Supplement – Baseline Risk Study Characteristics

Study ID	Study Design	Location Study Period	Population	COVID-19 diagnosis	Age	Male (%)	Prior VTE (%)	Anticoagulation prior to hospitalization (%)	D-dimer	Still in ICU at end of study (%)	Still in hospital at end of study (%) (May include ICU, if not specified.)	Number of patients on prophylactic intensity (N)	Prophylactic intensity description (drug, dose, duration)	RoB
Paolisso 2020	Retrospective chart review	Italy; 1 Mar 2020 – 10 Apr 2020	Consecutive patients admitted to Sant'Orsola Bologna University Hospital with laboratory-confirmed COVID-19	Positive SARS-CoV-2 test only	Median (IQR): 67 (55,79)	63	0.00	0.00	Median (IQR): 800 (500, 1500)	NR	NR	361	Standard deep vein thrombosis (DVT) prophylaxis enoxaparin treatment (40-60mg daily)	Low risk of bias for all relevant outcome(s), except for stroke, acute myocardial infarction, acute kidney injury
Al-Samkari 2020	Retrospective cohort study	USA; 1 Mar 2020 – 5 Apr 2020	All patients aged 18 years or more with confirmed COVID-19 who had a D-dimer test performed on initial presentation (non-critically ill patients)	Confirmed diagnosis	Median (IQR): 60 (23,99)	52.7	NR	NR	NR	NR	19.10	256	Enoxaparin, 40mg SC daily (or every 12 hours for BMI ≥41 or weight >120 kg) OR Unfractionated heparin 5000U SC every 8-12 hours (or 5000-7500 U SC every 8 hours for BMI ≥41 or weight >120 kg)	Low risk of bias for all relevant outcome(s)
Artifoni 2020	Retrospective study	France; 25 Mar 2020 – 10 Apr 2020	Acutely ill inpatients with COVID-19	Combination (ie confirmed and suspected)	Median (IQR): 64 (46,75)	60.6	7.04	0.00	Median (IQR): 790 (480,1610)	NR	NR	71	Enoxaparin 40 mg/day for BMI <30 kg/m^2, 60 mg/day for BMI 30-40 kg/m^2 and 40 mg BID for BMI >40 kg/m^2)	Low risk of bias for all relevant outcome(s)
Boari 2020	Retrospective cohort	Italy; 28 Feb 2020 - 31 Aug 2020	Consecutive patients with confirmed COVID-19 admitted to a medical ward	Confirmed diagnosis	Mean (SD): 71 (13.80)	67.1	NR	11.24	Mean (SD): 482.6 (910.41)	NA	0.00	258	Prophylactic dose of 4000 Units SC. once daily	Low risk of bias for all relevant outcome(s)
Campochiaro 2020	Retrospective study	Italy; NR	Patients hospitalized for confirmed COVID-19 with hyper-inflammation and severe respiratory involvement	Positive SARS-CoV-2 test only	Mean (SD): 63.75 (16.35)	86.2	NR	NR	NR	1.54	18.46	65	Enoxaparin 4000 UI subcutaneously once a day	Low risk of bias for all relevant outcome(s)

Mei 2020*	Retrospective study	China; 1 Jan 2020 – 23 Mar 2020	Non-critically ill patients not requiring ventilator support	Confirmed diagnosis	Median (IQR): 55.5 (0.5,87)	51.2	0.00	NR	Median (IQR): 510 (310,830)	NR	NR	211	All patients received VTE prophylaxis following standard protocols with LMWH or UFH or mechanical intermittent pneumatic compression device if contraindicated to anticoagulant	Low risk of bias for all relevant outcome(s)
Middeldorp 2020	Retrospective cohort study	Netherlands; 2 Mar 2020 – 12 Apr 2020	Acutely ill inpatients	Combination (ie confirmed and suspected)	Mean (SD): 60 (16.00)	58.5	7.32	9.76	Median (IQR): 1100 (700,1600)	NR	NR	123	Prophylactic intensity - (Nadroparin, 2850 IU OD) or (Nadroparin, 5700 IU for patients with a body weight of ≥100 kg)	Low risk of bias for all relevant outcome(s)
Pesavento 2020	Retrospective	Italy; 26 Feb 2020 – 6 Apr 2020	Acutely ill inpatients not requiring intubation, and could receive antithrombotic medication	Positive SARS-CoV-2 test only	Median (IQR): 71 (59,82)	55.9	5.24	0.00	NR	NR	NR	240	LMWH 40 mg OD or Fondaparinux 2.5 mg or UFH 5000 U TID	Low risk of bias for all relevant outcome(s)
Santoliquido 2020	Prospective cohort	Italy; 3 Apr 2020 – 10 Apr 2020	Acutely ill inpatients	Confirmed diagnosis	Mean (SD): 67.6 (13.50)	72.6	3.57	NR	Mean (SD): 4108 (7098.00)	NR	NR	84	Enoxaparin, 40 mg (4000 units), SC OD; Fondaparinux, 2.5 mg, SC OD	Low risk of bias for all relevant outcome(s)
Arachchillage 2021	retrospective	UK; 10 Apr 2020 – 23 Apr 2020	Patients admitted to a major tertiary NHS Trust in London	Confirmed diagnosis	Mean (SD): 65 (12.60)	59.6	NR	NR	NR	16.90	NR	171	Standard thromboprophylaxis: 40 mg of enoxaparin (20 mg of enoxaparin for patients with creatinine clearance < 30 mL/min)	Low risk of bias for all relevant outcome(s)
Dutch COVID & Thrombosis Coalition 2021	Cohort study	Netherlands; First wave: 24 Feb 2020 – 26 Apr 2020 Second wave: 1 Sep 2020 – 30 Nov 2020	All adults COVID-19 patients	Combination (ie confirmed and suspected)	First wave: Mean (SD): 67 (14.00) Second wave: Mean (SD): 66 (14.00)	First wave: 63 Second wave: 62	First wave: 4.50 Second wave: 5.50	First wave: 14 Second wave: 14	NR	NR	NR	First wave: 83 Second wave: 594	First wave: Nadroparin 2850 IU/d or 5700 IU/d if body weight >100 kg Second wave (varies by institution): Nadroparin 2850 IU/d or 5700 IU/d if body weight >100 kg; Nadroparin 5700 IU/d;: Dalteparin 5000 IU/d; Dalteparin 5000 IU/d or 5000 IU BID if body weight >100 kg; nadroparin 2850 IU/d for <70 kg, nadroparin 3800 IU/d	Low risk of bias for all relevant outcome(s)

													for 70-90 kg, nadroparin 5700 IU for >90 kg; nadroparin 2850 IU for BMI <30, nadroparin 5700 IU/d fir BMI >30; nadroparin 5700 IU for <100 kg, nadroparin 7600 IU/d for 100 kg	
Fortini 2020	Prospective, observational	Italy; 1 Apr 2020 – 30 Apr 2020	Patients with a laboratory-confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection	Confirmed diagnosis	Mean (SD): 75.9 (12.70)	49	NR	NR	Median (IQR): 1443 (576,5716)	NR	NR	85	95.3% were on low molecular weight heparin prophylaxis, mostly with 4000 or 6000 IU per day.	Low risk of bias for all relevant outcome(s), except for PE
Fujiwara 2021	retrospective cohort study	Japan; 1 Feb 2020 – 31 Aug 2020	We included all patients with COVID-19 admitted to our hospitals during the defined timeframe.	Confirmed diagnosis	Median (IQR): 41 (28,58)	62.1	NR	NR	NR	NR	NR	43	prophylactic anticoagulants (unfractionated intravenous heparin, subcutaneous heparin calcium, direct oral anticoagulants, and warfarin)	Low risk of bias for all relevant outcome(s)
Ierardi 2021	Cross-sectional screening study	Italy; 1 Mar 2020 – 5 Apr 2020	Random sample of patients with laboratory-confirmed COVID-19. We did not include patients who were diagnosed with COVID-19 during hospital stay, but were admitted for other medical conditions	Positive SARS-CoV-2 test only	Mean (SD): 63 (15.00)	66.5	3.00	NR	Median (IQR): 1332 (809,3779)	0.00	0.00	263	Prophylactic doses of weight-adjusted enoxaparin (100 international units per kilogram, once per day, the dose being halved in severe chronic kidney disease)	Low risk of bias for all relevant outcome(s)
Jimenez-Guiu 2020	Prospective non-randomized cohort	Spain; 1 Apr 2020 – 30 Apr 2020	Patients with COVID-19 pneumonia who were admitted to the emergency department and required hospitalization.	Confirmed diagnosis	Mean (SD): 71.3 (12.70)	50.9	0.00	NR	Mean (SD): 478.48 (249.08)	NR	NR	37	Prophylactic dosage (40mg of enoxaparin every 24 hours).	Low risk of bias for all relevant outcome(s)
Kevorkian 2021	Observational cohort study	France; 9 Jan 2020 – 30 Nov 2020	All successive non-critically ill COVID-19 patients requiring >1L/min-oxygen and admitted to our ward	Not reported	Median (IQR): 66 (54,75)	77.9	NR	NR	Mean (SD): 979.63 (709.46)	NA	NA	68	Prophylactic AC: anti-Xa inhibitor such as rivaroxaban or apixaban (58.82%), LMWH (41.17%).	Low risk of bias for all relevant outcome(s)

Martinelli 2021	Observational cohort	Italy; 9 Mar 2020 – 7 Apr 2020	Hospitalized in non-ICU settings (high intensity care and low intensity care wards)	Positive SARS-CoV-2 test only	Median (IQR): 59 (50,68)	63.4	NR	NR	Mean (SD): 1032.73 (210.86	NR	NR	93	Standard dose: enoxaparin 40 mg daily increased to 60 mg daily in obese.	Low risk of bias for all relevant outcome(s), except for VTE and bleeding
Moll 2020	Retrospective cohort study	USA; 7 Mar 2020 – 13 Apr 2020	COVID positive patients not spending time in the ICU during admission	Positive SARS-CoV-2 test only	Mean (SD): 59.94 (17.19)	38.9	4.60	NR	Median (IQR): 798.00 (408,1446)	NR	0.90	80	Enoxaparin 40mg sc daily, or UFH 5000 IU sc BID or TID	Low risk of bias for all relevant outcome(s)
Pancani 2020	Prospective observational cohort study	Italy; 27 Mar 2020 – 6 May 2020	Patients with COVID-19 related pneumonia not requiring endotracheal intubation	Confirmed diagnosis	Mean (SD): 74 (14.00)	57.6	4.40	NR	Mean (SD): 372 (512)	NR	24.20	68	LMWH: Enoxaparin 4000IU/day, Fondaparinux 2.5mg	Low risk of bias for all relevant outcome(s)
Piazza 2020	Retrospective observational cohort analysis	USA; 13 Mar 2020 – 3 Apr 2020	Consecutive patients 18 years or older who were tested positive for SARS-CoV-2 infection based on SARS and admitted to non-intensive care	Confirmed diagnosis	Mean (SD): 60.60 (18.00)	53.7	4.40	84.70	Mean (SD): 1156.50 (1410.20)	NR	1.80	229	Prophylactic dosages not specified (LMWH or UFH)	Low risk of bias for all relevant outcome(s)
Russo 2020	Retrospective cohort study	Italy; 15 Feb 2020 – 15 Mar 2020	COVID patients who were admitted to internal medicine units	Confirmed diagnosis	Mean (SD): 63.77 (4.53)	53.3	NR	NR	NR	NR	NR	46	Fondaparinux 2.5 units/day	Low risk of bias for all relevant outcome(s)
Soni 2020	Retrospective cohort study	India; 2 Apr 2020 – 24 Ju l2020	COVID-19 confirmed adult patients (18 years or older) who had a definite outcome (discharge or death) and moderate to severe disease where the respiratory rate was more than 24/min or SpO2 was less than 93%	Confirmed diagnosis	Median (IQR): 61 (51,71)	69.9	NR	NR	Median (IQR): 1120 (560,3280)	NR	0.00	483	All the COVID-19 patients requiring admission were given prophylactic low molecular weight heparin (LMWH)	Low risk of bias for all relevant outcome(s)

Sholzberg 2021 (RAPID)	The RAPID trial was an investigator-initiated, parallel, pragmatic, adaptive multi-center, open-label randomized controlled trial	Brazil, Canada, Ireland, Saudi Arabia, United Arab Emirates, United States of America; 29 May 2020 – 12 Apr 2021	Patients who were moderately ill and admitted to hospital wards for covid-19 with laboratory confirmed SARS-CoV-2 infection and had increased D-dimer levels within the first five days of admission.	Confirmed diagnosis	Mean (SD): 59.99 (14.82)	56.8	1.07	NR	51% with >=2xULN 26% with >=3xULN	NR	NR	237	Dose-capped prophylactic subcutaneous heparin (LMWH or UFH) adjusted for body mass index and creatinine clearance. **Intermediate-dose UFH or LMWH were not permitted in the control arm.**	Low risk of bias for all relevant outcome(s)
Lopes 2021 (ACTION)	pragmatic, open label (with blinded adjudication), multicentre, randomised, controlled trial	Brazil; 24 Jun 2020 – 26 Feb 2021	Patients >18 years old hospitalised with a confirmed diagnosis of COVID-19, with symptoms for up to 14 days before randomisation, and elevated D-dimer concentration (above the upper limit of normal reference range per local laboratory).	Confirmed diagnosis	Mean (SD): 56.6 (14.00)	59.8	1.00	0.00	73% with >=1xULN 27% with >=3xULN	0.00	4.10	304	Standard VTE prophylaxis with enoxaparin/UFH during hospitalisation and could receive **extended prophylaxis at the discretion of the treating physician**	Low risk of bias for all relevant outcome(s)
Marcos 2021 (BEMICOP)	Investigator initiated, open-label, multicenter, randomized, controlled trial in patients with COVID-19 hospitalized in a conventional ward.	Spain; 01 Oct 2020 – 31 May 2021	Patients >18 years-old, hospitalized at the conventional ward due to mild or moderate (CURB65< 2 points and Sat.O2>90%) COVID-19 pneumonia with baseline D-Dimer >500 ng/mL	Confirmed diagnosis	Mean (SD): 62.65 (12.83)	62.1	0.00	0.00	100% with >=2xULN	NR	28.78	33	Bemiparin sc **3,500 IU OD**	Low risk of bias for all relevant outcome(s)
Lawler 2021 (ATTACC, ACTIV-4a, REMAP-CAP)	International multiplatform randomized clinical trial	International (United States, Canada, the United Kingdom, Brazil, Mexico, Nepal, Australia, the Netherlands, and Spain); 21 Apr 2020 – 22 Jan 2021	Moderate COVID-19 (hospitalized but noncritically ill), which was defined as hospitalization for COVID-19 without the need of ICU-level care.	Positive SARS-CoV-2 test only	Mean (SD): 58.76 (14.01)	58.7	NR	0.00	37% with >=2xULN *(28% unknown)*	NR	NR	1054	Usual care pharmacological thromboprophylaxis, according to **local practice**	Low risk of bias for all relevant outcome(s)

*Baseline characteristics were based on overall population and may include data from ICU patients. HEP-COVID was not included in the BLR analysis as many patients were not on prophylactic intensity anticoagulation with population being indirect and at very high risk of VTE

Study ID	Study Design	Location Study Period	Population	COVID-19 diagnosis	Age	Male (%)	Prior VTE (%)	Anticoagulation prior to hospitalization (%)	D-dimer	Still in ICU at end of study (%)	Still in hospital at end of study (%) (May include ICU, if not specified.)	Anticoagulation group (N)	Anticoagulation description (drug, dose, duration)	Risk of Bias
Lopes 2021 (ACTION)	Pragmatic, open-label (with blinded adjudication), multicentre, randomised, controlled trial	Brazil; 24 Jun 2020 – 26 Feb 2021	Patients >18 years old hospitalised with a confirmed diagnosis of COVID-19, with symptoms for up to 14 days before randomisation, and elevated D-dimer concentration (above the upper limit of normal reference range per local laboratory).	Confirmed diagnosis	Mean (SD): 56.60 (14)	59.8	1.00	0.00	73% with >=1xULN 27% with >=3xULN	0.00	4.10	Therapeutic intensity (N=310)	Stable: oral **rivaroxaban 20 mg OD**. 15 mg OD with CrCl of 30–49 mL/min or taking azithromycin, until 30d. Unstable: enoxaparin SC at 1 mg/kg BID, or IV UFH target anti-Xa concentration (0·3–0·7 IU/mL) or a corresponding target aPTT (1·5–2·5 times the mean normal value). **When stable, transitioned to above**	Some concerns for all relevant outcome(s)
												Prophylactic intensity (N=304)	Standard VTE prophylaxis with enoxaparin/UFH during hospitalisation and could receive **extended prophylaxis at the discretion of the treating physician**	
Marcos 2021 (BEMICOP)	Open-label, multicenter, randomized, controlled trial	Spain; 01 Oct 2020 – 31 May 2021	Patients >18 years-old, hospitalized at the conventional ward due to mild or moderate (CURB65< 2 points and Sat.O2>90%) COVID-19 pneumonia with baseline D-Dimer >500 ng/mL	Confirmed diagnosis	Mean (SD): 62.65 (12.83)	62.1	0.00	0.00	100% with >=2xULN	NR	28.78	Therapeutic intensity (N=32)	Bemiparin sc **115 IU/Kg once daily**, adjusted to body weight (7,500 IU for 50-70 Kg; 10,000 IU for >70-100 Kg; 12,500 IU for >100 Kg)	High risk of bias for all relevant outcome(s)
												Prophylactic intensity (N=33)	Bemiparin sc **3,500 IU OD**	
Sholzberg 2021 (RAPID)	Parallel, pragmatic, adaptive multi-center, open-label randomized controlled trial	Brazil, Canada, Ireland, Saudi Arabia, united Arab Emirates, United States of America; 29 May 2020 – 12 Apr 2021	Moderately ill patients who were admitted to hospital wards for covid-19 with laboratory confirmed SARS-CoV-2 infection and had increased D-dimer levels within the first five days of admission.	Confirmed diagnosis	Mean (SD): 59.99 (14.82)	56.8	1.07	NR	51% with >=2xULN 26% with >=3xULN	NR	NR	Therapeutic intensity (N=228)	Therapeutic dosing of heparin (LMWH or UFH). UFH was administered IV as an infusion using a weight-based nomogram and the activated partial thromboplastin time (aPTT) or UFH anti-Xa titration according to **center-specific VTE treatment protocols**	Some concerns for all relevant outcome(s)
												Prophylactic intensity (N=237)	Dose-capped prophylactic subcutaneous heparin (LMWH or UFH) adjusted for body mass index and creatinine clearance**. Intermediate-dose UFH or LMWH were not permitted in the control arm.**	
Spyropoulos 2021 (HEP-COVID)*	Open-label, multi-center randomized active control trial with pseudo-blinding mechanisms.	United states of America; 08 May 2020 – 14 May 2021	Hospitalized nonpregnant adults 18 years or older with COVID-19 diagnosed by nasal swab or serologic testing who needed supplemental oxygen per investigator judgment with plasma D-dimer level greater than 4 times the upper limit of normal based on local laboratory criteria or a sepsis-induced coagulopathy score of 4 or greater.	Confirmed diagnosis	Mean (SD): 66.70 (14.00)	53.8	3.10	94.94	100% with >=4xULN	NR	NR	Therapeutic intensity (N=84)	**Enoxaparin 1mg/kg sc B**ID if CrCl was 30 mL/min/1.73m2 or greater **or 0.5 mg/kg BID** if CrCl was 15-29 mL/min/ 1.73m2	Some concerns for all relevant outcome(s)
												Prophylactic intensity (N=86)	**Prophylactic or intermediate-dose heparin** regimens per local standard and could include UFH, up to 22,500 IU sc (BID or TID); enoxaparin, 30 mg or 40 mg sc OD or BID (weight based enoxaparin 0.5mg/kg sc BID was permitted but strongly	

													discouraged); or dalteparin, 2500 IU or 5000 IU sc daily	
Lawler 2021 (ATTACC, ACTIV-4a, REMAP-CAP)	Open-label, international multiplatform randomized clinical trial with response-adaptive randomization	International (United States, Canada, the United Kingdom, Brazil, Mexico, Nepal, Australia, the Netherlands, and Spain); 21 Apr 2020 – 22 Jan 2021	Moderate COVID-19 (hospitalized but noncritically ill), which was defined as hospitalization for COVID-19 without the need of ICU-level care.	Positive SARS-CoV-2 test only	Mean (SD): 58.76 (14.01)	58.7	NR	0.00	37% with >=2xULN *(28% unknown)*	NR	NR	Therapeutic intensity (N=1190)	Initial pragmatic strategy of therapeutic-dose anticoagulation with heparin, according **to local protocols used for the treatment of acute VTE** for up to 14 days or until recovery	High risk of bias for all relevant outcome(s)
												Prophylactic intensity (N=1054)	Usual care pharmacological thromboprophylaxis, according to **local practice**	

*Baseline characteristics were based on overall population and may include data from ICU patients.