NICE Diagnostics Assessment Programme

Diagnostics North East Conference 2018

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NICE - aims

- Speed up NHS uptake of interventions that are both clinically and cost-effective
- Encourage better and more rational use of resources by focussing the provision of healthcare 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

Consistent vs Fair

NICE National Institute for Health and Care Excellence
Managing healthcare resources within a fixed budget

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
Centre for Health Technology Evaluation (CHTE)
Technology appraisals and guidance on diagnostics, medical technologies (and interventional procedures)

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)
Assessing diagnostics at NICE

Medical Technologies Topic Oversight Group

- Medical Technologies Evaluation Programme (MTEP)
- Diagnostics Assessment Programme (DAP)
- Technology Appraisals (TA)
- Interventional Procedures (IP)

Sponsors notify topics to NICE
The sponsor 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 MTTOG identify the most appropriate way to assess the value proposition of a selected product?

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

Assessment Methodologies
- Does the product impact on patient health outcomes?
- Is the product ‘unique’?
- Is the cost impact /saving readily identifiable?
- Is the clinical pathway complex; will it change the patient journey?
- Is the product potentially disruptive to the current clinical pathway?
- Are there other products achieving the same outcome at the same place in the clinical pathway?
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Routing of Selected Products

<table>
<thead>
<tr>
<th>Clinical Performance</th>
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<tbody>
<tr>
<td>Cost Impact</td>
<td>£ or £</td>
</tr>
<tr>
<td>Evaluation Method</td>
<td>Cost effectiveness (£/QALY)</td>
</tr>
<tr>
<td></td>
<td>Costs consequences (£)</td>
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<table>
<thead>
<tr>
<th>NICE Guidance Programme</th>
<th>Technology Appraisals Programme (TAP)</th>
<th>Diagnostics Assessment Programme (DAP)</th>
<th>Medical Technologies Evaluation Programme (MTEP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technologies</td>
<td>✓ Devices</td>
<td>✓ Diagnostics</td>
<td>✓ Devices ('Simple Diagnostics')</td>
</tr>
</tbody>
</table>

NICE National Institute for Health and Care Excellence
The value proposition

Fit with health system priorities
Justifiable Price
Improved health outcomes
Well constructed evidence base
Incremental benefit for patients
Impact on health system resources

Value varies depending on your perspective
NICE takes the perspective of the National Health Service (NHS) and Personal Social Services (PSS)
Diagnostics – Potential Value

System Benefits:
- Speed up recovery
- Reduce hospitalisation
- Reduce length of stay
- Different staff grade or type
- Reduce process time required

Patient Benefits:
- Improve compliance
- Decision or care nearer home
- Improve health outcome
- Enable self care
- Reduce unnecessary interventions
- Enhance dignity

Diagnostics Assessment Programme (DAP) examine the VALUE PROPOSITION of all types of diagnostics products (diagnosis, monitoring, prognosis, imaging, endoscopy)
The use and initial cost of a diagnostic test is often far removed from its impact and value.

Diagnostics – potential impact

- **True Positive**
  - CORRECT DIAGNOSIS
  - Patient: Optimal Treatment & Outcomes
  - System: Optimal Resource Usage & Outcome Metrics

- **False Positive**
  - OVER DIAGNOSIS
  - Patient: Potential Harms
  - System: Unnecessary Resource Usage

- **True Negative**
  - CORRECT DIAGNOSIS
  - Patient: No Treatment ( & Relief)
  - System: No Resource Usage

- **False Negative**
  - UNDER DIAGNOSIS
  - Patient: Late/No Treatment & Poorer Outcomes
  - System: Poor Outcome Metrics and increased resource usage on subsequent/late diagnosis

Diagnosis | Treatment | Outcomes
Clinical and cost-effectiveness - challenges for diagnostics

- Complexity and variation in diagnostic and care pathways
- Alternates i.e. more than 1 technology posing the same value proposition
- Real world implementation uncertainty
- Benefits typically result indirectly i.e. from treatments rather than directly from diagnostic procedures
- End to end clinical studies following patients from diagnosis through care to outcomes rarely available
- Rapid product evolution i.e. short product life cycles
- Lower level of resources available in diagnostic ‘sector’

Benefits typically result indirectly i.e. from treatments rather than directly from diagnostic procedures.
The Diagnostics Assessment Process

**Scoping (12 weeks)**
- Utilising input from stakeholders and specialist to lock down the question the NHS needs answering
- Inclusion of all relevant technologies

**Assessment (28 weeks)**
- Production of systematic review of clinical and cost effectiveness by Diagnostics Assessment Report by External Assessment Group
- Stakeholder comments

**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

Single technology notified and referred to DAP

DAP technical lead
- Diagnostic pathway
- Care pathway
- Alternative technologies
- Relevant population(s)
- Costs
- Outcomes
- Potential equality issues
- Potential implementation barriers

Draft scope

Scoping workshop
Registered stakeholders

Revised scope

ASG meeting
Specialist Committee members
Standing DAC member
Assessment Group

Final scope

Assessment of single or multiple technologies
Scoping

1. How is the condition managed in the NHS

2. Where does the technology fit in the care pathway

3. What does the technology deliver?
Understanding diagnostics benefits

- **Diagnostic Test**
  - **Positive**
    - Treatment
    - Improved survival/
      Quality of life
  - **Negative**
    - False negative?
    - False positive?
Diagnostic evidence requirements

- Systematic reviews of RCTs
- RCTs
- Controlled observational studies (e.g. case-control)
- Uncontrolled observational studies (e.g. case reports)
- Expert opinion

Observational Data

Other relevant data
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
Diagnostic tests: Outcomes data

<table>
<thead>
<tr>
<th>Condition as determined by “Gold Standard”</th>
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<tbody>
<tr>
<td>Condition positive</td>
<td>Condition negative</td>
</tr>
<tr>
<td>Test outcome positive</td>
<td>True Positive</td>
</tr>
<tr>
<td>Test outcome negative</td>
<td>False Positive</td>
</tr>
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Measurements of test accuracy are necessary:

- PPV
- NPV
- Sensitivity
- Specificity
Diagnostic tests: Outcomes data

ROC Curve

Cut off points
Diagnostic tests: Outcomes data

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

Test side effects should be included

Not possible

Identify studies on the effectiveness of those subsequent treatments

Use a systematic approach to identify relevant studies
Clinical and Cost-Effectiveness
DAP Approach to Diagnostics Challenges

LINKED EVIDENCE MODELLING

Diagnostic Accuracy → Impact on Treatment Decisions → Impact on Outcomes

- 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

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Clinical and Cost-Effectiveness: DAP & Diagnostics

New diagnostic more costly

New diagnostic DOMINANT
i.e. more effective and less costly than standard diagnostic practice (the comparator)

Cost per QALY threshold applied

New diagnostic more effective but more costly

New diagnostic less effective and less costly

(Cost savings may outweigh reduction in health benefits)

New diagnostic less costly

New diagnostic DOMINANT
i.e. more effective and less costly than standard diagnostic practice (the comparator)

Clinical and Cost-Effectiveness: DAP & Diagnostics

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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

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

DAC Standing Committee

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

Recommended for Routine Use
Further Research Recommended
Not Recommended for Routine Use

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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
A molecular diagnostics example......

Molecular testing strategies for Lynch syndrome in people with colorectal cancer

- Initial tumour tests and genetic testing for probands with colorectal cancer
- Cascade testing for relatives

- 10 diagnostic accuracy studies
- No end-to-end studies
- 10 testing strategies modelled
Molecular testing strategies for Lynch syndrome in people with colorectal cancer

Strategy 9

- MSI testing

or

Strategy 5

- IHC testing

MSI^+

BRAF V600E

- Negative

MLH1 promoter hypermethylation test

- Negative

Genetic testing of germline DNA

MLH1^ab

MSH2^ab

MSH6^ab

PMS2^ab
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)
Companion diagnostics

- Companion diagnostics are tests intended to assist health care professionals 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.
Companion diagnostics

- 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
Examples of companion diagnostics in DAP

• EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer

• Gene expression profiling and expanded immunohistochemistry tests for guiding adjuvant chemotherapy decisions in early breast cancer management

• Fluorouracil chemotherapy: The My5-FU assay for guiding dose adjustment

• Therapeutic monitoring of TNF-alpha inhibitors in Crohn’s disease
Any questions?