Health Technology Assessment and its impact across countries

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How do HTAs work (as a coverage/reimbursement tool)?

Similarities and differences in HTA across countries and relevance to oncology therapies

Conclusions and implications for Patient representatives

Background on pricing mechanisms for new drugs in Europe

1. **Rate of return** regulation: UK only
2. **Price control and negotiation** (predominantly through external price referencing (24/27 EU MS)
3. **Controlling use** (contract agreements with regulators focusing on price-volume trade-offs)
4. **Cost-effectiveness pricing** (UK, Sweden)
5. **Clinical efficacy** (France, Germany)

How do HTAs work (as a reimbursement tool)?

Similarities and differences in HTA across countries

Conclusions and implications for Patient representatives

Health Technology Assessments: An increasingly used tool to determine value, coverage and access

How do HTAs work?

- **Pricing and reimbursement** mechanism
- **Robust framework** (evidence based medicine)
- To assess a medicine's (clinical) **benefit**, and in some cases **costs** as well

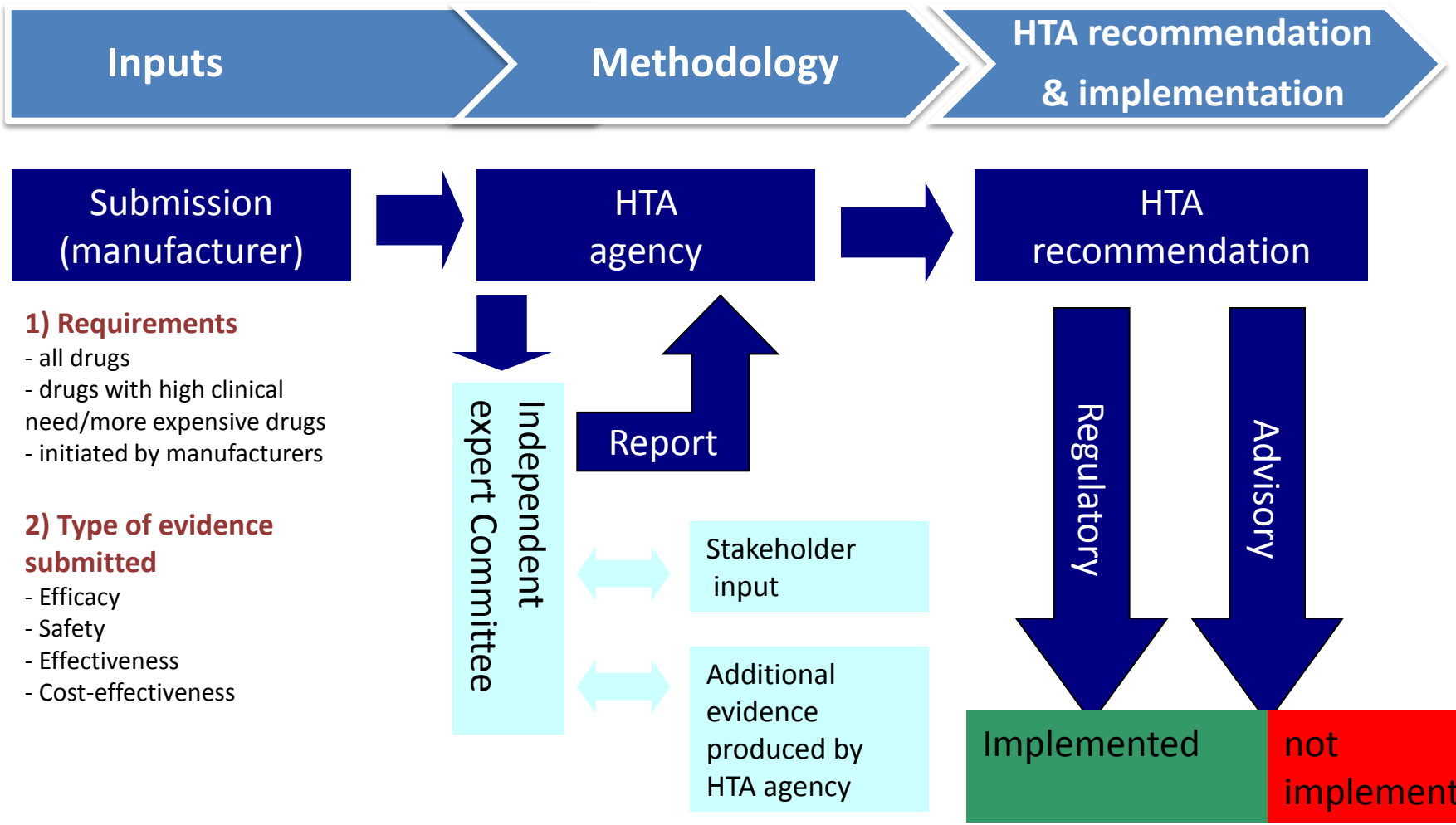
⇒ To reimburse **cost-effective drugs** or drugs that provide an **additional clinical benefit** compared to those available on the market

⇒ **Alleviate budgets** from cost-ineffective drugs or drugs that do not provide any additional benefit

⇒ Overall aim is to increase the **efficiency of healthcare resources**

Health Technology Assessments

How do HTAs work (as a reimbursement tool)?



Health Technology Assessments

Implications of a positive or negative reimbursement decision

Impact of a **positive reimbursement** outcome:

- Access to the patient
- Reward to the manufacturer
- Value for money to the payer

Impact of a **negative reimbursement** outcome:

- Cost-effective use of resources
- Budgets freed up to invest in other cost-effective treatments

BUT

- Limited access to the patient
  - Out-of-pocket
  - Not affordable
- May jeopardize the sustainability of the pharmaceutical industry (disincentive to the manufacture to further invest in R&D)
- When resubmission, time and resource consuming for all

What does cost-effectiveness mean?

When is a drug for a specific indication cost-effective?

A drug is **cost-effective** if:

$$\frac{\text{(cost new tx – cost comparator)}}{\text{(effect new tx – effect comparator)}} = \text{ICER} < \text{WTP}$$

ICER: incremental cost-effectiveness ratio
WTP: willingness-to-pay threshold

Examples of WTP:

- NICE in the UK = £20,000-£30,000/QALY
- TLV in Sweden: increases with disease severity

How do HTAs work (as a reimbursement tool)?

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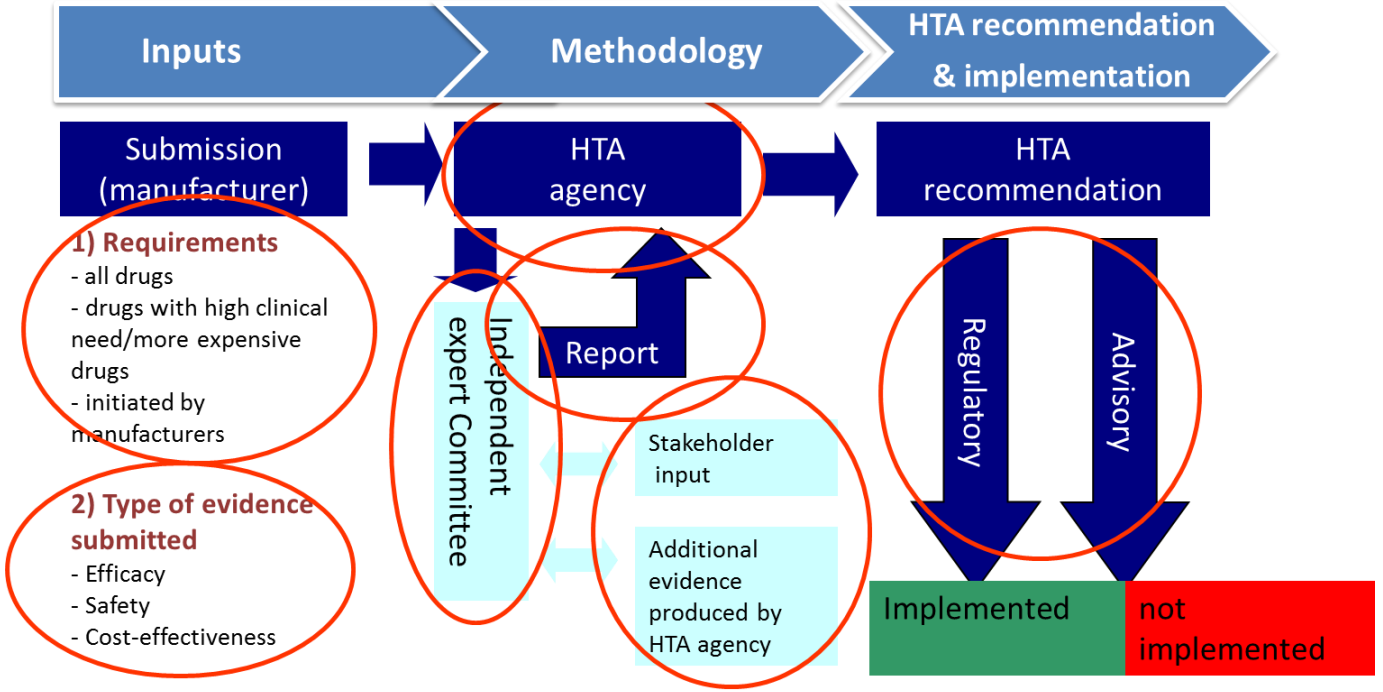
Health Technology Assessments

Similarities and differences in HTA outcomes across countries

Different studies show that the impact of HTAs varies greatly across countries, even though they are assessing a same drug and a same indication.

These differences can be seen at all stages of the process.



Health Technology Assessments - Methods

Research being conducted at the LSE

DATA

Database: all drug-indication pairs issued between January 2007 and December 2009

Country selection: England, Scotland, Sweden, Canada, Australia, (France)

Stratification per disease area: WHO ICD10 codes

HTA recommendation classification: List ("L"), List with Conditions ("LWC"), Do not list ("DNL")

Selection of disease areas: cancer, orphan, central nervous system indications

OBJECTIVE

To measure the level of agreement (kappa score) and associations (two-way correspondence analysis) in HTA recommendations issued across the study countries, and understand why HTA recommendations differ across settings (case studies).

Source: Elena Nicod and Panos Kanavos. Commonalities and differences in HTA outcomes: a comparative analysis of five countries and implications for coverage decisions. Health Policy 2012 (Accepted for publication).

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Health Technology Assessments

HTA agencies included in the study

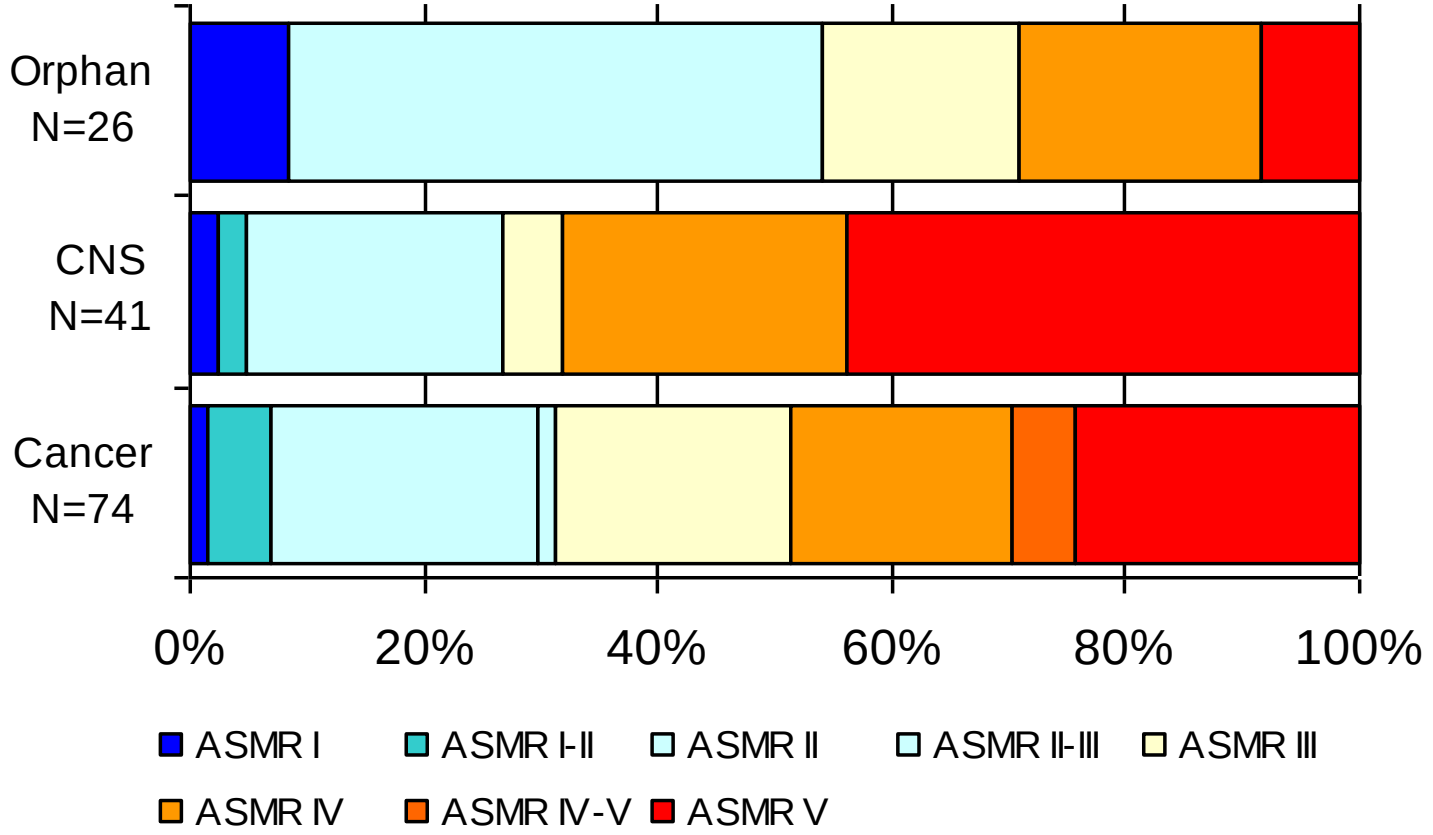
	HTA agencies
Canada	**CDR/CED** Common drug review (CDR), Canadian Agency for Drugs and Technologies in Health (CADTH) Committee to Evaluate Drugs (CED)
Australia	**PBAC** Pharmaceutical Benefits Advisory Committee Department of Health and Ageing (PBAC)
England	**NICE** National Institute for Clinical Excellence
Scotland	**SMC** Scottish Medicines Consortium
France	**HAS** Haute Autorité de Santé
Sweden	**TLV** Dental and Pharmaceutical Benefits Agency

Snapshot of our database - orphan therapies

Drug	Indication	ICD10	Canada CDR/CED	England NICE	Australia PBAC	Sweden TLV	Scotland SMC
Dasatinib	Chronic myeloid leukemia	C92.1	LWC	Ongoing	LWC	L	LWC
Sorafenib tosylate	Renal cell carcinoma	C64	DNL	DNL	DNL	L	DNL
Sorafenib tosylate	Hepatocellular carcinoma	C18-C21	LWC	DNL	LWC	LWC	DNL
Ambrisentan	Pulmonary arterial hypertension	I27	LWC		LWC	LWC	LWC
Imatinib mesylate	Chronic myeloid leukaemia	C	LWC	LWC		L	LWC
Imatinib mesylate	GIST	C16-18	LWC	LWC		L	DNL
Lenalidomide	Multiple myeloma	C90		LWC	LWC	LWC	DNL
Levodopa / carbidopa monohydrate	Parkinsons	G20	DNL		DNL	LWC	DNL
Miglustat	Gaucher Disease	E75.2	DNL		LWC	L	LWC
Nilotinib	Chronic myeloid leukemia	C92.1		Ongoing	LWC	L	LWC
Sildenafil citrate	Pulmonary arterial hypertension	I27	LWC		LWC	L	LWC
Sitaxsentan sodium	Pulmonary arterial hypertension	I27	DNL		LWC	L	LWC
Carmustine implant poliferprosan	Glioblastoma (newly diagnosed)	C71		LWC	DNL		L
Dasatinib	Acute lymphoblastic leukemia	C91.0			LWC	L	DNL
Eculizumab	Paroxysmal nocturnal haemoglobinuria	D59.5	DNL		DNL		DNL
Idursulfase (Iduronate-2-sulfatase)	MPS II, Hunter Syndrome	E76.1	DNL		DNL		DNL
Temsirolimus	Renal cancer	C64	DNL	DNL	DNL		

Health Technology Assessments

ASMR ratings issued per therapeutic class (in %), 2007-2009

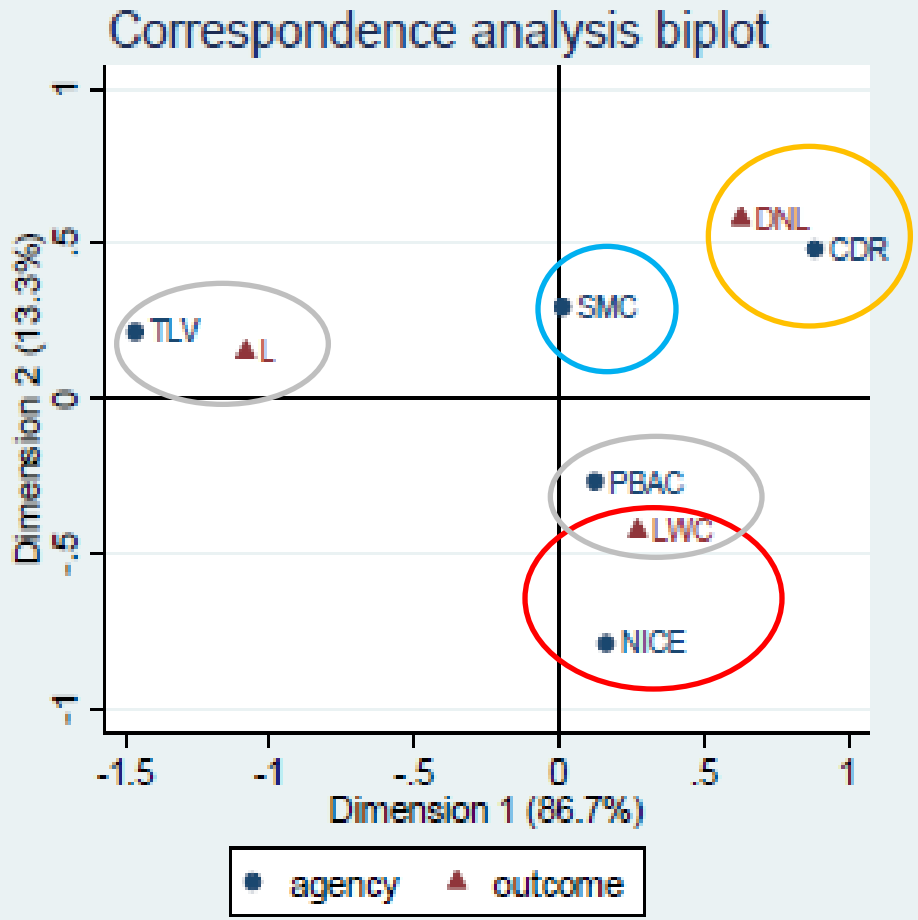


ASMR = relative improvement in clinical benefit (e.g. how much clinically better is the new treatment compared to its comparator?)

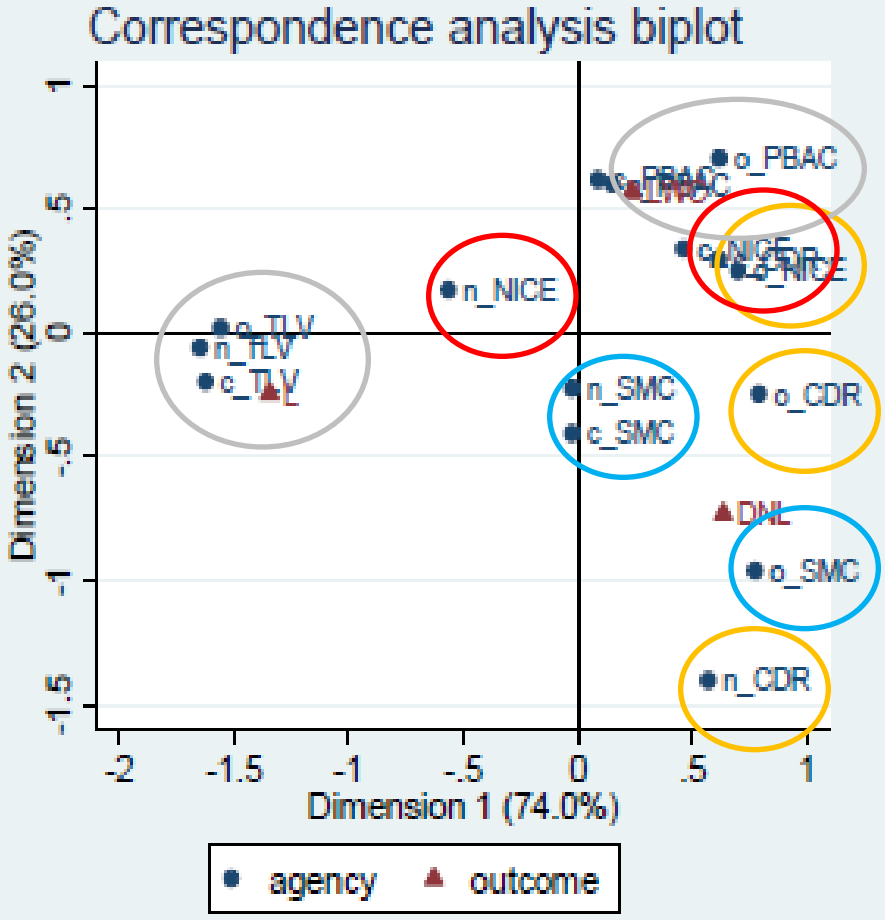
Ranges from ASMR I = highly innovative to ASMR V = no clinical improvement

Associations between HTA bodies and their recommendations

CORA for all drugs (N=287)



CORA for 3 therapy areas (N=141)



Legend: Recommendations/outcomes: L: list; LWC: restrict; DNL: reject;
HTA bodies: TLV - Sweden; SMC - Scotland; CDR - Canada; PBAC - Australia; NICE - England & Wales
Therapy areas: c – cancer; n- central nervous system; o- orphan indications

Source: Nicod E and Kanavos P, Health Policy 2012

Examples of reasons for differences identified in a number of case studies (e.g. metastatic colorectal cancer)

Differences are a consequence of:

- Context-specific considerations (e.g. national preferences, costs)
- HTA processes
  - Evidence (e.g. clinical expertise)
  - Methods (e.g. economic model, choice of comparator)
  - Interpretation (e.g. what constitutes acceptable levels of evidence, clinical endpoint)
  - Other considerations (e.g. disease severity, symptomatic/curative, existing treatment alternatives, orphan indication)

LESSONS FROM HTAs – METASTATIC COLORECTAL CANCER
HTA recommendations issued

Different HTA recommendations issued across HTA bodies

	Canada CED/CDR	England NICE	Australia PBAC	Scotland SMC	France HAS (ASMR)
Cetuximab W/chemotherapy, 1st line, wild-type KRAS gene		LWC	DNL	DNL	V
Bevacizumab W/chemotherapy, 1st line, wild-type KRAS gene	LWC	DNL	LWC	DNL	
Panitumumab 3rd line, wild-type KRAS gene	LWC		DNL	DNL	V

LESSONS FROM HTAs – METASTATIC COLORECTAL CANCER
Clinical evidence

QUESTION 1: Did the agencies consider the same clinical evidence in their appraisals?

Cetuximab	Bevacizumab	Panitumumab
YES, but … Both NICE and PBAC also considered additional studies Additionally, all agencies assessed placebo-controlled trials, **whereas PBAC only looked at indirect comparisons** (of the same trials with other placebo-controlled trials and comparators)	**YES, but…** Of the 3 clinical trials assessed by all agencies, **NICE** only appraised one of these trials, and additionally two other trials; **SMC** considered indirect comparisons in its last submission	**YES**

LESSONS FROM HTAs – METASTATIC COLORECTAL CANCER
Dealing with uncertainty

QUESTION 2: Did the agencies appraise the evidence and address the clinical uncertainties in the same manner?

Cetuximab	Bevacizumab	Panitumumab
No… mainly because of the nature of the clinical evidence **Posthoc analysis** ⇒Addressed by NICE through clinical expertise ⇒Rejected by SMC, HAS **Indirect comparison** ⇒non-inferiority not demonstrated for PBAC	**No… mainly because of the nature of the clinical evidence** **Generalizability and sample size** ⇒Addressed through patient registries for HAS ⇒Patient registries deemed insufficient for SMC, and inadequate for NICE	**No… mainly because of the interpretation of the clinical results** **Posthoc analysis + cross-overs across study arms + clinical endpoints** ⇒Uncertain clinical benefit for HAS and PBAC (also because the agencies requested additional endpoints – OS – not stat. sig.) ⇒Assessment based on primary endpoint PFS, where clinical benefit deemed demonstrated for CED

LESSONS FROM HTAs –METASTATIC COLORECTAL CANCER
Economic evidence

QUESTION 3: Did the estimates of cost-effectiveness from the economic models presented vary between the agencies, and if applicable, how were uncertainties addressed?

Cetuximab	Bevacizumab	Panitumumab
Different economic models… **Rejection by PBAC, SMC** •High and uncertain cost-effectiveness estimate (mainly because of clinical uncertainties) **Accepted by NICE** •Uncertainties addressed by **clinical expertise** •**Risk Sharing Agreement**	**Different economic models…** **Rejection by NICE, SMC** •High and uncertain cost-effectiveness estimate (mainly because of clinical uncertainties) **Accepted by PBAC, CED** •Resubmission with revised economic model (decreased price and narrowing down of indication) and **Patient Access Scheme** •Reimbursement through the **Cancer Care Ontario's New Drug Funding Program**, although drug cost-ineffective	**Similar economic models…** **Rejection by PBAC, SMC** •High and uncertain cost-effectiveness estimate (because of clinical uncertainties) **Accepted by CED** •Provides value for money (mainly because only minor uncertainties raised)

LESSONS FROM HTAs – METASTATIC COLORECTAL CANCER
Stakeholder involvement

	Canada CDR/CED	England & Wales NICE	Australia PBAC	Sweden TLV	France HAS	Scotland SMC
Professionals	Bevacizumab	Cetuximab				Bevacizumab
Specialists	Panitumumab	Bevacizumab				
Patient		Cetuximab				Cetuximab
Carers		Bevacizumab				Bevacizumab
Manufacturers		Cetuximab Bevacizumab	Panitumumab			
Other commentor organizations		Cetuximab Bevacizumab				

Little reference in the HTA reports on the type of input from stakeholders and how they can be useful

⇒ Need for a greater formal approach on stakeholder input and how it can, together with other levels of evidence, address clinical uncertainties?

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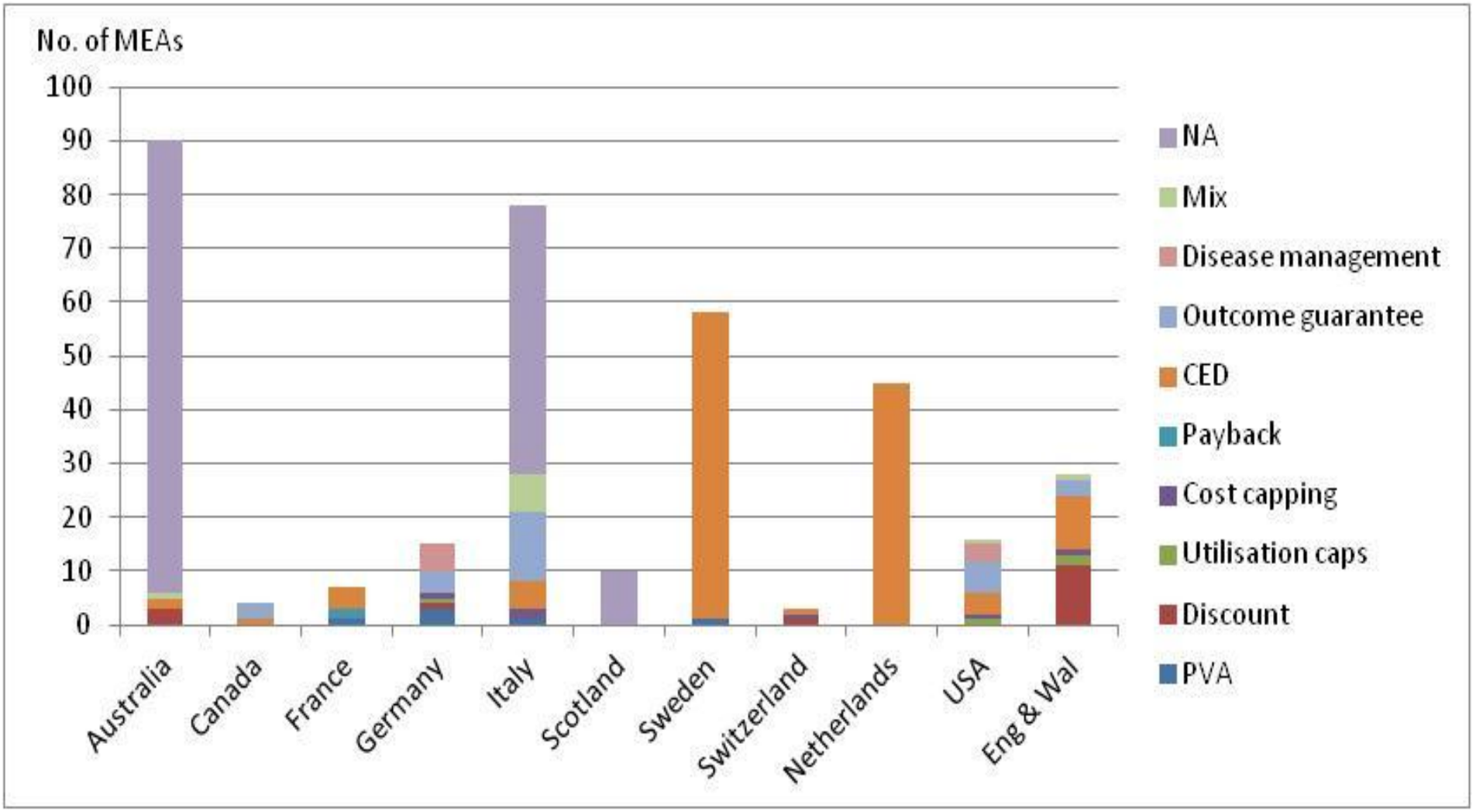
Risk sharing agreements in EU Member States by type, 2010-11



Source: Ferrario A and Kanavos P, Dealing with risk and uncertainty: Managed entry agreements for pharmaceuticals, forthcoming

How do HTAs work (as a reimbursement tool)?

Similarities and differences in HTA across countries

Discussion, conclusions and implications

HTA is an increasingly used tool to determine value, coverage and access in Europe and beyond

Inter-country variability in HTA recommendations:

- Low level of agreement between HTA agencies
- Differing associations between:
  - HTA bodies and recommendations issued
  - HTA bodies and recommendations issued per therapy area
- Differences are a consequence of:
  - Context-specific considerations (e.g. national preferences)
  - HTA processes (e.g. evidence, methods, evidence interpretation, other considerations)

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Significant methodological and empirical differences exist in its implementation

Aim of HTA:

- Efficiency in healthcare resource allocation
- Value for money

⇒ Therapy X is deemed cost-effective in country A, but not in country B because of, for example, different levels of evidence presented (e.g. clinical expertise)

⇒ *Does this imply that value for money is attained in country A but not in country B?*

⇒ *OR may reflect areas where HTA methods can be improved?*

Need to understand why such differences exist:

- Identify the reasons for these differences and differentiate when they are a consequence of:
  - National-specific considerations
  - HTA processes
- These preliminary findings have demonstrated that it is also important to differentiate HTA processes *per therapy area*

THANK YOU FOR YOUR ATTENTION