

Tackling chronic diseases in the UK

Comparative cost-effectiveness of therapies

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*Chronic Disease & Health Management
Bucharest, 6-7 October 2011*

A few words about NICE

- The independent organisation responsible for providing national guidance (in England & Wales) for the NHS* on the promotion of good health and the prevention and treatment of ill health
- NICE makes recommendations on:
 - new and existing medicines, treatments and procedures (TAs, IPs)
 - treating and caring for people with specific diseases and conditions (clinical guidelines , social care & quality standards)
 - how to improve people's health and prevent illness and disease*

* advice applies to local authorities, local authorities and other organisations in the public, private, voluntary and community sectors)

Core principles of all NICE guidance

- Based on the best evidence available (**clinical and economic**)
- Expert input
- Patient and carer involvement
- Independent advisory committees
- Genuine consultation
- Regular review
- Open and transparent process
- Social values and equity considerations

Criteria for decision-making – cost-effectiveness

1. How well does the technology work compared to standard practice in the NHS
2. How much does the technology cost compared to standard practice in the NHS
 - cost of technology, monitoring, length of inpatient or outpatient stay, costs of treating adverse events
3. Health gain is measured using quality adjusted life years (QALYs):

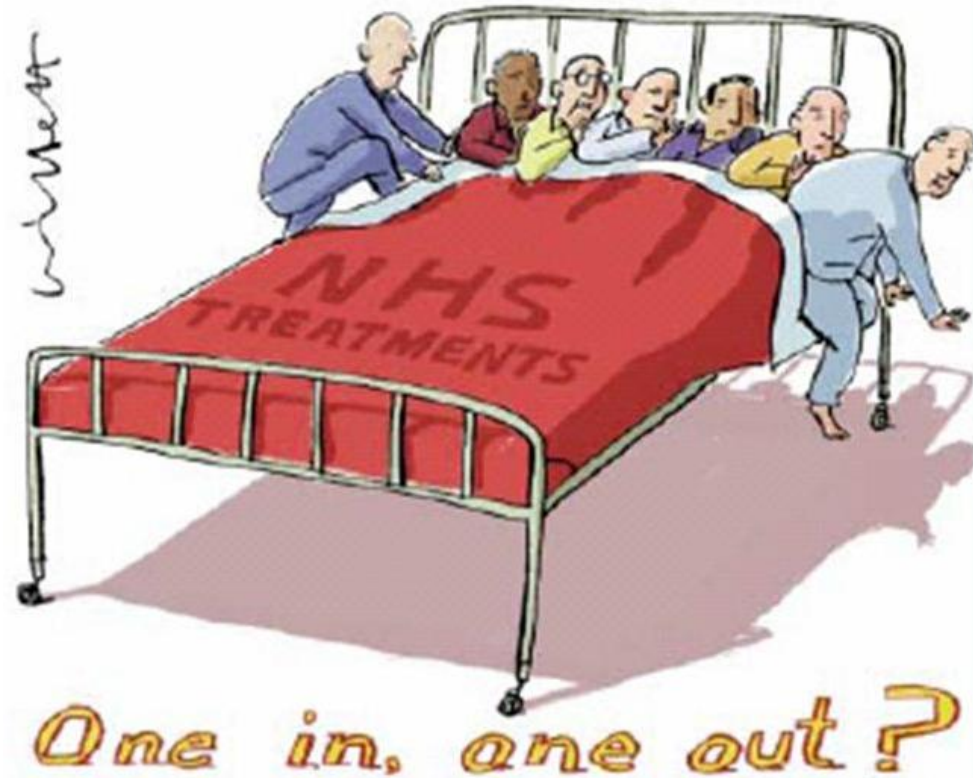
Difference in costs

Difference in effect

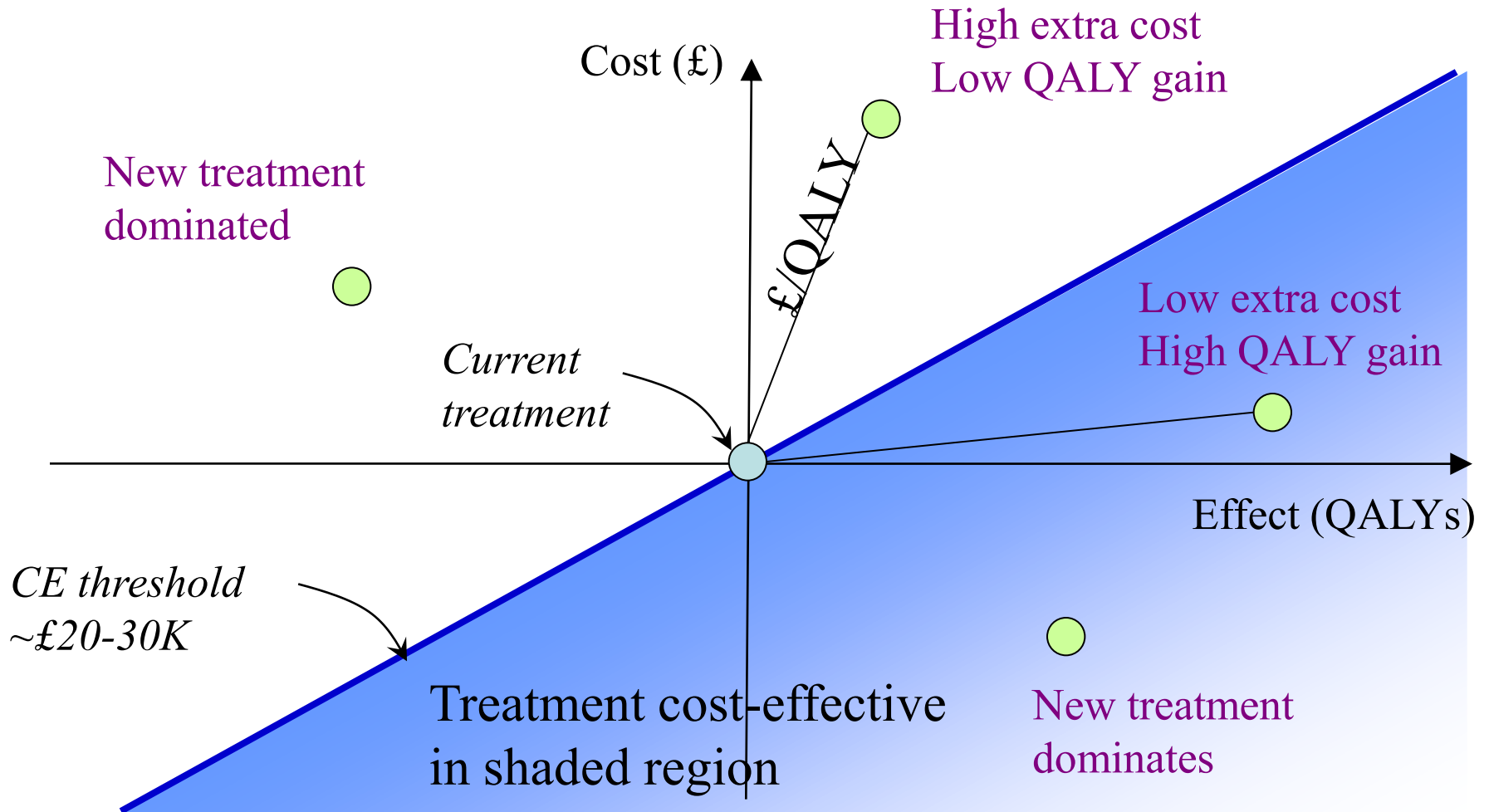
Cost Utility Analysis

Opportunity costs

- The NHS budget is limited
- It is about choice
- If the NHS spends more on one thing, it has to do less of something else
- Could we do more good by spending the extra money in other ways?



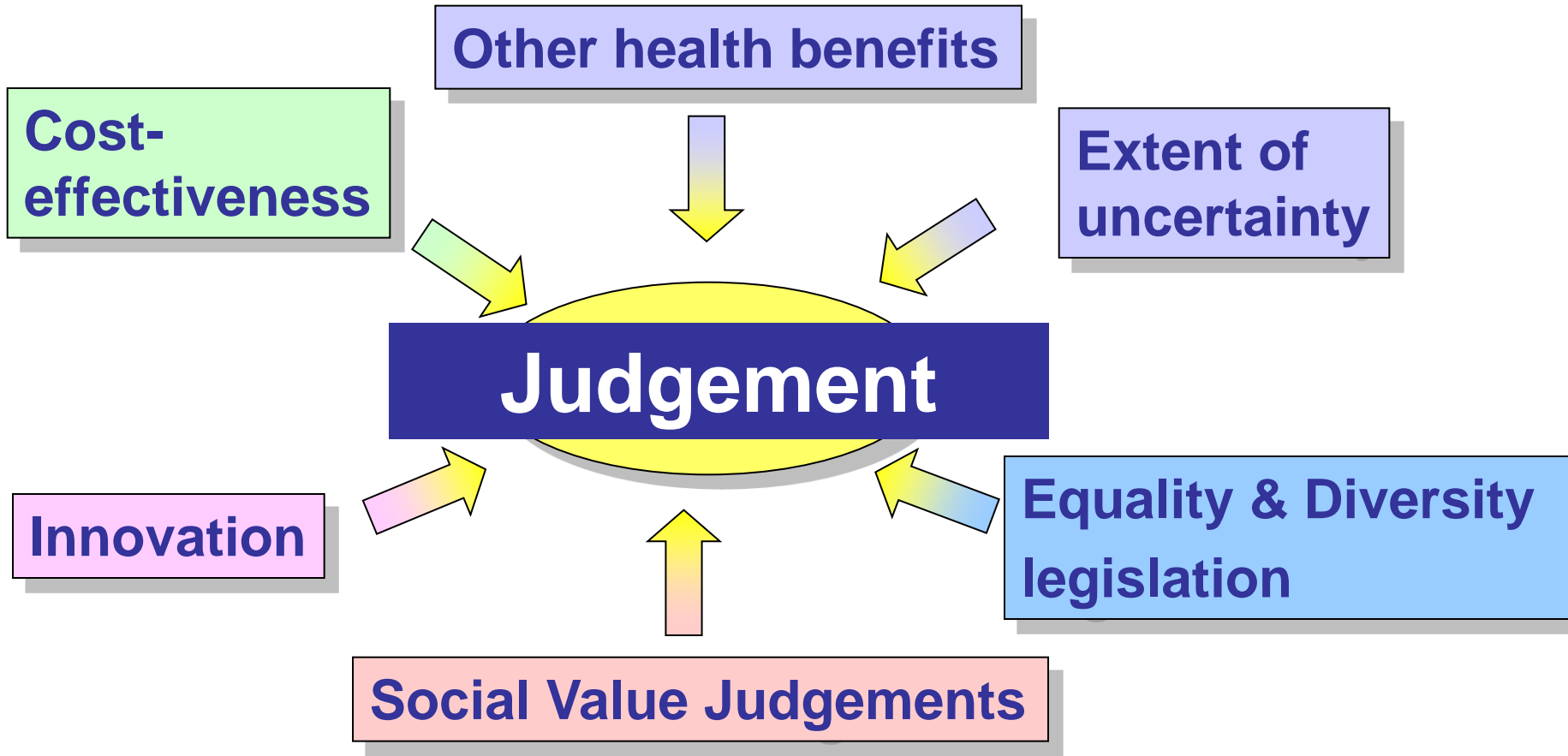
Assessing cost-effectiveness



The NICE reference case

Perspective on costs	National Health Service
Perspective on outcomes	All health effects on individuals
Measure of health effects	QALYs
Source of data for measurement of health related quality of life	Reported directly by patients and/or carers
Source of data for measurement of health related quality of life	Representative sample of the public
Discount rate	3.5% per year for costs and health effects
Equity weighting	An additional QALY has same weight for all patients

Why NICE doesn't have a fixed cost effectiveness threshold?



The case of Diabetes



Diabetes in the UK

Epidemiology

- 5% prevalence in England and 4.6 % in the UK*
- Over 2.6 millions people affected, of whom 85% of type 2 diabetes and numbers increasing (>4 Millions cases predicted in the UK in 2025)
- 4.2% mortality (♂) & 7.7% (♀); 10 – year reduction in life expectancy
- Many cases are undiagnosed (>500,000)
- Type-2 diabetes affect people > 40 years, but younger in south Asian and afro-carribean populations.

* Quality and Outcomes Framework (QOF) 2009

Diabetes: a heavy burden

Three major costs:

- Direct costs to the NHS & services for treating diabetes
 - Estimated to represent at least 5% of health expenditure in the UK, almost 10% of hospitals budgets
- Indirect economic costs, including impact on mortality and productivity loss
- Impact of diabetes complications on patients and their family

Treatment

- Diet and physical activity are first line treatments for Type 2 Diabetes
- But most people subsequently need sequential addition of oral glucose-lowering drugs:
 - Metformin widely used as first-line oral therapy
 - sulfonylureas added as second-line therapy if glycaemic control remains poor or deteriorate
 - Other oral drugs for lowering blood glucose include alpha-glucosidase inhibitors, thiazolidinediones and meglitinides.
- most people with type 2 diabetes eventually need insulin (long- or short-acting formulations, or a pre-mixed (biphasic) combination of short- and long-acting insulins)

NICE diabetes guidance (published)

Date	Type	Recommendations
2002	TA**	Long acting insulin analogues- Types 1 & 2 l'insuline glargine (TA53)
2003	TA	glitazones inType 2 diabetes (TA 63)
2003	TA	Patient education models (Type 1 &2) (TA60)
2008	TA	Insulin pump therapy(TA 151)
2010	TA	Liraglutide for Type 2 diabetes (TA203)
2002	RPC*	Type 2 diabetes blood glucose (G), blood pressure & blood lipids (H), kidney disease (F),retinopathy (E)
2004	RPC*	Type 1 diabetes _ diagnostic & management (CG 15)
2004	RPC*	Type 2 _ diabetes _Foot care (H)
2008	RPC*	Type 2 diabetes (CG 66) _ update of :G, F & E; TAs 53,60,63
2008	RPC*	Diabetes in pregnancy (CG 63)
2009	RPC*	Type 2 diabetes (CG 87)_partial update

Six more pieces of guidance in development

*Clinical guidelines ; ** Technology Appraisals; *** prevention

The NICE Type 2 diabetes Guideline (CG 87)_partial update

- A multidisciplinary Guideline Development Group
- Rescoping of the guideline CG66
- A systematic review of clinical literature and 'de novo' cost-effectiveness modelling by Aberdeen University
- Estimated through the use of a patient simulation model, the UKPDS* Outcomes Model
- A consultation with all relevant stakeholders

*UKPDS: United Kingdom Prospective Diabetes Study

The image shows the cover of a NICE short clinical guideline. The top right corner features the NHS logo and the text 'National Institute for Health and Clinical Excellence'. Below this, the issue date is listed as 'May 2009'. The main title is 'Type 2 diabetes: newer agents' in a large, bold font, followed by the subtitle 'Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes'. A paragraph of text explains that this guideline partially updates NICE clinical guideline 66 and combines recommendations with CG66. A smaller section dated 'September 2010' mentions the EMA's decision to suspend the marketing authorization for rosiglitazone. At the bottom, it identifies the guideline as 'NICE short clinical guideline 87' and notes it was developed by the Centre for Clinical Practice at NICE.

NHS
National Institute for
Health and Clinical Excellence

Issue date: May 2009

Type 2 diabetes: newer agents

Type 2 diabetes: newer agents for blood glucose control in type 2 diabetes

This short clinical guideline partially updates NICE clinical guideline 66. The recommendations have been combined with unchanged recommendations from CG66 in NICE clinical guideline 87

September 2010
In September 2010 the European Medicines Agency (EMA), the European Union (EU) body responsible for monitoring the safety of medicines, recommended the suspension of the marketing authorisation for rosiglitazone (Avandia, Avandia and Avaglim) from GlaxoSmithKline. The EMA has concluded that the benefits of rosiglitazone no longer outweigh its risks and the marketing authorisation should be suspended across the EU.
The EMA has advised that patients who are currently taking rosiglitazone-containing medicines should make an appointment with their doctor at a convenient time to discuss suitable alternative treatments. Patients are advised not to stop their treatment without speaking to their doctor. NICE does not recommend the use of drugs without marketing authorisation. Therefore, as a result of the EMA's decision, NICE has temporarily withdrawn its recommendations on the use of rosiglitazone in this guideline.

NICE short clinical guideline 87
Developed by the Centre for Clinical Practice at NICE

Interventions assessed

- Incretin enhancers (DPP-4 inhibitors): sitagliptin and vildagliptin
 - Incretin mimetics (GLP-1 analogues): exenatide
 - Thiazolidinediones: pioglitazone and rosiglitazone
 - Long-acting recombinant human insulin analogues: insulin detemir and insulin glargine
- There is an urgent need for guidance that determines the role of all of these agents and their place in the care pathway of blood glucose control for people with type 2 diabetes
 - The use of thiazolidinediones (rosiglitazone and pioglitazone) need detailed examination
 - safety concerns specifically in relation to rosiglitazone to be addressed regarding the risk of cardiovascular adverse events

The UKPDS Outcomes model

- computerised simulation to estimate life expectancy, quality adjusted life expectancy & costs of complications in people with T2D.
- uses equations and algorithms published in the UK Prospective Diabetes Study (UKPDS) - 3,642 patients followed up for between six and twenty years
- predicts likely outcomes using risk factors: age, sex, ethnicity, duration of diabetes, height, weight, smoking status, total cholesterol, HDL cholesterol, systolic blood pressure and HbA1c
- takes into account that patients are at risk of complications

Long-acting insulin analogues

- Insulin glargine versus NPH insulin

Male BMI 30	No complications			With complications		
	Glargine	NPH	Net	Glargine	NPH	Net
UKPDS QALYs	8.538	8.540	-0.002	8.331	8.333	-0.003
Total QALYs	8.464	8.457	0.007	8.258	8.253	0.006
Direct Drug Cost	£7,939	£6,111	£1,828	£7,727	£5,946	£1,780
Total Cost	£18,258	£16,402	£1,855	£18,778	£16,980	£1,798
ICER			£281,349			£320,029

Long-acting insulin analogues

- Insulin detemir versus insulin NPH

Male BMI 30	No complications			With complications		
	Detemir	NPH	Net	Detemir	NPH	Net
UKPDS QALYs	8.530	8.540	-0.010	8.316	8.333	-0.018
Total QALYs	8.472	8.457	0.015	8.259	8.253	0.006
Direct Drug Cost	£8,826	£6,111	£2,715	£8,585	£5,946	£2,638
Total Cost	£19,128	£16,402	£2,726	£19,621	£16,980	£2,641
ICER			£187,726			£417,625

Appropriate comparisons - the case of exenatide...

- The de novo analysis suggested that relative to *insulin glargine*, exenatide was potentially a highly cost-effective option at a starting BMI of 30 kg/m²

However...

- results could be sensitive to assumptions on patient weight
- results of the pair-wise comparison between insulin glargine and NPH insulin indicate that insulin glargine was highly cost ineffective compared with NPH insulin
- No cost effectiveness data on the comparison between NPH insulin and exenatide...

Long-acting insulin analogues – going beyond “cost per QALY”... (1)

- GDG not persuaded that exenatide should routinely be used at a starting BMI of less than 35 kg/m²...but could be “situations in which the benefits obtained would result in exenatide being a cost-effective choice.”
- a person should have a starting BMI of 35 kg/m² before being considered for treatment with exenatide.
- If <35.0 kg/m², exenatide therapy should be considered only for those in whom therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.
- exenatide therapy should be continued only if the person has had a beneficial metabolic response (a reduction of at least 1.0 percentage point in HbA1c and a weight loss of at least 3% of initial body weight at 6 months).

Long-acting insulin analogues – going beyond “cost per QALY”... (2)

- The long-acting insulin analogues (glargine and detemir) did not appear to be cost-effective options when compared with NPH insulin in the analysis undertaken by the Assessment Group.
- The advisory body “accepted that episodes of hypoglycaemia have the potential to be highly detrimental to a person's health-related quality of life”.
- Assessment group ‘attempted’ to include quality of life issues related to hypoglycaemia
- Advisory body → when starting basal insulin therapy NPH insulin should be preferred on the basis of its cost effectiveness and well-known safety profile.

Long-acting insulin analogues – going beyond “cost per QALY”... (3)

- it would be “more cost effective to target the use of the long-acting insulin analogues to people with type 2 diabetes most likely to benefit
 - people significantly restricted by symptomatic hypoglycaemic episodes.”
- “the healthcare resources spent on helping people who need assistance with their insulin injections would be reduced significantly
- the use of insulin analogues in this group is likely to be cost effective.”

Limitations of the UKPDS model...

- Predicts only the first event
- Not all relevant complications are included
- UKPDS may fail to capture the impact of weight changes on health-related quality of life, or infrequent diabetic complications
- Analysis attempted to
 - take into account potential direct quality of life gains associated with weight changes and the reduced fear of hypoglycaemic episodes.
 - to explore the impact of changing the baseline rate of complications

Further challenges with the analysis...

- The current available direct evidence did not include all the comparisons of interest.
 - Quite important in the case of exenatide
- One solution is to undertake an indirect / mixed treatment analysis
 - Initially attempted but there was concern that the degree of heterogeneity across the relevant studies would make such analysis difficult to undertake and interpret
 - There was concern over the validity of such an analysis
- Focus on available direct head-to-head pairwise comparisons

Summary

- It was helpful to make use of an ‘off the shelf’ model structured around a dataset from a UK relevant population
- But model had limitations...
- ...and extra work was needed to (partially) overcome these limitations
- Decision making a deliberative process
- Time could have been saved by relying on published economic evidence – so would have that been reasonable?
 - Probably not → technical reasons / stakeholder expectations

Suspension of rosiglitazone

- Sept 2010 the EMA recommended the suspension of the marketing authorisation for rosiglitazone from GlaxoSmithKline
- Benefits of rosiglitazone no longer outweigh its risks (MI and stroke)
- NICE does not recommend the use of drugs without marketing authorisation
- NICE has temporarily withdrawn its recommendations on the use of rosiglitazone in this guideline

Not everybody is happy with our decisions



Alzheimer's Society, London 2006

In conclusion

NICE is committed to using economic analysis in its decision making...But this is not the only criteria

- Should the QALY threshold be raised?
 - Yes - NICE should base its decisions on the public's willingness to pay.
 - No - The threshold should be based on opportunity costs in terms of displaced interventions
- NICE should develop a disinvestment programme based on identifying treatments with poor cost effectiveness
- Ongoing work: the 'threshold-searcher'

The New York Times

“As spending on drugs soared in many nations — often haphazardly — overall health often showed little improvement. So international aid agencies are advising governments to adopt British assessments and deliberations to improve their public’s health while lowering costs, and officials are listening — a trend that is likely to accelerate during the present global economic slowdown.”

December 2008

...Political support is key

“We conclude that NICE does a vital job in difficult circumstances. The development of more and more health technologies and procedures, alongside rising patient expectations and the ageing population, is going to make it even more difficult in the future. Healthcare budgets in England, as in other countries, are limited. Patients cannot expect to receive every possible treatment. NICE requires the backing of the Government. NICE must not be left to fight a lone battle to support cost- and clinical effectiveness in the NHS.”

Jan 2008 – UK Parliament – Health Select Committee

www.nice.org.uk