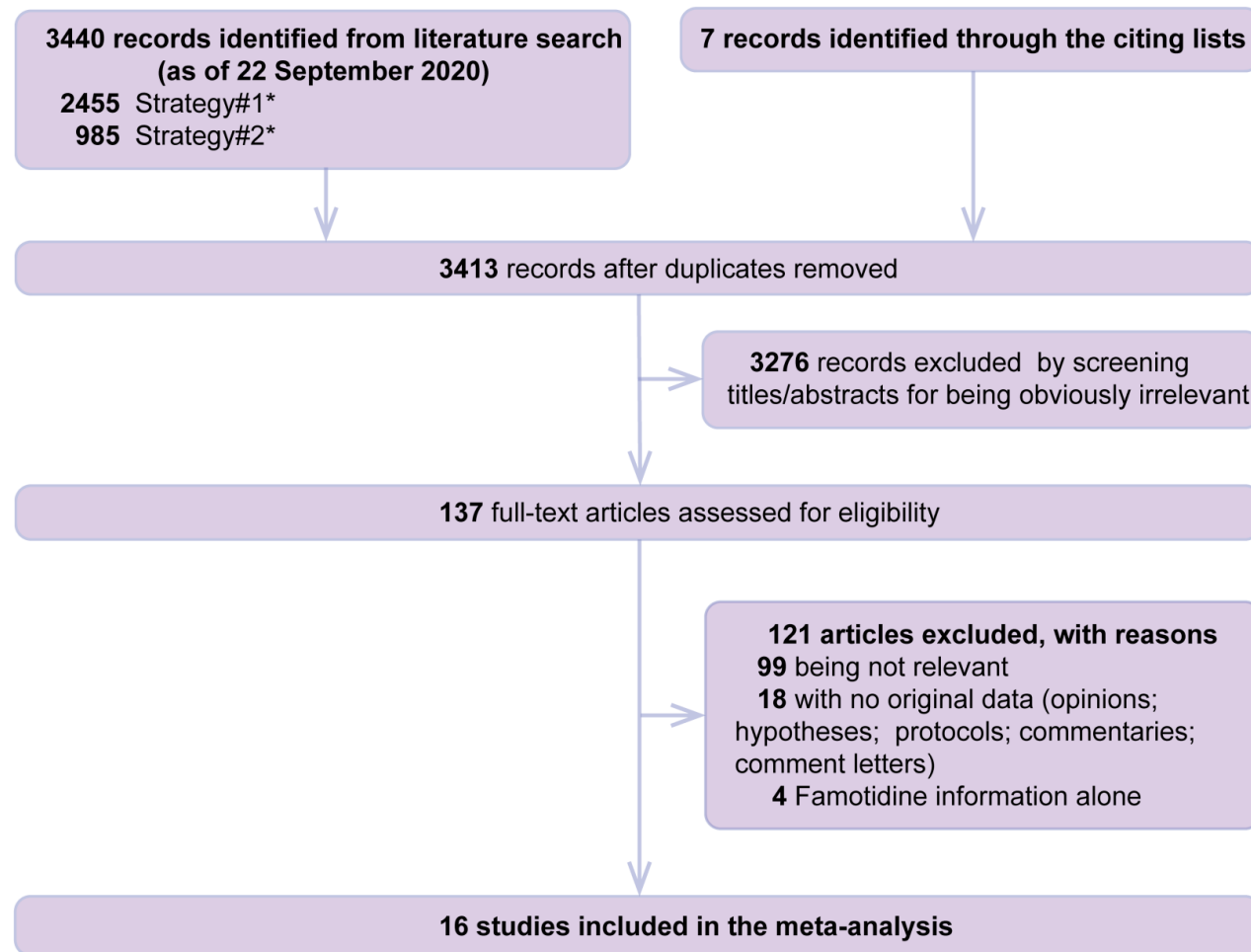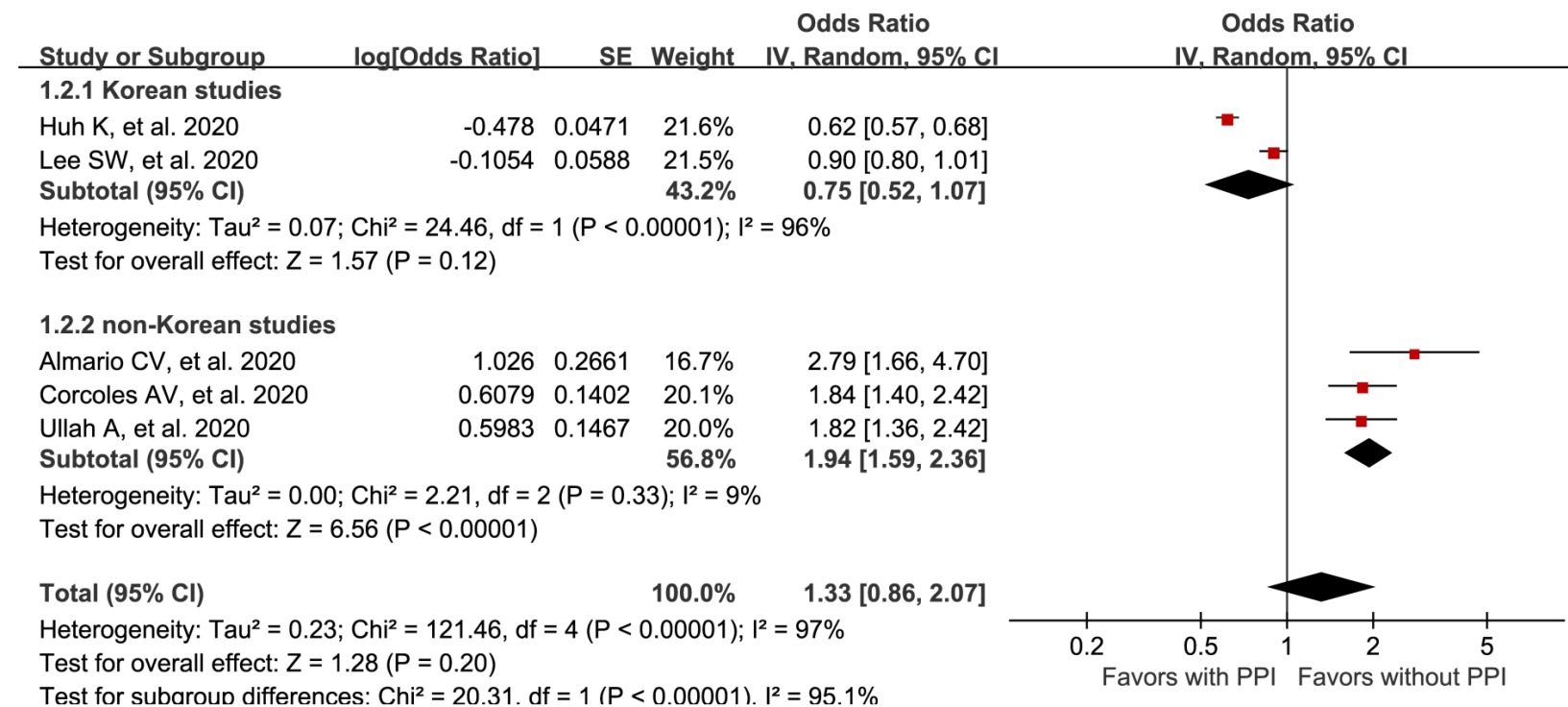**Supplementary figure 1: Flow chart for study selection**

Searches using strategy#1 ("proton pump inhibitor" or "PPI*" OR " H2-receptor antagonist*" OR hypochlorhydria OR "gastric acid" OR "gastric pH" OR omeprazole OR rabeprazole OR esomeprazole OR famotidine OR pantoprazole OR lansoprazole) or strategy#2 (gastrointestinal[title/abstract]) were performed in the COVID-19 Research Articles Downloadable Database by the US CDC (https://www.cdc.gov/library/researchguides/2019novelcoronavirus/researcharticles.html), which includes literature from 25 databases, such as Medline (Ovid and PubMed), Embase, Scopus, Cochrane Library, LitCovid, WHO COVID-19 website, medRxiv (preprints), bioRxiv (preprints), chemRxiv (preprints), and SSRN (preprints).

3440 records identified from literature search (as of 22 September 2020)
2455 Strategy#1*
985 Strategy#2*

7 records identified through the citing lists

3413 records after duplicates removed

3276 records excluded by screening titles/abstracts for being obviously irrelevant

137 full-text articles assessed for eligibility

121 articles excluded, with reasons
99 being not relevant
18 with no original data (opinions; hypotheses; protocols; commentaries; comment letters)
4 Famotidine information alone

16 studies included in the meta-analysis

Supplementary figure 1

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

Gut
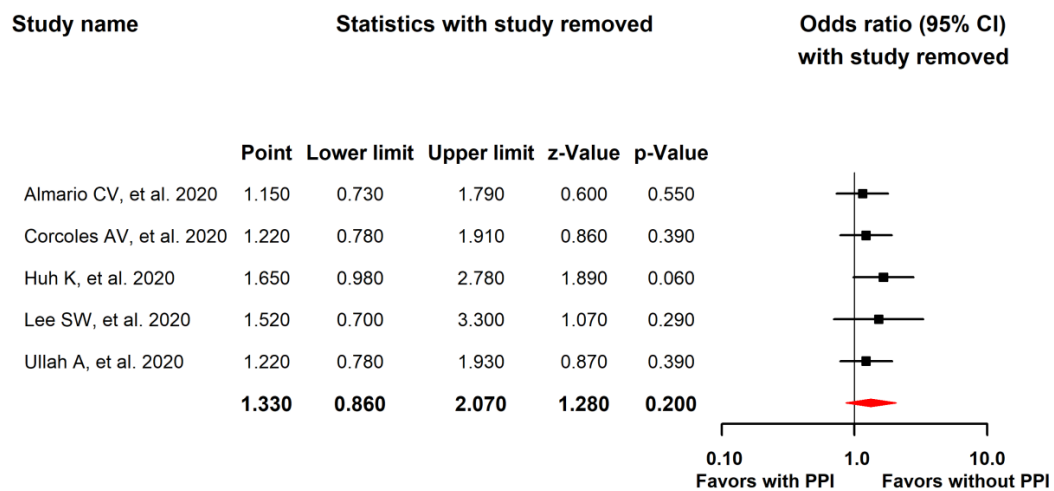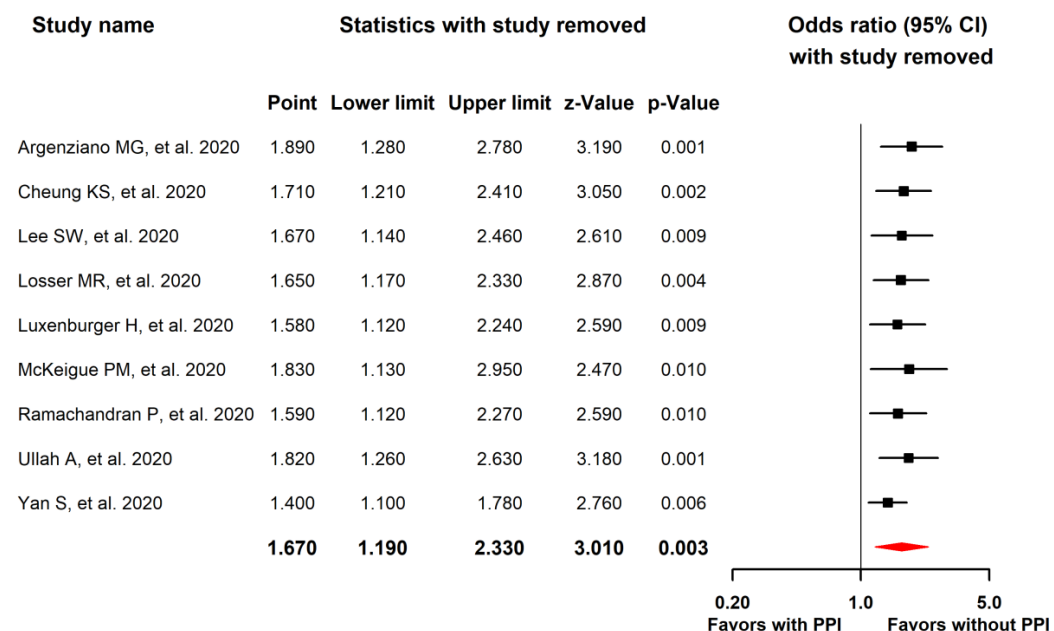
Supplementary figure 2: Subgroup analysis of Korean versus non-Korean cohorts for the association between PPI use and risk of SARS-CoV-2 infection

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
1.2.1 Korean studies				
Huh K, et al. 2020	-0.478	0.0471	21.6%	0.62 [0.57, 0.68]
Lee SW, et al. 2020	-0.1054	0.0588	21.5%	0.90 [0.80, 1.01]
Subtotal (95% CI)			43.2%	**0.75 [0.52, 1.07]**
Heterogeneity: Tau² = 0.07; Chi² = 24.46, df = 1 (P < 0.00001); I² = 96%				
Test for overall effect: Z = 1.57 (P = 0.12)				
1.2.2 non-Korean studies				
Almario CV, et al. 2020	1.026	0.2661	16.7%	2.79 [1.66, 4.70]
Corcoles AV, et al. 2020	0.6079	0.1402	20.1%	1.84 [1.40, 2.42]
Ullah A, et al. 2020	0.5983	0.1467	20.0%	1.82 [1.36, 2.42]
Subtotal (95% CI)			56.8%	**1.94 [1.59, 2.36]**
Heterogeneity: Tau² = 0.00; Chi² = 2.21, df = 2 (P = 0.33); I² = 9%				
Test for overall effect: Z = 6.56 (P < 0.00001)				
Total (95% CI)			100.0%	**1.33 [0.86, 2.07]**
Heterogeneity: Tau² = 0.23; Chi² = 121.46, df = 4 (P < 0.00001); I² = 97%				
Test for overall effect: Z = 1.28 (P = 0.20)				
Test for subgroup differences: Chi² = 20.31, df = 1 (P < 0.00001), I² = 95.1%				

Odds Ratio
IV, Random, 95% CI

0.2   0.5   1   2   5
Favors with PPI   Favors without PPI

Supplementary figure 3: Forest plot showing leave-one-out sensitivity analysis for the association of PPI use with incidence of SARS-CoV-2 infection

Study name	Statistics with study removed					Odds ratio (95% CI) with study removed
	Point	Lower limit	Upper limit	z-Value	p-Value	
Almario CV, et al. 2020	1.150	0.730	1.790	0.600	0.550	
Corcoles AV, et al. 2020	1.220	0.780	1.910	0.860	0.390	
Huh K, et al. 2020	1.650	0.980	2.780	1.890	0.060	
Lee SW, et al. 2020	1.520	0.700	3.300	1.070	0.290	
Ullah A, et al. 2020	1.220	0.780	1.930	0.870	0.390	
	1.330	**0.860**	**2.070**	**1.280**	**0.200**	

0.10   1.0   10.0
Favors with PPI   Favors without PPI

Supplementary figure 4: Forest plot showing leave-one-out sensitivity analysis for the association of PPI use with severe outcomes of COVID-19

Study name	Statistics with study removed					Odds ratio (95% CI) with study removed
	Point	Lower limit	Upper limit	z-Value	p-Value	
Argenziano MG, et al. 2020	1.890	1.280	2.780	3.190	0.001	
Cheung KS, et al. 2020	1.710	1.210	2.410	3.050	0.002	
Lee SW, et al. 2020	1.670	1.140	2.460	2.610	0.009	
Losser MR, et al. 2020	1.650	1.170	2.330	2.870	0.004	
Luxenburger H, et al. 2020	1.580	1.120	2.240	2.590	0.009	
McKeigue PM, et al. 2020	1.830	1.130	2.950	2.470	0.010	
Ramachandran P, et al. 2020	1.590	1.120	2.270	2.590	0.010	
Ullah A, et al. 2020	1.820	1.260	2.630	3.180	0.001	
Yan S, et al. 2020	1.400	1.100	1.780	2.760	0.006	
	1.670	**1.190**	**2.330**	**3.010**	**0.003**	

0.20   1.0   5.0
Favors with PPI   Favors without PPI

Supplementary table: Summary characteristics of the included studies

Study	Study design	Country or region	Timing of data collection	Mean or median age (years)	Male subjects (%)	Number of subjects	Number of PPI users	Clinical outcome	Confounder adjustment
Lee 2020[1]	Retrospective cohort	Korea	Jan 1 to May 15, 2020	48	51.0	132316	20405	SARS-CoV-2 infection; severe outcomes of COVID-19*	Yes
Almario 2020[2]	Retrospective cohort	USA	May 3 to Jun 24, 2020	NR	48	53130	16547	SARS-CoV-2 infection	Yes
Ullah 2020[3]	Retrospective cohort	UK	Feb 12 to Jun 12, 2020	57	43.9	15586	5908	SARS-CoV-2 infection; severe outcomes of COVID-19*	No
Corcoles 2020[4]	Retrospective cohort	Spain	May 1 to Apr 3, 2020	≥ 50	48.1	34936	11807	SARS-CoV-2 infection	No
Huh 2020[5]	Case-control	Korea	Up to Apr 8, 2020	49	48.7	65149	14167	SARS-CoV-2 infection	Yes
Tarlow 2020[6]	Retrospective cohort	USA	NR	NR	NR	84325	18240	SARS-CoV-2 infection	No
Ramachandran 2020[7]	Retrospective cohort	USA	Mar 1 to Apr 25, 2020	66	54.9	295	46	Severe outcomes of COVID-19*; duration of hospital stay	Yes
Luxenburger 2020[8]	Retrospective cohort	Germany	NR	65	56.6	152	62	Severe outcomes of COVID-19*	No
McKeigue 2020[9]	Case-control	Scotland	Up to Jun 6, 2020	NR	NR	41220	2715	Severe outcomes of COVID-19*	No
Argenziano 2020[10]	Retrospective cohort	USA	Mar 1 to Apr 5, 2020	63	59.6	1000	163	Severe outcomes of COVID-19*	No
Cheung 2020[11]	Retrospective cohort	Hongkong	Jan 1 to May 10, 2020	NR	NR	952	27	Severe outcomes of COVID-19*	Yes
Losser 2020[12]	Case series (individual)	France	Mar16 to Apr 12, 2020	70	58.8	17	6	Severe outcomes of COVID-19*	No
Yan 2020[13]	Retrospective cohort	China	Jan 22 to Mar 13, 2020	51	48.2	168	32	Severe outcomes of COVID-19*	No
Zhang 2020[14]	Retrospective cohort	China	Jan 20 to Mar 16, 2020	50	55.2	58	29	Duration of hospital stay	Yes

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance
placed on this supplemental material which has been supplied by the author(s)

Gut

Jimenez 2020[15]	Retrospective cohort	Brazil	NR		NR	NR	1357	242	Severe outcomes of COVID-19*	Yes
Freedberg 2020[16]	Retrospective cohort	USA	Feb 25 to Apr 13, 2020	NR		NR	1620	NR	Severe outcomes of COVID-19*	Yes

*Severe outcomes of COVID-19 consisted of admission to the intensive care unit, mechanical ventilation, acute respiratory distress syndrome, or death.

COVID-19, Coronavirus Disease 2019; NR, not reported; PPI, proton pump inhibitor; SARS-CoV- 2, severe acute respiratory syndrome coronavirus 2.