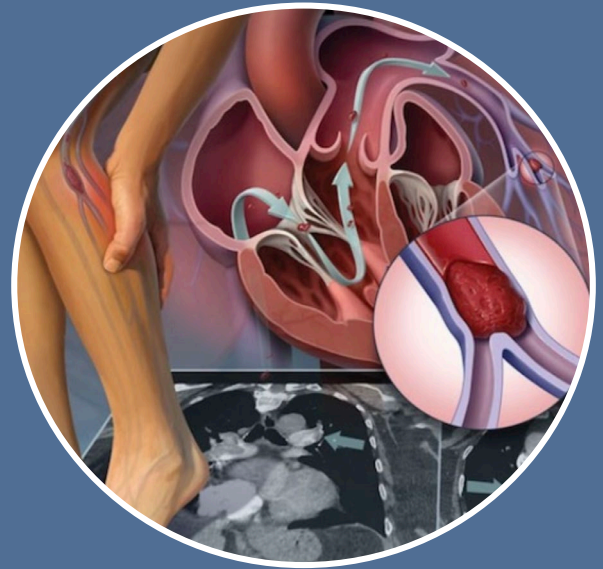


Overview of Diagnosis in Pulmonary Embolism



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Achieving Excellence in the Diagnosis of
Acute Cardiovascular Events:
A Virtual Workshop
April 23, 2021

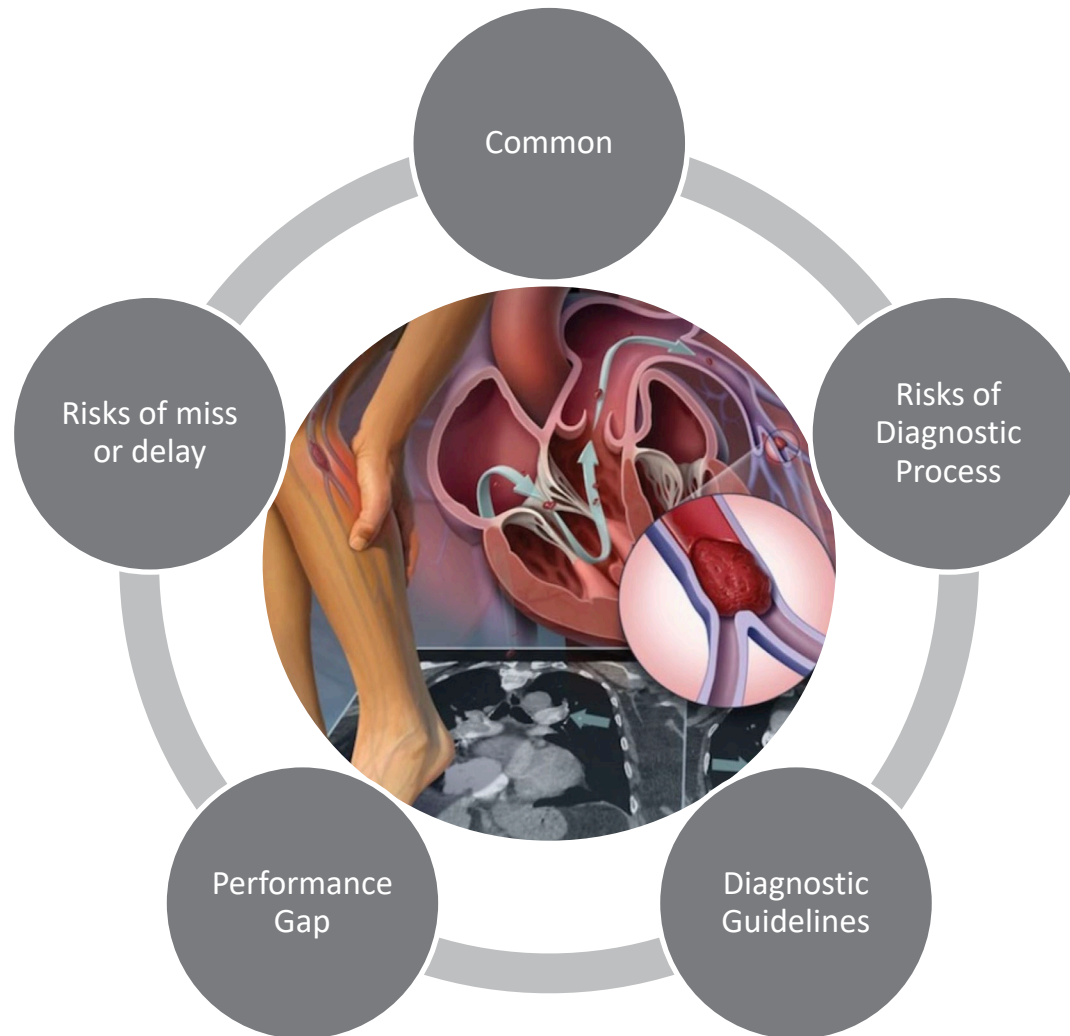
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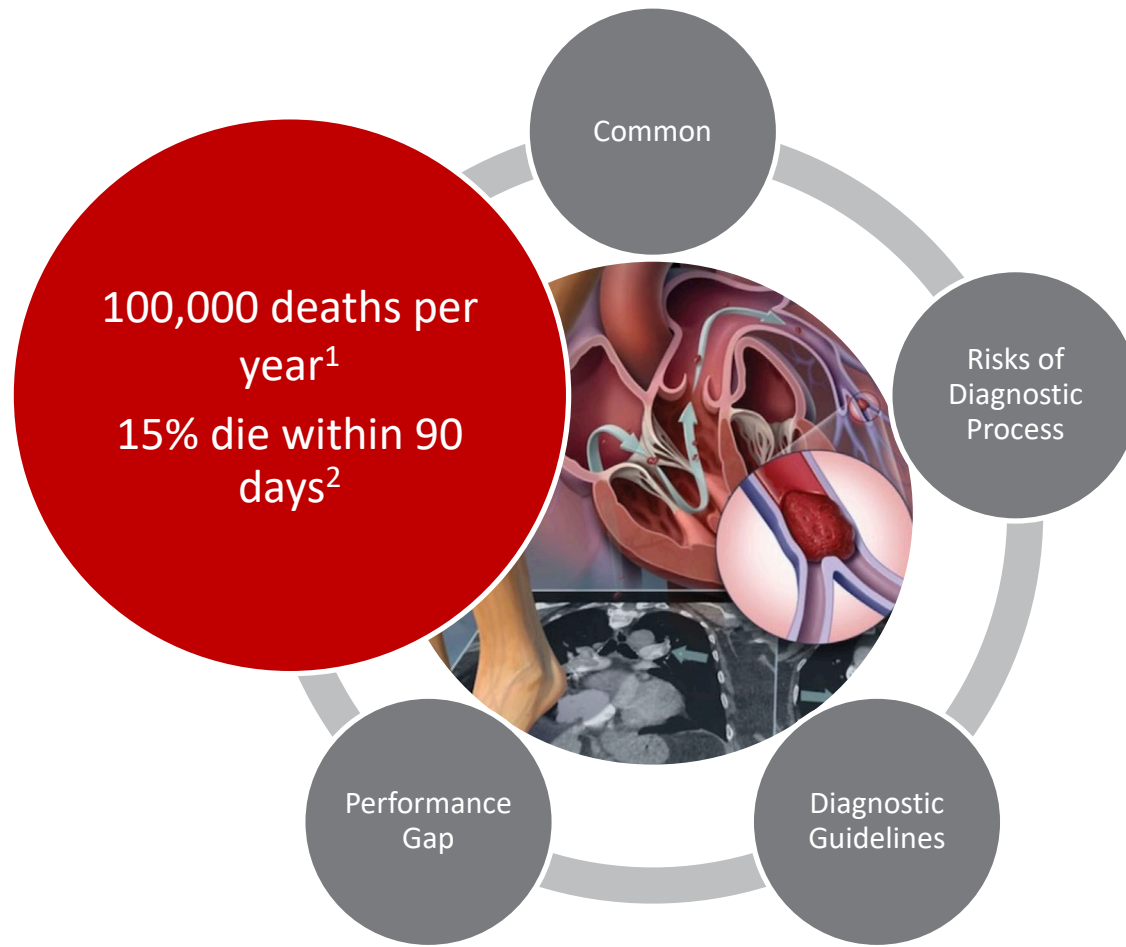
Disclosure

- I am currently funded by the Gordon and Betty Moore Foundation
- Project: Composite measure of diagnostic performance for Pulmonary Embolism
- Funding period: 12/19 – 12/22
- Yale Funding ID 20-002043
- Originating Sponsor Award Number AWD0004016

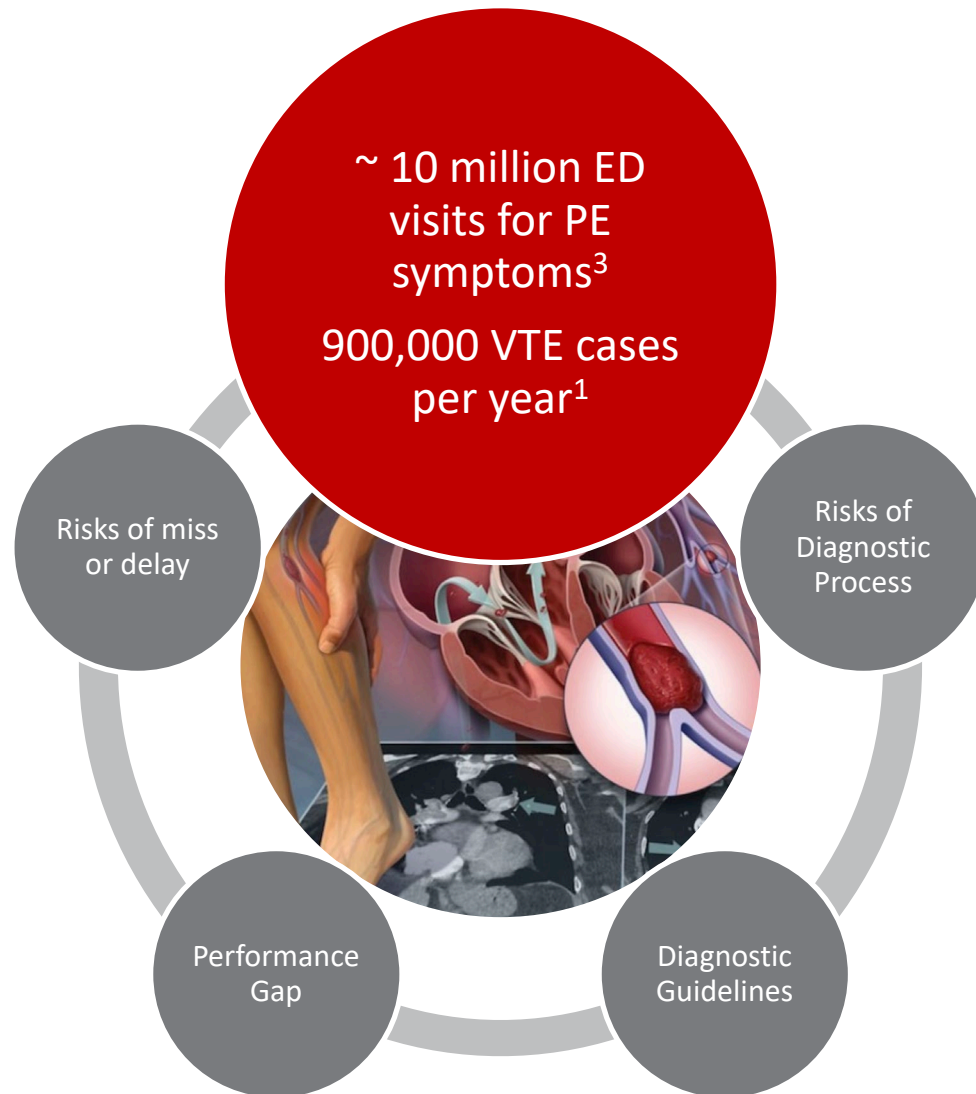
Pulmonary Embolism: Ideal test case



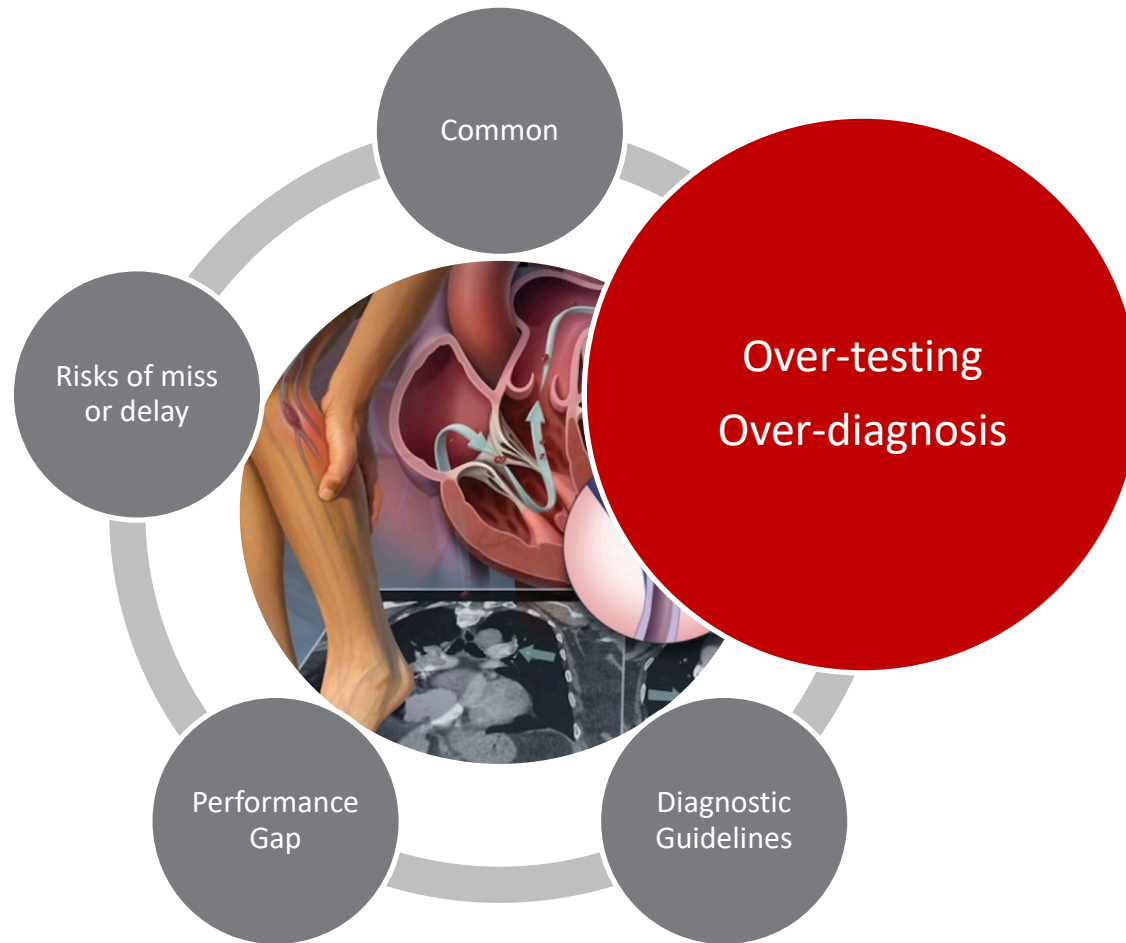
Pulmonary Embolism: Risk of miss/delay



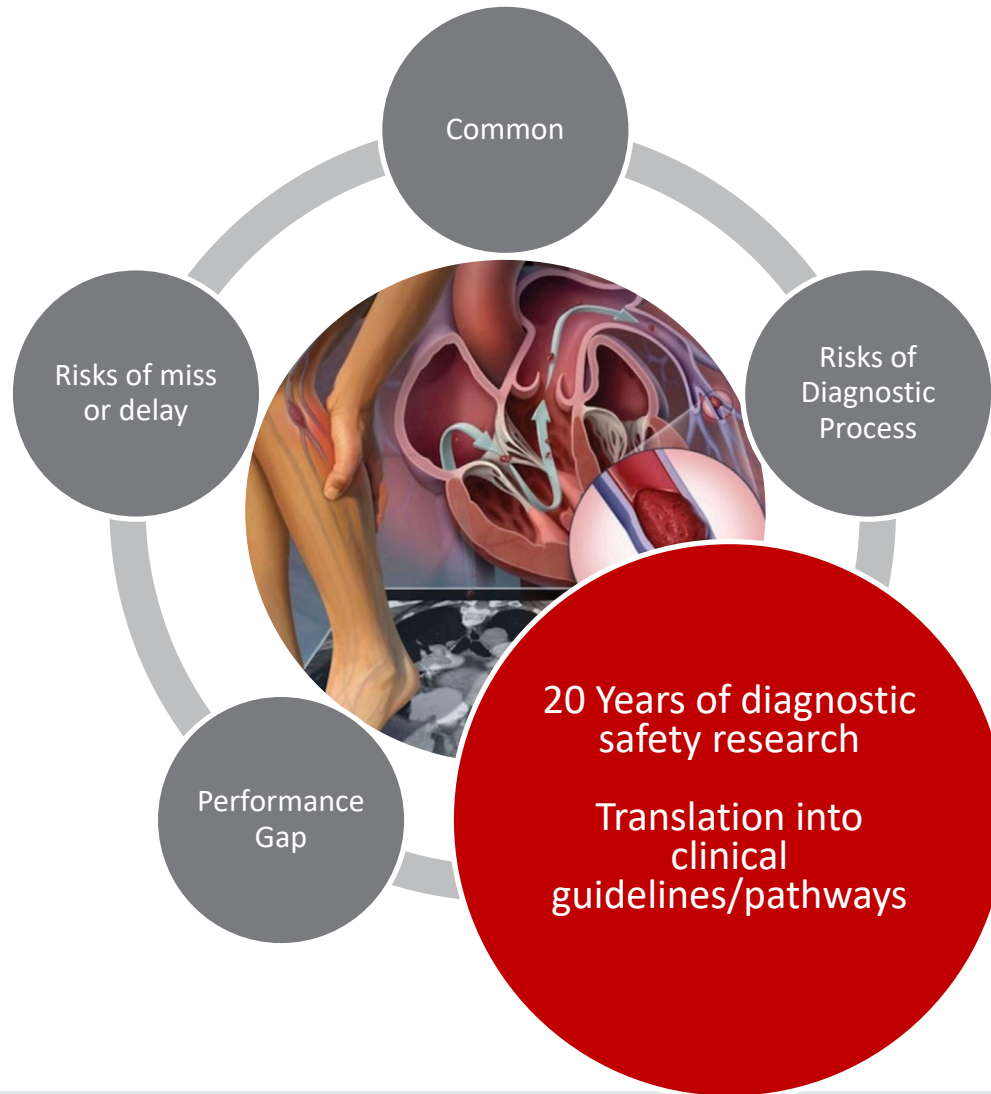
Pulmonary Embolism: Common



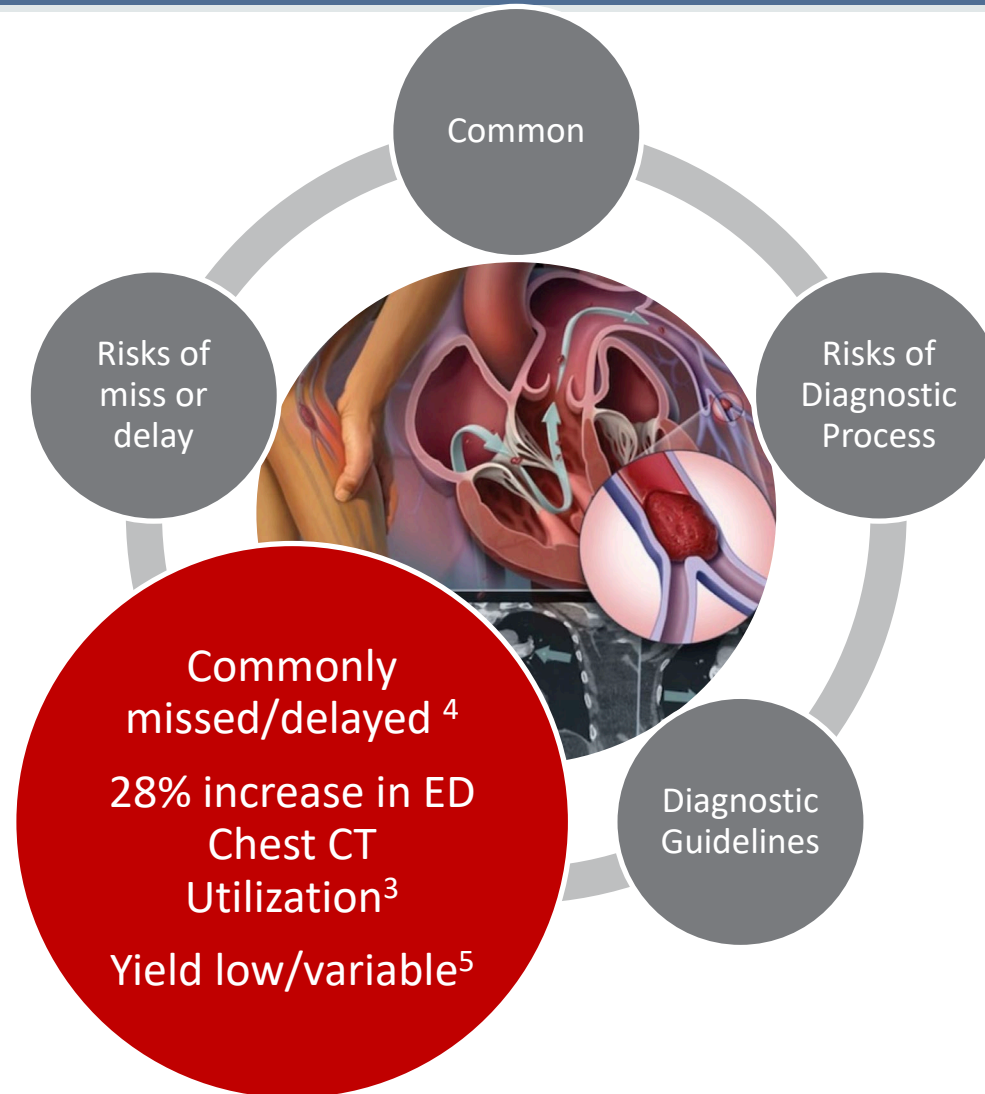
Pulmonary Embolism: Risk of diagnostic process



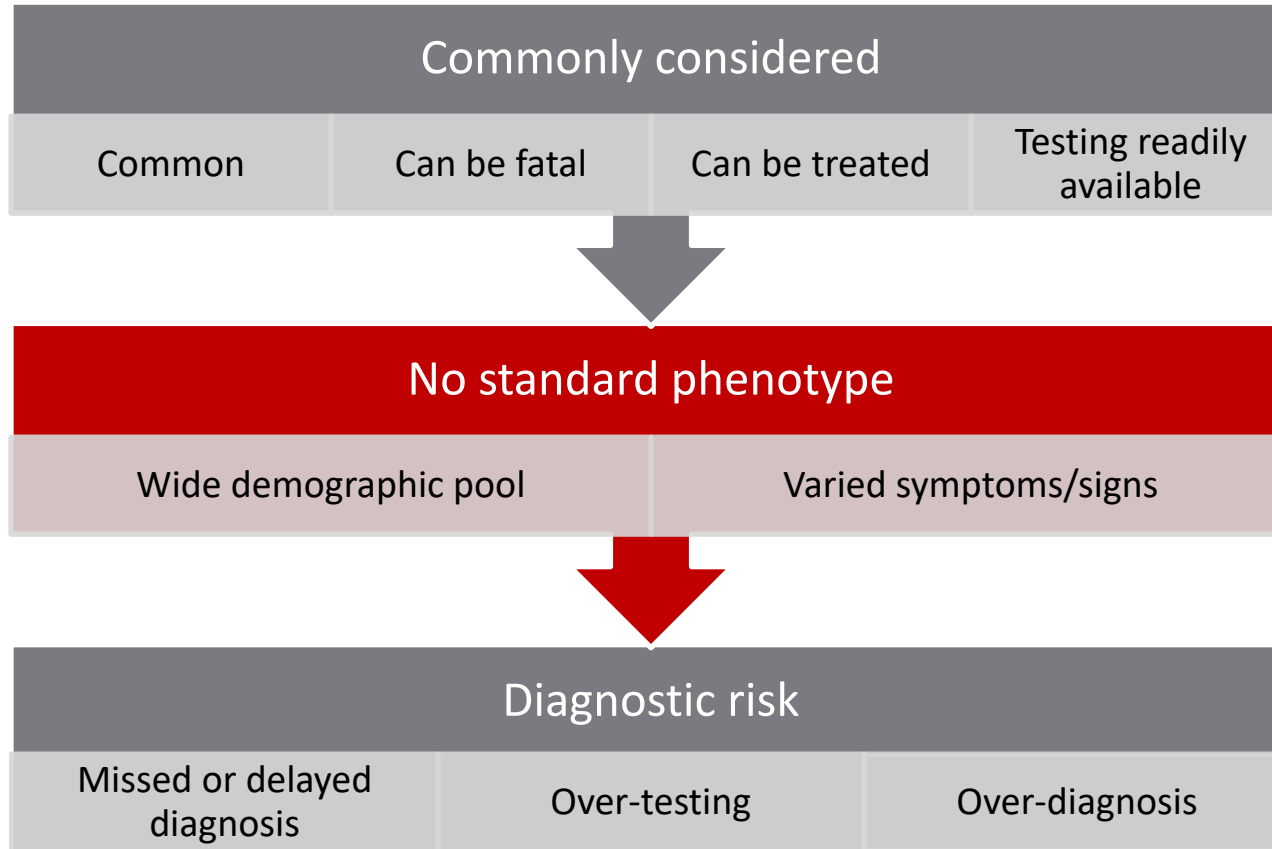
Pulmonary Embolism: Science



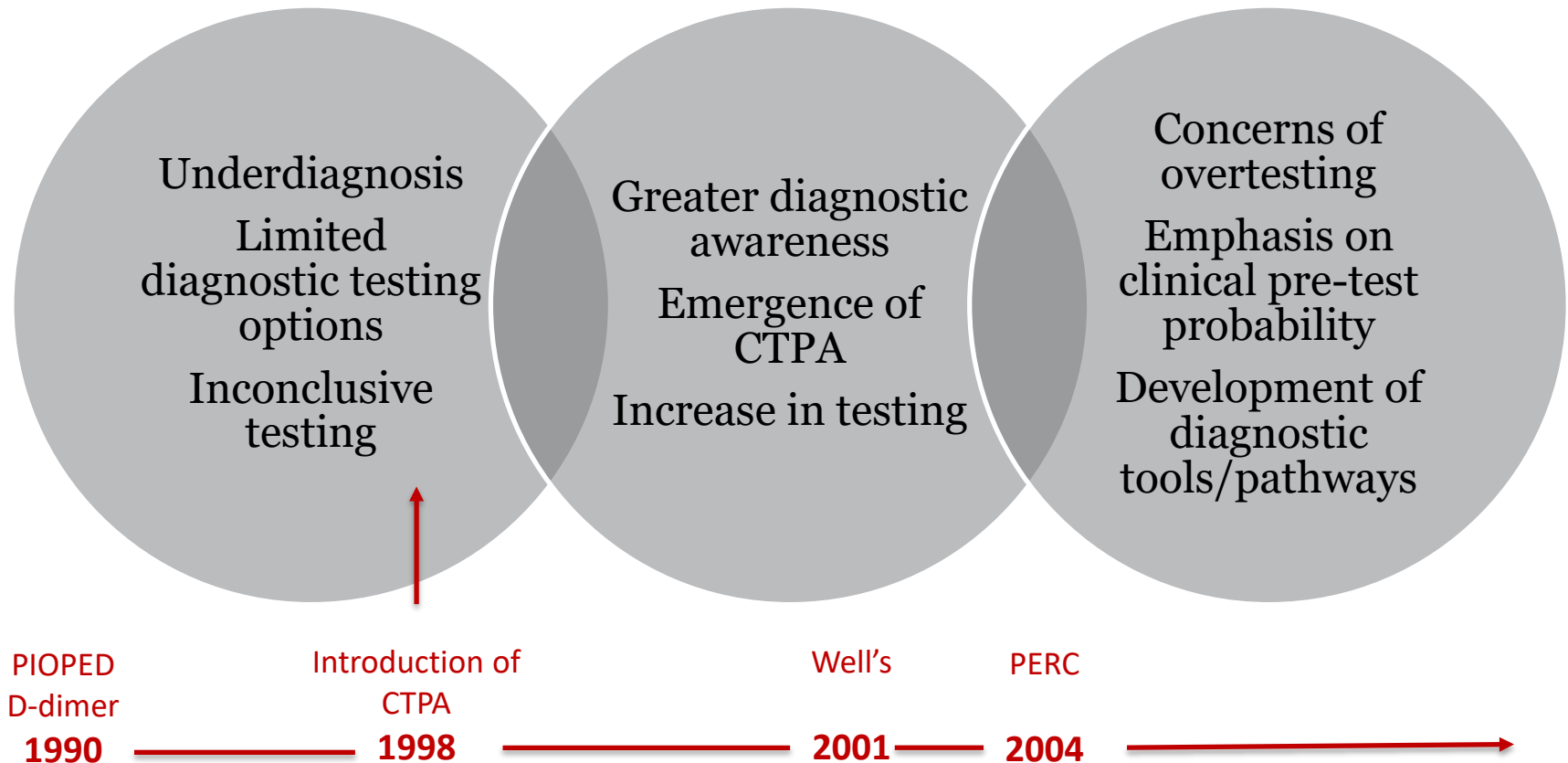
Pulmonary Embolism: Performance Gap



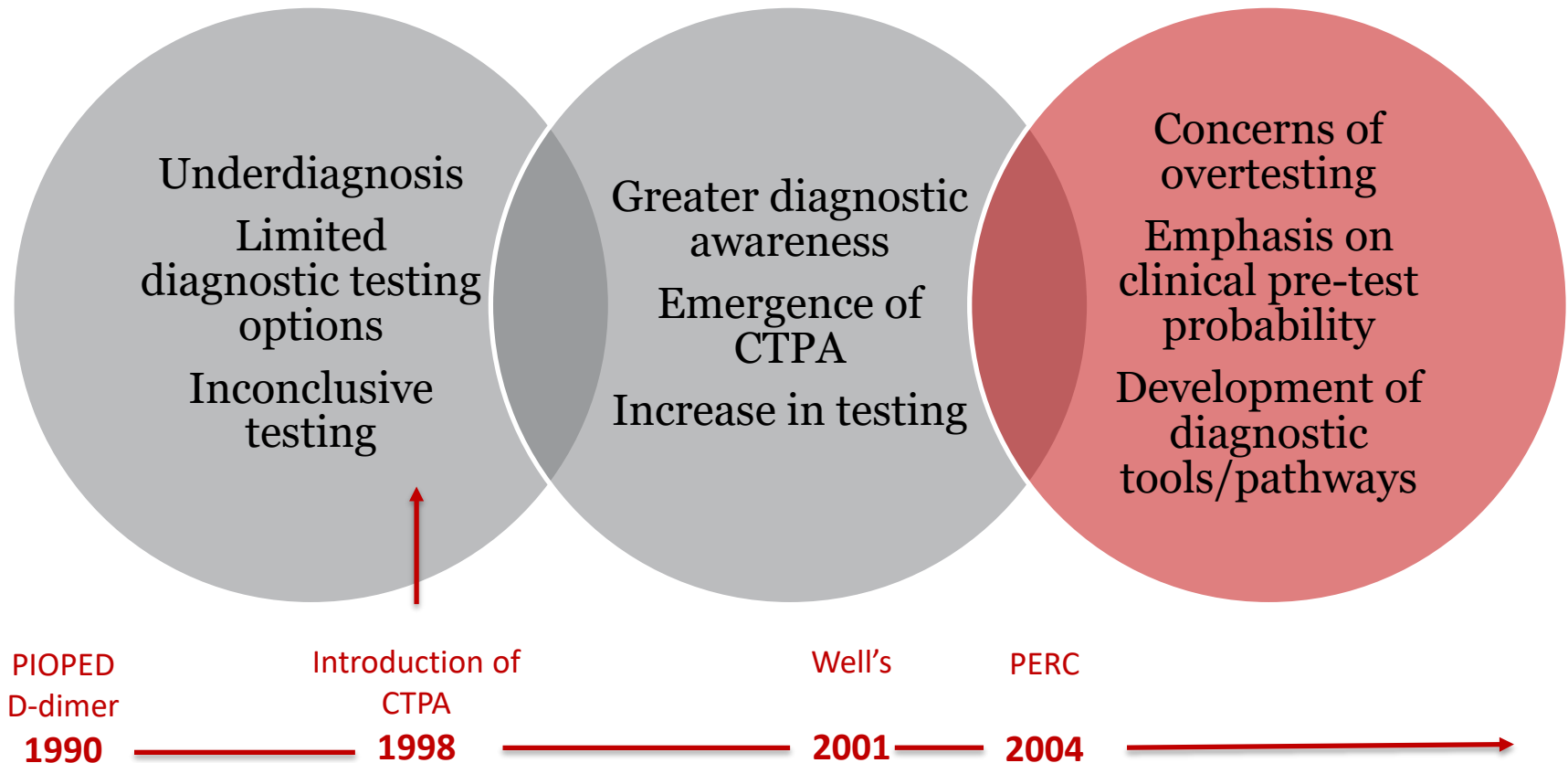
Why is PE diagnosis challenging?



Historical Context – 30 years of progress



Historical Context – 30 years of progress



Fundamental Lesson

- Equipoise in diagnosis
- To consider PE \neq test for PE
- If PE is considered, a clinical pre-test probability is assigned (Bayesian reasoning)
- When pre-test probability is lower than the test threshold, risk of harm from testing is greater than benefit from testing
- Accuracy is not the sole measure of diagnostic performance
- Diagnostic safety can only be optimized through this lens
- A large body of science has translated into clinical practice with respect of PE diagnosis

Probability assessment – PE Rule-out Criteria (PERC)⁶

Age ≥ 50	No 0	Yes +1
HR ≥ 100	No 0	Yes +1
O ₂ sat on room air <95%	No 0	Yes +1
Unilateral leg swelling	No 0	Yes +1
Hemoptysis	No 0	Yes +1
Recent surgery or trauma Surgery or trauma ≤ 4 weeks ago requiring treatment with general anesthesia	No 0	Yes +1
Prior PE or DVT	No 0	Yes +1
Hormone use Oral contraceptives, hormone replacement or estrogenic hormones use in males or female patients	No 0	Yes +1

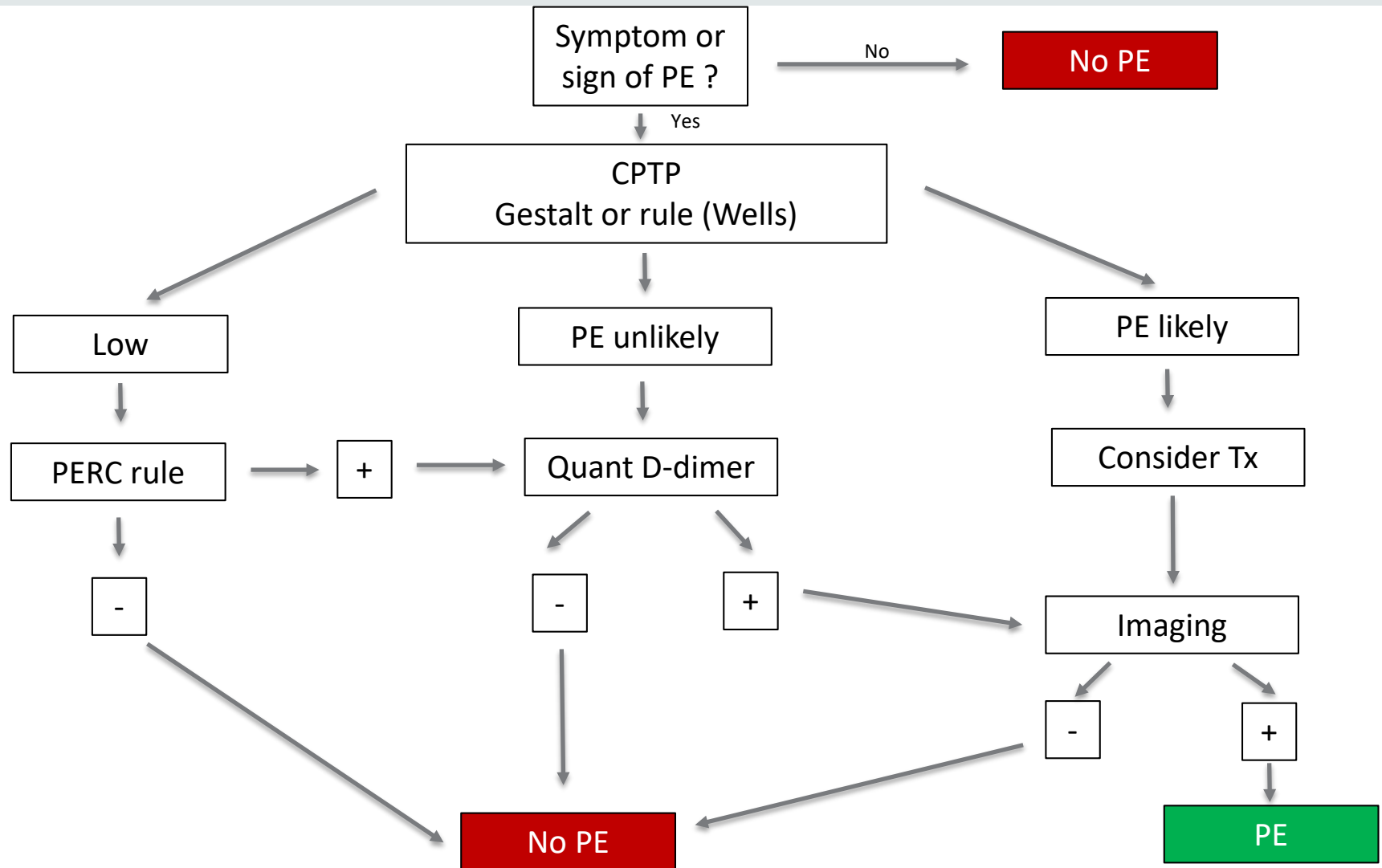
Probability assessment– Wells Criteria⁷

Clinical signs and symptoms of DVT	No 0	Yes +3
PE is #1 diagnosis OR equally likely	No 0	Yes +3
Heart rate > 100	No 0	Yes +1.5
Immobilization at least 3 days OR surgery in the previous 4 weeks	No 0	Yes +1.5
Previous, objectively diagnosed PE or DVT	No 0	Yes +1.5
Hemoptysis	No 0	Yes +1
Malignancy w/ treatment within 6 months or palliative	No 0	Yes +1

Two Tier Model

- Patient risk is determined to be “PE Unlikely” (0-4 points, 12.1% incidence of PE): consider high sensitivity d-dimer testing.
 - If the dimer is negative consider stopping workup.
 - If the dimer is positive consider CTA.
- Patient risk is determined to be “PE Likely” (>4 points, 37.1% incidence of PE): consider CTA testing.

Current diagnostic approach



Classification of PE

Classification of early mortality risk

Early mortality risk		Risk parameters and scores			
		Shock or hypotension	PESI Class III-V or sPESI ≥ 1	Signs of RV dysfunction on an imaging test	Cardiac laboratory biomarkers
High		+	(+)	+	(+)
Intermediate	Intermediate-high	-	+	Both positive	
	Intermediate-low	-	+	Either one (or none) positive	
Low		-	-	Assessment optional; if assessed, both negative	

Original and Simplified Pulmonary Embolism Severity Index (PESI)				
Variable		Score		
		Original PESI	Simplified PESI	
Age		Age in years	Age $\geq 80 = 1$	
Male sex		+10		
History of cancer		+30	1	
History of heart failure*		+10	1*	
History of chronic lung disease*		+10	1*	
Pulse ≥ 110 beats/min		+20	1	
Systolic blood pressure < 100 mm Hg		+30	1	
Respiratory rate ≥ 30 breaths/min		+20		
Temperature $< 36^{\circ}\text{C}$		+20		
Altered mental status		+60		
Oxygenation saturation $< 90\%$		+20	1	
PESI Score			SPESI ≥ 1 point warrants consideration of inpatient therapy	
Score	Class	30 day mortality		
< 65	I	0-1.6%		
66-85	II	1.7%-3.5%		
86-105	III	3.2%-7.1%		
106-125	IV	4.0%-11.4%		
> 125	V	10.0%-24.5%		

*The combination of heart failure and chronic lung disease defines cardiopulmonary disease

Challenge – Cognitive errors

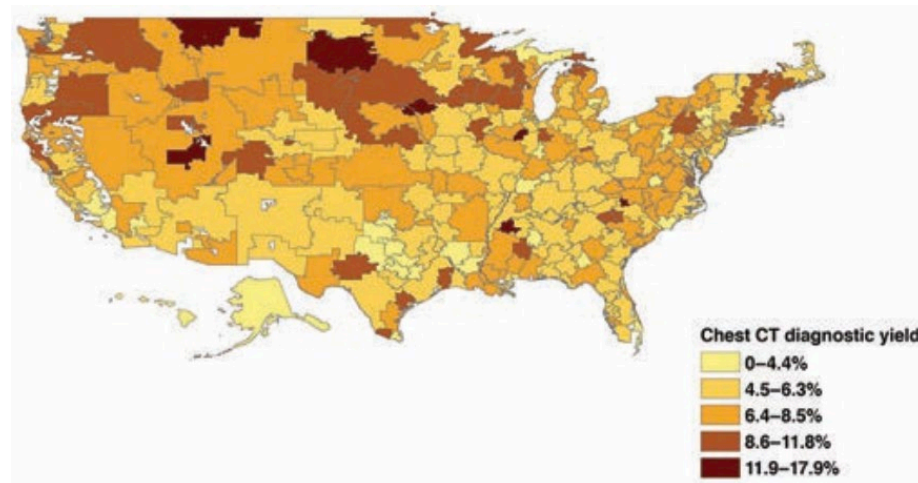
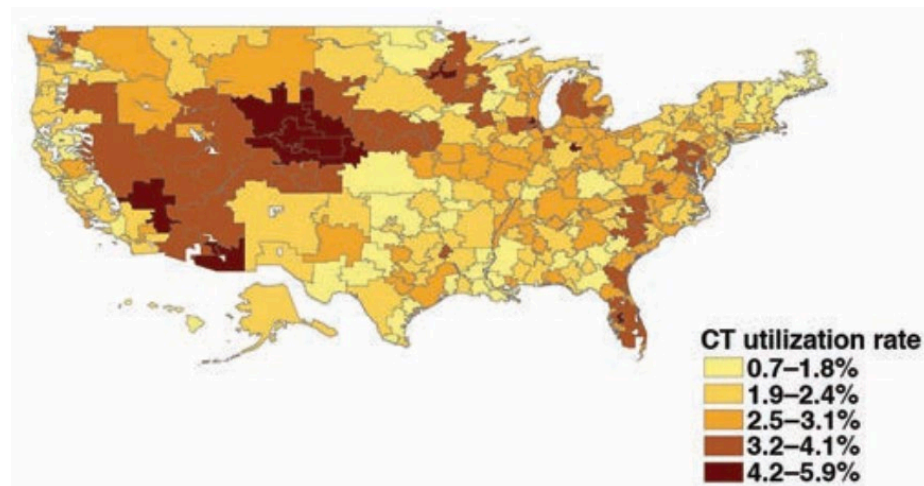
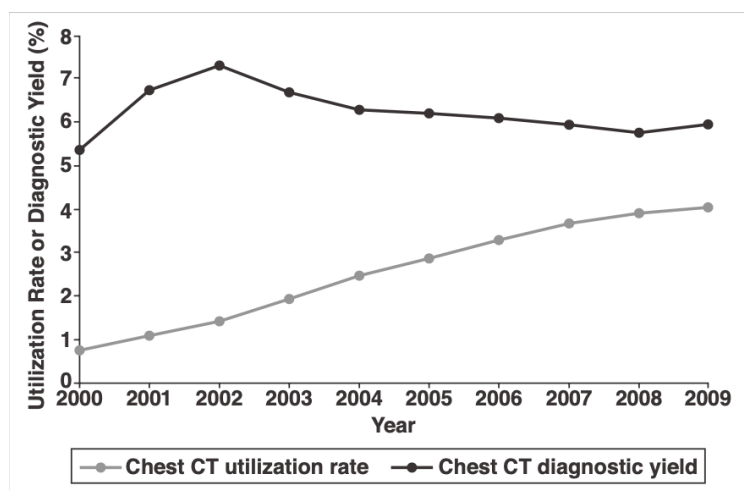
Missed or Delay Diagnosis

- Failure to consider diagnosis
- Test avoidance in select populations (pregnant)
- Missed or inaccurate classification of PE risk category

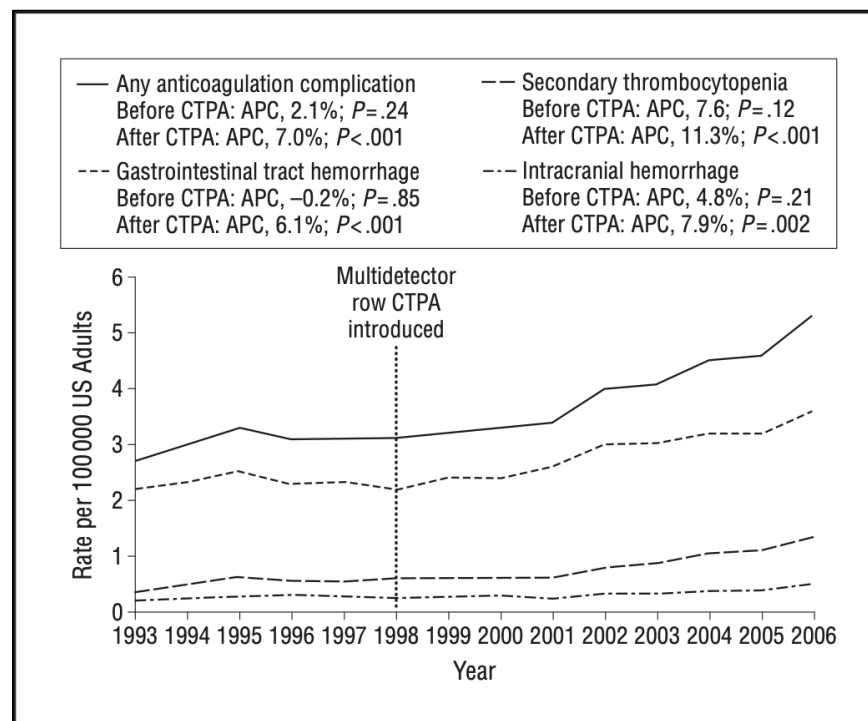
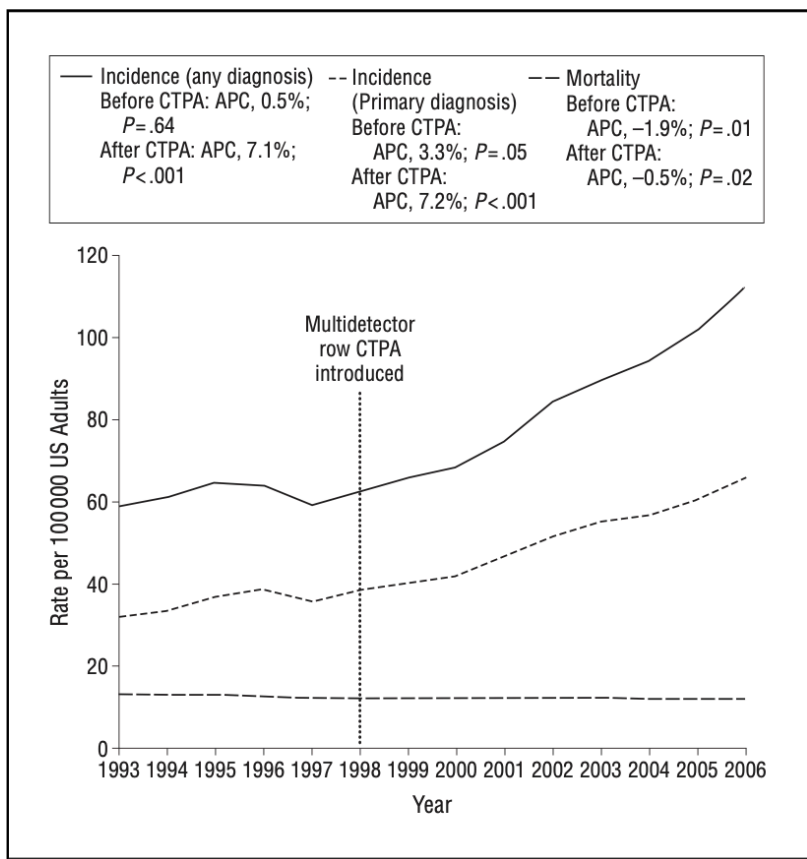
Overtesting/overdiagnosis

- Accurate assessment of clinical pre-test probability
- Knowledge/adherence to diagnostic guidelines
- Repeat testing in patients with prior PE

Challenge— Utilization and Yield of Imaging⁸



Challenge – Incidence, Mortality, Complications⁹



Challenge: Diagnostic accuracy gap

- Underdiagnosis:
 - Are we accurately diagnosing the class of PE?
 - Are we doing so in a timely manner?
 - Are we matching classification type to evidence-based therapies?
 - Thrombolytic therapy
 - Catheter directed therapies
 - Hemodynamic support
- Overdiagnosis:
 - Do subsegmental PEs warrant therapy?

Solution: Refining Pre-test probability^{10,11}

THE LANCET

Volume 390, Issue 10091, 15–21 July 2017, Pages 289–297



Articles

Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study

Tom van der Hulle MD ^a, Whitney Y Cheung MD ^c, Stephanie Kooij MD ^e, Ludo F M Beenen MD ^d, Thomas van Bommel MD ^f, Josien van Es MD ^g, Laura M Faber MD ^h, Germa M Hazelaar MD ⁱ, Christian Heringhaus MD ^b, Herman Hofstee MD ^k, Marcel M C Hovens MD ^j, Prof Karin A H Kaasjager MD ^l, Rick C J van Klink MD ^o, Marieke J H A Kruij MD ^m, Rinske F Loeffen MD ⁿ, Albert T A Mairuhu MD ^e, Prof Saskia Middeldorp MD ^c, Mathilde Nijkeuter MD ^l ... Antonio Iglesias del Sol

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JAMA Cardiology | **Original Investigation**

Derivation and Validation of a 4-Level Clinical Pretest Probability Score for Suspected Pulmonary Embolism to Safely Decrease Imaging Testing

Pierre-Marie Roy, MD, PhD; Emilie Friou, MD; Boris Germeau, MD; Delphine Douillet, MD; Jeffrey Allen Kline, MD, PhD; Marc Righini, MD, PhD; Grégoire Le Gal, MD, PhD; Thomas Moumneh, MD; Andrea Penalzoza, MD, PhD

Solution: Understanding at-risk populations

- Race
- Gender
- Vulnerable populations
 - Pregnancy
- Context
 - Outpatient
 - ED
 - Inpatient

Solution: Feedback and measure development

- Balanced measures to enhance performance
 - Accuracy
 - Overall
 - Classification of PE type
 - Utilization
 - Yield
- Leveraging IT and machine learning
 - Enhance risk assessment pre-diagnosis; augment gestalt
 - Promote guideline adherence
 - Define risk post-diagnosis

Summary

In many ways, 20 years of cumulative science examining the optimal diagnostic approach to pulmonary embolism illuminates the current diagnostic quality chasm for a wide spectrum of diseases.

By balancing the risk of missed diagnosis with the risk of testing and overdiagnosis, this science highlights the importance of a holistic approach to diagnostic safety.

Future initiatives should refine diagnostic pathways, develop balanced measures to enhance performance, and harness technology to complement clinician gestalt.

As cutting-edge treatments for high-risk PE continue to develop, careful attention diagnostic performance with respect to the timely risk classification holds the promise to decrease in mortality associated with PE.

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