FIFARMA Symposium

Managed Entry Agreements: A health policy mechanism to reconcile access to innovation with healthcare system sustainability

ISPOR Latin America 2019

FIFARMA

Federación Latinoamericana de la Industria Farmacéutica

FIFARMA

Agenda

- Opening and introduction by Rafael Andrés Díaz-Granados
- Multilateral perspective by Héctor Castro, MD.
- Academic perspective by Louis P. Garrison, Jr. PhD
- Industry perspective by Jens Grueger, PhD.
- Q&A moderated by Rafael Andrés Díaz-Granados

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Speakers

Hector Castro is the Global Leader of Health Financing, Technologies, Data and Impact at Management Sciences for Health (MSH) in Washington D.C. Doctor in medicine and surgery, MSc in Health Policy, Planning, and Financing from the London School of Hygiene & Tropical Medicine (LSHTM), joint degree with the London School of Economics & Political Science. Doctor in Public Health and Policy/Health Economics from the University of London and former Takemi Postdoctoral Fellow at the Harvard T.H. Chan School of Public Health.

Louis P. Garrison, Jr., PhD, is Professor Emeritus in the Pharmaceutical Outcomes Research and Policy Program in the School of Pharmacy, and Adjunct Professor in the Departments of Global Health and Health Services at the University of Washington. He also co-directs the Global Medicines Program in Global Health. Dr. Garrison received a BA in Economics from Indiana University, and a PhD in Economics from Stanford University. He has more than 100 publications in peer-reviewed journals. Louis was president-elect of ISPOR Board of Directors for the period 2015-2016.

Jens Grueger, PhD is the former VP Global Access at F. Hoffmann-La Roche, based in Basel, Switzerland. Jens was trained in mathematics and medicine, receiving a master's degree in medical statistics (1984) and a PhD in theoretical statistics (1986) from the Technical University of Dortmund in Germany. Jens is the president-elect for ISPOR Board of Directors for the period 2019-2020.

Moderator

Rafael Andrés Díaz-Granados serves as executive director of FIFARMA. Leveraging deep healthcare expertise and working closely with FIFARMA's member companies, associations and staff, Rafael is committed to FIFARMA's mission to foster access to pharmaceutical innovations for the benefit of patients in Latin America, and ensuring sustainable health systems in our region. Rafael has an economics degree from Harvard and a JD from Georgetown.

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Management Sciences *for* Health

Esquemas de Acceso Administrado

Managed Entry Agreements (MEAs)

Oportunidades Y Desafíos Para Países De Ingreso Medio/Bajo

Héctor E. Castro MD, MSc, DrPH
Practice Area Leader Health Financing, Technologies, Data & Impact

Prioridades que compiten

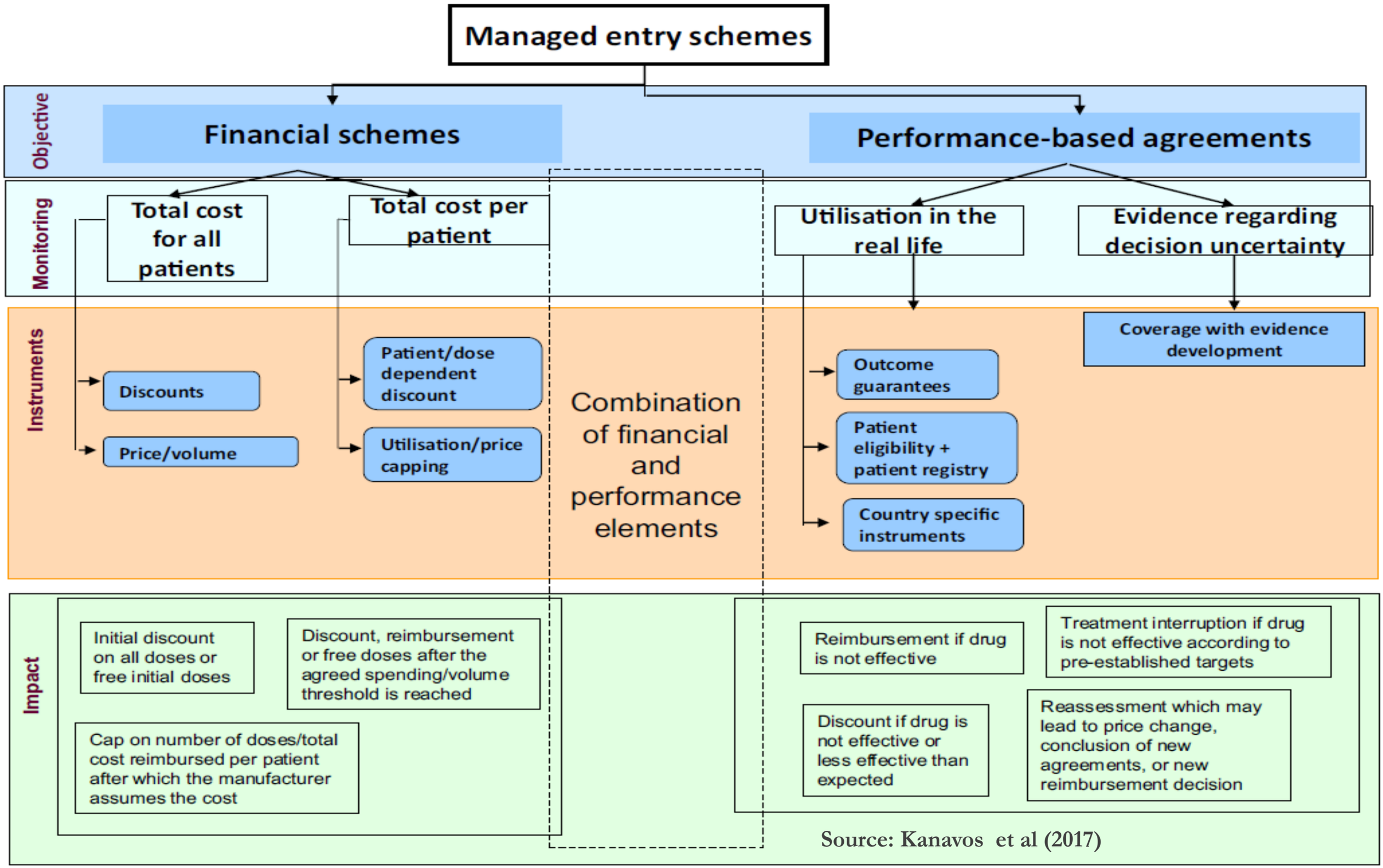
- De casi 60 millones de muertes en el mundo en 2015, 40 M estuvieron relacionadas con Enfermedades Crónicas No Transmisibles (ECNT). OMS (2018)
  - Cardiovasculares, el cáncer y la diabetes las tres mas frecuentes.
  - 75% de muertes anuales por ECNT ocurren en LMICs (30 millones).
- Pero además agendas inconclusas en ET&O, ET, Huérfanas.
- I&D para ha resultado efectiva y costo efectiva en muchos casos, pero <u>en otros no!</u>
- Incertidumbre respecto a efectividad e impacto financiero, especialmente de medicamentos innovadores puede retardar acceso a los pacientes… <u>Y en ocasiones llevar a medidas regulatorias desesperadas!</u>

Una oportunidad para los EAAs

Además de incertidumbre sobre beneficios vs. costos marginales… restricciones presupuestales… también presiones sociales y demográficas… tendencia global hacia cobertura universal (no solo amplitud, sino en profundidad).

- Oportunidad para que pagadores y desarrolladores compartan riesgo.
- **Esquemas de Acceso Administrado (EAAs)-** *Managed entry agreements/ schemes, risk sharing agreements, performance-based, patient access schemes, etc*: MEAs, son un tipo de arreglo institucional entre pagadores y fabricantes para compartir el riesgo asociado a la incertidumbre (en efectividad/impacto financiero) y para facilitar acceso a nuevas tecnologías (Ferrario & Kanavos, 2012).
  - Tipos (Carlson, Sullivan, et al, 2010):
    - No relacionados con desenlaces en salud
    - Relacionados con desenlaces en salud

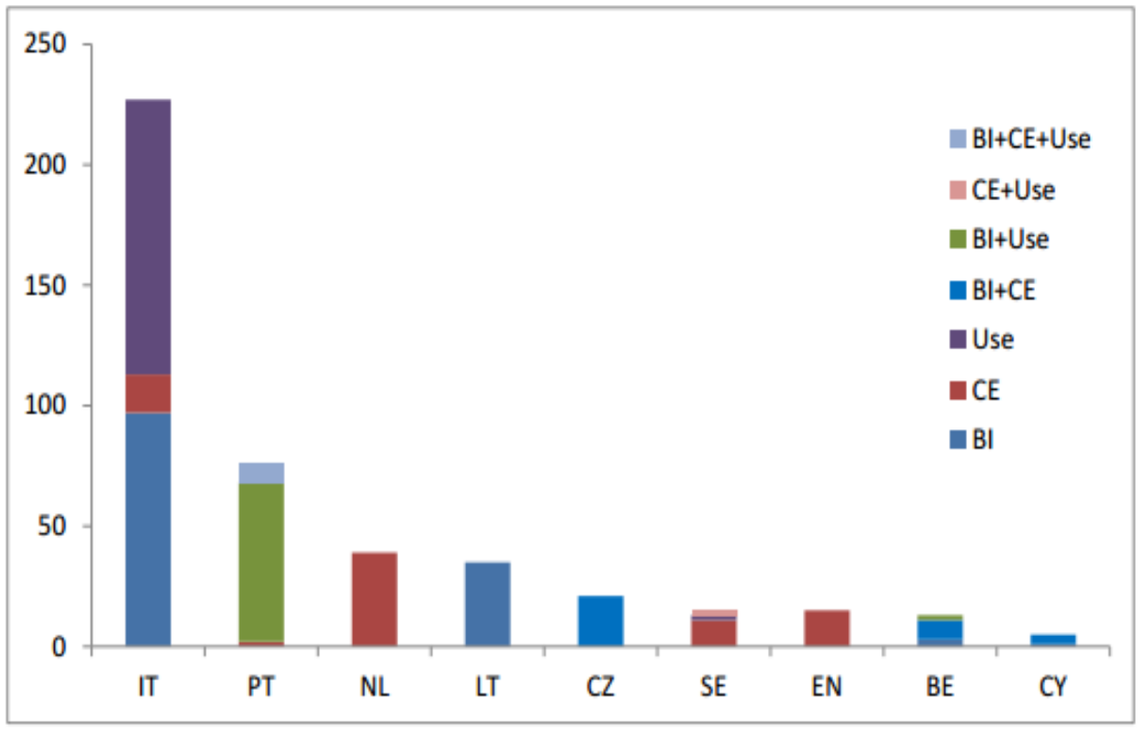
Taxonomía de los EAAs



Source: Kanavos et al (2017)

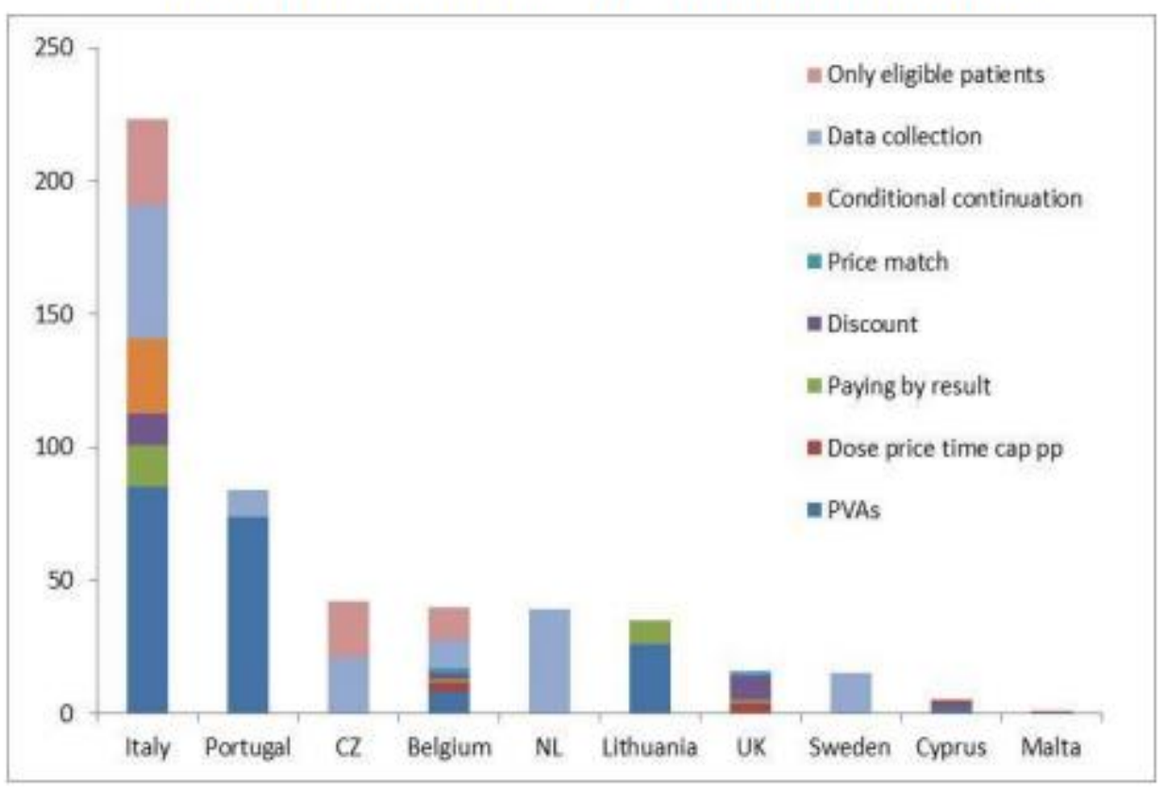
Una oportunidad para los EAAs

Objectives Member States are trying to achieve through MEAs overall and at country level



Legend: BI: Limit budget impact, CE: Address uncertainties regarding the cost-effectiveness, Use: Monitor use in clinical practice, Access+CE: Improve patient access and cost-effectiveness. BE: Belgium, CY: Cyprus, CZ: Czech Republic, EN: England, IT: Italy, LT: Lithuania, MT: Malta, NL: Netherlands, PT: Portugal, SE: Sweden

Common elements of MEAs overall and at country level

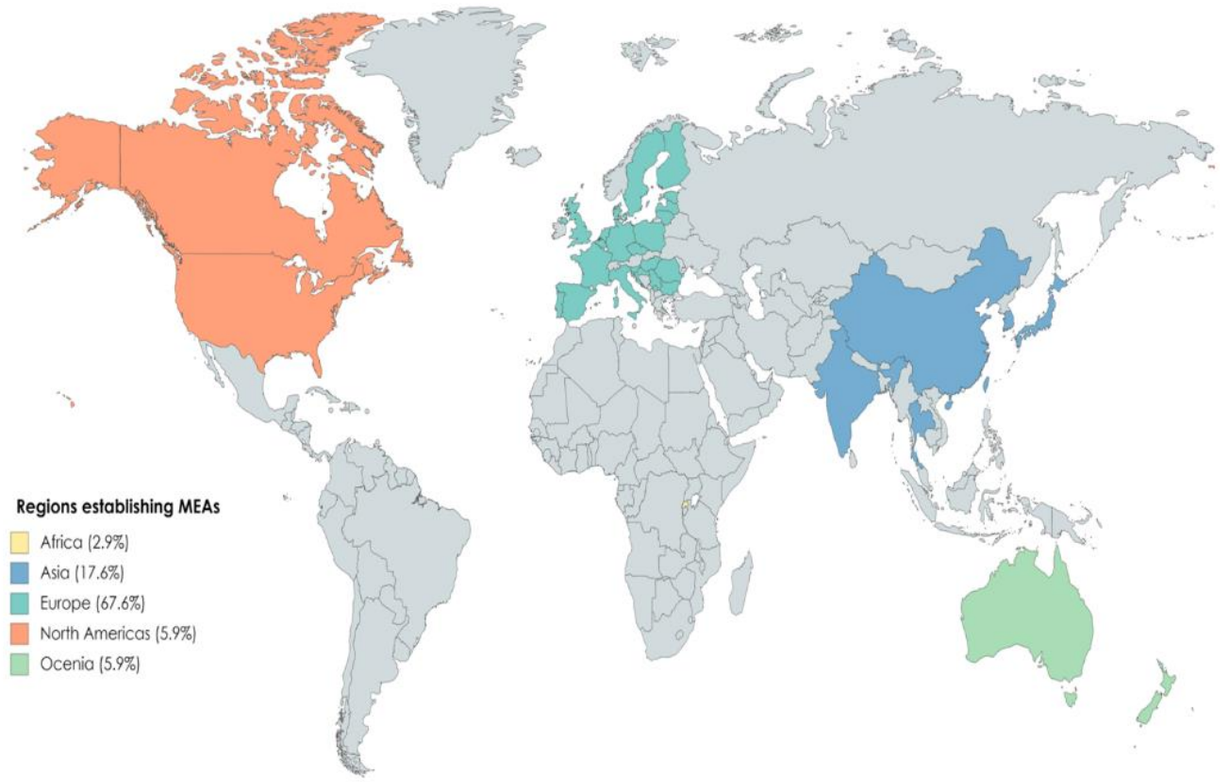


Proyecto reciente en EAAs

- Proyecto financiado por el Banco Mundial; piloto en 3 países (Colombia, Kenia, Ucrania)
- Actividad I: Identificar y evaluar los programas de acceso a medicamentos existentes, incluyendo para los de medicamentos genéricos
  - Revisión sistemática de la literatura publicada- Diciembre/ 2017- Febrero/2018
  - Revisión de la literatura no convencional ("literatura gris")- Enero- Febrero/2018
  - Entrevistas semiestructuradas con informantes clave en 3 países (Colombia, Kenia, Ucrania) – Febrero 2018
  - Triangulación con 5 expertos globales en EAAs - Mar/18
- Actividad II: Co-crear nueva evidencia para la toma de decisiones apropiadas en el contexto de LMICs.
- Actividad III: Desarrollar un compendio de "buenas prácticas" para estrategias de acceso a medicamentos.
- Actividad IV: Apoyo a la diseminación y uso de resultados

Resultados

- 285 esquemas fueron identificados en nuestra búsqueda.
- EAAs fueron identificados en 23 países en Europa (67.6%), 6 países de Asia (17.6%), 2 países de América del Norte, 2 países de Oceanía y 1 país de África (Ruanda).
- Es posible que muchos otros LMICs estén implementando EAAs pero que no hayan sido publicados o usen diferente terminología.
- Los esquemas financieros resultaron levemente más comunes (50.2%) que los esquemas basados en el desempeño (44.9%); 4.9% de los esquemas fueron modelos híbridos ambos acuerdos.
- La implementación de los esquemas financieros tiende a ser menos compleja que la implementación de esquemas basados en el desempeño.



Mayoría de esquemas para diferentes tipos cáncer (cáncer de mama, leucemia mielócitica crónica, cáncer colo-rectal)

Factores que ayudan/obstaculizan el uso de EAAs

- *Características del contexto:* Nivel de ingreso, tamaño del mercado, estabilidad política, niveles de corrupción, estructura del sistema de salud (centralizado o descentralizado), casos de éxito locales, cooperación internacional y esfuerzos de coordinación
- *Características del medicamento, evidencia e incertidumbre:* Suficiencia y calidad de la evidencia disponible sobre medicamento en un país en particular, incluyendo evidencia del mundo real, costo-efectividad y criterios de elegibilidad del paciente; posibilidad de generalización/ extrapolación de resultados clínicos en la población local
- *Capacidad del sistema de salud para regular y negociar:* Capacidad para recopilar, monitorear y evaluar datos. Para esquemas financieros, los sistemas de salud requieren capacidad para estimar volúmenes; para esquemas basados en desempeño, capacidad de sistemas de salud para evaluar resultados)
- *Existencia de marcos legales y de políticas que habiliten el uso de MEAs:* incluyendo requisitos legales sobre transparencia de los precios y los acuerdos confidenciales.

Factores que ayudan/obstaculizan el uso de EAAs

- *Existencia de reglas, roles, responsabilidades y planes de implementación claros dentro del sector de la salud,* particularmente en términos de pagadores y compañías farmacéuticas.
- *Conocimiento del uso y las limitaciones de MEAs por parte de los actores clave,* incluyendo entendimiento de la complejidad de la implementación de MEAs, la viabilidad y el atractivo del mercado
- *Aceptación y apoyo por parte de actores clave para el uso de MEAs como una solución normativa:* Inclusión de MEAs en la formulación e implementación de la agenda de política; formación de coaliciones y redes apoyo; apoyo financiero; existencia defensores ("campeones")
- *Nivel de confianza entre los pagadores y las compañías farmacéuticas* y la disposición al diálogo.
- *Actitudes frente a riesgo por parte de pagadores y compañías farmacéuticas: ("neutrales, evasores y buscadores")*; incluye las actitudes frente al riesgo hacia la incertidumbre, el incumplimiento del acuerdo, los efectos en los ingresos internacionales, y la garantía de compensar posibles grandes pérdidas.

Ventajas y Desventajas

- Pacientes: acceso temprano a nuevos tratamientos.
- Pagadores: avanzar acceso temprano y lidiando con incertidumbre (efectividad e impacto presupuestal).
- Compañías farmacéuticas: previsibilidad condiciones iniciales de precio y estimación tamaño del mercado (mas recursos = mayor innovación?).
- EAAs ayudan a crear un entorno más colaborativo entre pagadores y compañías farmacéuticas.
- EAAs proveen diferentes tipos de instrumento para abordar diferentes necesidades y mercados.
- EAAs pueden utilizarse en conjunto o pueden complementar otras estrategias de acceso.

- Percepciones negativas sobre EAAs pueden dificultar su implementación-
- EAA difieren entre países, lo que lleva a una confusión sobre su uso como estrategia para mejorar el acceso a medicamentos y sinergia con otras iniciativas.
- Carga para sistema de salud—administración, costo y recopilación y análisis de datos
- Implementación de EAAs es viable en países con marcos legales y políticos habilitantes.
- Confidencialidad de acuerdos limita capacidad de aprendizaje entre países y transparencia.
- Compañías farmacéuticas perciben que los AF no representan justamente el "valor" de sus innovaciones.

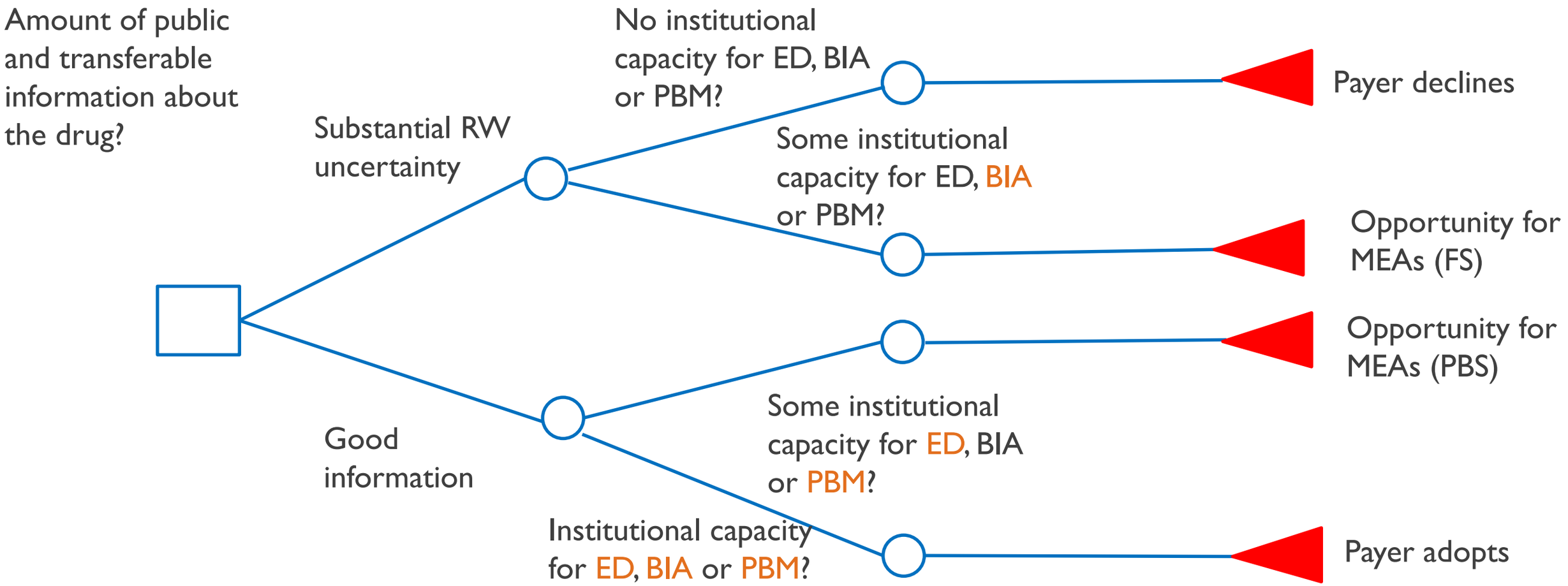
¿Una oportunidad para acercar posiciones?

El dialogo entre pagadores y compañías farmacéuticas es un paso fundamental para hacer viable el uso de EAAs en LMICs. Los modelos analíticos de decisión podrían facilitar ese dialogo permitiendo que las partes interesadas se familiaricen con los términos y conceptos, las opciones de diversos instrumentos y las concesiones antes de que el dialogo ocurra.

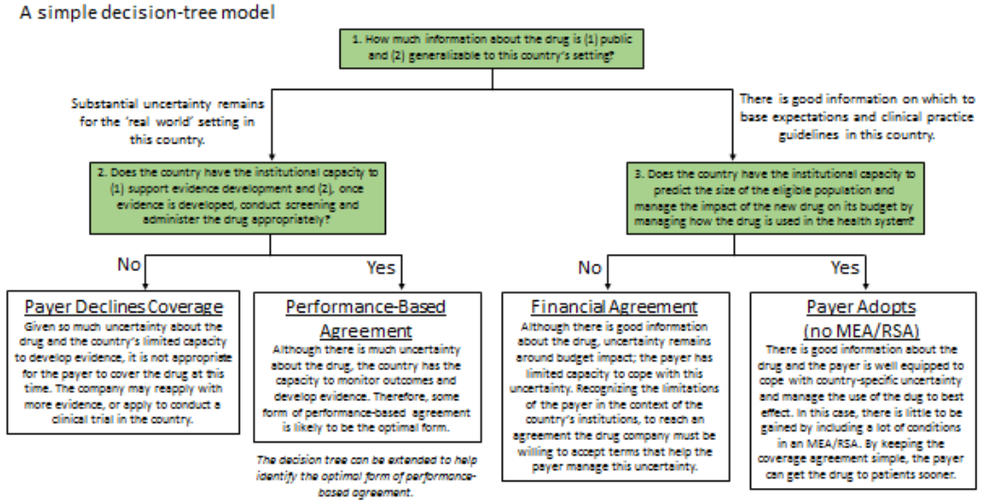
Tres modelos analíticos de decisión, fueron desarrollados conjuntamente por MSH y RTI International:

- Modelo estático de para explorar diferentes alternativas (snapshot model)
- Modelo dinámico para ilustrar la progresión del sistema y en relación a tipos de esquema adoptables ('bridge' model)
- Modelo cuantitativo para estimar precio, volumen y otras variables

Modelo estático para explorar diferentes alternativas (‘*snapshot’ model*)



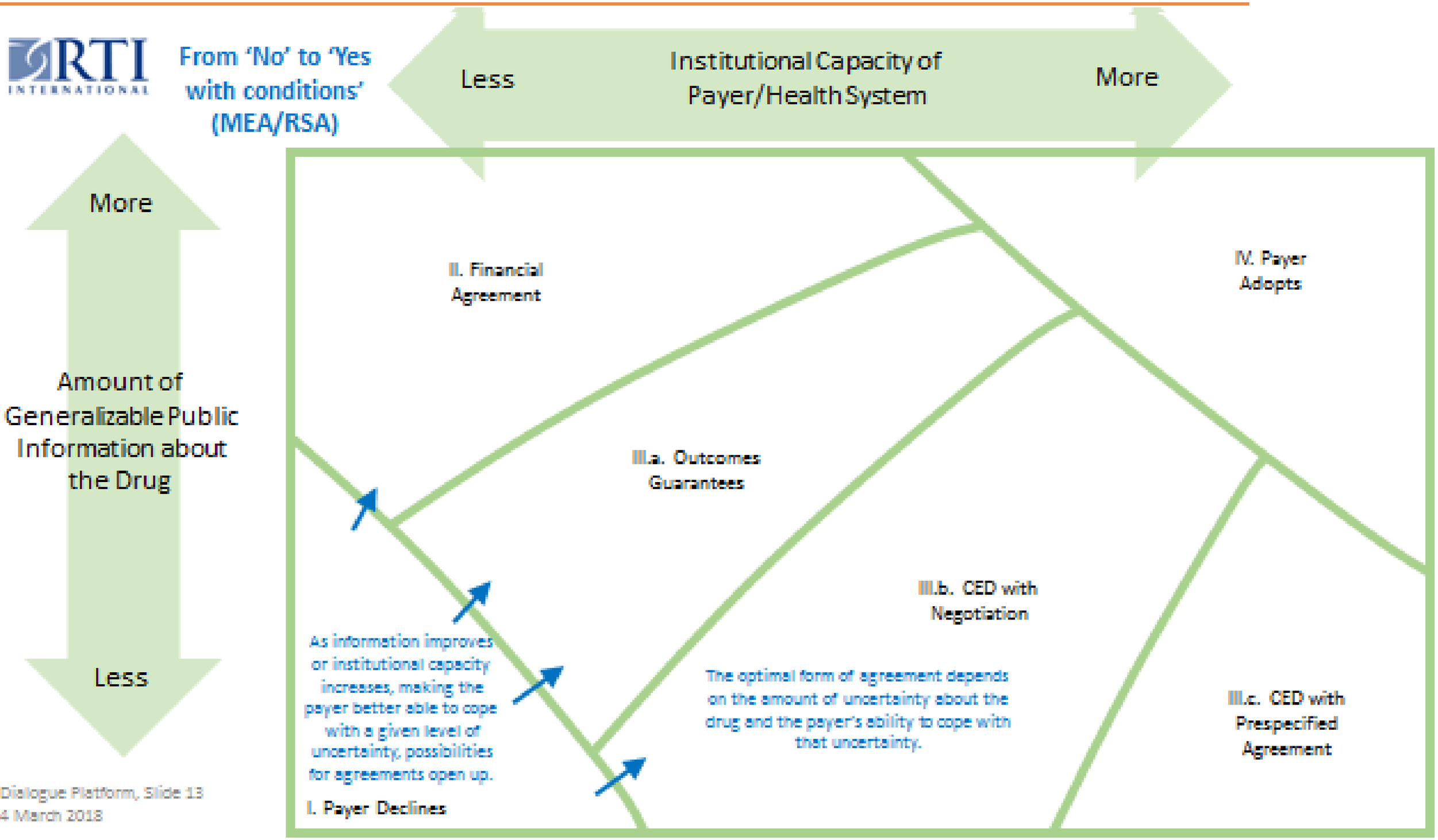
A simple decision-tree model



A simple matrix model

Amount of Generalizable Public Information about the Drug	Institutional Capacity of Payer/Health System: Limited	Institutional Capacity of Payer/Health System: Adequate
Adequate	Financial Agreement	Payer Adopts (no MEA/RSA)
Limited	Payer Declines Coverage	Performance-Based Agreement

Modelo dinámico progresión del sistema (*'bridge' model*)



Dialogue Platform, Slide 13
4 March 2018

Modelo cuantitativo para estimar precio, volumen y otras variables

D. New Drug Impact — Performance-Base Agreement

NOTE: In this version, modeling is limited to ***Outcomes Guarantees***. In future versions, the modeling can be extended to Coverage with Evidence Development.

1. Percentage of treated patients expected to respond:

55% expected positive response rate

2. Average health impact per responding patient

0.85 DALY per year of treatment

Assumptions:

Rebates will given for any non-responding patients. Rebates will be given at the reduced price as long as the total number of responding patients is greater than the number paying the negotiated price. If the number of responding patients falls short of the number paying the negotiated price, the difference between the number responding and the number paying the negotiated price will be rebated at the negotiated price.

—implies the following outcomes:

Buget Impact: 1,443,750 *USD* *per year*

(32% **increase)**

New average cost per HCPD patient per year:

351 *USD* *per year*

(23% **increase)**

Expected cost effectiveness:

1,029 *USD* per *DALY*

Recomendaciones para países con limitada experiencia y capacidad para implementar EAAs

- Aprender de experiencias de otros países, particularmente LMICs.
- Desarrollar las capacidades individuales y organizacionales necesarias para entender los tipos de acuerdos (EAAs).
- Priorizar una o dos enfermedades que podrían hacer parte de un piloto
- Identificar y elegir el mejor instrumento de EAA de acuerdo al contexto del país.
- Promover dialogo con compañías farmacéuticas.
- Implementar piloto y evaluar la experiencia para identificar las necesidades de capacidades necesarias para el futuro uso/implementación de EAAs.
- Publicar y difundir los resultados del piloto en un caso de estudio.
- Considerar una estrategia incremental de implementación de EAAs.
- Fortalecer capacidades adicionales para la implementación de EAAs (ETES, PBM y otras herramientas)
- Ajustar políticas sectoriales (e intersectoriales) que minimicen posibles obstáculos para implementación a largo plazo de los EAAs.

Conclusiones

- EAAs ofrecen una alternativa de política a las flexibilidades establecidas en los ADPIC (ej. concesión de licencias obligatorias), popular entre activistas internacionales, pero muy complejos políticamente y soluciones de corto plazo.
- EAAs pueden promover el desarrollo de capacidades duraderas y acuerdos institucionales para la toma de decisiones sostenibles sobre medicamentos para las ENT.
- El compendio de buenas prácticas producido para el BM recomienda estrategias para partes interesadas que estén considerando el uso de EAAs, y ofrece recomendaciones para y orientación práctica para futuro análisis http://pubdocs.worldbank.org/en/792561542818915277/MSH-RTI-GLOHI-Compendium-Final-Version-2-Nov-21-2018.pdf:
  - ***Recomendaciones para países con poca experiencia previa y capacidad limitada para implementar EAAs***
  - ***Recomendaciones para países con poca experiencia previa, pero con mayor capacidad (entorno favorable, infraestructura, voluntad política) para implementar EAAs***
  - ***Recomendaciones para futuro análisis y orientación práctica sobre el uso de EAAs en LMIC***

STRONGER HEALTH SYSTEMS. GREATER HEALTH IMPACT.



Photo credits*, l to r*: , Amy Niebling, Warren Zelman, Carmen Urdaneta

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Managed Entry Agreements in LatAm: An Academic Health Economist's Perspective

ISPOR Latin American Meeting

FIFARMA Symposium

Bogota, Colombia

Sept. 14, 2019

Lou Garrison, PhD

Professor Emeritus

The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute

School of Pharmacy, Univ. of Washington

Visiting Senior Fellow, Office on Health Economics, London, UK

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- Thanks for FIFARMA support for my participation in this symposium

- ISPOR Short Course material from Lou Garrison and Josh Carlson (University of Washington) and Adrian Towse (OHE)

- University of Washington (UW) Project Collaborators: Sean Sullivan, Josh Carlson, David Veenstra, Peter Neumann, Rick Carlson, Adrian Towse

- Sponsors of UW PBRSA Research Project: Novartis, Johnson & Johnson, GSK, GE Healthcare, Roche, Pfizer, Eli Lilly, Sanofi-Aventis, Abbott Laboratories, Amgen

- ISPOR PBRSA Task Force: Co-Chairs: Louis P. Garrison, Jr., Adrian Towse, England, UK; Members: Andrew Briggs, Gerard de Pouvourville, Jens Grueger, Penny Mohr, J.L. (Hans) Severens Paolo Siviero, Miguel Sleeper

Performance-Based Risk-Sharing Arrangements: A Variety of Names—Similar Concepts

- **managed entry agreements (MEA)**
- outcomes-based schemes
- risk-sharing agreements
- coverage with evidence development (CED)
- access with evidence development
- patient access schemes (PAS)
- conditional licensing
- pay-for-performance programs (P4P)
- value-based arrangements
- And others?

What makes innovative medicines unique economic goods? The relevance for MEAs?

1. Have global public goods properties:
   - Information/scientific knowledge can benefit everyone in the world.
   - Markets will tend to undersupply public goods.
     →Patents and subsidies
     →"Free-rider" problems
2. Regulated (benefit-risk comparison) for public safety
3. Risky, high fixed development costs with low marginal cost
   →Market failure: free-riding on real-world evidence
   →Optimal financing is global differential pricing

Starting Point

Lack of Real-World Data: A Market Failure for Medicines as Global Public Goods

Current global health system has very weak incentives to measure performance after a medicine is on the market.

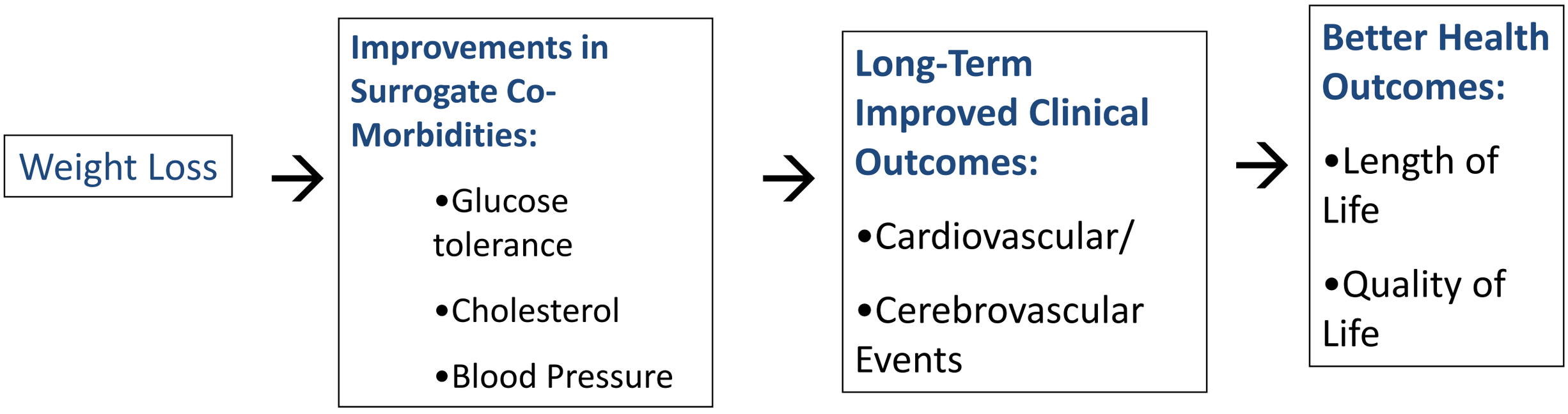
- This means that we do NOT operate as a “learning health care system.”

Basics of Innovative Medicines: The Pervasiveness of Uncertainty

- Drugs are approved, launched, and reimbursed under conditions of uncertainty, affecting many key parameters:
  - Efficacy (heterogeneity)
  - Effectiveness in real world
  - Risks (safety)
  - Models, including links between surrogate markers and long-term outcomes
  - Cost-effectiveness
  - Budget impact.

1. **Variability→Uncertainty (=Risk)**
2. **Gathering more evidence to reduce uncertainty is costly.**

Bioclinical Health Outcomes Framework: Which Outcomes to Measure? Where Is the Uncertainty?



Example: Obesity Disease-Treatment Model

The New York Times

Business

Pricing Pills by the Results

Illustration by The New York Times

By ANDREW POLLACK
Published: July 14, 2007

Drug companies like to say that their most expensive products are fully worth their breathtaking prices. Now one company is putting its money where its mouth is — by offering a money-back guarantee.

Johnson & Johnson has proposed that Britain's national health

VELCADE® Response Scheme (VRS) for patients with Multiple Myeloma at 1st relapse within the NHS in England, Wales and N.Ireland- Process Flow

Customer

Janssen-Cilag/Ortho Biotech

VRS Administrator

JC Drug Safety

Signs VRS agreement with JC

VRS claim forms are sent to Customer upon receipt of signed VRS agreement

Orders VELCADE

Evaluate response after a maximum of 4 cycles (≤16 vials) Response Y/N

No[2]

Hospital completes VRS claim form for replacement stock, credit or full cash refund for ≤16 vials. Fax/Post to JC

VRS Claim Form copied to JC Drug Safety Dept.

Drug Safety allocates a specific UK/DS Number and writes to clinician requesting more details on the non-response event

Yes[1]

Order further vials of VELCADE

Claim validated[3] Y/N

No

JC advises and discusses with customer

Yes

Instruction to despatch replacement stock, issue credit note or full cash refund

Replacement product delivered or credit note/cash refund issued to customer

VRS claim logged (Audit and Healthcare Compliance)

Notes:

1 Response defined as a patient, at first relapse, with a 50% or greater reduction in serum M-protein, within 4 cycles of treatment, compared to baseline level immediately prior to VELCADE treatment

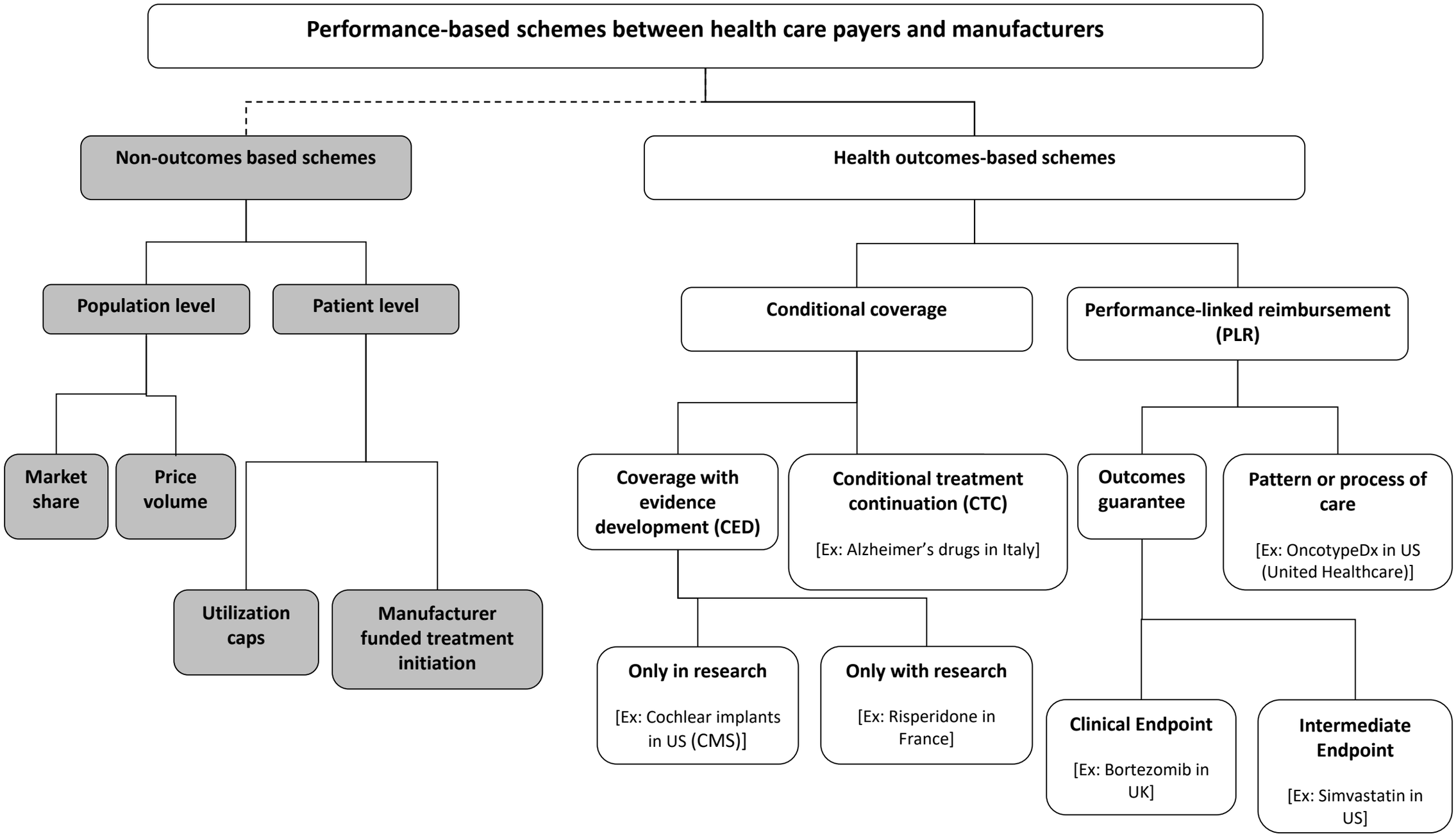
2 Non-response or minor response defined as a patient, at first relapse, having less than a 50% reduction in serum M-protein, within 4 cycles of treatment, compared to baseline level immediately prior to VELCADE treatment

NB: 15% - 20% of patients do not have measurable serum M-protein levels, and for this group Bence-Jones urine protein (urine free light chains) could be used. Response defined according to the standard EBMT (European Group for Blood and Marrow Transplantation) criteria, i.e. at least a 90% reduction, compared to baseline. This would be compared to baseline immediately prior to VELCADE treatment (and within 4 cycles).

3 Claim Validation to check:

- VRS claim form completed in full and signed

UW Taxonomy (Carlson et al.)



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ISPOR TASK FORCE REPORTS

Performance-Based Risk-Sharing Arrangements—Good Practices for Design, Implementation, and Evaluation: Report of the ISPOR Good Practices for Performance-Based Risk-Sharing Arrangements Task Force

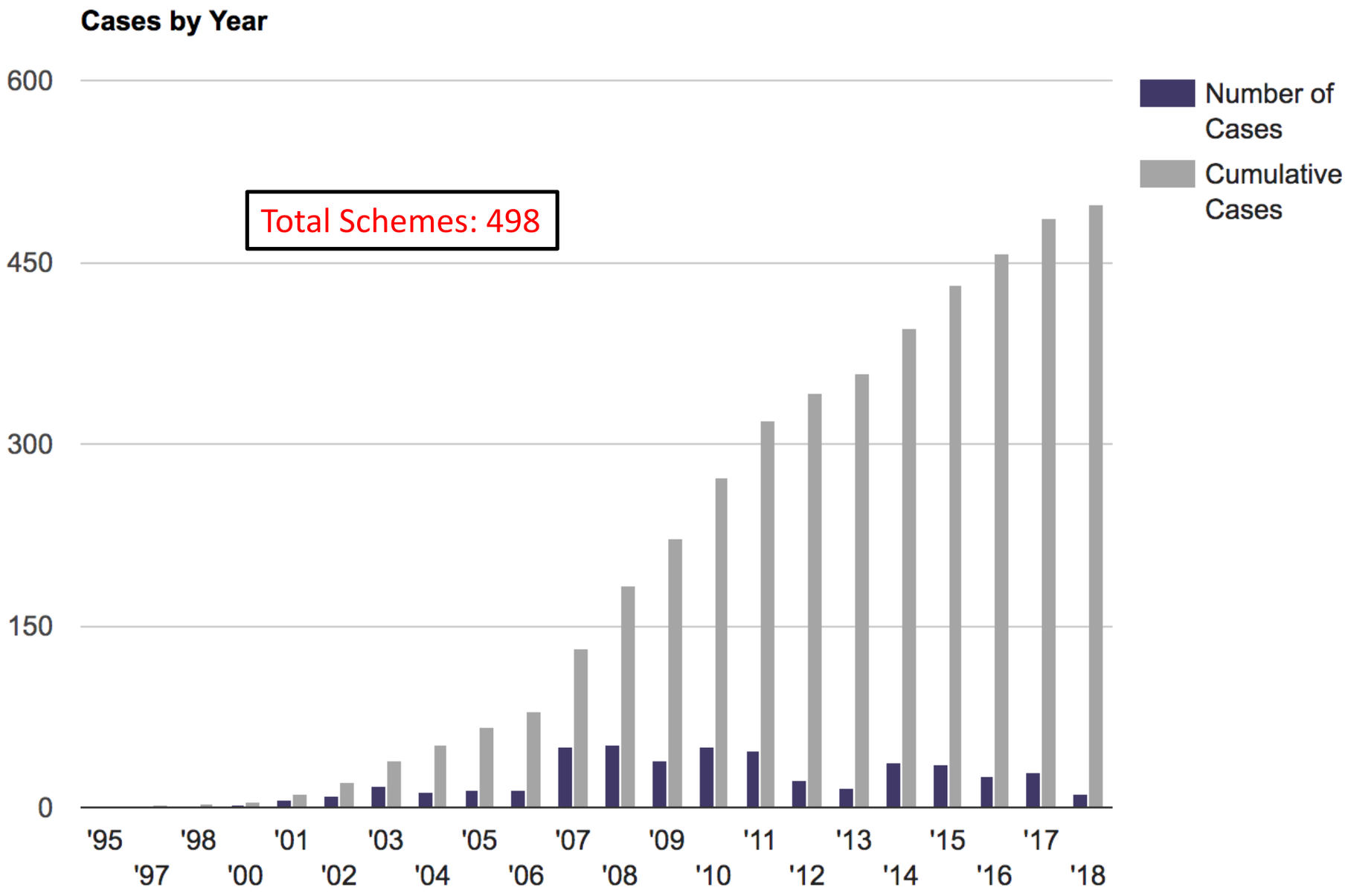
Louis P. Garrison Jr., PhD (co-chair)[1,*], *Adrian Towse, MA, MPhil (co-chair)*[2], *Andrew Briggs, MSc, DPhil*[3], *Gerard de Pouvourville, PhD*[4], *Jens Grueger, PhD*[5], *Penny E. Mohr, MA*[6], *J.L. (Hans) Severens, PhD*[7], *Paolo Siviero, BA*[8], *Miguel Sleeper, ACMA*[9]

[1]*Pharmaceutical Outcomes Research & Policy Program, Department of Pharmacy, University of Washington, Seattle, WA, USA;* [2]*Office of Health Economics, London, UK;* [3]*Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK;* [4]*ESSEC Business School, Cergy Pontoise, France;* [5]*F. Hoffmann - La Roche AG, Basel, Switzerland;* [6]*Center for Medical Technology Policy, Baltimore, Maryland, USA;* [7]*Institute of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, The Netherlands;* [8]*Agenzia Italiana del Farmaco, Rome, Italy;* [9]*Access to Medicines GlaxoSmithKline plc, Brentford, UK*

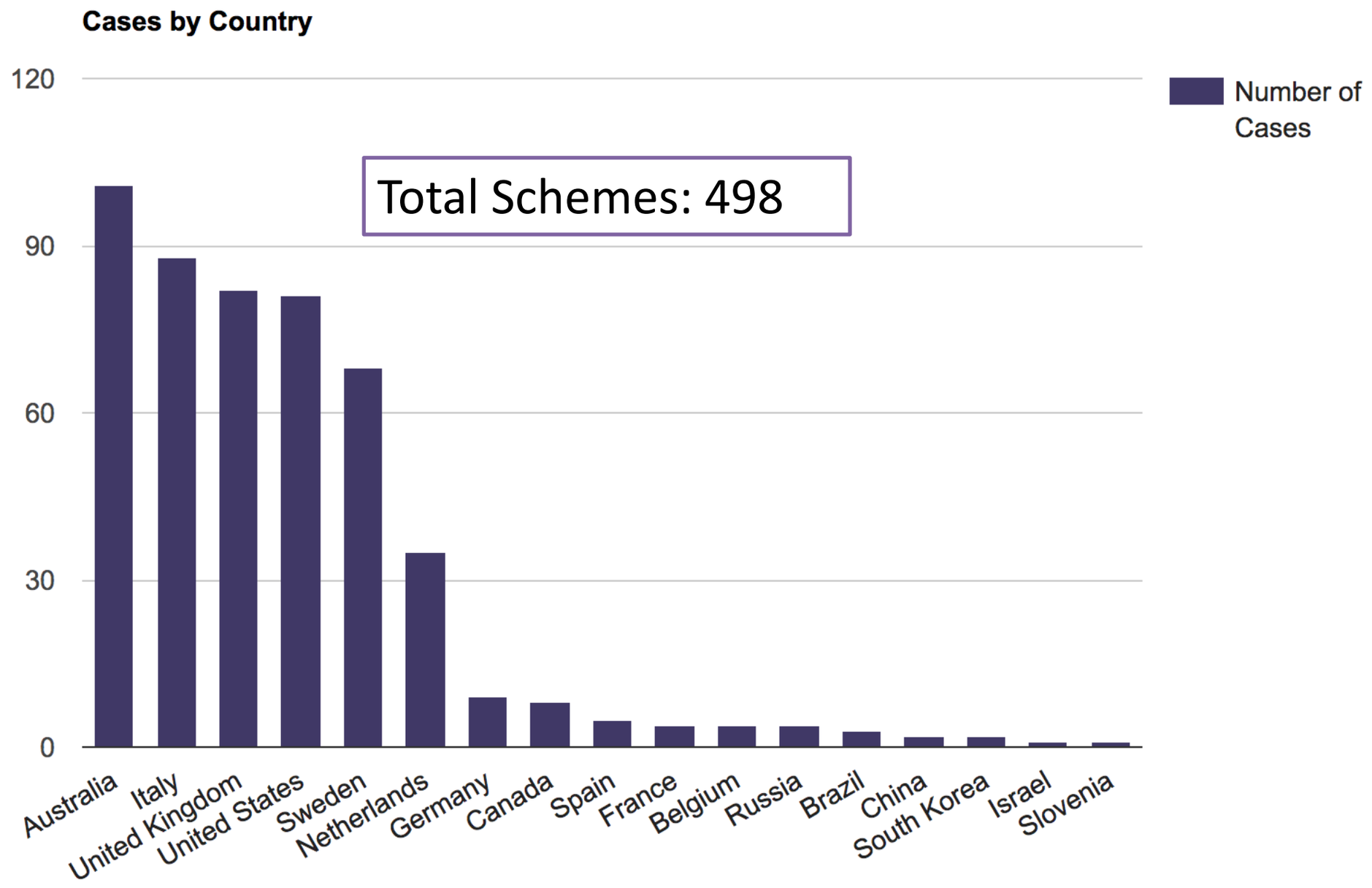
MEA (PBRSA)—Five Key Characteristics

1. ***There is a program of data collection*** agreed between the manufacturer (or provider, in some instances) and the payer..
2. ***This data collection is typically initiated during the time period following the regulatory approval*** (which may be full, conditional, or adaptive), and linked to post-launch coverage decisions..
3. ***The price, reimbursement, and/or revenue for the product are linked to the outcome of this program of data collection*** either <u>explicitly</u> by a pre-agreed rule or <u>implicitly</u> through an option to renegotiate coverage, price, and revenue at a later date
4. ***The data collection is intended to address uncertainty*** **about …. *For example:***
   - efficacy or effectiveness in the tested population as compared to current standard of care;
   - the efficacy or effectiveness in a broader, more heterogeneous population than used in registration trials or in pre-licensing testing;…
5. ***These arrangements provide a different distribution of risk*** **between the payer and the manufacturer than the historical manufacturer-payer relationship.**

Source: ISPOR PBRSA Task Force Report


Cases by Year
600
450
300
150
0
Total Schemes: 498
Number of Cases
Cumulative Cases
'95
'97
'98
'00
'01
'02
'03
'04
'05
'06
'07
'08
'09
'10
'11
'12
'13
'14
'15
'16
'17
'18

Cases by Country



Source: UW PBRSA Database


POLICY

Private Sector Risk-Sharing Agreements in the United States: Trends, Barriers, and Prospects

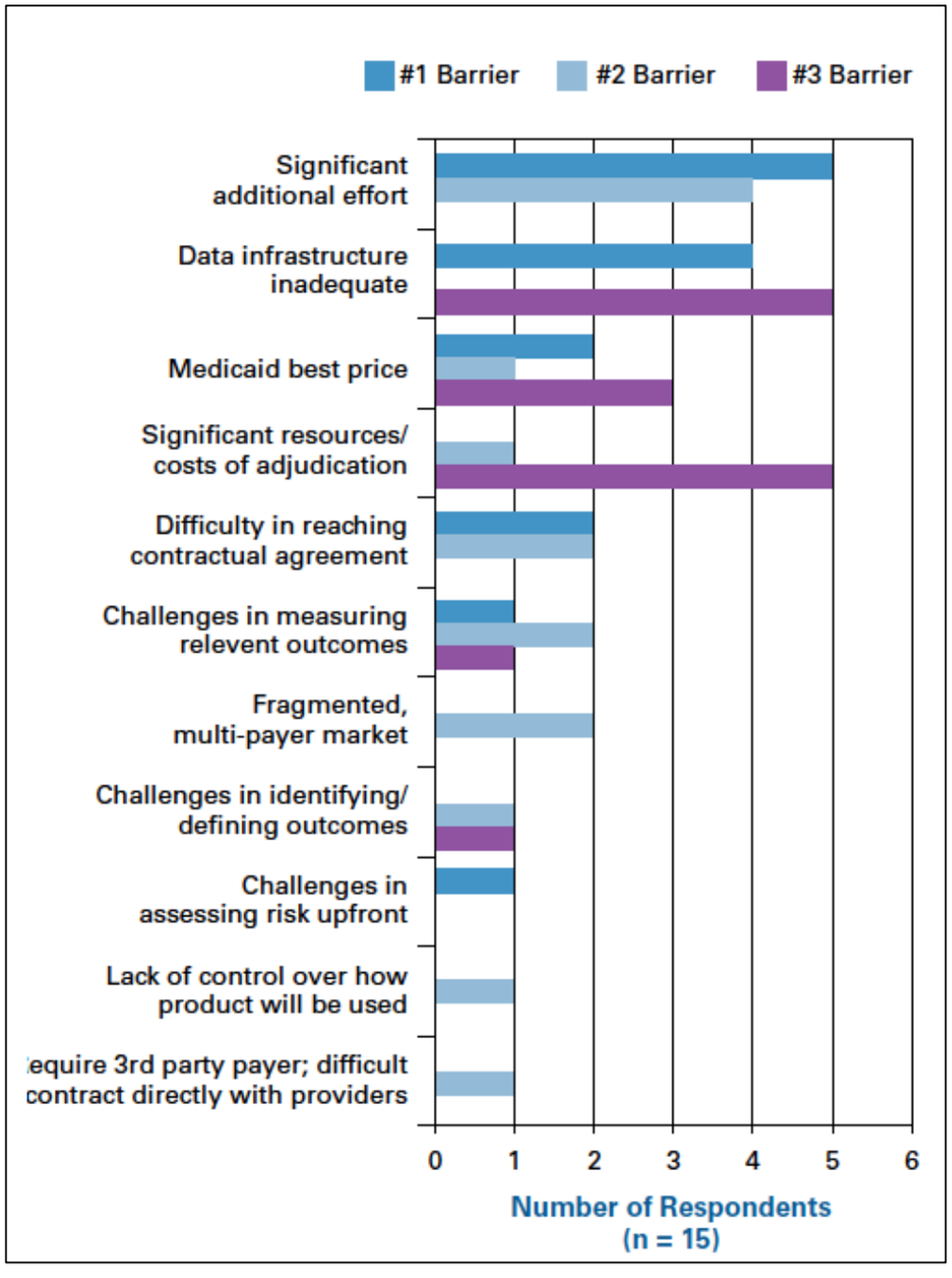
Louis P. Garrison, Jr, PhD; Josh J. Carlson, PhD; Preeti S. Bajaj, PhD; Adrian Towse, MA, MPhil; Peter J. Neumann, ScD; Sean D. Sullivan, PhD; Kimberly Westrich, MA; and Robert W. Dubois, MD, PhD

AJMC, 2015

Key findings:

- Lots of interest and talk by manufacturers
- Substantial implementation barriers
  - Need better data systems
  - Costs of negotiation
- More interest in financially-based RSAs
- Shift incentives? Via Accountable Care Organizations and government subsidies?

Figure 5. Survey Findings of Top Barriers to the Use of RSAs in the United States



AJMC, 2015

Value-Based Arrangements May Be More Prevalent Than Assumed

Nirosha Mahendraratnam, PhD; Corinna Sorenson, PhD, MHSA, MPH; Elizabeth Richardson, MSc; Gregory W. Daniel, PhD, MPH, RPh; Lisabeth Buelt, MPH; Kimberly Westrich, MA; Jingyuan Qian, MPP; Hilary Campbell, PharmD, JD; Mark McClellan, MD, PhD; and Robert W. Dubois, MD, PhD

TABLE. Outcome Measures and Payment Mechanisms Used in VBAs, by Sector, 2014-2017

	Manufacturer		Payer	
	Total VBAs (n = 88)	Company (n = 11)	Total VBAs (n = 122)	Company (n = 8[a])
Outcome measure				
Laboratory measures	25	5	19	6
Imaging measures	0	0	1	1
Other biomarker measures (eg, cytogenetic testing)	0	0	1	1
Survival	8	3	8	2
Disease progression	9	3	6	2
Symptom improvement	1	1	0	0
Other nonbiomarker clinical measures (proprietary)	0	0	10	1
Medical encounter process measures	8	3	15	5
Financial measures	13	3	28	4
Drug utilization measures	34	8	42	7
Other[b]	5	2	11	2
VBA incentive mechanisms				
Larger rebate to payer	70	10	85	6
Full refund to payer	13	3	6	2
Full or partial coverage of corrective services by manufacturer	0	0	2	2
Manufacturer receives bonus payment from payer	6	3	1	1
Manufacturer pays some portion of supportive product costs (eg, data analytics, follow-up testing)	6	1	18	1
Other[c]	0	0	19	2

VBA indicates value-based payment arrangement.

AJMC, 2019

Desirable Scheme Characteristics

- **Simple** to implement and evaluate
- **Clinically robust, clinically plausible, appropriate, and monitorable**
- **Operationally manageable** –without complex administration, monitoring, or excessive costs
- **Distribution on treatment restricted** to a limited number of outlets
- **Consistent with financial flows** in the healthcare system
- **Limited duration**—built-in review after not more than 2 years

Concluding Thoughts (1)

1. Almost no health system in the world has the data infrastructure to implement rapid monitoring of individual patient outcomes for clinical outcomes-based agreements.

1. So-called “financial agreements” include an element of outcomes—uptake and use in a population.

2. MEAs (aka PBRSAs) provide an important opportunity to generate the real-world evidence on product performance.

3. In the absence of adequate data infrastructure, the best solution may be CED (i.e., health services research to assess clinical effectiveness) to support re-negotiation of a locally feasible value-based price.

Concluding Thoughts (2)

4. The financially-based risk-sharing agreements can provide—via confidential discount—an important avenue for highly desirable differential pricing of medicines across countries with vastly different abilities to pay.

5. Financial agreements will do little to correct the global market failure of the undersupply of RWE that patients and their providers would like to have.

6. There remains the big global trade-off between access and innovation.

Implications for LatAm and LMIC countries:

- **MEAs can provide a useful vehicle to negotiate local value-based prices and contain costs in the aggregate.**
- **This supports global differential pricing, providing global support for greater innovation while improving access.**

Gracias!
Obrigado!

FIFARMA

Agenda

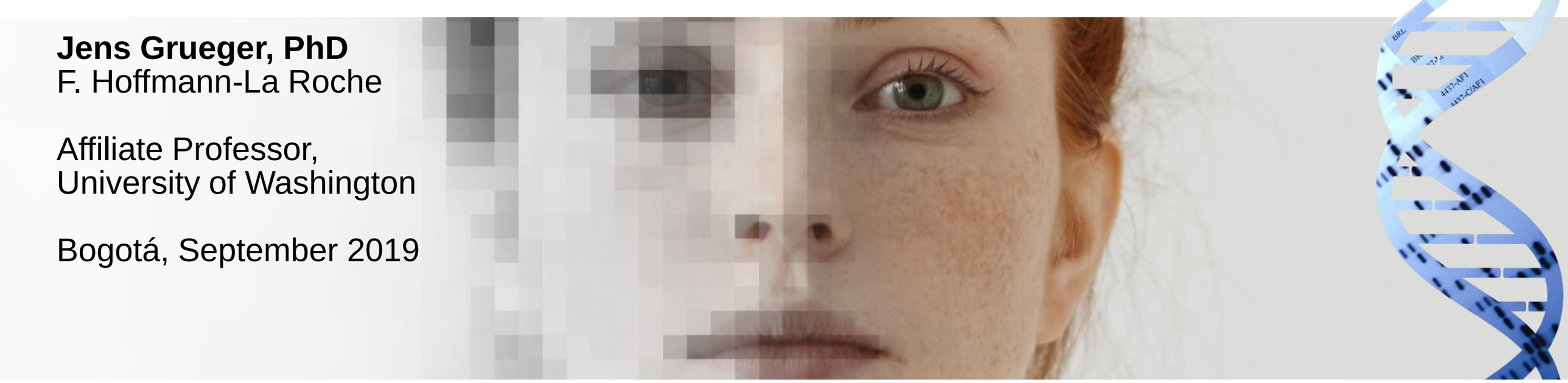
- Opening and introduction by Rafael Andrés Díaz-Granados
- Multilateral perspective by Héctor Castro, MD.
- Academic perspective by Louis P. Garrison, Jr. PhD
- **Industry perspective by Jens Grueger, PhD.**
- Q&A moderated by Rafael Andrés Díaz-Granados

Managed Entry Agreements in Latin America
An Industry Perspective

Jens Grueger, PhD
F. Hoffmann-La Roche

Affiliate Professor,
University of Washington

Bogotá, September 2019



Managed Entry Agreements

- MEAs are designed specifically to ensure access to medicines for which there is still uncertainty with respect to
  - their cost-effectiveness,
  - optimal and real-life clinical and health system utilization,
  - access pathways, and
  - impact on health sector expenditure

(Ferrario et al., 2017)

Overview

- Reasons to consider Managed Entry Agreements from an industry perspective
- When and how to design an MEA
- Practical considerations
- Measuring success
- Summary and conclusions

Managed Entry Agreements (MEA) were emerging in Europe in the early 2000s

- Uncertainty around clinical and cost-effectiveness
  - “we need proof, not promise”
- Increasing market access delays
  - Facilitate early access and continue data collection post-approval
- Concerns around appropriate utilization of new expensive treatments
  - Ensure that the right patients receive the right treatment
- Increasing price referencing and trade
  - Need to find country specific solutions that deliver differentiated price
- And more recently: managing financing of potential cures
  - How to smoothen large upfront payment?

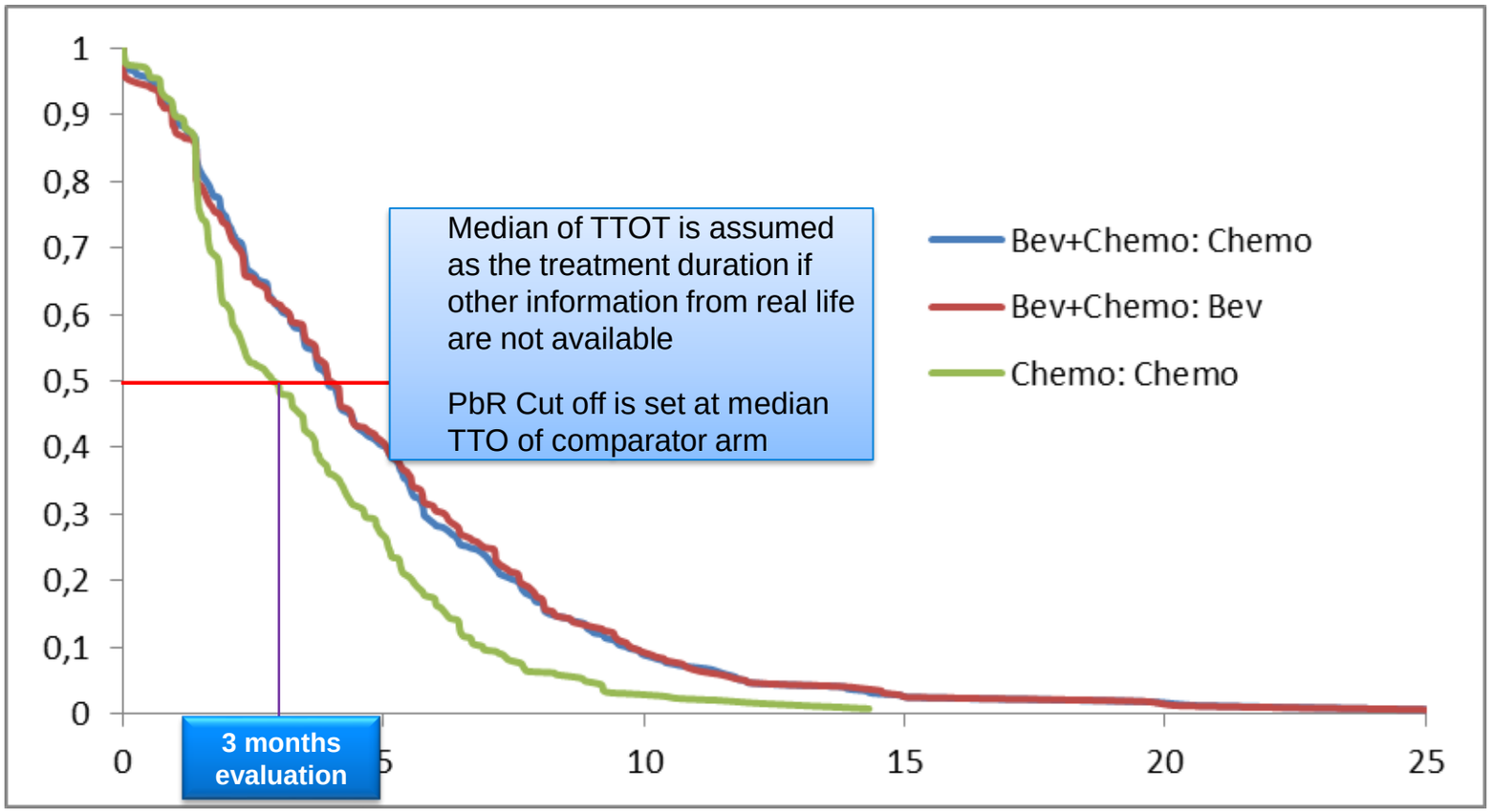
When and how to design an MEA

- Build this proactively into a product´s market access strategy, rather than as a reactive response to failure
- Focus on reducing decision uncertainty, rather than parameter uncertainty
- Use endpoints/success criteria that have been explored in pivotal trials and are included in marketing authorization
- Engage with all stakeholders early

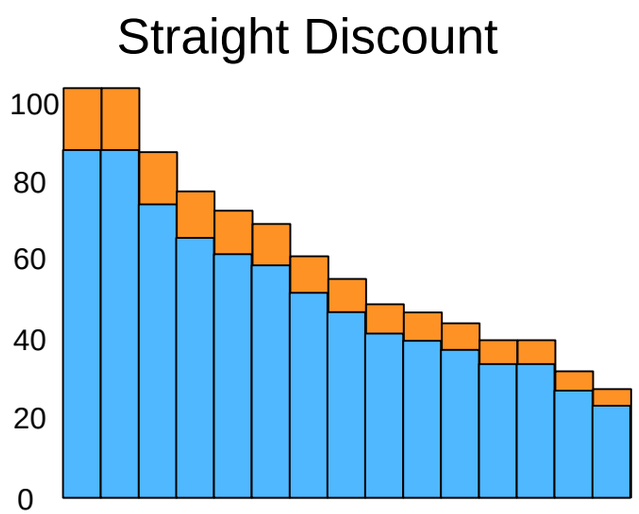
Performance based risk sharing criteria are often defined on the basis of “time to off-treatment” curve from RCTs

Avastin TML: PbR 3 months in Italy

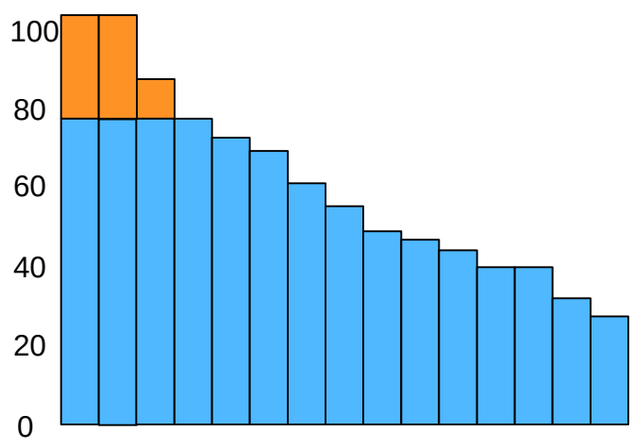
Example: Kaplan Meier Time To Off Treatment Avastin TML



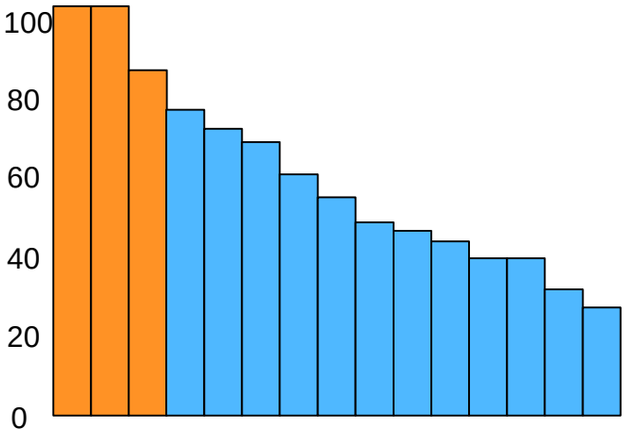
Different kinds of MEA deliver different levels of discount



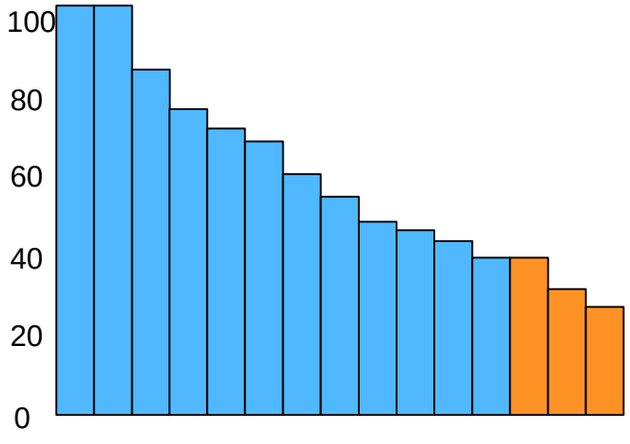
Straight Discount



Pay by Response



Free treatment Initiation



Episode of Care Cap

Practical considerations

- MEAs require efficient collection of data about drug utilization and patient outcomes
  - Countries like Italy have established a simple online treatment registry
- MEAs are easier to implement in National Health Services than in decentralized health systems
  - In a NHS, it may be sufficient to collect utilization and outcomes data for a representative sample of providers, whereas in decentralized systems every provider and hospital needs to collect the data
- MEAs can be used to differentiate net prices between and within countries
- In order to be successful, expectations need to be clear
  - MEAs are primarily around improving patient outcomes, and only then about managing utilization and reducing cost

What has been the impact of MEA on patient access?

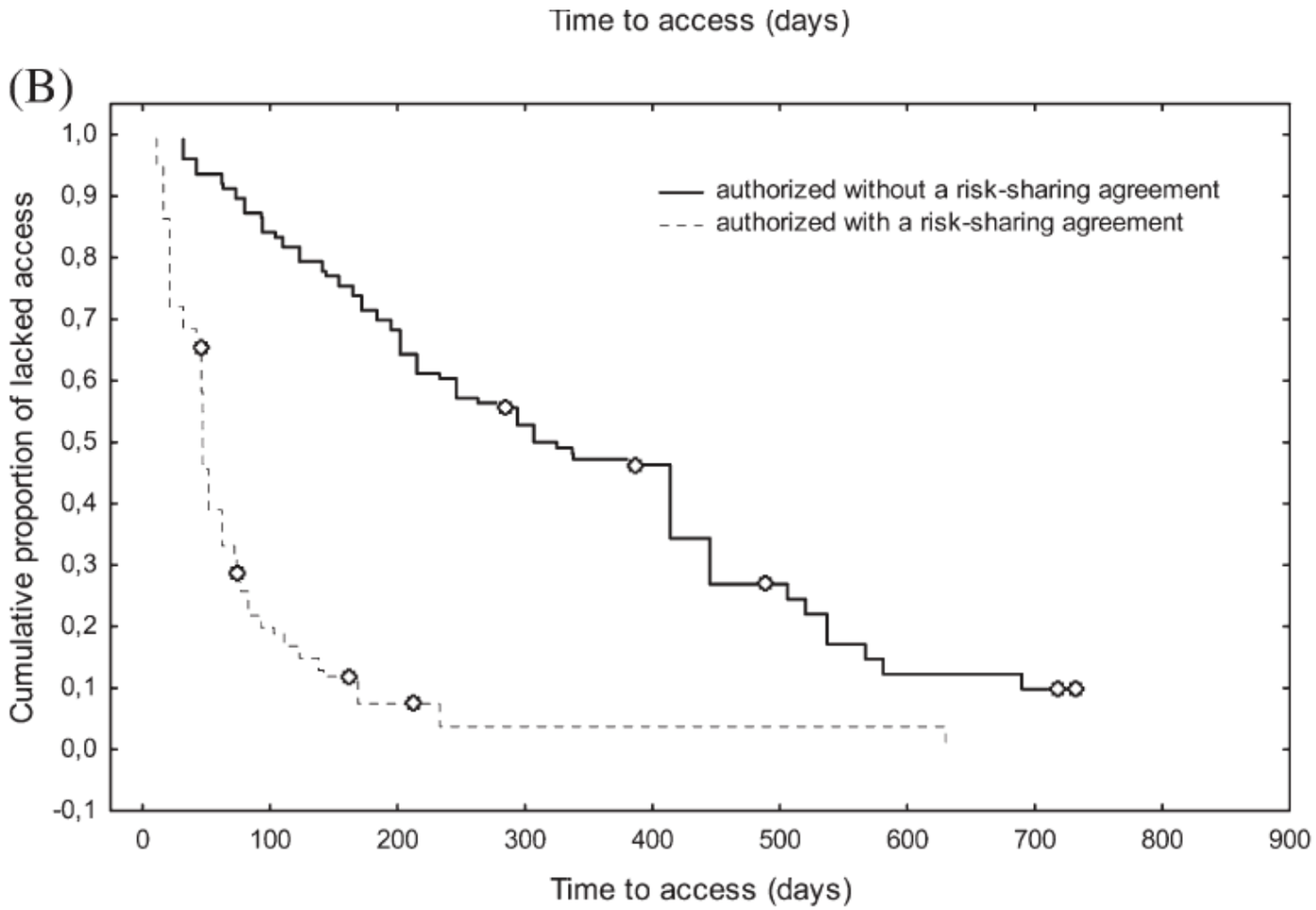


Figure 1. Kaplan–Meier analyses of time to regional patient access according to either the introduction in Region with or without a compulsory regional formulary (A) or authorization with or without a risk-sharing agreement (B).

Russo P, Mennini FS, Siviero PD, Rasi G. Time to market and patient access to new oncology products in Italy: a multistep pathway from European context to regional health care providers, Ann Oncol. 2010 Oct;21(10):2081-7

Experience in Latin America

Roche Breast Cancer Agreement in Uruguay (2017-2019)

- Single payer for high-cost medicines at a national level (FNR)
- Access to innovative medicines has been challenging due to budget constraints and uncertainty around financial impact
- Subscription model – fixed monthly payments to cover all Her2 breast cancer patients in Uruguay (includes Herceptin, Perjeta, Kadcyla)
- Guidelines have been agreed between all stakeholders (inclusion criteria, patient follow up, criteria for starting and stopping treatment)
- To monitor the agreement, a commission has been set up with representatives from payer, Roche, and Ministry of Health
- This agreement allows more than 1000 women to be treated.

Experience in Latin America

Brazil: risk sharing pilot for inclusion of Spinraza in SUS (April 2019)

- Uncertainty about cost-effectiveness and financial impact
- Aspects included in the agreement:
  - reduction of drug cost
  - description of the disease and eligibility criteria for the groups of patients who shall benefit from the agreement
  - expected results in terms of health and clinical effectiveness
  - maximum number of patients who will receive the drug per year (if number is exceeded, supplier shall bear the additional costs)
  - criteria for supply termination for patients whose treatment proves not to be efficient
  - frequency for the drug clinical effectiveness review

Source: http://www.mondaq.com/brazil/x/827944/Healthcare/Life+Sciences+Healthcare

Specific consideration for LatAm

- Do not reinvent the wheel
  - Build on experience in Europe
  - Not necessary to collect data again on longterm outcomes, rather focus on data that reduce uncertainty around effectiveness in your specific health system
- Collaboration between countries can generate the necessary capacity and avoid duplication
  - IT solutions for data collection and analysis may be used across countries
  - Not every country needs to collect the same data

Summary and conclusions

- Managed entry agreements are a potentially useful tool to improve patient access and outcomes, manage financial risks and design country specific solutions
- Implementation requires additional data collection, which may be burdensome for providers and patients
- Early engagement between all stakeholders is critical
- All stakeholders need to be clear about the objectives and expectations

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