

Andras Incze  
moderator



Akceso Advisors AG

Jaime Espin  
panelist



Escuela Andaluza de Salud Pública  
CONSEJERÍA DE SALUD

Lou Garrison  
panelist



Zoltan Kalo  
panelist



syréon  
Research Institute

## INTERNATIONAL REFERENCE PRICING: U.S. VS. REST OF WORLD—WHO IS SHOOTING WHOSE FOOT?

ISPOR ISSUE PANEL IP2  
Virtual Session May 18<sup>th</sup>, 2020

*The underlying research was financially supported by PhRMA*

1 | ISPOR – IRP US vs. RoW – Who is shooting whose foot? | May 18<sup>th</sup> 2020 |

## Session Presenters

*Panelists representing different perspectives*

Moderator:

- **Andras Incze**, PhD, MBA, University Lecturer Healthcare Management, Baden-Wuerttemberg State University, Germany; CEO Akceso Advisors AG, Basel, Switzerland  
[aincze@akceso.ch](mailto:aincze@akceso.ch)



Akceso Advisors AG

Panelists:

- **Lou Garrison**, PhD, Professor Emeritus, The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute Department of Pharmacy; University of Washington, Seattle, WA, USA  
[lgarrison@uw.edu](mailto:lgarrison@uw.edu)
- **Jaime Espin**, PhD, BLaw, MSChE, Professor, Andalusian School of Public Health, Granada, Spain  
[jaime@easp.es](mailto:jaime@easp.es)
- **Zoltan Kalo**, PhD, Professor of Health Economics, Center for Health Technology Assessment, Semmelweis University/Syreon Research Institute, Budapest, Hungary  
[zoltan.kalo@syreon.eu](mailto:zoltan.kalo@syreon.eu)



Escuela Andaluza de Salud Pública  
CONSEJERÍA DE SALUD



syréon  
Research Institute

2 | ISPOR – IRP US vs. RoW – Who is shooting whose foot? | May 18<sup>th</sup> 2020 |

## INTERNATIONAL REFERENCE PRICING: U.S. VS. REST OF WORLD—WHO IS SHOOTING WHOSE FOOT?

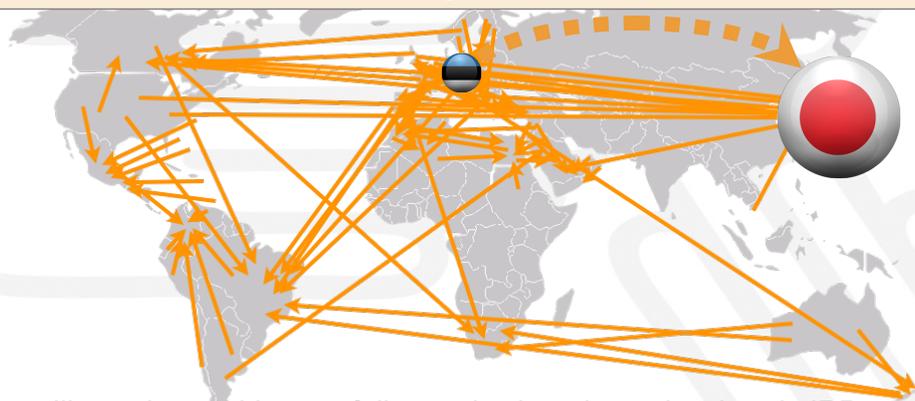
ISPOR ISSUE PANEL IP2  
Virtual Session May 18<sup>th</sup>, 2020

Introduction by Andras Incze, moderator

The underlying research was financially supported by PhRMA

### IRP\* of drugs makes the world interdependent *No matter how small a country, it can impact the largest ones*

**Estonia**  
even though 100 times smaller, can affect the price in  
**Japan**



Illustrative world map of direct price interdependencies via IRP

\*IRP: International Reference Pricing, also called External Reference Pricing

## Many new drugs are unavailable to patients due to no launch or extended negotiations

*Avoiding IRP spillover effect to other, higher-potential markets*

### Large difference in new drug availability between lower income and higher income countries

Median number of available new drugs in **lower income**:

11 (50%)



Median number of available new drugs in **higher income**:

18 (82%)



Lower income countries: the 1st tertile of 29 European countries by GDP/capita, average: \$14,937  
 Higher income countries: the 3rd tertile of 29 European countries by GDP/capita, average: \$62,893  
 Availability of drugs as regular treatments in March 2020 in European countries from 22 NCEs registered by EMA in the first half of 2015

## Pharma companies often apply an “Avoidance Strategy” supposedly to mitigate IRP effects

*Avoiding launch in lower-priced countries or even pulling out*



### Case of Greece cost containment, 2010

#### Avoided impact for a key modern insulin in 23 European IRP markets over 10 years 2010 – 2020

Avoided 10yr mean price erosion:

2.0%

Avoided yearly sales loss:

\$6m

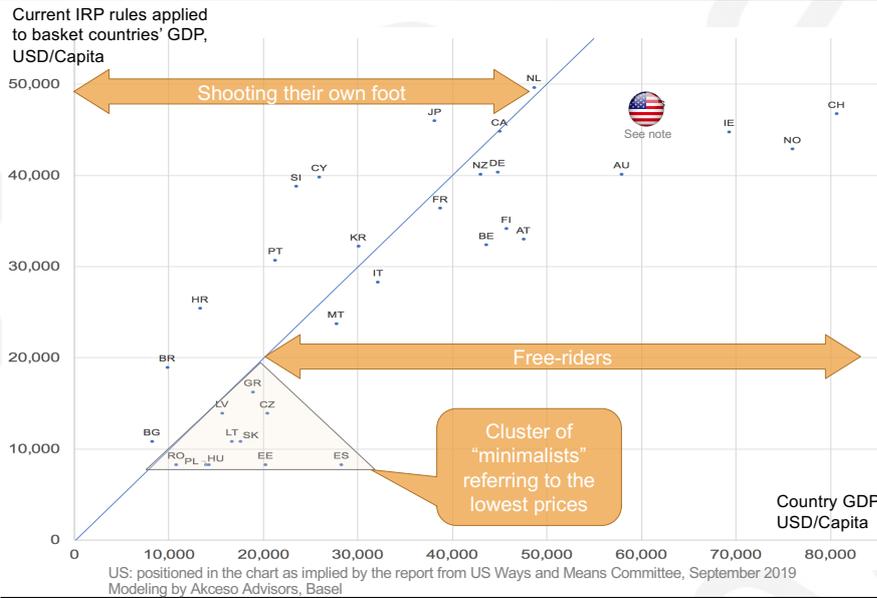
NPV of total avoided 10yr sales loss:

\$32m

Information obtained from public sources, situation decomposed, reverse-engineered and effects modeled and estimated by Akceso Advisors, Basel

## Many countries reference to an unlike basket

To what degree does each country compare its list price to similar Ability-to-Pay countries?



The imperfections of IRP mean that even free-riders shoot their own foot:

ultimately leading to unavailability of new drugs in the cluster of "minimalists" and others

## U.S. is considering the introduction of IRP

with several initiatives from all political sides



whose price control & coverage system is organized fundamentally differently from the ones it considers to price-reference

## What would be the effect of U.S. introducing IRP?

What would be the effect on

- Payers
- Pharma industry
- Patients

in

- U.S.
- Large, higher income European countries
- Lower income countries in Europe and worldwide



## International Reference Pricing: US vs. Rest of World— Who is Shooting Whose Foot?— A U.S. Health Economist Perspective

### Louis Garrison, PhD

- Professor Emeritus, CHOICE Institute, School of Pharmacy, University of Washington, Seattle WA, USA
- Visiting Senior Fellow, Office of Health Economics, London, UK

*ISPOR Issue Panel IP2  
Virtual Session  
May 18, 2020*



## U.S. Considering IRP

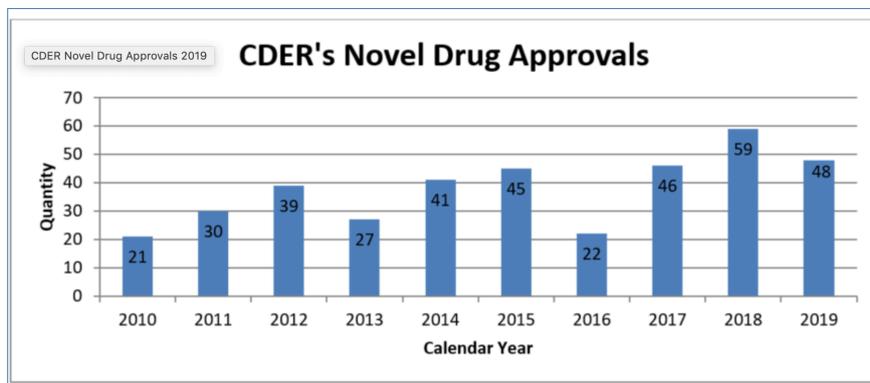
**H.R. 3**—U.S. House of Representatives passed the “Elijah E. Cummings Lower Drug Costs Now Act” Dec. 2019.

1. Lower patient out-of-pocket costs
2. Adjust prices for recent inflation
3. Sec. of HHS negotiates drug prices based on “**International Price Index**” (IPI). **Not exceed 120% of pricez of six countries.**
4. **CBO projects \$456 billion in savings over 10 years. And 8 fewer drugs in 2020-2029.**

### Trump Administration—Notices of Proposed Rule-Making

- HHS/CMS Blueprint Oct. 30, 2018—International Pricing Index Model for Medicare Part B
- Senate Finance Committee, Dec. 6, 2019—Inflation penalties for Part B & D; no IRP
- HHS/FDA Dec. 23, 2019—Proposed “Importation of Prescription Drugs” from Canada

2



In 2019:

- 20 of 48 (42%) as first-in-class
- 21 of 48 (44%) treat rare or “orphan” diseases
- 17 of 48 (35%) as Fast Track
- 13 of 48 (27%) as breakthrough therapies
- 28 of 48 (58%) were designated Priority Review

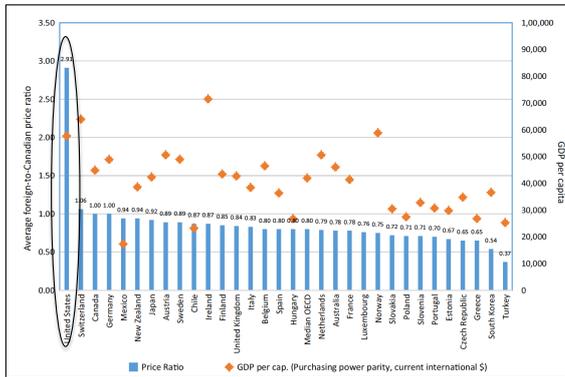
### New drugs:

- **Global public goods**
- **Few annually**
- **Productivity flat**
- **Mix constantly changing**

3

## Drug Prices: U.S. vs. ROW

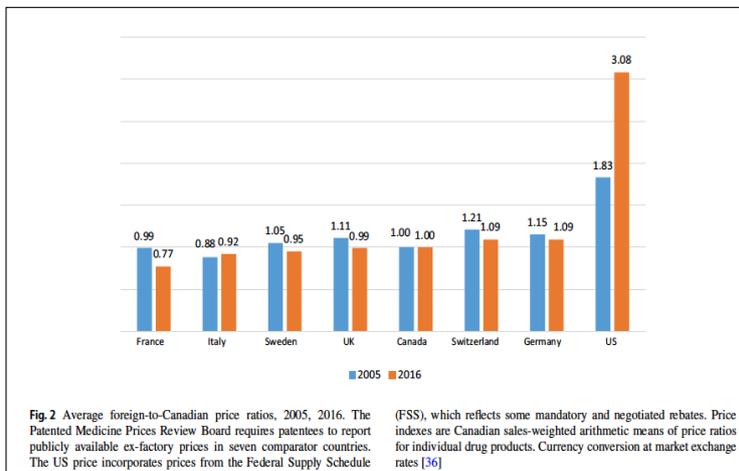
(Average Foreign-to-Canadian Price Ratios for Patented Drugs by Country, 2016)



US list price 3x higher  
Low correlation with GDP per capita

Source: Danzon,  
*PharmacoEconomics*, 2018

## Drug Price Changes: 2005 vs. 2016—8 Countries



U.S. prices rising—  
and faster over time

Source: Danzon,  
*PharmacoEconomics*, 2018

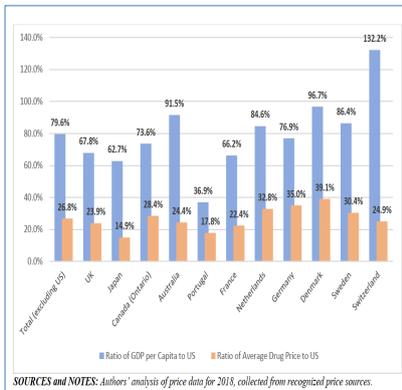


**A Painful Pill to Swallow:  
U.S. vs. International Prescription  
Drug Prices**

Prepared by Ways and Means Committee Staff  
September 2019

**U.S. Government  
Focus on Drug Price  
Differences**

**GDP per capita and  
Drug Prices relative to U.S.**



**Price Differential as a Rebate**

Table 2. U.S. Rebate Rate Required to Match Select Countries Ex-Factory Prices, 2018

Drug Prices Listed for Each Country			
Country	Average Price	US Rebate Rate Needed	Drugs Listed
U.S.	\$466.15	-	79
UK	\$105.45	77.4%	78
Japan	\$69.50	85.1%	58
Canada (Ontario)	\$132.59	71.6%	47
Australia	\$113.57	75.6%	62
Portugal	\$82.97	82.2%	37
France	\$104.51	77.6%	54
Netherlands	\$152.86	67.2%	61
Germany	\$165.01	64.6%	65
Denmark	\$182.29	60.9%	65
Sweden	\$143.91	69.1%	59
Switzerland	\$116.22	75.1%	72
Average	\$152.92	72.3%	61.4

SOURCES and NOTES: Authors' analysis of price data for 2018, collected from recognized price sources.



International Journal of Health Care Finance and Economics, 3, 183–205, 2003  
© 2003 Kluwer Academic Publishers. Manufactured in The Netherlands.

**Differential Pricing for Pharmaceuticals:  
Reconciling Access, R&D and Patents**

PATRICIA M. DANZON  
The Wharton School, University of Pennsylvania

ADRIAN TOWSE  
Office of Health Economics

**Economists have long argued for global  
differential pricing.  
Has equity implications as well.**

OUTLOOK NEGLECTED DISEASES NATURE | Vol 449 | 13 September 2007

**At what price?**

Differential pricing could make global medicines affordable in developing countries. But drugs for diseases that have no market in the developed world will require additional subsidies, says **Patricia M. Danzon**.

**F**or the general population in developing nations to have appropriate access to medicines, existing drugs must be affordable, and innovation is needed to develop new medicines. But this presents a potential conundrum: prices that are high enough to pay for research and development (R&D) may make medicines unaffordable in developing regions. Differential pricing (also known as price discrimination) can offer a solution to this dilemma, at least for drugs with considerable sales in the developed world. Prices in affluent countries — and to a lesser extent in middle-income countries — could gener-

for R&D. Pharmaceutical R&D can benefit patients globally, raising the question of how — which seems plausible for pharmaceuticals. A simulation\* comparing worldwide pharma-

## Achieving Optimal Innovation— The Goal of Dynamic Efficiency

- **Static Efficiency**—optimal use given today’s prices—e.g., by using cost-effectiveness analysis.
- **Dynamic Efficiency**—eliciting the **optimal rate of innovation over time**.
  - **Key Issue: What is the lifetime revenue elasticity of innovation? How responsive is innovation to the “expected market size”?**
- **Dubois, de Monzon, Scott-Morton (2015) estimate: 0.23→**”on average, \$2.5 billion is required in additional revenue to support the invention of one new chemical entity.”

### The Big Trade-Off: Innovation vs. Access

- Financing innovation by granting a monopoly implies a trade-off between the rate of innovation (i.e., “dynamic efficiency” and access (or equity)).
  - Monopoly returns elicit a greater supply of new drugs **IN THE LONG TERM.**
  - BUT**
  - Monopoly power results in higher prices and, thus, worse access **IN THE SHORT TERM.**

**But if new medicines aren’t invented, no one can access them IN THE LONG TERM.**

# Who's Shooting Whose Foot?

[With IRP, there's a good chance that U.S. would be shooting itself in foot—and everyone else as well.](#)

## **Likely effects:**

- On the one hand, globally, fewer drugs
- On the other hand, economics teaches us that "you can have too much of good thing." But would we lose the right ones?
- Higher prices outside U.S. and lower access
- Less cumulative scientific progress
  - With COVID-19, "Oh! if we'd only known a bit more."

## **An Alternative:**

- More movement toward value-based pricing that better aligns rewards with value delivered (i.e., effectiveness/real-world data) and operating with a broader concept of value (per the ISPOR Special Task Force on U.S. Value Frameworks).
- Better management of desirable and appropriate global differential pricing

10

**Thanks!**  
**Questions?**

lgarrisn@uw.edu

INTERNATIONAL REFERENCE PRICING:  
U.S. VS. REST OF WORLD—WHO IS SHOOTING WHOSE FOOT?  
Academic perspective of **European Union countries**

ISPOR ISSUE PANEL IP2  
Virtual Session May 18<sup>th</sup>, 2020



Jaime Espín, PhD  
Professor  
Andalusian School of Public Health

1

## Rationale or Theoretical Foundation

- **One of its main shortcomings is the lack of a clear rationale or theoretical foundation.** For instance, price control based on the **cost-plus** (or cost of production) criterion seeks to determine a price that allows producers to recover production costs and obtain a fair/acceptable profit. **Value-based pricing** assumes that the price of a drug should reflect its therapeutic or welfare-added value in relation to existing therapies. It also assumes that new products that do not bring any added value should not get a higher price than existing treatments.
- Although ERP does not have any clear rationale or theoretical foundation, the **implicit assumption** is that it reflects some of the following aims:
  - To **obtain prices similar** to – in fact, not higher than - those of a set of countries.
  - To obtain the same price as the **lowest price** in a set of countries.
  - To obtain **differential** - usually lower - prices in relation to those of a set of countries.

2

## Evidence of impact based on literature review (I)

- **Few articles in scientific journals that dealt directly with ERP**, often related to price comparisons (even if there are not using for ERP); very scarce information is available from low and middle income countries
- **Assessing the impact of ERP in relation to other pricing approaches is a difficult task**

(how far can an observed delay in the launch of new medicines in a given country be attributed to ERP and not to parallel trade or just to low prices, three situations which often appear together? )

- Some conclusions (Prof. Danzon): After adjusting for GNP per capita, **prices are higher in countries with lower income levels and regulated drug prices** (for example: Spain, Portugal and Greece) than in countries with high income levels (Japan, Germany and the UK)

3

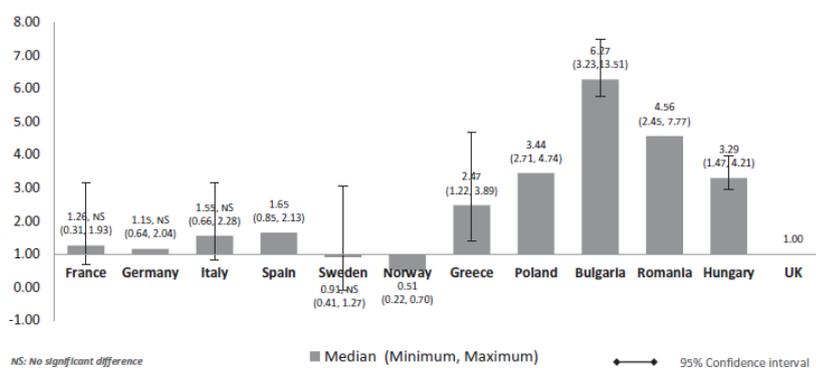


Figure 2. Relative cost ratios: adjusted using nominal GDP per capita (UK reference = 1).

Source: K. E. Young, I. Soussi & M. Toumi (2017) **The perverse impact of external reference pricing (ERP): a comparison of orphan drugs affordability in 12 European countries**. A call for policy change, Journal of Market Access & Health Policy, 5:1, 1369817

4

## Evidence of impact based on literature review (II)

- A study conducted by Stargardt and Schreyogg, using an **analytical model**, estimated that a **1€ reduction in German drug prices would lead to a reduction of between 0.15€ and 0.36€ in the EU-15 countries that use ERP** (Austria and Italy, respectively).
- The main alleged **negative effects** can be:
  - 1) higher prices in low-income countries
  - 2) delays in the launching new drugs in low-price countries

5

## Evidence of impact based on literature review (III)

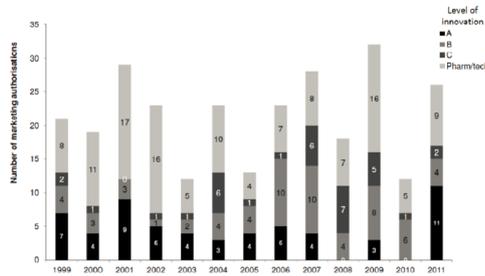
This was made evident in a European Commission report (Pharmaceutical Sector Inquiry – DG Competition) that asked companies to indicate which countries they preferred to use for launching new drugs. **Companies preferred to initiate their product launches in countries with free prices** (United Kingdom, Germany, Sweden). In contrast, countries with smaller markets, such as Cyprus or Malta, or with lower disposable income, such as Poland, Bulgaria, Lithuania, Latvia, Estonia, Hungary and Romania (20), are mentioned last.

6

## Should we really worry about “launch delays” of new drugs in OECD countries?

Livio Garattini · Simone Ghislandi

Considering the relatively small number of new medicines that actually make any substantial therapeutic contribution over existing ones, such delays in marketing might not necessarily be a bad thing



**Figure 4.3 Level of innovation of pharmaceuticals approved in Europe between 1999 and 2011.** All pharmaceuticals are new active substances that are approved through the centralised procedure in Europe. Classification of innovation according to Motola (73) A) important, B) moderate, C) modest or as Pharm or Tech) merely pharmacological / technological innovations. Source: (35).

Source: Minds Open – Sustainability of the European regulatory system for medicinal products RIVM Report

## Use of ERP – HAI/WHO Paper

Country	Price setting	Products - ERP	Countries	Price used	Criteria	Sources of information
<b>Brazil</b>	Agência Nacional de Vigilância Sanitária (ANVISA)	On patent (Category I)	USA, Canada, Portugal, <b>Spain</b> , France, Italy, Greece, New Zealand and Australia	Ex-factory	Minimum	Websites;
<b>Czech Republic</b>	SUKL(State Institute for Drug Control)- maximum prices/reimbursement prices/ Health funds - price negotiations	Reimbursable	For pricing: Estonia, France, Italy, Lithuania, Hungary, Portugal, Greece, and Spain For reimbursement: all EU countries	Ex-factory	Average	Websites; Manufacturer
<b>Hungary</b>	National Health Insurance Fund Administration (OEP)	Reimbursable (new active substances)	Countries in the European Union and European Economic Area	Ex-factory	Minimum	Websites; Manufacturer
<b>Iran</b>	Pricing Commission	On-patent and imported	Greece, <b>Spain</b> , Turkey and the country of origin	Ex-factory and wholesaler	Minimum	Manufacturer
<b>Jordan</b>	Pricing committee of the Jordan Food and Drug Administration (FJDA)	All products	Selected European countries (UK, France, <b>Spain</b> , Italy, Belgium, Greece and the Netherlands), the export price to Kingdom of Saudi Arabia, and the country of origin	Ex-factory price of the reimbursed price	Median	Websites; Manufacturer
<b>Lebanon</b>	Pricing Committee - MoH	On- and off-patent products	Region: Jordan, Kingdom of Saudi Arabia, Kuwait, Sultanate of Oman, United Arab Emirates, Bahrain and Qatar. Comparative: France, England, Belgium, Switzerland, Italy, <b>Spain</b> and Portugal	All	Minimum	Manufacturer
<b>South Africa</b>	Pharmaceutical Economic Evaluations (PEE) Directorate	On- and off-patent products	Australia, New Zealand, <b>Spain</b> , and Canada	Ex-factory and import	Minimum	Manufacturer
<b>Sultanate of Oman</b>	Directorate General of Pharmaceutical Affairs & Drugs Control	All products	Gulf Cooperation Council (GCC) countries: Kingdom of Saudi Arabia, United Arab Emirates, Bahrain, Kuwait, and Qatar	Import price CIF (cost, insurance & freight)	Minimum	Manufacturer
<b>United Arab Emirates</b>	Committee - MoH	All products (some exceptions)	Country of origin and Gulf Cooperation Council (GCC) countries: Kingdom of Saudi Arabia, Kuwait, Bahrain, Qatar, and the Sultanate of Oman	Ex-factory and import	Minimum	Websites; Manufacturer

Source: Espin J, et al. WHO/HAI project on medicine prices and availability-Working paper 1: external reference pricing (2011 May)

## Limitations and/or disadvantages

- **Price information is not always available.** Available prices are often heterogeneous (ex-factory, retail prices, etc.) and it is not always easy to adjust them to obtain the required type of price.
- **It is difficult to find transaction prices;** the prices that countries have access to are often not real prices, but virtual list/catalogue prices.
- There is no conclusive evidence about the impact of this practice, although **launch delays and the non-availability of new medicines in low-price countries seem to be a likely effect.** Price convergence, resulting from higher prices in lower-income countries, and decreasing price transparency are possible additional negative effects.

9

## Some Recommendations (I)

- ❖ Countries should consider using ERP as a method for negotiating or benchmarking the price of a medicine.
- ❖ Countries should consider using ERP as part of an overall strategy, in combination with other methods, for setting the price of a medicine.
- ❖ In developing an ERP system, countries should define transparent methods and processes to be used.
- ❖ Countries/payers should select comparator countries to use for ERP based on economic status, pharmaceutical pricing systems in place, published actual versus negotiated or concealed prices, exact comparator products supplied, and similar burden of disease.

## Some Recommendations (II)

- Preferably using some form of price regulation based on the value (**Value based pricing**)  
*See Kanavos, P., Nicod, E., Espin, J. and Van Den Aardweg, S.,. Short-and long-term effects of value-based pricing vs. external price referencing. EMiNet.*
- Open the space to **differential pricing**, trying to remove the legal and technical barriers
- **ERP** is not a panacea and **results** (savings, launch delays, etc.) always depend of how is implemented

11



Thank you very much for your attention.

[jaime@easp.es](mailto:jaime@easp.es)

12

# INTERNATIONAL REFERENCE PRICING: U.S. VS. REST OF WORLD WHO IS SHOOTING WHOSE FOOT? *- academic perspective of lower income European countries -*

Zoltán Kaló

*Professor of Health Economics*

1) Center for Health Technology Assessment, Semmelweis University

2) Syreon Research Institute  
Budapest, Hungary



**syreon**  
Research Institute

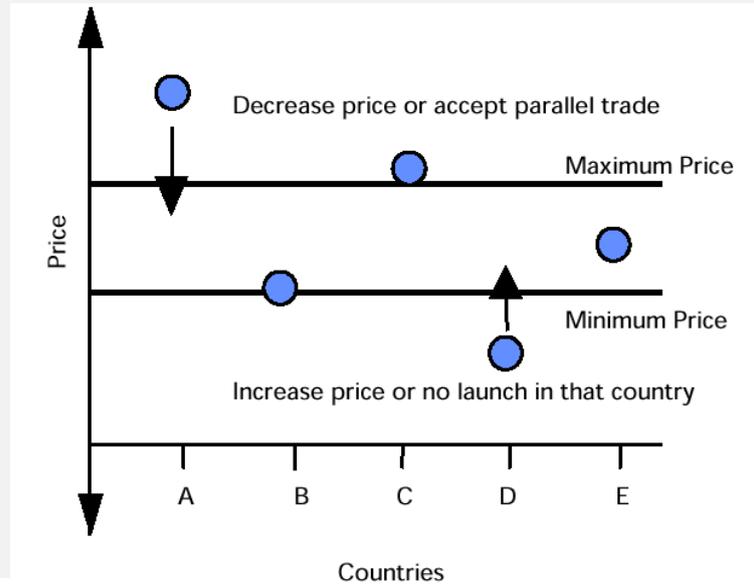
Today's research for tomorrow's health

## European external price referencing (EPR) system

	AT	BE	BU	CH	CY	CZ	DE	DK	EE	EL	ES	FI	FR	HR	HU	IE	IS	IT	LT	LU	LV	MT	NL	NO	PL	PT	RO	SE	SI	SK	UK	Add. countries	N. of countries
AT																																	24
BE																																	26
BU																																	12
CH																																	6
CY																																	4
CZ																																	19
DE																																	15
DK																																	9
EE																																	4
EL																																	22
ES																																	16
FI																																	29
FR																																	4
HR																																	3
HU																																	31
IE																																	9
IS																																	4
IT																																	27
LT																																	8
LU																																	1
LV																																	7
MT																																	11
NL																																	4
NO																																	9
PL																																	31
PT																																	3
RO																																	12
SE																																	n/a
SI																																	3
SK																																	27
UK																																	n/a
Reference frequency	16	15	9	2	10	13	17	15	12	13	16	15	19	5	13	13	3	15	14	9	11	8	15	6	10	13	10	13	13	16	17		

Source: Toumi M, Rémuzat C, Vataire AL, Urbinati D. External reference pricing of medicinal products: simulation based considerations for cross-country coordination. Report prepared for the European Commission. 2014

## Impact of external price referencing (and parallel trade) in the European Union: narrow pricing corridor for new medicines



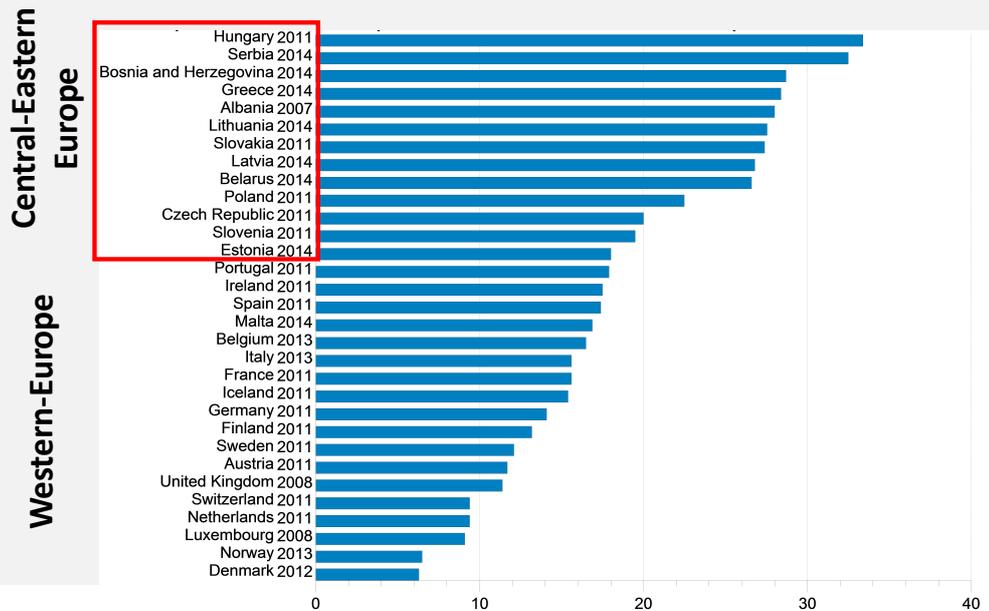
Today's research for tomorrow's health

## Consequence of narrow price corridor: pharmaceutical expenditure in higher vs lower income European countries (average values between 2000–2012)

	Higher income EU countries	Lower income EU countries
GDP per capita (1000 EUR)	34.2	14.6
Total health expenditure per GDP	8.8%	7.5%
Pharmaceutical expenditure per GDP	1.3%	<b>1.8%</b>
Pharmaceutical / total health expenditure	14.4%	<b>24.8%</b>

Ref: Elek P, Takács E, Merész G, Kaló Z. Implication of external price referencing and parallel trade on pharmaceutical expenditure: indirect evidence from lower-income European countries, *Health Policy and Planning*. 2017. 1. 32(3). 349-358.

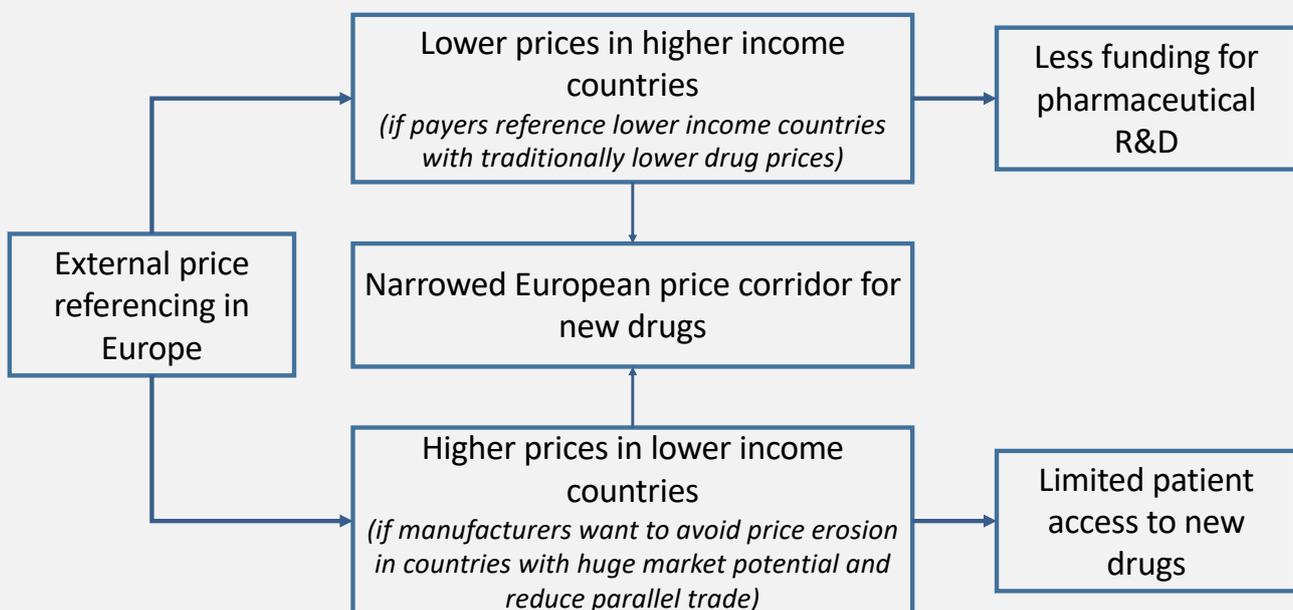
## Share of pharmaceutical expenditure in total health expenditure (last available year)



Today's research for tomorrow's health

Source: WHO Health For All European Database 2016

## Impact of external price referencing in Europe



Today's research for tomorrow's health

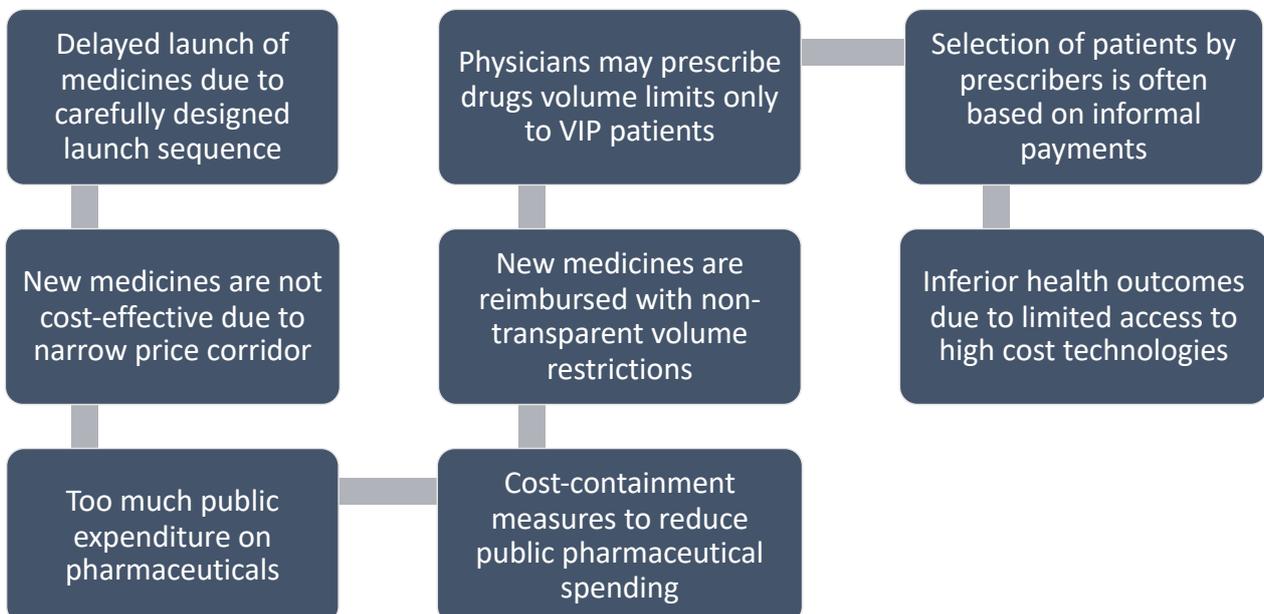
Adapted from: Ridley DB: *Pharmacoeconomics* 2005; 23 (7): 651-658

## WHO IS SHOOTING WHOSE FOOT? - perspective of lower income countries -

1. In the short-run not free-riding on prices in other countries creates damages in any lower income countries → race to the bottom
2. In the long-run, by contributing to the wide use of external price referencing, all lower income countries are shooting their own foot

Today's research for tomorrow's health

### Consequences of global implementation of external price referencing on lower income European countries



## Message to higher income countries

- Referencing drug prices of lower income countries reduces patient access, and consequently may even kill patients in the referenced countries
- More savings can be generated by referencing the salary of physicians and nurses in lower income countries, which can also reduce migration of health care professionals