The Emergence of RWE – Future Directions in the Regulatory and HTA space

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Disclosures

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The opinions, results and conclusions reported are those of the authors and are independent from the funding sources.

ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

"These pills will help you stay asleep. They change your dreams into Powerpoint presentations!"

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REAL-WORLD EVIDENCE
IS SO HOT RIGHT NOW!
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My 3 promises

1. You will better understand real-world evidence and the current landscape in Canada

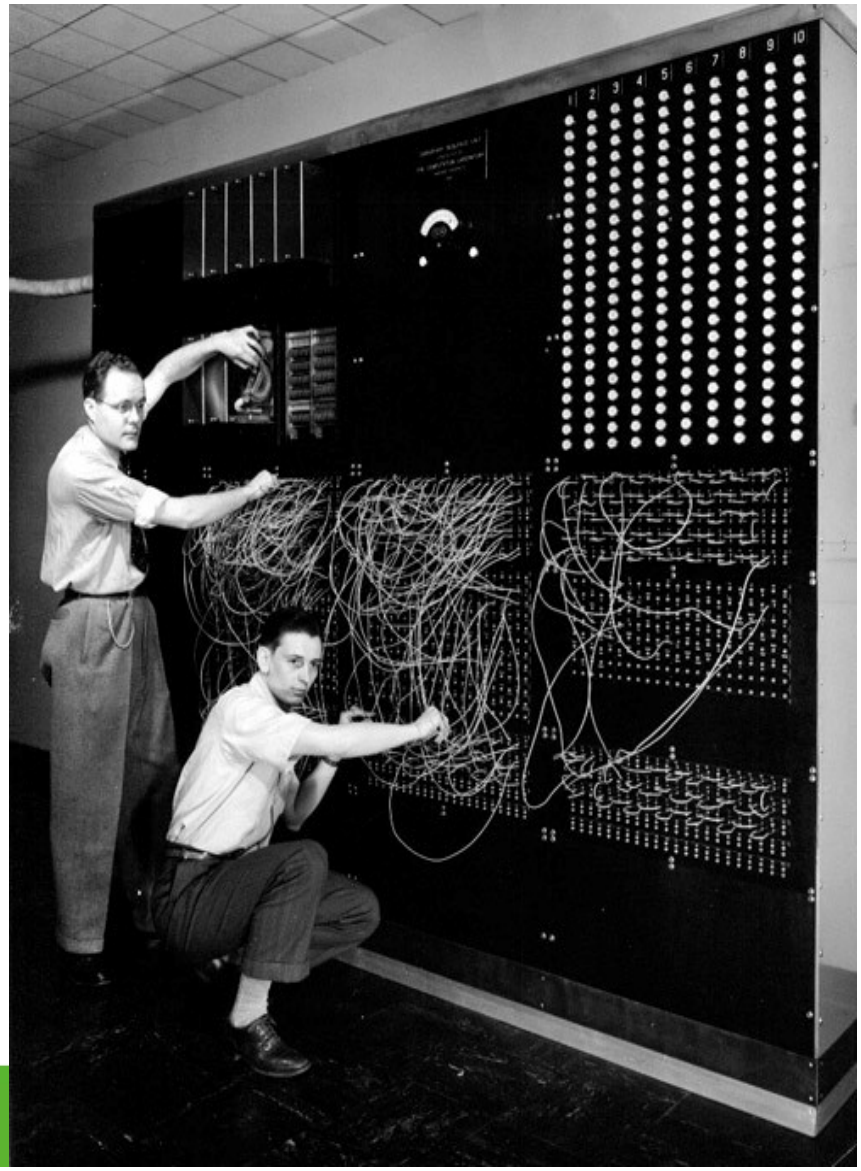
2. Understand how this will change the way we approve and use medications

3. Get some tips for appraisal and you will get sick of cartoons

What is big Data?

What is data?

- Data- facts and statistics collected for references and analysis
  - Big data is just like small data but bigger- way bigger!
- Simply- a set of values
  - List of names and phone numbers
  - Dates of evets
  - Identifying information
- Linking of information becomes powerful



Big Data Everywhere!

- Lots of data is being collected by businesses
  - Website data (number of clicks)
  - e-commerce (what you buy)
  - Purchases at department/ grocery stores
  - Bank/Credit Card transactions
  - Social Network (Facebook)
  - Healthcare data (Drugs, diagnosis)

What is Real-World Evidence (RWE)?

- Real-World Evidence (RWE) is using data collected from a variety of sources to help understand treatment approaches to improve patient health

- RWE provides important insights about patient experience and treatment implementation to be used in healthcare decisions

" RWE is not just "Big data" – it's the integration of multiple sources of data"

– NEHI 2015

Why Real-World Evidence (RWE)?

- Earliest use to assess post-marketing safety.
- Growing interest in integrating into reimbursement. Most evidence used for drug approval and reimbursement has been limited to clinical trial evidence
- Minimal generalizability to real-world populations
  - Healthy-user Bias
  - Polypharmacy
  - Various models of care
  - Off-label use
- Smaller Sample sizes
  - Post-approval studies often limited to studies of safety
  - Growing understanding and need for rare diseases and rarer indications

Sources of data (RWD) for RWE

- Data can include:
  - electronic medical records
  - health registries
  - administrative claims data

Administrative Claims Data

- Use of administrative data is a major area of opportunity to conduct RWE Studies

  Strengths:
  - Actual patterns of drug use in population
  - Large sample sizes and follow-up time
  - Quicker and less expensive

  Limitations:
  - Validity (billing versus research)
  - Limits in ability to assess some confounders (lifestyle, disease severity, OTC use etc.)
  - Confounder bias can impact data

- Continuing development of advanced methodology to address confounders and potential bias

Using Administrative Claims Data

- Secondary use of billing data: tracking claims

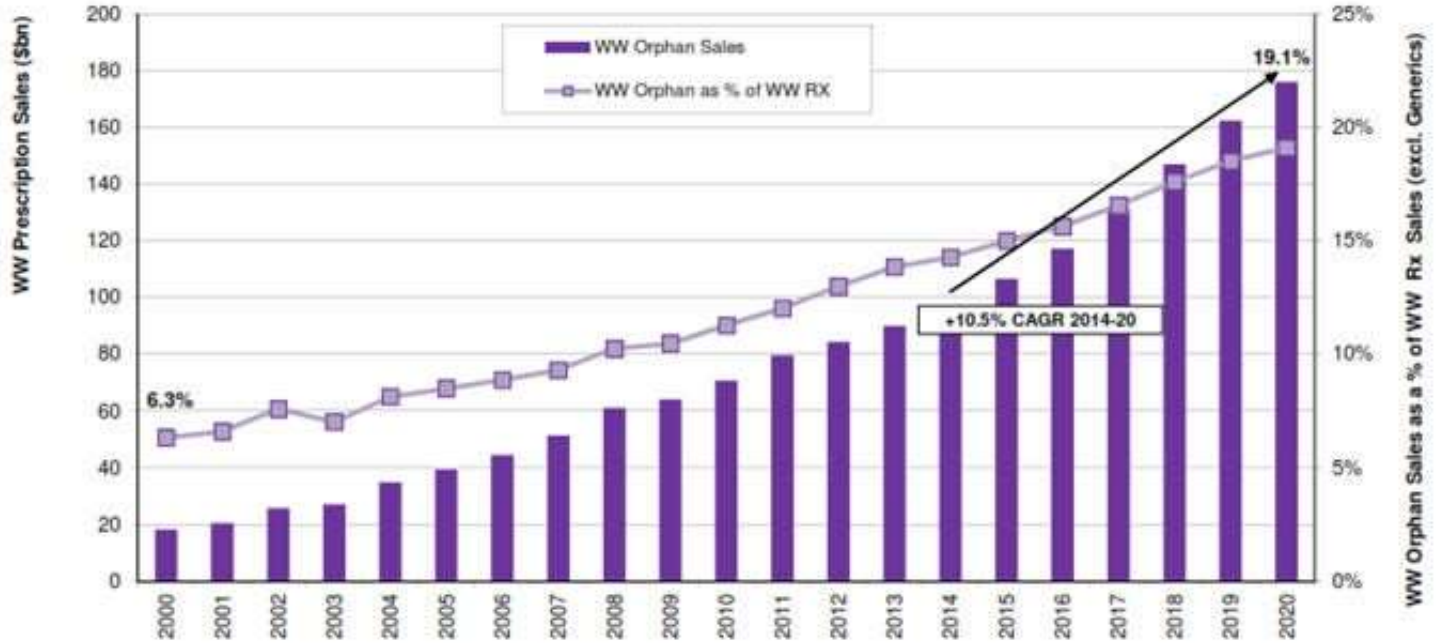
- Ability to link across pharmacy data, hospitalizations, Emergency rooms, visits to doctor's office, etc. This allows us to explore data such as:
  - Prescriptions
  - Cost (of medications and/or health services)
  - Demographics (age, sex, region)
  - Doctors visits
  - Past diagnoses and procedures

But Who cares and why now?

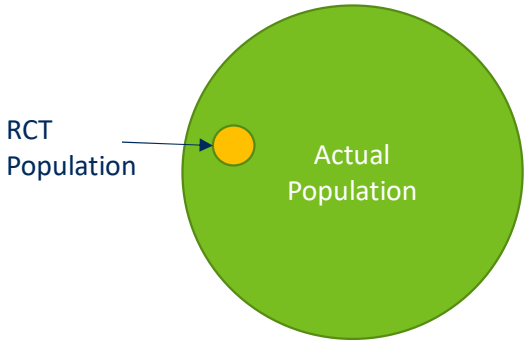
- Timing
  - Data flood
- Solves growing problems
  - Generalizability
  - Drugs for Rare diseases
  - Uncertainty
  - Value for money
- Promises unrealized
  - Formulary Modernization
  - Outcome-based re-imbursement
  - Optimal use of medicines

Rare is the new Normal

Worldwide Orphan Drug Sales & Share of Prescription Drug Market (2000-20)
Source: EvaluatePharma® (27 OCT 2014)



RCT Vs. RWE



A Drug Life- A tale of two cities

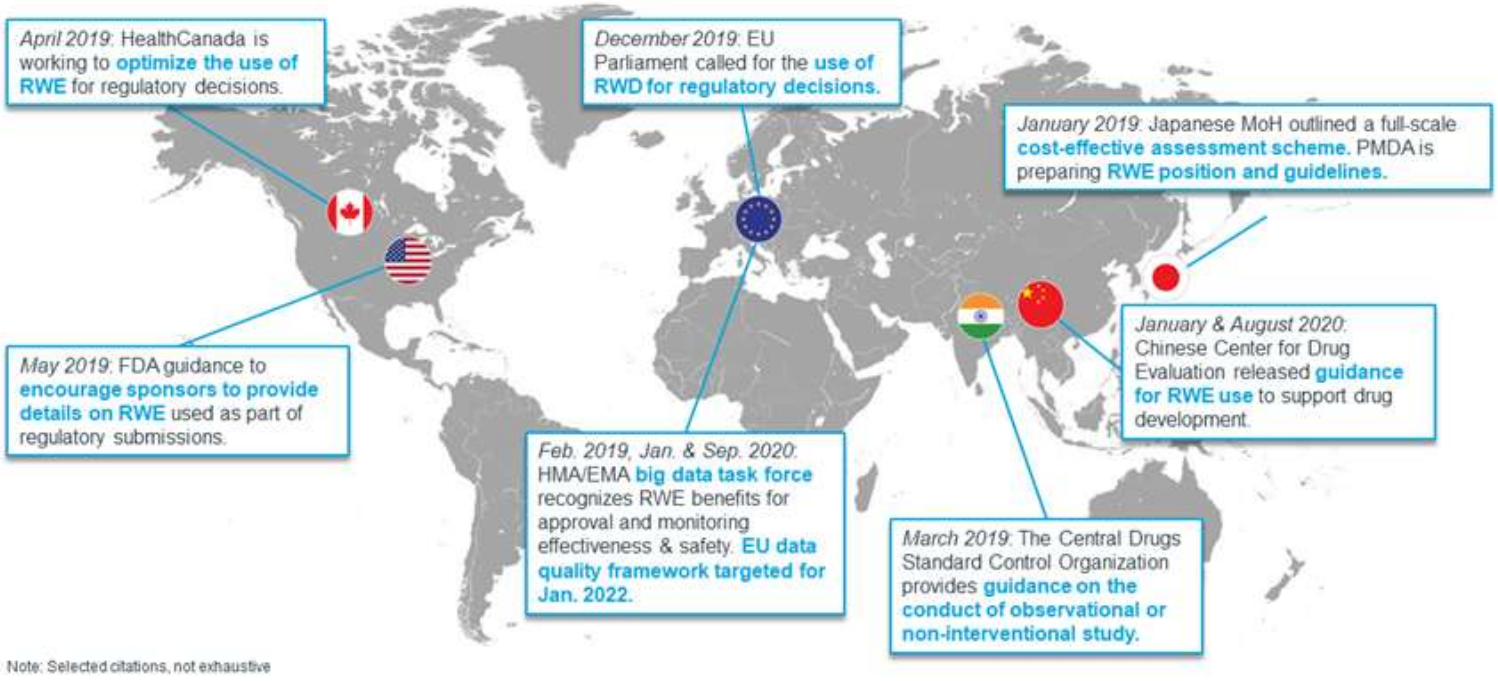
A Drug Life- A tale of two cities

- Currently less application
- Potential use in:
  - Budget Impact Analysis
  - Inputs into Economic Evaluations
  - Supplemental evidence submissions
- The golden grail is Outcome/performance based reimbursement
- The devil is in the details

A Drug Life- A tale of two cities

Re-Evaluation
and
Modernization

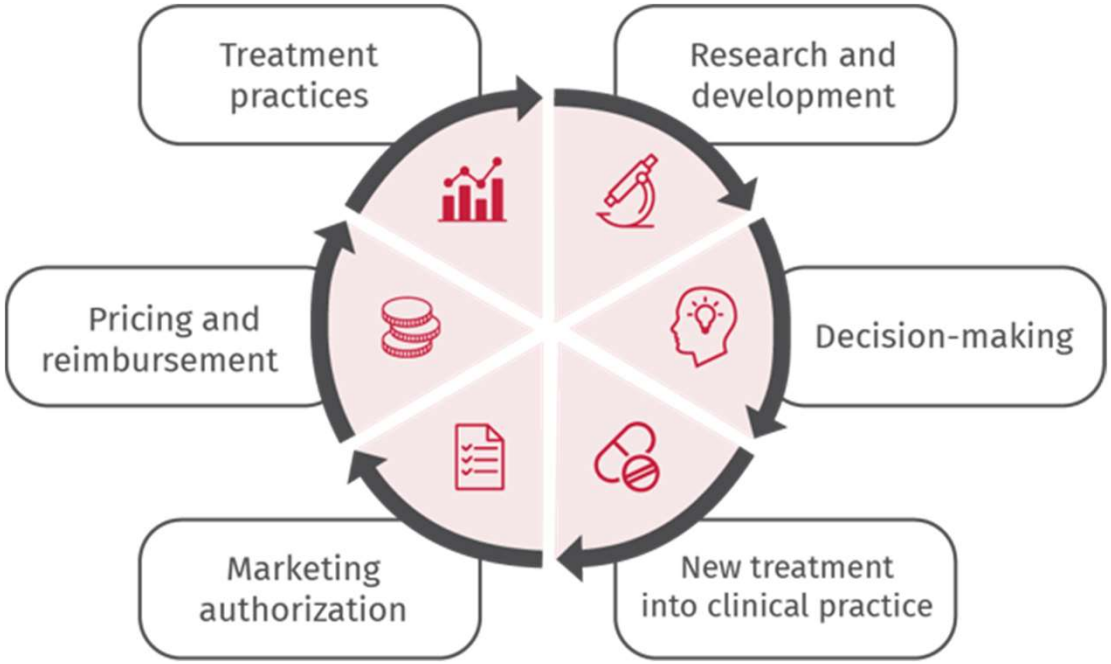
Global Flood of RWE



Note: Selected citations, not exhaustive

Source: IQVIA Global report

RWE is full drug lifecycle



Source: Medaaffcon

Okay- so what's next for RWE in Canada?

Holding pattern in Canada

Development of Canadian Guidance

To develop a Canadian RWE Guidance document to provide recommendations for both quality and reporting standards for all RWE submissions intended for use in any regulatory or health-technology submissions in Canada

Keep in Mind

Purpose – The guidance will provide recommendations for:

- Reporting standards
- Minimum standards for decision-grade RWE
- Regulatory or health-technology submissions
- Canadian context but aligned globally

Specific Target Users:

- Researchers conducting RWE studies for submission
- Employees of Health Technology and Pharmaceutical companies preparing submissions
- HTA and Regulatory Reviewers of submissions

Methods and Process

- Leveraged and updated on INESS Environmental of RWE tools and guidances
- Eliminated duplicate items and modified items into similar language to enhance usability and allow mapping of other important components

Translated into a questionnaire!

- Expert panelists completed the questionnaire, rating the importance of items for inclusion in the reporting guidance
- Importance rated on scale of 1-4 for inclusion
- Questionnaire determined what components should be included in draft guidance

Methods and Process

- Expert Panel discussed items that generated <70% ratings of agreement
    - Decision whether to keep, revise or omit each item
- General discussion on scope, content, and style of the guidance document
- Sub-group helped with usability of recommendations and construct of document

Methods and Process

- Additional in-depth discussion and asynchronous feedback were collected via email
- The insights from the first discussions and questionnaire were used by the Internal Team to draft the guidance
- Draft guidance was developed over the summer and shared with all for review and feedback in September
- The draft was posted for public and stakeholder review and feedback
- Proposed modifications will be reviewed in collaboration with the Expert Panel

Expert Panel Members

Canadian External

McGill
Robert Platt
Erin Strumpf

UofM
Lisa Lix

UNB
Ted McDonald

UBC
Mary De Vera

Laval University
Jason Guertin

IHE
Jeff Round

Dal
Sanja Stanojevic

CanREValue
Kelvin Chan

UofA,
RWE Consortium
Scott Klarenbach

Expert Panel Members

International

Harvard
Shirley Wang

NICE
Seamus Kent
Dalia Dawoud

Oxford (NDORMS)
Dani Prieto-Alhambra

FDA
Donna Riveria

Expert Panel Members

Internal Expert Members

CADTH
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Geneviève Plamondon
Tom Samaha

Stats Canada
Eric Dorff

Health Canada
Catherine Njue
Andrew Raven

CIHI
Roger Cheng

Authorship Leads
Mina Tadrous
Theresa Aves
Kaley Hayes

Results

Section (n=13 out of 15-panel members)	Number of questions	Overall Agreement	Drop
1. Study Design and Question	22	18 (82%)	2
2. Setting and Context	11	9 (82%)	0
3. Data Access and Cleaning methods	14	8 (57%)	1
4. Data Linkage	8	6 (75%)	2
5. Data Sources/Measurement	12	8 (67%)	0
6. Participants	22	22 (100%)	0
7. Exposure Definitions and Comparators	12	12 (100%)	0
8. Outcomes	18	12 (67%)	2
9. Variables (covariates and all variable measurement)	9	4 (44%)	0
10. Effect Modifiers	3	3 (100%)	0
11. Bias and Confounding	8	7 (88%)	2
12. Statistical Analysis	19	15 (79%)	0
13. Participant Characteristics	9	8 (89%)	0
14. Study Findings	12	12 (100%)	0
15. Limitations	9	8 (89%)	0
16. Interpretation and Generalizability	12	11 (92%)	2
OVERALL	**200**	**163 (82%)**	**11**

Stakeholder Feedback

- Public feedback open for 2 months November 2022- January 2023
- Reviewed all feedback internal and external
- Summarized major themes of feedback (response document)
  - Major changes- defined as changing the intent or messaging of the report were responded to
  - Methods-specific feedback was brought to experts and voted on for consensus (50+ points)- only 8 needed discussion.
  - Minor changes (ex. Typos/small word changes) were just made
  - CADTH, INESS, and Health Canada also developed responses for major feedback

Guidance screen shot

Home / Guidance for Reporting Real-World Evidence

Details

Files

Project Line:
Methods and Guidelines

Project Number:
MG0020-000

CADTH has partnered with Health Canada, the Institut national d'excellence en santé et en services sociaux (INESSS), and other health system stakeholders to advance the integration of real-world evidence (RWE) into decision-making. *Guidance for Reporting Real-World Evidence* lays the foundation for the use of RWE in regulatory approval and Health Technology Assessment (HTA) in Canada, starting with the principles for transparent reporting of RWE studies.

The development of this guidance was founded on the following main objectives:

- to ensure that regulators and HTA agencies have sufficient information to evaluate a study for its appropriateness of use for decision-making
- to provide core reporting standards for RWE studies that align with global standards
- to prioritize transparency in reporting while accounting for practical challenges related to RWD and RWE.

CADTH and Health Canada are the co-chairs of the **RWE Steering Committee**, which includes pan-Canadian health, government, and patient organizations; industry; academia; and data holders. The RWE Steering Committee provided support and oversight for this initiative and received quarterly updates from the *Guidance for Reporting Real-World Evidence* working group (WG). The *Guidance for Reporting Real-World Evidence* WG included a Methods Authorship Team, a Leadership Review Team, and an Expert Methods Panel including Stakeholder Panel members in Canada.

The *Guidance for Reporting Real-World Evidence* document includes a Recommendations Checklist, which can be used as a tool to ensure submissions adhere to the guidelines outlined in the document. This guidance was written in a manner that allows for flexibility in its use for a variety of RWE applications. As such, some recommendations in this document will not apply to all RWE studies. The summary lists of recommendations and the checklist are not intended to replace a careful review of the text, which contains critical information needed to develop adequate reporting.

A separate *Response to Stakeholder Feedback* report outlines the feedback received during the consultation process by theme and responses to feedback, including from regulatory and HTA perspectives.

For details on Health Canada's position on *Guidance for Reporting Real-World Evidence* and related documents to support the use of RWD/RWE in regulatory decision-making, please visit **Health Canada's website**.

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SO WHAT?

What does it Mean for regulators

Builds already on the status quo:

- Consider more NOC with conditions

- Further alignment with rare disease strategy

- Expansion of drug safety monitoring

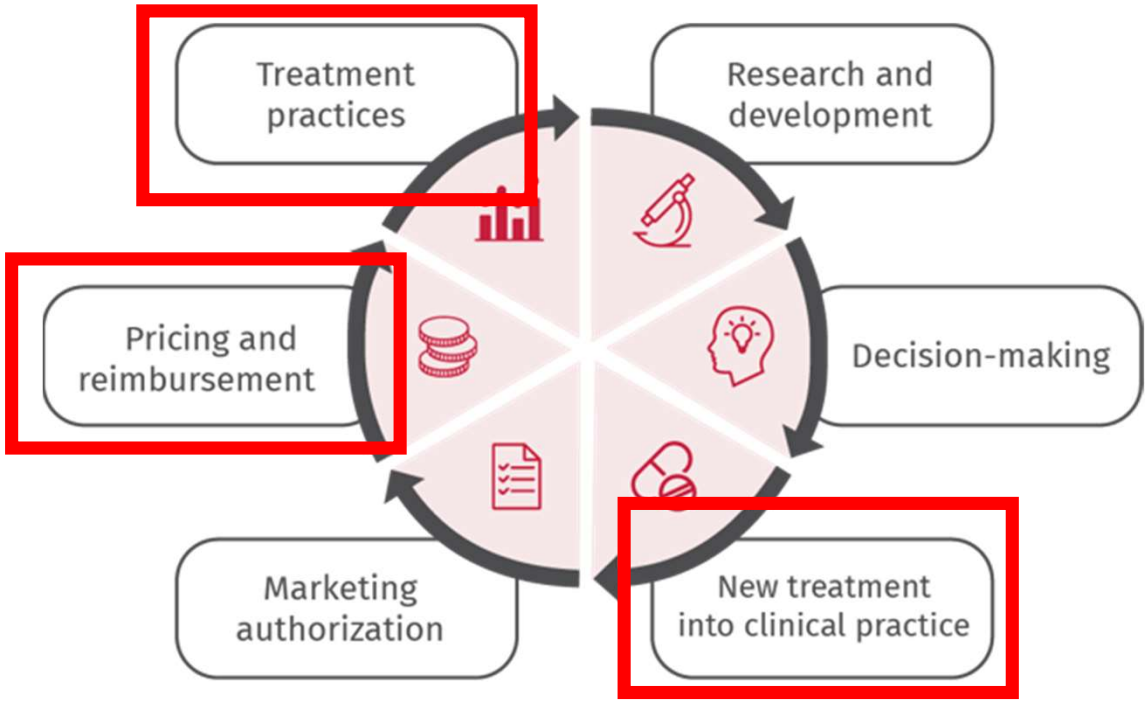
What does it Mean for HTA

Builds already on the status quo:

- inputs into models (ex. CEA models)

- Budge Impact Analysis

RWE is full drug lifecycle



Source: Medaaffcon

RWE re-shaping HTA (THE DREAM)

- Major Shifts we can dream of:
- re-evaluation and re-assessment
- Formulary Modernization
- Outcome-based agreements (OBA)
- Quality of inputs and more transparency

For Payers and Clinicians

- Change the way drugs are approved and evaluated
  - Potential faster access
  - De-listing
- Opportunity to join the data party
  - PSP data
  - Registry
  - Enrich data from pharmacies
- Evaluate Interventions and Health technology

For Patients

- Improved access to medications
- Optimal use for both safety and effectiveness
- Opportunity to feed into data easier for outcomes that matter (Patient-reported outcomes)

Important Thoughts

- RWD and RWE is changing fast
  - Solution is transparency
  - Think global.
- This is the first step
  - When to use this?
  - We will need to update/extend
- Time to train and build capacity
  - Internal reviews (HTA and Regulatory)
  - To conduct (opportunity for Canada)

Future steps for our team

- Need to establish a place to:
  - Bring people in this space together
  - Develop and tackle Public-Private Partnerships
  - Capacity building

Questions