Internationale Standards des HTA?

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Conflicts of Interest

- A Gutachten was commissioned by VFA – we had full editorial freedom
- Kleijnen Systematic Reviews Ltd has been commissioned by IQWiG for several assessments concerning non-drug questions
- We do only non-drug projects for public commissioners; we do projects concerning drugs/medicines only for pharmaceutical companies

Questions concerning German NICE (presentation in Berlin 28 April 2003)

- Will there be a transparent process?
- Will it be mandatory for industry to submit all evidence?
- Will it be seen as independent (not a tool for rationing)?
- Is there capacity to do the work, timely and at high quality?
- Will health care providers follow decisions?

International standards?

- HTA has elements which are country specific: costs / insurance system / organisation of care / delivery of care
- Best options for international standards for evidence systematic reviews
- Different questions often lead to different reviews – rarely the scope of two HTAs is identical

Process of NICE

- Involvement of relevant parties.
- Scoping process: written material and a meeting.
- Evidence assessment by an independent group.
- NICE performs the evidence appraisal and formulates recommendations.

Process of IQWiG

- IQWiG drafts the research protocol (Berichtsplan).
- IQWiG and the review team perform the evidence assessment jointly.
- Report plans and preliminary reports on the web for comments.
- IQWiG gives recommendations
- The Federal Joint Committee performs the appraisal.

Pre-school vision screening in Germany and the UK

Objectives

- A methodological comparison of two reports of vision screening programmes and tests (from the UK and from Germany).
- This project addressed the policy context, scope, methods, findings and conclusions of the two reports.

Policy Context

- UK: What is the clinical and cost effectiveness of screening programmes for amblyopia and squint?
- Germany: What is the effectiveness of screening programmes for visual deficiencies in children up to 6 years?

Similarities

- Populations: Pre-school children
- The main outcomes: the effectiveness of screening programmes, the diagnostic accuracy of screening tests, and the effectiveness of treatment.
- The optimum age for prevention, detection, and treatment.

Differences

- Condition: ‘amblyopia and squint’ versus ‘visual deficiencies that need treatment’.
- Cost-effectiveness of screening.

Scope (protocols)

- UK: To estimate the cost-effectiveness of screening options for amblyopia and squint in children using a decision model.
- Germany (3 goals):

  1. Comparison of a vision screening programme with no screening / or a different screening programme.

  2. Comparison of early versus late treatment.

  3. Assessment of the diagnostic test accuracy.

Similarities

- Populations: Pre-school children
- The main outcomes: the effectiveness of screening programmes, the diagnostic accuracy of screening tests, and the effectiveness of treatment.

Differences

- Germany:

- 3 Systematic Reviews (screening, diagnostic tests and treatment)

- UK:

- 7 Systematic Reviews to inform the economic model;

- Focus on cost-effectiveness

Method sections

- UK: Focus on decision model
- Germany: Focus on systematic reviews

Inclusion Criteria

Outcomes:

- UK: No specific outcomes reported; only HRQoL measures.
- Germany:

1. Prevalence of amblyopia; negative effects of screening/ diagnosis;
2. For diagnostic tests: data for 2x2 table
3. Health-related quality of life; vision; amblyopic risk factors; cognitive and educational limitations; adverse effects of screening or diagnostic tests; adverse treatment effects.

Inclusion Criteria

Study designs:

- UK: Potential screening test and papers reporting on the impact of screening programmes upon treatment outcomes were included, as were all potential diagnostic test studies.
- Germany: RCTs, non-randomised controlled studies, controlled cohort studies, and cross sectional studies.

Included diagnostic studies

- 5 studies included in both reports
- 6 studies included in UK report, excluded with reason in German report
- 4 studies included in UK report, not mentioned in German report
- 21 studies included in German report, not mentioned in UK report

Included screening studies

- 4 studies included in both reports
- 21 studies included in UK report, not mentioned in German report
- 1 studies included in German report, not mentioned in UK report

Included treatment studies

- 5 studies included in both reports
- 5 studies included in UK report, excluded with reason in German report
- 20 studies included in German report, not fulfilling inclusion criteria in UK report
- 14 studies included in UK report, not mentioned in German report
- 20 studies included in German report, not mentioned in UK report

Conclusions

- UK: the cost-effectiveness of screening for amblyopia is dependent on the long-term utility effects of unilateral vision loss. There was limited evidence on any such effect, though the authors' interpretation of the available literature is that the utility effects are likely to be minimal.
- Germany: there is no evidence to suggest there is benefit or harm from universal pre-school vision screening.

Do they fulfil each other's brief?

- UK report: fulfils most of the requirements.

- shortcoming: limited to UK data; reporting of the methodology of the systematic review process should be improved.

- German report: fulfils most requirements.

- shortcoming: lack of an economic assessment; does not address the question of effectiveness of treatment options beyond the relative effectiveness of early versus late treatment.

Ideal Report

- Germany:

- German report.

- UK:

- UK economic model based on German systematic reviews.

Conclusion

- The research questions were similar.
- The protocols were quite different.
- The methods allowed for considerable differences in studies to be included.
- Projects report different types of results.
- Both projects came to similar conclusions.

Observations about HTA

- Pharmaceutical companies have few new block busters in the pipeline
- Increasingly, one does not see a new drug for a specific disease, but an existing drug in search for an indication
- 4th hurdle process (reimbursement decisions) becoming more and more prominent
- Phase III trials programme in many companies not yet geared up towards reimbursement, still very much focussed on licensing
- Situation of just one RCT for a new reimbursement decision, with multiple possible comparator drugs

BMJ

RESEARCH

Methodological problems in the use of indirect comparisons for evaluating healthcare interventions: survey of published systematic reviews

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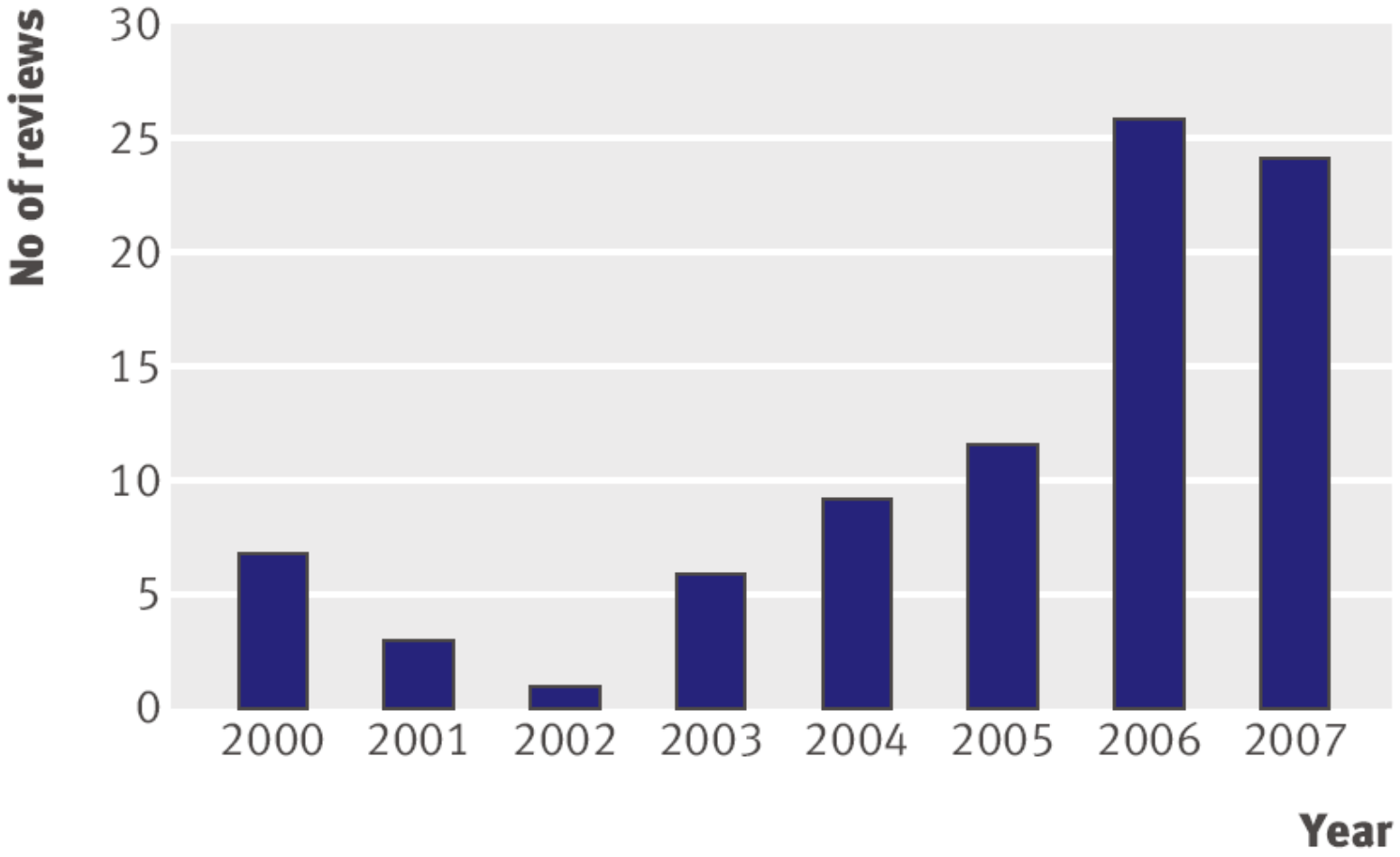

Fig 2 | Publication year of 88 review reports that explicitly used indirect comparison

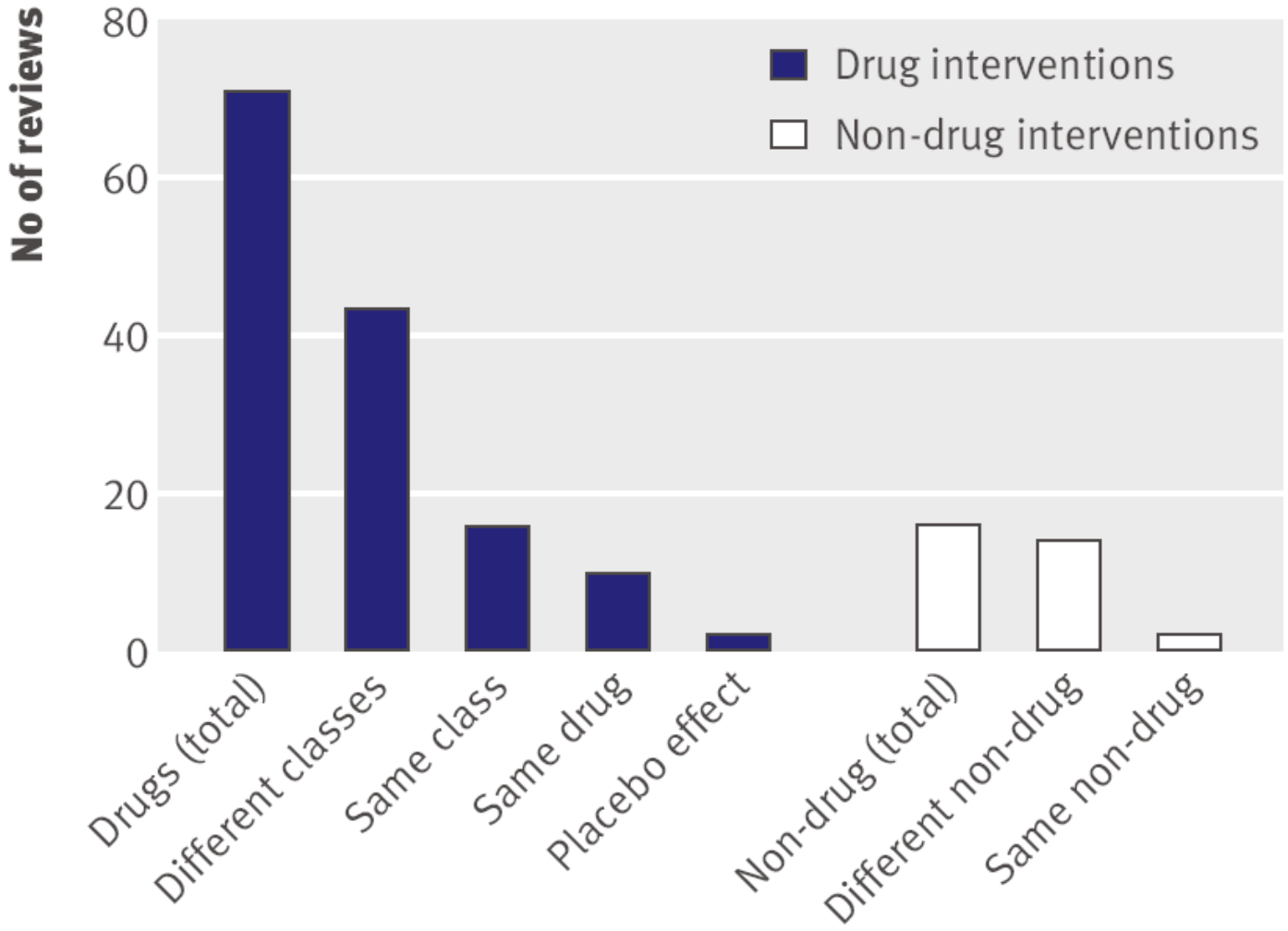

Fig 3 | Types of interventions indirectly compared in 88 review reports

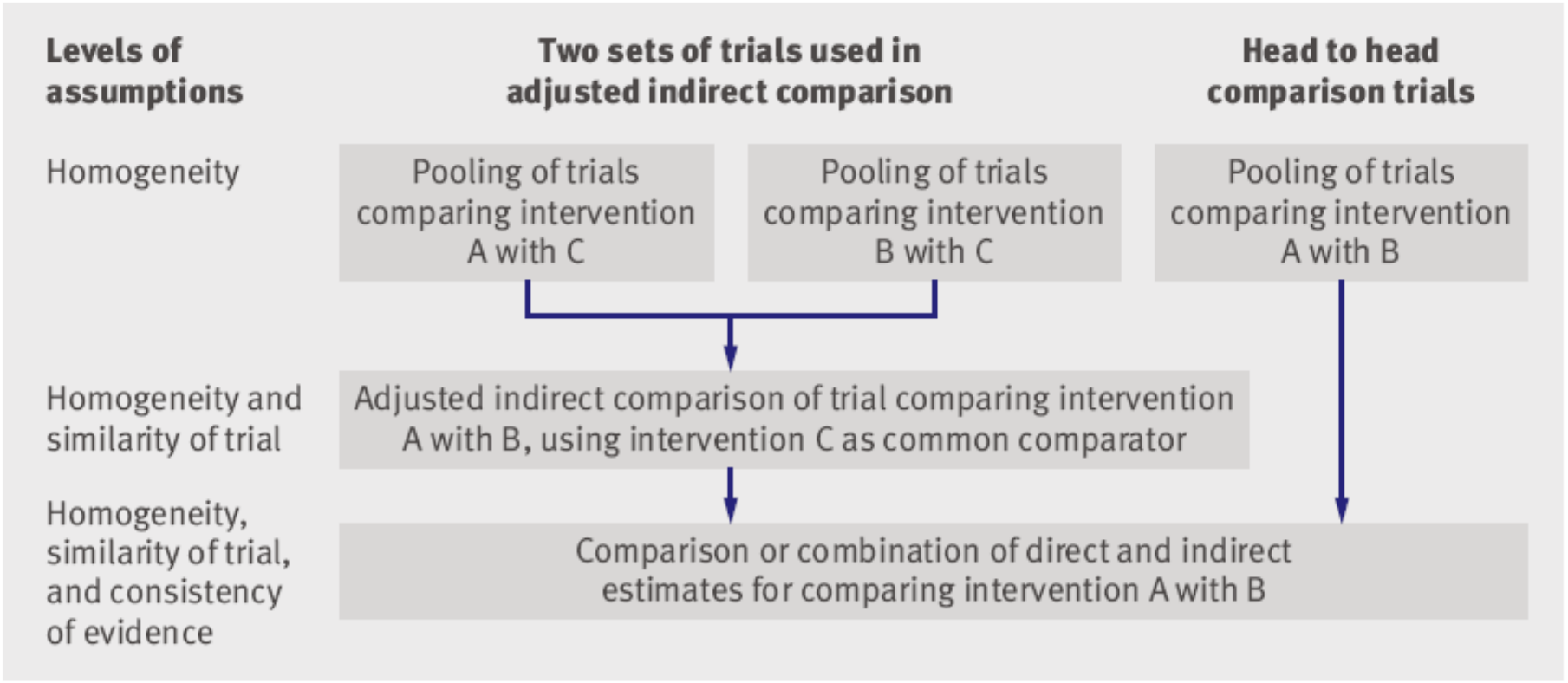

Fig 1 | Assumptions underlying adjusted indirect and mixed treatment comparison

Table 1 | Methods used for indirect comparison and availability of direct comparison evidence

Indirect comparison method	No (%) of included reviews	Direct comparison available	Comparison of indirect and direct evidence	Combination of indirect and direct evidence
Simple adjusted	49 (56)	15	11	2
Network or Bayesian approaches	18 (20)	16	9	15
Informal indirect	13 (15)	6	1	0
Naive indirect	6 (7)	2	1	0
Unclear	2 (2)	1	1	0
Total	88 (100)	40	24	17

WHAT IS ALREADY KNOWN ON THIS TOPIC

Indirect comparisons can be valid if some basic assumptions are fulfilled

The related but different methodological assumptions have not been clearly distinguished

WHAT THIS STUDY ADDS

Certain methodological problems may invalidate the results of evaluations using indirect comparison approaches

Understanding basic assumptions underlying indirect and mixed treatment comparison is crucial to resolve these problems

A framework can help clarify homogeneity, similarity, and consistency assumptions underlying adjusted indirect comparisons

BMC Medicine

BioMed Central

Research article

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Inhaled drugs to reduce exacerbations in patients with chronic obstructive pulmonary disease: a network meta-analysis

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Indirect comparisons

- Move towards network meta-analyses
- No international standards
- Various forms of indirect comparisons used by NICE (and IQWiG)

Assessments and appraisals

- "The assessment process consists of an objective analysis of the quality, findings and implications of the (mainly research) evidence available as it relates to the appraisal question and context. The appraisal process, in contrast, is a consideration of the outputs of the assessment process within the context of additional information supplied by relevant parties such as clinical specialists and patient experts. The appraisal decision is a judgment on the importance of a range of factors that differ from appraisal to appraisal"

Assessment and appraisal

- IQWiG performs assessments and gives recommendations
- G-BA performs appraisals

- Overlap between assessment and appraisal by IQWiG giving recommendations

- NICE performs technology appraisals
- The assessments are done by independent academic groups

Process - Scoping

- Scoping workshop to address PICOS questions – Patients, Interventions, Comparator, Outcomes, Study designs
- Scoping workshop to enable input from stakeholders, external experts, IQWiG and G-BA
- Scoping workshop enhances transparency

Process – External experts

- Report by independent external experts should be published
- This helps with transparency, it also helps with judgements about IQWiG's recommendations – what appraisal has taken place
- IQWiG produces final version of report themselves and submit it to G-BA

Process – open process of dealing with comments

- Comments from stakeholders and referees should be published
- IQWiG's decision about whether or not to take up the comments should be documented and be made public
- Names of all commentators should be published

Process – consequences for stakeholders

- Participation also comes with requirements:
  - Stakeholders need to make patient based data public, only confidentiality of economic data can be justified
  - A registry of all clinical trials is inevitable in the long term, best to put it in place as soon as possible
  - IQWiG is and should remain an independent body. All decisions about an assessment should ultimately be theirs
  - Stakeholder involvement is participation and exchange of opinions and knowledge
  - Stakeholder involvement is not a consensus process!

Methods – principle of best available evidence

- Scoping workshop will be crucial in defining the objectives of the assessment
- G-BA must take decisions, therefore best available evidence, whatever its level, needs to be summarised
- There is no empirical evidence that supports demanding a minimum number of studies needed for making decisions

Methods – Use of different study designs

- Applying the principle of best available evidence means that one cannot strictly always demand certain study designs such as randomised trials
- This needs to be addressed during scoping and decisions about the approach to be taken need to be made on a case-by-case basis, and possibly also within projects individually per different outcomes (categories)

The HRT controversy: observational studies and RCTs fall in line

For several years, we witnessed a disarraying debate about the conflicting messages between observational studies and randomised trials on the effect of hormone replacement therapy (HRT) on coronary heart disease and breast cancer. HRT seemed protective for coronary heart disease in observational studies, but randomised trials found an increase of coronary heart disease in the first years of use.[1] For breast cancer, combined oestrogen-progestin showed a lesser risk in the large Women's Health Initiative randomised trial than in observational studies such as the Million Women Study.[2,3] Unopposed oestrogens had a smaller breast cancer risk than combined preparations in observational studies, but carried no risk in the trial.[4] Observational research suffered a credibility crisis.

Recent reanalyses have brought the results from observational and randomised studies into line. The results

Methods - comparators

- Needs to be addressed in scoping workshop – careful decisions needed about:
  - Head to head comparisons
  - Comparisons with placebos
  - Co-interventions that are allowed
- Principle of including all relevant comparators
- The decisions should again be taken on a case-by-case basis

Confidential data

- Should only be allowed for economic data
- Not ethical to keep patient data confidential
- IQWiG's current approach makes sense

Trials register

- Unavoidable in the mid-term future, best to implement as soon as possible

10 years of NICE: still growing and still controversial

Peter Littlejohns, Sarah Garner, Nick Doyle, Fergus Macbeth, David Barnett, Carole Longson

The National Institute for Health and Clinical Excellence (NICE) will have existed for 10 years on April 1, 2009. Over the past decade, the institute's methodological approach to the development of guidance and assessment of the value of health-care interventions has received international interest and acclaim. Furthermore, individual decisions, in particular those made on new cancer drugs, have generated enormous controversy. An early example was the appraisal of irinotecan and oxaliplatin for colorectal cancer in 2002. In 2003, NICE described the rationale behind its decision making. The 10th anniversary of the institute provides an opportunity to review some of the key issues affecting cancer appraisals and to explain the development of other NICE guidance programmes relevant to the provision of cancer services.

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See Keynote Comment page 306

See Reflection and Reaction page 315

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Introduction

The National Institute for Health and Clinical Excellence (NICE) is the independent organisation that provides

a national review in 2007–08 to establish a 10-year vision of the NHS on its 60th anniversary,[5] the functions of the institute will expand further.

Conclusions

- HTA agencies should optimise transparency
- Scoping workshop with all parties involved is crucial
- External experts' report should be made public
- Openness of processes should be optimised
- Principle of best available evidence should be consistently applied
- Differentiated approach needed for use of study designs
- Comparators need careful consideration
- Trials register is needed, patient data should not be confidential
- There is no international standard for HTA, best possibilities for standardisation are with systematic review part of HTAs