

# W17: Risk-Sharing Arrangement: The Role of Real-World Evidence and Budget Impact Analysis

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# An Overview of International Efforts and Recent Development of Risk-Sharing Agreements

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Virtual ISPOR Asia Pacific Summit 2022

Concurrent Breakout Session 4. September 21, 2022

# The Concept of Risk-Sharing Agreements

- Risk-Sharing Agreements (i.e., outcomes-based contracts) have emerged as a promising mode engaging pharmaceutical manufacturers to share risk and improve patient access to medicines via evaluation of real-world outcomes
- Improving health outcomes, cost and financial risk reduction are the primary motivators for payers, while potential access or reimbursement gains are the key factors for pharmaceutical manufacturers, especially in areas of oncology and rare/orphan diseases
- Because RSAs are largely confidential and the complexity of the agreement itself, the trend and sustainability are unclear
- The high growth options are expected worldwide, including Asia Pacific countries and regions in the near future

# Advantage of Risk-Sharing Agreement

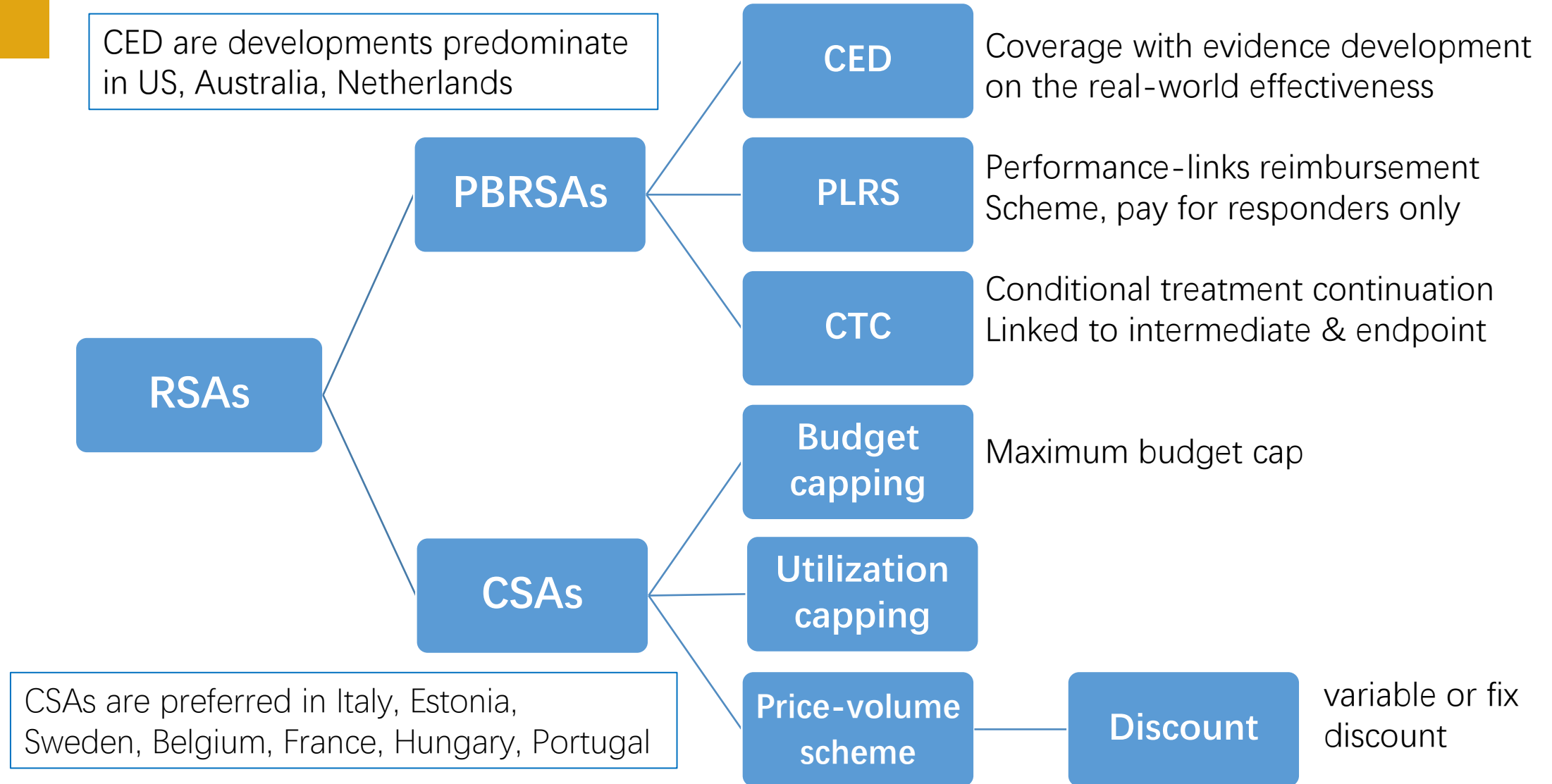
- Reducing uncertainty on clinical evidence and budget impact
- Pay only for patients responding to the therapy
- To boost overall efficiency
- Providing additional options to payer
- To promote rapid patient access to drugs

# Uncertainty Type, Scope & Considered Variables

Uncertainty type	Uncertainty scope	Considered Variables
Clinical	Efficacy, effectiveness, safety	<ul style="list-style-type: none"> <li>• Time frame fro treatment and follow-up</li> <li>• Clinical trial phase</li> <li>• Patient characteristics</li> <li>• Patient subgroup analysis</li> <li>• Primary endpoints</li> <li>• Surrogate endpoints</li> <li>• Active comparator</li> </ul>
Financial	Budget impact, cost-effectiveness	<ul style="list-style-type: none"> <li>• Treatment regimen</li> <li>• Potentially replaceable treatments</li> <li>• Net financial impact of treatments</li> <li>• Other modifications in use of resources linked to new treatment</li> <li>• Availability of CE or CU studies</li> </ul>

(Clopes A et al: 2014)

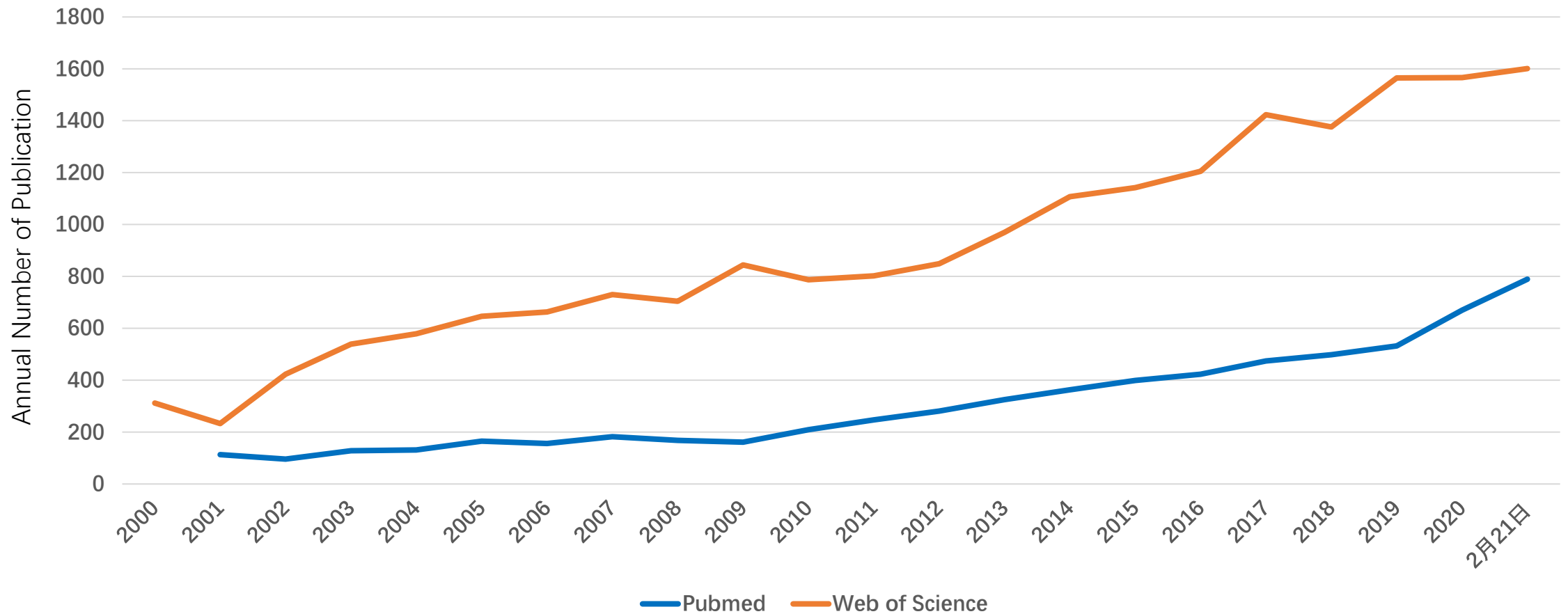
# The Taxonomy of Risk-Sharing Agreement



# The Prerequisite Condition for Implementing RSAs

- Need multiple disciplinary working group
- Establishing a specific RSA guideline or a best practice guideline
- Required a robust study design, implementation, evaluation and governance
- The outcome measures should be clear, measurable, objective, relevant and achievable
- Certain matters should be prespecified, including data collection and analysis, the evidence making a revised decision on price, revenue or coverage
- Reducing the implementation costs and building up the trust between payers and product manufactures

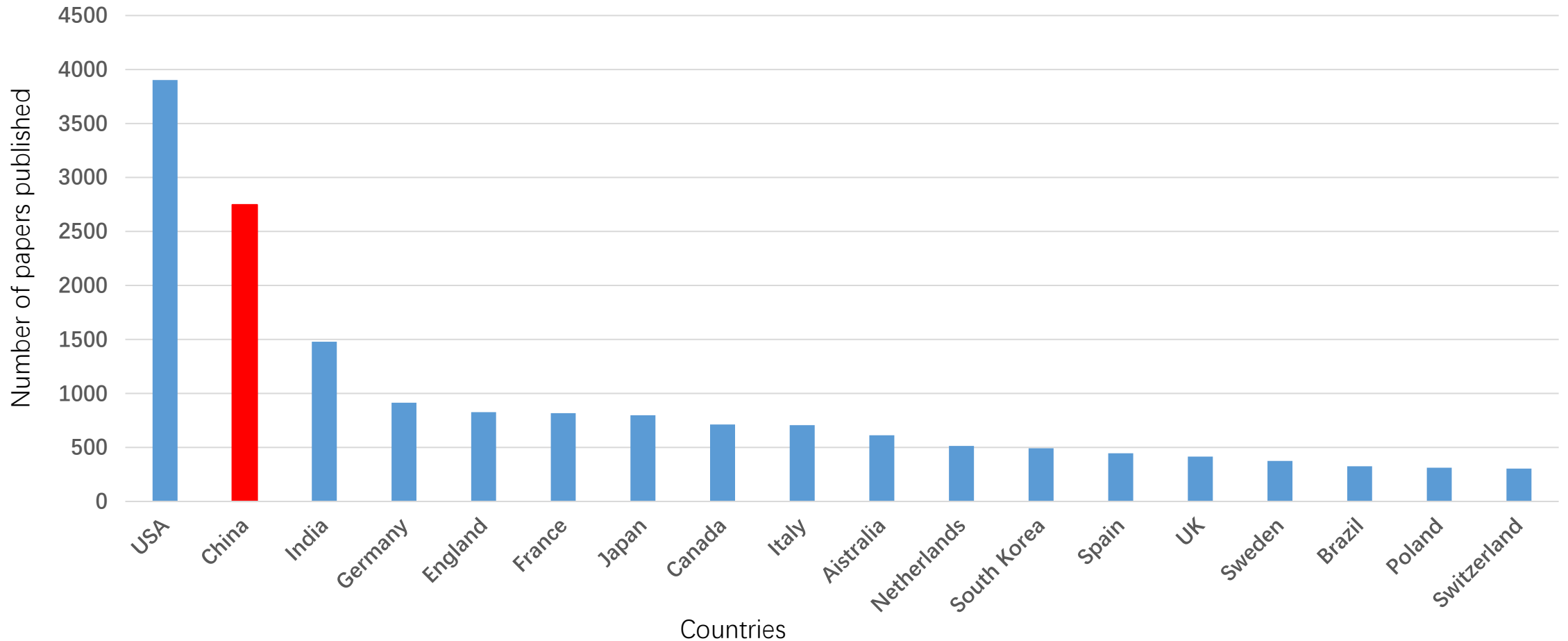
# The Number of RSA Articles Published in PubMed and Web of Science (2000-2021)



(Yang SS, Li RJ, Hu SL 2022)



# Total Number of RSAs Articles Published Between 2000 and 2021 (Web of Science)



(Yang SS, Li RJ, Hu SL 2022)

# PBRSA: An Updated International Review

- Professors Carison and Garrison performed a review of PBRSA from 1993 to 2016 using the University of Washington PBRSA database
- 185 out of 437 arrangements, 42% were categorized as currently active, five main types of PBRSA have been identified

PRSRAs	No. of cases	Percentage Performance-linked reimbursement (%)
Coverage with evidence development	149	41.9
Performance-linked reimbursement	104	23.8
Conditional treatment continuation	78	17.8
Financial or utilization	71	16.2
Hybrid schemes with multiple components	5	8.0

# Evaluation of Reimbursement for RSA Drugs in Italy

- Italy started first RSA contract in July 2006
- Pay back from RSA only 5% of total expenditure varies between drugs
- Management cost need to be taken into account, including cost for implementation and maintenance, time cost for hospital and consultation pharmacists, data available on the efficacy and safety
- Italy has three RSA categories
  - Cost sharing (discount)
  - Risk-sharing (partial reimbursement for eligible non-responders after a clinical evaluation)
  - Payment by results
- Because of the CSAs are easy to implementation, it is preferred in Italy, Estonia, Sweden, Belgium, France, Hungary and Portugal

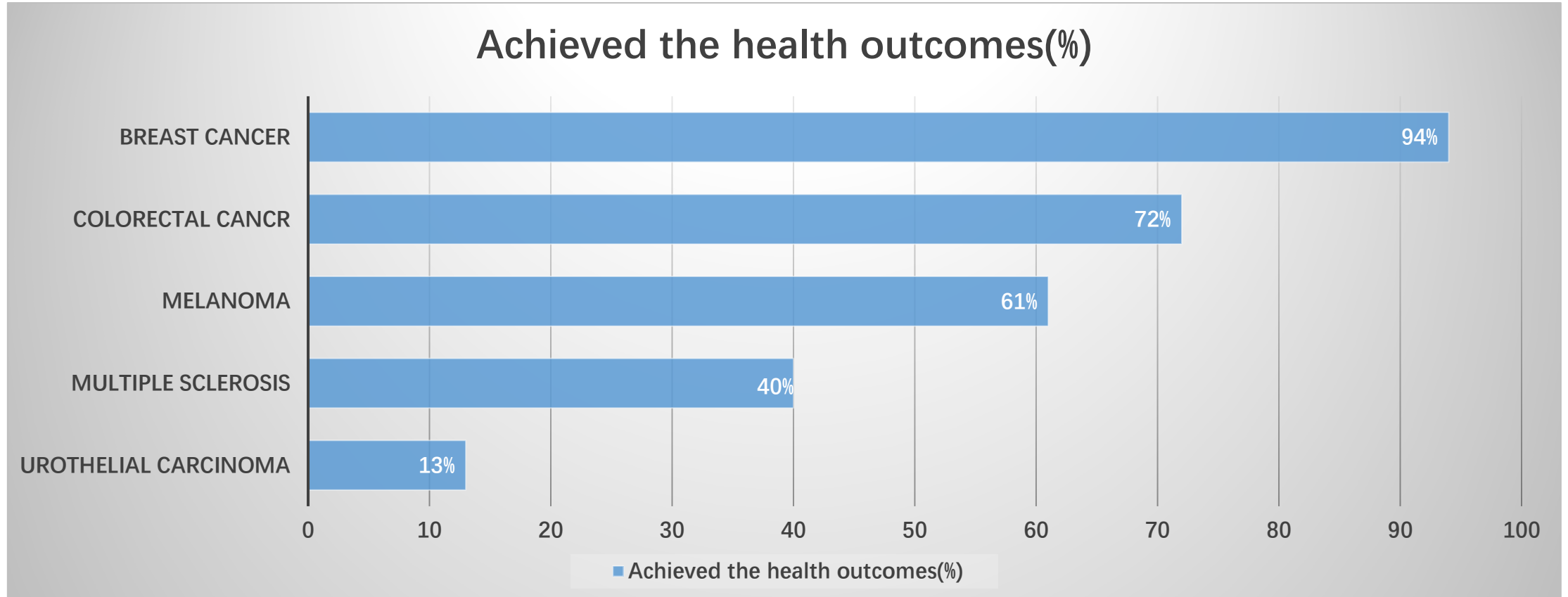
# Evaluation of Reimbursement for RSA Drugs in Spain

- Guarga L et al did retrospective descriptive analysis of RSAs from 2016 to 2019 in Catalan health service (CatSalut)
- Total 15 RSAs were implemented. 10 of which are still ongoing, risk-sharing arrangement by category as follows:

Disease therapeutic areas	Performance-linked reimbursement	Disease therapeutic areas	Cost-sharing arrangement
Colorectal cancer	PLRS 2016-ongoing	Lung carcinoma	Discount 2018-2019 Price-volume/year
Multiple sclerosis	PLRS 2017- ongoing	Multiple myeloma	Budget capping/year 2019-ongoing
Beast cancer	PLRS 2017-2019	Rare diseases	Budget capping/year 2018-ongoing
Melanoma	PLRS 2017- ongoing	Melanoma	Discount 2019-ongoing

(Guarga L et al: Implementing risk-sharing arrangements for innovative medicines: The experience in Catalonia (Spain) ViH 25(5) 803.2022)

# Health Outcomes by Disease in PLRS



(Guarga L et al: Implementing risk-sharing arrangements for innovative medicines : The experience in Catalonia (Spain) ViH 25(5) 803.2022)

# Evaluation of Reimbursement for RSA Drugs in Korea

- The regulatory approval started reimbursement of drugs through RSA since 2014 in South Korea
- Total 42 drugs (anticancer & rare disease) have been considered eligible for RSA pathway
- 21 drugs (50%) were categorized as “expenditure cap”, 12 drugs (28.6%) as “refund”
- The lag time from regulatory approval to actual reimbursement was shorten from 40 months in 2014 decreased to 17 months in 2019
- 24 out of 42 drugs (57%) have been listed under the waiver of CEA to improve patient access to medicines

# Conclusion

- Payment system reform of innovative drugs should be considered along with the rapid high-technology development and limitation of health insurance budgeting
- The risk-sharing agreement was applied to anticancer and rare disease drugs as a policy to improve patient accessibility
- The taxonomy for RSAs are largely divided into performance-based risk-sharing arrangements (PBRsAs) and cost-sharing arrangement (CSAs)
- In Asia-Pacific region except South Korea, China has interest in conducting risk-sharing agreements, however, it has not been implemented in the reality yet, it will be learning and practice in the near future

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2022

*Thank You!*





Virtual ISPOR Asia Pacific Conference  
September 20-21, 2022.

# Role of Real World Evidence and Budget Impact Analysis in Risk Sharing Arrangement

**Professor Shu Chuen Li**

BPharm, CertHealth Econ, GradDip Mgt (Tech Mgt), MAppIsc, MBA, PhD

Issue Panel: Risk-Sharing Arrangement: The Role of Real-World Evidence and Budget Impact Analysis.

- Risk sharing agreements

- An arrangement between a manufacturer and payer/provider that enables access to (coverage/reimbursement of) a health technology subject to specified conditions.
- These arrangements can use a variety of mechanisms to address uncertainty about the performance of technologies or to manage the adoption of technologies in order to maximize effective their use, or limit their budget impact.

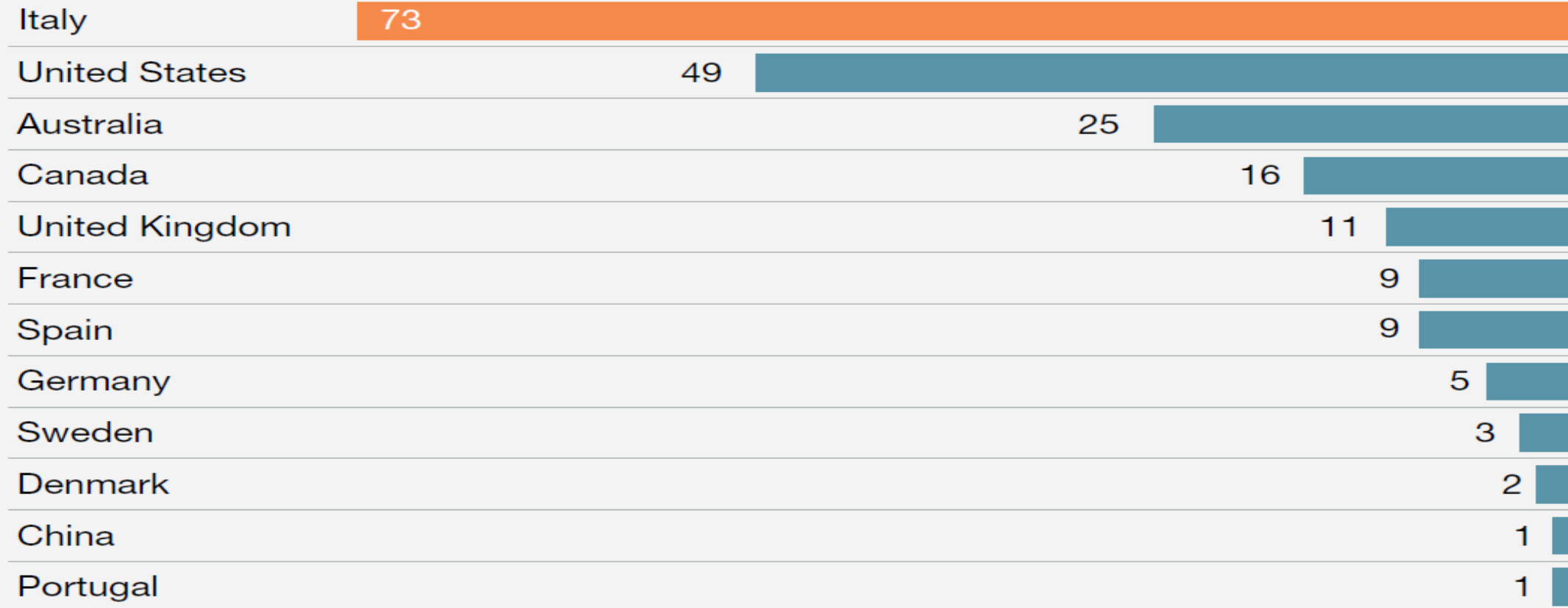
- **Managed Entry Agreements**

- Arrangements between firms and healthcare payers that allow for coverage of new medicines while managing uncertainty around their financial impact or performance.
- As a potential solution to address payer's restricted healthcare budgets.
- can broadly be categorised as finance-based or outcomes-based.

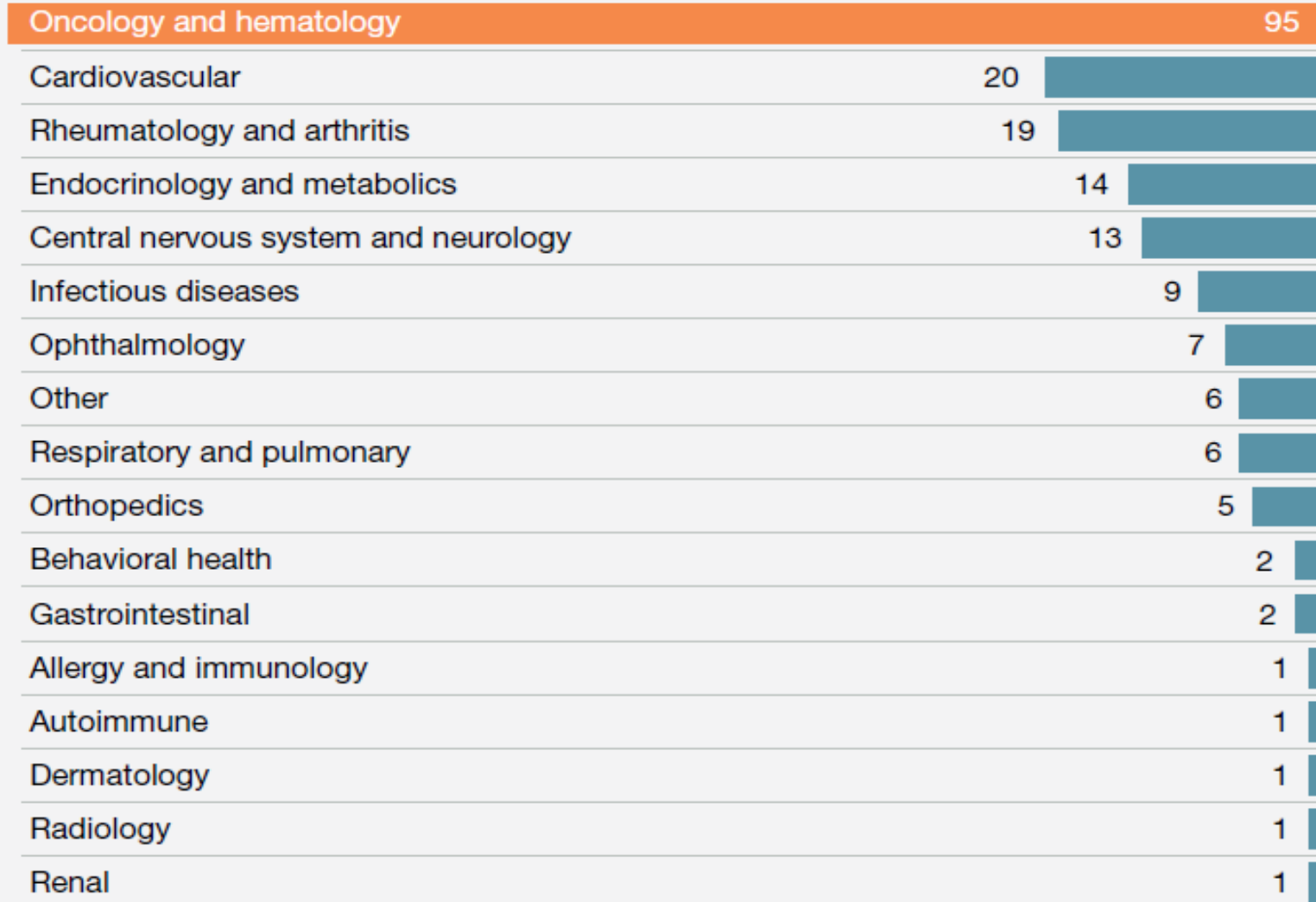
- **Innovative Pharmaceutical Agreements**

- Any arrangement outside traditional fixed-cost-per-unit and rebating practices
- Innovative contracts are flexible payment arrangements between biopharmaceutical companies and payers that can generally be divided into three categories: (1) results-based contracts, (2) alternative financing arrangements or (3) a hybrid of those two models.

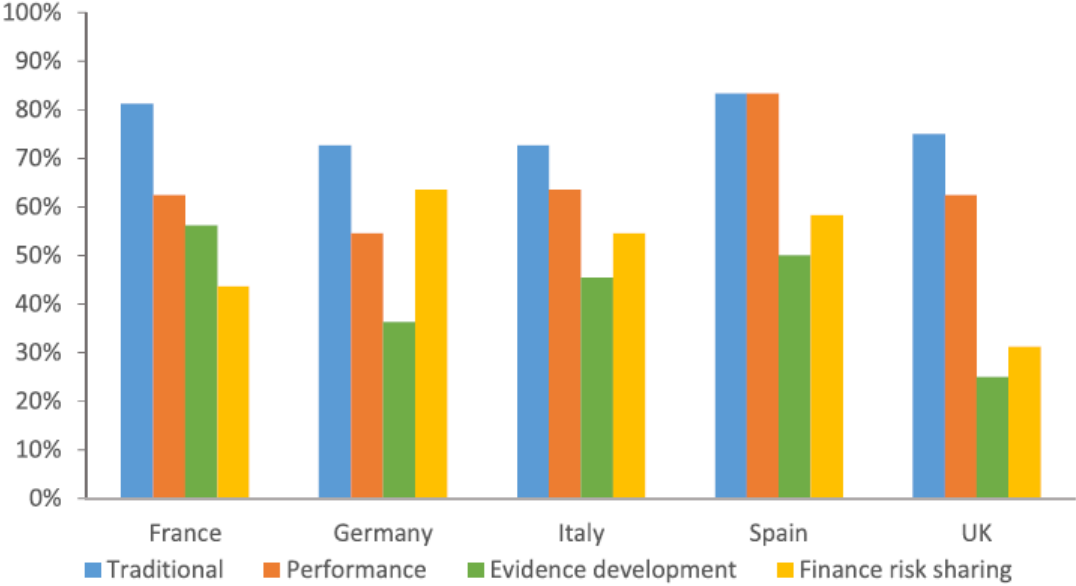
Innovative contracts by country since 1994,  
number of public contracts executed



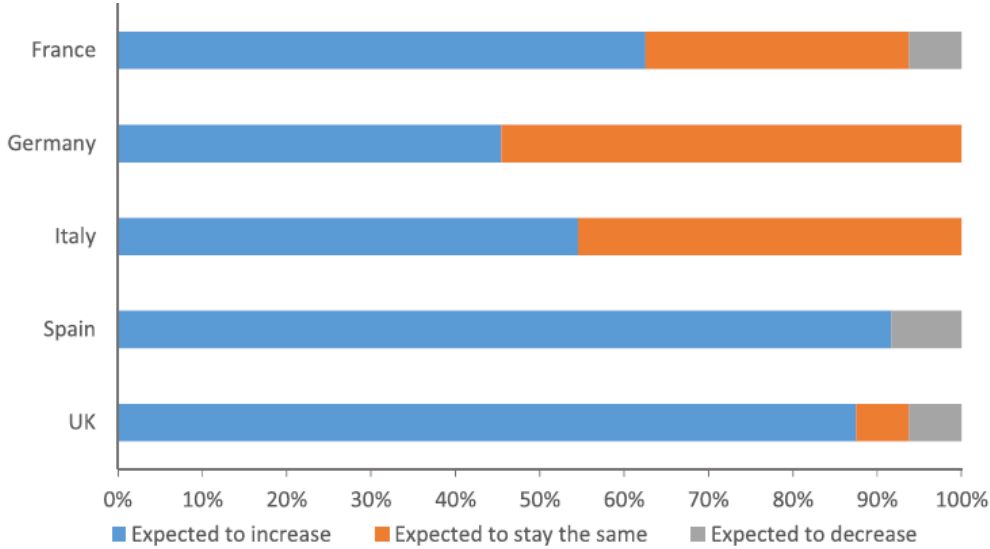
Global innovative contracts by therapeutic area since 1994,  
number of public contracts executed



# Stakeholders' Experience and Attitude to Risk Sharing Agreements in Five European Countries



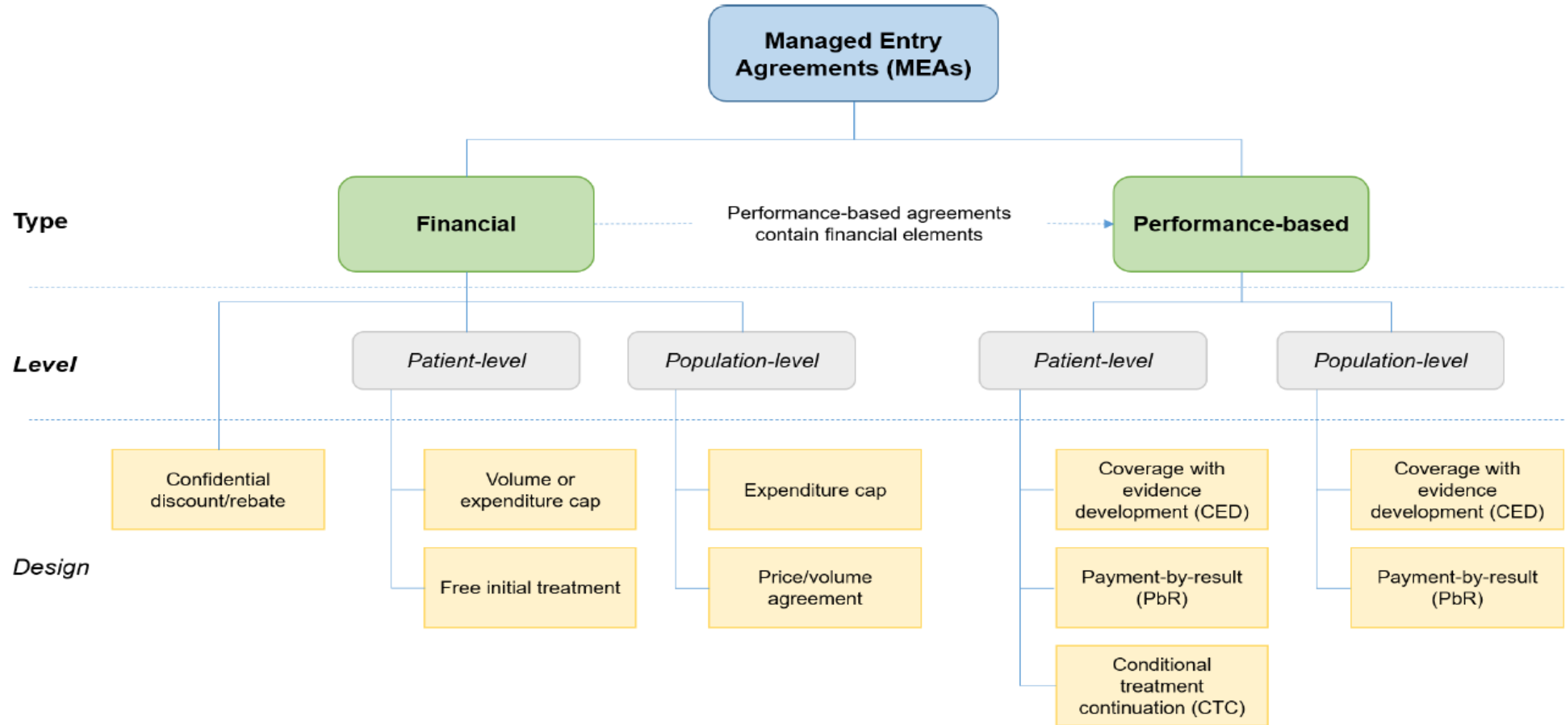
**Percentage of stakeholders with experience in different type of Risk sharing agreements (N=66)**



**Percentage of stakeholders selecting expectation in the change in utilization of Risk sharing agreements in the next five years (N=66)**

Source: Dunlop et al. Health Policy 2018.

# A Taxonomy of Managed Entry Agreements (MEAs)





# Some Common Approaches in Risk Sharing Arrangement

## Finance-based

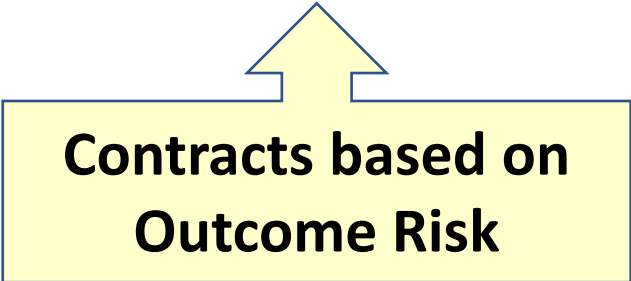
- Drug utilization caps
- Budget caps
- Fixed cost per patient
- Price volume agreements
- Patient access schemes with confidential discounts



**Contracts based on  
Financial Risk**

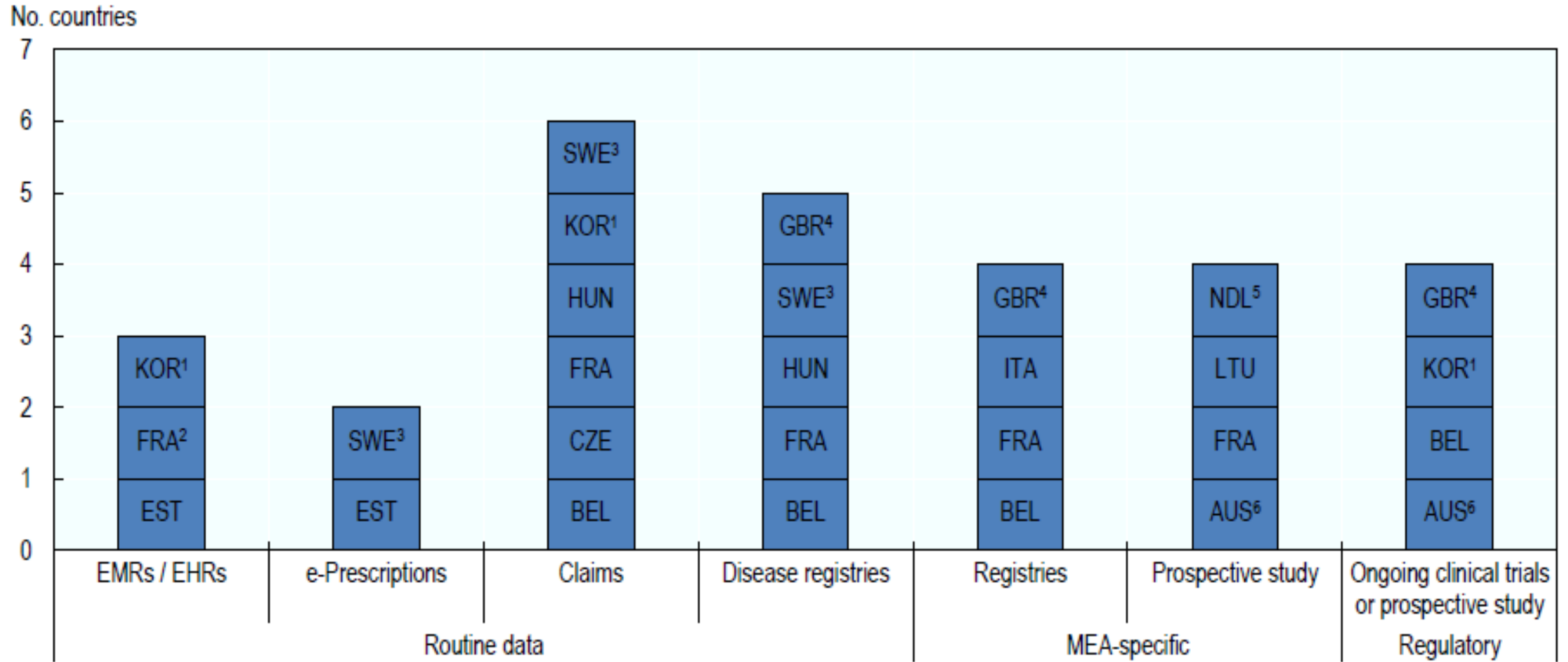
## Outcome-based

- Results-based agreements
- Conditional treatment continuation
- Coverage with evidence development agreements



**Contracts based on  
Outcome Risk**

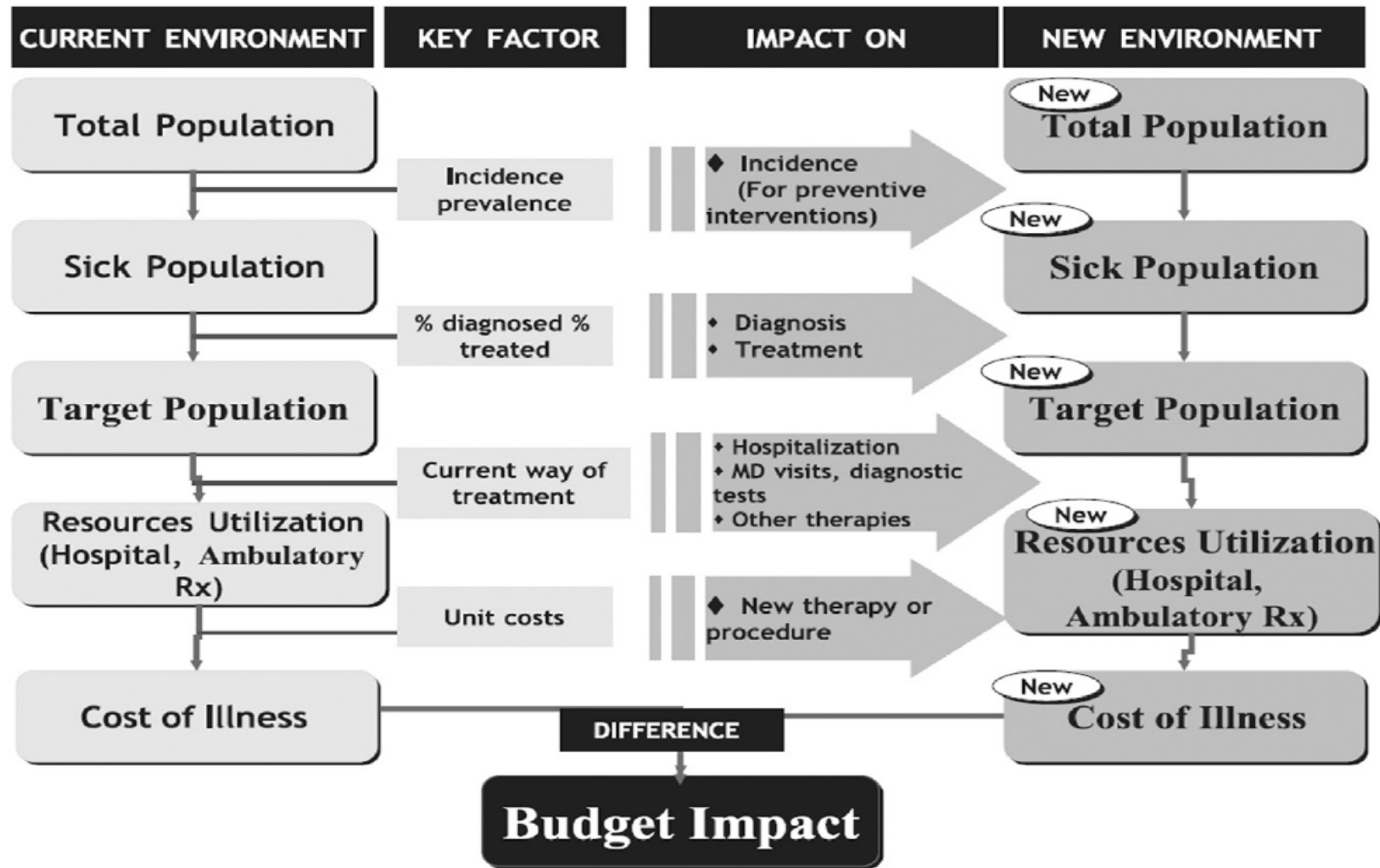
# Data sources used for the execution of performance-based MEAs



# Budget Impact Analysis

- A tool to predict the potential financial impact of the adoption and diffusion of a new technology into a healthcare system with finite resources.
- Provides an analysis of the added financial impact of a new health technology for a finite period that can be useful for resource or budget planning.

# ISPOR Framework of Budget Impact Analysis



# Data Requirement for Performing Budget Impact Analysis

- Population estimates
  - Total and targeted populations
- Incidence and prevalence data
  - Current and potential targeted subpopulations
    - Mortality data (when appropriate)
- Medication cost
  - Utilization of current and new medicine or technologies
- Unit cost of other healthcare services
  - Monitoring, diagnostics, GP and specialist visits, etc.
- Clinical and Patient reported outcomes
- Other input parameters
  - Annual growth rate etc.

# Real World Data (RWD) and Real World Evidence (RWE)

- Real-World Data (RWD) are data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources.
- Real-World Evidence (RWE) is the *clinical* evidence about the usage and potential benefits or risks of a medical product derived from analysis of RWD.

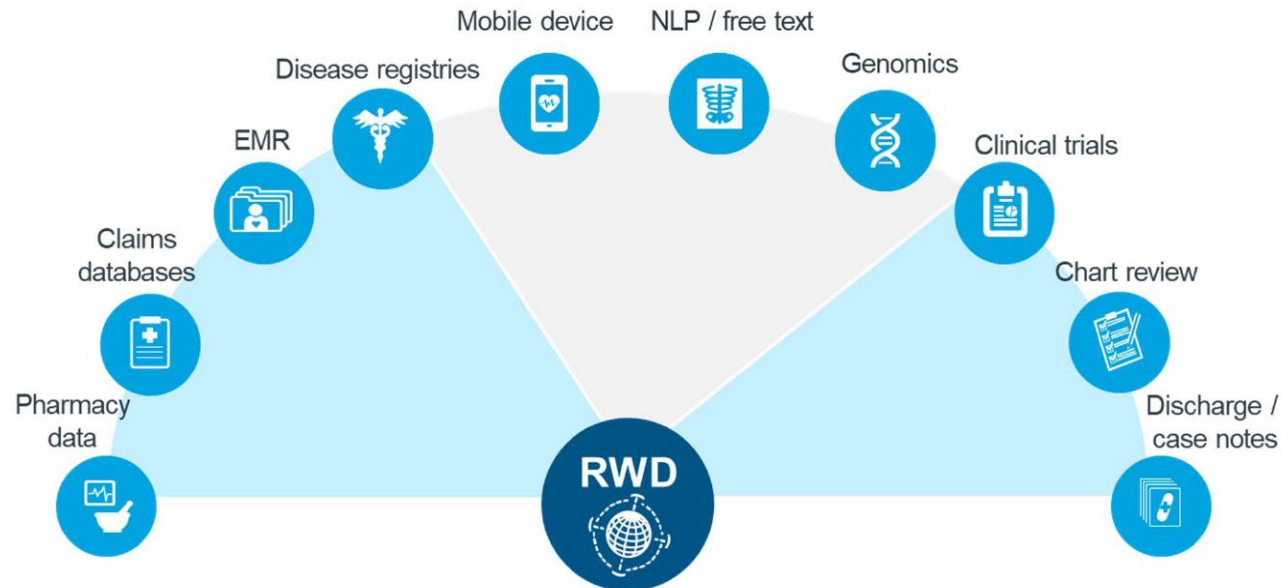
# Sources of Real World Data

Clinical data

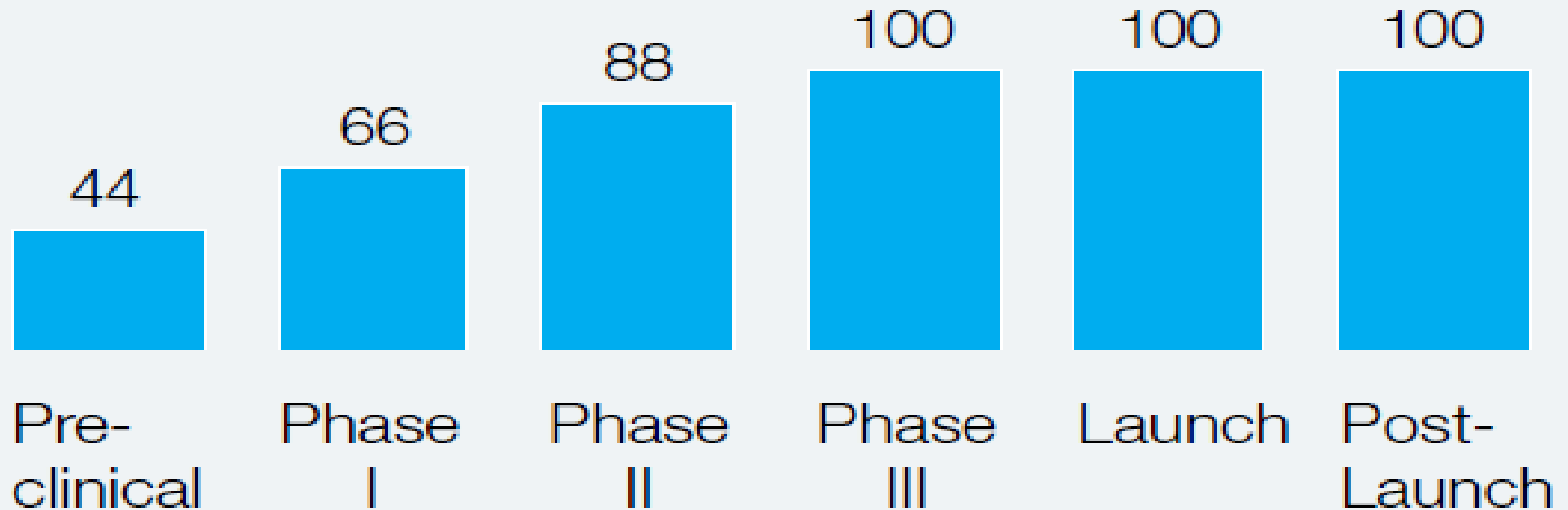
Administrative/claims data

Patient-generated/reported data

Non-traditional, health-related digital data sources



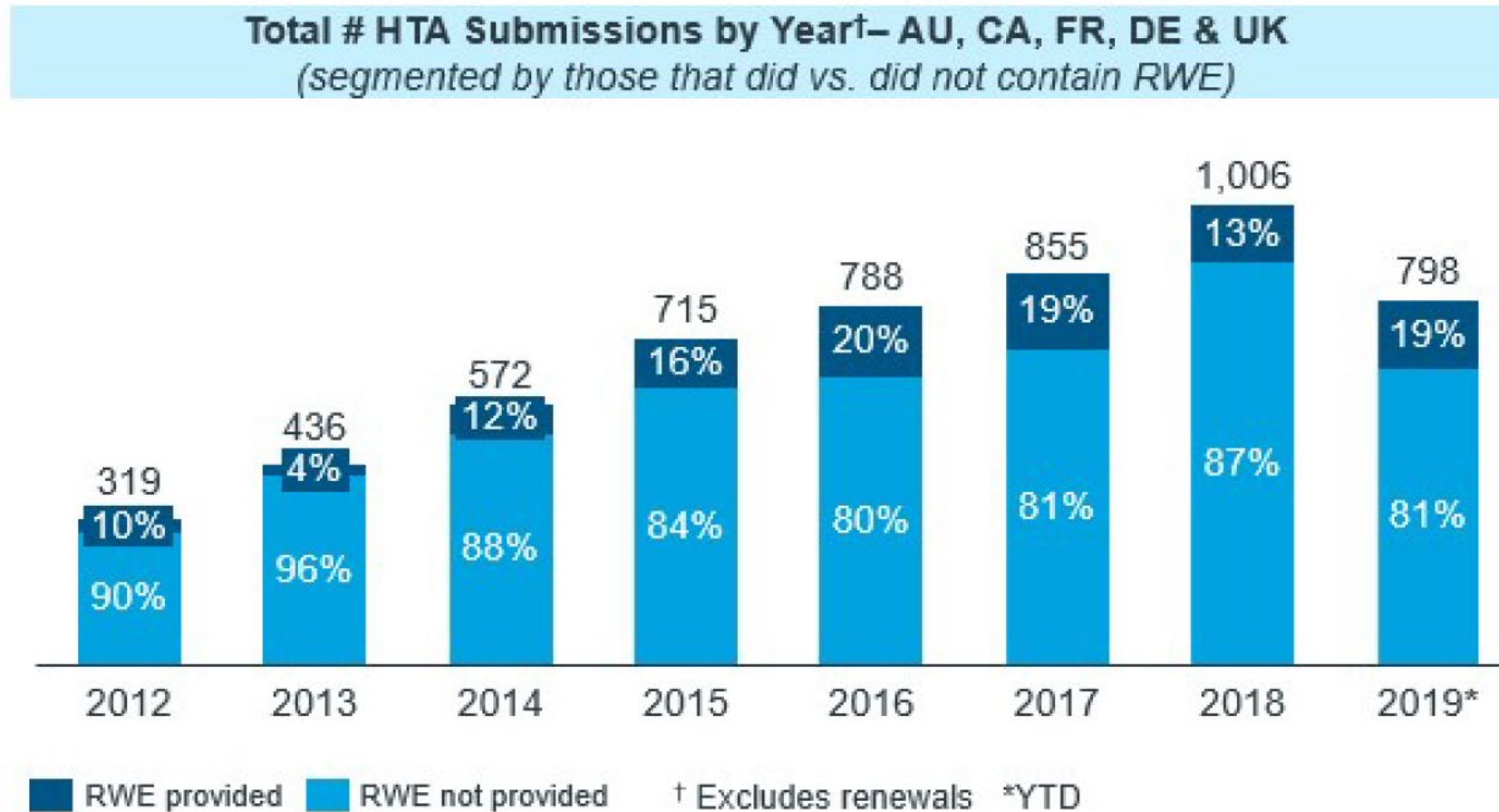
## RWE involvement of across life cycle (Percentage of Companies)



Source: McKinsey RWE Benchmarking (2017)



# Proportion of HTA Submissions containing RWE



Source: HTA Accelerator analysis of n=5,489 HTA submissions from 2012 to 2019 (YTD); includes all single drug assessments in HTAA from PBAC, HAS, NICE, CADTH, pCODR and G-BA in this timeframe

Source: Source: IQVIA HTA Accelerator

# Top 10 Pharm Industry Trends & Innovations in 2022

- Artificial Intelligence
- Big Data & Analytics
- Flexible Production
- Precision Medicine
- Additive Manufacturing
- Block Chain
- Extended Reality
- Real World Data
- Digital Therapeutics
- Curative Therapies

Source: [Startus-insight.com](https://www.startus-insight.com)

- Block Chain
- Investment in Real World Data
- Artificial Intelligence
- Flexible Production
- Digital Therapeutics
- Big Data & Analytics
- Additive Manufacturing
- Precision Medicine
- Curative Therapies
- Extended Reality

Source: [Kawawell.com](https://www.kawawell.com)

# Challenges in using RWE in healthcare coverage

- **Infrastructure and Process**

- Regulatory
  - what data can satisfy regulatory approval
  - What data can satisfy negotiation requirement
- interoperability
  - Linkage across healthcare system
- Information sharing
  - Confidentiality and data sharing
- Shortage of expertise

- **Data quality and availability**

- Accessibility of data
- “Fit for use” data
- Bias and confounding
- Incomplete data, unstructured data and inconsistency in reporting methods
- Lack of universally accepted methodological standard
  - Data mining – different models and different methods can produce different outcomes

# Risk-Sharing Arrangement: The Role of Real-World Evidence and Budget Impact Analysis

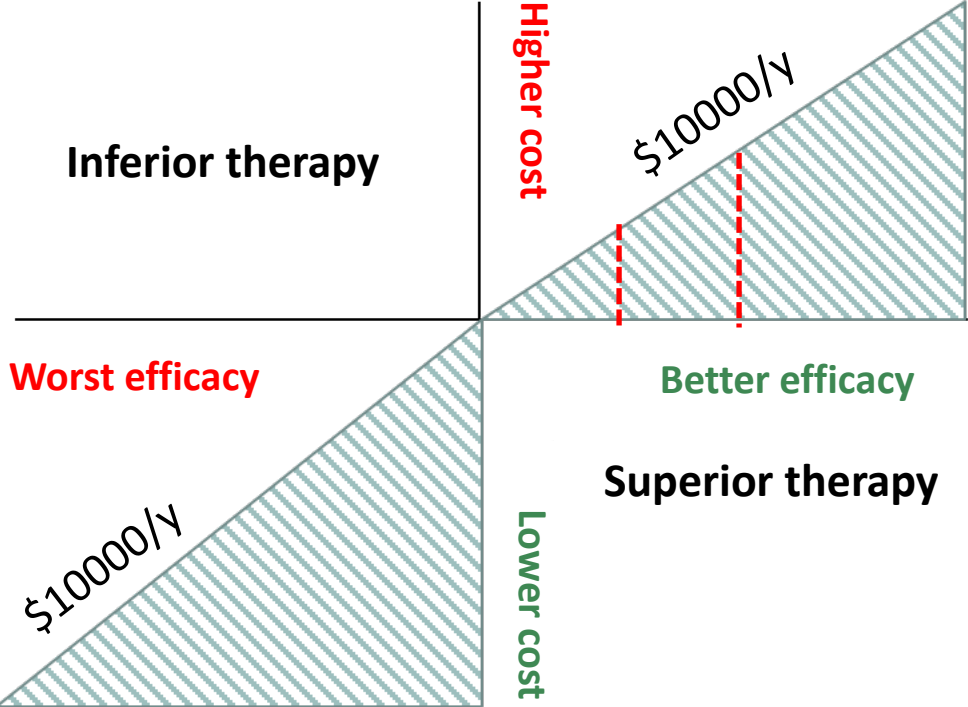
## CASE STUDIES

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Fei-Li Zhao, PhD  
2022-09-21

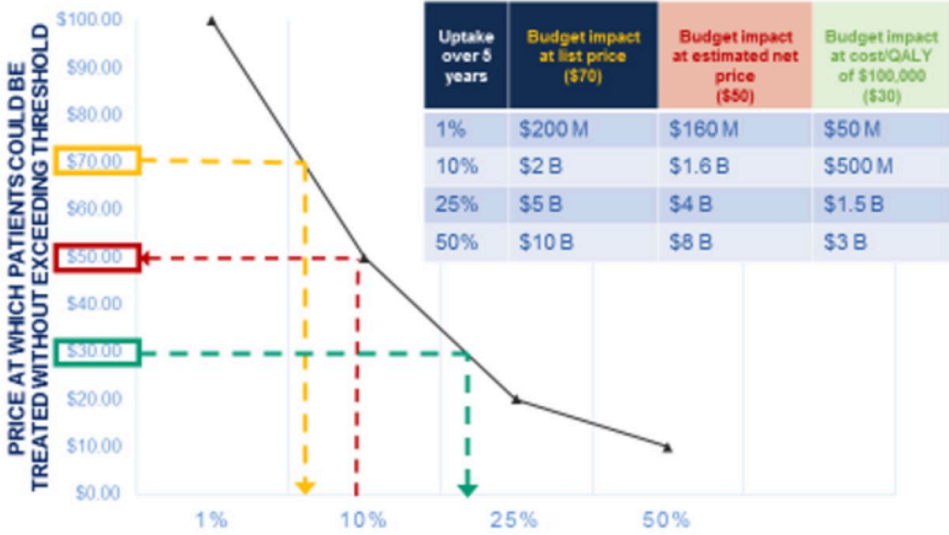
# Health Economics Evaluations & RSA: complement each other

## Cost-effectiveness analysis



## Budget Impact Analysis

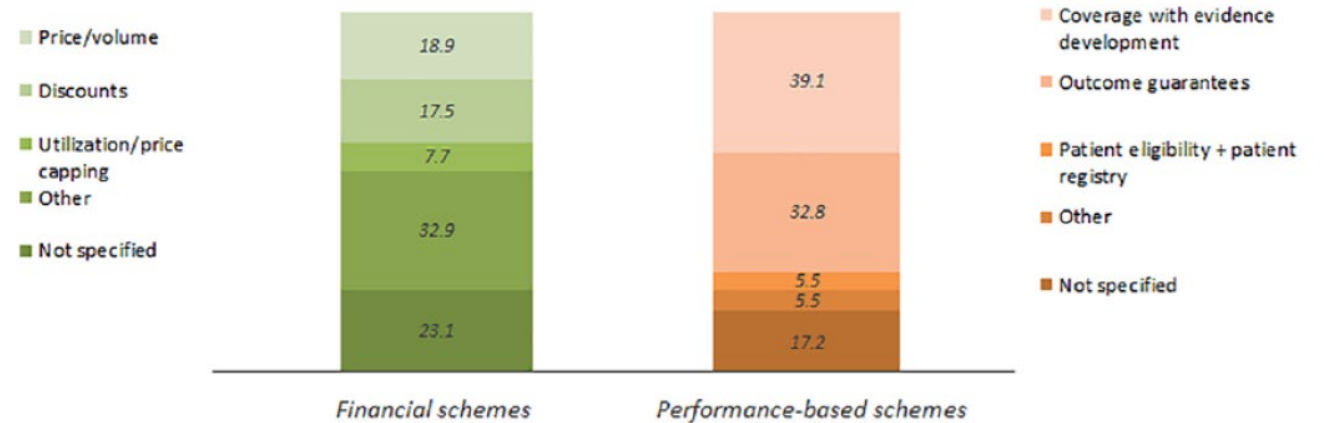
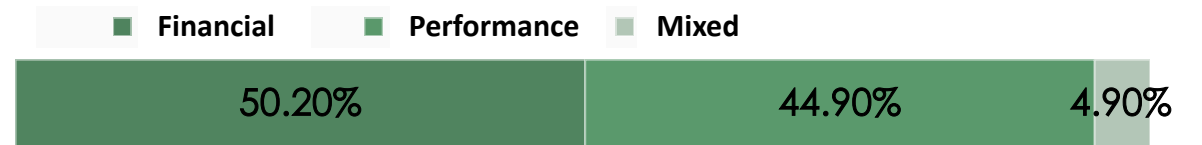
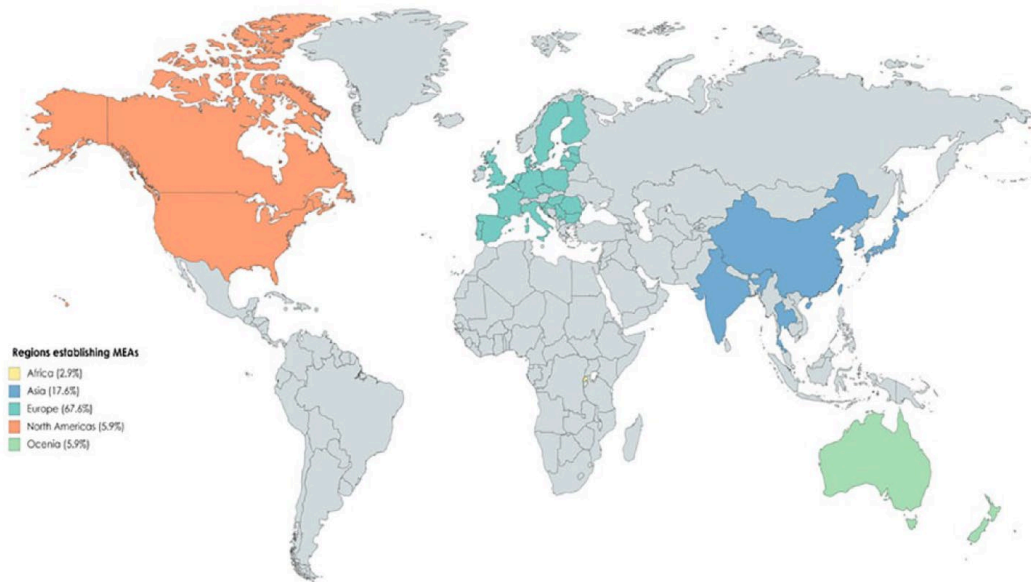
POTENTIAL BUDGET IMPACT SCENARIOS



Source: ICER 2019 report

# Snapshot of the Implementation of RSA

Castro et al. 2019

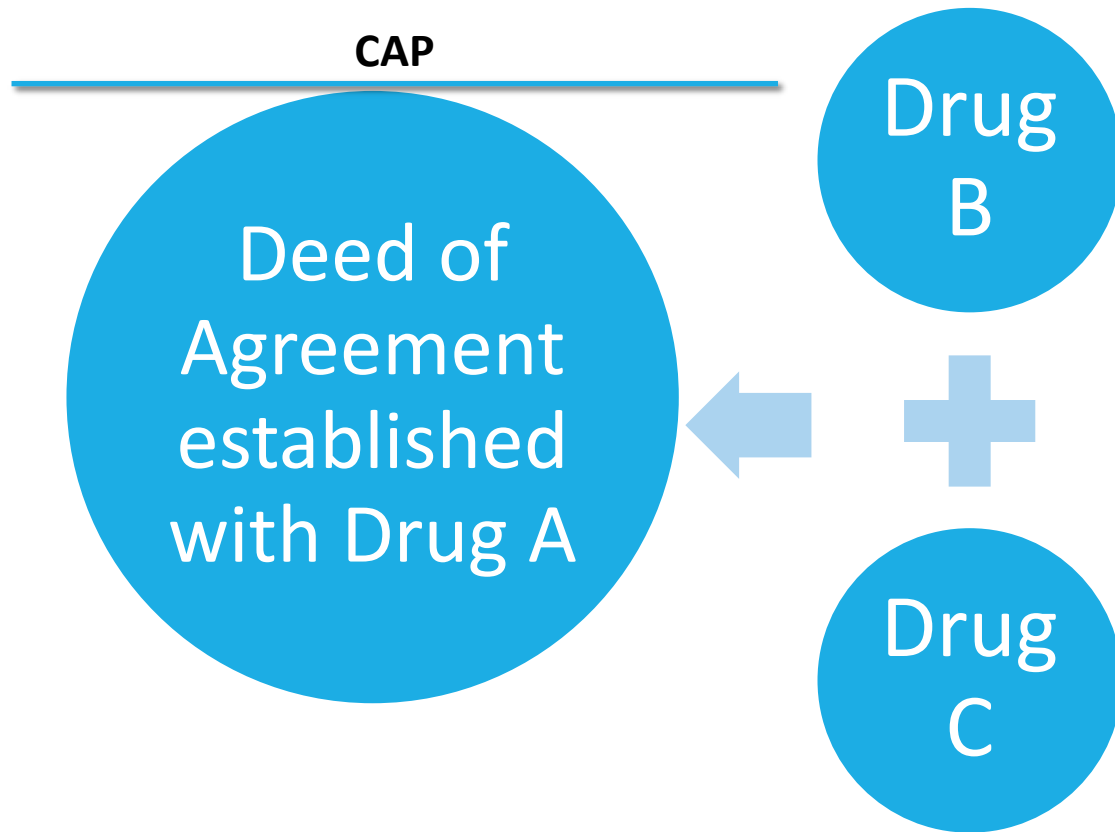


Source: Castro et al. 2019

# Case 1: BIA and RSA

## Cost sharing arrangement - Australia

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- B, C drugs are normally assessed with CMA with estimated cost neutral BIA to the government
- Cap can be set with Drug A BIA without adjustment when B, C listed
- Pros: manageable and predictable costs to the payer
- Cons: high risk of large rebate for the companies, delayed patient access due to negotiation



## Case 2: NICE RSA for multiple sclerosis disease modifying therapies (DMT)

2000, 2002 NICE recommendation on the first generation DMT: not cost-effective

- 5y model: £ 380,000 to £ 780,000/QALY
- 10y model : £ 190,000 to £ 425,000
- 20y model : £ 40,000 to £ 90,000

Given the efficacy of the therapy, the government, industry, healthcare, and patient organization worked together to reach a Risk Sharing Arrangement: following 5000 patients in 10 years with evaluating disease progression and regularly adjusted price with collected RWE.

> [BMJ](#). 2010 Jun 3;340:c1672. doi: [BMJ](#). 2003 Feb 15; 326(7385): 388–392.

doi: [10.1136/bmj.326.7385.388](https://doi.org/10.1136/bmj.326.7385.388)

PMCID: PMC1125245

PMID: [12586677](https://pubmed.ncbi.nlm.nih.gov/12586677/)

### Multiple sclerosis r failure

Problems with UK government's risk sharing scheme for assessing drugs  
for multiple sclerosis

James Raftery <sup>1</sup>

[Cathie L M Sudlow](#), Wellcome clinician scientist<sup>a</sup> and [Carl E Counsell](#), senior lecturer<sup>b</sup>

# Case 2: NICE RSA for multiple sclerosis disease modifying therapies (DMT)

BMJ



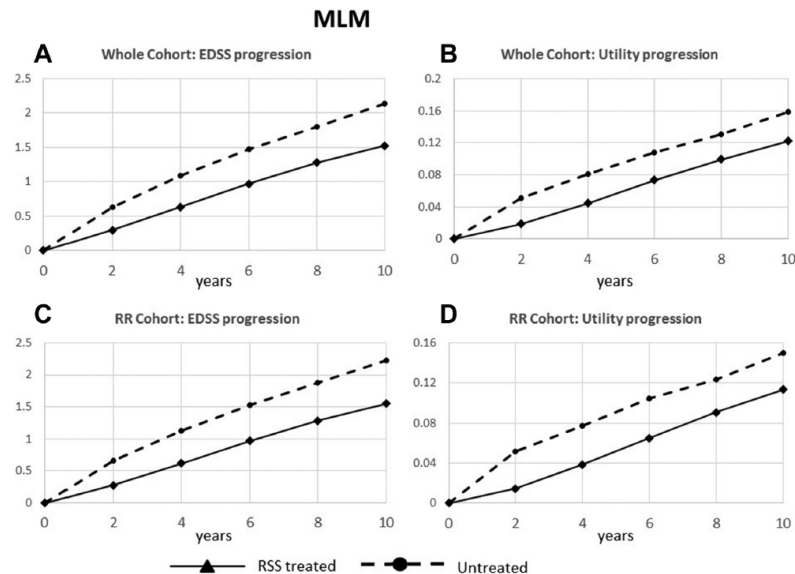
OPEN ACCESS

Palace J, et al. *J Neurol Neurosurg Psychiatry* 2019;**90**:251–260. doi:10.1136/jnnp-2018-318360

RESEARCH PAPER

## Assessing the long-term effectiveness of interferon-beta and glatiramer acetate in multiple sclerosis: final 10-year results from the UK multiple sclerosis risk-sharing scheme

Jacqueline Palace,<sup>1</sup> Martin Duddy,<sup>2</sup> Michael Lawton,<sup>3</sup> Thomas Bregenzer,<sup>4</sup> Feng Zhu,<sup>5</sup> Mike Boggild,<sup>6</sup> Benjamin Piske,<sup>4</sup> Neil P Robertson,<sup>7</sup> Joel Oger,<sup>5</sup> Helen Tremlett,<sup>5</sup> Kate Tilling,<sup>3</sup> Yoav Ben-Shlomo,<sup>3</sup> Richard Lilford,<sup>8</sup> Charles Dobson<sup>9</sup>



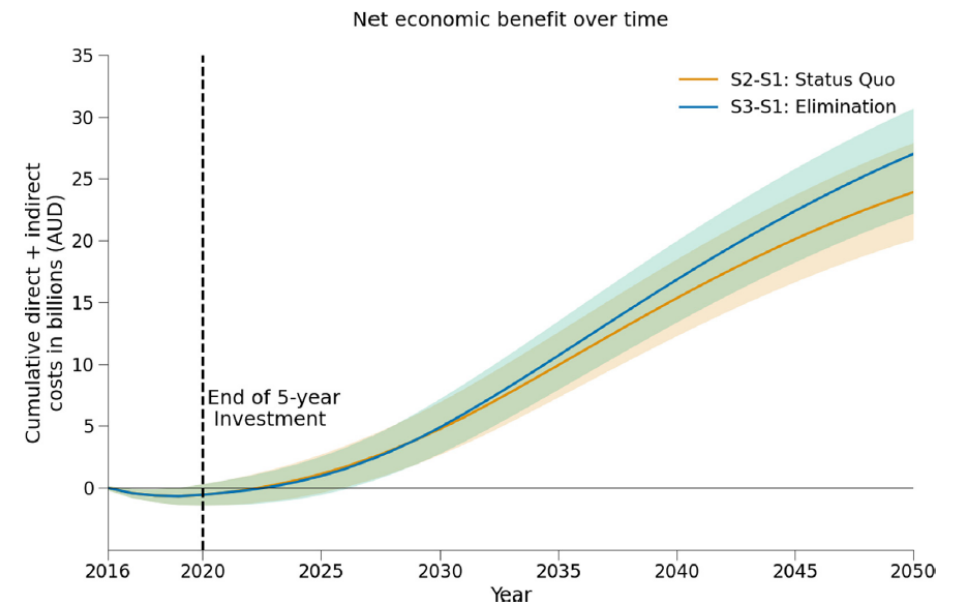
- Confirmed long term effectiveness and cost-effectiveness
- 18000 patients accessed the DMT timeline
- New DMTs can be listed following the
- MS disease management platform and systems being established
- Question: RSA management cost?

# Case 3: Hepatitis C direct-acting antiviral (DAA) treatments RSA in Australia – Impact assessment

- The Australian government committed a \$1.2 billion volume based RSA with sponsors for unlimited DAA treatment courses between March 2016 and February 2021 to achieve hepatitis C elimination

Scott et al. 2022: CEA assessment of this RSA

- A \$5,752 per QALY gained from a health systems perspective
- economic productivity gains from hepatitis C cure are estimated to be A\$6.17 over 2016-2030
- cost-saving from a societal perspective by 2022 with a net economic benefit of A\$5.70 billion by 2030
- More work needed to achieve elimination



# Challenges

## Management

- Administrative burden of managing deed
- Complicated negotiation process
- Coverage with evidence development
  - Time and possibility to validate uncertainties
  - Delisting challenge
  - Balance between promoting innovation and pricing adjustment

## Data

- Who is responsible to collect, manage, and analyze the data? Who should bear the costs?
- Data management:
  - Data privacy, and consent
  - Data infrastructure, eg, EMR
- RWD analyses:
  - Missing data
  - Bias and confounding factors
  - Quality of data

## Others

- Ethics compliance
- Barriers in implementation: country specific barriers

# Thank you

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Dr Fei-Li Zhao: [Feili.Zhao@newcastle.edu.au](mailto:Feili.Zhao@newcastle.edu.au)