Table of contents

1. Meta-analysis of Observational Studies in Epidemiology Checklist 2
2. Included and excluded studies 9
3. Incidence estimates for deep venous thrombosis 24
4. Incidence estimates for venous thromboembolism 27
Part 1: Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Checklist

Overall Goal
The specific aim of the project is to estimate the incidence of pulmonary embolism (PE) during hospitalization for COVID19 by performing a meta-analysis of the proportions of PE among published case series, cohort studies and controlled trials of hospitalized COVID19 patients. A secondary aim is to estimate the incidence of DVT and of VTE (the combined incidence of PE and DVT). The reason for doing the study is that the results might guide clinical decisions regarding the threshold for performing diagnostic studies and empiric treatment for acute PE. It may also inform decisions about the risk:benefit relationships regarding higher than standard doses of pharmacological prophylaxis.

Reporting of background
Problem definition
VTE has been reported in ranges from 0% to up to 53% of hospitalized or critically ill COVID19, which is higher than rates in non-COVID hospitalized patients, many hospitals use intensified thromboprophylaxis despite the absence of clear evidence regarding the risks and benefits of such measures.

Hypothesis statement
The rates of VTE among hospitalized COVID19 patients is comparable to the rate among similarly ill patients without COVID19. Among non-COVID hospitalized medical patients, the rate of PE is estimated at 3.9% and the rate of DVT is estimated at 6.7% (ACCP VTE prophylaxis guidelines 9th ed). Among patients in the ICU because of respiratory failure, the rate of PE is estimated at 18.7% and the rate of DVT is 19.9%. (Minet CCM 2012).

Description of study outcome(s)
Presentation with or development of objectively measured PE, with a secondary outcome of DVT and VTE.

Type of exposure or intervention used
Hospitalization for COVID-19, in ICU or in non-ICU wards

Type of study designs used
Case series, cohort studies, randomized control studies

Study population
Adults with COVID19 infection
Role of Project in the Overall Goal
A rigorous systematic review of published literature will provide the best available evidence regarding the actual incidences of PE, as well as DVT and VTE, during hospitalization for COVID19.

Methods

Reporting of search strategy
Qualifications of searchers
Licensed MDs with clinical training in pulmonary medicine, critical care medicine and hematology, as well as specialized training in literature review and data extraction.

Search strategy, including time period included in the synthesis and keywords
Search terms [(SARS-CoV2 OR COVID-19 OR Covid19) AND (trial OR series OR cohort OR incidence)] from December 1, 2019 to July 13, 2020.

Effort to include all available studies, including contact with authors
Peruse reference list of review manuscripts identified through the screening process (see below).

Databases and registries searched
U.S. National Library of Medicine MEDLINE database. The rationale for using MEDLINE as the sole database for the searches stems from its comprehensive nature (containing more than 30 million references) and the high-quality process by which the journal entries are selected, based on the recommendation of the Literature Selection Technical Review Committee (LSTRC) of the NIH and on separate NLM-initiated reviews, performed in consultation with an array of NIH and outside experts and external organizations with which NLM has or had special collaborative arrangements. (Source: https://www.nlm.nih.gov/pubs/factsheets/medline.html)

Search software used, name and version
PubMed search engine

Use of hand searching (eg, reference lists of obtained articles)
Peruse reference list of review manuscripts identified through the screening process

List of citations located and those excluded, including justification
Search strategy:
Search terms [(SARS-CoV2 OR COVID-19 OR Covid19) AND (trial OR series OR cohort OR incidence)] from December 1, 2019 to July 13, 2020.

Authors screen all study titles and abstracts and exclude those that do not include clinical data on adult patients with COVID-19.

Authors review the full text of the remaining articles and exclude those that met the following exclusion criteria.

Method of addressing articles published in languages other than English
None.

Method of handling abstracts and unpublished studies
None.

Description of any contact with authors
Email of authors with questions concerning study procedures

**Screening method**
Authors screen all study titles and abstracts and exclude those that do not include clinical data on adult patients with COVID19. The investigators record the number of the references from the total yield that were screened out for irrelevance on the basis of the title and abstract. The authors read the bibliography lists from review articles in the same fashion and included any additional references with clinical data from COVID19 patients.

The two authors review the full text of the remaining articles and exclude those that meet the exclusion criteria. The investigators record the number of references that are excluded.

The investigators apply predetermined criteria to exclude irrelevant manuscripts, relevant but poor-quality manuscripts and manuscripts that do not meet criteria for numerical inclusion in the results for other reasons. They record the number of manuscripts excluded by each criterion.

Inclusion Criteria: manuscripts with the following characteristics

1. The manuscript describes original primary clinical data from COVID-19 patients, rather than meta-analyses or literature reviews. (Literature reviews and meta-analyses will be saved so that their reference lists may be checked for additional studies.)
2. Population only includes patients >18 years of age
3. Articles must be written in English

Exclusion Criteria: Category of Quality

1. Not peer-reviewed
2. No defined study time interval
3. Did not describe and quantify hospitalized patients with confirmed diagnosis of COVID-19

Exclusion Criteria: Category of Imprecision

1. Did not describe a method whereby clinically detected VTE was tabulated
2. Did not report the VTE incidence (PE, DVT, or both) among the specified study population

Exclusion Criteria: Category of Enrichment of the Sample Population

1. Inclusion on the sample population was related to the clinical suspicion for VTE
2. Did not describe a consecutive case series or consecutive cohort studies or controlled trials with consecutive enrollment of subjects that met specific inclusion criteria

Studies excluded because of enrichment of the sample population are separately listed, along with a description of the method for enrichment.

The following characteristics do not result in exclusion of studies but are recorded and discussed as limitations

Limitation Characteristics

1. The study populations did not specify the proportions of non-ICU hospitalized patients and ICU patients (risk of imprecision)
2. Screening methods to initiate diagnostic work-up for VTE not specified (risk of bias)
3. Diagnostic methods for VTE not specified (risk of imprecision)
4. Thromboprophylaxis regimens not specified (risk of imprecision)
5. Thromboprophylaxis regimens were heterogenous within the study (risk of bias)
6. Thromboprophylaxis regimens were not standard for hospitalized or ICU patients (risk of bias)

**Extraction method**

Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested

Independent evaluation by two reviewers that the studies met no exclusion criteria and met quality criteria for inclusion. A third reviewer arbitrates differences.

Rationale for the selection and coding of data
Selection and coding of data regarding the diagnoses of PE, DVT and VTE follow sound clinical principles agreed upon by all clinical authors prior to data extraction. Controversies regarding data extraction for particular manuscripts are settled by consensus decision after group discussion.

Documentation of how data are classified and coded

Two raters for each article independently highlight and underline data within manuscript that will be extracted.

Independent extraction into Excel datasheets and comparison of extracted data between the two reviewers.

Confirmation of extracted data compared to manuscript text and adjudication of disagreements by a third investigator.

Presentation of source data and excel data extraction to entire group for confirmation.

Assessment of confounding

Group discussion of how comparable each included study and its corresponding data are to the experimental question.

Assessment of study quality

Credibility of VTE diagnosis is decided by group consensus.

Potential for missing clinically important VTE within the study population is decided by group consensus.

Assessment of heterogeneity

Three outcome measures of incidence are treated separately: PE, DVT and VTE. The incidence for each study is estimated as $\hat{p} = \frac{x}{N}$ where $x$ is the number of cases and $N$ is the number of patients at risk. The variance is $\hat{p}(1 - \hat{p})/N$, and 95% confidence intervals are estimated for display in forest plots. (2) In cases where a zero event is recorded, add 0.1 to both $x$ and $N$ to avoid division by zero. An arcsine transformation ($\arcsine[\sqrt{\hat{p}}]$) is applied in order to stabilize the variance if the values of $\hat{p}$ are strongly skewed. The variance of the transformed variable is $1/4N$ and the weight for each study is the inverse of the variance.

If ($\arcsine[\sqrt{\hat{p}}]$) is more than 3 standard deviations from the mean of the transformed distribution, then assumed that the study was drawn from a different population of studies, and exclude from subsequent analysis.

Combine estimates with random-effects method that accounts for heterogeneity between studies. (3) Summarize with the meta-analysis macro MA. (4) Back-transform the estimate, and its 95% confidence interval, to give the overall estimate of incidence and display in the forest plot. Assess heterogeneity by the I2 index. (5)
Analyze five relevant categorical variables: region (Europe, Asia, USA, Middle East, International), design (retrospective, prospective, mixed), observational (observational, interventional), site (single center, multicenter), ward/ICU (ward, ICU, both ward and ICU, other). Tabulate median and interquartile incidence for each category. Compare categories by the Wilcoxon or Kruskal-Wallis tests as appropriate. Fit meta-regression models to examine the effect of covariates on incidence. For each model the outcome is \( \text{arcsine}(\sqrt{\hat{p}}) \). The independent variables were a polynomial function of \( \log N \) and one categorical covariate. Display results as bubble plots where the size of the bubbles reflect the precision of each study.

**Results**

**Yield of screening and exclusion**

Summary of manuscript selection

Document the total number of manuscripts resulting from search of MEDLINE and the number of additional manuscripts identified through perusal of review manuscripts.

Document the number of manuscripts excluded for irrelevance.

Of the remaining manuscripts, document the number that met the inclusion and exclusion criteria listed above. Describe the studies excluded because of enrichment of the sample population.

Flow diagram of study selection.

**Study data**

Graphic summarizing individual study estimates and overall estimate

Bubble plots to illustrate the relationship between study precision and estimated incidence of PE and of DVT and VTE.

Separate bubble plots to illustrate the same relationship across categorical variables.

Forest plots to illustrate ranges and precision of reported incidence.

Table giving descriptive information for each study included

Summary table of study characteristics

Tables of subgroups for sensitivity testing

Statistical analysis of subgroups (described above)

Indication of statistical uncertainty of findings

Total incidence numbers and 95% CIs.

Incidence numbers and 95% CIs from the subgroups
Discussion
Quantitative assessment of bias and interpretation of the results regarding various forms of bias

Publication bias
Imprecision (not finding VTE if it was present)
Imprecision (study population not representative of hospitalized COVID19 population).

Justification for exclusion
Brief explanation of why some categories of study were excluded.

Assessment of quality of included studies
The overall impression of the study data.

Conclusions
Consideration of alternative explanations for observed results
Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)

Potential for change in clinical practice

Guidelines for future research

Speculation

Disclosure of funding source

Methodological References
1. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA: the journal of the American Medical Association*. 2000;283(15):2008-2012.
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4. Der G, Everitt B. *Applied medical statistics using SAS*. Boca Raton, FL: CRC Press; 2013.
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### Part 2: Included and excluded studies

| Author                  | Study               | Design          | Size       | Location | Population | Anticoagulation                                                                 |
|-------------------------|---------------------|-----------------|------------|----------|------------|--------------------------------------------------------------------------------|
| Al-Samkari(6)           | Retrospective       | Observational   | Multi center | USA      | Wards and ICU | Standard prophylaxis with LMWH or UFH (88.5%), intermediate or therapeutic dose (8.8%), mechanical prophylaxis (2.7%). |
| Artifoni(7)             | Retrospective       | Observational   | Multi center | Europe   | Wards      | Study inclusion criterion was weight adjusted enoxaparin (40 mg/day for BMI < 30 kg/m², 60 mg/day for BMI 30 to 40 kg/m² and 40 mg twice daily for BMI > 40 kg/m²). |
| Beigel(8)               | Prospective         | Interventional  | Multi center | International | Wards and ICU | No mention of anticoagulation. |
| Beun(9)                 | Retrospective       | Observational   | Single center | Europe   | ICU        | No mention of anticoagulation, only in group that had therapeutic dose for treatment of VTE. |
| Campochiaro(10)         | Retrospective       | Observational   | Single center | Europe   | Wards      | All received thromboprophylaxis (enoxaparin 4000 UI daily). |
| Cattaneo(11)            | Retrospective       | Observational   | Single center | Europe   | Wards      | All received 40 mg enoxaparin daily. |
| Criel(12)               | Retrospective       | Observational   | Single center | Europe   | Wards and ICU | All ICU patients received anticoagulation (Enoxaparin 2x40mg daily and if > 100 kg Enoxaparin 2x60mg daily). Non-ICU patients 94% received anticoagulation (Enoxaparin 1x40mg daily and if > 100 kg Enoxaparin 1x60mg daily). |
| Cui(13)                 | Retrospective       | Observational   | Single center | Asia     | ICU        | No anticoagulation was administered. |
| Davoudi-Monfared(14)    | Prospective         | Interventional  | Single center | Middle East | Wards and ICU | Prophylaxis in 95.3% of patients, no regimen or dose specified. |
| Demelo-Rodriguez (15) | Prospective | Observational | Single center | Europe | Wards | Standard prophylactic dose of enoxaparin 40mg daily or bemiparin 3500 UI (98.1%), no anticoagulant (SCDs) because of high bleeding risk (1.9%). |
|----------------------|-------------|---------------|---------------|--------|-------|-------------------------------------------------|
| Desborough (16)      | Retrospective | Observational | Single center | Europe | ICU   | All on thromboprophylaxis (dalteparin daily) adjusted for renal failure or weight (less than 50 kg or more than 100 kg), 17% upgraded to treatment dose due to atrial fibrillation or ECMO. |
| Devreese (17)        | Prospective | Observational | Single center | Europe | ICU   | Thromboprophylaxis doses of LMWH or UFH (61.5%), therapeutic doses (32%) or none (6.5%). |
| Faggiano (18)        | Retrospective | Observational | Single center | Europe | Wards | Mixture of thromboprophylaxis regimens: no prophylaxis (64%), enoxaparin 40mg once daily (20%), therapeutic doses (16%). |
| Fauvel (19)          | Retrospective | Observational | Multi center | Europe | Wards and ICU | Mixture of no anticoagulation (21.5%), prophylactic dose of daily low molecular weight heparin or twice daily subcutaneous unfractionated heparin (59.5%), intermediate doses of double the preventive dose (8.0%), and therapeutic doses (10.9%). |
| Fraisse (20)         | Retrospective | Observational | Single center | Europe | ICU   | Usual/prophylactic dose of anticoagulant (46.7%) or full/therapeutic dose (53.2%) according to |
| Name                          | Study Type   | Design   | Location      | Setting | Anticoagulation |
|-------------------------------|--------------|----------|---------------|---------|-----------------|
| Galeano-Valle (21)            | Prospective  | Observational | Single center | Europe  | Wards           |
|                               |              |          |               |         | Thromboprophylaxis with enoxaparin 40 mg per day or bemiparin 3500 UI per day (99.3%). |
| Goyal P (22)                  | Retrospective| Observational | Multi center | USA     | Wards and ICU   |
|                               |              |          |               |         | No mention of anticoagulation. |
| Grein (23)                    | Prospective  | Interventional trial | Multi center | International | Wards and ICU |
|                               |              |          |               |         | No mention of anticoagulation but suspect widely variable. |
| Guo (24)                      | Retrospective| Observational | Multi center | Asia    | Wards and ICU   |
|                               |              |          |               |         | No mention of anticoagulation |
| Gupta (25)                    | Retrospective| Observational | Multi center | USA     | ICU             |
|                               |              |          |               |         | Therapeutic anticoagulation (41.5%), the remainder are unspecified. |
| Hegerova (26)                 | Prospective  | Interventional trial | Multi center | USA     | ICU             |
|                               |              |          |               |         | No mention of anticoagulation. |
| Hekimian (27)                 | Retrospective| Observational | Single center | Europe  | ICU             |
|                               |              |          |               |         | All except one had received anticoagulation before PE diagnosis of varying doses and medications. |
| Helms (28)                    | Prospective  | Observational | Multi center | Europe  | ICU             |
|                               |              |          |               |         | Prophylactic dosed LMHW 4000 UI/day for LMWH or if contraindicated UFH at 5-8U/kg/h (70%), therapeutic heparin (30%). |
| Hippensteel (29)              | Retrospective| Observational | Single center | USA     | ICU             |
|                               |              |          |               |         | Therapeutic anticoagulation during hospitalization (54.3%) for various reasons, including unconfirmed suspicion of VTE or clinician concern for hypercoagulability (21.7%), acute onset atrial fibrillation (4.3%), elevated troponin (2.2%). |
| Huet (30)                     | Retrospective| Interventional trial | Single center | Europe  | Wards and ICU   |
|                               |              |          |               |         | No mention of anticoagulation. |
| Ibañez (31)                   | Prospective  | Observational | Single center | Europe  | ICU             |
|                               |              |          |               |         | All on thromboprophylaxis |
According to the local protocol (enoxaparin 40-60mg daily).

| Study | Study Type | Study Design | Location | Setting | Anticoagulation |
|-------|------------|--------------|----------|---------|-----------------|
| Inciardi(32) | Retrospective | Observational | Single center | Europe | Wards and ICU | Anticoagulation not routinely performed in patients in sinus rhythm. |
| Khamis(33) | Retrospective | Observational | Multi center | Middle East | ICU | No mention of anticoagulation. |
| Klok(34) | Retrospective | Observational | Multi center | Europe | ICU | All patients received at least standard doses thromboprophylaxis, although regimens differed between hospitals and doses increased over time. |
| Koleilat(35) | Retrospective | Observational | Single center | USA | Wards and ICU | Mixture of thromboprophylaxis anticoagulation regimens, therapeutic anticoagulation and no anticoagulation. |
| Larsen(36) | Prospective | Observational | Single center | Europe | Wards and ICU | Thromboprophylaxis on unspecified dose of LMWH (80%). |
| Li(37) | Retrospective | Observational | Single center | Asia | Wards and ICU | No mention of anticoagulation. |
| Llitjos(38) | Retrospective | Observational | Multi center | Europe | ICU | Anticoagulant dose, left to the discretion of the treating physician, was either prophylactic anticoagulation (31%) or therapeutic anticoagulation with LMWH or UFH (69%). |
| Lodigiani(39) | Retrospective | Observational | Single center | Europe | Wards and ICU | All ICU patients received thromboprophylaxis with LMWH: the dosage was weight-adjusted in 17 patients and therapeutic in two patients on ambulatory treatment with direct oral anticoagulants. A total of 246 (75%) patients admitted to general wards. |
received initial in-hospital thromboprophylaxis: a prophylactic dosage was used in 133 (41%) patients, 67 (21%) were treated with intermediate dosage thromboprophylaxis, and 74 (23%) received therapeutic dose anticoagulation, including 22 who continued ambulatory treatment for atrial fibrillation or prior VTE.

| Longchamp (40) | Prospective | Observational | Single center | Europe | ICU | Thromboprophylaxis at higher than standard doses (92%): either continuous intravenous heparin infusion (15 000 IU/24 h, or 20 000 IU/24 h for patients >100 kg), or once-daily subcutaneous enoxaparin injections (40 mg, or 60 mg for patients >100 kg). Two patients (8%) were on chronic therapeutic anticoagulation for atrial fibrillation. |
| Maatman (41) | Retrospective | Observational | Multi center | USA | ICU | Thromboprophylaxis with either 5000U subcutaneous UFH every 8 hours, 40mg Enoxaparin daily or 30mg Enoxaparin twice per day (94%). Full dose anticoagulation for other comorbidities of VTE diagnosed at presentation (6%). |
| Mei (42) | Retrospective | Observational | Single center | Asia | Wards and ICU | All patients received VTE prophylaxis following standard protocols with LMWH or UFH or |
| Study | Design | Setting | Region | Location | Details |
|-------|--------|---------|--------|----------|---------|
| Mestre-Gomez(43) | Retrospective | Observational | Single center | Europe | Wards | Thromboprophylaxis in patients admitted to general ward with COVID19, but doses and patient percentages not specified. |
| Middeldorp(44) | Retrospective | Observational | Single center | Europe | Wards and ICU | Ward patients received thromboprophylaxis with nadroparin 2850 IU once daily or 5700 IU for patients with a body weight of ≥100 kg. From April 3 onwards, patients in ICU received nadroparin 2850 IU twice daily for patients with a body weight <100 kg and 5700 IU twice daily for those ≥100 kg. |
| Nahum(45) | Prospective | Observational | Single center | Europe | ICU | All received anticoagulant prophylaxis at hospital admission however regimens and doses not specified. |
| Pagnesi(46) | Retrospective | Observational | Single center | Europe | Wards | No mention of anticoagulation |
| Poissy(47) | Retrospective | Observational | Single center | Europe | ICU | All patients received thromboprophylaxis according to current recommendations for critically ill patients. |
| Rieder(48) | Prospective | Observational | Single center | Europe | Wards and ICU | Not specified aside from 12 patients who were on therapeutic anticoagulation. |
| Santoliquido(49) | Prospective | Observational | Single center | Europe | Wards | All received prophylactic anticoagulation as per institution’s guidelines since first day of hospitalization (enoxaparin 40mg |
| Study | Design | Type | Setting | Region | Location | Anticoagulation | Findings |
|-------|--------|------|---------|--------|----------|----------------|----------|
| Shah (50) | Retrospective | Observational | Single | Europe | ICU | No mention of anticoagulation. | |
| Shekhar (51) | Retrospective and prospective | Observational | Single | USA | Wards and ICU | Mention of thromboprophylaxis in those with bleeding events only. | |
| Soumagne (52) | Retrospective | Observational | Multi | Europe | ICU | Details of anticoagulant doses were not reported but all patients received at least preventative doses. | |
| Spiezia (53) | Retrospective | Observational | Single | Europe | ICU | All on anticoagulant prophylaxis, but heparin doses not specified. Excluded patients already on therapeutic anticoagulation. | |
| Stoneham (54) | Retrospective | Observational | Single | Europe | Wards | No mention of anticoagulation except for 3 patients who received therapeutic dose after diagnosis of VTE as an example of "heparin resistance." | |
| Tavazzi (55) | Retrospective | Observational | Single | Europe | ICU | All on thromboprophylaxis weight based. | |
| Thomas (56) | Retrospective | Observational | Single | Europe | ICU | All on thromboprophylaxis (dalteparin) adjusted for weight and renal function. | |
| Voicu (57) | Prospective | Observational | Single | Europe | ICU | All on anticoagulation: prophylactic enoxaparin (73%), prophylactic unfractionated heparin (14%), therapeutic anticoagulation (13%) for atrial fibrillation and ECMO (13%). | |

Daily or fondaparinux 2.5mg daily. Excluded from study patients with indications for full anticoagulation.
| Study | Design | Type | Setting | Region | Outcome | Notes |
|-------|--------|------|---------|--------|---------|-------|
| Wang (58) | Prospective | Interventional trial | Multi center | Asia | Wards and ICU | No mention of anticoagulation. |
| Whyte (59) | Retrospective | Observational | Single center | Europe | Wards and ICU | Standard anticoagulation in wards, intermediate dose in ICU. |
| Wright (60) | Retrospective | Observational | Single center | USA | ICU | All patients received thromboprophylaxis with at least enoxaparin between 40 and 60 mg/d or UFH between 10,000 and 15,000 units/d. |
| Zhang (61) | Retrospective | Observational | Single center | Asia | Wards | Prophylactic anticoagulant of unspecified dose (37.1%), therapeutic LMWH after positive ultrasound studies for DVT (41.3%). |
| Ziehr (62) | Retrospective | Observational | Multi center | USA | ICU | No mention of anticoagulation. |

Table S1: Characteristics of included studies.
Herein, we present a series of eight confirmed cases of peripheral multifocal APE in a cohort of 20 hospitalized patients, who consecutively underwent CTPA between March 25 and April 21, 2020 because of abnormal D-Dimer levels (>1000 mg/L) and at least one among the following inclusion criteria: risk factors for APE, clinical signs of APE, severe pneumonia (requiring minimum oxygen support of 10 L/min and/or need for Non-Invasive Ventilatory Support, NIV)).

They were referred for CTPA at initial presentation because of hesitation between COVID-19 pneumonia and PE, after clinical probability assessment and D-dimer dosage, applying the same cut-off as for non-COVID patients.

A total of 172 patients were excluded due to no surveillance results on DVT or pharmacologic thromboprophylaxis before ICU admission.

"In patients with suspected or confirmed SARS-CoV-2 infection, chest CT scan was performed when clinical features of severe disease were present (e.g., requirement for mechanical ventilation [IMV]) or underlying comorbidities. Patients with non-contrast chest CT scans were excluded. “The main objective of our study was to evaluate pulmonary embolus in association with COVID-19 infection using pulmonary CT angiography."

"Of these 160 patients, 106 patients were classified as COVID-19 infection (97 patients by RT-PCR and 9 patients with positive CT and negative RT-PCR test). The reason for CT angiography in these patients was suspicion of pulmonary embolus in 67/106 (63%) patients and other CT indication in 39/106 (37%) patients."

"All patients according to internal protocol underwent a computed tomography pulmonary angiography (CTPA) to assess the pulmonary parenchyma and the possible occurrence of pulmonary vessels thrombosis (PVT). Furthermore, all patients underwent a Duplex scan of the veins and arteries of the upper and lower limbs to investigate the presence of peripheral thrombosis."

"During a one-month period, 328 patients positive on COVID-19 RT-PCR testing underwent pulmonary CT angiography."

"A manual chart review was conducted by the primary author (R.T.) on identified COVID-19 patients and who all underwent ultrasound evaluation for DVT were included...45 intubated patients with COVID-19 underwent ultrasound evaluation to identify DVT and were subsequently included in our study. “

Table S2. Studies excluded because the inclusion criteria were related to the clinical suspicion for PE, DVT or both.
| Author          | Incidence                                                                 | Patient inclusion criteria from study                                                                 |
|-----------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| Grandmaison(71) | VTE 23/58 (39.6%), Distal DVT 21/58 (36.2%), Proximal DVT 7/59 (11.8%), PE 4/58 (6.9%) | Cross-sectional study of compression ultrasound screening and CTPA for suspected PE in all COVID19 patients present in a university hospital with ARDS or pneumonia on April 7, 2020. |
| Ren(72)         | Distal DVT 36/48 (75%), Proximal DVT 5/48 (10.4%)                         | Cross-sectional study of compression ultrasound screening of all COVID19 patients present in two hospitals in Wuhan, China, from February 29, 2020 to March 2, 2020, |

**Table S3:** Studies excluded because they did not include consecutive patients admitted to ICUs or non-ICU wards.
Included and excluded study references

1. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA : the journal of the American Medical Association. 2000;283(15):2008-12.
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Part 3: Incidence estimates for deep venous thrombosis

There were 38 incidence estimates of deep venous thrombosis (DVT). They ranged from 0.000 to 0.794, with a median of 0.082. After excluding the highest (outlier) value, the combined estimate was 0.062 (95%CI: 0.050, 0.075).

Figure S1. The incidence of DVT against the number of hospitalized COVID19 patients at risk. The size of each bubble is proportional to the study weight (1/variance), which reflects the precision of the study. Panel A. Estimated incidence of DVT incidence decreases with study sample size. Panel B. DVT incidence decreases with study sample size and varies with clinical location (white circles - non-ICU wards, black circles - ICU, grey circles - combination of ICU and non-ICU wards). Panel C. DVT incidence decreases with study sample size and varies with geographic location (white circles - Asia, black circles - Europe, grey circles - USA). Middle East and International were too few to be included in the regression model. Panel D. DVT incidence plotted against study size but does not vary with anticoagulation regimen (white circles – at least 95% of patients were on standard prophylaxis regimens, black circles – mixed prophylaxis regimens, grey circles – not specified).
|                      |   |          |       |                      |
|----------------------|---|----------|-------|----------------------|
|                      |  $\hat{p}$ | Median   | IQR   | n       | P-value for Wilcoxon or Kruskal-Wallis |
| **Design:**          |   |          |       |                      |
| Retrospective        | 0.08 | 0.02, 0.17 | 12    | 0.808   |
| Prospective          | 0.07 | 0.02, 0.23 | 25    |          |
| **Observational:**   |   |          |       |                      |
| Interventional       | 0.01 | 0.02, 0.23 | 3     | 0.071   |
| Observational        | 0.10 | 0.02, 0.23 | 34    |          |
| **Site:**            |   |          |       |                      |
| Multi-site           | 0.02 | 0.01, 0.09 | 12    | 0.098   |
| Single-site          | 0.12 | 0.02, 0.23 | 25    |          |
| **Geography:**       |   |          |       |                      |
| Asia                 | 0.13 | 0.01, 0.41 | 6     | 0.472   |
| Europe               | 0.08 | 0.02, 0.14 | 24    |          |
| USA                  | 0.21 | 0.07, 0.25 | 5     |          |
| **Location:**        |   |          |       |                      |
| ICU                  | 0.16 | 0.05, 0.25 | 18    | 0.047   |
| Wards                | 0.12 | 0.02, 0.15 | 6     |          |
| Wards and ICU        | 0.02 | 0.01, 0.07 | 10    |          |

**Table S3. Comparison of DVT incidence by potential categorical predictors.**

Categories with two or fewer studies (e.g. ‘Middle East’ or ‘International’) were excluded.
Figure S2. Incidence of DVT among patients hospitalized for COVID19. The reported incidences of DVT among the included studies are represented by Forest plots.
Part 4: Incidence estimates for venous thromboembolism

There were 27 incidence estimates of VTE. They ranged from 0.0 to 0.415, with a median of 0.180. The combined estimate was 0.146 (95%CI: 0.117, 0.176).

**Figure S3. The incidence of VTE against the number of hospitalized COVID19 patients at risk.** The size of each bubble is proportional to the study weight (1/variance), which reflects the precision of the study. **Panel A.** Estimated incidence of VTE incidence decreases with study sample size. **Panel B.** VTE incidence decreases with study sample size and varies with clinical location (white circles - non-ICU wards, black circles - ICU, grey circles - combination of ICU and non-ICU wards). **Panel C.** VTE incidence decreases with study sample size and varies with geographic location (white circles - Asia, black circles - Europe, grey circles - USA). Middle East and International were too few to be included in the regression model. **Panel D.** VTE incidence plotted against study size but does not vary with anticoagulation regimen (white circles – at least 95% of patients were on standard prophylaxis regimens, black circles – mixed prophylaxis regimens, grey circles – not specified).
|                  | ˆp Median | IQR       | n   | P-value for Wilcoxon or Kruskal-Wallis |
|------------------|-----------|-----------|-----|--------------------------------------|
| **Design:**      |           |           |     |                                      |
| Retrospective    | 0.18      | 0.03, 0.21| 7   | 0.422                                |
| Prospective      | 0.17      | 0.08, 0.27| 20  |                                      |
| **Observational:**|           |           |     |                                      |
| Interventional   | 0.11      | 0.01, 0.20| 2   |                                      |
| Observational    | 0.18      | 0.08, 0.26| 25  |                                      |
| **Site:**        |           |           |     |                                      |
| Multi-site       | 0.18      | 0.09, 0.23| 9   | 0.939                                |
| Single-site      | 0.17      | 0.05, 0.26| 18  |                                      |
| **Geography:**   |           |           |     |                                      |
| Asia             | 0.21      | 0.01, 0.41| 4   | 0.789                                |
| Europe           | 0.15      | 0.08, 0.22| 15  |                                      |
| USA              | 0.23      | 0.09, 0.26| 7   |                                      |
| **Location:**    |           |           |     |                                      |
| ICU              | 0.23      | 0.18, 0.28| 14  | 0.026                                |
| Wards            | 0.13      | 0.03, 0.42| 3   |                                      |
| Wards and ICU    | 0.05      | 0.02, 0.12| 9   |                                      |

**Table S3. Comparison of VTE incidence by potential categorical predictors.**

Categories with two or fewer studies (e.g. ‘Middle East’ or ‘International’) were excluded.
Figure S4. Incidence of VTE among patients hospitalized for COVID19. The reported incidences of VTE among the included studies are represented by Forest plots.