European Experience and Perspective on Assessing Value for Oncology Products

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Outline of Presentation

- The European landscape on access to oncology products.
- The National Institute for Health and Clinical Excellence (NICE) and its approach to assessing value.
- Current issues and debates.

Some Background

- European healthcare systems are largely national health services, or based on social insurance.
- East/West divide in relation to GNP per capita.
- North/South divide in relation to the use of evidence-based medicine and health technology assessment.

Some Background (contd.)

- Hospitals funded by global budgets or, increasingly, casemix-related payments.
- Growth in the use of health technology assessment, particularly in relation to outpatient drugs.
- Promulgation of clinical practice guidelines, although almost none consider costs or cost-effectiveness.

Use of Health Technology Assessment in Europe

- Long history, especially in France, The Netherlands and Sweden.
- Recent growth in the use of HTA for reimbursement and coverage decisions.
- The latter considers only drugs, with the exception of The Netherlands, Ireland and the UK.

Jurisdictions Requiring Cost-Effectiveness Evidence for New Drugs

- Belgium
- Finland
- Germany*
- Hungary*
- Ireland*
- The Netherlands*
- Norway
- Portugal*
- Sweden
- Slovakia
- United Kingdom*

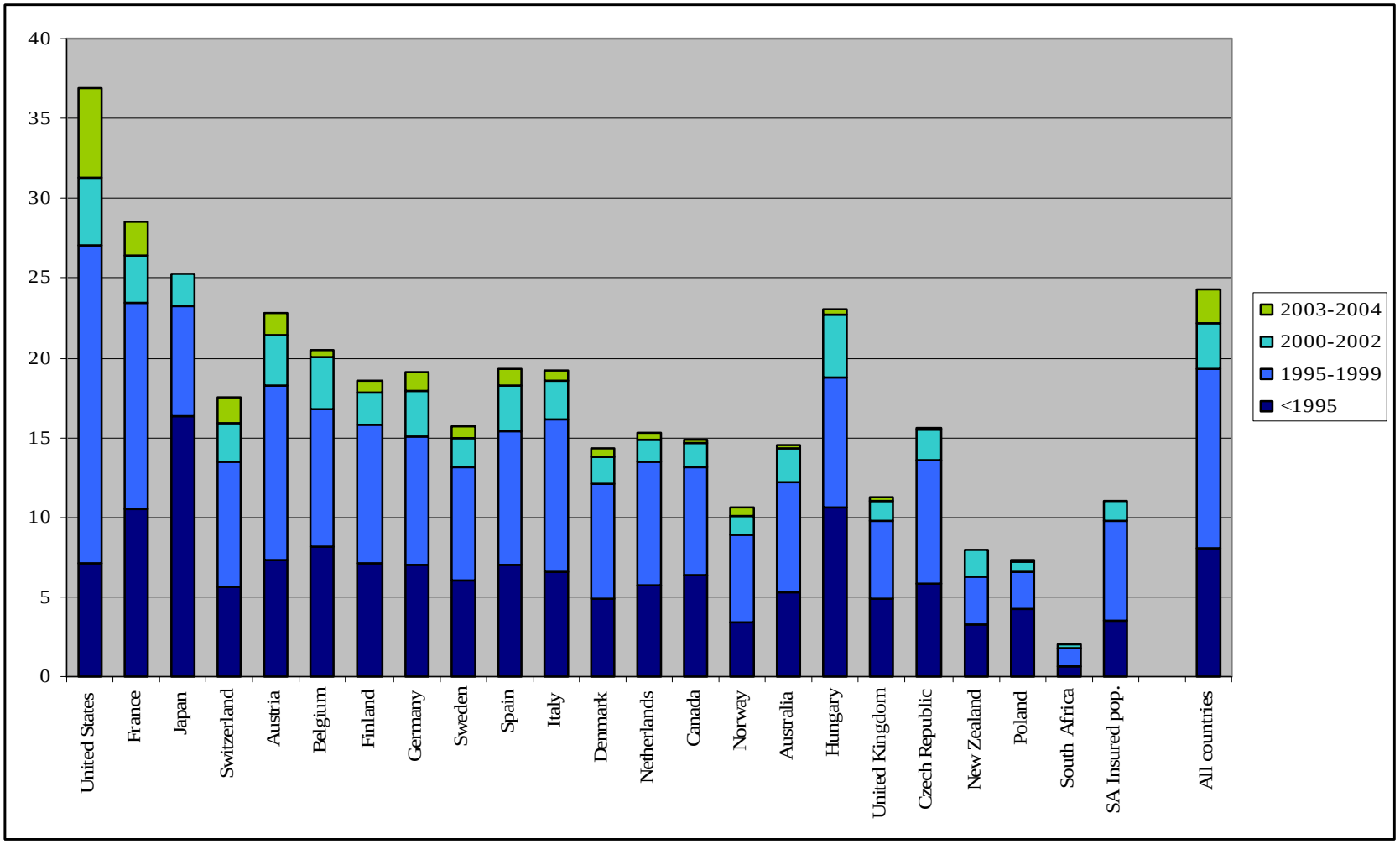
* In these jurisdictions only certain drugs are subjected to appraisal.

Karolinska Reports on Access to Cancer Drugs

- Two reports, in 2005 and 2007.
- Second report considered 19 countries in Europe, plus the US, Canada, Japan, Australia, New Zealand and South Africa.

- Reference: Jönsson B, Wilking N. *Annals of Oncology* 2007; 18 (supplement 3).

PPP-adjusted per capita cancer drug sales (€) in 22 of the study countries in 2005. Distributed on drugs of different “vintage”.

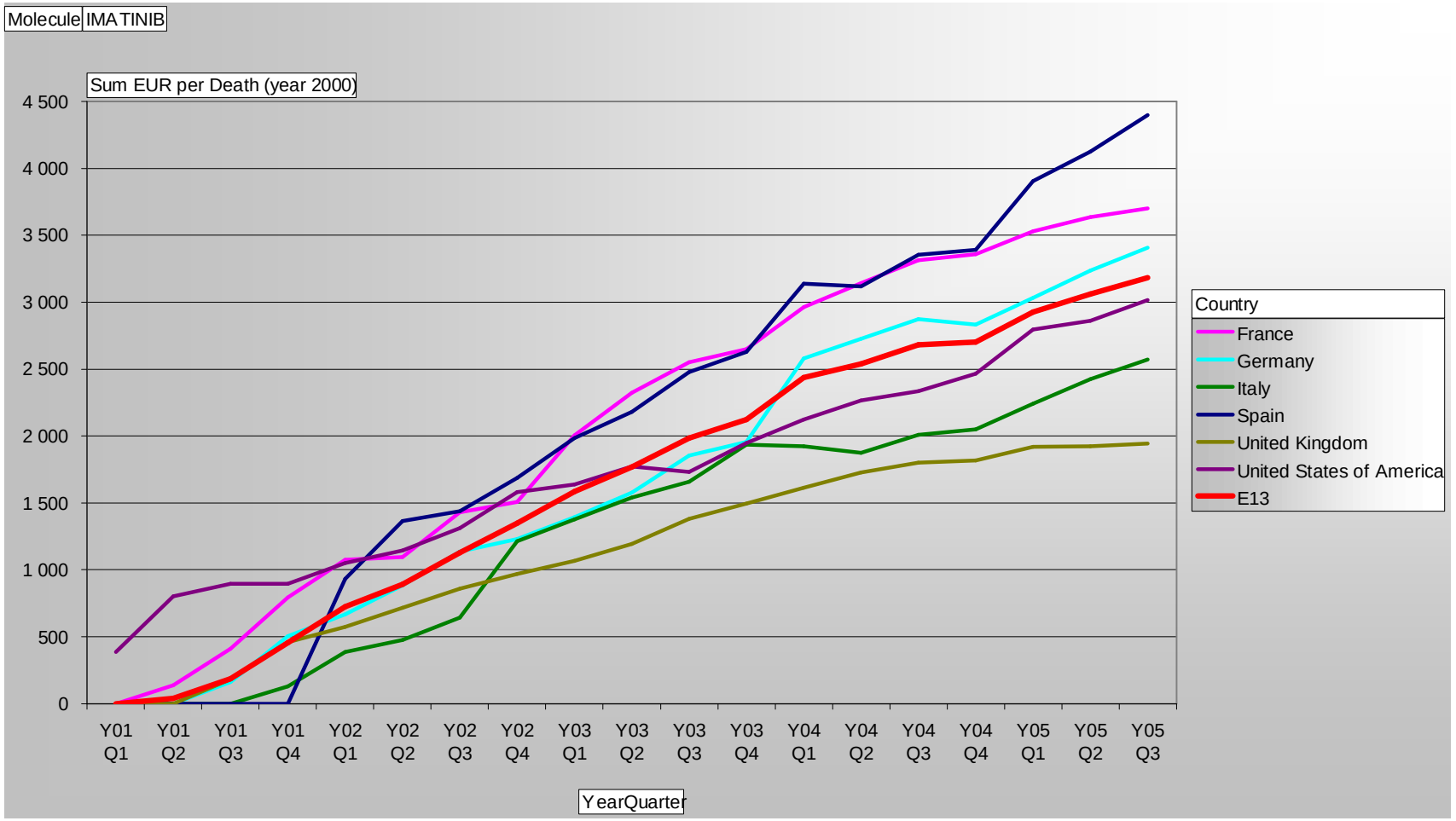


Source: Jönsson B, Wilking N. 2007.

Costs of Cancer Drugs in Perspective

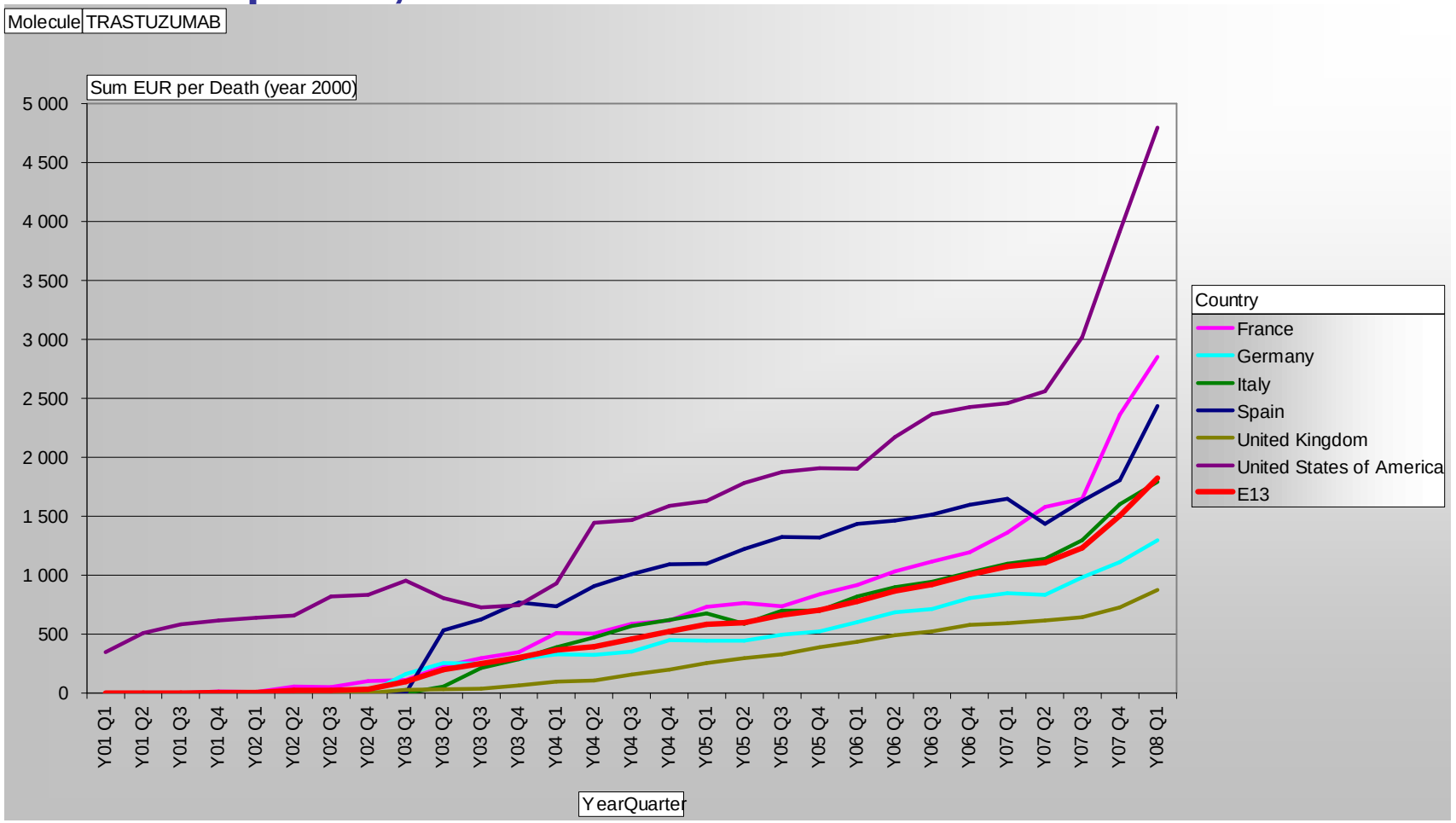
- Account for a minor, but growing, component (10-15% of total cancer care expenditure).
- Drug costs increase by 15-20% per year.

Imatinib Uptake in E13 (average European uptake), France, Germany, Italy, Spain, UK and USA Per Patient



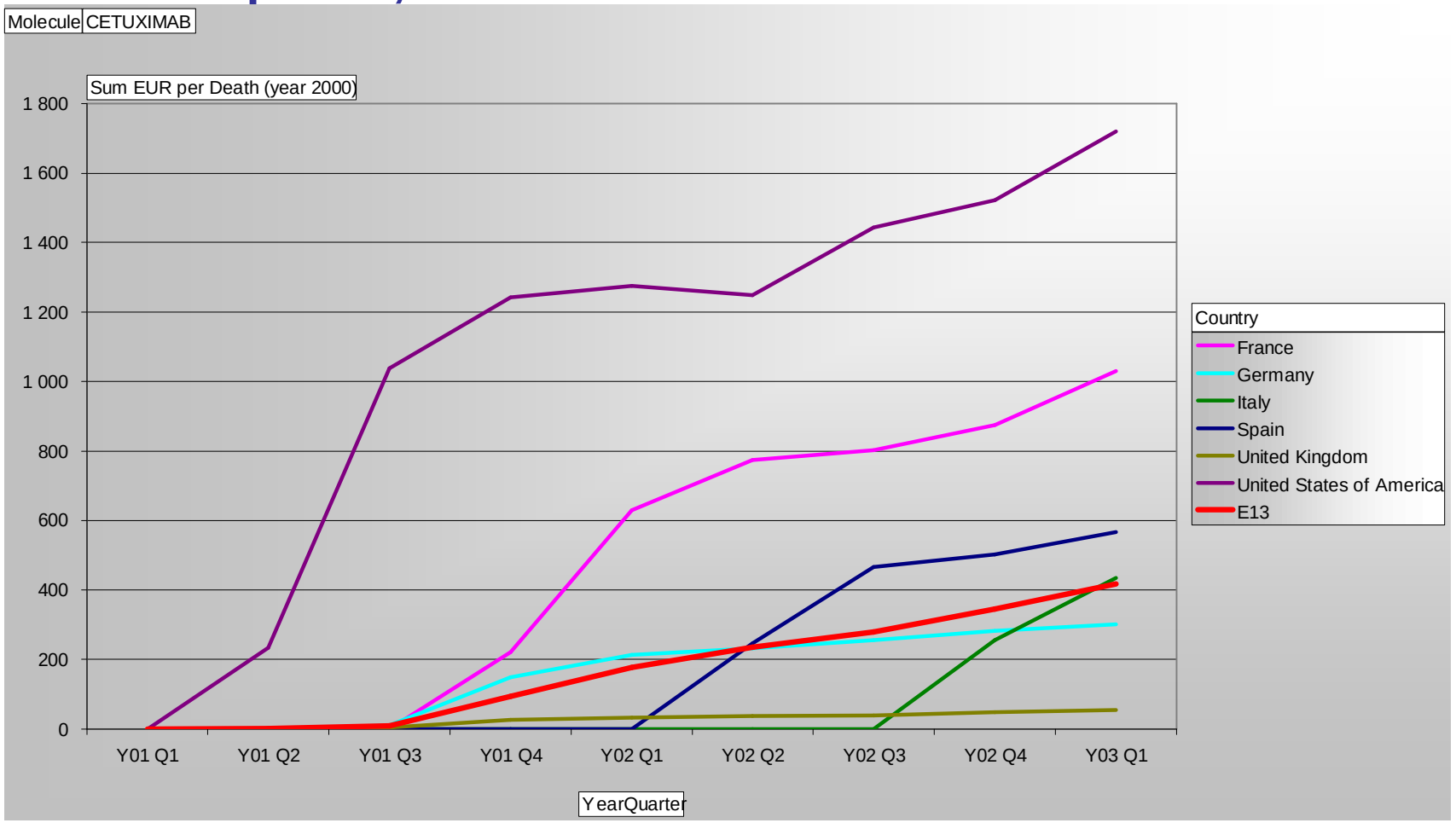
Source: Jönsson B, Wilking N. 2007.

Trastuzumab Uptake in E13 (average European uptake), France, Germany, Italy, Spain, UK and USA Per Patient



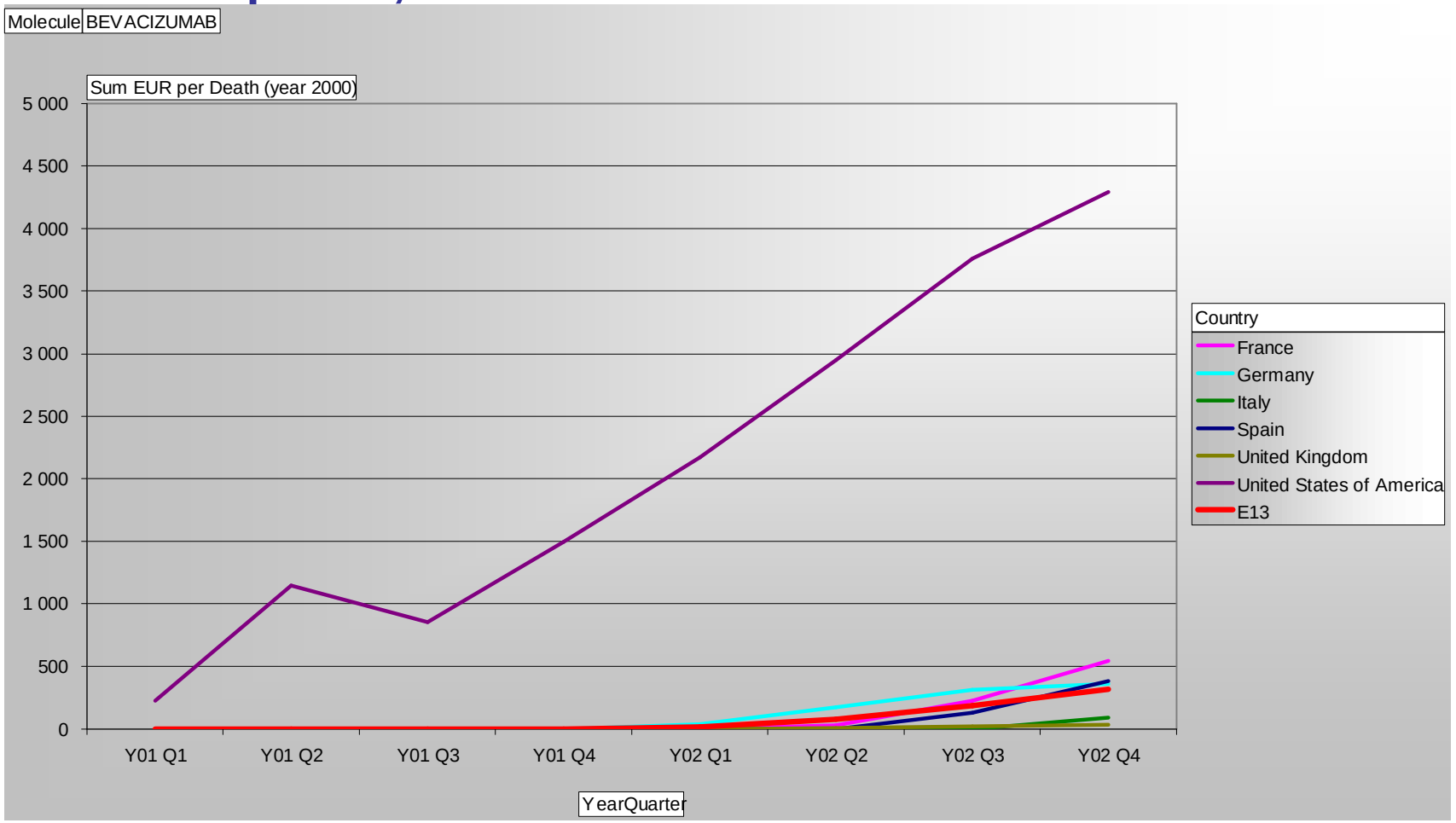
Source: Jönsson B, Wilking N. 2007.

Cetuximab Uptake in E13 (average European uptake), France, Germany, Italy, Spain, UK and USA Per Patient



Source: Jönsson B, Wilking N. 2007.

Bevacizumab Uptake in E13 (average European uptake), France, Germany, Italy, Spain, UK and USA Per Patient



Source: Jönsson B, Wilking N. 2007.

National Institute for Health and Clinical Excellence (NICE)

- Created in 1999.
- A Special Authority within the National Health Service (NHS).
- Programmes of work in:
  - health technology appraisal;
  - new investigational procedures;
  - clinical guidelines;
  - public health interventions.

Types of Technology Appraisal

- *Multiple Technology Appraisal (MTA)*
  - Several technologies appraised;
  - Full systematic review and economic model;
  - Takes 54 weeks.
- *Single Technology Appraisal (STA)*
  - Only one technology appraised;
  - Appraisal of company submission;
  - Takes 39 weeks.

NICE's Single Technology Appraisals

- A new 'fast track' procedure introduced in response to concerns over the time taken by NICE's standard approach.
- So far applies to drugs; in the main, cancer drugs.
- Places more emphasis on analyses submitted by the manufacturer and incorporates less external review.

NICE's Guidance on New Cancer Drugs: May 2000-March 2008: Methods

- Data sources
  - NICE published appraisals on cancer drugs;
  - EMEA/ MHRA licences / SPCs.
- Data extraction
  - Drug, indication, recommendations;
  - Stated justifications:
    uncertainty; methodological issues; trial evidence; ICER.
- For each drug evaluation
  - compare recommendation with licence;
  - classify recommendation as:
    - licence; restricted; no routine use; not licensed.
- Restricted / no routine use
  - 24/55 drug evaluations;
  - reasons for restrictions explored.

Mason A and Drummond M. *Eur.J.Cancer* (in press).

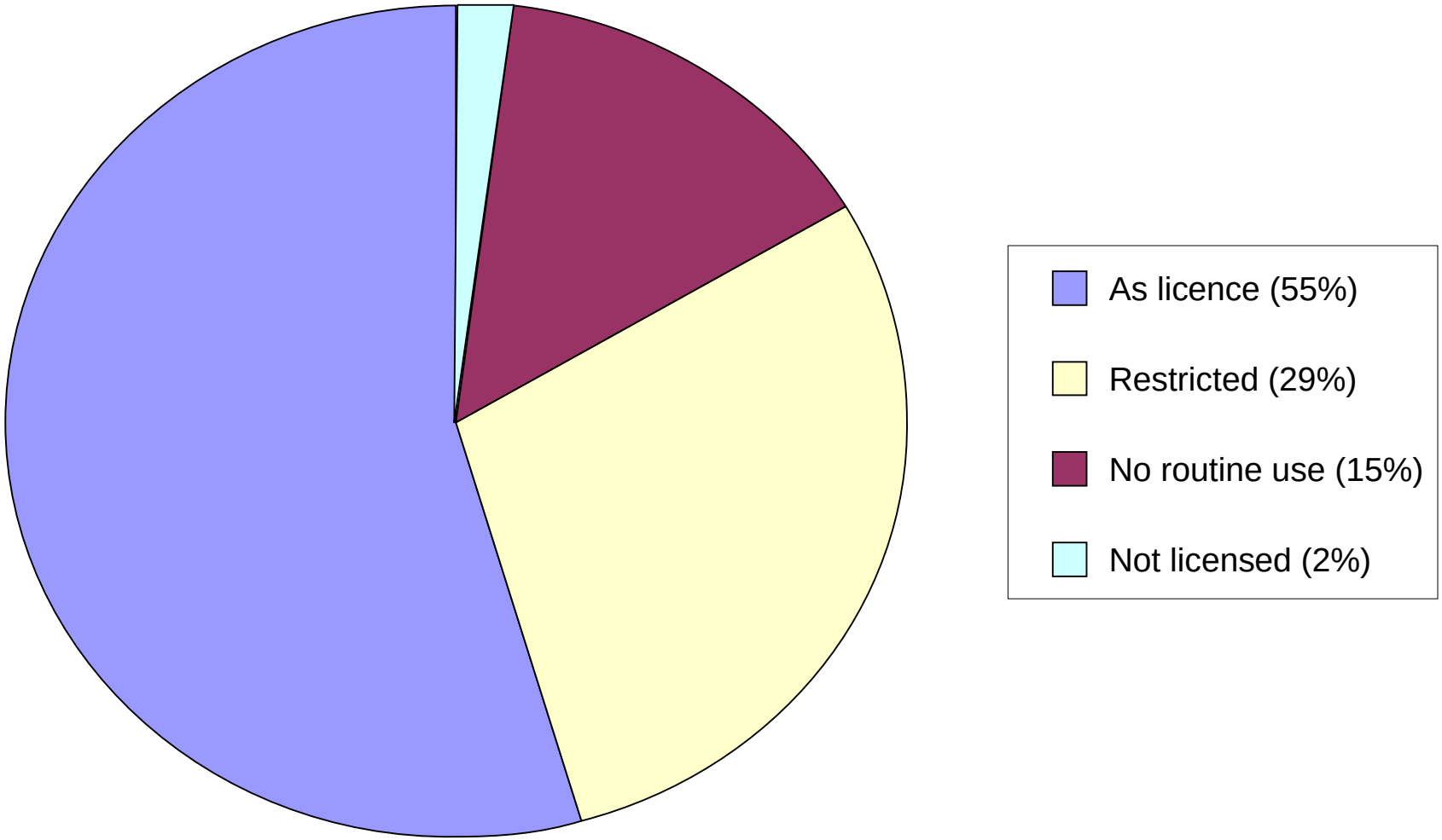
NICE Appraisal Committee Stated Criteria

- Recommendations for use made by Appraisal Committee:

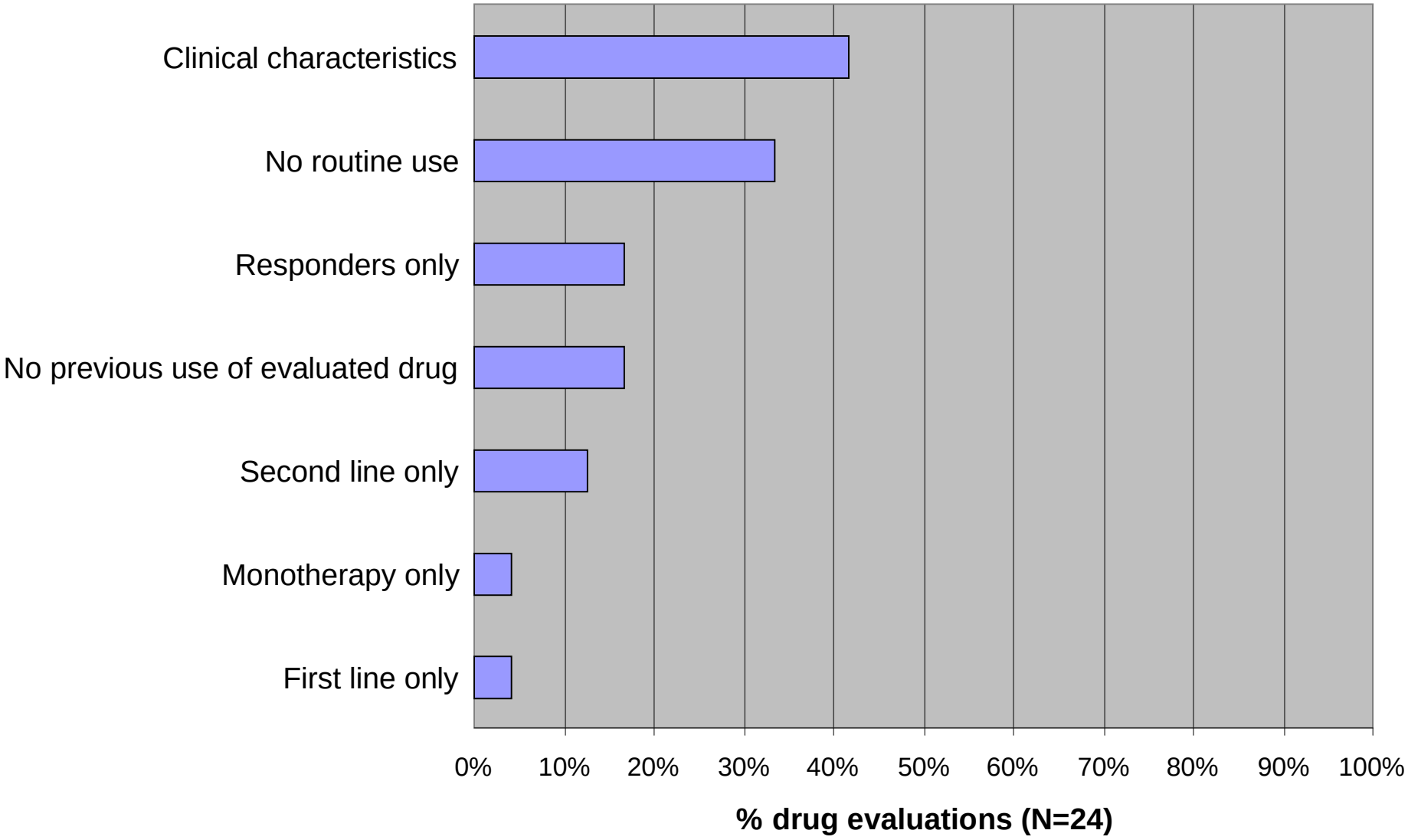
"The Committee reviewed the data available on the clinical and cost effectiveness of (drug x) for the treatment of (condition y), having considered evidence on the nature of the condition and the value placed on the benefits of (drug x) by patient representatives and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources."

- NICE stated threshold: cost/QALY: £20,000 to £30,000
  - Orlistat for obesity (March 2001).
- Actual threshold may be "somewhat higher".
  - Devlin N and Parkin D. (2004); *Health Economics* 13: 437-52.

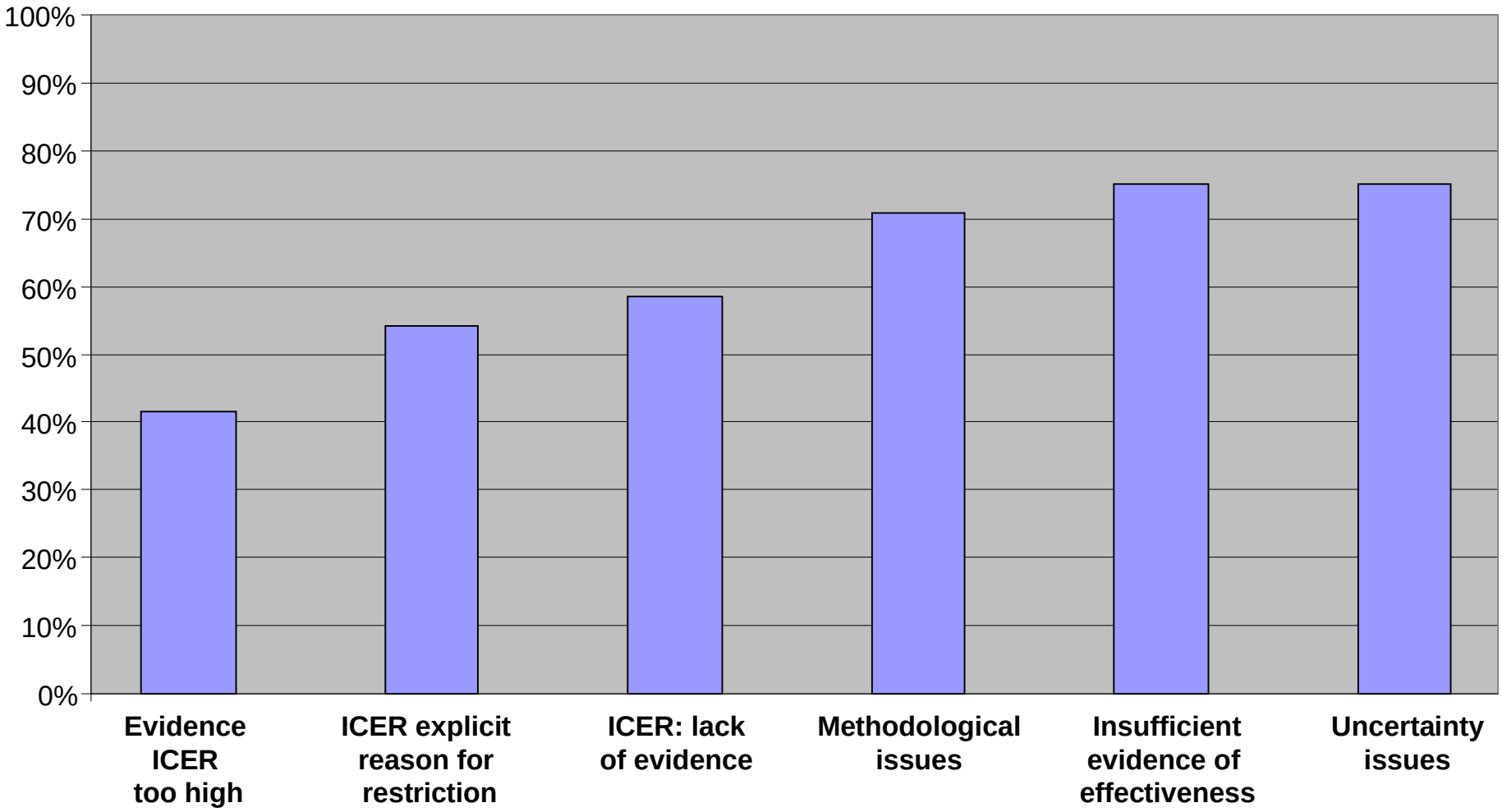
NICE Cancer Recommendations
% cancer drug evaluations (N=55)



NICE Cancer Recommendations
Types of restriction



Reasons for NICE Restrictions
% drug evaluations (N=24)



NICE's "Waiting List" (March, 2008)

DRUG	TUMOUR TYPE	UK LICENCE DATE
bevacizumab	Breast cancer (advanced & metastatic)	12/01/2005
bevacizumab	Lung cancer (non-small cell)	21/08/2007
bevacizumab	Renal cell carcinoma	14/12/2007
capecitabine	Pancreatic cancer	?
cetuximab	Colorectal cancer	29/06/2004
cetuximab	Head and neck cancer	29/03/2006
cetuximab	Lung cancer (non-small cell)	?
dasatinib	Acute lymphoblastic leukaemia	20/11/2006
dasatinib	Chronic myeloid leukaemia	20/11/2006
erlotinib	Lung cancer (non-small cell)	19/09/2005
gefitinib	Lung cancer (non-small cell)	?
irinotecan	Colon cancer (adjuvant)	?
lapatinib	Breast cancer (advanced or metastatic)	positive opinion: 13/12/2007
lenalidomide	Multiple myeloma - lenalidomide	14/06/2007
liposomal muramyl tripeptide phosphatidyl ethanolamine	Osteosarcoma (newly diagnosed, non-metastatic, resectable)	?
nilotinib	Acute lymphoblastic leukaemia	19/11/2007
nilotinib	Chronic myeloid leukaemia	19/11/2007
sorafenib	Renal cell carcinoma	19/07/2006
sunitinib	Renal cell carcinoma	19/07/2006
temozolomide	Advanced and metastatic melanoma	?
temsirolimus	Renal cell carcinoma	19/11/2007
topotecan	Relapsed small cell lung cancer	13/01/2006

Most Recent Controversy

- In August 2008, NICE published its Appraisal Consultative Document on four new drugs for treating advanced renal carcinoma: *bevacizumab, sorafenib, sunitinib, temsirolimus*.

- It recommended that none of the four drugs should be used in the NHS on the grounds that they were not cost-effective.

- Oncologists and patient organizations were outraged, since these drugs are widely used in many other countries and offer benefit to patients for whom no other effective treatments are available.

Independent Evaluation of Drugs for Advanced Renal Carcinoma

(First-line Treatments for Patients Suitable for Immunotherapy)

Drug	***Comparison***	***Cost***	***QALYs***	***Cost/QALY***
Sunitinib	*versus* IFN-alpha	£31,185	0.44	£71,462
Bevacizumab	*added to* IFN-alpha	£45,435	0.27	£171,301
Temsirolimus	*versus* IFN-alpha*	£22,272	0.24	£94,385

(* patients with poor prognosis)

Source: NICE, 2008

Is NICE Getting Nastier?

- NICE's decisions on cancer drugs from May 2000 to end May 2006 were compared with those from June 2006 to May 2008.
- The period from June 2006 contained all the STAs.
- NICE rejected a higher proportion of drugs in the second period (4/37 versus 5/18).
- It appears that the higher rejection rate in the second period is because the drugs reviewed were less cost-effective.
- There is no evidence that NICE has changed its criteria.
- The shift towards STAs may be one explanation of the difference in the rejection rate.

Mason A and Drummond M. *Eur.J.Cancer* (in press).

Current Issues and Debates

- Is NICE's threshold at the right level?
- Should oncology products be considered 'special'?
- What new policies could be considered?

Is NICE's Threshold Set at the Right Level?

- NICE admits that the current threshold range (ie £20-30,000 per QALY) is not based on research.
- Some research on current healthcare expenditure suggests that, if anything, the threshold may be too high.
- New research is attempting to ascertain what the UK population think a QALY is worth.

Supplementary Guidance for ‘End of Life’ Therapies

- **If the therapy**:

  -is for a small patient population with life expectancy of less than 24 months;

  -where no equivalent therapy exists;

  -where the therapy adds three months or more to life expectancy.

- **Then**:

  -the QALYs gained should assume full quality of life in the added months;

  -in addition the Committee can consider that the QALYs gained should be weighted sufficiently high for the therapy to be approved given NICE’s current threshold.

Would Risk-Sharing Offer a Solution?

- Useful in situations where there is uncertainty about the value of a product

  eg. where final outcome data are not available (PFS, not OS)

  where it is unclear which patients will benefit

- In these situations, limiting the payer's risk may make them more willing to reimburse the product

- One approach is to establish performance-related contracts

Recent Example of Risk-Sharing from the United Kingdom

Velcade (bortezomib) for Multiple Myeloma

- In the course of a NICE technology appraisal, an ‘outcome guarantee’ scheme was suggested by the manufacturer.
- The NHS will ensure that ‘all suitable patients’ will have access to the drug.
- In return, the manufacturer will refund treatment costs for patients who fail to respond.
- The details of the scheme, including the definition of ‘clinical response’ have now been agreed.

Would Value-Based Pricing Offer a Potential Solution?

- Value-based pricing was suggested by the UK's Office of Fair Trading in its report on the Pharmaceutical Price Regulation Scheme
- The idea is that the price of a drug is set in relation to the value it adds *in each indication*
- In theory it means the price of a drug could rise if a high-value indication were added

Hypothetical Example of How Value-based Pricing Might be Applied*

- According to NICE, sunitinib in first line treatment for advanced and/or metastatic renal cell carcinoma has an ICER of £71,462 per QALY
- At the current price proposed by the manufacturer (£3,363 per 30 capsules of 50mg per pack), the treatment cost is £31,185 more than IFN, of which the drug cost is £31,060
- Therapy with sunitinib results in a gain of 0.44 QALYs
- In order for the ICER to be below the top of the 'acceptable' range of cost per QALY, the price of sunitinib would need to be below £1410 per 30 capsules

* For the benefit of Pfizer's lawyers, this example is 'without prejudice'

Relevance of Value-Based Pricing in Oncology

- New drugs are often launched first for patients with end-stage disease, where it is difficult to show a large survival gain
- However, companies set prices high because it is usually impossible to raise them at a later stage, when survival gains may be greater
- With the high price, the drug will typically not give high value for money and may not be reimbursed

Conclusions

- Variations across Europe in access to cancer drugs and the rigor of any appraisal.
- NICE in the United Kingdom is the most widely-discussed HTA agency.
- NICE's evaluations do lead to restrictions on the use of drugs, based on value for money criteria.
- The key issues are those of what we consider to be 'good value for money' and whether cancer should be treated differently from other diseases.