Leids Universitair
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Subsegmental pulmonary embolism: treatment is *not* routinely needed

F.A. (Erik) Klok MD, PhD
Department of Medicine - Thrombosis and Hemostasis
LUMC, Leiden, Netherlands
✉ F.A.Klok@LUMC.nl

Disclosures

I have no conflicts of interest for this lecture

Affiliation/financial interest	**Company/party**
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Consultant:	–
Major stock/shareholder:	–
Advisory board:	–

Giant

- ✓ 2.10 m
- ✓ One of the brightest minds in VTE research land
- ✓ (future) key opinion leader

Giants do get it wrong sometimes….

Giants do get it wrong sometimes….

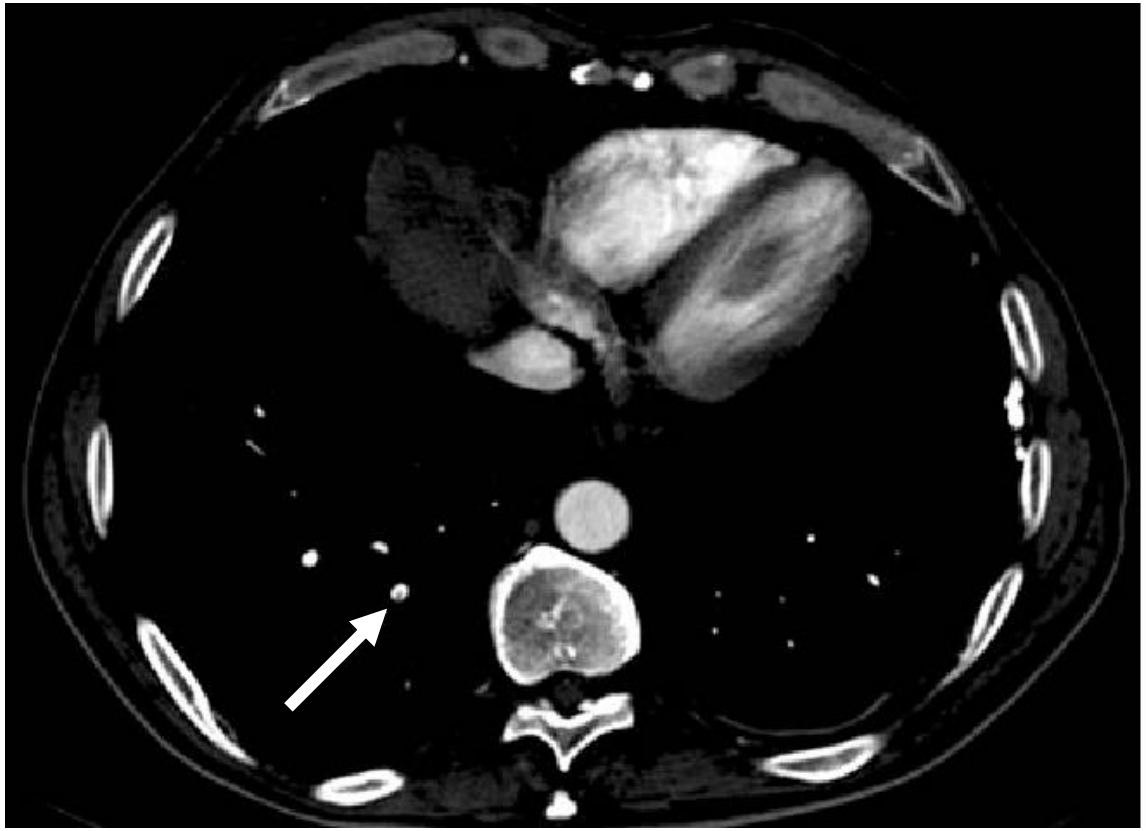
Case

26-year old man with subacute chest pain

- ✓ No relevant medical history
- ✓ Pleuritic left-sided chest pain that started 3 days ago
- ✓ No fever or notable dyspnea
- ✓ No symptoms of DVT

- ✓ BP 126/82, HR 68/min, sat 98%
- ✓ Physical examination: unremarkable
- ✓ ECG/lab/X-ray normal, CRP 16, D-dimer 508

Case



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- ✓ Physical examination: unremarkable
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- ✓ CTPA: small ssPE right

Case

Question

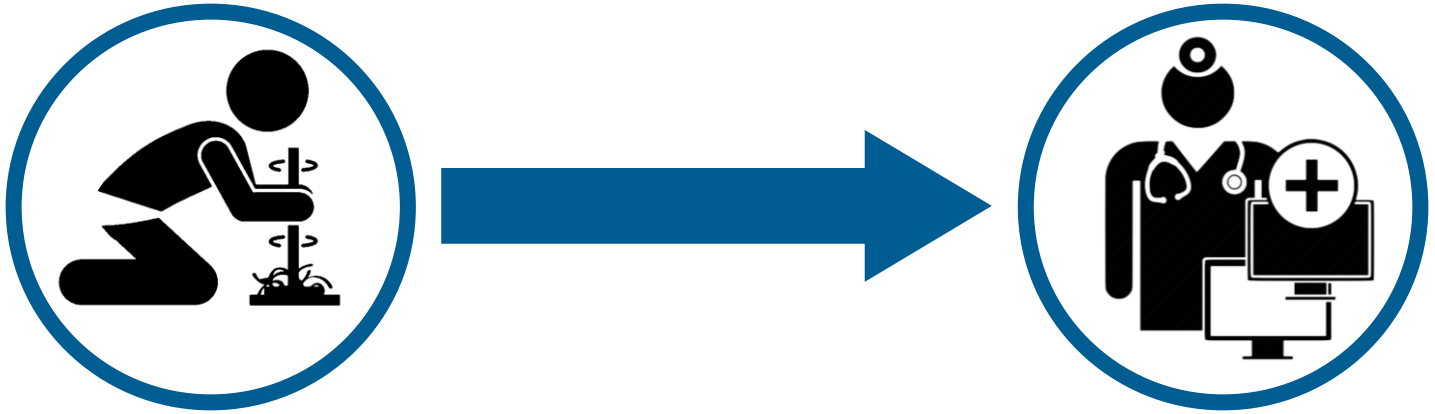
Would you initiate anticoagulant treatment?

Main issues in subsegmental PE

I would strongly consider not to….

1. Overdiagnosis
2. Evidence from intervention studies
3. Back-up from guidelines

Overdiagnosis: increasing prevalence over time



4.7%

15%

Carrier M *et al*, J Thromb Haemost 2010

Overdiagnosis: less ssPE with VQ vs CTPA

Table 2. Rates of Pulmonary Embolism and Deep Vein Thrombosis at Baseline and at 3 Months of Follow-up

	No. (%) of Baseline Patients	
	CTPA (n = 694)	V̇/Q̇ (n = 712)
PE alone	94 (13.5)	64 (9.0)
PE and DVT	29 (4.2)	19 (2.7)
DVT		
Total	10 (1.4)	18 (2.5)
Proximal	7 (1.0)	11 (1.5)
Total VTE[a]	**133** (19.2)	**101** (14.2)
	Three-Month Follow-up	
	(n = 561)	**(n = 611)**
PE total	2 (0.4)	4 (0.7)
Fatal PE	0	1 (0.2)
DVT	0	2 (0.3)
Total VTE[b]	**2** (0.4)	**6** (1.0)

Anderson DR *et al*, JAMA 2007

Overdiagnosis: less ssPE with VQ vs CTPA

7% ssPE

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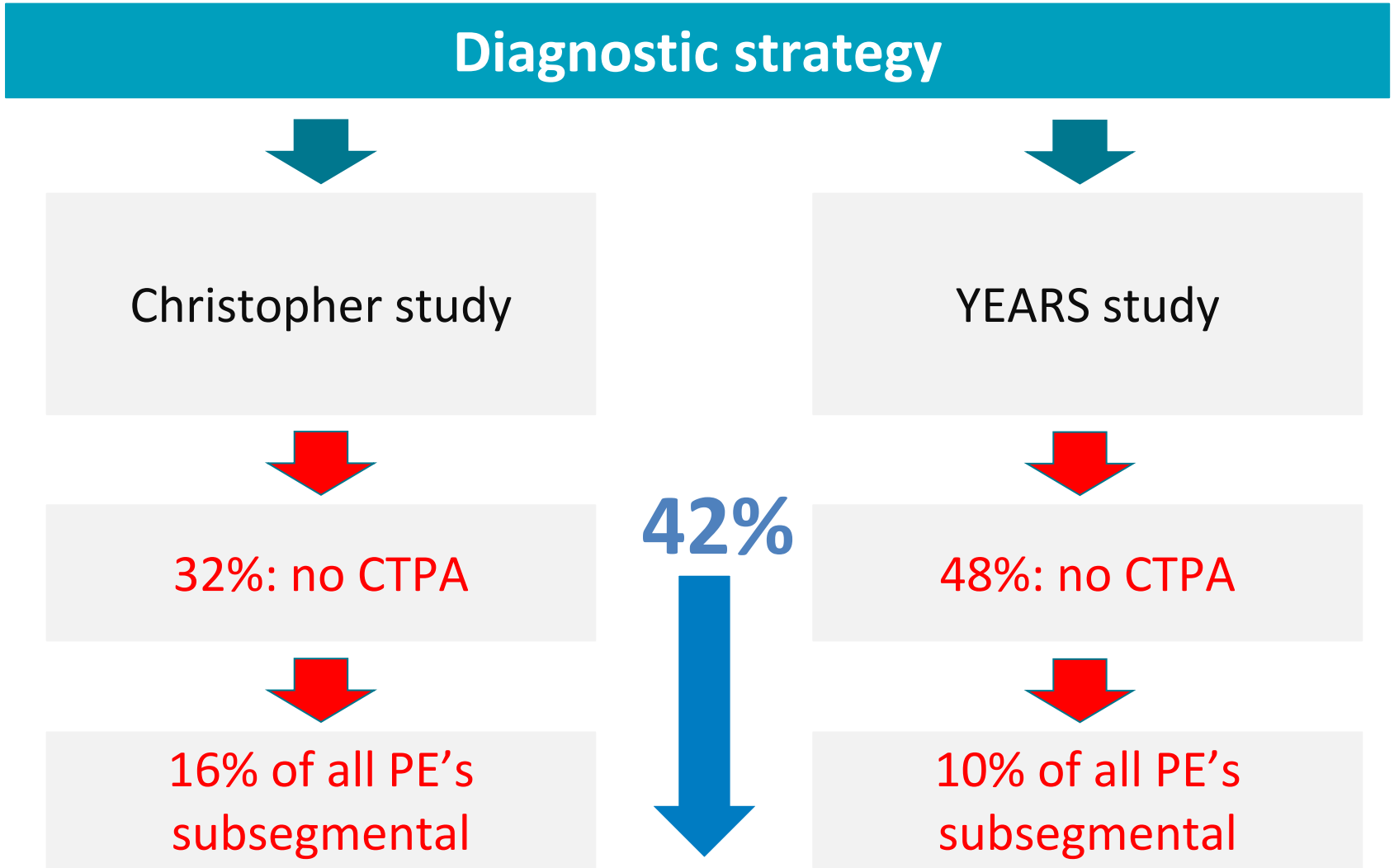
Anderson DR *et al*, JAMA 2007

Overdiagnosis: less ssPE with moderns algoritms



van Belle A *et al*, JAMA 2006; van der Hulle T *et al*, Lancet 2017; van der Pol L *et al*, Br J Hematol 2018

Evidence from clinical studies

Meta-analysis of published literature

✓ 126 patient left untreated:

- Risk of bleeding: 0%
- Risk of recurrent VTE: 3.9% (95%CI 1.8-13%)

✓ 589 patients treated:

- Risk of bleeding: 8.1% (95%CI 2.8-16%)
- Risk of recurrent VTE: 5.3% (95%CI 1.6-11%)

Bariteau A *et al*, Acad Emerg Med 2018

Evidence from clinical studies

Annals of Internal Medicine

ORIGINAL RESEARCH

Risk for Recurrent Venous Thromboembolism in Patients With Subsegmental Pulmonary Embolism Managed Without Anticoagulation

A Multicenter Prospective Cohort Study

Grégoire Le Gal, MD, PhD; Michael J. Kovacs, MD; Laurent Bertoletti, MD, PhD; Francis Couturaud, MD, PhD; Carole Dennie, MD; Andrew M. Hirsch, MD; Menno V. Huisman, MD, PhD; Frederikus A. Klok, MD, PhD; Noémie Kraaijpoel, MD, PhD; Ranjeeta Mallick, PhD; Amanda Pecarskie, BSc; Elena Pena, MD; Penny Phillips, BSc; Isabelle Pichon, BSc; Tim Ramsay, PhD; Marc Righini, MD; Marc A. Rodger, MD; Pierre-Marie Roy, MD, PhD; Olivier Sanchez, MD, PhD; Jeannot Schmidt, MD, PhD; Sam Schulman, MD; Sudeep Shivakumar, MD; Albert Trinh-Duc, MD; Rachel Verdet, BSc; Ulric Vinsonneau, MD; Philip Wells, MD; Cynthia Wu, MD; Erik Yeo, MD; and Marc Carrier, MD; on behalf of the SSPE Investigators*

Le Gal G *et al*, Ann Int Med 2021

Evidence from clinical studies

Exclusion criteria

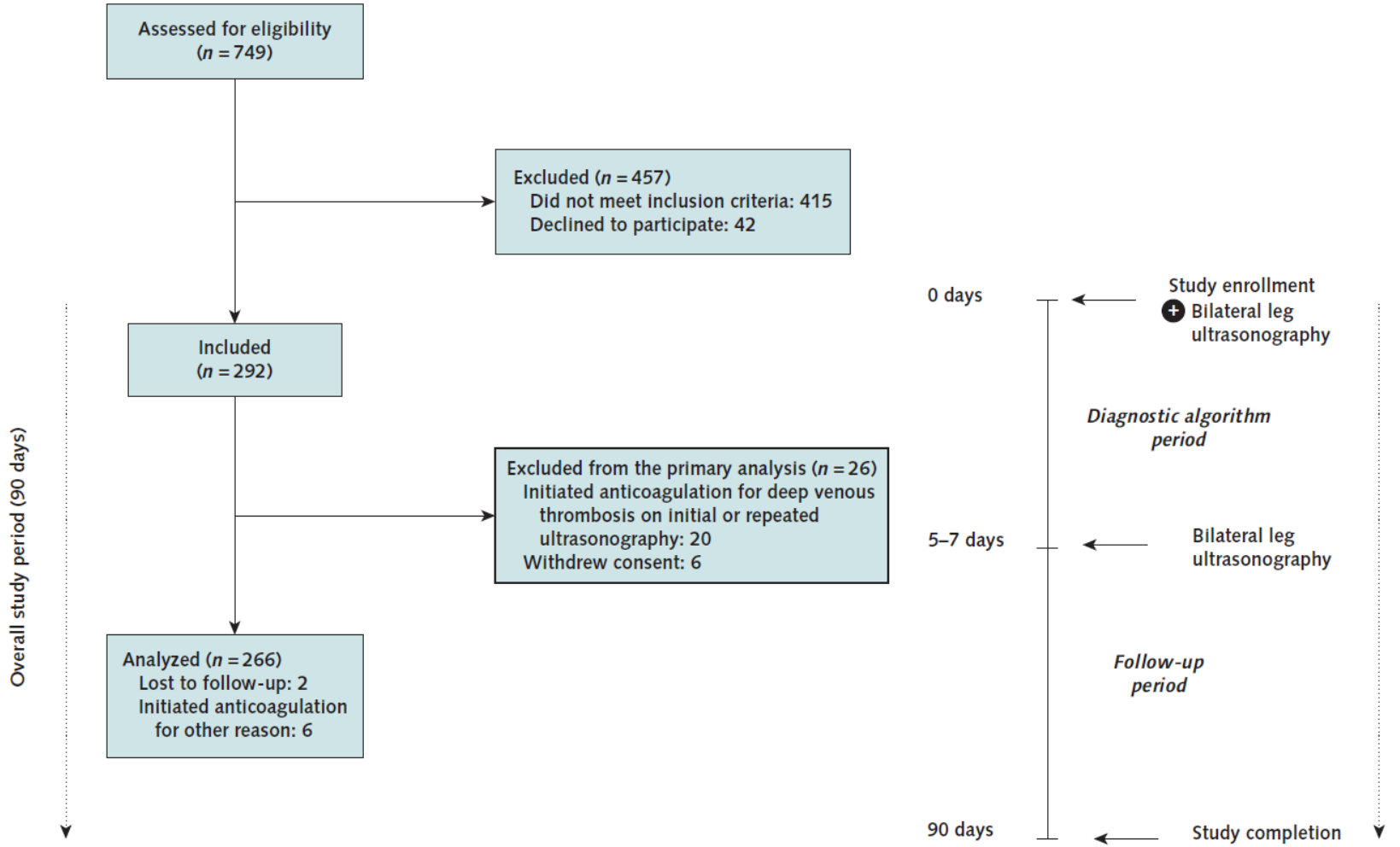




Le Gal G *et al*, Ann Int Med 2021

Evidence from clinical studies

Figure 1. Study flow diagram.



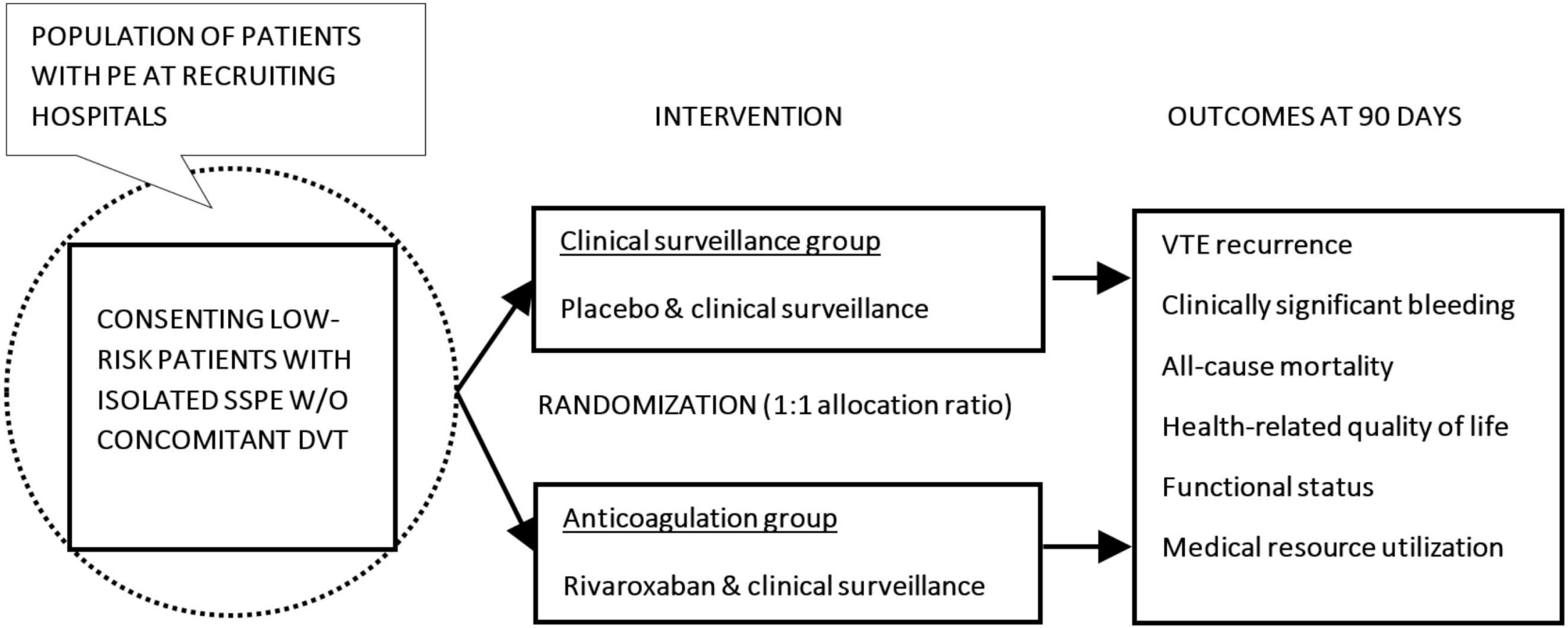
Le Gal G *et al*, Ann Int Med 2021

Evidence from clinical studies

- ✓ Primary outcome in 8 patients, cumulative 90-day incidence of 3.1% (95% CI, 1.6% to 6.1%)
- ✓ More frequently in single than multiple ssPE's (HR 2.7, 0.7-11)
- ✓ More frequently in elderly (>65 years) (HR 3.2, 0.8-14)

Le Gal G *et al*, Ann Int Med 2021

SAFE-ssPE study



Baumgartner C *et al*, BMJ open 2020

Back-up from guidelines

Whether to Anticoagulate Subsegmental PE

***19. In patients with subsegmental PE (no involvement of more proximal pulmonary arteries) and no proximal DVT in the legs who have a (i) low risk for recurrent VTE (see text), we suggest clinical surveillance over anticoagulation** (Grade 2C) **or (ii) high risk for recurrent VTE (see text), we suggest anticoagulation over clinical surveillance** (Grade 2C).

ACCP guideline 2016

Back-up from guidelines

3. In patients with subsegmental pulmonary embolism (PE) (no involvement of more proximal pulmonary arteries) and no proximal DVT in the legs who have a (i) low risk for recurrent VTE (see text), we suggest clinical surveillance over anticoagulation (weak recommendation, low-certainty evidence) or (ii) high risk for recurrent VTE (see text), we suggest anticoagulation over clinical surveillance (weak recommendation, low-certainty evidence).

ACCP guideline 2021

Back-up from guidelines

Recommendations	Class[a]	Level[b]
For patients with PE and cancer, weight-adjusted subcutaneous LMWH should be considered for the first 6 months over VKAs.[360–363]	IIa	A
Edoxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[366]	IIa	B
Rivaroxaban should be considered as an alternative to weight-adjusted subcutaneous LMWH in patients without gastrointestinal cancer.[367]	IIa	C
For patients with PE and cancer, extended anticoagulation (beyond the first 6 months)[c] should be considered for an indefinite period or until the cancer is cured.[378]	IIa	B
In patients with cancer, management of incidental PE in the same manner as symptomatic PE should be considered, if it involves segmental or more proximal branches, multiple subsegmental vessels, or a single subsegmental vessel in association with proven DVT.[376,377]	IIa	B

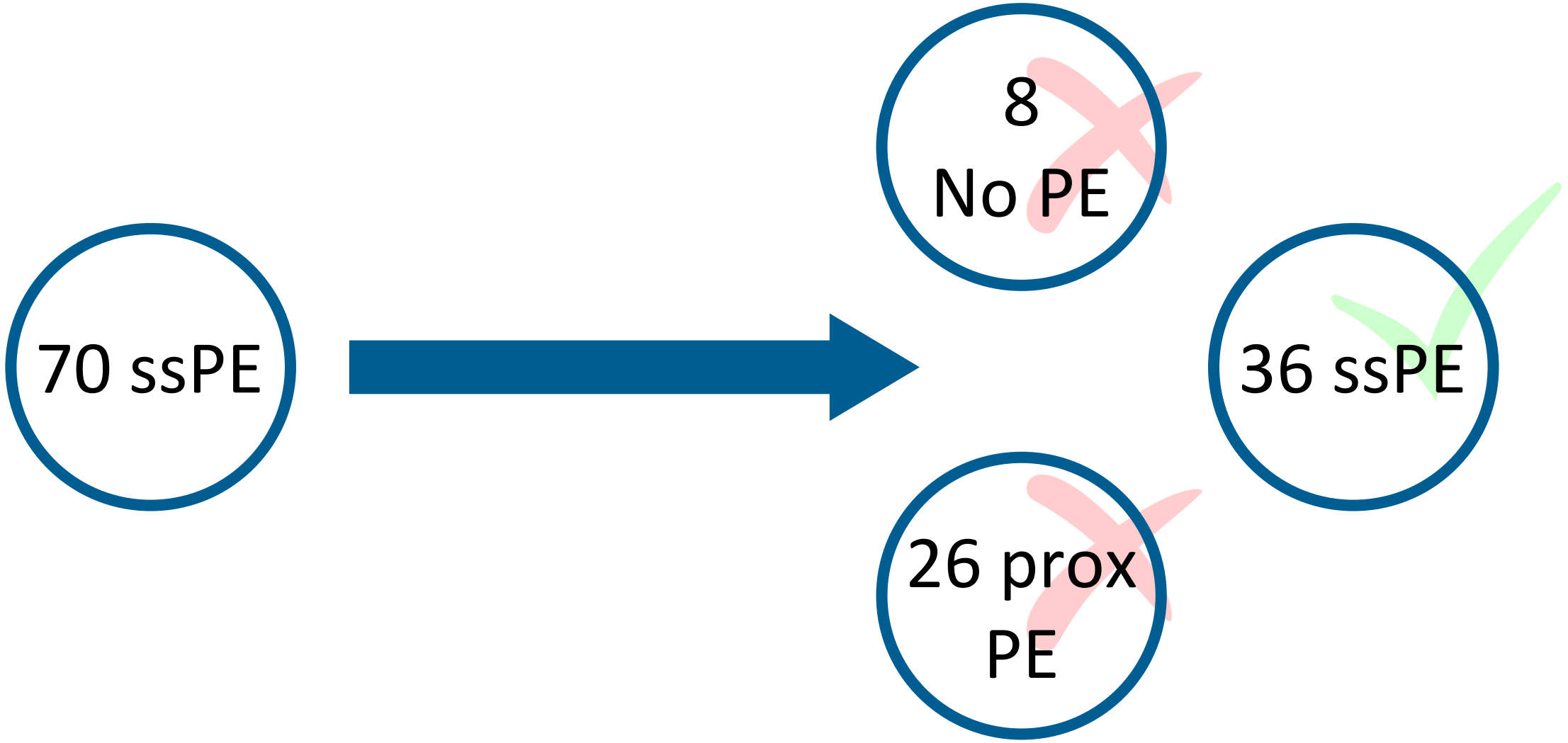
ESC guideline 2019

Reasonable approach

Subsegmental PE?

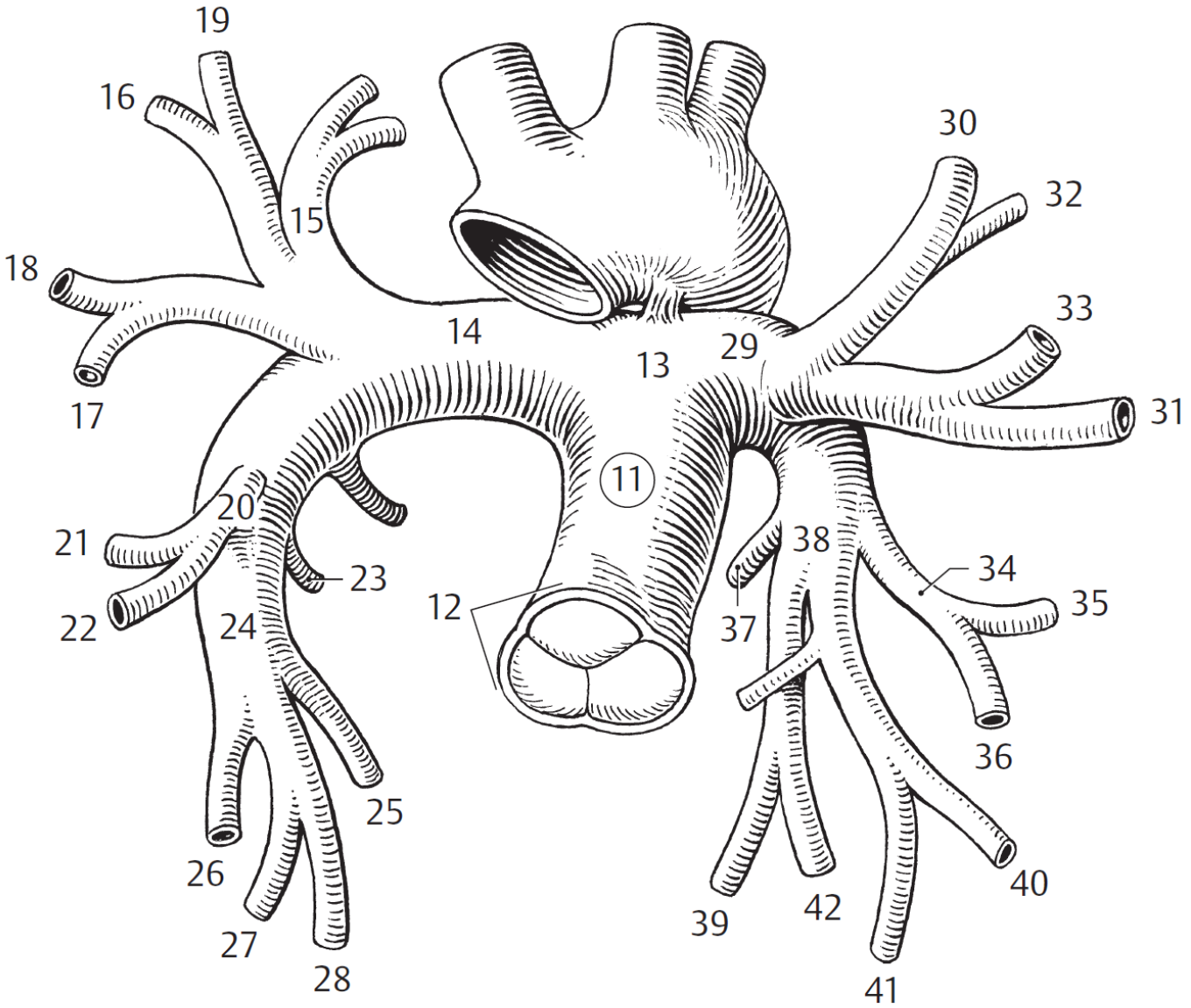
- ✓ Check with expert radiologist to confirm
- ✓ Assess risk factors of bleeding and recurrence
- ✓ Consider surveillance over anticoagulation if low risk subsegmental PE and no DVT

Poor interobserver agreement



Pena E *et al*, J Thromb Haemost 2012

Pulmonary artery anatomy



Hypothesis: definition of subsegmental PE

1. Anatomical location
2. Artery diameter
3. Technical quality of the scan

den Exter *et al,* Res Pract Thromb Haemost 2020

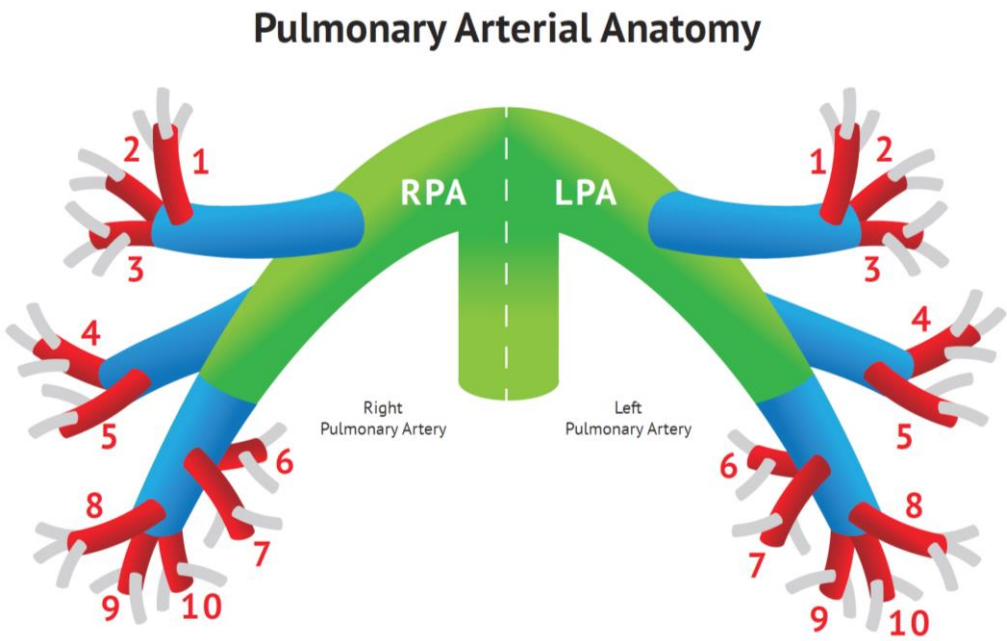
Delphi analysis

- ✓ Selection of experts based on publication records
- ✓ Multiple choice questions based on hypothesis
- ✓ As many rounds as needed to achieve >70% consensus

den Exter *et al,* Res Pract Thromb Haemost 2020

First Delphi round (radiological experts)

- ✓ 27/40 consented to participate
- ✓ 12 countries, most affiliated to Fleischner Society
- ✓ Consensus reached after 2 rounds



den Exter *et al,* Res Pract Thromb Haemost 2020

Most notable results

77%: diameter does not contribute

88%: definition only based on anatomical location

78%: filling defect visible in >1 subsequent axial slices

den Exter *et al,* Res Pract Thromb Haemost 2020

Most notable results

89%: desired max. reconstructed slice thickness is ≤1mm.

70%: perfusion imaging mostly does not contribute

93%: reading approach is systematically from center to periphery per lobe/segment

den Exter *et al,* Res Pract Thromb Haemost 2020

Final definition

A contrast defect in a subsegmental artery, i.e. the **first arterial branch division of any segmental artery** independent of artery diameter, **visible in at least two subsequent axial slices**, using a CT scanner with a **desired maximum collimator width of ≤1mm**

96%

den Exter *et al,* Res Pract Thromb Haemost 2020

Specific recommendations with consensus

- ✓ Presence of substantial motion artefacts should be excluded, preferable in the ‘lung window’
- ✓ Reviewer should make sure that contrast resolution is sufficient to identify contrast defects in the subsegmental level
- ✓ “Isolated subsegmental pulmonary embolism” refers to subsegmental pulmonary embolism in one subsegmental artery

96%

den Exter *et al,* Res Pract Thromb Haemost 2020

Second Delphi round (clinical experts)

- ✓ 40/51 consented to participate
- ✓ 11 countries
- ✓ Consensus reached after 2 rounds

den Exter *et al,* Res Pract Thromb Haemost 2020

Second Delphi round (clinical experts)

- ✓ Agreement on definition: **83%**
- ✓ Agreement on recommendation: **79%**

den Exter *et al,* Res Pract Thromb Haemost 2020

Second Delphi round (clinical experts)

✓ Agreement on treating ssPE in following circumstances (**>70%**)

✓ Agreement on not treating incidental ssPE in absence of these circumstances (**76%**)

den Exter *et al,* Res Pract Thromb Haemost 2020

Other notable results

95%: preferred drug class same as for proximal PE

77%: treatment duration same as for proximal PE

90%: Bleeding risk carries a greater weight in discontinuation AC than for proximal PE

den Exter *et al,* Res Pract Thromb Haemost 2020

Conclusion

- ✓ Radiological criteria for ssPE that can be applied both in clinical trials and practice
- ✓ Broad consensus among international experts
- ✓ Overview of best practice of ssPE management

den Exter *et al,* Res Pract Thromb Haemost 2020