



Navigating Market Access With Magnolia

Leveraging Real World Data in Vaccine Safety: Signal Detection and Confirmation for Market Access Stakeholders

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a medical knowledge group company

Magnolia Market Access: Today's Moderator & Speakers



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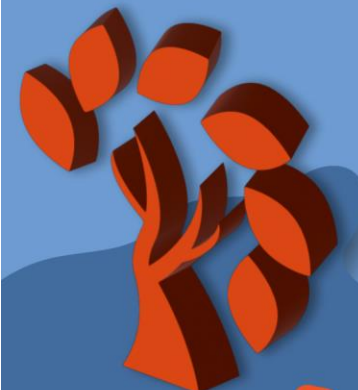
Methods to Assess Real-World Vaccine Data

5

Real-World Applications, Future Trends, & Discussion

Introduction

Vaccines in the Real World



The Critical Role of Ongoing Vaccine Safety Surveillance



Public Health

- Vaccines are cornerstone of public health
- Prevent disease, eliminate, and control outbreaks
- Ensuring vaccine safety is critical for public health and maintaining public trust

Healthcare Costs

- Preventing infections prevents direct medical costs
- Reduced use of long-term care, antibiotics
- Reduced outbreaks
- Increased productivity, reduced work and school absenteeism

Public Trust & Stability

- Trust increases vaccine uptake, especially in the context of rapid vaccine development
- Reduces spread of misinformation
- Supports ongoing innovation and development

Harnessing Real-World Data: Transforming Vaccine Safety Monitoring

Reviewing Real-World Data (RWD)



- Includes health-related data collected outside of traditional clinical trials—such as electronic health records (EHRs), insurance claims, registries, and patient-reported outcomes
- Provides insights into broader, more diverse populations over time, compared to clinical trials

RWD in Vaccine Safety



- Enables early detection of rare or long-term adverse events
- Vaccine performance and safety
- Assess effectiveness across subgroups
- Supports regulatory and public health decisions

Real-World Data Sources

Assessing Vaccine Safety

Unlocking Insights: The Essential Role of Real-World Data in Healthcare Decision-Making

Diverse Populations

- RWD allows for the analysis of vaccine safety in populations that may be excluded or underrepresented in clinical trials

Rare Adverse Events

- Clinical trials may not be adequately powered to detect rare adverse events

Long-Term Safety

- Patients can be observed for longer duration than a typical trial

Comparative Safety

- Compare safety profiles of different products to inform public health recommendations and medical decision-making

Comprehensive Surveillance Strategies for Vaccine Safety: Exploring Passive and Active Methods

Passive Surveillance

- Broad reach with emphasis on early detection and novel risks
- Relies on voluntary reporting
 - Health Care Providers
 - Manufacturers
 - General Public
- Vaccine Adverse Event Reporting System (CDC), EudraVigilance (EMA), VigiBase (WHO)



Active Surveillance

- Focused monitoring may target specific vaccines, populations or suspected adverse events (AEs)
- Makes use of existing data
 - Insurance Claims
 - Electronic Health Records
 - Registries
- Vaccine Safety Datalink (VSD) and Sentinel aggregate RWD for analysis

Vaccine Adverse Event Reporting System (VAERS): A Key Pillar in Monitoring Vaccine Safety and Confidence

Strengths & Limitations

- Established in 1990, jointly managed by FDA and CDC
- Strengths
 - Broad reach
 - Timely data
 - Novel adverse events
- Limitations
 - Underreporting and reporting bias
 - Unconfirmed outcomes
 - Lack of denominator data

Report an Adverse Event - Patient Information Instructions | en Español

Note: Fields marked with an * are essential and should be completed.

Item 1

Patient first name: Patient last name:

Street address:

City: State: County:

Zip code: Phone: Email:

Item 2 **Item 3**

* Date of birth mm/dd/yyyy or mm/yyyy * Sex: Male Female

Item 4

* Date of vaccination mm/dd/yyyy or mm/yyyy Time: AM PM

Item 5

* Date adverse event started mm/dd/yyyy or mm/yyyy Time: AM PM

Item 6 **Item 7**

* Age at vaccination years months Today's date:

Item 8

Pregnant at time of vaccination?
(If yes, describe the event, any pregnancy complications, and estimated due date if known in item 18)

Yes No Unknown

Successes & Controversies

- Bowel obstruction after rotavirus vaccine
- Autism reports
- COVID-19 misinformation
- A vaccine turned me into the **Incredible Hulk!?!?**



Vaccine Safety Datalink (VSD): Advancing Research and Enhancing Vaccine Safety Surveillance

- Established in 1990, collaboration between CDC and healthcare organizations across the US
- 11 sites provide EHR data on over 12 million patients
- Strengths
 - Data quality
 - Rapid Cycle Analysis
 - Algorithms to identify pregnancy and link mother/infant records
- Limitations
 - Generalizability / Selection bias
 - Signals require confirmation

Real World Impact

- Rapid Cycle Analysis of H1N1 vaccine
- Safety of influenza vaccine in special populations
- Febrile seizure after MMRV



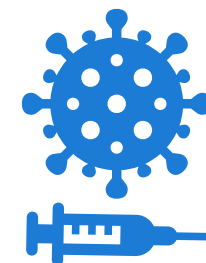
Sentinel Initiative: Enhancing Vaccine Safety with PRISM and BEST Systems

- Established by FDA in 2008
- 1.3 billion person-years of data
- >125MM patients currently accruing data
- Within Sentinel:
 - Post-Licensure Rapid Immunization Safety Monitoring: focus on vaccines
 - Biologics Effectiveness and SafeTy: broader focus on biologics

Strengths	Limitations
Large & diverse data	Complexity & cost
Advanced statistical methods	Data privacy & governance
Near real-time monitoring	

COVID Vaccine Safety

- Myocarditis and Pericarditis
- Thrombosis with Thrombocytopenia Syndrome (TTS)
- Anaphylaxis



From Signal to Action: Confirming Vaccine Safety with Regulatory and Industry Collaboration

- Signals found by surveillance systems need confirmation
- Regulators can require manufacturers to conduct post-market safety studies
 - Manufacturers collaborate with regulators on safety assessments and risk mitigation strategies
 - Studies may lead to labeling changes or recalls/safety alerts
- Full protocol-based epidemiology study
 - Cohort design, case-control, or self-control
 - RWD data sources such as claims, EHR, or registry
 - May involve chart review
 - Propensity-matched analysis or other methods to control for confounding

Comparative Data Needs: Navigating Signal Detection and Confirmatory Studies in Vaccine Safety

Signal Detection

- Emphasis on rapid access and broad coverage
- Large datasets needed to detect rare events
- Clinical details and confirmed outcomes are less important

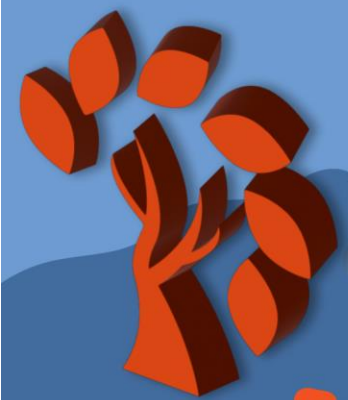


Signal Confirmation

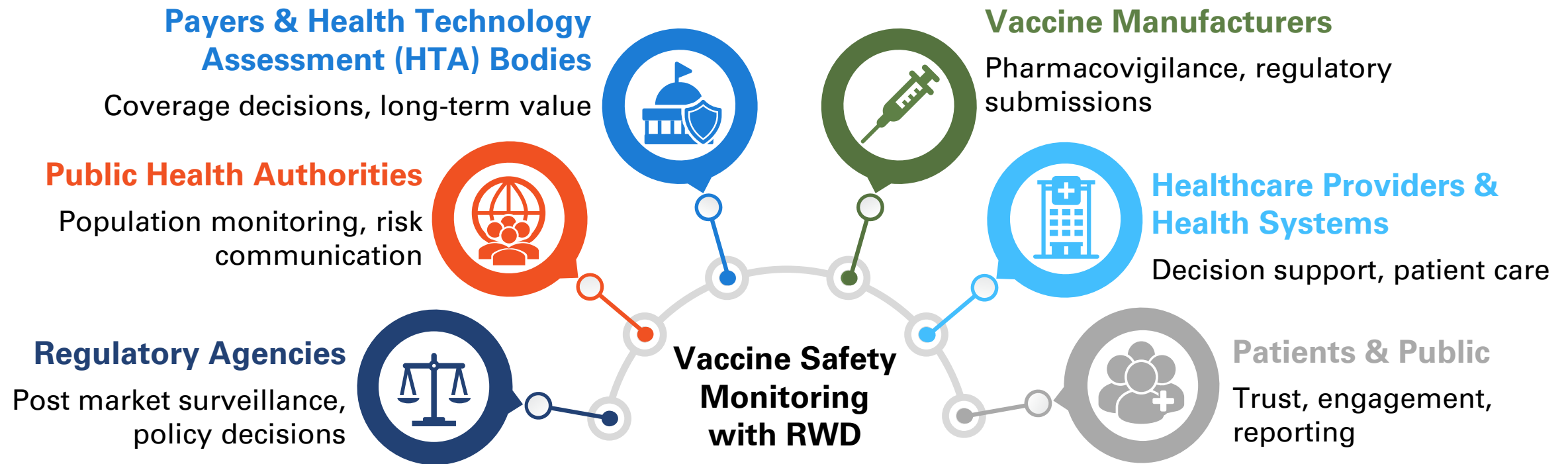
- Smaller datasets are feasible based on study design
- Detailed clinical data is needed
- May involve chart review to confirm outcomes



Stakeholder Perspectives

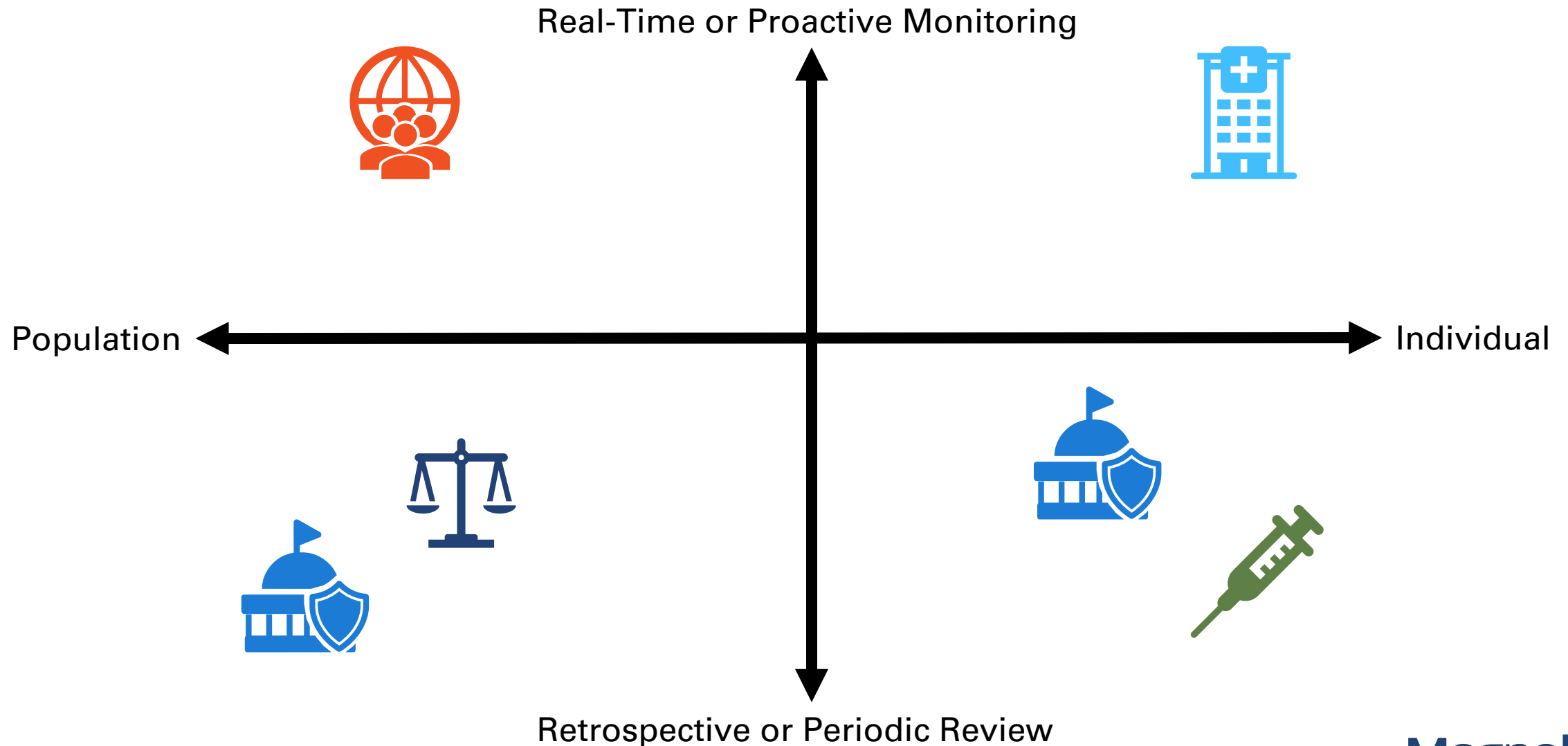


Integrating Diverse Perspectives: Enhancing Vaccine Real-World Data Through Stakeholder Collaboration

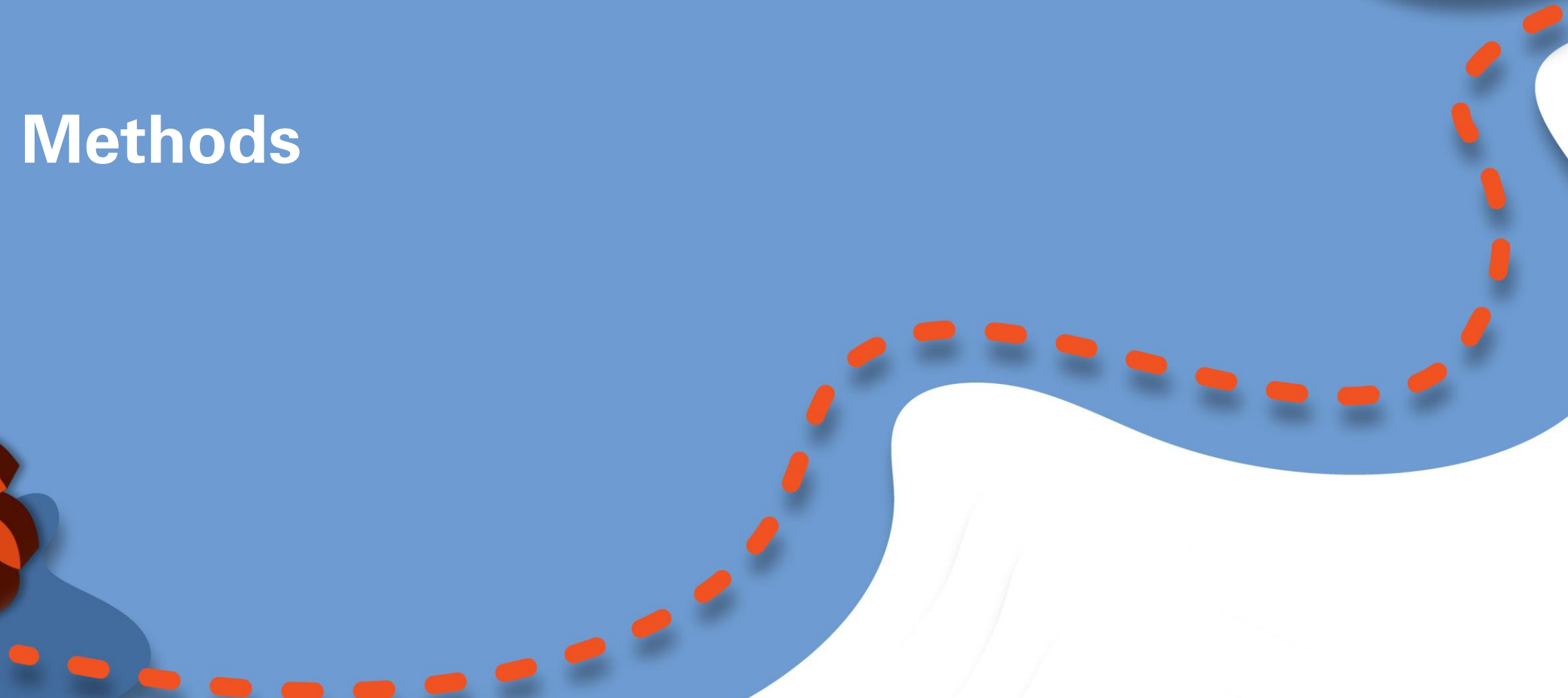
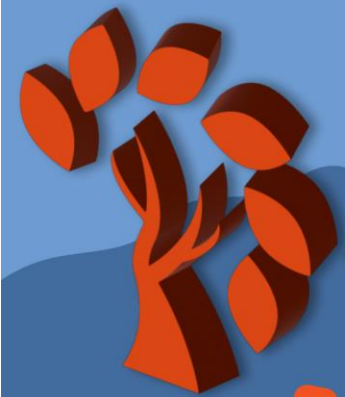


Collaboration, data sharing, and incentive alignment between and across stakeholders required for improvement of RWD surveillance.

Stakeholder Priorities in RWD for Vaccine Safety



Methods



Exploring Real-World Study Designs: Advancing Vaccine Safety and Effectiveness

Descriptive Studies

- Characterize patterns, trends, and frequencies
- Detect early warning signs
- Case series, cross-sectional, surveillance reports
- Signal detection in pharmacovigilance systems
- Hypothesis generation
- Rapid response and communication

Analytic Studies

- Establish associations between vaccines and outcomes
- Cohort and case-control studies
- Provide robust evidence
- Distinguish true signals
- Leverage longitudinal data for EHRs, medical claims, surveillance systems

Comparative Effectiveness

- Evaluate how different interventions work in real-world settings
- Propensity score matching
- Goes beyond clinical trials to assess safety in everyday use
- Monitors effectiveness and side effects across age groups, comorbidities, and geographies

Advanced Techniques for Identifying Vaccine Safety Signals: From AI to Clinical Expertise



- Identifying unusual patterns or potential safety concerns
- Signal refers to new or unknown AE that occurs more frequently than expected
- Key Methodologies:
 - Disproportionality Analysis
 - AI tools for automated signal detection from surveillance databases
 - Temporal pattern discovery
 - Expert clinical review



Confirmatory Study Methodologies in Vaccine Safety: Testing Hypotheses with Robust Epidemiological Approaches



Confirmatory studies test hypotheses generated during signal detection and establish or rule out causality using rigorous epidemiological methods

Use large population-based datasets, including comparators, control for confounding and biases via statistical methods

- Key Methodologies:
 - Retrospective cohort studies
 - Case-control studies
 - Interrupted time-series
 - Self-controlled case series (SCSS)



Continuous Safety Monitoring in RWD: Long-Term Approaches for **Confirmatory Vaccine Studies**



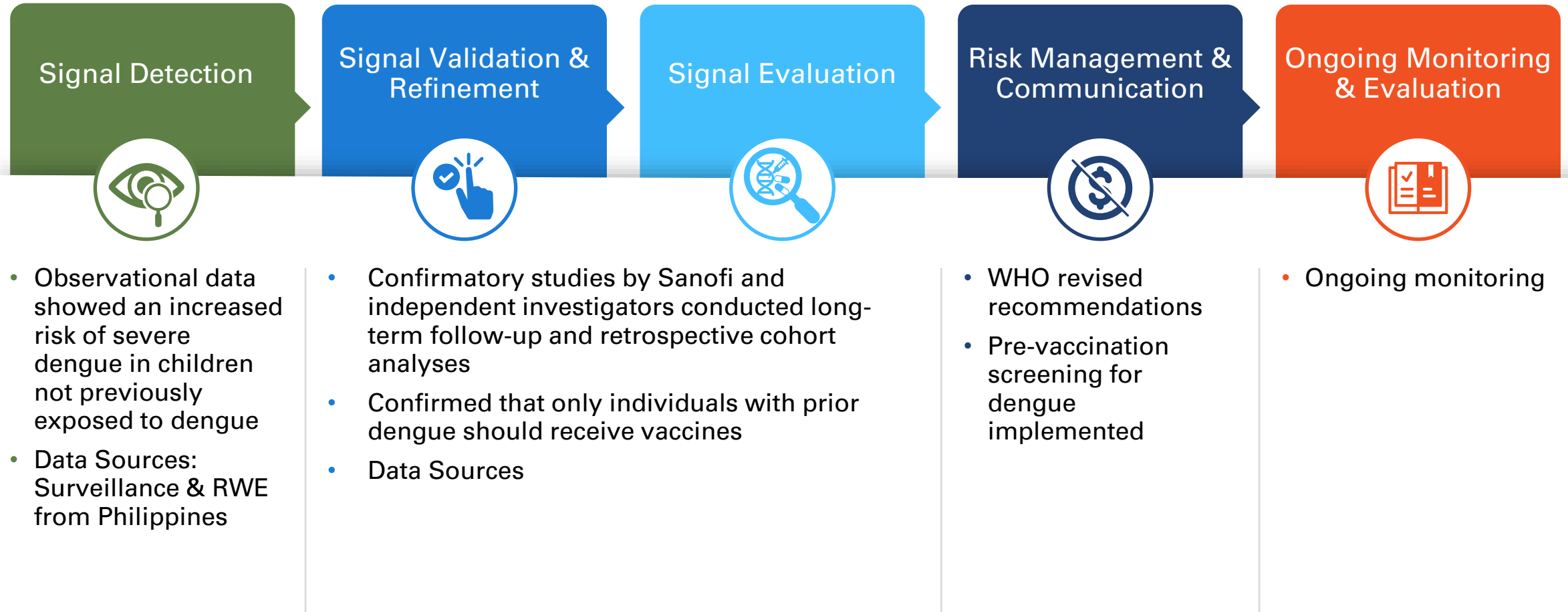
- Continuously monitor and track safety post-response.
- Focus on long-term effects, new at-risk populations
- Key Methodologies:
 - Enhanced surveillance
 - Registry follow-up
 - Post-marketing studies



Real World Applications

Case Studies, Future Trends, Innovation Opportunities, & Discussion

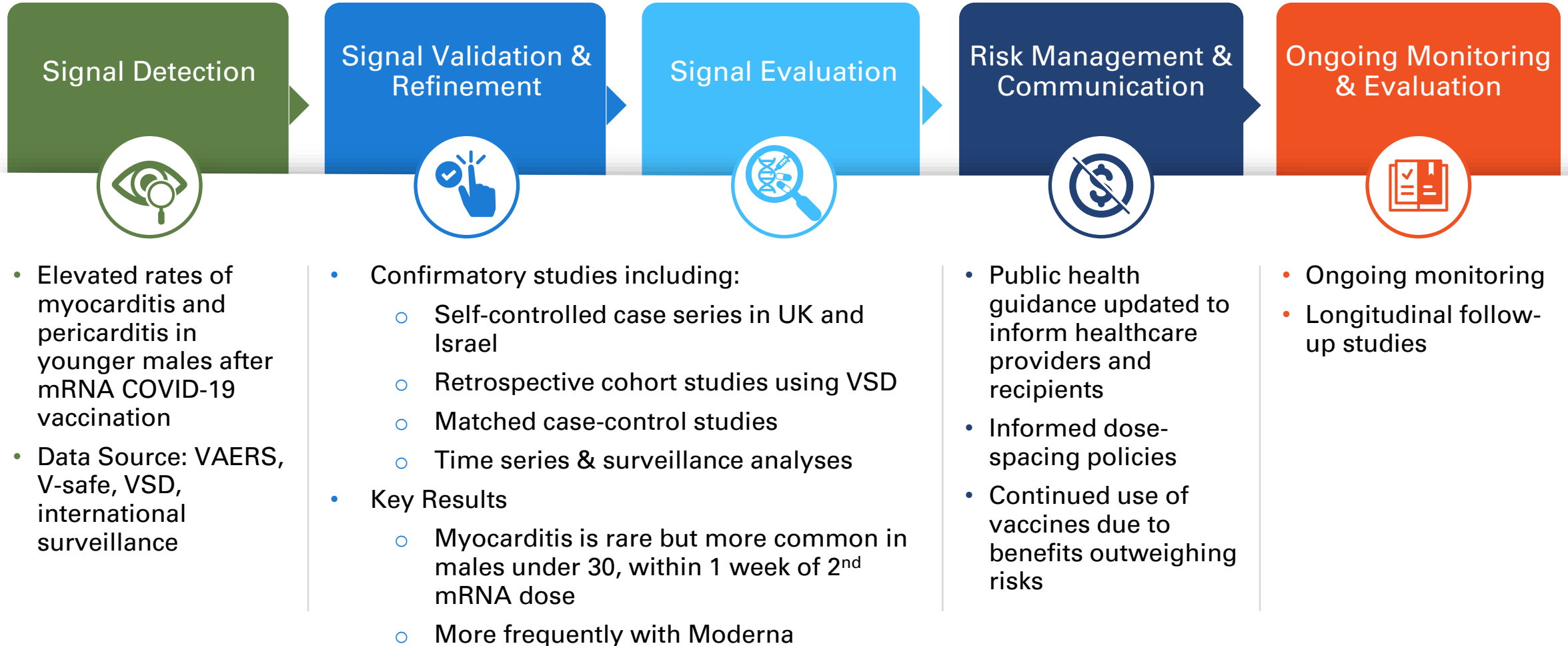
Dengvexia and Severe Dengue (2017)



WHO-ATC, World Health Organization Anatomical Classification System

1. [CO PDAB 2023 Eligible Drug Dashboard](#). 2. [Affordability Review Summary Report: Stelara](#). June 7, 2024.

COVID-19 Vaccines and Myocarditis



WHO-ATC, World Health Organization Anatomical Classification System

1. [CO PDAB 2023 Eligible Drug Dashboard](#). 2. [Affordability Review Summary Report: Stelara](#). June 7, 2024.

Future Trends & Innovation Opportunities

AI and Machine Learning for Signal Detection

01

Global Data Integration

02

Real-Time, Patient-Generated Data

03



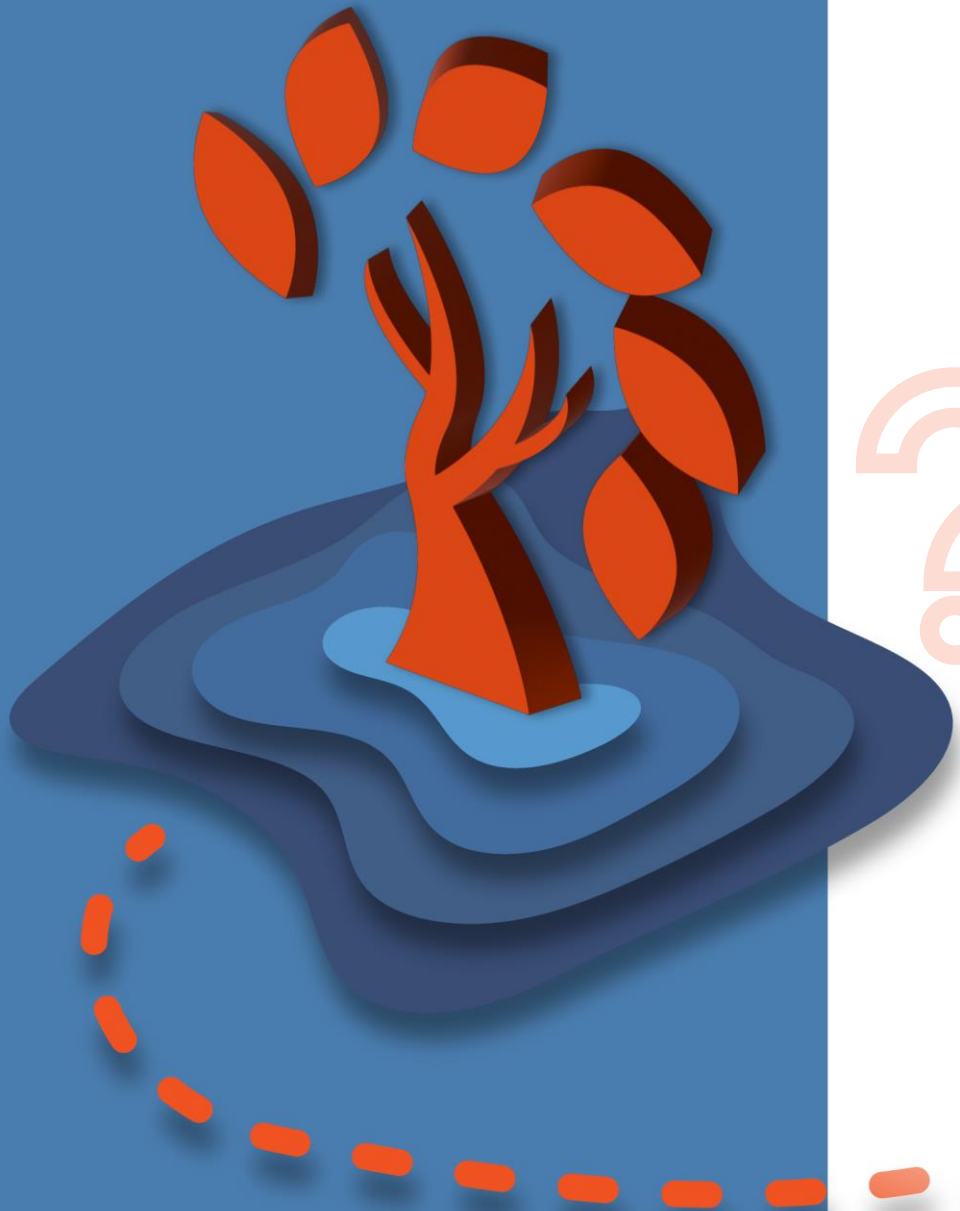
07 Integration of Equity & Subpopulation Analyses

06 Personalized Safety Monitoring

05 Broader Use of Pragmatic & Hybrid Trials

04 Enhanced Data Linkage & Interoperability

Discussion



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Navigating Market Access with Magnolia

How Can the Congressional Budget Office Improve Its Methodology Used to Score Healthcare Legislation?

Thursday, May 22, 2025
12:00 PM to 1:00 PM Eastern

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