IMPACT OF RARE DISEASES ON HEALTH ECONOMICS

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Disclosure of Interests

- Astellas Pharma (consultancy role)

- International Federation of Pharmaceutical Manufacturers & Associations (consultancy role)

Presentation Outline

- Historical timeline of orphan drugs development

- HTA and patient access

- Economic Evaluation

- Impact of disease rarity on cost - effectiveness

- England: NICE approach and HST programme

- HTA challenges with orphan drugs

- Multiple Criteria Decision Analysis

Historical timeline of orphan drug development

- 1962 Kefauver Harris Amendment or "Drug Efficacy Amendment": requirement of efficacy for a new drug to be approved in addition to rising safety standards →**R&D costs of new drugs increased**

- Rare diseases (**RDs**) as a **risky area**: low number of patients, lower expected sales, recuperation of R&D costs?

- Rare disease area ignored leading to unmet needs → "**orphans**"

- 1983 **Orphan Drug Act**: to amend the Federal Food, Drug, and Cosmetic (FD&C) Act to facilitate the development of RDs drugs

- In the **EU legislations to incentivise** R&D and commercialisation of orphan drugs (government grants for R&D, fast-track regulatory assessment with reduced fees, to tax credits and prolonged market exclusivity)
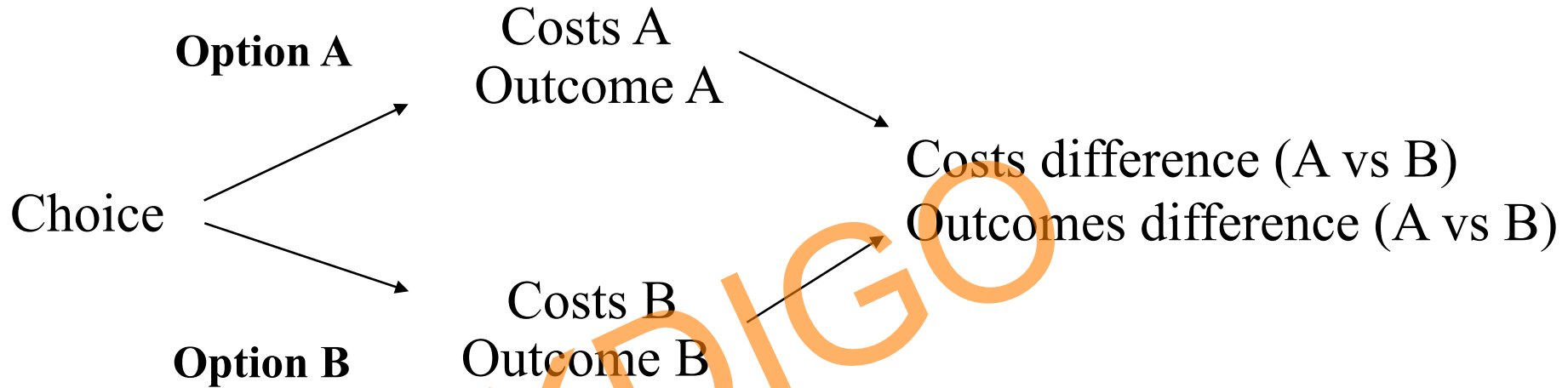
HTA and patient access

- Marketing authorisation of a new product by clinical regulators (e.g. FDA, EMA) is not sufficient to secure patient access

- Once the clinical efficacy and safety of a new product is approved, Health Technology Assessment agencies act as gate-keepers on behalf of the payers

- Licensing and coverage decisions have traditionally been compeltely different processes, with some efforts to align them only very recently (e.g. the collaboration of EMA and EUnetHTA on evidence requirements)

Economic Evaluation

- **Objective**: *make choices that maximise utility/welfare*

- **Constraint**: *scarcity of resources*

- **Question**: *how to allocate resources that maximise utility* (best "value for money")?

→ Need to *quantify and compare* the benefits and costs of alternative options to help allocate available resources ***efficiently***

➢ Economic evaluation: a set of techniques to assemble evidence on the effects (outputs) and costs (inputs) of alternative options

❖ Opportunity cost: the potential utility/welfare that could have been derived, if the resources had been used in an alternative way

Source: adapted from Alistair McGuire (2015)

Economic Evaluation

Option A

Costs A
Outcome A

Choice

Costs difference (A vs B)
Outcomes difference (A vs B)
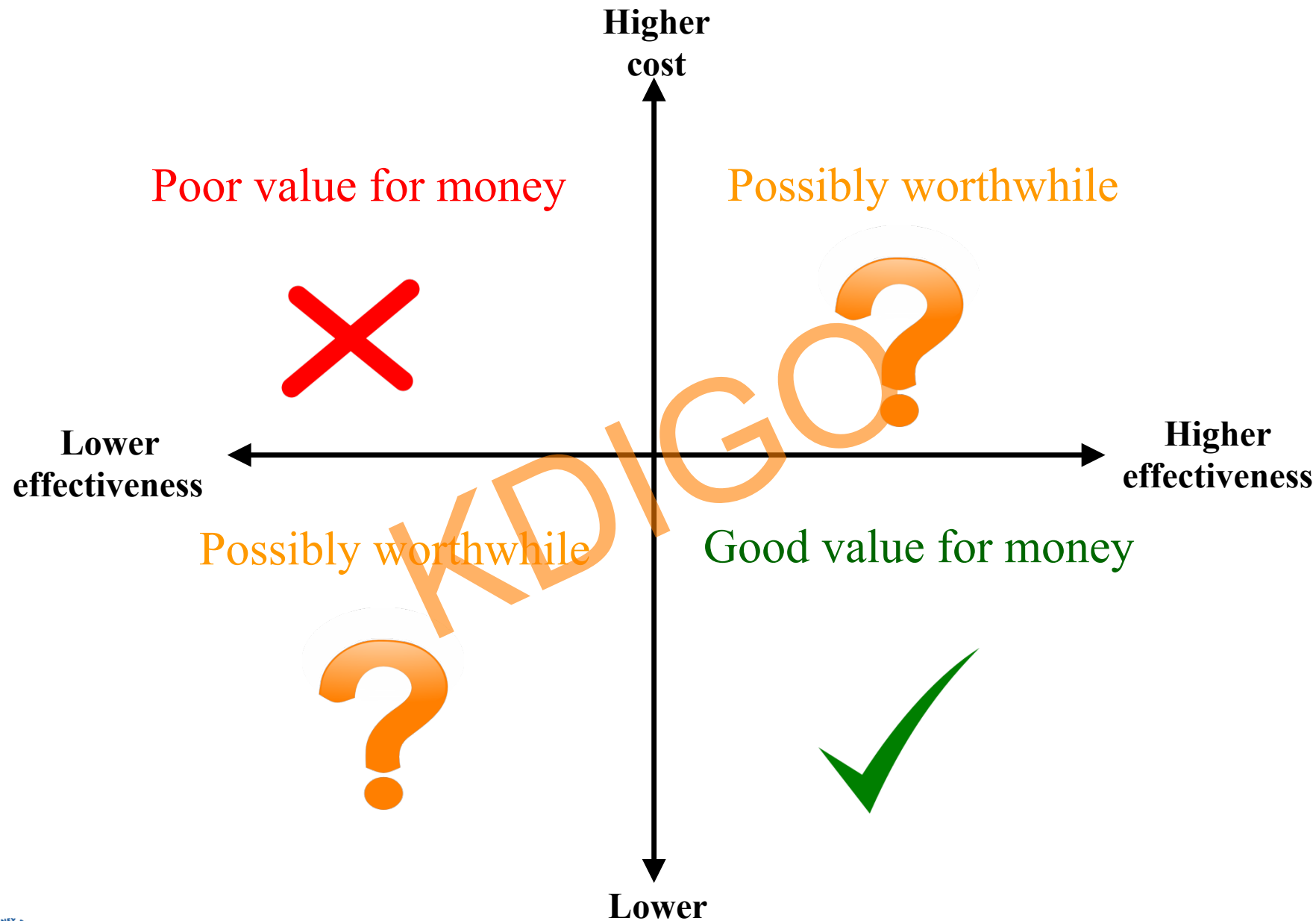
Costs B
Outcome B

Option B

The difference in costs is compared with the difference in outcomes,
to assess the cost per unit of outcome of the intervention of interest

$$ICER = \frac{C_a - C_b}{E_a - E_b} = \frac{\Delta C}{\Delta E}$$

Source: adapted from Alistair McGuire (2015)

Analysis	Costs	Outcomes/Effects	Results
Cost-Minimisation	$	<u>identical</u> (therefore not analysed)	cost per patient over 12 months: $50 (A) vs. $150 (B) • Cost savings
Cost-Effectiveness Analysis (CEA)	$	<u>natural units</u> (some physical measure of the health outcome associated with intervention, e.g. changes in blood pressure, changes in survival, etc.)	$10,000 per LYG per patient over 10 years of patient's life • Relative efficiency (i.e. the incremental cost per incremental effectiveness)
Cost-Utility Analysis (CUA)	$	<u>individuals' preferences</u> (effects measured in physical units weighted by utility measure, i.e. adjusted for quality of life)	$15,000 per quality adjusted life year (QALY) per patient •Relative efficiency (i.e. incremental cost per incremental QALYs gained)
Cost-Benefit Analysis (CBA)	$	<u>monetary terms</u> (usually through willingness to pay)	$10,000 worth of outcomes for a cost of $5,000 •Net monetary value (i.e. if effects > costs, then the programme is worth undertaking)

Source: adapted from Alistair McGuire (2015)

Impact of disease rarity on cost-effectiveness

❖ *Disease rarity* has a **negative impact on ICER**, resulting in poor value for money

• *cost dimension*: manufacturers have to assign relatively **high prices** to recoup the development costs due to low expected volumes

• *effects dimension*: relatively small number of patients enrolled in clinical trials might give **insignificant improvement** in clinical benefit

➢ According a *utilitarian approach* to efficiency (total health gain for the greatest number of people), orphan drugs seem to be **"doomed to fail"** because of the particularities of RDs

Impact of disease rarity on cost-effectiveness

❖ Absence of an appropriate evaluation framework for orphan medicines creates a **methodological, conceptual and policy gap** (Drummond and Towse, 2014):

- *Payers* recognise that because of high prices **orphan drugs cannot be approved** for coverage based on cost-effectiveness grounds…
- *Manufacturers* realise that their end products once developed (through orphan incentives) **cannot secure reimbursement**…
- *Patients* **cannot get access** to treatments for their rare condition even though available options exist on the market…

➢ **Medicines are produced that enter the market but that cannot be accessed by the patients!**

Impact of disease rarity on cost-effectiveness

❖ But, *should we* treat cost-effectiveness estimates of orphan medicines **differently** to others?

❖ The justification of a *special status* of a disease based solely on its prevalence would be **questionable**, as it entails valuing one disease differently to another one because it is a less common disorder or a more common disorder (McCabe et al, 2005).

❖ A possible justification for providing special status to RDs could be on equity grounds, using the rationale that "Patients suffering from rare conditions *should be entitled* to the **same quality of treatments** as other patients" (European Parliament, 2000).

❖ **In other words, take into account the unmet need *arising* from the rarity of a disease, i.e. unavailability of treatments.**

England: Value Based Pricing consultation

A new value-based approach to the pricing of branded medicines (DH, 2010)

- ➢ **Aim:** "to ensure NHS funds are used to gain the greatest possible value for patients"

- ➢ **Concept:** "value of new products would be assessed and their benefits compared with the benefits that could be gained if the funds required were used to help patients elsewhere in the NHS"

- ➢ **How:** "apply weightings to the benefits provided by new medicines, which would imply a range of price thresholds or maximum prices, explicitly adjusted to reflect a broader range of relevant factors"

- ➢ **What (factors):**
  - • the more the medicine is focused on diseases with unmet need or which are particularly severe (**burden of illness**), the higher the threshold;
  - • higher thresholds for medicines that can demonstrate greater **therapeutic innovation** and improvements compared with other products;
  - • higher thresholds for medicines that can demonstrate **wider societal benefits**
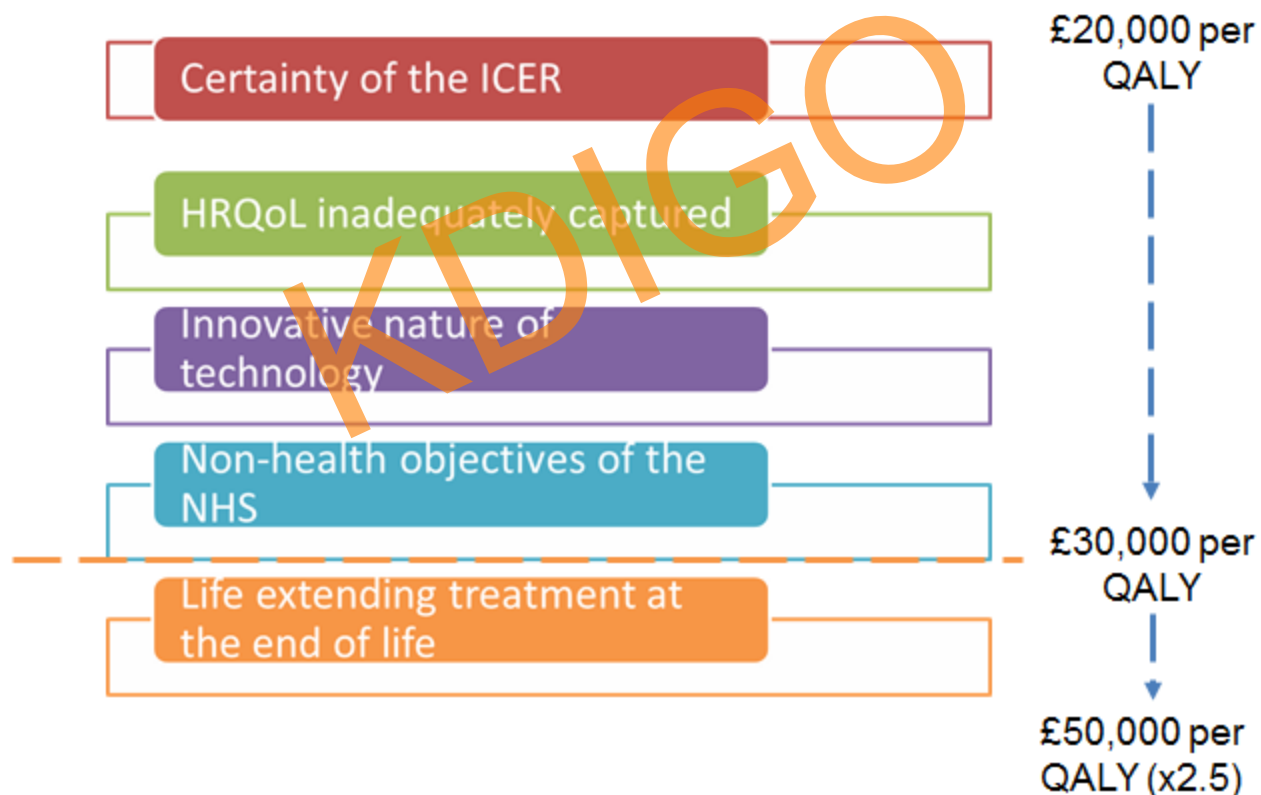
England: Value Based Assessment consultation

Value Based Assessment of Health Technologies (NICE, 2014)

➢ **Aim:** "how to change the way we make recommendations on the use in the NHS of health technologies for use in the NHS, taking into account the new terms of reference for value based assessment"

➢ **Concept:** "discretion to consider whether the NHS should accept a higher opportunity cost (threshold) than they would normally recommend, when something might offer the same overall health gain than it will displace, but has other elements of value not captured in the QALY"

• E.g. life-extending treatments, used at the end of life (x2.5 implicitly)

➢ **How:** "more explicitly and systematic framework"

➢ **What (modifiers):**

• **burden of illness**: loss (or shortfall) in quality and length of life, measured in QALYs (quality adjusted life years), which occurs as a consequence of having a disease or condition

• **wider societal impact:** loss (or shortfall) in a person's capacity to engage with society as a result of living with the disease or condition

VBA consultation: current approach

Flexible decision-making: current approach

- Certainty of the ICER
- HRQoL inadequately captured
- Innovative nature of technology
- Non-health objectives of the NHS
- Life extending treatment at the end of life

£20,000 per QALY

£30,000 per QALY

£50,000 per QALY (x2.5)

VBA consultation: suggested approach

Flexible decision-making: new approach

- Burden of illness
- Wider societal impact
- Certainty of the ICER
- HRQoL inadequately captured
- Innovative nature of technology
- Non-health objectives of the NHS

20,000 per QALY

£50,000 per QALY or 2.5
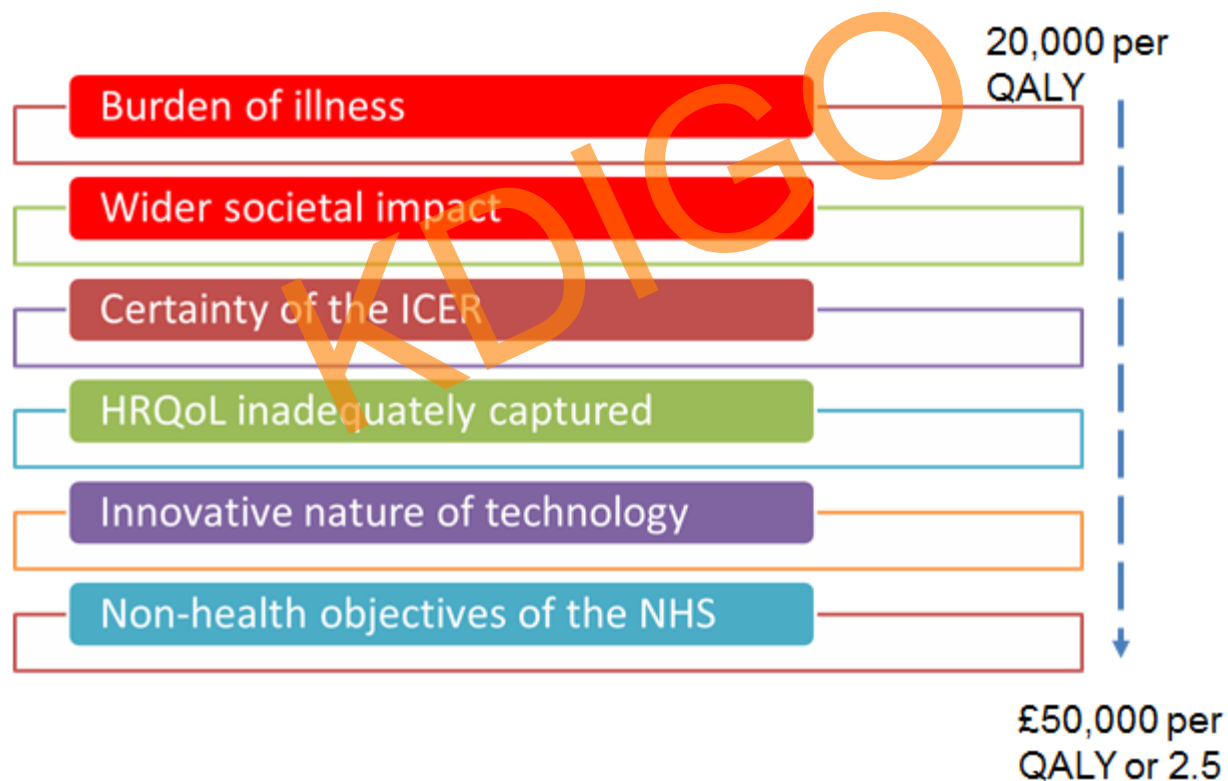
VBA consultation: LSE response

Does proportional QALY shortfall appropriately reflect burden of illness?

"Our current understanding is that BoI considers disease severity in the form of QALY loss (i.e. proportional QALY shortfall). We believe that proportional QALY shortfall is a logical and practical way to quantify disease severity. However, the definition of BoI should be *expanded beyond disease severity and include unmet clinical need*, for example, in the form of treatment availability. We feel this is an important consideration and, as such, it reflects societal values as evidenced by public preferences in the UK (Linley and Hughes, 2013)."

Highly Specialised Technology programme

❖ In England, the National Institute of Health and Care Excellence (**NICE**) has been investigating the construction of a new framework for the evaluation of *ultra-orphan drugs* known as Highly Specialised Technology (HST) programme.

❖ An independent evaluation committee makes recommendations to NICE regarding the benefits and costs of HSTs for national commissioning.

❖ The committee has discretion to consider factors that relate both to *Scientific* and *Social Value Judgements* through a decision making framework that takes into account a **range of evaluation criteria** including:

      -the nature of the condition
      -impact of the technology (beyond direct health benefits)
      -cost to NHS and personal social services
      -value for money
      -cost of R&D? (for the case of eculizumab for aHUS)

HTA challenges with orphan drugs

A number of weaknesses in the current orphan drugs policy and legislative framework need to be addressed (Kanavos and Nicod, 2012):

- *poor value for money* because of high prices
- *uncertain evidence* because of the small patient populations (obtaining statistical power, recruitment)
- *heterogeneous* nature of the conditions

➢ improvements in **data collection** with the creation of registries,

➢ **definition** of what is "sufficient" and "excessive" profits,

➢ overall a **better and more holistic value assessment framework** that explicitly accounts for the peculiarities of rare diseases in the context of value based assessment

HTA challenges with new medicines

- Economic evaluation **does not adequately capture** a number of value dimensions

- Increasing evidence that Decision Makers are reluctant to base decisions on economic evaluation alone, **seeking broader assessment**

- Different stakeholders attach different **value judgements** to the criteria considered

- **What additional benefits to incorporate, how to establish their relative importance, and whose preferences to consider?**

HTA challenges with new medicines

➢ Adopt an alternative methodological approach for value assessment

➢ Develop comprehensive and transparent framework potentially overcoming the previous limitations
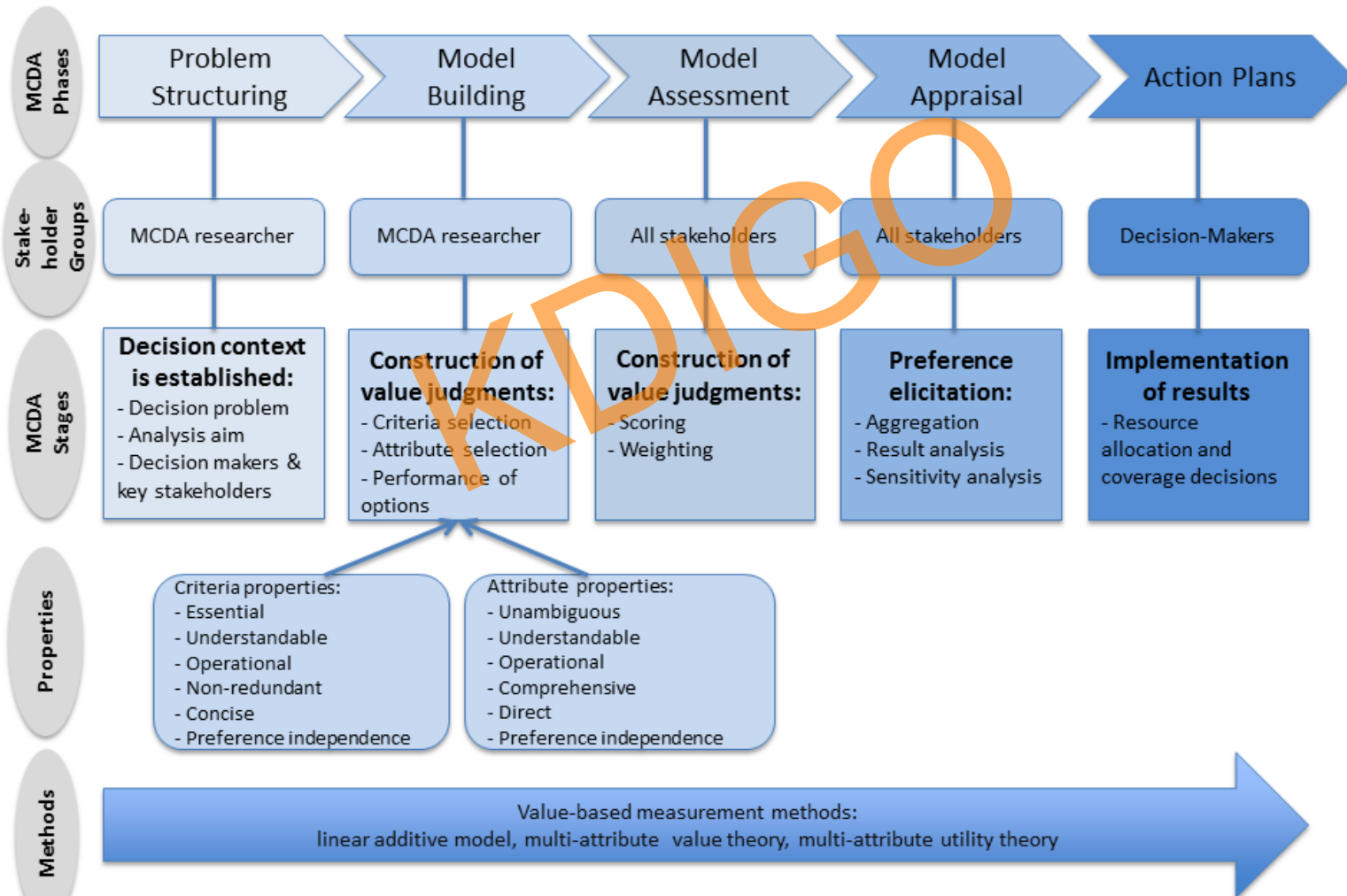
➢ Contribute to a more efficient resource allocation

Multiple Criteria Decision Analysis

➢ Multiple Criteria Decision Analysis "*is both an approach and a set of techniques, with the goal of providing an overall ordering of options*" by looking at the extent to which a set of objectives are achieved.
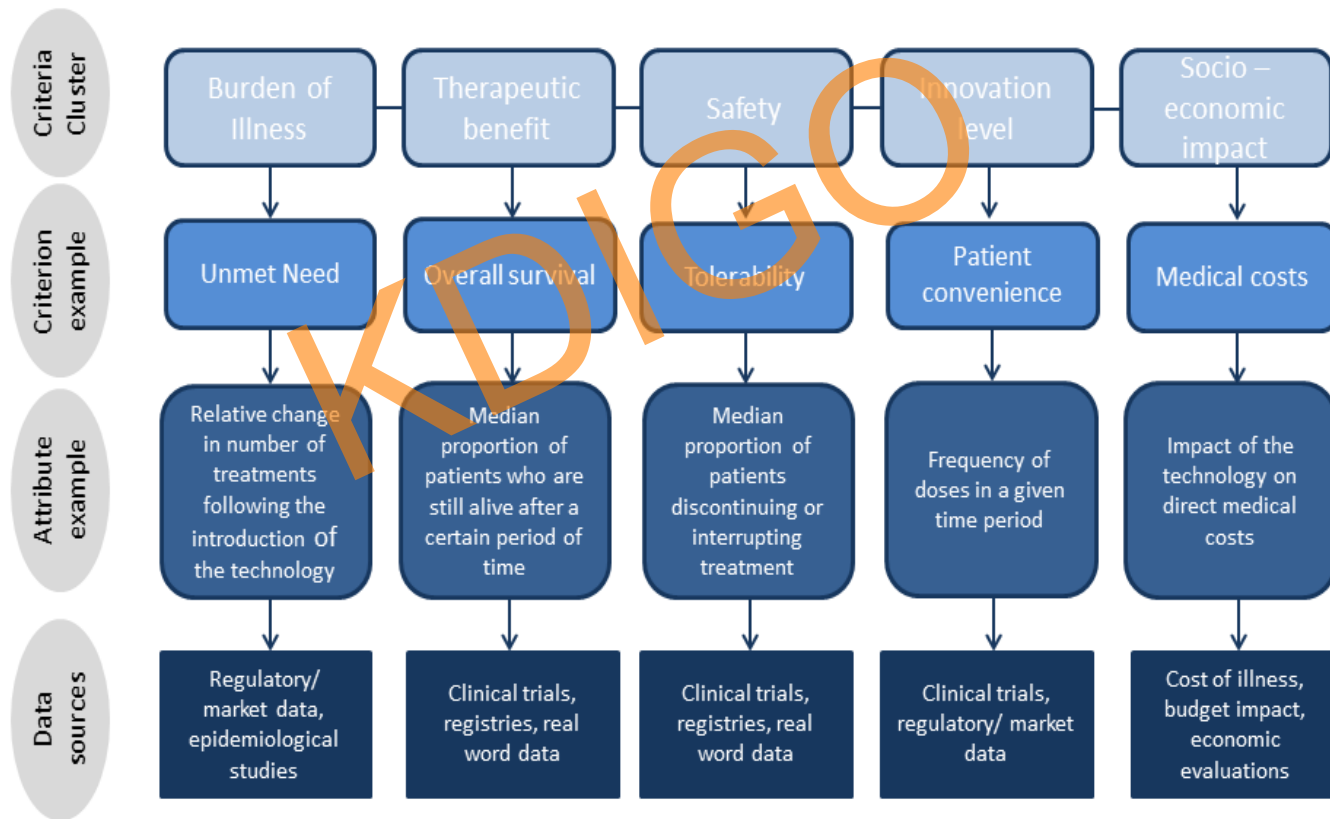
Analyse complex situations characterised by a mix of objectives:

- disaggregate a complex problem into simpler components
- measure the extent to which certain options achieve the objectives
- weight these objectives
- re-assemble the components to show an overall picture

MCDA in the context of HTA

MCDA in the context of HTA

	Burden of Illness	Therapeutic benefit	Safety	Innovation level	Socio – economic impact
Criteria Cluster	Burden of Illness	Therapeutic benefit	Safety	Innovation level	Socio – economic impact
Criterion example	Unmet Need	Overall survival	Tolerability	Patient convenience	Medical costs
Attribute example	Relative change in number of treatments following the introduction Of the technology	Median proportion of patients who are still alive after a certain period of time	Median proportion of patients discontinuing or interrupting treatment	Frequency of doses in a given time period	Impact of the technology on direct medical costs
Data sources	Regulatory/ market data, epidemiological studies	Clinical trials, registries, real word data	Clinical trials, registries, real word data	Clinical trials, regulatory/ market data	Cost of illness, budget impact, economic evaluations

Source: Angelis and Kanavos, 2016

MCDA in the context of HTA

- MCDA could generate a more holistic metric of value

- Incorporation of costs can then produce a metric of efficiency, involving incremental cost per incremental MCDA value unit, that can be used for reimbursement and coverage decisions

- Overall, the MCDA approach provides improved comprehensiveness, flexibility, and transparency

- Attention should be paid on the theoretical foundations of DA so that the results are meaningful and decision recommendations robust

Source: Angelis and Kanavos, 2016

Thank you

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