

# NICE methods of technology appraisal

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# The background: why NICE was set up

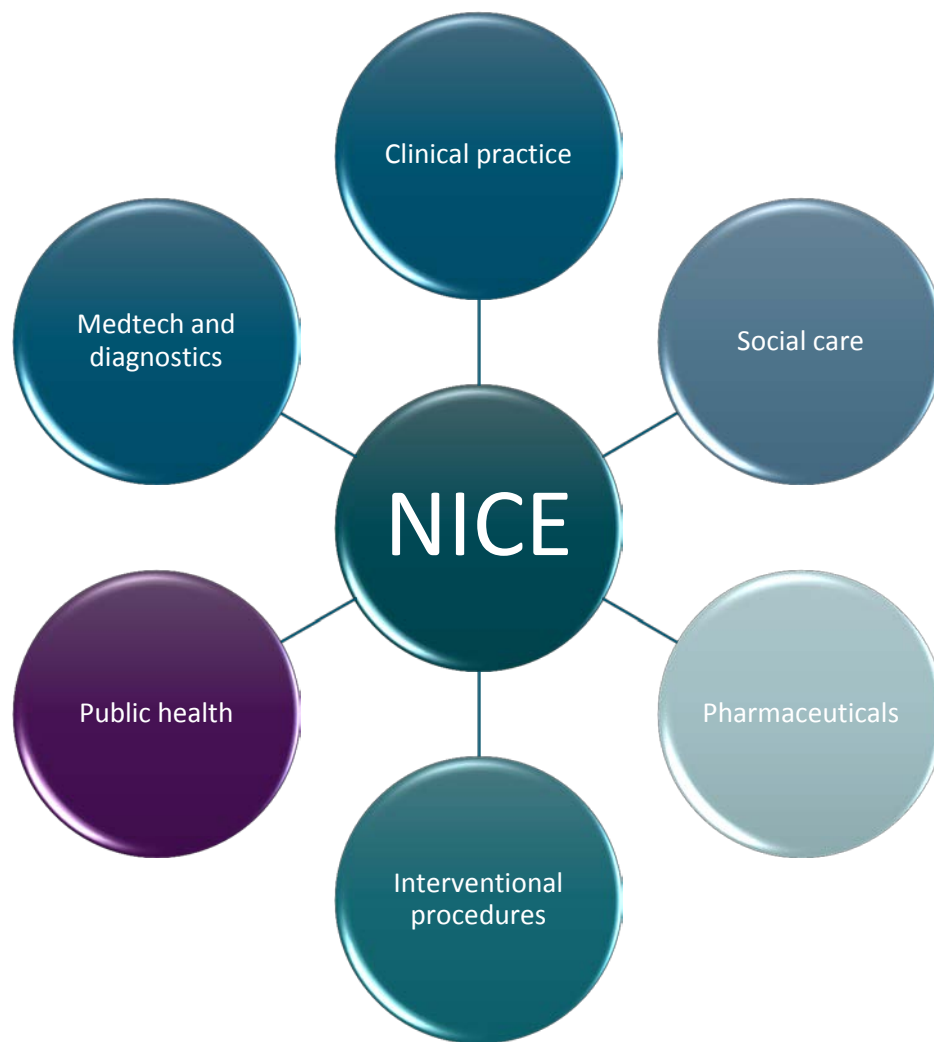
- Established in 1999
- To reduce variation in the availability and quality of treatments and care
- To resolve uncertainty about which medicines and treatments work best and which represent best value for money for the NHS



# Improving outcomes for people

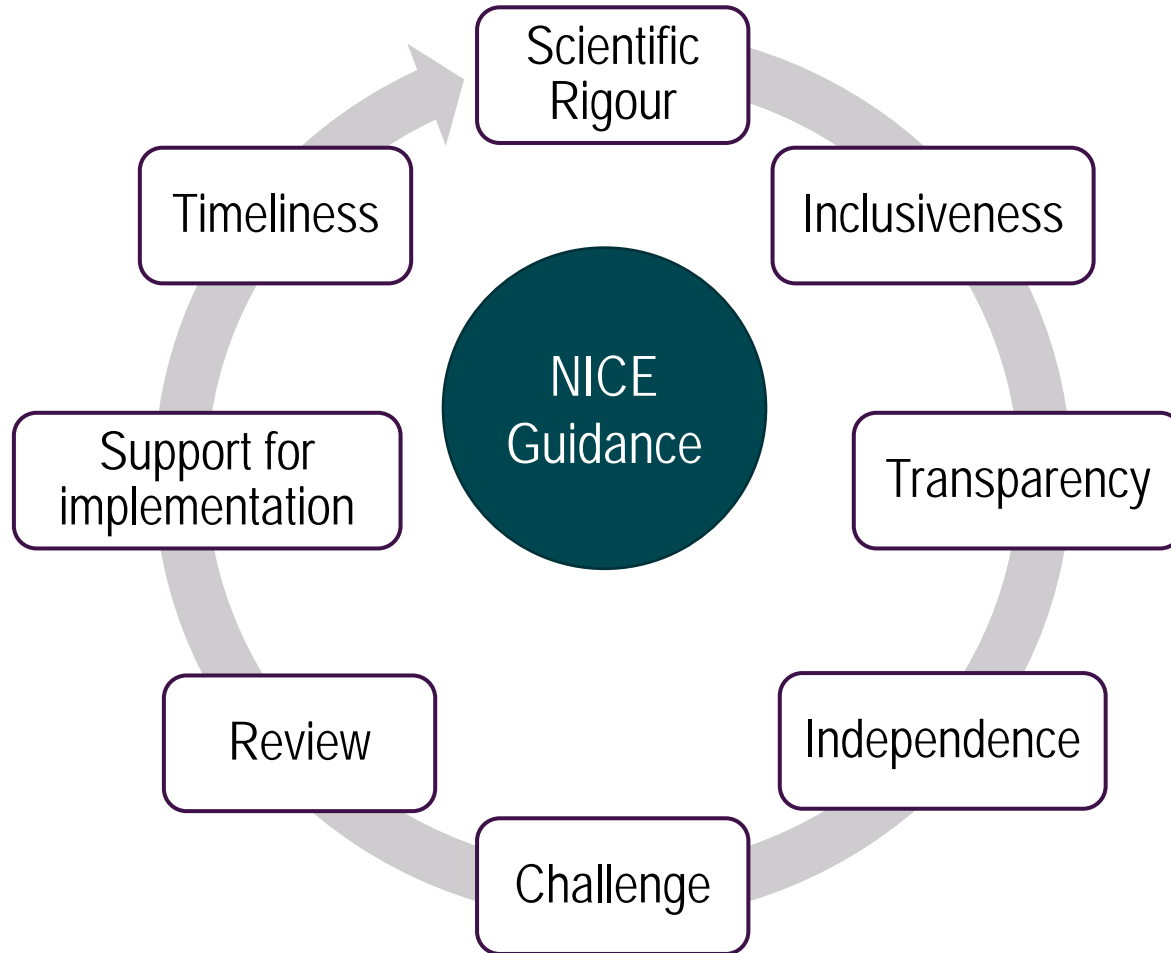


# Areas where guidance and advice is produced



Different NICE programmes have different methods

# Procedural principles for guidance development



# NICE Technology Appraisals

- A review of clinical and economic evidence leading to recommendations on the appropriate use of new and existing technologies for the NHS in England
- Final decision made by independent Committee
- Mandatory funding direction for recommended technologies
- HTA either provided by Industry and evaluated by an academic group (STA) or HTA completed by an academic group (MTA).

**NICE** National Institute for  
Health and Care Excellence



Ceritinib for previously treated  
anaplastic lymphoma kinase positive non-  
small-cell lung cancer

Technology appraisal guidance  
Published: 22 June 2016  
[nice.org.uk/guidance/ta395](https://www.nice.org.uk/guidance/ta395)

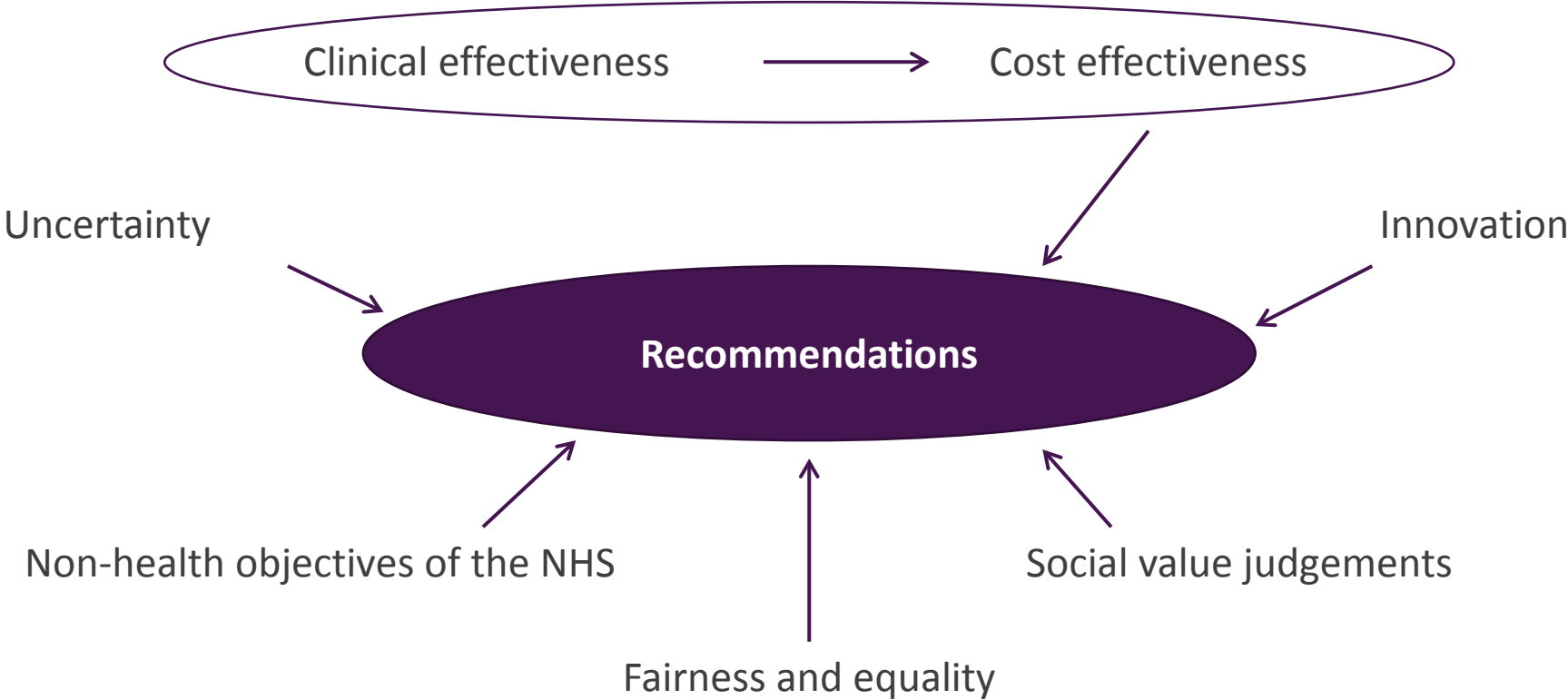
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# The NICE Technology Appraisal methods guide

- Describes key principles of assessment and appraisal methodology
  - General methodological concepts underlying each stage of the appraisal process
  - What is required of participants submitting evidence to NICE
  - How the Appraisal Committee appraises the evidence and makes the judgements that lead to its final conclusions
- Work of the academic groups should be in line with the NICE TA methods guide, but they will also follow general guidelines for systematic review that are developed by the Centre for Reviews and Dissemination at the University of York



# Decision making framework



# Decision problem

Aspect	Technology Appraisal focus
Technology	Licensed indication of the technology: <ul style="list-style-type: none"><li>• Non-licensed indications considered only with agreement from Department of Health</li></ul>
Population	Licensed population for the indication: <ul style="list-style-type: none"><li>• Company can submit only for a subgroup</li><li>• Decision problem may specify specific subgroups for analysis</li></ul>
Comparator	All potentially relevant comparators: <ul style="list-style-type: none"><li>• Committee will decide the most appropriate</li><li>• Can include branded, generic and biosimilar</li></ul>
Outcomes	Health benefits and adverse effects that are important to patients and/or their carers <ul style="list-style-type: none"><li>• survival or health-related quality of life that translates into quality-adjusted life years (QALYs) for cost effectiveness</li></ul>

# Reference case

Element of HTA	Reference case
Decision problem	As per the scope developed by NICE
Comparators	As listed in the scope developed by NICE
Perspective on outcomes	All direct health effects whether for patients or where relevant for caregivers
Perspective on costs	National Health Service and Personal Social Services and valued using costs relevant to NHS and PSS
Type of economic evaluation	Cost utility analysis with fully incremental analysis
Time horizon	Long enough to capture all important differences in costs or outcomes of technologies being compared
Synthesis of evidence	Systematic review
HRQOL	Reported directly by patients and/or caregivers and valued by a representative sample of UK population

# Assessment of benefits and harms

- Aim of the assessment: Quantify the effect of the technology and of the relevant comparator technologies on survival and health-related quality of life so that this can be used to estimate a QALY in economic evaluation
- Evidence quantifying the effect should:
  - Reflect the decision problem and reference case
  - Not be limited by type of study or other study design parameters – best available evidence
  - Assembled systematically and be reproducible
  - Be analysed in a way that minimises bias

# A specific note on harms

- Assessment and appraisal of harms is limited to consideration of the need to include them in economic analysis and their quantification where their inclusion is considered relevant for economic modelling.

# Appraisal of clinical effectiveness

- Discretion to take account of the full range of clinical studies and the Committee is not expected to restrict itself to considering only certain categories of evidence
  - Includes observational studies, qualitative evidence and expert statements
- Judgements on clinical effectiveness may include:
  - Nature and quality of the evidence
  - Uncertainty generated by the evidence and relevance to practice
  - Differential effects in subgroups
  - Patient perspective of benefits and harms
  - Position of technology in pathway of care
- Extent to which the factors are taken into account in making judgements is a matter for the Committee's discretion

# Study design and publication status

- All study designs both published and unpublished can be submitted
  - The importance given to an particular study type depends on its suitability to address issues under consideration
- In general, greater importance is given to evidence derived from high-quality studies with methodology designed to minimise bias where available
- RCTs preferred for relative treatment effect
- Evidence from other studies is often used for the valuation of health effects over time into QALYs, and for costs

# Indirect comparison methods

- Data from head-to-head RCTs should be presented in the reference-case analysis
- Network meta-analysis can be presented if the technologies being compared have not been evaluated in a single RCT
  - Randomisation must be preserved
  - Methods and individual studies must be described
  - Heterogeneity and consistency should be explored
- The Committee will take into account the additional uncertainty associated with the lack of direct evidence
- A series of technical documents are available to support Industry to provide appropriate analyses



# Surrogate outcomes

- Clinical end points that reflect how a patient feels, functions, or how long a patient survives are regarded as more informative than surrogate end points
- When the use of 'final' clinical end points is not possible and 'surrogate' outcomes are used evidence of the surrogate-to-final end point outcome relationship must be provided
- Usefulness of the surrogate end point will be greatest when there is strong evidence that it predicts health-related quality of life and/or survival
- Uncertainty associated with the relationship between the end point and health-related quality of life or survival should be explored and quantified

# Subgroup analysis

- Characteristics of the group must be clearly defined and identifiable
- When possible, potentially relevant subgroups will be identified at the scoping stage before the assessment starts
- Subgroups may be defined based on relative risk or absolute baseline risk of specific health outcomes
- Evidence supporting biological or clinical plausibility for a subgroup effect should be submitted
- Details of statistical analysis must be provided and use of IPD is preferred
- When considering subgroups attention is paid to legal obligations on equality and human rights

# Observations and conclusions

- IQWiG methods in general seem more prescriptive in terms of procedures and rules that guide assessment and appraisal
- When our organisations receive non-randomised data, indirect comparisons, surrogate outcomes and post-hoc subgroups, our consideration of these doesn't seem fundamentally different
  - Differences in how far we will take these data
- These differences likely to arise from our differing remits, functions and requirements of our procedures rather than a fundamentally different understanding of what is acceptable evidence