PULMONARY EMBOLISM
Supporting information

This guideline has been prepared with reference to the following:

NICE. Venous thromboembolic diseases: diagnosis, management and thrombophilia testing. 2023. London. NICE

https://www.nice.org.uk/guidance/ng158

Konstantinides SV, Meyer G, Becattini C et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41:543-603

https://academic.oup.com/eurheartj/article/41/4/543/5556136

Giri J, Sista AK, Weinberg I et al. Interventional Therapies for Acute Pulmonary Embolism: Current Status and Principles for the Development of Novel Evidence: A Scientific Statement From the American Heart Association. Circulation. 2019;140:e774-e801

https://www.ahajournals.org/doi/10.1161/CIR.0000000000000707?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

Luke SGEH, Steven B, Robin C et al. British Thoracic Society Guideline for the initial outpatient management of pulmonary embolism (PE). Thorax. 2018;73(Suppl 2):ii1-ii29

https://thorax.bmj.com/content/73/Suppl_2/ii1

Kearon C, Akl EA, Comerota AJ et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141:419S-94

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278049/

Recognition and assessment

Pulmonary thromboembolism (PE) is rare in patients <40 years in the absence of risk factors?
A 2020 review found that the overall incidence of PE among patients aged between 20 and 40 years of age was 16 cases per 100,000 person years in women and 7 cases per 100,000 person years in men (Jarman, 2020).
Analysis of data from 1029 patients treated at 2 large Swiss centres (Righini, 2000) showed that the under-40s accounted for the smallest percentage of PEs (12%). The over-80s were the worst-affected group (44%).
A study of 175730 admissions to a tertiary care hospital in the US (Stein, 1999) revealed an incidence of PE of 0.23% in all age groups (400 cases). Patients below the age of 40 accounted for only 49 of these, equating to an overall incidence of 0.11% amongst women in this age group and 0.12% in men.

Jarman AF, Mumma BE, Singh KS et al. Crucial considerations: Sex differences in the epidemiology, diagnosis, treatment, and outcomes of acute pulmonary embolism in non-pregnant adult patients. J Am Coll Emerg Physicians Open. 2021;2:e12378
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7839235/

Righini M, Goehring C, Bounameaux H, et al. Effects of age on the performance of common diagnostic tests for pulmonary embolism. Am J Med 2000;109:357-61

Stein PD, Huang H, Afzal A, et al. Incidence of acute pulmonary embolism in a general hospital: relation to age, sex, and race. Chest 1999;116:909-13
http://journal.publications.chestnet.org/article.aspx?articleid=1078217

Evidence Level: IV

Do most episodes of PE follow popliteal/iliofemoral DVT?
Lower limb DVT is "responsible for over 90% of pulmonary emboli" (Kearon, 2003).
In a series of 78 patients who had evidence of PE on pulmonary arteriograms but no findings in the legs, venography (or radionuclide venography) showed that 24 patients (31%) had asymptomatic DVT of the superficial femoral or popliteal vein (Ferris, 1992).
An autopsy series (Havig, 1977) showed that two-thirds of emboli described as "contributing to death" originated in the proximal iliofemoral veins.
Bilateral DVT resulted in the worst outcomes in a study of 1913 patients (Seinturier, 2005), with survival at 2 years of 65% for bilateral proximal disease, compared to 80% for unilateral distal disease.

Ferris EJ. Deep venous thrombosis and pulmonary embolism: correlative evaluation and therapeutic implications. Am J Roentgenol 1992;159:1149-55
http://www.ajronline.org/doi/pdf/10.2214/ajr.159.6.1442374

Havig O. Deep vein thrombosis and pulmonary embolism: an autopsy study with multiple regression analysis of possible risk factors. Acta Chir Scand Suppl 1977;478:1-120

Kearon C. Natural history of venous thromboembolism. Circulation 2003;107:I22-30
http://circ.ahajournals.org/cgi/pmidlookup?view=long&pmid=12814982

Seinturier C, Bosson JL, Colonna M, et al. Site and clinical outcome of deep vein thrombosis of the lower limbs: an epidemiologic study. J Thromb Haemost 2005;3:1362-7
http://onlinelibrary.wiley.com/doi/10.1111/j.1538-7836.2005.01393.x/full

Evidence Level: V

What are the risk factors for PE?
A prospective cohort study in 1239 patients (Wells, 1998) was used as the basis for an algorithm to determine the pretest probability of PE. Of 102 patients graded as "high risk", 78.4% had PE. Risk factors used in the calculation of the algorithm were:

- Surgery within 12 weeks
- Immobilisation (complete bedrest) for 3 or more days in the previous 4 weeks
- Previous DVT or objectively diagnosed PE
- Fracture of a lower extremity and immobilisation within 12 weeks
- Strong family history of DVT/PE
- Cancer (treatment ongoing, or within last 6 months)
- Postpartum period
- Lower-extremity paralysis

A case-control study in 625 patients (Heit, 2000) identified the following risk factors:

- Surgery (OR 21.7; 95% CI 9.4-49.9)
- Trauma (OR 12.7; 95% CI 4.1-39.7)
- Hospital/nursing home confinement (OR 8.0; 95% CI 4.5-14.2)
- Malignant neoplasm (OR 4.1; 95% CI 1.9-8.5)
- Malignant neoplasm treated by chemotherapy (OR 6.5; 95% CI 2.1-20.2)
- Central venous catheter or pacemaker (OR 5.6; 95% CI 1.6-19.6)
- Superficial vein thrombosis (OR 4.3; 95% CI 1.8-10.6)
- Neurological disease with extremity paresis (OR 3.0; 95% CI 1.3-7.4)

Heit JA, Silverstein MD, Mohr DN, et al. Risk factors for deep vein thrombosis and pulmonary embolism: a population-based case-control study. Arch Intern Med 2000;160:809-15

Wells PS, Ginsberg JS, Anderson DR, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. Ann Intern Med 1998;129:997-1005

Evidence Level: III

COPD is a minor risk factor for PE?

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A 2025 systematic review of 22 studies revealed that the prevalence of pulmonary embolism in the AECOPD was 17.82% (Li, 2025).
A 2021 systematic review found that the prevalence of PE in patients with acute exacerbations of COPD (AE-COPD) to be 12.9% (95% CI: 8.9%-18.4%) [Wang, 2021]. This study pooled the data of 5035 patients with AE-COPD.
A 2018 systematic review identified a total of 5 articles which demonstrated a prevalence of PE among patients with a clinical diagnosis of AE-COPD that ranged from 3.3 to 29.1% (Pourmand, 2018). Sample sizes varied from 49-197 patients. Studies occurred in both emergency department and inpatient settings, including intensive care units. Among the studies that reported patient characteristics associated with PE in AE-COPD, both obesity and immobility were important.

Li M, Jiang Y, Xu Y et al. The prevalence and risk factors of pulmonary embolism in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. Thromb J. 2025;23:42
https://pmc.ncbi.nlm.nih.gov/articles/pmid/40301960/

Pourmand A, Robinson H, Mazer-Amirshahi M e al. Pulmonary Embolism Among Patients With Acute Exacerbation Of Chronic Obstructive Pulmonary Disease: Implications For Emergency Medicine. J Emerg Med. 2018;55:339-46

Wang J & Ding YM. Prevalence and risk factors of pulmonary embolism in acute exacerbation of chronic obstructive pulmonary disease and its impact on outcomes: a systematic review and meta-analysis. Eur Rev Med Pharmacol Sci. 2021;25:2604-16
https://www.europeanreview.org/article/25424

Evidence Level: IV

Following V/Q scan, what is the percentage probability of PE for a high, intermediate, low or very low result?
Data from the PIOPED study (Anon, 1990) has been used to calculate probabilities for the diagnosis of PE. A random sample of 933 of 1493 patients was studied prospectively. 88% of high-probability patients had PE, 33% of intermediate, and 12% in the low-probability group. However, only 41% of patients with PE had high-probability scans, another 41% had intermediate-probability scans, 16% had low-probability scans and 2% had near-normal scans. Dependence on low-probability scan results alone to rule out PE would thus result in failure to treat 1 in 5 of patients actually having one (Ralph, 1994). The original criteria have since been revised to improve their accuracy (Sostman, 1994), resulting in a significant reduction of 15.4% ($p<.001$) in the number of scans classed as “intermediate” probability.

Anon. Value of the ventilation/perfusion scan in acute pulmonary embolism: results of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED). JAMA 1990;263:2753-9

Ralph DD. Pulmonary embolism: the implications of prospective investigation of pulmonary embolism diagnosis. Radiol Clin N Am 1994;32:679-87

Sostman HD, Coleman RE, DeLong DM, et al. Evaluation of revised criteria for ventilation-perfusion scintigraphy in patients with suspected pulmonary embolism. Radiology 1994;193:103-7

Evidence Level: III

A normal V/Q scan result effectively rules out PE?
A prospective study was conducted on 515 patients with clinically suspected PE but with normal perfusion scans (Hull, 1990). Impedance plethysmography was performed in the 493 patients in whom it was possible (22 had leg casts, amputations, etc) and proximal-vein thrombosis was found in only 5 (1%).
Pooled data from 693 patients in this and 2 other studies (van Beek, 1995; Kipper, 1982) show a total event rate of 0.2% (95% CI 0.1-0.4%) for patients with a normal scan.

Hull RD, Raskob GE, Coates G, et al. Clinical validity of a normal perfusion lung scan in patients with suspected pulmonary embolism. Chest 1990;97:23-6
http://journal.publications.chestnet.org/data/Journals/CHEST/21605/23.pdf

Kipper MS, Moser KM, Kortman KE, et al. Longterm follow-up of patients with suspected pulmonary embolism and a normal lung scan: perfusion scans in embolic subjects. Chest 1982;82:411-5

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http://journal.publications.chestnet.org/data/Journals/CHEST/21316/411.pdf

van Beek EJ, Kuyer PM, Schenk BE, et al. A normal perfusion lung scan in patients with clinically suspected pulmonary embolism: frequency and clinical validity. Chest 1995;108:170-3
http://journal.publications.chestnet.org/article.aspx?articleid=1068818

Evidence Level: III

Immediate treatment

Paracetamol is unlikely to provide adequate analgesia in pleuritic chest pain associated with massive PE, in which case indomethacin is indicated?
A single study on indometacin for pleuritic pain has been identified (Klein, 1984). This stated: "Indomethacin (50 mg every eight hours) was given to 17 selected patients with pleurisy to control pain. Eleven of 17 obtained good to excellent relief of pain within 24 hours. Pain was not relieved in three patients and was only partly relieved in three others. Potentially serious side effects developed in two patients but resolved quickly. In selected patients indomethacin appears to be a reasonable initial choice for relief of pleural pain."

Klein RC. Effects of indomethacin on pleural pain. South Med J 1984;77:1253-4

Evidence Level: V

Treatment with diuretics is dangerous in a patient with PE?
A 2021 RCT concluded that in normotensive patients with intermediate-risk PE (n=276), a single bolus of furosemide improved the primary efficacy outcome at 24 h (absence of oligo-anuria and normalization of a simplified PE Severity Index) and maintained stable renal function (Lim, 2021). In the furosemide group, urine output increased, without a demonstrable improvement in heart rate, systolic blood pressure, or arterial oxygenation. The primary outcome occurred in 68/132 patients (51.5%) in the diuretic and in 49/132 (37.1%) in the placebo group (relative risk = 1.30, 95% confidence interval 1.04-1.61; P = 0.021). Major adverse outcome at 48 h occurred in 1 (0.8%) patients in the diuretic group and 4 patients (2.9%) in the placebo group (P = 0.19).
Diuretic drugs can cause clumping or aggregation of red blood cells (Roberts, 1966) and have been associated with thromboembolic complications in a number of case reports (Green, 1988; Robinson, 1980). Dilation of the venous system by diuretics may also cause pre-existing clots to break loose (Robinson, 1980).

Green ST, Ng, JP, Callaghan M. Metolazone and axillary vein thrombosis. Scott Med J 1988;33:211-2

Lim P, Delmas C, Sanchez O et al. Diuretic vs. placebo in intermediate-risk acute pulmonary embolism: a randomized clinical trial. Eur Heart J Acute Cardiovasc Care. 2021: epub ahead of print

Roberts BE, Smith PH. Hazards of mannitol infusions. Lancet 1966;ii:421-2

Robinson GS, Wiese WH. Pulmonary embolism during mannitol therapy. Chest 1980;77:432-3
http://journal.publications.chestnet.org/article.aspx?articleid=1051679

Thrombolysis is appropriate in patients with PE who present with life-threatening features?
According to recommendations of the European Society of Cardiology, the use of catheter-directed thrombolysis should be restricted to high-risk patients with contraindications to systemic thrombolysis or failure of systemic thrombolysis, or to patients with an intermediate high-risk PE presenting with hemodynamic deterioration (Konstantinides, 2019). Based on newer data, recent consensus documents advocate a more liberal approach considering certain red flags associated with clinical deterioration (Pruszczyk, 2019 & Ghanem, 2023).
An updated Cochrane review of 17 RCTs (Watson 2014) found that thrombolysis also has a place in the treatment of DVT, with complete clot lysis occurring significantly more often in the standard anticoagulant treatment group; early follow up (risk ratio (RR) 4.91; 95% confidence interval (CI) 1.66 to 14.53, P = 0.004) and at intermediate follow up (RR 2.37; 95% CI 1.48 to 3.80, P = 0.0004).

Ghanem A, Andrassy M, Dürschmied D et al. Interventionelle Therapie und multidisziplinäre Managementstrategien für die akute Lungenembolie. Die Kardiologie. 2023;17:141–59

Konstantinides SV, Meyer G. The 2019 ESC Guidelines on the Diagnosis and Management of Acute Pulmonary Embolism. Eur Heart J. 2019;40:3453–5
https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Acute-Pulmonary-Embolism-Diagnosis-and-Management-of

Pruszczyk P, Klok FA, Kucher N et al. Percutaneous treatment options for acute pulmonary embolism: a clinical consensus statement by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function and the European Association of Percutaneous Cardiovascular Interventions. EuroIntervention. 2022;18:e623–e38
https://pmc.ncbi.nlm.nih.gov/articles/PMC10241264/

Watson L, Broderick C, Armon MP. Thrombolysis for acute deep vein thrombosis. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No.: CD002783.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002783.pub3/full

Evidence Level: I

Subsequent management (non-pregnant patients)

Following proven PE, heparin treatment reduces the risk of recurrence?
A randomised trial in 73 patients with proven PE (Barritt, 1960) found that the group treated with 10000 units of iv heparin, 6 hrly for 6 doses (n=54) had no deaths from recurrences, compared to 5 deaths in the untreated group (n=19).

Barritt DW, Jordan SC. Anticoagulant drugs in the treatment of pulmonary embolism: a controlled trial. Lancet 1960;i:1309-12

Evidence Level: II

Do removable vena cava filters have a role in the prevention of PE where anticoagulation is contraindicated?
2014 guidance from the European Society of Cardiology states that Inferior vena cava (IVC) filters are suggested in patients with acute PE who have absolute contraindications to anticoagulant drugs (Konstantinides, 2014).
A Cochrane systematic review of 6 RCTs (Young, 2020) failed to come to any firm conclusions about the value of filters.
A 2023 systematic review of 5 RCTs (including 1137 patients) found no significant differences between patients with vena cava filters and those without vena cava filters for the risk of PE, major bleeding, and all-cause mortality, while the risk of DVT was significantly increased for patients treated with vena cava filters (Miao, 2023).

Konstantinides S, Torbicki A, Agnelli G et al. 2014 Guidelines on the diagnosis and management of acute pulmonary embolism. The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2014; 35: 3033–80
http://eurheartj.oxfordjournals.org/content/ehj/35/43/3033.full.pdf

Miao HT, Li XY, Zhou C et al. Efficacy and safety of vena cava filters in preventing pulmonary embolism: A systematic review and meta-analysis. Phlebology. 2023;38:474-83

Young T & Sriram KB. Vena caval filters for the prevention of pulmonary embolism. Cochrane Database of Systematic Reviews 2020, CD006212
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD006212.pub5/full

Evidence level: II

Discharge policy

Warfarin at a dose that maintains INR between 2 and 3 reduces risk of recurrent PE?
In the randomised, multi-centre trial in 897 patients with a first episode of thromboembolism (Schulman, 1995) referred to in the evidence for the previous question, INR was maintained between 2.0 – 2.85. NNT to prevent recurrence within 2 years was 12 (8 – 24).

Schulman S, Rhedin AS, Lindmarker P, et al. A comparison of six weeks with six months of oral anticoagulant therapy after a first episode of venous thromboembolism. N Engl J Med 1995;332:1661-5

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Evidence Level: II

Following a first PE, the risk of recurrence is low after 3 months of warfarin?
The annual cumulative incidence of recurrence in PE treated with anticoagulants ranges from 4-17% in prospective studies, and from 4-8% in studies published since 1992 (Pinede, 2001). A multicentre randomised study from the Warfarin Optimal Duration Italian Trial Investigators (Agnelli, 2003) concluded that patients with PE had a substantial risk of recurrence (RR 0.99, 95% CI 0.45-2.16) after discontinuation of warfarin, regardless of the duration of treatment. In a study of 826 patients (Kyrle, 2004), men were at higher risk of recurrence than women (RR 3.6; 95% CI 2.3-5.5).

Agnelli G, Prandoni P, Becattini C, et al. Extended oral anticoagulant therapy after a first episode of pulmonary embolism. Ann Intern Med 2003;139:19-25

Kyrle PA, Minar E, Bialonczyk C, et al. The risk of recurrent venous thromboembolism in men and women. N Engl J Med 2004;350:2558-63

Pinede L, Ninet J, Duhaut P, et al. Comparison of 3 and 6 months of oral anticoagulant therapy after a first episode of proximal deep vein thrombosis or pulmonary embolism and comparison of 6 and 12 weeks of therapy after isolated calf deep vein thrombosis. Circulation 2001;103:2453-60
http://circ.ahajournals.org/content/103/20/2453.long

Evidence Level: III

In a pregnant woman with suspected PE, does the risk of harm from unnecessary heparin treatment outweigh the risk of mortality if the condition remains untreated?
The mortality rate for untreated PE in pregnancy has not been accurately assessed, with most PE occurring in the postpartum period (151.8 vs. 47.9 per 100,000 (Heit, 2005)), but has been assumed to average 15% (range, 10% - 50%) (Doyle, 2004).
A review on the subject (Tapson, 2008) concluded that “Pregnant patients with acute venous thromboembolism require the same initial approach as other patients with regard to the need for parenteral anticoagulation”.
The use of LWMH in such patients is generally held to be effective and safe (Kher, 2007).
A prospective case control study was conducted in 143 women who had an antenatal PE and 259 matched controls (Knight, 2008). Nine women who had a PE “should have received antenatal thromboprophylaxis with LMWH according to national guidelines” but only three (33%) had. Six women (4%) had a PE despite receiving prophylaxis, but three of these (50%) were given lower than the recommended doses.

Doyle NM, Ramirez MM, Mastrobattista JM, et al. Diagnosis of pulmonary embolism: a cost-effectiveness analysis. Am J Obstet Gynecol 2004;191:1019-23

Heit JA, Kobbervig CE, James AH, et al. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. Ann Intern Med 2005;143:697-706
http://www.copacamu.org/IMG/pdf/Heit-ann_int_med.pdf

Kher A, Bauersachs R, Nielsen JD. The management of thrombosis in pregnancy: role of low-molecular-weight heparin. Thromb Haemost 2007;97:505-13

Knight M. Antenatal pulmonary embolism: risk factors, management and outcomes. Br J Obstet Gynaecol 2008;115:453-61
http://onlinelibrary.wiley.com/doi/10.1111/j.1471-0528.2007.01622.x/full

Tapson VF. Acute pulmonary embolism. N Engl J Med 2008;358:1037-52

Evidence Level IV

How many patients develop pulmonary hypertension (CTPH) after suffering a PE?
A 2018 systematic review of cohort studies found that the overall incidence of CTPH after acute pulmonary embolism, with a median follow-up from 6 to 94.3 months, was 3.13% (95% CI: 2.11-4.63%) [Zhang, 2018].

Zhang M Wang N, Zhai Z et al. Incidence and risk factors of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: a systematic review and meta-analysis of cohort studies. J Thorac Dis. 2018;10:4751-63
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6129909/

Evidence Level: III

What are the risk factors for developing CTPH?
A 2018 review identified the following risk factors for developing CTPH:

• VA shunt	Odds ratio (OR) 19.49 (95% CI 2.47 to 2520)
• Splenectomy	OR 22.09 (95% CI 2.97–2824)
• Massive/submassive PE	OR 13.03 (p = .004)
• VTE history	OR 49.01 (p < .001)
• Recurrent VTE	OR 45.02 (95% CI 21.00–114.73)
• Thyroid replacement	OR 5.41 (95% CI 2.70–12.23)
• Hypothyroidism	OR 4.3 (95% CI 1.4–13.0)
• Prior VTE	OR 19.36 (95% CI 11.66–33.79)
• APS/lupus AC	OR 3.28 (95% CI 1.58–7.50)
• Non-blood group O	OR 3.12 (p < .001)
• Unprovoked PE	OR 20.0 (95% CI 2.7–>100)
• RV dysfunction at diagnosis	OR 4.1 (95% CI 1.4–12.0)
• Symptoms >2 weeks prior to PE diagnosis	OR 7.9 (95% CI 3.3–19.0)
• Age >60 years	OR 2.9 (95% CI 1.2–7.2)

Fernandes T, Auger W, Fedullo P. Epidemiology and risk factors for chronic thromboembolic pulmonary hypertension. Thromb Res. 2018;164:145-9

Evidence Level III

Is follow-up of PE patients for CTPH cost-effective and if so, how should it be carried out?
A 2025 Dutch study analysed 11 different PE follow-up algorithms and one hypothetical scenario without a dedicated CTPH follow-up algorithm using a Markov model (Luijten, 2025). The lifelong costs per CTPH patient were compared and related to quality-adjusted life-years (QALYs) for each scenario. Compared to not performing dedicated follow-up, the integrated follow-up algorithms are associated with an estimated increase of 0.89 to 1.2 QALYs against an incremental cost-effectiveness ratio (ICER) of EUR 25,700 to 46,300 per QALY per CTPH patient. When comparing different algorithms with each other, the maximum differences were 0.27 QALYs and EUR 27,600. The most cost-effective algorithm was the InShape IV algorithm, with an ICER of EUR 26 700 per QALY compared to the next best algorithm. The authors of this study concluded that subjecting all PE survivors to any of the currently established dedicated follow-up algorithms to detect CTPH is cost-effective and preferred above not performing a dedicated follow-up, evaluated against the Dutch acceptability threshold of EUR 50 000 per QALY.

Luijten D, van den Hout WB, Boon H et al. Cost-effectiveness of follow-up algorithms for chronic thromboembolic pulmonary hypertension in pulmonary embolism survivors. ERJ Open Res. 2025;11
https://pmc.ncbi.nlm.nih.gov/articles/pmid/39811556/

Evidence Level: I

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