What are the regulatory needs in terms of registry data?

Joint HMA/EMA multi-stakeholder workshop on Patient Registries
12 – 13 February 2024

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An agency of the European Union

RCT's and RWD

RCTs gold standard for providing information regarding drug efficacy and safety

Value of RWD is increasingly acknowledged

- Transform, accelerate and de-risk decision making
- Improve efficiency in design and conduct of trials
- Increase public health impact

Marketing Authorisation

- Contextualize study results
- Ensure generalisability of results to target population

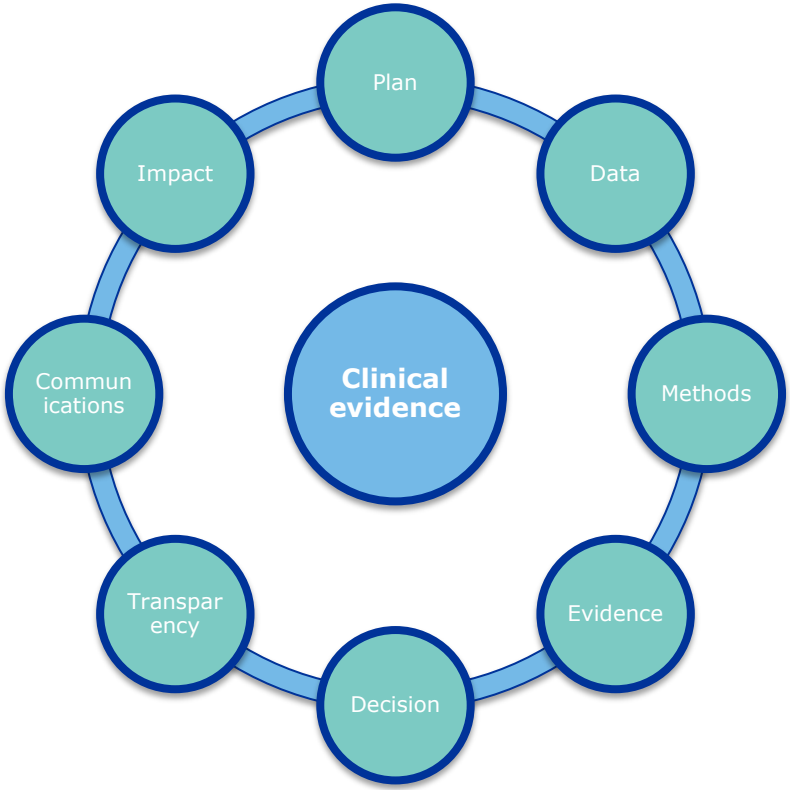
Post-Authorisation

- Appreciate real-world value
- Long-term B/R balance

Treachery of Images (1929) by René Magritte

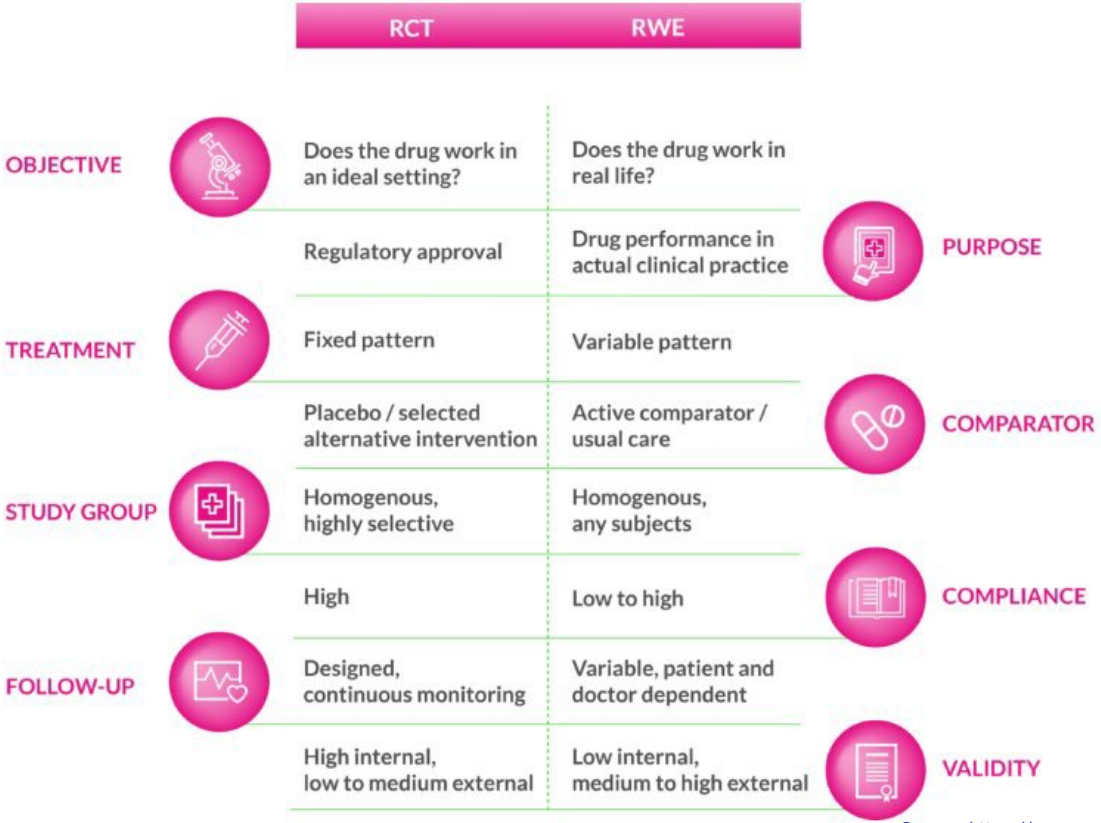
The vision: Clinical evidence 2030

- Evidence generation is planned and guided by data, knowledge and expertise
- Research question drives evidence choice: embraces spectrum of data and methods
- **Clinical trials remain core but are bigger, better and faster**
- **Real world evidence is enabled, and value is established**
- The patient voice guides every step of the way
- Healthcare systems are supported in their choices
- High levels of transparency underpin societal trust



Adapted from Peter Arlett

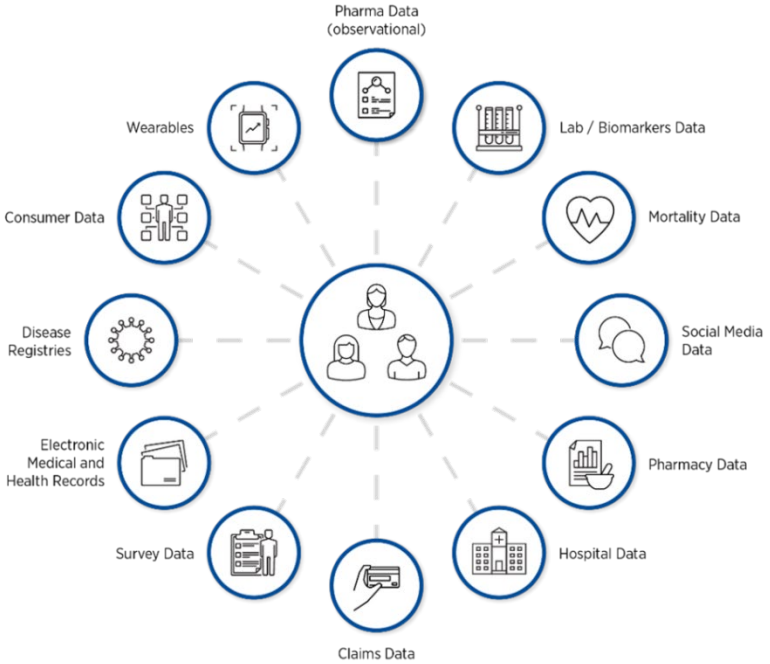
Key diferences between RCT's and RWE



Source: https://www.medengine.fi/opinion/what-is-your-real-world-data-strategy/

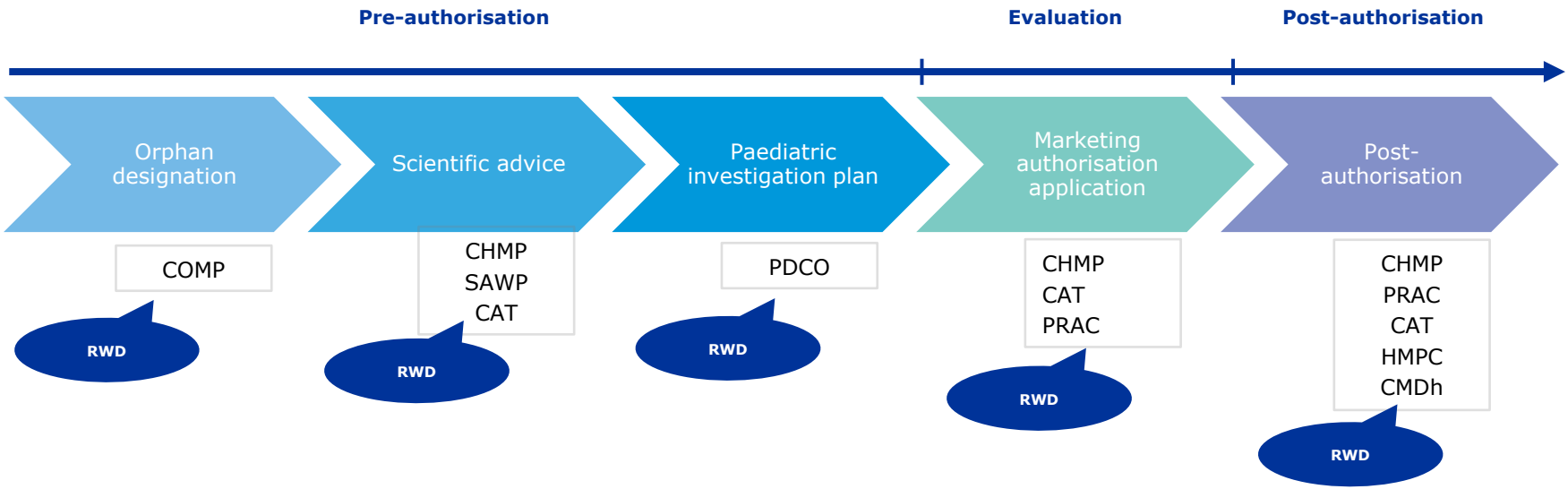
RWD

- Personalised medicine – smaller target populations
  RWD could complement RCT evidence
- Various types of RWD
- Regulators largely rely on patient registries:
  Systematic, curated, disease-specific data in clinical practice with good quality standards while reflecting real-world behaviors and effects
- Traditionally regulators use RWD for safety evaluation and long-term B/R, <u>but…</u>
- Exposure to RWD across all phases of drug development is increasing.



https://premier-research.com/blog-what-is-real-world-data-and-evidence-and-how-it-can-facilitate-clinical-development/

RWD use across the medicinal product lifecycle



Adapted from Peter Arlett

Three main areas for which RWD analyses can support EMA committees' decision-making

1 Understand the clinical context

- Disease epidemiology
- Clinical management
- Drug utilisation

2 Support the planning and validity

- Design and feasibility of planned studies
- Representativeness and validity of completed studies

3 Investigate associations and impact

- Effectiveness and safety studies
- Impact of regulatory actions

Adapted from Peter Arlett

Combining PRE- and POST-marketing authorisation use of registries

PRE-marketing authorization use of a registry (RWD)

- For a better knowledge on ***disease*** characteristics
  - Disease course, natural or with SOC
  - Identification of biomarkers

POST-marketing authorization use of a registry (RWD)

- For a better knowledge on the ***medicine's or treatment's*** characteristics
  - Refine benefit (quantitative, comparative)
  - Increase safety data
  - Further optimize treatment (posology)
  - Identification of surrogates for treatment effect

RWD: real world data; SOC: standard of care

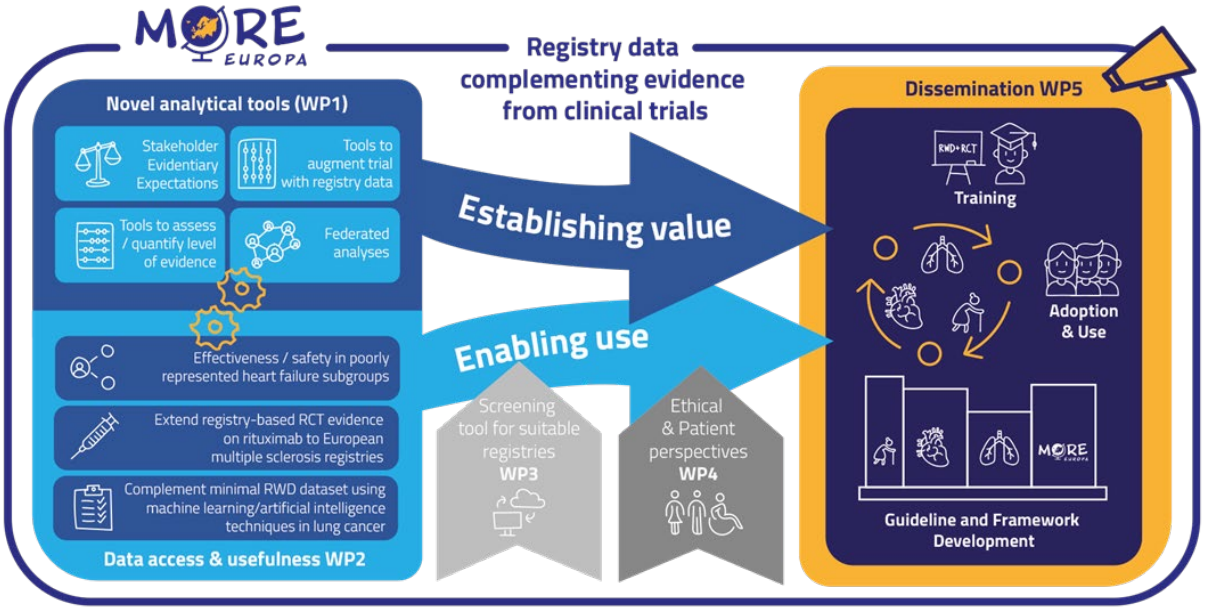
Adapted from Harald Enzmann

Use cases

Medicinal product	Indication	Authorisation	Use of RWE
Zolgensma (onasemnogene abeparvovec) ATMP	For the treatment of spinal muscular atrophy and a specific mutation in patients <2 years of age	2020	Data from a single-arm study. Data from two natural history studies provided the information of the natural course of the disease.
Rybelsus (semaglutide)	For the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise	2020	Medullary Thyroid Carcinoma Surveillance Study: a Case-Series Registry to evaluate further a potential association between treatment with long-acting GLP-1 RAs and the occurrence of medullary thyroid carcinoma in humans.
Nulibry (fosdenopterin)	To treat patients with molybdenum cofactor deficiency (MoCD) type A	2022	The outcome results in patients treated with Nulibry were compared with historical data from studies involving patients who did not receive Nulibry or any other treatment.

Adapted from Carla Jonkers and Carla Torre

The More-EUROPA project



More-EUROPA Kick-Off Meeting May 2023

WP1/WP5: Web based survey study to get insight on the views of diferent players on the topic of evidence needs, more specifically the role of real-world data and patient registries in their line of work.

Web based survey study – Preliminary results (WP 1 team)

108 regulators

Age groups:

18-30 years: 2%

31-40 years: 19%

41-50 years: 30%

51-60 years: 31%

61-70 years: 15%

71+ years: 1%

Gender: 63% women

Work experience:

<2 years: 12%

3-5 years: 13%

6-10 years: 17%

>10 years: 57%

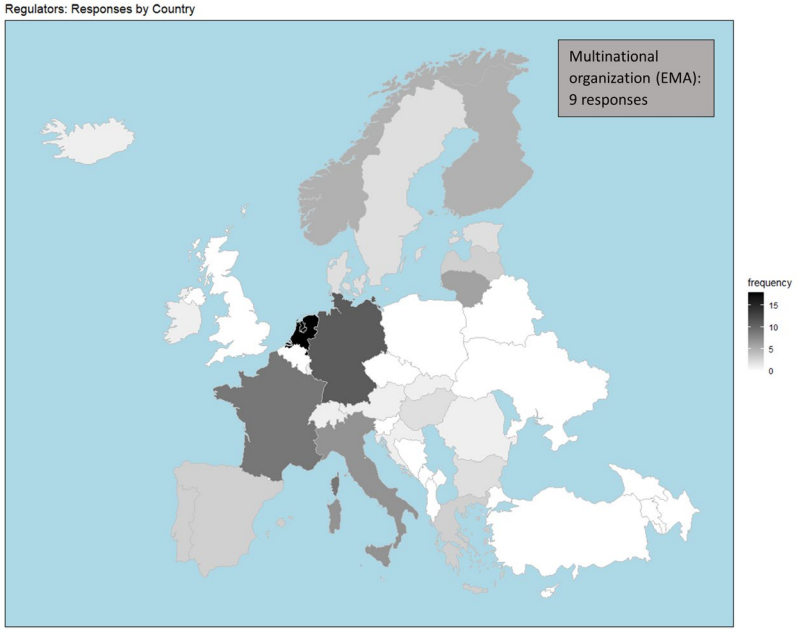
Other responders:

n= 95

27 HTA/payers

28 Industry

40 Academia/others

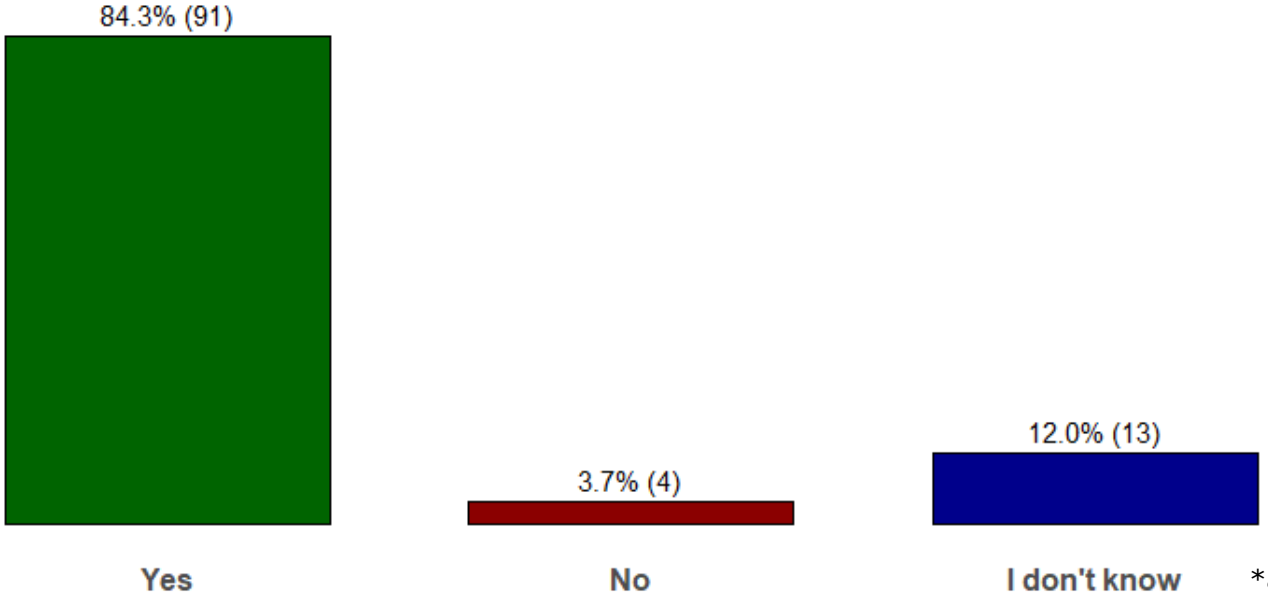


**percentages do not round up to 100 because of rounding and/or missing data*

Slides are a courtesy of Sieta de Vries and More-EUROPA WP 5 Team

EU-regulators agreement with the definition of patient registries

"An organized system that collects uniform data (clinical and other) to identify specified outcomes for a population defined by a particular disease, condition or exposure"

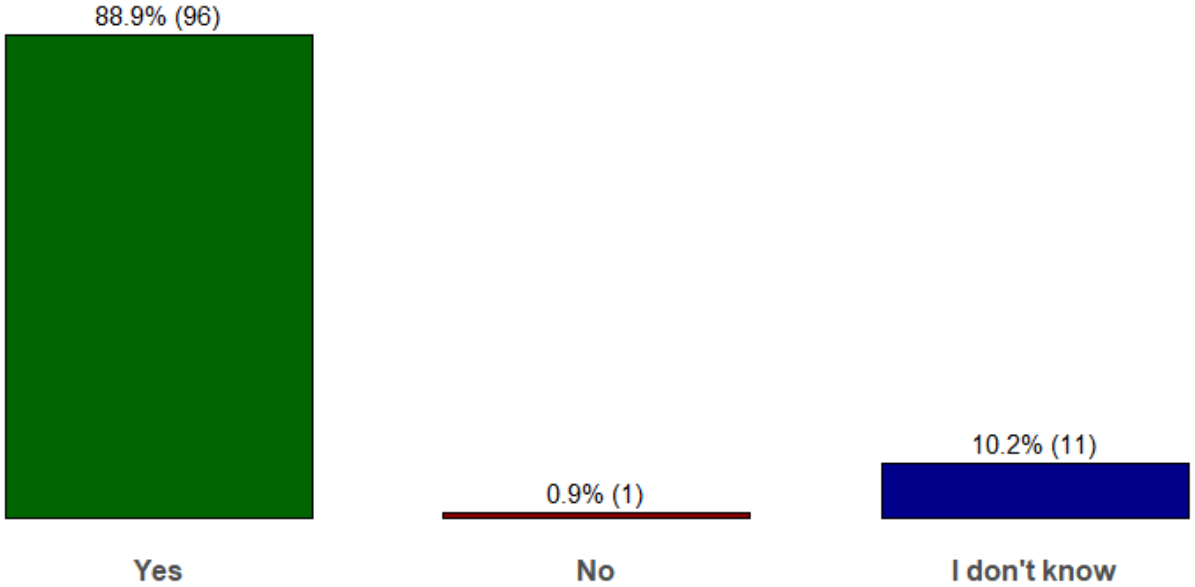


*absolute frequency in brackets

Slides are a courtesy of Sieta de Vries and More-EUROPA WP 5 Team

EU-regulators agreement with the definition of registry-based registries

"The investigation of a research question using the data collection infrastructure or patient population of one or more patient registries"



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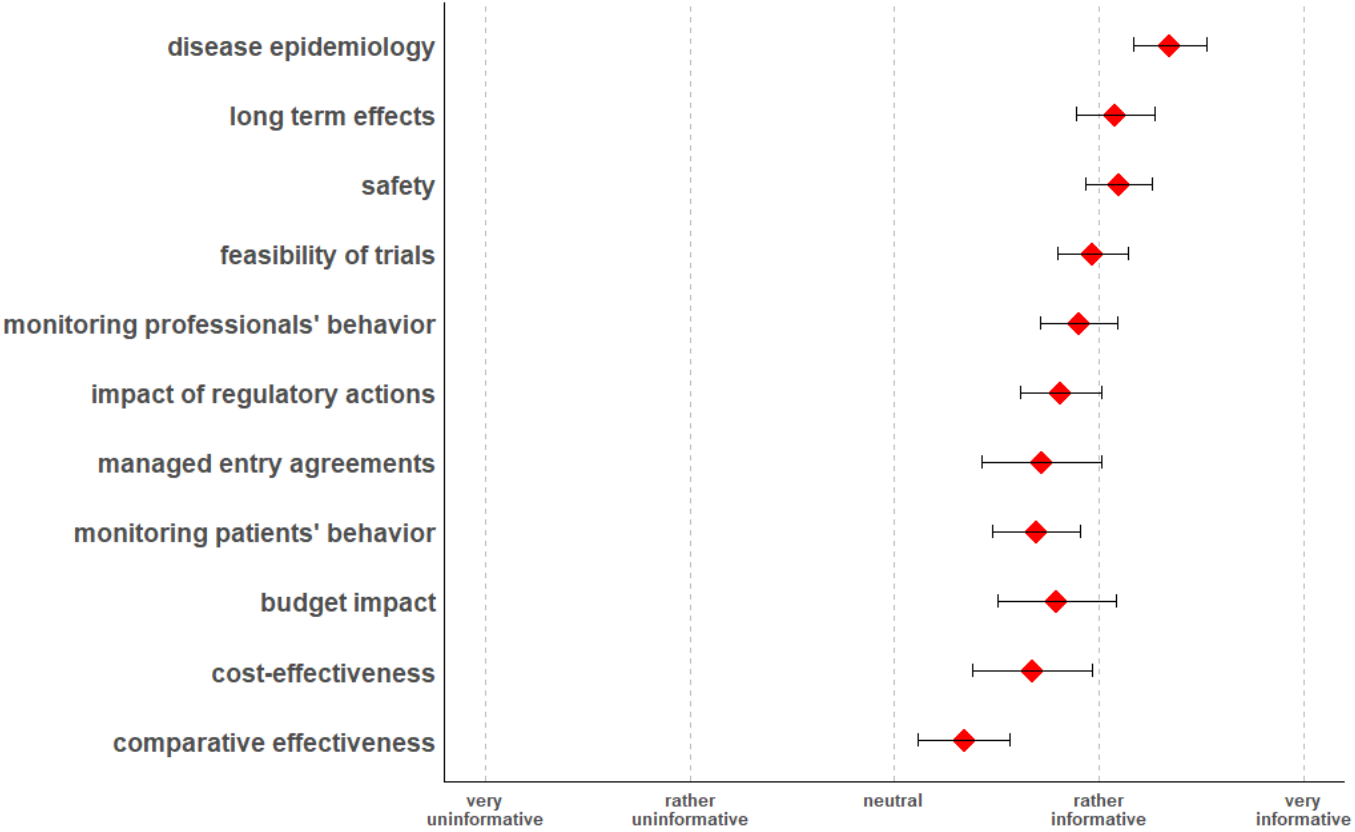
In your view, how informative are patient registry data for studying the following aspects?



*displaying means and standard deviations

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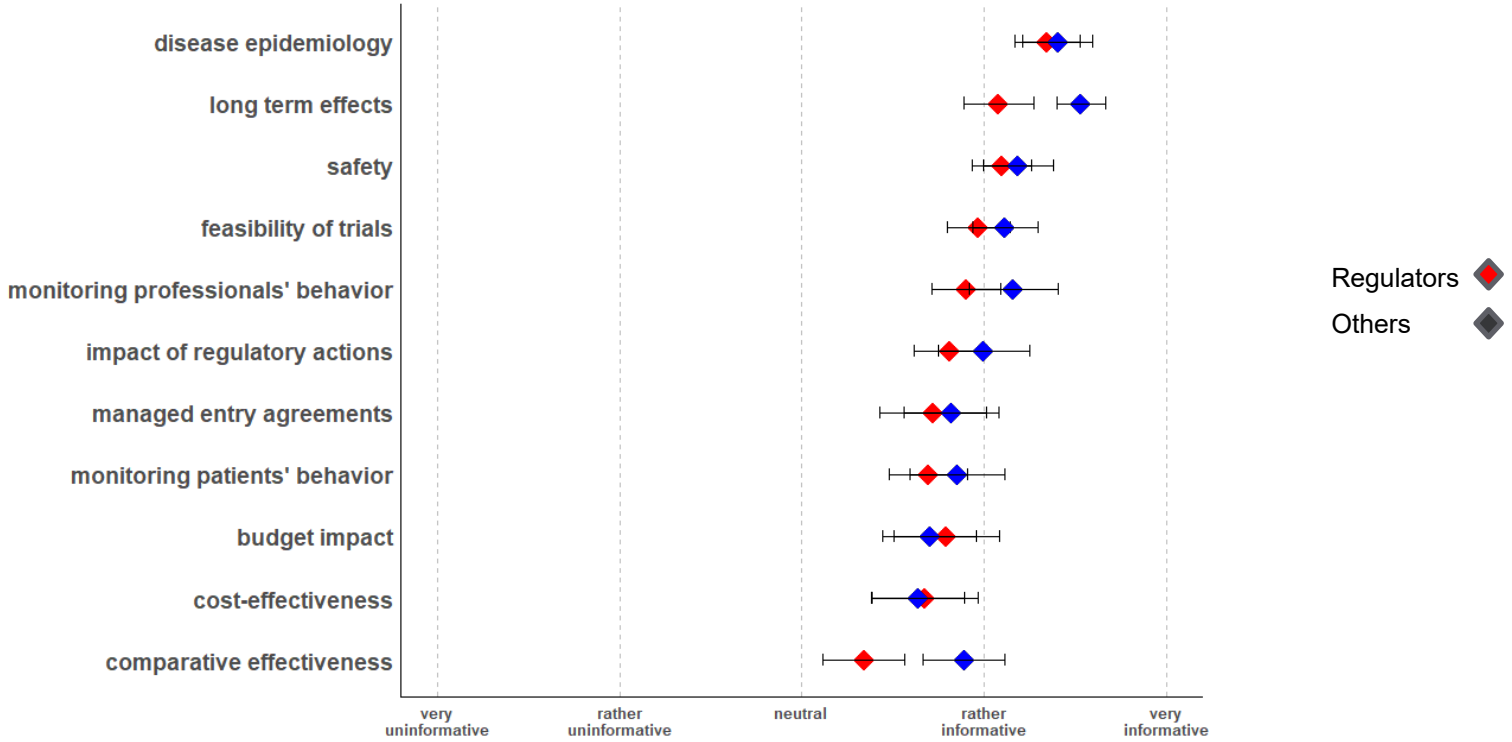

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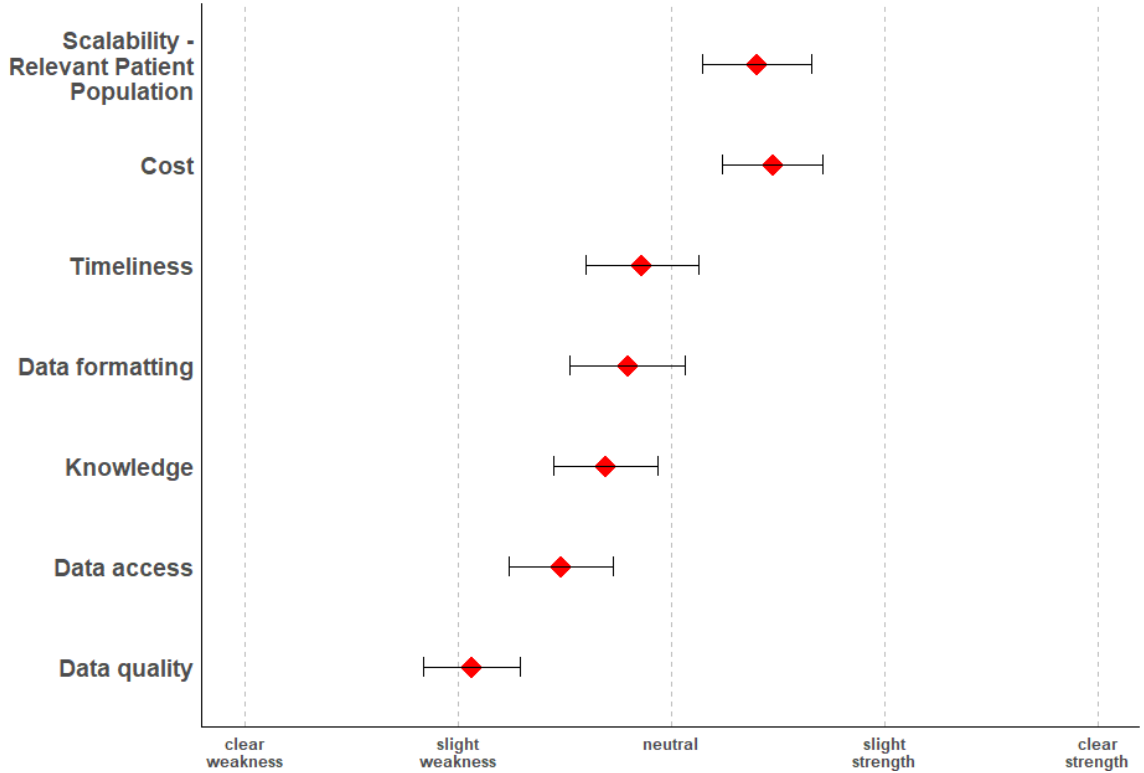
Do you view each of these aspects as a potential weakness or strength of using data from existing patient registries for decision-making?



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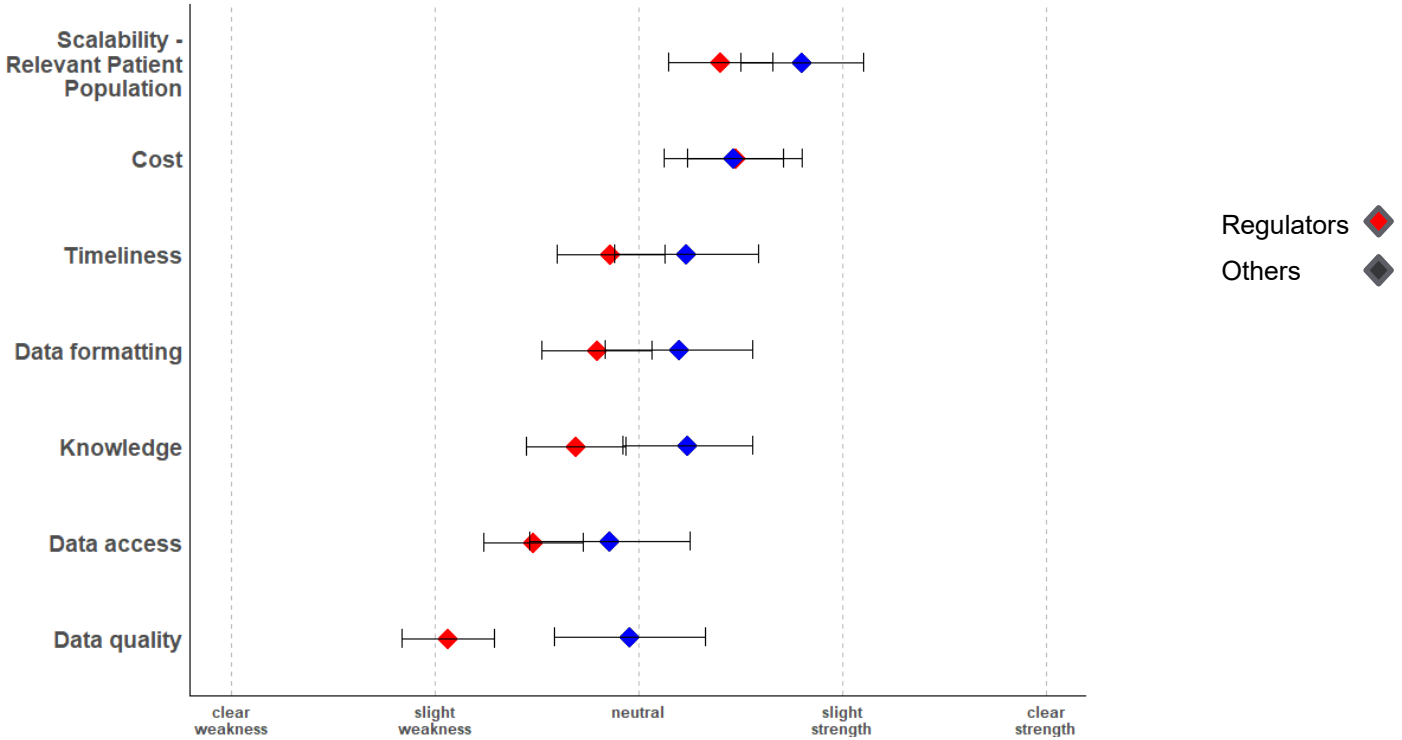

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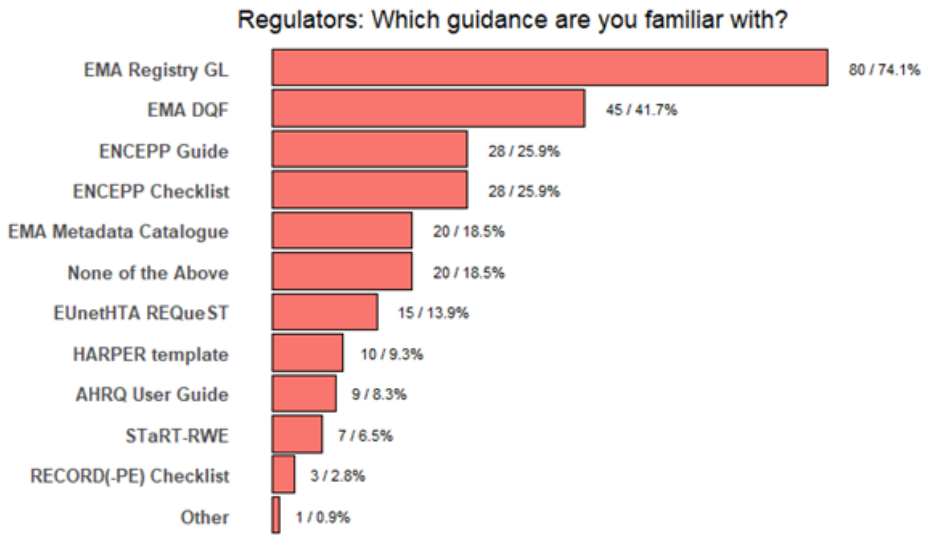
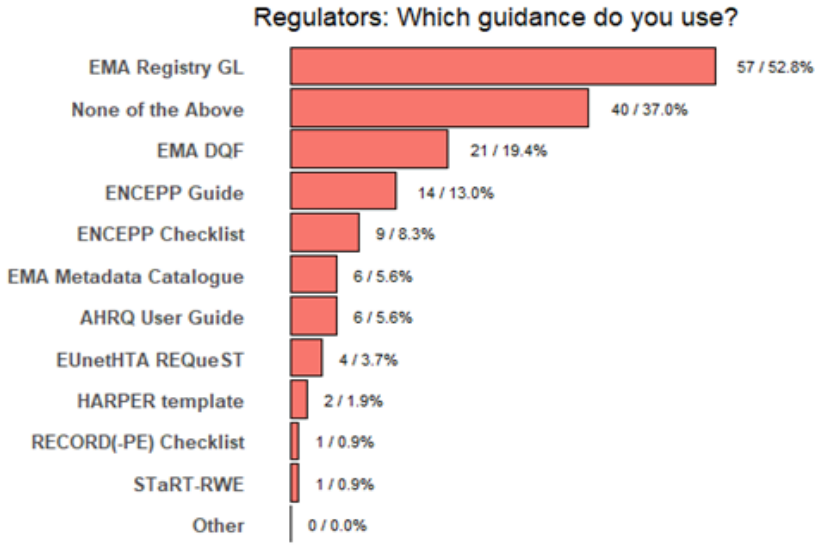
EU regulators' familiarity with guidance documents



Use of guidance documents when assessing registry-based evidence



Slides are a courtesy of Sieta de Vries and More-EUROPA WP 5 Team

Conclusions

- RWE in supporting the evaluation of medicines across different phases of development has been evolving, driven by the ability to answer specific research questions

- There is large agreement with EMA-definitions for patient registries and registry based studies

- In general patient registries are considered informative to study disease epidemiology, long term effects, and safety
    - Other responders a bit more positive regarding its use for assessing long term effects and comparative effectiveness

- Scalability – relevant patient population and cost are considered as slight strengths of registries

- Data quality and data access are considered as slight weakness of patient registries
    - Other responders generally a bit more positive except for costs

- Regulators are familiar with EMA and ENCEPP registry-guidance, but there is less actual use
    - Surprisingly large number reports using none of the guidances

Take Home Messages from the Regulator Perspective

- RWE have been used and will continue to be used (Regulators cannot afford not to use these data)

- Data (or registry) quality and transaparency is crucial

  The crucial regulatory need

- Powerful tool when used in complement to RCTs

- Enabling the use of RWE and establishing its value supports safer and more effective use of innovative medicines

Source:https://copperbowl.de/Chess-Pieces-Tier-List-Cape-Fear-Games-61289.html