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PEARLS OF LABORATORY MEDICINE

Optimal Reporting of Diagnostic Accuracy Studies

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CCTC Clinical Chemistry Trainee Council

Diagnostic Accuracy Studies: Design

Figure A: Single Set of Eligibility Criteria

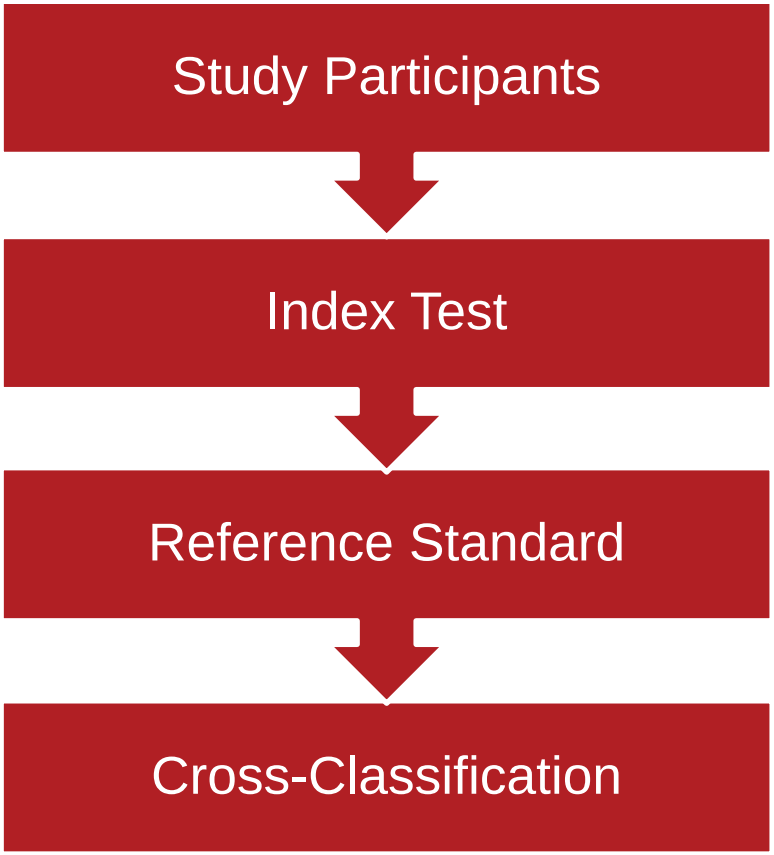
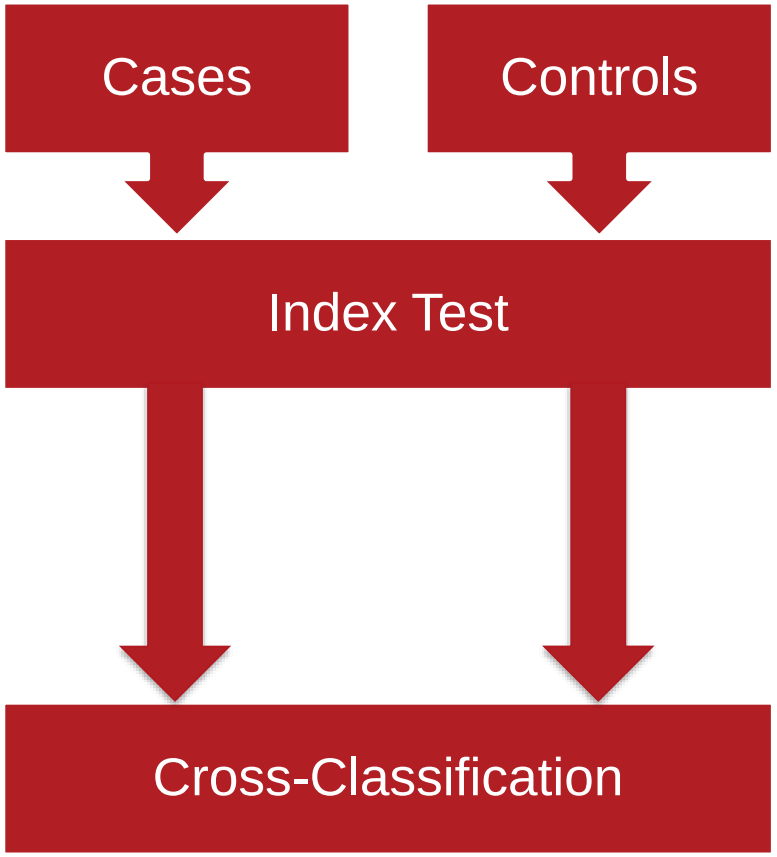


Figure B: Multiple Sets of Eligibility Criteria



Diagnostic Accuracy Studies: Results

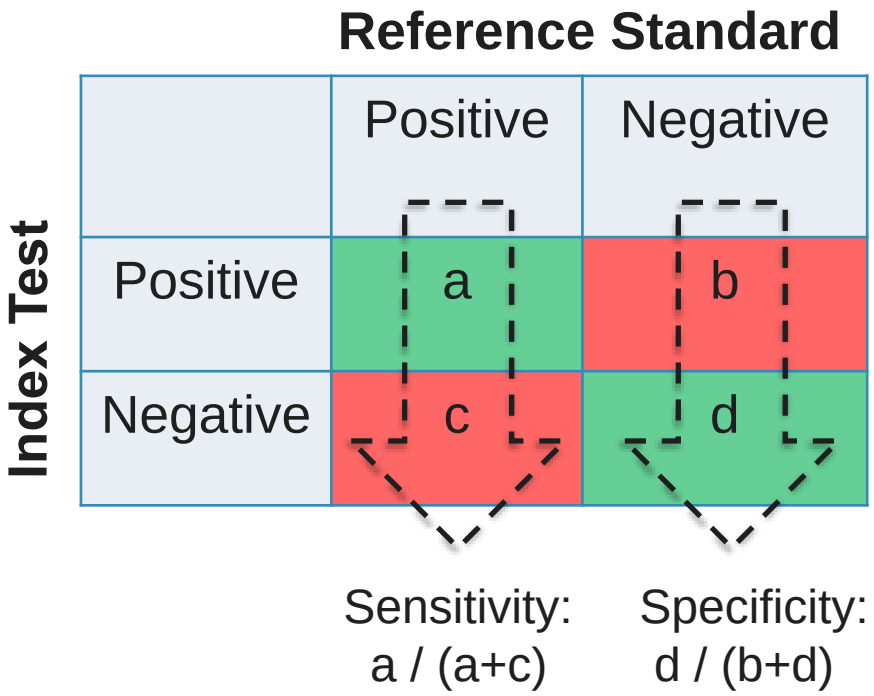


Figure A: 2x2 Table

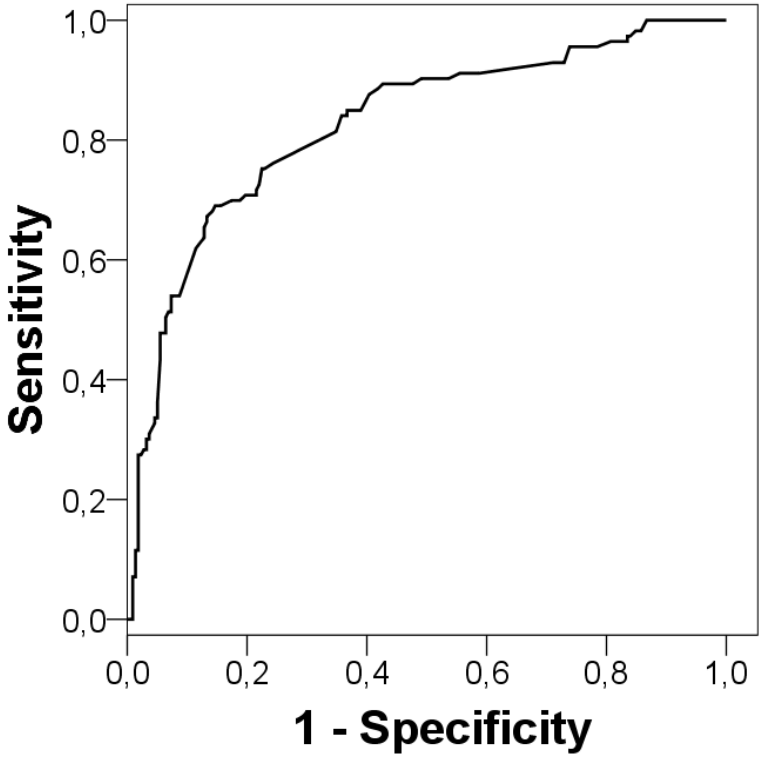


Figure B: ROC curve

Diagnostic Accuracy Study: Example

"Patients suspected of having acute hemispheric stroke"

↓

"plasma glial fibrillary acidic protein"

↓

"Final diagnosis at hospital discharge"

↓

Cross-classification

Figure A: Example Study Design

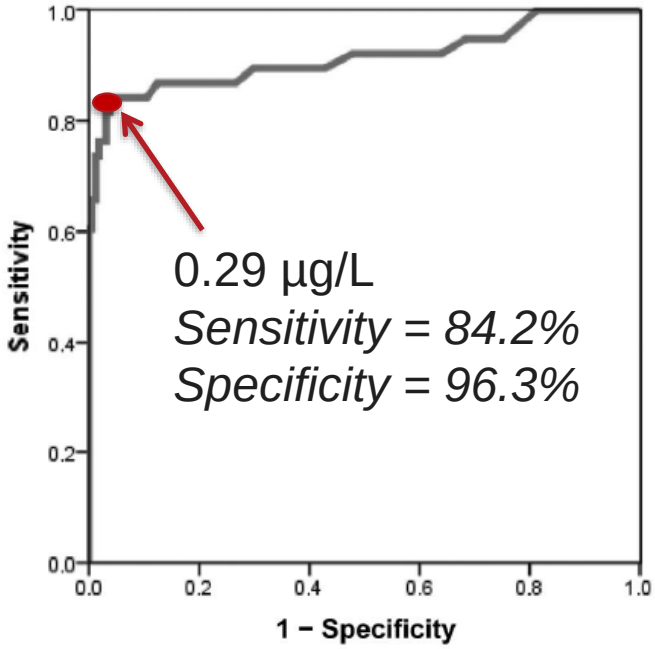


Figure B: Example of Study Results

Foerch C, Niessner M, Back T, et al. Diagnostic accuracy of plasma glial fibrillary acidic protein for differentiating intracerebral hemorrhage and cerebral ischemia in patients with symptoms of acute stroke. *Clin Chem* 2012;58:237-45.

Interpreting Diagnostic Accuracy Studies

- **Sources of Bias:**
  - Study design (case-control studies)
  - Masking (unblinded reading of test results)
  - And many others…
- **Sources of Variation:**
  - Patient characteristics
  - Disease prevalence
  - Previous testing
  - How tests are performed and interpreted

Reporting Diagnostic Accuracy Studies

- Individuals who read reports of diagnostic accuracy studies should be able to assess:
  - Study validity
  - Study applicability
- Reports of diagnostic accuracy studies are often insufficiently informative
- **STARD (STAndards for Reporting Diagnostic accuracy)** aims to improve the quality of reporting of diagnostic accuracy studies

STARD 2015 Update

Section & Topic	No.	Item
TITLE OR ABSTRACT		
	1	Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)
ABSTRACT		
	2	Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts)
INTRODUCTION		
	3	Scientific and clinical background, including the intended use and clinical role of the index test
	4	Study objectives and hypotheses
METHODS		
Study design	5	Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study)
Participants	6	Eligibility criteria
	7	On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry)
	8	Where and when potentially eligible participants were identified (setting, location and dates)
	9	Whether participants formed a consecutive, random or convenience series
Test methods	10a	Index test, in sufficient detail to allow replication
	10b	Reference standard, in sufficient detail to allow replication
	11	Rationale for choosing the reference standard (if alternatives exist)
	12a	Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory
	12b	Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory
	13a	Whether clinical information and reference standard results were available to the performers/readers of the index test
	13b	Whether clinical information and index test results were available to the assessors of the reference standard
Analysis	14	Methods for estimating or comparing measures of diagnostic accuracy
	15	How indeterminate index test or reference standard results were handled
	16	How missing data on the index test and reference standard were handled
	17	Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory
	18	Intended sample size and how it was determined
RESULTS		
Participants	19	Flow of participants, using a diagram
	20	Baseline demographic and clinical characteristics of participants
	21a	Distribution of severity of disease in those with the target condition
	21b	Distribution of alternative diagnoses in those without the target condition
	22	Time interval and any clinical interventions between index test and reference standard
Test results	23	Cross tabulation of the index test results (or their distribution) by the results of the reference standard
	24	Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)
	25	Any adverse events from performing the index test or the reference standard
DISCUSSION		
	26	Study limitations, including sources of potential bias, statistical uncertainty, and generalisability
	27	Implications for practice, including the intended use and clinical role of the index test
OTHER INFORMATION		
	28	Registration number and name of registry
	29	Where the full study protocol can be accessed
	30	Sources of funding and other support; role of funders

Figure: STARD 2015
List of Essential Items

Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *Clin Chem* 2015;61:1446-52.

STARD documents available at:

http://www.equator-network.org/reporting-guidelines/stard

STARD Item 1: Title or Abstract

- ***Item***: "Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC)."
- ***Rationale***: Identification of diagnostic accuracy studies in research repositories (e.g. PubMed) is often difficult.
- ***Example***: "Diagnostic Accuracy of Serum Ceruloplasmin in Wilson Disease: Determination of Sensitivity and Specificity by ROC Curve Analysis among ATP7B-Genotyped Subjects."

Mak CM, Lam CW, Tam S. Diagnostic accuracy of serum ceruloplasmin in Wilson Disease: determination of sensitivity and specificity by ROC curve analysis among ATP7B-genotyped subjects. *Clin Chem* 2008;54:1356-62.

STARD Item 9: Participants

- ***Item***: "Whether participants formed a consecutive, random or convenience series."
- ***Rationale***: In a convenience sample, patients may not represent a random sample of the targeted population, which may jeopardize the generalizability, and could lead to bias.
- ***Example***: "A total of 510 consecutive patients with an MI referred to the Luxembourg Heart Institute for emergent percutaneous coronary intervention (PCI) with acute and ongoing chest pain for 12 h and clinically significant ST-T changes were included in the study."

Devaux Y, Vausort M, Goretti E, et al. Use of circulating microRNAs to diagnose acute myocardial infarction. *Clin Chem* 2012;58:559-67.

STARD Item 12a: Test Methods

- ***Item***: "Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory."
- ***Rationale***: Future studies should be able to reproduce test positivity cut-offs; clinicians should be able to apply them in practice; exploratory cut-offs are often biased.
- ***Example***: "We used ROC curve analysis to calculate diagnostic accuracy of GFAP. [..] We predefined a GFAP plasma concentration of 0.29 µg/L [..] as the cut-off."

Foerch C, Niessner M, Back T, et al. Diagnostic accuracy of plasma glial fibrillary acidic protein for differentiating intracerebral hemorrhage and cerebral ischemia in patients with symptoms of acute stroke. *Clin Chem* 2012;58:237-45.

STARD Item 13a: Test Methods

- ***Item***: "Whether clinical information and reference standard results were available to the performers/readers of the index test."
- ***Rationale:*** Reading of the index test may be influenced if the reader is aware of the results of the reference standard (test review bias).
- ***Example***: "The investigators performing the molecular analysis on the blood samples were blinded to the patients' clinical diagnosis."

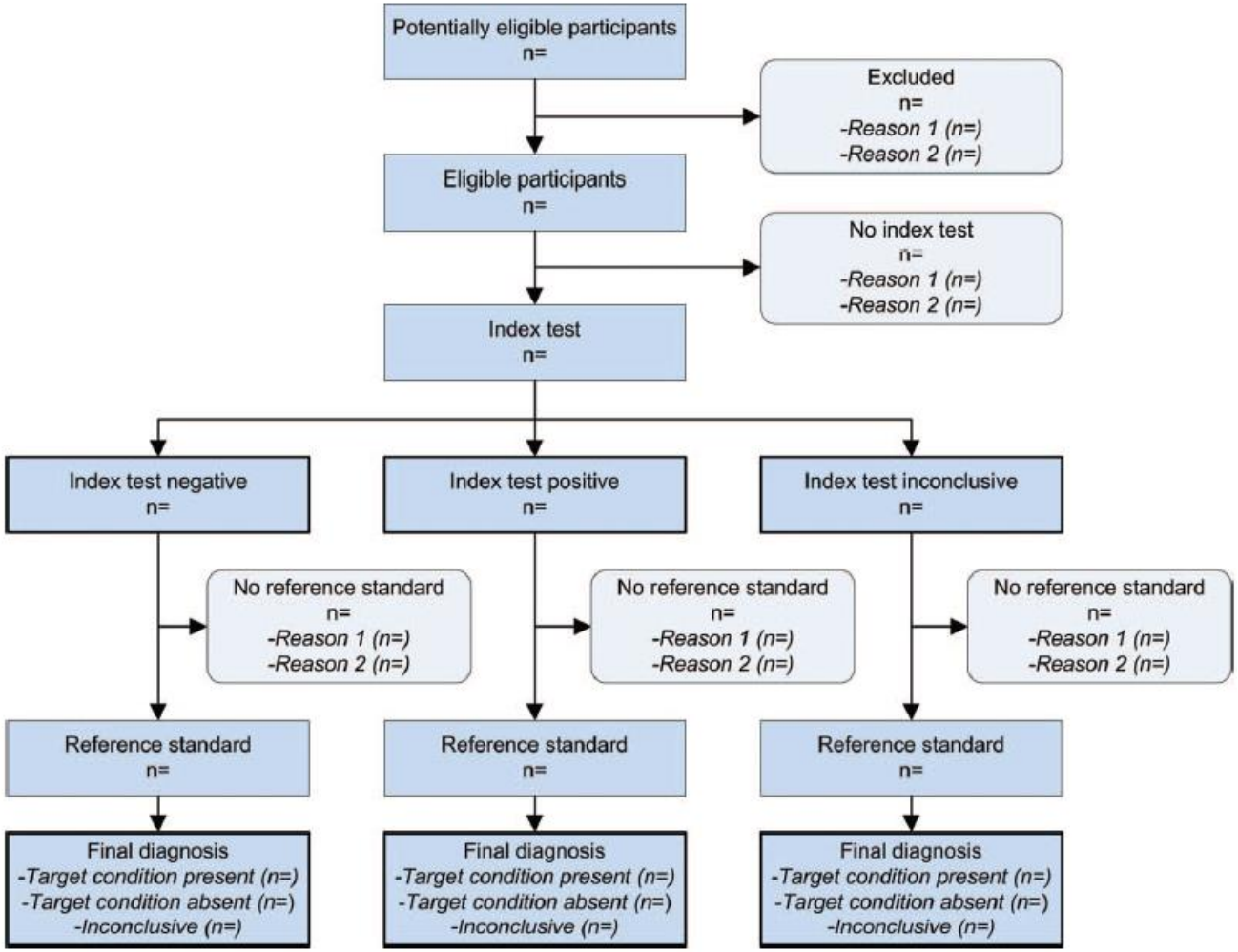
Liu R, Chen X, Du Y, et al. Serum microRNA expression profile as a biomarker in the diagnosis and prognosis of pancreatic cancer. *Clin Chem* 2012;58:510-8.

STARD Item 19: Results

- ***Item***: "Flow of participants, using a diagram."
- ***Rationale***: Estimates of diagnostic accuracy may be biased if not all eligible participants undergo the desired reference standard, or if many participants have missing or inconclusive test results.
- ***Example***: See STARD 2015 flow diagram prototype on next slide.

Bossuyt PM, Reitsma JB, Bruns DE, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *Clin Chem* 2015;61:1446-52.

STARD 2015 Flow Diagram Prototype



STARD Item 24: Test Results

- ***Item***: "Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals)."
- ***Rationale***: The smaller the number of included patients, the larger the uncertainty will be that the identified accuracy estimates actually represent the 'true' values.
- ***Example***: "[..] the sensitivity and specificity at an optimal cut-point of 18.4 were 93% (95% CI, 77%-99%) and 71% (95% CI, 20%-96%), respectively."

Debray FG, Mitchell GA, Allard P, et al. Diagnostic accuracy of blood lactate-to-pyruvate molar ratio in the differential diagnosis of congenital lactic acidosis. *Clin Chem* 2007;53:916-21.

Utilization of STARD 2015

- **Potential Users of STARD:**
  - Authors
  - Peer reviewers
  - Journal editors
- **Potential Advantages of Using STARD:**
  - Improve visibility and utility of study
  - Positive associations with citation rates
  - Positive associations with journal impact factor
  - Endorsed by >200 journals:
    - *Clinical Chemistry: "*For studies of diagnostic accuracy of tests, complete the STARD Checklist for Evaluations of Diagnostic Accuracy electronically upon submission."

Conclusions

- Suboptimal reporting of clinical diagnostic accuracy studies is a major source of research waste, but 100% preventable
- Authors, peer reviewers, and journal editors should make efforts to make sure that study reports are sufficiently informative
- STARD 2015 aims to improve the quality of reporting of diagnostic accuracy studies

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Disclosures/Potential Conflicts of Interest

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