11:20-13:00 **ACCESO E INNOVACIÓN**

Modera: Javier de Urquía Martí. Patrono Fundación CEFI

- **Acceso a la innovación. Plan Nacional de Terapias Avanzadas. Medicamentos CAR-T.**
  Enrique Ruiz Escudero. Consejero de Sanidad CAM
- **Registro de datos de ensayos y de práctica real. Valtermed.**
  Ponente pendiente de confirmar
- **Acceso a la innovación. Incertidumbres regulatorias entre autorización de comercialización y reembolso. Soluciones en otros países de la UE.**
  Jordi Faus Santasusana. Abogado socio Faus & Moliner Abogados
- **Medicamentos en espera de precio, sin interés comercial y desabastecimientos.**
  Lourdes Fraguas Gadea. Secretaria General y Directora Departamento Jurídico y RRHH Farmaindustria

DR. JORGE MESTRE-FERRÁNDIZ

CONSULTOR ECONÓMICO

PROF ASOCIADIO, UNIVERSIDAD CARLOS III, MADRID

A LITTLE ABOUT ME…

- Economist by training
- Currently working as a freelancer
- Used to work for the Office of Health Economics, London
- Areas of interest: pharmaceutical policy
- Research/academia and consulting experience

AGENDA

- Context
- Use of real-world data/evidence (RWD/E)
- Addressing the challenges: role of RWD/E
- RWD/E Framework
- Barriers to RWD/E use
- **Valtermed: el caso Español**
- Some final reflections

THE LIFE SCIENCES INDUSTRY: VIRTUOUS CYCLE (OR "VICIOUS")?

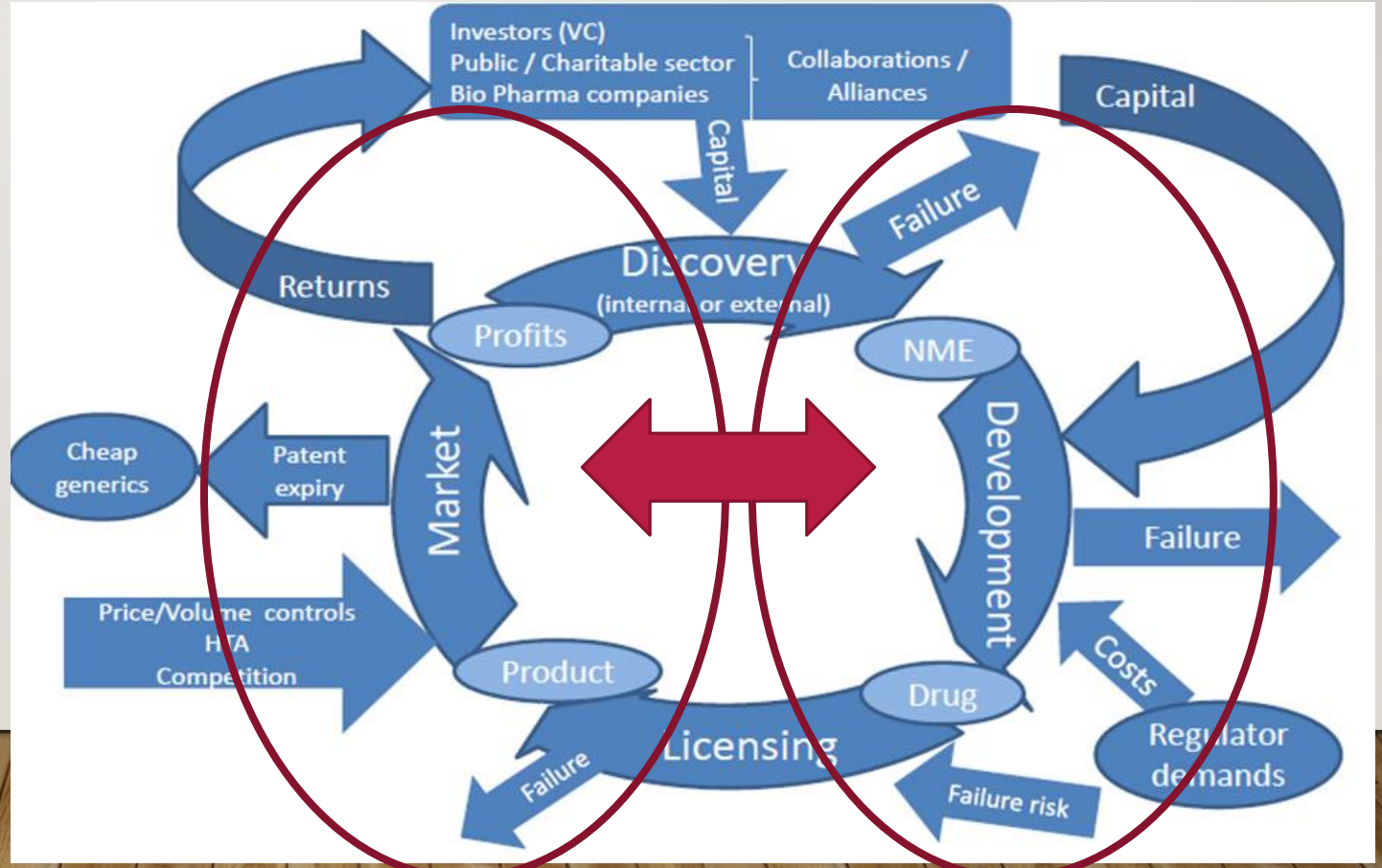
FIVE GLOBAL CHALLENGES

- **Demand side**

Challenge 3: Closer benefit-risk monitoring by regulators over a medicines' life cycle
Challenge 4: Increase in demand for **RWE** of relative effectiveness by HTA, payers and regulators
Challenge 5: Disconnect between regulators and (across) payers/HTA bodies evidence needs

- **Supply side**

Challenge 1: Increasing importance of specialised and stratified medicines
Challenge 2: Rising drug development costs



CONTEXT (1/2): OUR SPECIFIC CHALLENGE

- Many decisions, including regulatory and pricing/reimbursement and access decisions, are taken with limited evidence, and usually based on outcomes that do not matter to patients or represent clinical practice
- At the same time, there is increased pressure to try to make (cost-) effective treatments available earlier
  - For example, a medicine could be approved on the basis of preliminary/limited clinical data (such as surrogate endpoints [e.g. biomarkers or response rates], phase II trials, or limited patient population), which would ultimately need to be verified with the help of clinical data reflecting actual patient benefit
- After regulatory approval (based on clinical trials), the clinical/economic assessment starts. The requirements from the HC systems to give access, price & reimbursement differs from regulatory assessment (given different remits), BUT also within different HC systems
- Payers, understandably, might be reluctant to implement new access mechanisms, which could lead to (at least perceived) higher uncertainty
- **Key question: What is the role of real-world data/evidence (RWD/E) in this setting? How could it be used to reduce the evidence gaps and increase access?**

CONTEXT (2/2): RWD/E COMPLEMENTING RCTS

- Conventional RCTs remain the gold standard way for researchers to collect evidence for new treatments' safety and efficacy, and will continue to do so in the foreseeable future…
- …but there is need to build on trial outcomes, with recognition of the part played by evidence in clinical practice to support access
- Thus, RCTs alone may not provide sufficient evidence of "value" to support access, price and reimbursement decision-making
- Timing: When do we start collecting "real-world data"?
  - Currently, it is difficult to collect RWE before Marketing Authorisation
  - However, the landscape is changing: for instance, new types of studies (such as pragmatic trials) could collect evidence in real-life settings, before authorisation, for authorisation (and later on for access/P&R)
- RWD is neither a panacea nor a replacement for RCTs
- **So how can RWD/E complement RCTs, and under which circumstances will this be needed?**

THE QUESTION OF HOW TO USE RWE IS NOT A NEW ONE (1/2)…

Advancing Evidence Generation for New Drugs
IMI GetReal's Recommendations on Real-World Evidence

For instance, **IMI GetReal** has recently "identified **seven key themes that require attention and actions** by stakeholders and policy makers regarding the use of RWD/E in effectiveness research for new drugs":

1. Integrity, quality, access and privacy protection of RWD sources
2. Guidance on RWE study design, evidence synthesis and interpretation in decision making
3. Standards for decision makers' use of RWE in decision making
4. RWE training and education
5. Broader involvement of stakeholders, especially patients and healthcare professionals, in RWE generation and use of RWD
6. Emphasis on a joint (regulatory/HTA/payer) scientific advice process
7. Construction of a standing forum and linking with ongoing initiatives

'Advancing Evidence Generation for New Drugs'. Available at: https://www.imi-getreal.eu/Portals/1/Documents. Accessed March 2019.

THE QUESTION OF HOW TO USE RWE IS NOT A NEW ONE (2/2)…

Harnessing the Power of Real-World Evidence (RWE): A Checklist to Ensure Regulatory-Grade Data Quality

Rebecca A. Miksad[1] and Amy P. Abernethy[1]

[1]Flatiron Health, Inc., New York, New York, USA. Correspondence: A.P. Abernethy (amy@flatiron.com)

advance online publication 6 December 2017. doi:10.1002/cpt.946

VOLUME 103 NUMBER 2 | FEBRUARY 2018 | www.cpt-journal.com

CHECKLIST FOR REGULATORY-GRADE RWE

As with all scientific evidence, RWE, both retrospective and prospective, must be fit for purpose. We propose a checklist to ensure regulatory-grade data quality. In all cases, policies and procedures must be well documented, each dataset tested, and results reported when appropriate.

1) High quality

The provenance of each datapoint must be clear, traceable, and auditable. Data quality must be systematically measured with predetermined frameworks (e.g., interrater reliability) and against benchmarks (e.g., stage distribution in Surveillance, Epidemiology and End Results (SEER)).

2) Complete

Completeness requires predefined rules for abstraction of structured and unstructured data, data harmonization, and quality monitoring. Completeness needs to be benchmarked to appropriate gold standards (e.g., National Death Index for date of death).

3) Transparent

Transparent study designs and analysis plans are critical for robust RWE. In particular, the specific aims and cohort selection criteria need to be precisely defined. Study design considerations include retrospective vs. prospective data collection, the need for matching or propensity scores to facilitate comparisons, and endpoint validation.

4) Generalizable

RWE is often based on a broad range of patients, which can translate into better generalizability. Potential biases (e.g., geographic representation) must be identified and reported to allow for appropriate statistical adjustments and clinical interpretations.

5) Timely

RWE reflects daily clinical decisions. Thus, reliable RWE needs to be recent and timely. Details about the timepoint that the data analysis represents must be reported (e.g., time period, last update, number of potential candidates, etc.).

6) Scalable

Data challenges become exponentially more complicated as the number of patients and variables increase. Therefore, scaling requires 1) a balance between high touch and automation; 2) a modular data model that can be used in multiple contexts and facilitates model evolution (e.g., frequency of intravenous regimens); and 3) unambiguous variable definitions, particularly for endpoints.

AND LET'S NOT FORGET RWE IS ALREADY BEING USED (1/3)…

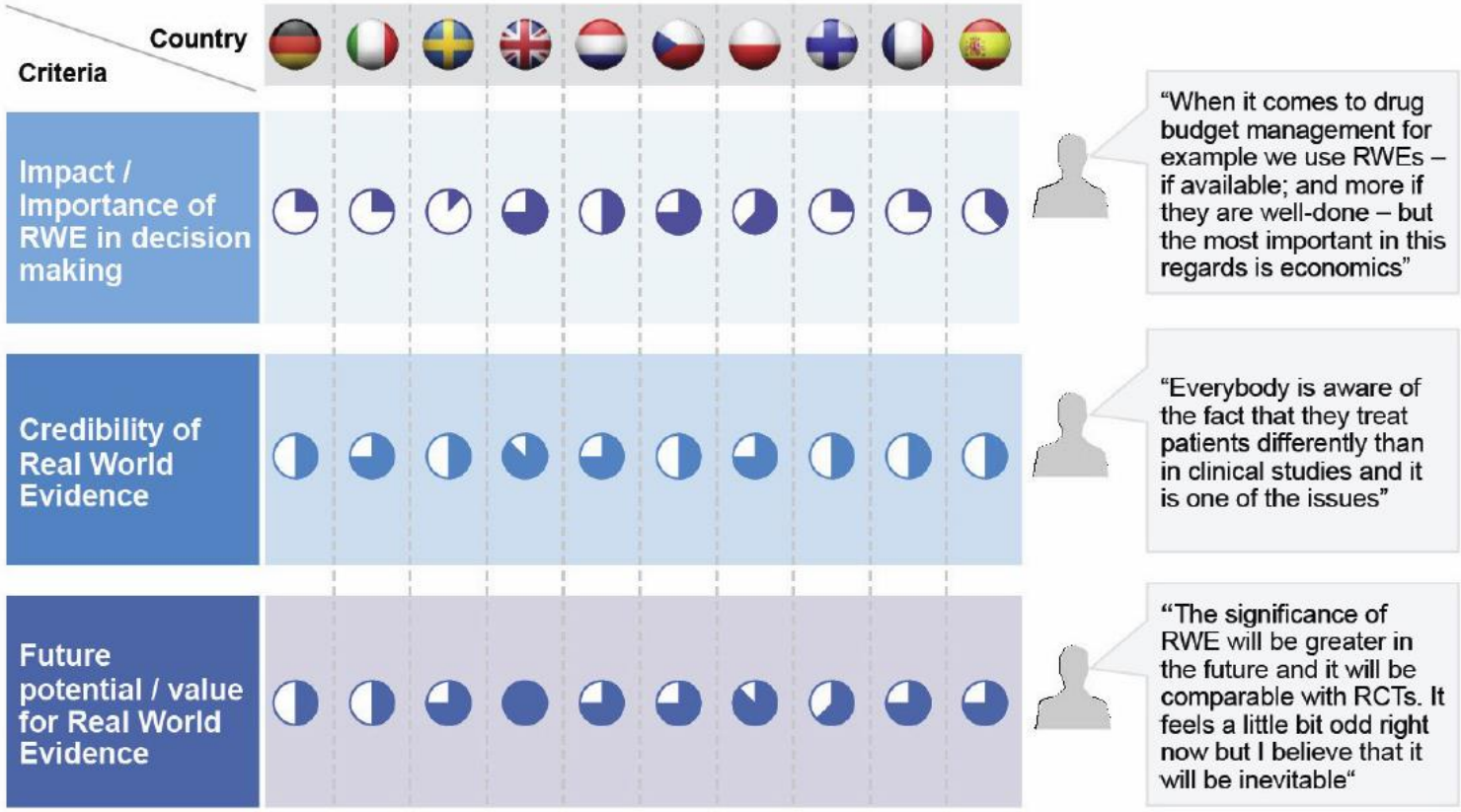
RWE is already in routine use in the EU

- Particularly true for marketed products and for safety monitoring and drug utilisation
- Increasing interest in the use of RWE for efficacy, outcomes for HTA, and rapid cycle evaluation of medicines
- There is major potential to increase the use of RWE to support lifecycle product development and monitoring, and to improve decision-making for regulation and HTA

Source: EMA, Update on Real World Evidence Data Collection, STAMP, 10 March 2016

AND LET'S NOT FORGET RWE IS ALREADY BEING USED (2/3)…ALTHOUGH DIFFERENT STARTING POINTS ON IMPORTANCE OF RWE IN DECISION-MAKING:

Figure 1: Opinions of RWE use across ten European countries



'The use of Real World Evidence in the European context'. Available at: http://eprints.lse.ac.uk/68442/1/RWE_in_Europe_Paper1.pdf. Accessed March 2019.

AND LET'S NOT FORGET RWE IS ALREADY BEING USED (3/3): THE CASE OF THE US

Current use of RWE in the US:

- Drug development
- Regulatory approval decisions
- Post-approval monitoring of safety signals
- HTA assessments and payer coverage decisions – initial decisions
- HTA assessments and payer coverage decisions – reassessments
- Outcomes-based contracting

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Office of Health Economics Research

Real World Evidence for Coverage Decisions: Opportunities and Challenges

A Report from the 2017 ICER Membership Policy Summit

March 2018

Grace Hampson, MSc
Senior Economist
Office of Health Economics

Adrian Towse, MPhil
Director
Office of Health Economics

Bill Dreitlein, PharmD, BCPS
Director of Pharmaceutical Intelligence
Institute for Clinical and Economic Review

Chris Henshall, PhD.
Independent Consultant

Steven D. Pearson, MD, MSc
President
Institute for Clinical and Economic Review

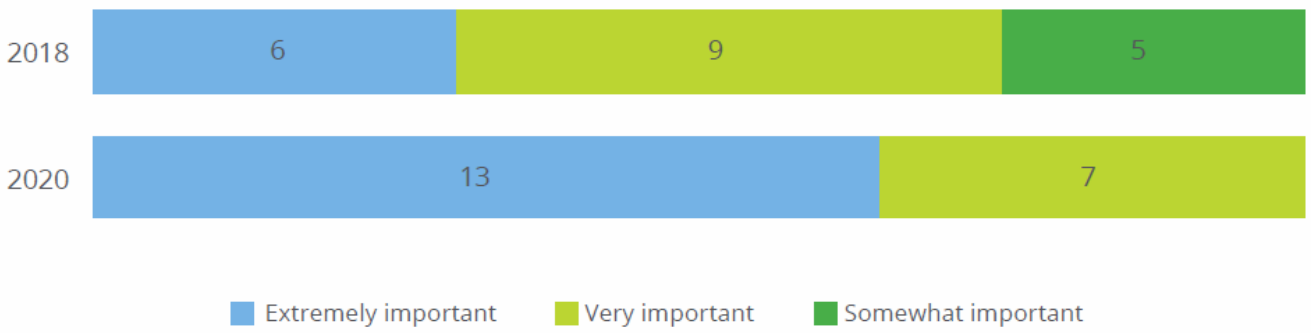
…AND WHAT IS THE INDUSTRY DOING ABOUT IT?

This year, we found that the visibility and importance of RWE initiatives are increasing at the executive level. Most respondents are leveraging RWD across the enterprise to not just generate evidence but also support other research, corporate, and commercial objectives. They report that this is being driven by pressure to demonstrate value for access and reimbursement, the need to better understand the patient journey, increased data availability, and greater acceptance of RWE among regulators.

SURVEY METHODOLOGY

Deloitte conducted its second annual real-world evidence (RWE) survey to explore the perceived value, capabilities, and barriers to utilizing RWE. Between January and April 2018, Deloitte surveyed and conducted interviews with RWE, IT, scientific, medical, and business executives from global life sciences companies. The 2018 study includes 20 respondents, up from 15 respondents in 2017. The larger sample enabled us to create a broader understanding of RWE investments, applications, and operationalization across the industry.

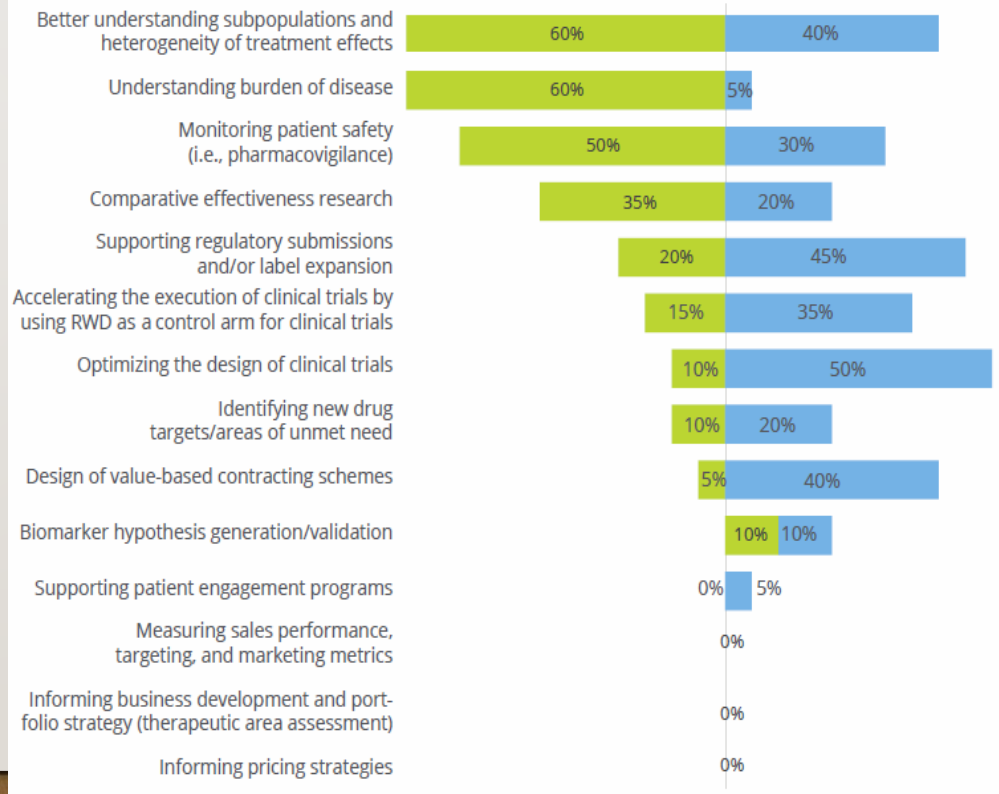
Figure 1. What level of importance do members of the executive leadership team place on the use of RWE as part of the organization's strategy? How important will they consider it to be in the next two years?



Source: Deloitte's 2018 RWE Benchmarking Survey.

Deloitte Insights | deloitte.com/insights

Figure 4. Please rank the three most impactful areas of current and future RWE application within your organization



Note: The figure denotes current and future application areas ranked amongst the top three by respondents and expressed as a percentage.

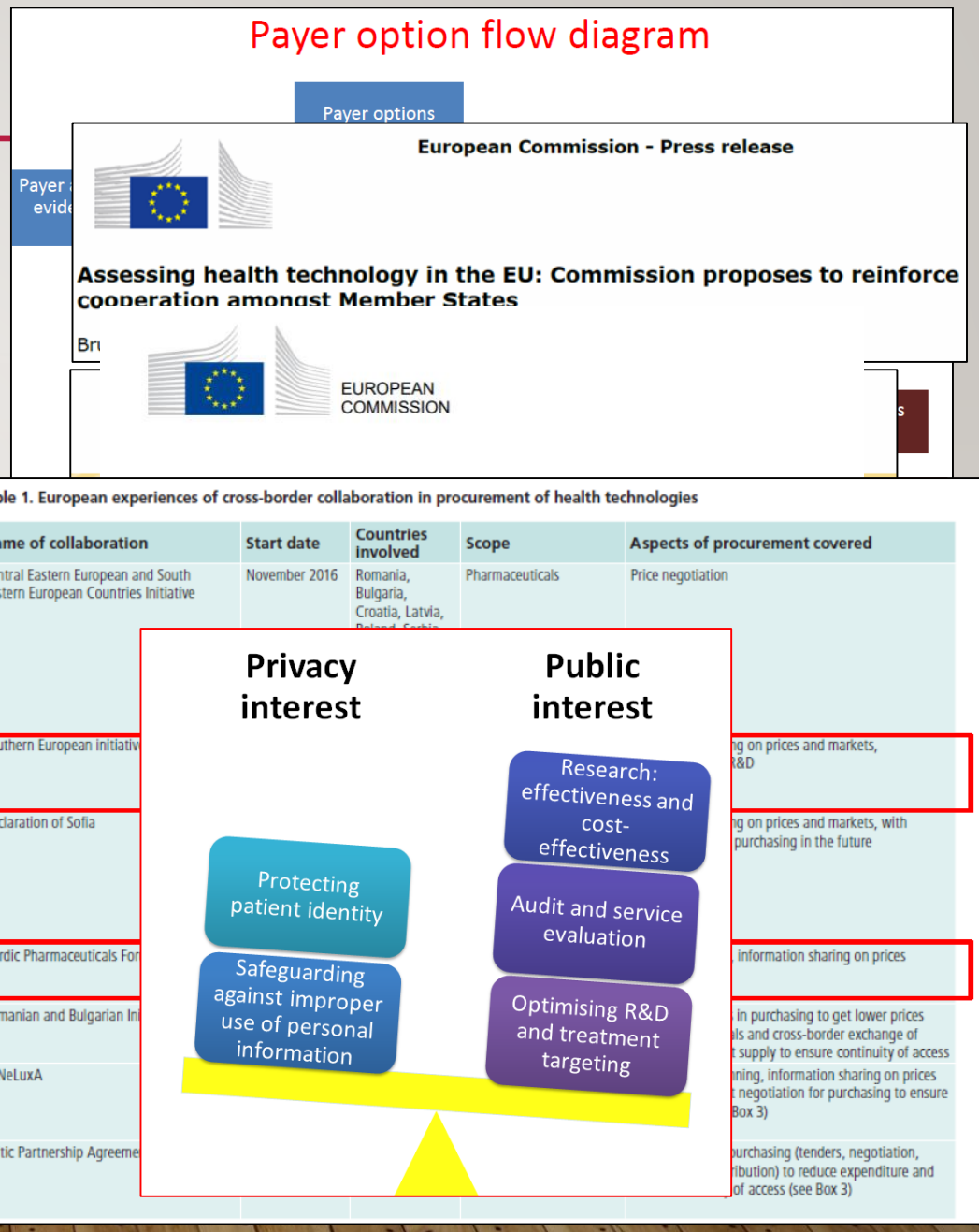
Source: Deloitte's 2018 RWE Benchmarking Survey.

Deloitte Insights | deloitte.com/insights

ADDRESSING THE CHALLENGES…

1. "Managed entry agreements" (*resolving uncertainties*)
2. More alignment between regulators and HTA/payers, and across HTA/payers (*more efficient evidence generation*) [impact of JCA?]
3. European-wide initiatives – procurement
4. RWE (*measuring if treatment works in real life*)
    1. Governance models: who has access to data, for what purpose, and under what conditions?
    2. What are the appropriate methods to ensure robust, transparent, and relevant findings?

Information based on speaker's experience



USES OF RWE: LIFE-CYCLE APPROACH

How can RWE be used in medicines development?

RWE has an important role in decision-making related to authorisation and access to new medicines and reimbursement. It can be used for:

- **understanding 'real-world' settings** such as treatment populations, patterns of care and the burden of disease
- **assessing the effectiveness of current therapies** using existing data
- **refining or supplementing evidence** from conventional trials of new medicines
- **providing new evidence of relative effectiveness** of new medicines.

RWD has conventionally been used to understand and characterise treatment populations, patterns of care and burden of disease. It is also used to describe the natural history of disease, project long-term outcomes, and define and validate new measures of outcome of relevance to patients.

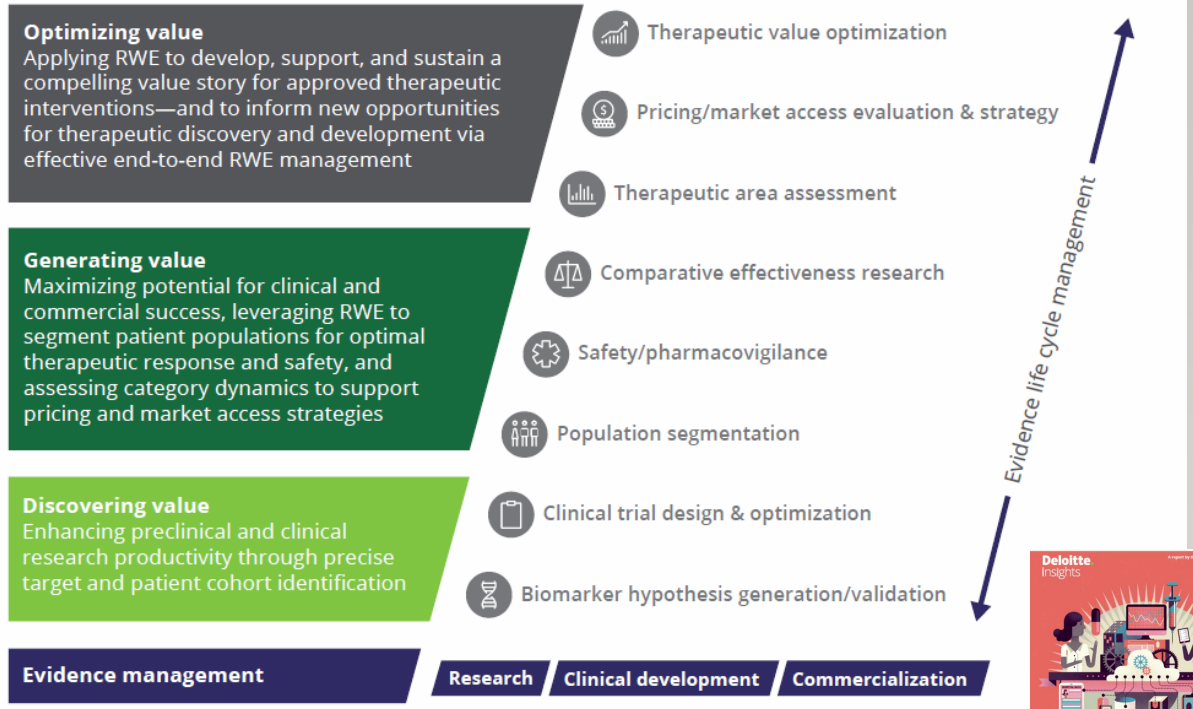
RWE of the effectiveness of existing therapies will usually be available to help plan studies of new medicines. In some situations it may be possible to generate new RWE ('early' estimates) of the effectiveness of a new medicine, in time to inform reimbursement decision-making.

RWE Navigator

Get Real

Figure 3. End-to-end evidence management approach

Pharma companies can maximize the value of their data by using it for decision-making at an enterprise level (vs. traditional siloed approaches)

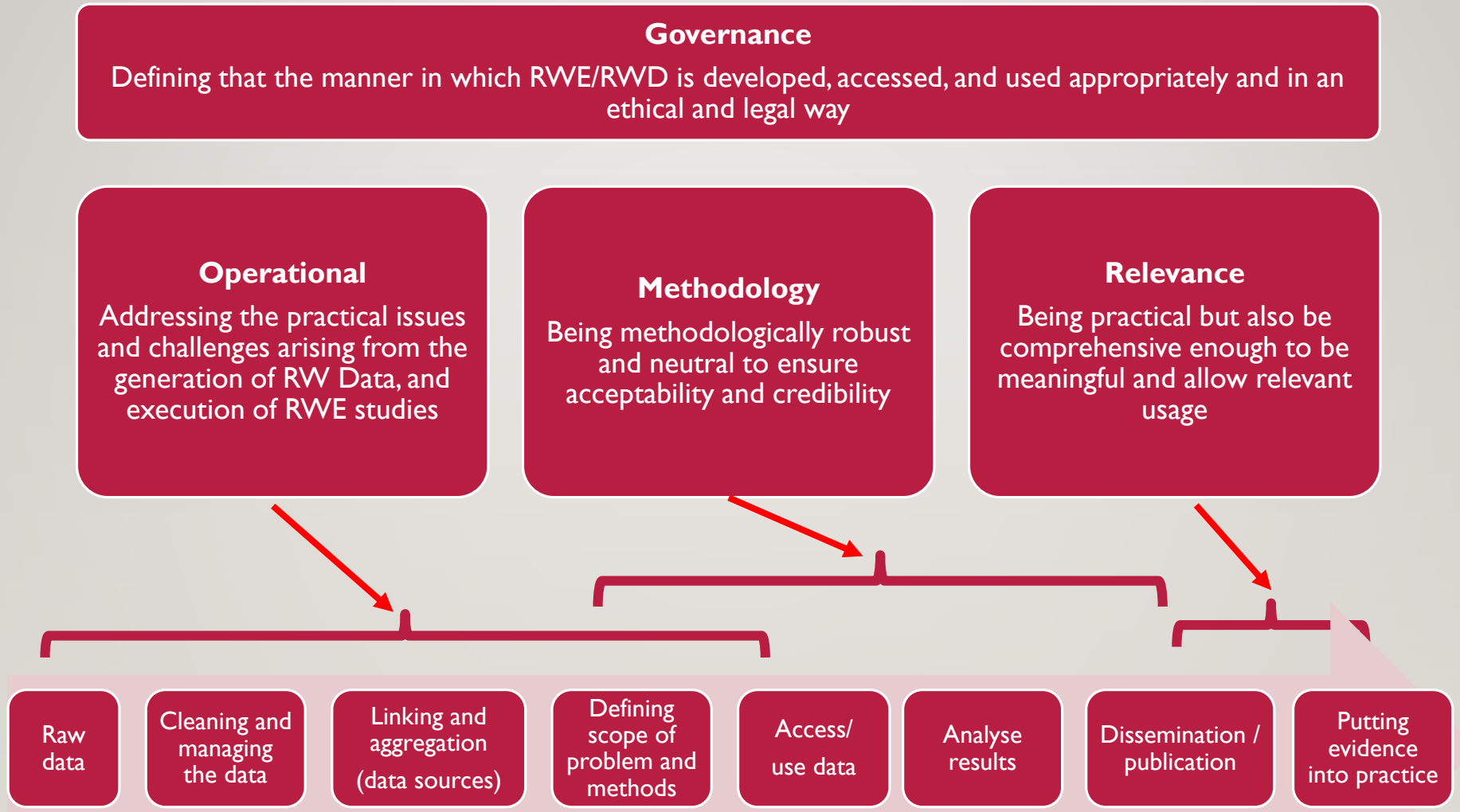


Source: Deloitte analysis.

Deloitte Insights | deloitte.

1. 'Real-world evidence and its importance in medicines development'. Available at: https://rwe-navigator.eu/rwe-importance-in-medicine-development/. Accessed March 2019. 2. Real-world evidence: Four shifts ushering in a new era of evidence in life sciences and health care. Available at: https://blogs.deloitte.com/centerforhealthsolutions/real-world-evidence-life-sciences-industry/. Accessed March 2019.

A RWD/E FRAMEWORK: OPTIMAL DEVELOPMENT AND USE OF RWD/E TO SUPPORT ACCESS AND P&R DECISIONS



Information based on speaker's experience

SO WHAT QUESTIONS ARE WE TRYING TO ADDRESS?

- What should be the role of RWD/E in **Access & Price/Reimbursement decisions** (i.e. coverage and payment)?

⇒ ***How*** can RWD/E be integrated as a key element within the Access, Price & Reimbursement process submission, *as well as* post-launch (to maintain/enhance reimbursement)?

- ⇒ Acceptability of RWD/E into decisions on "access (coverage)/price & reimbursement (payment)" – life-cycle approach
- ⇒ What RWD/E will fit into payer decision-making framework: "access decision criteria"

⇒ ***How*** can RWD/E be a key element to address some of the **gaps/lack of information** in PRICING process (*given wider use of RWD/E for Reimbursement*)?

- ⇒ Types of studies
- ⇒ What outcomes to measure
- ⇒ "Patient-based RWE": is it accepted, and how does it fit?
- ⇒ …

BARRIERS TO RWE INITIATIVES (1/2)

- Bias & confounding
- Incomplete data
- Data mining
- Access to data
- Lack of universally accepted methodological standards
- Lack of investigator expertise
- Obsolete evidence hierarchies


Real-world evidence for coverage decisions: opportunities and challenges

Grace Hampson*[,1], Adrian Towse[1], William B Dreitlein[2], Chris Henshall[1,3] & Steven D Pearson[2]

[1]Office of Health Economics, Southside, London, SW1E 6QT, UK
[2]Institute for Clinical & Economic Review, Boston, MA, 02109, USA
[3]Independent Consultant, UK

Journal of Comparative Effectiveness Research

- Incomplete access to electronic healthcare data from different MSs and a lack of hospital in-patient data
- Variable data quality and a lack of harmonisation
- The need to develop methods for efficacy and HTA outcomes
- Delays to start studies
- Fragmentation of EU efforts to harness the potential

Source: EMA, Update on Real World Evidence Data Collection, STAMP, 10 March 2016

BARRIERS TO RWE INITIATIVES (2/2)

- Respondents noted that health care stakeholder receptivity to industry-generated RWE and lack of an internal understanding of where RWE analyses can be applied are the key barriers to RWE initiatives.

Figure 11. What are the top three challenges to the success of your RWE efforts?

1 — **75%** respondents

Lack of receptivity by industry stakeholders (payers, providers, etc.)

2 — **70%** respondents

Lack of understanding among internal stakeholders about where RWE analyses can be applied broadly

3 — **65%** respondents

Lack of access to external data necessary to make RWE analyses valuable

Note: Chart shows top three barriers calculated as the percentage of respondents who ranked the barrier in the top three.

Source: Deloitte's 2018 RWE Benchmarking Survey.

Deloitte Insights | deloitte.com/insights

…AND HOW CAN WE MOVE FORWARD IN THE USE OF RWD?

Data Rich, Information Poor: Can We Use Electronic Health Records to Create a Learning Healthcare System for Pharmaceuticals?

Hans-Georg Eichler[1], Brigitte Bloechl-Daum[2], Karl Broich[3], Paul Alexander Kyrle[2], Jillian Oderkirk[4], Guido Rasi[1], Rui Santos Ivo[5], Ad Schuurman[6], Thomas Senderovitz[7], Luke Slawomirski[4], Martin Wenzl[4] and Valerie Paris[4]

Judicious use of real-world data (RWD) is expected to make all steps in the development and use of pharmaceuticals more effective and efficient, including research and development, regulatory decision making, health technology assessment, pricing, and reimbursement decisions and treatment. A "learning healthcare system" based on electronic health records and other routinely collected data will be required to harness the full potential of RWD to complement evidence based on randomized controlled trials. We describe and illustrate with examples the growing demand for a learning healthcare system; we contrast the exigencies of an efficient pharmaceutical ecosystem in the future with current deficiencies highlighted in recently published Organisation for Economic Co-operation and Development (OECD) reports; and we reflect on the steps necessary to enable the transition from healthcare data to actionable information. A coordinated effort from all stakeholders and international cooperation will be required to increase the speed of implementation of the learning healthcare system, to everybody's benefit.

Eichler HG, et al. Clin Pharmacol Ther. 2019;105(4):912–922.

VALTERMED (1/2)

Patricia Lacruz @PatLacruz · 22 ene.
Hoy hemos mantenido en @sanidadgob una reunión con las CCAA para avanzar con #VALTERMED

Avanzamos.

#SNSmásFuerte

> **diariofarma** @diariofarma
> Ministerio y CCAA trabajan en Valtermed, un sistema para medir el valor en fármacos /Sanidad hace público el Proyecto de RD que regulará el 'Nodo SNS' - mailchi.mp/diariofarma/po...

3 14 25

Jorge Mestre-Ferrand @JorgeMestreFerr · 23 ene.
Suena bien! Pero estaría incluso mejor ver algún detalle de la propuesta...espero que estéis "usando" economistas de la salud! ;) @AesSecretaria

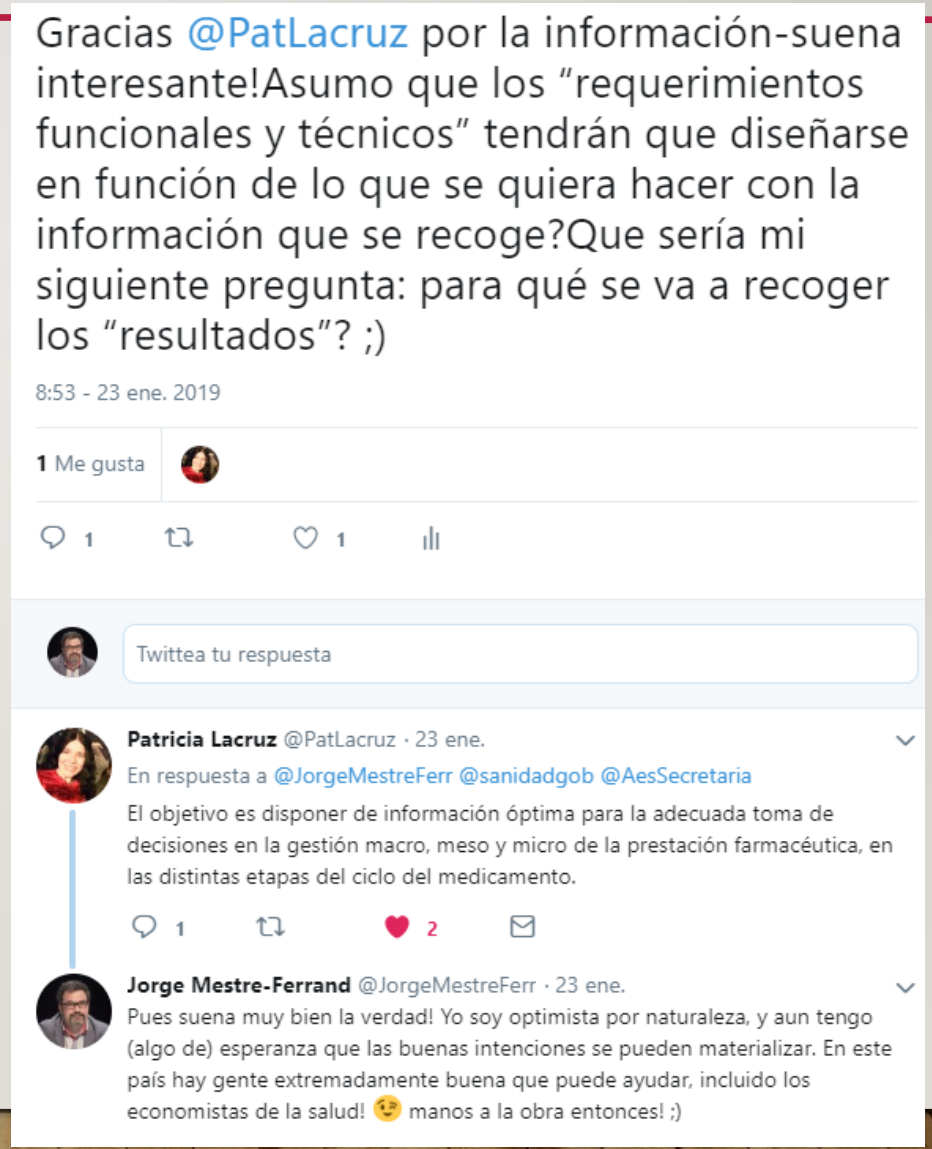
1 1 2

Patricia Lacruz @PatLacruz · 23 ene.
Actualmente estamos diseñando el SI en lo que a los requerimientos funcionales y técnicos se refiere.

Para cada medicamento se definirá el protocolo de medición de resultados en el seno de la Comisión Permante de Farmacia.

#SNSmásFuerte

1 3



Gracias @PatLacruz por la información-suena interesante!Asumo que los "requerimientos funcionales y técnicos" tendrán que diseñarse en función de lo que se quiera hacer con la información que se recoge?Que sería mi siguiente pregunta: para qué se va a recoger los "resultados"? ;)

8:53 - 23 ene. 2019

1 Me gusta

1 1

Twittea tu respuesta

Patricia Lacruz @PatLacruz · 23 ene.
En respuesta a @JorgeMestreFerr @sanidadgob @AesSecretaria
El objetivo es disponer de información óptima para la adecuada toma de decisiones en la gestión macro, meso y micro de la prestación farmacéutica, en las distintas etapas del ciclo del medicamento.

1 2

Jorge Mestre-Ferrand @JorgeMestreFerr · 23 ene.
Pues suena muy bien la verdad! Yo soy optimista por naturaleza, y aun tengo (algo de) esperanza que las buenas intenciones se pueden materializar. En este país hay gente extremadamente buena que puede ayudar, incluido los economistas de la salud! 😉 manos a la obra entonces! ;)

VALTERMED (2/2)

ELGLOBAL

Editorial/Opinion | Política Sanitaria | Farmacia | Industria Farmacéutica | Suplementos y

Con la venia:

Sobre Valtermed

Temas relacionados:

Con la Venia - Valtermed

+ 3

Herramientas

Imprimir

Enviar

Jordi Faus Abogado y socio de Faus & Moliner | 10 may 2019 - 12:44 h | ElGlobal.net

El 16 de enero, en respuesta a un tuit de la SEFH, Patricia Lacruz hizo público, también en Twitter, que el Ministerio y las CCAA habían empezado a trabajar en Valtermed, un sistema de información "para medir el valor terapéutico en la práctica clínica real de los medicamentos de alto impacto sanitario". Ya se sabe que las ideas que prosperan son las que se apoyan en recursos humanos y financieros, y si además se presentan con una

Jorge Mestre-Ferrand @JorgeMestreFerr · 11 may.

spot on @FausJordi como siempre! Claro, conciso, y concreto ;) será ahora el momento donde despeguen de verdad todos estos mecanismos novedosos? parece que empezamos a tener las herrmamientas...y q conste que @PatLacruz tambien me contestó a mi! #valtermed

Sobre Valtermed

El 16 de enero, en respuesta a un tuit de la SEFH, Patricia Lacruz hizo público, también en Twitter,...

elglobal.es

5

En definitiva, vincular la financiación y precio de un medicamento a su valor terapéutico no es nuevo, lo cual tampoco debería sorprender. Cualquiera sabe que cuando pagamos un precio por un producto, el valor que este nos aporta es muy relevante en nuestra decisión de compra. La novedad que supone Valtermed, parece, es que será un sistema de información que permitirá medir ese valor; y es imprescindible que se vayan dando pasos para conseguir que el Ministerio disponga de los recursos humanos y financieros precisos para su viabilidad. También será importante generar complicidades con todos los implicados, porque Valtermed no puede ser una herramienta contra nadie. Por cierto, tampoco estaría mal que alguien se empiece a preocupar por ordenar el contenido de la web del Ministerio, para que tenga el valor informativo que nos merecemos todos los contribuyentes.

FINAL REFLECTIONS

There is a need for:

- Better planning of RWD/E collection and analysis throughout the life cycle, delivered through:
  - Scientific advice for products in development
  - Benefit risk management planning at initial and post-authorisation
- Many ongoing initiatives, but fragmented: need better coordination between existing initiatives, leveraging outputs and identifying gaps
- Cross-stakeholder collaborative approach to fill the gaps for RWE access and analysis (trust critical!)
- **Y para España en particular: !la necesidad de tener buenas herramientas si queremos modelos más innovadores basado en datos de vida real!**

Thanks for your attention!

Dr Jorge Mestre-Ferrandiz

Independent Economics Consultant

Profesor Asociado, Universidad Carlos III, Madrid

Visiting Fellow, Office of Health Economics

Profesor de Health Economics de FT/Instituto de Empresa (IE) Business School

Director, Oxford Martin Programme on Affordable Medicines, Oxford Martin School, University of Oxford

Honorary Visiting Lecturer, Department of Economics, City University London

Views expressed are my own

Email: jormesfer13@gmail.com