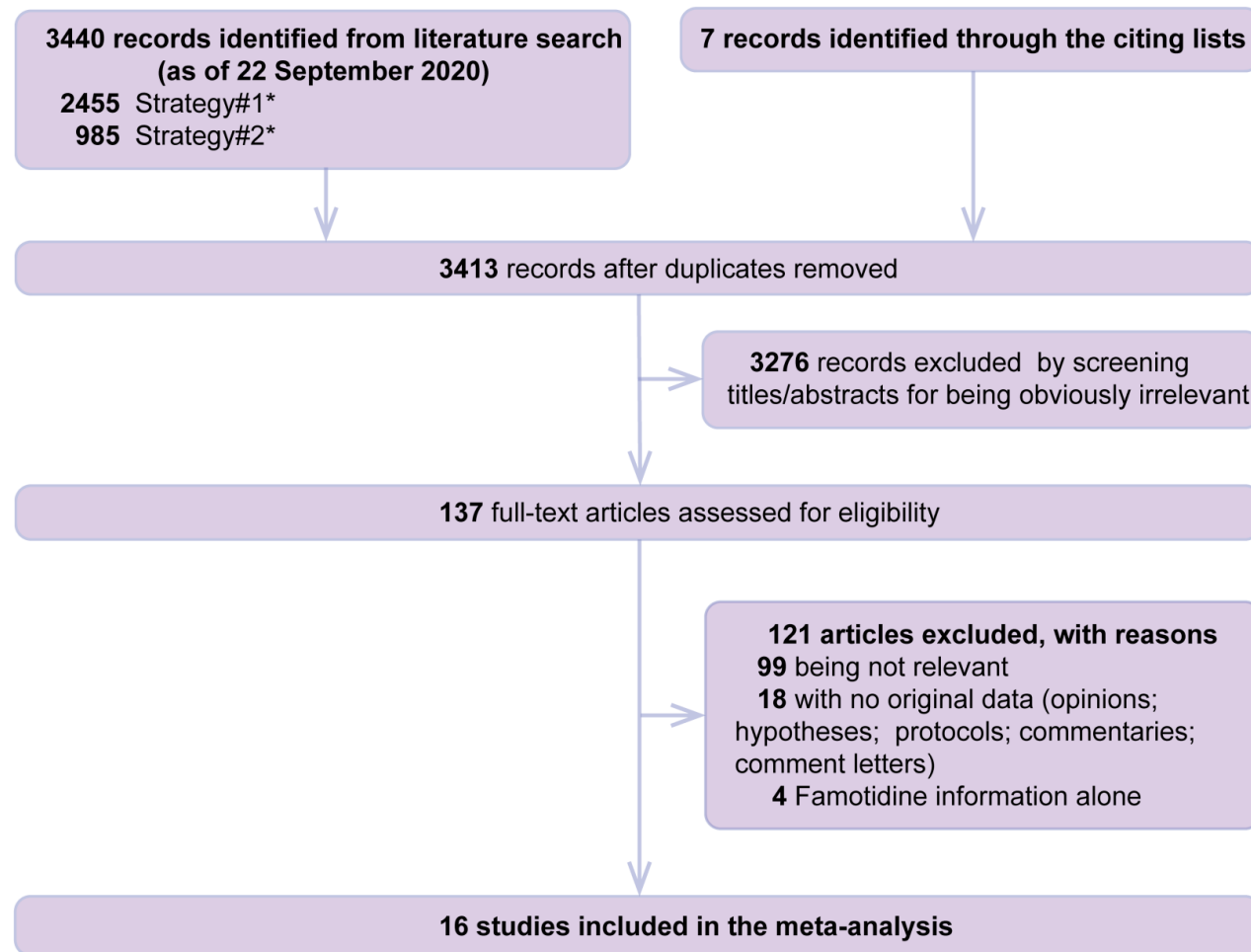


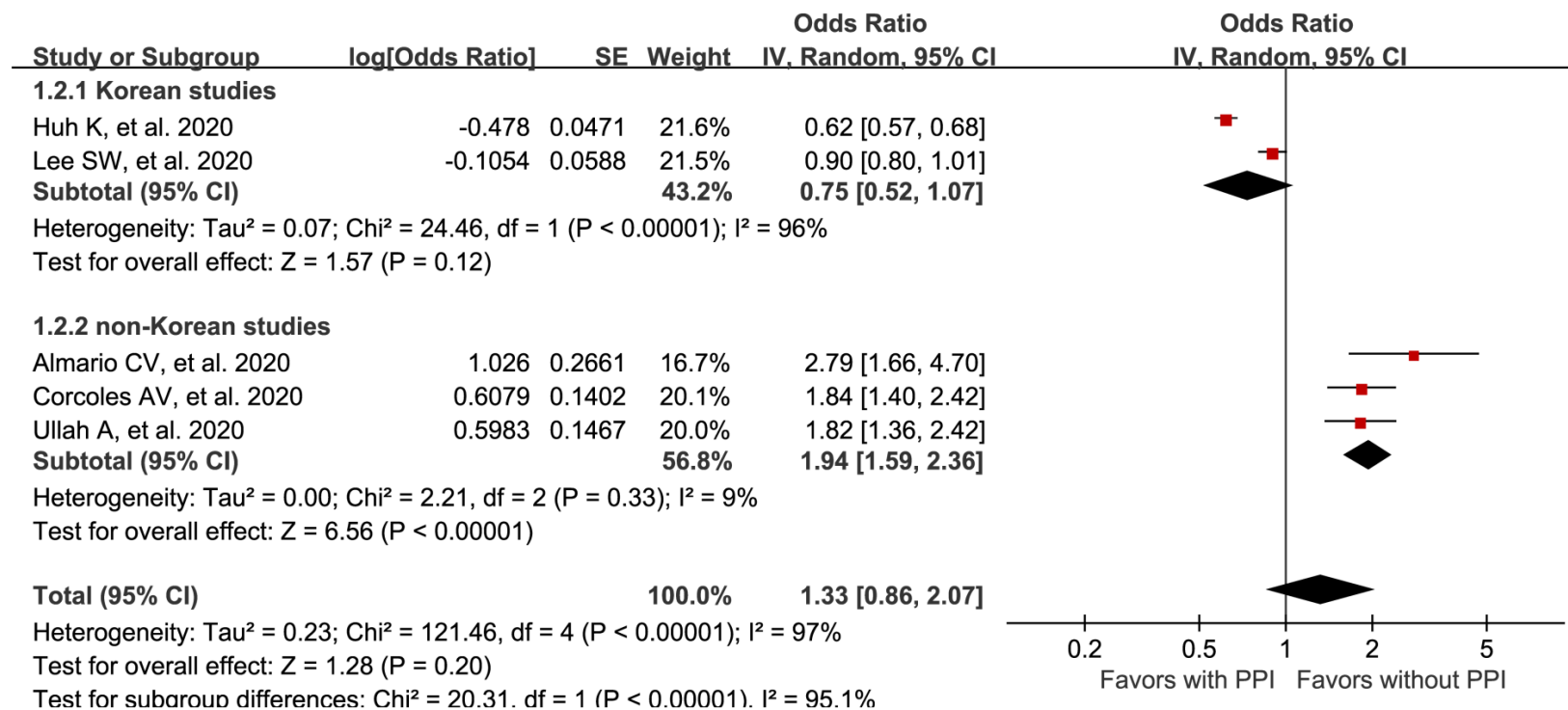
Supplementary figure 1: Flow chart for study selection

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).

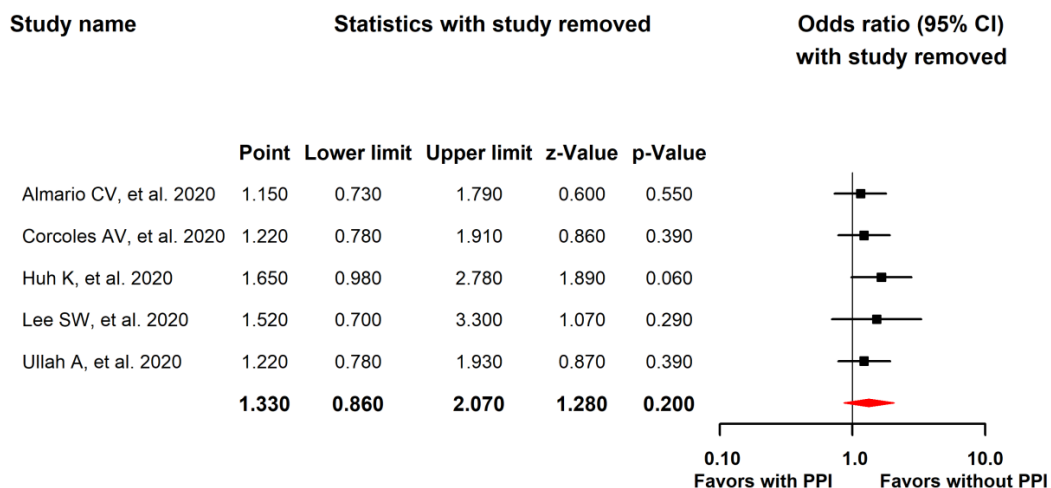


Supplementary figure 1

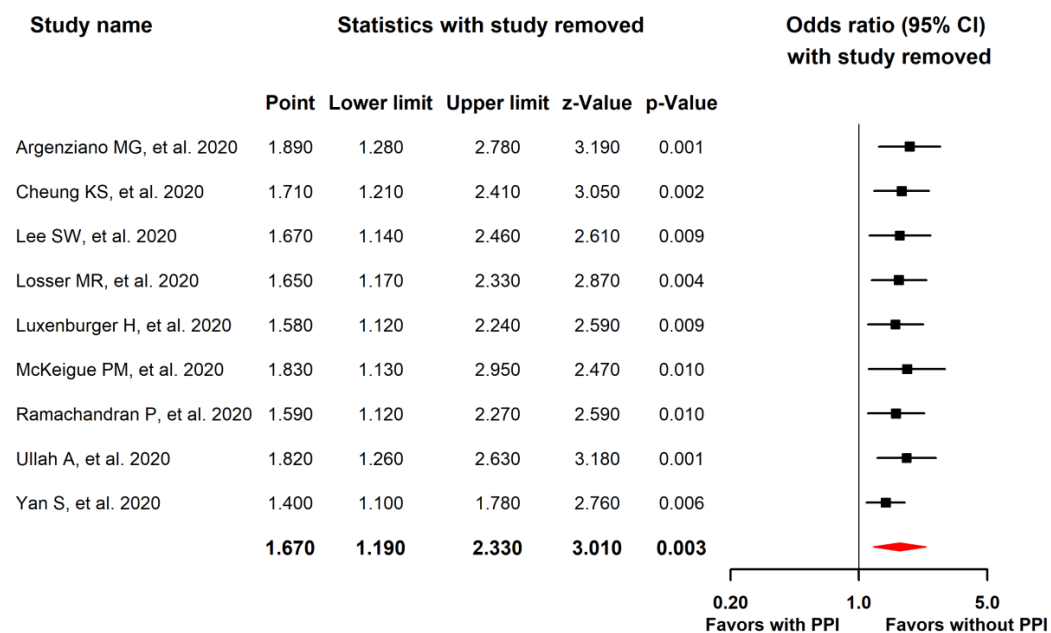
Supplementary figure 2: Subgroup analysis of Korean versus non-Korean cohorts for the association between PPI use and risk of SARS-CoV-2 infection



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



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



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	Mar 16 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

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.