Mapping the landscape and quality of TB diagnostic research

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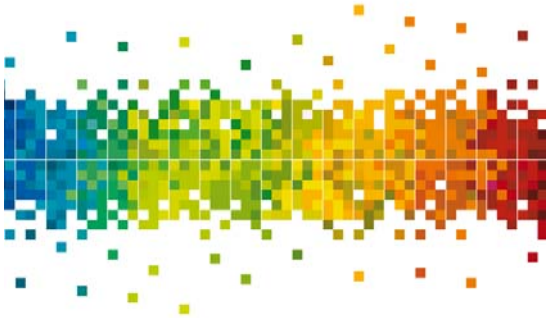
Goals of this project by STP RM & NDWG

- Map the landscape of current TB diagnostic research
  - What % of TB research is focused on diagnosis?
  - Where is the research output from?
  - What tests are being evaluated?
  - What outcomes are commonly reported?
- Assess the quality of TB diagnostic accuracy studies
  - Methodological quality of TB diagnostic accuracy studies
  - Quality of reporting

Methods

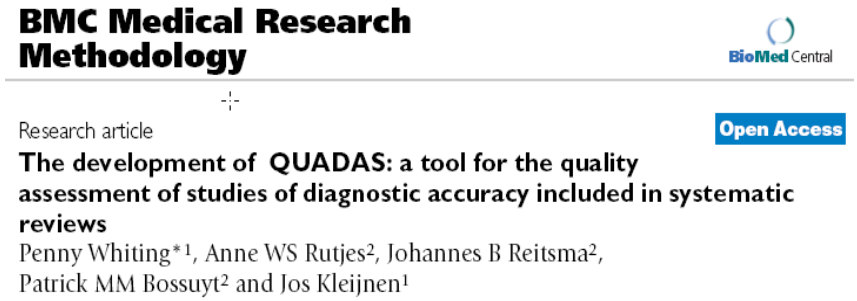
- Map the landscape of current TB diagnostic research
  - Bibliometric analysis of citations:
    - PubMed and EMBASE were searched by a librarian for all original TB citations in a two year period – 2007–2008
  - All citations (titles and abstracts) were read and coded by a trained researcher after pilot testing and standardization
  - Health Research Classification System (HRCS) was used to retrieve details on the type of research of each study.
  - Additional information was collected for the diagnosis studies on: study design and type of outcome reported, purpose of the test, technology platform, study population, reporting of HIV status, country where study was done, etc.

UK Clinical Research Collaboration
Health Research Classification System



Methods

- Assess the quality of TB diagnostic accuracy studies
  - We used QUADAS and STARD checklists to assess the methodological and reporting quality of TB diagnostic studies published in a 3 year period [2004 – 2006]



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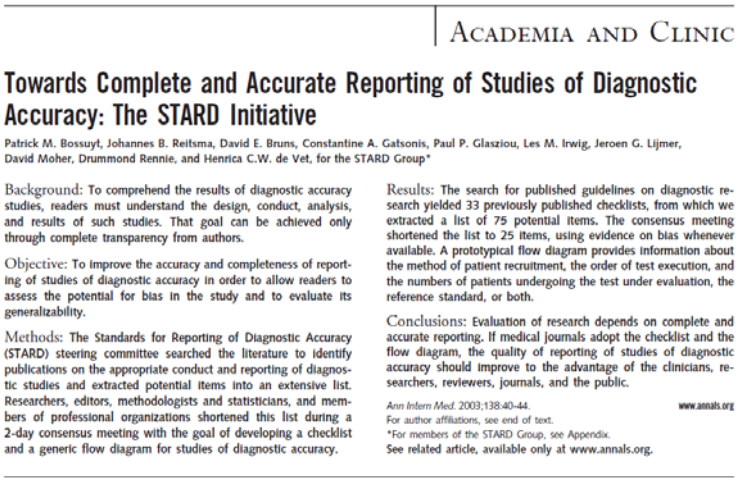
The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews

Penny Whiting*[1], Anne WS Rutjes[2], Johannes B Reitsma[2], Patrick MM Bossuyt[2] and Jos Kleijnen[1]



ACADEMIA AND CLINIC

Towards Complete and Accurate Reporting of Studies of Diagnostic Accuracy: The STARD Initiative

Patrick M. Bossuyt, Johannes B. Reitsma, David E. Bruns, Constantine A. Gatsonis, Paul P. Glasziou, Les M. Irwig, Jeroen G. Lijmer, David Moher, Drummond Rennie, and Henrica C.W. de Vet, for the STARD Group*

Background: To comprehend the results of diagnostic accuracy studies, readers must understand the design, conduct, analysis, and results of such studies. That goal can be achieved only through complete transparency from authors.

Objective: To improve the accuracy and completeness of reporting of studies of diagnostic accuracy in order to allow readers to assess the potential for bias in the study and to evaluate its generalizability.

Methods: The Standards for Reporting of Diagnostic Accuracy (STARD) steering committee searched the literature to identify publications on the appropriate conduct and reporting of diagnostic studies and extracted potential items into an extensive list. Researchers, editors, methodologists and statisticians, and members of professional organizations shortened this list during a 2-day consensus meeting with the goal of developing a checklist and a generic flow diagram for studies of diagnostic accuracy.

Results: The search for published guidelines on diagnostic research yielded 33 previously published checklists, from which we extracted a list of 75 potential items. The consensus meeting shortened the list to 25 items, using evidence on bias whenever available. A prototypical flow diagram provides information about the method of patient recruitment, the order of test execution, and the numbers of patients undergoing the test under evaluation, the reference standard, or both.

Conclusions: Evaluation of research depends on complete and accurate reporting. If medical journals adopt the checklist and the flow diagram, the quality of reporting of studies of diagnostic accuracy should improve to the advantage of the clinicians, researchers, reviewers, journals, and the public.

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For author affiliations, see end of text.

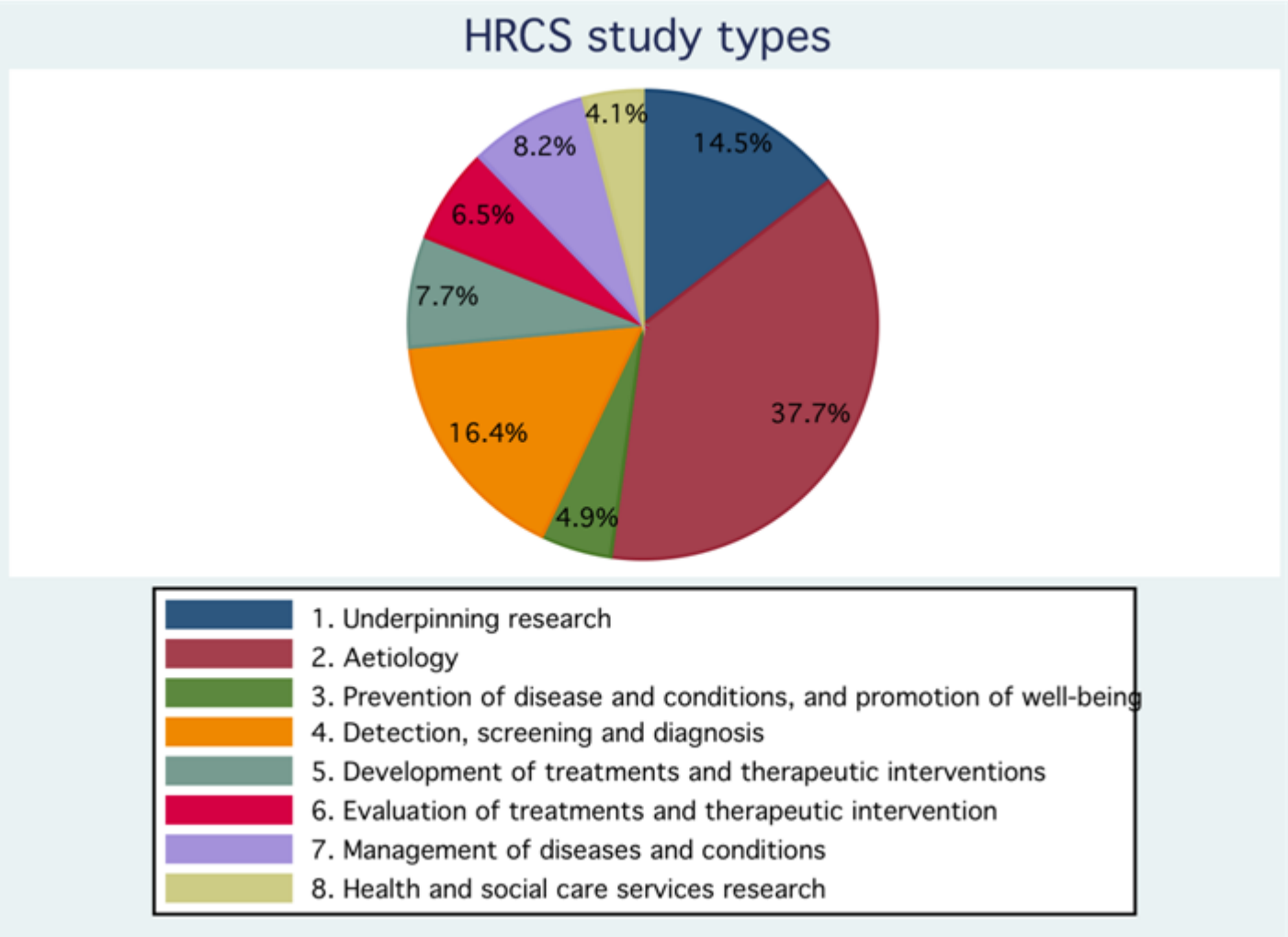
*For members of the STARD Group, see Appendix.

See related article, available only at www.annals.org.

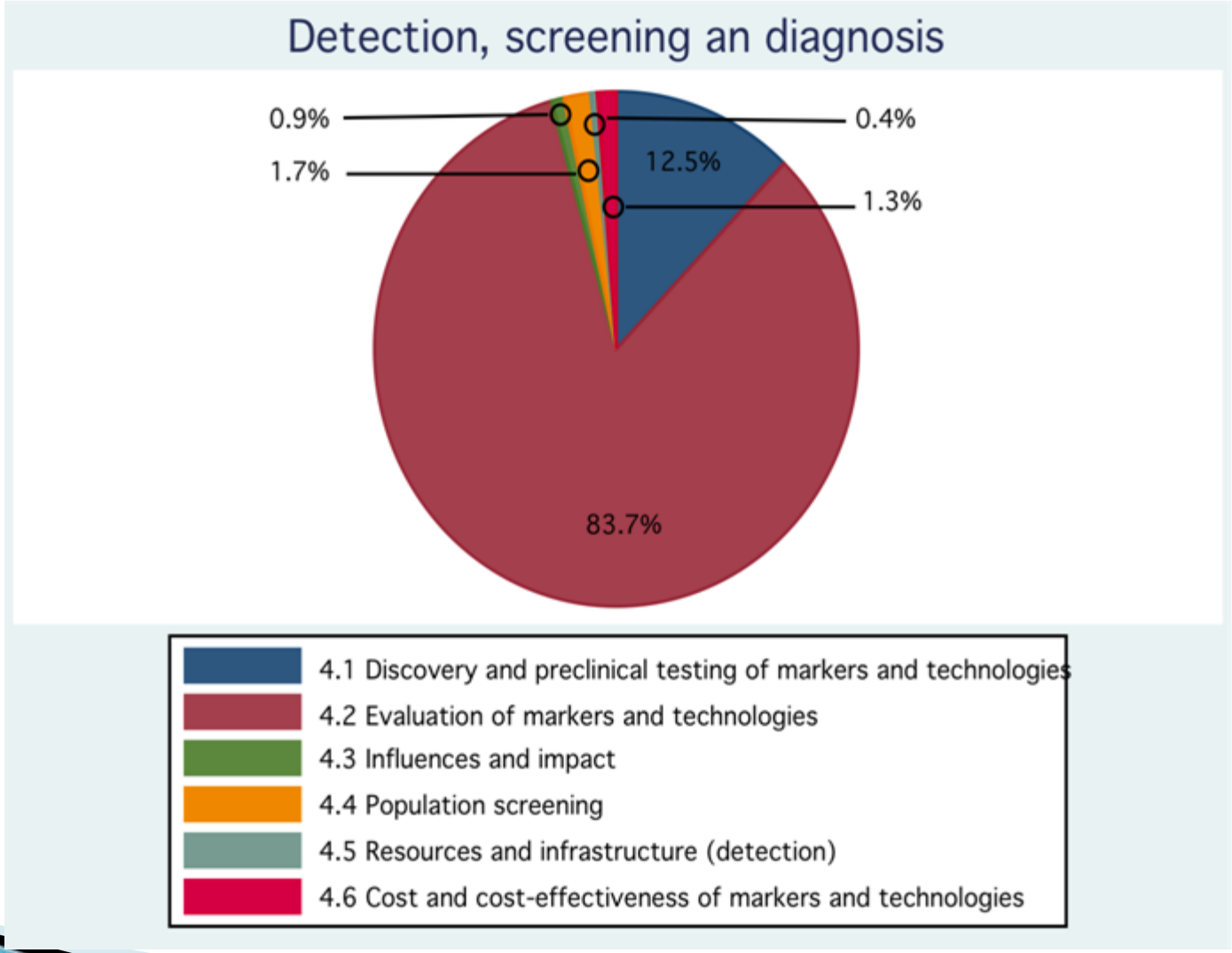
Results: bibliometric/citation analysis


Total unique citations on TB [from PubMed & Embase for 2007-2008] 6459
Citations excluded: No abstract available 1021 (15.8%)
Abstracts available 5438 (84.2%)
Abstracts excluded: Not original study 215 (4.0%) Case reports or case series 957 (17.6%)
Original Study 4266 (78.4%)
Coded as per UK Health Research Classification System (HRCS)
1. Underpinning Research 619 (14.5%)
1.1 Biological 545 (88.8%)
1.2 Psycological, Socioeconomic 1 (0.1%)
1.3 Chemical, Physical 9 (1.5%)
1.4 Methodology 52 (8.5%)
1.5 Ressources 7 (1.1%)
2. Aetiology 1607 (37.7%)
2.1 Biological 482 (30.1%)
2.2 Environmental 259 (16.2%)
2.3 Psychological, social, economic 92 (5.7%)
2.4 Distribution 708 (44.2%)
2.5 Methodology 60 (3.7%)
2.6 Resources 2 (0.1%)
3. Prevention of Disease and Conditions, and Promotion of Well-Being 209 (4.9%)
3.1 Behaviour 1 (0.5%)
3.2 Environmental 14 (6.7%)
3.3 Nutrition, Chemoprevention 0 (0%)
3.4 Vaccines 194 (92.8%)
3.5 Resources 0 (0%)
4. Detection, Screening and Diagnosis 699 (16.4%)
4.1 Preclinical 84 (12.0%)
4.2 Evaluation 584 (83.7%)
4.3 Impact 6 (0.9%)
4.4 Population Screening 12 (1.7%)
4.5 Resources 3 (0.4%)
4.6 Cost 9 (1.3%)
5. Development of Treatments and Therapeutic Interventions 328 (7.7%)
5.1 Pharmaceutical 316 (96.4%)
5.2 Cellular/gene 3 (0.9%)
5.3 Medical device 0 (0%)
5.4 Surgery 4 (1.2%)
5.5 Radiotherapy 1 (0.3%)
5.6 Psychological Behavioural 0 (0%)
5.7 Physical 0 (0%)
5.8 Complementary 2 (0.6%)
5.9 Resources 2 (0.6%)
6. Evaluation of Treatments and Therapeutic Interventions 279 (6.5%)
6.1 Pharmaceutical 189 (68.2%)
6.2 Cellular/gene 1 (0.4%)
6.3 Medical device 8 (2.9%)
6.4 Surgery 66 (23.8%)
6.5 Radiotherapy 3 (1.1%)
6.6 Psychological Behavioural 1 (0.4%)
6.7 Physical 0 (0%)
6.8 Complementary 5 (1.8%)
6.9 Resources 4 (1.4%)
7. Management Of Diseases and Conditions 349 (8.2%)
7.1 Individual care needs 155 (44.4%)
7.2 End of life Care 1 (0.3%)
7.3 Management 191 (54.7%)
7.4 Resources 2 (0.6%)
8. Health and Social Care Services Research 176 (4.1%)
8.1 Organisation Delivery of Services 104 (59.4%)
8.2 Health, welfare Economics 19 (10.9%)
8.3 Policy, ethics Research Governance 43 (24.6%)
8.4 Methodology 9 (5.1%)
8.5 Resources 0 (0%)

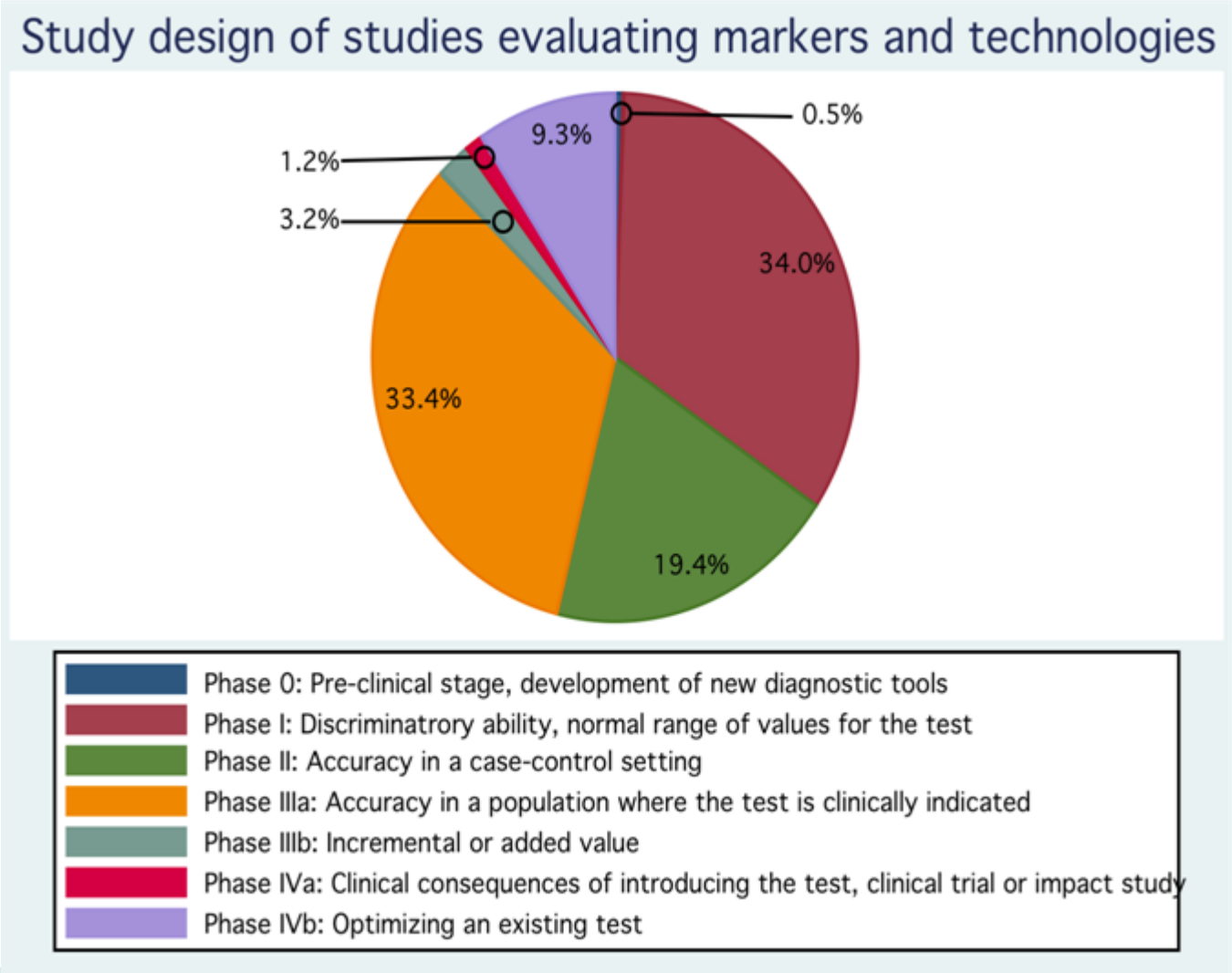
Distribution of major types of TB research activities [N=6459]



Distribution of study types within diagnostic research [N=**699**]



Distribution of phases within evaluation studies of diagnostics [N=584]

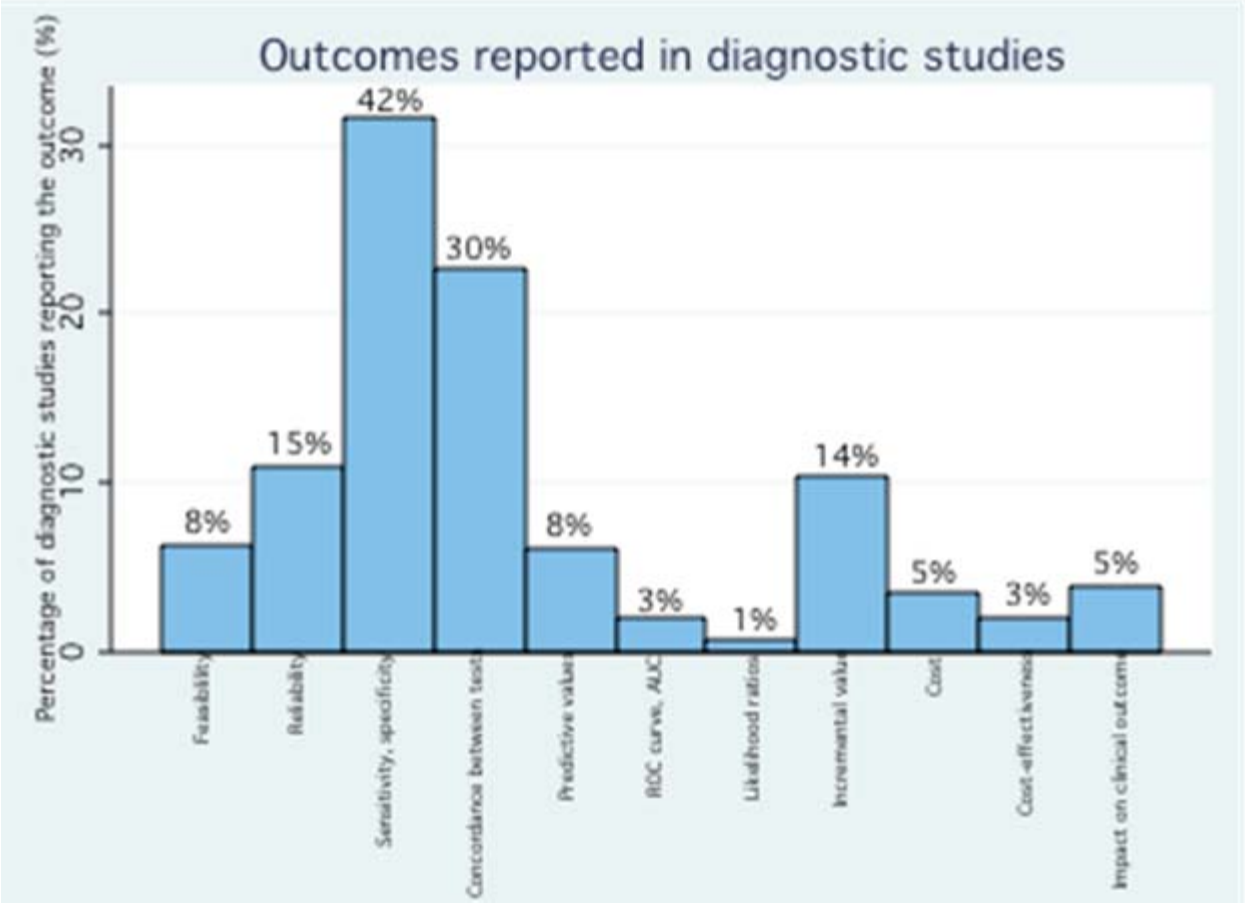


Countries accounting for the majority of diagnostic studies

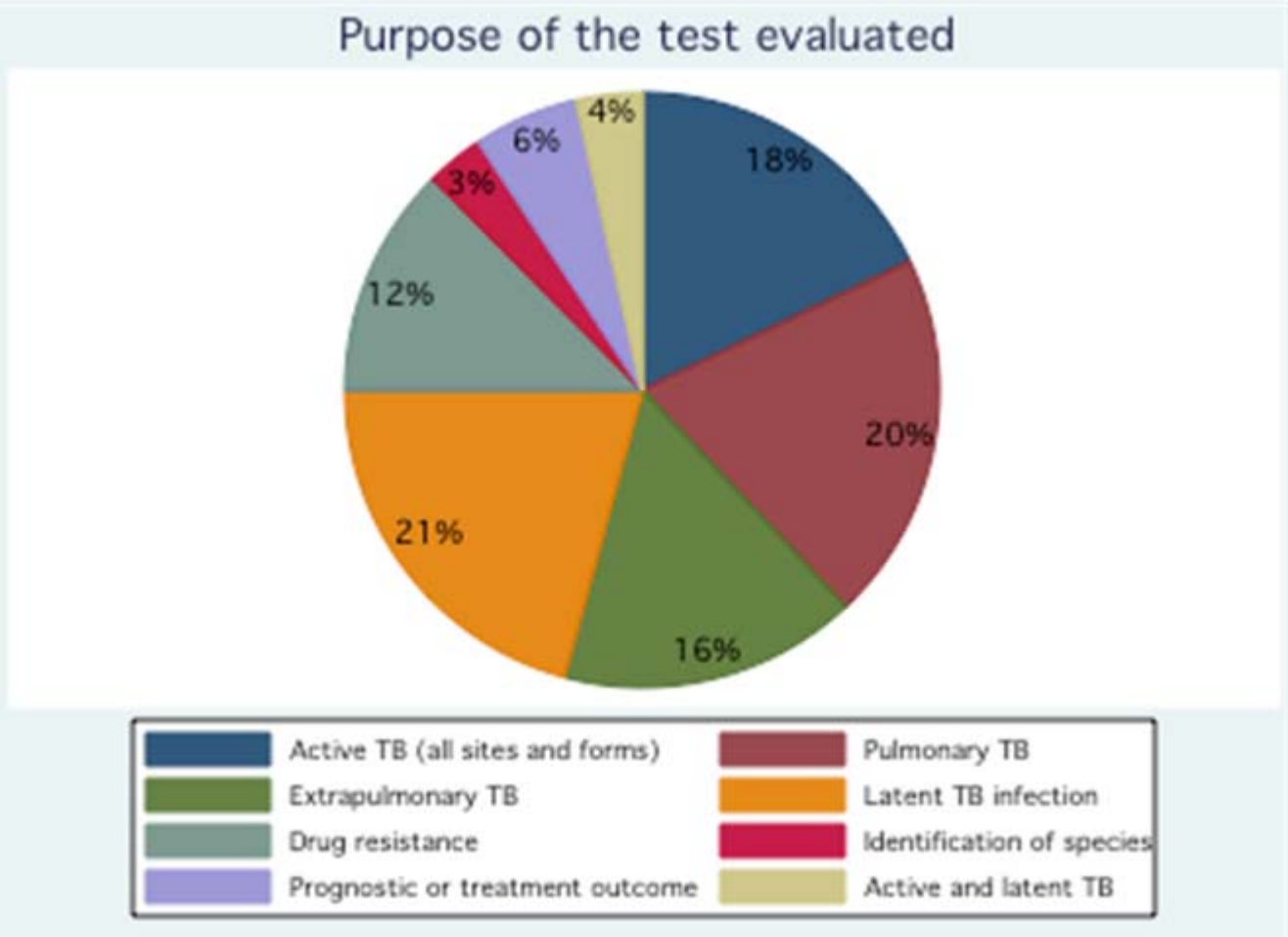
Country	N	%
India	86	12.3
China	50	7.1
USA	47	6.7
Japan	44	6.3
Brazil	36	5.1
Russia	36	5.1
South Africa	30	4.3
Turkey	29	4.1
Republic of Korea	23	3.3

Country	N	%
Germany	19	2.7
Italy	19	2.7
Peru	17	2.4
UK	15	2.1
Taiwan	14	2.0
Netherlands	13	1.8
Spain	12	1.7
Iran	10	1.4

Distribution of outcomes reported in abstracts of diagnostic studies [N=**699**]



Distribution of the purpose of the test within diagnostics studies [N=**699]**



Results: quality and reporting of diagnostic accuracy studies

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PLoS one

Quality and Reporting of Diagnostic Accuracy Studies in TB, HIV and Malaria: Evaluation Using QUADAS and STARD Standards

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Abstract

Background: Poor methodological quality and reporting are known concerns with diagnostic accuracy studies. In 2003, the QUADAS tool and the STARD standards were published for evaluating the quality and improving the reporting of diagnostic studies, respectively. However, it is unclear whether these tools have been applied to diagnostic studies of infectious diseases. We performed a systematic review on the methodological and reporting quality of diagnostic studies in TB, malaria and HIV.

Methods: We identified diagnostic accuracy studies of commercial tests for TB, malaria and HIV through a systematic search of the literature using PubMed and EMBASE (2004–2006). Original studies that reported sensitivity and specificity data were included. Two reviewers independently extracted data on study characteristics and diagnostic accuracy, and used QUADAS and STARD to evaluate the quality of methods and reporting, respectively.

Findings: Ninety (38%) of 238 articles met inclusion criteria. All studies had design deficiencies. Study quality indicators that were met in less than 25% of the studies included adequate description of withdrawals (6%) and reference test execution (10%), absence of index test review bias (19%) and reference test review bias (24%), and report of uninterpretable results (22%). In terms of quality of reporting, 9 STARD indicators were reported in less than 25% of the studies: methods for calculation and estimates of reproducibility (0%), adverse effects of the diagnostic tests (1%), estimates of diagnostic accuracy between subgroups (10%), distribution of severity of disease/other diagnoses (11%), number of eligible patients who did not participate in the study (14%), blinding of the test readers (16%), and description of the team executing the test and management of indeterminate/outlier results (both 17%). The use of STARD was not explicitly mentioned in any study. Only 22% of 46 journals that published the studies included in this review required authors to use STARD.

Conclusion: Recently published diagnostic accuracy studies on commercial tests for TB, malaria and HIV have moderate to low quality and are poorly reported. The more frequent use of tools such as QUADAS and STARD may be necessary to improve the methodological and reporting quality of future diagnostic accuracy studies in infectious diseases.

Quality of TB accuracy studies using QUADAS [N=45]

Quality item	45 studies n (%)
Adequate spectrum composition	26 (58)
Clear description of selection criteria	21 (47)
Adequate reference standard	44 (98)
Absence of disease progression bias	42 (93)
Absence of partial verification bias	44 (98)
Absence of differential verification bias	42 (93)
Absence of incorporation bias	45 (100)
Absence of index test review bias	6 (13)
Absence of reference test review bias	7 (16)
Absence of clinical review bias	14 (31)
Report of uninterpretable results	9 (20)
Description of withdrawals	3 (7)

Fontela et al. PLoS One 2009

Summary of findings

- About 15% of all TB papers were mainly focused on TB diagnosis.
- Of these, about 85% were evaluation studies of tests and markers.
- Of these evaluation studies, about 85% are early phase studies of test accuracy
- There are very little data on patient outcomes, cost-effectiveness and impact in real world settings.
- Most test accuracy studies are of moderate to low quality and are poorly reported.
- Essential methodological and design elements are often either not reported or poorly reported.
- These results have important implications for evidence-based policy making

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