

Supplementary Appendix

Supplement Table 1 GRADE evaluation of outcomes and summary of findings

Certainty assessment							Number of patients	of Effect	Certainty	Importance		
No. of studies	Study Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Pandemic period	Pre-pandemic period	Relative (95% CI)	Absolute (95% CI)		
Incidence of fibrinolysis (assessed with: Odds Ratio)												
14	observational studies	very serious	very serious	serious.	not serious.	publication bias strongly suspected all plausible residual confounding would suggest spurious	207/15209 (1.4%)	275/35144 (0.8%)	OR -- to 2.75)	-- per 1,000 (from 1 more to 13 more)	⊕○○○	CRITICAL

effect,
while no
effect was
observed.

Incidence of Fibrinolysis in HICs (assessed with: OR)

7	observati onal studies	very serio us	not serious.	not serious.	serious.	all plausible residual confoundin g would suggest spurious effect, while no effect was observed.	102/37 17 (2.7%)	237/189 66 (1.2%)	OR -- -- (0.70 to 1.15)	-- -- per (from 4	⊕○○ ○ Very low fewer to 2 more)	IMPORTA NT
---	------------------------------	---------------------	-----------------	-----------------	----------	--------------------------------------------------------------------------------------------------------------------------------	------------------------	-------------------------	-----------------------------------------	-----------------------------------	---------------------------------------------------	---------------

Incidence of fibrinolysis in LMICs (assessed with: Odds Ratio)

7	observati onal	very serio	very serious	very serious	not serious	strong association	105/11 425	88/1602 8 (0.5%)	OR -- -- (2.18	-- -- per 1,000	⊕○○ ○	IMPORTA NT
---	-------------------	---------------	-----------------	-----------------	----------------	-----------------------	---------------	---------------------	--------------------------	-------------------------------------	----------	---------------

studies us all (0.9%) to (from Very
 plausible 12.22) 6 more low
 residual to 58
 confoundin more)
 g would
 suggest
 spurious
 effect,
 while no
 effect was
 observed

All-cause Mortality (assessed with: Odds Ratio)

13 observati very serious. serious. not publication 795/15 2406/34 **OR -- -- per ⊕○○ CRITICAL**
 onal serio serious. serious. bias 050 913 (0.87 **1,000** ○
 studies us strongly (5.3%) (6.9%) to (from Very
 suspected 1.37) 8 low
 all fewer
 plausible to 23
 residual more)
 confoundin

g would
 suggest
 spurious
 effect,
 while no
 effect was
 observed

All-cause mortality in studies showing significantly increased incidence of fibrinolysis (assessed with: Odds Ratio)

5	observati onal studies	very serio us	not serious	not serious	very serious	all plausible residual confoundin g would suggest spurious effect, while no effect was observed	25/376 (6.6%)	23/487 (4.7%)	OR -- -- (0.67 to 4.06)	-- per 1,000 (from 15 fewer to 120 more)	⊕○○ ○ Very low	CRITICAL
---	------------------------------	---------------------	----------------	----------------	-----------------	-------------------------------------------------------------------------------------------------------------------------------	------------------	------------------	----------------------------------	------------------------------------------------------------	-------------------------	----------

All-cause mortality in studies showing no significant change in the incidence of fibrinolysis (assessed with: Odds Ratio)

8	observati onal studies	very serio us	not serious	not serious	very serious	all plausible residual confoundin g would suggest spurious effect, while no effect was observed	770/14 674 (5.2%)	2383/34 426 (6.9%)	OR -- -- (0.83 to 1.33)	-- -- per 1,000 (from 11 fewer to 21 more)	⊕○○ ○ Very low	IMPORTA NT
---	------------------------------	---------------------	----------------	----------------	-----------------	-------------------------------------------------------------------------------------------------------------------------------	-------------------------	--------------------------	-----------------------------------------	-------------------------------------------------------------------------------	-------------------------	---------------

All-cause mortality in HICs (assessed with: Odds Ratio)

6	observati onal studies	very serio us	very serious	not serious	very serious	all plausible residual confoundin g would suggest spurious effect,	256/36 25 (7.1%)	1750/18 885 (9.3%)	OR -- -- (0.76 to 1.66)	-- -- per 1,000 (from 21 fewer to 52 more)	⊕○○ ○ Very low	IMPORTA NT
---	------------------------------	---------------------	-----------------	----------------	-----------------	-----------------------------------------------------------------------------------------	------------------------	--------------------------	-----------------------------------------	-------------------------------------------------------------------------------	-------------------------	---------------

while no
effect was
observed

All-cause mortality in LMICs (assessed with: Odds Ratio)

7 observational studies very seriously serious very serious not all plausible residual confounding suggest a spurious effect, while no effect was observed

539/11 656/160 OR -- -- per 1,000 (1.03 to 1.30) 1 more to 12 more)

⊕○○○ IMPORTA
○ NT
Very low

HICs: High-income countries; LMICs: Low-and middle-income countries.

MOOSE checklist

Reporting Criteria

Reported (Yes/No)

Reported on Page

Reporting of Background

Problem definition	Yes	1
Hypothesis statement	Yes	2
Description of Study Outcome(s)	Yes	3
Type of exposure or intervention used	Yes	2
Type of study design used	Yes	3
Study population	Yes	2
Reporting of Search Strategy		
Qualifications of searchers (e.g., librarians and investigators)	No	
Search strategy, including time period included in the synthesis and keywords	Yes	2
Effort to include all available studies, including contact with authors	Yes	2-3
Databases and registries searched	Yes	2
Search software used, name and version, including special features used (e.g., explosion)	Yes	2-3
Use of hand searching (e.g., reference lists of obtained articles)	Yes	2
List of citations located and those excluded, including justification	Yes	4

Method for addressing articles published in languages other than English	Not applicable	
Method of handling abstracts and unpublished studies	Yes	?
Description of any contact with authors	Yes	
Reporting of Methods		
Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	Yes	4
Rationale for the selection and coding of data (e.g., sound clinical principles or convenience)	Yes	3-4
Documentation of how data were classified and coded (e.g., multiple raters, blinding, and interrater reliability)	Yes	3-4
Assessment of confounding (e.g., comparability of cases and controls in studies where appropriate)	Yes	10
Assessment of study quality, including blinding of quality assessors; stratification or regression on possible	Yes	10

predictors of study results	Yes	10-13
Assessment of heterogeneity	Yes	13
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	Yes	3
Provision of appropriate tables and graphics	Yes	4-13
Reporting of Results		
Table giving descriptive information for each study included	Yes	5-7
Results of sensitivity testing (e.g., subgroup analysis)	Yes	13
Indication of statistical uncertainty of findings	Yes	
Reporting of Discussion		
Quantitative assessment of bias (e.g., publication bias)	Yes	11-12
Justification for exclusion (e.g., exclusion of non-English-language citations)	Yes	4
Assessment of quality of included studies	Yes	10

Reporting of Conclusions		
Consideration of alternative explanations for observed results	Yes	14
Generalization of the conclusions (e.g., appropriate for the data presented and within the domain of the literature review)	Yes	14-15
Guidelines for future research	Yes	15
Disclosure of funding source	Yes	16

From: **Stroup DF**, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000; **283**: 2008-2012 [PMID: 10789670doi: 10.1001/jama.283.15.2008]

Detailed quality assessment using Newcastle-Ottawa scale:

Studies **Selection** **Comparability** **Outcome (Max** **Total stars**
(Max: ★ ★ ★ (Max ★★) ★★ ★)
★)

	<i>Case-Control studies</i>			
Daoulah, 2021	★★	★	★★	6
Leng, 2021	★★★★	★★	★★	7
Song, 2021	★★★★	★	★★	6
Wang, 2020	★★★★	★★	★★	7
Xiang, 2020	★★★★	★	★★	6

Zhang, 2021	★★		★★	4
Erol, 2020	★★	★	★★	5
Mesnier, 2020	★★	★	★	4
Balghith, 2020	★★★	★	★★	6
Clifford, 2021	★★★★	★★	★★★★	8
Rodriguez- Leor, 2020	★★	★	★★	5
Calvao, 2021	★★★★	★	★★★★	7
	<i>Cohort studies</i>			
Huang, 2020	★★★★	★	★	5
Wu, 2020	★★★★★	★★	★★	8



Supplementary Figure 1 Quality assessment of included studies using the Newcastle-Ottawa scale.

Search strategies

PubMed:

((("st elevation myocardial infarction"[MeSH Terms] OR ("st"[All Fields] AND "elevation"[All Fields] AND "myocardial"[All Fields] AND "infarction"[All Fields]) OR "st elevation myocardial infarction"[All Fields] OR (("standards"[MeSH Subheading] OR "standards"[All Fields] OR "st"[All Fields]) AND ("elevate"[All Fields] OR "elevated"[All Fields] OR "elevates"[All Fields] OR "elevating"[All Fields] OR "elevation"[All Fields] OR "elevational"[All Fields] OR "elevations"[All Fields]))) OR (("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("myocardial infarction"[MeSH Terms] OR ("myocardial"[All Fields] AND "infarction"[All Fields]) OR "myocardial infarction"[All Fields])) OR ("acute coronary syndrome"[MeSH Terms] OR ("acute"[All Fields] AND "coronary"[All Fields] AND "syndrome"[All Fields]) OR "acute coronary syndrome"[All Fields]) OR ("st elevation myocardial infarction"[MeSH Terms] OR ("st"[All Fields] AND "elevation"[All Fields] AND "myocardial"[All Fields] AND "infarction"[All Fields]) OR "st elevation myocardial infarction"[All Fields] OR "STEMI"[All Fields] OR "STEMIS"[All Fields])) AND ("thrombolytic therapy"[MeSH Terms] OR ("thrombolytic"[All Fields] AND "therapy"[All Fields]) OR "thrombolytic therapy"[All Fields] OR ("thrombolytic therapy"[MeSH Terms] OR ("thrombolytic"[All Fields] AND "therapy"[All Fields]) OR "thrombolytic therapy"[All Fields] OR ("fibrinolytic"[All Fields] AND "therapy"[All Fields]) OR "fibrinolytic therapy"[All Fields]) OR ("fibrinolytic agents"[Pharmacological Action] OR "fibrinolytic agents"[MeSH Terms] OR ("fibrinolytic"[All Fields] AND "agents"[All Fields]) OR "fibrinolytic agents"[All Fields]) OR ("fibrinolysis"[MeSH Terms] OR "fibrinolysis"[All Fields] OR "fibrinolyses"[All Fields]) OR "thrombolysis"[All Fields] OR ("tissue plasminogen activator"[MeSH Terms] OR ("tissue"[All Fields] AND "plasminogen"[All Fields] AND "activator"[All Fields]) OR "tissue plasminogen activator"[All Fields] OR "alteplase"[All Fields]) OR ("streptokinase"[MeSH Terms] OR "streptokinase"[All Fields] OR "streptokinases"[All Fields]) OR ("reteplase"[Supplementary Concept] OR

"reteplase"[All Fields]) OR ("tenecteplase"[MeSH Terms] OR "tenecteplase"[All Fields]))
 AND ((english[Filter]) AND (2020:2022[pdat]))

Scopus:

("ST elevation myocardial infarction" OR "ST elevation" OR "acute myocardial infarction" OR "acute coronary syndrome" OR STEMI) AND ("thrombolytic therapy" OR "fibrinolytic therapy" OR "fibrinolytic agents" OR fibrinolysis OR thrombolysis OR alteplase OR Streptokinase OR reteplase OR tenecteplase).

Web of Science:

(ST elevation myocardial infarction OR ST elevation OR acute myocardial infarction OR acute coronary syndrome OR STEMI) AND (thrombolytic therapy OR fibrinolytic therapy OR fibrinolytic agents OR fibrinolysis OR thrombolysis OR alteplase OR Streptokinase OR reteplase OR tenecteplase)

Cochrane:

(ST elevation myocardial infarction OR ST elevation OR acute myocardial infarction OR acute coronary syndrome OR STEMI) AND (thrombolytic therapy OR fibrinolytic therapy OR fibrinolytic agents OR fibrinolysis OR thrombolysis OR alteplase OR Streptokinase OR reteplase OR tenecteplase)