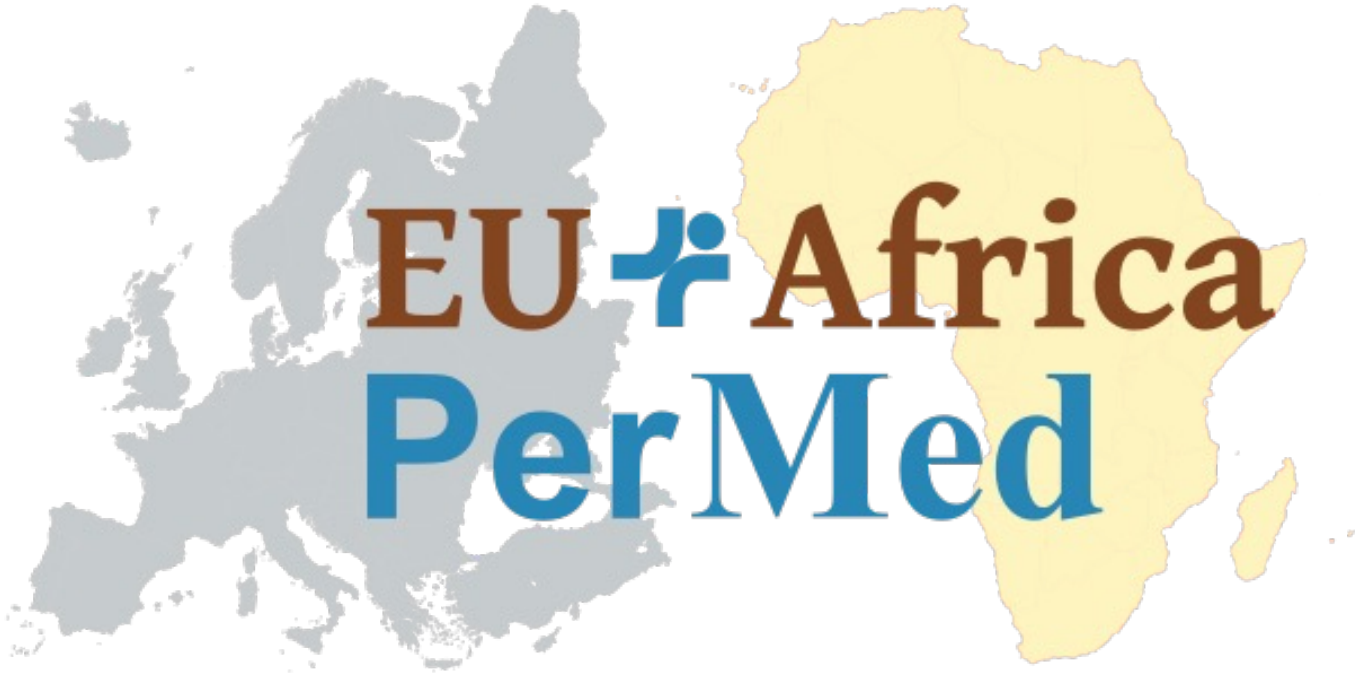
5th Webinar

"The role of Health Technology Assessment (HTA) under the Personalised Medicine (PM) approach"



FRIDAY, 14th April 2023

Dr Ramiro Gilardino

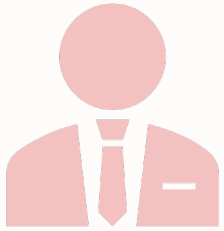
BUILDING LINKS BETWEEN EUROPE AND AFRICA IN PERSONALISED MEDICINE

EU-Africa PerMed has received funding from the European Union's Horizon 2020 Research and Innovation programme under grant agreement No 964333

5th Webinar “The role of Health Technology Assessment (HTA) under the Personalised Medicine (PM) approach”

- What is HTA?
- What is the aim of HTA ?
- How HTA and value assessment could support PM approaches?

Disclaimer



I am employed by MSD International

My company was not involved in the development or sponsoring of this session

Opinions and view in this presentation are my own

Health Technology Assessment

A multidisciplinary process that uses explicit methods to determine the **value** of a **health technology** at different points in its lifecycle.

The purpose is to **inform decision-making** in order to promote an equitable, efficient, and high-quality health system.

O'Rourke et al. (2020) Int J Technol Assess Health Care. Jun;36(3):187-190.
Tsoi B, Masucci L, Campbell K, et al. (2013) Expert Rev Pharmacoecon Outcomes Res. Aug;13(4):497–511.

Differences between Regulatory and HTA

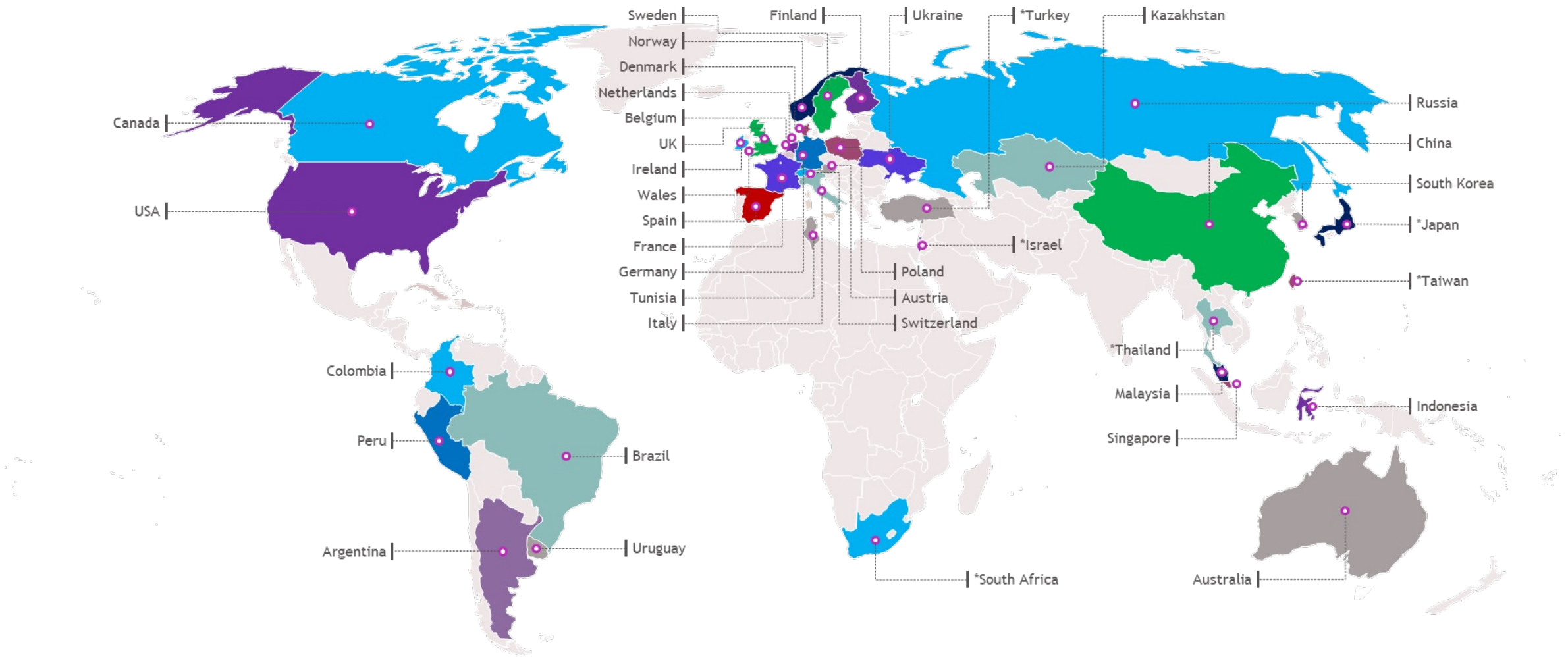
	Regulatory Approval	HTA / Coverage
Legal Authority	Typically **defined in national public health legislation** with a **regulatory body** accountable to the government in their jurisdiction. In the European Union (EU), there are two main routes for authorizing medicines: a **centralized** route and a **national** route.	Typically defined **within the rules and regulations of the health care system** in which decision are made and are **accountable to the health care system within which they operate**. In certain circumstances, **its role** and **responsibilities** are **defined in legislation** and, as such, the **body may be accountable to the government**.
Primary Role	**Market authorization** of a product in the relevant jurisdiction on the basis of an assessment on safety, quality, efficacy, and risk-benefit profile.	**Coverage/reimbursement of a product within a particular health care system** on the basis of assessment on relative effectiveness, costs and in some, system affordability, value for money, priorities, and values within the system
Decision	Does the product do **more good than harm** for patients with **defined target indication**? Should this technology **be available**?	Does product offer **useful**, **appropriate** (and **affordable**) **benefits for all** or a **select subgroup** of patients in this health care system **compared to what is most commonly used in the disease area**? Should we **buy this technology at the current price**?
Type of Evidence	**Safety** **Efficacy** **Quality** (i.e. good manufacturing practices)	**Safety** **Relative Effectiveness** **Economics** and **budgetary impact** **Social**, **ethical**, **legal**, **organizational impact**

Tsoi B, Masucci L, Campbell K, et al. (2013) Expert Rev Pharmacoecon Outcomes Res. Aug;13(4):497–511.

HTA is Cost-Effectiveness

An economic evaluation (like cost-effectiveness assessment) could be part of the HTA process, but it does not constitute itself as HTA.

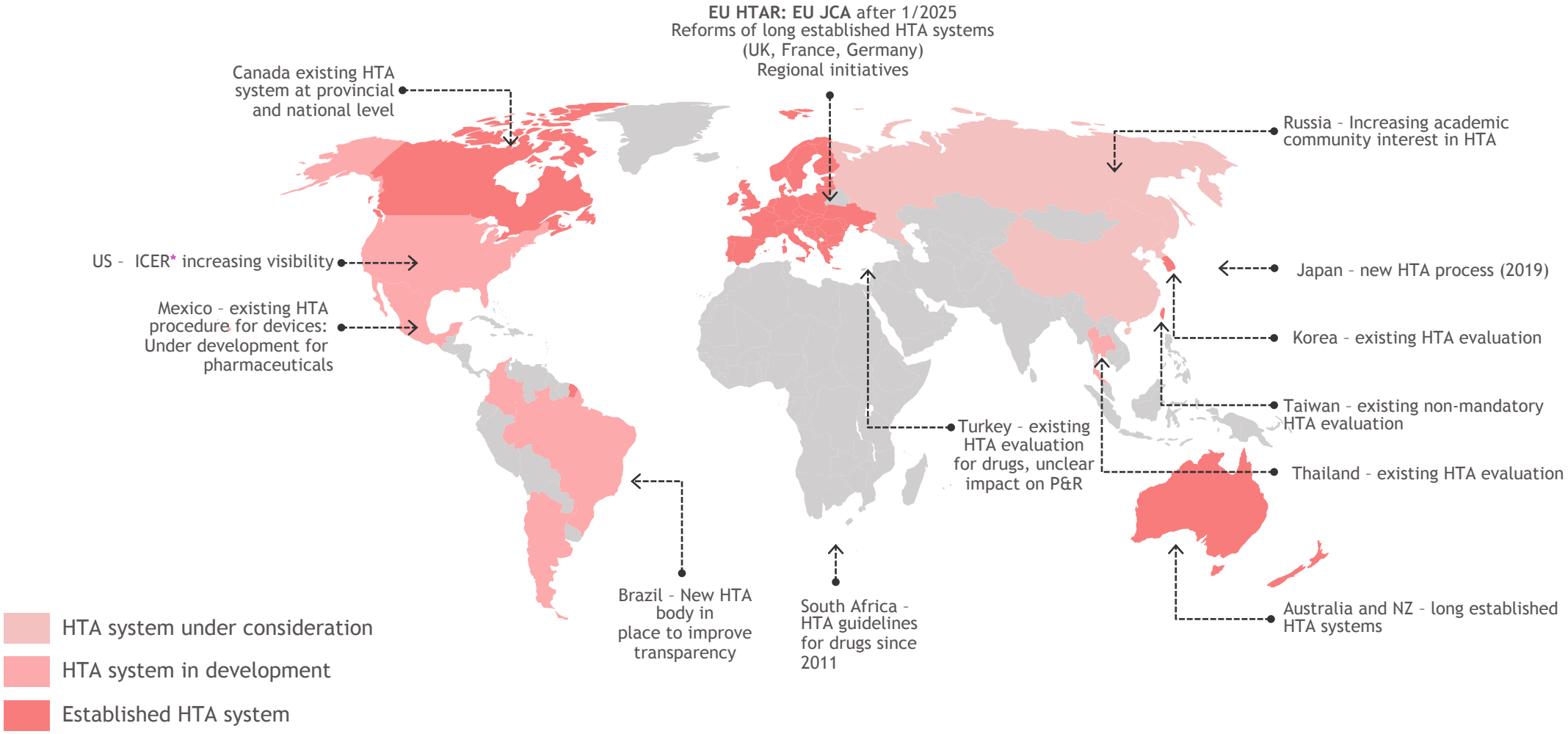
HTA Agencies Global Landscape



HTA organisations currently listed as members of HTAi or INAHTA

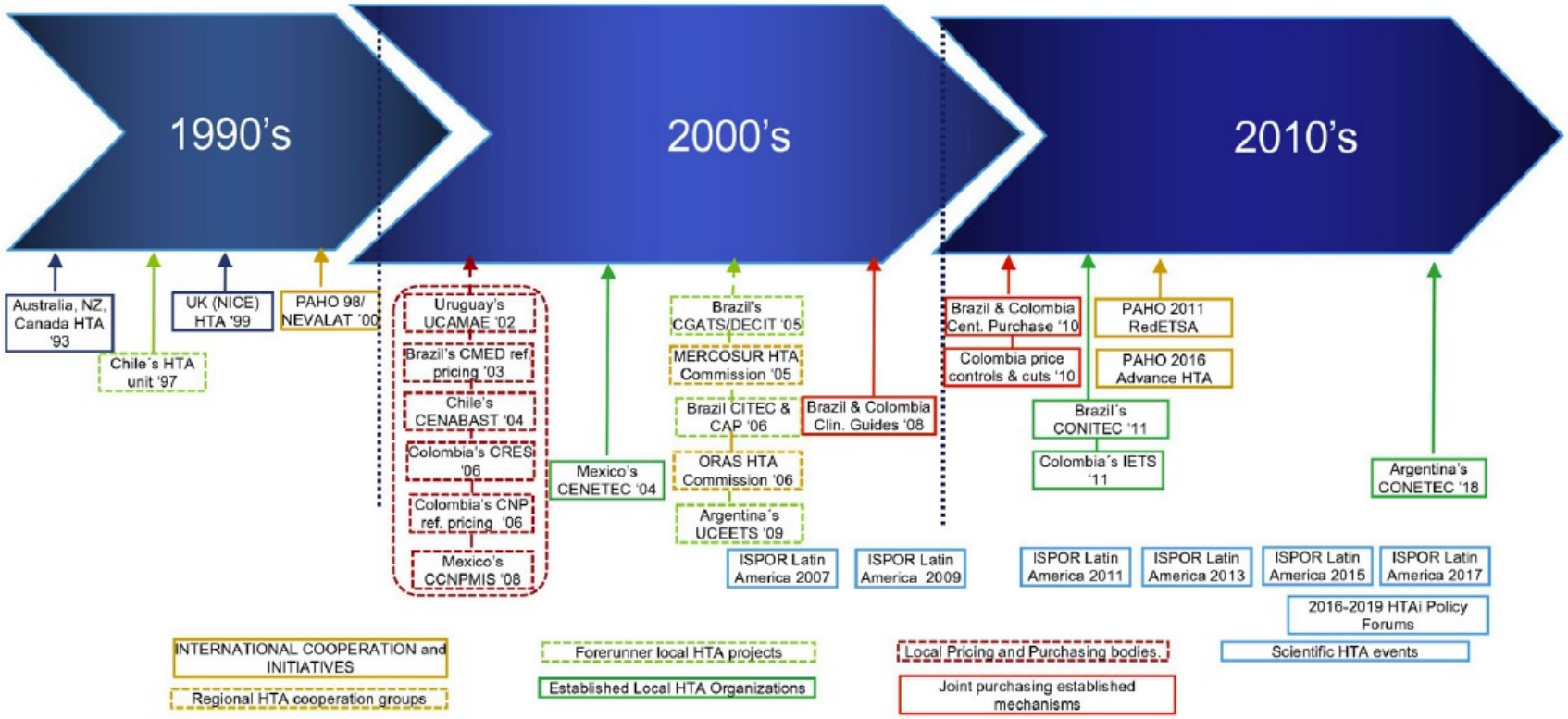
*Non currently listed by HTAi or INAHTA

However, HTA bodies are in different stages of development



*ICER is an example of a non-governmental HTA organisation without any explicit reimbursement decision-making power

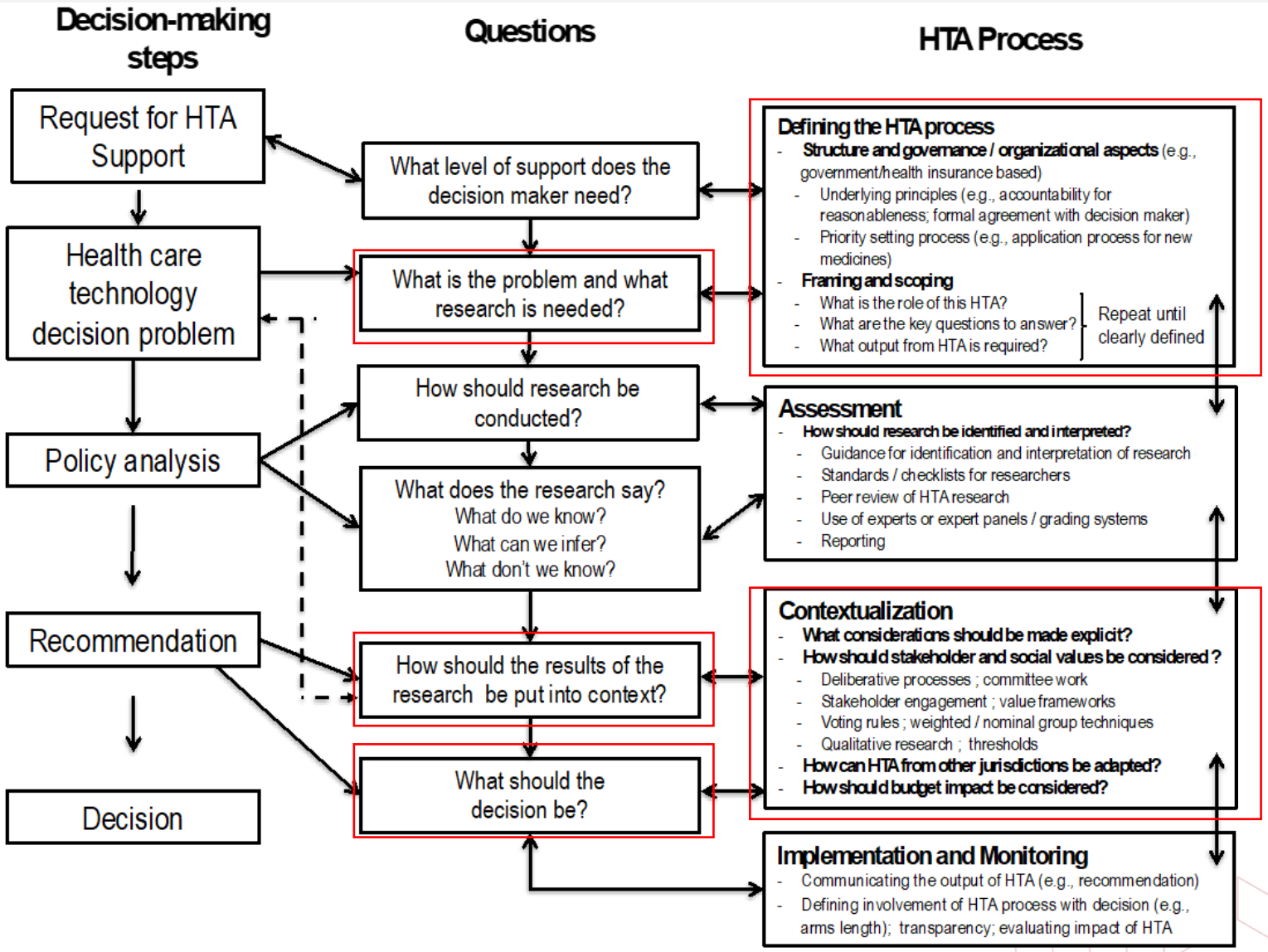
Natural evolution of HTA in an emergent region: LATAM



UCAMAE: Unidad Centralizada de Adquisición de Medicamentos y Afines del Estado; CMED: Câmara de Regulação do Mercado de Medicamentos; CENABAST: Central de Abastecimiento del Sistema Nacional de Servicios de Salud; CCNPMIS: Comisión Coordinadora para la Negociación de Precios de Medicamentos e Insumos para la Salud; DECIT-CGATS: Coordenação Geral de Avaliação de Tecnologias em Saúde; Departamento de Ciência e Tecnologia; CITEC: Comissão de Incorporação de Tecnologias do Ministério da Saúde; UCEETS: Unidad Coordinadora de Evaluación y Ejecución de Tecnologías en Salud.; ORAS: Organismo Andino de Salud. CONETEC: National Commission of Health Technology Assessment HTAi: Health Technology Assessment International

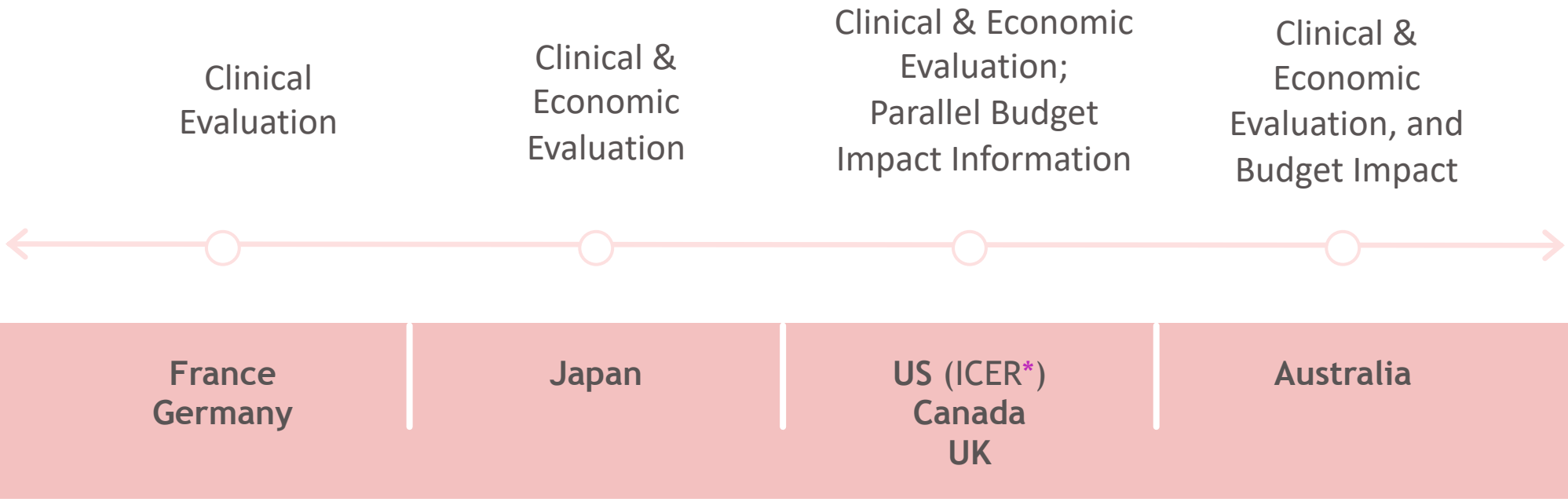
Gilardino R, Mejia Ae, Rey-Ares L et al. (2020) Val Healt Reg Issues; 23: 6-12

Components of HTA within the Healthcare Decision-Making Process



Børlum Kristensen F, Husereau D, Huić M, et al. (2019) Value Health Jan;22(1):13-20.

HTA does not have a single assessment framework

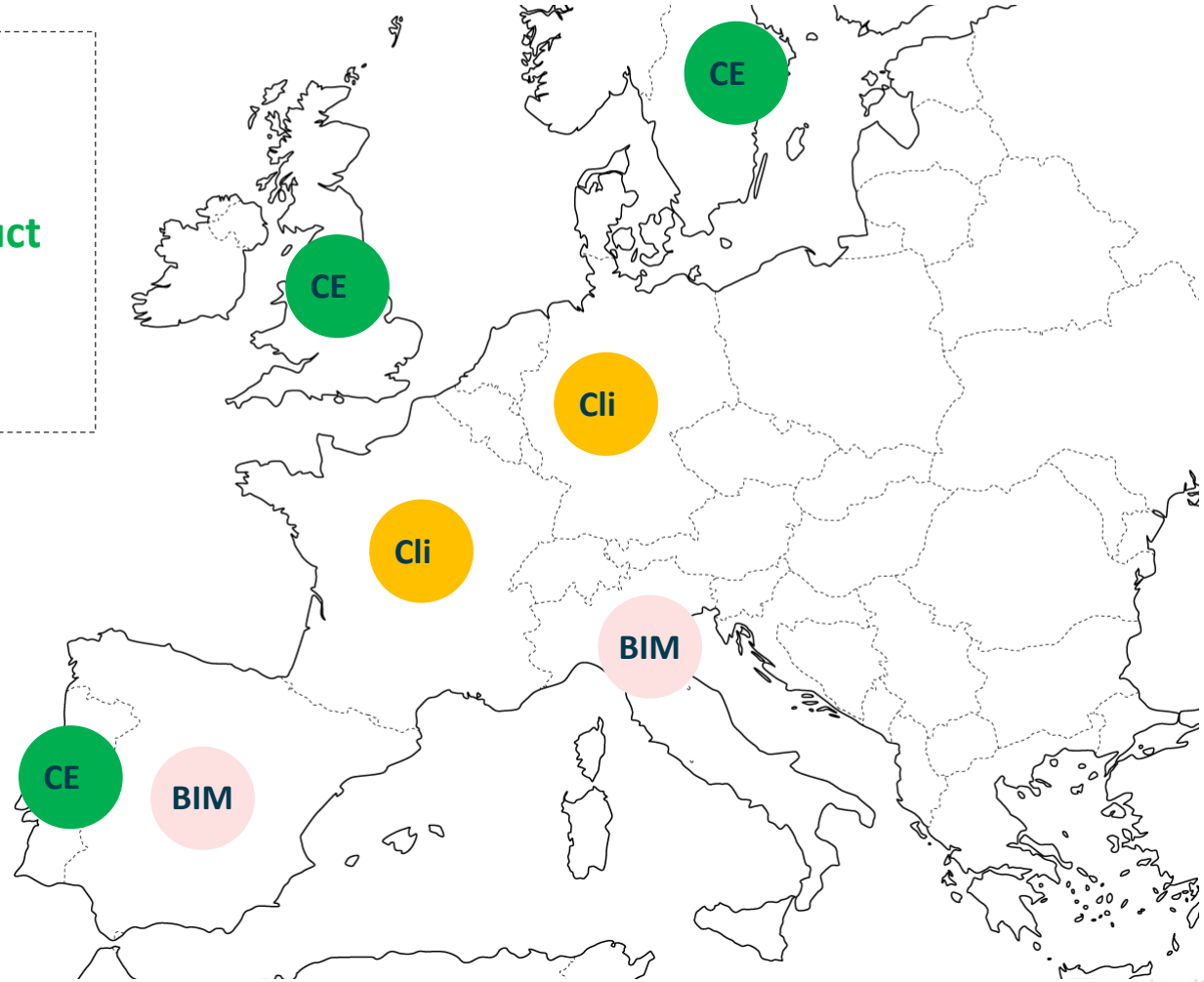


*ICER is an example of a non-governmental HTA organisation without any explicit reimbursement decision-making power
Source: White paper from the USC Schaeffer Center- HTA for the US Healthcare System, February 2020

Differences of HC systems model and value assessment priorities, among other characteristics, leads to different payer archetypes

- HTA body: NICE
- Key value driver: **cost-effectiveness of the product**
- CE = Benefit of the intervention / cost

- HTA body: MoH and regions (decentralized)
- Key value driver: **Budget Impact Model** (price driven)



- HTA body: IQWIG and GBA
- Key value driver: **clinical efficacy**, patient reported outcomes

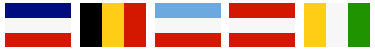
- HTA body: HAS
- Key value driver: **clinical efficacy**

https://www.who.int/teams/health-product-policy-and-standards/assistive-and-medical-technology/medical-devices/assessment

Activities:
- Horizon scanning
- HTA
- Information sharing
- Pricing and reimbursement (potentially) leading to joint negotiations
- Six assessments and two pilots on joint pricing concluded

Beneluxa

Countries involved:
The Netherlands, Belgium, Luxembourg, Austria, Ireland



42 M citizens –
Started:2014

Activities:
- Participation in expert meetings
- Exchanging information
- Organizing pilot negotiations

The fair pricing Initiative (FAAP)

Countries involved:
Hungary, Poland, Slovakia, Lithuania, Czech Republic (observer), Latvia (invited)

69 M citizens –
Started: May 2017

Activities:
- Share information and good practice
- Identify areas of cooperation, objectives and scope of work
- Joint assessment and negotiation for selected medicines

La Valletta

Countries involved:
Croatia, Cyprus, Greece, Ireland, Italy, Malta, Portugal, Romania, Slovenia, Spain

160 M citizens –
Started: May 2017

Activities:
- HTA
- Health economic assessment
- Information sharing
- Pricing and reimbursement (potentially) leading to joint negotiations
- Six assessments and two pilots on joint pricing concluded

Finose

Countries involved:
Norway, Sweden, Finland (Denmark)

20,5 M citizens –
Started: March 2018

Activities:
- COVID-19,
- Collaboration with regulators,
- Work-sharing and efficiency gains,
- Digital Heath and AI
- Future proofing of HTA systems.

Multi Country Collaboration

Countries involved:
Australia, Canada, Ireland, United Kingdom

130M citizens –
Started:
Sept 2022

2014 — **2016** — **2017** — **2018** — **2020** — **2022**

EUNETHTA JOINT ACTION III (2016-2020)

Started: Follows and builds on EUNETHTA JAI (2010-2012) and II (2012-2015)
Involves 83 partners (medicines agencies, payers, health ministries…) from across Europe

EU HTA Regulation mandate under DG Sante (EUnetHRA 21 secretariat)

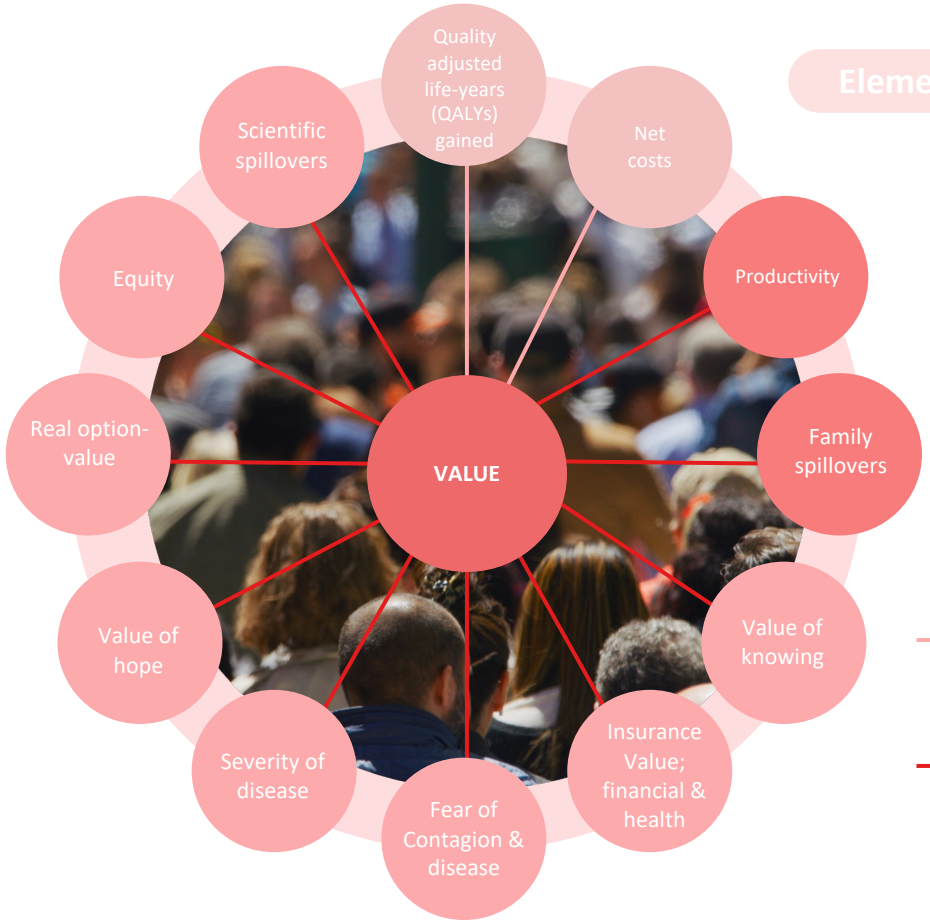
Value, Dimensions of Value and Value Frameworks

Value in healthcare

- Value is what someone is (actually) willing to pay or forgo to obtain something (opportunity cost).
- Value varies over time and value measurement in healthcare is difficult.

The dimensions of value

- Dimensions can include clinical and economic dimensions, in addition to ethical, social, cultural, legal issues, organizational / environmental aspects, and wider implications for the patient, relatives, caregivers, and the population.
- Are assessed by examining the intended and unintended consequences of using a health technology compared with existing alternatives.



Adapted from Garrison L; Value in Health, 20(2017) 213 – 216

What is included under the definition of HTA?

A Health Technology[1]

- is an intervention developed to **prevent**, **diagnose**, or **treat** medical conditions; **promote health**; **provide rehabilitation**; **or organize healthcare delivery**.
- The intervention can be a **test**, **device**, **medicine**, **vaccine**, **procedure**, **program**, or **system**

The dimensions of value[1]

- Are assessed by examining the **intended and unintended consequences** of using a health technology **compared with existing alternatives**.
- These dimensions often include **clinical effectiveness**; **safety**, **costs**, and **economic implications**; **ethical, social, cultural and legal issues**; and **organizational** and **environmental aspects**, as well as wider implications for the patient, relatives, caregivers, and the population.
- The overall value may vary depending on the perspective taken, the **stakeholders involved**, and the **decision context**.

The process[1]

- is **formal**, **systematic**, and **transparent**, and it uses **state-of-the-art methods** to consider the **best available evidence**

Can be applied[1]

- At **different points in the lifecycle of a health technology**

(ie, pre-market, during market approval, post-market, and through to the disinvestment of a health technology)

Definition of value differs greatly by country and HTA agency

	Country	Germany	France	UK	Australia	Canada[1]	USA	South Korea	Japan
	HTA agency	*IQWiG/ DAHTA*	*HAS/CEPS*	*NICE, SMC, AWMSG*	*PBAC*	*CADTH*	*ICER*	*HIRA*	*Chuikyo/C2H*
Elements used to input into value decisions	Unmet need	✓	✓	✓	✓	✓	✓	✓	✓
	Comparative clinical effectiveness	✓	✓	✓	✓	✓	✓	✓	✓
	Cost-effectiveness	✗	✓	✓	✓	✓	✓	✓	✓
	Budget impact	✗	✓	✓	✓	✓	✓	✓	✗
	Formal patient input	✗	✓	✓	✓	✓	✓	✓	✗
	Level of innovation	✗	✓	✗	✗	✓	✓	✗	✗
	Equity considerations	✗	✗	✓	✓	✓	✗	✗	✗
	Direct medical	✓	✓	✓	✓	✓	✓	✓	✓
	Direct non-medical (e.g., transportation/day care)	✗	✗	✗	✗	✗	✗	✗	✗
	Indirect (e.g., time lost from work)	✗	✗	✗	✗	✗	✗	✗	✗
	Intangible (e.g., pain and suffering)	✗	✗	✗	✗	✗	✗	✗	✗

AWMSG: All Wales Medicines Strategy Group; , C2H: Core 2 Health; CADTH: Canadian Agency for Drugs and Technologies in Health; CEPS: Economic Committee of Health Products; Chuikyo: Central Social Insurance Medical Council; DAHTA: German Agency for HTA; HAS: Haute Autorité de Santé; HIRA: Health Insurance Review and Assessment service; ICER: Institute for Clinical and Economic Review; IQWiG: Institute for Quality and Efficiency in Healthcare. NICE: National Institute for Health and Care Excellence; PBAC: Pharmaceutical Benefits Advisory Committee; SMC: Scottish Medicines Consortium.

What are those attributes of value?

	Terkola (2017) US / Ex-US	Brogan (2019) US / Ex- US	Jakab (2021) US
Core Element of Value	Efficacy and Effectiveness	Patient improvement in outcomes	
	Safety (side effects)	Clinical Benefit	
		Cost per QALY	
Common Element of Value	Resource and cost implications associated with complications	Budget Impact	
	Investment on treatment	PRO linked to cost	
		Comparative Effectiveness	
		Treatment options	
Potential New Elements of Value	Dignity of individualism of patient	KOL	Real Option Value
	Patient time to feeling well	Site of care	Value of Hope
			First treatment options
			Severity of Disease
			Caregiver QoL

Yes Partial No

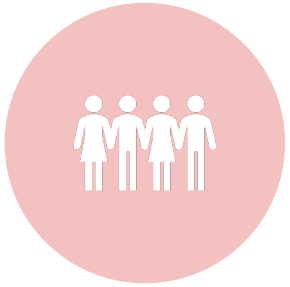
1. Terkola R, Anto anzas F, Postma M. Eur J Hosp Pharm. 2017; doi:10.1136/ejhpharm-2017-001295.
2. Brogan A, Hogue SL, Vekaria R, et al. J Manag Care Spec Pharm. 2019;25(12):1319-27
3. Jakab I, Whittington MD, Franklin E, et al. Front. Pharmacol. 2021; 12:690021.doi: 10.3389/fphar.2021.690021

HTA fits for Personalized Medicine

- HTA on PM focuses on assessing the effectiveness, safety, and cost-effectiveness of diagnostic tools and treatments that are tailored to individual patients based on their genetic, environmental, and lifestyle factors.
- HTA can provide important information to support decision-making in the adoption, funding, and use of these technologies in clinical practice.

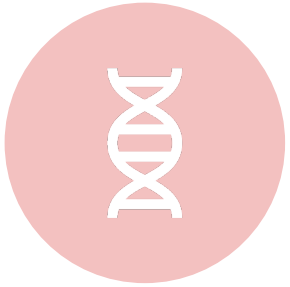
HTA fits for PM?

Current approaches to economic evaluation to support decision making are largely focused on reimbursement of drugs.



Drug reimbursement evaluations are typically population based, involving single interventions in single populations.

Because PM, leads to restricted populations or individual care there are questions as to whether current approaches to economic evaluation are adequate for PM interventions.

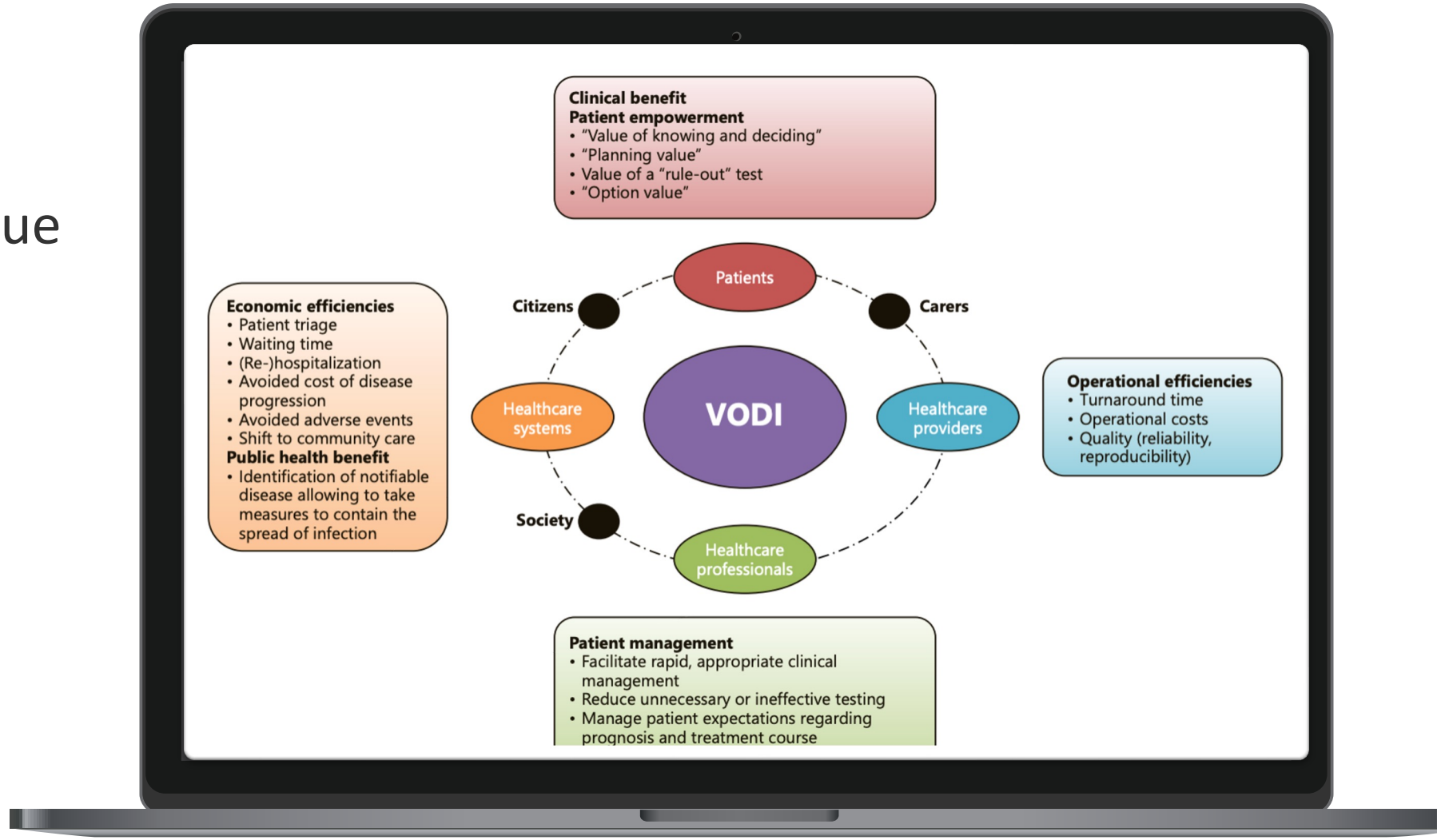


HTA agencies' experience of PM has primarily been with diagnostic and companion diagnostic tests (those that identify biomarkers correlated with treatment response such as the HER2 receptor protein for breast cancer)

Love-koh, J. PharmacoEconomics (2018) 36:1439–1451

Value of Diagnostic Information (VODI) Framework

- An approach to demonstrate the value of diagnostic tests.



Wurcel et al. Public Health Genomics 2019;22:8–15 DOI: 10.1159/000501832

Example of VODI system level approach

Value of Knowing for Patients

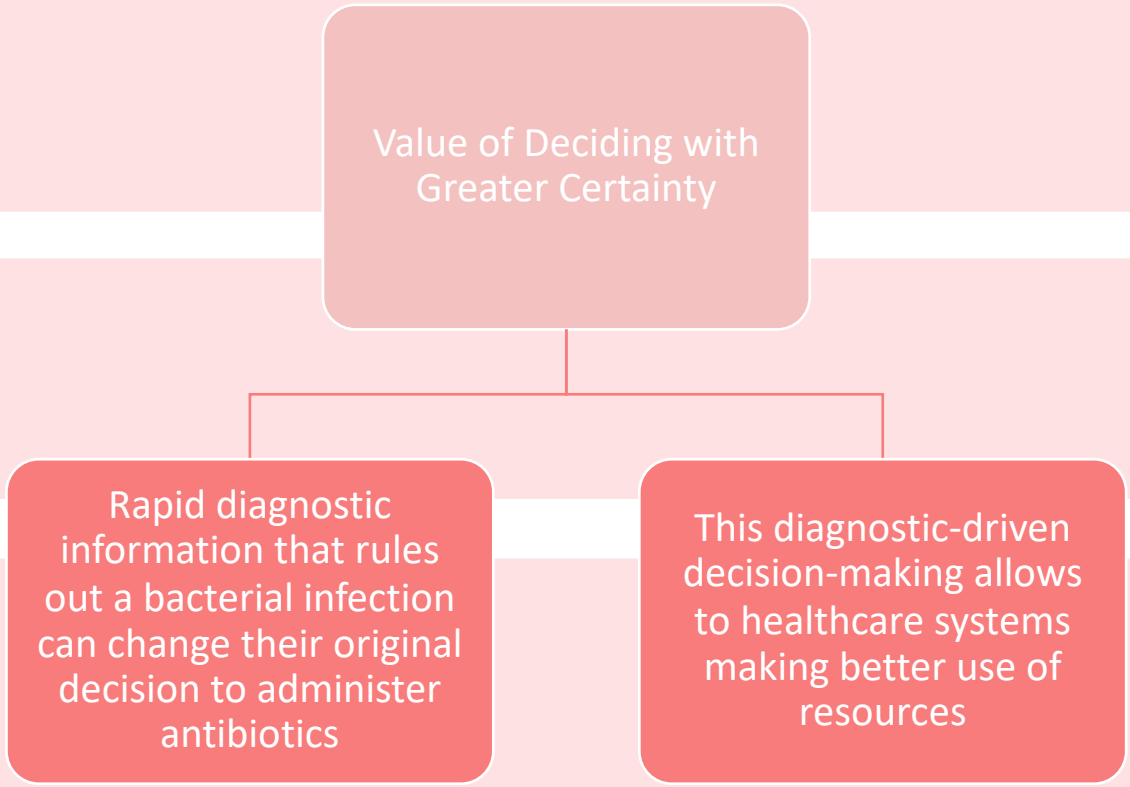
- The well-being value comes from the reassurance or the sense of self-control provided by knowing.
- The dimension of "knowledge and understanding" is the most cited reason for taking the test (38%), followed by life planning (17%)
- The patient receiving diagnostic information about the presence of a chronic condition (e.g., high cholesterol, diabetes) may attempt to pursue a healthier lifestyle.

Relevant Patient Outcomes Facilitated by Diagnostic Information

- Knowing health status or prognosis empowers patients' choices about their own health status, and on reproduction, work, retirement, long-term health, and end-of-life management ("value of knowing and deciding").
- Empowerment and an increased sense of well-being and satisfaction due to being in charge of their health

VODI for Health Systems

- Reduce costs related to in-hospital stay and outpatient visits, through early identification and prevention
- Improve the efficiency of care delivery by better targeting of treatment and monitoring of "at risk" individuals
- Maximising the cost-effectiveness of available treatments by selecting the population that will most likely respond and be less likely to experience adverse events



Wurcel et al. Public Health Genomics 2019;22:8–15 DOI: 10.1159/000501832

Experience with treatments with prospect of cure, has further validated the Value Flower

Value of hope

Many patients are willing to sacrifice some life expectancy for the chance for a cure

Severity of disease

Greater willingness to pay for more severe diseases (beyond the QALY loss)

Fear of contagion

A psychic externality due to worry about spread of infectious disease (e.g., Covid and Zika viruses)

Insurance value

- Financial risk protection AND
- Health risk protection
- Can adjust for severity and rarity;
- In “Extended CEA” used in global health

Reduction in uncertainty due to Dx test (also called “Value of Knowing”)

- Test-drug combination more valuable
- Value in prognosis

Real option value

- Investing in a life-extending treatment provides more value in disease area with more promising pipeline

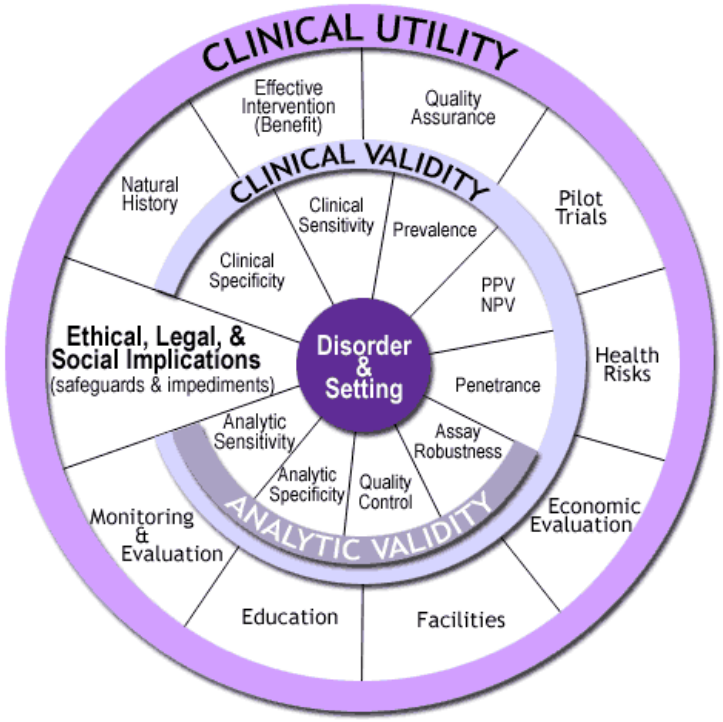
International Journal of
Environmental Research and Public Health

MDPI

Review

A Systematic Review of the Value Assessment Frameworks Used within Health Technology Assessment of Omics Technologies and Their Actual Adoption from HTA Agencies

Ilda Hoxhaj [1,†], Laurenz Govaerts [2,3,*,†], Steven Simoens [3], Walter Van Dyck [2,3], Isabelle Huys [3], Iñaki Gutiérrez-Ibarluzea [4,‡] and Stefania Boccia [1,5,‡]



Twenty-two frameworks, which addressed genetic and/or genomic technologies, evaluating analytical validity, clinical validity and clinical utility domains.

3.4. HTA Reports

We identified forty-five HTA reports [39–83] conducted from agencies in 15 different countries, mainly in Europe and Canada. The subjects of the assessment were predominantly the commercial transcriptomic prognostics Mammaprint, OncotypeDx, Endopredict and Prosigna (48%), and the genomic technology—next generation sequencing (22%). Based on the definition of HTA, the following evaluation domains in the assessment reports were considered [9]: clinical effectiveness (38/45; 84%); costs and economic evaluation (33/45; 73%); description and technical characteristics (31/45; 69%); health problems (28/45; 62%); safety (49/45; 49%); organizational aspects (14/45; 31%); ethical analysis (10/45; 22%) and social aspects (10/45; 15%). Although most of the HTA reports utilized the concepts within the ACCE evaluation framework, only three reports referenced its use in the methodology (Figure 2). Five reports mentioned EGAPP and only one report mentioned EUnetHTA HTA core model (Supplementary Table S1).

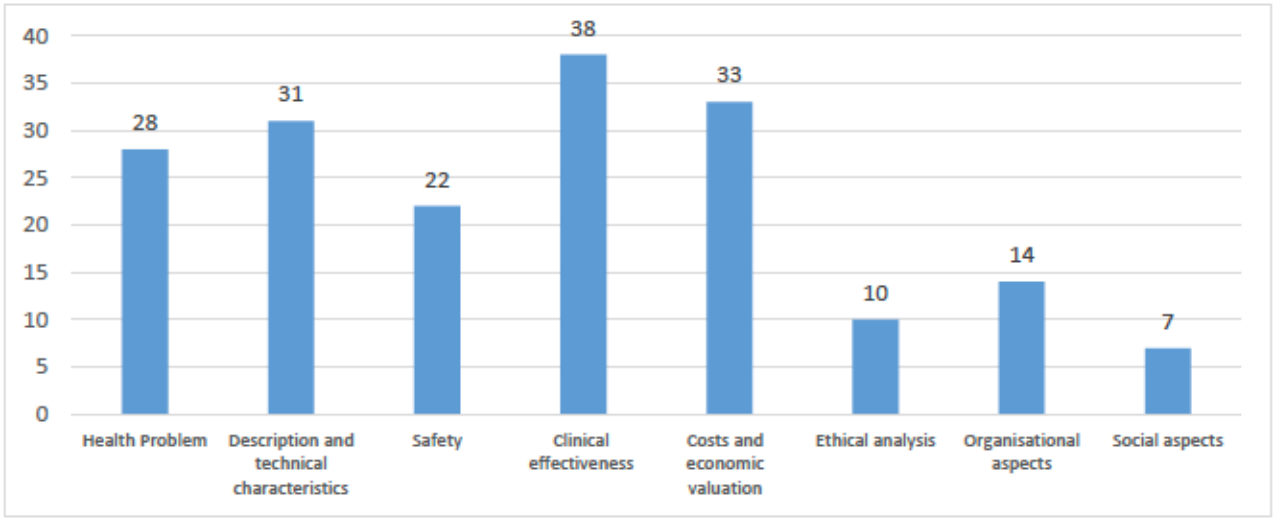


Figure 2. Characteristics of the available forty-five health technology assessment reports on omics technologies.

ACCE Model Process for Evaluating Genetic Tests Available at https://www.cdc.gov/genomics/gtesting/acce/index.htm

Hoxhaj I, Govaerts L, Simoens S, et. al. (2020) Int. J. Environ. Res. Public Health 17, 8001; doi:10.3390/ijerph17218001

Still… Not fit for purpose

Gene Therapy Evidence Generation and Economic Analysis: Pragmatic Considerations to Facilitate Fit-for-Purpose Health Technology Assessment

*Tingting Qiu[1], Michal Pochopien[2], Shuyao Liang[1], Gauri Saal[3], Ewelina Paterak[2], Justyna Janik[2] and Mondher Toumi[1]**

[1] Département de Santé Publique, Aix-Marseille Université, Marseille, France, [2] Department of Health Economics and Outcomes Research, Creativ-Ceutical, Warsaw, Poland, [3] Department of Health Economics and Outcomes Research, Apothecom, London, United Kingdom

Gene therapies (GTs) are considered to be a paradigm-shifting class of treatments with the potential to treat previously incurable diseases or those with significant unmet treatment needs. However, considerable challenges remain in their health technology assessment (HTA), mainly stemming from the inability to perform robust clinical trials to convince decision-makers to pay the high prices for the potential long-term treatment benefits provided. This article aims to review the recommendations that have been published for evidence generation and economic analysis for GTs against the feasibility of their implementation within current HTA decision analysis frameworks. After reviewing the systematically identified literature, we found that questions remain on the appropriateness of GT evidence generation, considering that additional, broader values brought by GTs seem insufficiently incorporated within proposed analytic methods. In cases where innovative methods are proposed, HTA organizations remain highly conservative and resistant to change their reference case and decision analysis framework. Such resistances are largely attributed to the substantial evidence uncertainty, resource-consuming administration process, and the absence of consensus on the optimized methodology to balance all the advantages and potential pitfalls of GTs.

Keywords: gene therapies, health technology assessment, economic analysis, recommendations, affordability

PharmacoEconomics (2021) 39:771–788
https://doi.org/10.1007/s40273-021-01010-z

SYSTEMATIC REVIEW

Guidance for the Harmonisation and Improvement of Economic Evaluations of Personalised Medicine

Heleen Vellekoop[1] · Simone Huygens[1] · Matthijs Versteegh[1] · László Szilberhorn[2] · Tamás Zelei[2] · Balázs Nagy[2] · Rositsa Koleva-Kolarova[3] · Apostolos Tsiachristas[3] · Sarah Wordsworth[3] · Maureen Rutten-van Mölken[1,4] on behalf of the HEcoPerMed Consortium

3.4.5 Additional Elements of Value

It has been argued that the QALY insufficiently captures the full value interventions may have. The ISPOR Value Assessment Framework Special Task Force identified a list of additional value elements to be included in a cost-effectiveness analysis, including scientific spill-overs, equity, real option value, value of hope, severity of disease, insurance value, fear of contagion and reduction in uncertainty [20]. A related concept that has been suggested is "personal utility", which is generally used either to describe the value of knowledge (e.g. knowledge of a test outcome) or as an umbrella term for the non-health outcomes that individuals might value [51, 52]. Patients may indeed value outcomes of healthcare beyond increased health. Diagnostic information, for example, may allow patients to make better life decisions or cause psychological effects such as alleviated (or increased) anxiety [53]. However, the suggested additional value elements raise several concerns.

Key points to keep discussing

- Value assessment plays a promising role in sustaining access to innovative therapeutics
- Decision rules to grant coverage still are based on traditional valuation: costs and benefits
- Societal perspective, caregiver burden, and value of hope are promising elements to demonstrate long-term value, rewarding investment in curative therapies
- Early economic modeling may narrow delays in time to access, but this still requires further exploration

Thank you!

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