
Optimizing
Pregnancy Registries
Public Workshop
MAY 7-8, 2026
Virtual & In-Person
FDA

U.S. FOOD & DRUG ADMINISTRATION

# Welcome

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# Session 3: Partnerships and Future Directions

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# Strategically Coordinated Registry Networks (CRNs):

## Levers for Optimizing Pregnancy Registry Infrastructure

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Office of Clinical Evidence and Analysis (OCEA)

Center for Devices and Radiological Health (CDRH)

# Distinct Evidence Needs in Pregnancy

- Care Delivery (clinical practice)
  - Focus: how pregnancy and delivery care are provided
  - Includes procedures, devices, and care pathways
  - Best addressed through professional society registries (e.g., ACOG)
- Medical Product Exposure in Pregnancy
  - Focus: safety and effectiveness of drugs, biologics, and devices
  - Includes treatment of conditions during pregnancy
  - Requires exposure-based cohorts

**These are distinct but overlapping needs**

# The **GOOD NEWS!**

We are not starting from scratch!

## There are many efforts to leverage

- ASPE/FDA Investments in infrastructure for Registries
- ONC/FDA collaboration on registries/EHRs certification

## The broad context also faciliates

- Other clinical societies registries
- CRN Learning Community
- International registries/consortia
- HL7 FHIR Efforts

ASPE- Assistant Secretary for Planning and Evaluation
ONC- Office of the National Coordinator for Health Technology

# Outline

- Context: Registries as RWD for regulatory decision making
- Evolution of legacy registries to CRNs and their role in building RWE infrastructure
- Lessons learned from other clinical areas
- Toward building the national pregnancy RWE  infrastructure

# Outline

01

**Context: Registries as RWD for regulatory decision making**

02

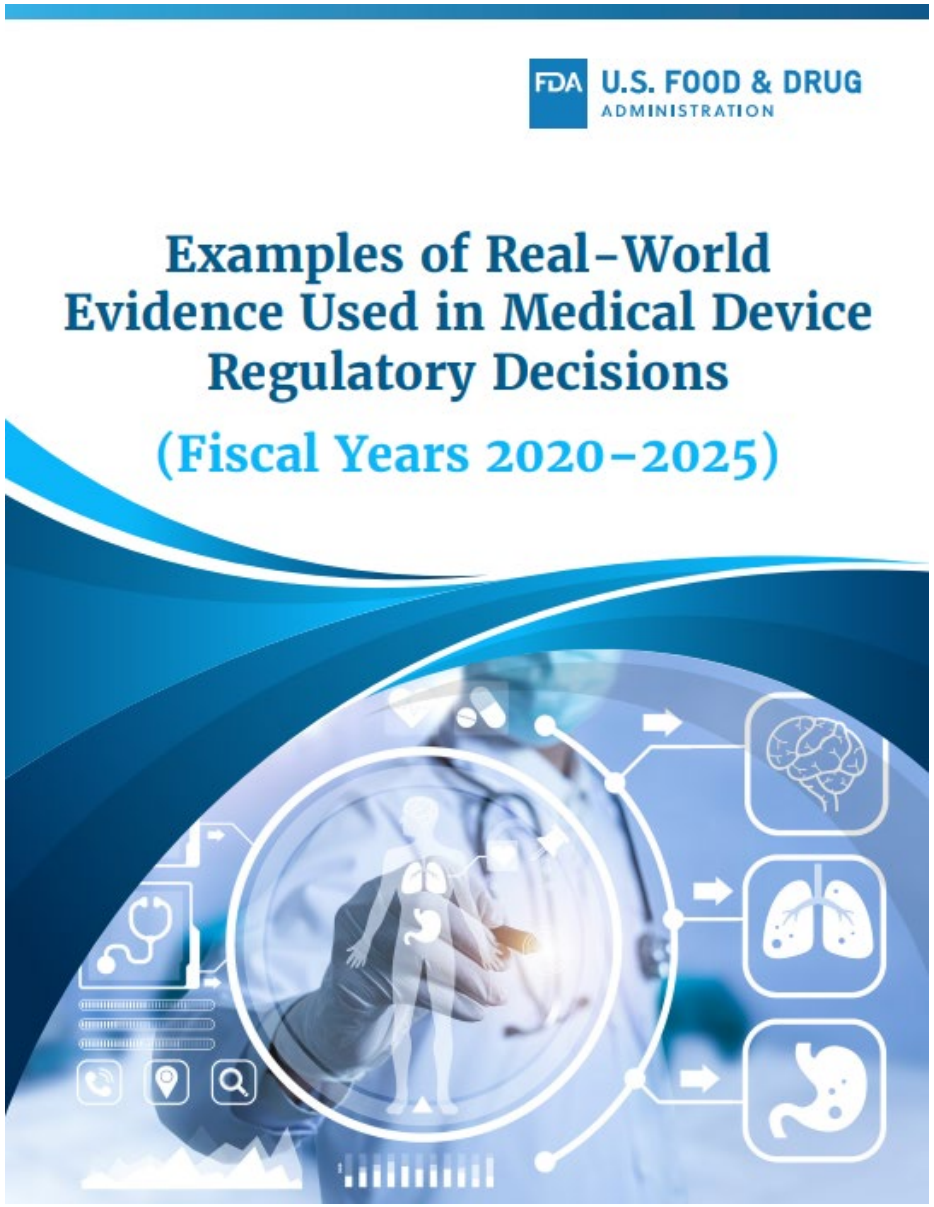
Evolution of legacy registries to CRNs and their role in building RWE infrastructure

03

Lessons learned from other clinical areas

04

Collaborative steps toward building the national pregnancy RWE infrastructure




# Overview of FDA/CDRH RWE Examples

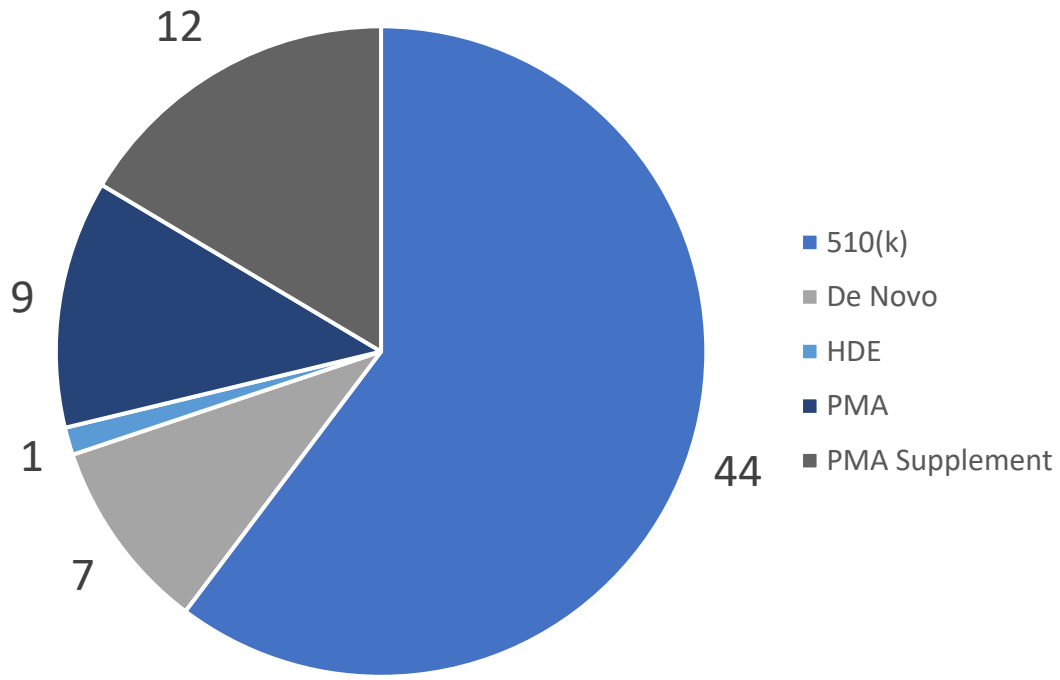
- 73 new examples
- Fiscal years 2020 – 2025
- Publicly available data
- New sections:
  - Device-generated data
  - Public health surveillance

https://www.fda.gov/media/191805/download

https://www.fda.gov/media/146258/download

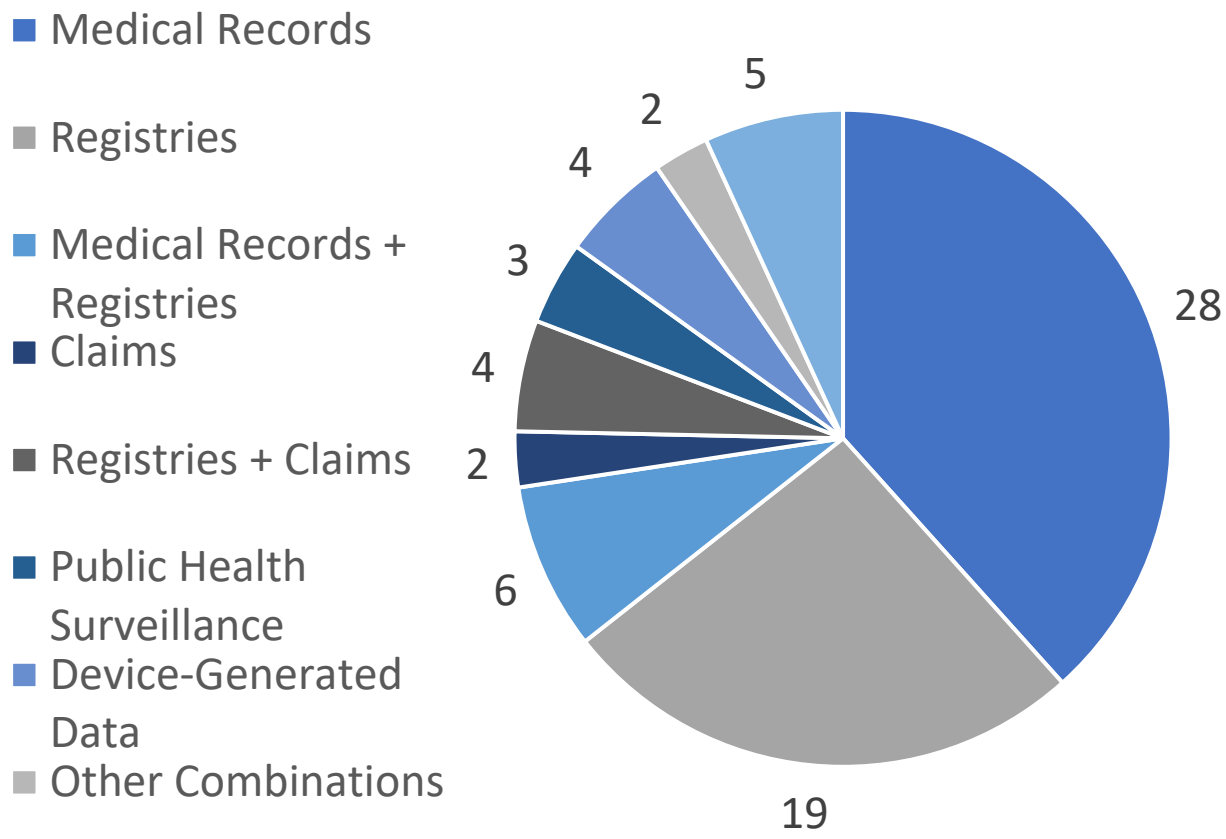
# RWE Examples by the Submission Type and Data Source

## Submission Type




PMA Premarket Approval - approval process for Class III devices
HDE Humanitarian Device Exemption
510 (k) Submission to demonstrate substantial equivalence with legally marketed predicate device
De Novo Submission – provides marketing pathway to classify novel devices for which there are no legally marked predicates and general or special controls are adequate

## Data Source



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# Registries/CRNs: Intersections with FDA, national and international ecosystems

THE VISION FOR NATIONAL SYSTEM LAUNCHED

MDEpiNet Launch

International Consortium of Orthopedic Registries (ICOR)

International Consortium of Vascular Registries (ICVR)

**Reports:**
- Planning Board
- Registry Task Force
- IMDRF

MDIC MEDICAL DEVICE INNOVATION CONSORTIUM
About Projects News & Events MDICx Series 2016
MDIC NEST Coordinating Center

NEST Data Collaborators Network

2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020

MDEpiNet



CRN Community of Practice

CRN Leearning Communities

IMDRF

International Medical Device Regulators Forum

Title: Principles of International System of Registries Linked to Other Data Sources and Tools

Authoring Group: IMDRF Patient Registries Working Group

Date: 30 September 2016

IMDRF IMDRF

Title: Methodological Principles in the Use of International Medical Device Registry Data

Authoring Group: IMDRF Patient Registries Working Group

Date: 16 March 2017

Tools for assessing the Usability of Registries for Regulatory Decision Making , March 2018

MDEpiNet – Medical Device Epidemiology Network
NEST – National Evaluation System for Health Technology
IMDRF – International Medical device Regulators Forum

# National Experts Agreed : Birth of the CRN Concept


Strategically Coordinated Registry Networks (CRN) Principles:

- **Link complementary sustainable registries/e-repositories** (Professional society registries, EHRs, Claims data, PCORI- CDRNs)
- **TPLC approach as a true continuum leveraging "real world" evidence**
- **"Dual purpose" existing national, regional or other large scale efforts**

# CRNs were defined by National Medical Device Registry Task Force (NMDRTF) as:

"strategically partnered electronic health information systems that support

1) the implementation of structured device identifiers, core minimum data elements and definitions, and
2) 2) the ability to share complementary data across information systems."

# Partnership between the FDA/CDRH and Office of the Assistant Secretary for Planning and Evaluation (ASPE)

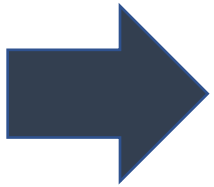
- Office of the Assistant Secretary for Planning and Evaluation (ASPE). Developing a Strategically Coordinated Registry Network (CRN) for Women's Health Technologies. https://aspe.hhs.gov/developing-strategically-coordinated-registry-network-crn-womens-health-technology.
- Office of the Assistant Secretary for Planning and Evaluation (ASPE). Bridging the PCOR Infrastructure and Technology Innovation through Coordinated Registry Networks (CRN) Community of Practice. https://aspe.hhs.gov/bridging-pcor-infrastructure-and-technology-innovation-through-coordinated-registry-networks-crn-community-practice


https://www.mdepinet.net/coordinated-registry-networks

# Use Case for Women's Health Technology CRN

**Single Purpose Registries**

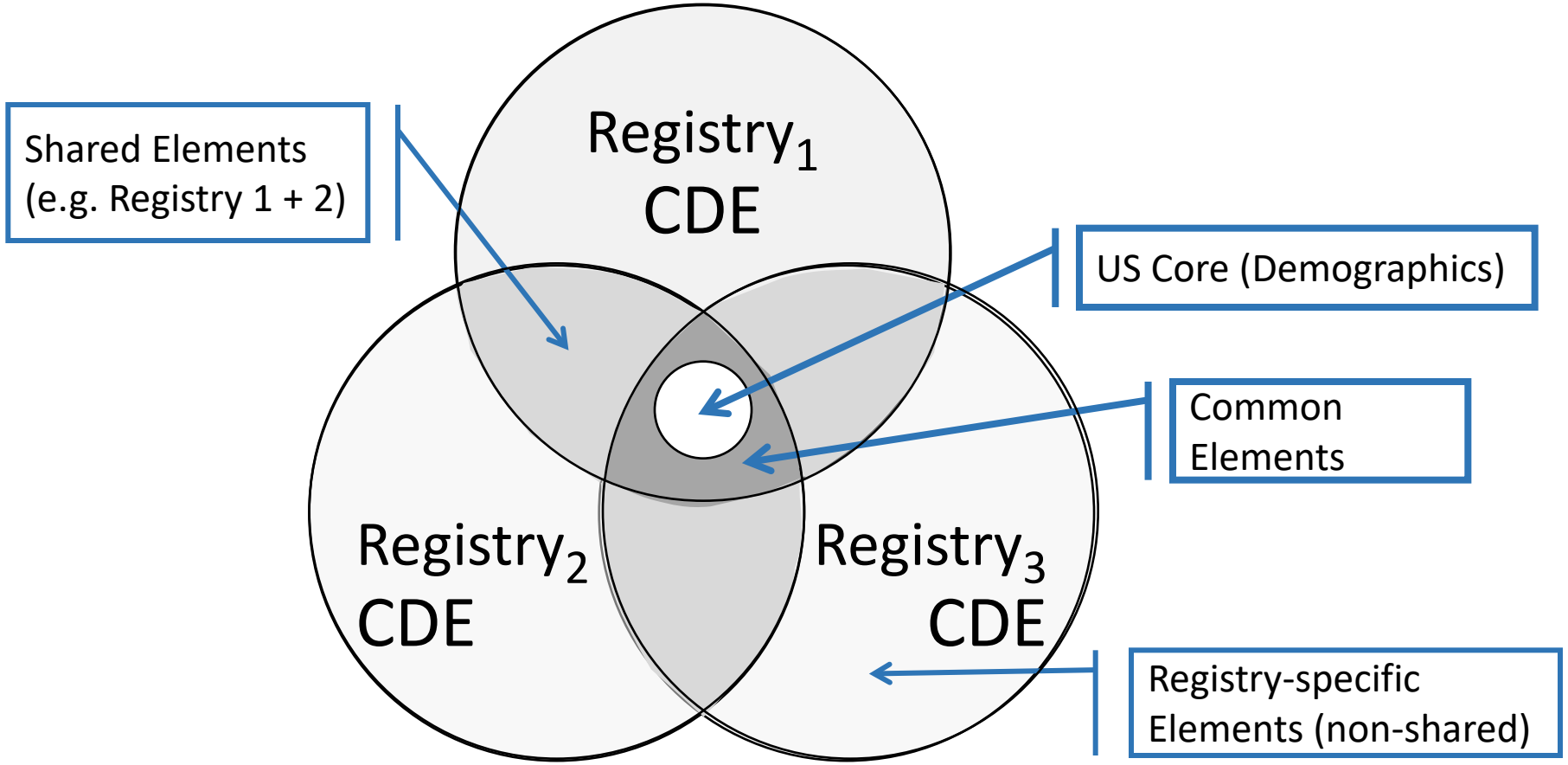
- Singular focus
- Time/Cost-intensive
- Challenging to address questions involving multiple therapies
- Stand-alone design: interoperability issues due to registry-specific data collection / normalization



**Coordinated Registry Network for Women's Health Technologies**

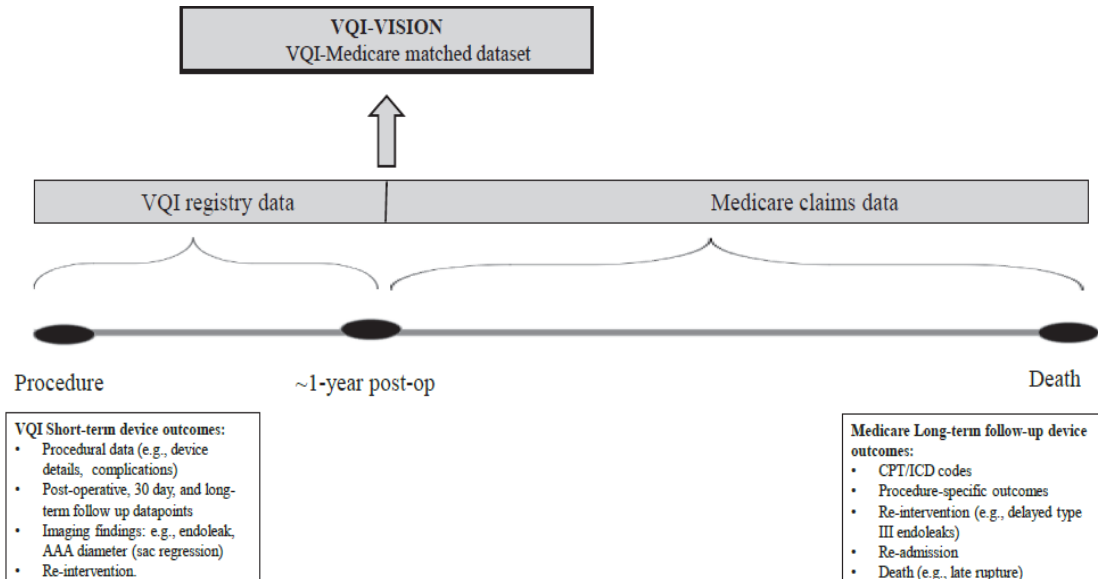
- Support assessment of real-world combinations of care for
  - Uterine fibroids
  - Pelvic Floor disorders (pelvic organ prolapse and stress urinary incontinence)
  - Sterilization/LARC (long acting reversible contraceptives)
- Harmonized, interoperable platform to support standardized data capture
- Address priority research questions from stakeholders
- Improve longitudinal evidence generation and reduce cost

# CRN CDE Collection – Target Endpoint



# VQI-VISION: Vascular Implants Surveillance & Interventional Outcome Network

- Society of Vascular Surgeons (SVS) Vascular Quality Initiative (VQI) consists of 14 registries containing demographic, clinical, procedural and outcomes data ( up to 1 year) from more than a million vascular procedures performed across the United States, Canada and Singapore
- VISION CRN adds long-term data analytics capabilities via linkage to claims data.

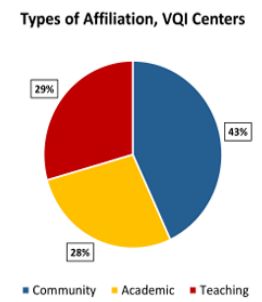


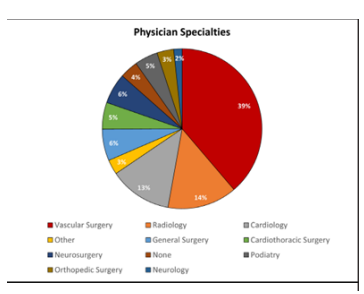

928 clinical sites
7000+ physicians
> 200 types of devices

| VISION's Medicare-Derived Late Outcomes |
|---|
| Death – verified by Social Security Death Index. 100% complete |
| Reintervention |
| Readmission |
| Procedure-Specific Adverse Event<br>- Stroke (validated 2024)<br>- Amputation (validated 2022)<br>- Rupture |
| Imaging |
| Cost |

| Total Procedures Captured as of 5/1/2025 | 1,366,581 |
|---|---|
| Peripheral Vascular Intervention | 477,911 |
| Carotid Endarterectomy | 232,646 |
| Carotid Artery Stent | 152,281 |
| Endovascular AAA Repair | 96,662 |
| Infra-Inguinal Bypass | 95,992 |
| Hemodialysis Access | 88,104 |
| Varicose Vein | 72,744 |
| Thoracic and Complex EVAR | 39,556 |
| Lower Extremity Amputations | 37,004 |
| Supra-Inguinal Bypass | 29,855 |
| Open Aorta | 20,494 |
| IVC Filter | 20,328 |
| Vascular Medicine Consult | 2,667 |
| Venous Stent | 337 |

Linkage Breadth:
88 % of all EVAR patients
93 % of all AAA patients




https://www.vqi.org/wp-content/uploads/2025-Detailed-Annual-Report-FINAL.pdf

# The Vascular Implant Surveillance and Interventional Outcomes Network (VISION)

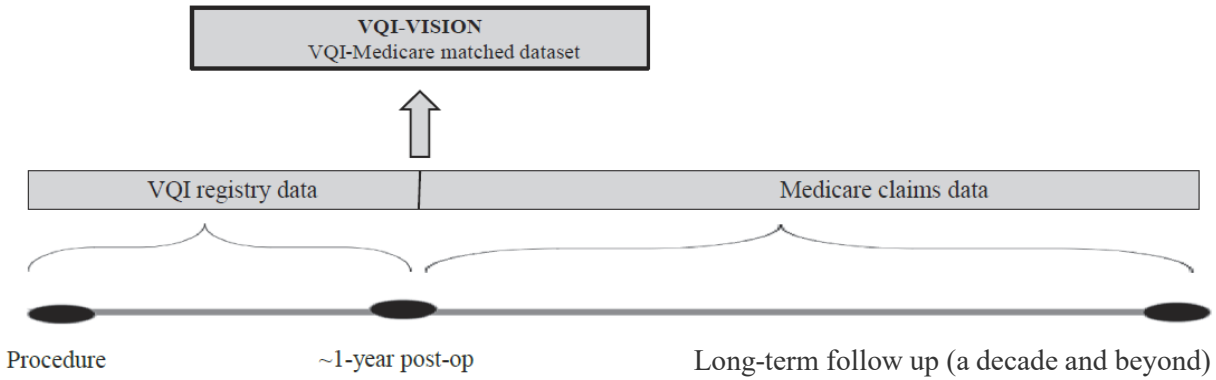
Clinical and technical **VQI registry data** about patients, procedures, and devices

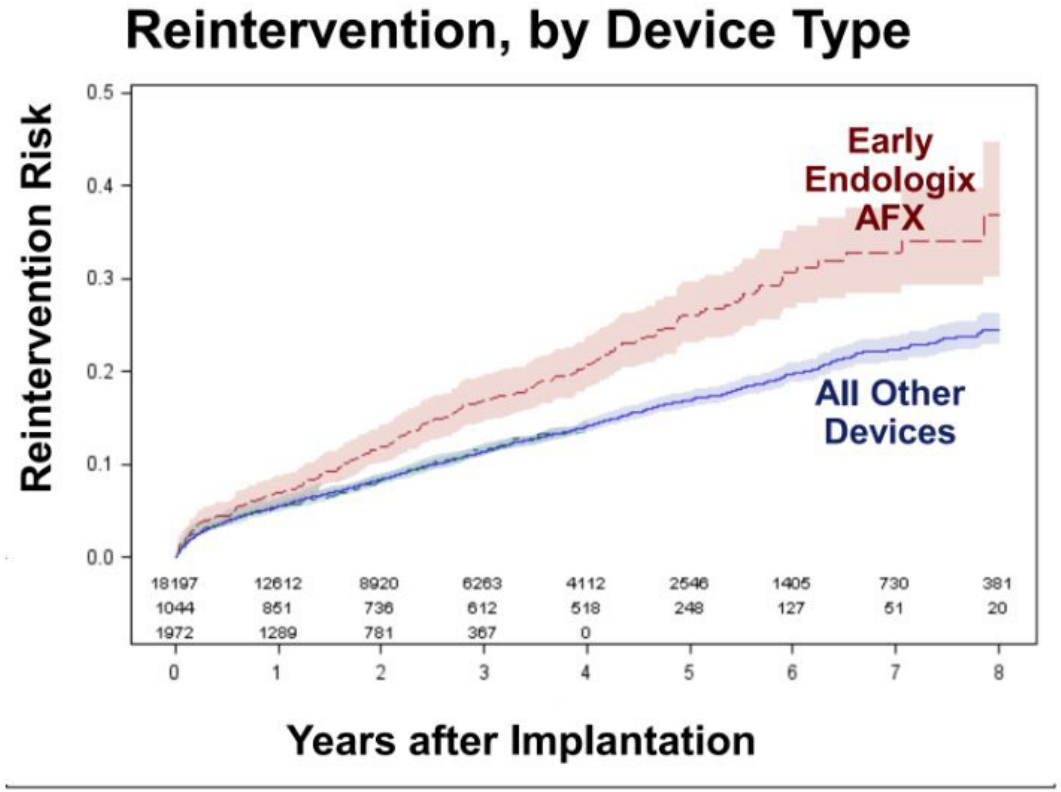
+

Long-term, generalizable follow-up linked to **Medicare claims data**

=

National repository of linked clinical-claims analytical **VQI-VISION datasets**



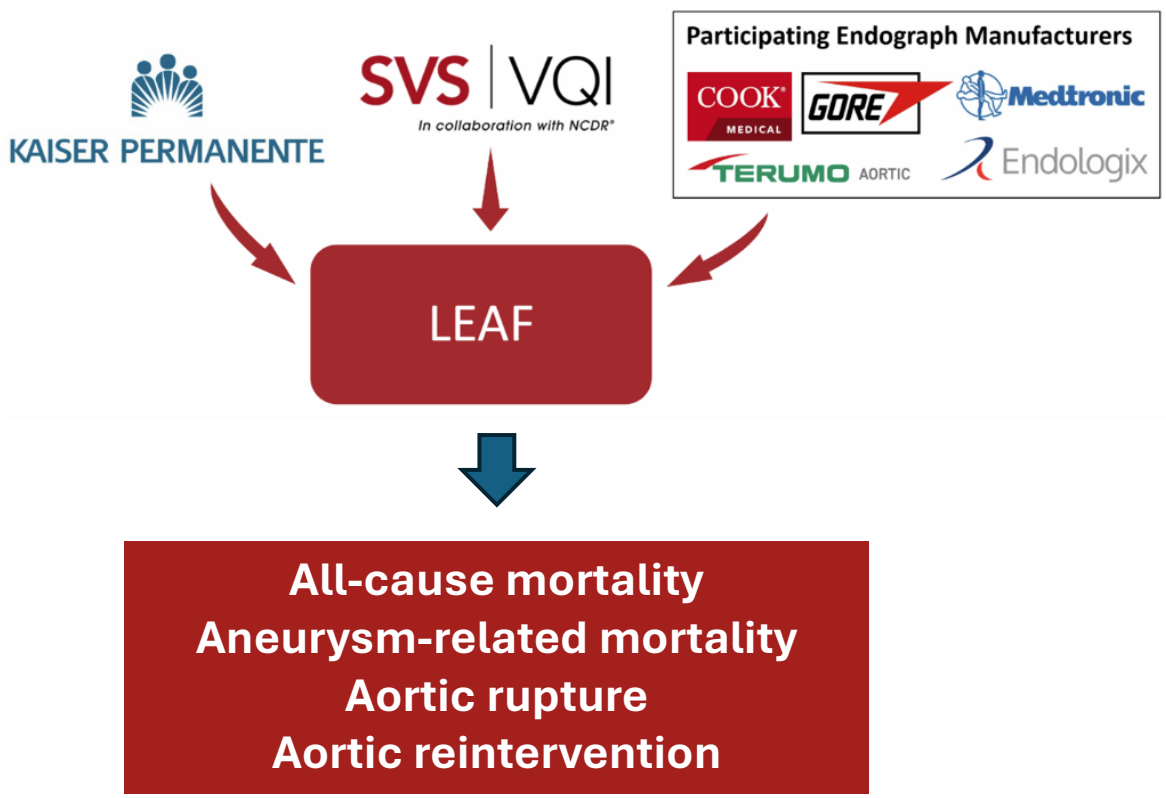



# The Long-Term EVAR Assessment and Follow-Up (LEAF) Surveillance System

'A real-world surveillance system should be created to collect data through 10 years post-EVAR. The surveillance system should assess the following clinical endpoints: all-cause mortality, aneurysm-related mortality, aortic rupture, and aortic reintervention.'

– *FDA Advisory Panel Recommendations on Lifelong Surveillance and Long-Term Postmarket Data Collection for Patients with AAA Endovascular Aortic Repair – Letter to Health Care*

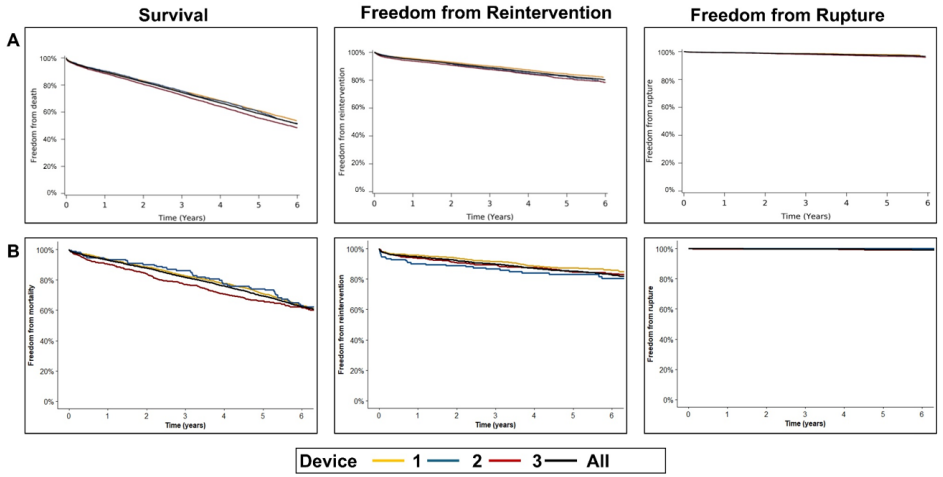
Figure 1. The LEAF Surveillance System combines data from VQI VISION's registry-claims linked datasets, Kaiser Permanente, and participating Endograph manufacturers




SVS | VQI VASCULAR QUALITY INITIATIVE · VISION SVS | VQI · KAISER PERMANENTE · fivos · FDA U.S. FOOD & DRUG ADMINISTRATION

# What lies ahead?

- Use of **improved registry-claims linkage algorithm** using updated diagnosis and procedure codes.
- **2026 LEAF practice management paper** provides a framework for expanding this methodology:
  - Inform development of other long-term device monitoring protocols
  - Serve as benchmark for future surveillance programs in other areas

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6-Year Lifetable Estimates

| | All | Device 1 | Device 2 | Device 3 |
|---|---|---|---|---|
| Survival | 53.2% | 55.4% | 52.3% | 50.0% |
| Freedom from Reintervention | 80.7% | 82.9% | 79.7% | 79.0% |
| Freedom from Aneurysm Rupture | 97.1% | 97.8% | 96.7% | 96.2% |
| Freedom from Imaging Surveillance Failure | 34.0% | 33.5% | 34.1% | 34.6% |

## VQI-VISION is a *System in Evolution*

*time*

| Year | Funding | Key Step | Key Publication |
|---|---|---|---|
| 2012 | ARHQ R21 (Goodney) | Probabilistic Linkages, 2-year outcomes | Wallaert et al, JVS 2016 |
| 2014 | NIH U01 (Skinner) | Multi-procedure outcomes | Bekelis et al, BMJ 2016 |
| 2015 | NIH U01 (Skinner)<br>FDA U01 (Sedrakyan) | Direct Linkages | Hoel et al, JVS 2017 |
| 2017 | NIH U01 (Skinner)<br>FDA U01 (Sedrakyan)<br>PCORI (O'Malley) | Validation with clinical data (single site), 5-year outcomes | Columbo et al, JAMA Open 2018, JVS 2018 |
| 2018 | FDA U01 (Sedrakyan)<br>PCORI (O'Malley)<br>AHA SFRN (Goodney)<br>P01 (Skinner) | Manufacturer-specific outcomes, cost data, under-65 populations, long-term mortality assessments | Columbo et al, JAMA Open 2018<br>Columbo et al, Ann Surg 2019<br>Wanken et al, Circulation 2019<br>Ramkumar et al, 2019 NEJM<br>Mao JVS 2022<br>Tsougranis JVS 2021 |
| 2019<br>2021 | NESTcc Supplement<br>NHLBI R01 Application<br>FDA, SVS PSO fundings | Long-term reintervention studies,<br>Disparities in vascular care<br>Validation analyses | |
| 2022 | FDA Panel on RWE | Transition to industry reporting<br>FDA commissioned PAS | FDA PAS |
| 2023 | LEAF Endologix | | SVS PSO Foundation Award |
| 2024 | LEAF Proposal | Transition to industry reporting<br>FDA commissioned PAS | FDA Commissioned PAS |

SVS | VQI VASCULAR QUALITY INITIATIVE
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KAISER PERMANENTE
fivos
FDA U.S. FOOD & DRUG ADMINISTRATION
SVS Society for Vascular Surgery
m2st

# Maturity Model for CRNs: 7 Key Domains, 5 Levels

***Product Identification***:

Precise identification of medical devices and their attributes

***Data collection efficiency***:

Structured data capture, mobile apps and automation with interoperability solutions

***Data Quality***:

Coverage, completeness of enrollment & records at both baseline and follow-up, and periodic audits.

***Total Product Life Cycle***:

Infrastructure for conducting research and surveillance at different stages of device evaluation. Important role for data linkages

***Governance and Sustainability***:

Engage major stakeholders: societies, payers, various states. Obtain major & diverse funding

***Healthcare Quality Improvement***:

Device technologies require continuous evaluation: Feedback, benchmarking and outlier assessments

***Engaging patients and incorporation of patient generated data:***

Engage, evaluate preferences and measure general and disease specific PROs

**Level 1. Early Learner**
**Level 2. Making progress**
**Level 3. Defined path to success**
**Level 4. Well managed**
**Level 5. Optimized**

For example: Level 5 - Optimized Data Collection Efficiency

Technologies are in place (e.g., structured data extraction from EHR; mobile apps for all core minimum data elements, and there is a full adoption and integration of data and terminology standards (assumes complete interoperability)

Advancing the Real-World Evidence for Medical Devices through Coordinated Registry Networks, BMJ SIT

# US CRN Learning Community

| CCR | CRN Name | Clinical Area (current phase) |
|---|---|---|
| 1. | Women's Health Technology Coordinated Registry Network (WHT-CRN) | Women's Health Women's Health (uterine fibroids, pelvic organ prolapses, stress urinary incontinence, sterilization) |
| 2. | Vascular Implants Surveillance and Outcomes Network (VISION-CRN) | Vascular |
| 3. | Cardiac Devices Coordinated Registry Network (CD-CRN) | Cardiac |
| 4. | Orthopedic Devices Coordinated Registry Network (Ortho-CRN) | Orthopedic |
| 5. | Devices Intended for Acute Ischemic Stroke Intervention (DAISI-CRN) | Acute ischemic stroke |
| 6. | Venous Access National Guideline & Registry Development Coordinated Registry Network (VANGUARD-CRN) | Venous access |
| 7. | Robotic Surgery Coordinated Registry Network (Robotic-CRN) | Robotic surgery |
| 8. | Study of Prostate Ablation Evidence Development (SPARED-CRN) | Prostate ablation |
| 9. | Temporo-mandibular Joint Coordinated Registry Network (TMJ-CRN) | Temporomandibular joint |
| 10. | National Breast Implants Registry (NBIR) | Breast implants |
| 11. | Obesity CRN | Obesity devices |
| 12. | End Stage Kidney Disease Coordinated Registry Network (ESKD-CRN) | End stage Kidney disease |
| 13. | Abdominal Core | Abdominal Core |

- **Crosspollination areas**: clinical, data science, epidemiology/statistics, digital tools, blockchain, imaging, international
- **16 tools shared and applied** : (a) harmonization efforts in CRN architecture and data exchange ( logic model for clinical work flow), (2) methods ( validation, data linkages, outcomes studies, ROI, ML/AI ), (3) mobile apps ( patient and provider-based) and others

# Federal agencies work collaboratively to facilitate the flow of data between the registries and EHRs

- The HHS/Office of the National Coordinator (ONC) has the statutory authority to certify health IT (EHRs) and develop certification criteria that can be referenced by other HHS programs in executing their authorities ( including FDA).
- The 21st Century Cures Act includes additional requirements for EHRs to be capable of transferring data electronically to and from the registries.
  - Specifically, Section 4005 of the 21st Century Cures Act ensures that these certified EHRs can effectively transmit and receive data to and from registries, emphasizing their role in improving patient care and safety.
- **Goal : FDA and ONC collaborate to advance the use of certified health IT and aligning data standards across the ecosystem, while also improving the quality, usability, and fidelity or real-world data derived from registries.**

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# CRNs - Key Advantages

## Embedded in routine practice (better, faster , cheaper)

## Strategically coordinated/harmonized within the ecosystem

- Clinical core data sets (including PRO where possible)
- Informatics solutions (including UDI, SDC)
- Sustainability (value propositions, ROI, maturity models)

## Network

- Term was ” Coined” for registries - but applies beyond

## Include national and international/global opportunities

# CRNs: Pragmatic Efficiencies

## Existing systems participating in CRNs:

- Minimize re-engineering (cost, time to implement)
- Leverage established clinical work flow
- Established governance & sustainability

## Strategic data sharing across participating CRN systems:

- Flexibility in design:  accommodate emerging e-systems
- Customizable across medical product, stakeholder and other diversity
- Builds architectural consistency (use/re-use of structured data sets & data sharing solutions across device areas)

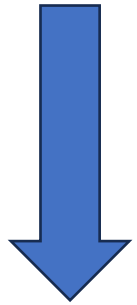
# CRNs - Key Limitations

Organized around specific clinical domains, which constrains their ability to represent the full complexity of patients whose care spans multiple specialties.

Less well-suited, in their current form, to support “whole patient” models of RWE that seek to integrate diverse clinical, physiological, and contextual variables across the continuum of care.

Variability in maturity across CRNs, incomplete coverage of clinical domains (particularly primary care and community health), and the need for sustained investment in governance and interoperability infrastructure may limit scalability in the near term.

# Outline



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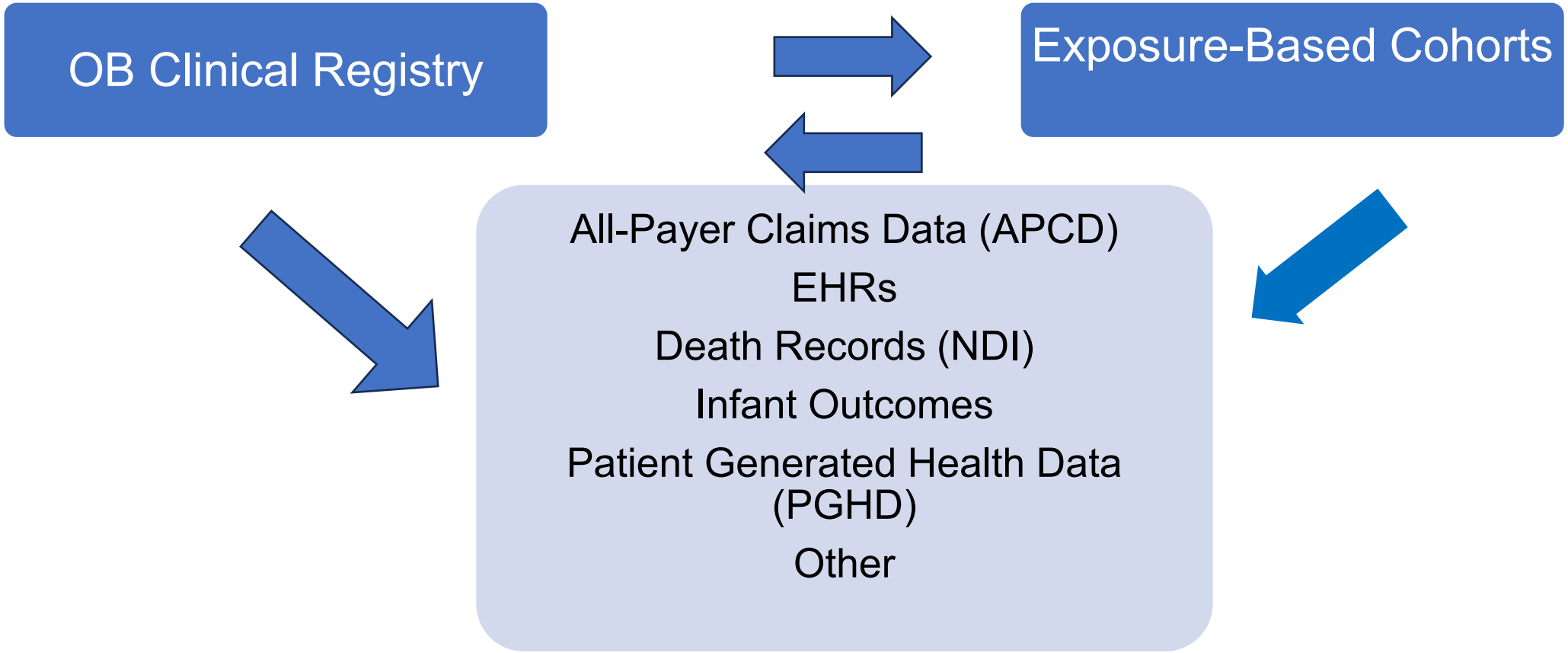
# One Integrated RWE Ecosystem




- **Both models require well-characterized cohorts and longitudinal follow-up**
- **Linkage enables complete outcome assessment**
- **Integration creates richer, more inclusive data**

# Complementary Strengths

OB Clinical Registry

- Deep clinical context
- Clinician-defined variables
- Strong for care delivery and device evaluation

Exposure Cohorts

- Product-specific focus
- Direct regulatory relevance
- Captures non-OB conditions

**Each model addresses gaps the other cannot**

# Why CRN ?

- **Granular, clinically relevant data**
  - Clinician engagement in variable specification and use, enabling rapid adaptation to changes in care and linkage to complementary datasets.
- **Sustainability**
  - Ability to generate evidence more efficiently than traditional studies.
  - The “collect once, use many times” principle distributes costs across stakeholders and supports reinvestment in infrastructure
- **Collaborative organizational structure**
  - Data remain locally controlled but aligned through shared standards and improvement goals, with expert-driven oversight ensuring continued clinical relevance.
  - Governance across networks celebrate adoption of innovations.

# Strategic Next Steps

- Bring together multi-stakeholder public private partnership for pregnancy
- Develop shared vision and framework for pregnancy RWE infrastructure

**Building pregnancy RWE infrastructure supports many needs!**

# Thank y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# After hearing the meeting yesterday, I had to change my presentation

# Coordinated Registry Networks (CRNs)

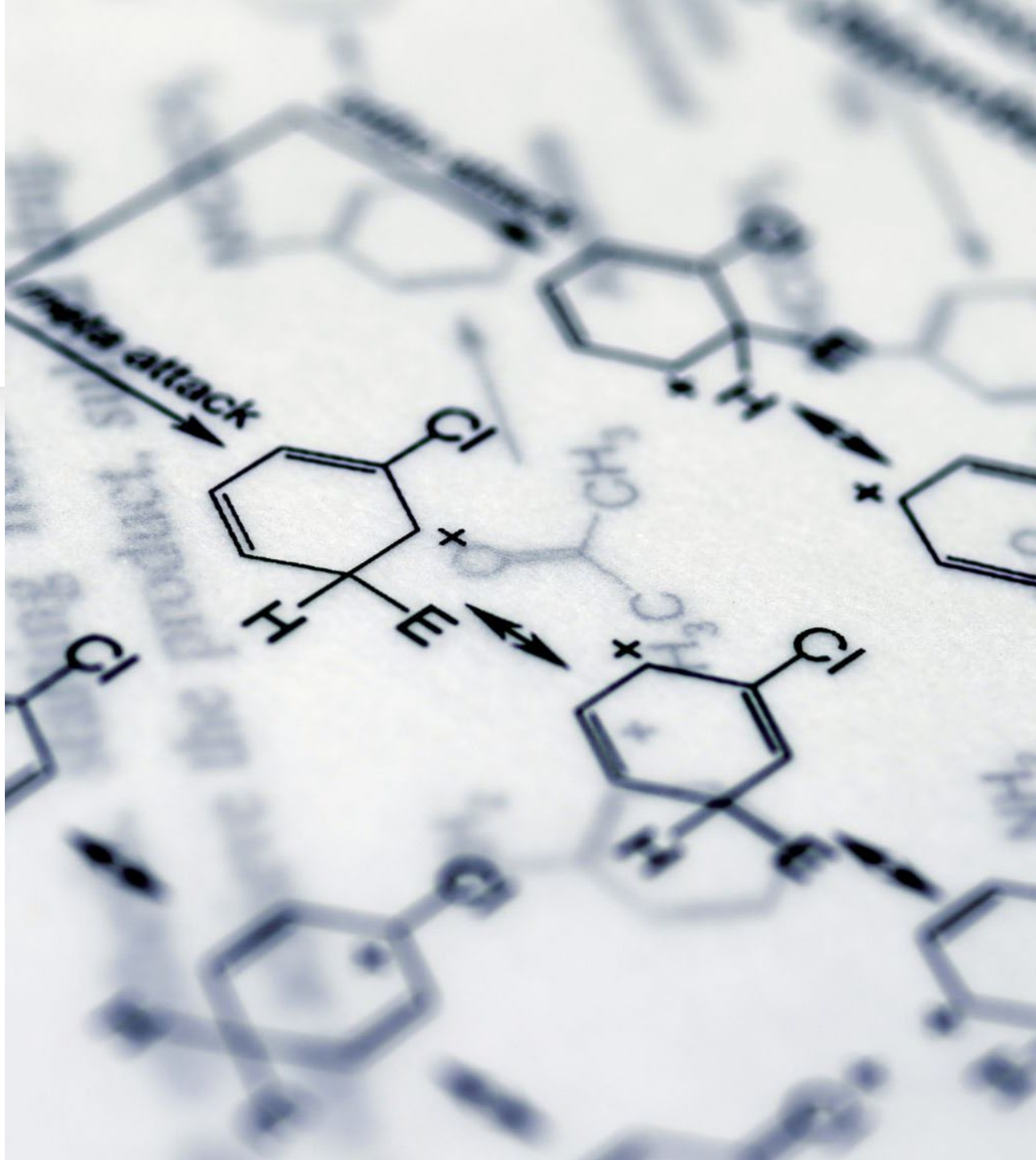
- Clinically curated registries led by professional societies (primary care included)
- Prospective definition of data elements and standards
- Clinician governance maintains clinical meaning across large networks
- Data extracted and curate by clinicians who create and understand the data
- Linkage to claims, mortality, and other datasets.

# CRN are a unique type of organization

- Complex problems need unique solution
- Social Science has recognized this problem and described organizations that are uniquely suited to the coordination problem need
  - Hage J. 2020. Knowledge Evolution and Societal Transformations. London: Anthem Press.
  - Hage J, Hadden WC. 2025. Solving Crises in Capitalism and Democracy. London: Routledge.
- CRN conform to that organizational design
  - Yogurtcu, Osman Nuri, et al. "Building Real-World Evidence Infrastructure to Improve Health and Healthcare in the United States: Part I—Coordinated Registry Networks and Systemic Coordinated Inter-Organizational Networks." International Journal of Translational Medical Research and Public Health 9.Suppl 1 (2025): S15-S25.
  - Yogurtcu, Osman Nuri, et al. "Building Real-World Evidence Infrastructure to Improve Health and Healthcare in the United States: Part II—How Coordinated Registry Networks Operate Like Systemic Coordinated Inter-Organizational Networks." International Journal of Translational Medical Research and Public Health 9.Suppl 1 (2025): S26-S36.
  - Yogurtcu, Osman Nuri, et al. "Building Real-World Evidence Infrastructure to Improve Health and Healthcare in the United States: Part III—Questions for Translational Science and Action Theory." International Journal of Translational Medical Research and Public Health 9.Suppl 1 (2025): S37-S45.

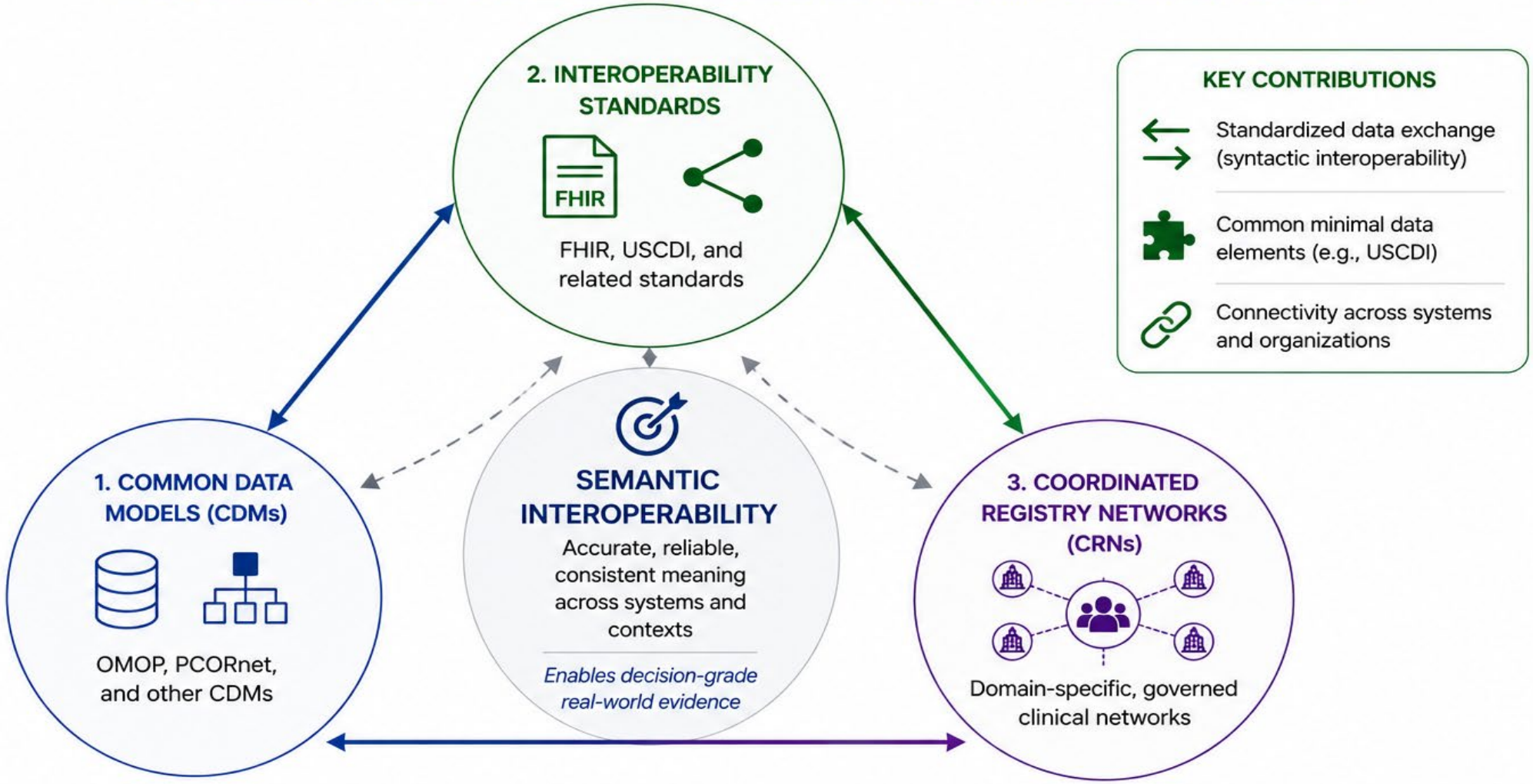
# How CRNs Generate Decision-Grade Evidence

- Granular clinically relevant data identified by clinicians and other users of the data
- Sustainable 'collect once, use many times' model.
  - Gressler, Laura Elisabeth, et al. "A comprehensive framework for evaluating the value created by real-world evidence for diverse stakeholders: the case for coordinated registry networks." Therapeutic Innovation & Regulatory Science 58.6 (2024): 1042-1052.
- Collaborative governance across clinicians and institutions
- Link to complementary national datasets.



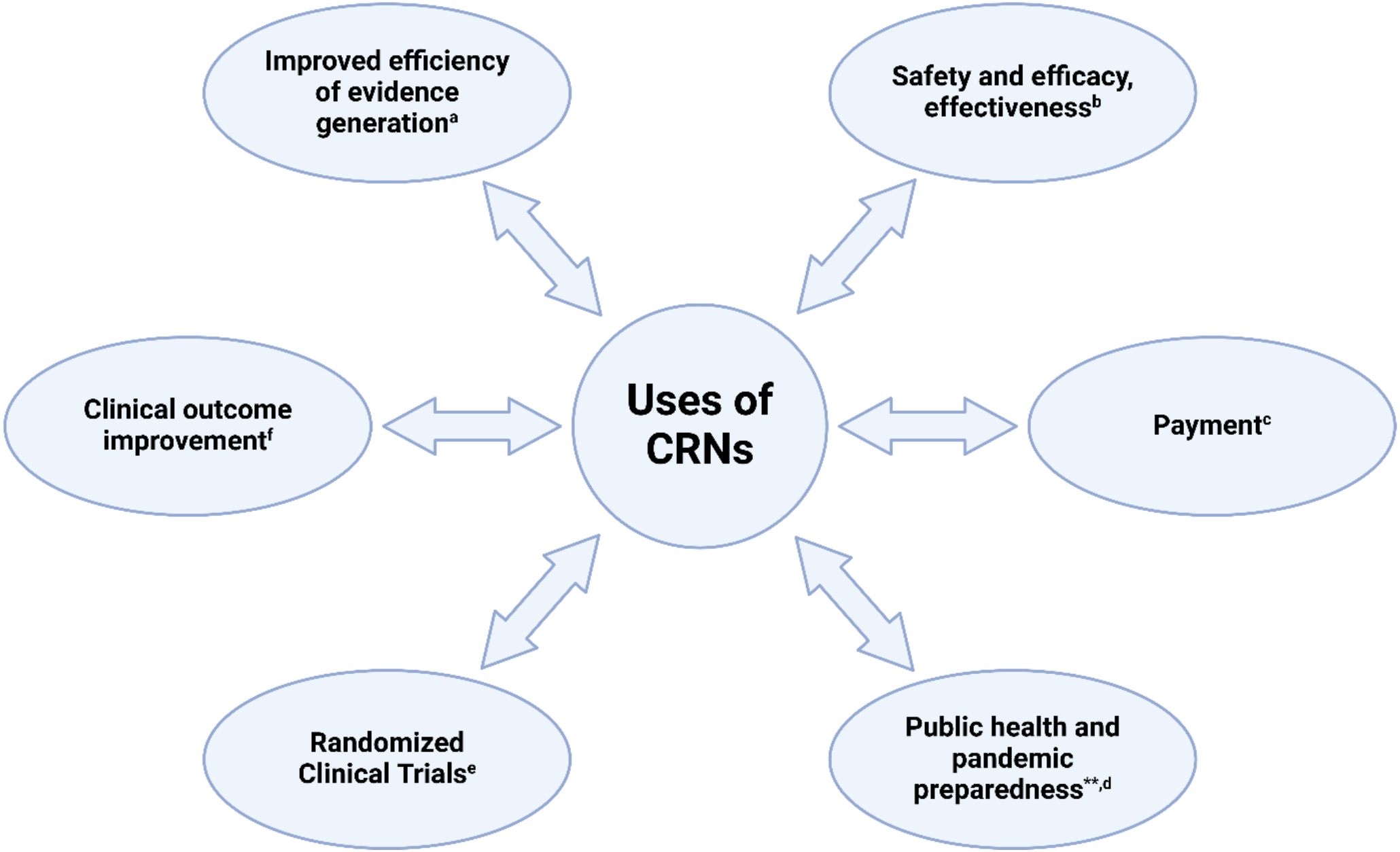
# Complementary Functions Enabling Semantic Interoperability in Real-World Data

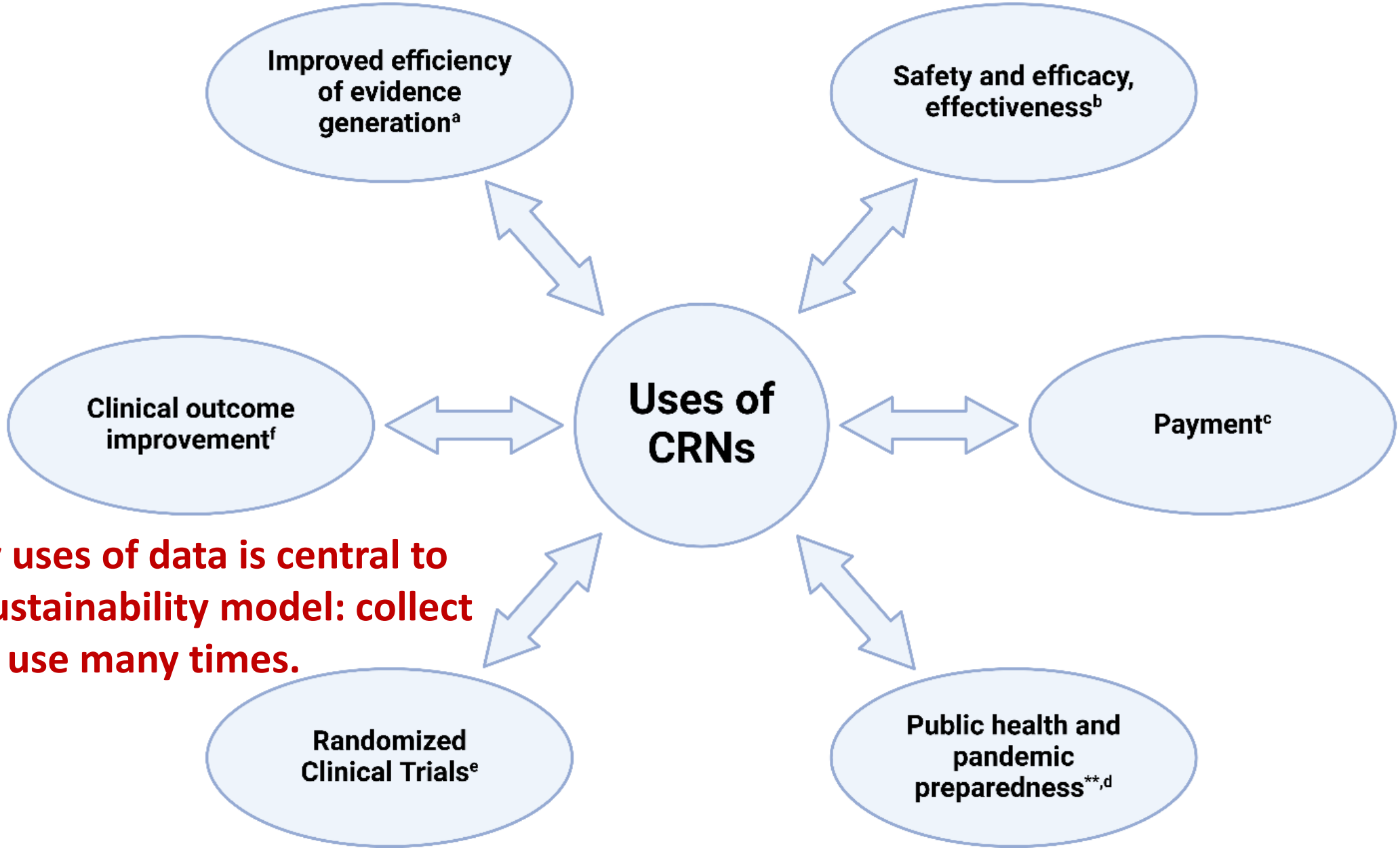
*Interoperability requires coordination across structural, technical, and semantic domains.*




**THESE FUNCTIONS OPERATE ACROSS THE DATA LIFECYCLE**

Interdependent and reinforcing—enabling the creation, exchange, and use of interoperable clinical data.

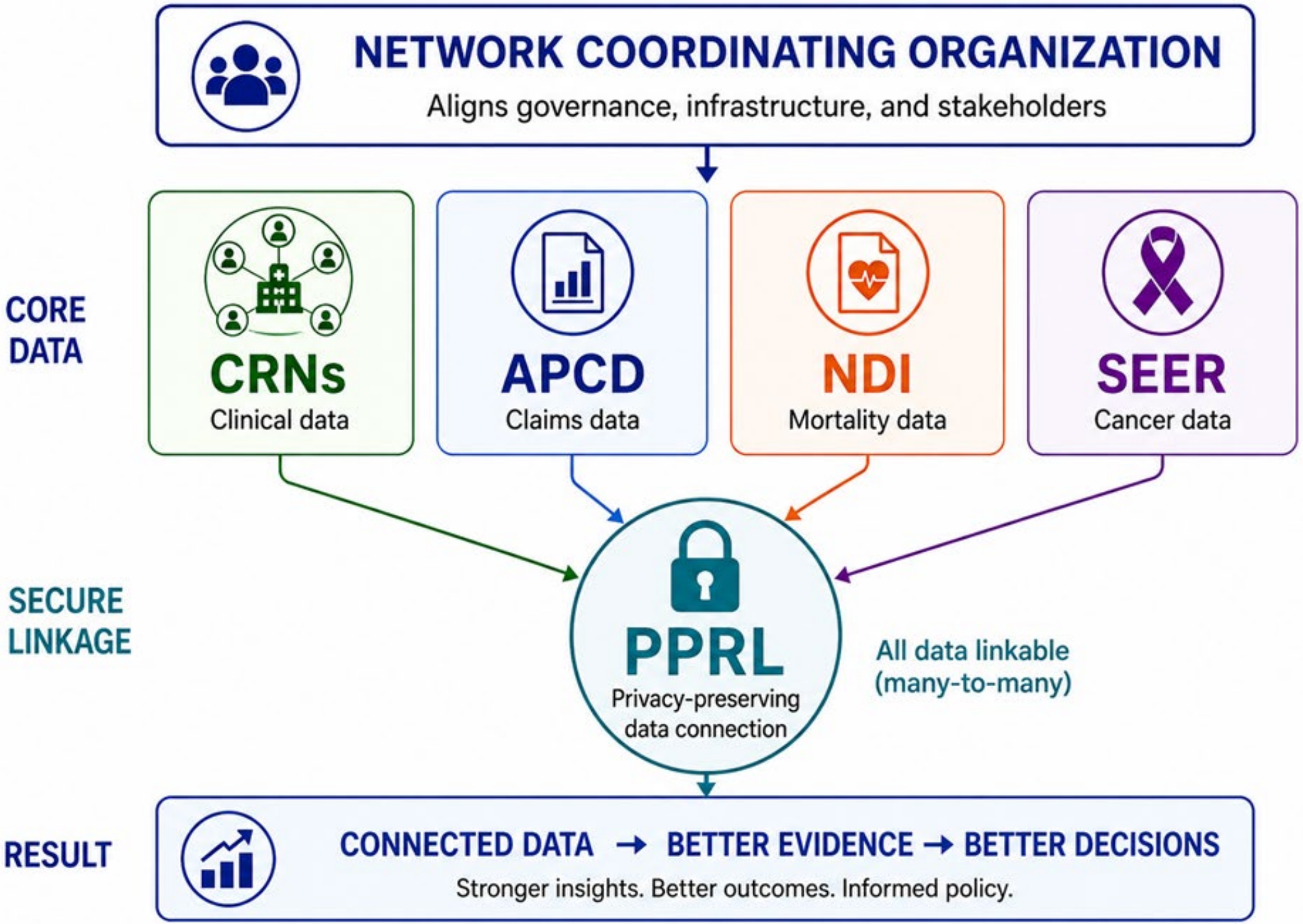

Improved efficiency of evidence generation[a]
Safety and efficacy, effectiveness[b]
Clinical outcome improvement[f]
Uses of CRNs
Payment[c]
Randomized Clinical Trials[e]
Public health and pandemic preparedness**,[d]




**Many uses of data is central to the sustainability model: collect once, use many times.**

# Vision for a National RWE Ecosystem

- Federated ecosystem centered on CRNs.
  - Sedrakyan, Art, and Suvekshya Aryal. "Maturity framework and select approaches for developing coordinated registry networks (CRNs): medical device epidemiology network (MDEpiNet) supplement." *BMJ Surgery, Interventions, & Health Technologies* 4.Suppl 1 (2022): e000148.
- Alignment with interoperability standards and governance.
- Integration with claims, mortality, and specialty datasets (linkage)
- National Coordinating Organization.


NETWORK COORDINATING ORGANIZATION
Aligns governance, infrastructure, and stakeholders
CORE DATA
CRNs
Clinical data
APCD
Claims data
NDI
Mortality data
SEER
Cancer data
SECURE LINKAGE
PPRL
Privacy-preserving data connection
All data linkable (many-to-many)
RESULT
CONNECTED DATA → BETTER EVIDENCE → BETTER DECISIONS
Stronger insights. Better outcomes. Informed policy.

# Key Enabling Technologies

- FHIR (HL7) and USCDI+ interoperability standards (ONC)
  - CRN work with standards to improve efficiency
- OMOP and other common data models
  - Guide the societies on how to create and code their variables
- Privacy-preserving record linkage (PPRL).
- Secure data governance and cybersecurity policies.
- Integration of AI tools within curated clinical workflows.

# Towards a National OB CRN

- There are models in other specialty area
  - Other specialty areas started with many pieces
  - Harmonized them into a working whole (a share minimum data set) then models
  - This also saves money in overhead
- One unique feature is the double purpose needed
  - To improve outcomes
  - To evaluation the effect of medical products used during pregnancy
- Medicine needs to harness IT (not the other way around)
  - Building data collection into the work flow to decrease the amount of time collecting data and improve care

# Towards a National OB CRN

- Needs to be part of a larger ecosystem
  - All CRN depend on many aspects of the wider ecosystem
- This is a task for leadership that
  - Can bring the profession together around this goal
  - Bring together existing pieces
  - Work with the other parts of medicine and partner to build the ecosystem
- Must start with a vision
  - It will not take as long as it did in the past
- Will need a lot of advocacy

# Thank you

# Lessons Learned from Public-Private Partnerships

Kourtney J Davis, PhD, MSPH, FISPE

Vice President

Global Epidemiology, Innovative Medicine

Office of the Chief Medical Officer

Johnson and Johnson

# Disclosure

I am a full-time employee and shareholder of Johnson & Johnson.

These remarks reflect my personal experience and do not represent an official company position.

# Great Expectations:
# Public Private Partnerships (PPP)

Patients, data owners, data access providers, academics, industry and health authorities benefit

**Build**

capabilities and capacity supporting robust and more timely evidence

**Advance**

accessible longitudinal data sources with core elements, common data model

**Generate**

evidence about historically under-represented groups

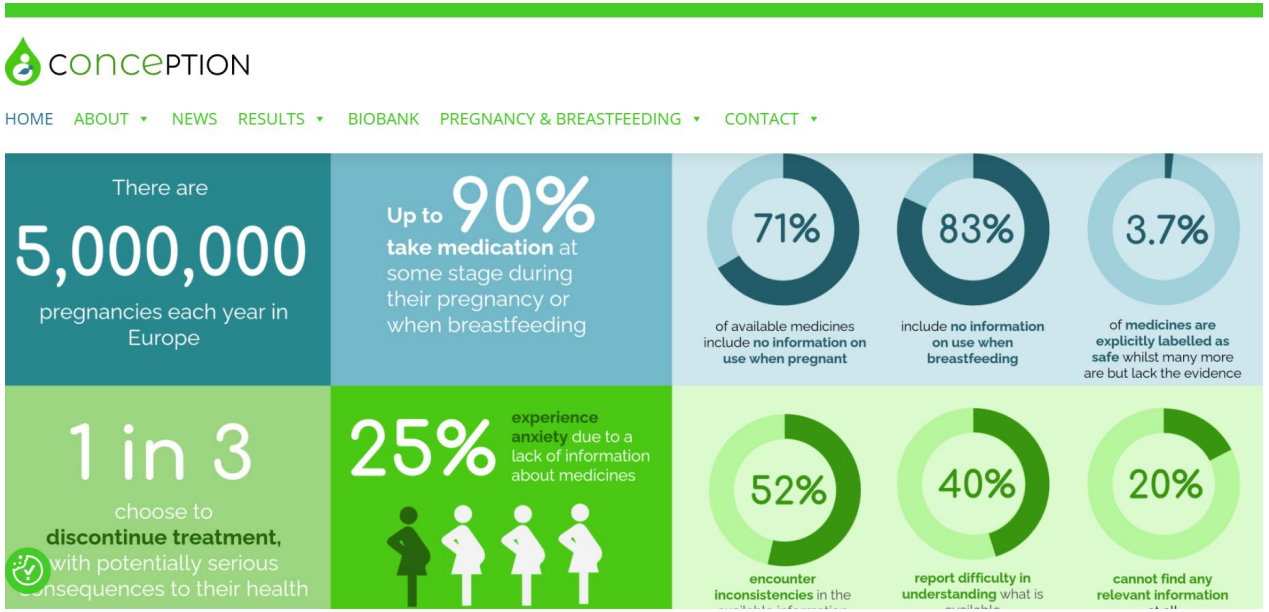
# Innovative Medicines Initiative (IMI) ConcePTION

Continuum of Evidence from Pregnancy Exposures, Reproductive Toxicology, and Breastfeeding to Improve Outcomes Now

- EU PPP from 2019 –2024

*Building an ecosystem for better monitoring and communicating of medical safety in pregnancy and breastfeeding:*

*validated and regulatory endorsed workflows for fast, optimized evidence generation.*




*www.ihi.Europa.edu/projects-results/project-factsheets/conception*

# **ConcePTION Lessons Learned**, 1/3

Diverse stakeholder groups aligned on common needs with dedicated resources can produce useful guidance, infrastructure, and tools

Drug Safety (2024) 47:227–236
https://doi.org/10.1007/s40264-023-01384-3

ORIGINAL RESEARCH ARTICLE

**Improving Data Collection in Pregnancy Safety Studies: Towards Standardisation of Data Elements in Pregnancy Reports from Public and Private Partners, A Contribution from the ConcePTION Project**

Guillaume Favre[1,2] · Jonathan L. Richardson[3,4] · Alan Moore[5] · Yvonne Geissbühler[5] · Valentine Jehl[5] · Alison Oliver[3] · Svetlana Shechtman[6] · Orna Diav-Citrin[6] · Maya Berlin[7] · Tal De Haan[7] · David Baud[2] · Alice Panchaud[8,9] · Anil Mor[10] · Meritxell Sabidó[11] · Sabrina de Souza[11] · Christina Chambers[12] · Yrea R. J. van Rijt-Weetink[13] · Eugène P. van Puijenbroek[13] · Laura M. Yates[14,15] · François Girardin[1] · Michael Stellfeld[16] · Ursula Winterfeld[1]

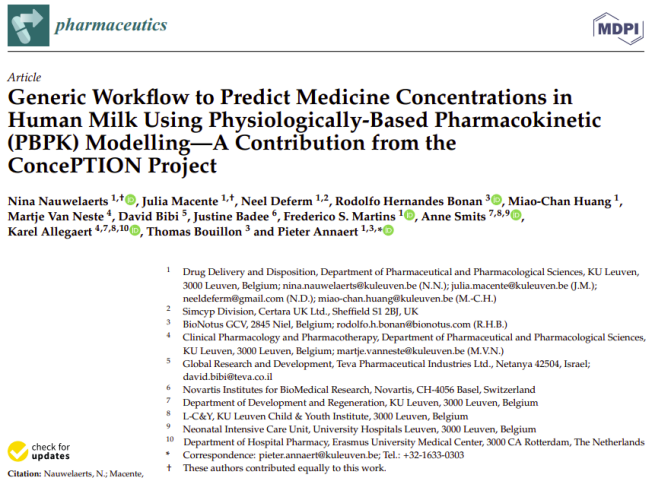
Accepted: 15 November 2023 / Published online: 19 December 2023


*Review Article*

**Drug Utilization Studies in Pregnant Women for Newly Licensed Medicinal Products: A Contribution from IMI ConcePTION**

Sandra Lopez-Leon[1,2] Anja Geldhof[3] Julie Scotto,[4] Keele Wurst[5] Meritxell Sabidó[6] Jingping Mo,[7] Ditte Molgaard-Nielsen,[8] Jorieke E. H. Bergman[9] Xuan Anh Phi,[9] and Sue Jordan[10]

[1]Novartis Pharmaceuticals, East Hanover, NJ, USA
[2]Rutgers Center for Pharmacoepidemiology and Treatment Science, Rutgers University, New Brunswick, NJ, USA
[3]Janssen Biologics B.V., Leiden, Netherlands
[4]Bristol Myers Squibb, Princeton, NJ, USA
[5]GlaxoSmithKline, Research Triangle Park, North Carolina, USA
[6]Merck Healthcare KGaA, Darmstadt, Germany
[7]Pfizer Inc., New York, NY, USA
[8]Novo Nordisk, Søborg, Denmark
[9]Department of Genetics, University of Groningen, University Medical Center Groningen, Groningen, Netherlands
[10]Faculty of Medicine, Health and Life Sciences, Swansea University, Swansea, Wales, UK



*pharmaceutics* MDPI

*Article*

**Generic Workflow to Predict Medicine Concentrations in Human Milk Using Physiologically-Based Pharmacokinetic (PBPK) Modelling—A Contribution from the ConcePTION Project**

Nina Nauwelaerts [1,†], Julia Macente [1,†], Neel Deferm [1,2], Rodolfo Hernandes Bonan [3], Miao-Chan Huang [1], Martje Van Neste [4], David Bibi [5], Justine Badee [6], Frederico S. Martins [1], Anne Smits [7,8,9], Karel Allegaert [4,7,8,10], Thomas Bouillon [3] and Pieter Annaert [1,3,*]

1 Drug Delivery and Disposition, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, 3000 Leuven, Belgium; nina.nauwelaerts@kuleuven.be (N.N.); julia.macente@kuleuven.be (J.M.); neeldeferm@gmail.com (N.D.); miao-chan.huang@kuleuven.be (M.-C.H.)
2 Simcyp Division, Certara UK Ltd., Sheffield S1 2BJ, UK
3 BioNotus GCV, 2845 Niel, Belgium; rodolfo.h.bonan@bionotus.com (R.H.B.)
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7 Department of Development and Regeneration, KU Leuven, 3000 Leuven, Belgium
8 L-C&Y, KU Leuven Child & Youth Institute, 3000 Leuven, Belgium
9 Neonatal Intensive Care Unit, University Hospitals Leuven, 3000 Leuven, Belgium
10 Department of Hospital Pharmacy, Erasmus University Medical Center, 3000 CA Rotterdam, The Netherlands
* Correspondence: pieter.annaert@kuleuven.be; Tel.: +32-1633-0303
† These authors contributed equally to this work.

check for updates

Citation: Nauwelaerts, N.; Macente,

Full list of 58 peer-reviewed publications: https://www.imi-conception.eu/results/papers/

# **ConcePTION Lessons Learned**, 2/3

Research questions of interest and obligations may differ by stakeholder

Need to align on roles and extent of independent vs collaborative tasks

Industry preference to engage scientifically, not restricted to only funding

# **ConcePTION Lessons Learned**, 3/3

## Fundamental shared principles: trust and transparency

scientific partners engage with committed resources, subject matter experts included

access to resources and deliverables for all partners

## ‘Look around corners’ to optimize sustainability

actively monitor and mitigate risks to reduce partner attrition

incentivize extension of expanded capabilities to benefit all partners

# **Lessons Learned from COVID-19 collaboration**, 1/2

## Unique challenges and incentives for innovation to generate post-authorization pregnancy safety data

- C-VIPER proposed as a multi-sponsor, global, site-less registry[1]

## Innovation required adaptation

- cross-pharma studies encouraged by regulators; not easily supported by framework
- joint MAH protocol/SAP submission to health authorities
- separate product timelines, regulatory review cycles, report frequency, geography
- unprecedented pace of change in external landscape drove amendments

[1]Wyszynski DF, Bhattacharya M, Martínez-Pérez O, Scialli AR, Tassinari M, Bar-Zeev N, Renz C, Hernández-Díaz S. The COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER): Protocol and Methodological Considerations. Drug Safety (2023) 46:297–308 https://doi.org/10.1007/s40264-022-01271-3.

# **Lessons Learned from COVID-19 collaboration**, 2/2

| | | | | |
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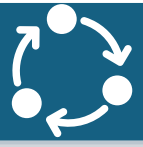
|  |  |  |  |  |
| Initiate consortia early to allow for MAH discussions | Consider joint regulatory review of common study documents | Anticipate study amendments, particularly in dynamic environment | Recognize complexity of underlying operational infrastructure | Leverage multi-stakeholder collaborations to increase future efficiency[1] |

[1]MacDonald SC, Guignard AP, Munoz FM, Dareng EO, Davis KJ, Machado MAA, Shmuel S, Taddei L and Marcelon L (2025) Post-approval safety studies of vaccines in pregnancy: available regulatory guidance and next steps towards the more efficient generation of safety evidence. Front. Drug Saf. Regul. 5:1648854. doi: 10.3389/fdsfr.2025.1648854

# Bright Future: Collectively Applying Lessons Learned

- Improve operational efficiency of evidence generation
- Increase relevance and representativeness of study populations
- Reduce attrition and maintain high engagement
- Democratize data collection with patient-centered platforms

# Opportunity to Change the Status Quo

- Increased demand for evidence to inform safe medication use in pregnancy and lactation
- Innovation and standardization in data collection, analysis, reporting
- Overcome challenges too large or complex for any single group
    - PPP, patient advocacy groups, professional societies
- Build trust in evidence through engagement and radical transparency

# Partnership Models for Accelerating Pregnancy Health

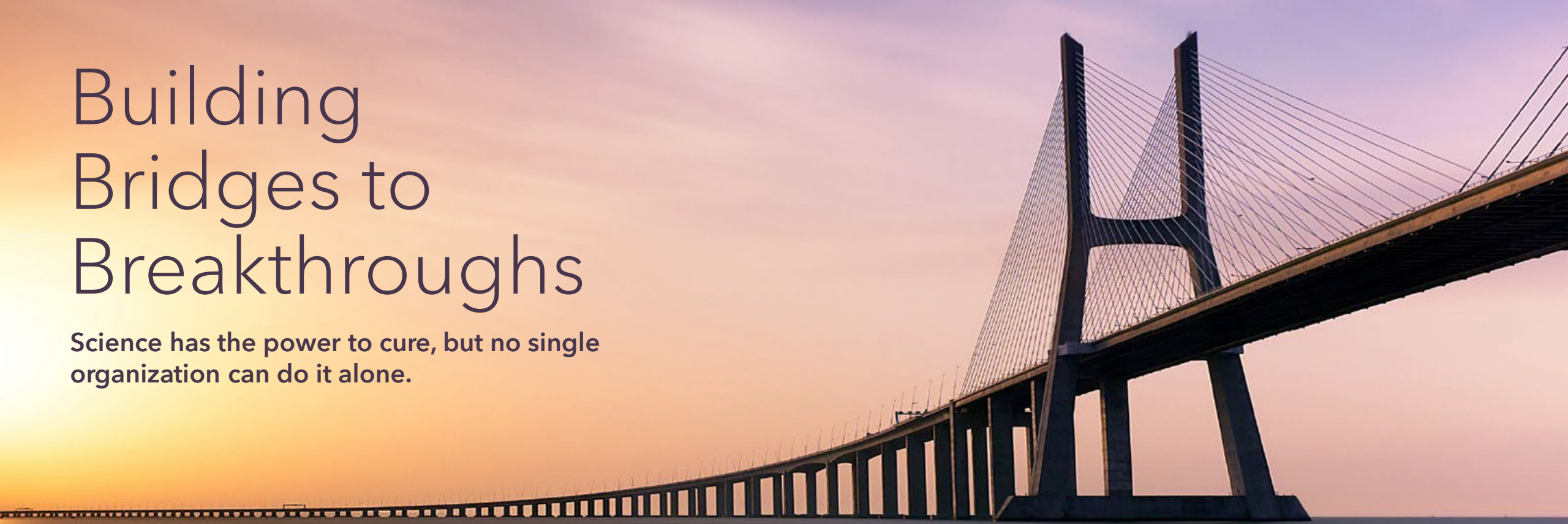
## Optimizing Pregnancy Registries Public Workshop

May 8, 2026

Tania Nayak Kamphaus, PhD
Associate Vice President, Science Partnerships
Foundation for the National Institutes of Health

FNIH

# Building Bridges to Breakthroughs



**Science has the power to cure, but no single organization can do it alone.**

We connect world-leading NIH researchers with the ingenuity and expertise of public and private sector leaders to accelerate medical breakthroughs.

The FNIH is a non-profit organization charted by congress and launched in 1996 to support the mission of NIH.

FNIH

# FNIH builds bridges from your goals to the impact you want to achieve

We have a proven track record of success at every step in the pathway from a goal to achieving impact

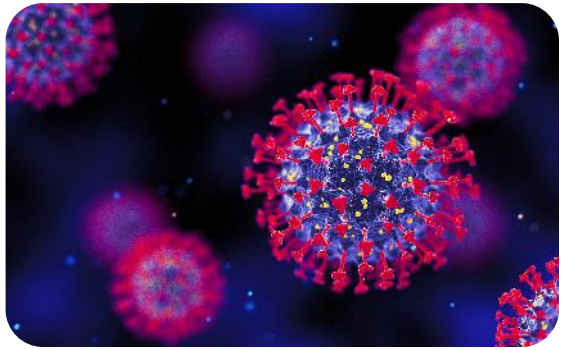
# Advancing breakthroughs across all areas of human health

From cancer to metabolic disorders to rare diseases, we want all people to have the opportunity to live longer, healthier lives

**CANCER**

**CARDIOVASCULAR**

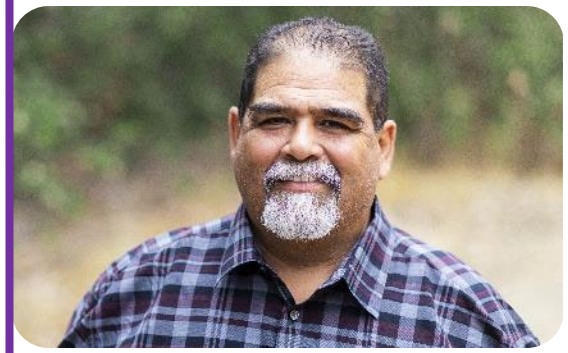
**INFECTIOUS DISEASES**



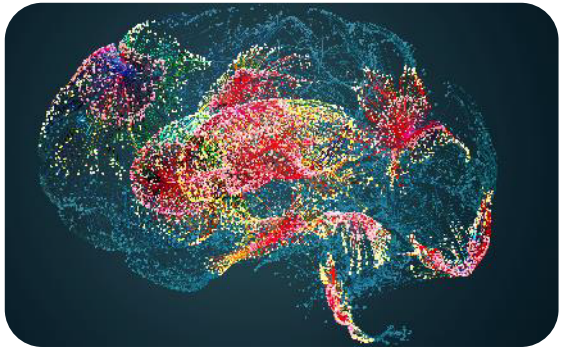
**INFLAMMATION + IMMUNOLOGY**

**MATERNAL CHILD + NEWBORN HEALTH**

**METABOLIC DISORDERS**



**NEUROLOGICAL DISEASE**



**RARE DISEASES**

FNIH

# Partnering with world-class organizations to tackle the most pressing health challenges

Long-standing relationships with renowned public and private sector institutions.

## NIH & OTHER GOVERNMENT AGENCIES


**We support the mission of the nation's premier biomedical research agency, driving discoveries that improve health and save peoples' lives**

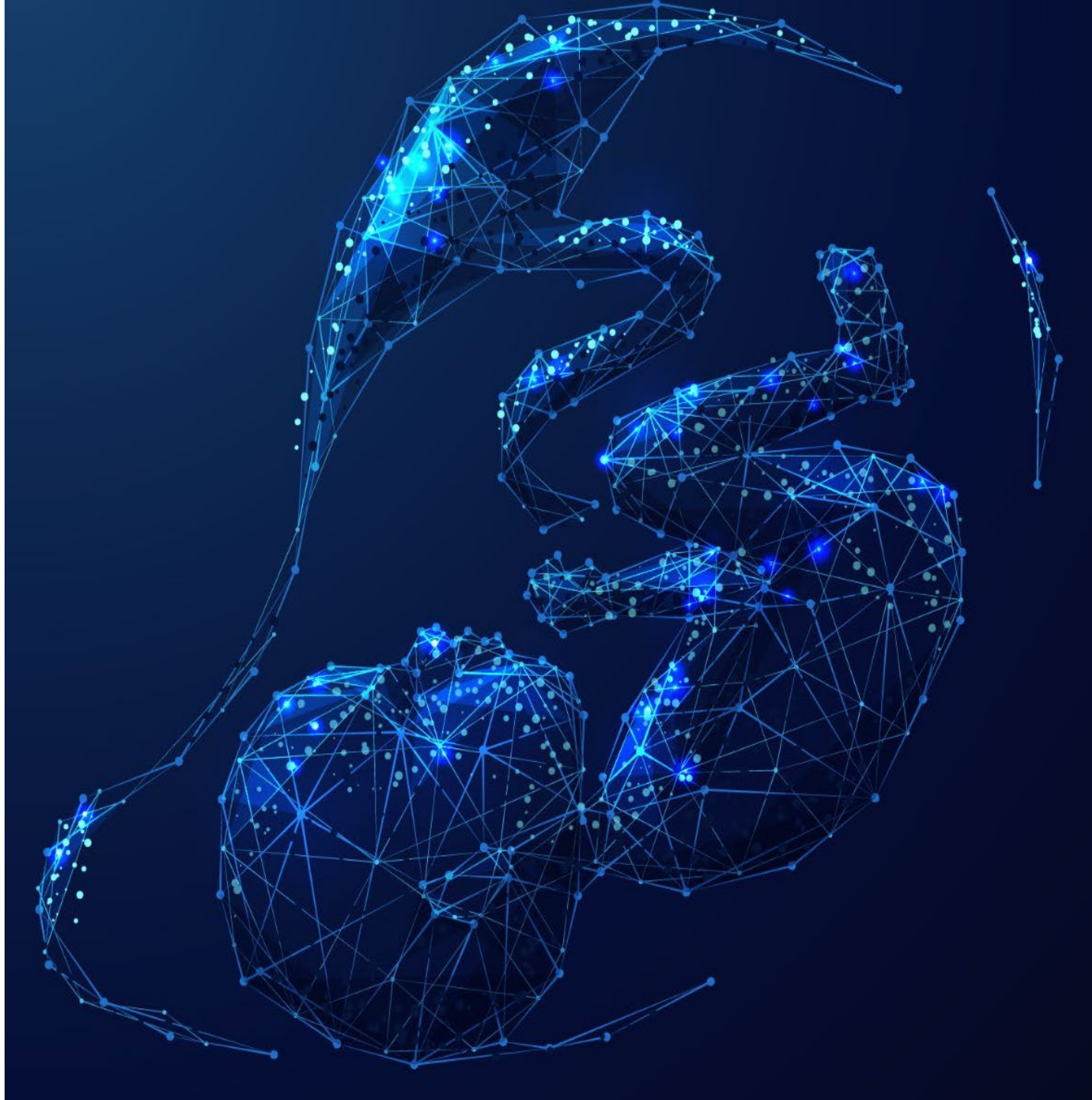
## LIFE SCIENCES COMPANIES & ACADEMIA

**We collaborate with leading R&D organizations to advance research that will lead to new therapies, diagnostics, and potential cures**

## FOUNDATIONS & PATIENT ORGANIZATIONS

**We work with foundations and patient organizations to address urgent issues in global health and accelerate biomedical innovation across a range of diseases**

# Biomarkers for Risk Stratification and Detection of Early-Onset Preeclampsia



FNIH

# Project Goal and Specific Aims

**Overall Goal:**

Leverage existing datasets and biosamples available through collaboration with the NIH and other resources to employ commercially available kits to evaluate the diagnostic and predictive ability of these biomarkers in a US population.

**Specific Aim #1:**

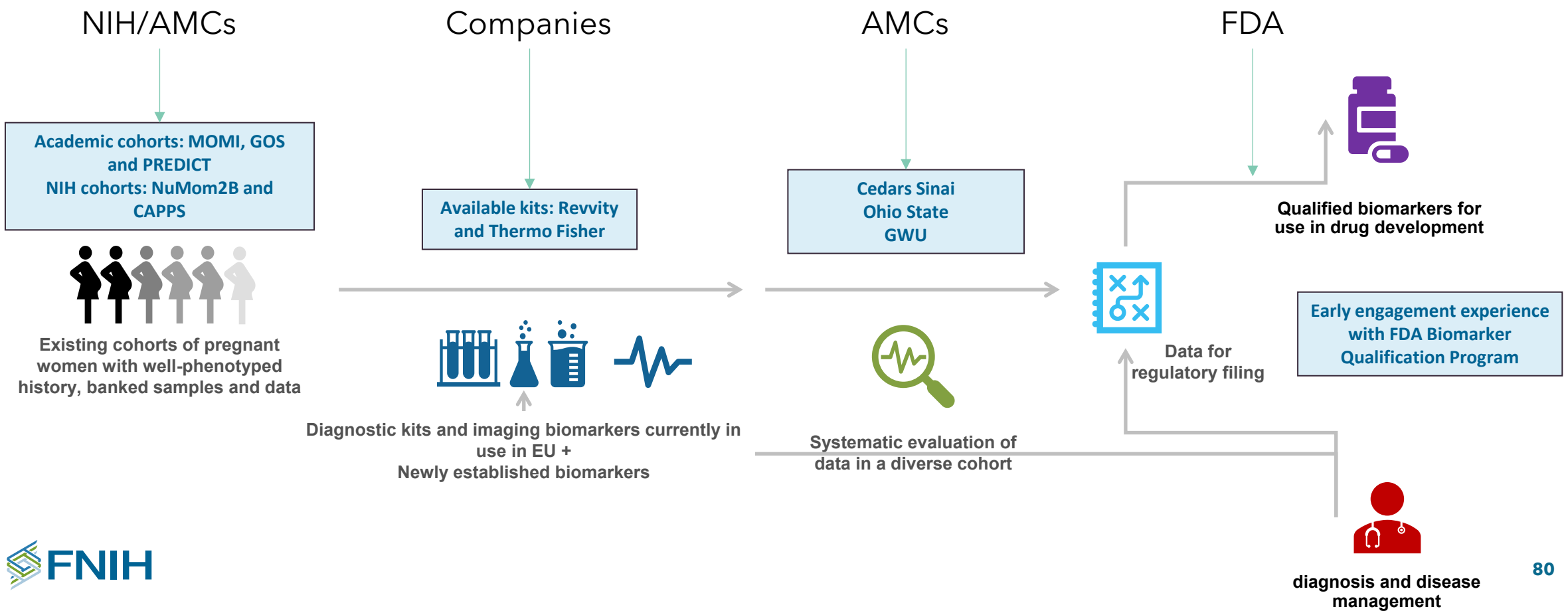
To validate biomarkers (from commercial kits for PlGF, PAPP-A) in a representative, racially diverse cohort of pregnant North American individuals in early pregnancy (10-14 weeks) in pregnant individuals who subsequently develop or do not develop early onset preeclampsia (<34 weeks) using existing biospecimens and datasets.

**Specific Aim #2:**

Validate an algorithm/model based on these findings for both early and mid-pregnancy combining biomarkers and maternal risk factors (blood pressure, race, BMI) to PE<34 weeks.

FNIH

# FNIH Biomarkers Consortium:
## Leveraging Public and Private Sector Resources to Diagnose Early Onset Preeclampsia



# Preeclampsia Project Team

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development
Healthy pregnancies. Healthy children. Healthy and optimal lives.

ThermoFisher SCIENTIFIC

revvity

Bill & Melinda Gates foundation

MERCK for Mothers

FNIH Foundation for the National Institutes of Health

Cedars Sinai

GW

The Ohio State University

## Strategic Partners

PREECLAMPSIA™ FOUNDATION

FDA

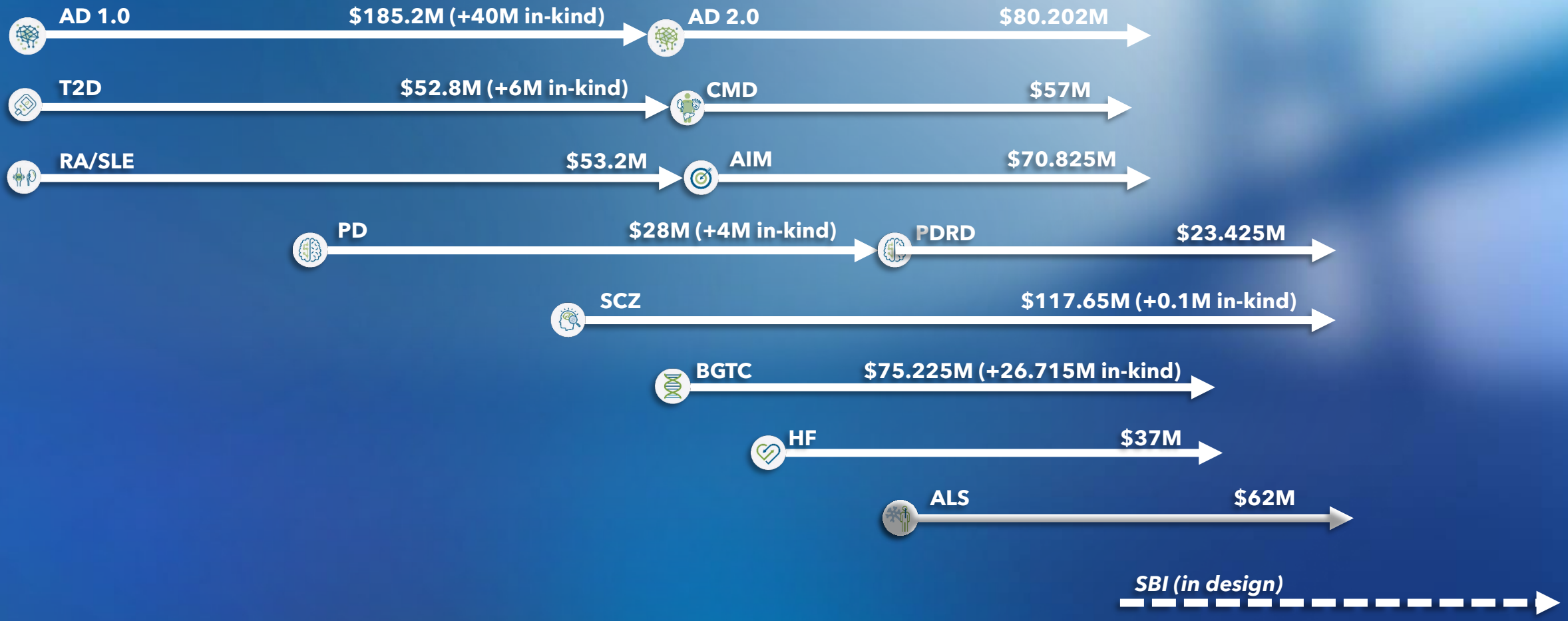
# Accelerating Medicines Partnership® (AMP®)

A PRECOMPETITIVE PUBLIC-PRIVATE COLLABORATION started in 2014, the program unites the resources of the National Institutes of Health (NIH) and private partners to improve our understanding of disease pathways and transform current models for developing new treatments by:

- Identifying new targets, biomarkers and development paradigms
- Developing leading-edge tools and technologies
- Collecting large scale datasets and supporting analytics for open analysis by the public
- Generating consensus platforms and procedures

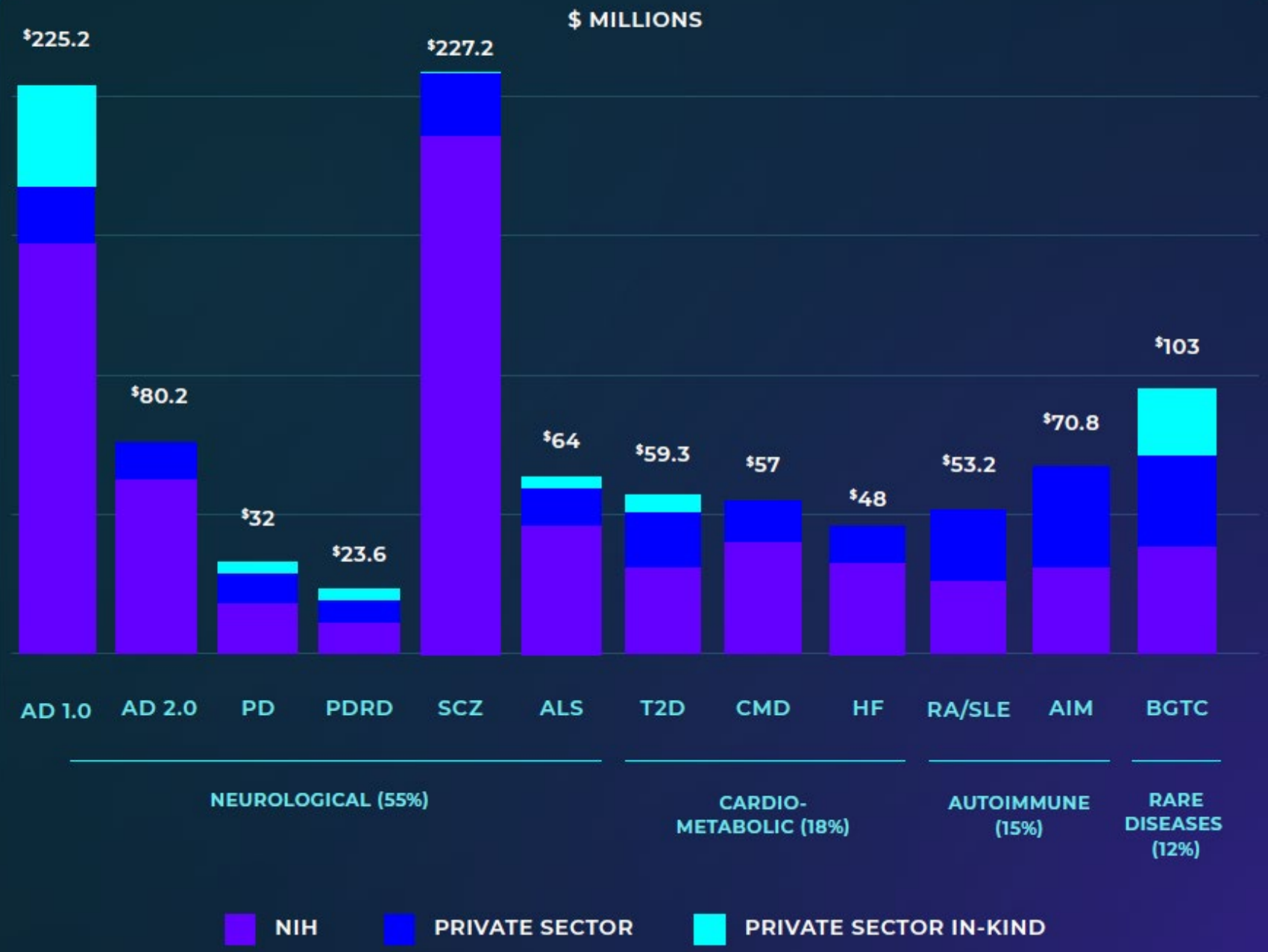

FNIH

# AMP® Program Development




FNIH

# PROGRAM FUNDING




The AMP program leverages the leadership and subject matter expertise of

**16** NIH INSTITUTE & CROSS-INSTITUTE PROGRAMS

**36** INDUSTRY PARTNERS

**35** NON-PROFITS

Collectively, the NIH and the private sector have invested more than

**$1B**

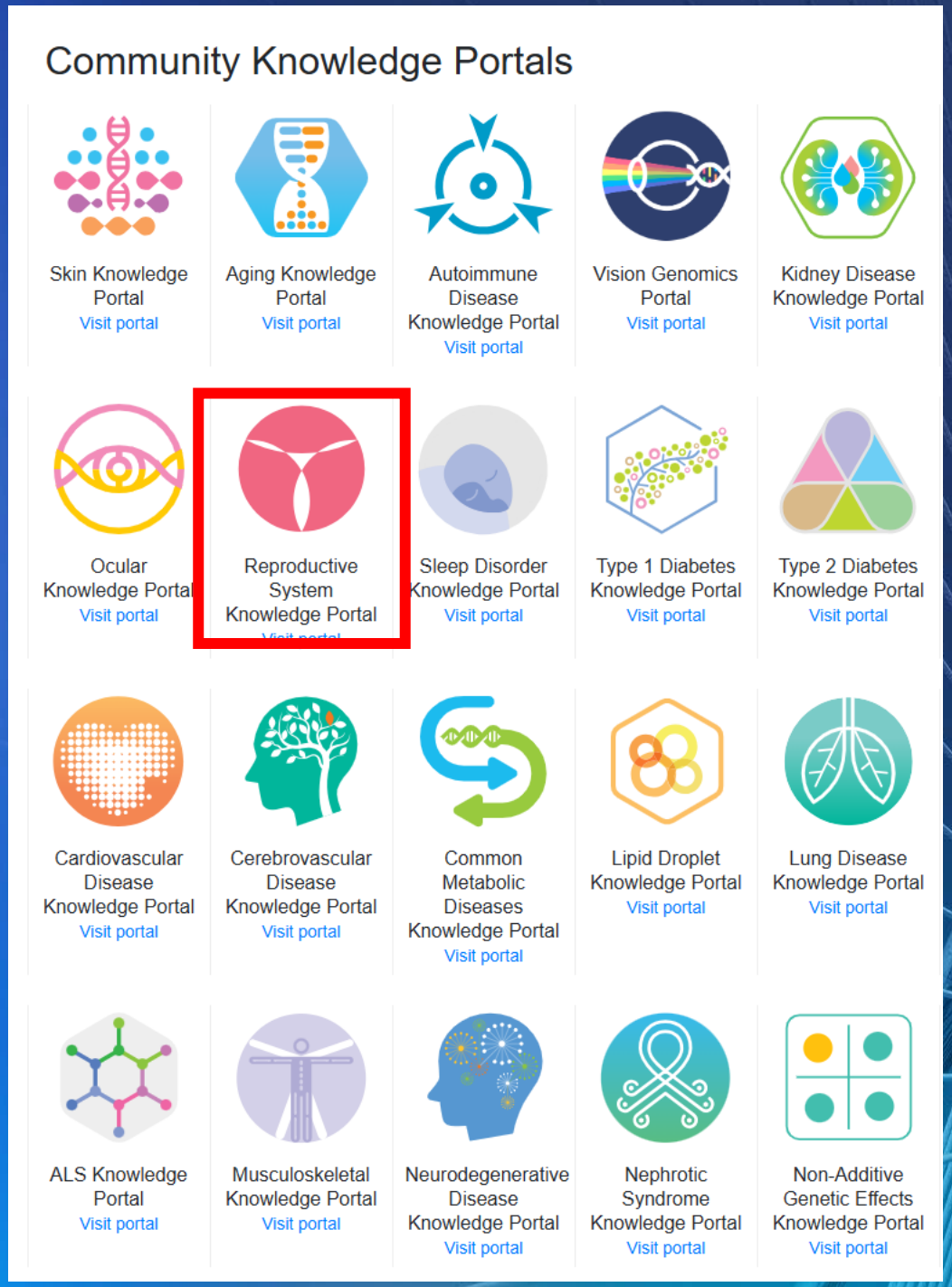
in project funding and in-kind donations, supporting over

**675**

researchers through AMP-funded projects

# AMP® Common Metabolic Diseases

Providing data and tools to promote understanding and treatment of common metabolic diseases





https://reproductive.hugeamp.org/

# How does FNIH help the FDA?

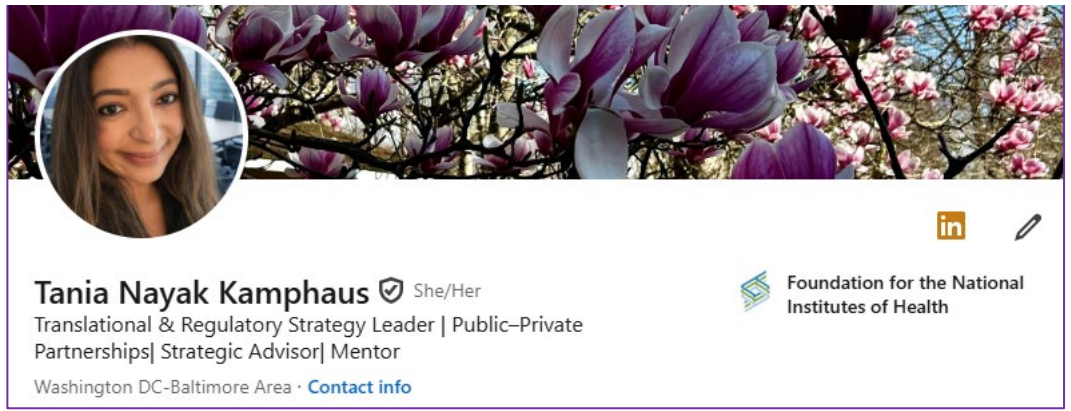
- **Provide regulator-ready, fit-for-purpose, and cutting-edge biomarker, endpoint, and assessment datasets with input from FDA" reduce risk/uncertainty for device and drug approvals**
- **Enhance quality data and evidence for project-related regulatory submissions**
  - Promote/educate all sectors on optimal use of FDA's BEST (https://pubmed.ncbi.nlm.nih.gov/31367046/), well-defined, fit-for-purpose and validated Tools for use in trials & IND packages
- **Preeminent convening role to strengthen FDA regulatory frameworks and new/improved Guidance(s).**
  - Primary focus on biomarkers for validation and qualification (Safety, Surrogate Endpoints, Multicomponent, Imaging, Remote Technologies, DHTs)
  - Policy/Guidance/Program development [(Evidentiary Stds – BQP, DHTs – ISTAND), BMx Controls/Stds, Master Protocols, Pediatrics and Rare Diseases (trial design/efficiencies)]
- **Provide a safe platform for transparent engagement with stakeholders and experts who use the tools validated/qualified by FDA**
  - Better understand real-world, user perspectives, concerns, and application for continuous improvement of practices/policies/interpretations
- **We are a trusted and experienced collaborator to FDA and the drug development, biomarker validation, and clinical trial execution community, translate FDA priorities, guidance, and regulatory expectations into actionable strategies—providing clarity where regulators cannot speak directly.**
  - 20 Yrs, >45 projects, a diversity of impactful co-convenings, our leadership, partnership acumen, nimble and flexible program management structures that include FDA voice and representation at executive, steering, and working committee levels is invaluable and required for the advancement of biomarker and regulatory science.

# Foundation for the National Institutes of Health

Forging powerful alliances that support the mission of the NIH and advance breakthrough biomedical discoveries.

Non-profit Organizations · North Bethesda, MD · 16K followers · 51-200 employees

**www.fnih.org**



U.S. FOOD & DRUG ADMINISTRATION

# BREAK

REAGAN-UDALL FOUNDATION FOR THE FDA

# Building RWD infrastructure to assess medical product safety and effectiveness in pregnancy: Lessons learned from network initiatives to develop coordinated population cohorts

Carla V. Rodriguez, PhD, MPH
Director of Research

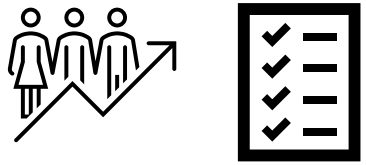
IMEDS

# AGENDA

- Different Registry Types
- Experience with RWD post-market pregnancy safety studies
- Real World Challenges & Lessons Learned in doing post-market pregnancy studies
  - Relevance & Reliability of Data – QCARD
  - Relevance & Reliability of algorithms – ACE-IT
- Visioning: Is it time for a coordinated effort?

# Heterogeneity in how “registry” is defined

prospective



“registry studies”

retrospective

“database studies”

**RWD**

Source Data

- Insurance
- Care Delivery

## Define Population

pregnancy-based

condition-based

product-based

# Pros | Cons of Prospective & Retrospective

Journal of Women's Health

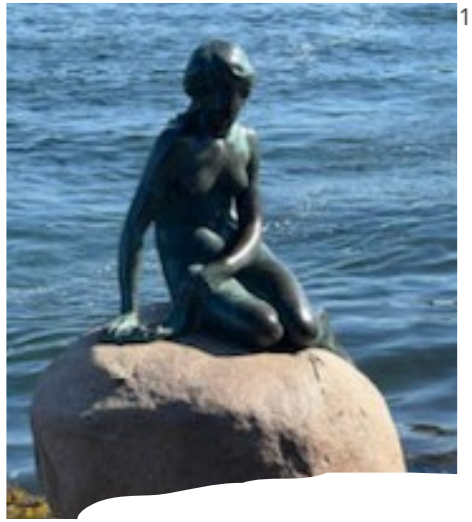
Mary Ann Liebert | Society for Women's Health Research

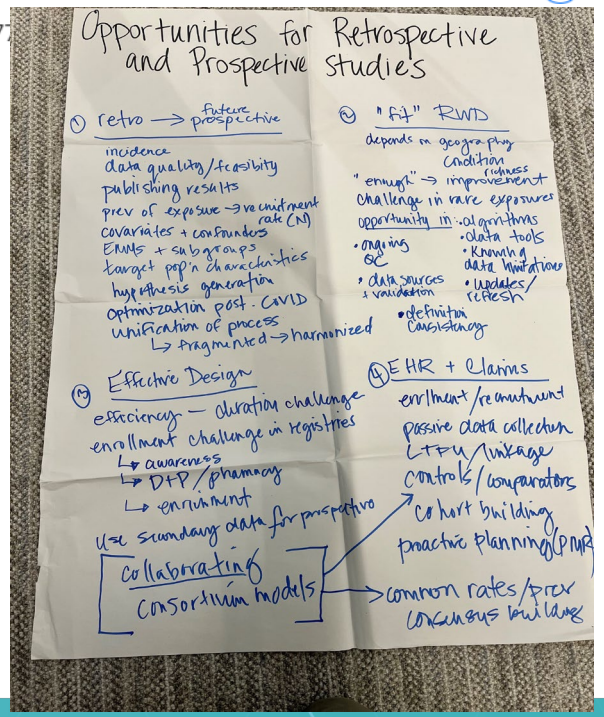
Journal indexing and metrics | Journal Homepage | Submission Guidelines

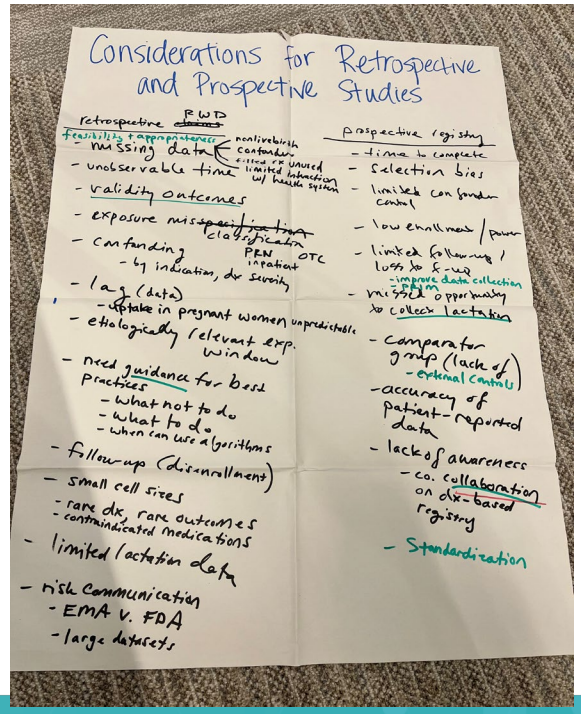
Free access | Article commentary | First published online April 23, 2026 | Request permissions

## Opportunities and Challenges to Leveraging Real-World Data for Post-Market Safety Studies in Pregnancy and Lactation: Meeting Proceedings

Carla Rodriguez-Watson, PhD, Kaylan Ware, MPH, [...], and Kristin Palmsten, ScD +3 View all authors and affiliations





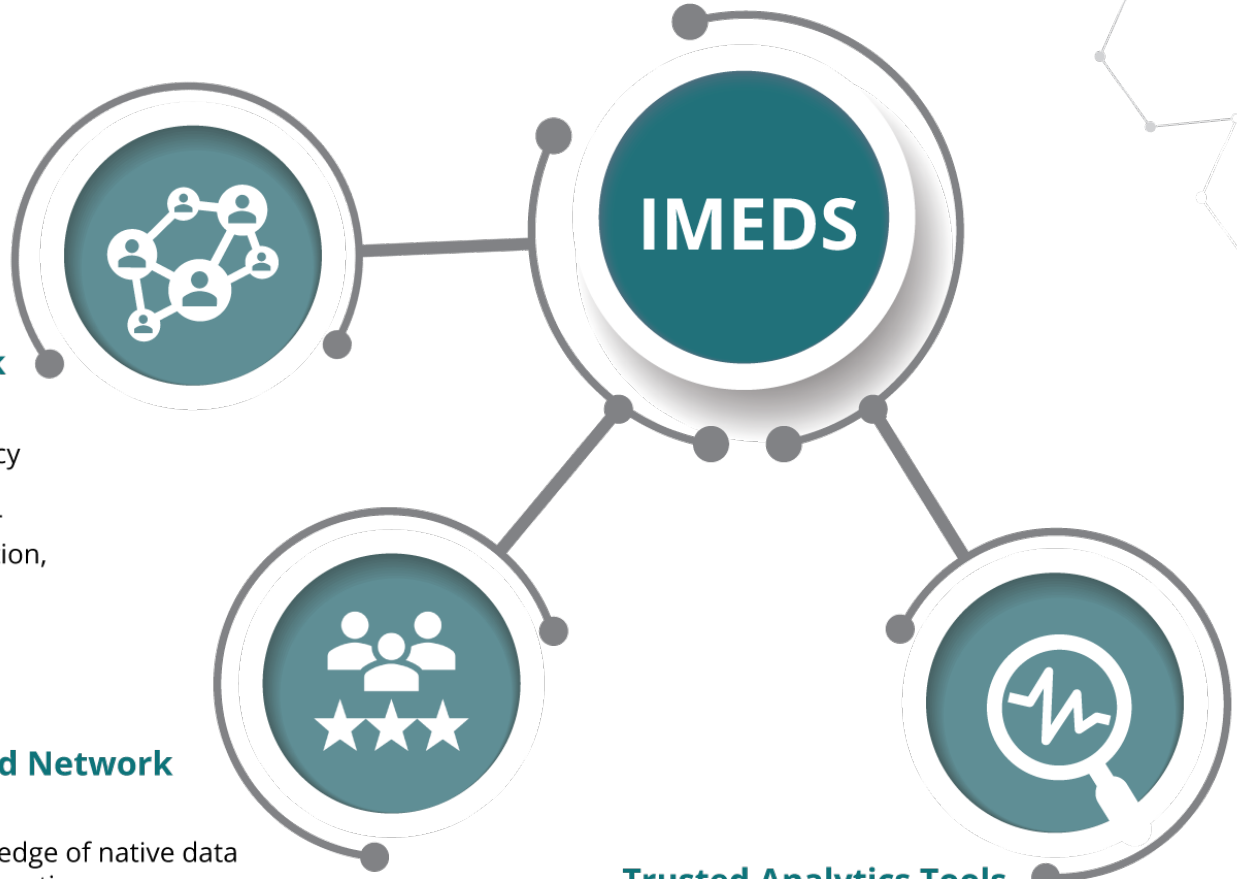



# Prospective registry challenges that RWD cohorts seek to address

- long timelines to identify and ‘recruit’ sample size
- limited representativeness
- small sample size / limited power

## RWD not without its challenges

# Experience with post-market required pregnancy safety studies in IMEDS




**Distributed Network Framework**

- Data protection & privacy
- Partner autonomy
- Central coordination for contracting, administration, and analysis

**Experienced Network Partners**

- Deep knowledge of native data
- Scientific expertise
- Geographically representative of all US states and territories

**Trusted Analytics Tools**

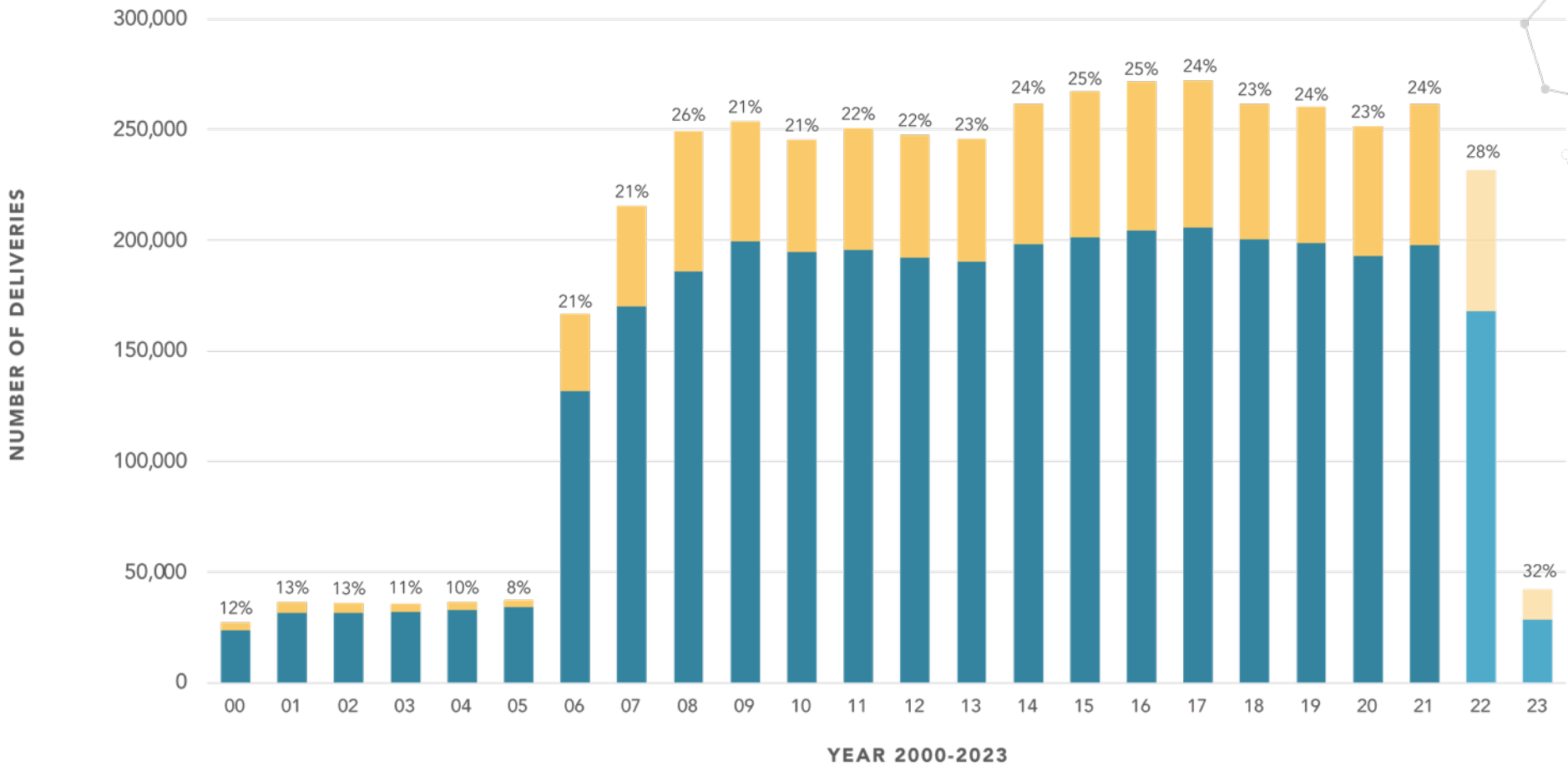
- Developed by FDA Sentinel
- Ensures relevance & reliability of results

- Uses Sentinel 2.0+ tools
- RWD cohort from **9** health plans (~30M covered lives per year)
- **2** Active post-market regulatory studies in pregnancy:
  - IBD
  - Psoriasis
- **7** years of experience

REAGAN-UDALL FOUNDATION FOR THE FDA

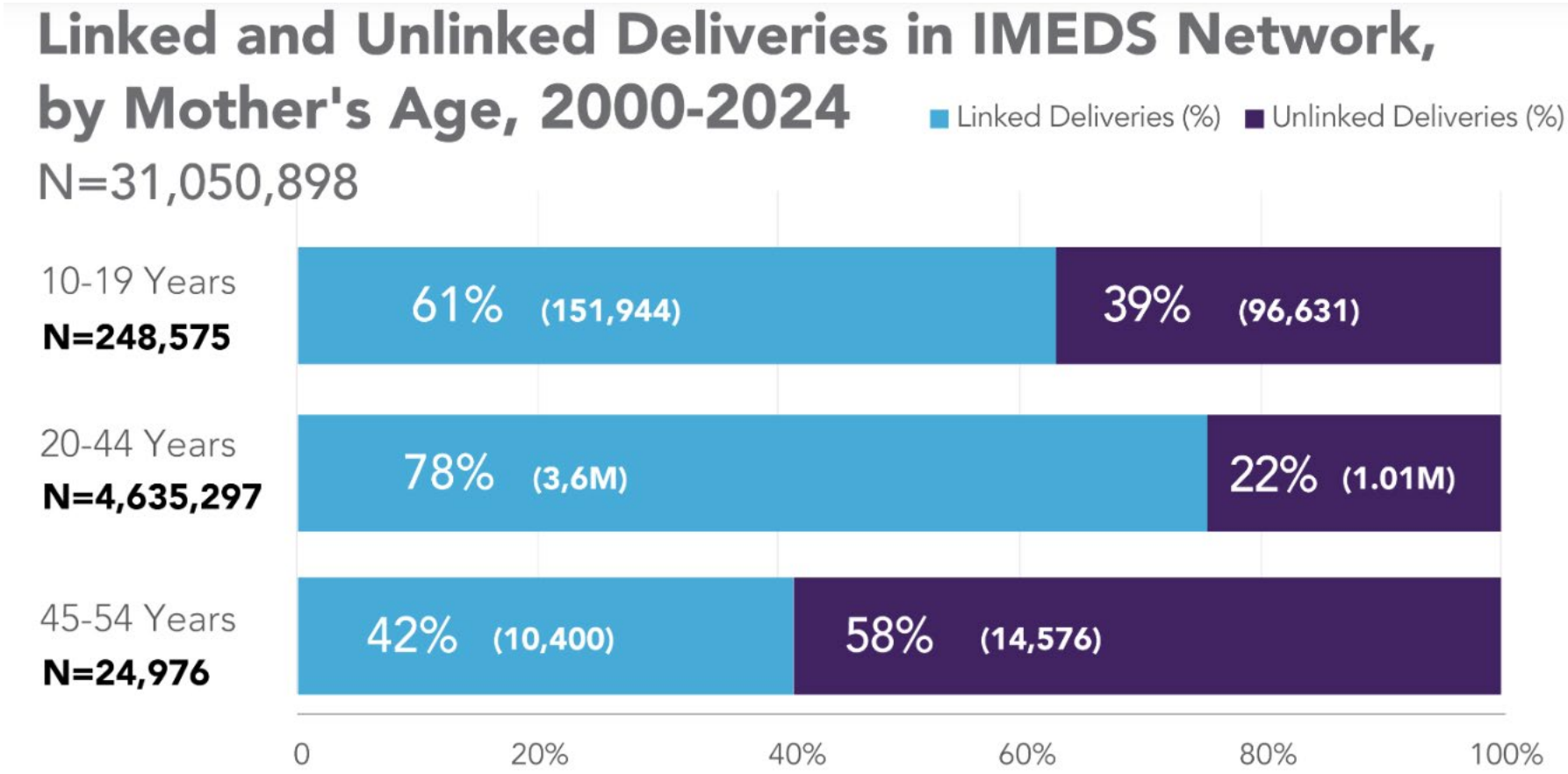
# IMEDS and Pregnancy Data

## Numbers of Deliveries in IMEDS Network, by Year and Linkage Status



REAGAN-UDALL FOUNDATION FOR THE FDA

# IMEDS and Pregnancy Data



# Ahh, but even with large cohort RWD and investigators inculcated into a culture of rigorous data quality assessment vis-à-vis the use and development of FDA tools

- Mom-baby linkage?
- Data reliability (do the data represent what we think they represent? Missingness, Provenance, syntactic, semantic accuracy)
- Accuracy of algorithms/c-phenotypes to define population, covariates, outcomes, exposure
- STILL sample size issues when we pursue questions of rare exposure for even rarer outcomes

# Develop and Deploy Regulatory Science Tools to Support Real-World Pregnancy Studies

PDS Pharmacoepidemiology & Drug Safety

ispe Official Journal of the International Society for Pharmacoepidemiology

ORIGINAL ARTICLE | Open Access

## The Oncology QCARD Initiative: Fostering efficient evaluation of initial real-world data proposals

Donna R. Rivera, Joy C. Eckert, Carla Rodriguez-Watson, Catherine C. Lerro, Monica M. Bertagnolli, Rebecca A. Hubbard, Lawrence H. Kushi, Jennifer L. Lund, Deborah Schrag ... See all authors

First published: 27 October 2024 | https://doi.org/10.1002/pds.5818 | VIEW METRICS

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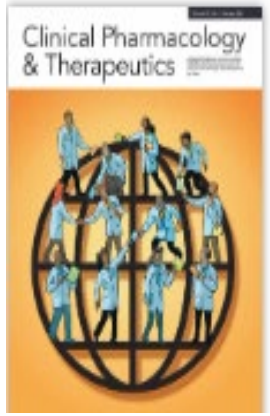



Volume 119, Issue 1
January 2026
Pages 131-138

## Developing and Refining the Pregnancy Algorithm CErtaInty Tool (ACE-IT) for Validating Pregnancy Outcomes

Sonal Singh, Hsiao-Ching Huang, Susan E. Andrade, Lesley Butler, Sangmi Kim, Maryline Le Noan-Lainé, Simone Pinheiro, Laura Shaughnessy, Ollie Desrochers, Carla Rodriguez-Watson

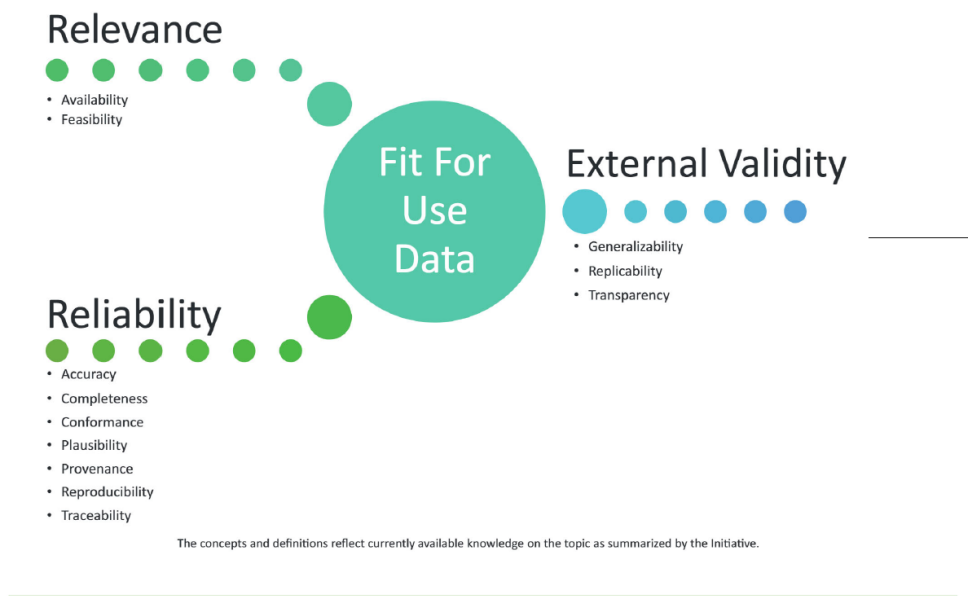
First published: 18 August 2025 | https://doi.org/10.1002/cpt.70036 | VIEW METRICS

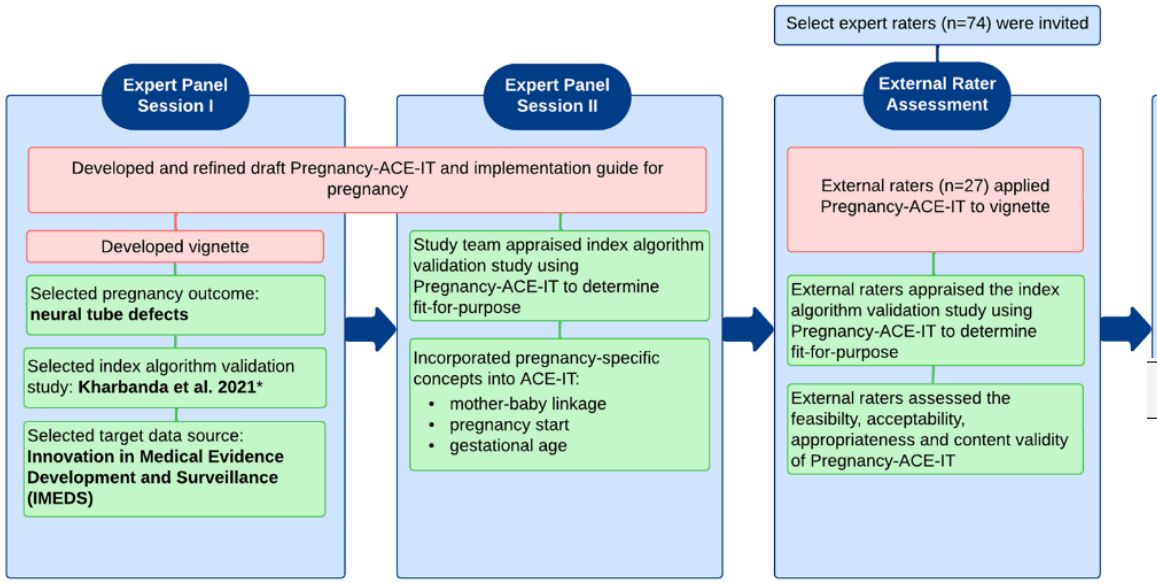
# The Oncology QCARD Initiative: Fostering efficient evaluation of initial real-world data proposals

**TABLE 2** (Continued)

| Section II. Study design parameters | |
|---|---|
| F. MEASUREMENT OF KEY COVARIATES<br>A variable, other than the exposure of interest, expected to potentially influence the outcome variable(s) to be analyzed. | |
| (1) Key covariates | Including and not limited to demographic, baseline, and clinical covariates. Please include a brief statement about available data to address intercurrent events or post-baseline confounding factors, as feasible, if applicable to the study. |
| G. STATISTICAL ANALYSIS | |
| (1) Brief summary of the planned main statistical analyses of the primary endpoint(s) | Including principal methods to control for bias and confounding, where applicable. |
| H. DATA QUALITY ASSURANCE | |
| (1) Auditing plan | Source data auditing feasibility in accordance with Good Clinical Practice such that source records (i.e., original records or certified copies) are available to FDA and data integrity assurance is provided in accordance with Bioresearch Monitoring (BIMO) and Guidance on 21 CFR 11. |
| (2) Data provenance documentation plan | Any available provenance documentation planned/under development (brief summary 250 words max) or already established for the relevant data source(s). For example, documentation to ensure that the relationship between records, source data, and all associated metadata can be preserved in a secure and traceable manner.[37,38] |
| (3) Data quality control plan | A description or reference to a description of any established data quality control plans planned/under development (brief summary 250 words max) or already established for the relevant data source(s). For example, policies and procedures in place to address issues such as errors in coding or interpretation of source documents, data entry, cleaning, transfer, and linkage. |
| (4) Missing data plan | A brief summary of data missingness and plans for evaluating and addressing missingness that are planned/under development (brief summary 500 words max). |








*Kharbanda EO, Vazquez-Benitez G, DeSilva MB, et al. Developing algorithms for identifying major structural birth defects using automated electroni Drug Safety. 2021;30(2):266-274.

Clinical Pharmacology & Therapeutics

Article | Full Access

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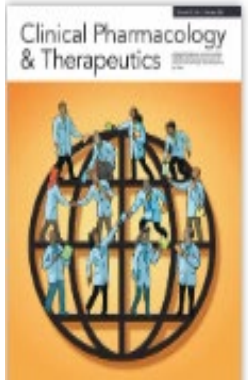
| | | | | | |
|---|---|---|---|---|---|
| | | ***Study Population*** | | | |
| 3 | **Are inclusions and exclusions of study participants in the index algorithm validation study adequately reported and justified?** | We included this item as the inclusion and exclusion of participants may result in a selection bias that may influence accuracy measures. Studies should describe the number of included and excluded participants and the reasons for inclusion and exclusion. The individual evaluating fit for purpose will need to assess the characteristics of included participants and differences with those of excluded participants if those are available. The individuals must also determine how these influence measures of accuracy. Sensitivity analysis may be conducted to determine the influence measures of accuracy. These may be acceptable if the amount of missing data is small and unlikely to impact findings. For example, if chart retrieval for algorithm validation is <100%, non-random capture of charts could introduce sampling bias. Pregnancy outcome validation studies should clarify whether pregnancy episodes and start date were identified based on electronic health care data recorded during the prenatal window (e.g., gestational age (GA) was calculated by the health care provider relying on self-reported last menstrual period) or estimated based on recorded services as ICD-10-CM codes or based on the pregnancy outcomes [5]. | Yes ☐ | No ☐ | N/A ☐ |


ONE RING TO RULE
THEM ALL

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# Fit for use/ Fit for purpose

# Visioning for a coordinated effort

## Opportunities

# Totality of Evidence Approach

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- Integrated research system:
  - Retrospective healthcare utilization data to identify eligible populations
  - Prospectively recruit
  - Link claims and EHR data at health care level to ease data collection burden (for patients/clinicians)
- Technological Considerations
  - Mobile platforms → Remote participation
  - Blue-button technology to ease consent
  - Tokenization
- Pre-competitive Collaboration
  - One registry for all drugs or pregnancy/condition registry to reduce duplication and patient burden of separate drug registries
- Policy and Regulatory Science Practice
  - Increase Sentinel or other reliable electronic data cohort use prior to PMR
  - Publicly Sponsored Disease Registries
  - Build Pregnancy Study Network
  - Increase understanding of "Fit RWD"
    - Algorithm/Data Development Frameworks, Catalog and Updates • Guidance for when chart validation is needed

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# Thank you! Let's keep the discussion going!

crodriguezwatson@reaganudall.org

# Pregnancy Registries (different types) and RWD have complimentary roles in RWE generation

| Randomized, Interventional Study | | Nonrandomized, Interventional Study | Nonrandomized, Noninterventional Study |
|---|---|---|---|
| **Traditional randomized trial using RWD in planning** | **Trial in clinical practice settings, with pragmatic elements** | **Externally controlled trial** | **Observational study** |
| RWD used to assess enrollment criteria and trial feasibility<br><br>RWD used to support selection of trial sites | Selected outcomes identified using, e.g., health records data, claims data, or data from digital health technologies<br><br>RCT conducted using, e.g., electronic case report forms for health records data or claims data | Single-group trial with external control group derived from RWD | Cohort study<br><br>Case–control study<br><br>Case–crossover study |

Generation of RWE

Increasing reliance on RWD

*Concato J, Corrigan-Curay J. Real-World Evidence - Where Are We Now? N Engl J Med. 2022 May 5;386(18):1680-1682. doi: 10.1056/NEJMp2200089. Epub 2022 Apr 30. PMID: 35485775.*

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# The IMEDS Network

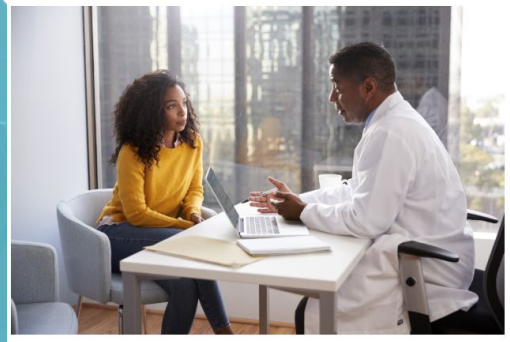
- CVS Healthspire Life Sciences Solutions
- Harvard Pilgrim Health Care
- Carelon Research, Inc.
- Health Partners Institute
- Humana Healthcare Research
- Kaiser Permanente Washington Health Research Institute
- Marshfield Clinic Health Systems
- Vanderbilt University Medical Center
- University of Massachusetts Chan Medical School Division of Health Systems Science

# **IMEDS** Post Market Requirement Studies

## Risankizumab Study in Crohn's with AbbVie

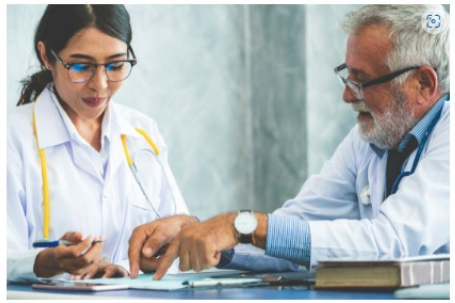
**Project Title:** Pregnancy Exposures and Outcomes in Women with Crohn's Disease Treated with Risankizumab: A Cohort Study Utilizing Large Electronic Healthcare Databases with Mother-Baby Linkage in the United States
**Project Sponsor:** AbbVie
**Project Status:** Current
**Product:** Risankizumab
**Conditions:** Crohn's Disease
**Summary:** To help fulfill a requirement from the European Medicines Agency (EMA), IMEDS was contracted to help design and execute a study to assess the safety of Risankizumab among women with Crohn's Disease during pregnancy. The risk of pre-specified pregnancy and outcomes will be estimated in pregnant women with Crohn's Disease and are exposed to Risankizumab, as well as in those exposed to comparator biologics (anti-tumor necrosis factor (TNF), integrin receptor antagonist biologics or their biosimilars [comparator biologic-exposed group]).

## Entresto® Study with Novartis



**Project Title:** Database cohort study to assess the risk of serious angioedema with LCZ696 (sacubitril/valsartan; Entresto®) use in Black patients with heart failure in the United States
**Project Sponsor:** Novartis
**Project Status:** Current
**Product:** LCZ696 (sacubitril/valsartan; Entresto®)
**Conditions:** Serious angioedema, Heart failure
**Summary:** The Reagan-Udall Foundation for the FDA (FDA Foundation PI: Carla Rodriguez-Watson) was recently awarded a contract to assess the risk of serious angioedema in association with LCZ696 (sacubitril/valsartan; Entresto®) use in Black patients with heart failure in the United States. This unique study leverages data from the Innovation in Medical Evidence Development and Surveillance (IMEDS) Network and the Center for Medicare and Medicaid (CMS). The research activities are a collaborative effort between the Novartis research team, the IMEDS Operations Center at FDA Foundation, the IMEDS Analytic Center at HPHCI, and participating IMEDS Network Partners.

## Ertugliflozin Study with Merck



**Project Title:** Post-authorization safety study to assess the risk of diabetic ketoacidosis among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents (AHA)
**Project Sponsor:** Merck
**Project Status:** Current
**Product:** Ertugliflozin
**Conditions:** Diabetic ketoacidosis, Type 2 diabetes mellitus
**Summary:** The Reagan-Udall Foundation for the FDA (FDA Foundation PI: Carla Rodriguez-Watson) was recently awarded a contract to leverage data from the Innovation in Medical Evidence Development and Surveillance (IMEDS) Network to continue implementation of a study titled: "Post-authorization safety study to assess the risk of diabetic ketoacidosis among type 2 diabetes mellitus patients treated with ertugliflozin compared to patients treated with other antihyperglycemic agents (AHA)" (EU PAS Register number: EUPAS31378). This work is being conducted to fulfill a requirement from the European Medicines Agency (EMA). The research activities are a collaborative effort between the Merck research team, the IMEDS Operations Center at FDA Foundation, the IMEDS Analytic Center at the Harvard Pilgrim Health Care Institute, and participating IMEDS Network Partners.

- Click to view the European Union electronic Register of Post-Authorisation Studies (EU PAS) register number (EUPAS31718)

## Risankizumab Study in Psoriasis with AbbVie

**Project Title:** Pregnancy Exposures and Outcomes in Women with Psoriasis Treated with Risankizumab: A Cohort Study Utilizing Large Electronic Healthcare Databases with Mother-Baby Linkage in the United States
**Project Sponsor:** AbbVie
**Project Status:** Current
**Product:** Risankizumab
**Conditions:** Psoriasis, Pregnancy
**Summary:** To help fulfill a requirement from the European Medicines Agency (EMA), IMEDS was contracted to help design and execute a study to assess the safety of Risankizumab among pregnant women with psoriasis. The risk of pregnancy, birth and infant outcomes will be estimated in pregnant women exposed to Risankizumab, as well as in those exposed to comparator biologics including anti-tumor necrosis factor (TNF), interleukin (IL)-17 biologics or their biosimilars (comparator biologic-exposed group).

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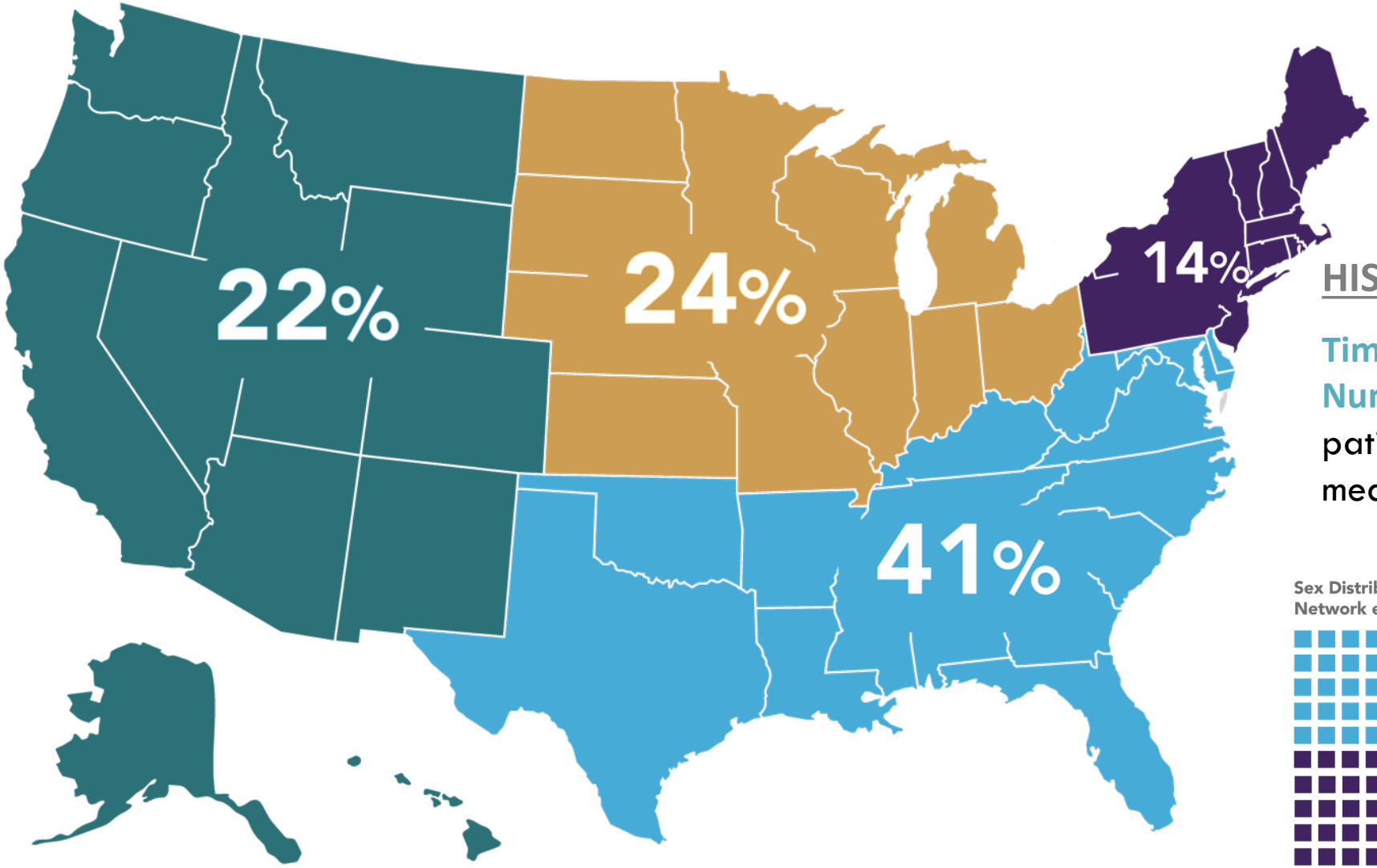
# Data are representative of the insured U.S population

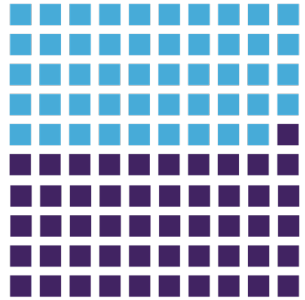


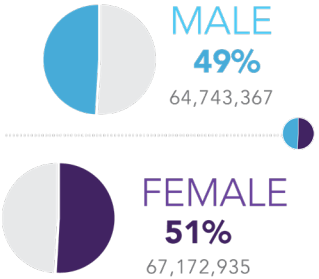

## HISTORICAL DATA

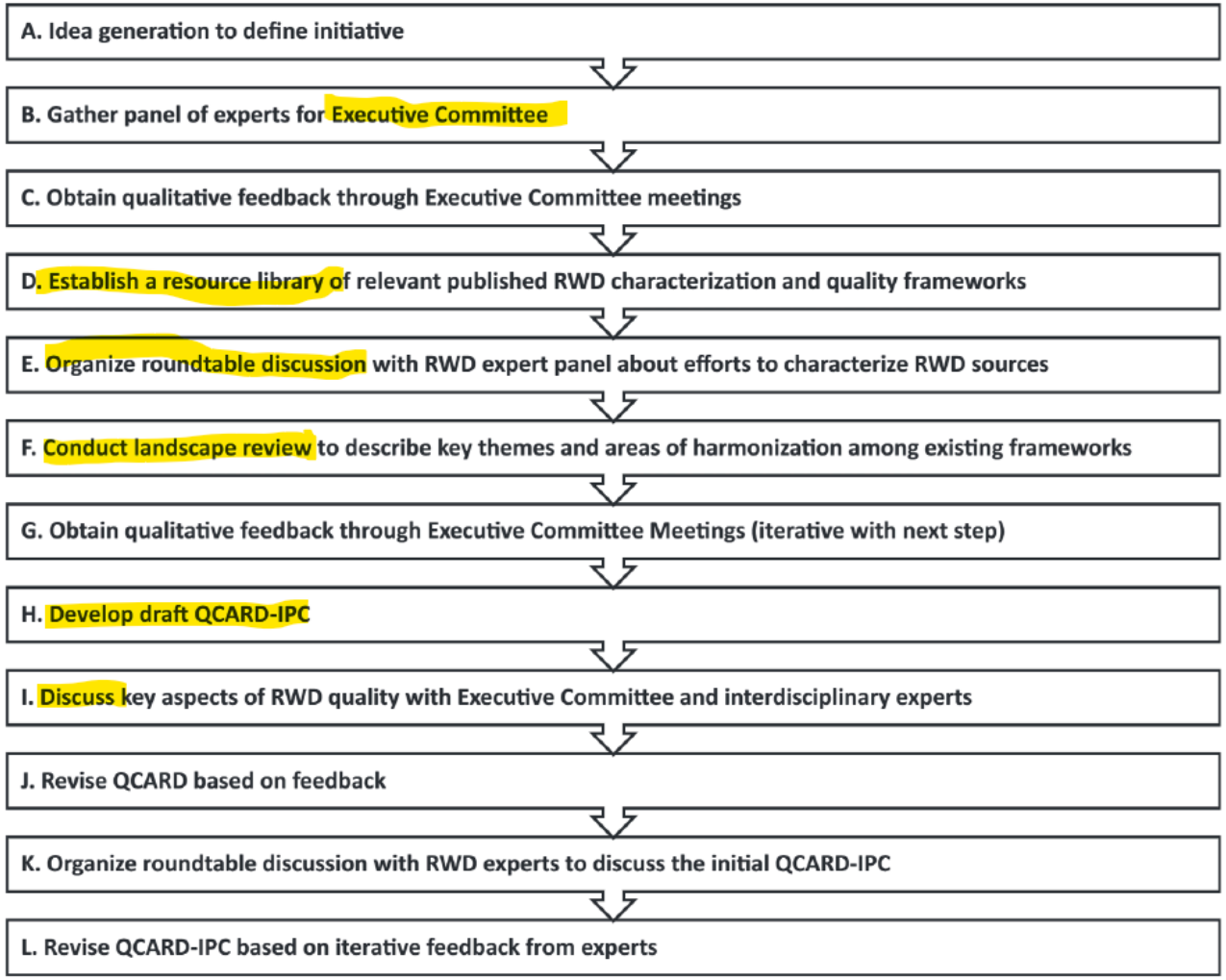
**Timespan** = 2000 - 2024

**Number of Patients** = 110M patients with at least **6** months of medical coverage

**Sex Distribution of Patients in the IMEDS Network ever enrolled, 2000-2024**








Oncology QCARD development process.

## QCARD PROCESS

**Discuss.**
**Gather Resources.**
**Review landscape.**
**Discuss. Draft.**
**Discuss. Revise.**
**Discuss. Finalize.**

*Beyond multi-product registries and registry networks:*

# Can a single, national pregnancy registry fill knowledge gaps more efficiently and quickly?

**Optimizing Pregnancy Registries Public Workshop**

May 7–8, 2026

**Christina Chambers, MPH, PhD**

Professor, Department of Pediatrics
School of Medicine
University of California San Diego

# Disclosures

Receive/d research funding from AbbVie, Amgen, AstraZeneca, Bristol Myers Squibb, CSL, Gerber Foundation, Gilead, GSK, J&J, Leo, Lilly, Novartis, Pfizer, Regeneron, Roche, Sanofi, Sun, Takeda, UCB

# The Scale of the Problem

**70%**

of pregnant people
take ≥1 medication

**<1%**

of drug trials
include pregnant patients

**2.6**

avg medications
per pregnancy

**4M+**

births annually
in the US

- Observational studies including pregnancy registries are a key source of safety data for new medications

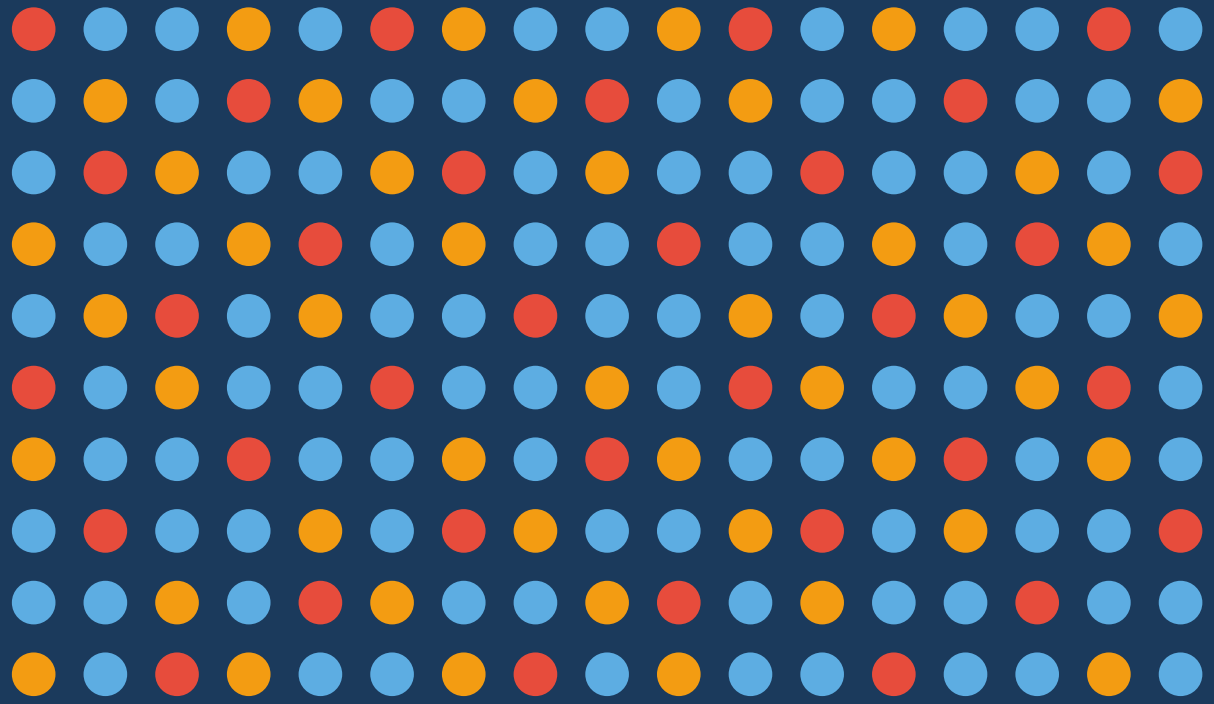
# Relative Advantages of a Pregnancy Registry

| Pregnancy Registry | EHR Data | Claims / Admin Data |
|---|---|---|
| **Drug exposure**<br>Directly from mother — exact gestational timing, dose, indication, brand | May be recorded; often incomplete or missing | Prescription or fill only — no data on adherence, shared or out of network medications |
| **Covariates & confounders**<br>Prospective — OTC use, supplements, smoking, alcohol, folic acid, demographics | Partially recorded; inconsistent across sites | Very limited — lifestyle factors, OTC, others not captured |
| **Prospective design**<br>Prospective — enrolled before outcome known, eliminates some recall bias | Retrospective but not reliant on voluntary consent | Retrospective but not reliant on voluntary consent |
| **Maternal interview**<br>Structured interviews capture key data and can be adapted for specific circumstances | No structured interview — provider notes only | No interview — billing codes only |
| **Pregnancy outcomes**<br>Loss, preterm delivery, malformations, growth, development, and can be adapted | Variable completeness; may require manual chart review | Relies on accurate coding of outcomes |

*Registry data is not a replacement for EHR or claims — it is the layer that captures what no administrative system records: the mother's voice, the full exposure story, and the infant outcomes.*

# The Current Reality: 170+ Fragmented Registries

*170+ single-drug registries currently active in the US*



## What providers & patients face today

**Is there even a registry for my drug?**

*170+ options — or none at all for many drugs*

**How do I find the right registry?**

*Someone has to search*

**Does my patient / do I even qualify?**

*Registries have different eligibility criteria*

**Why share confidential data if results are years away?**

*Drug-specific registries often slow to enroll*

**Will my contribution actually matter?**

*Single-drug registries may never achieve interpretable N*

→ *Fragmentation breeds confusion, erodes trust, and slows enrollment — leaving clinicians without the safety evidence they need to counsel pregnant patients.*

# What if We Established One Nationwide Universal Registry?

# Operational Advantages of a Universal Registry

### Simple enrollment for patients & providers

One registration portal - patients enroll once; providers refer to a single workflow — reducing confusion and improving participation rates

### Faster time to usable data

Continuous enrollment across all drugs; periodic review and analysis when thresholds are met; appropriate comparator pregnancies.

### No artificial sample size targets

Grows continuously, eliminating arbitrary enrollment targets. Further, all drug exposures (new and older) are eligible for study

### Adaptable to specific drug or new safety concerns

When a new drug or safety signal emerges, the existing platform can expand to capture

### Incorporates new data types and capture technologies

Integrates data from EHR and claims for those in the registry; complementary data from EHR and claims for context; data capture technologies (e.g., wearables) added; biorepository

### Cost savings through economies of scale

One system costs a fraction of running dozens of isolated registries.

### Build trust & reduce burden for providers and patients

A single, visible registry demonstrates that contributions lead to clinically relevant safety data as quickly as possible — building the trust needed to sustain long-term enrollment from providers and patients.

# Scientific Advantages of a Universal Registry

## Common Data Elements (CDEs)

A universal registry mandates a shared set of data definitions, variable names, and measurement standards across all drugs. CDEs ensure that:

- Data from different drugs are directly comparable
- Regulatory submissions use consistent, accepted terminology
- Findings are unambiguous and auditable

### Cross-drug comparability

Direct comparison of outcomes across drug classes, revealing patterns invisible to siloed registries.

### Auditable & transparent methods

Registry process open to external scrutiny and peer review.

## Rigor & Reproducibility

A single protocol with standardized methods enables scientific reproducibility — a cornerstone of evidence-based medicine. This means:

- Outcomes defined prospectively
- Independent researchers can replicate and validate findings
- Reduced risk of selective reporting or publication bias
- Higher evidentiary standard for FDA label changes

### Foundation for secondary research

A standardized dataset enables pharmacoepidemiology, machine learning, and hypothesis generation beyond drug safety.

### Companion biorepository

A linked biorepository of maternal/infant blood, urine, saliva, stool, milk, etc., enables further research

# MotherToBaby: A Working Model

## MotherToBaby National Pregnancy Cohort

*Existing single national cohort study with one umbrella IRB approved protocol*

**Drug A Registry**

**Drug B Registry**

**Drug C Registry**

Drug D Registry

Sponsor D

**+ More...**

*Each registry separately managed & separately sponsored*

mothertobaby.org/pregnancy-studies

## Key Features

- Prospective observational cohort — women enrolled before outcome known
- Mother is primary source of exposure & covariate data via structured interviews
- Standard follow-up protocol: phone interviews during pregnancy + post-delivery
- Medical records, birth outcomes, and infant follow-up collected for all participants
- Results update drug labeling and inform clinical guidance resources (LactMed, TERIS, Reprotox)
- Linked to national breast milk biorepository

# MotherToBaby: One Cohort, Many Exposures

*The MotherToBaby national pregnancy cohort has generated safety evidence across a wide range of exposure categories — demonstrating that a single platform can address multiple simultaneous research questions:*

## Vaccines and Antivirals

Influenza · COVID-19 · Tdap · Meningococcal ·Vaccines

## Autoimmune & Biologic Drugs

TNF inhibitors · IL-X inhibitors · vedolizumab · small molecules MS medications

## Asthma & Allergy Medications

Inhaled corticosteroids · montelukast ·

## Secondary Data Analyses

Medications to treat nausea and vomiting

## Secondary Data Analyses

Disease severity; consequences of discontinuing treatment

## Secondary Data Analyses

Prescription opioid use for pain

# The Cost Efficiency Argument

## $2.5 Billion

Estimated cost of 170 pregnancy registries @ $15M each over 10 years

## $680 Million

Estimated cost of one pregnancy registry with shared comparators

## One System vs. Dozens

Running a single universal registry eliminates redundant infrastructure costs across multiple drug-specific registries and could save ~72% of costs over 10 years.

# Benefits to the Pharmaceutical Industry

*A universal registry would not a burden on industry — it is shared infrastructure that delivers direct value to every pharmaceutical sponsor.*

- **Fulfills postmarketing commitments**
- **Shared infrastructure = lower cost**
- **Faster path to label update**
- **Accelerates drug development**
- **Reduced litigation exposure**
- **Supports global regulatory alignment**
- **Targeted signal detection**
- **Builds patient & prescriber trust**
- **Scalable to new products**

# How Could a Universal Pregnancy Registry Be Funded?

## Stream 1 — Collaboration Across Existing Registries

***Consolidation rather than duplication (Coordinated Registry Network)***

## Stream 2 — Pooled Industry Resources

***Shared cost; proportional to market share (Public-Private Partnership)***

## Stream 3 — PDUFA VIII User Fee Commitment

***A small portion of user fees could be allocated for this purpose***

→ *The three streams are complementary and could operate simultaneously creating a durable funding model.*

# The Real Consequences of "Business as Usual”

- Prescribers left without guidance
- Subtherapeutic treatment harms mothers
- Potential fetal risk from un- or under-treated disease
- "No data" ≠ "safe"

# PRGLAC Recommendations: Optimize Pregnancy Registries

*Task Force on Research Specific to Pregnant Women and Lactating Women · HHS Report to Congress & Secretary · September 2018*

**RECOMMENDATION 13: Optimize Registries for Pregnancy and Lactation**

**User-friendly registry listing**

**Registry standards & common data elements**

**Transparency & data access**

**Disease/condition -focused registries**

→ *A universal pregnancy registry directly fulfills PRGLAC Rec. 13.*

# Thank You

MotherToBaby
PREGNANCY STUDIES

mprint

VAMPSS
Vaccines and Medications
in Pregnancy Safety Studies

Mommy's Milk
HUMAN MILK RESEARCH BIOREPOSITORY

UC San Diego
Health Sciences

BRIDGE
Better Research, Information and
Data Generation for Empowerment
of Women of Childbearing Age

U.S. FOOD & DRUG ADMINISTRATION

# Session 3: Future Directions Panel Discussion

U.S. FOOD & DRUG ADMINISTRATION

# Workshop
# Closing Remarks