



## **“Statistics on Health Decision Making: State of the art”**

**Prescription: Cost-Effectiveness – Does it make sense?**

**José Aranda da Silva**

## COMPETENT NATIONAL AUTHORITIES OR EUROPEAN AUTHORITIES

- Quality
- Safety
- Efficacy



**Marketing Authorization**

## Competent national authorities - INFARMED

- Exclusive competence for price and financing decisions

## FINANCING EVALUATION AND DECISION

- Decisive to ensure patient access to medicines.
- The Economic Evaluation and the determination of the Added therapeutic value are intended to justify the decision regarding medicine's reimbursement by NHS.
- It consists of determining the added value of the medicinal product in the following aspects:
- Added Therapeutic value;
- Economic advantage.

**Marketing  
Authorization**



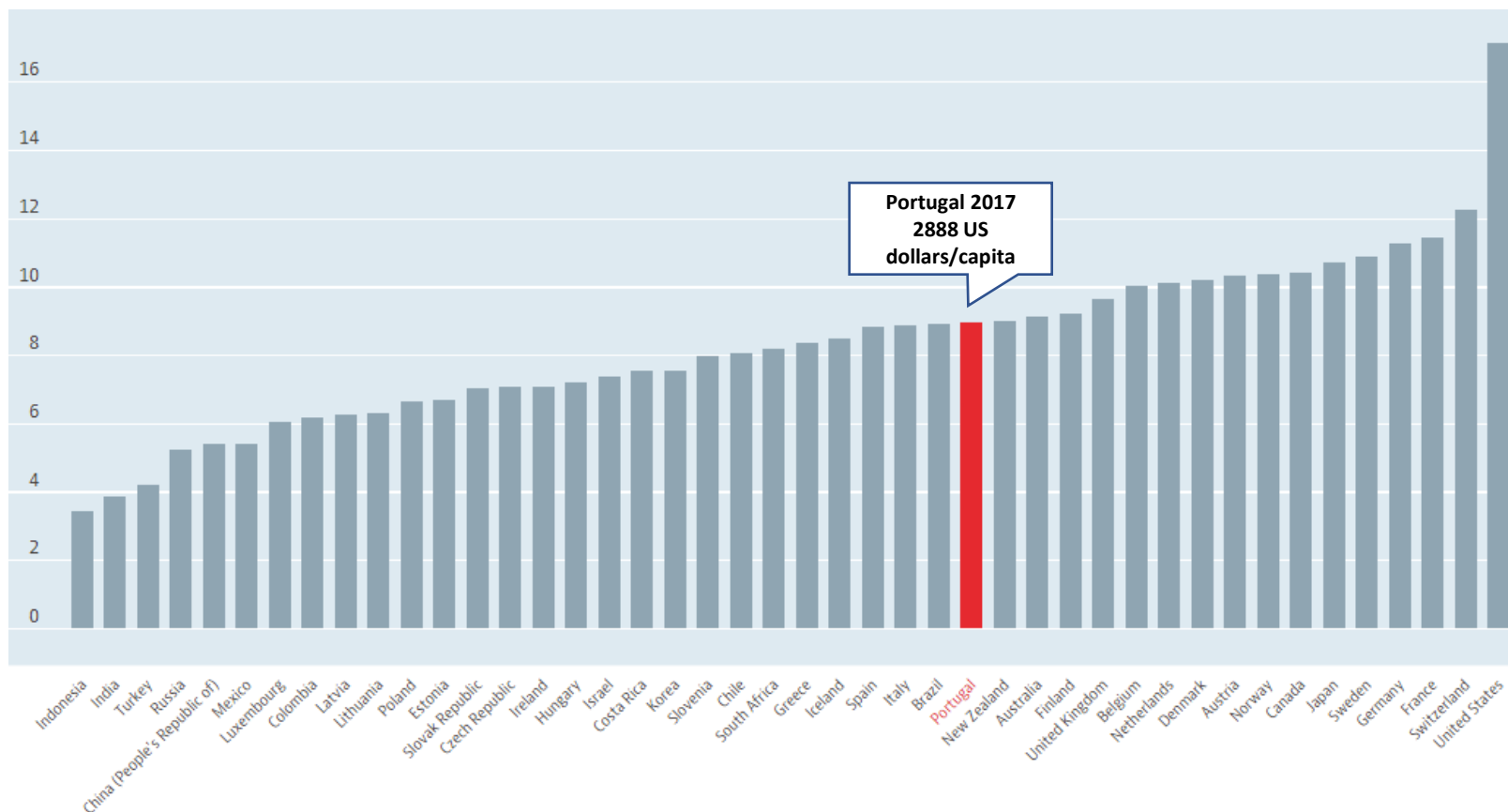
**Outpatient:**

**Price** → **Reimbursement with price setting**

**Hospital: Prior evaluation with price setting**

# HEALTH SPENDING

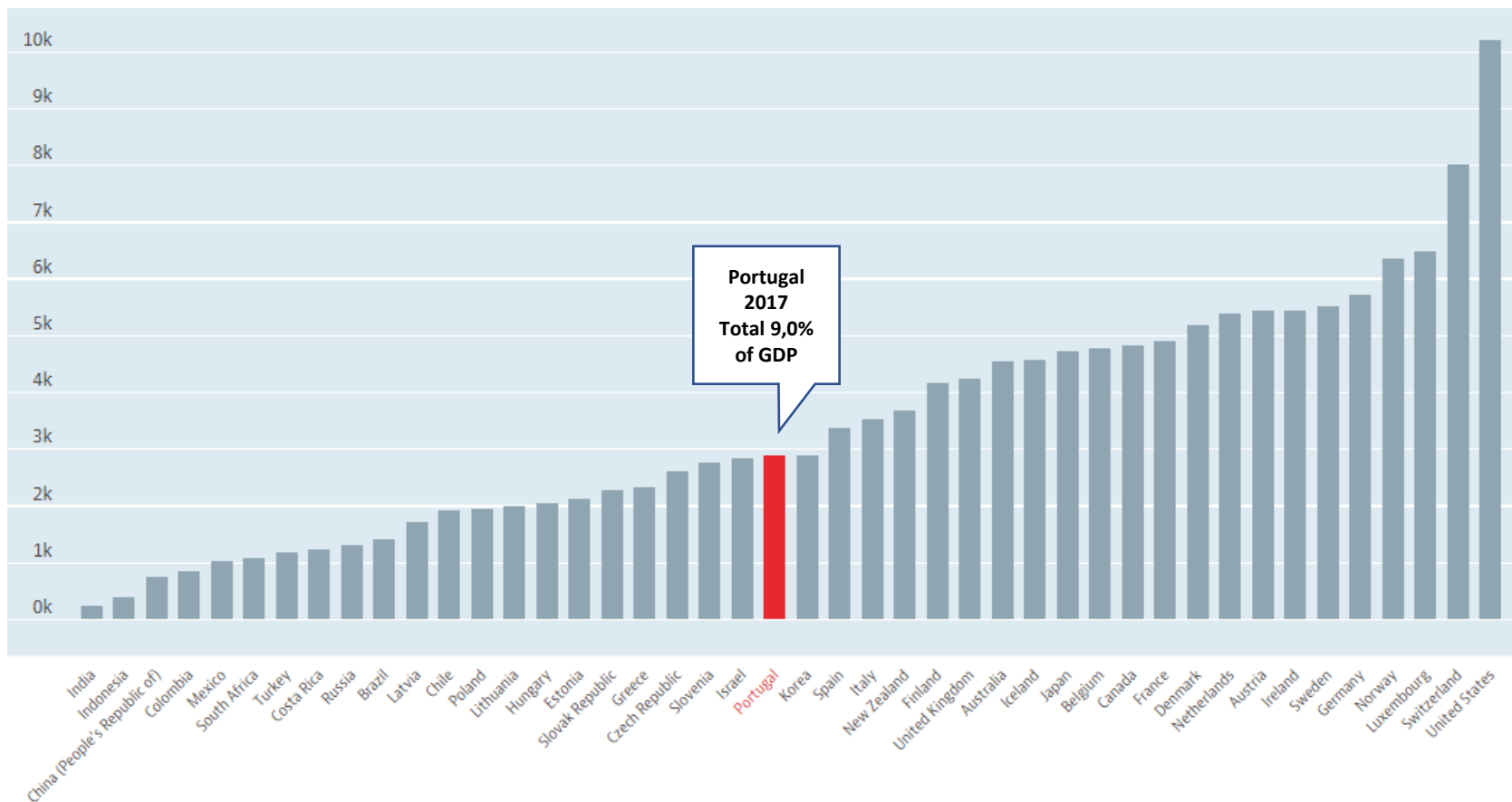
## TOTAL, % OF GDP, 2017 OR LATEST AVAILABLE



Source: Health expenditure and financing: Health expenditure indicators: <https://data.oecd.org/healthres/health-spending.htm>

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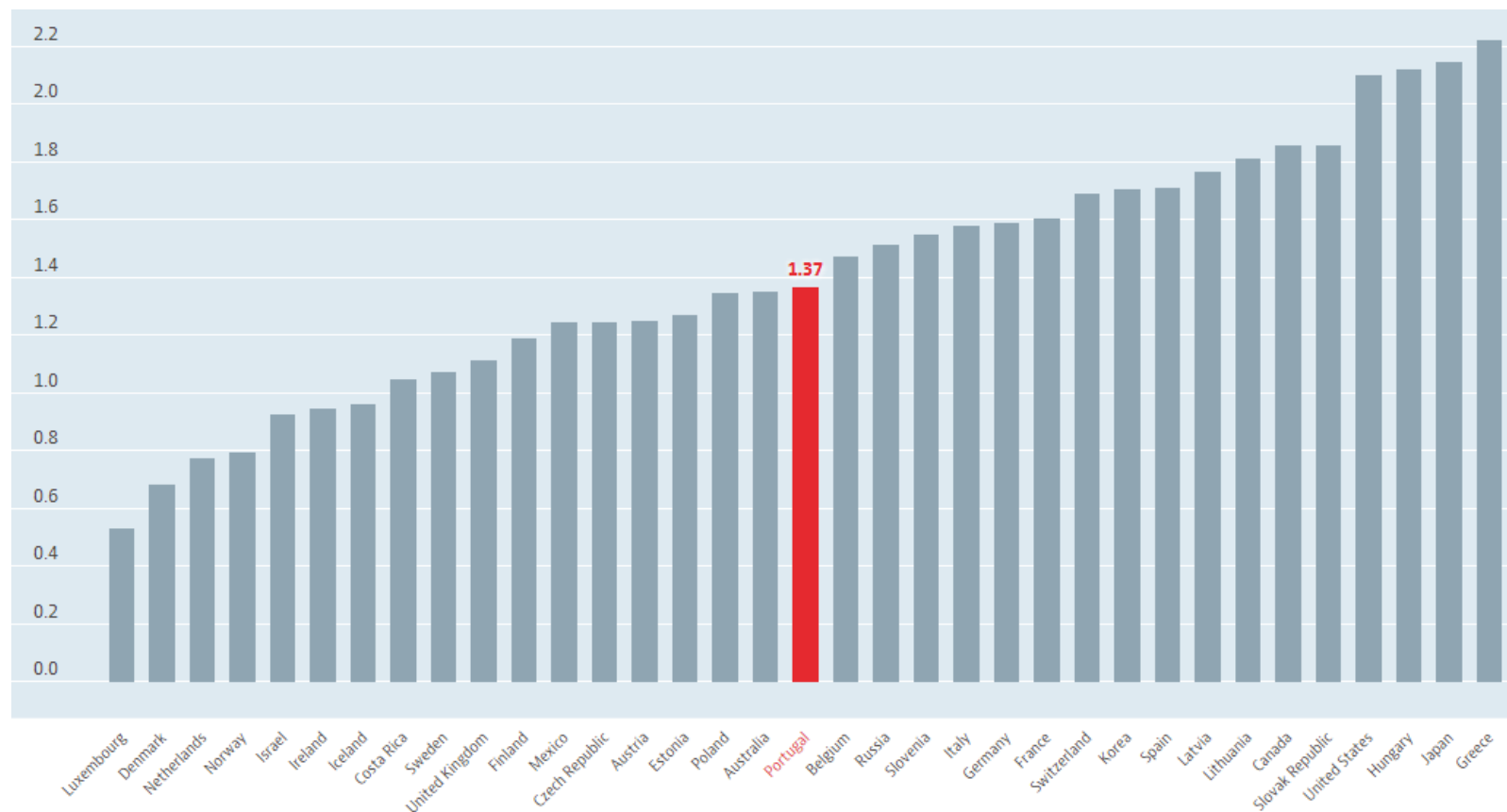
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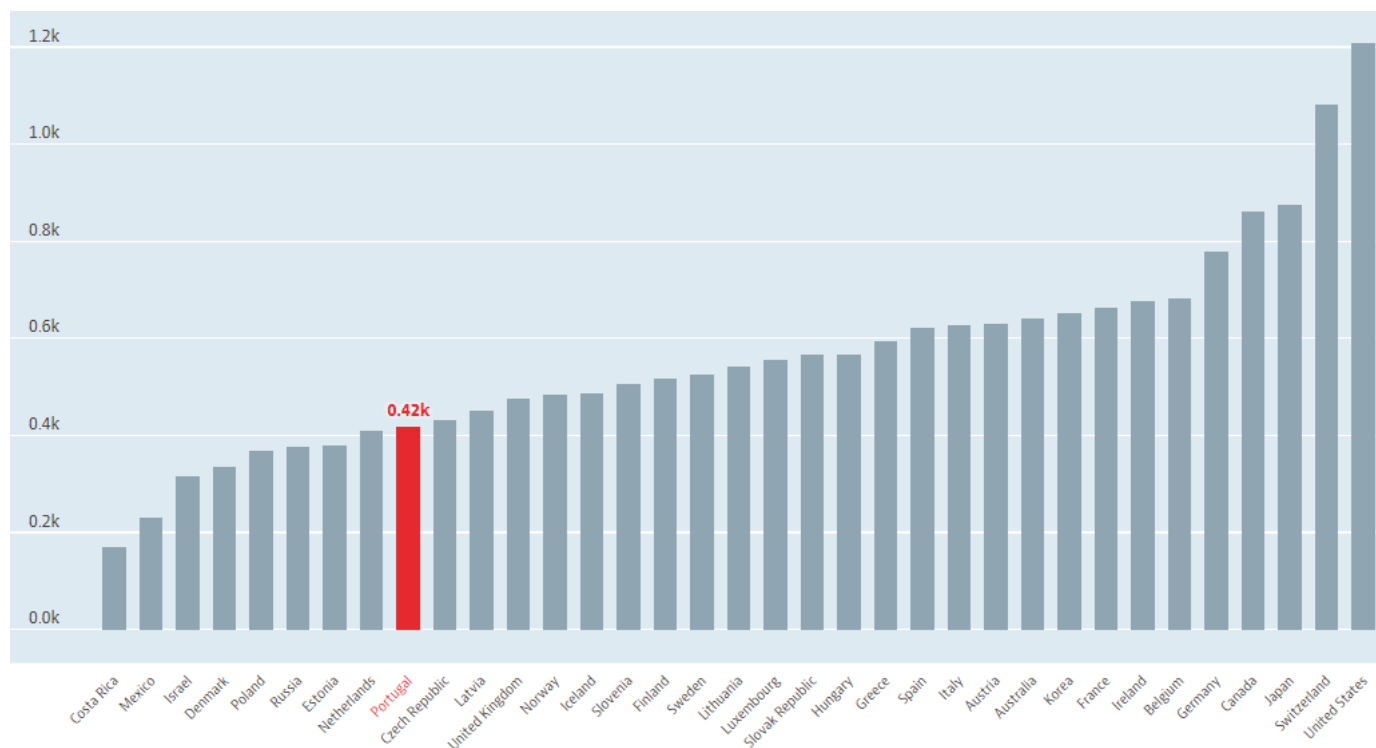
TOTAL, % OF GDP, 2017 OR LATEST AVAILABLE



Source: Health expenditure and financing: Health expenditure indicators: <https://data.oecd.org/healthres/pharmaceutical-spending.htm#indicator-chart>

# HEALTH SPENDING

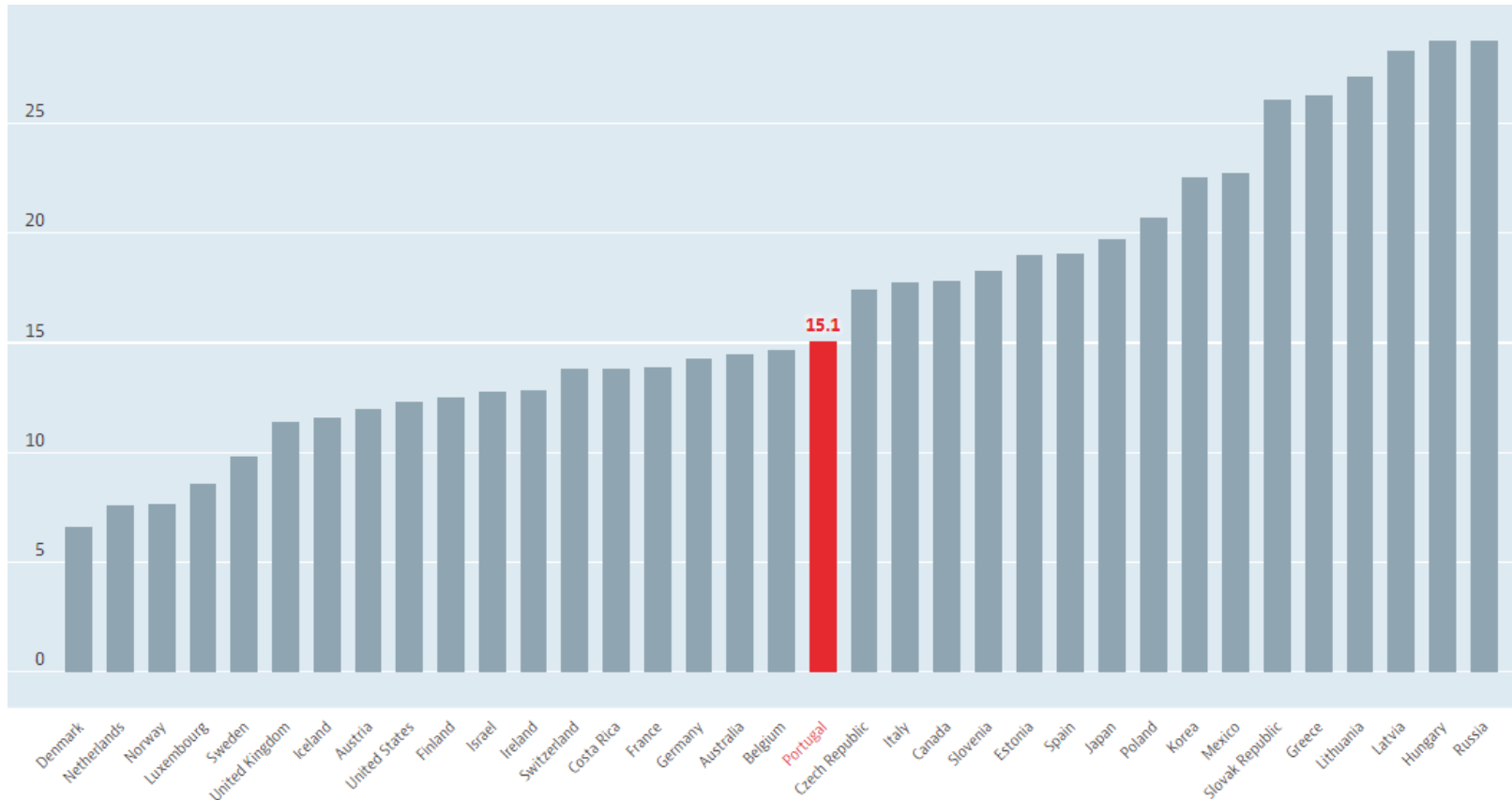
TOTAL, % OF GDP, 2017 OR LATEST AVAILABLE



Source: Health expenditure and financing: Health expenditure indicators: <https://data.oecd.org/healthres/pharmaceutical-spending.htm#indicator-chart>

# PHARMACEUTICAL SPENDING

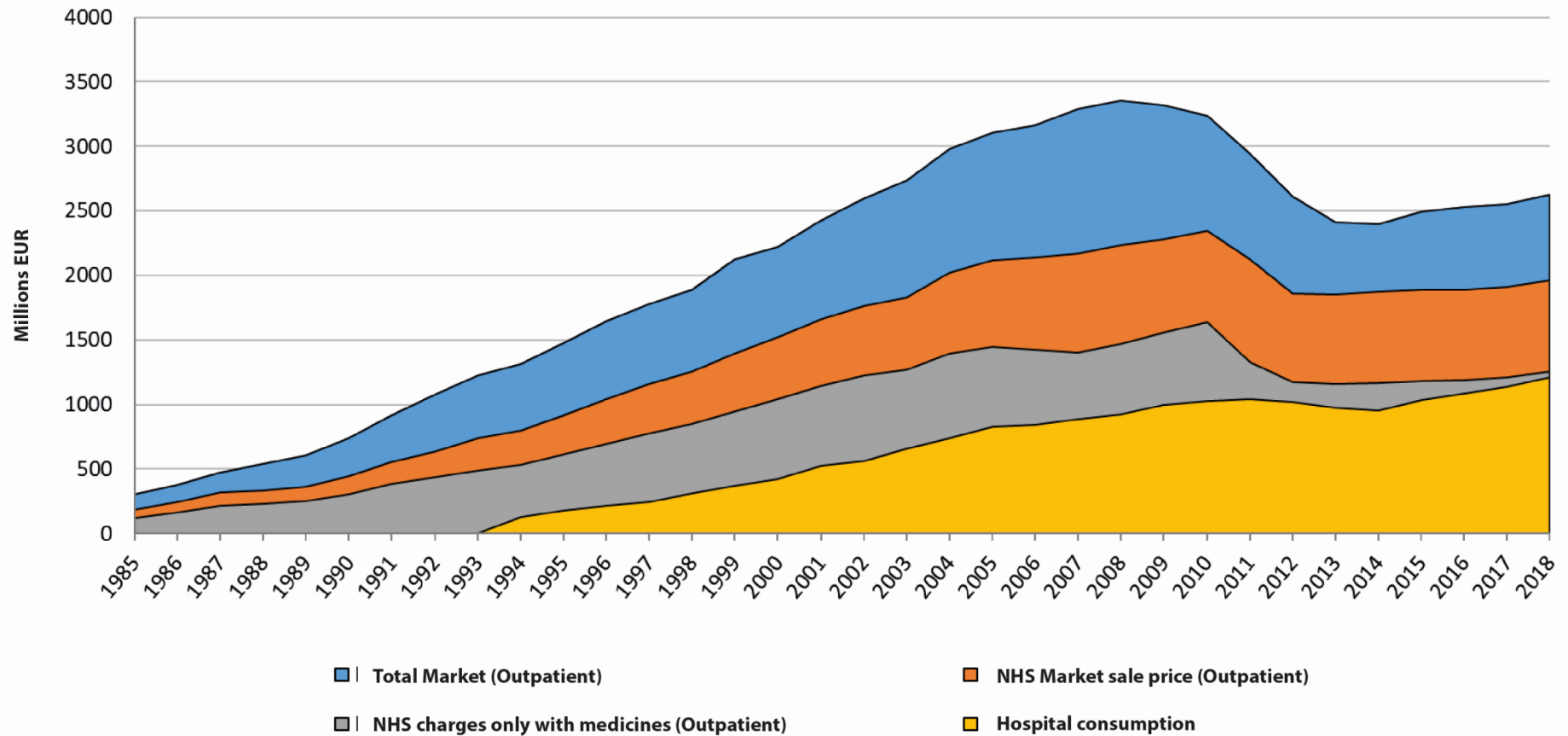
TOTAL, 5 OF HEALTH SPENDING (YEARLY), 2017 OR LATEST AVAILABLE



Source: Health expenditure and financing: Health expenditure indicators: [https://data.oecd.org/HEALTHRES/PHARMACEUTIC\\_SPENDING.HTM](https://data.oecd.org/HEALTHRES/PHARMACEUTIC_SPENDING.HTM)



# FINANCING EVALUATION AND DECISION



## EFFICACY – EFFECTIVENESS GAP: WHAT WE DON'T KNOW

### Efficacy

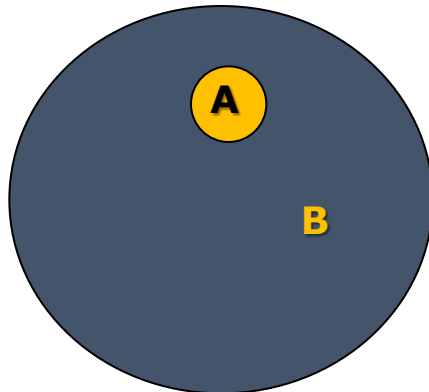
*Capacity for producing desired results under optimum conditions*

Ex. Controlled environment of a clinical trial

### Effectiveness

*Capacity for producing desired results under real conditions*

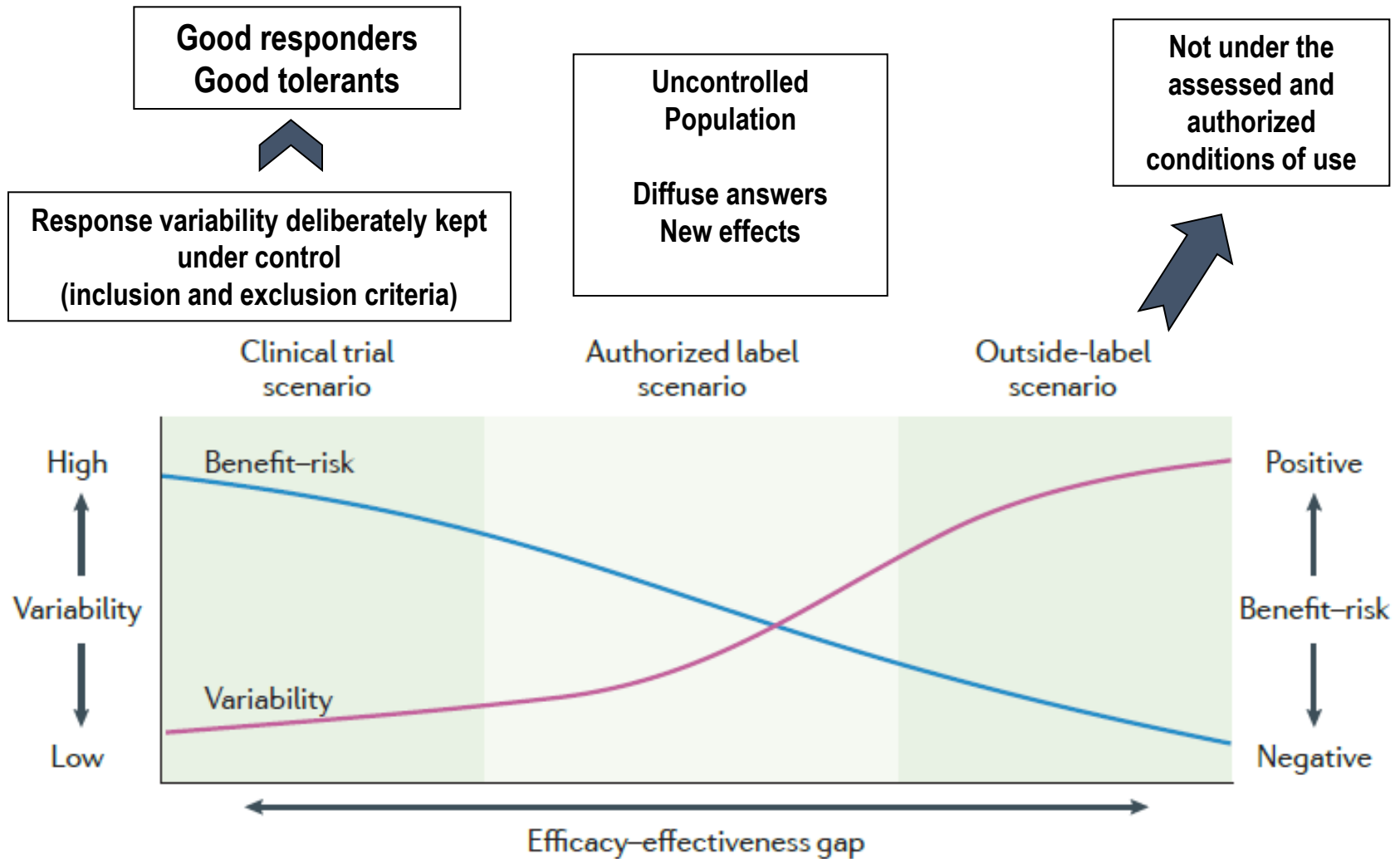
Ex. Population in general without any differentiation



*Internal validity  $\neq$  External validity*

*The results established for population "A" are not necessarily reproduced when we subject population "B" to the same conditions!*

# EFFICACY – EFFECTIVENESS GAP: WHAT WE DON'T KNOW



Fonte: Eichler, et al. Bridging the efficacy-effectiveness gap: a regulator's perspective on addressing variability of drug response. Nature reviews Drug discovery, 2011, 10.7: 495.

## EFFICACY – EFFECTIVENESS GAP: WHAT WE DON'T KNOW

Optimizing the individual therapeutic response should be at the center of clinical decision-making, but for most medicines there is very little information on the factors (individual or external) that influence the outcome.

For example, antihypertensive and antidyslipidemic agents are prescribed extensively but only a fraction of the treated patients achieve target blood pressure and the desired lipid profile. Why?

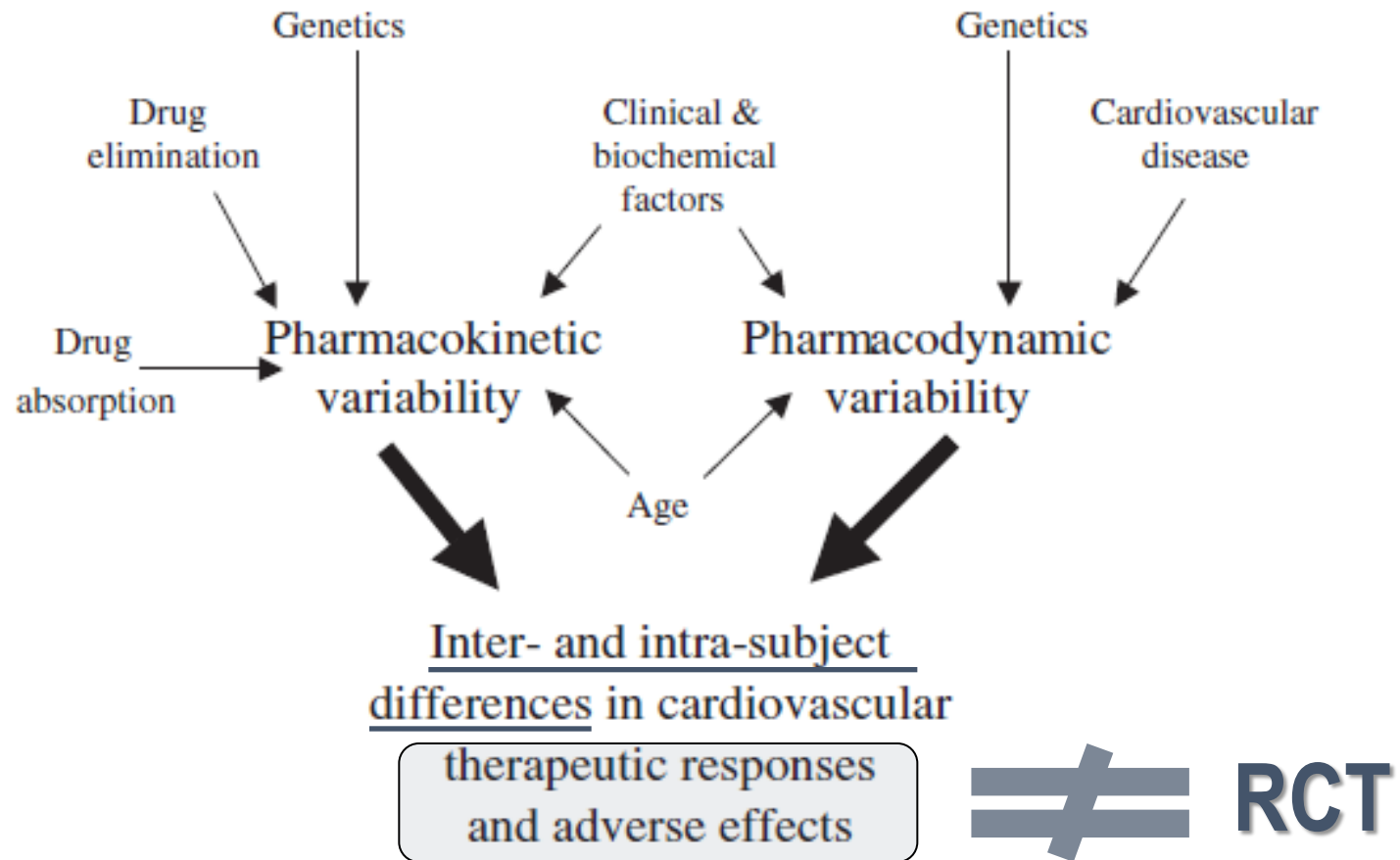
Clinical options regarding medicines, namely the dosage selection, the sequencing of different therapeutic options, association of different active substances, can have a strong [empirical component!](#)

# VARIABILITY OF THE INDIVIDUAL RESPONSE TO PHARMACEUTICALS AS A CAUSE OF TOXICITY OR LACK OF EFFICACY

Source of variability	Mechanism	Drug	Description of problem
<b>Biology</b>			
Genomics	Individual patients' genomic make-up influences PK and PD, affecting medicine concentration profile at the target site and the likelihood and magnitude of desired and adverse effects	Trastuzumab	PD: only effective in patients overexpressing HER2 Receptor on tumour cells
		Abacavir	PD: High risk of severe hypersensitivity reaction in patients with HLA-B*5701 allele
		Codeine	PK: lack of analgesia in carriers of nonfunctional CYP2D6 alleles, toxicity with multiple CYP2D6 gene copies
Other intrinsic and extrinsic factors	Comorbidity, baseline severity of disease, other altered physiological states, or external factors influencing PK and/or PD	Insulin	PD: glucose control and risk of hypoglycaemia affected by stress or physical activity
		Several medicine	PK: increased toxicity due to increased absorption with concomitant consumption of grapefruit juice
<b>Behaviour</b>			
Prescribing and medicine's utilization	Inappropriate or off-label prescribing, co-prescribing with an interacting medicine, continued prescription to non-responders or medication errors	Cerivastatin	Rhabdomyolysis due to high starting doses
		Gemfibrozil	Interactions in medicine label ignored
		Mibefradil	Toxicity due to drug–drug interactions, label often ignored
Patient adherence	Poor adherence to prescribed medicine regimen, discontinuation (non-persistence), 'drug holidays' or inadvertent overdosing	Anti-hypertensives	Non-adherence or non-persistence perceived as treatment-resistant hypertension
		Anti-infective medicine	medicine holidays leading to the development of resistance

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## EFFICACY – EFFECTIVENESS GAP: WHAT WE DON'T KNOW



# WHAT DO STUDIES DETERMINING PHARMACODYNAMIC AND PHARMACOKINETIC TELL US ABOUT MEDICINES?

## PHARMACODYNAMIC

Information on pharmacological mechanisms and actions.

- Interactions with cellular components (receptor or target site);
- Effects at the site of action;
- Relationship between concentration and effect;
- Modification of disease progression;
- Secondary effects;
- Pharmacological interactions

## PHARMACOKINETIC

Information of the medicine route in the body (absorption, distribution, metabolism and excretion).

- Absorption from the administration site;
- Distribution to the site of action;
- Metabolization and elimination;
- Time until effect onset;
- Duration of effect;
- Accumulation in repeated administration;
- Pharmacological interactions.



**Intra and interpersonal variations**



## EFFICACY – EFFECTIVENESS GAP: WHAT WE DON'T KNOW

### Efficacy

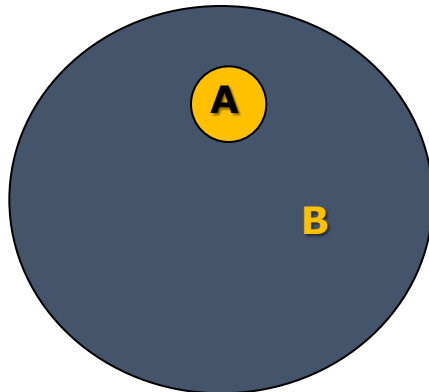
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## THE FUTURE IS NOW

Quality concerns – 1930/1960 ( Sulfanilamide syrup USA)

Safety issues – 1960/1990 (Thalidomide)

Efficacy accuracy– 1990/2010 (RCT regulations)

**Effectiveness** issues – 2010/... (EUnetHTA 2019)

**Economic** issues – 2010/... (EUnetHTA 2019)

# THE FUTURE IS NOW

**Effectiveness** issues – 2010/... (EUnetHTA 2019)

**Economic** issues – 2010/... (EUnetHTA 2019)

## Tools

- Observational studies (RWD)
- Treatment of the existing data in the health system
- Specific database development (RON; ReumaPt; ...)