NICE approach to point of care tests for antimicrobials

11th December 2018, Mumbai

Dr Grace Jennings – Senior scientific adviser, NICE Scientific Advice
Introduction to NICE & Health Technology Assessment (HTA)
The background: why NICE was set up

• Established in 1999
• Aim: to reduce variation in the availability and quality of treatments and care (the so-called ‘postcode lottery’)
• To resolve uncertainty about which medicines and treatments work best and which represent best value for money for the NHS
What is NICE?

An independent institute that identifies how to:

• prevent, diagnose and treat disease and ill health in most effective ways

• reduce inequalities and variation

• ensure quality and value for money for the NHS
Opportunity cost
NICE: Improving outcomes for people

- **Evidence-based guidance and advice** for health, public health and social care
- **Information services** for commissioners, practitioners and managers
- **Quality standards and performance metrics** for those providing and commissioning health, public health and social care
What is Health Technology Assessment (HTA) ?

- Product
- Evidence

- Market
- Policy-making

Evidence-based
Includes the efficient allocation of health care resources
Difficulties faced by medtech/diagnostic companies

- Complex decision-making processes
- Many stakeholders – may delay change
- Difficulty getting peer reviewed research
- Competing with long-established practice – may act as a block to change
- Funding
Scarce resources = difficult decisions

HTA

Health Technology Assessment
Triple E of Healthcare Technologies

- **Efficacy**: Does it work in clinical trials?
- **Effectiveness**: Does it work in clinical practice?
- **Efficiency**: Does it contribute to the efficient use of resources?

NICE
What does NICE value?

Value

- Clinical effectiveness
- Cost effectiveness
- Non-health objectives
- Equity
- End of life
- Degree of need
- Innovation
The same evidence can lead to different decisions
Two key questions asked by NICE

How well does the technology work compared to standard practice in the National Health service (NHS)?

How much does this course of action cost compared to standard practice in the NHS?
AMR Point of Care tests and NICE
Prescribing policy in the NHS

Antibiotic items prescribed in primary care per 1,000 people, England

<table>
<thead>
<tr>
<th>Year</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>2013</td>
<td>170</td>
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<tr>
<td>2014</td>
<td>170</td>
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<td>2015</td>
<td>161</td>
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<tr>
<td>2016</td>
<td>157</td>
</tr>
<tr>
<td>2017</td>
<td>151</td>
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AMR at NICE

Common Infections Guidance from NHS England:
• Rapid guidance within an ongoing programme to promote appropriate antimicrobial use

NICE Guidance:
• Antimicrobial stewardship: changing risk-related behaviours in the general population (NG63)
• Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (NG15)
• Antimicrobial stewardship (QS121)
NG15 – relevant sections

1.1.22 Ensure that laboratory testing and the order in which the susceptibility of organisms to antimicrobials is reported is in line with: national and local treatment guidelines, the choice of antimicrobial in the local formulary, the priorities of medicines management and antimicrobial stewardship teams.

1.1.25 When deciding whether or not to prescribe an antimicrobial, take into account the risk of antimicrobial resistance for individual patients and the population as a whole.

1.1.26 When prescribing any antimicrobial, undertake a clinical assessment and document the clinical diagnosis (including symptoms) in the patient's record and clinical management plan.

1.1.27 For patients in hospital who have suspected infections, take microbiological samples before prescribing an antimicrobial and review the prescription when the results are available.
NG15 – relevant sections

1.1.28 For patients in primary care who have recurrent or persistent infections, consider taking microbiological samples when prescribing an antimicrobial and review the prescription when the results are available.

1.1.29 For patients who have non-severe infections, consider taking microbiological samples before making a decision about prescribing an antimicrobial, providing it is safe to withhold treatment until the results are available.

1.1.30 Consider point-of-care testing in primary care for patients with suspected lower respiratory tract infections as described in the NICE guideline on pneumonia in adults.
Previous NICE publications related to AMR PoC

3 MIBs:
- Alere Afinion CRP for C-reactive protein testing in primary care [MIB81]
- QuikRead go for C-reactive protein testing in primary care [MIB78]
- Xpert Carba-R to identify people carrying carbapenemase-producing organisms [MIB52]

All 2016

1 DG
- Procalcitonin testing for diagnosing and monitoring sepsis (ADVIA Centaur BRAHMS PCT assay, BRAHMS PCT Sensitive Kryptor assay, Elecsys BRAHMS PCT assay, LIAISON BRAHMS PCT assay and VIDAS BRAHMS PCT assay) [DG18]
  October 2015

NOT ENOUGH EVIDENCE FOR GUIDANCE
Decision making
Summary of the NICE reference case

Decision problem defined as per NICE scope

Health effects
- Patients/carers perspective
- QALYs (EQ-5D)
- Reported by patients, valued by public
- QALY = QALY = QALY
- Discounted at 3.5%

Costs
- NHS and PSS perspective
- Discounted at 3.5%

Economic model
- Cost–utility analysis with fully incremental analysis
- Time horizon long enough to reflect all important differences in costs or outcomes

ICER
Economic evaluation

\[
\text{ICER} = \frac{\text{difference in cost (current treatment vs new treatment)}}{\text{difference in effect (current treatment vs new treatment)}}
\]

**I** Incremental: extra, additional

**C** Cost: how much do we have to pay?

**E** Effectiveness: what do we get (in QALYs)?

**R** Ratio: unit per unit (e.g. km/h) – we use cost per QALY

Does the value of health gain justify the additional resources required for the new treatment compared to the current treatment?
Committee decision making

Make **explicit reference** to:
- Degree of certainty
- HRQL adequately captured?
- Innovative nature
- Social value judgment
- Equalities

Need to identify an **increasingly strong case**

Criteria for **life-extending, end-of-life treatments**
- Life expectancy <24mo
- Life extension >3mo
- Robust estimate of extension to life

**Probability of rejection**

- Probably cost effective

**Cost per QALY (£’000)**
Why doesn’t NICE have a fixed threshold?
Decision-making approach

- Certainty of the ICER
- HRQOL inadequately captured
- Innovative nature of technology
- Non-health objectives of the NHS
- Life extending treatment at the end of life

- £20,000 per QALY
- £30,000 per QALY
- £50,000 per QALY (x2.5)
Understanding value
What is a value proposition?

A clear and credible set of claims for which evidence can be developed that provide value to healthcare providers and users.
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 benefits: diagnostics

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

**Diagram:**
- Positive branch:
  - Treatment
    - Improved survival/
      - Quality of life

- Negative branch:
  - False negative?
  - False positive?
Understanding benefits: diagnostics

Patient benefits rarely arise from the diagnostic directly – they come mainly from treatments informed by the diagnostic.

The treatment pathway or the range of pathways must be understood for the value of the diagnostic to be assessed.

Need to know the reference test.

Test side effects should be included.
What makes a good value proposition?

• Think about your audience

• What represents value in healthcare systems and in particular the NHS?
  - Is your VP actually giving payers what they want?

• A value proposition aimed at NICE, healthcare commissioners and professionals differs from that a company might use for potential investors
Proving your value proposition

- Can be even harder to get the evidence to justify the claim
  - Does it work in clinical trials?
  - Does it work in clinical practice?
  - Does it contribute to more efficient use of resources?
Key elements of value proposition development

1. Describe the issue being faced [in the NHS] in relation to this indication and current clinical practice.

2. Explain how the technology in question can provide a solution to this problem.

3. Detail the clinical benefits for patients delivered by the product over and above current clinical practice.

4. Detail the resource use and cost savings for the healthcare system delivered by the product over and above current clinical practice.

5. Remember the need to provide evidence to substantiate the claims.
Are these good value propositions?

Empowers patients to treat their own disease

Excellent for orthopaedic work

Test identifies which patients presenting with head injury have a life threatening condition requiring urgent admission enabling others to be discharged

Leads to earlier discharge from ICU

9 out of 10 doctors prefer to use...

Improves quality of life for the patient and their family

It’s the most technologically advanced and robust system on the market

No need for repeat surgery

Improved design has been clinically proven to enhance patient outcomes in a number of studies

Easy and convenient to use

Avoids the need for an MRI scan

NICE
The PICO framework
### Defining the clinical question

<table>
<thead>
<tr>
<th>P</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Intervention</td>
</tr>
<tr>
<td>C</td>
<td>Comparator</td>
</tr>
<tr>
<td>O</td>
<td>Outcomes</td>
</tr>
</tbody>
</table>

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>P</td>
<td>Usually the patients indicated in the marketing authorisation</td>
</tr>
<tr>
<td>I</td>
<td>Technology to be appraised</td>
</tr>
<tr>
<td>C</td>
<td>Established practice in the NHS</td>
</tr>
<tr>
<td>O</td>
<td>Outcomes which have an impact on:</td>
</tr>
<tr>
<td></td>
<td>- survival</td>
</tr>
<tr>
<td></td>
<td>- health related quality of life (HRQL)</td>
</tr>
</tbody>
</table>
Define the target patient population as precisely as possible:

- Who is the product intended for?
- Disease
- Severity or treatment stage
- Presenting symptoms
- Genetic factors
- Other patient characteristics

Conduct your studies in the relevant target population.
Population - Subgroups

- Effectiveness and cost effectiveness may differ because of some characteristic of the patients

For example:
- A companion diagnostic test may identify the subgroup of patients who will respond best
- The patient may have a different baseline risk of having a certain event

Think in advance about identifying any subgroups
Intervention

• The intervention is the actual technology (test or device) proposed by the manufacturer for a **specific purpose**

• I also stands for index diagnostic test

• Be precise about how it is used:
  - in what setting?
  - who uses it?
  - when?
Comparator(s)

The comparator(s) is a treatment or test that is commonly used as part of current management

- There may be more than one comparator
- The comparator may be ‘best supportive care’
- Diagnostics: there can be multiple tests or variants or test sequences in common use and all would be relevant comparators
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

Outcomes vary depending on population

- Different prior probabilities of disease
- Test accuracy can vary in differing populations, disease stage
- Differences in impact of treatment, side effect and complications

Alternative follow-up/confirmatory tests
Cut-off point on the receiver operating characteristic (ROC) curve used.
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.

Test side effects should be included.

Use a systematic approach to identifying relevant studies.
**Diagnostic tests: Outcomes data**

Measurements of test accuracy are necessary:

<table>
<thead>
<tr>
<th>Condition as determined by “Gold Standard”</th>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Condition positive</strong></td>
<td><strong>Condition negative</strong></td>
</tr>
<tr>
<td>Test outcome positive</td>
<td><strong>True Positive</strong></td>
</tr>
<tr>
<td></td>
<td><strong>False Positive</strong></td>
</tr>
<tr>
<td>Test outcome negative</td>
<td><strong>False negative</strong></td>
</tr>
<tr>
<td></td>
<td><strong>True Negative</strong></td>
</tr>
</tbody>
</table>

- **PPV**: Positive Predictive Value
- **NPV**: Negative Predictive Value
- **Sensitivity**
- **Specificity**
Diagnostic tests: Outcomes data

Cut off points
Fitting your product into the treatment pathway

What is the current pathway(s) in NHS?
- How did you obtain this information?

Your product:
- Does it replace or act as alternative to an existing technology?
- Does it add or remove a step in the pathway?
- Is it aimed at specific subgroup?

Think about how your product might fit in the pathway, and how this affects the value proposition and the evidence you need to collect to support it.
How does a diagnostic test change the pathway of care?

Usually benefits come from changes to the subsequent treatments and tests which in turn changes the outcomes for the patient and the overall costs

The test may target treatment to those who are likely to respond best

Patients are less likely to receive ineffective or unnecessary treatments

Subsequent treatments, any side effects and their treatments may be avoided

Patient benefits rarely arise from the diagnostic directly – they come mainly from treatments informed by the diagnostic
Diagnostics: consider whole treatment pathway

- Test inaccuracy
- Test harms
- Medical test
  - Diagnostic decision
  - Treatment decision
  - Patient outcomes
  - Therapeutic yield
  - Test accuracy
  - Diagnostic yield

NICE
Programmes at NICE
NICE HTA programmes

Centre for Health Technology Evaluation

- Technology Appraisals
- Diagnostics Assessment
- Medical Technologies Evaluation
- Highly Specialised Technologies
MedTech publications

• **NICE guidance**
  – Interventional Procedures Guidance
  – Medical Technologies Guidance
  – Diagnostics Guidance
  – Technology Appraisals Guidance
  – Highly Specialised Technologies Guidance

• **NICE guidelines**
  – Clinical conditions
  – Social care
  – Public health

• **NICE advice**
  – Medtech innovation briefing
  – Health app briefing
Options for NICE consideration of medtech value propositions

<table>
<thead>
<tr>
<th>Clinical performance</th>
<th>Better</th>
<th>Non-inferior</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>Higher</td>
<td>Less overall</td>
</tr>
<tr>
<td>Evaluation method</td>
<td>Cost effectiveness (QALY)</td>
<td>Cost consequences</td>
</tr>
<tr>
<td>NICE guidance programme</td>
<td>Technology Appraisals Programme (TA)</td>
<td>Diagnostics Assessment Programme (DAP)</td>
</tr>
<tr>
<td>Technologies</td>
<td>✓ Devices</td>
<td>✓ Diagnostics</td>
</tr>
</tbody>
</table>
Potential journey

Interventional procedures guidance
- Procedure specific
- Pseudo regulatory
- Focus on safety and efficacy only
- No cost considerations
- Procedure specific recommendations

Medtech Innovation Briefing
- Product specific
- Summary of key clinical evidence
- Summary of existing economic models (if available)
- No recommendations

NICE guidance
- Product specific
- Systematic review of clinical & cost evidence
- De novo economic modelling
- Product specific recommendations

NICE guideline
- Condition/population specific
- Systematic review of clinical evidence
- Key areas prioritised for economic modelling
- Recommendations unlikely to be product specific

~33 weeks
~15 weeks
~38+ weeks
bespoke timeline
Value proposition

→ Evaluation

→ Guidance

‘Same/better performance at lower cost’

Cost consequences analysis

Based on reducing healthcare resource use

‘Better performance at higher cost’

Cost utility analysis

Based on incremental benefits to patients
AIMS: Identify > Evaluate > Promote adoption
Novel .... or apparently under-used techs

- Aim to identify promising technologies early
- Permissive approach to clinical evidence
- Good expert advice is vital
- “Promise” and plausibility important
- Comparison with current management
- Clinically non-inferior and no more costly
- Modelling for cost consequences
- Single technologies (products)
### Cost model - examples

<table>
<thead>
<tr>
<th>Category</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acquisition costs</td>
<td>System savings (e.g., change in setting, staff grade/time)</td>
</tr>
<tr>
<td>Running costs eg disposables</td>
<td>Reduced costs of improved health outcomes</td>
</tr>
<tr>
<td>or concomitant treatment</td>
<td></td>
</tr>
<tr>
<td>Staffing costs</td>
<td>Improved ease of use or patient acceptability</td>
</tr>
</tbody>
</table>

Considered as part of the overall evidence but not valued.
After guidance: Adoption support

• Develop resources to support the adoption of selected NICE guidance
• Focus is on guidance where adoption barriers have been identified
• Resources provide practical support to organisations to help them put the guidance recommendations into practice
• Tools to estimate the resource impact
Medtech Innovation Briefing (MIB)

The aim of MIBs is to provide objective information on medical technologies as an aid to local decision-making by clinicians, commissioners and procurement professionals.
MIBs do

• Provide a rapid, responsive service that gives objective information on device, diagnostic and health app technologies to aid local decision-making by clinicians, managers and procurement professionals.

• Use publically available information.
MIBs do not:

• Constitute guidance from NICE
• Contain a recommendation or judgement about the technology
• Preclude guidance being developed in future
MTEP vs DAP

Medical Technologies Evaluation Programme

- Single product evaluated
- Early stage evidence
- Innovative devices and diagnostics
- More benefit for the same cost or same benefit for less cost

Diagnostic Assessment Programme

- Multiple products evaluated
- More cost for more benefit
- Complex care pathways

DAP and MTEP encourage further research into promising technologies
Diagnostics Assessment Programme

Specialist programme to undertake complex assessments of diagnostic technologies

Decision making by independent Diagnostics Advisory Committee

Assessment of single or multiple technologies

No formal manufacturer submission required

Systematic review of evidence and modelling to estimate outcome benefits and cost effectiveness is undertaken as part of the assessment
Overview of assessment process

- Guidance topic referred to DAP from MTEP
- Scoping
- Assessment of evidence by external assessment group
- Draft recommendations developed by DAC
- Draft recommendations released for public consultation
- DAC consider feedback and develop final recommendations
- Final recommendations approved by GE for publication
- Guidance released for resolution period
- Guidance published
NICE Guidelines

- Clinical conditions
- Social care
- Public health

- Systematic review of all relevant evidence
- Recommendations made by committee
- Very unlikely to recommend specific products
- Economic modelling on prioritised areas
- Evidence needs to be well developed
- Bespoke development timelines
Medtech Publications

Not mandatory - except TA/HST
Not needed for use in NHS. Decisions can be made
• Locally
• Regionally (e.g. CCGs)
• Nationally (e.g. NHSE)

Topics identified in many ways:
• Core library of conditions, diseases, population groups
• Referrals from other organisations (e.g. NHSE)
• Horizon scanning (e.g. HealthTechConnect, UK pharmascan, NIHR innovation observatory)
• Notifications from clinicians/companies
NICE’s selection considerations

What are the benefits compared with current management?
- Patient outcomes/experience
- Use of resources - facilities, staff, tests

Do the benefits matter?
- Will it change how patients are managed?
- Are the benefits meaningful to patients/staff/carers

What does it cost?

Is evidence available?
Other potential adoption mechanisms into the NHS

Commissioning through Evaluation
Individual Clinical Commissioning Group decisions
Commissioning through Evaluation

- Limited programme for access to treatments that are not currently funded by the NHS but show significant promise for the future
- Collection of clinical and patient experience data within a formal evaluation programme
- Phase 1
  - Patients are recruited, with NICE assistance to determine the scope of the scheme
- Phase 2
  - Analysis phase of varying length (usually not longer than 24 months)
- Once data are available, NHS England reviews the published policy
NICE programmes and PoC tests for AMR

At the moment, the same methodology applies

• Establish the current treatment pathway
• Describe effects on downstream clinical outcomes
• Discuss clinical acceptability
• Determine QALYs and subsequent ICERs
  • Can be very difficult to develop models and generate QALYs/ICERs

DAP committee flexibility

• - Purpose of NICE is to ensure good value for the NHS
Point of care tests – questions to think about

• What does Point of Care mean?
• What is the relevant setting?
• Who should be making the decision to request a test?
• Who should be conducting the test?
• How long does the test process take?
• How accurate is the test?
• What is the evidence that the result affects the treatment pathway?
AMR PoC tests

Think in terms of the value proposition:
• Accuracy compared to established tests
• Speed

Very difficult to develop linked evidence
• Potentially for antimicrobial prescribing reduction
• Not for AMR reduction

Adoption issues:
• Space
• Training of staff
• Credibility

**PoC is only meaningful if it affects the treatment pathway**
Engaging with NICE
NICE’s ‘offer’

NICE Office for market access
First point of contact for talking to NICE

NICE META tool
Gap analysis

NICE Scientific advice
Advice on generating evidence

NICE Guidance and advice
Critical assessment of the evidence

NICE Adoption & Impact
Overcome barriers to adoption

NICE Research facilitation
Generates new evidence
**The changing landscape**

*Exciting times!.......*

Very strong pipelines of products with potential for major patient benefits
Patients and healthcare systems need access to clinically and cost effective products as quickly as possible
Personalised/precision medicine becoming a reality...

**Challenges:**
High cost of some products
Timely patient access while the evidence is still emerging
New initiatives in the landscape

**Effective engagement necessary to address challenges:**
The Office for Market Access
NICE Scientific Advice
NICE Office for Market Access (OMA)

NICE OMA • ‘SAFE HARBOUR PRINCIPLE’
From multi stakeholder to focused perspective
Multifaceted opportunity for exploration of key system access questions

- Covers all life sciences products:
  - Pharmaceuticals, biopharmaceuticals, medical devices, diagnostics & digital (if patient benefit)

- Tailored engagement and expert advice to help companies optimise the journey through NICE

- OMA provides opportunities to engage with NICE at any stage in the product development to adoption pathway

- Every company’s needs are different, so we offer bespoke services tailored to requirements
  - Fees are charged on a not-for-profit basis (varying in scale to reflect the resources required).
NICE Scientific Advice

Why seek Scientific Advice?
Understand the perspective of decision makers
Understand pros and cons of different trial /study options
Maximise relevance of trial programme outputs
Explore alternative strategies to address data gaps
Integrate cost effectiveness considerations into early decision making
De-risking strategy
International Knowledge Transfer Services

• These services offer advice, support and insight into NICE processes. By sharing our experiences we can help you to:
  ✓ assess your healthcare programmes
  ✓ develop your own methods, processes and strategies
  ✓ identify areas for risk assessment and review
  ✓ develop new healthcare strategies
• We also offer bespoke services including seminars workshops, capability building...
• Fee for service on cost recovery basis

• [www.nice.org.uk/about/what-we-do/international-services/knowledge-transfer](http://www.nice.org.uk/about/what-we-do/international-services/knowledge-transfer)
The META tool

In collaboration with GMAHSN and their partner TRUSTECH
HOW THE SERVICE WORKS

1. Create account / Sign in
2. Select organisation to facilitate
3. Complete short form (general information)
4. Request call back to discuss process
5. Make payment
6. Complete online synopsis form
7. Facilitation
8. META report

NICE
Find out more at:
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Any questions?
Additional slides
Useful Links

- NHS England antimicrobial stewardship
- Notify a medical technology to NICE
- NICE Diagnostics Assessment Programme
- Diagnostics Assessment Programme manual
- Technology Appraisals Programme
- 2013 Guide to the methods of technology appraisal
- NHS Commissioning through Evaluation
- Scientific Advice Programme
- META tool
- HealthTech Connect
Useful resources to help with trial design

CAMPUS database (http://campus.ecrin.org/)
ECRIN MD outcomes measure database (http://ecrin.org/tools/medical-device)
Ideal, Development, Exploration, Assessment, Long-term follow-up (IDEAL) collaboration (www.ideal-collaboration.net)
National Institute for Health Research (NIHR) Clinical Trials Toolkit http://www.ct-toolkit.ac.uk/
European Clinical Research Infrastructure Network (www.ecrin.org)
Assessment evidence requirements
What data do you need?

Regulator

**Product safety**: laboratory testing with clinical trial data for devices with greatest risk

**Evidence of efficacy**: does the device meet its intended purpose? (not necessarily from comparative studies)

HTA

**Evidence on clinical effectiveness** *(compared to established practice)*: trials, evidence synthesis

**Evidence on cost effectiveness**: trials, modelling

Evidence on relative safety/adverse events

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*Trueman P et al 2011*
Evidence- how much is needed?

It depends.....

Uncertainties about **the disease** and how it is best managed
Uncertainties about **the technology** and how it works
Uncertainties about **the benefits** and what value they have
Etc....

High uncertainty = more evidence
Low uncertainty = low evidence
Evidence requirements

Varies by programme, but in general....

Any evidence from any country
No design/quality thresholds
• Published and in-press research (academic/commercial in confidence)
• Unpublished data
• Real world data, register data, audits, post market surveillance
• Forthcoming trial results
  Each technology/potential benefit assessed on case by case basis
Evidence considerations

The ideal evidence would be a good quality ‘end-to-end’ study – follows patients from testing, through treatment, to final outcomes

- Typically not available for diagnostics
- Search for data on test accuracy, direct outcomes from the test, indirect health outcomes from the test result, and costs
- Identified evidence can then be combined through a linked evidence approach
Evidence hierarchy

- Systematic reviews of RCTs
- RCTs
- Controlled observational studies (e.g. case-control)
- Uncontrolled observational studies (e.g. case reports)
- Expert opinion
Evidence on devices and diagnostics from research/clinical studies...

... typically sparse and poor:

- Little regulatory demand (unlike drugs)
- Many manufacturers inexperienced
- RCTs challenging on devices
- Evaluation often early in trajectory

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
Discussion with stakeholders for market access
Routes for engagement with stakeholders

- Budget impact test and managed implementation
- Patient access support liaison unit (PASLU)
- Managed access agreements (MAA)
- Office for market access (OMA)
- Scientific Advice
Features of a good Managed Access Agreement

• simple,
• reproducible,
• has the capacity to be consistently applied
• will not unduly add to the administrative burden of the process for NICE or its stakeholders

CDF: Plausible potential but evidence not robust enough to be considered for routine commissioning

...an example – the Cancer Drugs Fund (CDF)

CDF decision consists of 2 key elements:
• Data Collection Arrangement
• CDF Commercial Agreement, determining the cost of the drug during the managed access period; cost of the drug reflects the decision uncertainty.
Budget impact test and managed implementation

Reconcile the roles of **NICE** and **NHS England**

→ Clinical & cost effectiveness  → Effective service delivery

Flexibility in the adoption of cost-effective, high budget impact technologies

- Balance value and affordability

**Budget impact threshold: £20m/year in first 3 years**

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<thead>
<tr>
<th>Negotiate access arrangements</th>
<th>Variation to the 90 day funding direction</th>
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NICE
## Cost effectiveness vs. Resource impact

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<thead>
<tr>
<th>Cost-utility analysis</th>
<th>Cost-impact analysis</th>
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</thead>
<tbody>
<tr>
<td>Is it <em>value</em> for money?</td>
<td>How much it will <em>cost</em>?</td>
</tr>
<tr>
<td>Cost per health gain for <em>one</em> (hypothetical) patient</td>
<td>Total cost for <em>England</em></td>
</tr>
<tr>
<td>Used to <em>inform</em> recommendations</td>
<td>Used for <em>planning and implementation</em> of recommendations</td>
</tr>
<tr>
<td><strong>Lifetime</strong> time horizon</td>
<td>Short time horizon <em>(1 to 5 years)</em></td>
</tr>
</tbody>
</table>
Budget impact and NICE decisions

• A high budget impact will mean that the NICE committee will want to be very confident, i.e. more certain that an intervention is cost effective

• The NICE committee cannot decide not to recommend something just because it has a high budget impact
Guidance Executive will consider a request from NHS England to vary the timescale for the funding requirement, taking into account whether:

- the budget impact test been met;
- all reasonable opportunities for reaching a commercial agreement been pursued;
- the request is in proportion with the magnitude of the budget impact;
- the request takes account of the severity and acuity of the condition to which the guidance relates;
- consideration has been given to NHS England’s and NICE’s duties under equalities legislation;
- an interim commissioning policy been developed to provide phased funding for and access to the technology during the extended funding variation period.
Managed access agreements
Commercial and Managed Access Programme

- Responsible for managed access activities including CDF and PASLU
- Support commercial engagement between companies and NHS England when a CAA or PAS is required to address specific uncertainties within a topic
- Commercial dialogue can be conducted:
  - before formal invitation to participate in the appraisal (for example during scoping)
  - at the decision problem meeting
  - on receipt of the evidence submission
  - at clarification
  - during technical report consultation
  - during ACD consultation.
Managed Access Agreements

A proposal that addresses a significant uncertainty

Fixed duration, and agreement for what happens next

Defined starting and stopping criteria

Data collection proposal

Financial risk management

Patient and clinician involvement

Time limited

Agreed with stakeholders
Issues for consideration

- Is the scheme feasible to implement?
- Is the scheme practical to operate?
- Is the company’s estimated administrative burden reasonable?
- Are the financial flows & governance arrangements of the scheme consistent with the PPRS?
- Is there unmet need for the population?
- Would the scheme avoid unduly complex monitoring?
- Uncertainty of benefits of the scheme?
More information on engaging with NICE
OMA engagement meetings under safe-harbour principles

Supported by rules of engagement to ensure a broad, open and free flowing discussion within a confidential framework

Collaborative event, including participation from a range of stakeholders

Designed to help companies deliver a market access plan that is patient & healthcare system focussed.
We would like our company to learn more how NICE can help us?

How should we optimize our value proposition?

What are the potential routes our product might follow through NICE?

How does our current thinking on market access sit with NICE /healthcare landscape partners?

NICE Office for Market Access
Our company develops products for orphan diseases, conventional approaches to evidence generation do not always work, what does NICE think about it?

We are discussing our registration package with the FDA this month, do we need to talk to EMA, NICE and other agencies?

We want to discuss our product with MHRA, Should we also talk to NICE?

We are developing a life-saving gene therapy, Should we talk to NICE?

Where can I learn about NICE methods for product evaluation?

We are working on a health economics model for a product, can we discuss it with NICE?
META stages

Company completes synopsis form

Facilitator reviews form and identifies any specific areas to focus on during session

90 – 120 minute guided facilitated gap analysis where company reflects on the strength of their value proposition, supporting evidence and level of preparedness for evaluation

Production of concise gap analysis report
Overview of META

Section 5

Welcome to the META tool

The META tool has been designed to help identify the evidence gaps you will need to fill in order to make a convincing argument to a payer or commissioner for your product. It also enables you to think through any issues in your development plans with an experienced facilitator.

Different technologies will be at different stages of evidence generation. How long it takes to complete the synopsis form will depend on the stage you are at in the development process.

Do not worry if you do not have information to answer a question. However, if you are not clear on why we are asking a particular question please highlight that this is the case so that we can discuss it with you during the facilitation.

There are 10 sections left to complete. They include:
- high-level, overview questions on the technology itself
- detailed questions about the clinical context in which your technology will be placed (the ‘treatment pathway’)
The META report

• Concise!
  - A couple of pages
  - Summarises the outcomes of the discussion
  - Record areas of strengths and weaknesses in the client’s value proposition and supporting evidence base
  - Record of potential next steps

Provides a gap analysis
What META is not designed for

- A META tool report is **not** meant to:
  - Provide advice
  - Act as an action plan
  - Endorse the product for potential investors
The META Report

Key assessment points

Summary

Regulatory and HTA requirements

Value proposition

Clinical treatment pathway

The PICO statement

Measuring clinical effectiveness

Economic data collection

Adoption and impact

Value proposition graph