Value of Real-World Data for Patient-Centred Affordable/Accessible Advanced Therapies for Rare Diseases

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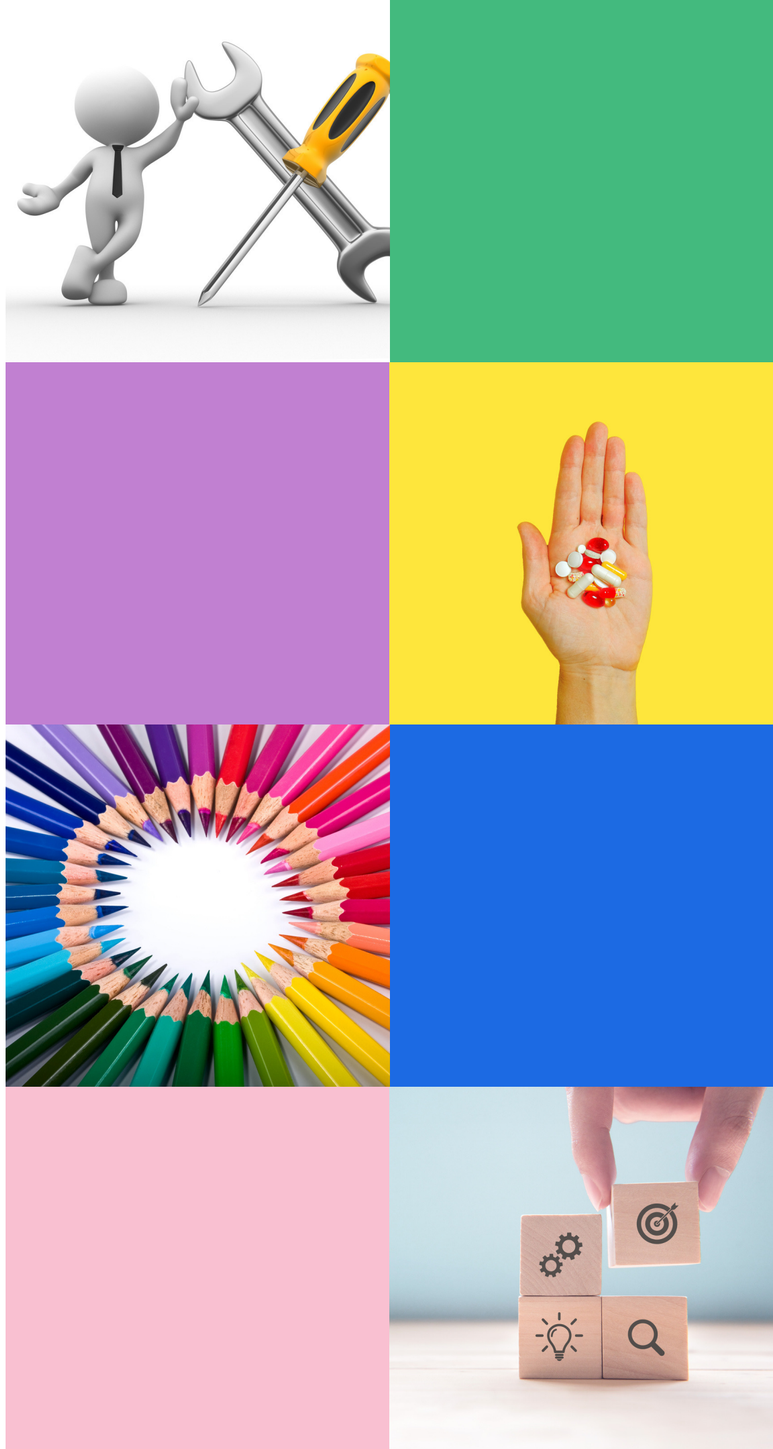
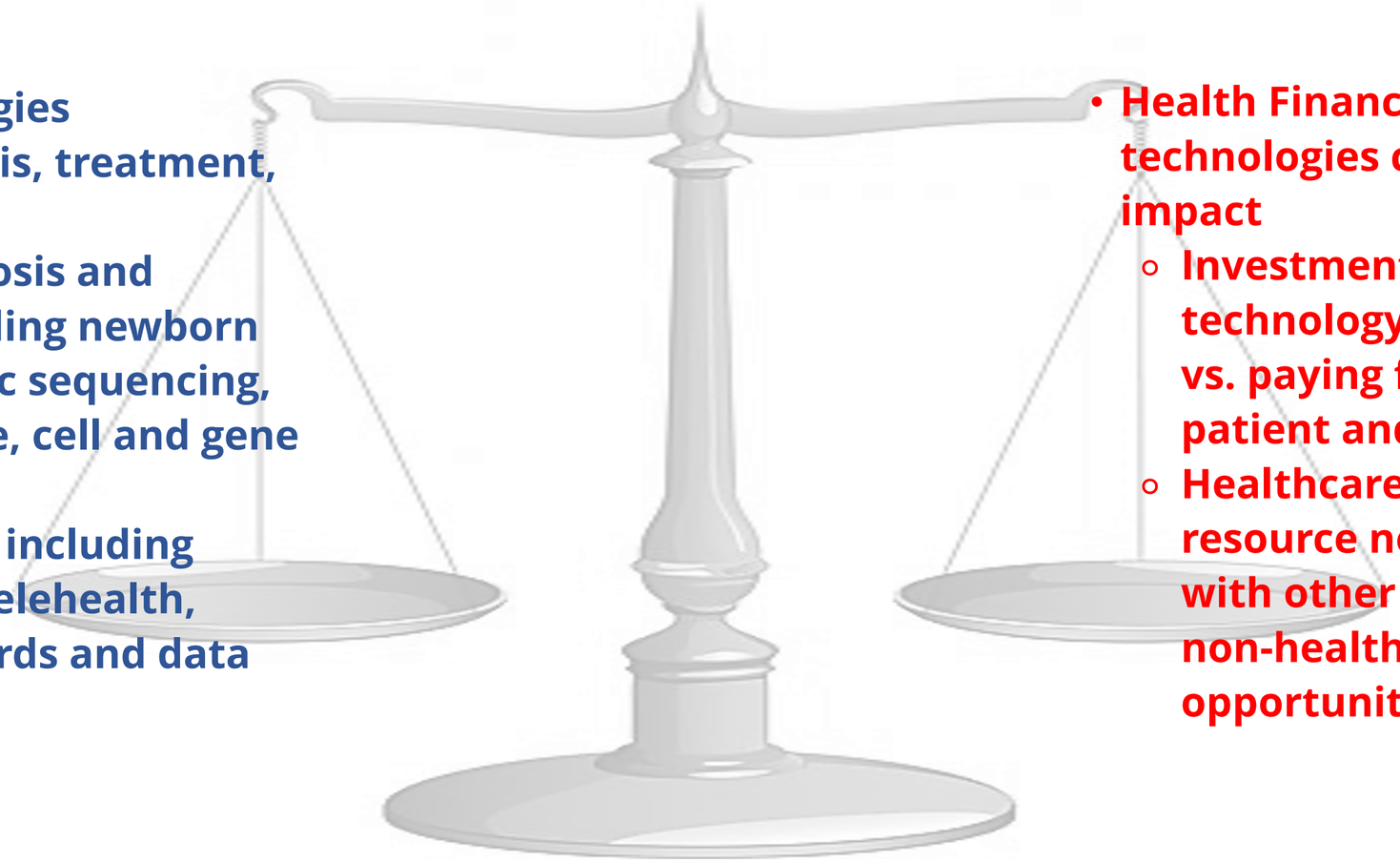


Drivers of Healthcare Ecosystem Impacting Innovative Rare Drug Access

- **Innovative Technologies accelerating diagnosis, treatment, and prevention**
  - Gene-based diagnosis and treatments, including newborn screening, genomic sequencing, precision medicine, cell and gene therapies
  - Digital-enhanced care including wearables, e-health, telehealth, electronic health records and data registries
- Health Financing of innovative technologies challenged by budget impact
  - Investment in health fueled by technology (prevention, well-being) vs. paying for treatment driven by patient and HCP needs
  - Healthcare competing with other resource needs: among diseases, with other societal priorities, with non-health investment opportunities

New Technology or Balanced Budgets? Or Can We Have It All?



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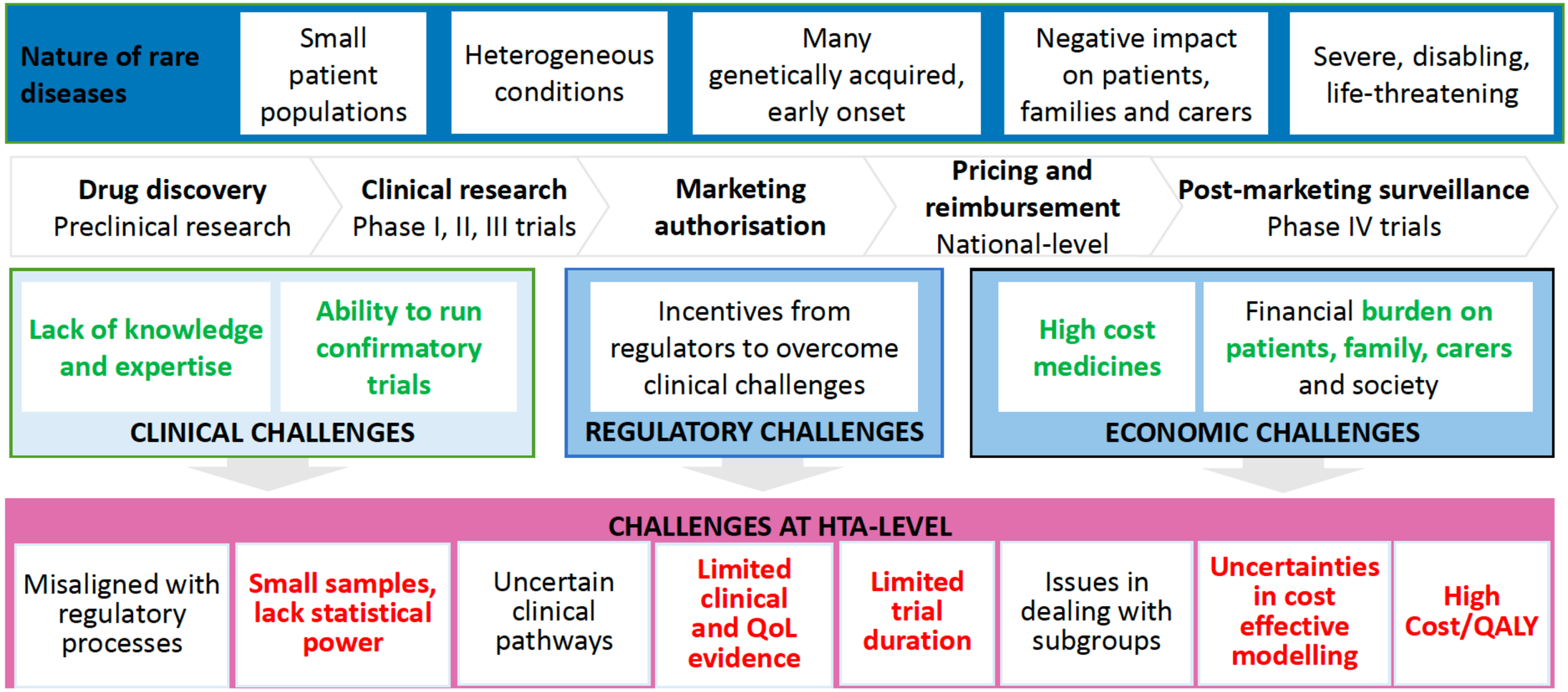
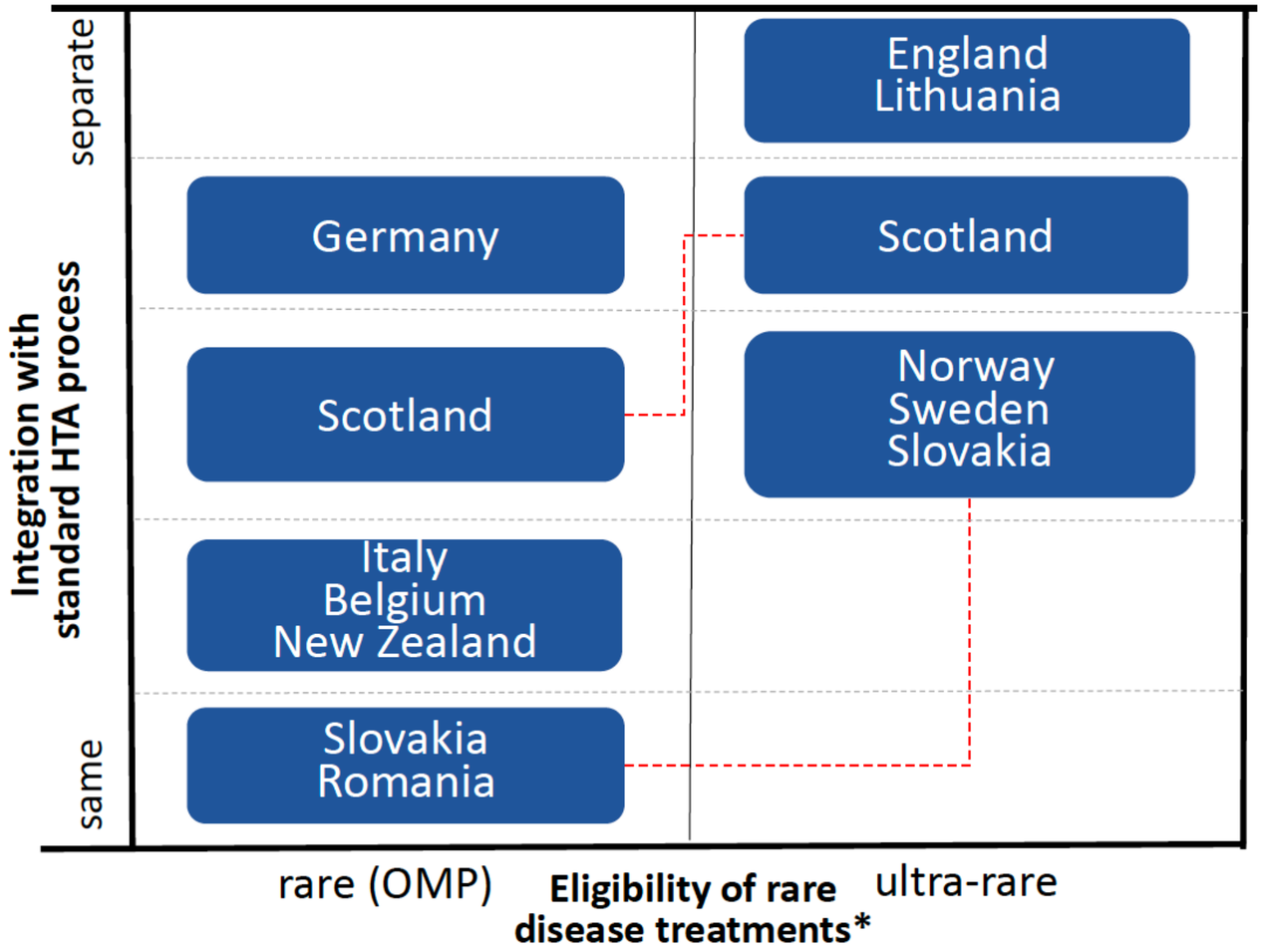
Difficulties developing rare disease treatments leading to HTA challenges



IMPACT HTA

Source: Nicod E, Annemans L, Bucsics A, Lee A, Upadhyaya S, Facey K. HTA programme response to the challenges of dealing with orphan medicinal products: Process evaluation in selected European Countries. Health Policy, 2019

13 (41%) of the 32 participating countries have some form of special HTA appraisal process informing routine use of medicines for rare diseases



Separate

Partially separate

Adapted

Expedited

Rarity weighted

Exempt from HTA
Latvia, Bulgaria

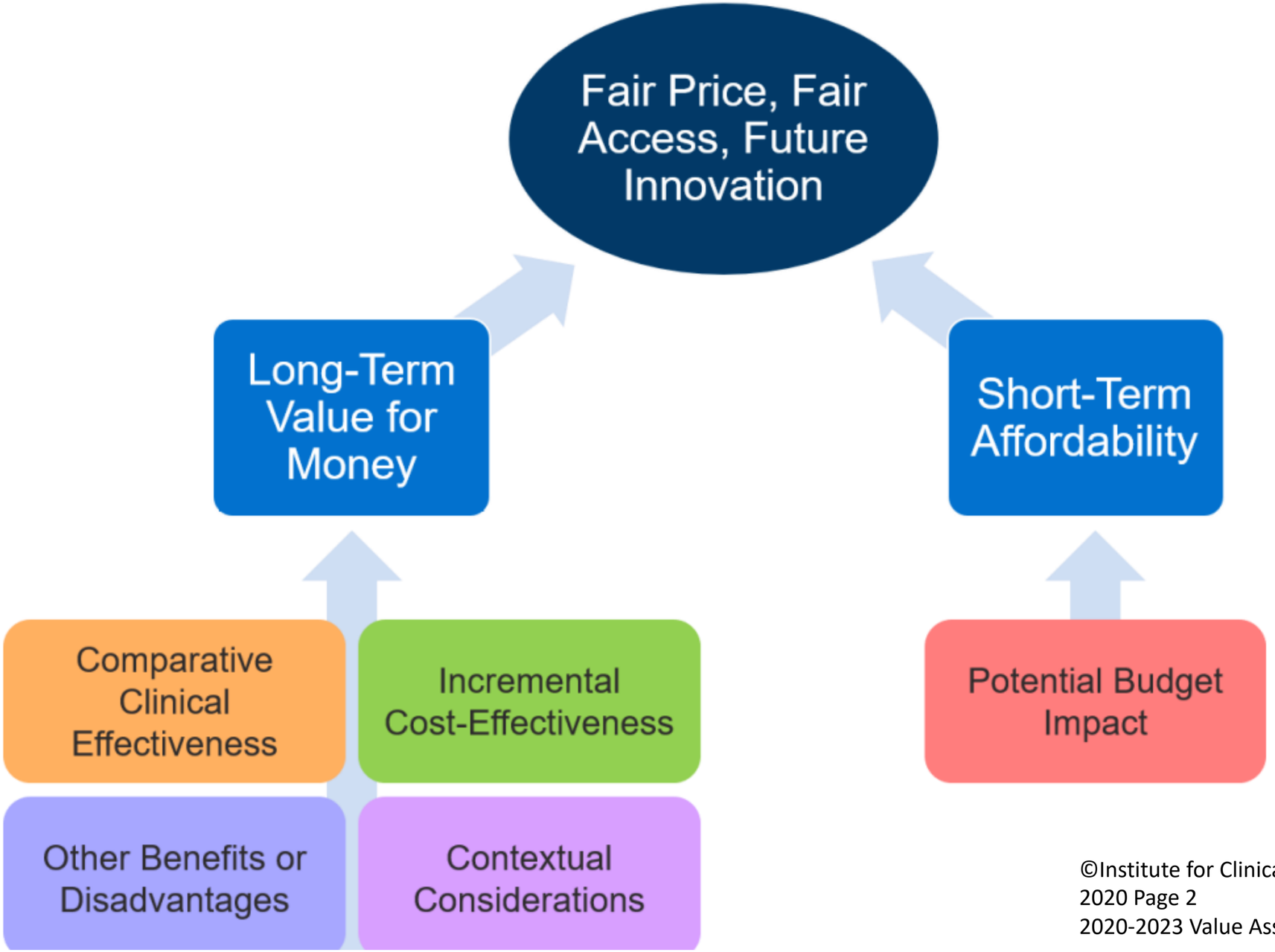
32/37 countries included:

- 41% special process
- 53% standard process
- 6% other programs applicable to rare disease treatments

* Rare disease treatment with orphan designation from European Medicines Agency ("Orphan Medicinal Product", OMP); ultra-rare disease treatments defined by individual country definitions

Source: Nicod E, Whittal A, Drummond M, Facey K. Are supplemental appraisal/reimbursement processes needed for rare disease treatments? An international comparison of country approaches. Orphanet Journal of Rare Diseases, 2020; 15:189

Figure 1.1. Conceptual Structure of the ICER Value Assessment Framework

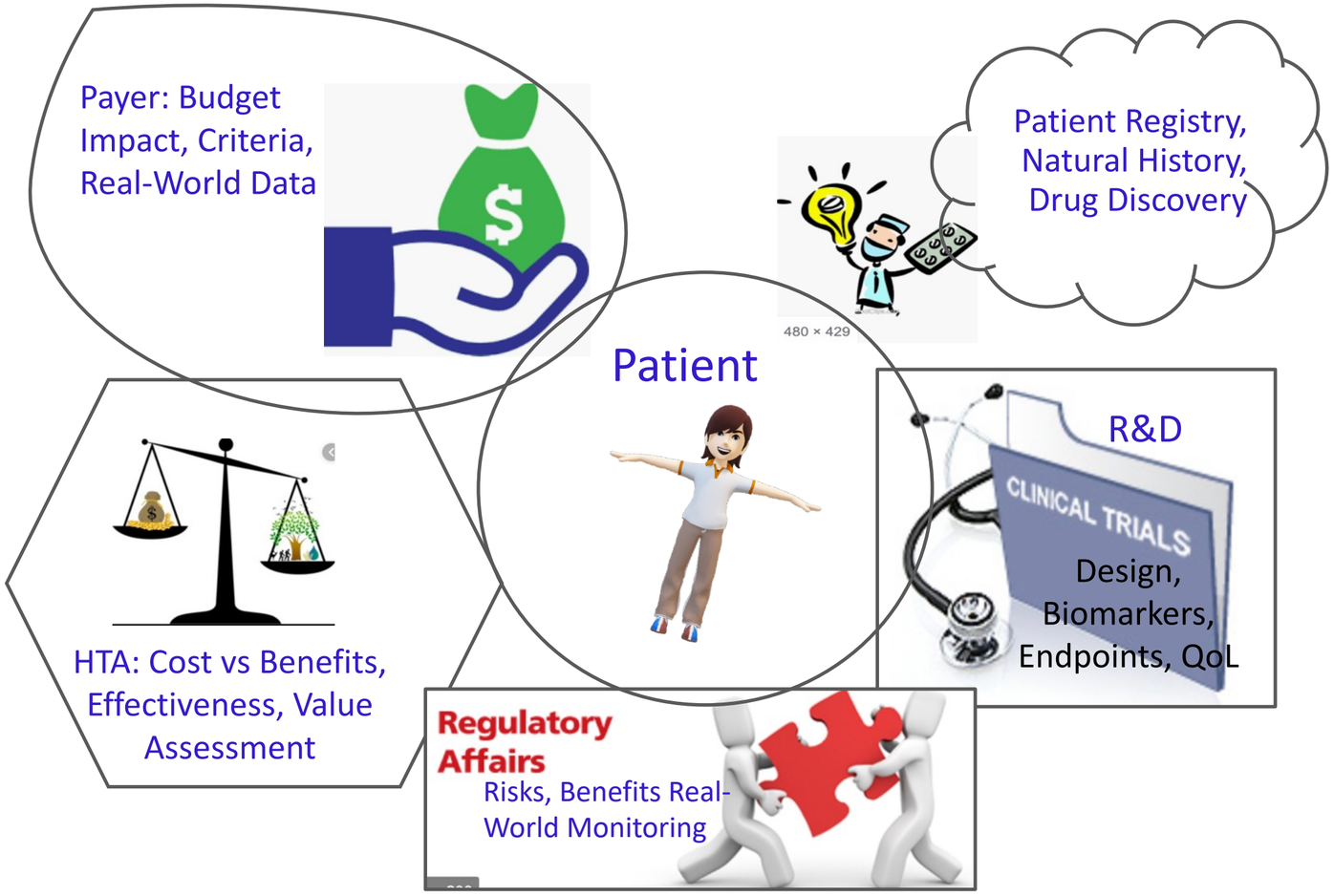


The Way Forward: A Framework for Reasonableness

Careful for tunnel vision towards orphan vs. non-orphan drugs
Always balance ethical with more quantitative criteria

Adopt a principle of fairness behind the treatment of orphan vs. non- orphan drugs. For instance, if patient hearings are organised, do so equally for both categories

Key to Access: Patient Engagement Throughout Drug Lifecycle?



RWD Studies can Generate Value and Information Across the Various Stages of the Product Lifecyle

Identify and respond to unmet needs

- Identify disease burden, epidemiology, global standard of care, healthcare resource uses, financial costs of disease

First application in patient settings

- Understand how efficacious and costly drugs are in the real-world
- Study the natural evolution of the rare disease
- Inform clinical trials, study designs, clinical disease characteristics

Long-term follow up in patients

- Understand patient satisfaction, preferences and outcomes on treatment and disease
- Determine the long-term impact of treatment to the patients

RWD studies can be used at all stages of the product lifecycle and can generate a plethora of evidence in favor of new therapies along with providing information to support clinical guidelines, regulatory decisions, and reimbursement decisions

Pro Relix Research. Real World Evidence Studies: Introduction, Purpose, and Data Collection Strategy: https://prorelixresearch.com/real-world-evidence-studies-introduction-purpose-and-data-collection-strategy/#:~:text=Purpose%20of%20RWE%20throughout%20the,regulatory%20decisions%2C%20and%20reimbursement%20decisions. (Accessed October 2023).

Variety of Real World Data Sources

Various Data Sources Collected to Inform Disease and Treatment Effectiveness, Patient Experience, Quality of Life etc.

Clinical

Collect **laboratory data** (i.e., Factor XIII levels, brain imagining) and replicate results from clinical trials[1]

Medication

Types of medicine, **method of drug administration**, and concomitant therapies[2]

Claims

Billing database with length of medication filled, **cost for doctor visits**, and **drug-drug** interactions[1]

Molecular Profiling

Availability of **patient genetic data**, for patients who are open to sharing their health information[2]

Mobile Health

Provides opportunity for **continuous monitoring, and real-time transition capabilities** not typically available from routine clinical care[2]

Patient Reported

Patient satisfaction to treatment, **quantify patient's health status (i.e., level of pain),** and signal potential exposure to outcomes relationship[1]

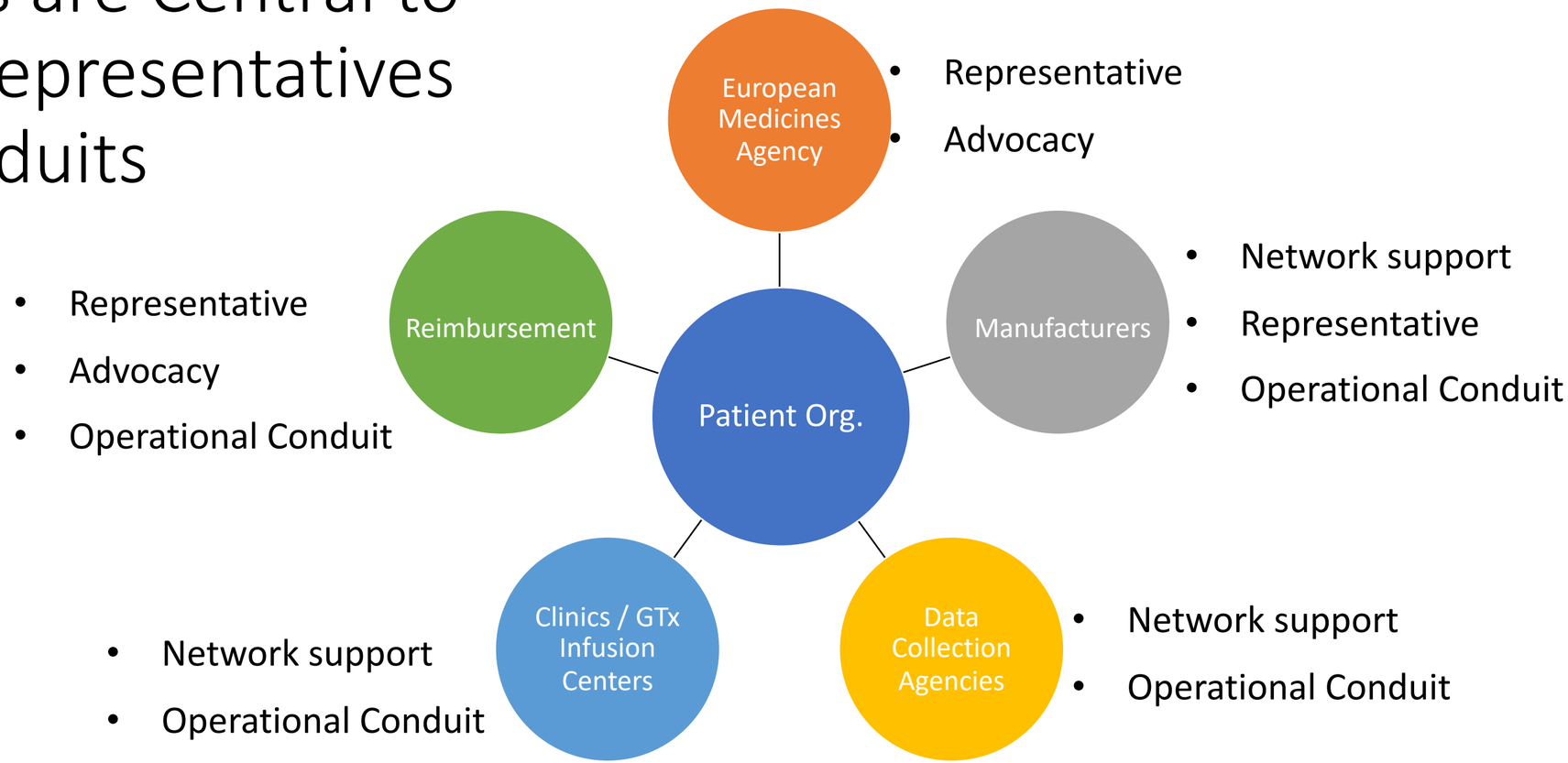
Social Media

Listen to **patient's public view** on health topics such as patient's impression of adverse events, patient experience with doctor visits and drug treatment[3]

Figure adapted from Liu F, Panagiotakos D. *BMC Med Res Methodol* 2022;22(1):287.

1. Liu F, Panagiotakos D. *BMC Med Res Methodol* 2022;22(1):287; 2. Swift B, et al. *Clin Transl Sci* 2018;11(5):450–60; 3. Dang A. *Pharmaceut Med* 2023;37(1):25–36.

Patient Organizations are Central to serve as Networks, Representatives and Operational Conduits



Stakeholders

Clinicals | Manufacturers | Reimbursement & Regulatory bodies | Patients & Caregivers

Ideas

Patient Organizations

Partnering with patient organizations to become the central connecting point

Patient commitment to long-term follow up

Infrastructure/care network-sharing models

Customize infrastructure/care network-sharing models where both benefit and risk is shared across involved parties

Unique Challenges for Patients of Real-World Data in Drug Development

- Limited data sources: patient registries, natural history studies, research, previous clinical trials
  - Heterogeneity of RD: genetic/genomic variations, symptoms, progression and outcomes.
  - Lack Treatment Protocols: lack consensual care pathways, use of experimental or off-label treatments, lack documentation of effectiveness
- Traditional clinical trial designs not suitable due to small numbers an limited data; need for alternative designs and (RW) data sources
  - Engaging patient communities to gathering data and patients' experiences, preferences, and quality of life concerns.
  - Data Security and Privacy: rarity (small numbers) create higher risk of privacy breaches, identification and discrimination
  - Integration of data from various sources, e.g. HCPs, registries, research studies, with different formats and standards, validity of data
  - Need for (early) collaboration among academic institutions, pharmaceutical companies, patient advocacy groups, regulatory agencies plus HTA and payers

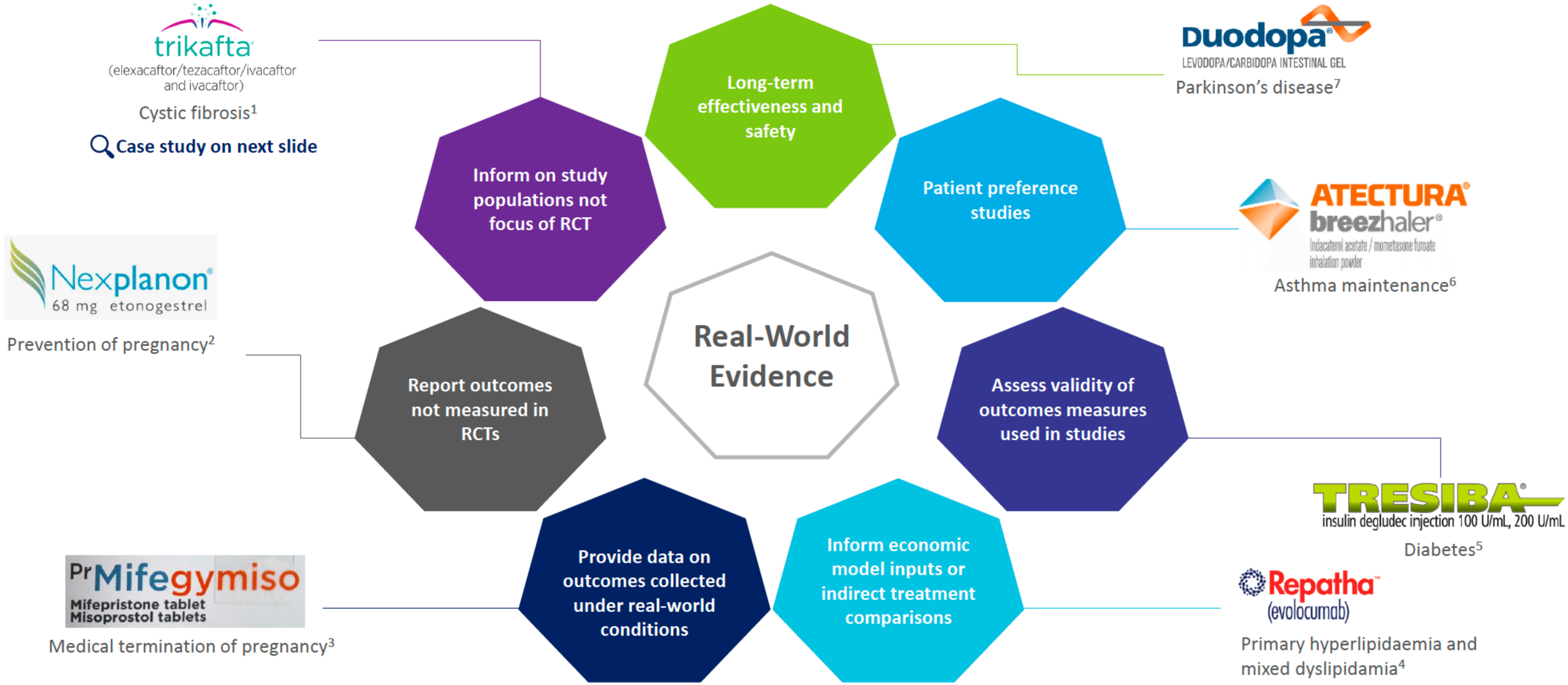
Benefits of real-world data collection and analysis throughout lifecycle

- Data on outcomes of importance to patients, including disease management and quality of life
- Monitoring in real life to know how well treatment is working, or not, across patients not included in clinical rials
- Long-term monitoring for safety and effectiveness, especially with limited historical data (on extended lifespan)
- Subgroups of patient responders (super to ineffective) and individual response guide personalized treatment decisions.
- Comparisons between different treatment options, helping patients and clinicians make more informed choices
- Contribution to knowledge pool (for others like me)
- Demonstration of value (or not)

Risks/negatives of real-world data collection

- Data quality/reliability: various sources, incomplete or inaccurate data, patient selection bias
- Lack controlled trial design: challenging to draw valid conclusions about treatment efficacy and safety
- Heterogeneity of patients: difficult to account for differences in respond based on RWD alone
- Risks of data privacy breaches and identification based on small #’s
- RWD may show ambivalent, inclusive, minimal or no benefit without good explanation
- RWD may show potential harm, unanticipated or rare negative outcomes without good explanation
- Data may value of benefit/risk does not support (high) price based on limited time horizon and some thresholds

Results: How RWE Has Been Used to Support CADTH Reimbursement Reviews



1. https://www.cadth.ca/elexacaftor-tezacaftor-ivacaftor-and-ivacaftor; 2. https://www.cadth.ca/etonogestrel-0; 3. https://www.cadth.ca/mifepristone-and-misoprostol-0; 4. https://www.cadth.ca/evolocumab-0; 5. https://www.cadth.ca/insulin-degludec; 6. https://www.cadth.ca/indacaterol-mometasone-furoate; 7. https://www.cadth.ca/levodopa-carbidopa-drug-plan-submission.

CADTH = Canadian Agency for Drugs and Technologies in Health; RCT = randomised controlled trial; RWE = real-world evidence

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