Managed entry agreements and pricing consideration for medicines across countries – building on the European experience

Alessandra Ferrario

LSE (until April 2017), Harvard (from July 207)

MURIA 3

Windhoek, 28 June 2017

Outline

- Background on pricing and reimbursement (P&R) to understand the need for managed entry agreements (MEAs)
- To present the European experience with MEAs, in particular their sustainability in facilitating access
- Current challenges with P&R and why MEAs are not a sustainable solution
- Conclusions

Drug development and market access

Search for new molecular targets

Pre-clinical studies

Phase I clinical trials

Phase II clinical trials

Phase III clinical trials

Licensing: safety, efficacy, quality

Pricing and reimbursement: costs and effectiveness

Rational use, pharmacovigilance, data collection

EVIDENCE

UNCERTAINTY : Where does the balance lie?

Value-for-money

Opportunity cost

GATEKEEPERS

POST-MARKETING ACTIVITIES

Pricing methods

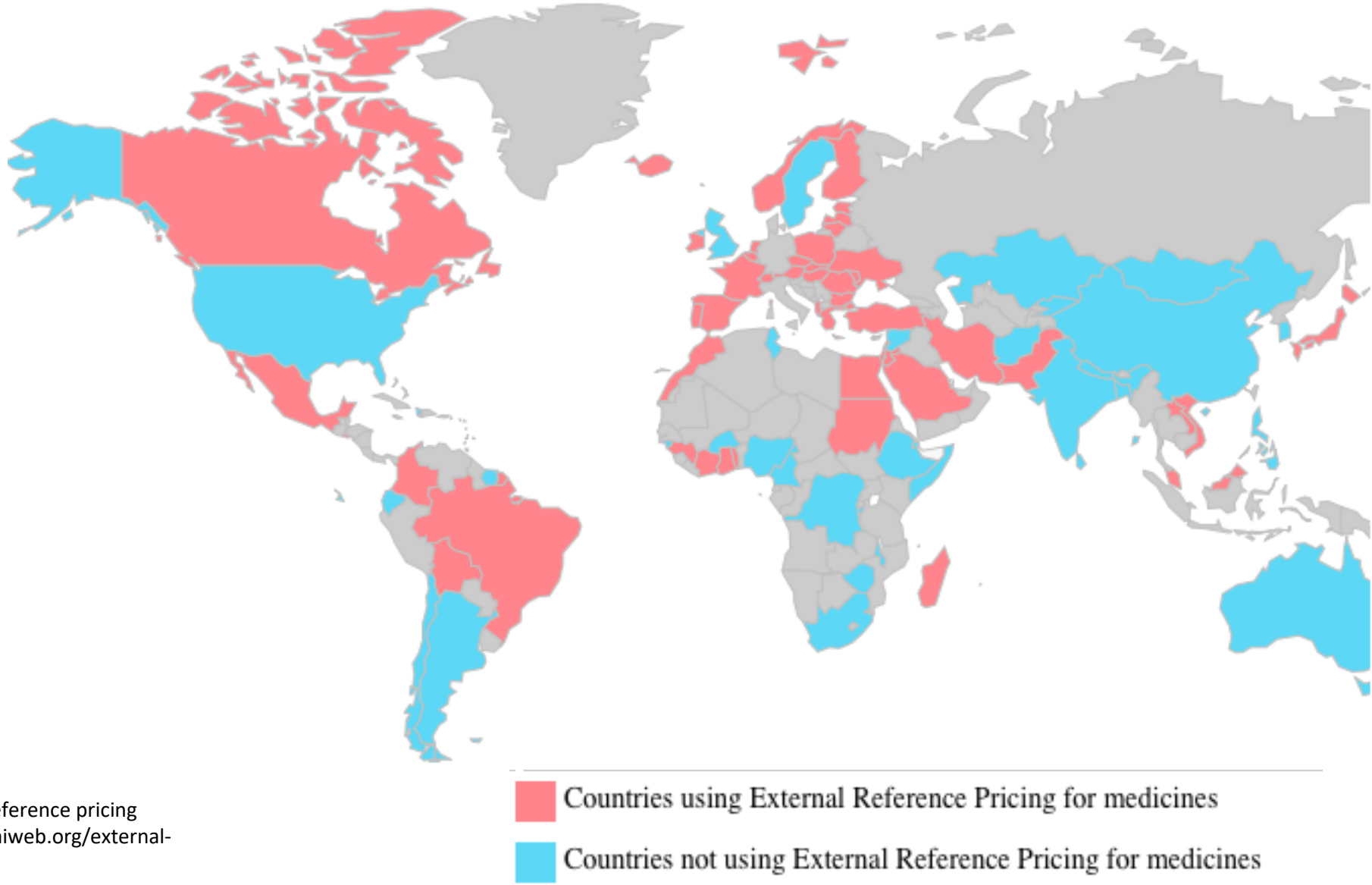
- External reference pricing
  - Widely used worldwide
- Free pricing
- Rate-of-return regulation
- Cost-plus pricing
- Value-based pricing

External or International reference pricing

- The practice of using the prices of a pharmaceutical product in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country.
- External price referencing is different from Internal or Therapeutic Price Referencing

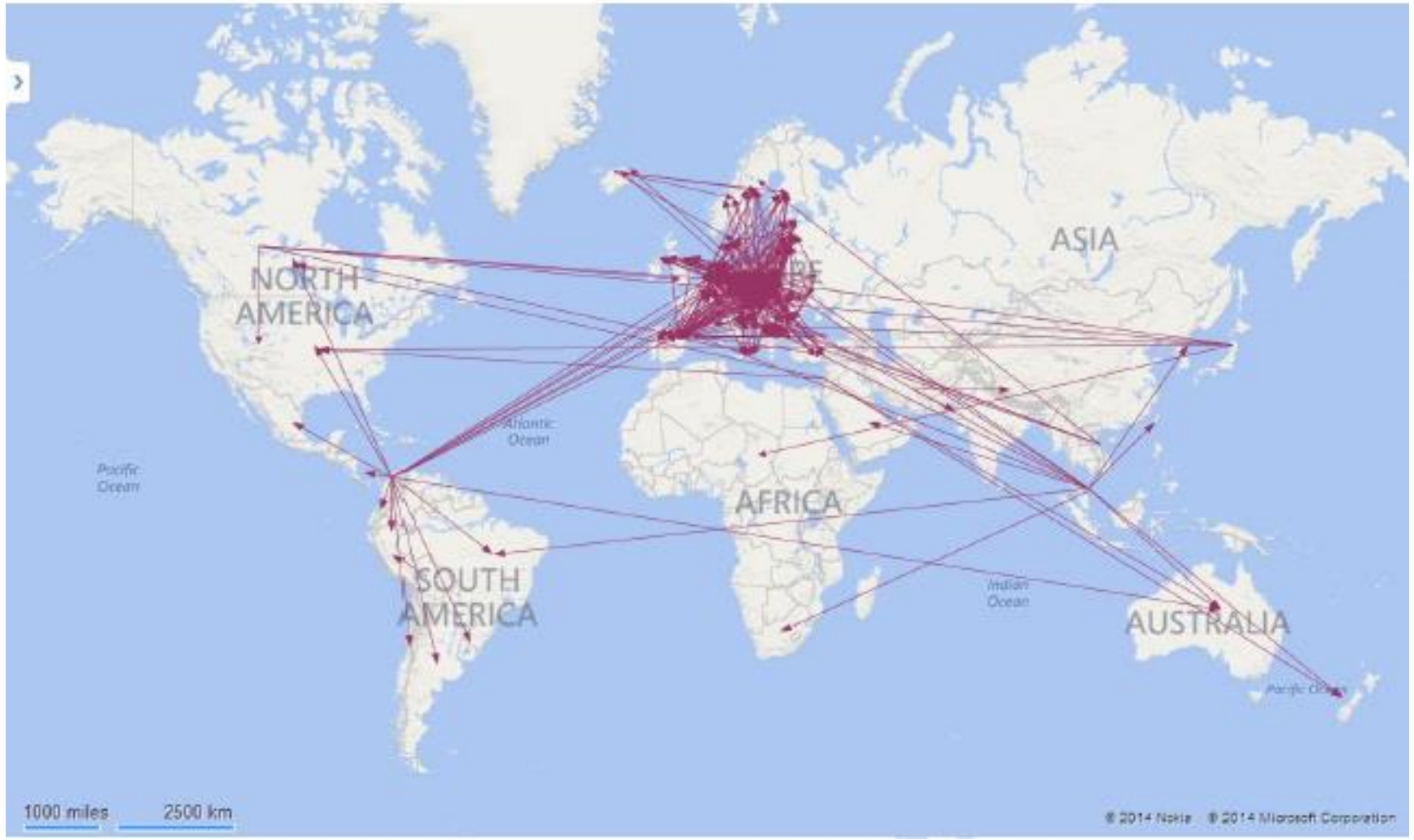
Source: PPRI glossary (http://whocc.goeg.at/Glossary/Search)

HAI study on external reference pricing



Source: Espin, Rovira, Ewen, Laing, Mapping external reference pricing practices for medicines, working paper, 2014; http://haiweb.org/external-reference-pricing-map/

Use of ERP globally showing countries referenced to



Source: Espin, Rovira, Ewen, Laing, Mapping external reference pricing practices for medicines, working paper, 2014; http://haiweb.org/external-reference-pricing-map/

Use of ERP in Europe showing countries referenced to

Source: Espin, Rovira, Ewen, Laing, Mapping external reference pricing practices for medicines, working paper, 2014; http://haiweb.org/external-reference-pricing-map/

The impact of ERP

Positive

- Studies have shown that it can generate savings for public payers

Negative

- Delayed launches or no launches in low-priced countries
- Manufacturers are not willing to grant lower list prices -> Widespread use of confidential discounts -> Erosion of price transparency -> Who wins who loses?
- Can be require considerable administrative efforts to implement

Vogler, Lepuschütz, Schneider, Stühlinger, Study on enhanced cross-country coordination in the area of pharmaceutical product pricing, 2015, European Commission
http://ec.europa.eu/health/sites/health/files/systems_performance_assessment/docs/pharmaproductpricing_frep_en.pdf

Reimbursement

Why is it important? Lack of reimbursement may…

- … limit access to cost-effective medicines
- … expose individuals to catastrophic health expenditure or impoverishment as a result of purchasing medicines

Tools to guide coverage decisions

- Health technology assessments (HTA): what is the added value?
- Budget impact: can the health system afford it?

HTA as tool to support universal health coverage

- WHO identified HTA as tool to inform decision makers in support of universal health coverage
- Universal health coverage is defined as ensuring that all people have access to needed promotive, preventive, curative and rehabilitative health services, of sufficient quality to be effective, while also ensuring that people do not suffer financial hardship when paying for these services[1].
- A medicine may not be universally reimbursed either because not included in the list of reimbursable medicines or because not all the population is covered by universal health insurance

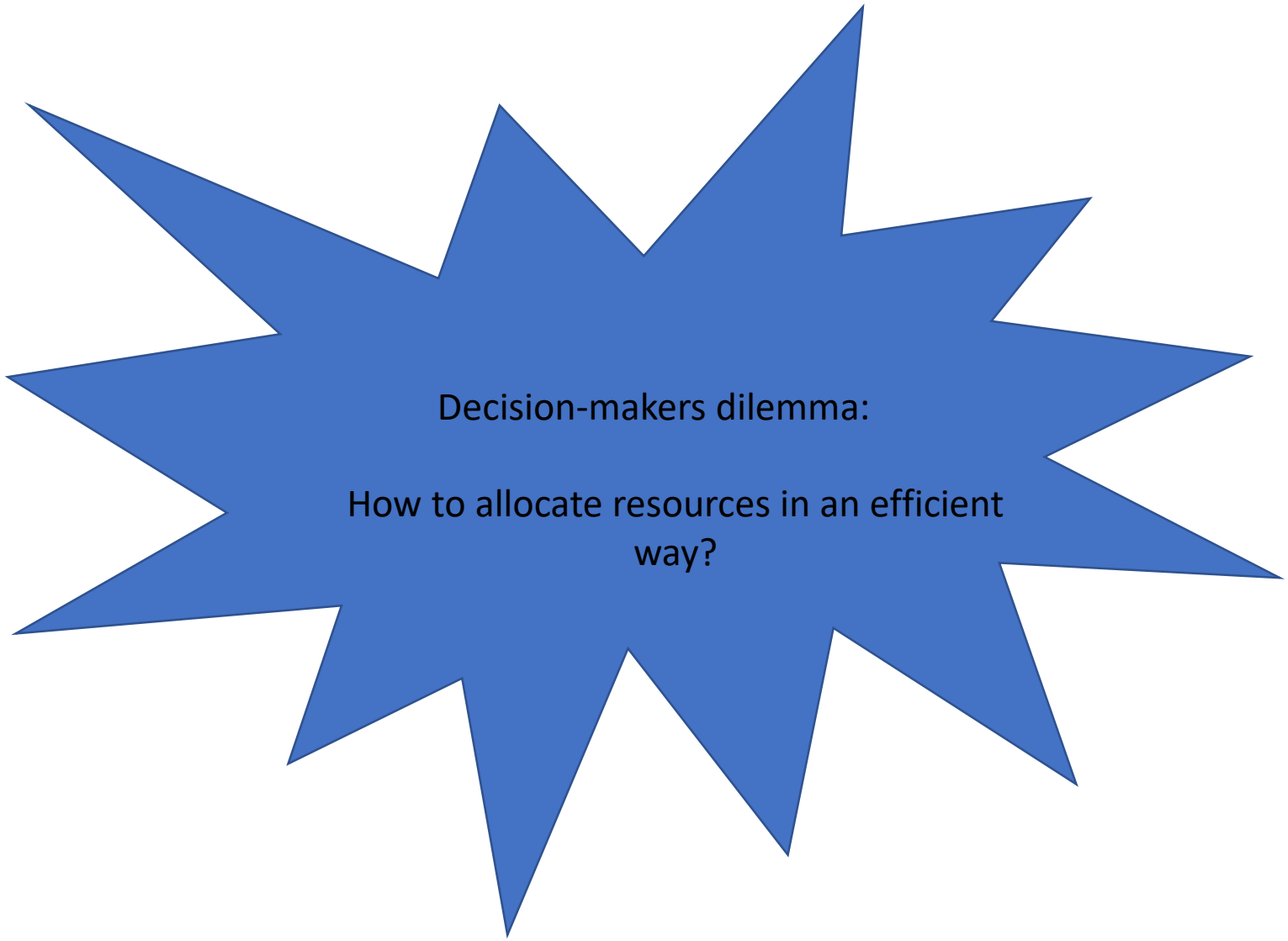
[1]http://www.who.int/healthsystems/universal_health_coverage/en/

Rationale for HTA

- How often should people over 50 year old be screened for colorectal cancer?
- Is the higher cost of a new medicine, in comparison to the current standard of care, justified in the light of the additional health benefits?

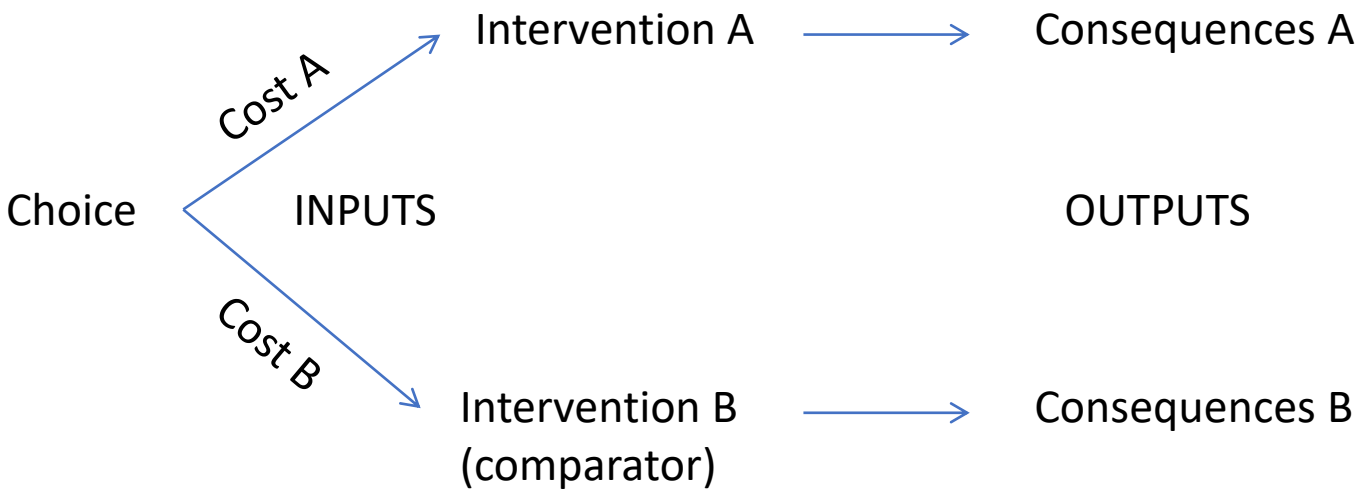
Why is it important to make these decisions?

- Scarce resources: needs > available resources
- Opportunity cost: We need to ensure that if we decide to launch an annual screening programme for diabetes these funds would not have been better spent delivering a hypertension programme


Decision-makers dilemma:
How to allocate resources in an efficient way?

Economic evaluation

- The comparative analysis of alternative courses of action in terms of both their costs and consequences (Drummond et al. 2005)



Adapted from Drummond et al. 2005

Drummond MF, et al. Methods for economic evaluation of health care programmes, 3rd Ed. Oxford University Press, 2005

Health technology assessment (HTA)

Incremental cost-effectiveness ratio (ICER)

$$\text{ICER} = \frac{\text{Cost of the new drug} - \text{Cost of current best practice}}{\text{Effect of the new drug} - \text{Effect of current best practice}}$$

Is it cost effective?

It depends…
on the country's willingness to pay (WTP) for the additional cost of gaining an extra unit of effect

HTA methods

$$\mathrm{ICER} = \frac{\Delta \mathrm{Costs}}{\Delta \mathrm{Effects}} < \mathrm{WTP}$$

Cost-effectiveness (CE)

- Natural units (e.g. a year of life, cm of growth, etc.) -> *Cost of per unit*

Cost-utility (CU)

- Quality adjusted life years (QALY) -> *Cost per QALY*

Cost-benefit

- Values health gains in monetary terms -> *How much do we get out of every Euro spent?*

Cost-minimisation

- Evidence shows that the two interventions are equally effective -> *Which of the two interventions costs less?*

Effect

$$\text{ICER} = \frac{\Delta \text{Costs}}{\Delta \text{Effects}} < \text{WTP}$$

- How is it measured?
  - Natural units (CE) vs. QALY (CU)
- Health outcomes
  - Variables:
    - Hard endpoints: overall survival, progression free survival
    - Surrogate markers: reduction in serum M-protein level (multiple myeloma), cholesterol reduction as a proxy for reduced risk of heart disease
  - Sources: RCTs, meta-analysis, observational studies, expert opinion or a combination
- Utility
  - Measuring health status: EuroQoL (EQ5D), Short-Form 6D (SF6D), Health Utilities Index (HUI), etc.

Costs

$$ICER = \frac{\Delta Costs}{\Delta Effects} < WTP$$

- Which costs are included?
  - Health sector: e.g. drug cost, health care staff time, etc.
  - Other sectors: e.g. nursing home care
  - Patient/family: e.g. transportation costs, carers time
  - Productivity losses

  -> It depends on the perspective of analysis (health system vs. societal) and varies across countries
- How are they measured
  - Marginal cost, average cost
- Data sources
  - Country specific

Willingness to pay (WTP)

$$\mathrm{ICER} = \frac{\Delta \mathrm{Costs}}{\Delta \mathrm{Effects}} < \mathrm{WTP}$$

- Country specific
- Generally countries are willing to pay more for end-of-life treatment, conditions with high unmet medical need
- England: £20,000-£30,000, higher for end-of-life
- Sweden: Variable
- Poland, Hungary: 2-3 times national gross domestic product (GDP) per QALY or life year gained
- Slovakia: €18,000-26,500

The role of other factors

	Belgium	England	Netherlands	Spain	Sweden
Cost-effectiveness	√	√	√	√	√
Budget impact	√		√	√	
Price	√				
Added therapeutic value			√		
Need and solidarity					√
Human value principle					√
Therapeutic value	√				
Therapeutic and social need	√			√	
Disease characteristics		√		√	
Specific needs of certain group of people				√	
Existence of alternative treatments				√	
Innovation				√	

Impact

- List
- Reject
- List with conditions:
  - Restriction on eligible patient population (i.e. more limited than marketing authorisation)
  - Temporary listing with request to provide real-life evidence -> **managed entry agreements**

Health technology assessment bodies

- National Institute of Health and Care Excellence (NICE) in England
- Scottish Medicines Consortium (SMC)
- Swedish Dental and Pharmaceutical Benefit Agency (TLV) in Sweden
- Agency for Health Technology Assessment in Poland (AHTAPol)

The role of NICE

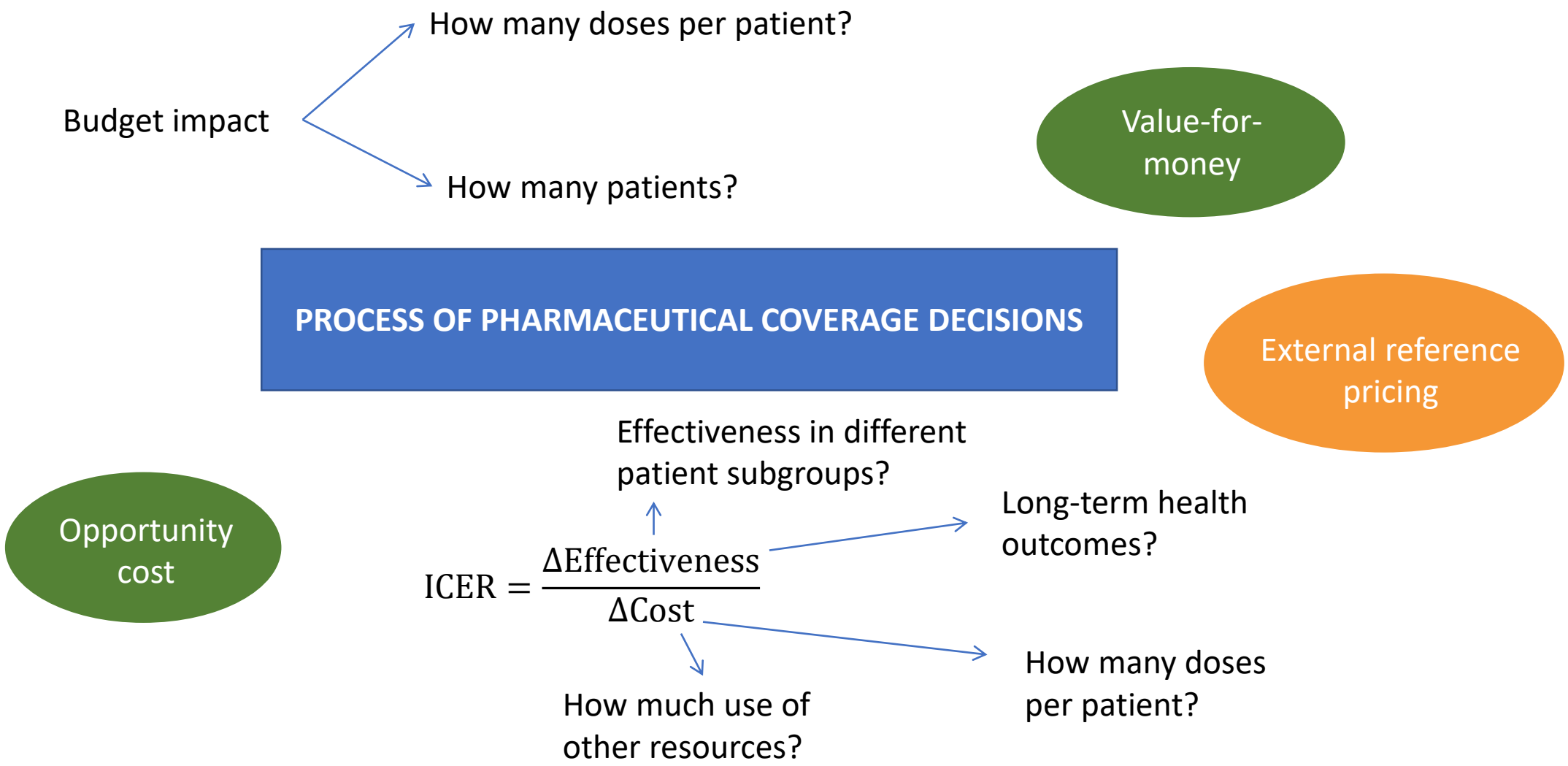
- In addition to **set standards and developing clinical guidelines,** NICE **assesses medical technologies** including medicines, medical devices, diagnostics, surgical procedures and health promotion activities
- Based on **clinical effectiveness** and **economics evidence**, it then makes a recommendation on whether a particular technology or procedure should be used routinely, and if yes under which conditions, in the NHS
- Local authorities are then legally obliged to make the necessary funds available to purchase the technology within 3 month of the publication of NICE recommendation
- Local authorities can still decide to make available technologies which have not been recommended by NICE. This is usually done on an individual basis by a committee assessing individual patient requests

http://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance

Impact

- List
- Reject
- List with conditions:
  - Restriction on eligible patient population (i.e. more limited than marketing authorisation)
  - Temporary listing with request to provide real-life evidence -> **managed entry agreements**

The context in which MEAs are introduced



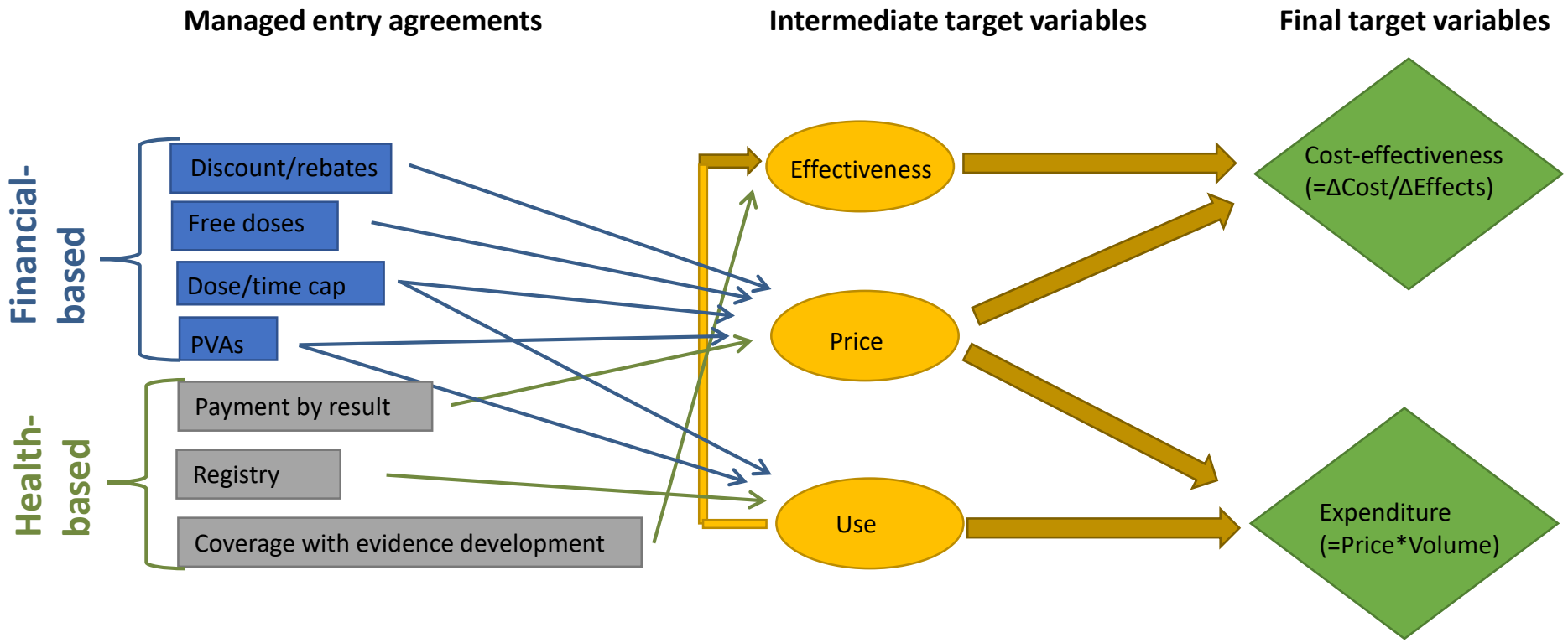
Managed entry agreements (MEAs)

- A MEA is an arrangement between a manufacturer and payer/provider that enables the reimbursement of a medicine subject to specific conditions (Klemp, *et al.* 2011)

- MEAs aim to:
  - mitigate the impact of uncertainty and high prices on cost-effectiveness and expenditure
  - enable patients to access promising new drugs in a context of uncertainty
- Two main groups:
  - health outcome based
  - financial based

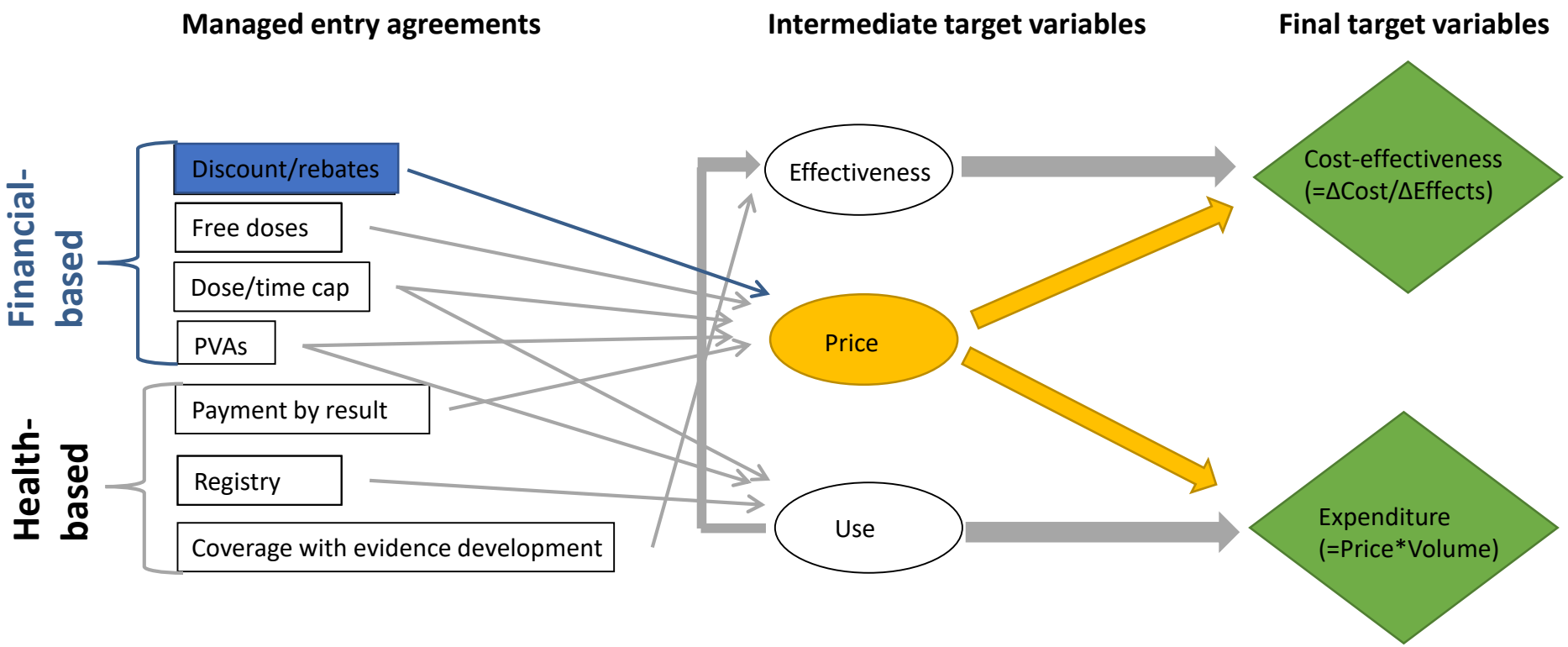
Klemp, M, KB Frønsdal, K Facey, and HTAi Policy Forum. 2011. What principles should govern the use of managed entry agreements? *Int J Technol Assess Health Care* 27 (1):77-83

How MEAs influence key parameters



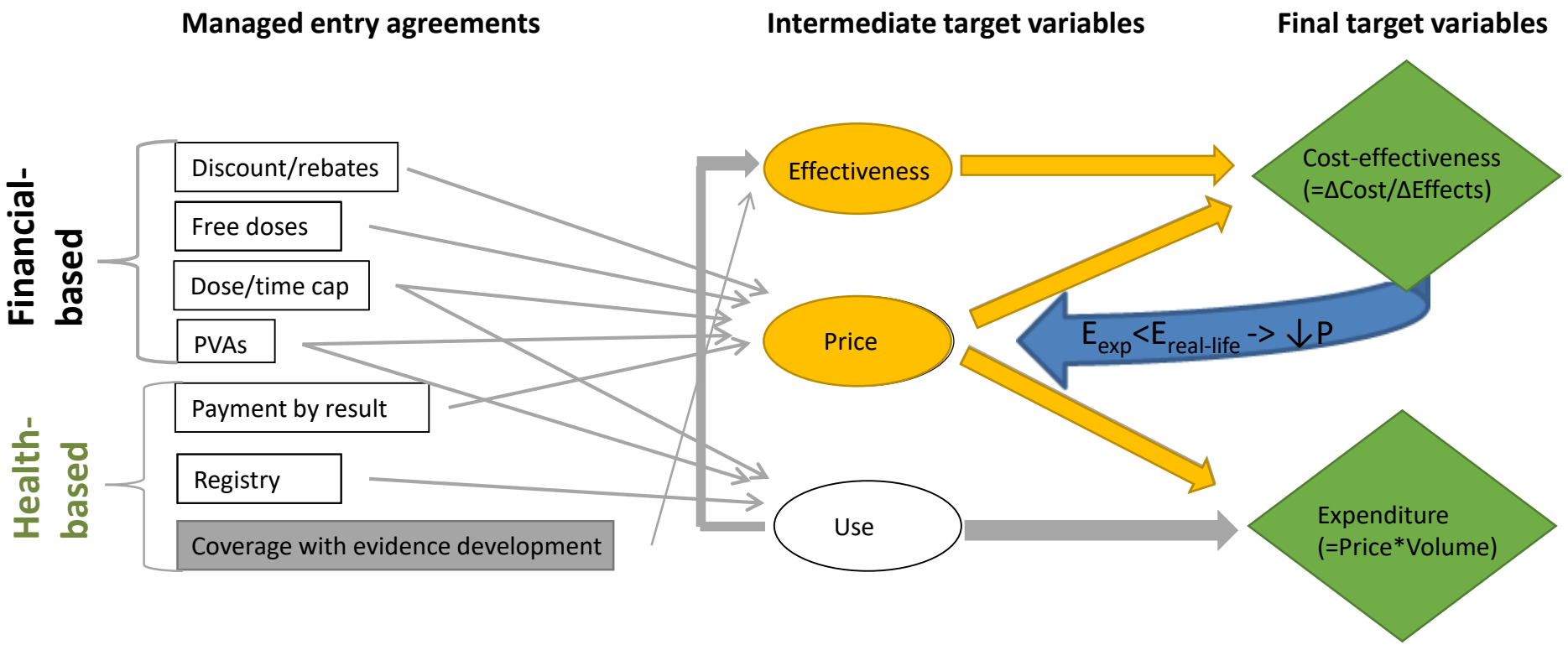
Source: Ferrario, A and Kanavos, P (2014), 'Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden', Social Science and Medicine

Example: Patient access schemes in England involving confidential discounts



Source: Ferrario, A and Kanavos, P (2014), 'Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden', Social Science and Medicine

Example: Coverage with evidence development in Sweden



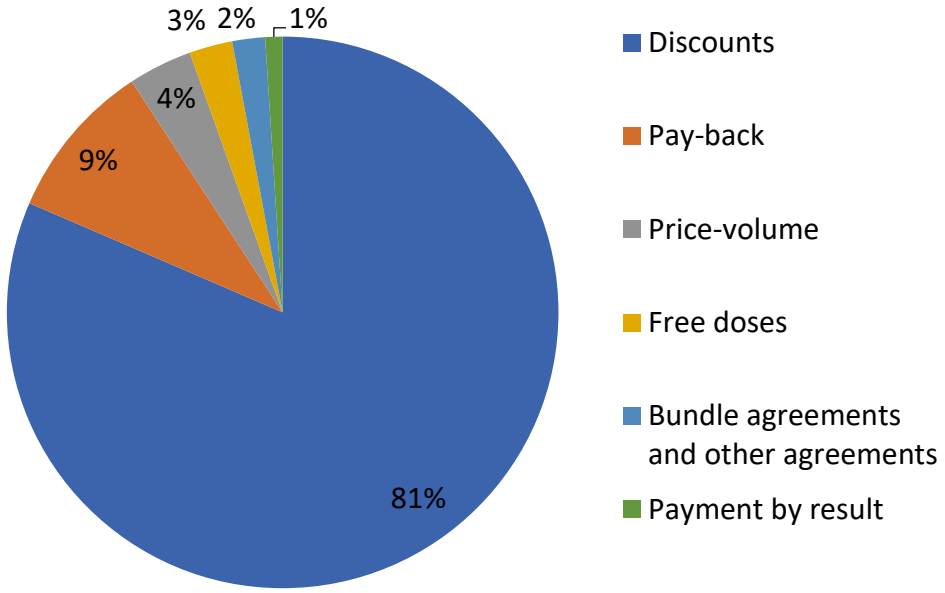
Levodopa/Carbidopa (Duodopa®) 2003-2008[1]

Temporal component

Source: Alessandra Ferrarioand Panos Kanavos (f2014), 'Dealing with uncertainty and high prices of new medicines: A comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden'; [1]Willis, M, Persson U, Zoellner Y, and Gradl B. Reducing Uncertainty in Value-Based Pricing Using Evidence Development : the case of continuous intraduodenal infusion of levodopa/carbidopa (Duodopa®) in Sweden. Appl Health Econ Health Policy. 2010;8(6):377-86

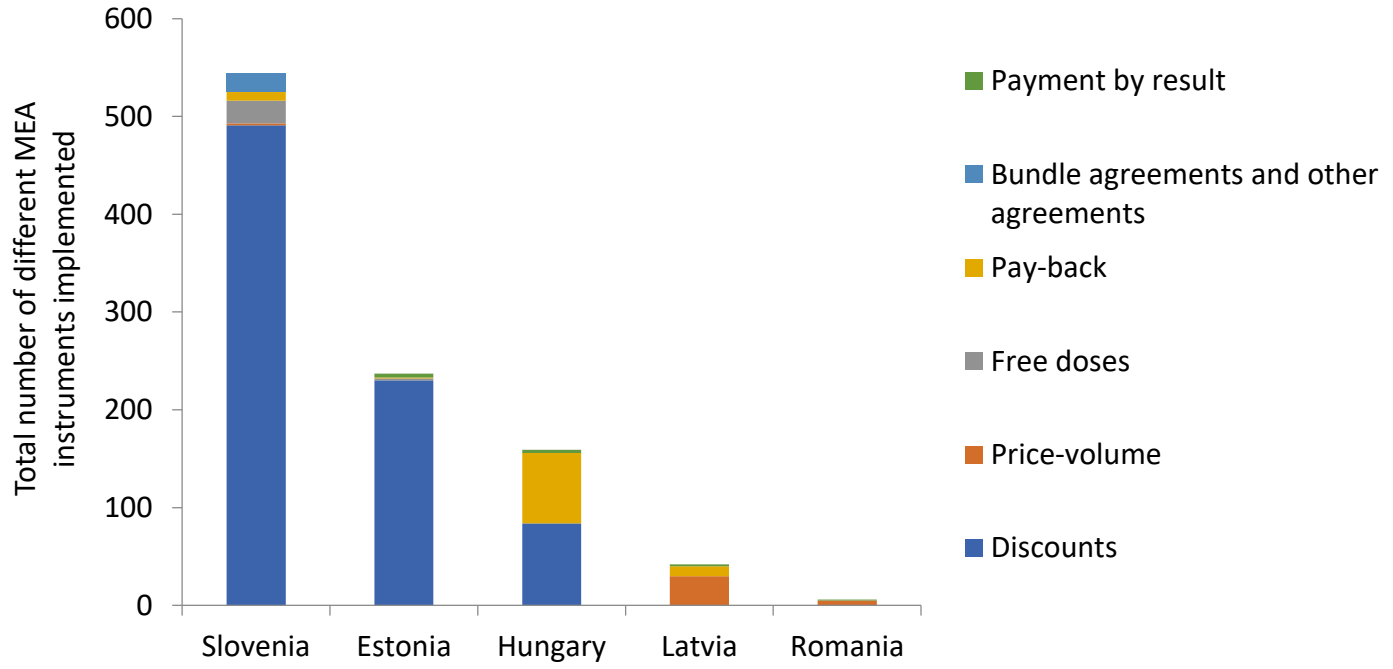
Types of MEAs - Overall

- Most frequently implemented MEA instruments in Slovenia, Hungary, Latvia, Estonia and Romania in 2016



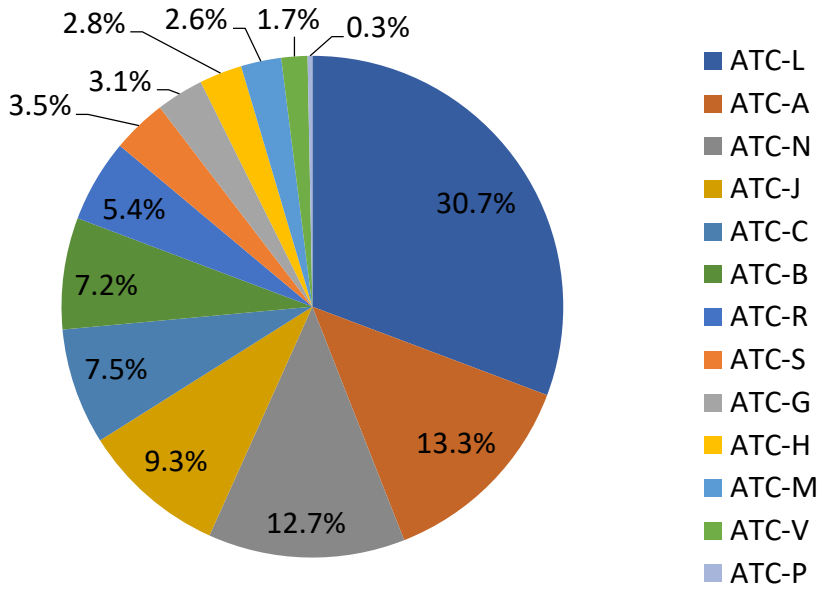
Types of MEAs – By country

- Number of MEA instruments implemented in Slovenia, Hungary, Latvia, Estonia and Romania in 2016



Therapeutic groups - Overall

- Therapeutic groups most frequently involved in MEAs in Bulgaria, Hungary, Lithuania, Latvia, Serbia, Estonia and Romania in 2015/16



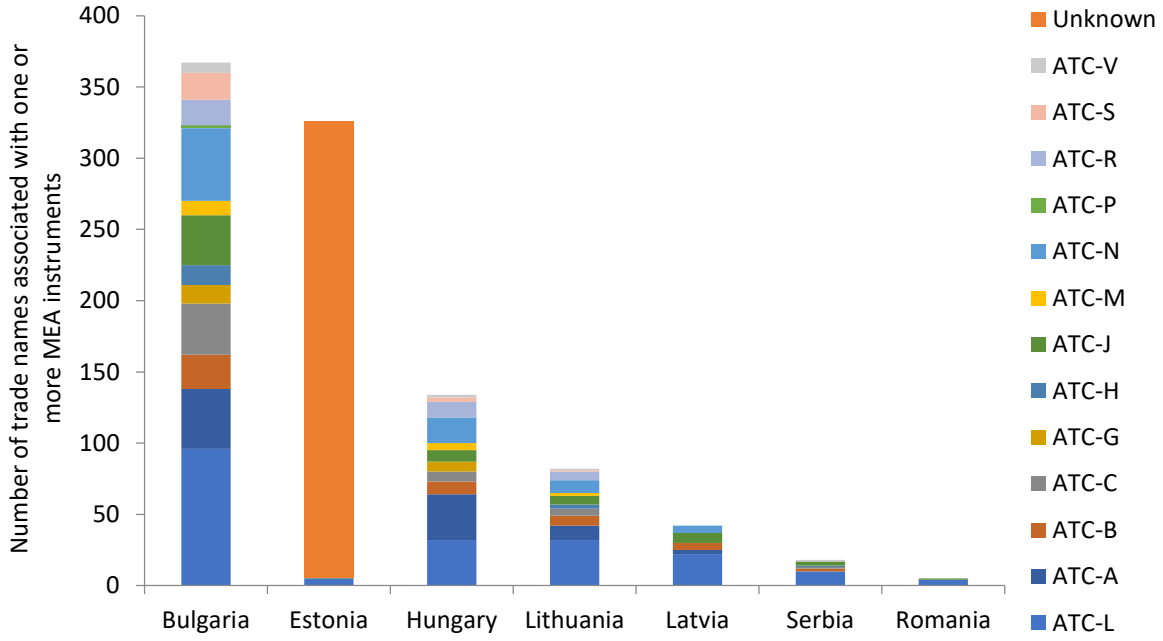
Note on Hungary

- Data in the pie chart include the outpatient sector only
- There are about 35 MEAs in the hospital sector
- About 25 of them were for oncology treatments (ATC-L01/02) and 10 contracts for other biologicals.

Data for Hungary, Latvia, Serbia, Estonia and Romania refer to 2016 while data for Bulgaria and Lithuania refer to 2015

Therapeutic groups – By country

- Therapeutic groups most frequently involved in MEAs in Bulgaria, Hungary, Lithuania, Latvia, Serbia, Estonia and Romania in 2015/16



Note on Hungary

- Data in the pie chart include the outpatient sector only
- There are about 35 MEAs in the hospital sector
- About 25 of them were for oncology treatments (ATC-L01/02) and 10 contracts for other biologicals.

Data for Hungary, Latvia, Serbia, Estonia and Romania refer to 2016 while data for Bulgaria and Lithuania refer to 2015

The situation is similar in Western Europe where financial agreements

- England, Scotland -> the majority of agreements are confidential discount agreements
- Netherlands -> started implementing coverage with evidence development then later moved to financial agreements
- Performance-based agreements are implemented only in a limited number of countries, for example:
  - Italy -> monitoring registries
  - Catalonia (Region of Spain)
  - Sweden -> financial agreements usually include a monitoring component through the Swedish quality registries

Issues with MEAs

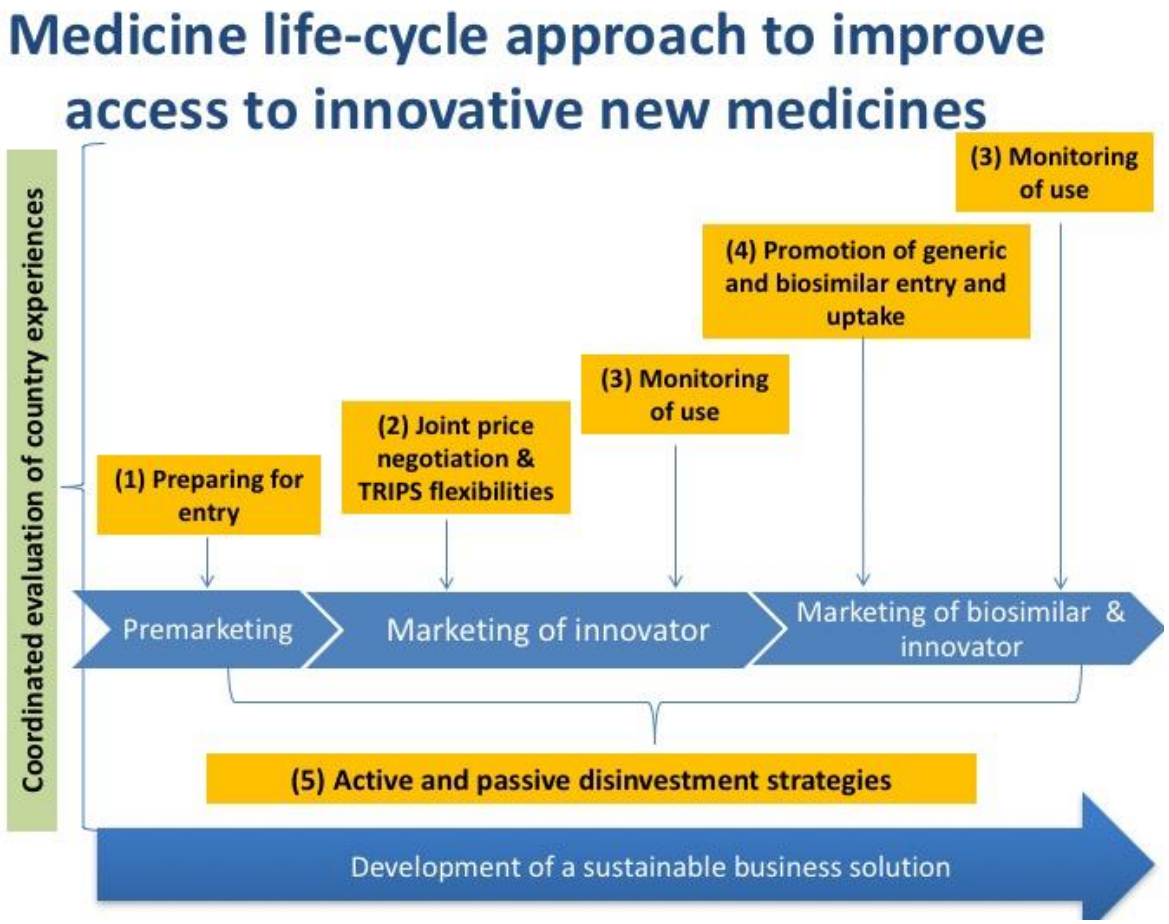
- Most agreements are confidential price agreements…and industry tells each country they got a really good deal…only industry knows prices in all countries…
- Even with discounts, prices are still very high and the number of patients treated may be more limited than per marketing authorisation due to budgetary restrictions

➢Inequalities in access

➢Threat to financial sustainability of health and pharmaceutical systems

- WHO fair pricing forum
- OECD consultation on sustainable access to innovative therapies
- Many proposals with limited implementation: de-link final price from R&D costs, voluntary pooled licensing
- Bottom-line, there is still no agreed upon solution

Possible way forward to promote sustainable access and use of medicines



Source: Ferrario A, Wirtz V, Improving access to innovative therapies: Expanding existing solutions and promoting new models, submission to the OECD consultation on sustainable access to innovative therapies, 29 April 2017

Thank you!

Alessandra Ferrario
a.ferrario@lse.ac.uk
a.ferrario@sunrise.ch