

Prevention, Diagnosis, and Treatment of VTE in Patients With Coronavirus Disease 2019

CHEST Guideline and Expert Panel Report

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e-Appendix 1.

PICO question 1

(1) Choice of anticoagulant (acutely ill hospitalized patient / critically ill patients)

P: Patients with COVID-19

I: Standard dose UFH, LMWH, Fondaparinux

C: Placebo

O: VTE, major bleeding, mortality

Search strategies

Ovid MEDLINE

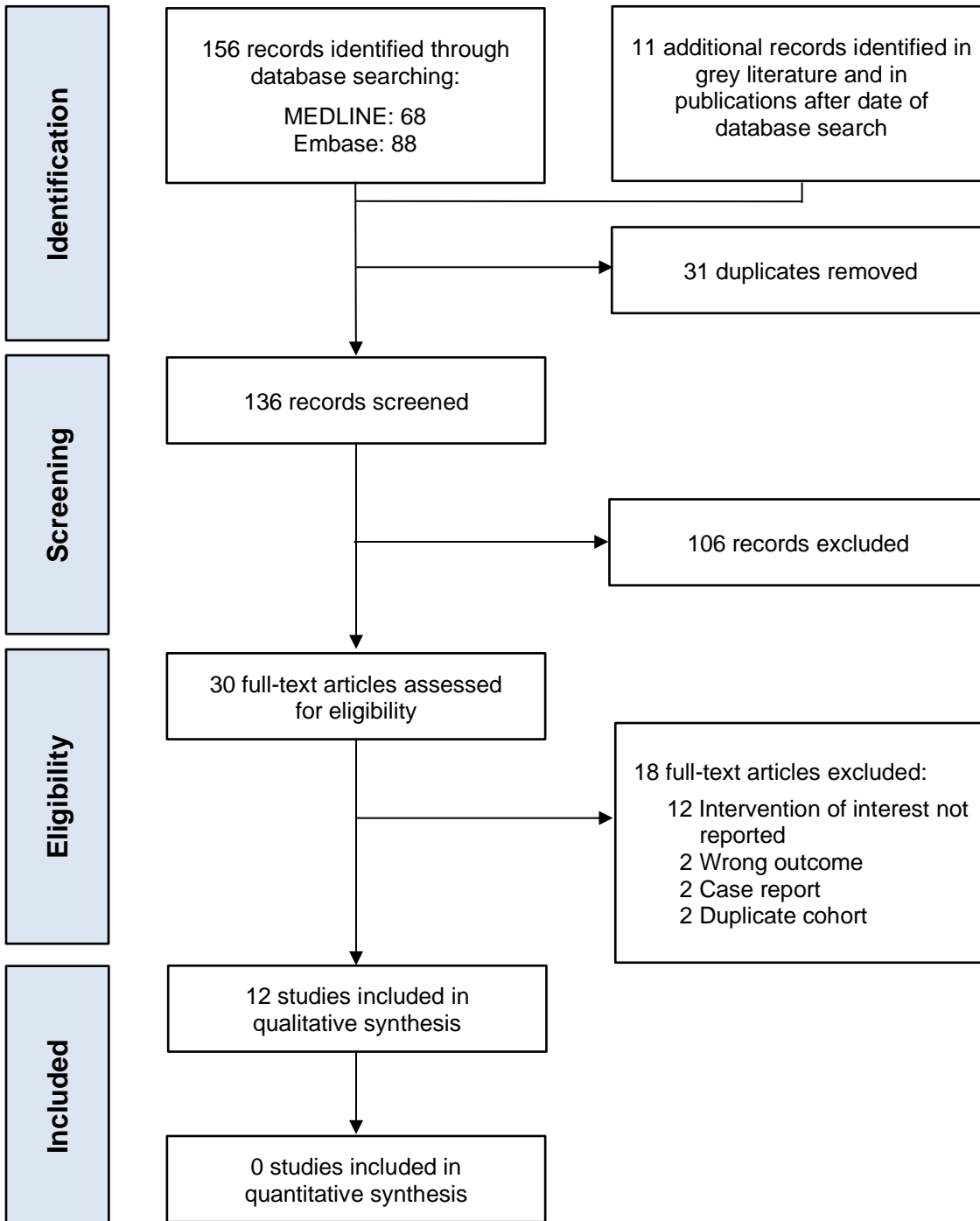
- 1 (exp coronavirus/ or coronavirus*.mp. or corona virus*.mp.) and (wuhan or beijing or shanghai).mp.
- 2 ((coronavirus or corona virus) adj3 "2019").tw.
- 3 covid.tw,kw.
- 4 covid19.tw,kw. or covid 19.kw.
- 5 sars cov 2.tw,kw.
- 6 (ncov or n cov).tw,kw.
- 7 novel coronavirus.tw,kw.
- 8 sars cov2.tw,kw.
- 9 Coronavirus Infections/ and Pandemics/
- 10 or/1-9
- 11 exp Heparin, Low-Molecular-Weight/
- 12 Fondaparinux.tw,kw.
- 13 exp Heparin/
- 14 (lmwh or heparin*).tw,kw.
- 15 thromboprophyla*.tw,kw.
- 16 exp Anticoagulants/
- 17 (liquemin or liquaemin).tw,kw.
- 18 (dalteparin or fragmin or enoxaparin or clexane or lovenox or nadroparin or fraxiparin or fondaparinux or arixtra or bemiparin or semuloparin or sulodexide).tw,kw.
- 19 Vitamin K/ai [Antagonists & Inhibitors]
- 20 (vitamin k adj2 antagonist*).tw.
- 21 (Coumadin or warfarin or phenprocoumon or marcoumar or acenocoumarol or Sintrom).tw,kw.
- 22 exp Factor Xa Inhibitors/
- 23 (rivaroxaban or apixaban or edoxaban or betrixaban or danaparoid or darexaban).tw,kw.
- 24 exp Antithrombins/
- 25 antithrombin*.tw,kw.
- 26 or/11-25
- 27 exp "embolism and thrombosis"/
- 28 (thrombo* or emboli*).tw,kw.
- 29 27 or 28
- 30 Hemorrhage/
- 31 (h?emorrhag* or bleed*).tw,kw.
- 32 30 or 31
- 33 Mortality/
- 34 Death/
- 35 mortality.tw,kw.
- 36 33 or 34 or 35

37 29 or 32 or 36
38 10 and 26 and 37
39 10 and 26
40 10 and 29
41 10 and 32
42 38 or 39 or 40 or 41
43 limit 42 to yr="2019 -Current"

Embase Classic + Embase

1 (exp coronavirus/ or coronavirus*.mp. or corona virus*.mp.) and (wuhan or beijing or shanghai).mp.
2 ((coronavirus or corona virus) adj3 "2019").tw.
3 covid.tw.
4 covid19.tw.
5 sars cov 2.tw.
6 (ncov or n cov).tw.
7 novel coronavirus.tw.
8 sars cov2.tw.
9 or/1-8
10 Coronavirus infection/
11 limit 10 to yr="2019 -Current"
12 9 or 11
13 exp anticoagulant agent/
14 exp blood clotting factor 10a inhibitor/
15 (rivaroxaban or apixaban or edoxaban or betrixaban or danaproid or darexaban).tw.
16 thrombosis prevention/
17 thromboprophyl*.tw.
18 antithrombin/
19 dabigatran.tw.
20 antivitamin K/
21 (Coumadin or warfarin or phenprocoumon or marcoumar or acenocoumaro).tw.
22 (dalteparin or fragmin or enoxaparin or clexane or lovenox or nadroparin or fraxiparin or fondaparinux or arixtra or bemiparin or semuloparin or sulodexide).tw.
23 (heparin* or liquemin or liquaemin).tw.
24 or/13-23
25 exp thromboembolism/
26 (thrombo* or embolism*).tw.
27 25 or 26
28 exp bleeding/
29 (h?emorrhag* or bleed*).tw.
30 28 or 29
31 exp mortality/
32 death/
33 mortality.kw,tw.
34 31 or 32 or 33
35 27 or 30 or 34
36 12 and 24 and 35
37 12 and 24
38 12 and 27
39 12 and 30
40 36 or 37 or 38 or 39
41 limit 40 to yr="2019 -Current"

PRISMA flow diagram PICO question 1



PICO questions 2, 3 and 6

(2) Intermediate-dose anticoagulant prophylaxis (acutely ill hospitalized patient / critically ill patients; biomarker(s) to select patients?)

P: Patients with COVID-19

I: Intermediate-dose anticoagulant thromboprophylaxis

C: Standard-dose anticoagulant thromboprophylaxis

O: VTE, major bleeding, mortality

(3) Full-dose anticoagulant prophylaxis (acutely ill hospitalized patient / critically ill patients; biomarker(s) to select patients?)

P: Patients with COVID-19

I: Full-dose anticoagulant thromboprophylaxis

C: Standard-dose or intermediate-dose anticoagulant thromboprophylaxis

O: VTE, bleeding, mortality

(6) Mechanical prophylaxis (acutely ill hospitalized patient / critically ill patients)

P: Patients with COVID-19

I: Combined mechanical and anticoagulant prophylaxis

C: Anticoagulant prophylaxis

O: VTE, bleeding, mortality

Search strategies

PubMed (Legacy)

```
(((((thromboembolic[tiab] OR thromboembolism[tiab] OR hemotologic OR haemotologic OR hemotol*[tiab] OR haemotol*[tiab] OR coagulation[tiab] OR coagulate[tiab] OR thromboembolism[MeSH] OR VTE[tiab] OR venous thromboembolism[tiab] OR "venous thrombosis"[MeSH Terms] OR venous thromboembolism[MeSH] OR pulmonary embol*[tiab] OR "pulmonary embolism"[MeSH Terms] OR thrombosis[tiab] OR thrombosis[MeSH] OR venous thrombosis[tiab] OR thrombus OR DVT[tiab] OR deep vein thromb*[tiab] OR "Venous Thromboembolism"[Mesh] OR "Thromboembolism"[Mesh] OR "Thromboembolism/drug therapy"[Mesh] OR Embolism and Thrombosis[MeSH] OR microemboli OR emboli[tiab] OR coagulation disorder[tiab] OR coagulopathy[tiab] OR thromboprophylaxis OR Therapeutic anticoagulation OR therapeutic anticoag*[tiab] OR chemoprophylaxis OR full therapeutic intensity[tiab] OR thromboprophylac*[tiab] OR mechanical prophyla*[tiab] OR sequential compression device*[tiab] OR TEDS[tiab] OR TED hose[tiab] )))) AND (((wuhan OR hubei OR hunan[tiab]) AND ("coronavirus"[MeSH Terms] OR coronavirus[All Fields] OR severe acute respiratory[tiab] OR pneumonia)) OR ((wuhan OR hubei OR hunan[tiab]) AND (outbreak[tiab] OR pandemic)) OR ("Coronavirus"[Mesh] OR COVID19 OR "covid" OR "CoV2" OR "CoV 2" OR "nCoV" OR "sarscov2" OR "novel CoV" OR coronavirus OR corona virus[tiab] OR coronavirinae[tiab] OR coronaviridae[tiab] OR betacoronavirus OR COVID-19 OR coronavirus OR SARS-CoV-2 OR 2019-nCoV[All Fields] OR 2019nCoV[All Fields] OR COVID-19[all fields] OR SARS-CoV-2[All Fields] OR novel coronavirus[tiab] OR coronavirus pandemic[tiab] OR "COVID-19"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "spike glycoprotein, COVID-19 virus"[Supplementary Concept] OR "Betacoronavirus"[Mesh] OR "Coronavirus Infections"[Mesh])) AND ("2019/12/01"[PDAT] : "3000/12/31"[PDAT]))) NOT (((("Animals"[Mesh] AND "Humans"[Mesh]))))
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Embase (Elsevier)

- #1 'coronavirus disease 2019'/exp OR 'covid 19':ti,ab OR ((covid NEAR/2 19):ti,ab) OR ((sars NEAR/2 'cov 2'):ti,ab) OR '2019 ncov':ti,ab OR ((wuhan:ti,ab OR hubei:ti,ab) AND coronavirus*:ti,ab) OR ([2019-2020]/py AND (new:ti,ab OR novel:ti,ab OR pandemic:ti,ab OR epidemic:ti,ab) AND ('coronavirus infection'/exp OR coronavirus*:ti,ab OR 'corona virus*':ti,ab)) OR covid19 OR covid OR 'cov 2' OR ncov:ab,ti,kw OR sarscov2:ab,ti,kw OR 'novel cov' OR 'coronavirinae'/exp OR 'coronavirinae' OR 'coronaviridae'/exp OR 'coronaviridae' OR 'coronaviridae infection'/exp OR 'coronaviridae infection' OR 'betacoronavirus'/exp OR betacoronavirus OR 'covid 19'/exp OR 'covid 19':ab,ti,kw OR 'coronavirus'/exp OR coronavirus:ab,ti,kw OR '2019 ncov':ab,ti,kw OR '2019 ncov2':ab,ti,kw OR 'sars cov 2':ab,ti,kw OR 'severe acute respiratory syndrome coronavirus 2'/exp OR 'severe acute respiratory syndrome coronavirus 2':ab,ti,kw
- #2 'thromboembolism'/exp OR 'thromboembolism':ab,ti,kw OR 'vein thrombosis'/exp OR 'venous thromboembolism'/exp OR 'venous thromboembolism':ab,ti,kw OR 'vein thrombosis':ab,ti,kw OR vte:ab,ti,kw OR dvt:ab,ti,kw OR 'deep vein thrombosis'/exp OR 'deep vein thrombosis':ab,ti,kw OR 'thromboembolic risk' OR thromboembolic:ab,ti,kw OR 'pulmonary embolism and thrombosis'/exp OR 'lung embolism'/exp OR 'pulmonary embolism':ab,ti,kw OR 'thrombosis'/exp OR 'thrombosis':ab,ti,kw OR 'blood clotting'/exp OR 'blood clotting':ab,ti,kw OR 'thrombus'/exp OR 'thrombus':ab,ti,kw OR 'microembolism'/exp OR 'microemboli*':ab,ti,kw OR 'blood clotting disorder'/exp OR 'chemoprophylaxis'/exp OR 'chemoprophylaxis':ab,ti,kw OR 'fibrinolytic agent'/exp OR thrombolytic:ab,ti,kw OR 'd dimer'/exp OR 'd dimer test' OR 'd dimer blood level' OR 'd dimer assay' OR 'anti xa assay' OR 'mechanical prophylaxis':ab,ti,kw OR 'sequential compression device'/exp OR 'sequential compression device':ab,ti,kw OR 'ted hose':ab,ti,kw OR teds:ab,ti,kw OR ((therapeutic NEAR/2 anticoagul*):ab,ti,kw) OR 'full therapeutic intensity':ab,ti,kw OR anti?coagulation:ab,ti,kw OR anti?coagulant*:ab,ti,kw OR thromboprevention:ab,ti,kw OR 'venous thromboprophylaxis':ab,ti,kw OR 'thromboprophylaxis':ab,ti,kw OR heparin:ab,ti,kw OR lovenox:ab,ti,kw OR enoxaparin:ab,ti,kw
- #3 [30-11-2019]/sd NOT [28-11-2021]/sd
- #4 #1 AND #2 AND #3

Web of Science

- #1 TS=(Coronavirus OR covid19 OR covid OR cov 2 OR ncov OR sarscov2 OR novel cov OR coronavirinae OR coronaviridae OR "coronaviridae infection" OR betacoronavirus OR "covid 19" OR coronavirus OR "2019 ncov" OR "2019 ncov2" OR "sars cov 2" OR "severe acute respiratory syndrome coronavirus 2" OR "novel coronavirus" OR "coronavirus pandemic" OR "coronavirus outbreak" OR "spike glycoprotein coronavirus" OR "coronavirus infections")
- #2 TS=(thromboembolism OR thrombosis OR thrombus OR embolism OR microembolism OR microemboli OR VTE OR venous thromboembolism OR deep vein thrombosis OR DVT OR coagulant OR hypercoagulable OR full therapeutic intensity OR heparin OR lovenox OR enoxaparin OR anticoagulant OR anticoagulation OR anti-coagulation OR chemoprophylaxis OR mechanical prophylaxis OR sequential compression device OR TEDS OR TED Hose OR Venous thromboprophylaxis OR Thromboprevention OR thrombolytics)
- #3 #1 and #2
- Dates 2019-2020

Science.gov

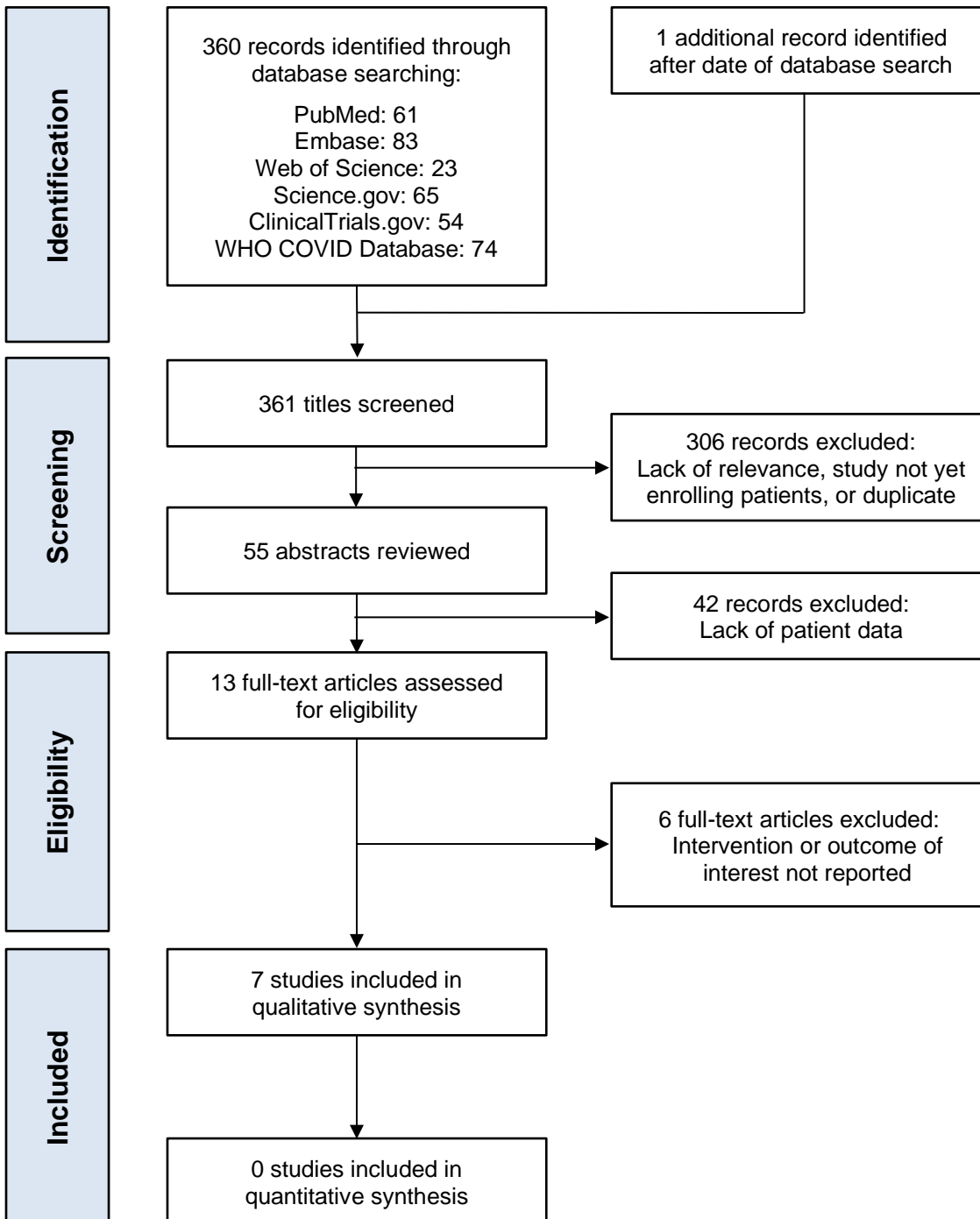
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WHO COVID-19 database

<https://search.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/>

hypercoagulability OR thromboembolism OR thrombolytic OR chemoprophylaxis OR anticoagulation OR anticoagulant OR heparin OR lovenox OR coagulant OR coagulate OR coagulation OR embolism OR emboli OR VTE OR DVT

PRISMA flow diagram PICO questions 2, 3 and 6



PICO question 4

(4) Duration of anticoagulant prophylaxis

P: Patients with COVID-19

I: Extended duration (45 days)

C: 10 days (or duration of hospitalization)

O: VTE, bleeding, mortality

Search strategies

Ovid MEDLINE

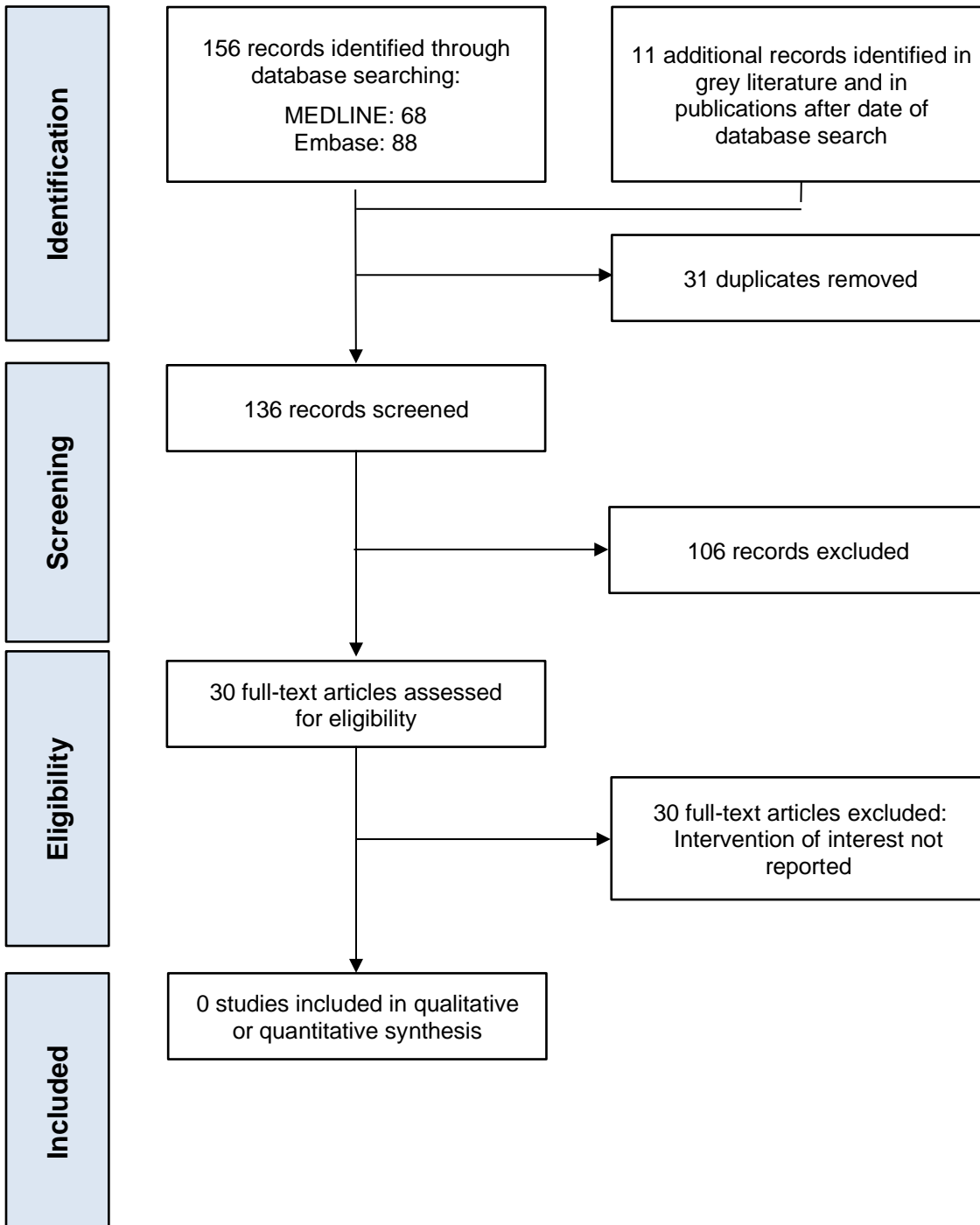
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- 2 ((coronavirus or corona virus) adj3 "2019").tw.
- 3 covid.tw,kw.
- 4 covid19.tw,kw. or covid 19.kw.
- 5 sars cov 2.tw,kw.
- 6 (ncov or n cov).tw,kw.
- 7 novel coronavirus.tw,kw.
- 8 sars cov2.tw,kw.
- 9 Coronavirus Infections/ and Pandemics/
- 10 or/1-9
- 11 exp Heparin, Low-Molecular-Weight/
- 12 Fondaparinux.tw,kw.
- 13 exp Heparin/
- 14 (lmwh or heparin*).tw,kw.
- 15 thromboprophyla*.tw,kw.
- 16 exp Anticoagulants/
- 17 (liquemin or liquaemin).tw,kw.
- 18 (dalteparin or fragmin or enoxaparin or clexane or lovenox or nadroparin or fraxiparin or fondaparinux or arixtra or bemiparin or semuloparin or sulodexide).tw,kw.
- 19 Vitamin K/ai [Antagonists & Inhibitors]
- 20 (vitamin k adj2 antagonist*).tw.
- 21 (Coumadin or warfarin or phenprocoumon or marcoumar or acenocoumarol or Sintrom).tw,kw.
- 22 exp Factor Xa Inhibitors/
- 23 (rivaroxaban or apixaban or edoxaban or betrixaban or danaparoid or darexaban).tw,kw.
- 24 exp Antithrombins/
- 25 antithrombin*.tw,kw.
- 26 or/11-25
- 27 exp "embolism and thrombosis"/
- 28 (thrombo* or emboli*).tw,kw.
- 29 27 or 28
- 30 Hemorrhage/
- 31 (h?emorrhag* or bleed*).tw,kw.
- 32 30 or 31
- 33 Mortality/
- 34 Death/
- 35 mortality.tw,kw.
- 36 33 or 34 or 35
- 37 29 or 32 or 36
- 38 10 and 26 and 37
- 39 10 and 26

40 10 and 29
41 10 and 32
42 38 or 39 or 40 or 41
43 limit 42 to yr="2019 -Current"

Embase Classic + Embase

1 (exp coronavirus/ or coronavirus*.mp. or corona virus*.mp.) and (wuhan or beijing or shanghai).mp.
2 ((coronavirus or corona virus) adj3 "2019").tw.
3 covid.tw.
4 covid19.tw.
5 sars cov 2.tw.
6 (ncov or n cov).tw.
7 novel coronavirus.tw.
8 sars cov2.tw.
9 or/1-8
10 Coronavirus infection/
11 limit 10 to yr="2019 -Current"
12 9 or 11
13 exp anticoagulant agent/
14 exp blood clotting factor 10a inhibitor/
15 (rivaroxaban or apixaban or edoxaban or betrixaban or danaproid or darexaban).tw.
16 thrombosis prevention/
17 thromboprophyl*.tw.
18 antithrombin/
19 dabigatran.tw.
20 antivitamin K/
21 (Coumadin or warfarin or phenprocoumon or marcoumar or acenocoumaro).tw.
22 (dalteparin or fragmin or enoxaparin or clexane or lovenox or nadroparin or fraxiparin or fondaparinux or arixtra or bemiparin or semuloparin or sulodexide).tw.
23 (heparin* or liquemin or liquaemin).tw.
24 or/13-23
25 exp thromboembolism/
26 (thrombo* or embolism*).tw.
27 25 or 26
28 exp bleeding/
29 (h?emorrhag* or bleed*).tw.
30 28 or 29
31 exp mortality/
32 death/
33 mortality.kw,tw.
34 31 or 32 or 33
35 27 or 30 or 34
36 12 and 24 and 35
37 12 and 24
38 12 and 27
39 12 and 30
40 36 or 37 or 38 or 39
41 limit 40 to yr="2019 -Current"

PRISMA flow diagram PICO question 4



PICO question 5

(5) Antiplatelet Agents (Acutely ill hospitalized patient / critically ill patients)

P: Patients with COVID-19

I: Antiplatelet agent

C: No antiplatelet agent

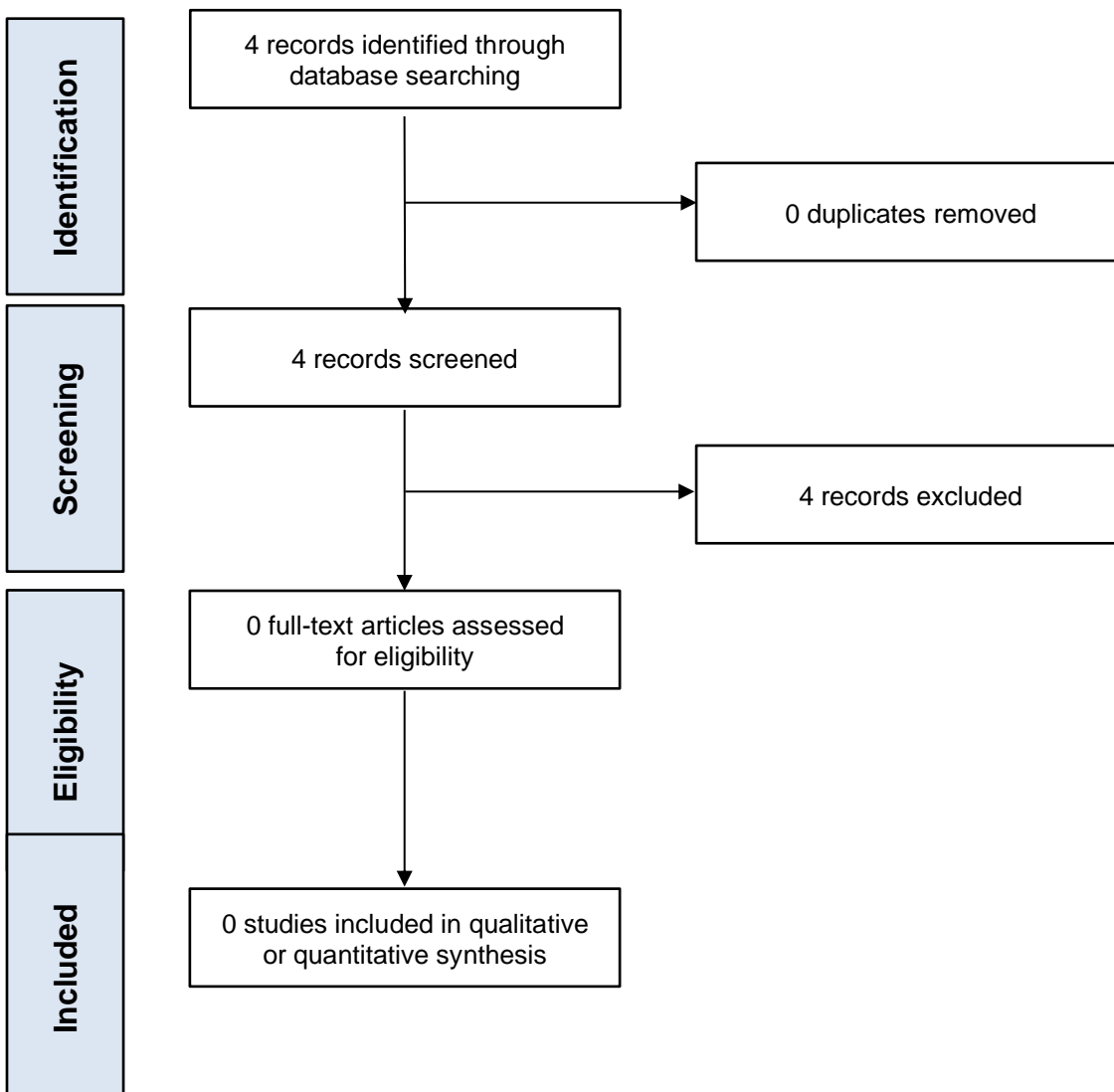
O: VTE, bleeding, mortality

Search strategy

PubMed

(2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) OR (2019 AND novel AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])) AND (antiplatelet drug* OR antiplatelet agent* OR aspirin OR dipyridamole OR clopidogrel OR ticagrelor OR cangrelor OR prasugrel OR vorapaxar OR ticlopidine)

PRISMA flow diagram PICO question 5



PICO question 7

(7) Choice of anticoagulant (acutely ill hospitalized patient / critically ill patients)

P: Patients with COVID-19 and objectively confirmed VTE

I: LMWH, Fondaparinux, DOAC

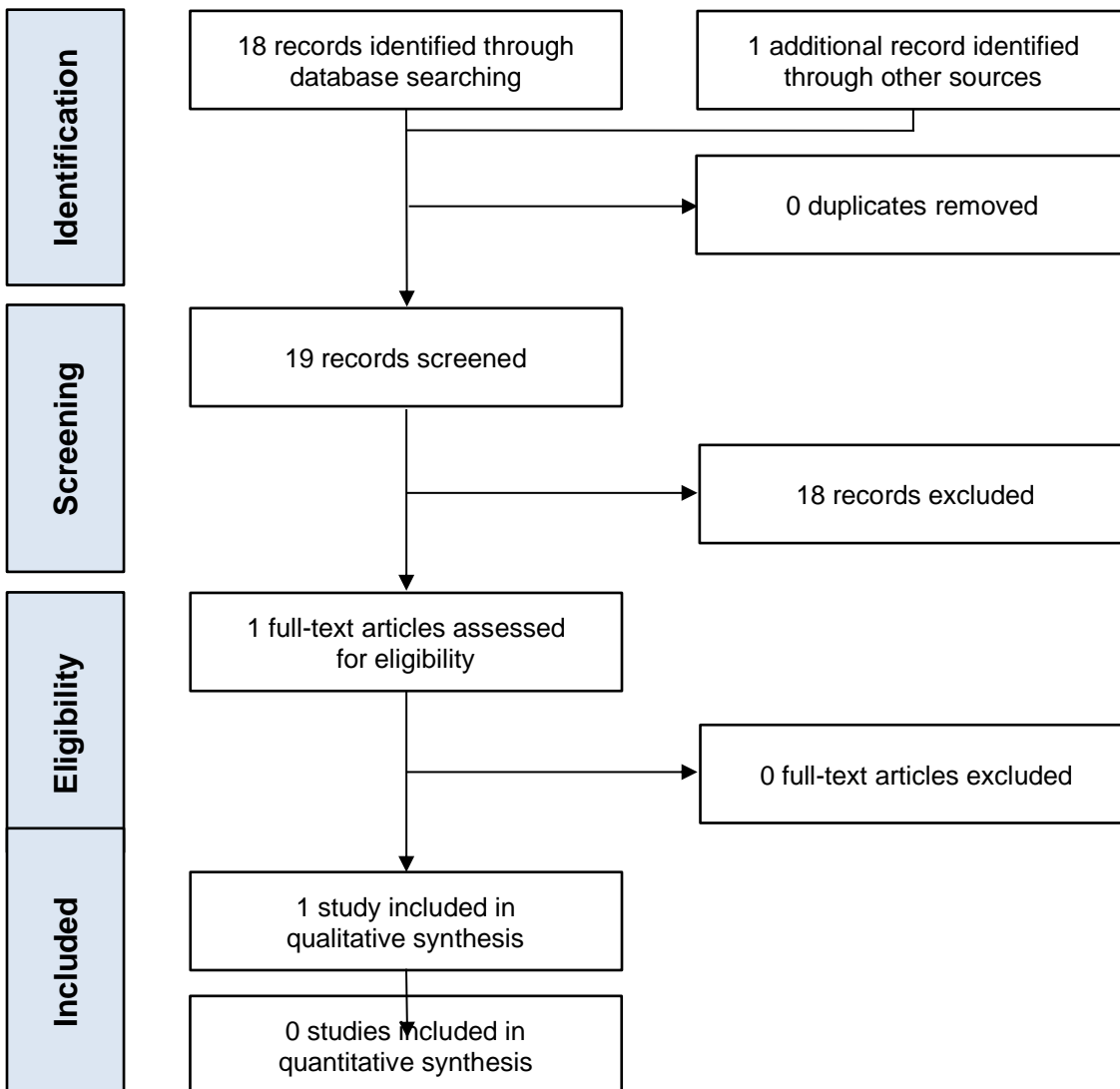
C: UFH

O: VTE, major bleeding, mortality

Search strategy

PubMed
 (2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) OR (2019 AND novel AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])) AND (anticoagulant drug* OR anticoagulant agent* OR heparin OR unfractionated heparin OR low-molecular-weight heparin OR fondaparinux OR direct oral anticoagulant* OR apixaban OR rivaroxaban OR dabigatran OR edoxaban)

PRISMA flow diagram PICO question 7



PICO question 8

(8) Thrombolytic therapy

P: Patients with COVID-19 and objectively confirmed PE

I: Thrombolytic therapy

C: No thrombolytic therapy

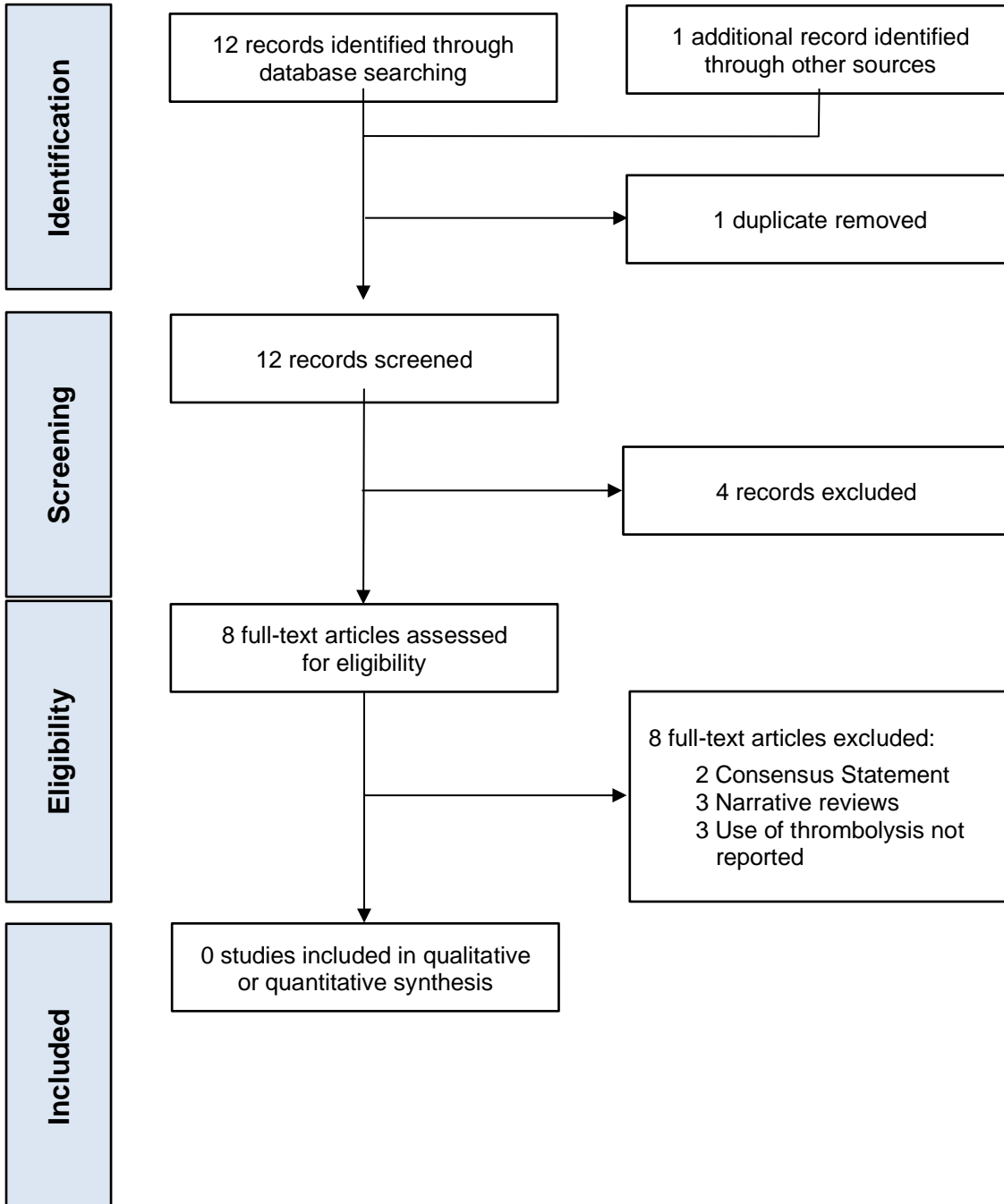
O: VTE, bleeding, mortality

Search strategy

Ovid MEDLINE, Embase Classic + Embase, Cochrane Controlled Register of Trials (CENTRAL)

- 1 exp Venous Thromboembolism/
- 2 exp Venous Thrombosis/
- 3 Pulmonary embolism.mp. or exp Pulmonary Embolism/
- 4 Deep vein thrombosis.mp.
- 5 Coronavirus Infections/
- 6 COVID.mp.
- 7 COVID-19.mp.
- 8 SARS-CoV-2.mp.
- 9 exp Thrombolytic Therapy/
- 10 exp Fibrinolytic Agents/
- 11 thrombolytic.mp.
- 12 Tissue Plasminogen Activator/
- 13 TPA.mp.
- 14 alteplase.mp.
- 15 reteplase.mp.
- 16 r-PA.mp.
- 17 exp Streptokinase/
- 18 streptokinase.mp.
- 19 prourokinase.mp.
- 20 Urokinase-Type Plasminogen Activator/
- 21 or/1-4
- 22 or/5-8
- 23 or/9-20
- 24 21 and 22 and 23

PRISMA flow diagram PICO question 8



PICO questions 9 and 10

Management of incident VTE on anticoagulant prophylaxis (acutely ill hospitalized patient / critically ill patients)

(9)

P: Patients with COVID-19 and objectively confirmed VTE while on standard or intermediate-dose anticoagulant thromboprophylaxis

I: 125-130% dose LMWH (UFH)

C: Full-dose UFH, LMWH, fondaparinux, DOAC, argatroban

O: VTE, bleeding, mortality

(10)

P: Patients with COVID-19 and objectively confirmed VTE while on full-dose anticoagulant thromboprophylaxis

I: 125-130% dose LMWH (UFH)

C: Full-dose UFH, LMWH, fondaparinux, DOAC, argatroban

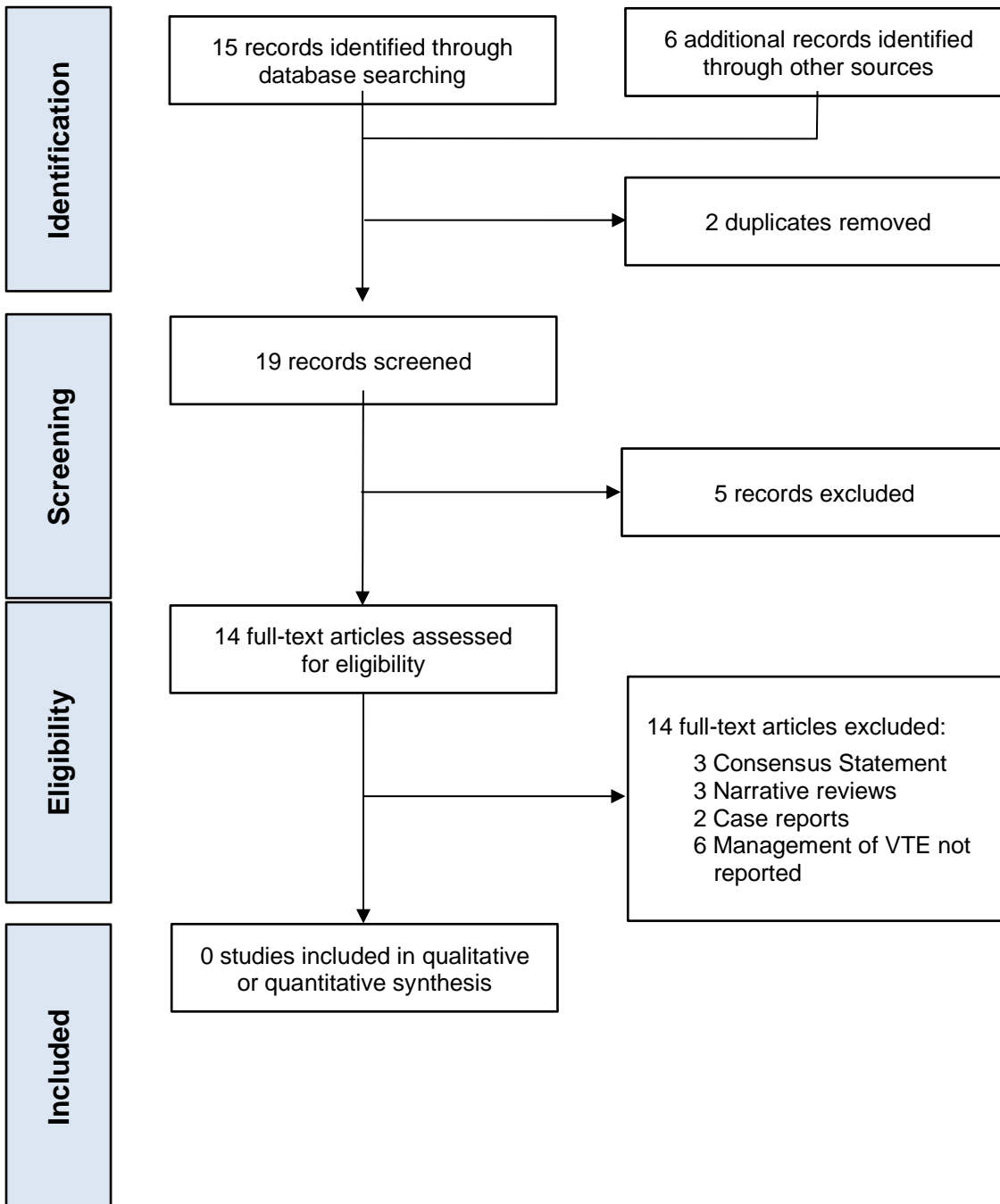
O: VTE, bleeding, mortality

Search strategy

Ovid MEDLINE, Embase Classic + Embase, Cochrane Controlled Register of Trials (CENTRAL)

- 1 exp Venous Thromboembolism/
- 2 exp Venous Thrombosis/
- 3 Pulmonary embolism.mp. or exp Pulmonary Embolism/
- 4 Deep vein thrombosis.mp.
- 5 Coronavirus Infections/
- 6 COVID.mp.
- 7 COVID-19.mp.
- 8 SARS-CoV-2.mp.
- 9 exp Anticoagulants/
- 10 exp Heparin/
- 11 exp Heparin, Low-Molecular-Weight/
- 12 exp Rivaroxaban/
- 13 apixaban.mp.
- 14 exp Dabigatran/
- 15 direct oral anticoagulant.mp.
- 16 DOAC.mp.
- 17 exp Fondaparinux/
- 18 argatroban.mp.
- 19 exp Warfarin/
- 20 or/1-4
- 21 or/5-8
- 22 or/9-19
- 23 20 and 21 and 22

PRISMA flow diagram PICO questions 9 and 10



PICO question 11

(11) Role of screening ultrasound (acutely ill hospitalized patient / critically ill patients)

P: Patients with COVID-19

I: Screening ultrasound of deep veins

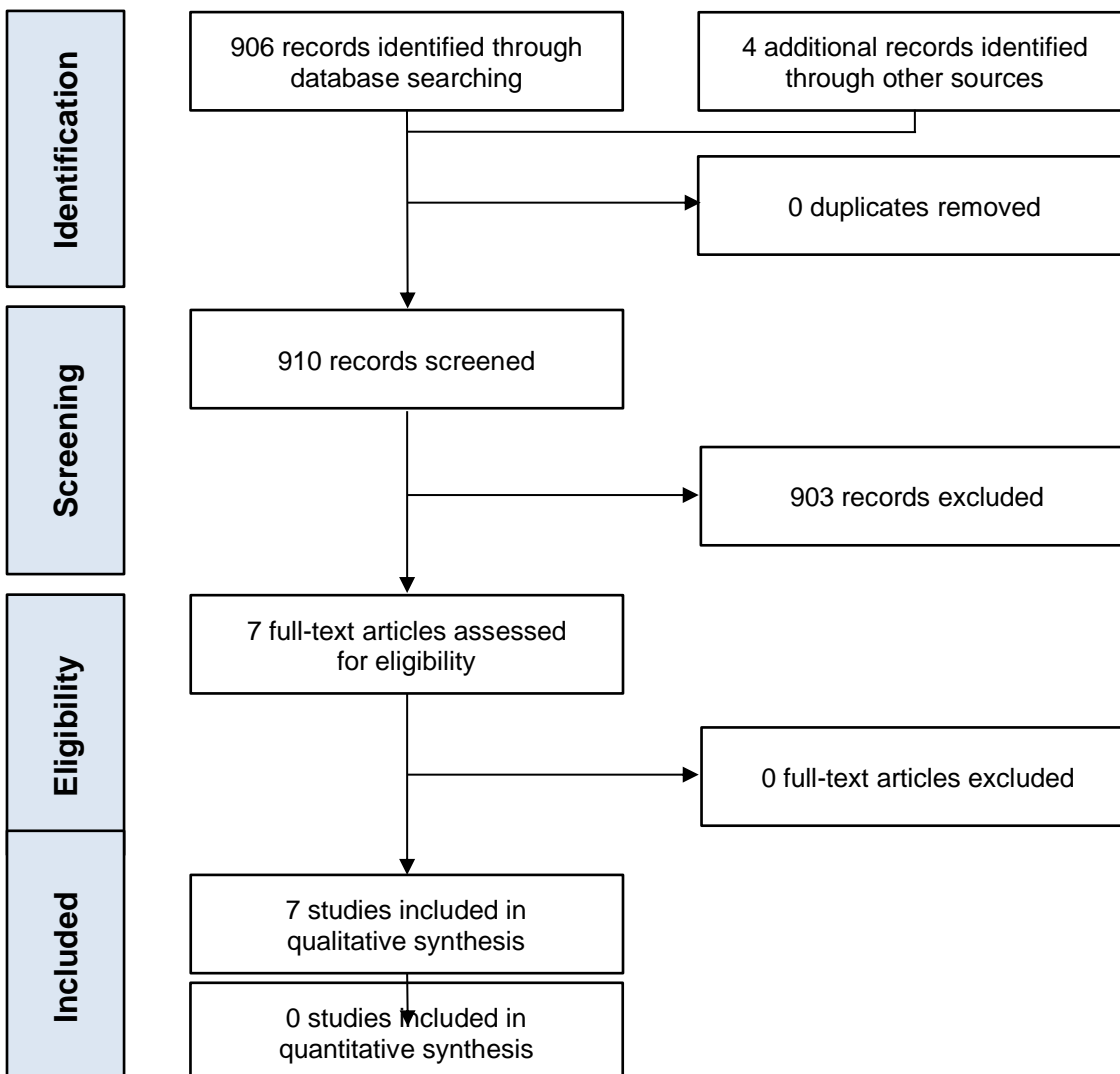
C: No screening ultrasound

O: Symptomatic VTE during follow-up (or prevalence/incidence of VTE at screening and during follow-up)

Search strategy

Pubed
(2019-nCoV OR 2019nCoV OR COVID-19 OR SARS-CoV-2 OR ((wuhan AND coronavirus) OR (2019 AND novel AND coronavirus) AND 2019/12[PDAT]:2030[PDAT])) AND (venous thromboembolism OR thromboembolism OR venous embolism OR embolism OR pulmonary embolism OR thrombosis OR thrombo* OR venous thrombo*)

PRISMA flow diagram PICO question 11



PICO question 12

(12) Static versus dynamic D-dimer for diagnosis of VTE

P: Patients with COVID-19

I: Rapidly rising D-dimer

C: Elevated D-dimer (above some cutoff)

O: Sensitivity, specificity, false negative, false positive, failure rate (i.e., VTE confirmed during follow-up), efficiency (i.e., no. of patients with negative D-dimer per total patients)

Search strategies

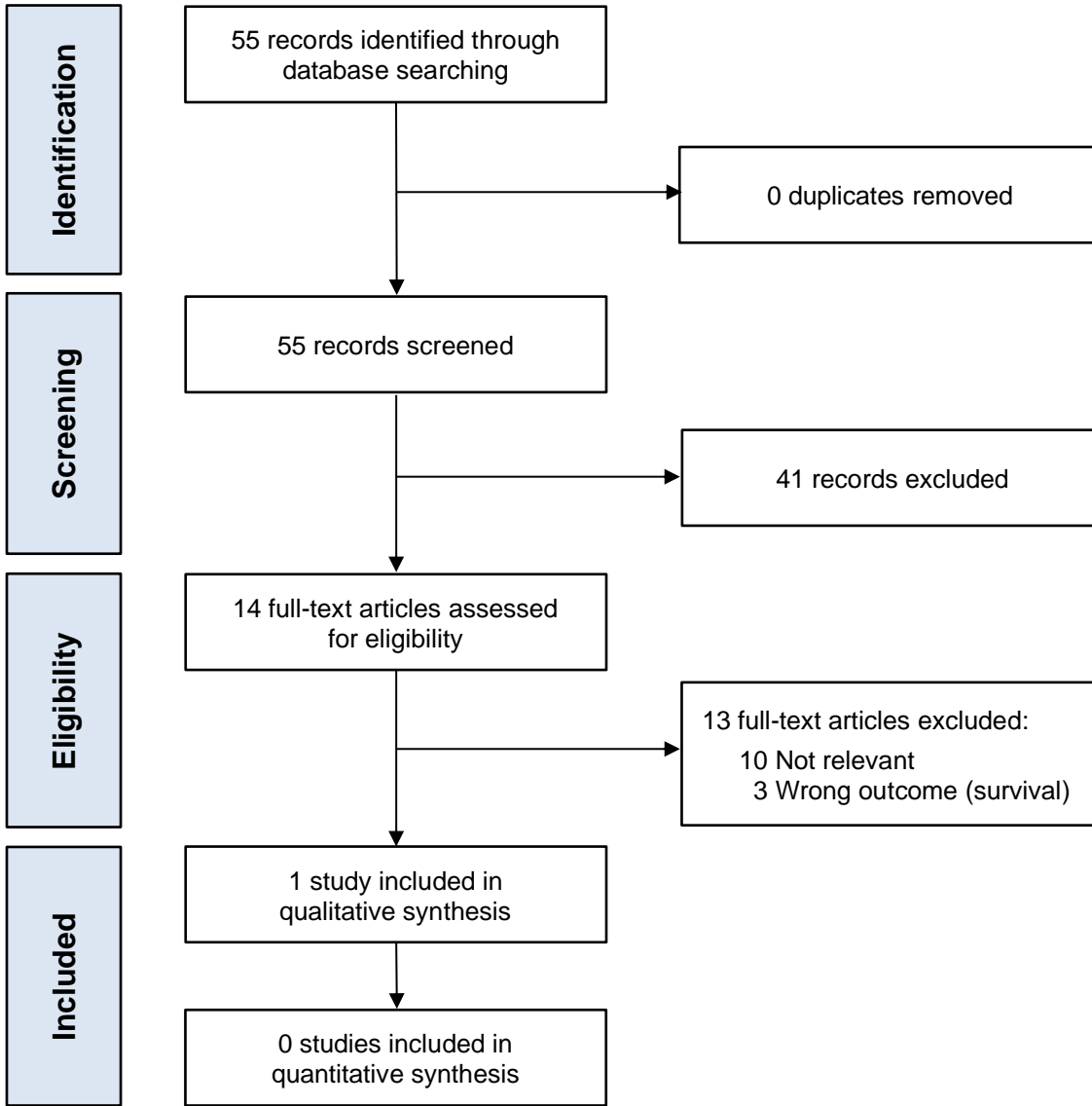
PubMed (Strategy #1)

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((((d dimer) OR (fibrin fragment D)) OR (fibrin fragment D [Supplementary Concept])) AND (((("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019 ncov"[All Fields]) OR 2019nCoV[All Fields] OR ("COVID"[All Fields] OR "Covid19" OR "COVID-2019"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields]) OR (((("Wuhan"[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND (2019/12[PDAT] OR 2020[PDAT]))))))))
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PubMed (Strategy #2)

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("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019 ncov"[All Fields]) OR 2019nCoV[All Fields] OR ("COVID-19"[All Fields] OR "COVID-2019"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields] OR ((("Wuhan"[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND (2019/12[PDAT] OR 2020[PDAT]))) OR ("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "sars cov 2"[All Fields]) OR (wuhan[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) OR (2019[All Fields] AND novel[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND ("fibrin fragment D"[Supplementary Concept] OR "fibrin fragment D"[All Fields] OR "d dimer"[All Fields])
```

PRISMA flow diagram PICO question 12



PICO question 13

(13) Biomarkers for Diagnosis of VTE (acutely ill hospitalized patient / critically ill patients)

P: Patients with COVID 19

I: Fibrinogen, PTT, INR, TT, AT, FVIII, TEG, DIC score

C: D-Dimer

O: Sensitivity, specificity, false negative, false positive, failure rate (i.e., VTE confirmed during follow-up), efficiency (i.e., no. of patients with negative D-dimer per total patients)

Search strategies

PubMed (Strategy #1)

("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019 ncov"[All Fields]) OR 2019nCoV[All Fields] OR ("COVID-19"[All Fields] OR "COVID-2019"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields] OR (("Wuhan"[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND (2019/12[PDAT] OR 2020[PDAT])) OR ("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "sars cov 2"[All Fields]) OR (wuhan[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) OR (2019[All Fields] AND novel[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND (("fibrin fragment D"[Supplementary Concept] OR "fibrin fragment D"[All Fields] OR "d dimer"[All Fields]) OR ("fibrinogen"[MeSH Terms] OR "fibrinogen"[All Fields]) OR PTT[All Fields] OR ("international normalized ratio"[MeSH Terms] OR ("international"[All Fields] AND "normalized"[All Fields] AND "ratio"[All Fields]) OR "international normalized ratio"[All Fields] OR "inr"[All Fields]) OR ("thrombin time"[MeSH Terms] OR ("thrombin"[All Fields] AND "time"[All Fields]) OR "thrombin time"[All Fields]) OR (("antithrombins"[Pharmacological Action] OR "antithrombins"[MeSH Terms] OR "antithrombins"[All Fields] OR "antithrombin"[All Fields] OR "antithrombin iii"[MeSH Terms] OR ("antithrombin"[All Fields] AND "iii"[All Fields]) OR "antithrombin iii"[All Fields]) AND ("time"[MeSH Terms] OR "time"[All Fields])) OR ("factor viii"[MeSH Terms] OR ("factor"[All Fields] AND "viii"[All Fields]) OR "factor viii"[All Fields] OR ("factor"[All Fields] AND "eight"[All Fields]) OR "factor eight"[All Fields]) OR TEG[All Fields] OR (DIC[All Fields] AND score[All Fields]))

PubMed (Strategy #2)

(thrombo* or embolism) AND (((("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019 ncov"[All Fields]) OR 2019nCoV[All Fields] OR ("COVID"[All Fields] OR "COVID-2019"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields]) OR (((("Wuhan"[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields])) AND (2019/12[PDAT] OR 2020[PDAT])))))

PubMed (Strategy #3)

((thrombo* or embolism) AND (((("severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "2019 ncov"[All Fields]) OR 2019nCoV[All Fields] OR ("COVID"[All Fields] OR "COVID-2019"[All Fields] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome

coronavirus 2"[All Fields] OR "2019-nCoV"[All Fields] OR "SARS-CoV-2"[All Fields] OR "2019nCoV"[All Fields]) OR (((("Wuhan"[All Fields] AND ("coronavirus"[MeSH Terms] OR "coronavirus"[All Fields]))) AND (2019/12[PDAT] OR 2020[PDAT]))) AND (((("Biomarkers"[Mesh]) OR (biomarker*[Title/Abstract])) OR (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR diagnos*[Title/Abstract] OR diagnosis[MeSH:noexp] OR diagnostic * [MeSH:noexp] OR diagnosis,differential[MeSH:noexp] OR diagnosis[Subheading:noexp]))))

PRISMA flow diagram PICO question 13

