Appendix list:

Appendix I: search strategy

Appendix II: References of included studies

Appendix III: forest plots

Appendix IV: sensitivity analyses

Appendix I Search strategy

PubMed

("COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "COVID-19 diagnostic testing"[Supplementary Concept] OR (("Coronavirus"[MeSH Terms] OR "Coronavirus Infections"[Mesh:NoExp] OR pneumonia virus*[tiab] OR cov[tiab]) AND (outbreak[tiab] OR wuhan[tiab] OR novel[all] OR 19[tiab] OR 2019[tiab] OR epidem*[tiab] OR epidemy[all] OR epidemic*[all] OR pandem*[all] OR new[tiab])) OR coronavirus*[tiab] OR corona virus*[tiab] OR ncov[tiab] OR 2019ncov[tiab] OR covid19[tiab] OR "covid 19"[tiab] OR "sars cov 2"[tiab] OR sars2[tiab] OR "ncov 2019"[tiab] OR "sars coronavirus 2"[tiab] OR "sars corona virus 2"[tiab] OR "severe acute respiratory syndrome cov 2"[tiab] OR "severe acute respiratory syndrome cov2"[tiab] OR severe acute respiratory syndrome cov*[tiab] OR cov2[tiab])

AND
Cohort Studies[Mesh] OR Case-Control Studies[MeSH] OR Cross-Sectional Studies[MeSH] OR Follow-Up Studies[MeSH] OR Retrospective Studies[MeSH] OR case control study[tiab] OR case series[tiab] OR cohort study[tiab] OR comparative study[tiab] OR comparison study[tiab] OR descriptive study[tiab] OR cross-sectional study[tiab] OR follow-up study[tiab] OR observational study[tiab] OR retrospective analysis[tiab] OR retrospective observational study[tiab] OR retrospective single-center study[tiab] OR retrospective study[tiab] OR ((enrol* OR include*[tiab]) AND (cases[tiab] OR patients[tiab] OR study[tiab])) OR ((collect* OR extract*) AND data[tiab]) OR Risk Factors[MeSH] OR risk factor*[tiab]

NOT
"Case Reports" [Publication Type] OR "Letter" [Publication Type] OR case report*[tiab] OR letter to editor[tiab] OR letter to the editor[tiab]

AND
(("2020/05/05"[PDAT] : "3000/12/31"[PDAT]) OR 2020/05/05:3000/12/31[Date - Entry])

Embase Ovid

1 exp Coronavirus/
2 exp Coronavirus Infections/
3 (coronavirus* or corona virus* or OC43 or NL63 or 229E or HKU1 or HCoV* or ncov* or covid* or sars-cov* or sarscov* or Sars-coronavirus* or Severe Acute Respiratory Syndrome Coronavirus*).mp.
4 (or/1-3)
5 4 not (SARS or SARS-CoV or MERS or MERS-CoV or Middle East respiratory syndrome or camel* or dromedar* or equine or coronary or coronal or covidence* or covidien or influenza virus or HIV or bovine or calves or TGEV or feline or porcine or BCoV or PED or PEDV or PDCoV or FIPV or FCoV or SADS-CoV or canine or CCov or zoonotic or avian influenza or H1N1 or H5N1 or H5N6 or IBV or murine corona*).mp. [line 5 removes noise in the search results]
6 ((pneumonia or covid* or coronavirus* or corona virus* or ncov* or 2019-ncov or sars*).mp. or exp pneumonia/) and Wuhan.mp.
7 (coronavirus disease 2019 or 2019-ncov or ncov19 or ncov-19 or 2019-novel CoV or severe acute respiratory syndrome coronavirus 2 or sars-cov2 or sars-cov-2 or sarscov2 or sarscov-2 or Sars-coronavirus2 or Sars-coronavirus-2 or SARS-like coronavirus* or coronavirus-19 or covid19 or covid-19 or covid 2019 or ((novel or new or nouveau) adj2 (CoV or nCoV or covid or coronavirus*

or corona virus or Pandemi*2)) or ((covid or covid19 or covid-19) and pandemic*2) or (coronavirus* and pneumonia)).mp.

8 (coronavirus disease 2019 or severe acute respiratory syndrome coronavirus 2).sh,dj.

9 (or/6-8) [Lines 6 to 8 are specific to Covid-19]

10 5 or 9

11 cohort analysis/ OR exp case control study/ OR cross-sectional study/ OR follow up/ OR retrospective study/ OR case control study.ti,ab,kw. OR case series.ti,ab,kw. OR cohort study.ti,ab,kw. OR comparative study.ti,ab,kw. OR comparison study.ti,ab,kw. OR descriptive study.ti,ab,kw. OR cross-sectional study.ti,ab,kw. OR follow-up study.ti,ab,kw. OR observational study.ti,ab,kw. OR retrospective analysis.ti,ab,kw. OR retrospective observational study.ti,ab,kw. OR retrospective single-center study.ti,ab,kw. OR retrospective study.ti,ab,kw.

12 ((enrol*.ti,ab. OR include*.ti,ab.) AND (cases.ti,ab. OR patients.ti,ab. OR study.ti,ab.)) OR ((collect*.ti,ab. OR extract*.ti,ab.) AND data.ti,ab.) OR risk factor/ OR risk factor*.ti,ab.

13 11 OR 12

14 10 AND 13

15 14 NOT (case report/ OR Case Report*.ti,ab,kw. OR letter.pt)

16 15 AND 20200505:20301231.(dc).

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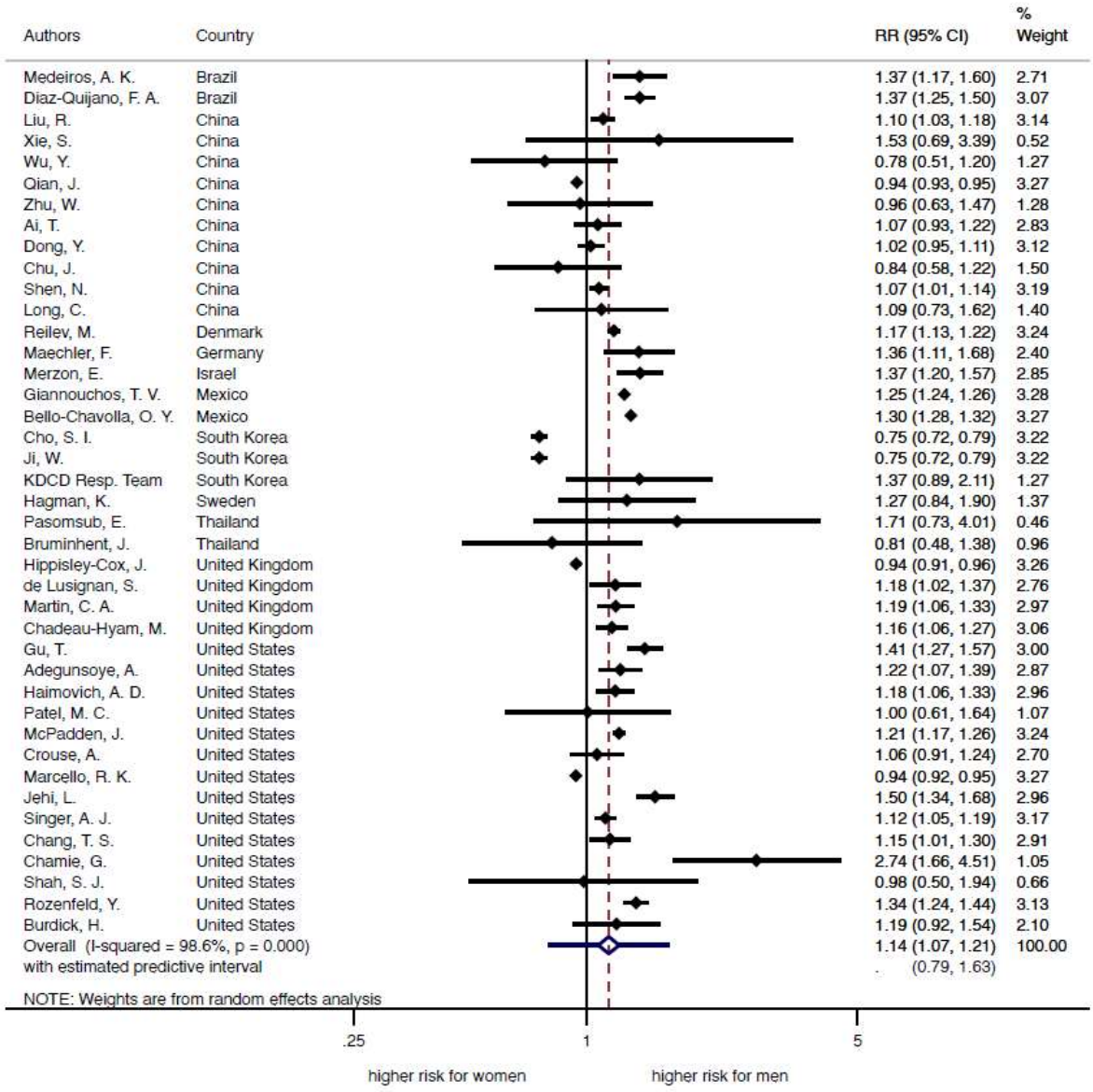
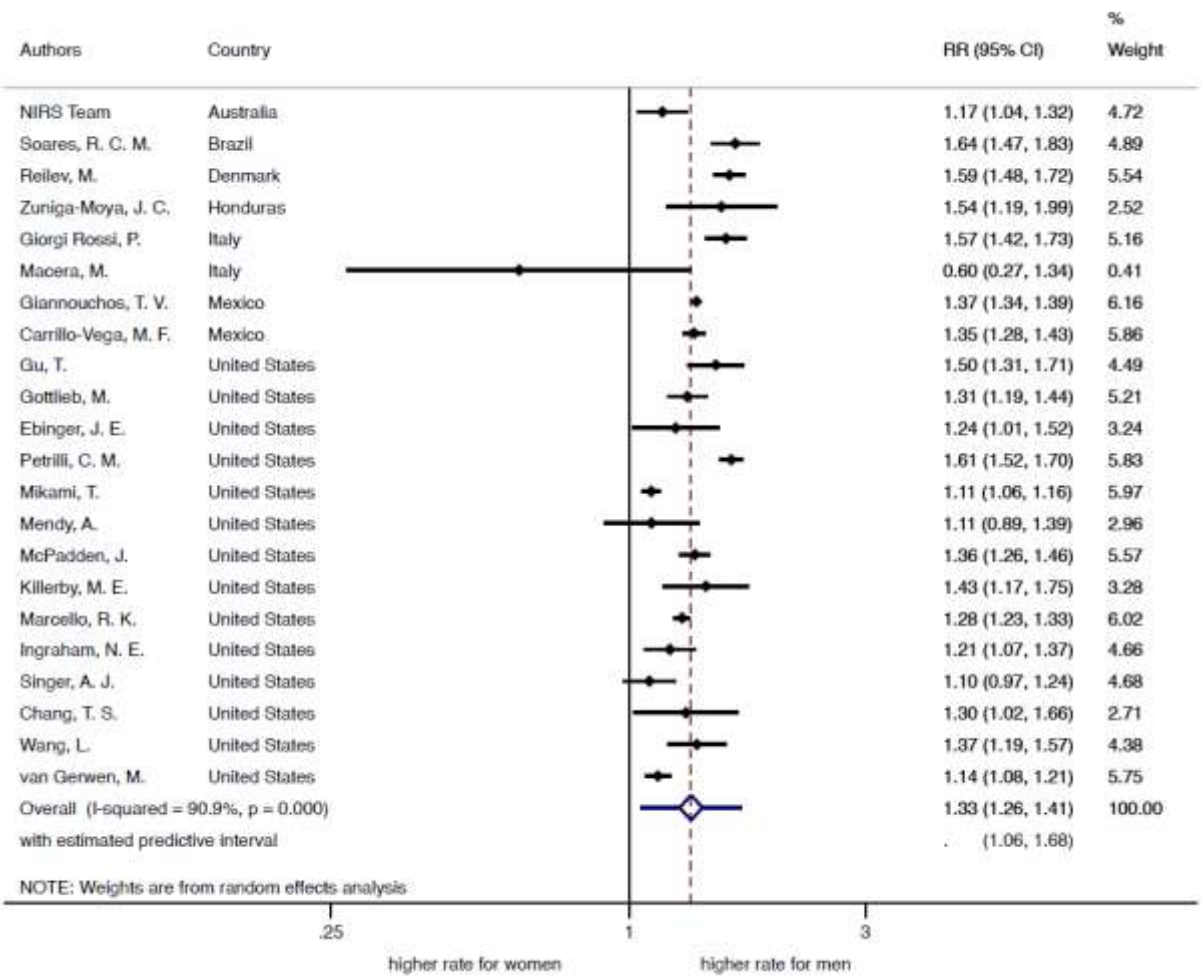
Appendix III: Forest Plots

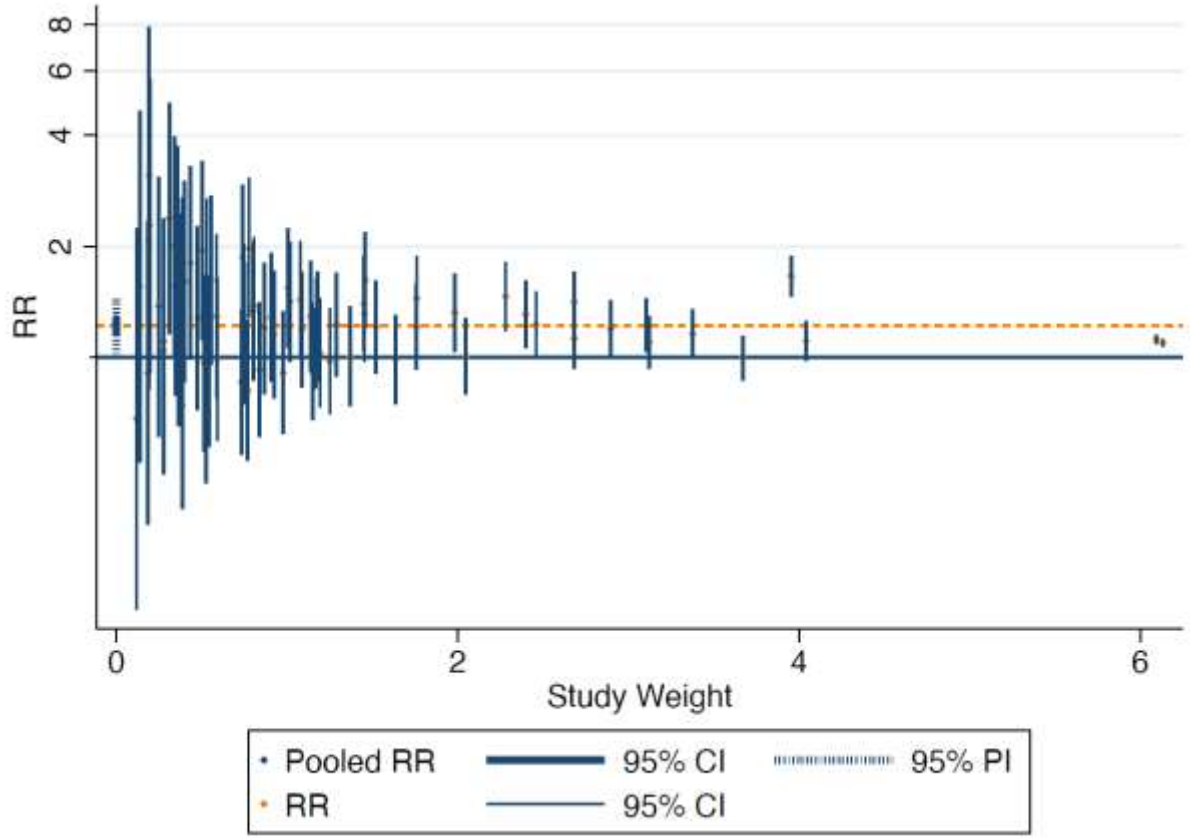
Infection:



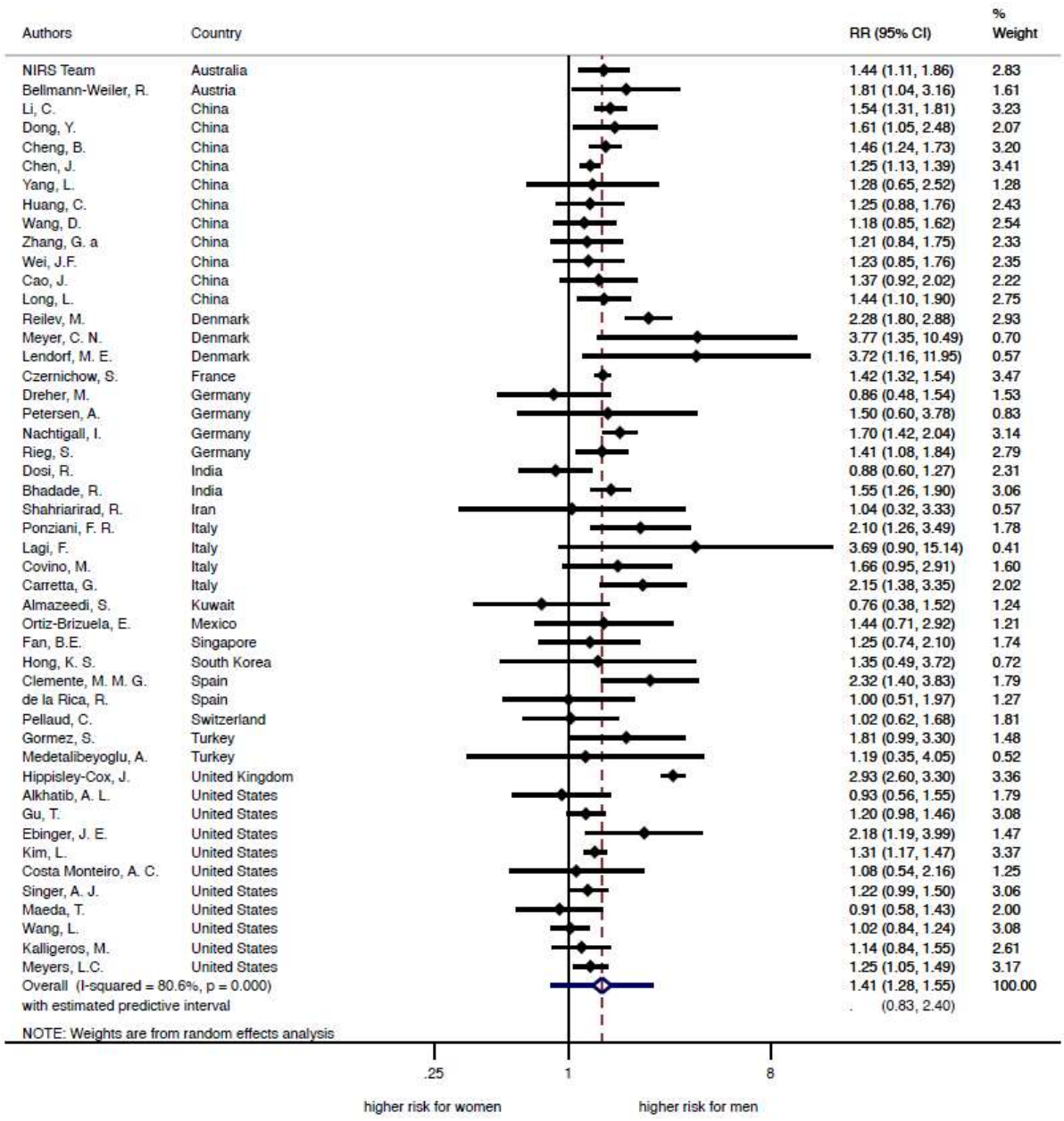
Hospitalization:



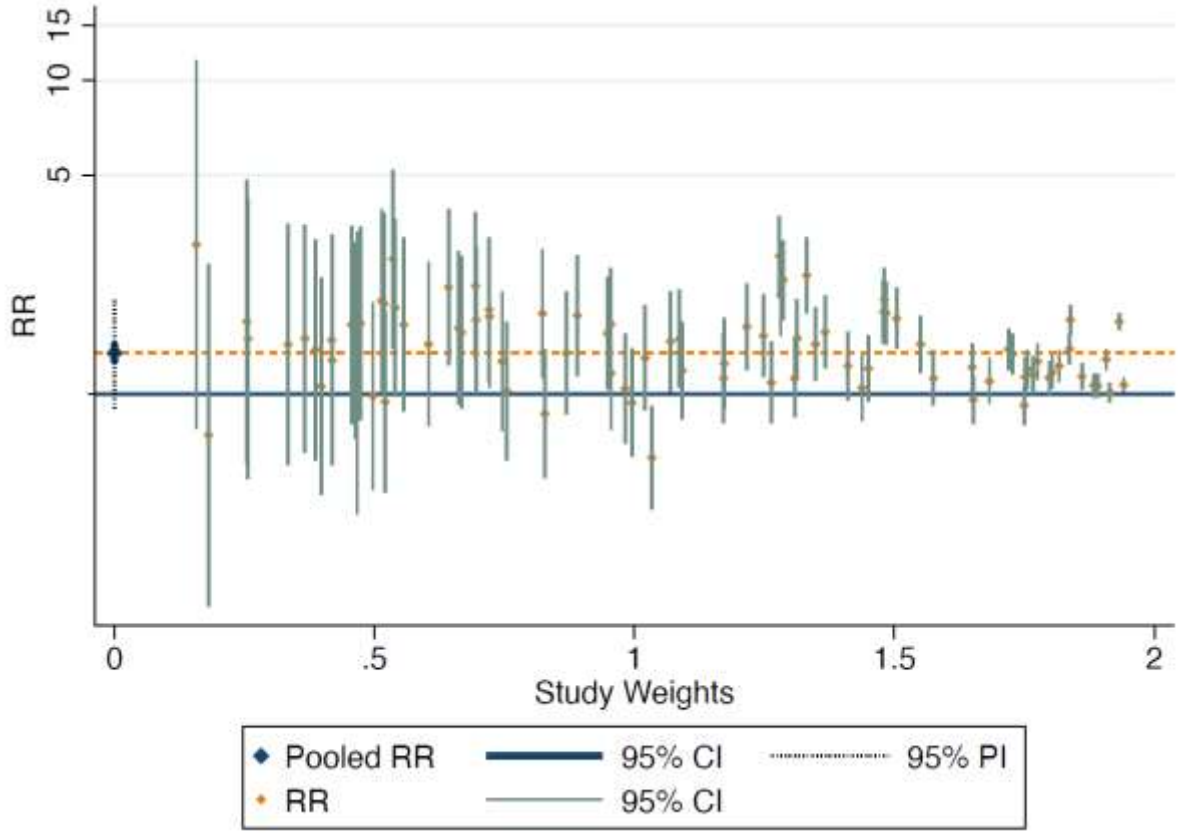
Severe disease:



ICU admission:



Death:



Appendix IV: sensitivity analysis

In primary outcomes, we observed moderate to substantial heterogeneity so that some discussion about the possible reasons for the differences between the studies is deserved. In the following, we report the results of several subgroup and meta-regression analyses per outcome. For meta-regression analyses, we used Knapp-Hartung modification approach in calculation of standard errors, p-values, and confidence intervals for the regression weights.

Infection to COVID-19

The meta-regression analysis shows that there was a significant positive association between the log relative risk and study start date (b = 0.003, 95%CI: 0.001 to 0.005) with p-value = 0.017. This means, in a month window, for example, the relative risk of infection for men was about 9% higher than that of women (i.e., exp(30×0.003) = 1.09), hence the greater the risk of infection for men over the pandemic period that we have studied. We even further confirmed this finding by performing a cumulative meta-analysis based on the study start date (not shown). For the meta-regression analysis, the corresponding R^2 indicated that 12% of the between-study variance is explained by the study start day (Table A1), resulting in a decreased estimated value of the between-study variance $\hat{\tau}^2$= 0.021, compared with $\hat{\tau}^2$= 0.031 before adjusting for the start study date.

Table A1: Meta-regression analysis on study start date for the relative risk of confirmed COVID-19 infection among the general population

```
Meta-regression                                 Number of obs  =      37
REML estimate of between-study variance         tau2           =  .02087
% residual variation due to heterogeneity       I-squared_res  =  94.84%
Proportion of between-study variance explained  Adj R-squared  =  12.23%
With Knapp-Hartung modification
```

logES	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
Start	.0025839	.0010275	2.51	0.017	.000498	.0046698
_cons	-56.60297	22.56431	-2.51	0.017	-102.4109	-10.79499

Moreover, the subgroup analysis based on clinical setting (hospital vs general population) revealed a decrease of the heterogeneity measure for the studies conducted in hospital (I^2 = 58%, compared with 99% for combined studies), but the estimated effect size remained unaffected (RR = 1.15, 95%CI: 1.08 to 1.22), see Figure A1.

Hospitalization due to COVID-19

Various meta-regression analyses on study size, total quality score, study duration and study start date did not reveal any association with the effect size. We further partitioned studies based on geographical location (i.e., Europe, North America and Central/South America). For Europe and Central/South America the I^2 statistics dropped to 65% and 73%, respectively, resulting in a slight increase of the effect size (RR = 1.54, 95%CI: 1.36 to 1.76 for Europe and RR = 1.42, 95%CI: 1.33 to 1.52 for Central/South America). In contrast, the effect size for the North America subgroup decreased trivially (RR = 1.28, 95%CI: 1.19 to 1.38). Nevertheless, all results were fairly close to that of the base analysis (RR = 1.33, 95%CI: 1.27 to 1.41), see Figure A2.

Severe COVID-19 disease

The meta-regression analysis showed a significant association with start study date (b = 0.002, 95%CI: 0.001 to 0.003) with p-value < 0.001, where the estimated value of $\hat{\tau}^2$was zero, so the start study date explained almost all of the variation between the studies (i.e., the overall 46% heterogeneity is almost explained by the start study date), see Table A2.

Table A2: Meta-regression analysis on study start date for the relative risk of severe COVID-19 disease among hospitalized patients with a confirmed infection

```
Meta-regression                                   Number of obs  =      69
REML estimate of between-study variance           tau2           =       0
% residual variation due to heterogeneity         I-squared_res  =  10.93%
Proportion of between-study variance explained    Adj R-squared  = 100.00%
With Knapp-Hartung modification
```

logES	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
Start	.001635	.0004575	3.57	0.001	.0007219	.0025481
_cons	-35.69802	10.02113	-3.56	0.001	-55.70028	-15.69576

Admission to ICU

We performed the meta-regression analysis on study duration and found a significant positive association between the effect size and study duration (b = 0.004, 95%CI: 0.001 to 0.007) with p-value = 0.005. This implies the longer the duration of the study, the higher the relative risk of admission to ICU for men than women, see Figure A3. For this model, 32% of the between-study variance is explained by the study duration, where the estimated between-study variance reduced marginally by half ($\hat{\tau}^2$= 0.038 compared with $\hat{\tau}^2$=0.067 before adjusting for study duration). We further investigated the effect of geographical location and total study quality score on the effect size through subgroup analyses, but none explained considerable between-study heterogeneity.

Death due to COVID-19

The results of a meta-regression analysis showed a significant negative association between the log relative risk and study start date, i.e., the later the start of the study, the lower the relative risk of death for men than women (b = -0.004, 95%CI: -0.006 to -.002) with p-value < 0.001. More specifically, in the pandemic period that we have studied, the relative risk of death due to COVID-19 for men decreased about 11% as compared to women in a month window (i.e., exp(30×-0.004) = 0.89), see Figure A4. Moreover, the study start date explained 29% of the between-study variance, resulted in a decreased estimate of the between-study variance from $\hat{\tau}^2$= 0.042 (before adjusting for covariate) to $\hat{\tau}^2$= 0.032 (after adjusting for covariate), see Table 3. There was no further evidence for the effect of study size, total quality score, study duration, and geographical location on the effect size.

Table A3: Meta-regression analysis on study start date for the relative risk of death due to COVID-19 among hospitalized patients with a confirmed infection

```
Meta-regression                                 Number of obs  =      88
REML estimate of between-study variance         tau2           =  .03198
% residual variation due to heterogeneity       I-squared_res  =  66.88%
Proportion of between-study variance explained  Adj R-squared  =  29.08%
With Knapp-Hartung modification
```

logES	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
Start	-.0037384	.0010112	-3.70	0.000	-.0057485	-.0017283
_cons	82.38067	22.20484	3.71	0.000	38.23891	126.5224