NIHR Diagnostic Evidence Co-operative Oxford

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Four Diagnostic Evidence Co-operatives (DEC)

➔ Facilitate development clinically relevant IVDs

- Interactions with industry
- DEC-specific themes

Diagnostic Evidence Co-operatives: NHS organisations and clinical themes

NIHR Leeds Teaching Hospitals NHS Trust DEC
Generating high quality evidence on protein and cellular biomarker-based IVDs for the clinical management of musculoskeletal, urological, liver and colorectal diseases and oncology
www.leeds.dec.nihr.ac.uk

NIHR Newcastle upon Tyne Hospitals NHS Foundation Trust DEC
Generating high quality evidence for new diagnostics tests for cancer, cardiovascular, liver, musculoskeletal and respiratory diseases, stroke, genetics, infections and transplantation
www.newcastle.dec.nihr.ac.uk

NIHR Oxford Health NHS Foundation Trust DEC
Generating high quality evidence for primary care IVDs across a range of common diseases and improving "bench to bedside" processes to implement IVDs into primary care
www.oxford.dec.nihr.ac.uk

NIHR Imperial College Healthcare NHS DEC
Generating high quality evidence for point-of-care in vitro diagnostic tests for gut health, primary and general care, respiratory disease, infectious disease, metabolic medicine, cardiovascular disease, cancer, women's health and paediatrics
www.london.dec.nihr.ac.uk

General Practice– the "perfect storm" for innovation in diagnostic tests

- 'Front door" to NHS
- Multiple lab tests
- Ageing population
- Multi-morbidity
- Chronic disease management
- Cost-containment – reducing unnecessary referrals
- Misdiagnosis malpractice
- Little current use of IVDs
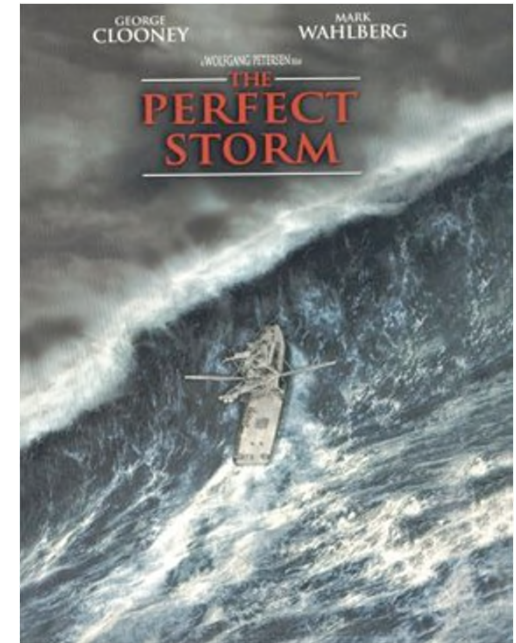
Oxford DEC strategy

Theme 1:   New and emerging diagnostic technologies

Theme 2:   Unmet diagnostic test needs in primary care

Theme 3:   Rapid testing to improve decision-making in community care

Theme 4:   Patient, carer & professional attitudes to implementing IVDs in primary care

Theme 5:   Improved methods for deriving and translating evidence for diagnostic tests

Industry liaison programme

Diagnostics industry collaborations

- Monthly meetings
  - New diagnostic technology

- Industry support service
  - Evidence reports
  - Needs assessment
  - Laboratory accuracy studies
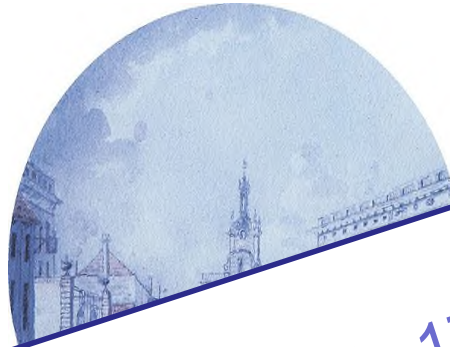 - Clinical field studies
  - Joint bids for funding

Goals for this course

Evidence and policy decisions

J Int Med, October 1991:289, Reprinted in Ann Intern Med 1992;117:30

Evidence and policy decisions

Coffee was forbidden in Sweden in 1794 and again in 1822.

83+

83

'Industry-research-clinical-commissioning' disconnect
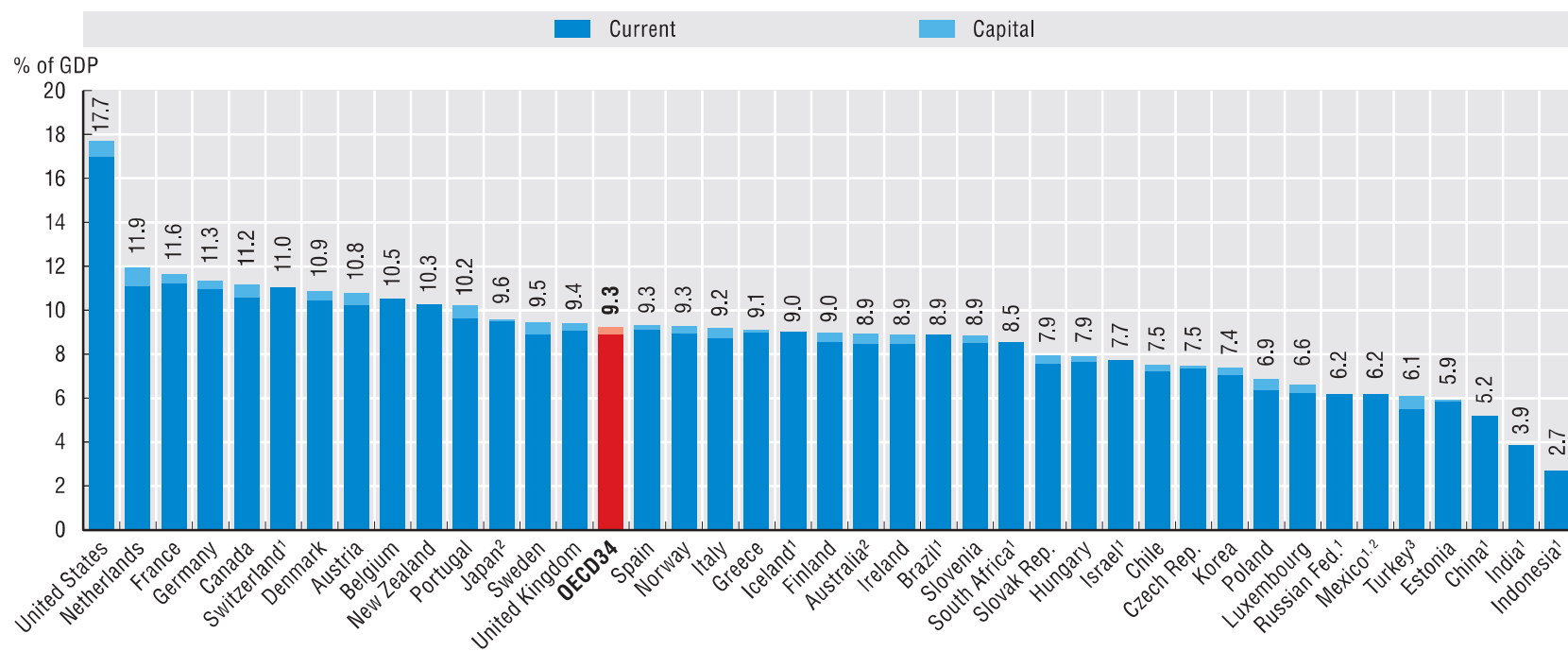
Available IVDs & technical capabilities.
Accuracy/ease/size/
speed/range/bundling

Current clinical practice.

Minimal test dissemination and adoption in primary care

Health is priceless

Legend: Current, Capital

% of GDP

Country	Value
United States	17.7
Netherlands	11.9
France	11.6
Germany	11.3
Canada	11.2
Switzerland[1]	11.0
Denmark	10.9
Austria	10.8
Belgium	10.5
New Zealand	10.3
Portugal	10.2
Japan[2]	9.6
Sweden	9.5
United Kingdom	9.4
OECD34	9.3
Spain	9.3
Norway	9.3
Italy	9.2
Greece	9.1
Iceland[1]	9.0
Finland	9.0
Australia[2]	8.9
Ireland	8.9
Brazil[1]	8.9
Slovenia	8.9
South Africa[1]	8.5
Slovak Rep.	7.9
Hungary	7.9
Israel[1]	7.7
Chile	7.5
Czech Rep.	7.5
Korea	7.4
Poland	6.9
Luxembourg	6.6
Russian Fed.[1]	6.2
Mexico[1,2]	6.2
Turkey[3]	6.1
Estonia	5.9
China[1]	5.2
India[1]	3.9
Indonesia[1]	2.7

From health question to evidence

- Could the test be accurate?

- Is the test accurate in real patients?

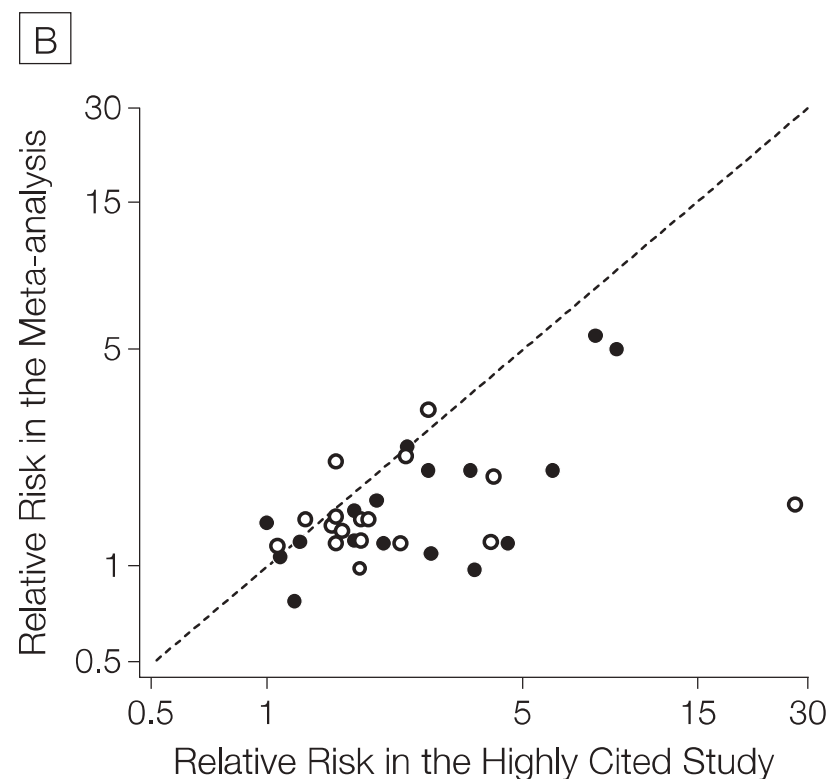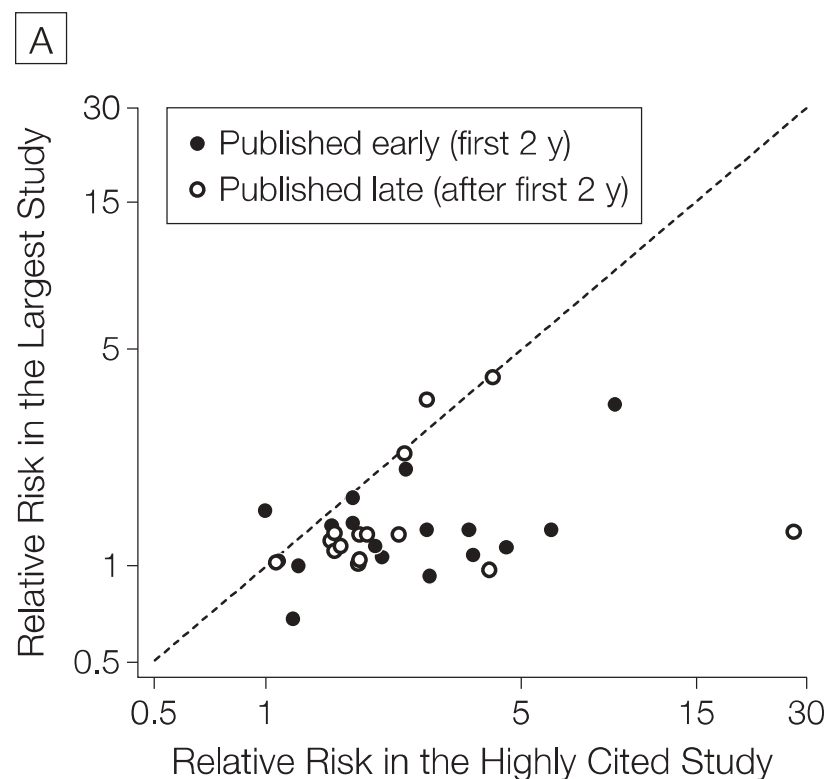- Are patients better off with the test?

- At what costs?

The winner's curse

Ioannidis JAMA 2011

Figure. Relative Risks in the Highly Cited Studies vs the Corresponding Largest Studies and in the Highly Cited Studies vs the Corresponding Meta-analyses

Statistically significant 'positive' results are:

- More likely to be published
  - **publication bias**

- More likely to be published rapidly
  - **time lag bias**

- More likely to be published in English
  - **language bias**

- More likely to be cited by others
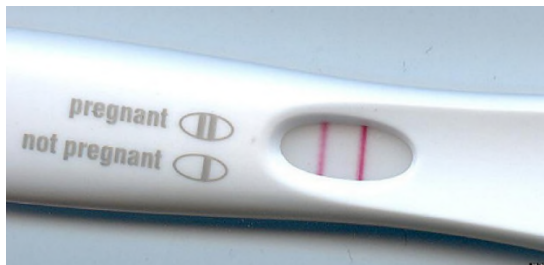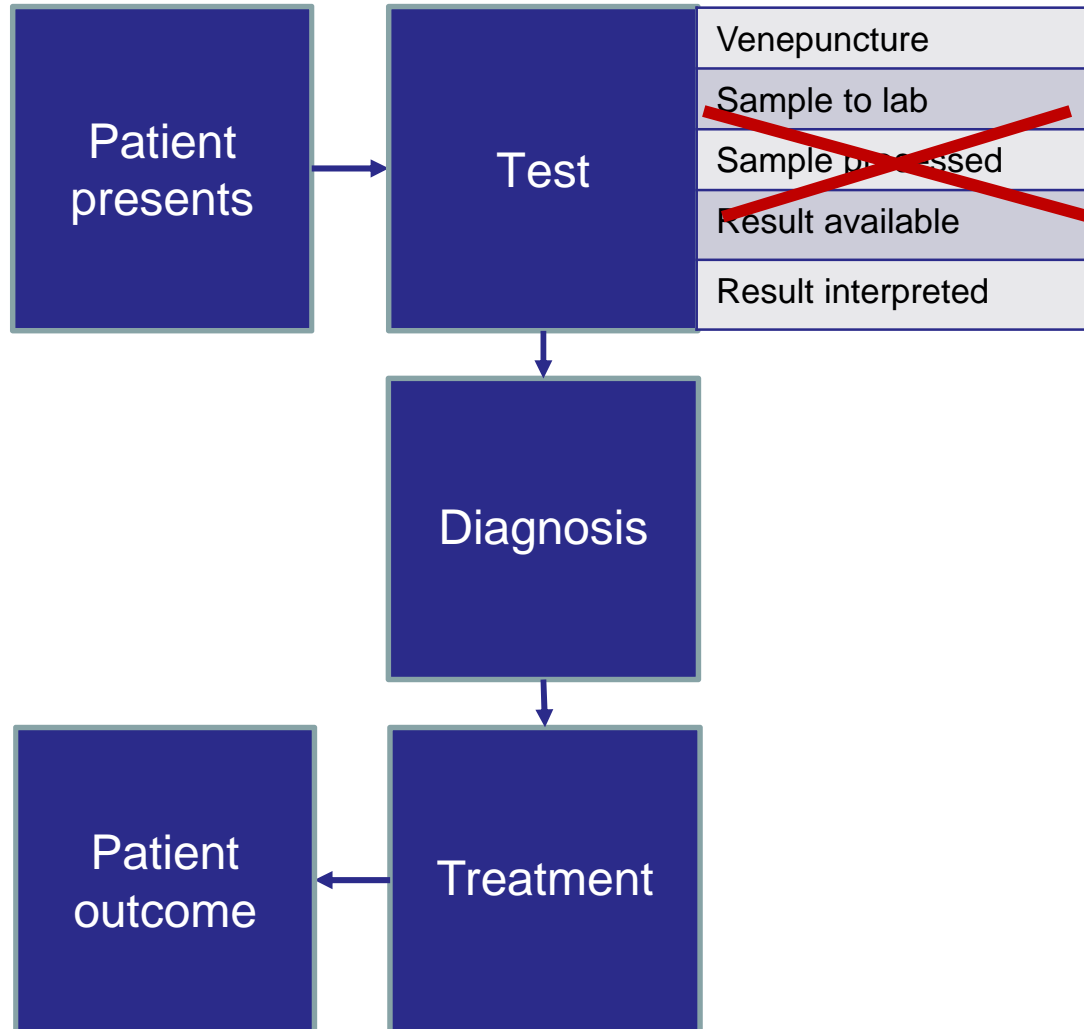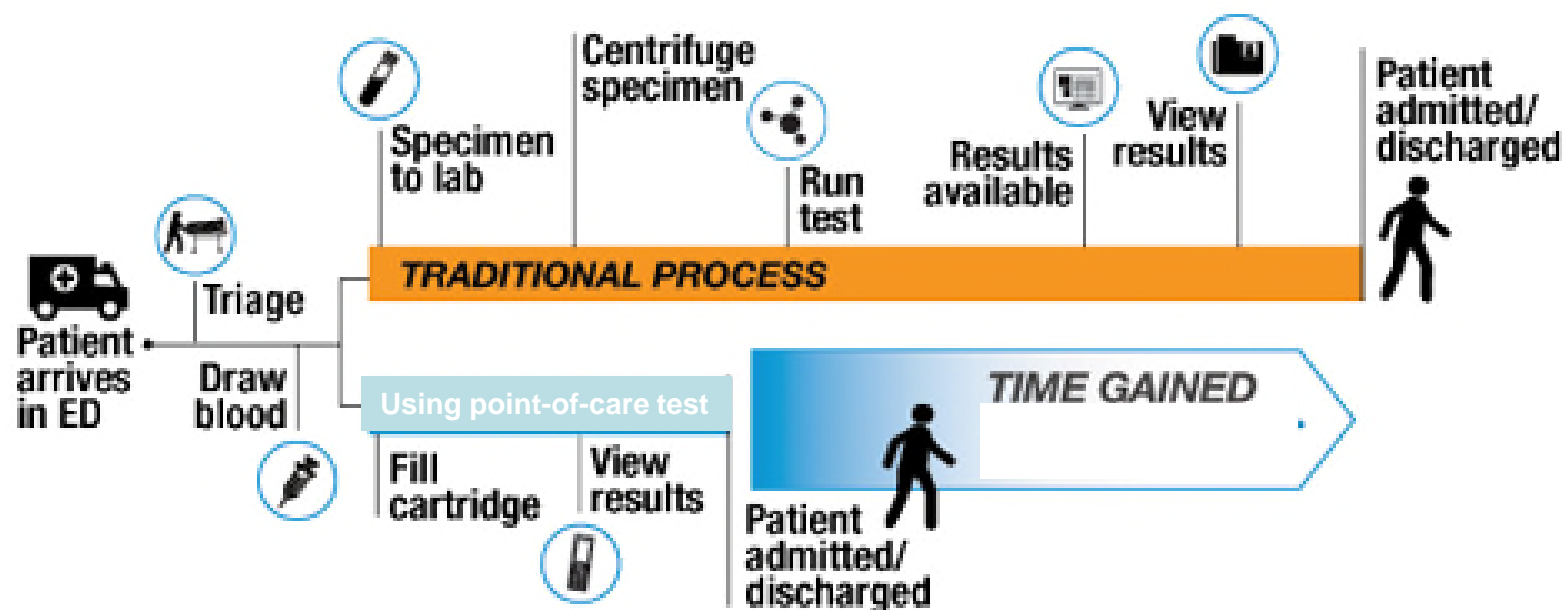 - **citation bias**
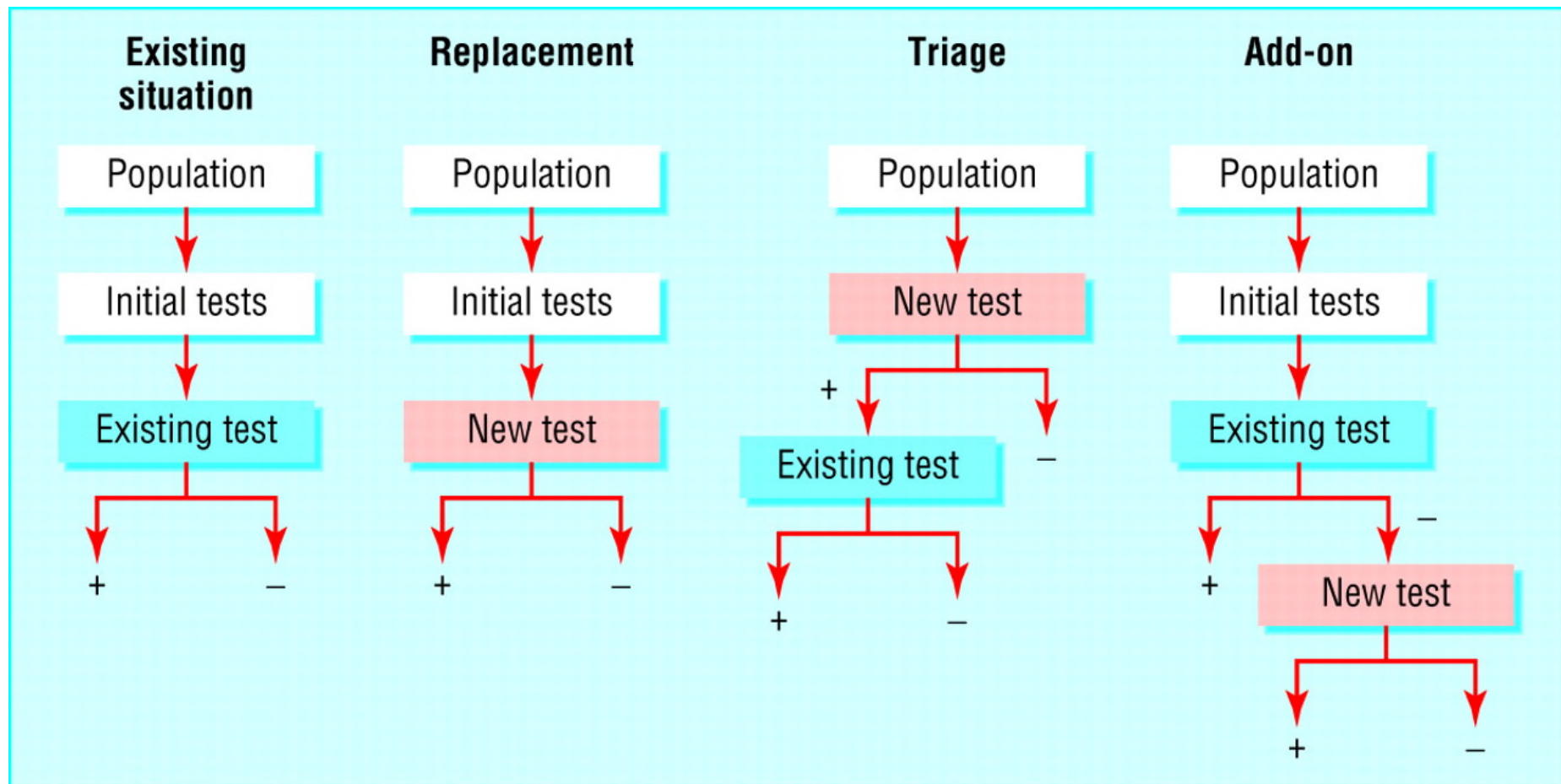
Point-of-care tests

- At the bedside of the patient / in the doctor's surgery / in the patient's home

- Single test - miniature labs - handheld ultrasound

- Results rapidly available

Changes the diagnostic process

Randomised controlled trial evidence

TABLE 13 Successful discharge home (primary outcome)

	PoC [n (%)]	SC [n (%)]
Successfully discharged	358 (32)	146 (13)
Not successfully discharged	767 (68)	972 (87)

Reason for no successful discharge

In hospital 4 hours after arrival and no decision has bee~
discharge
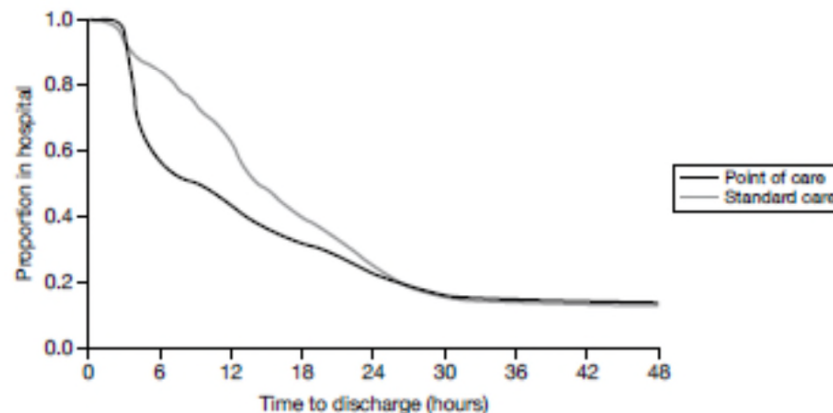
Initially discharged but re-attended with major adverse

Discharge success by initial status

Initially discharged

Not in hospital at 4 hours

In hospital at 4 hours; decision made to discharge

PoC, point of care; SC, standard care.

FIGURE 3 Duration from arrival to discharge from hospital (all centres).

Goodacre S 2011. RATPAC trial: point-of-care cardiac markers in the ED for patients with chest pain.

Time-related effects

Process outcomes

- Faster throughput

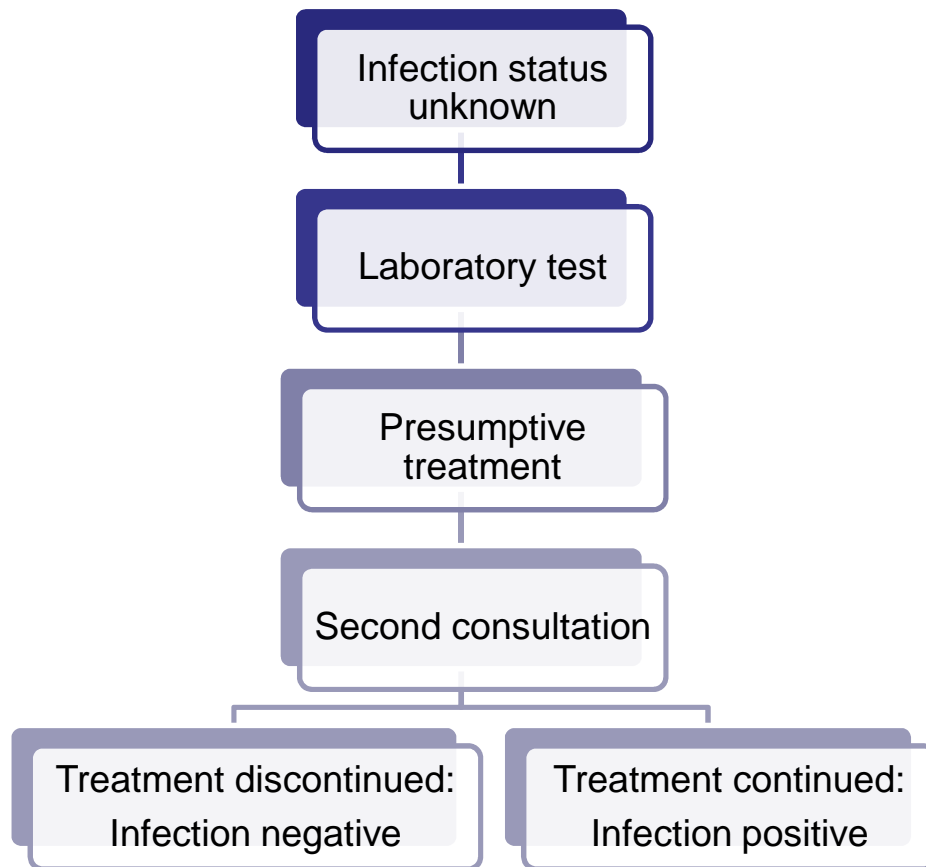- Waiting times target

- Repeat consultations for lab result

Patient outcomes

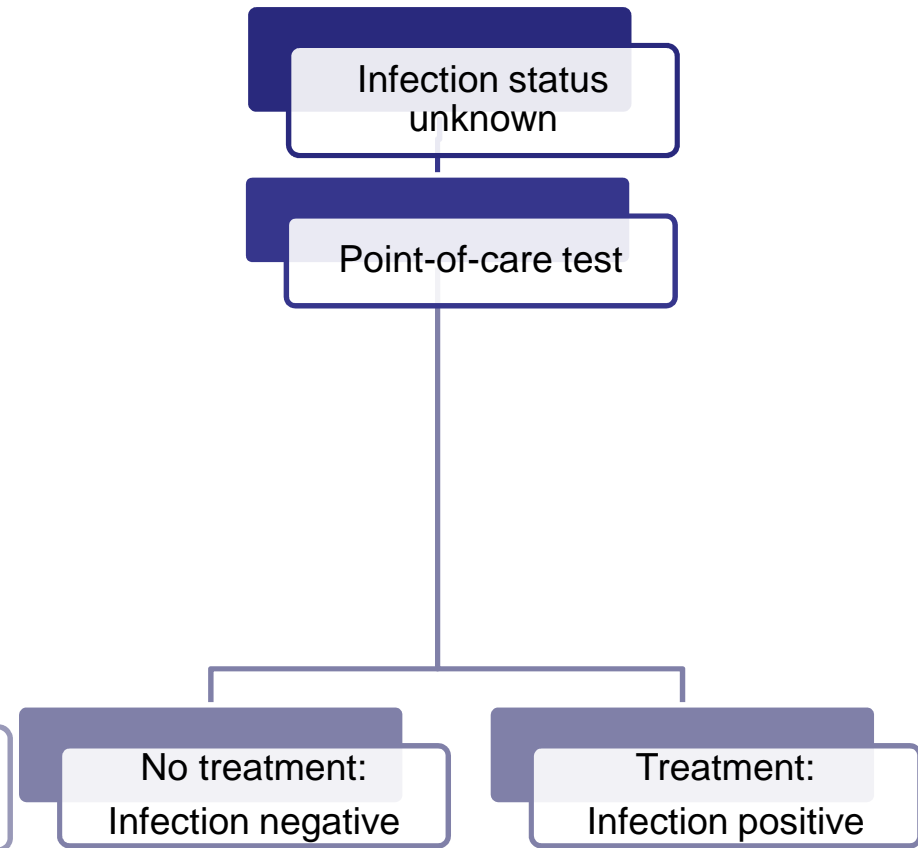- Faster diagnosis

- Faster treatment

- Patient satisfaction

Time-related downstream effects

Chlamydia and gonorrhoea – usual care pathway

Chlamydia and gonorrhoea – point-of-care pathway

Infection status unknown

Laboratory test

Presumptive treatment

Second consultation

Treatment discontinued: Infection negative

Treatment continued: Infection positive

Infection status unknown

Point-of-care test

No treatment: Infection negative

Treatment: Infection positive

Is it just about time?

Changes the diagnostic process
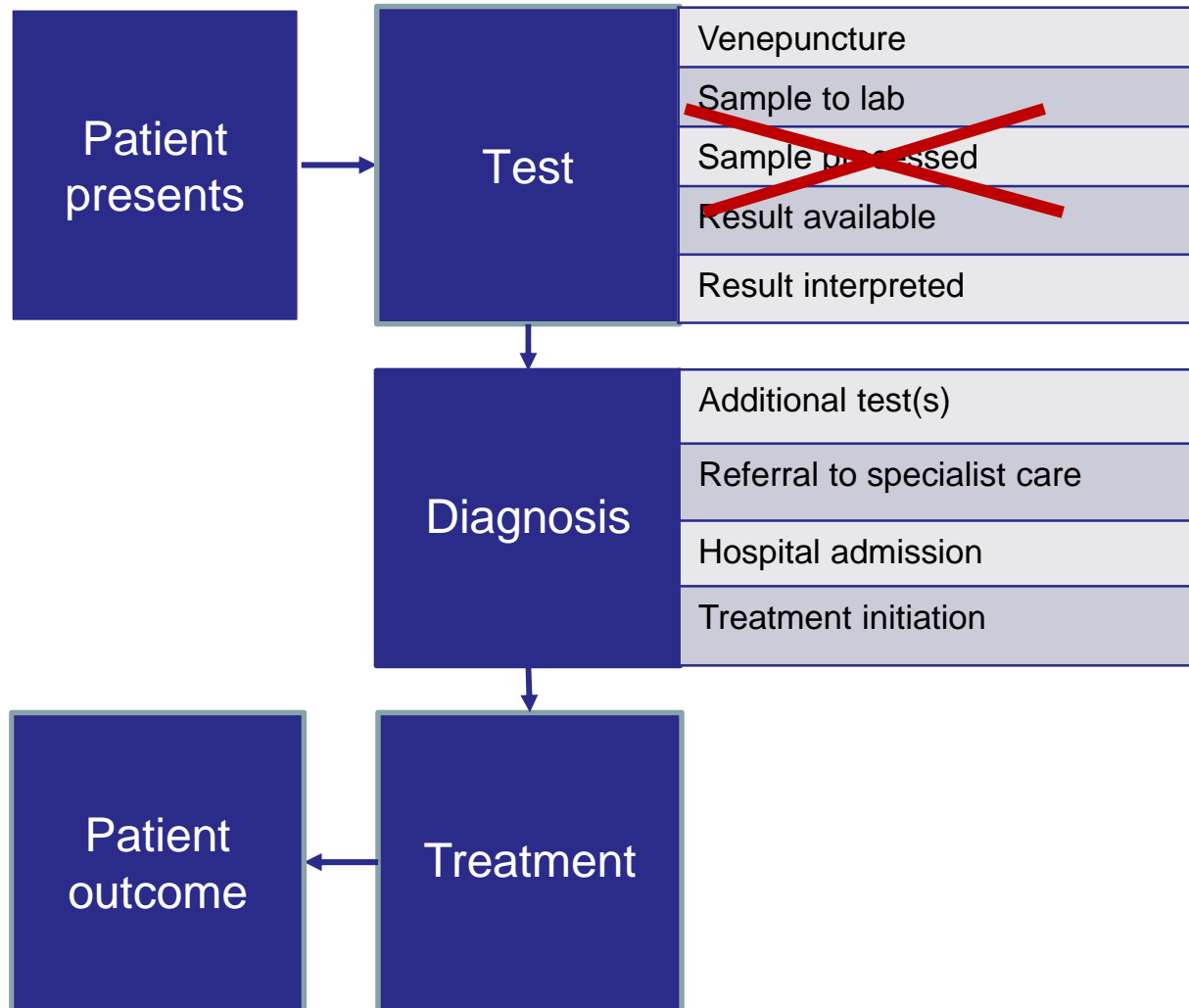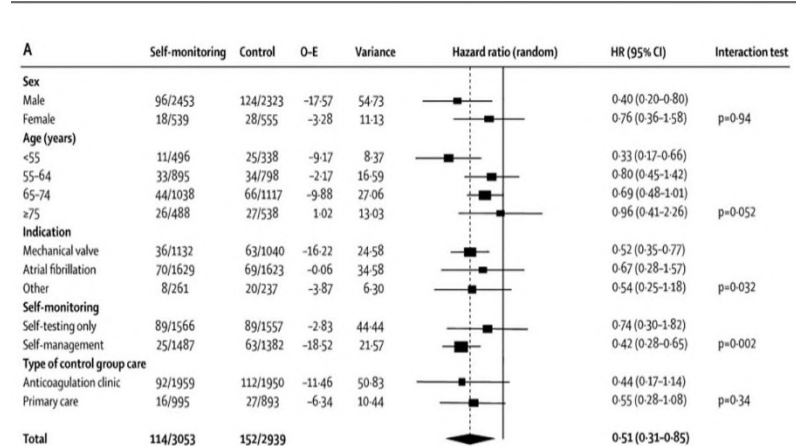
Changes to clinical pathway

- Shift from primary care to patient's home

➔ Way tests are used changes

INR self-management

Heneghan C 2012: Self-monitoring of oral anticoagulation

Changes to clinical pathway

- **Shift from secondary to primary care**

➔ Impact on referrals to next level of care

- BNP for suspected heart failure

- Modelling of costs:
  - 40% reduction in referral to cardiology outpatient departments
  - 25-40% cost-saving
  - NICE estimated whole pathway saving of £3.8 million

- In reality:
  - Echocardiography referrals went up

Spectrum effects

Test threshold lowers:

- More easily available
  - More people get tested

- Less invasive
  - Different people get tested

This will lead to:

- Lower prevalence of target condition

→ More false positives

- Less or differently selected population

→ Spectrum shift

→ Different treatment efficacy

Changes to clinical pathway

- Point-of-care test fills clinical gap:
  - 'Classic' lab test too slow to have impact
  - Point-of-care test in new patient group ➜ Effects on patient outcome unknown

Table 3 Effects of interventions on antibiotic prescribing at index consultation and antibiotic prescribing and reconsultation follow-up

Variables	Intervention groups		Control groups		P value†
	No of patients	Percentage (crude 95% CI*)	No of patients	Percentage (crude 95% CI*)	
C reactive protein test:	n=227		n=204		
Antibiotics at index consultation	70	30.8 (21.8 to 39.8)	108	52.9 (43.0 to 62.8)	0.02
Antibiotics at days 1 to 28	102	44.9 (35.2 to 54.6)	119	58.3 (48.5 to 68.1)	<0.01
Reconsultation within 28 days	79	34.8 (28.3 to 41.3)	62	30.4 (23.8 to 37.0)	0.50

Cals J 2009. Point-of-care testing for C-reactive protein on antibiotic use in lower respiratory tract infections.

Direct impact on patient

- Less invasive
  - Less adverse events from testing

- Treatment adherence

- Anxiety

- Sense of control

"We wanted to make the stress test as realistic as possible."

Direct impact on clinician

- Direct result=direct interpretation
  - No time to think
  - More certainty
  - Enhanced confidence
- Clinical practice effects
  - Fewer re-consultations
  - Undermining of clinical expertise
- Patient-clinician relationship
  - Opportunity for shared decision making
  - Better communication

Implications for research

- Different or new spectrum of patients
  - Diagnostic accuracy?
  - Treatment efficacy?
- Different place in clinical pathway
  - Downstream effects healthcare resources?
- Direct effects on patient outcome
  - Adverse events?
  - Patient satisfaction?

➔ Complex intervention:
  - Modelling - linked evidence approach
  - Randomised controlled trial

In conclusion

- Diagnostic tests used for a variety of purposes
- Evaluation should take a wider system approach
  - Effects on patient
  - Effects on clinician
  - Effects on healthcare system

Thank you!