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UK Diagnostics Forum 2013

Improving evidence for diagnostic tests:

How much evidence is enough?

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Outline

- Consequences of testing:
  - Intended effects
  - Unintended effects
- Identifying all important tests effects
- RCTs
- A more practical solution: Framework of Test Effects
- How much evidence is enough?

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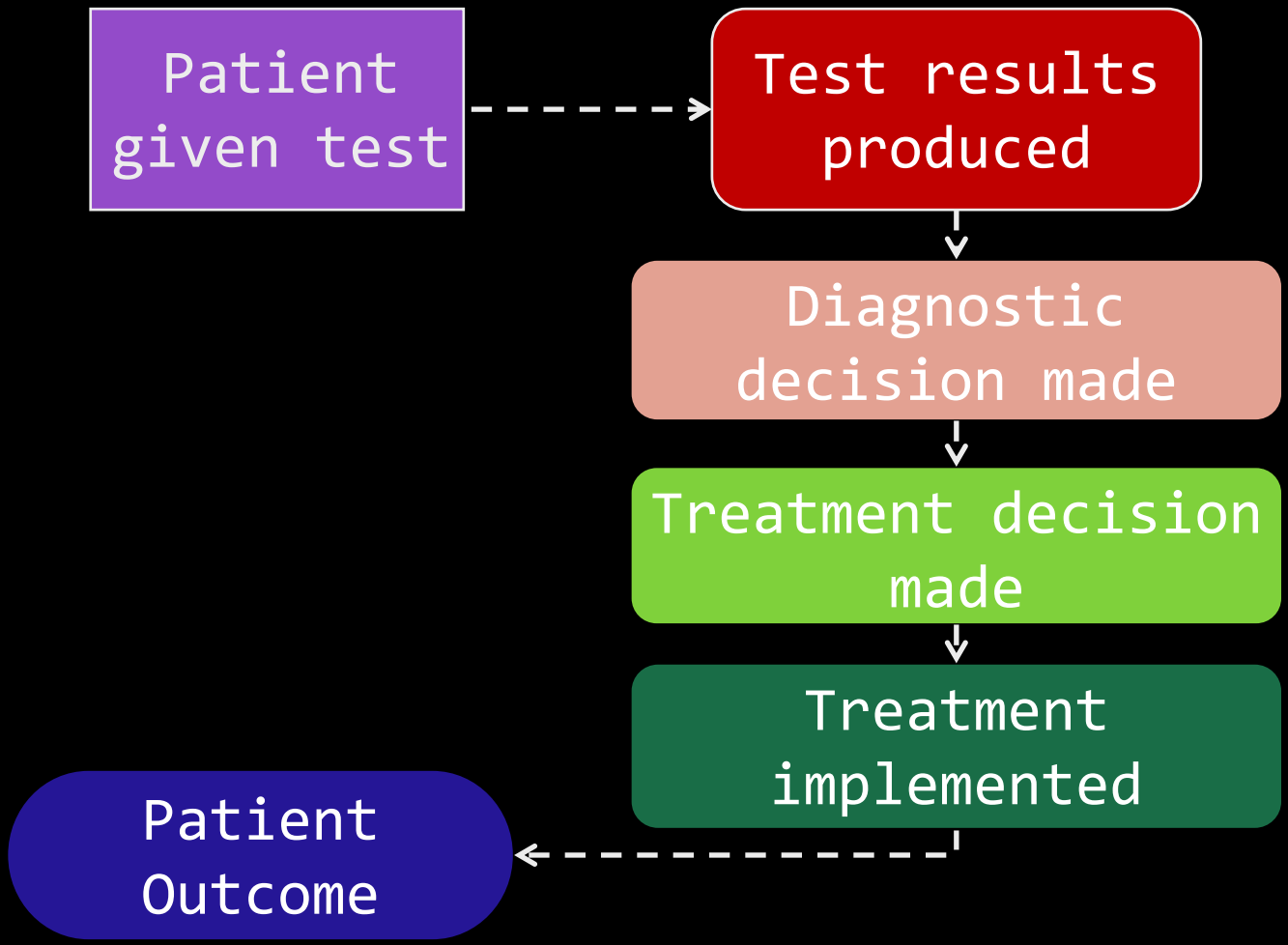
Tests as packages of care



Adapted from Bossuyt and Lijmer 1999

Evaluating how tests change patient health

INTENDED BENEFITS

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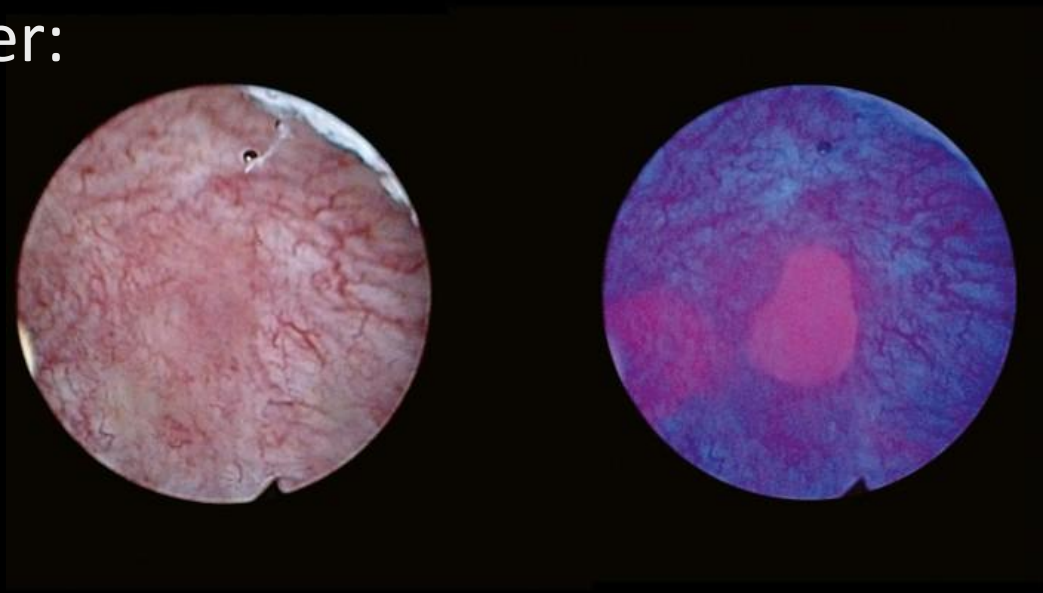
Changing decisions:
accuracy, diagnostic yield & therapeutic yield

Detecting bladder cancer:



- **White Light Cystoscopy**
  - Ambient lighting
  - High recurrence rate
  - ?missed tumours
- **Blue Light Cystoscopy**
  - Fluorescence lighting
  - Increased contrast
  - ?more accurate tumour detection

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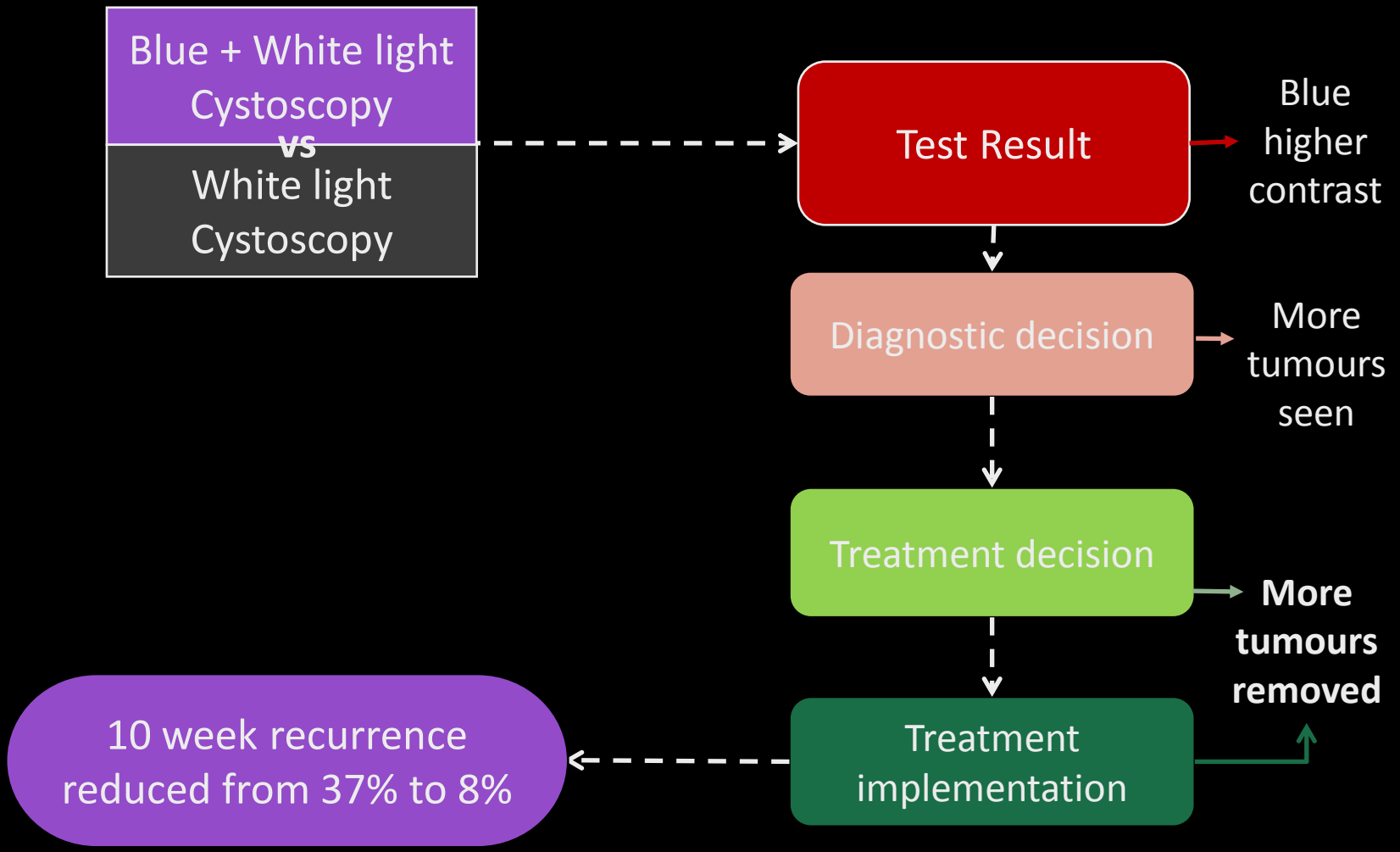
Babjuk et al. BJU International 2005;96:768-802

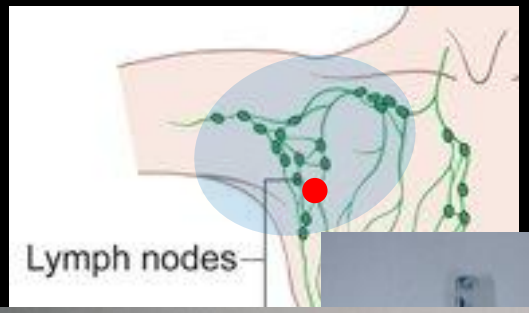


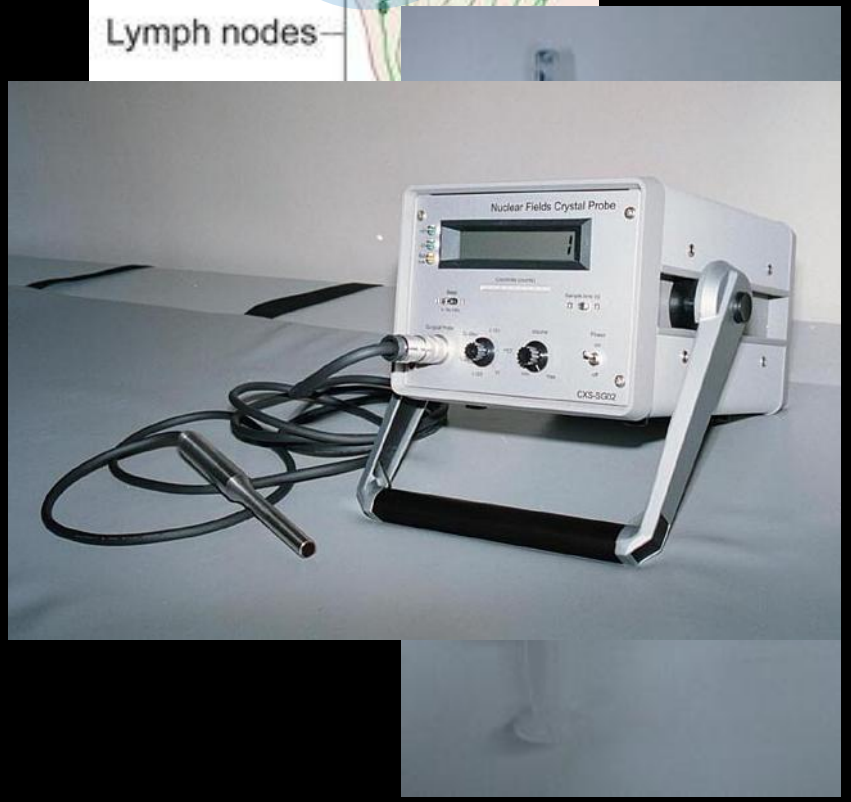
Enhanced accuracy leads to more appropriate diagnostic and therapeutic decision–making

Preventing patient harm:
direct test effects

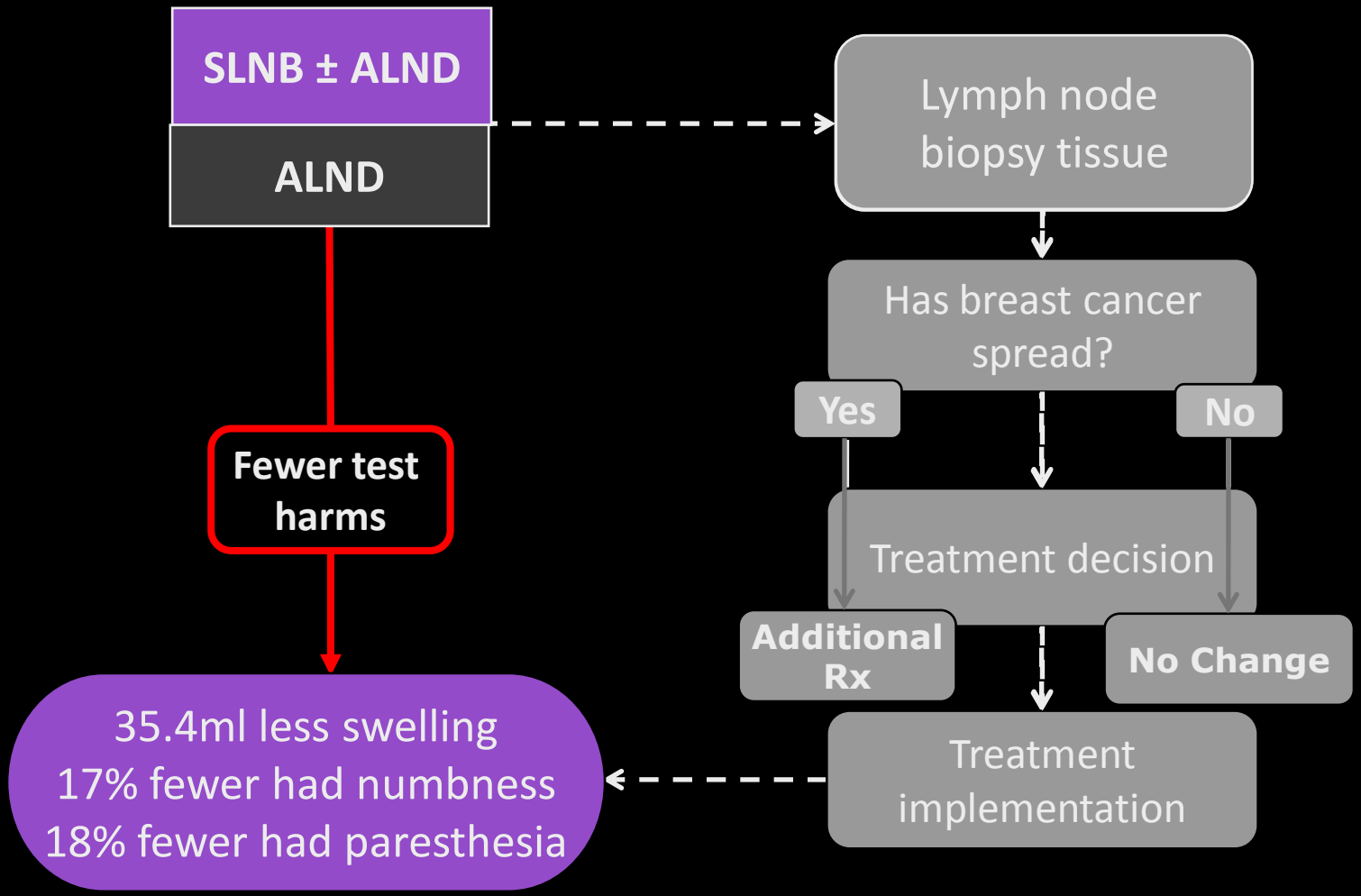
Staging early breast cancer:

- Axillary Lymph Node Dissection:
  - Diagnostic & therapeutic
  - High complication rate
- Sentinel Lymph Node Biopsy
  - Diagnostic
  - Removal of one node
  - ?Less invasive procedure





Purushotham et al. J Clin Oncol 2005;23:4312-4321

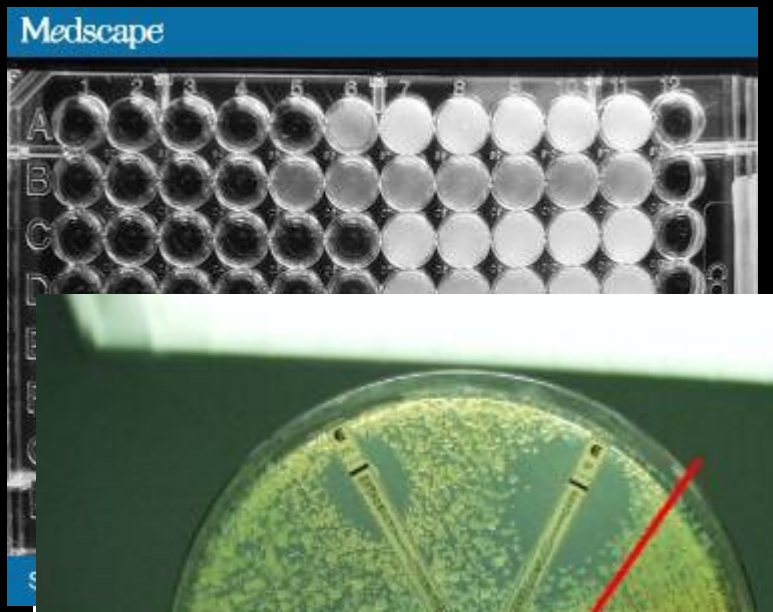


Less invasive triage test spares test-negative patients harms of more invasive test (though trade-off with accuracy)

Changing timeframes:
timing of testing, diagnosis & treatment

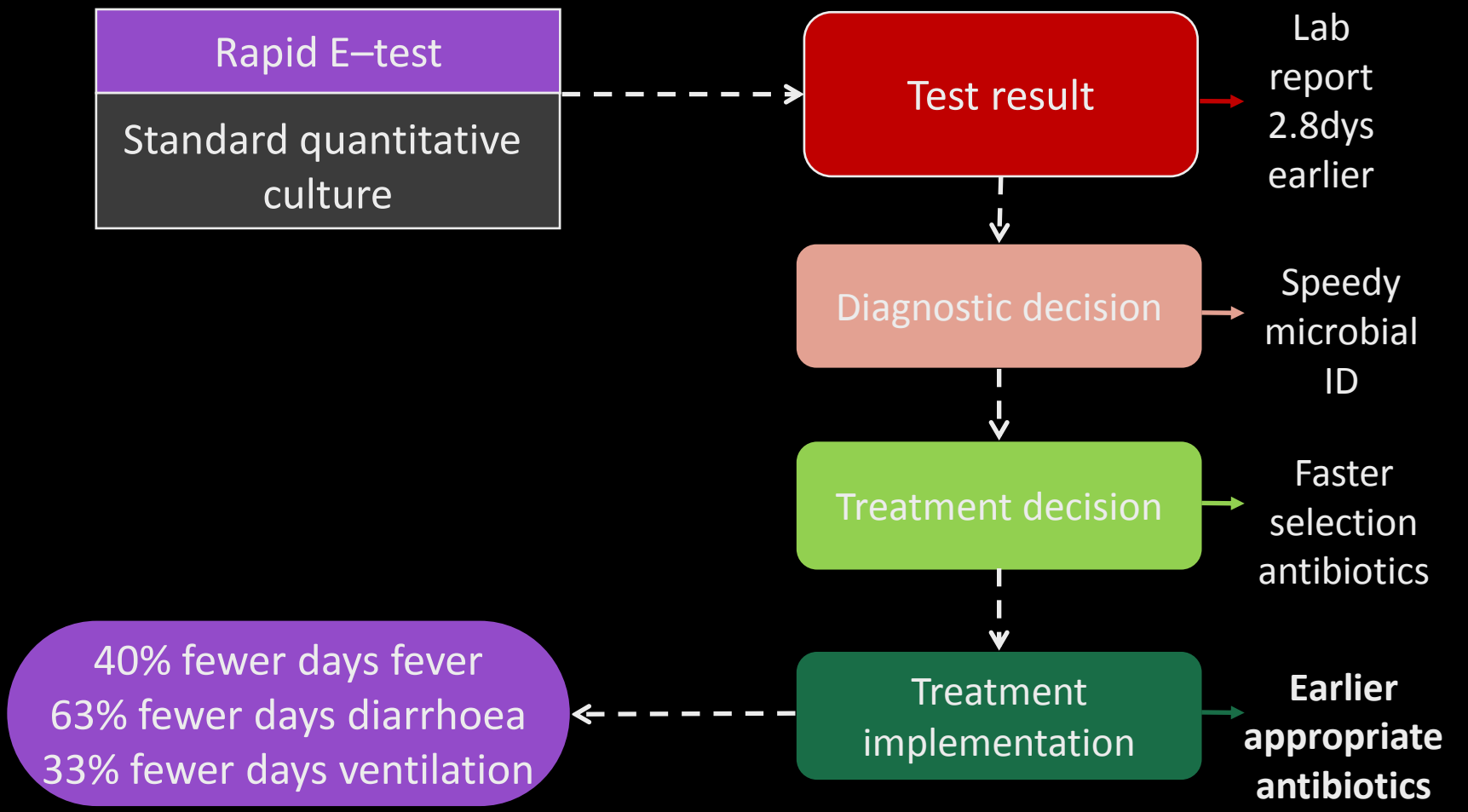
Confirming the cause of pneumonia:

- Quantitative culture
  - antimicrobial susceptibility
  - Lengthy process
- Rapid E–test
  - Antibiotic strips
  - Quicker to process
  - ? Speeds up time to treatment



http://dx.doi.org/10.1016/j.diagmicrobio.2006.12.021

Bouza *et al. Clin Infect Dis 2007;44:382-87*



Quicker turn–around time allows faster diagnosis and treatment

Evaluating how tests change patient health

UNINTENDED EFFECTS

...when good tests don't work

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Unintended effects:
diagnostic confidence

Staging lung cancer:

- Thoracotomy
  - Resect tumour
  - Definitive staging
  - ‘Futile’ procedure if cancer inoperable
- PET
  - Pre–surgical staging
  - Highly accurate
  - ?identification of more patients with inoperable disease

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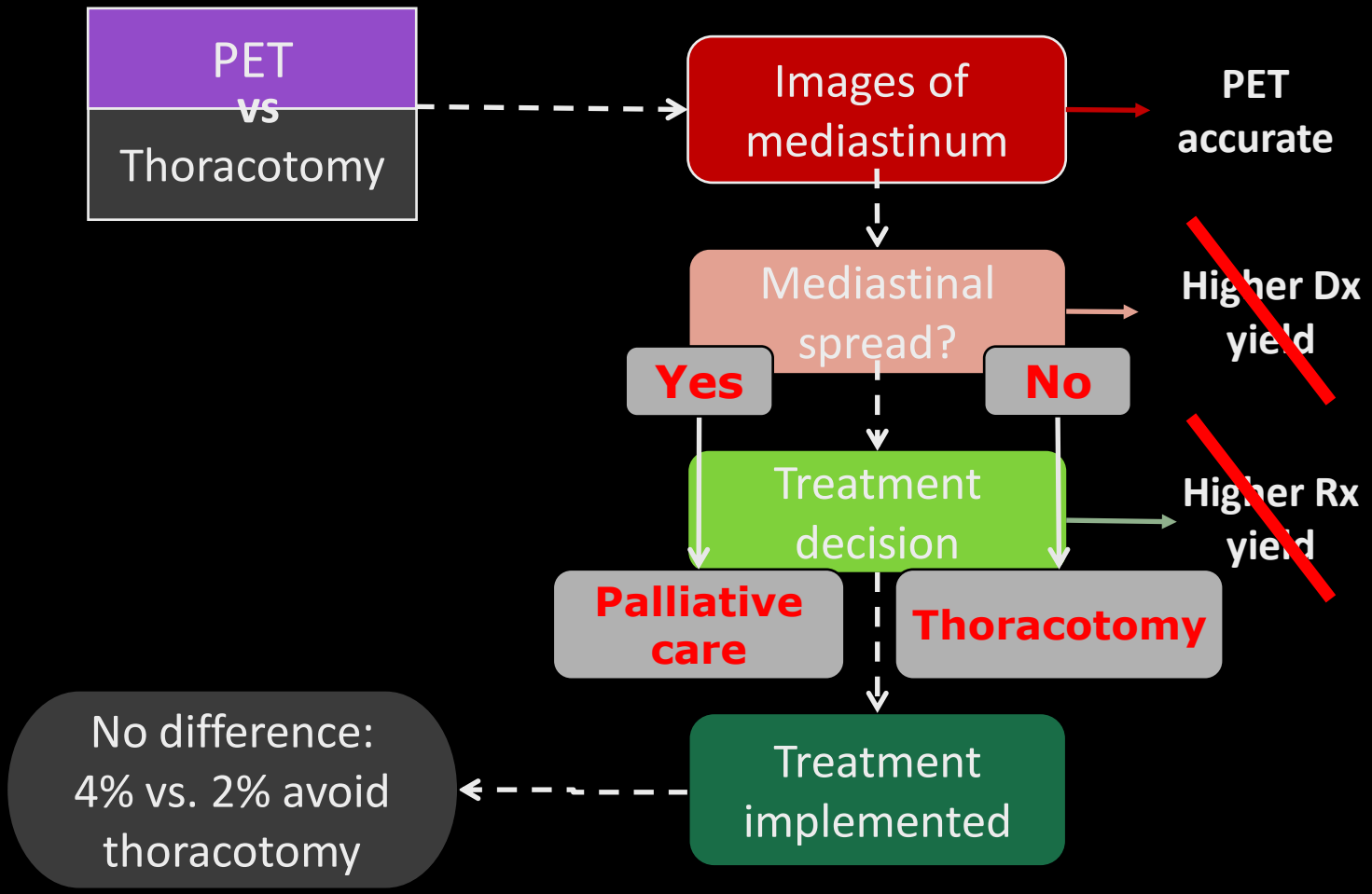
Unintended effects:
diagnostic confidence

Viney et al. J Clin Oncol 2004;22:2357-2362



Enhanced accuracy fails to change diagnostic decisions as surgeons lack confidence in PET results.

Are RCTs the answer?

- Well designed RCTs can measure all effects
  - Intended and unintended
- ...but 'test-treatment RCTs' are not always feasible:
  - Large sample sizes
  - Clinican adherence is problematic
  - Difficult to eliminate bias (e.g. Blinding)
  - Rapid advance vs. long–term follow–up

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A more practical solution?

BMJ

BMJ 2012;344:e686 doi: 10.1136/bmj.e686 (Published 21 February 2012)

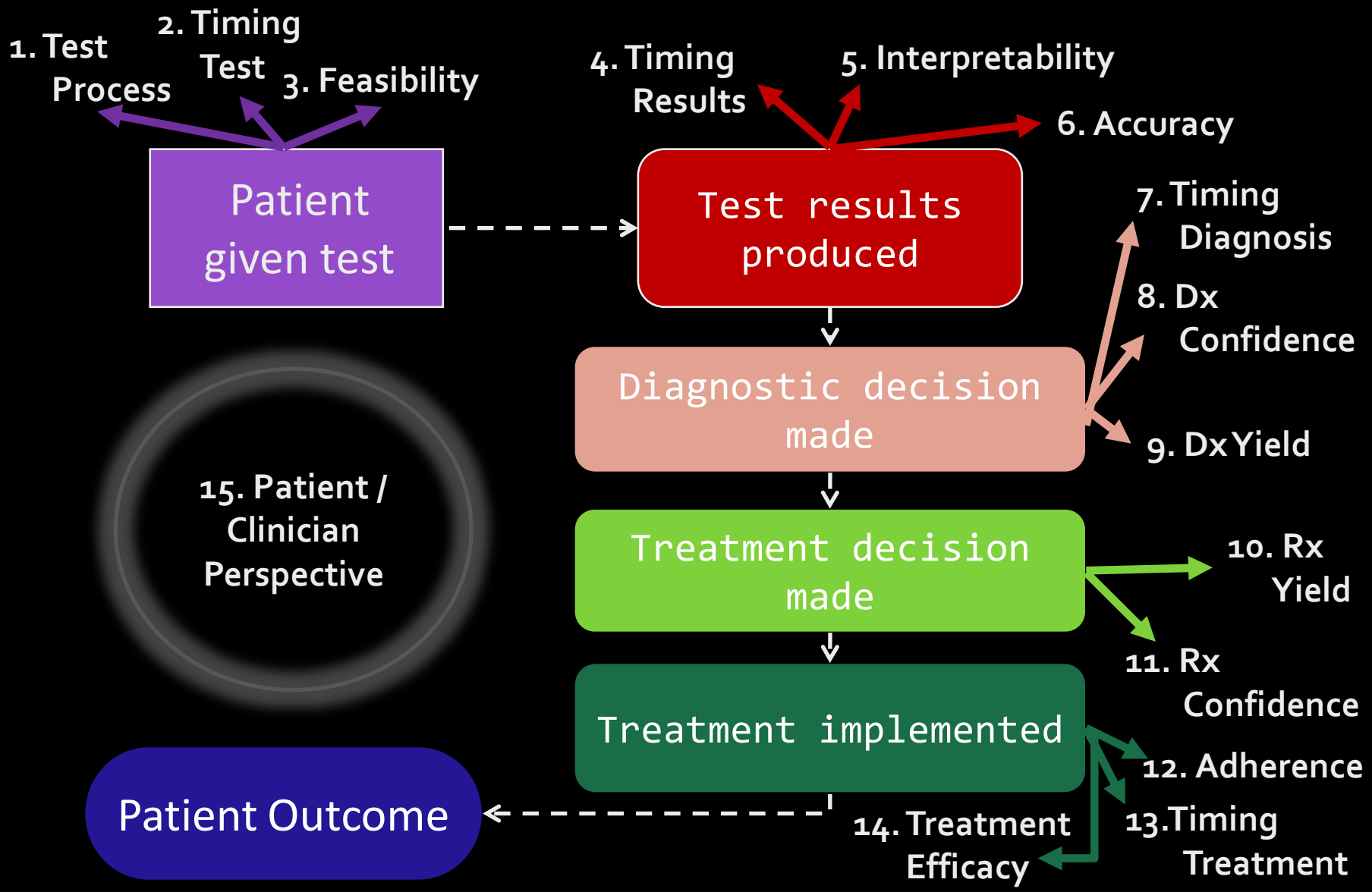
RESEARCH METHODS & REPORTING

Assessing the value of diagnostic tests: a framework for designing and evaluating trials

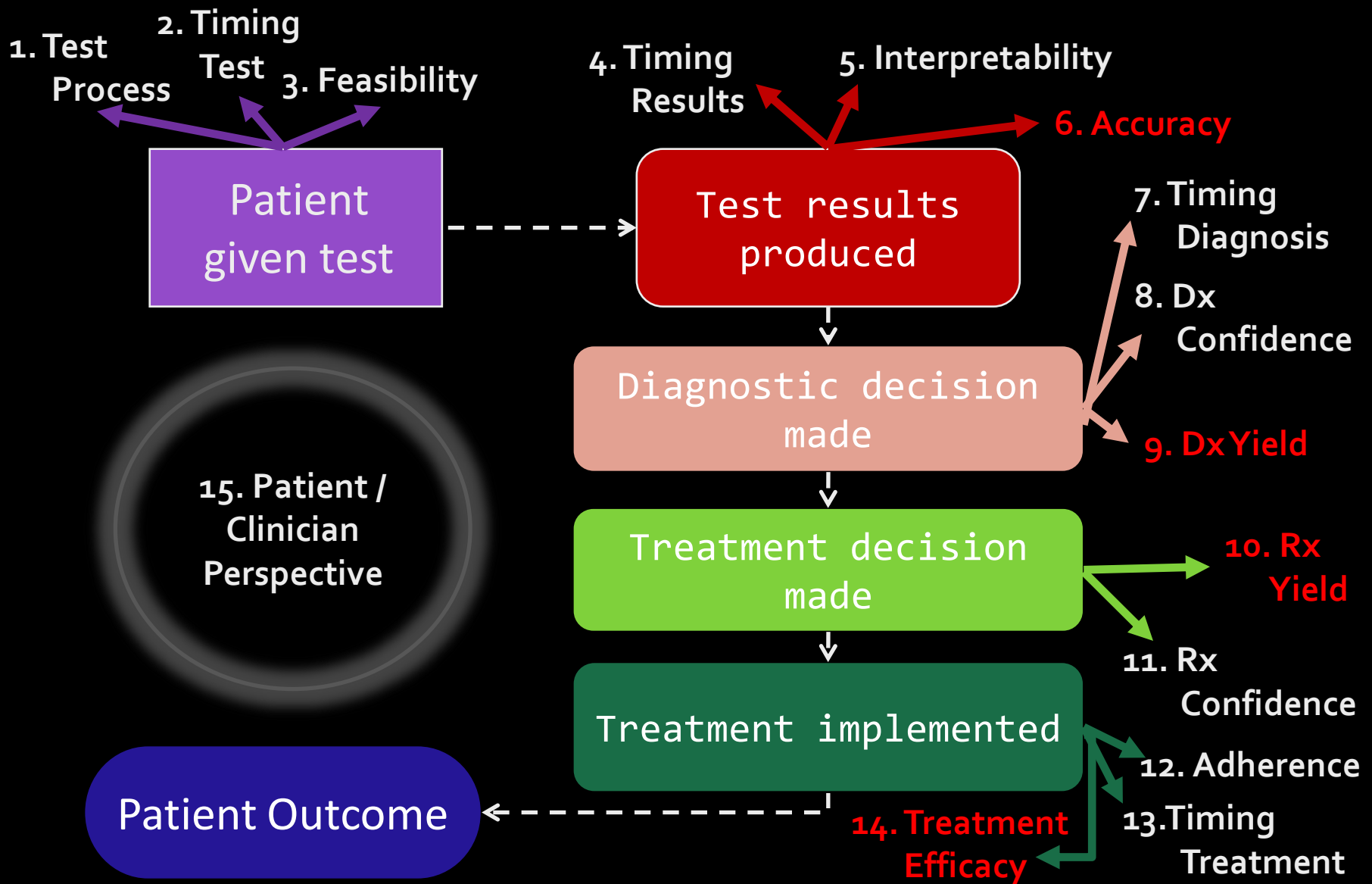
The value of a diagnostic test is not simply measured by its accuracy, but depends on how it affects patient health. This article presents a framework for the design and interpretation of studies that evaluate the health consequences of new diagnostic tests

Lavinia Ferrante di Ruffano *research fellow*[1], Christopher J Hyde *professor of public health and clinical epidemiology*[2], Kirsten J McCaffery *associate professor and principal research fellow*[3], Patrick M M Bossuyt *professor of clinical epidemiology*[4], Jonathan J Deeks *professor of biostatistics*[1]

A more practical solution?



A more practical solution?



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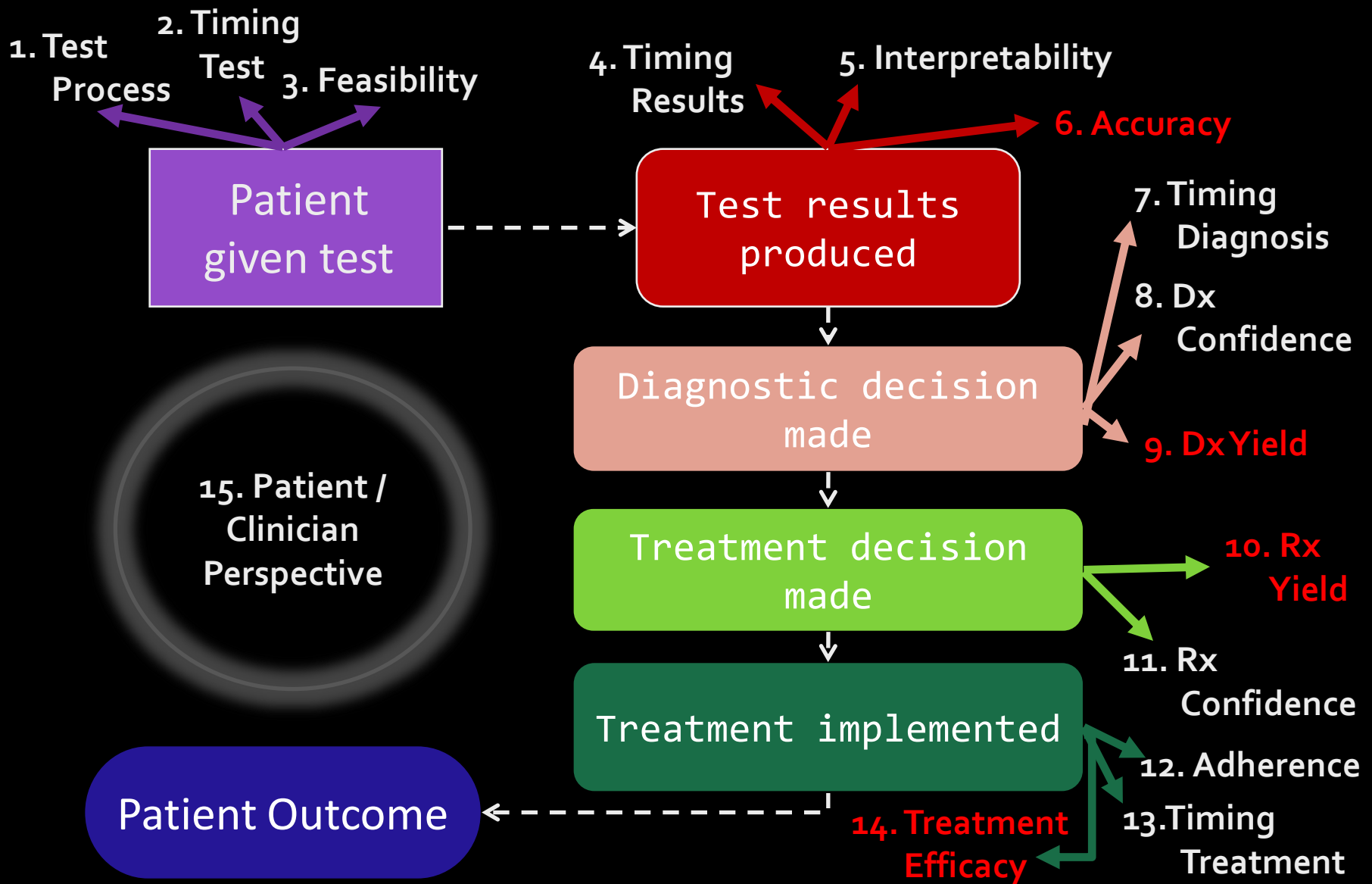

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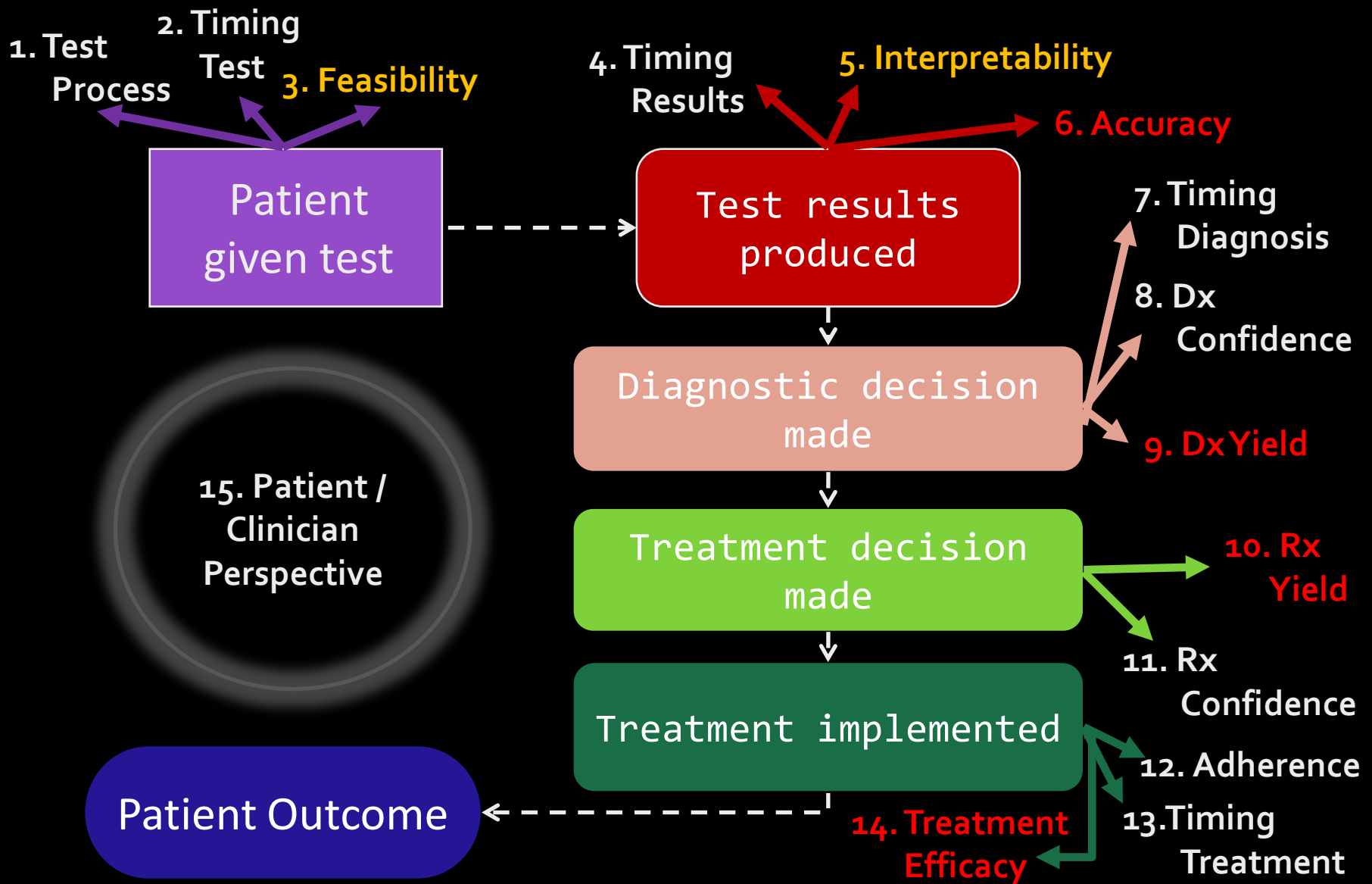

	Might there be an important difference between the existing and new test strategies in:				Y/N/?
Test Delivery	Timing of test:	a.	Time to test delivery?	Do the diagnostic strategies administer testing within comparable timeframes, e.g. does the new strategy administer a diagnostic test considerably earlier than its comparator?	
	Feasibility:	b.	Acceptability?	Is one test likely to be more/less acceptable to patients than the other test, e.g. does one test carry a significantly increased risk of harm?	
		c.	Clinical contra-indications?	Is one test likely to be suitable to different proportions of the relevant patient group, e.g. might one test be contraindicated in additional/fewer patients?	
		d.	Technical failure rates?	Do the two test processes produce different proportions of failed procedures, e.g. does the process of one test tend to fail more frequently than the other?	
	Test Process:	e.	Procedural harms or benefits?	Do the two tests differ in how they affect patients during their application both physically or psychologically, e.g. is one test more intrusive than the other, does one test have a higher procedural-related morbidity than the other?	
		f.	Placebo effect?	Could one diagnostic strategy give patients a different perspective on being investigated than the other, e.g. might one test give greater encouragement to patients as to the thoroughness of their investigation?	
Test Result	Interpretability:	g.	Ease of interpretation?	Do the two test processes produce different frequencies of clearly interpretable test results, e.g. once the test has been completed successfully, does one test tend to produce a higher frequency of indeterminate or unreadable results?	
	Accuracy:	h.	Accuracy?	Do the tests correctly identify the target condition in different patients, e.g. does one test have a proven or hypothesised ability to identify a higher proportion of diseased &/or non-diseased patients than the other?	
	Timing of results:	i.	Time to produce a result?	Does the speed with which test data are processed differ between tests, e.g. is the turn-around-time between administration of test and production of results considerably different between tests?	

How much evidence is enough?

- Evidence of intended and unintended effects
  - Portfolio of smaller primary studies, e.g.
    - Diagnostic impact study
      (Accuracy, Diagnostic/Therapeutic decision–making)
    - Qualitative research
      (patient acceptability, clinician interpretation of tests)
    - Short–term RCTs
      (diagnostic processes)
  - Combine evidence from multiple studies using decision–analytic modelling

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Summary

- Effects of tests are numerous, indirect & complicated
- Key task is to identify how new test could benefit and harm patients:
  - Definition of where test ‘fits’ within a care pathway
  - Comparison to current care pathway
  - Consideration of differences between the two
  - Identification of all possible effects
    - ↳ Intentional and unintentional consequences

- *...BUT complex trade–offs between effects may require RCTs*

Acknowledgements

Jon Deeks

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Patrick Bossuyt

Kirsten McCaffery

- Ferrante di Ruffano L, et al. Assessing the value of diagnostic tests: a framework for designing and evaluating trials. BMJ 2012;344:e686

Thank you for listening…

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