Appendix S1. Search strategies

PUBMED. The following search strategy was used: i) 'coronavirus' (Mesh) OR 'COVID-19' (Mesh) OR 'SARS-CoV-2' (Mesh); ii) 'coronavirus' (All Fields) OR 'covid 2019' (All Fields) OR 'SARS2' (All Fields) OR 'SARS-CoV-2' (All Fields) OR 'SARS-CoV-19' (All Fields) OR 'novel cov' (All Fields) OR '2019ncov' (All Fields) OR 'sars cov2' (All Fields) OR 'cov2' (All Fields) OR 'ncov' (All Fields) OR 'covid-19' (All Fields) OR 'covid19' (All Fields) OR 'coronaviridae' (All Fields) OR 'corona virus' (All Fields)); iii) i OR ii; iv) 'IFITM3' (All Fields) OR 'interferon-inducible transmembrane protein 3' (All Fields); v) iii AND iv.

EMBASE. The following search strategy was used: i) coronavirus:ti,ab,kw OR 'covid 2019':ti,ab,kw OR sars2:ti,ab,kw OR 'sars cov 2':ti,ab,kw OR 'sars cov 19':ti,ab,kw OR 'novel cov': ti,ab, kw OR 2019ncov:ti,ab, kw OR 'sars cov2': ti,ab, kw OR cov2:ti, ab, kw OR ncov:ti, ab, kw OR 'covid 19': ti, ab, kw OR covid19: ti, ab, kw OR coronaviridae: ti, ab, kw OR 'corona virus':ti, ab, kw; ii) 'coronavirinae'/exp OR 'coronavirus infection'/exp OR 'coronavirus disease 2019'/exp; iii) I OR ii; iv) ifitm3 OR ('interferon inducible' AND transmembrane AND protein AND 3); v) iii AND iv.

China National Knowledge Infrastructure. The following search strategy was used: (xin guan OR xin xing guan zhuang bing du) AND (IFITM3) (in Chineses).

Wanfang. The following search strategy was used: (xin guan OR xin xing guan zhuang bing du) AND (IFITM3) (in Chineses).

bioRxiv and Medrxiv. The following search strategy was used: IFITM3.

Appendix S2. Checklist for Meta-analyses of Observational Studies.

Item	Recommendation	Where mentioned
Reporting of background should include		
1	Problem definition	3
2	Hypothesis statement	3
3	Description of study outcome(s)	3, 4
4	Type of exposure or intervention used	3, 4
5	Type of study designs used	4
6	Study population	3, 4
Reporting of search strategy should include		
7	Qualifications of searchers (e.g., librarians and investigators)	3
8	Search strategy, including time period included in the synthesis and key words	3, Appendix 1
9	Effort to include all available studies, including contact with authors	3, 4
10	Databases and registries searched	3
11	Search software used, name and version, including special features used (e.g., explosion)	Appendix 1
12	Use of hand searching (e.g., reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	2, Table I, Fig. 1
14	Method of addressing articles published in languages other than English	3
15	Method of handling abstracts and unpublished studies	3
16	Description of any contact with authors	-
Reporting of methods should include		
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	4
18	Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	4
19	Documentation of how data were classified and coded (e.g., multiple raters, blinding and interrater reliability)	4
20	Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	4, Table I
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	4, Appendix 4
22	Assessment of heterogeneity	4
23	Description of statistical methods (e.g., complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	4
24	Provision of appropriate tables and graphics	Tables I-III, Figs. 1-3
Reporting of results should include		
25	Graphic summarizing individual study estimates and overall estimate	Figs. 2-3
26	Table giving descriptive information for each study included	Table I
27	Results of sensitivity testing (e.g., subgroup analysis)	6, Table III
28	Indication of statistical uncertainty of findings	5, 6
29	Quantitative assessment of bias (e.g., publication bias)	6
30	Justification for exclusion (e.g., exclusion of non-English language citations)	4
31	Assessment of quality of included studies	5, Appendix 4
Reporting of conclusions should include		
32	Consideration of alternative explanations for observed results	6, 7

Appendix S2. Continued.

Item	Recommendation	Where mentioned
33	Generalization of the conclusions (i.e., appropriate for the data presented and within the domain of the literature review)	6
34	Guidelines for future research	6
35	Disclosure of funding source	8

Stroup DF, Berlin JA, Morton SC, *et al*, for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group. Meta-analysis of Observational Studies in Epidemiology. A Proposal for Reporting. JAMA. 2000;283(15):2008-2012. doi: 10.1001/jama.283.15.2008.

Appendix S3. Definition of severe COVID-19 of included studies

Zhang et al (1) and Pan et al (2). Mild disease was defined as COVID-19 with the presence of fever, respiratory symptoms, and pneumonia at imaging. Severe disease was defined as COVID-19 with the additional presence of significant respiratory distress (>30 breaths/min), blood oxygen saturation <93%, ratio of arterial oxygen pressure to fraction of inspired oxygen <300 mmHg, respiratory failure with mechanical ventilation, shock, or other organ failure requiring intensive care in the intensive care unit (3).

Alghamdi et al (4). The definition of severity was not supplied. Genotype data was grouped by hospitalization or not, and death or not.

Cuesta-Llavona et al (5). The definition of severity was not supplied. Genotype data was grouped by ICU admission or not, and death or not.

Schönfelder et al (6). Clinical outcome was defined as follows according to the criteria of the European Centre for Disease Prevention and Control (ECDC) (7): Moderate, outpatients and hospitalized patients and serious, hospitalized patients admitted to an intensive care unit and/or dependent on mechanical ventilation and all cases of COVID-19-associated deaths during the hospital stay (7). By contrast with the ECDC classification, where patients are counted up to three times, every patient was only counted once according to the worst clinical outcome observed during the hospital stay in the study.

Appendix S4. Quality of included studies assessed using the Newcastle Ottawa Scale (8).

Study	Selection	Comparability	Exposure	Total score
Zhang *et al*, 2020 (1)	****	*	***	8
Pan *et al*, 2021 (2)	****	*	***	8
Alghamdi *et al*, 2021 (4)	****	**	***	9
Cuesta-Llavona *et al*, 2021 (5)	****	**	***	9
Schönfelder *et al*, 2021 (6)	****	**	***	9

A study can be awarded a maximum of four stars for Selection, two stars for Comparability, and three stars for Exposure. The total scores ranged from 0 to 9 and a score ≥7 indicates high quality.

References

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2. Pan Y, Li F, Wang X, Liang Z, Cui S, Peng X, Lu G, Zhao J, Liu Y, Wang Q and Zhang D: Association between rs12252 polymorphism in IFITM3 gene and COVID-19. Int J Virology 28: 192-195, 2021.
3. The National Health Commission of China: The diagnosis and treatment of COVID-19. http://www.nhc.gov.cn/yzygj/s7653p/202203/b74ade1ba4494583805a3d2e40093d88.shtml. Accessed 1 April 2022, 2022.
4. Alghamdi J, Alaamery M, Barhoumi T, Rashid M, Alajmi H, Aljasser N, Alhendi Y, Alkhalaf H, Alqahtani H, Algablan O, *et al*: Interferon-induced transmembrane protein-3 genetic variant rs12252 is associated with COVID-19 mortality. Genomics 113: 1733-1741, 2021.
5. Cuesta-Llavona E, Albaiceta GM, García-Clemente M, Duarte-Herrera ID, Amado-Rodríguez L, Hermida-Valverde T, Enríquez-Rodriguez AI, Hernández-González C, Melón S, Alvarez-Argüelles ME, *et al*: Association between the interferon-induced transmembrane protein 3 gene (IFITM3) rs34481144/rs12252 haplotypes and COVID-19. Curr Res Virol Sci 2: 100016, 2021.
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8. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M and Tugwell P: The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute, Ottawa, ON, 2000. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.