NICE National Institute for Health and Care Excellence

Evidence for implementation in routine practice

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NICE - aims

Speed the uptake by the National Health Service (NHS) of interventions that are both clinically effective and cost effective

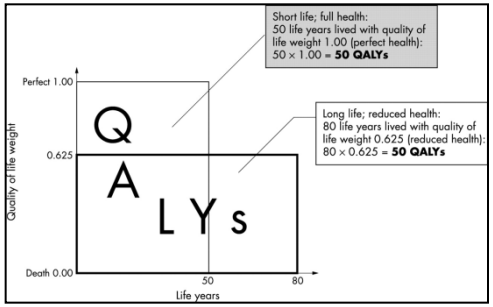
Encourage better and more rational use of available resources by focussing the provision of health care on the most cost-effective interventions

Encourage more equitable access to healthcare (reduce post-code lottery of care)

Encourage the creation of new and innovative technologies.

Economic evaluation of new drugs, medical technologies and clinical practice

vs



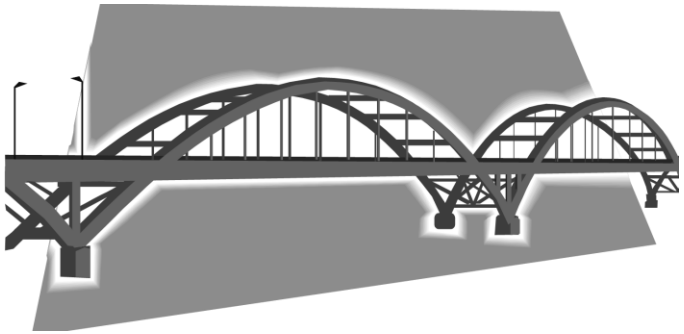
Consistent

Fair

Managing healthcare resources within a fixed budget

Evidence

Product



Market

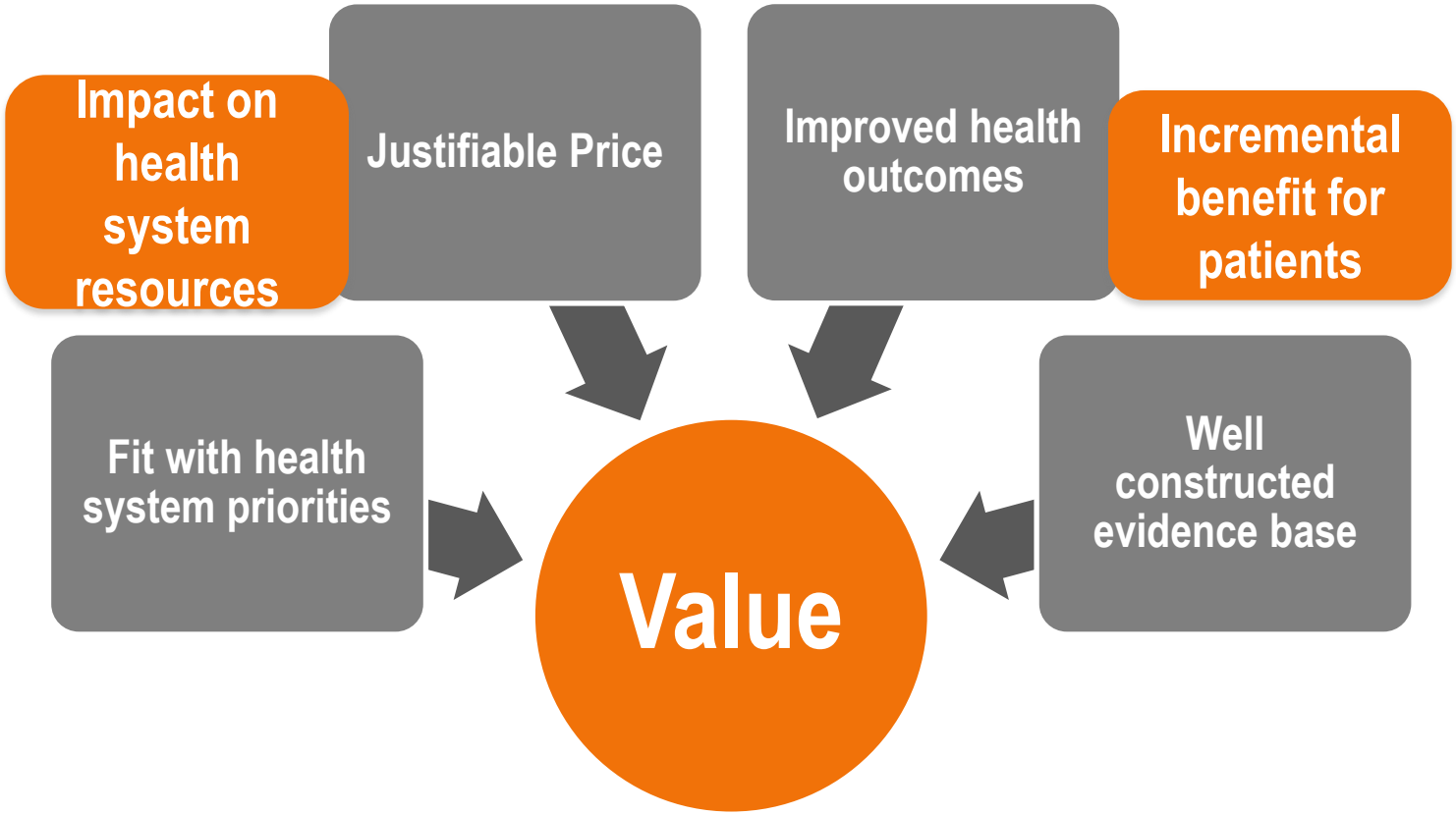
Policy-making

Health Technology Assessment (HTA) is an evidence-based way of guiding the efficient allocation of health care resources

NICE - core guidance principles

- Based on best available evidence
- Expert input
- Patient and carer involvement
- Independent advisory committees
- Genuine consultation
- Regular review
- Open and transparent process

The Value Proposition



Value varies depending on your perspective

NICE takes the perspective of the National Health Service (NHS) and Personal Social Services (PSS)

NICE - who does what?

Centre for Clinical Practice

Clinical guidelines = evidence based recommendations

‘ appropriate treatment and care of people with specific diseases and conditions’

Health and Social Care Directorate

Quality standards & social care guidance

‘QS markers of high quality, cost-effective patient care’

Centre for Health Technology Evaluation

Technology appraisals and guidance on diagnostics, medical technologies and interventional procedures.

NICE ‘Centres’ – Who does what?

Centre for Health Technology Evaluation (CHTE)

Technology appraisals and guidance on *diagnostics*, *medical technologies* (and interventional procedures)

BIVDA

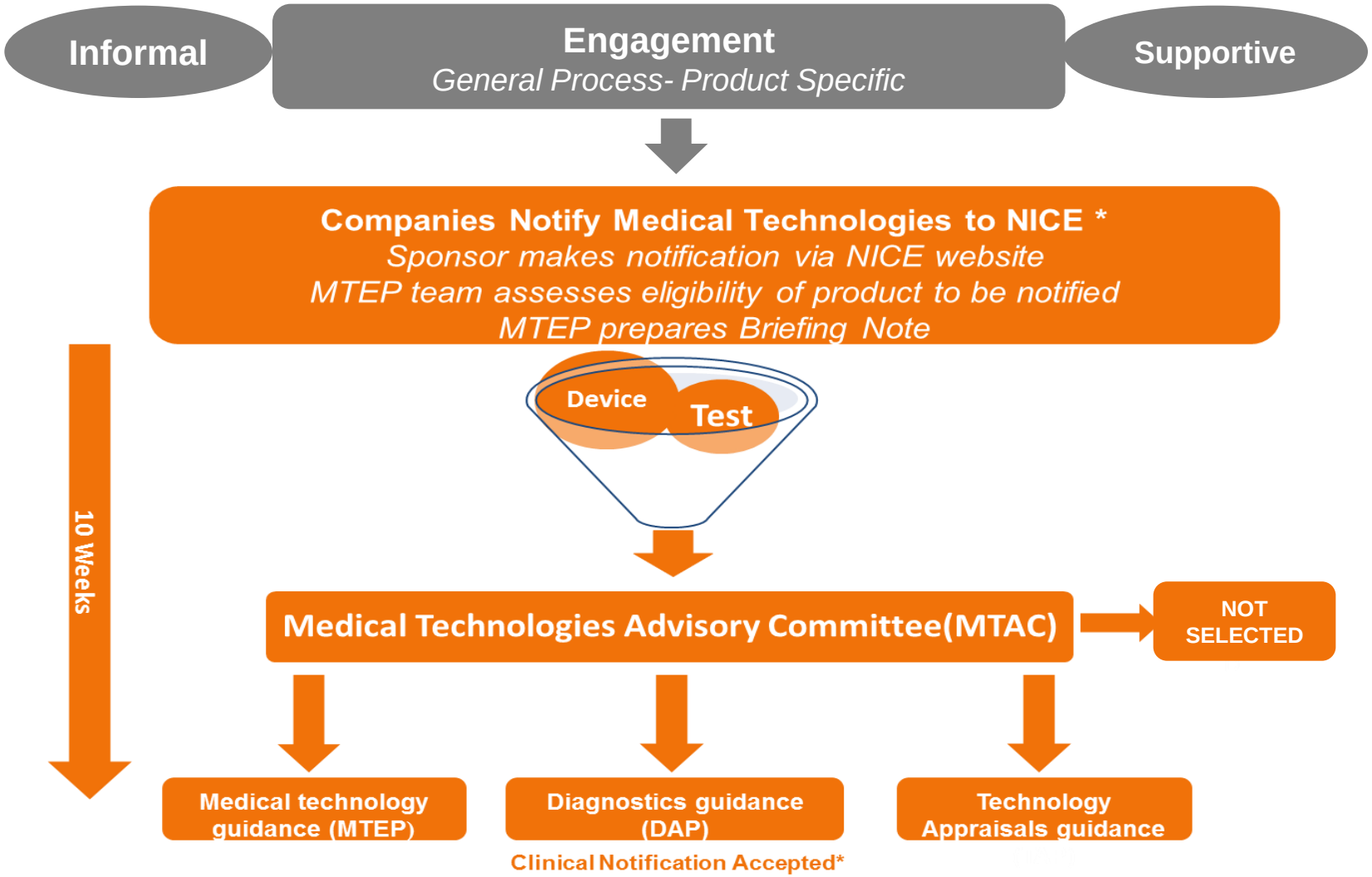
AXrEM

abhi

Two programmes established in 2010:

- driven by notification of technologies by companies/ sponsors
- aiming to improve the timeliness and consistency of adoption of medical technologies and diagnostics with the potential to:
  - Improve patient outcomes
  - Reduce costs
  - Provide system benefits (e.g. facilitate service redesign)

Medical Technologies – Product Selection



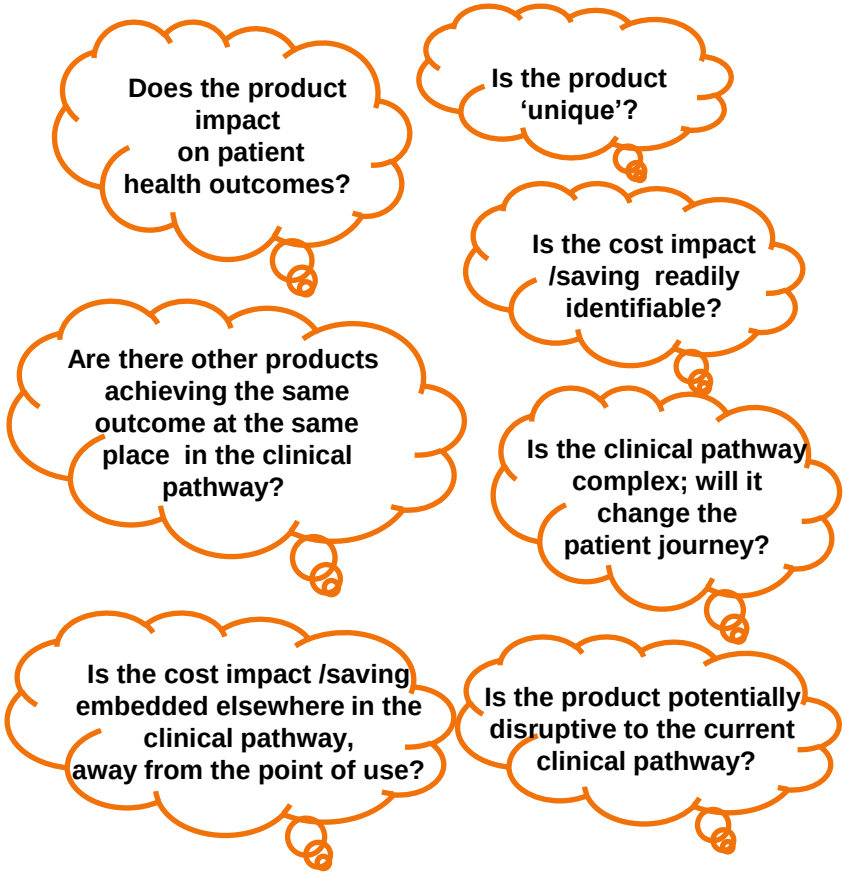
Product Selection

The Company submits a **notification form** to Medical Technologies Evaluation Programme that details:

- Product description
- Patient population
- Current management and comparator(s)
- Claimed patient benefit
- Claimed healthcare system benefit
- Claimed sustainability benefit
- Costs
- Patient safety

Medical Technologies(Devices & Diagnostics) Routing of Selected Products

How does MTAC identify the most appropriate way to assess the value proposition of a selected product?



Assessment Methodologies

Cost Consequences

- Non –inferior clinical performance i.e. health outcomes remain unchanged
- Demonstrates cost impacts i.e. cost saving vs. current standard of care

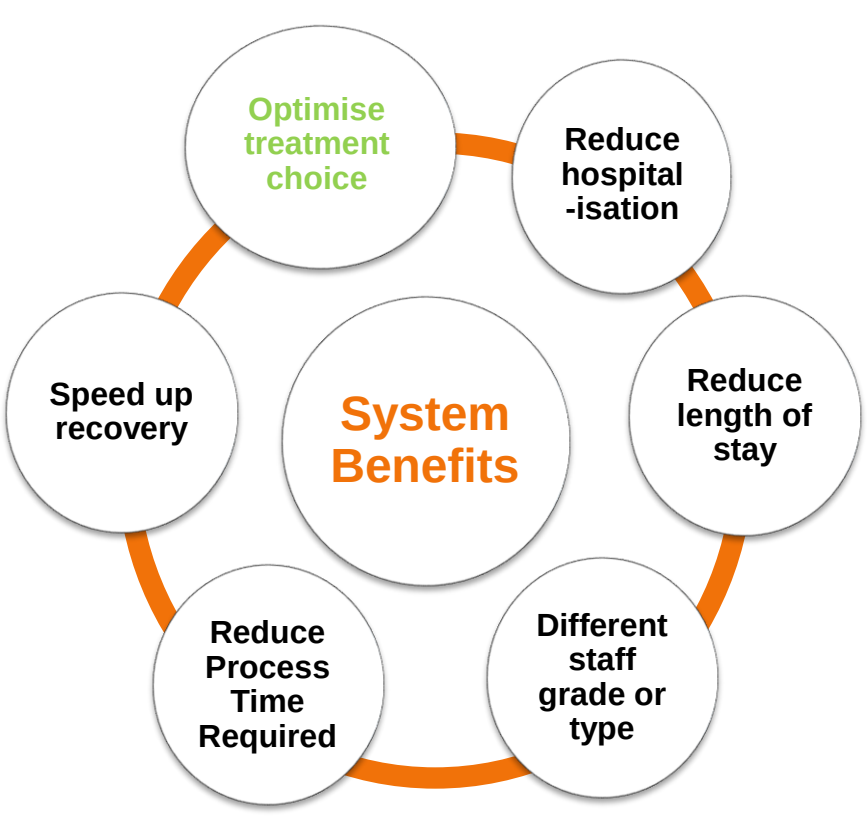
Cost Effectiveness

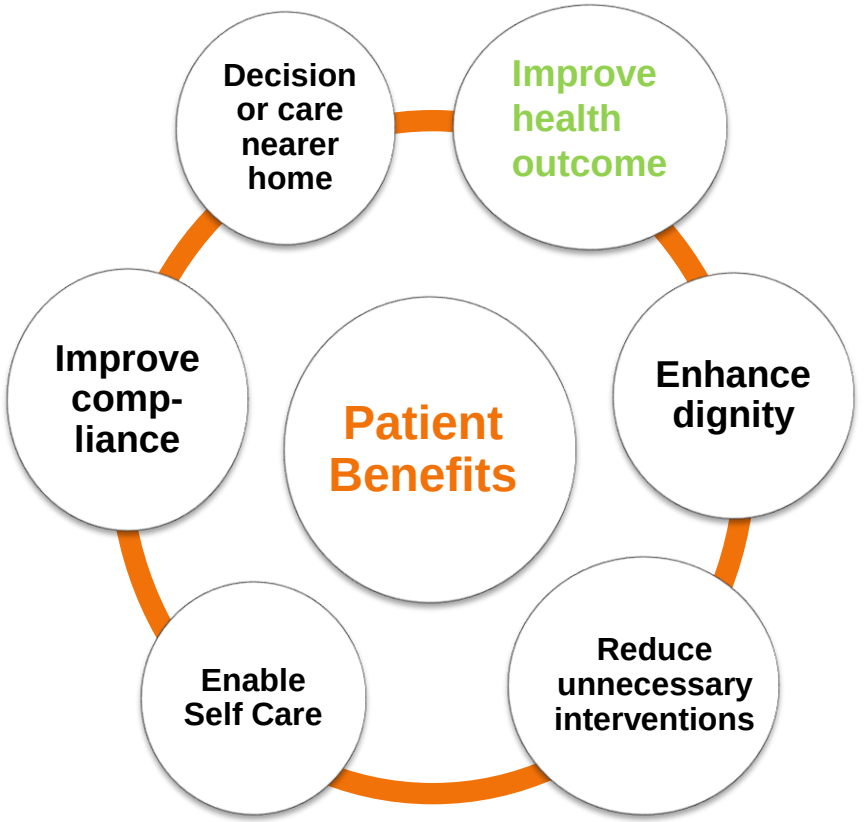
- Assesses impact on health benefits i.e. increases (or decreases) and
- the associated cost impacts i.e. cost saving (or cost increasing) vs. current standard of care

Routing of Selected Products

Clinical Performance	↑		=
Cost Impact	£↓ or ↑		£↓
Evaluation Method	*Cost effectiveness (£/QALY)*		*Costs consequences (£)*
NICE Guidance Programme	*Technology Appraisals Programme (TAP)*	*Diagnostics Assessment Programme (DAP)*	*Medical Technologies Evaluation Programme (MTEP)*
Technologies	✓ ***Devices***	✓ ***Diagnostics***	✓ ***Devices*** ✓ ***('Simple Diagnostics')***

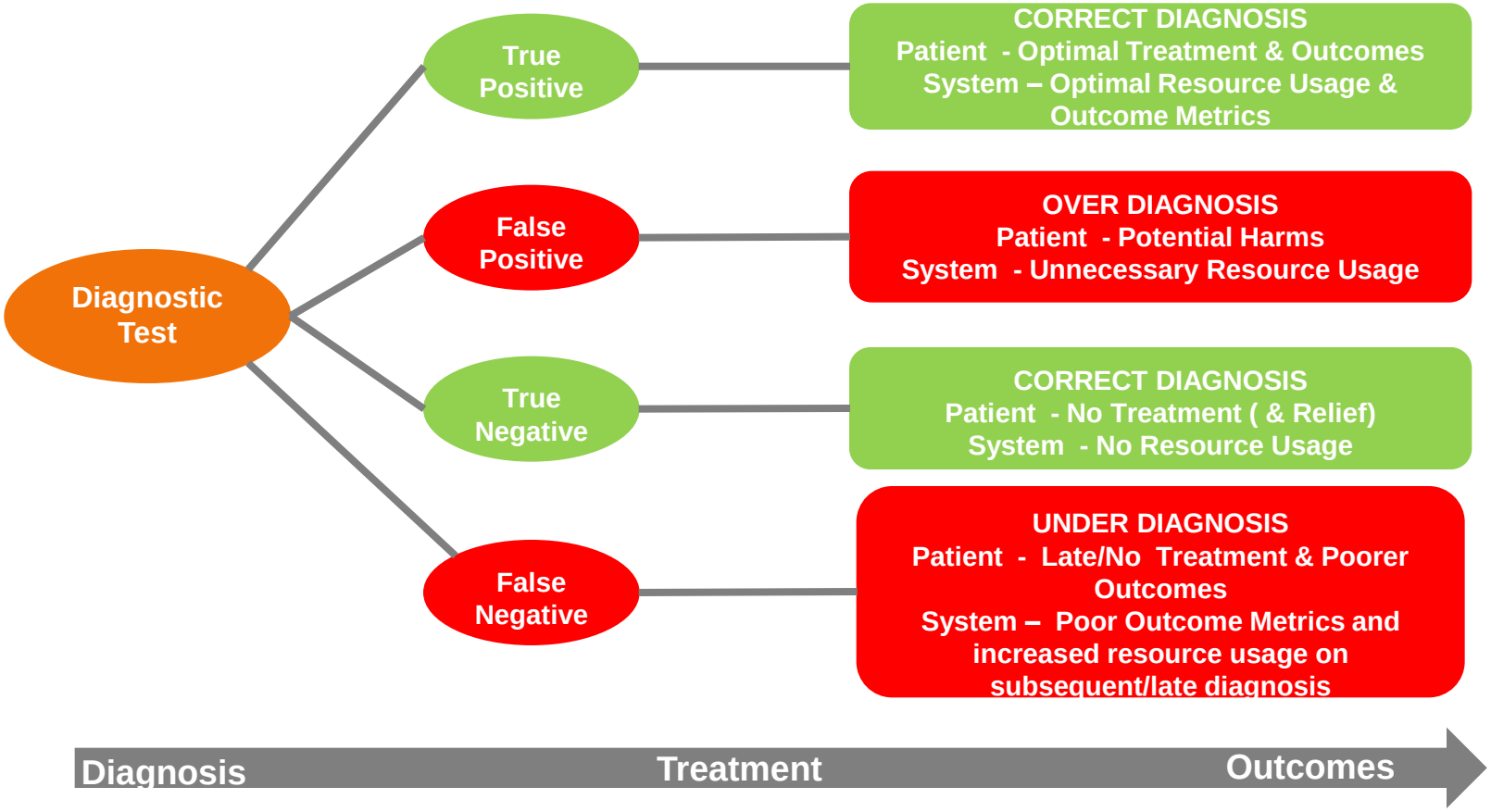
Diagnostics – Potential Value





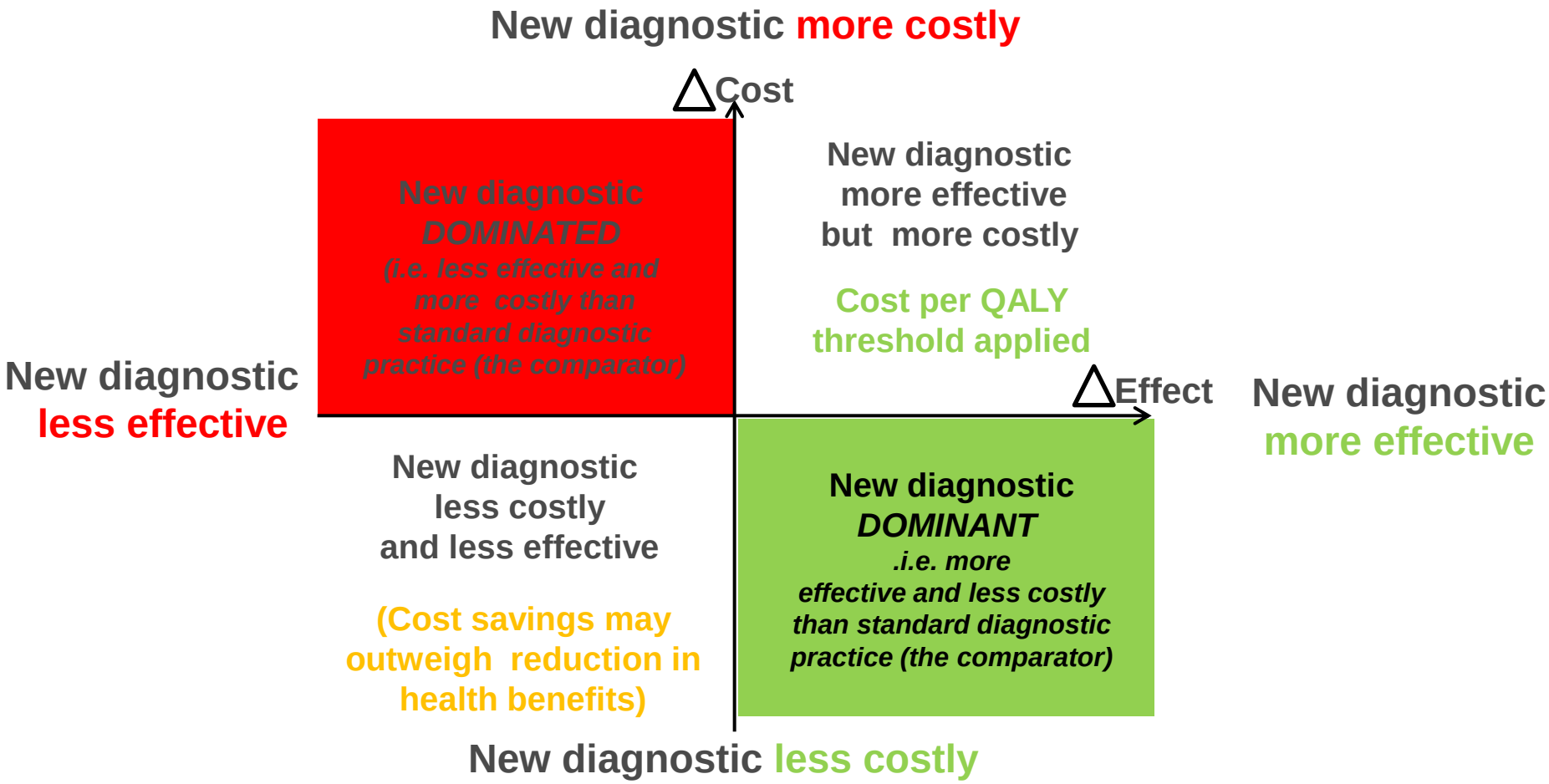
Diagnostics Assessment Programme(DAP) assesses the value proposition of diagnostic technologies .i.e. pathological tests, imaging, endoscopy, algorithms or test combinations, physiological measurement and genetic/molecular tests

Diagnostics – Potential Impact

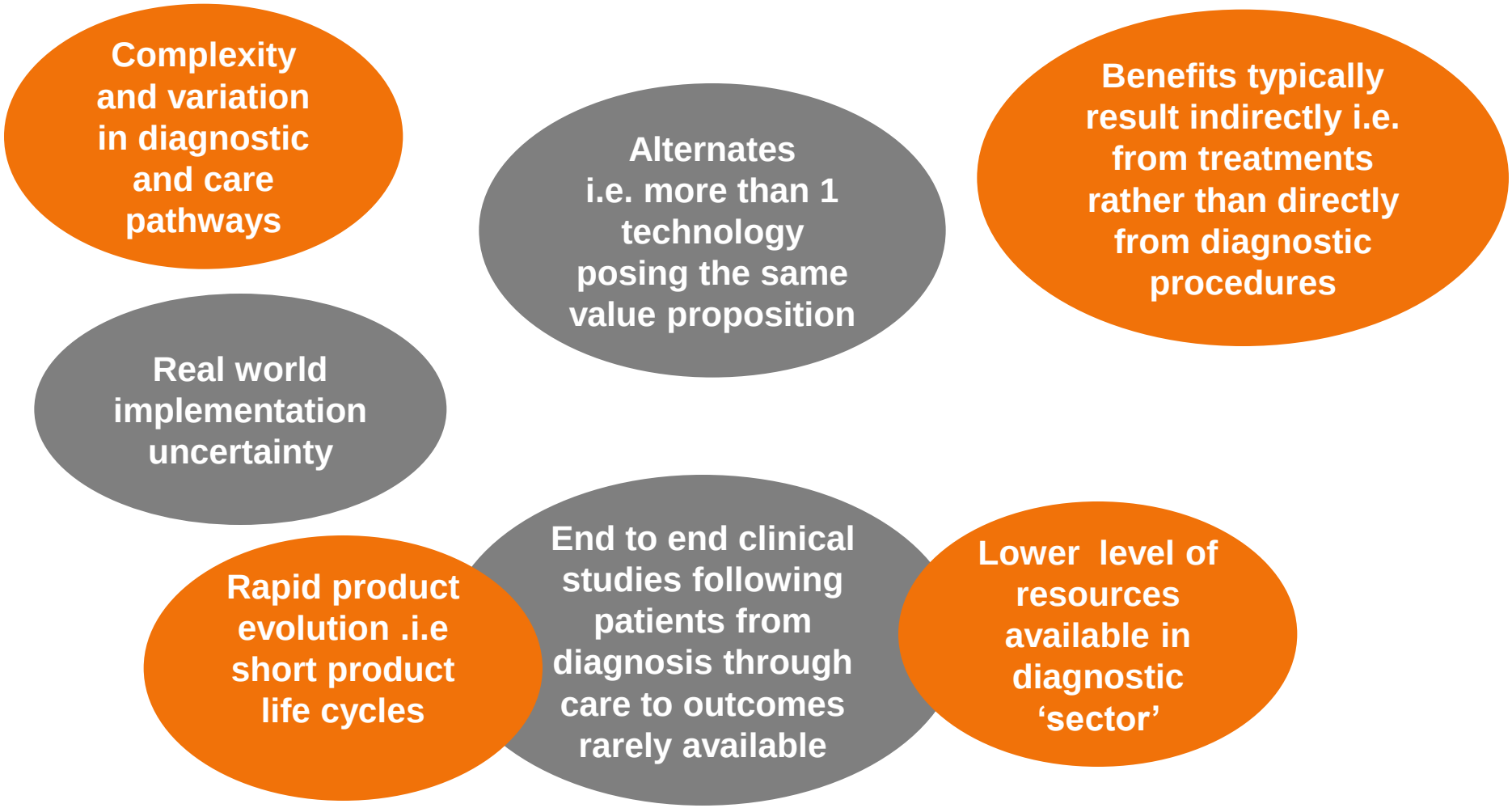


The use and initial cost of a diagnostic test is often far removed from its impact and value

Clinical and Cost-Effectiveness DAP & Diagnostics



Clinical and Cost-Effectiveness Challenges for Diagnostics



Clinical and Cost-Effectiveness DAP Approach to Diagnostics Challenges

Utilises existing evidence for parts of the care pathway to develop models

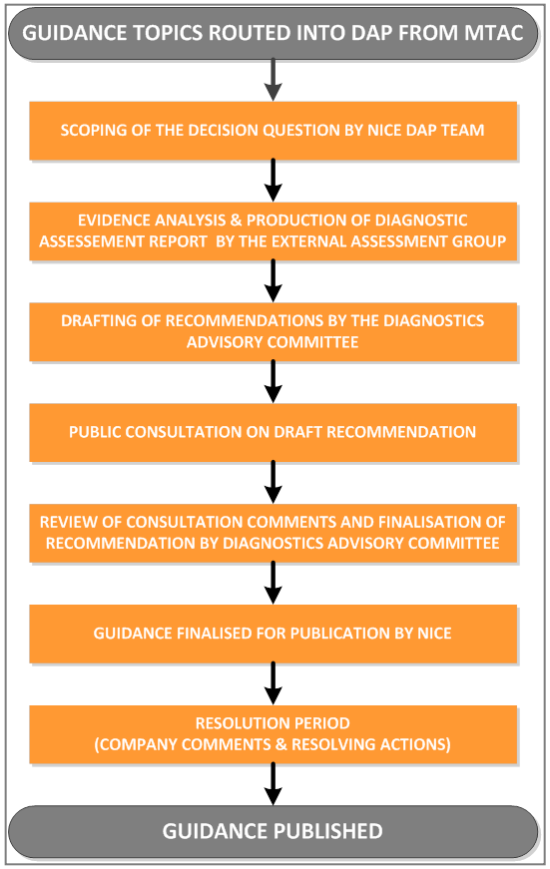
Can utilise existing models (directly or with modification)

Topic/clinical expert input into model structure and evidence gaps

Robust diagnostic accuracy data is a minimum requirement for linked evidence modelling

No company dossier submission – systematic review of clinical and cost-effectiveness developed entirely by external assessment group

The Diagnostics Assessment Process



Scoping (12 weeks)

- Utilising input from stakeholders and specialist to lock down the question the NHS needs answering

Assessment (28 weeks)

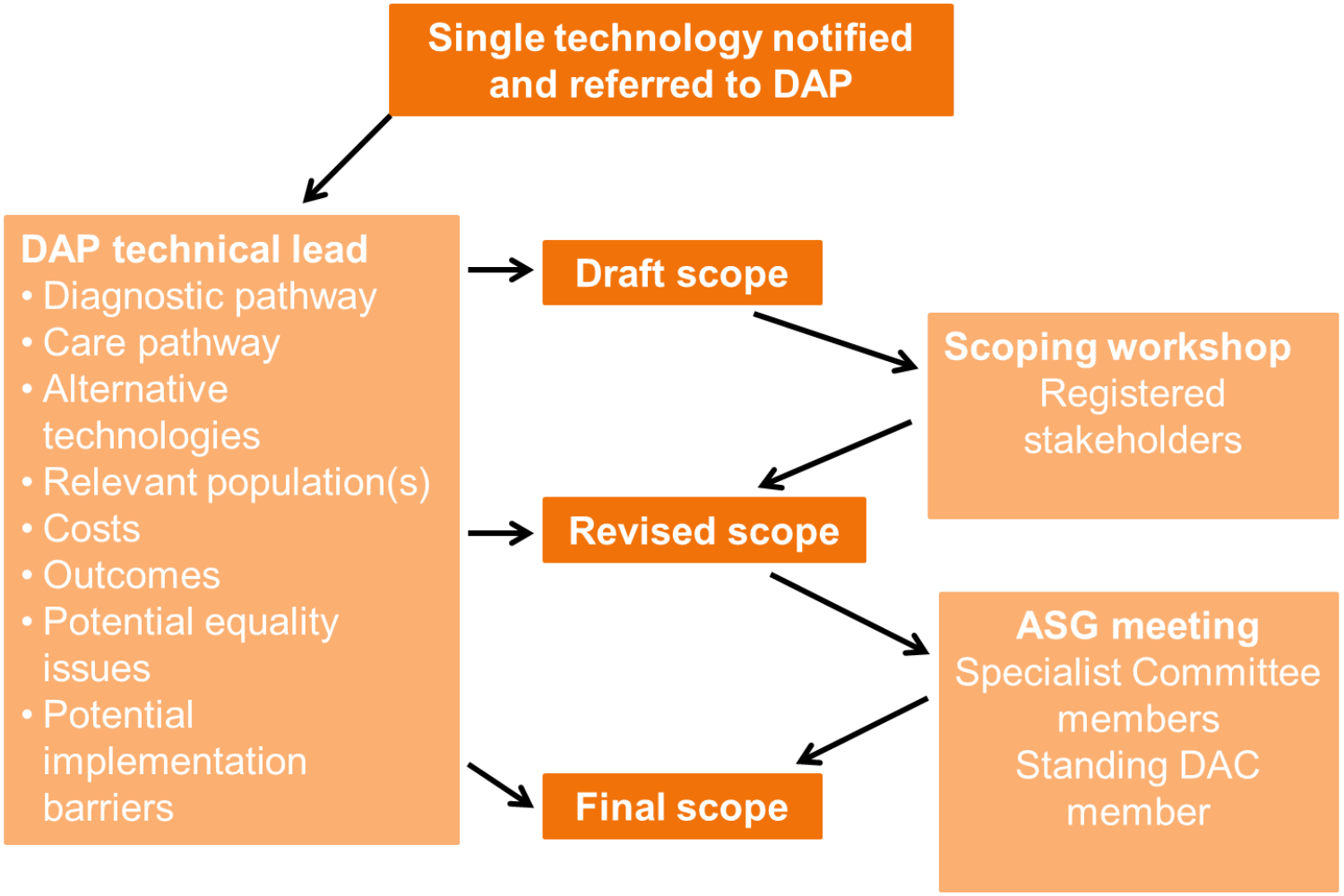
- Production of systematic review of clinical and cost effectiveness by Diagnostics Assessment Report by External Assessment Group

Guidance Production (23 weeks)

- Production of draft recommendations
- Public consultation and finalisation of recommendations
- Resolution period & guidance publication

DAP process methodology is tailored to take account of the specific challenges relating to how diagnostics 'deliver their impact' for patients and the healthcare system

Scoping



Assessment of single or multiple technologies

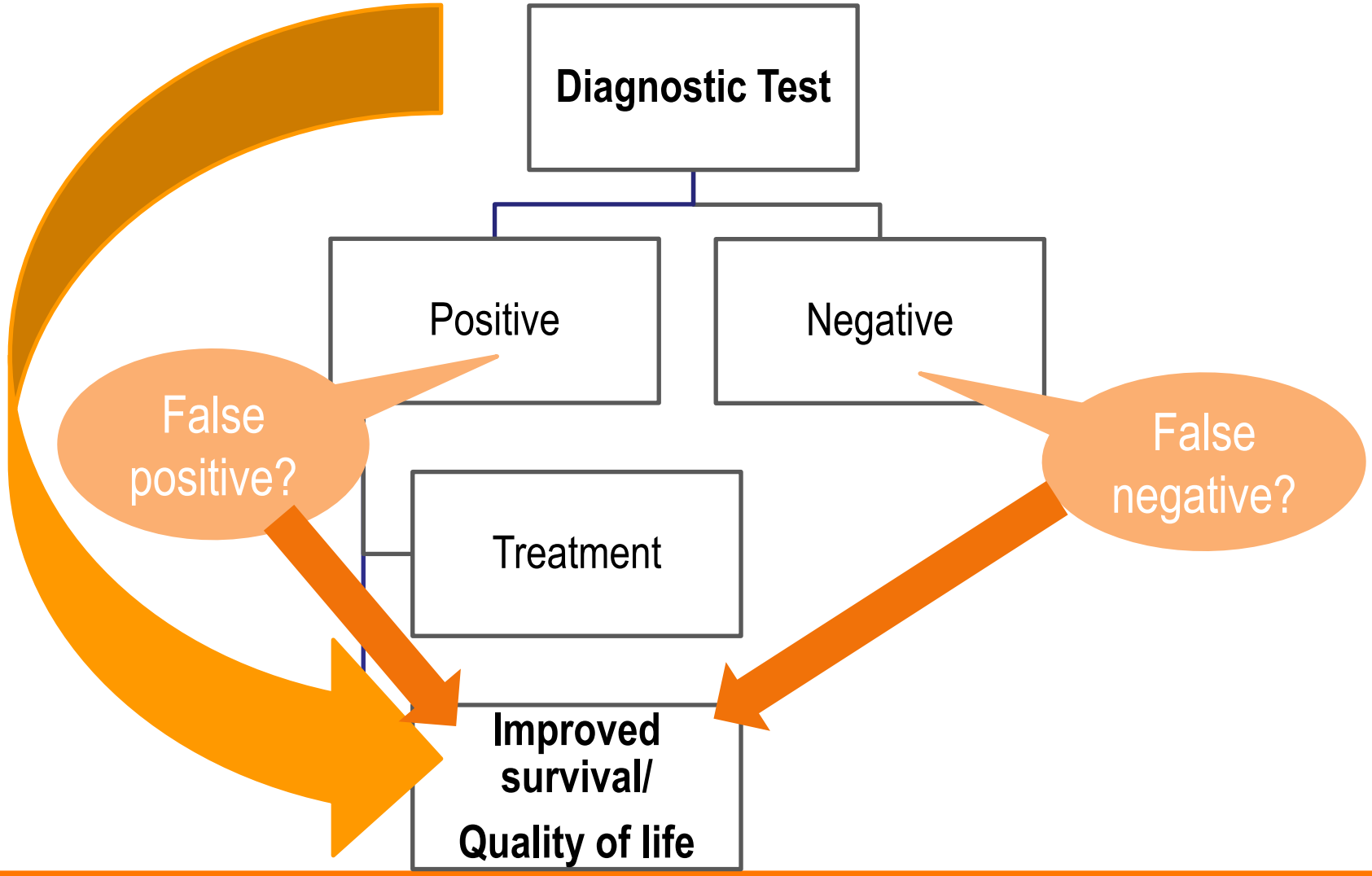
Scoping

1. How is the condition managed in the NHS?

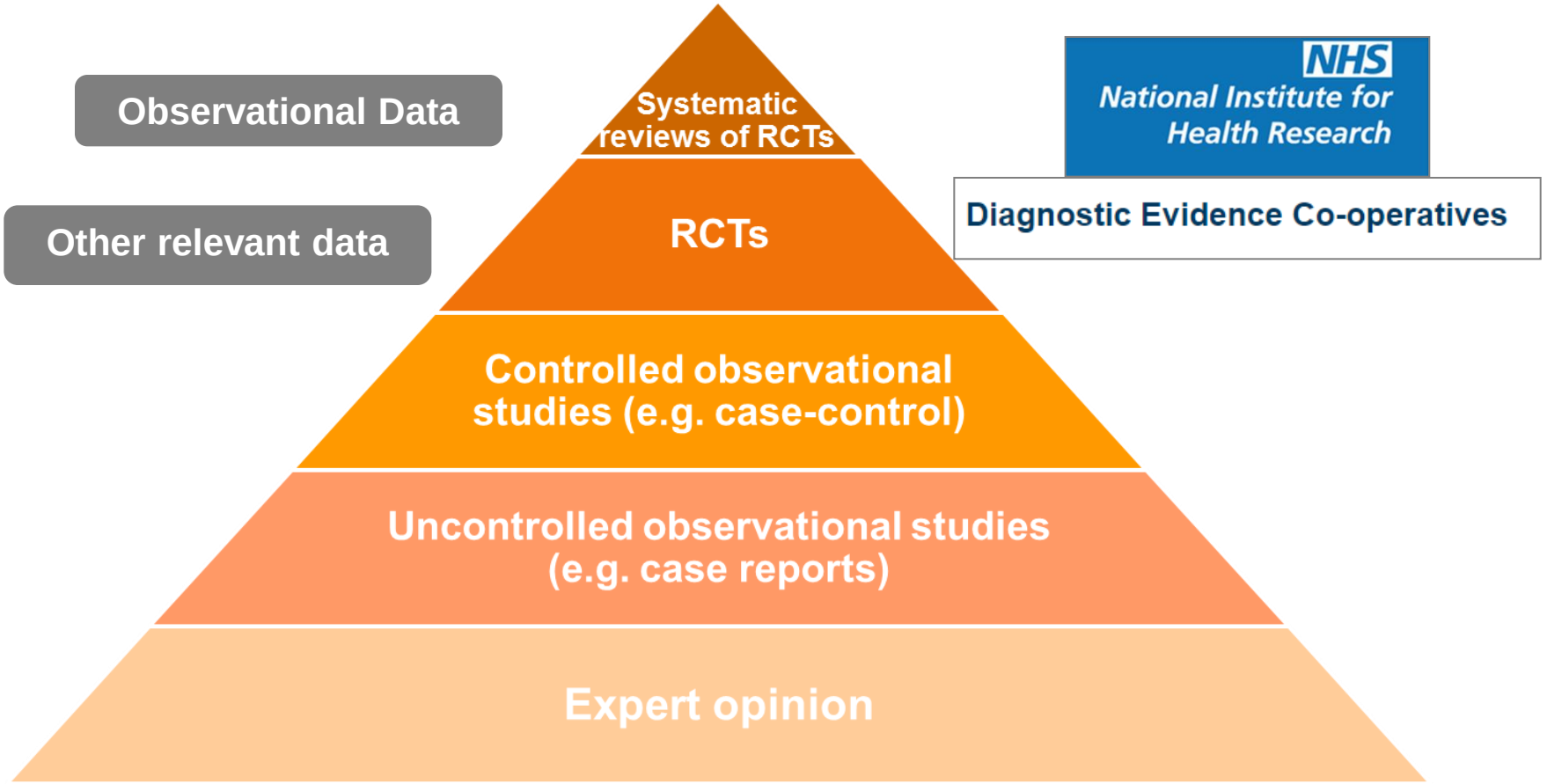
2. Where does my product fit in the care pathway?

3. What does my product deliver?

Understanding diagnostics benefits



Diagnostics evidence requirements



Study design

- **Outcomes**: patient focussed outcomes are particularly important, as opposed to intermediate or surrogate outcomes
  - e.g. a reduction in tumour size will be given less weight than evidence about clinical benefit such as improved survival or quality of life
- **Size**: Studies with larger numbers of patients will usually be preferred as estimates of benefits and harms will be more accurate
- **Duration:** Studies should have sufficient follow up to capture final outcomes where possible
  - e.g. very important for prognostic tests

Diagnostic tests: Outcomes data

Ideally comparative 'end-to-end' clinical studies including the test and subsequent treatments should be conducted

Not possible

Identify studies on the effectiveness of those subsequent treatments

Use a systematic approach to identifying relevant studies

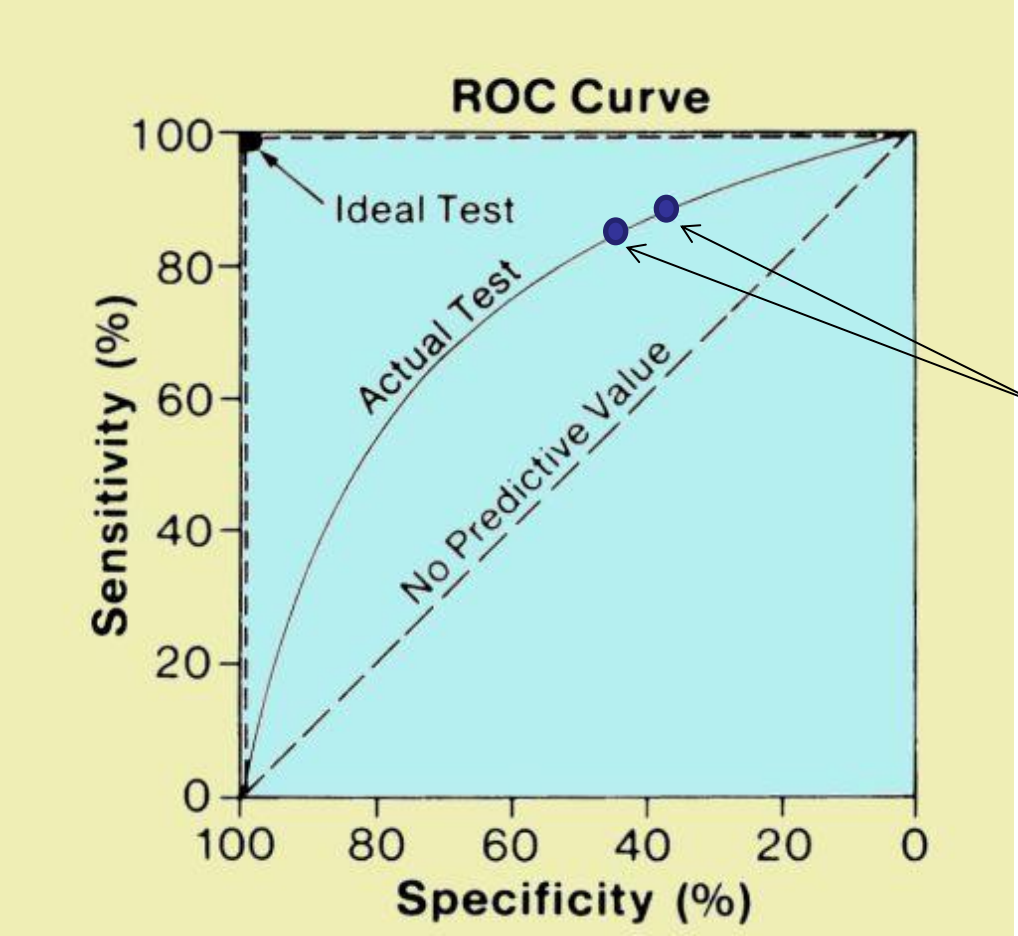
Test side effects should be included

Diagnostic tests: Outcomes data

		Condition as determined by "Gold Standard"		
		Condition positive	Condition negative	
Test outcome	Test outcome positive	**True Positive**	**False Positive**	**PPV**
	Test outcome negative	**False negative**	**True Negative**	**NPV**
		Sensitivity	**Specificity**	

Measurements of test accuracy are necessary:

Diagnostic tests: Outcomes data



Cut off points

A diagnostics example……

SonoVue (sulphur hexafluoride microbubbles)
Contrast agent for contrast-enhanced ultrasound imaging of the liver

- Characterising incidentally detected focal liver lesions
- Detection of potential liver metastases
- Characterising focal liver lesions (cirrhosis)

No end-to-end studies available

High quality accuracy data – SonoVue vs CT and MRI

Relevant evidence on care pathway and outcomes

NICE Scientific Advice

- **Enables companies to:**
  - **present prospective clinical development plan**
  - **ask questions on population, trial design, relevant outcomes, comparators, health-related quality of life data collection, economic analysis, cost effectiveness modelling, extrapolation, resource use and costs**
- **Receive bespoke advice to support decision making and help develop an evidence base which can be used in future NICE evaluations or discussions with payers/ commissioners**

Light Scientific Advice (for SMEs)
11-13 week process
Option for additional adoption advice
Clarification teleconference
Light advice letter
Clarification teleconference (optional)

Clinical and Cost-Effectiveness DAP Approach to Diagnostics Challenges

The Diagnostics Advisory Committee (DAC):

independent decision making body basing its recommendations on a review of clinical and economic evidence

22 Standing members - all assessments
Unique experience in diagnostics decision making

+

Specialist Committee Members:

- 5 – 7 for each individual assessment topic
- Recruited for expertise in the diagnostic and/or care pathway
- Clinicians, researchers ,healthcare professionals, lay persons with a perspective on the condition(s) being diagnosed
- Input is critical to crystallising the question to be answered and linked evidence modelling development

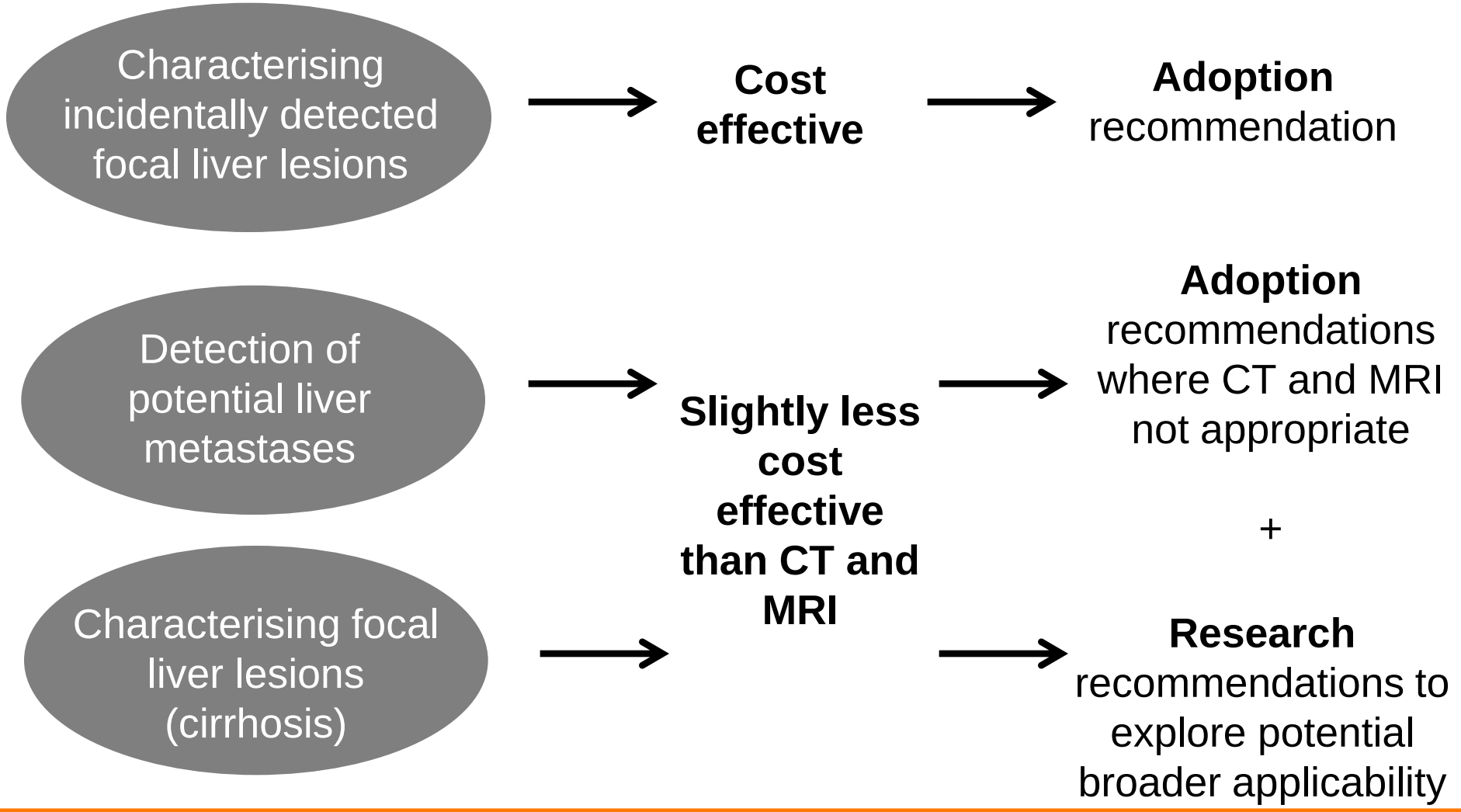
Recommended for Routine Use ← – – → **Further Research Recommended** ← – – → **Not Recommended for Routine Use**

MTEP Research Commissioning

Guidance development

- Decision making in presence of uncertainty
- Public consultation can change decision making
- Clarity in recommendations on indication
  - Rule-in / rule-out / diagnosis / monitoring
  - Setting
  - ➢ Supported by evidence, minimise risk of indication creep and inappropriate use of tests that may lead to misdiagnosis
  - ➢ Cost-effective use of NHS resources
- ‘Committee considerations’ describe uncertainties and rationale behind decision-making.

SonoVue (sulphur hexafluoride microbubbles) Contrast agent for contrast-enhanced ultrasound imaging of the liver……again



Post Guidance Research Facilitation

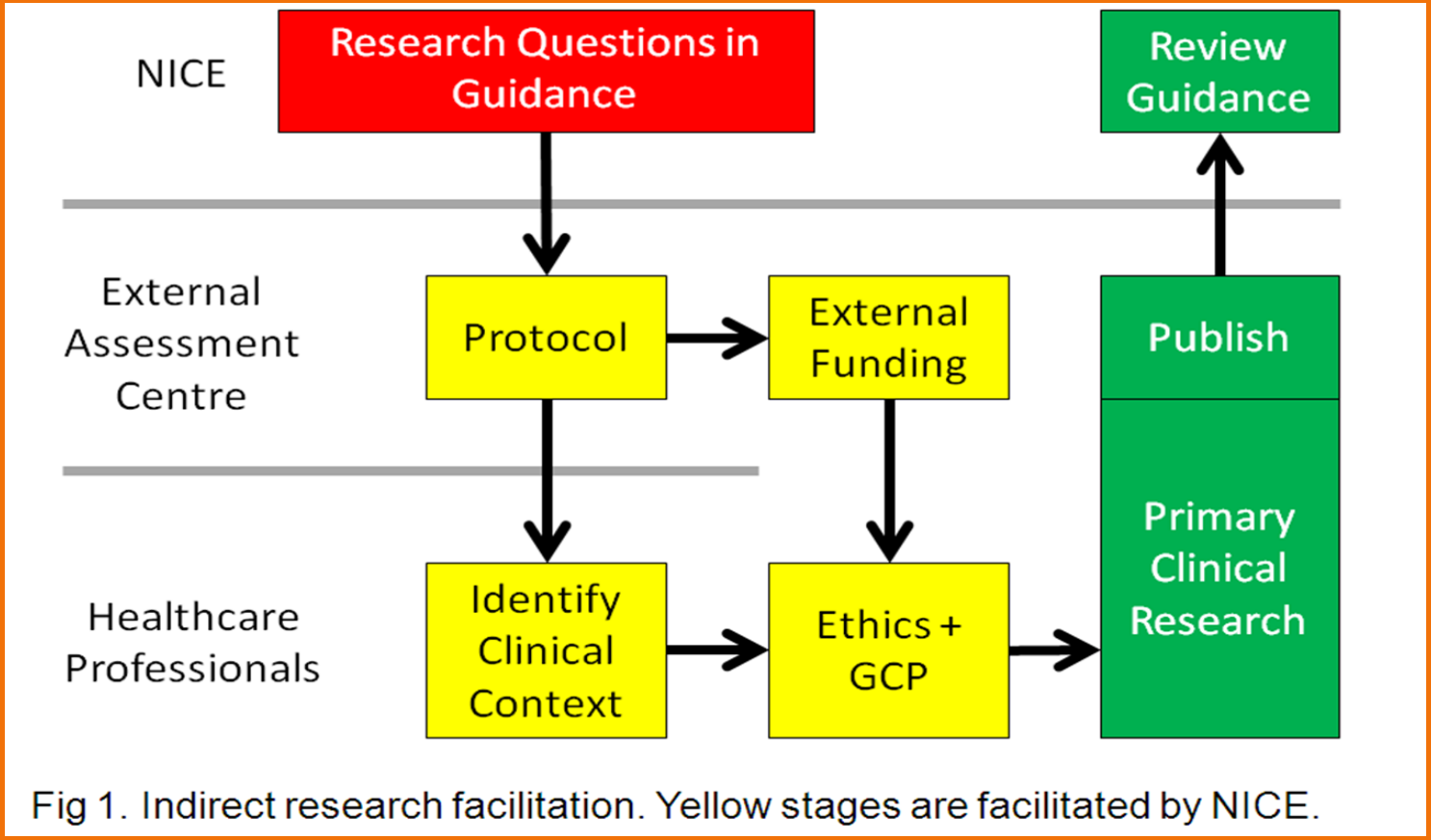


Fig 1. Indirect research facilitation. Yellow stages are facilitated by NICE.

Pomfrett C.J.D, Campbell B, Pugh P.J, Campbell M, Marlow M. Medical Technologies Evaluation II: catalysing the development of primary clinical evidence for promising technologies. HTAI Bilbao 2012

NICE: Companion diagnostics (CDx)

- Companion diagnostics are assays (a test or measurement) intended to assist physicians in making treatment decisions for their patients
- They do so by elucidating the efficacy and/or safety of a specific drug or class of drugs for a targeted patient group or sub-groups
- There are two main groups of companion diagnostics that include:
  - Tests that have been developed after a drug has come to market
  - Tests that are being developed in conjunction, or as a companion to the drug

NICE: Companion diagnostics (CDx)

- In January 2013, NICE published update to the Technology Appraisals methods guide
  - Costs of CDx testing incorporated into evaluation of clinical and cost effectiveness
  - Sensitivity analysis to assess impact of CDx cost on cost effectiveness of pharmaceutical
  - Diagnostic accuracy can be examined and incorporated in cost effectiveness analysis
  - Potential issues of alternative CDx can be highlighted in guidance without assessment of evidence

Example of CDx in TA programme

TA 208 Trastuzumab for HER2-positive metastatic gastric cancer

- MA included testing with fluorescence in situ hybridisation (FISH) then revised to include silver in situ hybridisation (SISH)
  - Timing of MA meant that only FISH was included in NICE appraisal
- Trial used parallel testing strategy
- Sequential testing strategy in manufacturer's model
  - Only ICH2 positive received FISH test
- ERG scenario analyses for both sequential and parallel testing strategies
  - Sequential ICER £66,982 per QALY
  - Parallel ICER £71,637 per QALY due to increased incremental costs
- Committee concluded that sequential testing was most appropriate for people with metastatic gastric cancer

Example of CDx in DAP programme

- EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer
- **Evidence**
  - Two tests used in clinical trials
  - Three tests had accuracy data
    - Linked to clinical trial data
  - Remaining tests had no trial or accuracy data
  - Included a survey of labs providing EGFR-TK testing
    - test characteristics and costs
  - Data from an EGFR-TK national external quality assurance scheme study

EGFR testing - Recommendations

- 5 tests recommended but insufficient evidence to make recommendations for others
- Key issues:
  - Test validation
  - Competent execution
  - Participation in external quality assurance scheme
- Research recommendation
  - Studies comparing different EGFR-TK mutation methods that link to patient outcomes
- Many assumptions in assessment

Diagnostics guidance (http://www.nice.org.uk/dg9)

Key contacts

- ***NICE DAP***
  - **Sarah Byron** (sarah.byron@nice.org.uk)
  - http://www.nice.org.uk/About/What-we-do/Our-Programmes/NICE-guidance/NICE-diagnostics-guidance
- ***NICE Medical Technologies Evaluation Programme***
  - **Jessica Linville-Boud**(Jessica.Linville-Boud@nice.org.uk
  - http://www.nice.org.uk/About/What-we-do/Our-Programmes/NICE-guidance/NICE-medical-technologies-evaluation-programme
- ***NICE Scientific Advice***
  - Richard Chivers (richard.chivers@nice.org.uk)
  - http://www.nice.org.uk/about/What-we-do/Scientific-advice

Thank – you very much for your attention!