NIHR CRSU

Complex Reviews Support Unit

Diagnostic Test Accuracy (DTA) Meta-analysis

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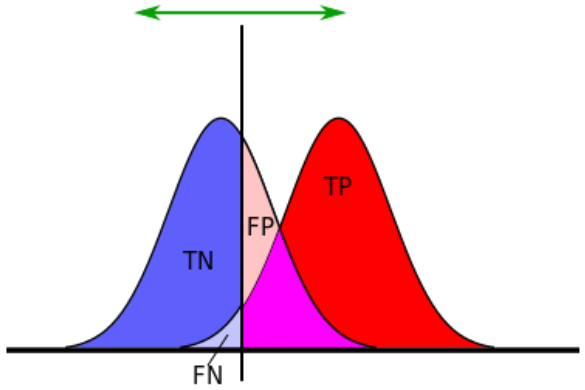
Sensitivity and Specificity

	Subject Positive	Subject Negative
Test Positive	True positive	False Positive
Test Positive	False Negative	True Negative

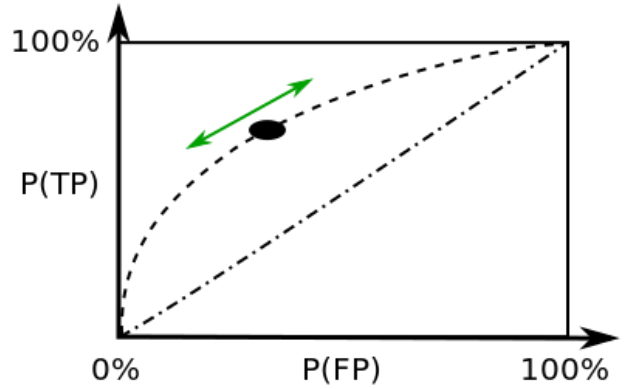
Sensitivity (probability of detection) = Prob. True Positive / Prob. Positive

Specificity (True negative rate) = Prob. True Negative / Prob Negative

Receiver Operator Curves (ROC)
Shows variation of sensitivity and specificity with test threshold



TP	FP
FN	TN



Sensitivity

Specificity

https://en.wikipedia.org/wiki/Receiver_operating_characteristic

An example Diagnostic Test Accuracy Review

Review

Cerebrovascular Diseases

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Diagnostic Accuracy of CT Perfusion Imaging for Detecting Acute Ischemic Stroke: A Systematic Review and Meta-Analysis

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Methodology

- Bivariate approach simultaneously models the sensitivity and specificity from studies, thereby incorporating any correlation [at the study level] that might exist
- Random effects approach allows for heterogeneity beyond chance due to clinical and methodological differences between studies.
- Covariates were added to the bivariate model to examine whether sensitivity and/or specificity were different depending on specific study characteristics.

Meta-Analysis of Sensitivity and Specificity

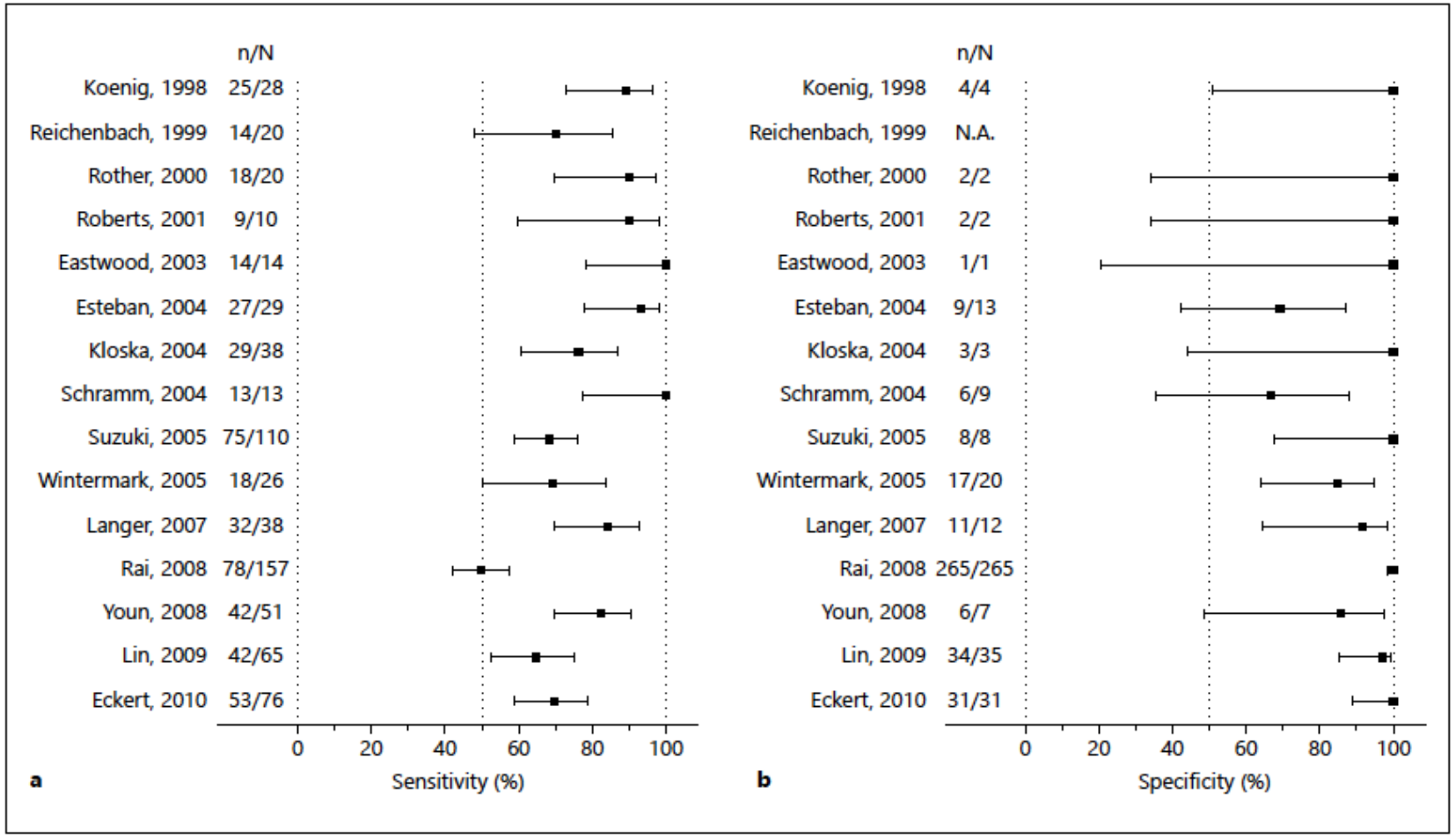


Fig. 2. a Sensitivity of CTP for detecting ischemic stroke. n = Number of true positives; N = number of true positives + number of false negatives. **b** Specificity of CTP for detecting ischemic stroke. n = Number of true negatives; N = number of true negatives + number of false positives.

Meta “ROC” plots

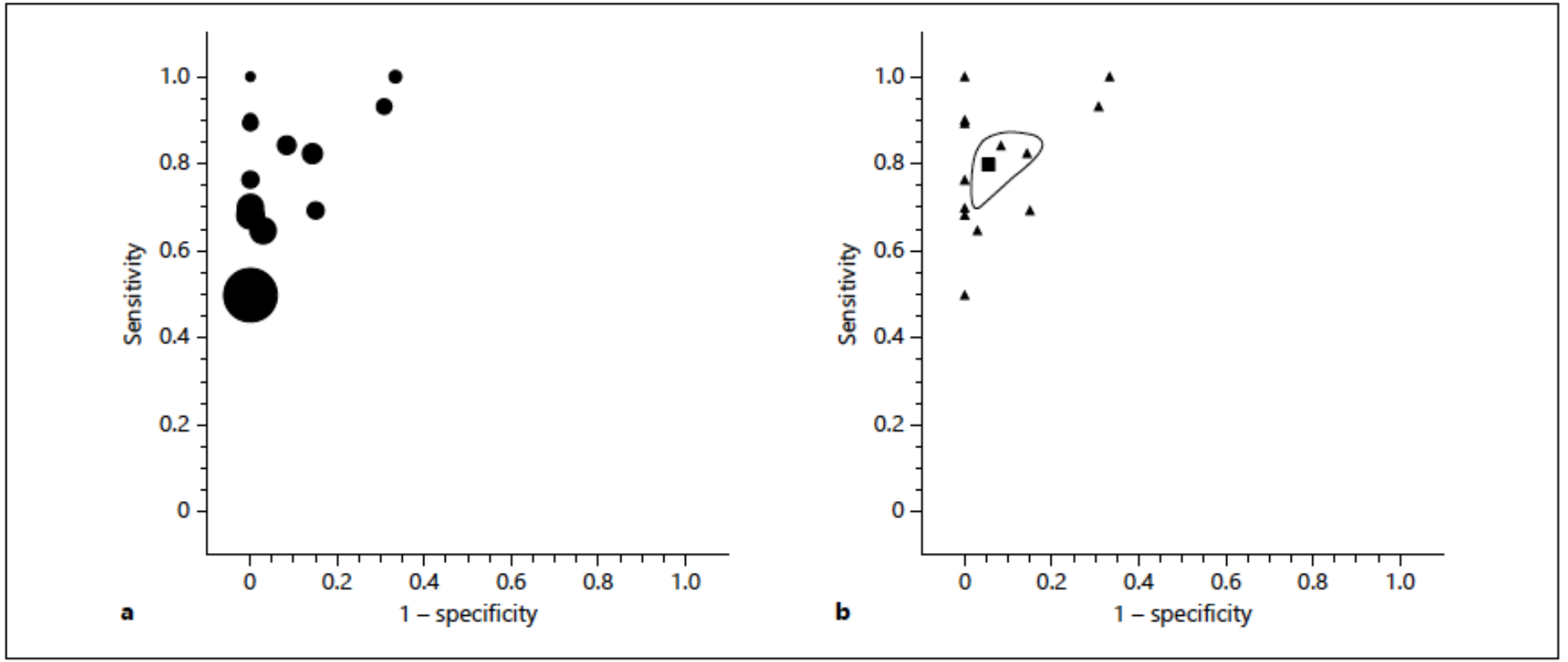


Fig. 3. a Diagnostic accuracy of the included studies for detecting ischemic stroke. The circle size represents the sample size of the corresponding study. **b** 95% confidence ellipse around mean sensitivity and specificity, which is represented by the square. The triangles represent the sensitivity and specificity of each included study.

Sensitivity Analyses

Table 3. Pooled analyses

	Studies	Patients	Sensitivity, % (95% CI)	Specificity, % (95% CI)
All studies	15	1,107	80 (72–86)	95 (86–98)
Prospective study design	8	309	85 (75–92)	97 (77–100)
<6 h between symptom onset and CTP acquisition	8	357	83 (73–90)	94 (76–99)
After exclusion FN due to limited coverage	13	536	89 (81–94)	90 (79–96)

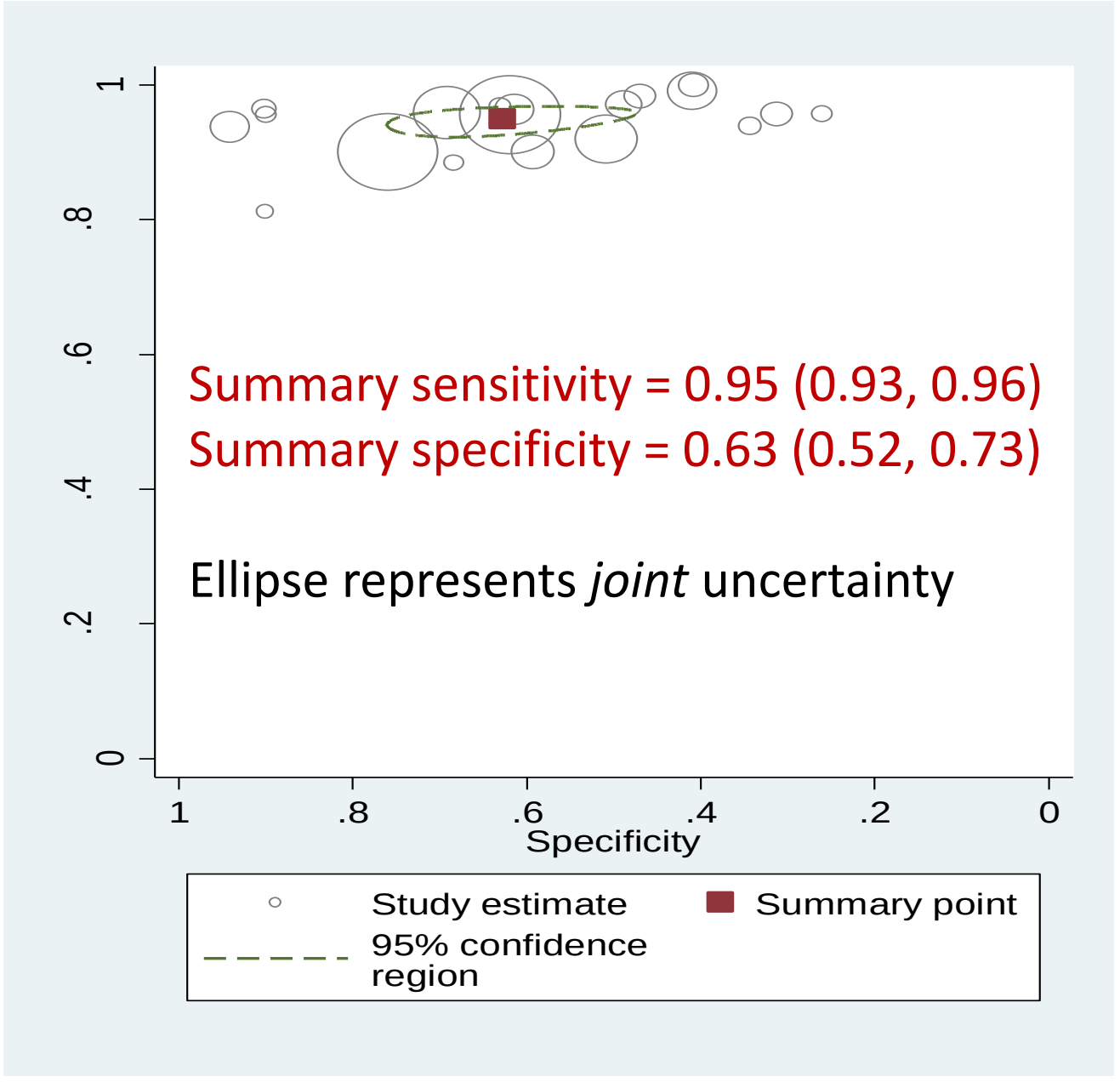
FN = False negatives.

Conclusions

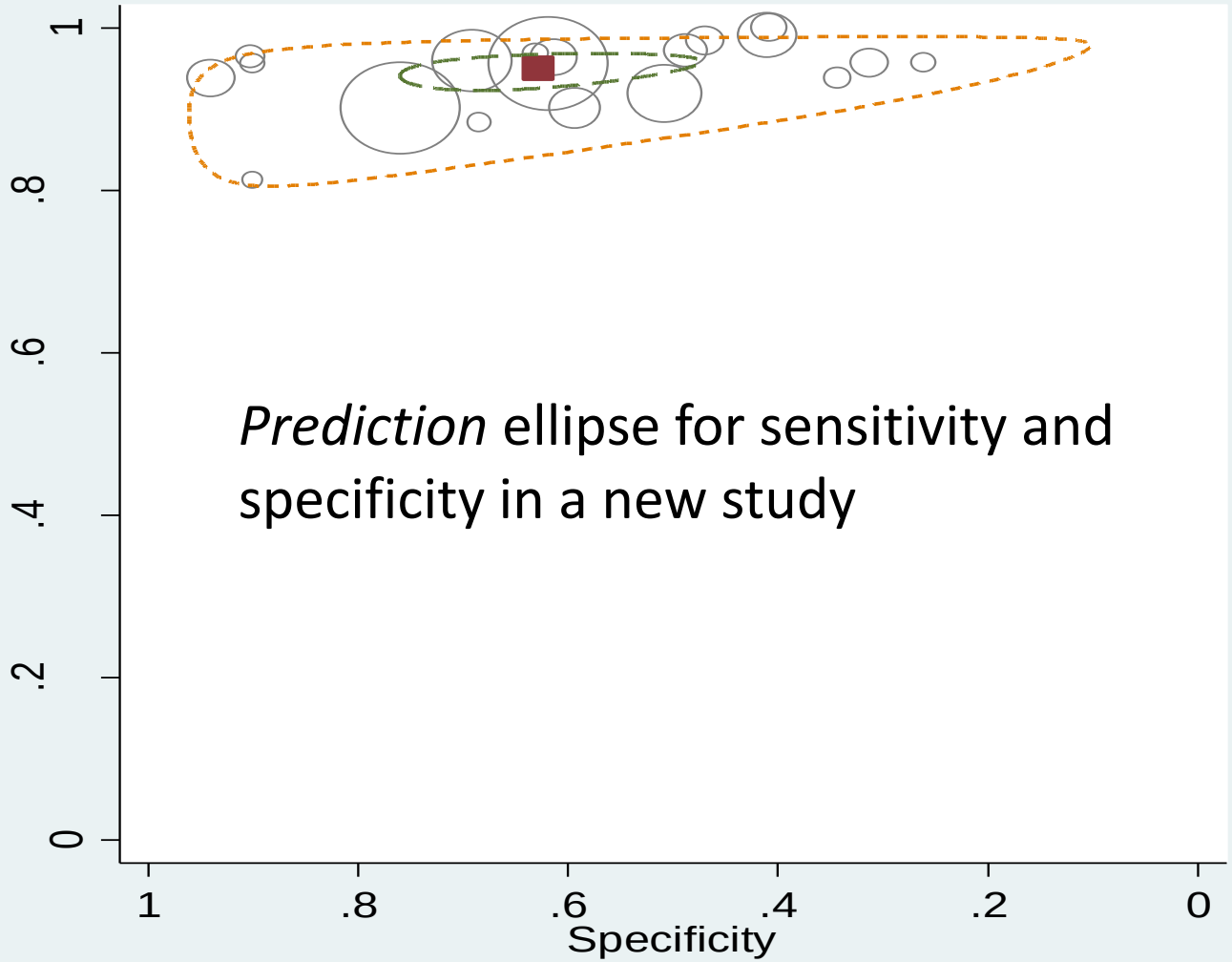
- CTP has a very high specificity and a high sensitivity for the diagnosis of ischemic stroke
- False negatives mainly occurred in cases of small lacunar infarcts. Other causes for false negatives were limited brain coverage and motion artifacts.
- The sensitivity of CTP varied considerably between studies, which is probably due to the heterogeneity in:
  - proportion of patients with lacunar infarcts varied between studies
  - maximum time between symptom onset and CTP scan acquisition varied between studies.
  - Proportion of patients with a confirmed diagnosis of ischemic stroke ranged from 37 to 100%,
  - coverage and temporal resolution of CTP imaging varied between studies
  - Post-processing of the raw CTP data

Some methodological issues

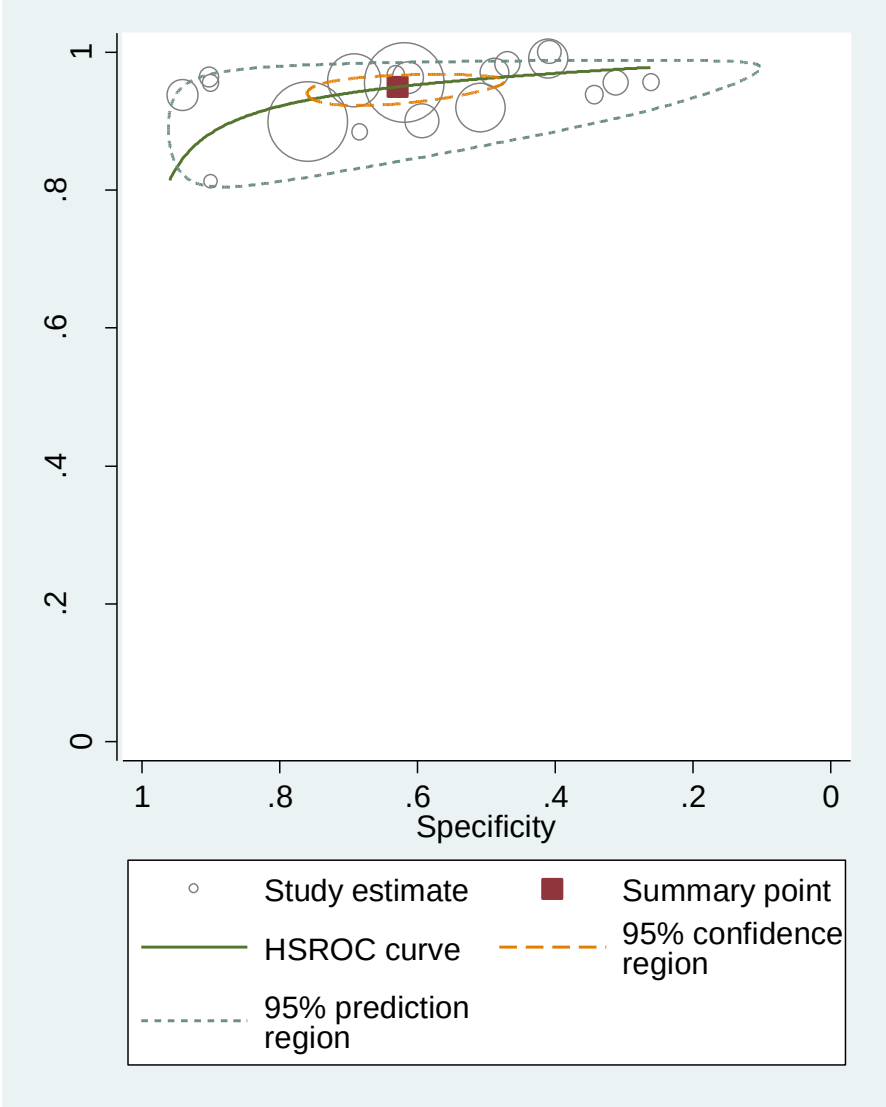
Mean Estimate from Bivariate Effects Analysis



95% prediction region



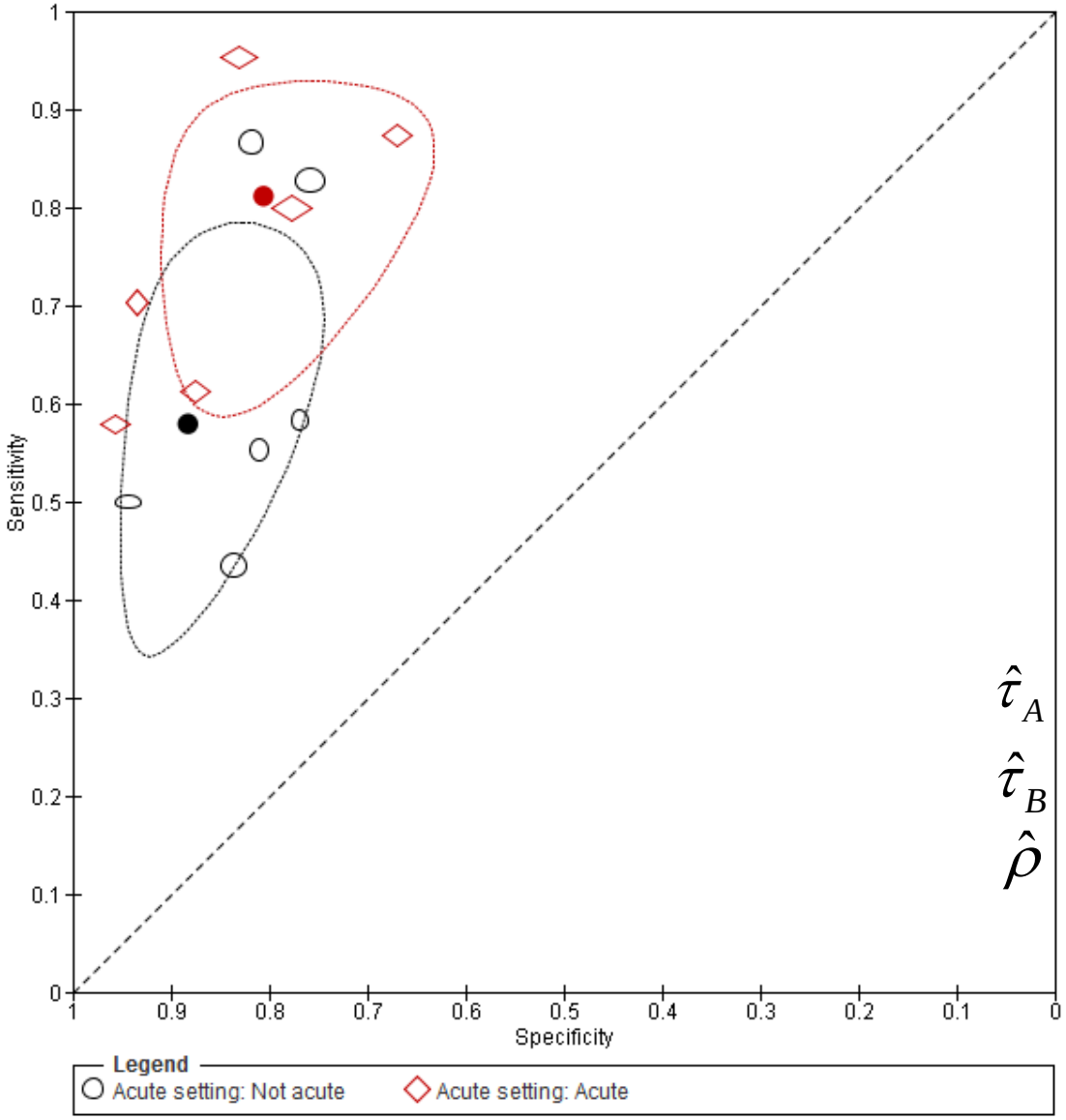
Hierarchical summary ROC (HSROC)



Exploring heterogeneity

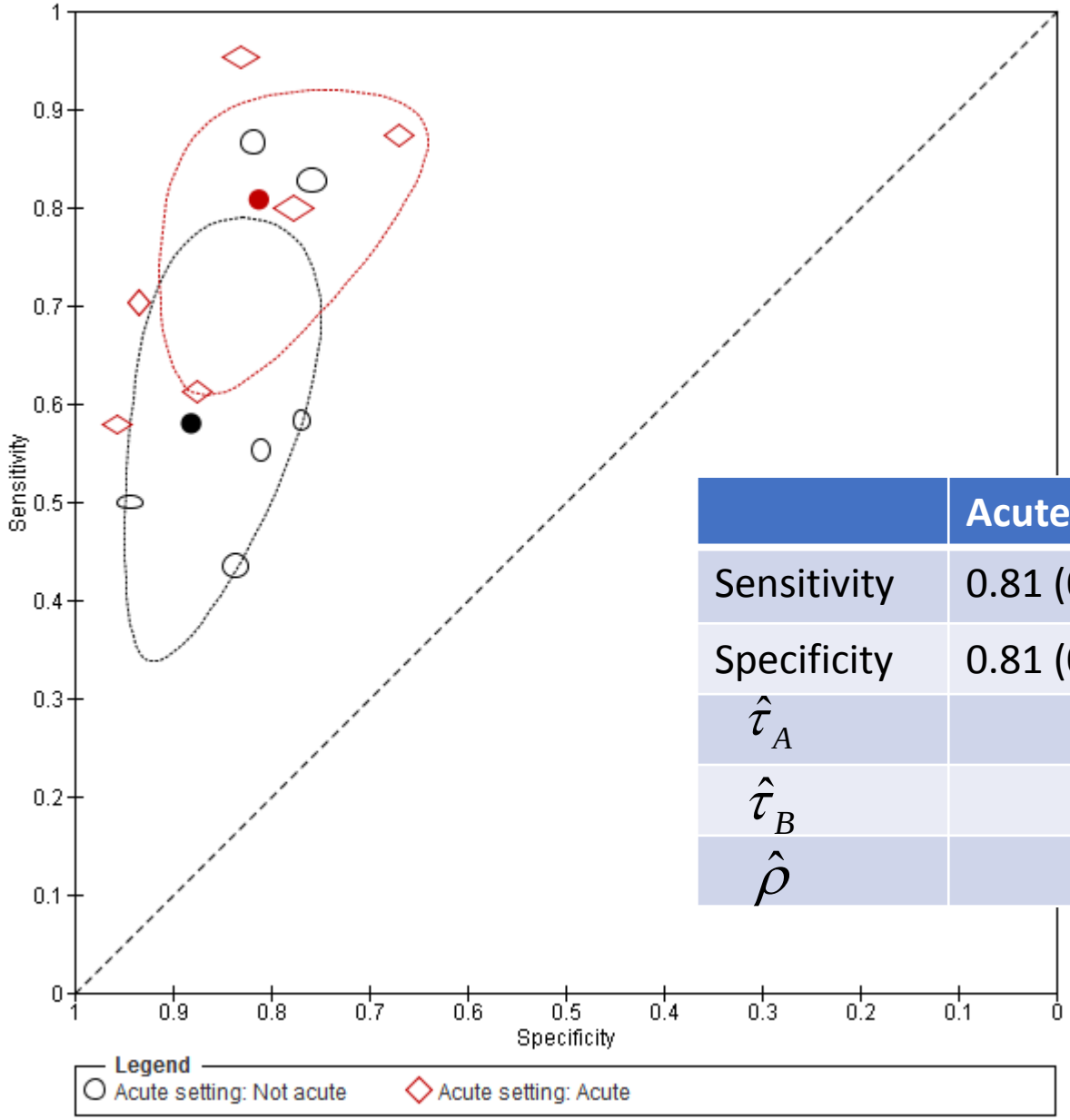
- Typically a large amount of heterogeneity in DTA meta-analysis
- The more unexplained heterogeneity, the less meaningful are the summary measures!
- Often more studies in DTA meta-analysis – potentially more scope for investigating reasons for heterogeneity

Subgroup analysis



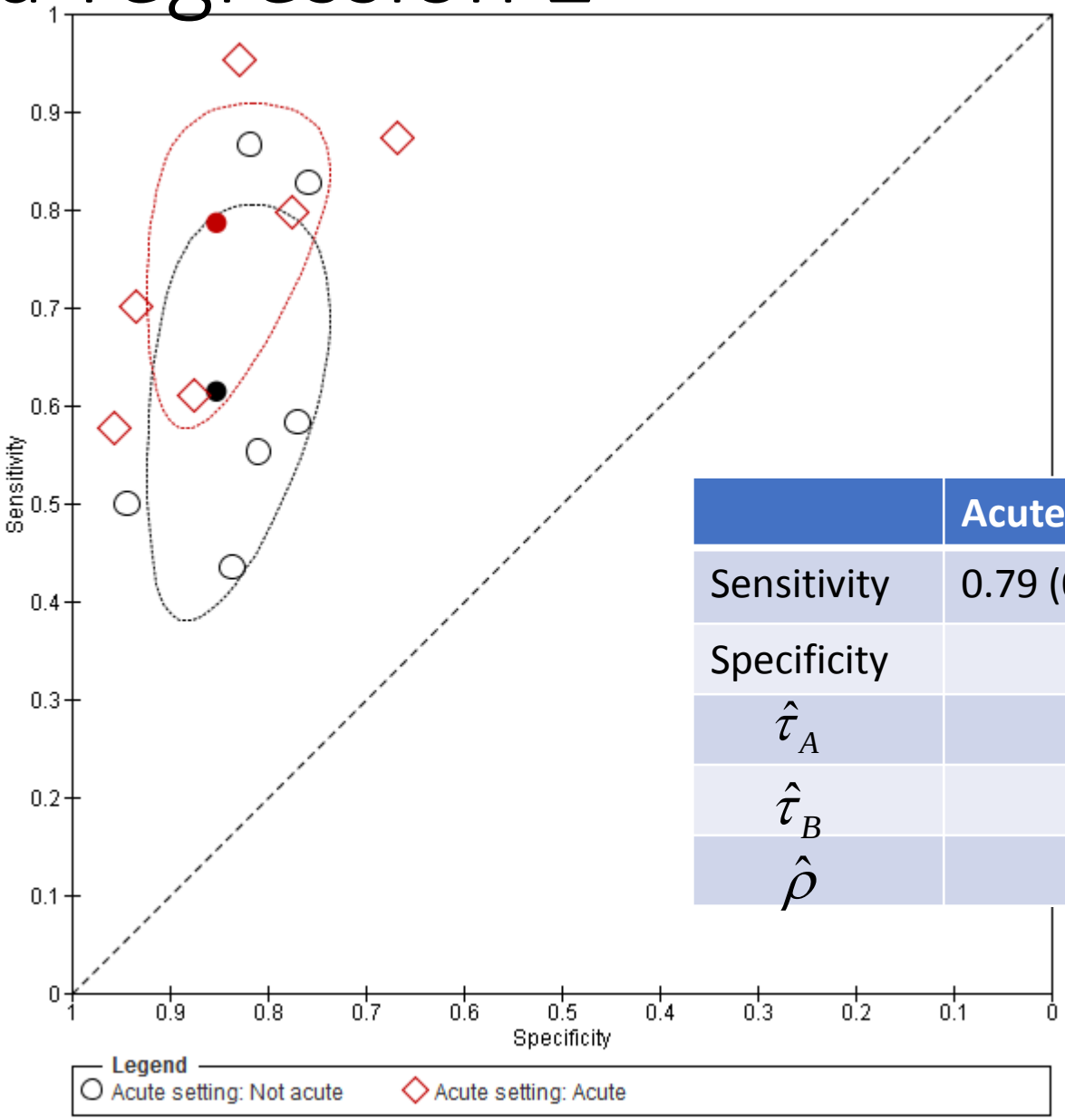
	Acute	Not acute
Sensitivity	0.81 (0.71, 0.89)	0.58 (0.45, 0.70)
Specificity	0.81 (0.72, 0.87)	0.88 (0.82, 0.93)
	0.58 (0.23, 1.45)	0.47 (0.20, 1.14)
	0.39 (0.14, 1.12)	0.47 (0.17, 1.31)
	-0.57 (-0.99, 0.90)	-0.82 (-1.00, 0.99)

Meta-regression 1



	Acute	Not acute
Sensitivity	0.81 (0.71, 0.88)	0.58 (0.45, 0.70)
Specificity	0.81 (0.73, 0.87)	0.88 (0.82, 0.92)
$\hat{\tau}_A$	0.51 (0.27, 0.96)	
$\hat{\tau}_B$	0.45 (0.23, 0.86)	
$\hat{\rho}$	-0.77 (-1.00, 0.76)	

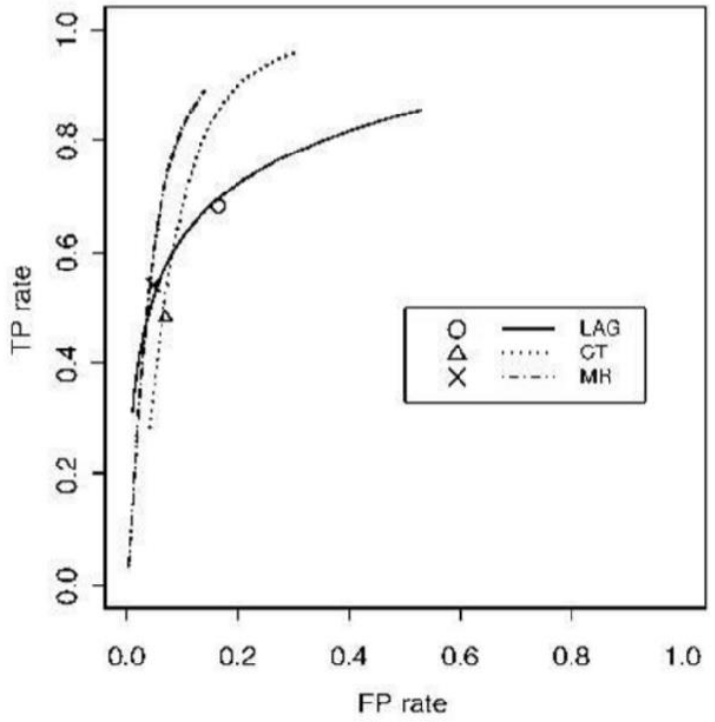
Meta-regression 2



	Acute	Not acute
Sensitivity	0.79 (0.69, 0.86)	0.61 (0.49, 0.72)
Specificity	0.85 (0.80, 0.89)	
$\hat{\tau}_A$	0.54 (0.28, 1.01)	
$\hat{\tau}_B$	0.54 (0.29, 0.97)	
$\hat{\rho}$	-0.78 (-0.99, 0.62)	

Test as a covariate

- Simple approach to comparing the performance of tests: test as a covariate
- Compare summary points / area under curve / sensitivity and specificity at particular threshold?
- Should single test studies contribute to such comparisons?



e.g. Rutter & Gatsonis, 2001: Comparison of the accuracy of lymphangiography (LAG), computed tomography (CT) and magnetic resonance imaging (MR) in identifying lymph node metastasis in women with cervical cancer

Some other methodological issues

- Choice of optimal threshold
- Combination of tests (rule-in, rule-out)
- Comparison of tests
- Lack of ”gold standard”

Implementation

- *R / Stata packages – some limitations + coding required*
  - metandi (Stata) fits the bivariate model (also presents HSROC summary) but no covariables
- *WinBUGS*
  - *Flexibility but no documentation*
- *DTA-MetaInsight App –*
  - *Uses R routines, no coding required*

DTA MA

An interactive web-based tool for conducting meta-analysis of diagnostic test accuracy studies

https://crsu.shinyapps.io/dta_ma/