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Market Access considerations in asset valuations

Future and current business

28/10/15

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Topics

- Brief introduction
- Health economics rationale
  - Current landscape
  - HE introduction
  - Meta-analysis
  - Value-of-information
  - Real World Data
  - Pricing
- Issues affecting reimbursement
- Checklist

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Introduction

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Mapi

- Founded 41 Years Ago
- Pioneered many of the practices that are now standard in the industry:
  - Patient centered research-PROs and Linguistic Validation
  - Acquired Registrat in 2010—pioneered registries
  - Acquired several of Optum's businesses in Dec 2014 (RWE, HEOR, SRS)
  - Established Mapi Research Trust—non profit information clearing house for researchers

Mapi's Patient-Centered Global Research Services

Real World Strategy & Analytics

- Identification of evidence required for all key stakeholders
- Market access challenges for specialty products and rare diseases
- Stakeholder Insights
- Evidence that supports value story and market access strategy
- Communication & evidence generation
- Real-world data (retrospective, prospective) & analytics
- Literature review / meta-analyses

Real World Evidence

- IV & Observational Studies
- Registries
- Outcomes
- REMS/EU-RMPs
- Safety Surveillance/PASS
- Expanded Access
- Direct To Patients (ProClinica)
- Patient Recruitment
- Patient Retention and Engagement
- Patient Insights
- Retrospective Chart Research

Language Services

- Cultural & Linguistic Validation
- Translatability Assessment
- Research Materials Localization
- eCOA screen shot reviews

Strategic Regulatory Services

- Leads clients through the drug registration process
- Advises clients subsequent to approval to maintain drug compliance
- Provides native knowledge through the regulatory process
- Provides post-approval pharmacovigilance and clinical auditing

Mapi Research Trust

- PRO & PRM Newsletters
- PROQOLID and PROLabels
- COA Questionnaire Licensing
- COA Questionnaire Distribution
- Data Extractions on COA research and endpoints
- Instrument Author Collaboration

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Situational analysis

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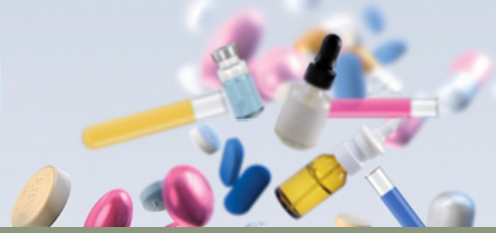
Current situation in the pharma market

- Products developed without regard to their commercialisation
- 2009 to 2012, ~ $75b will evaporate as products go generic
- Clinical development programmes insufficiently productive
- Development programmes are becoming increasingly expensive (~ $1.2bn)
- Many new products targeted to narrow patient populations
- New products sourced from smaller companies, licensed in at various stages of development
- Premium-price is still expected
- Effective patent life time is decreasing



Reality for individuals in licencing

- More complex deals as owners increasingly want to retain some level of control or license out to several partners
- Increasing risk as products get licensed in earlier affecting:
  - Deal valuation
  - Cost of additional trials
  - Likelihood of reimbursement
  - Investments (total value)
- Increasing regulatory demands
- More stringent payer requirements
- Pricing pressures due to complex reimbursement and payer environment

Complex payer landscape in Europe

Drug expenditure outpaces GDP in high income countries with limited budgets

The need for prioritisation

- Rising healthcare costs due to ageing population
- Economic crisis – Cost containment
- Governments seeking **VALUE FOR MONEY**

Fundamental changes in policy

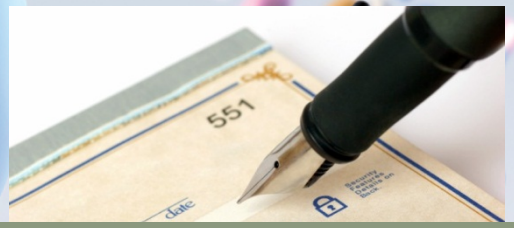
- Healthcare reform
- Changes in reimbursement / pricing policies

Entry of new generics

- Continued pressure to reduce prices

Dynamic market with novel entrants

- Often high-price treatments



Different Payer archetypes in EU

- **Market Access Clinical Assessment**- (e.g. TC, AIFA)
- **HTA groups/bodies** –(e.g. NICE, IQWIG, HAS)
- **Price & Reimbursement agencies** – (e.g. AIFA, Spain MOH, CEPS, Tenders)
- **Budget Holders** (Regional/sub-regional) – (e.g. Regional Health Authorities, Primary Care Trusts, Spain /Italy regions)
- **Reimbursement Funds -** (e.g. Sickfunds, Mutuelles, ZIN)

Payers ask questions in addition to those asked by regulators

Does the new therapy provide benefit over current standards of care?

For which population is the new therapy appropriate?

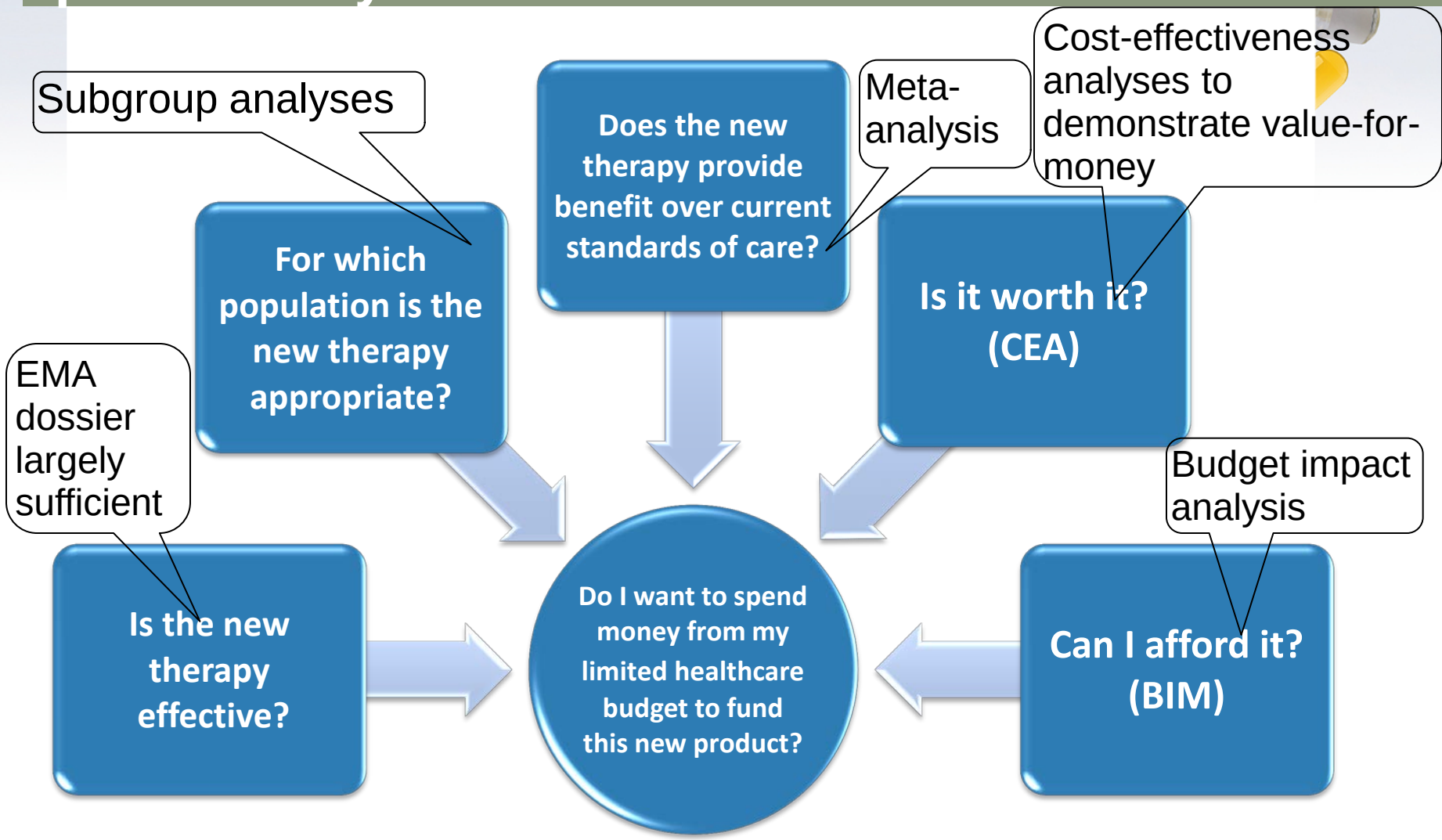
Is it worth it?

Is the new therapy effective?

Do I want to spend money from my limited healthcare budget to fund this new product?

Can I afford it?

Answers to these questions are (often) provided by Health Economic evidence



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Evidence development

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Cost-effectiveness analysis: value-for-money

- Cost-effectiveness analysis is a structured way of analysing *costs* and *effects* in an attempt to answer the question:

Does the drug provide value for money compared to the standard of care?

- Models developed in using *Excel* or other software
- Comparing new intervention to current standard of care
- Cornerstone of most reimbursement submissions
- Often expressed as cost per quality-adjusted life years gained or cost per life year gained

Budget impact modelling: affordability

- Often requested to complement cost-effectiveness analysis
- CE analysis measures ‘value-for-money’
- Budget impact analysis estimates the actual cost of implementing a new treatment within a specific population

An intervention may be considered cost-effective but it may still be unaffordable in specific circumstances or health care settings

- Takes into account both the **number of people eligible for treatment** and the **expected rate of uptake in that population (market share)**
- A new treatment with a relatively high ICER may have a relatively low budget impact due to a small population

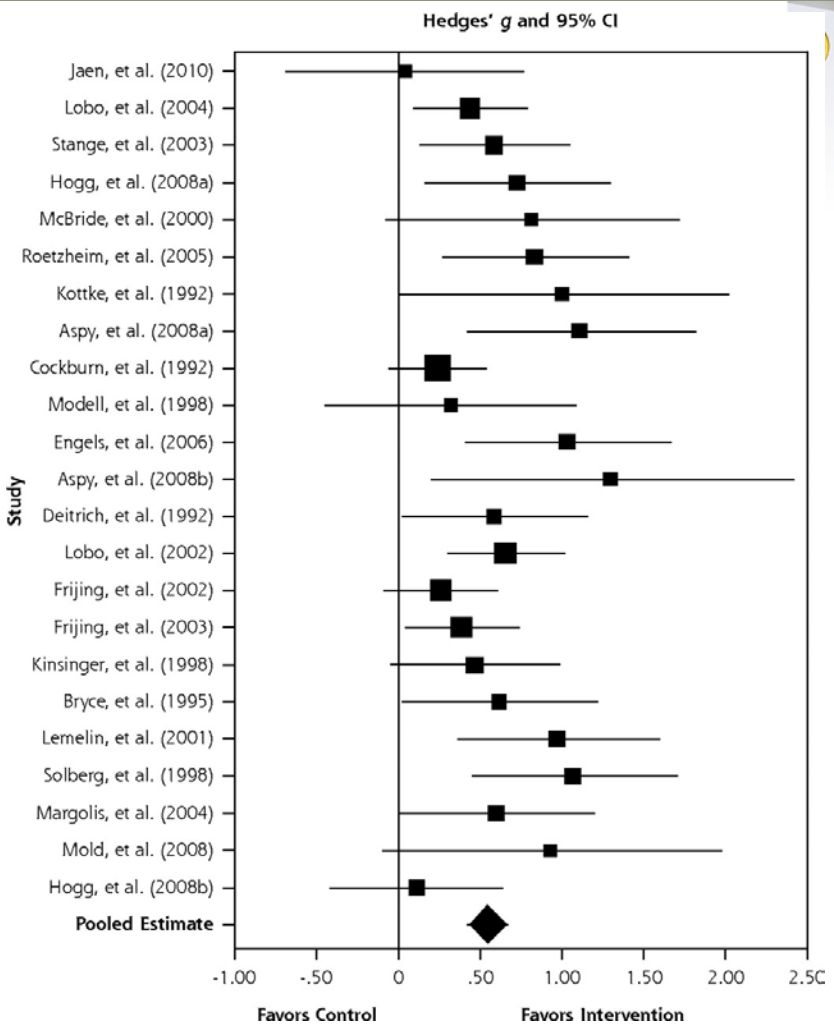
Significant differences between CEA and BIM Budget impact analysis vs. CE analysis

	CEA	BIM
Objective	Is it value for money?	Can the system afford it?
Framework	Comparisons of two strategies	“World with” vs. “World without”
Level of analysis	Individuals or groups of given characteristics	Covered population
Primary emphasis	Incremental cost and incremental effectiveness	Incremental costs and cost offsets
Market share over time	Usually ignored	Usually considered
Time horizon	Long enough for all relevant outcomes	Typically matched to budget cycle

Budget impact and cost-effectiveness analysis are data intensive and require local data from published sources

Meta-analysis to compare all evidence of efficacy and safety

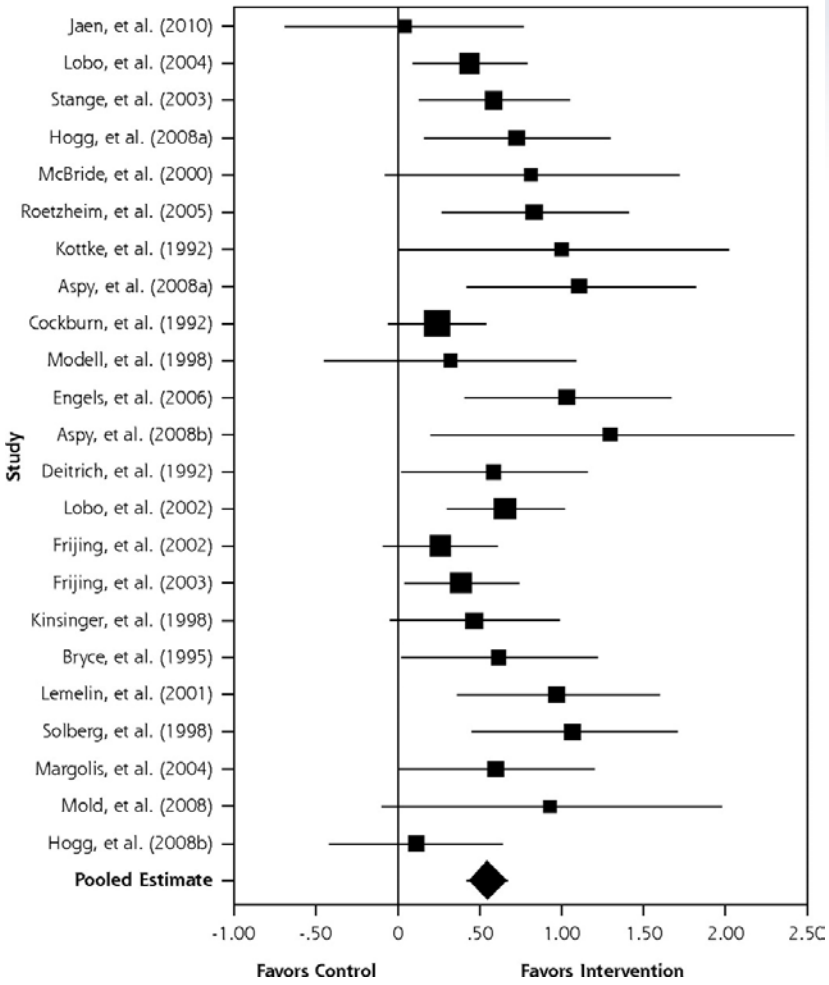
- Requested by most HTA agencies
- Ensure that clinical data for economic evidence include all available data and all relevant comparators
- Avoids “cherry picking” of evidence
- More robust estimates of efficacy and safety



Meta-analysis – direct comparison

Direct meta-analysis

- All evidence involves the same treatment
- Identification of evidence using a systematic literature review
- Pooling of evidence
  - Several methods but most used in inverted variance method and Bucher methods



Meta-analysis – indirect comparison

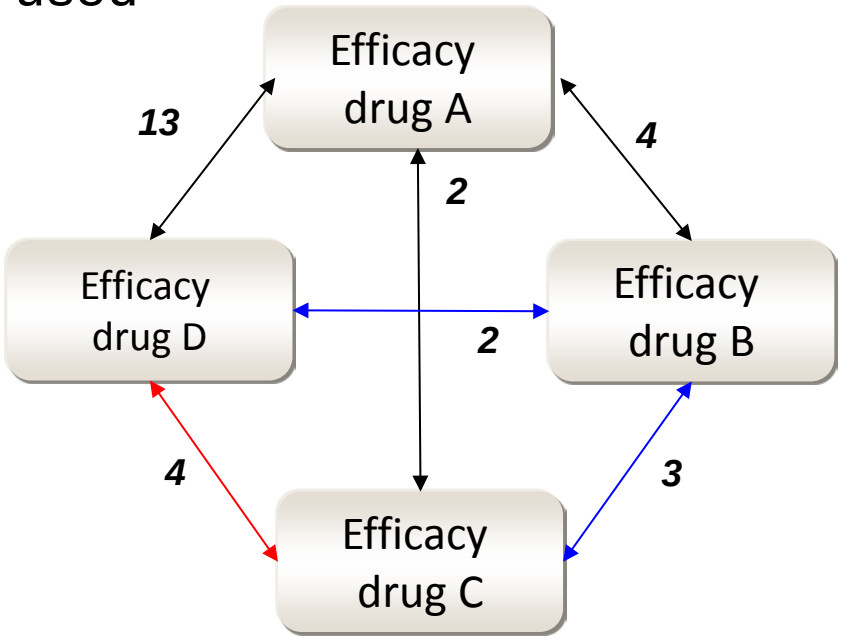
- Using one common comparator
- All evidence will come from a systematic literature review
- Valuable method if you have a few treatments (up to 3) that need to be synthesised and compared

Evidence	Direct comparison	Indirect comparison
Trial 1: Drug A vs. placebo Trial 2: Drug A vs. placebo Trial 3: Drug B vs. placebo Trial 4: Drug A vs. placebo Trial 5: Drug B vs. placebo Trial 6: Drub B vs. placebo Trial 7: Drug C vs. placebo Trial 8: Drug C vs. placebo ….	Pairwise analysis Drug A vs. placebo Drug B vs. placebo Drug C vs. placebo	Pairwise analysis Drug A vs. Drug B Drug A vs. Drug C Drug B vs. Drug C

Meta-analysis: network meta-analysis

- Network meta-analysis (NMA) s is a generalisation of standard pair-wise meta-analysis
- Used when comparing multiple treatment options (3 or more)
- Mixture of comparators
- Ideally a closed network is used

A		C	D	**1 trial**
	B	C	D	**1 trial**
A	B			**4 trials**
A		C		**1 trial**
A			D	**12 trials**
	B	C		**2 trials**
	B		D	**1 trial**
		C	D	**2 trials**



The cost and value of future research - VOI

- For licensed-in assets in Ph I or Ph II/b additional clinical evidence will be needed
- To assess how much these trial should cost - **Value-of–Information (VOI) analysis**
- How much to spend on add evidence? Dependent of effect on:
  - Efficacy and safety
  - Probability of reimbursement
  - Profitability
- Bayesian statistical analyses; based on what “perfect information” adds in decision making process

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Real world data

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Real World Data (RWD)

- RWD the latest trend in pharma
- RWD include any data that are not captured within the context of a clinical trial
- RWD are considered “big data” when vast in quantity and multiple sources are combined
- RWD is complex, diverse and can be obtained (sometimes) within minimal time
- Can provide information on substantial number of research questions
- Methodological considerations

Groves P, Kayyali B, Knott D, Van Kuiken S. The ‘big data’ revolution in healthcare. McKinsey & Company. Center for US Health System Reform Business Technology Office. January 2013.
Using real world data for coverage and payment decisions: The ISPOR real world data task for report. Accessed via: http://www.ispor.org/workpaper/rwd_tf/rwtfmanuscript.pdf

RWD: Sources and outcomes

- RWD can be used for a multitude of purposes
- In licencing can provide information on unmet need or population size

Sources

- Late phase studies
- Registries
- Pragmatic clinical trials
- Claims / admin databases
- Health surveys
- EMRs
- Medical chart reviews

Outcomes

- Clinical
- Health-related quality of life (HRQoL)
- Patient reported outcomes (PRO)
- Economic

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Pricing

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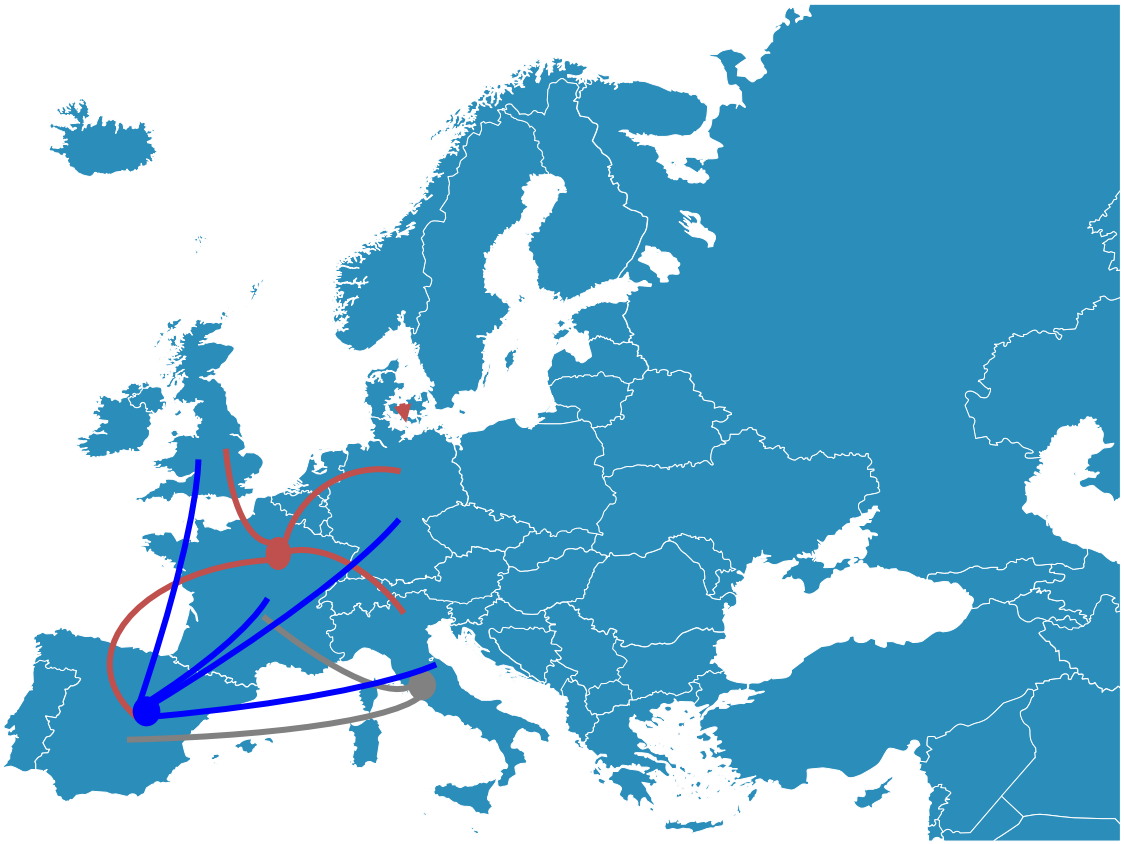
Pricing archetypes that you can encounter

Free pricing	UK (sort of)
Value-based pricing	(UK DE FR) pricing so that the product's price is in line with its value
Internal reference priding	(NL DE BE DK FR IT PT ES) – where products in the same reference category have the same price; mostly for non-innovative products
International reference pricing	All Eur countries except DE UK SE DK
Negotiations	Possible at the national and regional/local level. Happens in most countries for hospital products but at the national/regional level in UK DE, IT, ES

Example of international price comparisons – France, Spain, Italy

- Complex and interlinked
- Continually changing



Aspects to consider in price setting

Launch sequence

- Will determine ultimate price due to reference pricing
- To be determined based on items below
- Complex and subject to uncertainty

Time to reimbursement

- Substantial differences between countries – may interfere with launch sequence and thus price
- Requires in-depth local knowledge
- Can depend on price level

Price corridor

- Range between which all prices in all countries should fall;
- Considers int. reference pricing and launch sequences;
- Developed by pricing department
- If price fall outside this corridor then consider not launching

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Issues affecting reimbursement

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What are the challenges that can effect reimbursement?

Contrasting perspectives

Regulators

- Evaluates efficacy vs. placebo
- Rewards areas of high unmet need (e.g. orphan drugs)
- Increasing focus on comparison against other therapeutic options
- Unmet medical need

Payers

- Evaluate efficacy vs. comparators
- Concerned with innovation
- Concerned with burden of illness
- Concerned with unmet need
- Value-for-money

Manufacturers

- Utilise pipeline
- Return on investment
- Focus on burden of illness
- Effective patent life

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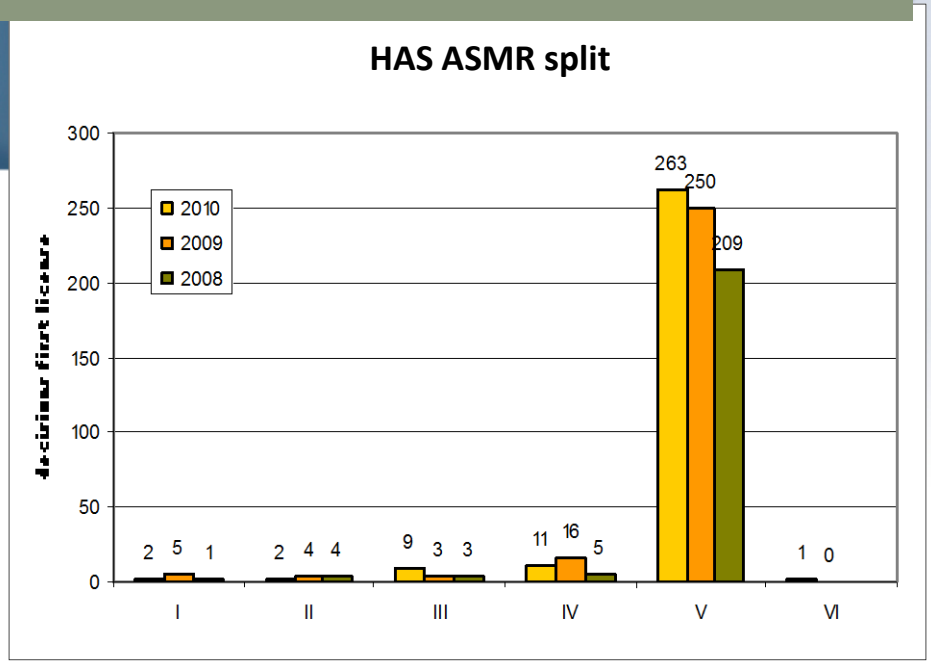
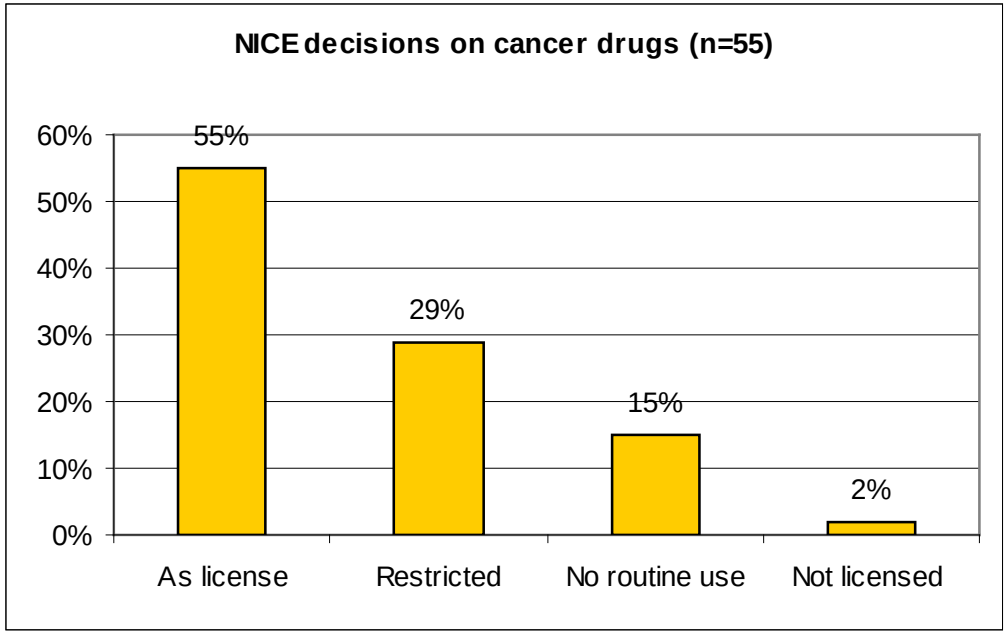
It is hard to be considered innovative

- NICE is selective in recommending drugs
- Only 55% of cancer drugs were recommended by NICE as licenced
- 29% were restricted





- Between 2008 and 2010 HAS has been selective in awarding products with status of innovation or (significant) therapeutic benefit
- No difference since then
- HCV treatments which have curative potential: ASMR II and III

(Premium) Pricing considerations that may affect reimbursement

Efficacy does not warrant high price (non-inferiority)

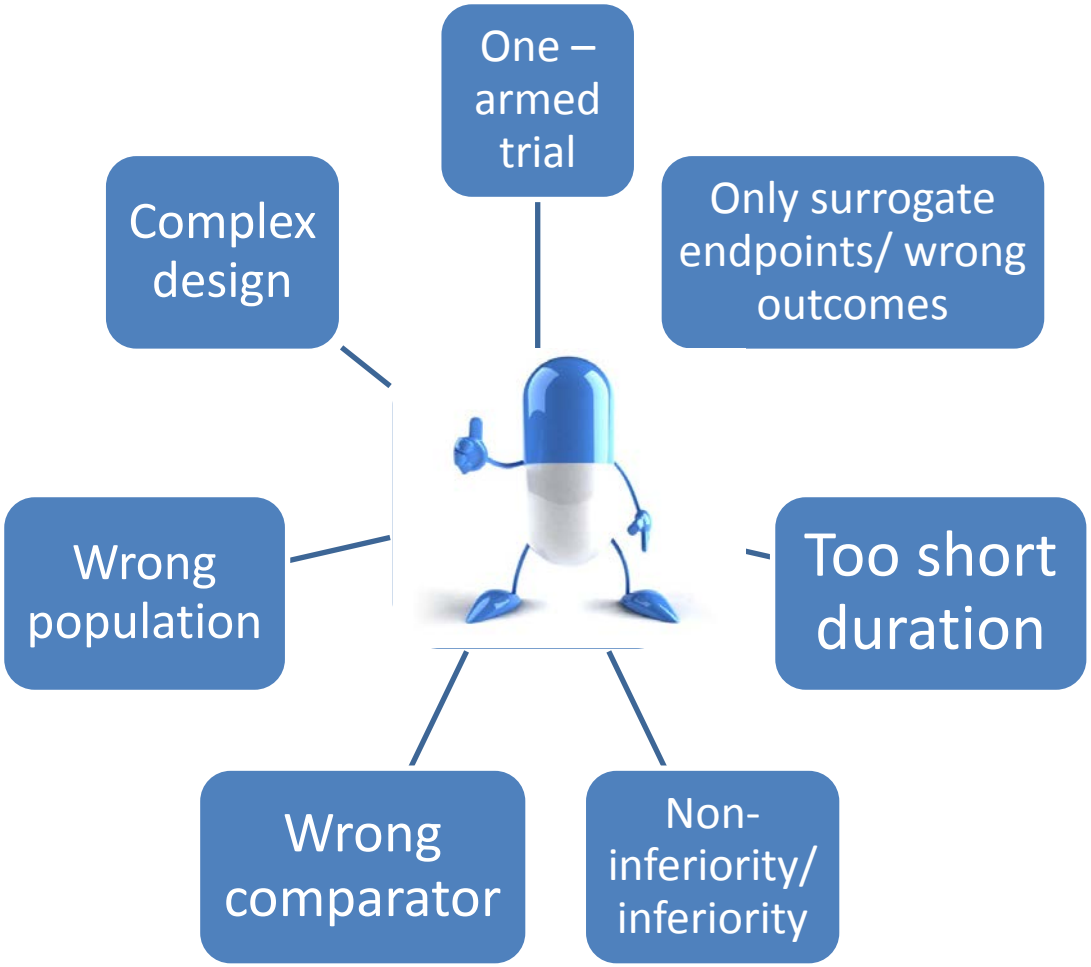
Comparator is a generic

Product is a me-too

High price will results in reimbursement delays

It will be severely restricted….

Challenges related to efficacy that may affect reimbursement



Issues related to safety which may affect reimbursement

Efficacy **Safety**

Rare but very expensive AEs	Different types of AEs than comparator
More AEs than comparator	No difference in AEs

Is your product innovative?

- Once daily/sustained release
- New administration route
- New treatment pathway
- Uses a device
- Novel process
- Patient preferences

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Possible solutions and checklist

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What you can do…..early scientific advice

- Licensors may ask licensees to provide an overview of HE evidence and likelihood of reimbursement as part of the due diligence
- Early assessment is now possible for both regulatory and Health Economic evidence
  - No panacea
  - No guarantee of reimbursement but will provide early indication of where issues lie and what can be done to resolve them

Overview of early scientific advice

Agency	Type of advice
EMA-HTA parallel/joint scientific advice	EMA and EUNetHTA agencies
SEED multi-HTA early dialogue	14 HTA bodies from the Belgium, Denmark, France, Germany, Hungary, Ireland, Italy, Netherlands, Spain, UK
NICE Scientific advice	HTA-only advice; In parallel with EMA or MHRA
G-BA consultation	HTA-only advice (no economic advice), to be done in parallel with EMA
HAS early encounter	HTA-only advice; to be carried out in parallel with EMA

Check list for health economic evidence when assessing reimbursability potential

- Critical assessment of (relative) efficacy & safety data
- Understanding of future needs for clinical trials and ideal design
- Maximum spend on additional data (VOI analysis)
- Mini landscape assessment

- Understanding of main competitors
- Benefits of current treatment over SOC
- Assessment of possible innovation
- HE evidence summary (prelim)
- Probability of reimbursement at highest price
- Early scientific advice

Thoughts or questions?

Thank You

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