

Appendix I: Composite reference standard used in AMUSE-2

PE confirmed	PE refuted – no anticoagulant treatment.
Spiral CT scanning demonstrating central, or (sub) segmental PE	Spiral CT scanning demonstrating no signs of PE, plus 3 months of uneventful follow-up in primary care
Ventilation-perfusion scanning findings demonstrating PE, in accordance with the PIOPED II study protocol #	Ventilation-perfusion scanning findings without signs of PE, in accordance with the PIOPED II study protocol #, plus 3 months of uneventful follow-up in primary care
Digital subtraction angiography demonstrating PE	Digital subtraction angiography without signs of PE, plus 3 months of uneventful follow-up in primary care
Compression ultrasonography demonstrating proximal deep vein thrombosis in a patient with clinical symptoms and signs of PE	If no imaging test was performed in secondary care ¥, PE was also considered refuted if uneventful follow-up of at least three months in primary care demonstrated no signs of acute venous thrombo-embolism §
Wells-PE rule ≤ 4 AND negative quantitative D-dimer test, but with a VTE event during 3 months of follow-up in primary care	Wells-PE rule ≤ 4 AND negative quantitative D-dimer test, and 3 months of uneventful follow-up in primary care

§ Patients received follow-up in primary care; follow-up was considered uneventful if a patient was not diagnosed with acute PE or deep vein thrombosis during 3 months of follow-up

¥ For example because of a low clinical probability assessment plus a negative D-dimer test as performed in secondary care, or because after referral an alternative diagnosis was found that completely explained the symptoms of an included patient (at the discretion of the attending physician)

Sostman, H.D., et al., *Acute pulmonary embolism: sensitivity and specificity of ventilation-perfusion scintigraphy in PIOPED II study*. Radiology, 2008. **246**(3):941-6.