is a consultant for the MHRA Vaccine Benefit Risk Expert Working Group. He filed for a patent on a test for bacterial meningitis based on a blood test (No. GB1606537.7 14th April 2016). He was on the Data Safety Monitoring Committee of the GSK Study to Evaluate the Safety and Immunogenicity of a Candidate Ebola Vaccine in Children GSK3390107A (ChAd3 EBO-Z) vaccine. He chaired the Siemens Healthineers Clinical Advisory Board (1) Data safety monitoring board: Study of Ebola vaccine ChAd3-EBO-Z - Commercial entity. He holds shares in Medefer Solutions. Benedict Michael has received payment for a lecture for Valneva. All other authors declare no competing interests.

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Clinical Research Training Fellowship (no award/grant number). ME and TS are supported by the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections at University of Liverpool in partnership with Public Health England, in collaboration with Liverpool School of Tropical Medicine and the University of Oxford (NIHR200907). IK is supported by the Medical Research Council (Dementias Platform UK Grant MR/L023784/2) and the Oxford Health Biomedical Research Centre (no award/grant number). DA is supported by the Faculty of Medicine, Chulalongkorn University, Thailand (no award/grant number). AGR is supported by the Royal College of Physicians of Edinburgh, John, Margaret, Alfred and Stewart Sim Fellowship 2018-2020 (no award/grant number). BDM is supported by the UKRI/MRC COVID-CNS Grant (MR/V03605X/1), the MRC-CSF (MR/V007181/1), and the MRC/AMED grant (MR/T028750/1). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Ethics Approval

This study is secondary research that synthesised the results of original papers; as such, it is exempt from ethical approval.

Figures

Figure 1: PRISMA flow diagram

Figure 2: Study design trends

Figure 3: Geographical distribution of studies

Figure 4: Forest plots for prevalence of five most commonly studied symptoms, subgrouped by disease severity. A – headache. B – myalgia. C – fatigue. D – anosmia. E – dysgeusia.

Supplementary material

Supplementary methods 1: Full search strategy

Supplementary table 1: PRISMA checklist

Supplementary table 2: List of extracted variables

Supplementary table 3: Full list of included studies

Supplementary table 4: comparison of proportion estimation models

Supplementary table 5: Subgroup analysis by country of origin

Supplementary figures 1-20: Forest plots for individual symptoms

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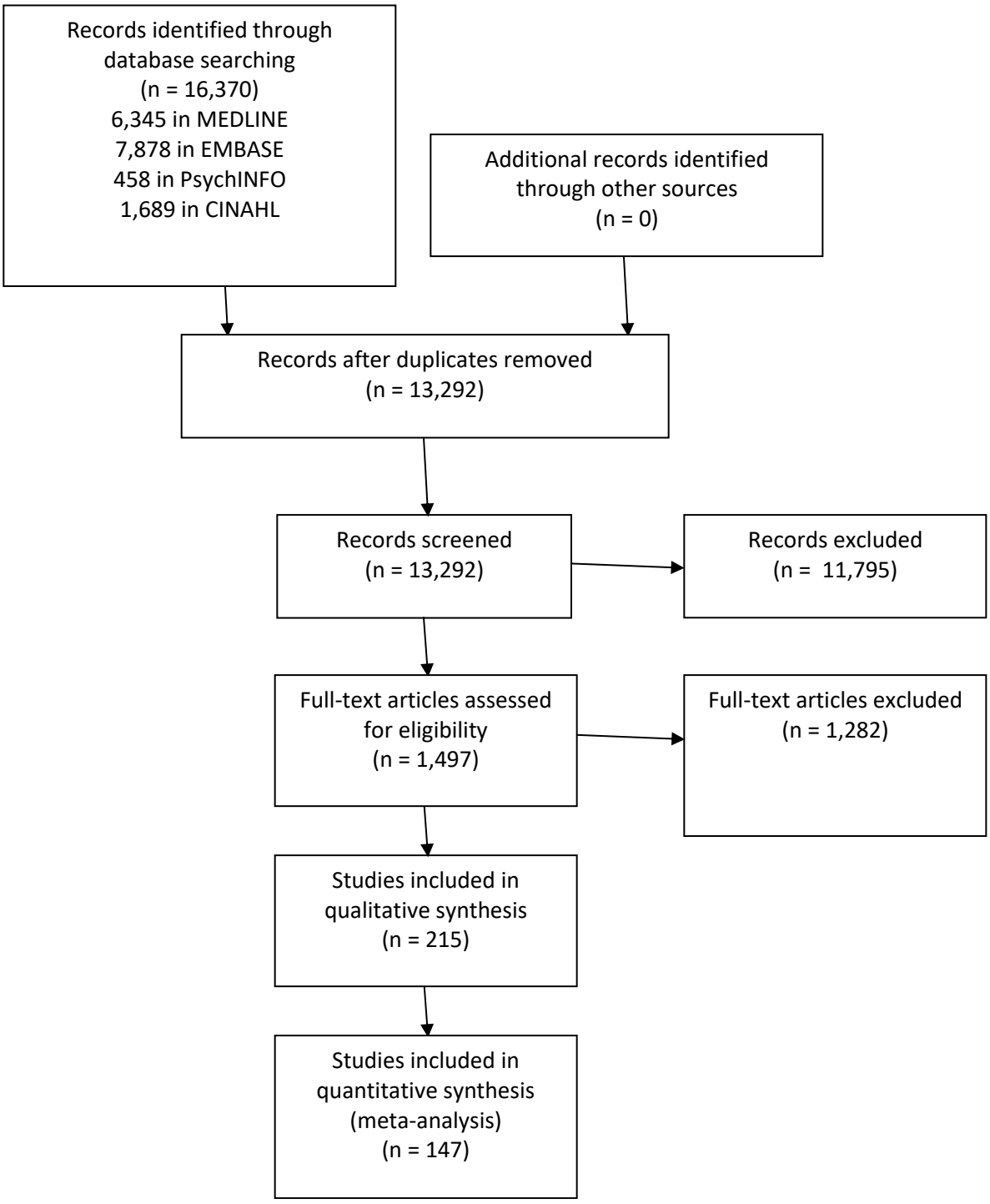
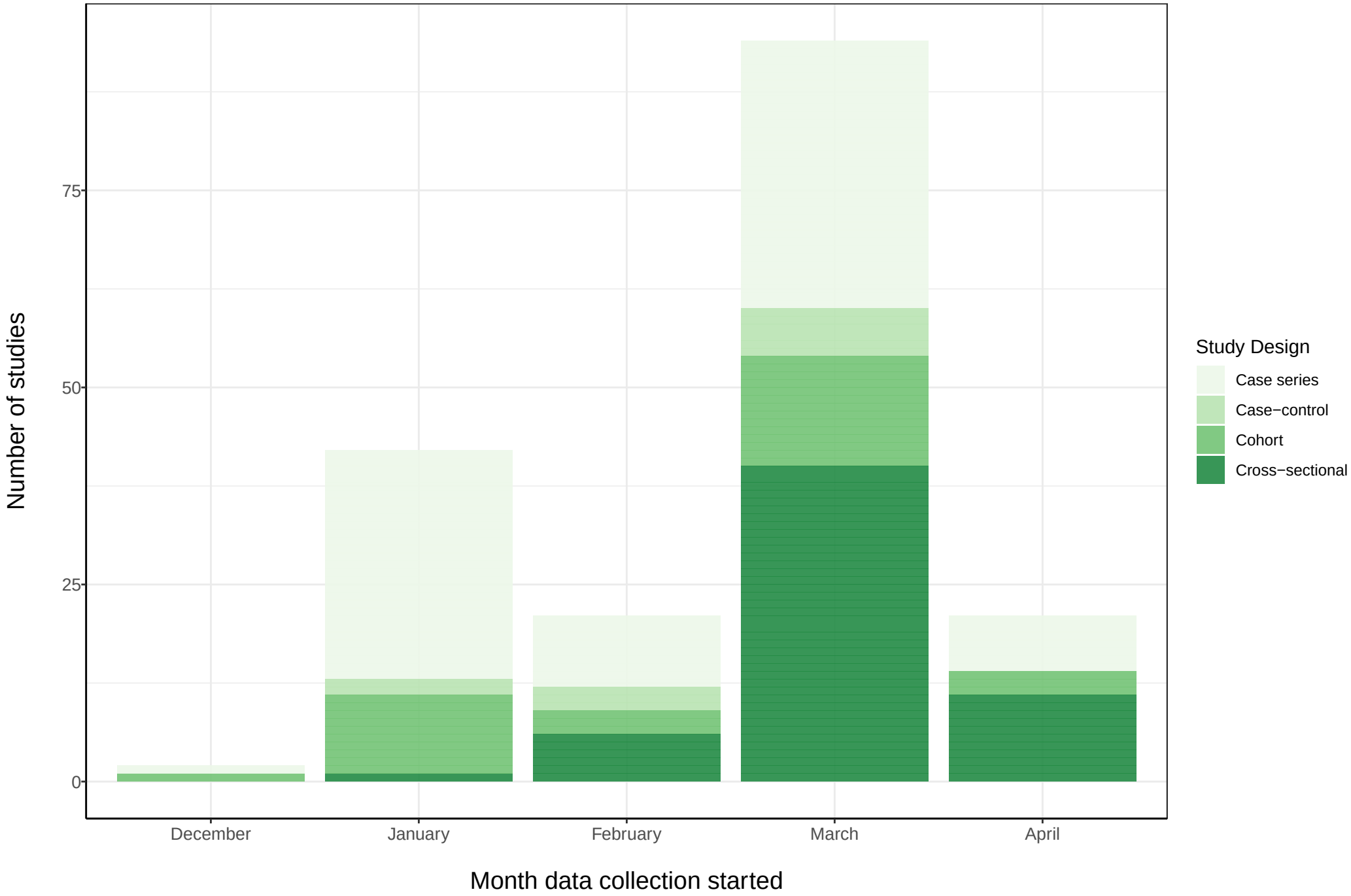
Figure 1: PRISMA flow diagram

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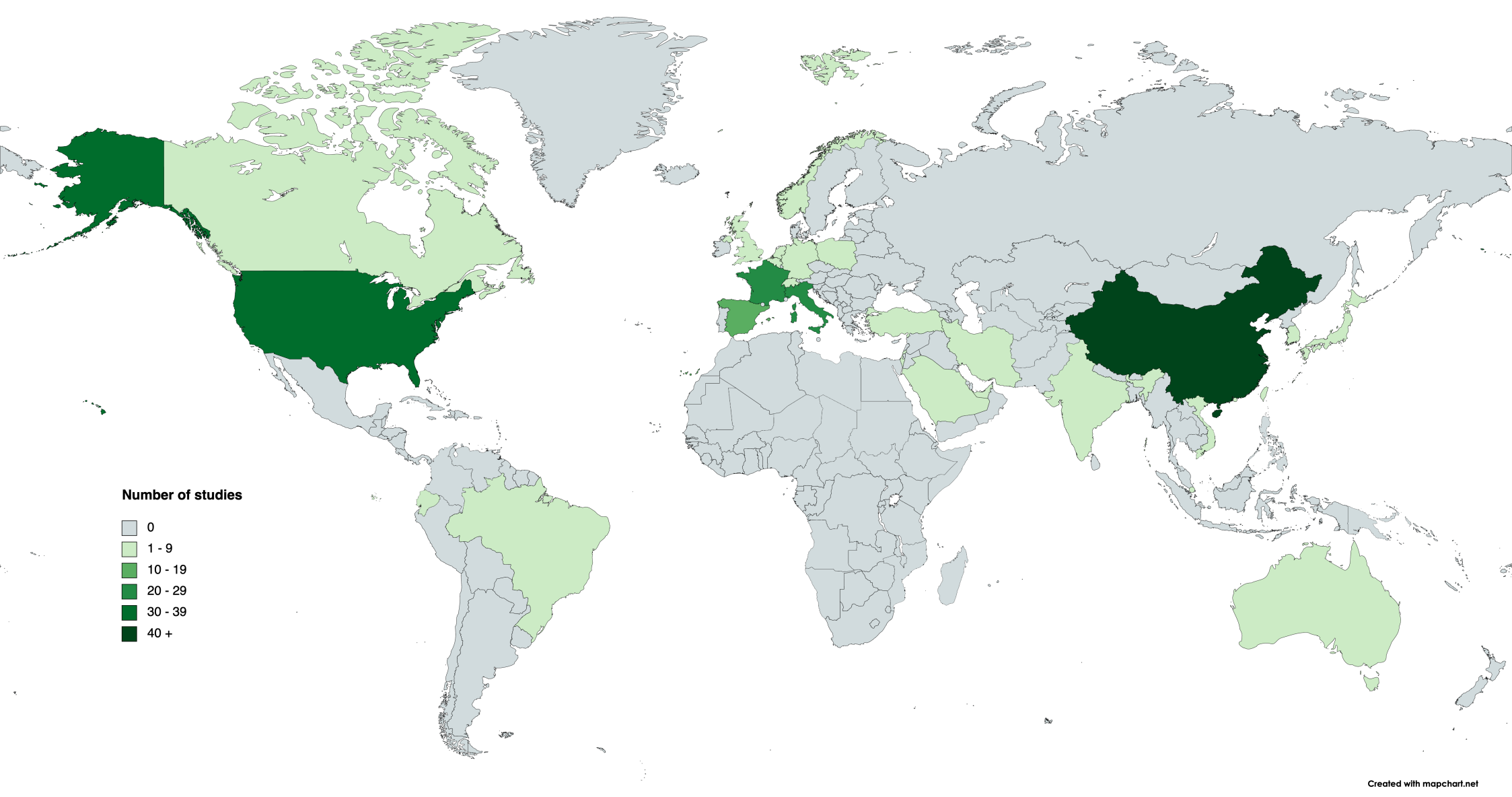
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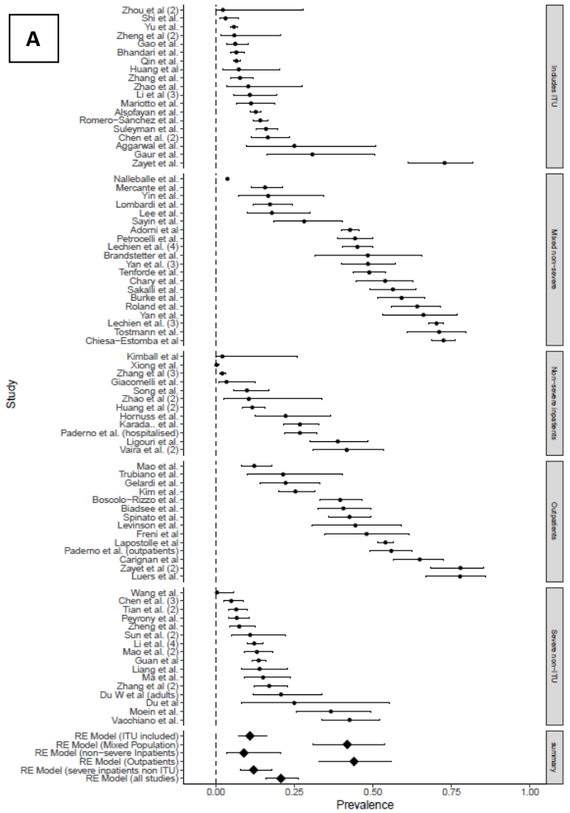
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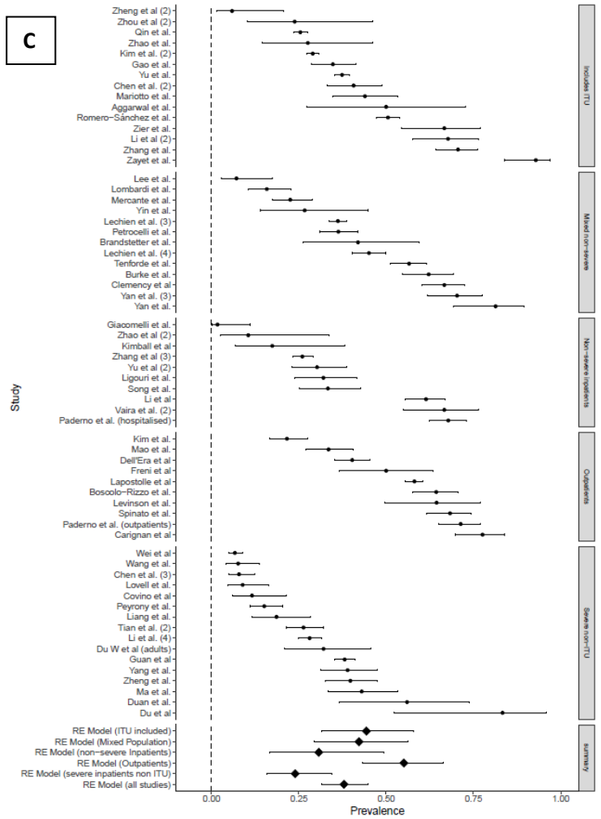
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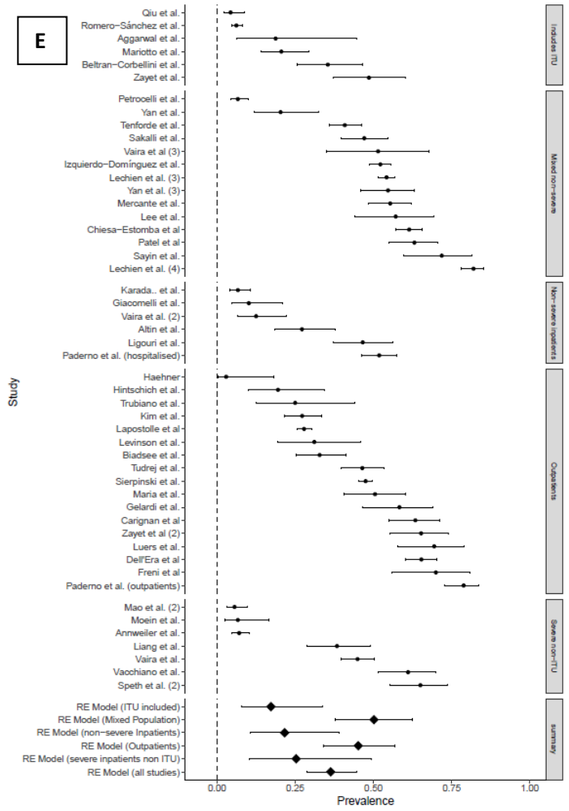
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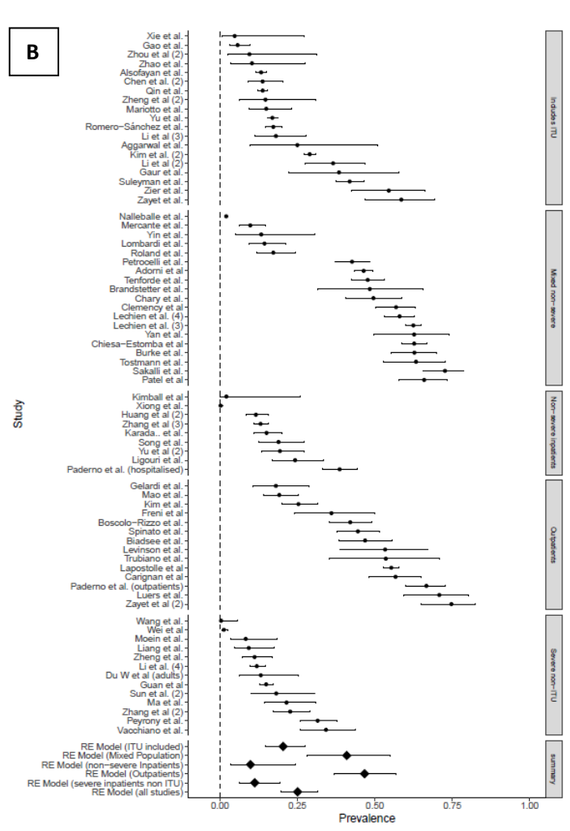
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Zayet et al (2)
Wang et al.
Wei et al
Moein et al.
Liang et al.
Zheng et al.
Li et al. (4)
Du W et al (adults)
Guan et al
Sun et al. (2)
Ma et al.
Zhang et al (2)
Peyrony et al.
Vacchiano et al.
RE Model (ITU included)
RE Model (Mixed Population)
RE Model (non−severe Inpatients)
RE Model (Outpatients)
RE Model (severe inpatients non ITU)
RE Model (all studies)
Includes ITU
Mixed non−severe
Non−severe inpatients
Outpatients
Severe non−ITU
summary
0.00
0.25
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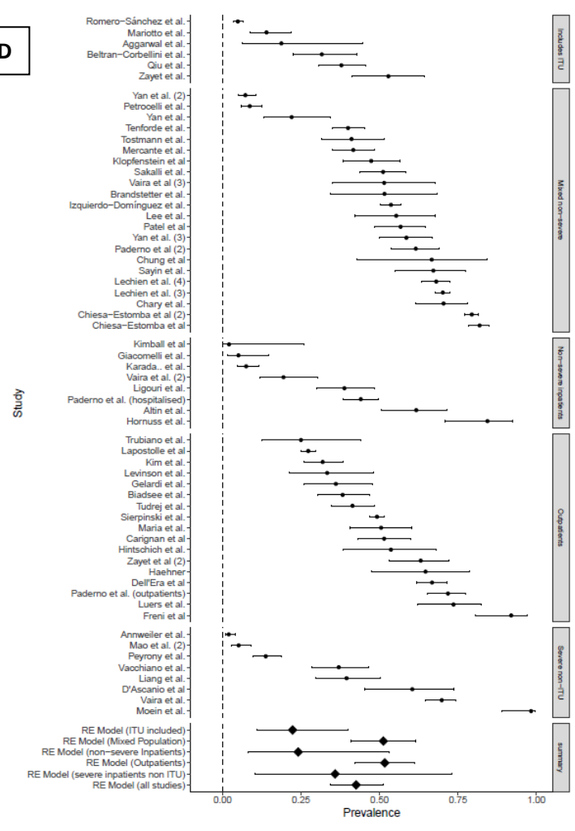
0.75
1.00
Prevalence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Study
Romero−Sánchez et al.
Mariotto et al.
Aggarwal et al.
Beltran−Corbellini et al.
Qiu et al.
Zayet et al.
Yan et al. (2)
Petrocelli et al.
Yan et al.
Tenforde et al.
Tostmann et al.
Mercante et al.
Klopfenstein et al.
Sakalli et al.
Vaira et al (3)
Brandstetter et al.
Izquierdo−Domínguez et al.
Lee et al.
Patel et al
Yan et al. (3)
Paderno et al (2)
Chung et al
Sayin et al.
Lechien et al. (4)
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Chary et al.
Chiesa−Estomba et al (2)
Chiesa−Estomba et al
Kimball et al
Giacomelli et al.
Karada.. et al.
Vaira et al. (2)
Ligouri et al.
Paderno et al. (hospitalised)
Altin et al.
Hornuss et al.
Trubiano et al.
Lapostolle et al
Kim et al.
Levinson et al.
Gelardi et al.
Biadsee et al.
Tudrej et al.
Sierpinski et al.
Maria et al.
Carignan et al
Hintschich et al.
Zayet et al (2)
Haehner
Dell'Era et al
Paderno et al. (outpatients)
Luers et al.
Freni et al
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Mao et al. (2)
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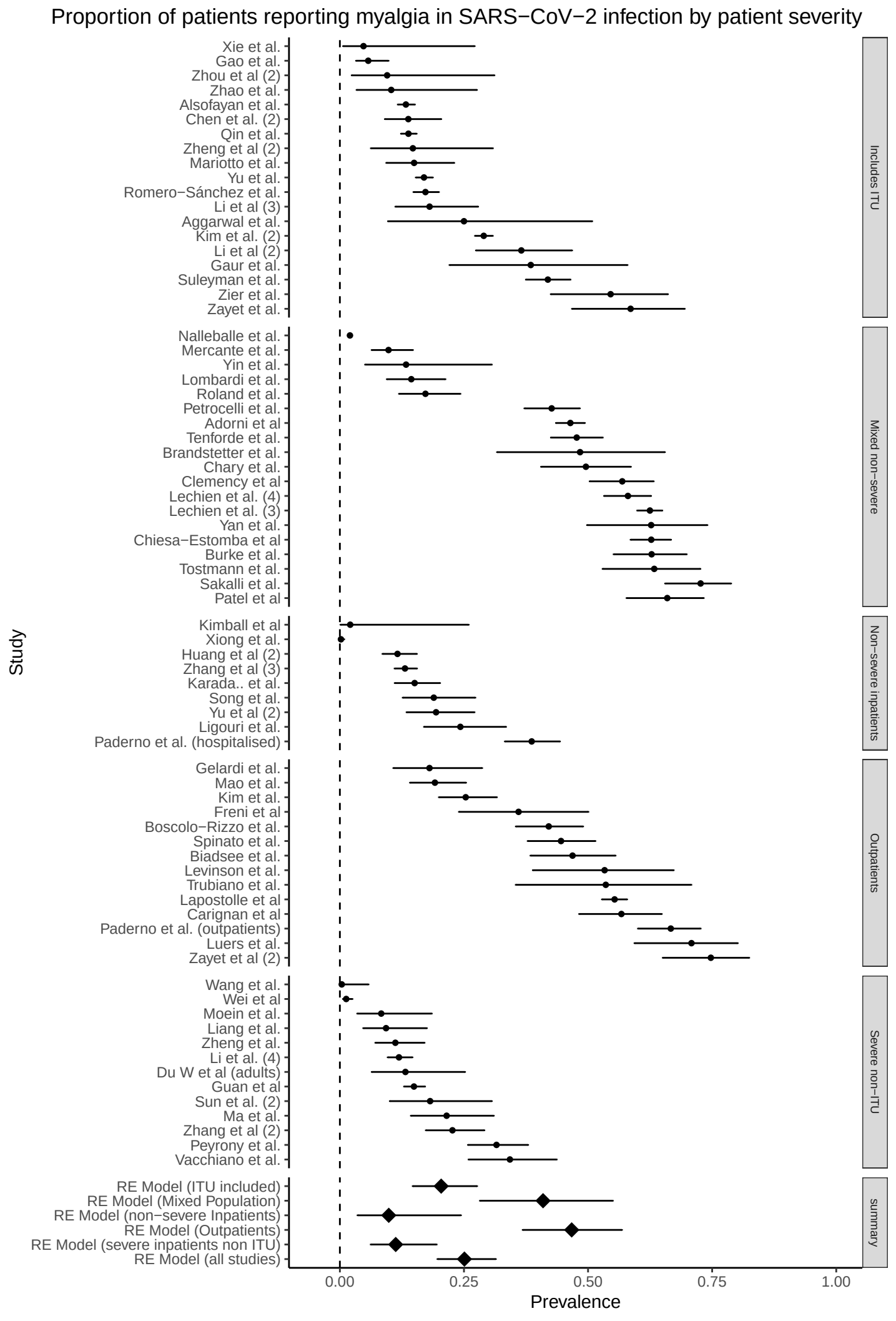
Prevalence


Proportion of patients reporting myalgia in SARS−CoV−2 infection by patient severity
Study
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Gao et al.
Zhou et al (2)
Zhao et al.
Alsofayan et al.
Chen et al. (2)
Qin et al.
Zheng et al (2)
Mariotto et al.
Yu et al.
Romero−Sánchez et al.
Li et al (3)
Aggarwal et al.
Kim et al. (2)
Li et al (2)
Gaur et al.
Suleyman et al.
Zier et al.
Zayet et al.
Includes ITU
Nalleballe et al.
Mercante et al.
Yin et al.
Lombardi et al.
Roland et al.
Petrocelli et al.
Adorni et al
Tenforde et al.
Brandstetter et al.
Chary et al.
Clemency et al
Lechien et al. (4)
Lechien et al. (3)
Yan et al.
Chiesa−Estomba et al
Burke et al.
Tostmann et al.
Sakalli et al.
Patel et al
Mixed non−severe
Kimball et al
Xiong et al.
Huang et al (2)
Zhang et al (3)
Karada.. et al.
Song et al.
Yu et al (2)
Ligouri et al.
Paderno et al. (hospitalised)
Non−severe inpatients
Gelardi et al.
Mao et al.
Kim et al.
Freni et al
Boscolo−Rizzo et al.
Spinato et al.
Biadsee et al.
Levinson et al.
Trubiano et al.
Lapostolle et al
Carignan et al
Paderno et al. (outpatients)
Luers et al.
Zayet et al (2)
Outpatients
Wang et al.
Wei et al
Moein et al.
Liang et al.
Zheng et al.
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Severe non−ITU
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RE Model (Outpatients)
RE Model (severe inpatients non ITU)
RE Model (all studies)
summary
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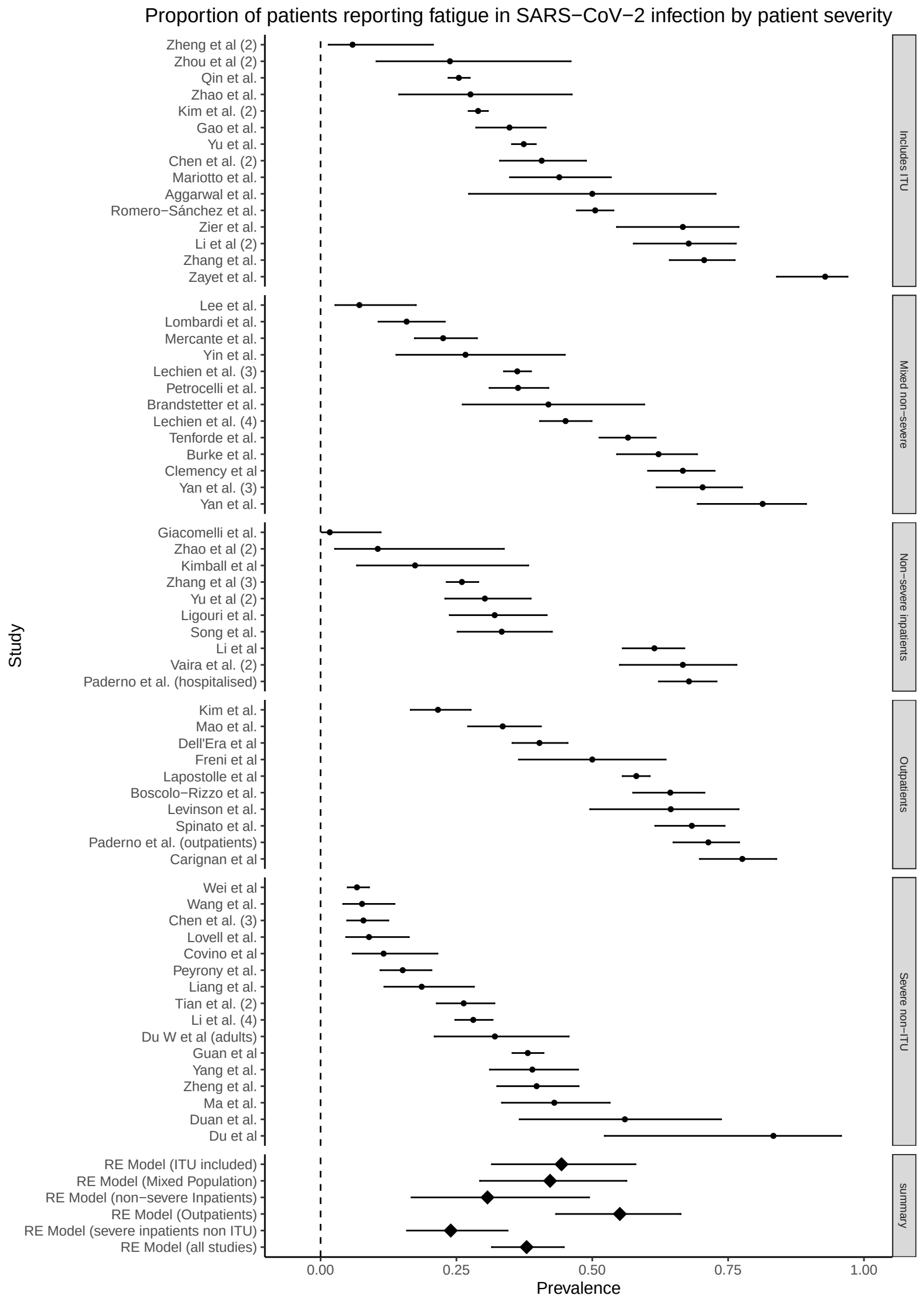
Prevalence


Proportion of patients reporting fatigue in SARS−CoV−2 infection by patient severity
Study
Zheng et al (2)
Zhou et al (2)
Qin et al.
Zhao et al.
Kim et al. (2)
Gao et al.
Yu et al.
Chen et al. (2)
Mariotto et al.
Aggarwal et al.
Romero−Sánchez et al.
Zier et al.
Li et al (2)
Zhang et al.
Zayet et al.
Includes ITU
Lee et al.
Lombardi et al.
Mercante et al.
Yin et al.
Lechien et al. (3)
Petrocelli et al.
Brandstetter et al.
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Tenforde et al.
Burke et al.
Clemency et al
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Mixed non−severe
Giacomelli et al.
Zhao et al (2)
Kimball et al
Zhang et al (3)
Yu et al (2)
Ligouri et al.
Song et al.
Li et al
Vaira et al. (2)
Paderno et al. (hospitalised)
Non−severe inpatients
Kim et al.
Mao et al.
Dell'Era et al
Freni et al
Lapostolle et al
Boscolo−Rizzo et al.
Levinson et al.
Spinato et al.
Paderno et al. (outpatients)
Carignan et al
Outpatients
Wei et al
Wang et al.
Chen et al. (3)
Lovell et al.
Covino et al
Peyrony et al.
Liang et al.
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Guan et al
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Zheng et al.
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Severe non−ITU
RE Model (ITU included)
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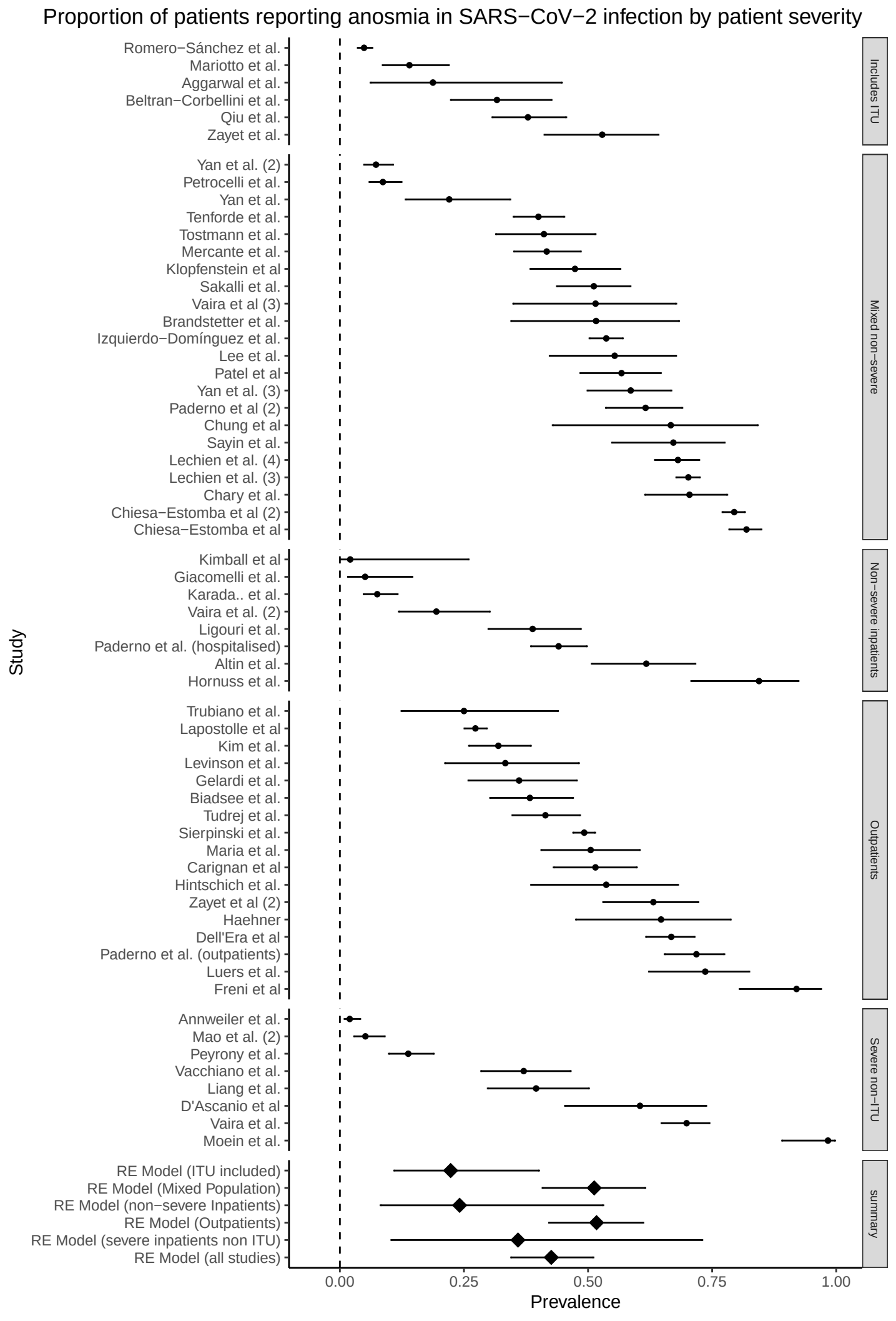
Prevalence


Proportion of patients reporting anosmia in SARS−CoV−2 infection by patient severity
Study
Romero−Sánchez et al.
Mariotto et al.
Aggarwal et al.
Beltran−Corbellini et al.
Qiu et al.
Zayet et al.
Includes ITU
Yan et al. (2)
Petrocelli et al.
Yan et al.
Tenforde et al.
Tostmann et al.
Mercante et al.
Klopfenstein et al
Sakalli et al.
Vaira et al (3)
Brandstetter et al.
Izquierdo−Domínguez et al.
Lee et al.
Patel et al
Yan et al. (3)
Paderno et al (2)
Chung et al
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Chary et al.
Chiesa−Estomba et al (2)
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Mixed non−severe
Kimball et al
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Severe non−ITU
RE Model (ITU included)
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RE Model (Outpatients)
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RE Model (all studies)
summary
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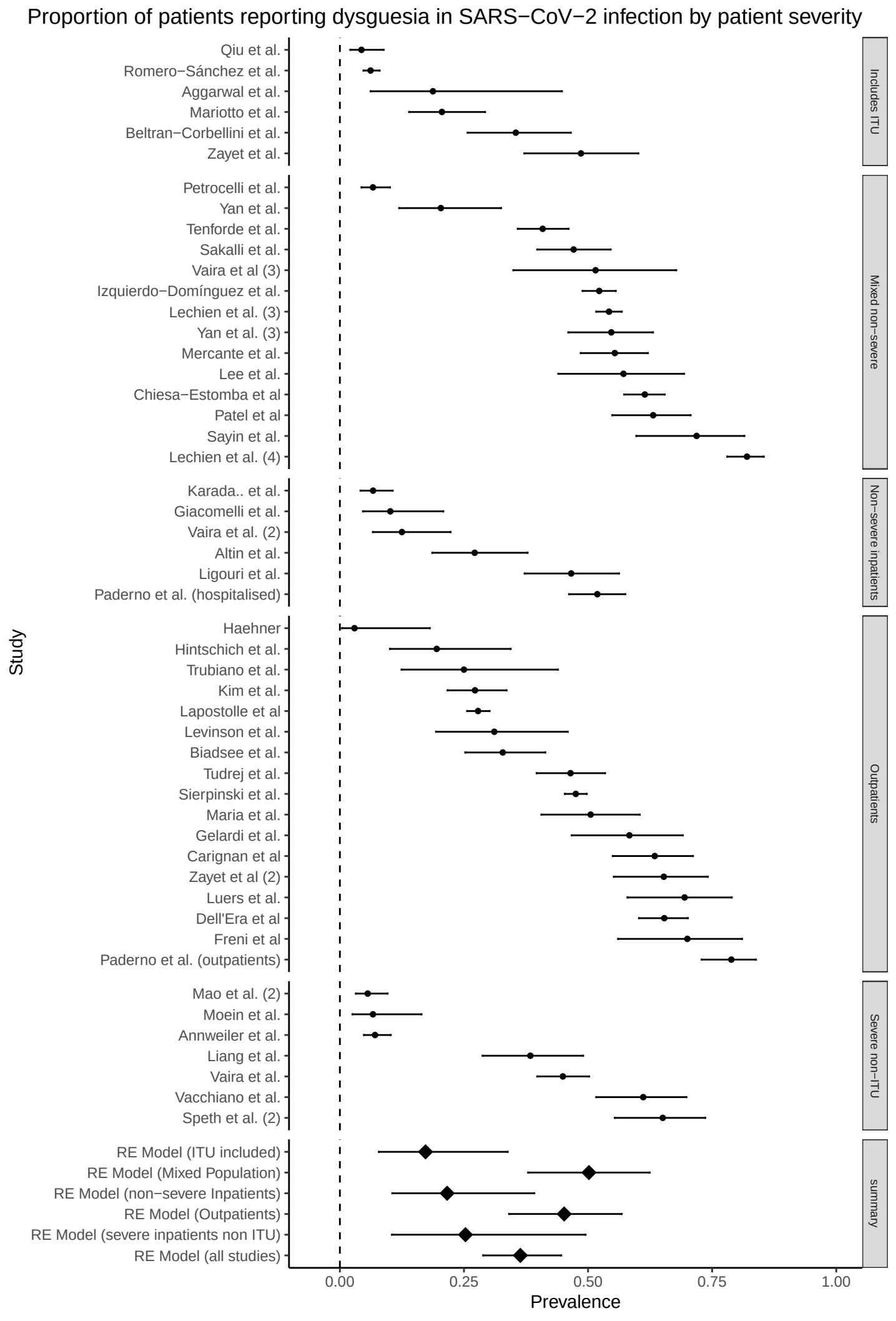
Prevalence


Proportion of patients reporting dysguesia in SARS−CoV−2 infection by patient severity
Study
Qiu et al.
Romero−Sánchez et al.
Aggarwal et al.
Mariotto et al.
Beltran−Corbellini et al.
Zayet et al.
Petrocelli et al.
Yan et al.
Tenforde et al.
Sakalli et al.
Vaira et al (3)
Izquierdo−Domínguez et al.
Lechien et al. (3)
Yan et al. (3)
Mercante et al.
Lee et al.
Chiesa−Estomba et al
Patel et al
Sayin et al.
Lechien et al. (4)
Karada.. et al.
Giacomelli et al.
Vaira et al. (2)
Altin et al.
Ligouri et al.
Paderno et al. (hospitalised)
Haehner
Hintschich et al.
Trubiano et al.
Kim et al.
Lapostolle et al
Levinson et al.
Biadsee et al.
Tudrej et al.
Sierpinski et al.
Maria et al.
Gelardi et al.
Carignan et al
Zayet et al (2)
Luers et al.
Dell'Era et al
Freni et al
Paderno et al. (outpatients)
Mao et al. (2)
Moein et al.
Annweiler et al.
Liang et al.
Vaira et al.
Vacchiano et al.
Speth et al. (2)
RE Model (ITU included)
RE Model (Mixed Population)
RE Model (non−severe Inpatients)
RE Model (Outpatients)
RE Model (severe inpatients non ITU)
RE Model (all studies)
Includes ITU
Mixed non−severe
Non−severe inpatients
Outpatients
Severe non−ITU
summary
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0.75
1.00
Prevalence

Supplementary methods 1: Full search strategy

Per phase one of our strategy and for the current manuscript we populated the database with a search extending from 1st Jan 2020 to 18th July 2020. Future phases will update the database on a progressively shortening basis. To enable this we will continuously run the processes described below. Successive iterations of the database will be version and date-controlled.

Information sources

We searched Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily, EMBASE (via Ovid), APA PsycInfo (via OVID) and CINAHL (via EBSCO) from 1st Jan 2020 to 18th July 2020. Individualised search strategies for each database were deposited with CRD. Reference lists of systematic review articles were examined and cross-checked against our database and eligibility criteria. We noted foreign language papers but did not translate these.

Search Strategy

MEDLINE

(Coronavirus or corona virus or coronavirinae or coronaviridae or betacoronavirus or Covid19 or Covid 19 or Covid-19 or nCoV or CoV 2 or CoV2 or CoV-2 or Sarscov2 or SARS-CoV-2 or 2019nCoV or novel CoV or Wuhan virus or ((Wuhan or Hubei or Huanan) and (respiratory or pneumonia or virus))).mp. or exp Coronavirus/ or exp Coronavirus Infections/ or Coronaviridae.mp.

AND

(neurol* or nervous or brain or CNS or encephal* or mening* or Cranial* or myeli* or demyeli* or ADEM or ataxi* or dysphasi* or aphasi* or stroke or guillain-barre or Miller-Fisher or paresis or palsy or cerebr* or crani* or epilep* or seizure or headache* or migraine* or dysgeusia or anosmia or taste or smell or psych* or neuropsych* or mania or manic or psycho* or delusion* or hallucin* or functional or catatoni* or cognit* or dement* or delir* or depress* or anxi* or obsess* or post-traum* or posttraum* or PTSD or behaviour or behavior or fatigue* or MRI or CT or neuroimag* or scan* or neurotrop* or neuroinvas* or neuropath* or cerebrospinal* or cerebro-spinal* or confus* or conscious* or letharg* or psychomotor* or psycho-motor* or agitat*).mp. or exp Neurology/ or exp Nervous System/ or exp Nervous System Diseases/ or exp Neurologic Manifestations/ or exp Psychiatry/ or exp Mental Disorders/ or exp Mental Processes/ or exp Behavioral Symptoms/ or exp Psychological Phenomena/

EMBASE

(Coronavirus or corona virus or coronavirinae or coronaviridae or betacoronavirus or Covid19 or Covid 19 or Covid-19 or nCoV or CoV 2 or CoV2 or CoV-2 or Sarscov2 or SARS-CoV-2 or 2019nCoV or novel CoV or Wuhan virus or ((Wuhan or Hubei or Huanan) and (respiratory or

pneumonia or virus))).mp. or exp Coronavirinae/ or exp Coronavirus Infection/ or exp Coronaviridae/ or exp Coronaviridae infection/ or exp SARS Coronavirus/

AND

(neurol* or nervous or brain or CNS or encephal* or mening* or Cranial* or myeli* or demyeli* or ADEM or ataxi* or dysphasi* or aphasi* or stroke or guillain-barre or Miller-Fisher or paresis or palsy or cerebr* or crani* or epilep* or seizure or headache* or migraine* or dysgeusia or anosmia or taste or smell or psych* or neuropsych* or mania or manic or psycho* or delusion* or hallucin* or functional or catatoni* or cognit* or dement* or delir* or depress* or anxi* or obsess* or post-traum* or posttraum* or PTSD or behaviour or behavior or fatigue* or MRI or CT or neuroimag* or scan* or neurotrop* or neuroinvas* or neuropath* or cerebrospinal* or cerebro-spinal* or confus* or conscious* or letharg* or psychomotor* or psycho-motor* or agitat*).mp. or exp Neuroscience/ or exp Nervous System/ or exp Neurologic Disease/ or exp Psychiatry/ or exp Mental Disease/ or exp Behavior/ or exp Mental Function/ or exp Confusion/ or exp Psychophysiology/

PsycINFO

(Coronavirus or corona virus or coronavirinae or coronaviridae or betacoronavirus or Covid19 or Covid 19 or Covid-19 or nCoV or CoV 2 or CoV2 or CoV-2 or Sarscov2 or SARS-CoV-2 or 2019nCoV or novel CoV or Wuhan virus or (Wuhan or Hubei or Huanan)).mp.

AND

(neurol* or nervous or brain or CNS or encephal* or mening* or Cranial* or myeli* or demyeli* or ADEM or ataxi* or dysphasi* or aphasi* or stroke or guillain-barre or Miller-Fisher or paresis or palsy or cerebr* or crani* or epilep* or seizure or headache* or migraine* or dysgeusia or anosmia or taste or smell or psych* or neuropsych* or mania or manic or psycho* or delusion* or hallucin* or functional or catatoni* or cognit* or dement* or delir* or depress* or anxi* or obsess* or post-traum* or posttraum* or PTSD or behaviour or behavior or fatigue* or MRI or CT or neuroimag* or scan* or neurotrop* or neuroinvas* or neuropath* or cerebrospinal* or cerebro-spinal* or confus* or conscious* or letharg* or psychomotor* or psycho-motor* or agitat*).mp OR exp Psychiatry/ OR exp Mental Disorders/ OR exp Sensory System Disorders/ OR exp Sense Organ Disorders/ OR exp Nervous System Disorders/ OR exp Neurosciences/ OR exp Neurocognitive Disorders or exp Emotional States

CINAHL

(Coronavirus or corona virus or coronavirinae or coronaviridae or betacoronavirus or Covid19 or Covid 19 or Covid-19 or nCoV or CoV 2 or CoV2 or CoV-2 or Sarscov2 or SARS-CoV-2 or 2019nCoV or novel CoV or Wuhan virus or ((Wuhan or Hubei or Huanan) and (respiratory or pneumonia or virus))) OR (MH "Coronavirus+") OR (MH "Coronavirus Infections+") OR (MH "Coronaviridae+")

AND

((neurol* or nervous or brain or CNS or encephal* or mening* or Cranial* or myeli* or demyeli* or ADEM or ataxi* or dysphasi* or aphasi* or stroke or guillain-barre or Miller-Fisher or paresis or palsy or cerebr* or crani* or epilep* or seizure or headache* or migraine* or dysgeusia or anosmia or taste or smell or psych* or neuropsych* or mania or manic or psycho* or delusion* or hallucin* or functional or catatoni* or cognit* or dement* or delir* or depress* or anxi* or obsess* or post-traum* or posttraum* or PTSD or behaviour or behavior or fatigue* or MRI or neuroimag* or scan* or neurotrop* or neuroinvas* or neuropath* or cerebrospinal* or cerebro-spinal* or confus* or conscious* or letharg* or psychomotor* or psycho-motor* or agitat*) OR) OR (MH "Neurology") OR (MH "Nervous System+") OR (MH "Nervous System Diseases+") OR (MH "Neurologic Manifestations+") OR (MH "Psychiatry+") OR (MH "Mental Processes+") OR (MH "Diagnosis, Neurologic+") OR ((MH "Behavioral and Mental Disorders+"))

Supplementary Methods 2: Author contributions

Author	Contribution(s)
All authors	● Made a substantial intellectual contribution to the study ● Approved the final manuscript
Dr Jonathan P Rogers	● Led and coordinated final phase of study ● Wrote manuscript ● Conducted quality assessment ● Sorted references ● Calculated descriptive statistics ● Consulted on study inclusion ● Arbitrated with quality assessment ● Checked completed manuscript
Dr Cameron Watson	● Conducted meta-analysis ● Screened studies for eligibility ● Extracted data
Mr James Badenoch	● Screened studies for eligibility ● Extracted data ● Checked data extraction ● Conducted quality assessment ● Checked adherence to PRISMA guidelines ● Made PRISMA flowchart ● Sorted references ● Drafted limitations of study ● Checked completed manuscript
Dr Benjamin Cross	● Screened studies for eligibility ● Extracted data ● Checked data extraction ● Conducted quality assessment
Dr Matthew Butler	● Screened studies for eligibility ● Consulted on screening studies ● Checked data extraction ● Conducted quality assessment ● Compared to other systematic reviews ● Drafted limitations of study ● Checked citations ● Checked completed manuscript
Dr Jia Song	● Screened studies for eligibility ● Consulted on screening studies ● Checked data extraction ● Conducted quality assessment ● Checked completed manuscript

Mr Danish Hafeez	• Screened studies for eligibility • Extracted data • Checked data extraction • Conducted quality assessment • Assisted in creating figure illustrating change in study design
Dr Hamilton Morrin	• Extracted data • Checked data extraction • Conducted quality assessment
Dr Emma Rachel Rengasamy	• Screened studies for eligibility • Extracted data • Checked data extraction • Assisted in writing results • Made supplementary table with complete list of studies
Miss Lucretia Thomas	• Screened studies for eligibility • Extracted data • Checked data extraction • Conducted quality assessment
Dr Silviya Ralovska	• Extracted Data • Checked data extraction • Conducted quality assessment
Ms Abigail Smakowski	• Checked data extraction • Conducted quality assessment • Supervised quality assessment • Arbitrated quality assessment
Miss Ritika Dilip Sundaram	• Extracted data • Checked data extraction • Conducted quality assessment
Ms Camille Kaitlyn Hunt	• Checked data extraction • Conducted quality assessment
Dr Mao Fong Lim	• Checked data extraction • Conducted quality assessment • Arranged funding statements
Dr Daruj Aniwattanapong	• Checked data extraction
Ms Vanshika Singh	• Conducted quality assessment • Drafted implications for clinicians
Dr Zain Hussain	• Conducted quality assessment • Assisted with creating tables of results

Miss Stuti Chakraborty	• Conducted quality assessment
Miss Ella Burchill	• Conducted quality assessment • Adapted to house style
Katrin Jansen	• Supported with meta-analysis methods • Conducted some of the meta-analyses
Prof Dr Heinz Holling	• Supported with meta-analysis methods • Advised on meta-analysis
Dr Dean Walton	• Conducted quality assessment • Provided senior review of manuscript
Dr Thomas A Pollak	• Conducted quality assessment • Provided senior review of manuscript
Dr Mark Ellul	• Conducted quality assessment • Provided senior review of manuscript
Dr Ivan Koychev	• Conducted quality assessment • Provided senior review of manuscript
Professor Tom Solomon	• Provided senior review of manuscript
Dr Benedict Daniel Michael	• Provided senior review of manuscript
Dr Timothy R Nicholson	• Conceived the study • Provided senior leadership and advice throughout • Conducted quality assessment • Provided senior review of manuscript
Dr Alasdair G Rooney	• Conceived the study • Led and coordinated early phases of study • Wrote manuscript • Screened studies • Consulted on screening studies • Checked data extraction • Conducted OCEBM ratings • Conducted quality assessment • Provided senior review of manuscript

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	pg 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	pg 5
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	pg 6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	pg 6-7
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	pg 7
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	pg 7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	pg 7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary methods 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	pg 8
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	pg 8
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Supplementary Table 2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	pg 8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	pg 8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	pg 8-9

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	pg 8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	pg 8-9
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Supplementary Table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	pg 9-11; Supplementary Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figures 4-8; Supplementary Figures 1-20
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	pg 11-12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	pg 11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	pg 12-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	pg 14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	pg 15

PRISMA 2009 Checklist

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	pg 15-18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	pg 17-18

Supplementary table 2: Comprehensive list of fields which were extracted from eligible studies

(*asterisk denotes variables for which outcome measures were collected*)

Data items	Prevalences	Mechanistic data	Analytical statistics
Title of study	Headache	C-reactive protein	Results from statistical tests reported by a study
CEBM Levels of Evidence	Myalgia	D-dimer	
Date of date collection	Asthenia	Antibodies	
Funding source	Dizziness/ vertigo	Cytokines	
Country of origin	Tinnitus	Creatine kinase	
Ethics statement	Hearing impairment	Computed tomography	
Number of recruitment settings	Ataxia	Magnetic resonance imaging	
Study design (including retrospective/ prospective)	Paresis	Electroencephalography	
Number of infected participants	Obsessions	Cerebrospinal fluid analysis	
Number of control participants	Palsy	Post-mortem findings	
Description of control group	Paraesthesia/numbness		
Population age (mean/median, sd/range)	Speech/aphasia		
Population sex (number male)	Focal neurological deficit		
Method of COVID-19 diagnosis	Seizures		
Stage of COVID-19 pathway	Neuralgia		
Severity of COVID-19	Ophthalmoplegia		
COVID-19 outcome	Visual defect		

Follow-up period	Fatigue*		
Time-point in relation to infection	Impaired smell*		
Treatments for neuropsych manifestations	Impaired taste*		
Neuropsychiatric and other relevant comorbidities	Cognitive impairment*		
Methodological limitations as noted by the authors	Depression*		
temporal onset of neuropsych complication (in relation to COVID-19 disease)	Anxiety*		
Method of ascertaining prevalence	Post-traumatic stress disorder*		
Nature of sample	Impaired consciousness/delirium/ encephalopathy*		
	Stroke		
	Meningoencephalitis		
	Guillain-Barre syndrome		
	Central demyelinating disorders		
	Motor neuropathy		
	Migraine		
	Sleep disorder		
	Catatonia		
	Dementia		
	Mania		
	Functional neurological disorder		
	Psychosis		

	Post-intensive care unit neuropsychiatric abnormality		
	Myopathy		
	Movement disorder		

Supplementary Table 1: Summary table of studies reporting neuropsychiatric outcomes of COVID-19 infected patients.

	Study	Setting	Population	Design	Infected sample (cases)	Mean Age (S.D.)	Male (%)	Outcomes
(1)	Nie et al. (2020)	China	Inpatient	Cross-sectional	78	58.4 (13)	33 (42.3%)	Depression 28 (35.9%), Anxiety 30 (38.5%), Depression and Anxiety 19 (24.3%)
(2)	Radmanesh et al. (2020)	USA	Mixed	Case series	242	68.7 (16.5)	150	Headache 5 (2%), Weakness 2 (0.8%), Dizziness/Vertigo 79 (32.6%), Focal neurological deficit 30 (12.4%), Altered mental status 102 (42.1%), Acute haemorrhagic stroke 11 (4.5%), Nonspecific white matter microangiopathy 134 (55.4%), Chronic infarct 47 (19.4%), Acute or subacute ischemic infarct 13 (5.4%)
(3)	Wei Y et al. (2020)	China	Outpatient	Cross-sectional	628	53 (14.8)	296	Myalgia 8 (1.3%), Dizziness/Vertigo 1 (0.2%), Fatigue 42 (6.7%)
(4)	Haehner et al. (2020)	Germany	Outpatient	Cross-sectional	34	-	227	Impaired smell onset 22 (64.7%), Impaired taste onset 22 (2.94%)
(5)	Beltran-Corbellini et al. (2020)	Spain	Inpatient	Cross-sectional	79	61.6 (17.4)	48	Impaired smell and taste 31 (39.2%), Impaired smell onset 25 (31.7%), Impaired smell at follow-up 13 (16.5%), Impaired taste at onset 28 (35.4%)
(6)	Renaud et al. (2020)	France	Outpatient	Case series	347	37* (-)	113	Impaired smell onset 345 (99.4%), Impaired taste at onset 123 (35.4%)
(7)	Gao et al. (2020)	China	Inpatient	Case series	210	71* (-)	101	Headache 13 (6%), Myalgia 12 (6%), Fatigue 73 (5%), Ischaemic stroke 3 (1%)

(8)	Abalo-Lojo et al. (2020)	Spain	-	Case series	131	50.4 (-)	56	Headache 51 (38.9%), Myalgia 61 (46.6%), Asthenia 76 (58%), Impaired smell onset 77 (58.8%), Impaired taste at onset 74 (56.5%)
(9)	Adorni et al. (2020)	Italy	Volunteers	Cross-sectional	170175 856	47.4 (14.5)	68767	Headache 485 (56.7%), Myalgia 527 (61.6%), Smell and/or taste 507 (59.2%)
(10)	Roland et al. (2020)	USA	Volunteers (online)	Cross-sectional	157	40 (13)	51	Headache 93 (64%), Myalgia 25 (77%), Smell or taste 95 (66%)
(11)	Aggarwal et al. (2020)	USA	Inpatient	Case series	16	65.5 (Range 38-95)	12 (75%)	Headache 4 (25%), Myalgia 4 (25%), Dizziness/Vertigo 3 (19%), Fatigue 8 (50%), Impaired smell 3 (19%),
(12)	Alsofayan Y.M. et al. (2020)	Saudi Arabia	Mixed	Cross-sectional	1519	36 * (-)	825	Headache 193 (27.3%), Myalgia 202 (28.6%)
(13)	Romero-Sanchez et al. (2020)	Spain	Inpatient	Case series	841	66.4 (15.0)	473	Headache 119 (14.1%), Myalgia 145 (17.2%), Asthenia 425 (51%), Dizziness/Vertigo 51 (6.1%), Seizures 6 (0.7%), Ophthalmoplegia 1 (0.1%), Impaired smell onset 41 (4.9%), Impaired taste at onset 52 (6.2%), Depression 44 (5.2%), Anxiety 68 (8.1%), Impaired consciousness 165 (19.6%), Ischaemic stroke 11 (1.3%), Haemorrhagic stroke 3 (0.4%), Meningoencephalitis 1 (0.1%), Guillain-Barre syndrome and variants 1 (0.1%), Sleep disorders 109 (13%), Psychosis 11 (1.3%), Myopathy 26 (3.1%), Movement disorder 6 (0.7%)
(14)	Sakalli et al. (2020)	Turkey	Mixed	Cohort	172	37.8 (12.5)	84	Headache 97 (56.4%), Myalgia 125 (72.7%), Anosmia and Dysgeusia 72 (41.9%), Impaired smell onset 88 (51.2%), Impaired smell follow-up 68 (39.5%), Impaired taste onset 81 (47.1%), Impaired taste follow-up 62 (36%)

(15)	Salmon Ceron et al. (2020)	France	Outpatient	Cohort	51	34* (Range 22-61)	24	Headache 38 (69.1%), Myalgia 17 (30.9%), Asthenia 28 (56%), Impaired smell onset 55 (100%), Impaired smell follow-up 35 (63.6%), Impaired taste onset 46 (83.6%)
(16)	Chen et al. (2020)	China	Inpatient	Case series	145	47.5 (14.6)	54.50%	Headache 24 (16.6%), Myalgia 20 (13.8%), Dizziness/Vertigo 29 (20%), Hearing impairment 2 (1.4%). Fatigue 59 (40.7%), Anorexia 62 (42.8%), Hypoacusis 2 (1.4%)
(17)	Chen et al. (2020)	China	Inpatient	Cohort	203	54 * (IQR 41-68)	108 (53.2%)	Headache 10 (4.9%), Dizziness/Vertigo 4 (2%), Myalgia or Arthralgia 54 (26.6%), Fatigue 16 (7.9%), Anorexia 6 (3%)
(18)	Liu et al. (2020)	China	Inpatient	Case-control	21	43.1 (2.6)	9	Suspected Depression 21 (100%), Suspected Anxiety 21 (100%)
(19)	Chiesa-Estomba et al. (2020)	South America	Online/outpatient	Cross-sectional	542	34 (11) (Range 18-88)	218 (40.2)	Headache 393 (72.5%), Myalgia 340 (62.7%), Total anosmia 78 (14.4%) Impaired smell onset 444 (81.9%), Impaired smell follow-up 183 (33.8%), Impaired taste onset 333 (61.4%)
(20)	Lombardi et al. (2020)	Italy	Healthcare workers	Case-control	139	44.5 (-)	57	Headache 24 (17.3%), Myalgia 20 (14.4%), Asthenia 22 (15.8%), Ophthalmoplegia 13 (9.3%), Anosmia and Dysgeusia 20 (14.3%)
(21)	Oualha et al. (2020)	France	Inpatient	Case series	27	6* (Range 0.2-17.8)	10	Paresis 1 (4%), Focal neurological deficit 1 (4%), Stupor and Reduced GCS 1 (4%), Haemorrhagic stroke 2 (7.4%), Meningoencephalitis 1 (4%)

(22)	Paderno et al. (2020)	USA	Mixed	Cross-sectional	508	*Group A* (hospital) = 61.9 (12.8), *Group B* (home) = 44.7 (12.1)	Group A (hospital) = 204 Group B (home) = 81	Headache 198 (38.9%), Myalgia 256 (50.4%), Asthenia 352 (69.3%), Impaired smell onset 283 (71.8%), Impaired smell follow-up 29 (19.7%), Impaired taste onset 321 (63.1%), Impaired taste follow-up 35 (19.7%)
(23)	Kim et al. (2020)	South Korea	Inpatient	Cohort	2491	62* (25)	1326	Myalgia 722 (29.1%), Fatigue 722 (29.1%), Encephalitis 151 (6.1%), Central demyelinating disorders 151 (6.1%)
(24)	Kim et al. (2020)	South Korea	Community	Cross-sectional	213	26 * (-)	66	Headache 54 (25.3%), Myalgia 54 (25.3%), Dizziness/Vertigo 32 (15%), Fatigue 46 (21.6%), Impaired smell onset 68 (31.9%), Impaired taste onset 58 (27.2%)
(25)	Kimball et al. (2020)	USA	Inpatient	Cohort	23	80.7 (8.4)	7	Dizziness/Vertigo 1 (4.4%), Fatigue 4 (17.4%)
(26)	Klopfenstein et al. (2020)	France	Mixed	Case series	114	-	-	Anosmia and Dysgeusia 46 (38%). Impaired smell onset 54 (47.4%)
(27)	Lovato et al. (2020)	Italy	Telephone survey-Mild/mixed	Cross-sectional	121	46.7 (-)	49	Anosmia and Dysgeusia 121 (83%)
(28)	Chiesa-Estomba et al. (28)	South America	Mixed	Cohort	1221	41 (13)	-	Impaired smell onset 970 (79.4%), Impaired smell follow-up 381 (50.7%)
(29)	Chougar et al. (29)	France	Inpatient	Case series	308	61.8 (14.9)	64	Fatigue 33 (10.7%), Focal neurological deficit 45 (14.6%), Seizures 16 (5.2%) , Visual defect 6 (19.5%), Impaired smell onset 28 (%), Impaired consciousness 89 (28.9%), Guillain-Barre syndrome and variants 3 (1%)

(30)	Chung et al. (2020)	Hong Kong	Inpatient (mild)	Cross-sectional	18	28 (19)	41	Anosmia and Dysgeusia 9 (52.9%), Impaired smell onset 12 (67%)
(31)	Gaur et al. (2020)	India	Inpatient	Cohort	26	37.6 (-)	16 (61.5%)	Headache 8 (30.8%), Myalgia 10 (38.5%),
(32)	Altin et al. (2020)	Turkey	Inpatient	Case-control	81	54.2 (17.0)	41 (50.6%)	Impaired smell onset 50 (61.7%), Impaired taste onset 22 (27.2%)
(33)	Annweiler et al. (2020)	France	Mixed	Cross-sectional	353	84.7 (7)	160 (45.3%)	Impaired smell onset 7 (2%), Impaired taste onset 25 (7.1%), Altered consciousness 37 (10.5%)
(34)	Gómez-Iglesias et al. (2020)	Spain	Population	Cross-sectional	909	34.7 (-)	283 (31.1%)	Myalgia 296 (32.5%), Smell and Taste 824 (90.7%), Impaired smell onset 888 (97.7%), Impaired taste onset 845 (93%)
(35)	Clemency et al. (2020)	USA	Outpatients – HCWs	Cross-sectional	225	-	-	Myalgia 128 (56.8%), Smell and Taste 110 (48.9%), Fatigue 150 (66.7%)
(36)	Coelho et al. (2020)	USA	General population	Cohort	260	-	-	Headache 76 (81.7%), Myalgia 75 (80.6%), Fatigue 81 (87.1%), Smell or Taste 3 (3.2%)
(37)	Gorzkowski et al. (2020)	France	Mixed	Cohort	229	39.7 (13.7)	82 (35.8%)	Smell or Taste 140 (61.1%), Impaired smell at onset 124 (54.2%), Impaired smell at follow-up 6 (2.6%), Impaired taste at onset 140 (61.1%)
(38)	Han et al. (2020)	China	Inpatient	Cohort	32	44 (-)	12 (37.5%)	Myalgia or Fatigue 13 (52%)

(39)	Lovell et al. (2020)	UK	Inpatients (referred to palliative care)	Case series	101	82 (IQR 72-89)	64 (63.3%)	Seizures 1 (1%), Fatigue 9 (8.9%), Delirium 24 (23.8%)
(40)	Lu et al. (2020)	China	Discharged or deceased	Cohort	304	44* (IQR 33-59)	182 (59.9%)	Seizures 2 (0.7%), Anxiety 1 (0.3%), Shock 8 (2.60%), Other cerebrovascular accident 4 (1.3%)
(41)	Sayin et al. (2020)	Turkey	Mixed	Case-control	64	38.6 (10.1)	48 (75%)	Headache 18 (39.1%), Smell or Taste 46 (71.9%), Impaired smell onset 43 (67.2%), Impaired taste onset 46 (71.9%)
(42)	Schmithausen et al. (2020)	Germany	Mild cases – home quarantined	Cross-sectional	41	40* (Range 18-92)	20 (49%)	Smell and/or taste 28 (68%)
(43)	Scullen et al. (2020)	USA	Inpatient	Case series	27	59.8 (Range 35-91)	14 (52%)	Headache 2 (2.63%), Weakness 1 (3.,7%), Focal neurological deficit 10 (13.2%), Impaired taste at onset 1 (1.32%), Altered mental status 26 (34,2%), Other cerebrovascular accident 4 (14.8%)
(44)	Belani et al. (2020)	USA	Inpatients undergoing neuroimaging for suspected stroke	Case-control	34	-	-	Stroke 19 (56%)
(45)	Bhandari et al. (2020)	India	Inpatient	Cohort	522	35.4 (-)	318 (60.91%)	Headache 139 (26.7%)
(46)	Hernández-Fernández et al. (2020)	Spain	Inpatient	Case series	1683	66.8 (-)	18 (1.1%)	Ischaemic stroke 17 (1.0%), Haemorrhagic stroke 5 (0.3%), Other cerebrovascular accident 1 (0.1%)

(47)	Covino et al. (2020)	Italy	Inpatient	Case series	69	84* (IQR 82-89)	37 (53.6%)	Fatigue 8 (11.6%)
(48)	Biadsee et al. (2020)	Israel	Self-isolating/non-hospitalised	Cross-sectional	128	36.3 (Range 18-73)	58 (45.3%)	Headache 52 (40%), Myalgia 60 (47%), Weakness 61 (48%), Impaired smell onset 49 (38%), Impaired taste onset 42 (32%)
(49)	Hintschich et al. (2020)	Germany	Home quarantine	Case-control	41	37 (-)	12 (29.3%)	Smell and Taste 18 (44%), Impaired smell onset 22 (54%), Impaired taste onset 8 (20%)
(50)	Sierpinski et al. (2020)	Poland	Self-isolating	Cross-sectional	1942	50* (-)	773 (39.8%)	Smell and Taste 825 (42.5%), Impaired smell onset 956 (49.2%), Impaired taste onset 923 (47.5%)
(51)	Paderno et al. (2020)	Italy	Mixed	Cohort	151	45 (Range 18-70)	56 (37%)	Impaired smell onset (complete anosmia) 93 (74%), Impaired taste (complete dysgeusia) 95 (70%)
(52)	Hornuss et al. (2020)	Germany	Inpatient	Case-control	45	56 (16.9)	25 (55.6%)	Headache 10 (22%), Impaired smell onset 38 (84.4%)
(53)	Boscolo-Rizzo et al. (2020)	Italy	Outpatient - mild	Cross-sectional	202	56*(-)	99 (49%)	Headache 80 (39.6%), Myalgia 85 (42%), Dizziness/vertigo 25 (12.3%), Smell or Taste 113 (55.9%), Fatigue. 130 (64.3%)
(54)	Huang et al. (2020)	China	Inpatient	Cohort	41	49 (-)	30 (73.2%)	Headache 3 (8%), Myalgia or Fatigue 18 (44%)
(55)	Huang et al. (2020)	China	Inpatient	Case series	336	43 (IQR 30-54)	182 (54.1%)	Headache 39 (11.6%), Myalgia 39 (11.6%), Weakness OR Fatigue 83 (24.7%), Impaired consciousness/delirium/encephalopathy 1 (0.3%)

(56)	Parra et al. (2020)	Spain	Inpatient	Case series	10	54.1(10.7)	6 (60%)	Psychosis 10 (100%)
(57)	Luers et al. (2020)	Germany	Outpatient	Cross-sectional	72	38 (-)	41(56.9%)	Headache 56 (77.8%), Myalgia 51 (70.8%), Impaired smell onset 53 (73.6%), Impaired taste onset 50 (69.4%)
(58)	Somekh et al. (2020)	Israel	Outpatient	Cross-sectional	73	-	-	Smell or Taste 37 (51%)
(59)	Song et al. (2020)	China	Inpatient	Case series	111	55*(/IQR 44-67)	62(55.9%)	Headache 11 (9.9%), Myalgia 21 (18.9%), Fatigue 37 (33.3%)
(60)	Immovilli et al. (2020)	Italy	Inpatient	Case series	19	76.1 (8.8)	10 (52.6%)	Ischaemic stroke 17 (89.5%), Haemorrhagic stroke 2 (10.5%)
(61)	Pastor et al. (2020)	Spain	Inpatient	Case-control	20	63.9 (-)	17 (85%)	Impaired consciousness/delirium/encephalopathy 18 (90%)
(62)	Izquierdo-Domínguez et al. (2020)	Spain	Mixed	Cross-sectional	846	56.8 (15.7)	446 (52.1%)	Smell and Taste 399 (47.2%), Impaired smell onset 454 (53.7%), Impaired taste onset 442 (52.2%)
(63)	Ma et al. (1) (2020)	China	Inpatients	Case series	93	67* (/IQR 54-72)	51 (54.8%)	Headache 14 (15.1%), Myalgia 20 (21.5%)
(64)	Ma et al. (2) (2020)	China	Inpatient	Cross-sectional	770	50.4 (13.1)	370 (48.0%)	Depression 332 (43.1%)
(65)	Mao et al. (2020)	China	Outpatient	Case series	188	46* (-)	94 (50%)	Headache 23 (12%), Myalgia 36 (19%), Fatigue 63 (34%)

(66)	Marinho et al. (2020)	Brazil	Outpatients (majority physicians)	Case series	12	- (Range 25-69)	6 (50%)	Asthenia 12 (100%), Impaired smell onset 11 (91.7%)
(67)	Mariotto et al. (2020)	Italy	Inpatient	Cross-sectional	107	65.8 (11.9)	82 (76.6%)	Headache 12 (17.4%), Myalgia 16 (23.2%), Dizziness/vertigo 6 (8.7%), Fatigue 47 (68.1%), Impaired smell onset 15 (21.7%), Impaired taste onset 22 (31.9%), Impaired consciousness/delirium/encephalopathy 13 (18.8%)
(68)	Mathian et al. (2020)	France	-	Case series	17	53.5* (Range 27-69)	4 (23.5%)	Headache 10 (59%), Myalgia 8 (47%), Impaired smell onset 5 (29%), Impaired taste onset 5 (29%), Impaired consciousness/delirium/encephalopathy 1 (6%)
(69)	McLoughlin et al. (2020)	UK	Inpatient	Cross-sectional	71	61 (Range 24-91)	51(71.8%)	Impaired consciousness/delirium/encephalopathy 31 (43.7%), Sleep disorders 16 (22.5%), Psychosis 5 (7%)
(70)	Patel et al. (2020)	UK	Mixed	Cross-sectional	141	45.6 (-)	83	Myalgia 93 (66%), Impaired smell onset 80 (56.7%), Impaired taste onset 89 (63.1%)
(71)	Mehrpour et al. (2020)	Iran	Inpatient	Case series	10	75.6 (9.6)	5 (50%)	Ischaemic stroke 9 (90%), Haemorrhagic stroke 1 (10%)
(72)	Mei et al. (2020)	China	Inpatient	Case series	494	40 /IQR 27-59)	266 (53.8%)	Smell and Taste 39 (7.9%)
(73)	Brandstetter et al. (2020)	Germany	Healthcare workers	Cross-sectional	31	-	5 (16%)	Headache 15 (48.4%), Myalgia 15 (48.4%) Fatigue 13 (41.9%)

(74)	Jäckel et al. (2020)	Germany	Inpatient	Case series	20	65.5 (11.0)	16 (80%)	Delirium 13 (65%)
(75)	Jalessi et al. (2020)	Iran	Post-discharge	Cross-sectional	92	52.9 (13.3)	62 (67.4%)	Headache 20 (21.7%), Myalgia 57 (62%), Smell and Taste 15 (16.3%), Impaired smell onset 22 (23.9%), Impaired smell follow-up 1 (1%)
(76)	Joffily et al. (2020)	Brazil	Outpatient	Cross-sectional	159	(70% under 39)	50 (31.4%)	Smell and Headache 116 (73%), Impaired smell onset 159 (100%), Impaired smell follow-up 88 (55.3%), Impaired taste onset 147 (92.5%)
(77)	Kai Chua et al. (2020)	Singapore	Presenting to ED with acute respiratory symptoms	Case series	31	-	-	Impaired smell onset 7 (22.6%)
(78)	Kandemirli et al. (2020)	Turkey / USA	ICU	Case series	235	-	-	50 (21%) developed neurological symptoms
(79)	Karadaş et al. (2020)	Turkey	Inpatient	Cohort	239	46.5 (15.4)	133 (55.7%)	Headache 64 (26.7%), Myalgia 36 (15.1%), Dizziness/vertigo 16 (6.7%), Tinnitus 5 (2.1%), Hearing impairment 3 (1.3%), Visual defect 8 (3.3%), Smell and Taste 11 (4.6%), Impaired smell onset 18 (7.5%), Impaired taste onset 16 (6.7%), Impaired consciousness/delirium/encephalopathy 23 (9.6%), Ischaemic stroke 7 (2.9%), Haemorrhagic stroke 2 (0.8%), Guillain-Barre syndrome 1 (0.4%), Sleep disorders 30 (12.6%)
(80)	Carignan et al. (2020)	Canada	Outpatient	Case-control	134	57.1 (/IQR 41-65)	64 (47.8%)	Headache 87 (64.9%), Myalgia 76. (56.7%), Asthenia 104 (77.6%), Dizziness/vertigo 27 (20.1%) Visual defect 6 (4.5%), Smell and/or Taste 87 (64.9%), Impaired smell onset 69 (51.5%), Impaired taste onset 85 (63.4%)

(81)	Meini et al. (2020)	Italy	Discharged from ITU 1 month ago	Cross-sectional	100	65 (15)	39 (39%)	Smell and Taste 28 (28%), Impaired smell onset 29 (29%), Impaired smell follow-up 5 (5%), Impaired taste onset 41 (41%), Impaired taste follow-up 7 (7%)
(82)	Menni et al. (2) (2020)	UK / USA	App users	Cohort	7178	41.6(-)	(-)	Smell and Taste 4668 (65%), Fatigue 2093(29.2%), Impaired consciousness/delirium/encephalopathy 1323 (18.4%)
(83)	Korkmaz et al. (2020)	Turkey	Paediatric cases presenting to ED	Case series	79	9.5 (IQR 3–15)	48 (60.8%)	Headache 11(14%), Fatigue or Myalgia 15 (19%), Impaired smell onset 1 (1%)
(84)	Mercante et al. (2020)	Italy	Mixed	Cross-sectional	204	52.6 (14.4)	110 (53.9%)	Headache 32 (15.7%), Myalgia 20 (9.9%), Dizziness/vertigo 43 (21.1%), Fatigue 46 (22.6%), Impaired smell onset 85 (41.7%), Impaired taste onset 113 (55.4%)
(85)	Speth et al. (2020)	Switzerland	Mixed	Cross-sectional	114	44.6 (16.1)	52 (45.60%)	PHQ-2 and GAD-2 scores increased significantly from baseline (adjusted incidence rate ratio 1.40 [1.10 - 1.78], p=0.006)
(86)	Speth et al. (2) (2020)	Switzerland	Mixed	Cross-sectional	103	46.8 (15.9)	50 (48.5%)	Impaired smell onset 63 (61.2%), Impaired tastel onset 67 (65%)
(87)	Kremer et al. (2020)	France	Inpatient	Case series	37	61 (12)	30 (81.0%)	Headache 4 (11%), Focal neurological deficit 4 (11%), Seizures 5 (14%), Impaired consciousness/delirium/encephalopathy 27 (73%), Haemorrhagic stroke 11 (29.7%), Other cerebrovascular accident 9 (24%), Sleep disorders 15 (41%), Post ICU neuropsychiatric abnormality 15 (41%)
(88)	Spoldi et al. (2020)	Italy	Inpatient undergoing head CT	Cross-sectional	63	77.8 (17.8)	39 (61.9%)	Olfactory cleft opacification 16 (25%)

(89)	Sun et al. (2020)	China	Mixed	Case series	55	44 (IQR 34-56)	31 (56.4%)	Headache 6 (10.9%), Myalgia 10 (18.2%), Dizziness/Vertigo 6 (10.9%)
(90)	Sweid et al. (2020)	USA	Acute cerebrovascular disease	Case series	22	59.5 (16)	10 (45.4%)	Ischaemic stroke 19 (86.4%), Haemorrhagic stroke 3 (13.6%)
(91)	Chary et al. (2020)	France	Mixed	Cohort	115	47 (-)	34 (29.6%)	Headache 62 (54%), Myalgia 57 (50%), Smell and Taste 38 (33%), Impaired smell onset 81 (70%), Impaired smell follow-up 29 (25.2%)
(92)	Lapostolle et al. (2020)	France	Outpatient	Cross-sectional	1487 (data missing for 35)	44(M),41 (F)* IQR 32-57 (M) IQR 30-54 (F)	700 (47.7%)	Headache 803 (55.3%), Myalgia 823 (6.7%), Asthenia 864 (59.5%), Impaired smell onset 406 (28%), Impaired taste onset 414 (28.5%)
(93)	Lechien et al. (2020)	Belgium	General population	Cross-sectional	78	40.6 (11.2)	32 (41.0%)	Impaired smell onset 78 (100%), Impaired taste onset 53 (67.9%)
(94)	Lechien et al. (2) (2020)	Belgium	Outpatient	Cross-sectional	16	36 (10)	8 (50%)	Headache 5 (31.3%), Myalgia 4 (25%), Asthenia 7 (44%)
(95)	Lechien et al. (3) (2020)	Europe	Mixed	Cross-sectional	702	40.3 (11.8)	206 (29.3%)	Headache 447 (63.7%), Myalgia 371 (52.9%), Asthenia 519 (73.9%)
(96)	Lechien et al. (4) (2020)	Europe	Mixed	Cross-sectional	1420	39.2 (12.1)	458 (32.3%)	Headache 998 (70.3%), Myalgia 887 (62.5%), Asthenia 514 (36 %), Smell and Taste 875 (61.6%), Impaired smell onset 997 (70.2%), Impaired smell follow-up 429 (30.2%), Impaired taste onset 770 (54.2%), Impaired taste follow-up 332(23.4%)

(97)	Lechien et al. (5) (2020)	Europe	Mixed	Cross-sectional	2013	39.5 (12.1)	684 (34.0%)	Headache 1411 (70.1%), Myalgia 1244 (61.8%), Impaired smell onset 1751 (87%), Impaired smell follow-up 282 (14%), Impaired taste onset 1135 (56.4%)
(98)	Lechien et al. (6) (2020)	Belgium	Outpatient	Cross-sectional	86	41.7 (11.8)	30 (34.9%)	Headache 42 (60%), Myalgia 30 (42.9%), Asthenia 51 (72.9 %), Speech/aphasia 17 (24.3%), Visual defects 18 (25.7%), Fatigue 51 (73%), Impaired smell onset 86 (100%), Impaired taste onset 44 (51%)
(99)	Khan et al. (2020)	UAE	Inpatient	Case series	22	46.3 (11.1)	20 (90.9%)	Ischaemic stroke 22 (100%)
(100)	Khira et al. (2020)	USA	Inpatients who had CT angiogram	Case series	31	64.9 (15.7)	68	Stroke 31 (100%)
(101)	Lee et al. (2020)	Canada	Inpatient	Case-control	56	38 (/IQR 32–53)	23 (41.10%)	Headache 10 (17.9%), Smell and Taste 20 (35.7%), Fatigue 4 (7.1%), Impaired smell onset 31 (55.4%), Impaired taste onset 32 (57.1%)
(102)	Lee et al. (2) (2020)	USA	General population	Cross-sectional	61	-	-	Dysfunctional coronavirus anxiety associated with coronavirus infection (OR 3.04 [1.28-7.25])
(103)	Lee et al. (3) (2020)	Korea	Inpatients	Case series	98	72* (IQR 68-79)	44 (44.9%)	Focal neurological deficit 7 (9%)
(104)	Lee et al. (4) (2020)	Korea	Mixed	Cohort	3,191	44 (e/IQR 25.–58.)	1,161 (36.4%)	Smell and Taste 488 (15.3%)
(105)	Li et al. (2020)	China	Inpatient	Case series	219	53.3 (15.9)	89 (40.6%)	Ischaemic stroke 10 (4.6%), Haemorrhagic stroke 1 (0.5%)

(106)	Merkler et al. (2020)	USA	Mixed	Case series	1916	64* (IQR 51-76)	1101 (57.5%)	Ischaemic stroke 31 (1.6%)
(107)	Moein et al. (2020)	Iran	Inpatient	Case-control	60	46.6 (12.2)	40 (66.7%)	Headache 22 (37%), Myalgia 5 (8%),Tinnitus 1 (2%), Smell OR Taste 21 (35%), Impaired smell onset 59 (96.3%) , Impaired taste onset 4 (7%),
(108)	Moro et al. (2020)	Italy	Online- survey of neurologists	Cross-sectional	-	-	-	Most frequently reported neurological findings: headache (61.9%), myalgia (50.4%), anosmia (49.2%), ageusia (39.8), impaired consciousness (29.3%), psychomotor agitation (26.7%), encephalopathy (21.0%), acute cerebrovascular disorders (21.0%)
(109)	Nalleballe et al. (2020)	USA	Mixed	Cohort	40,469	-	18,364 (45.4%)	Headache 150 (3.7%), Myalgia 821 (2%), Dizziness/vertigo 379 (0.9%), Focal neurological deficit 392 (1%), Seizures 258 (0.6%), Smell and Taste 477 (1.2%), Depression 1549 (3.8%), Anxiety 1869 (4.6%), Impaired consciousness/delirium/encephalopathy 937 (2.3%), Other cerebrovascular accident 406 (1.%), Sleep disorders 1394 (3.4%), Other movement disorders 277 (0.7%), Suicidal ideation 63(0.2%)
(110)	Li et al. (2020)	China	Inpatient	Cross-sectional	280	104 (51-65)	135 (48.2%)	Fatigue 172 (61.4%), Depression 114 (40.7%), Anxiety 174 (62.1%), Sleep disorders 178 (63.6%)
(111)	Li et al. (2) (2020)	China	Inpatient	Case series	93	51 (17.5)	41 (44.1%)	Myalgia 34 (37%), Fatigue 63 (68%)
(112)	Li et al. (3) (2020)	China	Inpatient	Case series	83	45.5 (12.3)	44 (53.0%)	Headache 9 (10.8%), Myalgia 15 (18.1%)

(113)	Paterson et al. (2020)	UK	Inpatient	Case series	43	Summarised according to clinical presentation) Encephalopathy: 57.5, inflammatory CNS syndromes: 53, stroke: 62.5, GBSL 56, plexopathy: 60, miscellaneous and uncharacterised: 20	Reported % male: Encephalopathy: 40, inflammatory CNS syndromes: 33, stroke: 75, GBS: 100, plexopathy: 100, miscellaneous and uncharacterised: 40	Encephalopathy 10 (23%), inflammatory CNS syndromes 12 (28%), ischaemic stroke 8 (19%), peripheral neurological disorders 8 (19%), miscellaneous CNS disorders 5 (12%)
(114)	D'Ascanio et al. (2020)	Italy	Mixed	Case-control	43	58.1 (15.6)	29 (67.4%)	Impaired smell onset 26 (60.4%)
(115)	Dawson et al. (2020)	USA	Household study of patients with positive swabs and those they lived with	Cross-sectional	42	31* (Range <1 - >90)	69 (-)	Headache 32 (76%), Myalgia 24 (57%), Light-headed 3 (7%), Smell OR Taste 16 (38%), Fatigue 15 (36%), Impaired smell onset 18 (43%), Impaired taste onset 24 (57%)
(116)	Dell'Era et al. (2020)	Italy	Outpatient	Cross-sectional	355	50* (IQR 40-59.5)	192 (54.1%)	Fatigue 143 (40.3%), Impaired smell onset 237 (66.8%) , Impaired smell follow-up 88 (24.8%), Impaired taste onset 232 (65.4%), Impaired taste follow-up 84 (36.2%)
(117)	Tabata et al. (2020)	Japan	Inpatient	Case series	104	68*(IQR 47-75)	54 (51.9%)	-
(118)	Tian et al. (2020)	China	Inpatient	Case series	751	64 (IQR 57-69)	372 (49.5%)	Headache 37 (5%)
(119)	Tostmann et al. (2020)	Netherlands	Healthcare workers	Cross-sectional	90	-	19 (21.1%)	Headache 64 (71.1%), Myalgia 57 (63.3%), Impaired smell onset 37 (46.8%)

(120)	Du et al. (2020)	China	Inpatient	Case series	12	45.3 (Range 23-79)	7 (58.3%)	Headache 3 (25%), Fatigue 10 (83%)
(121)	Du W et al (2020)	China	Inpatient	Case series	67	34.1* (0-65)	32 (47.8%)	Headache 1 (7.1%), Myalgia 1 (7.1%), Fatigue 1 (7.1%)
(122)	Trubiano et al. (2020)	Australia	Outpatient	Cross-sectional	28	55* (IQR 46-64)	14 (50%)	Headache 6 (21.4%), Myalgia 15 (53.6%), Smell and Taste 3 (10.7%), Impaired smell onset 7(25%)
(123)	Guan et al. (2020)	China	Inpatient	Case series	1099	47 (IQR 35-58)	637 (58%)	Headache 150 (13.6%), Myalgia 164 (14.9%), Fatigue 419 (38.1%)
(124)	Escalard et al (2020)	France	Inpatient	Case series	10	59.5 (IQR 54-72)	8 (80%)	Ischaemic stroke 10 (100%)
(125)	Farahani et al. (2020)	Iran	Inpatient	Cohort	10	50* (-)	7 (70%)	Headache 10 (100%), Fatigue 10 (100%)
(126)	Freni et al. (2020)	Italy	Outpatient	Cohort	50	37.7 (17.9)	30 (60.0%)	Headache 24 (48%), Myalgia 18 (36%), Asthenia 25 (50%), Impaired smell onset 46 (92%), Impaired smell follow-up 9 (18%), Impaired taste onset 35 (70%), Impaired taste follow-up 4 (8%)
(127)	Galanopoulou et al. (2020)	USA	Inpatient	Case series	22	63.2 (11.9)	14 (63.6%)	Seizures 14 (63.6%), Impaired consciousness/delirium/encephalopathy 15 (68.2%)
(128)	Tudrej et al. (2020)	France	Outpatient	Cross-sectional	198	45*(IQR 28)	284 (143.0%)	Smell and Taste 58 (29.3%), Impaired smell onset 82 (41.4%), Impaired taste onset 92 (46.5%)

(129)	Vacchiano et al. (2020)	Italy	Inpatient	Cohort	108	59*(Range 18-83)	62 (57%)	Headache 46 (43%), Myalgia 37 (34%), Dizziness/vertigo 11 (10%), Impaired smell onset 40 (37%), Impaired taste onset 66 (61%)
(130)	Vaira et al. (2020)	Italy	Mixed	Cross-sectional	345	48.5 (12.8)	146 (42.3%)	Impaired smell onset 241(70%), Impaired taste onset 155 (44.9%)
(131)	Vaira et al. (2020)	Italy	Inpatient	Cross-sectional	72	49.2 (13.7)	27 (37.5%)	Headache 30 (41.6%), Asthenia 48 (66.7%), Smell and Taste 30 (41.7%), Impaired smell onset 14 (14.4%), Impaired taste onset 9 (12.5%), Impaired taste follow-up 9 (12.5%)
(132)	Boscolo-Rizzo et al. (2020)	Italy	Self-isolating	Cross-sectional	54	-	-	Smell or Taste 34 (63%)
(133)	Burke et al. (2020)	USA	Mixed	Case series	164	50 (-)	92 (56%)	Headache 97 (59%), Myalgia 103 (63%), Smell or Taste 36 (24%), Fatigue 102 (62%)
(134)	Cecchetti et al. (2020)	Italy	Inpatients referred for EEG	Case series	18	-	11 (61.1%)	Seizures 0 (0%)
(135)	Chen et al. (2020)	China	Inpatient	Case series	12	14.5 (IQR 9--16)	6 (50.0%)	Dizziness/vertigo 2 (16.7%), Fatigue 1 (8.3%)
(136)	Chen et al. (2) (2020)	China	Inpatient	Case series	113	68 (IQR 62-77)	83 (73.5%)	Headache 11 (10%), Myalgia 21 (19%), Dizziness/vertigo 10 (9%), Fatigue 64 (57%), Impaired consciousness/delirium/encephalopathy 25 (22%)

(137)	Denis et al. (2020)	France	Other	Cross-sectional	2,477,174	39.1, 37*, (IQR 15-99)	-	Asthenia 1,154363 (46.6%), Smell or Taste 325,910 (17.1%)
(138)	Duan et al. (2020)	China	Inpatient	Case series	25	52 (19.3)	15 (60.0%)	Fatigue 14 (56%)
(139)	Fraisse et al. (2020)	France	Inpatient (ICU only)	Case series	92	61*(IQR 55-70)	73 (79.3%)	Ischaemic stroke 2 (2.2%), Haemorrhagic stroke 2 (2.2%)
(140)	Gaborieau et al. (2020)	France	Inpatient	Cohort	157	0.5*(IQR 0.125 – 10)	94 (59.9%)	Smell or Taste 7 (4.5%)
(141)	Garrazzino et al. (2020)	Italy	Mixed	Case series	168	5 (IQR 0.3-9.6)	94 (56.0%)	Seizures 3 (1.8%), Fatigue 3 (1.8%)
(142)	Guo et al. (2020)	China	Inpatient	Case-control	103	42.5 (12.5)	59 (57.3%)	Depression 62 (60.2%), Anxiety 59 (55.3%), PTSD 1 (10%)
(143)	Kaye et al. (2020)	USA	Other	Cross-sectional	237	39.6 (14.6)	108 (45.6%)	Headache 88 (37%), Impaired smell onset 173 (73%), Impaired smell follow-up 65 (27%)
(144)	Li et al. (2020)	China	Inpatient	Case series	655	-	367 (56.0%)	Headache 80 (12.2%), Myalgia 78 (11.9%), Fatigue 184 (28.1%)
(145)	Liang et al. (2020)	China	inpatients	Cross-sectional	86	25.5 (Range 6-57)	44 (51.2%)	Headache 12 (14%), Myalgia 8 (9.3%), Tinnitus 3 (3.5%), Smell and Taste and Tinnitus 44 (51.2%), Fatigue 16 (18.6%), Impaired smell onset 34 (39.5%), Impaired taste onset 33 (38.4%)

(146)	Liu et al. (2020)	Taiwan	Imported cases from abroad	Case series	321	-	151 (47%)	Headache 34 (10.6%), Myalgia 14 (12.5%), Dizziness/vertigo 6 (1.9%), Smell or Taste 42 (13.1%), Fatigue 52 (16%), Ophthalmic symptoms 6 (1.9%)
(147)	Luo et al. (2020)	China	Mixed	Case series	60	43.6 (M) (2.7) 50.0 (F) (1.8)	32 (53.3%)	Headache 8 (12.7%), Dizziness/vertigo 12 (20%), Fatigue 23 (38%), Impaired taste onset 8 (12.7%)
(148)	Mao et al. (2020)	China	Inpatients	Case series	214	52.7 (15.5)	87 (40.7%)	Headache 28 (13.1%), Dizziness/vertigo 36 (16.8%), Ataxia 1 (0.5%), Seizures 1 (0.5%), Neuralgia 5 (2.3%), Visual defects 3 (1.4%), Impaired smell onset 11 (5.1%), Impaired taste onset 12 (5.6%), Impaired consciousness 16 (7.5%), Other cerebrovascular accident 6 (2.8%), Myopathy 23 (10.7%)
(149)	Myrstad et al. (2020)	Norway	Inpatients	Cohort	66	67.9 (Range 30-95)	38 (57.6%	Impaired consciousness/delirium/encephalopathy 11 (16.7%), New confusion 11 (16.7%)
(150)	Naeini et al. (2020)	Iran	Mixed	Cross-sectional	49	45.1 (12.2)	27 (55.1%)	Headache 35 (71.4%), Fatigue 31 (63%), Impaired smell onset 49 (100%), Impaired taste onset 37 (75.5%)
(151)	Nguyen et al. (2020)	Vietnam	Outpatient	Cross-sectional	1387	-	-	Participants with COVID-19 more likely to have depression (OR 2.88, $p<0.001$) and lower average HRQOL ($p<0.001$)
(152)	Pati et al. (2020)	USA	Inpatient (severe)	Case series	10	61.3 (-)	5 (50.0%)	Cerebral Performance Category <2 (poor outcome): 5 (50%); 3-5 (good outcome): 5 (50%)

(153)	Paz et al. (2020)	Ecuador	Outpatient	Cross-sectional	306	38.3 (11.0)	149 (48.7%)	Depression and anxiety 49 (16%), Depression 17 (22.9%), Anxiety 74 (24.2%)
(154)	Petrescu et al. (2020)	France	Inpatients undergoing EEG	Case series	36	69.1 (-)	26 (72.2%)	Confusion or fluctuating alertness 23 (58%), delayed awakening after ceasing sedation 6 (15%)
(155)	Petrocelli et al. (2020)	Italy	Healthcare workers	Cohort	300	43.6 (12.2)	75 (25.0%)	Headache 133 (44.3%), Myalgia 128 (42.7%), Asthenia 109 (36.3%), Smell and Taste 164 (54.7%), Impaired smell onset 26 (8.7%), Impaired taste onset 20 (6.7%)
(156)	Peyrony et al. (2020)	France	Inpatient	Cohort	225	62 (whole population) (IQR 48-71)	241 (107%)	Headache 15 (6.7%), Myalgia 71 (31.6%), Dizziness/vertigo 8 (3.6%), Fatigue 34 (15.1%), Impaired smell onset 31 (13.8%), Impaired consciousness/delirium/encephalopathy 15 (6.7%)
(157)	Pinna et al. (2020)	USA	Inpatient	Case series	50	59.6 (-)	29 (58.0%)	Headache 12 (24%), Ataxia 1 (2%), Palsy 3 (6%), Paraesthesia 1 (2%), Seizures 13 (26%), Hypogeusia and Dysgeusia 5 (10%), Impaired smell onset 3 (6%), Altered mental status 30 (60%), Ischaemic stroke 10 (20%) , Haemorrhagic stroke 4 (8%), SAH 4 (8%), TIA 1 (2%), Hypoxic ischemic brain injury 7 (14%), Meningoencephalitis 2 (4%), Myopathy 6 (12%), Short term memory loss 12 (24%), Extra -ocular muscle abnormalities 5 (10%)
(158)	Pons-Escoda et al. (2020)	Spain	Inpatient	Case series	103	74 (IQR 50-90)	63 (61.2%)	Seizures 3 (2.9%), Ischaemic stroke 3 (2.9%), Haemorrhagic stroke 8 (7.7%), Hematoma 6 (5.8%), Guillain-Barre syndrome 1 (1%)
(159)	Porta-Etessam et al. (2020)	Spain	Healthcare workers previously infected	Cross-sectional	112	43.4 (11.4)	21 (18.8%)	Headache 112 (100%), Photophobia 32 (28.6%), Impaired smell onset 11 (9.8%)

(160)	Qin et al. (2020)	China	Inpatient	Case series	1875	63 (IQR 51-70)	945 (50.4%)	Headache 123 (6.6%) , Myalgia 259 (13.8%), Dizziness/vertigo 87 (4.6%), Fatigue 477 (25.4%), Impaired consciousness/delirium/encephalopathy 16 (0.9%), Phonophonbia 46 (41.1%), Allodynia 5 (4.5%), Autonomic Symptoms 22 (19.6%)
(161)	Qiu et al. (2020)	China, France, Germany	Inpatient	Case series	161	38.8 (IQR 23-53)	92 (57.1%)	Smell and Taste 93 (24%), Impaired smell onset 61 (15%), Impaired taste onset 7 (2%)
(162)	Radmanesh et al. (2020)	USA	Inpatient	Case series	11	53 (Range 38-64)	9 (81.8%)	Impaired consciousness/delirium/encephalopathy 11 (100%)
(163)	Reddy et al. (2020)	USA	Inpatient	Case series	12	56.3	6 (50.0%)	Ischaemic stroke 10 (83.3%), Haemorrhagic stroke 2 (16.7%)
(164)	Shi et al. (2020)	China	Inpatient (ICU only)	Case series	161	59.4 (16.6)	104 (64.6%)	Headache 5 (3.1%), Fatigue and Myalgia 17 (10.6%)
(165)	Soltani et al. (2020)	Iran	Inpatient (Paeds)	Cohort	30	6 (5)	14 (46.7%)	Impaired consciousness/delirium/encephalopathy 4 (13.3%)
(166)	Spinato et al. (2020)	USA	Outpatients (mild)	Cross-sectional	202	56 (IQR 45-67)	97 (48.0%)	Headache 86 (42.6%), Myalgia 90 (44.6%), Smell or Taste 130 (64.4%), Fatigue 138 (68.3%)
(167)	Su et al. (2020)	-	Inpatients (Resp sx)	Case series	14	42.9 (Range 30-72)	8 (57.1%)	Fatigue 3 (21.4%)

(168)	Sun et al. (2020)	China	Inpatients (>60)	Case-control	244	Discharged: 67* (IQR 64-72) Deceased: 72* (IQR 66-78)	51 (41.5%) discharged 82 (67.8%) deceased	Consciousness disorders 32 (13.1%)
(169)	Tenforde et al. (2020)	USA	Mixed	Cross-sectional	350	43* (IQR 32-57)	165 (47.1%)	Headache 171 (60%) Myalgia 167 (58%), Smell and/or Taste 163 (56%), Fatigue 198 (69%), Impaired smell onset 140 (49%), Impaired taste onset 143 (50%), Confusion 41 (14%)
(170)	Vaira et al. (2020)	Italy	Healthcare workers	Cross-sectional	33	51.8 (-)	11 (33.3%)	Smell and Taste 13 (39.4%), Impaired smell onset 17 (51.5%), Impaired taste onset 17 (51.5%)
(171)	Varatharaj et al. (2020)	UK	Inpatient	Case series	153	71 (Range 23-94)	73 (47.7%)	Focal neurological deficit 1 (0.8%), Seizures 1 (0.8%), Cognitive impairment 6 (4.8%), Depression 3 (2.4%), Impaired consciousness/delirium/encephalopathy 9 (7.2%), Ischaemic stroke 57 (45.65), Haemorrhagic stroke 9 (7.2%), Other cerebrovascular accident 11 (8.8%), Meningoencephalitis 7 (5.6%), Guillain-Barre syndrome 4 (3.2%), Catatonia 1 (0.8%), Mania 1 (0.8%), Psychosis 10 (8%), Myasthenic crisis 1 (0.8%)
(172)	Vargas-Gandica et al. (2020)	Germany, USA, Venezuela, Bolivia	Mixed	Case series	10	48 (-)	3 (30.0%)	Headache 3 (30%), Weakness 4 (40%), Impaired smell onset 8 (80%), Impaired taste onset 9 (90%), Polyarthralgia 2 (20%)
(173)	Vespignani et al. (2020)	France	Inpatient	Case series	26	Specified for only 5/26 patients: 67 (-)	Specified for only 5/26 patients: 4 (15.4%)	Seizures 1 (20%), Impaired smell onset 1 (20%)
(174)	Wang et al. (2020)	China	Inpatients	Cohort	131	49* (Range 18-88)	59 (45%)	Dizziness/vertigo 2 (1.5%), Fatigue 10 (7.6%)

(175)	Wu et al. (2020)	France	Inpatient	Cross-sectional	14	-	7 (50.0%)	Fatigue 8 (57.1%), Anxiety 13 (92.9%)
(176)	Xiao et al. (2020)	China	Inpatient	Cross-sectional	66	-	34 (51.5%)	Headache 11 (16.7%) Myalgia 16 (24.2%), Fatigue 26 (39.3%), Ischaemic stroke 5 (3.3%)
(177)	Xie et al. (2020)	China	Inpatient	Case series	21	54 (15.4)	13 (61.9%)	Myalgia 1 (4.8%), Weakness 4 (19%)
(178)	Xiong et al. (2020)	China	Inpatient	Cohort	917	48.7 (17.1)	504 (55.0%)	Headache 2 (0.2%), Myalgia 2 (0.2%), Syncope 3 (0.3%), Neuralgia 1 (0.1%), Delirium 7 (0.8%), Other cerebrovascular accident 10 (1.1%)
(179)	Yan et al. (2020)	USA	Mixed	Cross-sectional	59	-	29 (49.2%)	Headache 39 (66.1%), Myalgia 37 (62.7%), Fatigue 48 (81.4%), Impaired smell onset 13 (22%), Impaired smell follow-up 40 (67.8%), Impaired taste onset 12 (20.3%), Impaired taste follow-up 42 (71.2%)
(180)	Yan et al. (2) (2020)	USA	Mixed	Cross-sectional	316	-	-	Impaired smell onset 23 (7.3%), Impaired smell follow-up 18 (23%)
(181)	Yang et al. (2020)	China	Inpatient	Case series	136	56 (/IQR 44-64)	66 (48.5%)	Dizziness/vertigo 12 (8.8%), Fatigue 53 (39%), Sleep disorders 49 (36%)
(182)	Yin et al. (2020)	China	Mixed	Cohort	30	52.7 (15.1)	19 (63.3%)	Headache 5 (16.7%), Myalgia 4 (13.3%), Fatigue 8 (26.7%)
(183)	Yu et al. (2020)	China	Inpatient	Case series	1859	59 (IQR 45-68)	934 (50.2%)	Headache 107 (6%), Myalgia 315 (17%), Fatigue 695 (37%)

(184)	Yu et al. (2020)	China	Inpatient	Case series	129	64 (/IQR 56-69)	56 (43.4%)	Myalgia 25 (19.4%), Fatigue 39 (30.2%)
(185)	Yuan et al. (2020)	China	Self-isolating	Cross-sectional	96	47.1 (13.2)	47 (49.0%)	Depression 42 (43.8%)
(186)	Zarghami et al. (2020)	Iran	Mixed	Cross-sectional	82	40.3 (14.4) (Hospitalised) 43.6 (15.8) (Non-Hospitalised)	32 (39.0%)	Depression 3 (3.7%), Anxiety 5 (6.1%), Sleep disorder 24 (29.3%)
(187)	Zayet et al. (2020)	France	Mixed	Cross-sectional	70	56.7 (19.3) (Range/19-96)	29 (41.4%)	Headache 51 (72.9%), Myalgia 41 (58.6%), Tinnitus 7 (10%), Hearing loss 4 (5.7%), Blurred vision 3 (4.3%), Fatigue 65 (92.9%), Impaired smell onset 37 (52.9%), Impaired taste onset 34 (48.6%)
(188)	Zayet et al. (2) (2020)	France	Outpatient	Case series	95	39.8 (12.2) (Range 18-73)	16 (16.8%)	Headache 74 (77.7%), Myalgia 71 (74.7%), Smell and/or Taste 70 (73.7%), Impaired smell onset 60 (63.2%), Impaired taste onset 62 (65.3%)
(189)	Zhang et al. (92020)	China	Mixed	Cohort	221	55*(IQR 39-67)	108 (48.9%)	Headache 17 (7.7%), Fatigue 156 (70.6%)
(190)	Zhang et al. (2) (2020)	China	Inpatient	Cohort	194	48.3*(IQR 33-56)	108 (55.7%)	Headache 33 (17.0%), Myalgia 44 (22.7%)
(191)	Zhang et al. (3) (2020)	China	Inpatient	Case series	869	51* (IQR 40-58)	377 (43.4%)	Headache 18 (2.1%), Myalgia 114 (13.1%), Dizziness/vertigo 12 (1.4%), Fatigue 226 (26%)

(192)	Zhao et al. (2020)	China	Inpatient	Cohort	29	56 (IQR 32 -66)	14 (48.3%)	Headache 3 (10.3%), Myalgia 3 (10.3%), Fatigue 8 (27.6%)
(193)	Zhao et al. (2) (2020)	China	Inpatient	Case series	19	48*(IQR 27-56)	11 (57.9%)	Headache 2 (10.5%), Fatigue 2 (10.5%)
(194)	Zheng et al. (2020)	China	Inpatient	Cohort	161	45*(IQR 33.5-57)	80 (49.7%)	Headache 12 (7.5%), Myalgia 18 (11.2%), Fatigue 64 (39.8%)
(195)	Zheng et al. (2) (2020)	China	Inpatient	Case series	34	66*(IQR 58-76)	23 (67.6%)	Headache 2 (5.9%), Myalgia 5 (14.7%), Fatigue 2 (5.9%)
(196)	Zhou et al. (2020)	China	Inpatient	Case-control	29	47 (10.5)	18 (62.1%)	No significant differences between total scores on Trail Making Test, Sign Coding Test, Continuous Performance Test and Digital Span Test among recovered COVID-19 patients compared to healthy controls.
(197)	Zhou et al. (2) (2020)	China	Inpatient	Cohort	21	66.1 (13.9)	13 (61.9%)	Myalgia 2 (9.5%), Fatigue 5 (23.8%)
(198)	Mahammedi et al. (2020)	Italy	Inpatient	Case series	108	71*(IQR 60.5-79)	69 (63.9%)	Headache 13 (12%), Myalgia 13 (12%), Ataxia 2 (2%), Seizures 10 (9%), Neuralgia 3 (3%), Impaired smell onset 2 (2%), Impaired consciousness/delirium/encephalopathy 64 (59%), Ischaemic stroke 34 (31%), Haemorrhagic stroke 6 (5.6%), Guillain-Barre syndrome 2 (20%), Central demyelination 2 (10%)
(199)	Solomon et al. (2020)	USA	Inpatient	Case series	18	62 (IQR 53-75)	14 (77.8%)	Headache 2 (11.1%), Myalgia 3 (16.7%), Impaired taste onset 1 (5.5%)
(200)	Levinson et al. (2020)	Israel	Isolation unit	Cross-sectional	45	34 (Range 15-82)	23 (51.1%)	Headache 20 (48%), Myalgia 24 (57%), Dizziness/vertigo 9 (21%), Fatigue 29 (69%), Impaired smell onset 15 (36%), Impaired smell follow-up 4 (8.9%), Impaired taste onset 14 (33%), Impaired taste follow-up 2 (2.2%)

(201)	Kotabagi et al. (2020)	UK	Inpatient (Pregnant women)	Cross-sectional	11	31(Range 18-39)	0 (0.0%)	PHQ-9 and GAD-7 scores highest at time of institution of lockdown rules
(202)	Yaghi et al. (2020)	USA	Inpatient	Case series	3556	62.5 (IQR 52-69.3) (in events)	23 (71.9%) (in events)	Stroke 32 (0.9%)
(203)	Yan et al. (2020)	USA	Mixed	Case series	128	53.5* (IQR 40-65)	9 (7.0%)	Headache 62 (48.4%), Fatigue 90 (70.3%), Impaired smell onset 75 (58.6%), Impaired taste onset 70 (54.7%)
(204)	Tian et al. (2020)	China	Inpatient	Case series	262	47.5*(Range 1-94)	127 (48.5%)	Headache 17 (6.5%), Fatigue 69 (26.3%)
(205)	Helms et al. (2020)	France	Inpatient (with ARDS)	Case series	58	63*(-)	-	Focal neurological deficit 39 (67%), Cognitive impairment 14 (36%), Confusion 26 (44.8%), Ischaemic stroke 3 (5%)
(206)	Suleyman et al. (2020)	USA	Mixed	Case series	463	57.5 (16.8)	204 (44.1%)	Headache 74 (16%), Myalgia 194 (42%)
(207)	Zier et al. (2020)	USA	Inpatient	Case series	66	58*(Range 23-87)	43 (65.2%)	Myalgia 36 (55%), Fatigue 44 (67%)
(208)	Dogra et al. (2020)	USA	Inpatient (ICH)	Case series	33	62*(Range 37-83)	26 (78.8%)	Speech/aphasia 1 (3%), Focal neurological deficit 7 (21.2%), Seizures 2 (6.1%), Impaired consciousness/delirium/encephalopathy 17 (51.1%), Haemorrhagic stroke 31 (93.9%), Other cerebrovascular accident 11 (33.3%), Meningoencephalitis 8 (24.2%)

(209)	Lechien et al. (2020)	Europe	Mixed	Cross-sectional	417	36.9 (11.4)	154 (36.9%)	Headache 188(45%), Myalgia 242 (58%), Asthenia 188 (45%), Impaired smell onset 284 (79.6%), Impaired taste onset 342 (88.8%)
(210)	Parma et al. (2020)	USA	Outpatients	Cross-sectional	4039	41.4 (12.2)	1118 (27.7%)	Mean reductions in smell (-79.7±28.7), taste (-69.0±32.6) and chemesthetic function (-37.3±36.2) during COVID-19
(211)	De Maria et al. (2020)	Italy	outpatients	Cross-sectional	95	-	-	Impaired smell onset 48 (50.5%), Impaired taste onset 48 (50.5%)
(212)	Ligouri et al. (2020)	Italy	Inpatient	Cross-sectional	103	55 (14.7)	59 (57.3%)	Headache 40 (38.3%), Myalgia 25 (24.7%), Dizziness/vertigo 27 (26.2%), Hearing impairment 2 (1.9%), Paraesthesia 6 (5.8%), Fatigue 33 (32%), Impaired smell onset 40 (38.3%), Impaired taste onset 48 (46.6%), Depression 39 (37.9%), Anxiety 34 (33%), Impaired consciousness/delirium/encephalopathy 23 (22.2%), Sleep disorders 51 (49.5%)
(213)	Wee et al. (2020)	Singapore	Mixed	Cohort	154	-	-	Smell or Taste 35 (22.7%)
(214)	Giacomelli et al. (2020)	Italy	Inpatient	Cross-sectional	59	60* (IQR 50-74)	40 (67.8%)	Headache 2 (3.4%), Asthenia 1 (1.7%), Smell and Taste 11 (28.9%), Impaired smell onset 3 (5.1%), Impaired taste onset 6 (10.2%)
(215)	Gelardi et al. (2020)	Italy	Outpatient	Cohort	72	49.7 (Range 19-70)	39 (54.2%)	Headache 16 (22%) , Myalgia 13 (18%), Weakness 29 (40%), Impaired smell onset 26 (36.1%), Impaired taste onset 42 (58.3%)

Outcomes refer to all COVID-19 infected patients. Mean age given, where median age used, illustrated by *, IQR/Range specified.

HCW = Health Care Workers. ICH = intracranial haemorrhage. ICU = Intensive Care Unit. MRI = Magnetic resonance imaging. ED = Emergency Department. CT = Computed tomography. CT Angiogram = Computed tomography angiography. SAH = Subarachnoid haemorrhage. TIA = Transient ischaemic attack. CNS = Central Nervous System.

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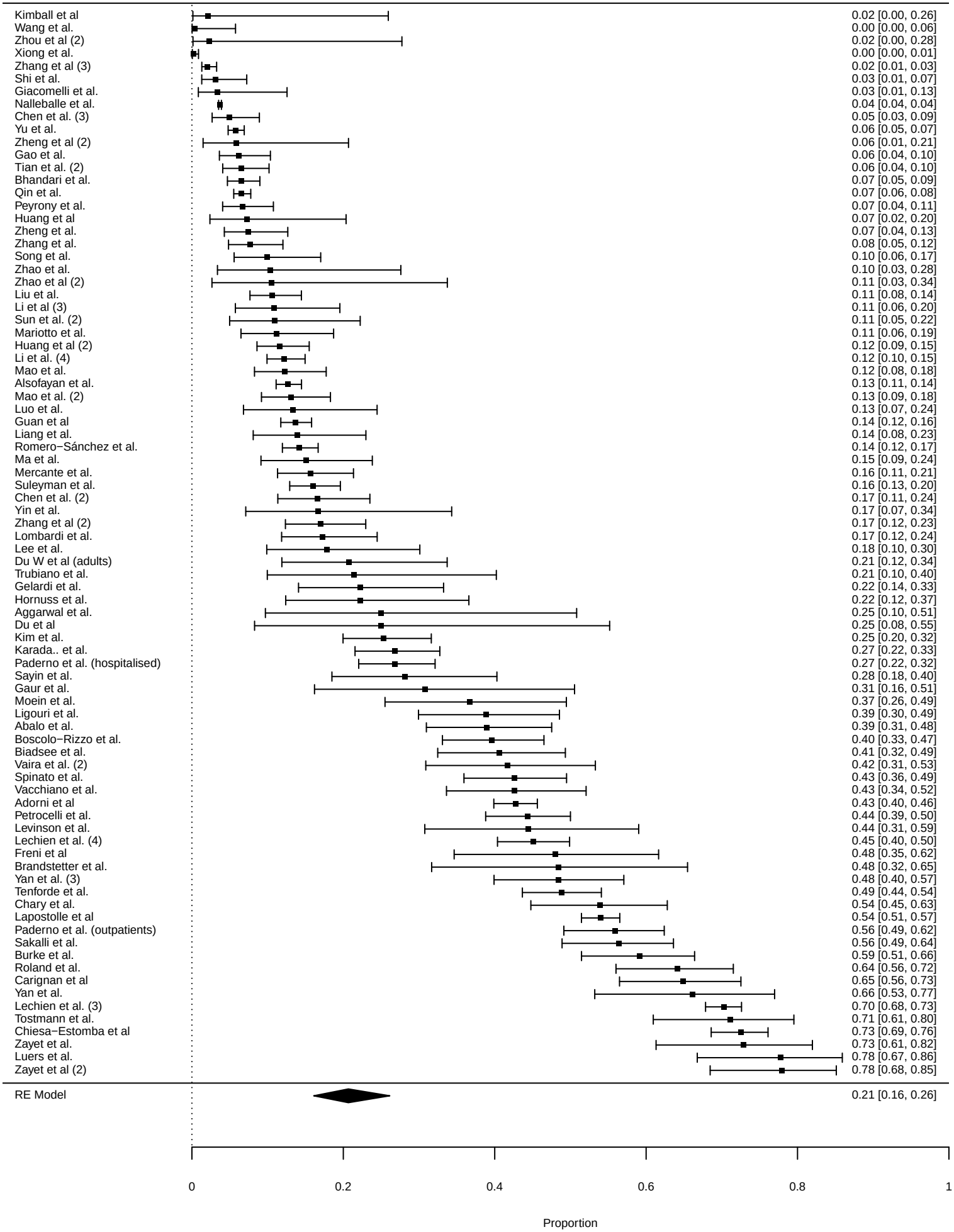
Supplementary Table 4: Comparison of proportion estimation models

	GLMM			Double-arcsine transformation		
Symptom/Syndrome	Prevalence (%)	95% CI	I^2	Prevalence (%)	95% CI	I^2
Headache	20.7	16.1 - 26.1	99.0%	24.3	19.6 - 29.4	99.2%
Myalgia	25.1	19.8-31.3	99.1%	28.6	23.5 - 33.9	99.3%
Anosmia	43.1	35.2 – 51.3	98.8%	45.0	37.8 - 51.5	98.6%
Fatigue	35.7	29.2 – 42.9	98.4%	37.1	30.9 - 43.5	98.4%
Dysgeusia	37.2	29.8 – 45.3	98.6%	39.5	32.8 - 46.5	98.5%

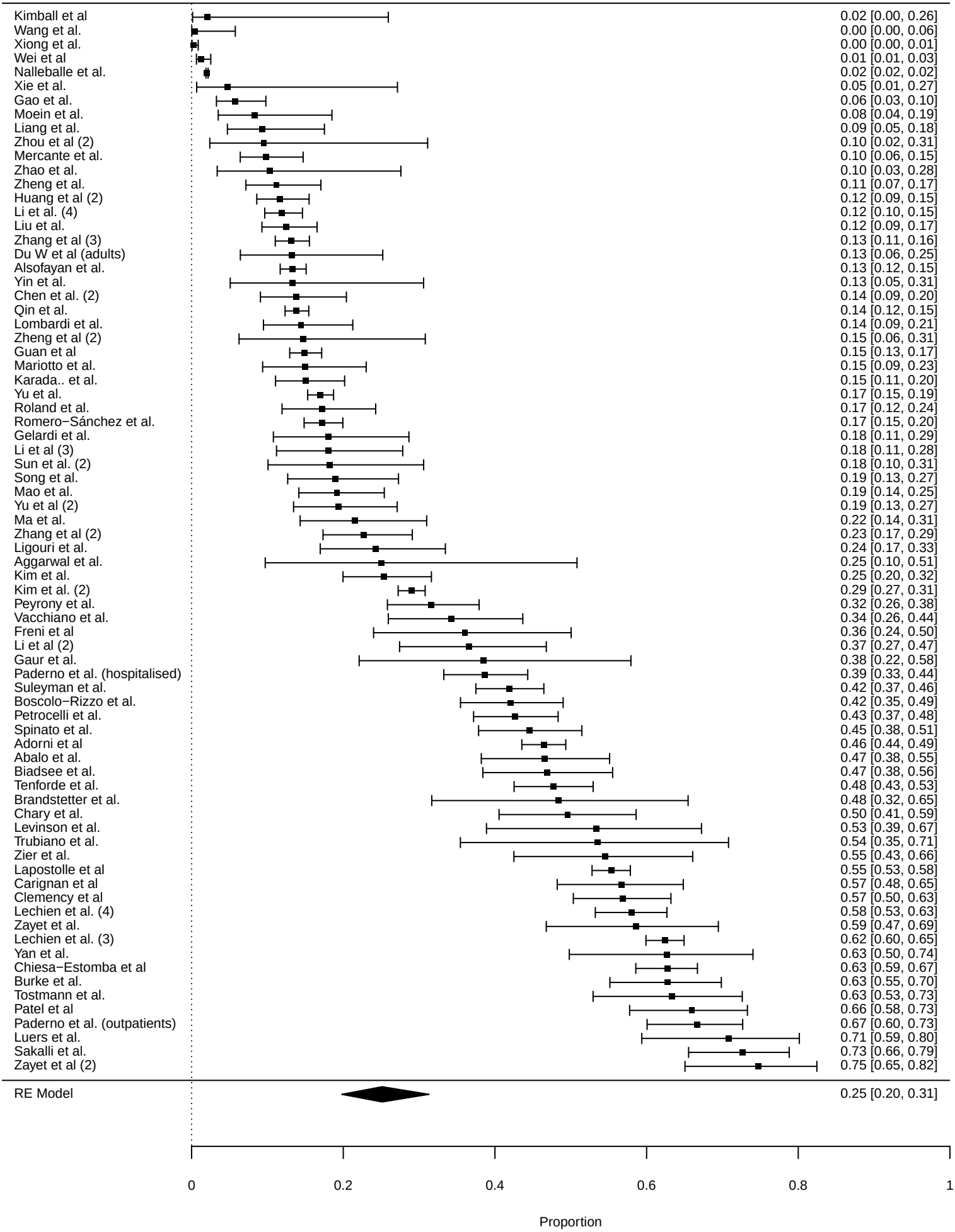
Supplementary table 5: Subgroup analysis by country of origin

Outcome	Country (*N* studies)	Prevalence %	95% CI	*p*
Headache (84 studies)	China (32)	7.8	5.7-10.4	(reference)
	Italy (12)	28.0	19.4-38.6	<0.001
	USA (12)	32.6	18.4-51.0	<0.001
Myalgia (76 studies)	China (27)	10.4	7.1-15.1	(reference)
	USA (13)	34.0	19.1-52.9	0.001
	Italy (10)	26.4	18.7-35.9	<0.001
Fatigue (67 studies)	China (30)	31.2	24.5-38.8	(reference)
	Italy (11)	31.1	18.9-46.8	1.00
	USA (11)	64.2	56.7-70.9	<0.001
Anosmia (63 studies)	Italy (15)	41.1	26.7-57.1	(reference)
	France (9)	35.5	18.4-57.4	0.67
	USA (8)	27.2	12.1-50.5	0.31
Dysgeusia (52 studies)	Italy (13)	39.1	26.0-54.1	(reference)
	France (6)	39.1	21.3-60.4	1.00
	USA (6)	45.0	27.8-63.4	0.63

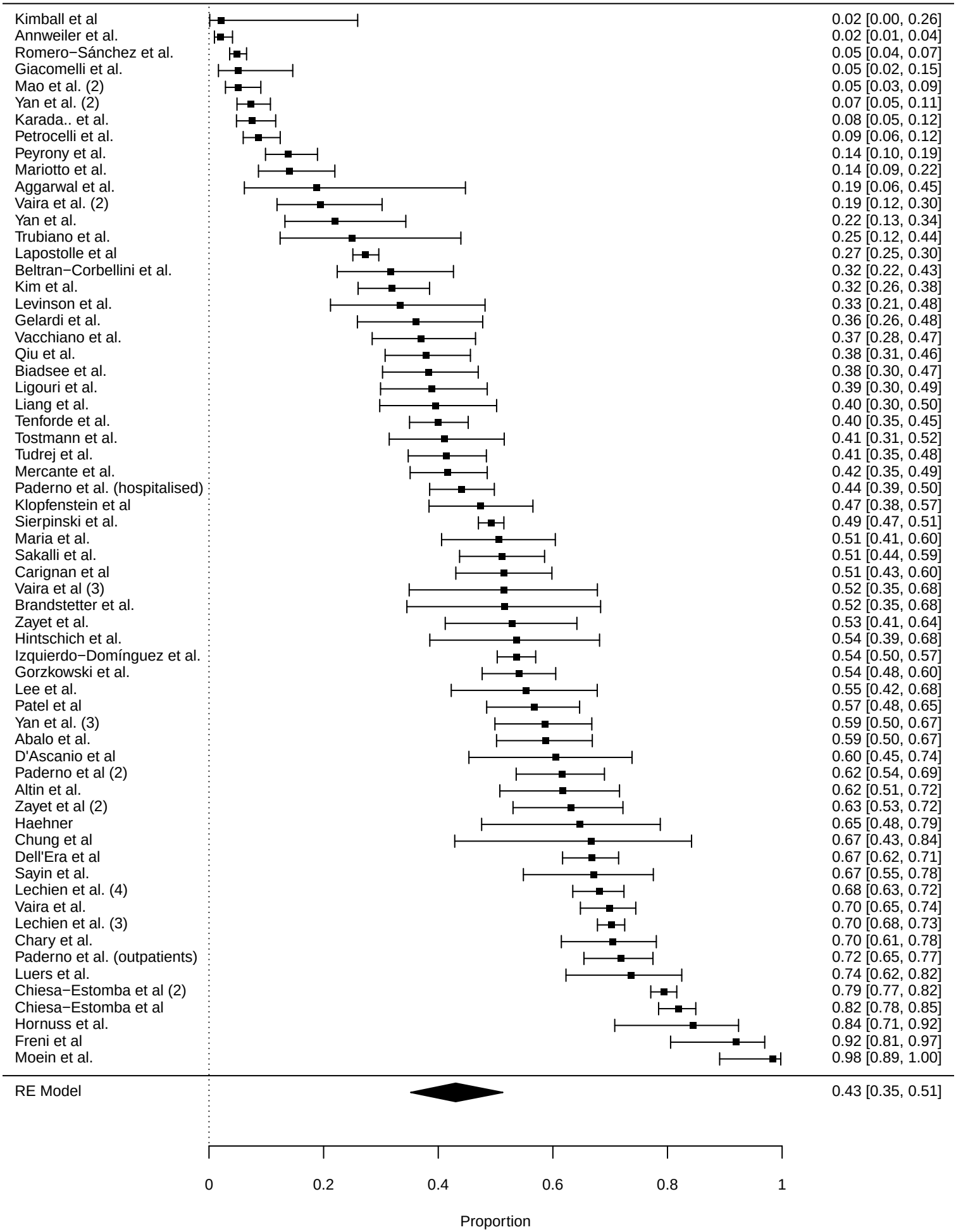
Proportion of patients reporting headache in SARS−CoV−2 infection



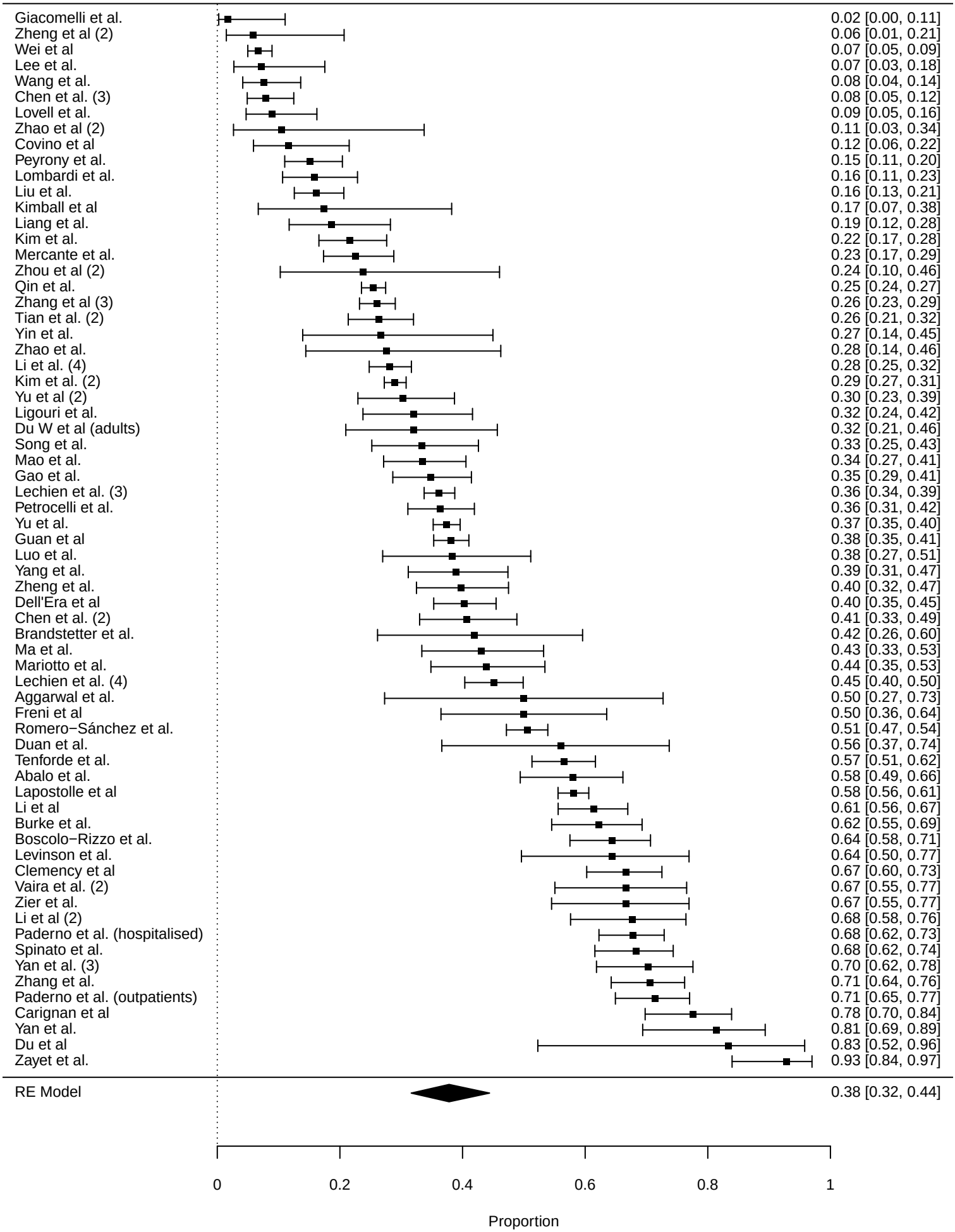
Proportion of patients reporting myalgia in SARS−CoV−2 infection



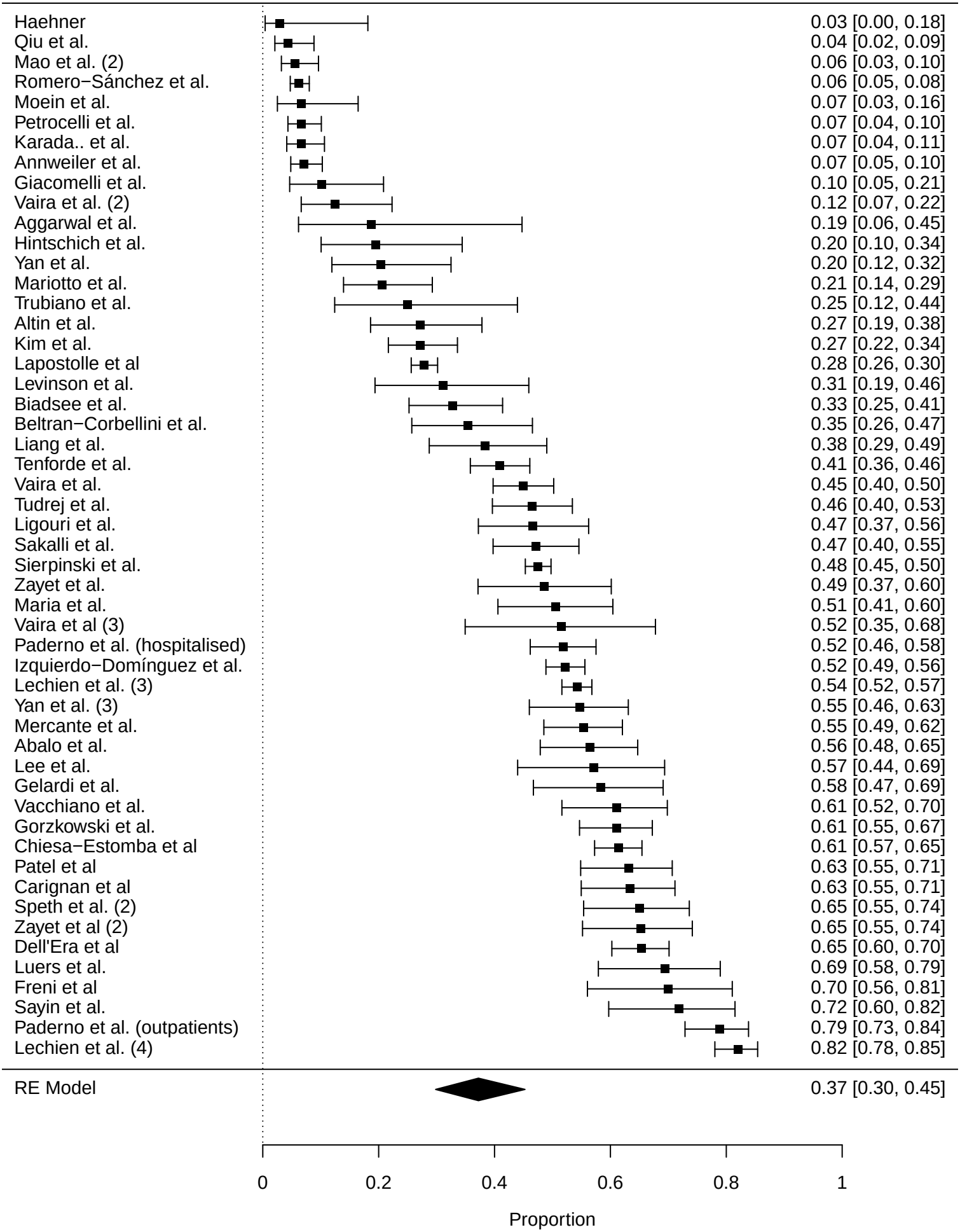
Proportion of patients reporting anosmia in SARS−CoV−2 infection



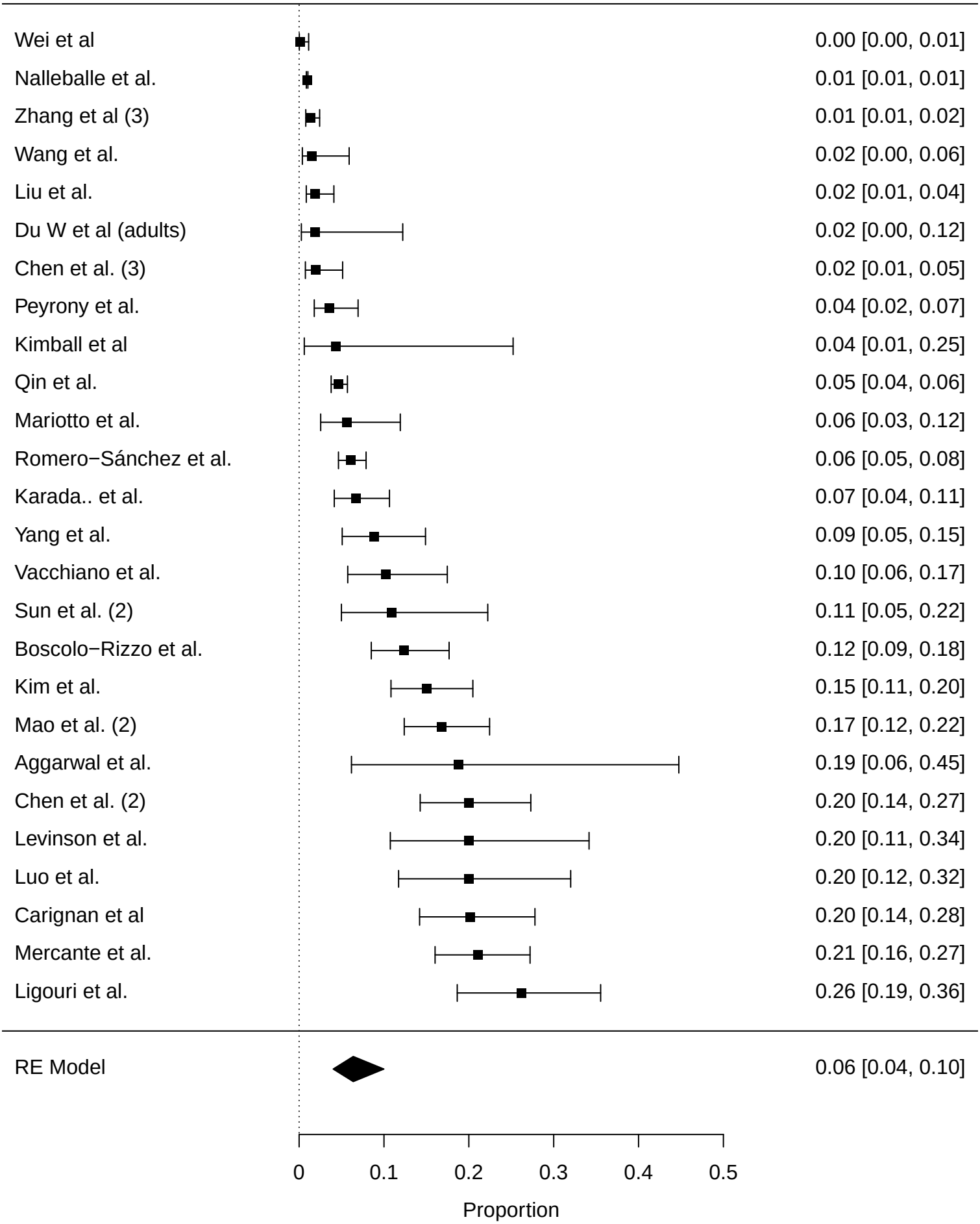
Proportion of patients reporting fatigue in SARS−CoV−2 infection



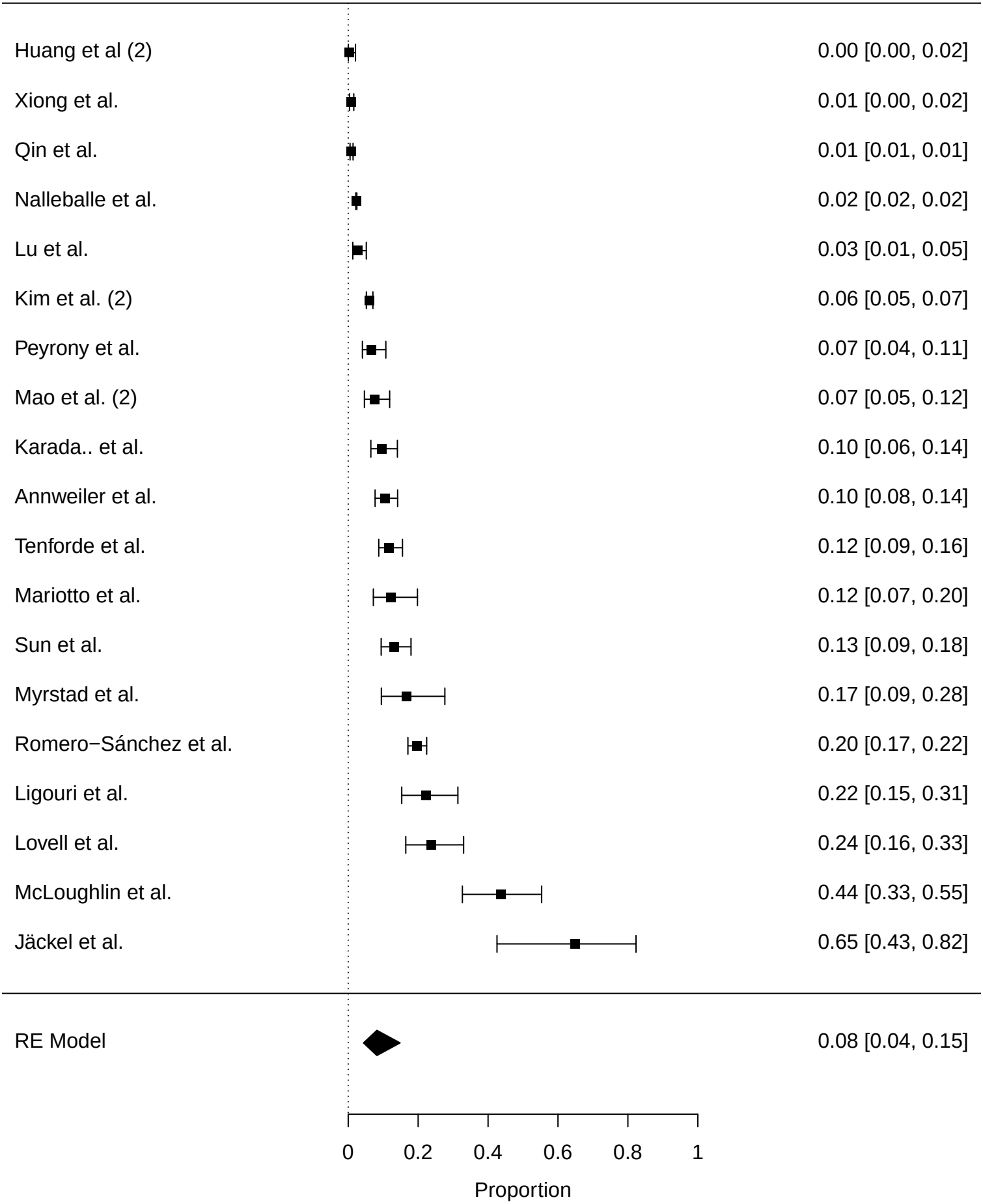
Proportion of patients reporting dysguesia in SARS−CoV−2 infection



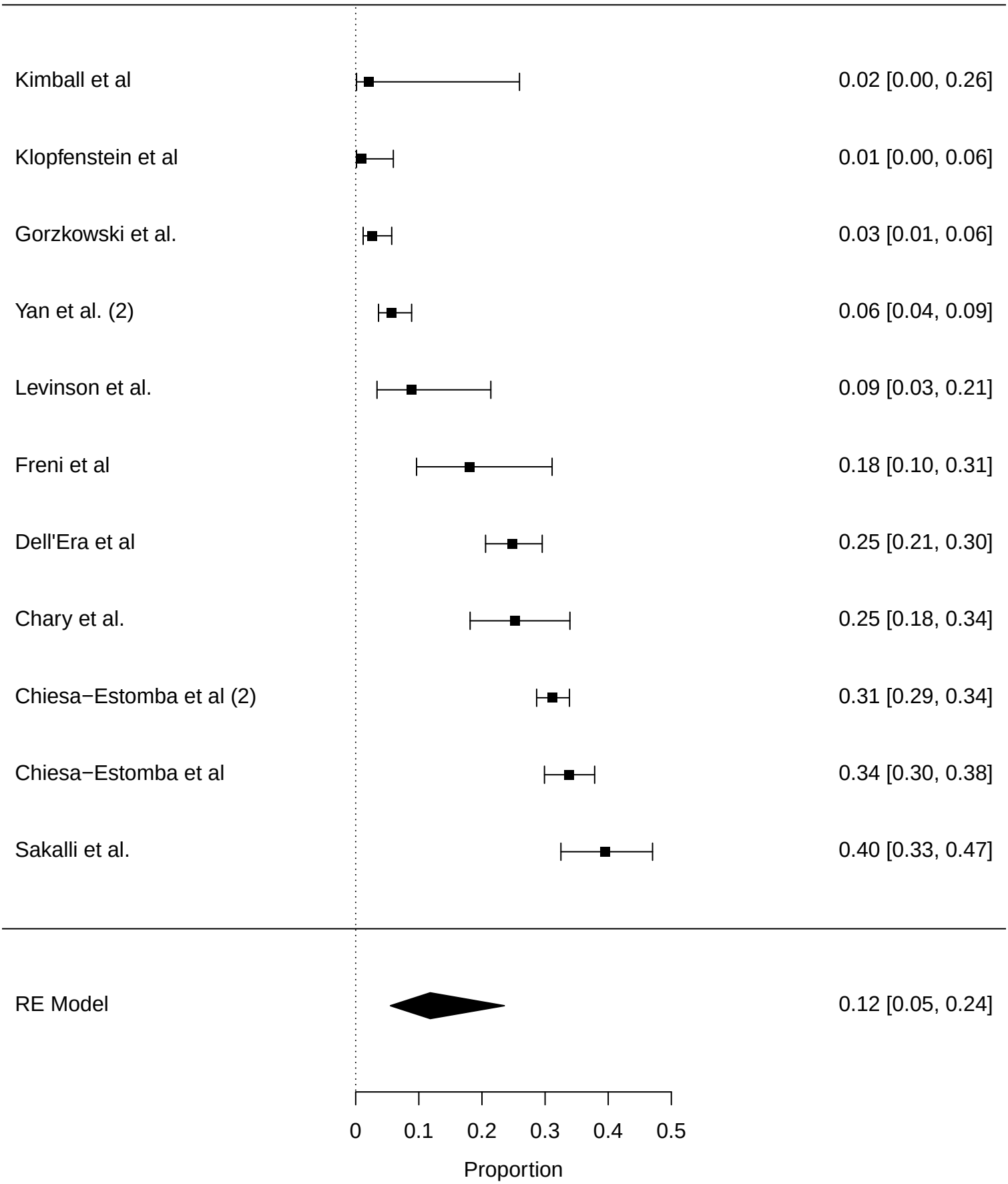
Proportion of patients reporting dizziness/vertigo in SARS−CoV−2 infection

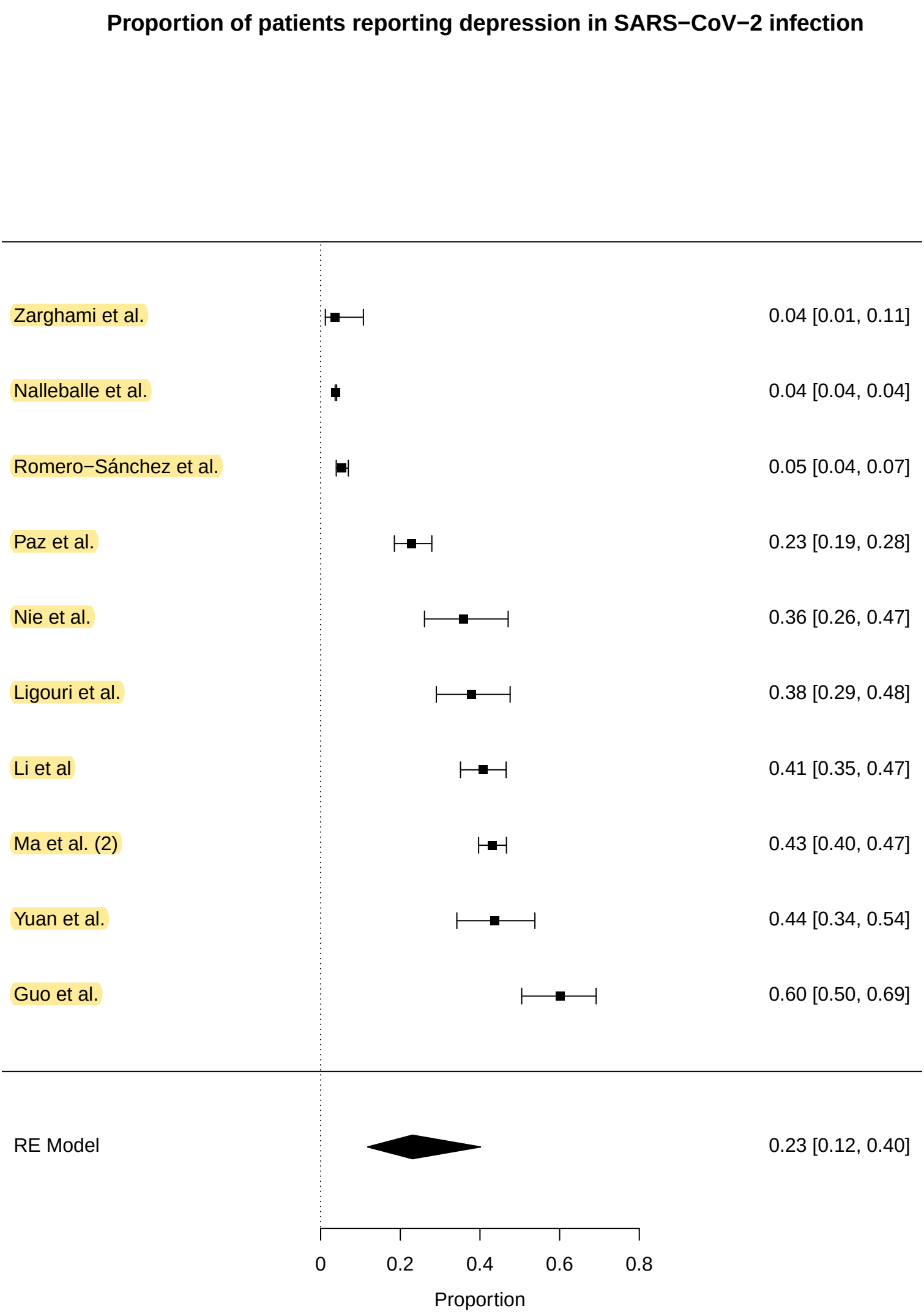


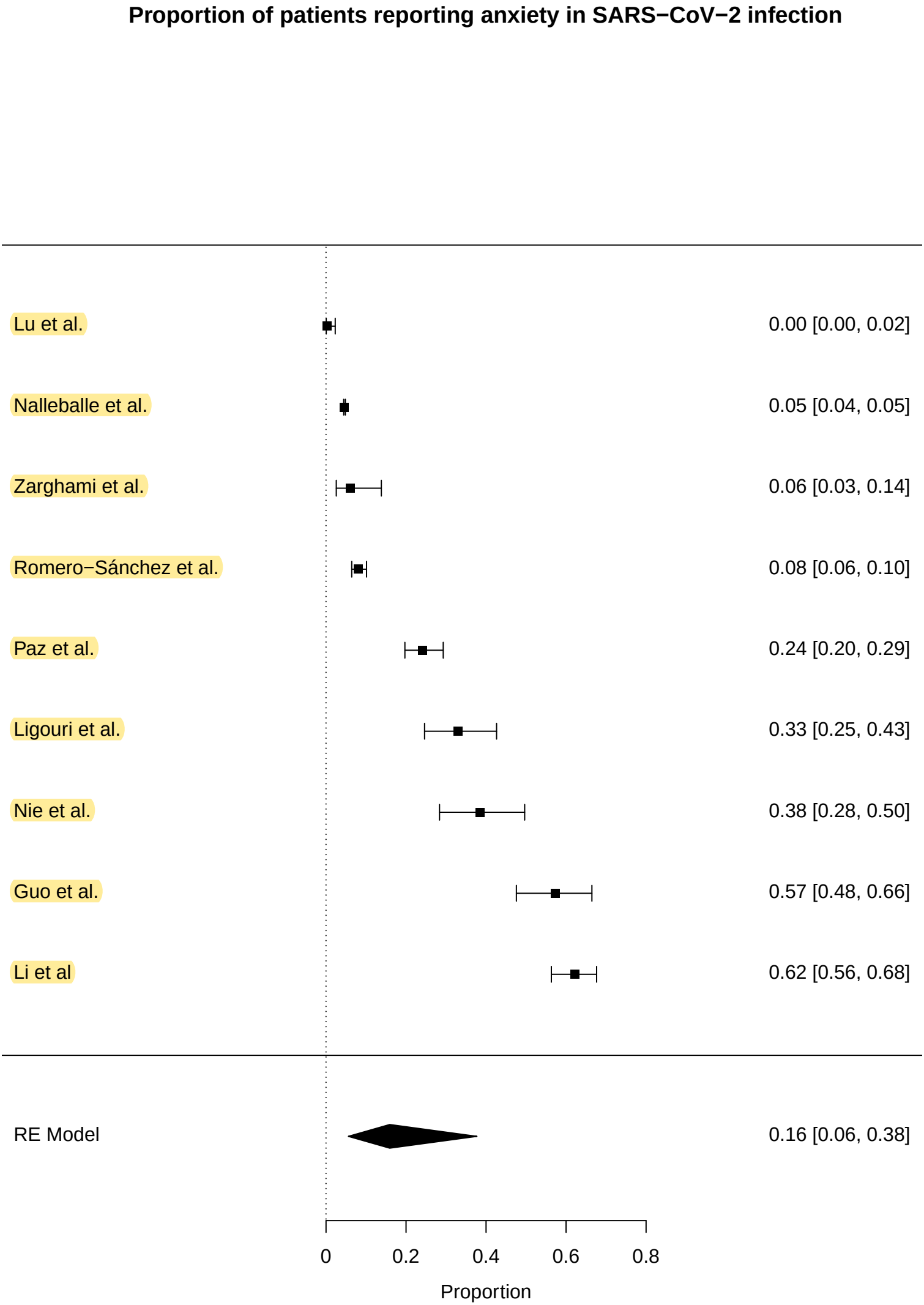
Proportion of patients reporting altered mental status in SARS−CoV−2 infection

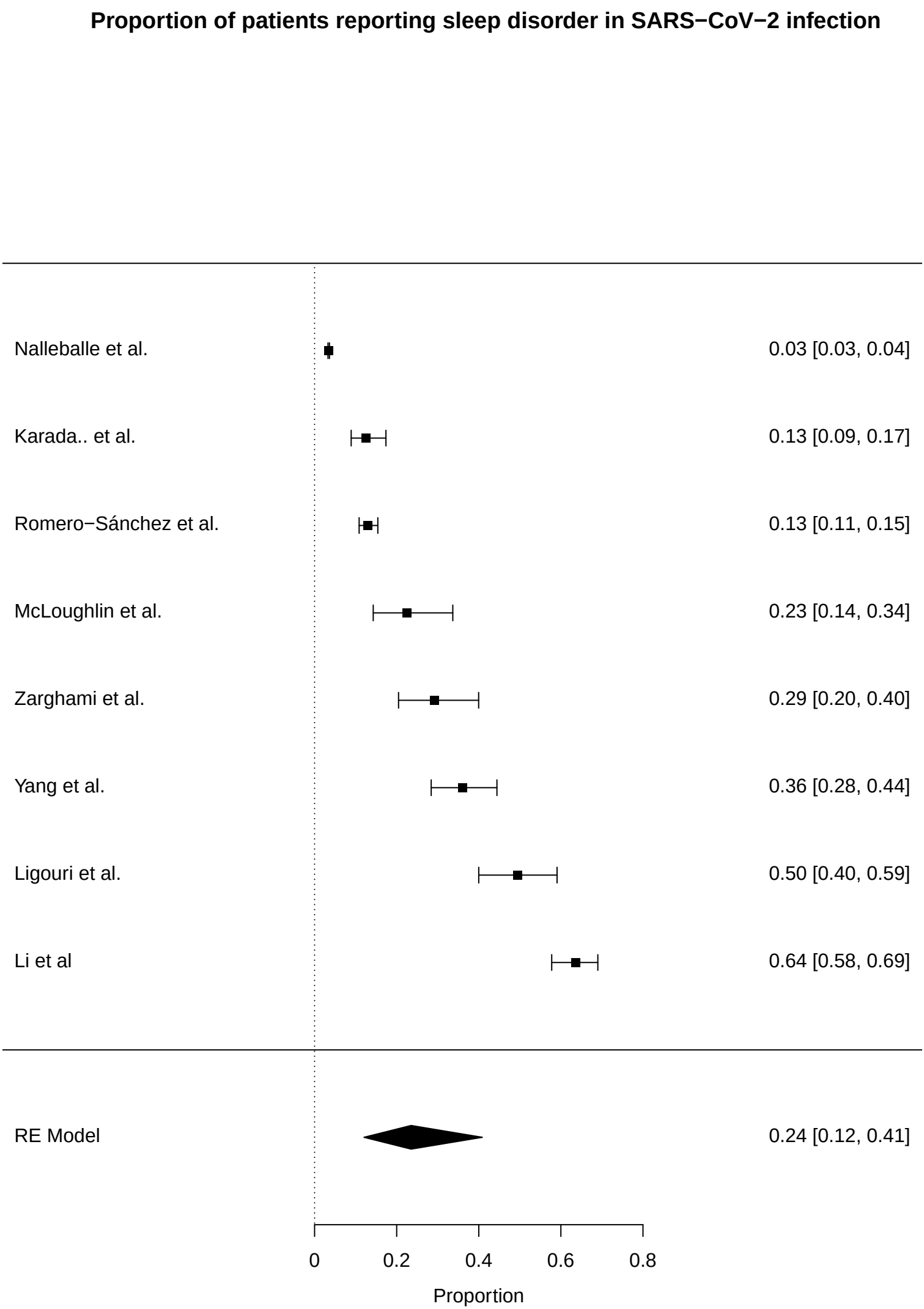


Proportion of patients reporting anosmia at follow−up in SARS−CoV−2 infection

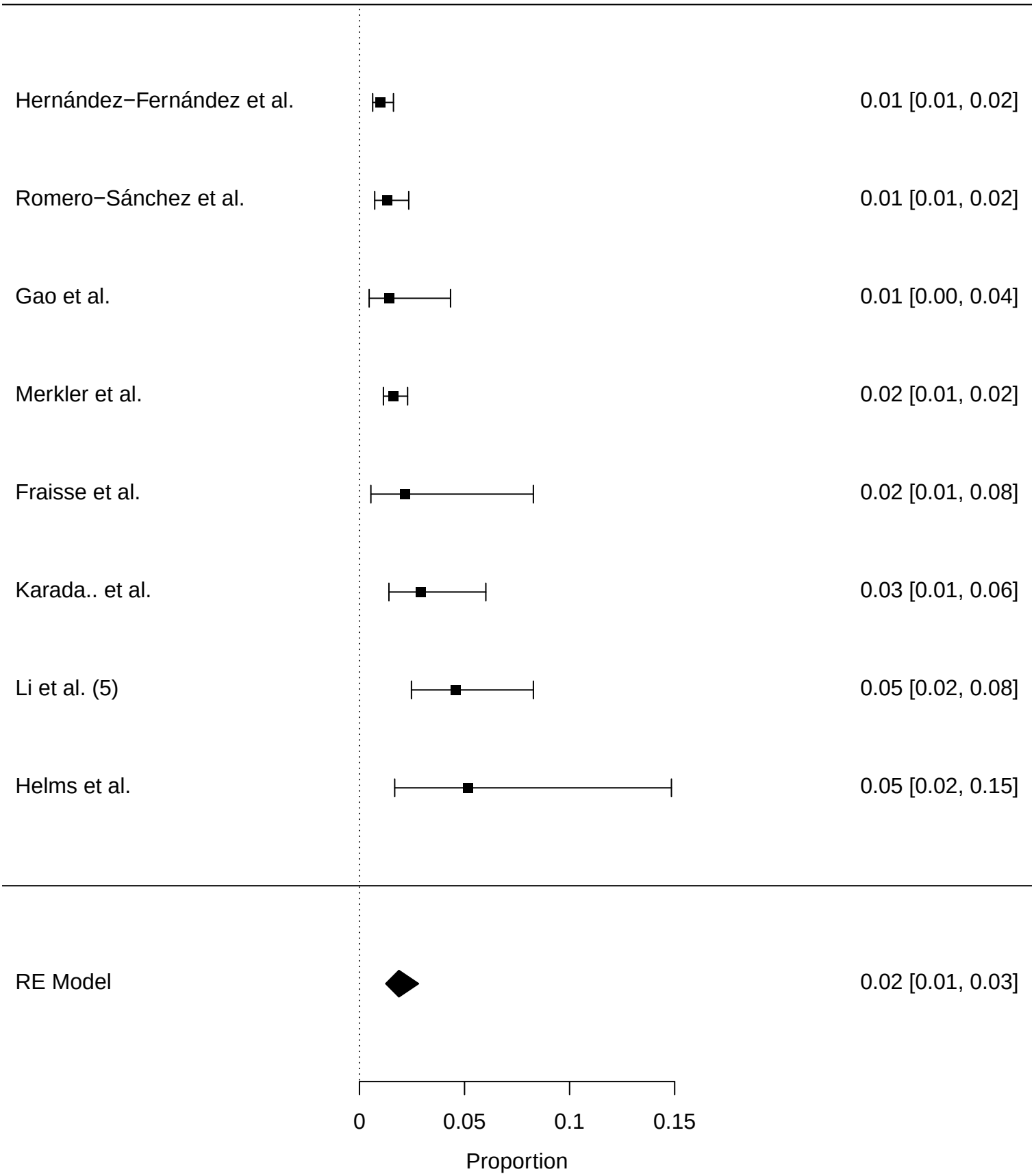



Proportion of patients reporting depression in SARS−CoV−2 infection
Zarghami et al.
0.04 [0.01, 0.11]
Nalleballe et al.
0.04 [0.04, 0.04]
Romero−Sánchez et al.
0.05 [0.04, 0.07]
Paz et al.
0.23 [0.19, 0.28]
Nie et al.
0.36 [0.26, 0.47]
Ligouri et al.
0.38 [0.29, 0.48]
Li et al
0.41 [0.35, 0.47]
Ma et al. (2)
0.43 [0.40, 0.47]
Yuan et al.
0.44 [0.34, 0.54]
Guo et al.
0.60 [0.50, 0.69]
RE Model
0.23 [0.12, 0.40]
0
0.2
0.4
0.6
0.8
Proportion

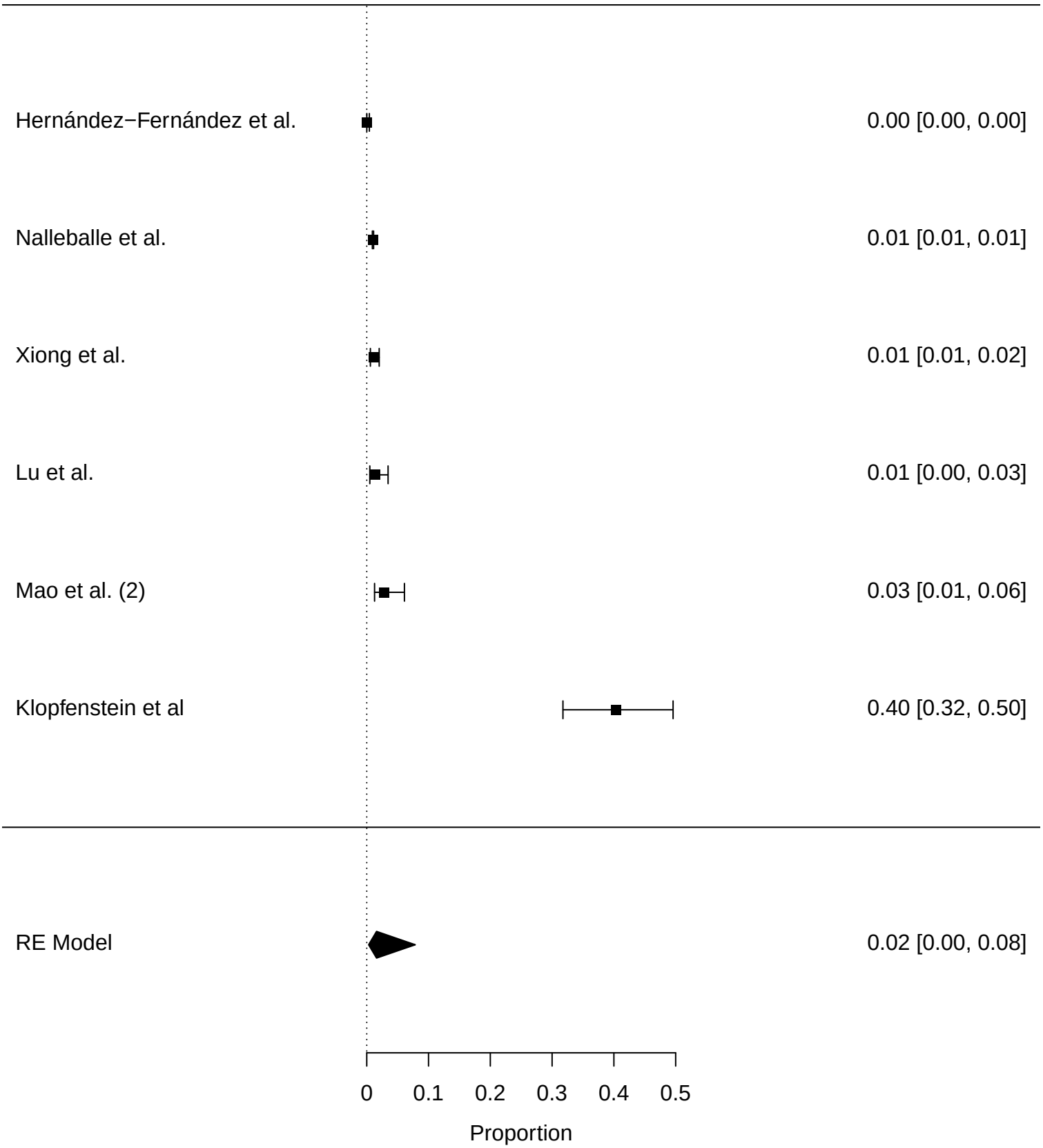

Proportion of patients reporting anxiety in SARS−CoV−2 infection
Lu et al.
Nalleballe et al.
Zarghami et al.
Romero−Sánchez et al.
Paz et al.
Ligouri et al.
Nie et al.
Guo et al.
Li et al
RE Model
0.00 [0.00, 0.02]
0.05 [0.04, 0.05]
0.06 [0.03, 0.14]
0.08 [0.06, 0.10]
0.24 [0.20, 0.29]
0.33 [0.25, 0.43]
0.38 [0.28, 0.50]
0.57 [0.48, 0.66]
0.62 [0.56, 0.68]
0.16 [0.06, 0.38]
0
0.2
0.4
0.6
0.8
Proportion


Proportion of patients reporting sleep disorder in SARS−CoV−2 infection
Nalleballe et al.
0.03 [0.03, 0.04]
Karada.. et al.
0.13 [0.09, 0.17]
Romero−Sánchez et al.
0.13 [0.11, 0.15]
McLoughlin et al.
0.23 [0.14, 0.34]
Zarghami et al.
0.29 [0.20, 0.40]
Yang et al.
0.36 [0.28, 0.44]
Ligouri et al.
0.50 [0.40, 0.59]
Li et al
0.64 [0.58, 0.69]
RE Model
0.24 [0.12, 0.41]
0
0.2
0.4
0.6
0.8
Proportion

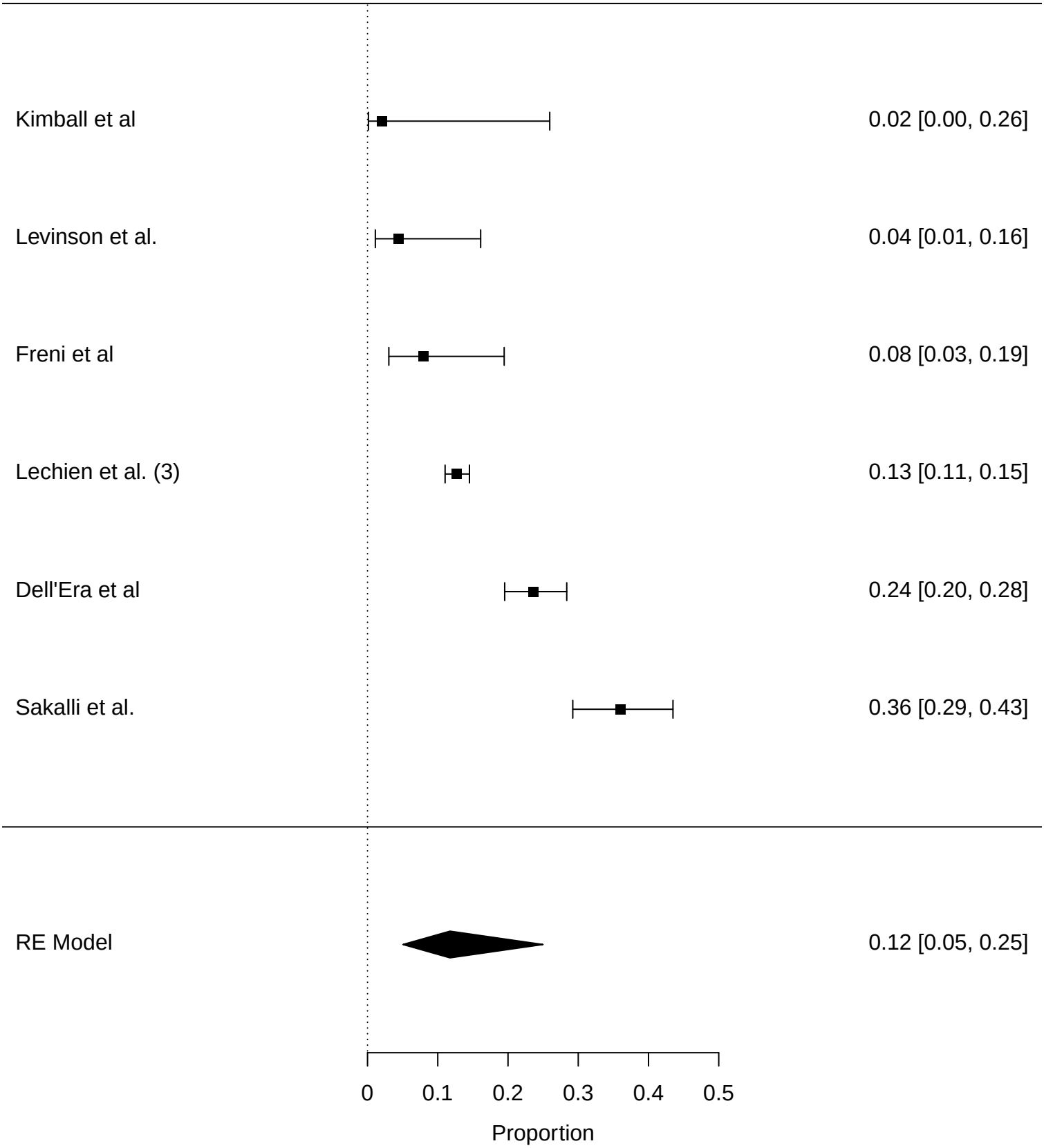
Proportion of patients with ischaemic stroke in SARS−CoV−2 infection

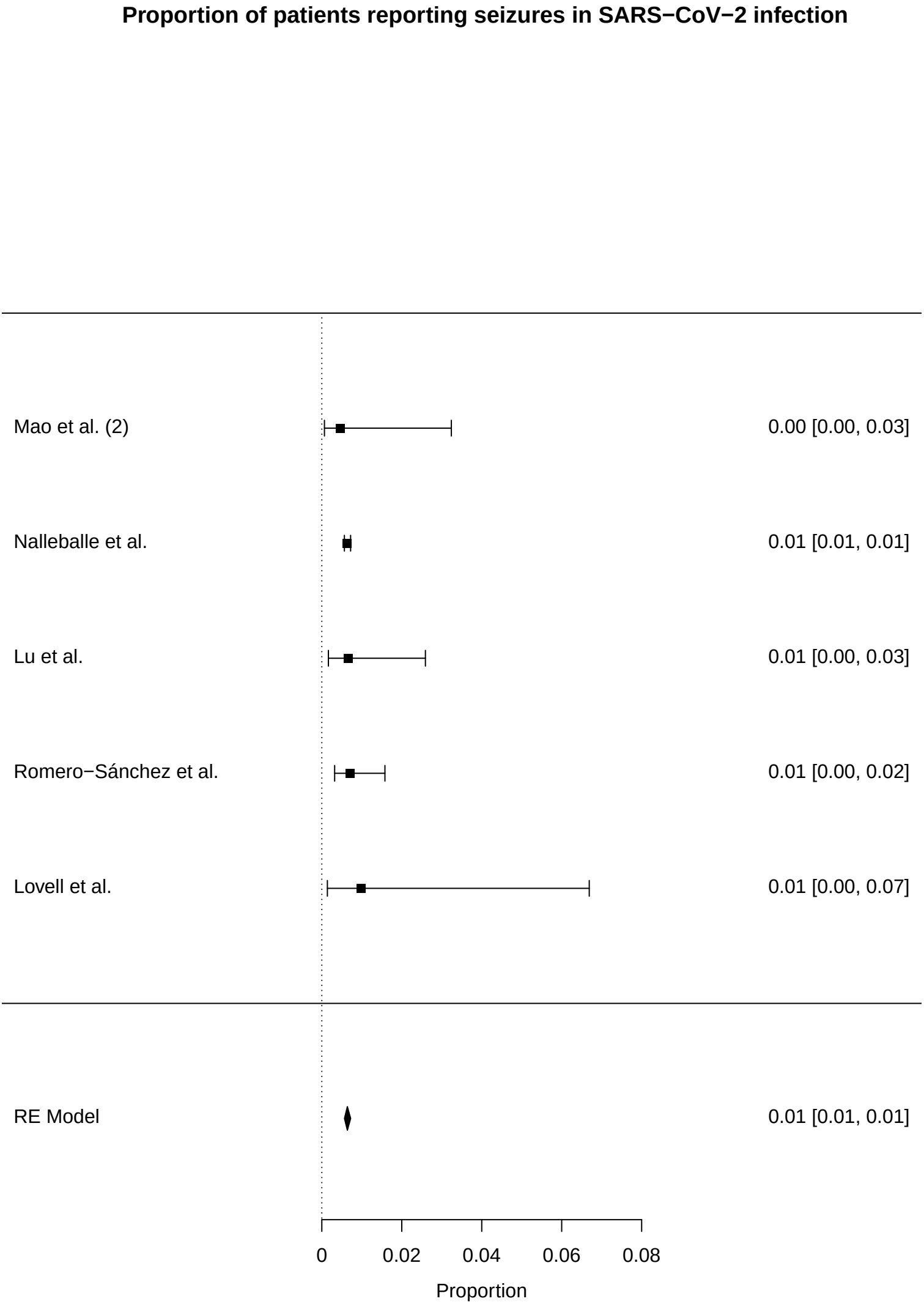


roportion of patients with unsecified cerebrovascular accident stroke in SARS−CoV−2 infe

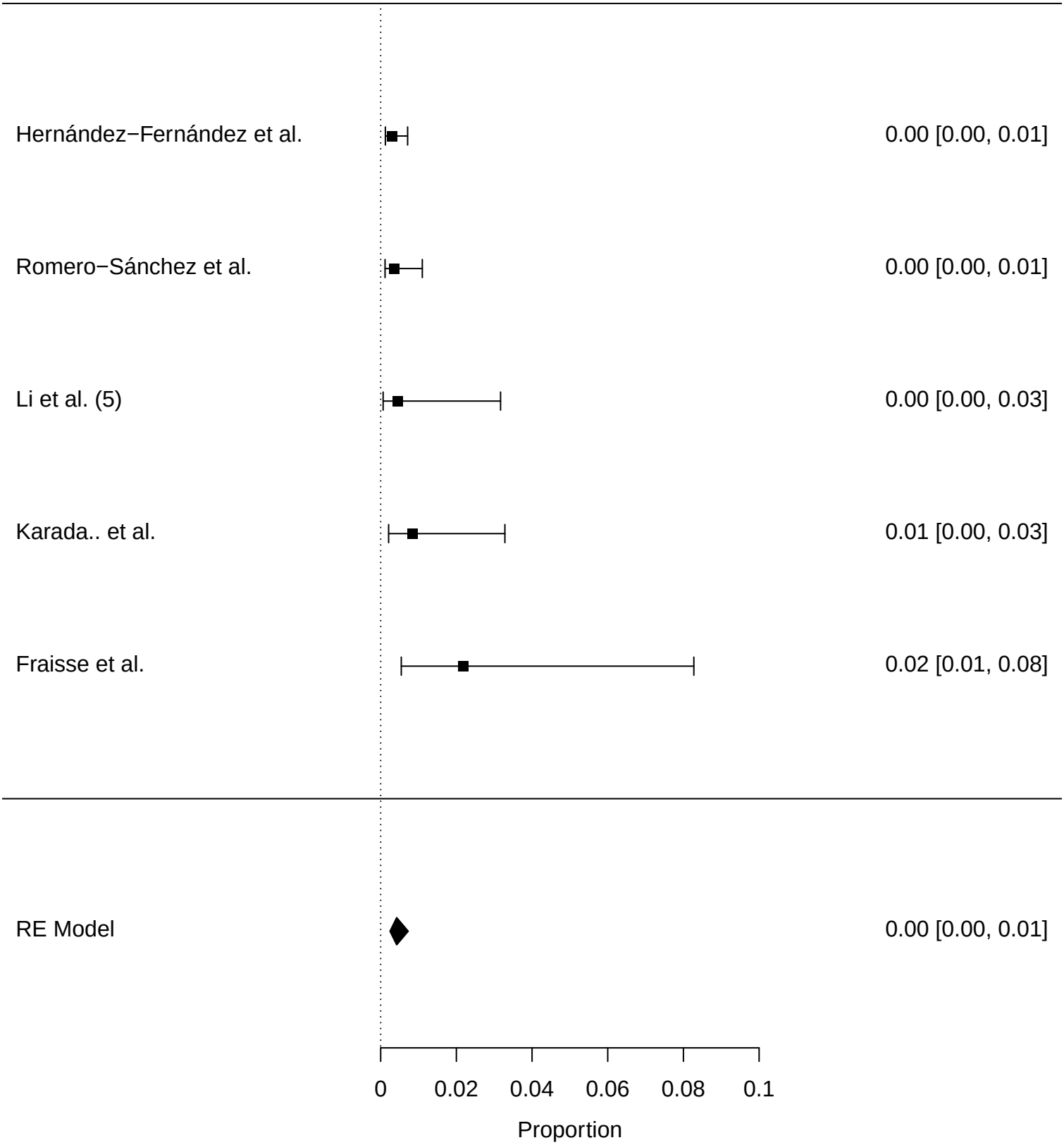


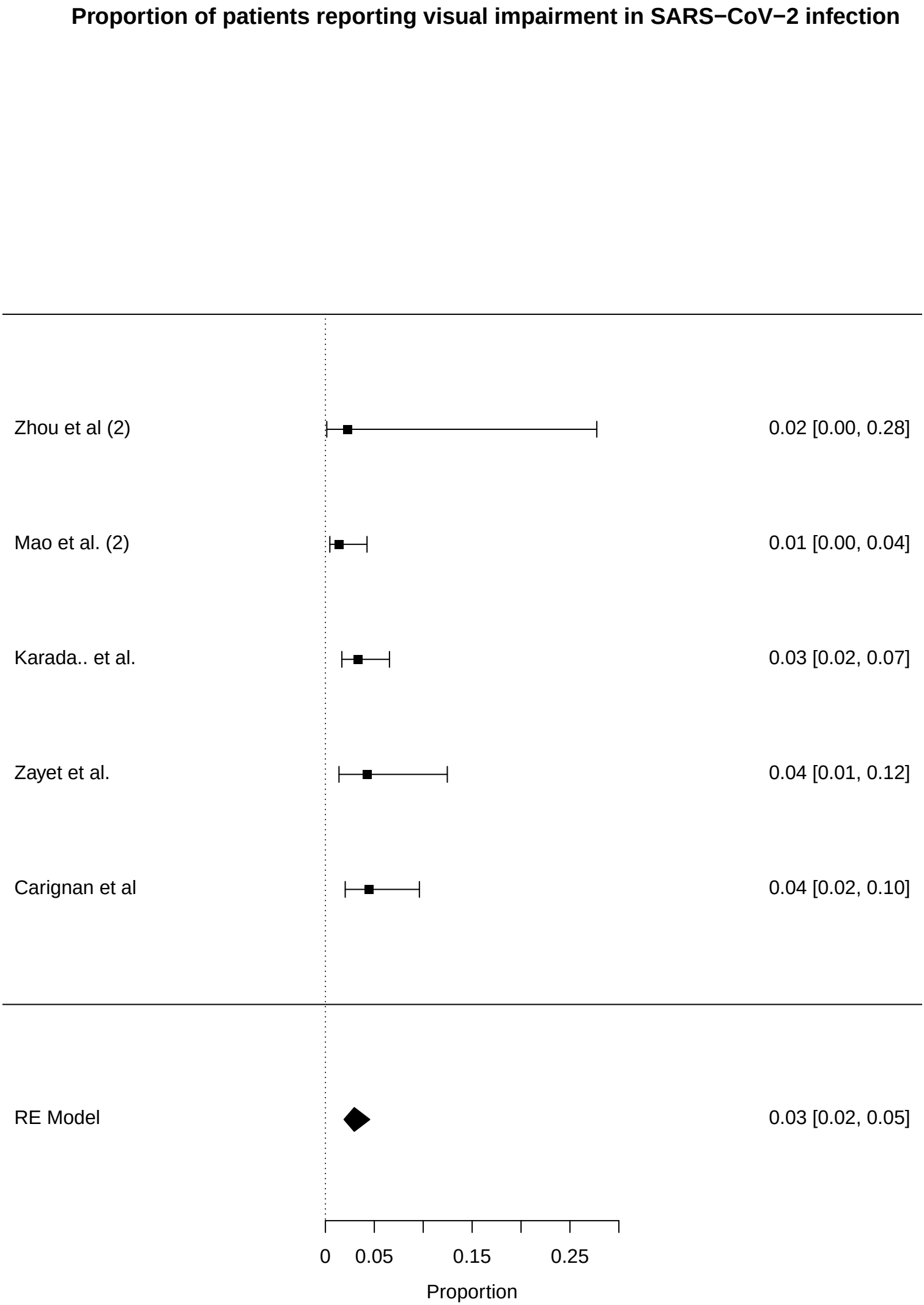
Proportion of patients reporting dysguesia at follow−up in SARS−CoV−2 infection



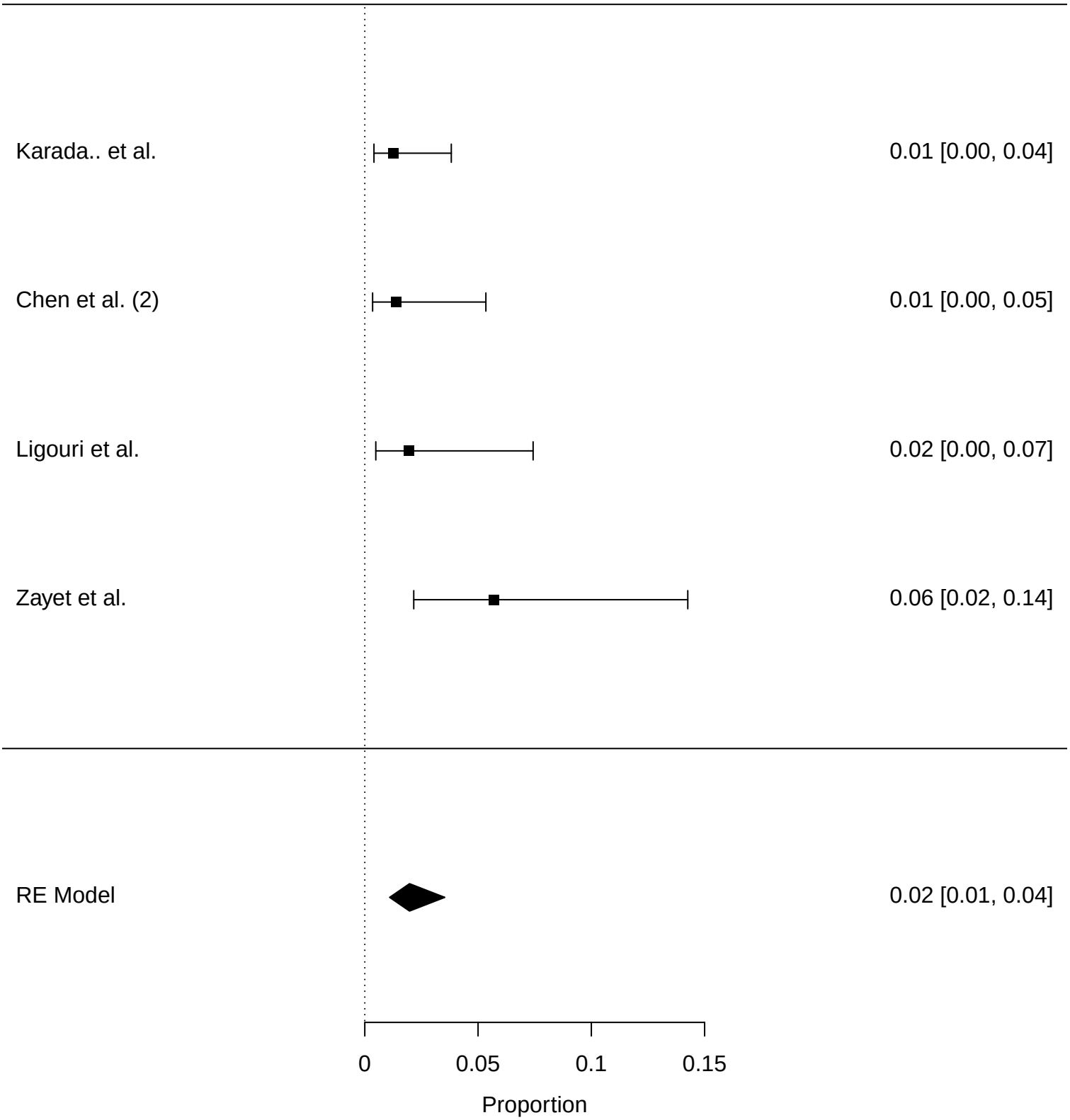

Proportion of patients reporting seizures in SARS−CoV−2 infection
Mao et al. (2)
0.00 [0.00, 0.03]
Nalleballe et al.
0.01 [0.01, 0.01]
Lu et al.
0.01 [0.00, 0.03]
Romero−Sánchez et al.
0.01 [0.00, 0.02]
Lovell et al.
0.01 [0.00, 0.07]
RE Model
0.01 [0.01, 0.01]
0
0.02
0.04
0.06
0.08
Proportion

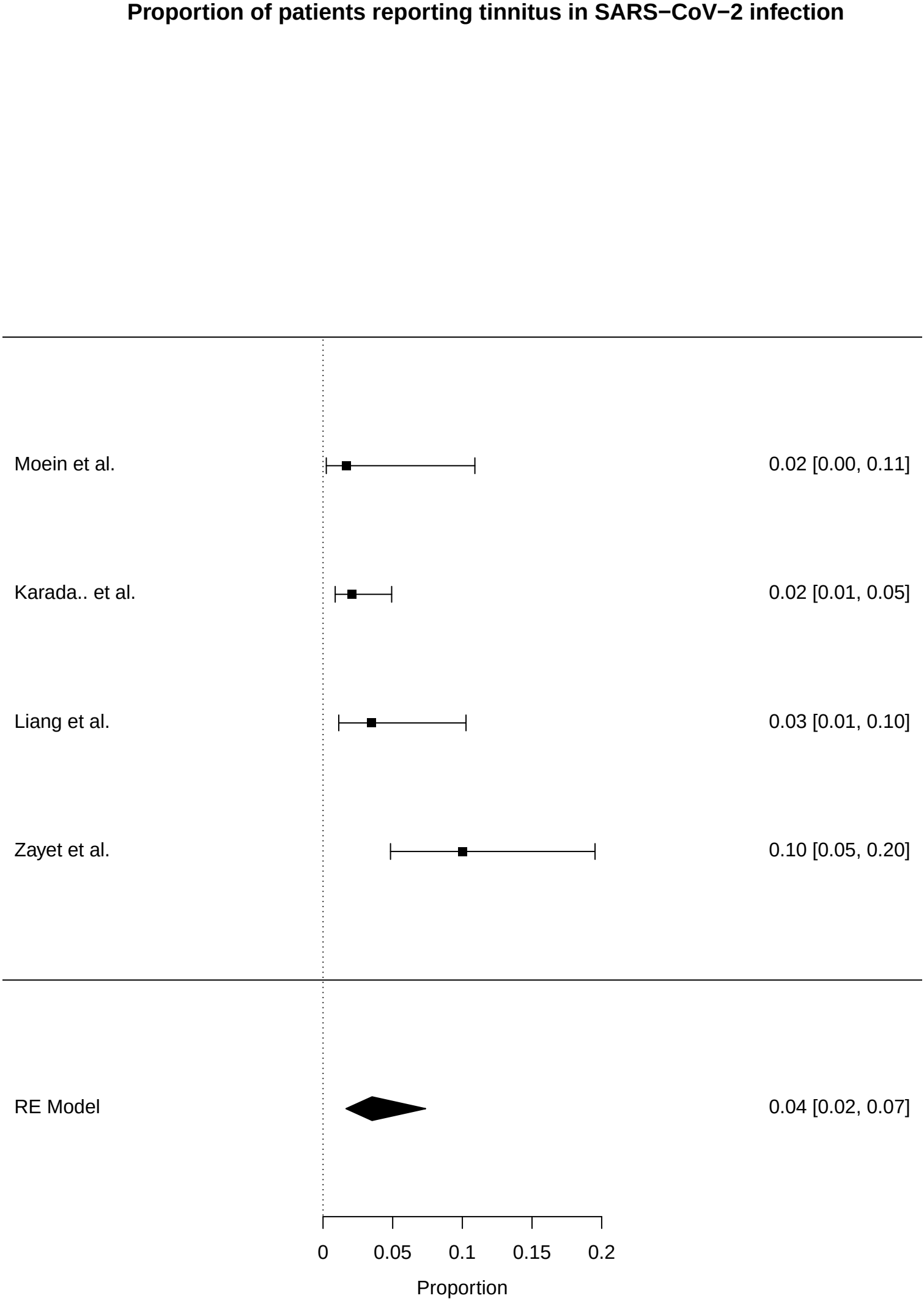
Proportion of patients with haemorrhagic stroke in SARS−CoV−2 infection

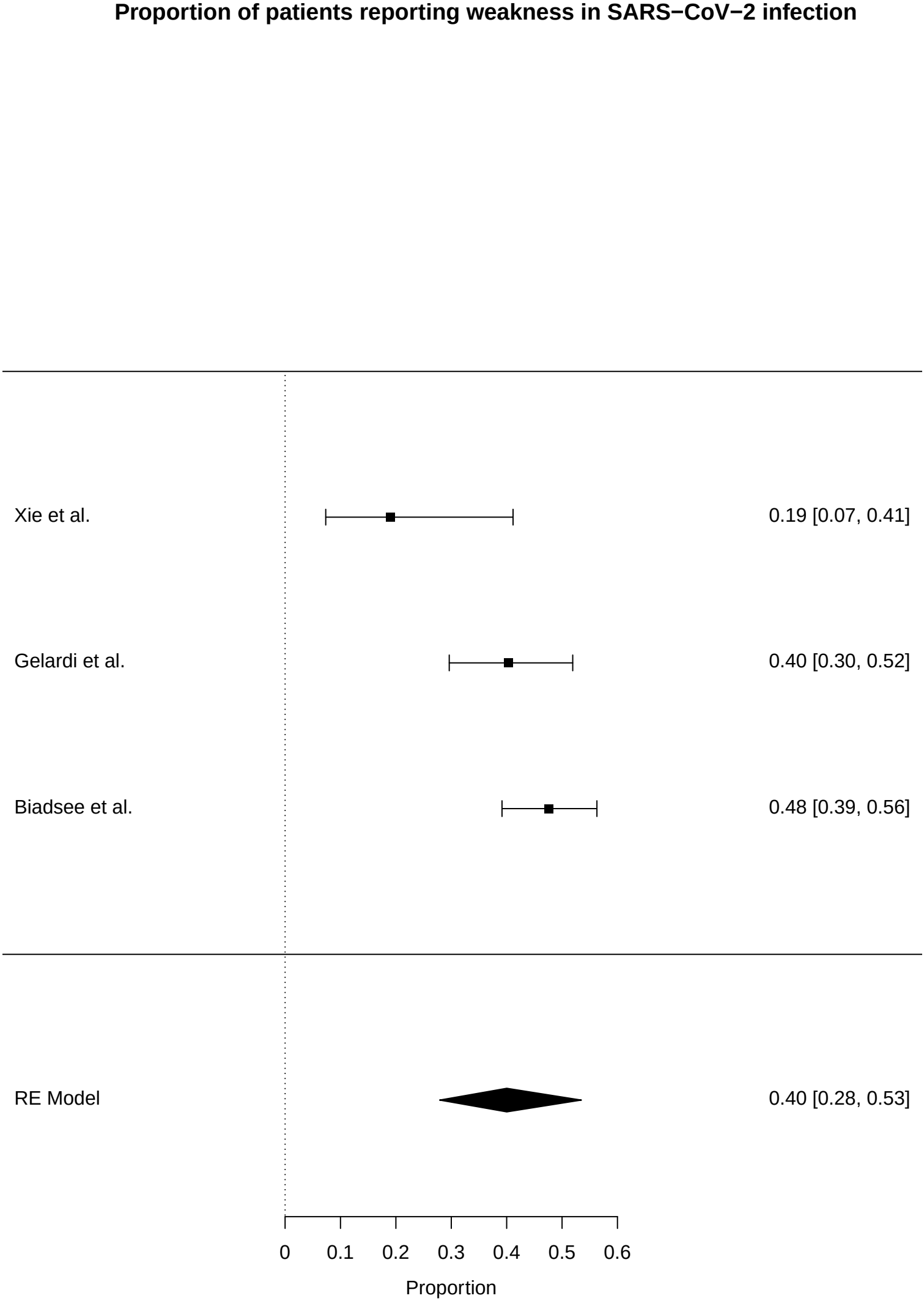



Proportion of patients reporting visual impairment in SARS−CoV−2 infection
Zhou et al (2)
0.02 [0.00, 0.28]
Mao et al. (2)
0.01 [0.00, 0.04]
Karada.. et al.
0.03 [0.02, 0.07]
Zayet et al.
0.04 [0.01, 0.12]
Carignan et al
0.04 [0.02, 0.10]
RE Model
0.03 [0.02, 0.05]
0
0.05
0.15
0.25
Proportion

Proportion of patients reporting hearing impairment in SARS−CoV−2 infection




Proportion of patients reporting tinnitus in SARS−CoV−2 infection
Moein et al.
0.02 [0.00, 0.11]
Karada.. et al.
0.02 [0.01, 0.05]
Liang et al.
0.03 [0.01, 0.10]
Zayet et al.
0.10 [0.05, 0.20]
RE Model
0.04 [0.02, 0.07]
0
0.05
0.1
0.15
0.2
Proportion


Proportion of patients reporting weakness in SARS−CoV−2 infection
Xie et al.
0.19 [0.07, 0.41]
Gelardi et al.
0.40 [0.30, 0.52]
Biadsee et al.
0.48 [0.39, 0.56]
RE Model
0.40 [0.28, 0.53]
0
0.1
0.2
0.3
0.4
0.5
0.6
Proportion