Making Value-Based Agreements a Reality in Canada Through RWE

CAPT 2020 Conference

October 26, 2020

Welcome!

Objective

- To share information on how researchers and policy makers can collaborate to make value-based agreements (VBAs) a reality in Canada through real-world evidence (RWE) generation and frameworks.

Speaker Introductions

- Dr. Winson Cheung – Oncologist, University of Calgary, Alberta Health Services, Oncology Outcomes (O2)

- Barry Stein – President, Colorectal Cancer Canada

- Dr. Parneet Cheema – Oncologist, William Osler Health System, University of Toronto

- Sylvie Bouchard – Director of Drug Evaluation and Technology Assessment for Reimbursement, INESSS

- Dr. Judith Glennie – J.L. Glennie Consulting Inc. (moderator)

Housekeeping

- Please feel free to enter questions into the chat room.
  - We will pull from these for the Q&A segment.
- Presentations will be made available on the CAPT web site after the session.
- An evaluation survey will be sent out after the conference.
  - Feedback on this session and the whole event would be greatly appreciated.

Setting the Stage

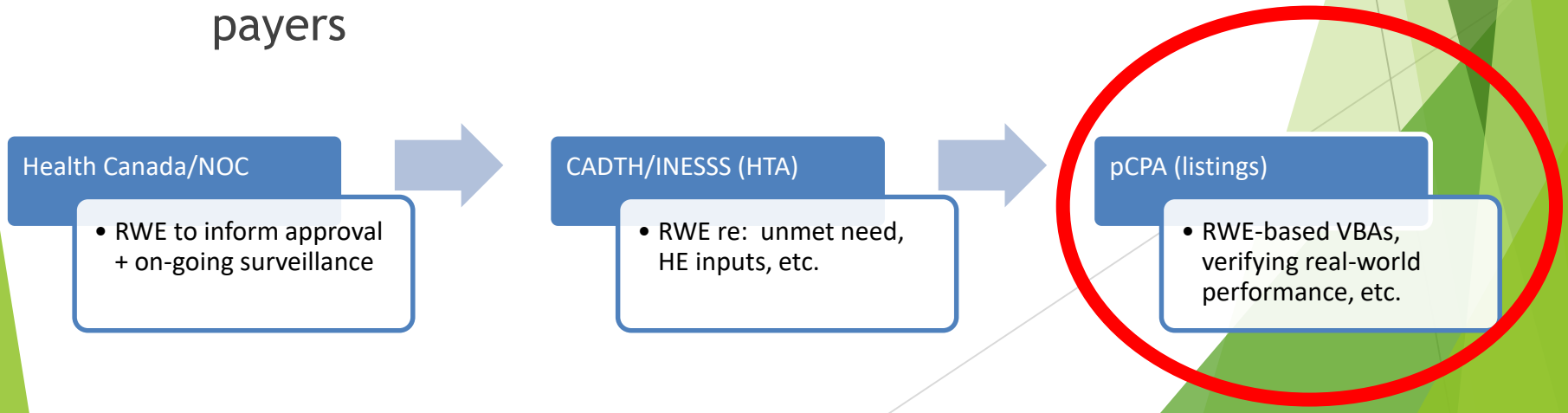
Dr. Judith Glennie

Background – Why are we doing this?

- Key area of policy change in Canada:
  - Determining the role of real-world evidence (RWE) generation and its relation to reimbursement decision making
- Processes appears to be stuck in neutral
  - Need for collaborative development of concrete frameworks so that we can move forward with this concept

Background – What is a VBA?

- For purposes of today's discussion, a value-based agreement (VBA) is:
  - A listing (i.e., funding) agreement that leverages real-world evidence (RWE) as a means of demonstrating the value of a product to decision-makers
  - Concept involves on-going data collection and analysis to address uncertainties regarding the value of the product that are of importance to payers



Background – Merits of VBAs?

Payer stakeholders see only a highly-limited and well-defined role for RWE-based VBAs.*

*Feairs, Glennie et al. CAPT 2019

- Allows payers to confirm value and adjust funding as appropriate
- Provides an evidence-based policy option:
  - In situations where there are high levels of clinical and economic uncertainty
  - In therapeutic areas where there is a genuine challenge in developing high quality research (e.g., rare diseases; rare cancers)

Pharmaceutical Managed Entry Agreements – Lessons Learned from Europe, the United States, Canada, and Australia (Grubert and MORSE; December 13, 2018)

So, our goal for today….

- To advance discussions on policies that will help define the role of RWE-based VBAs in patient access to medications

How can we collaborate to make VBAs a reality through RWE generation and frameworks?

Agenda:

1. Presentations on RWE and VBAs from different perspectives
   - Researcher
   - Patient
   - Clinician
   - Decision-maker/HTA
2. Audience Q&A

RWE and VBAs – An RWE Researcher Perspective

Dr. Winson Cheung

Why RWE now?

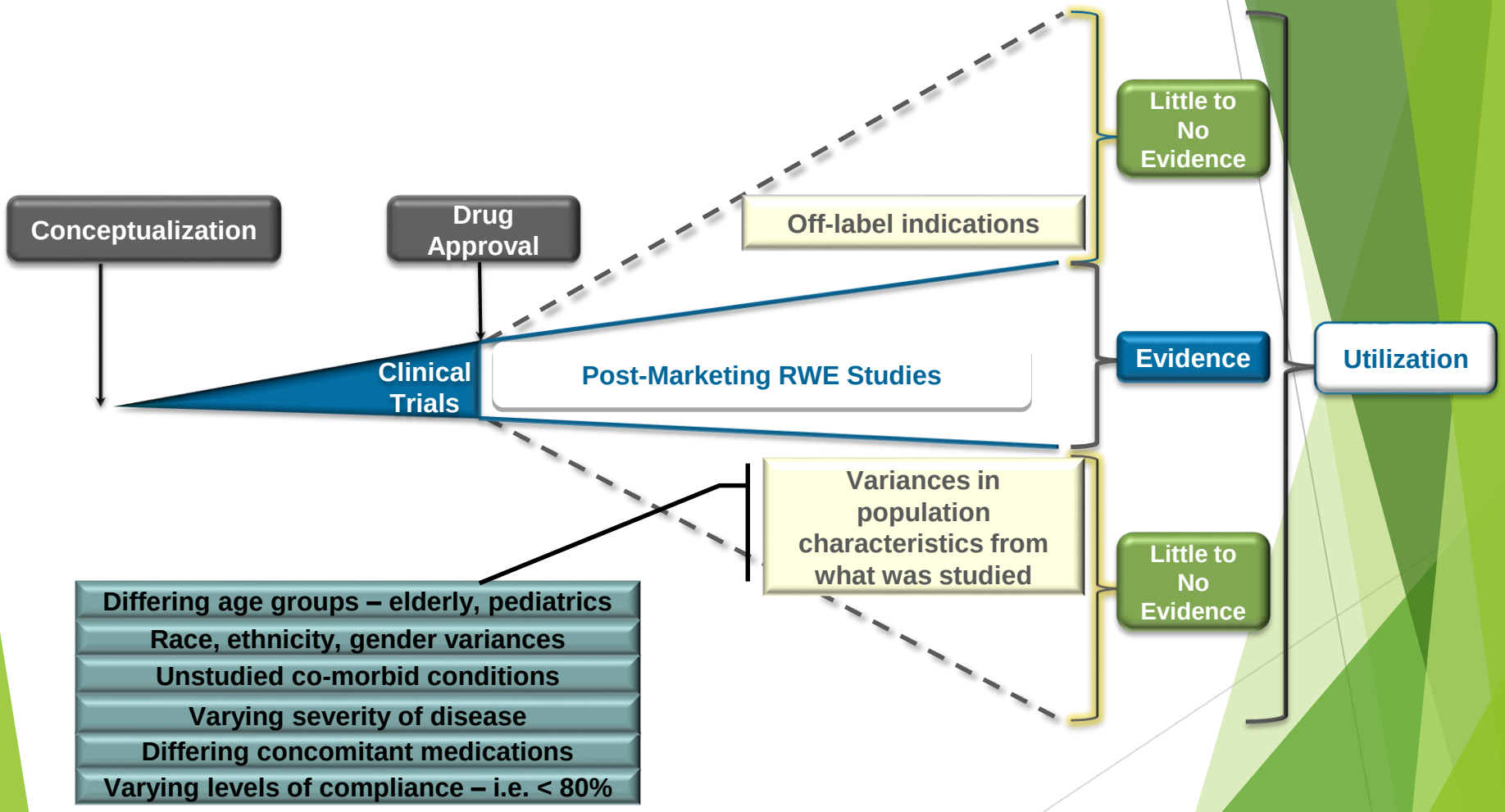
Controlled Setting

Real World

RCTs vs. RWE

Clinical Trials	Real World Cohorts
Internal validity	**External** validity
Young and **fitter** patients	**Older** and **frailer** patients
Finite follow-up	**Longitudinal** follow-up
Tumor-**specific**	Tumor-**agnostic**
Singular primary endpoints	**Multiple** potential endpoints
Limited cost and healthcare use information	**Comprehensive** cost and healthcare use information
Granular data on **selected** patients	**General** data on **unselected** patients
Resource **intensive**	Relatively **inexpensive**

Value of RWE


Conceptualization
Drug Approval
Clinical Trials
Post-Marketing RWE Studies
Off-label indications
Variances in population characteristics from what was studied
Differing age groups – elderly, pediatrics
Race, ethnicity, gender variances
Unstudied co-morbid conditions
Varying severity of disease
Differing concomitant medications
Varying levels of compliance – i.e. < 80%
Little to No Evidence
Evidence
Little to No Evidence
Utilization

Common RWE Themes

Intersection Between RWE and HTA/Payer Bodies

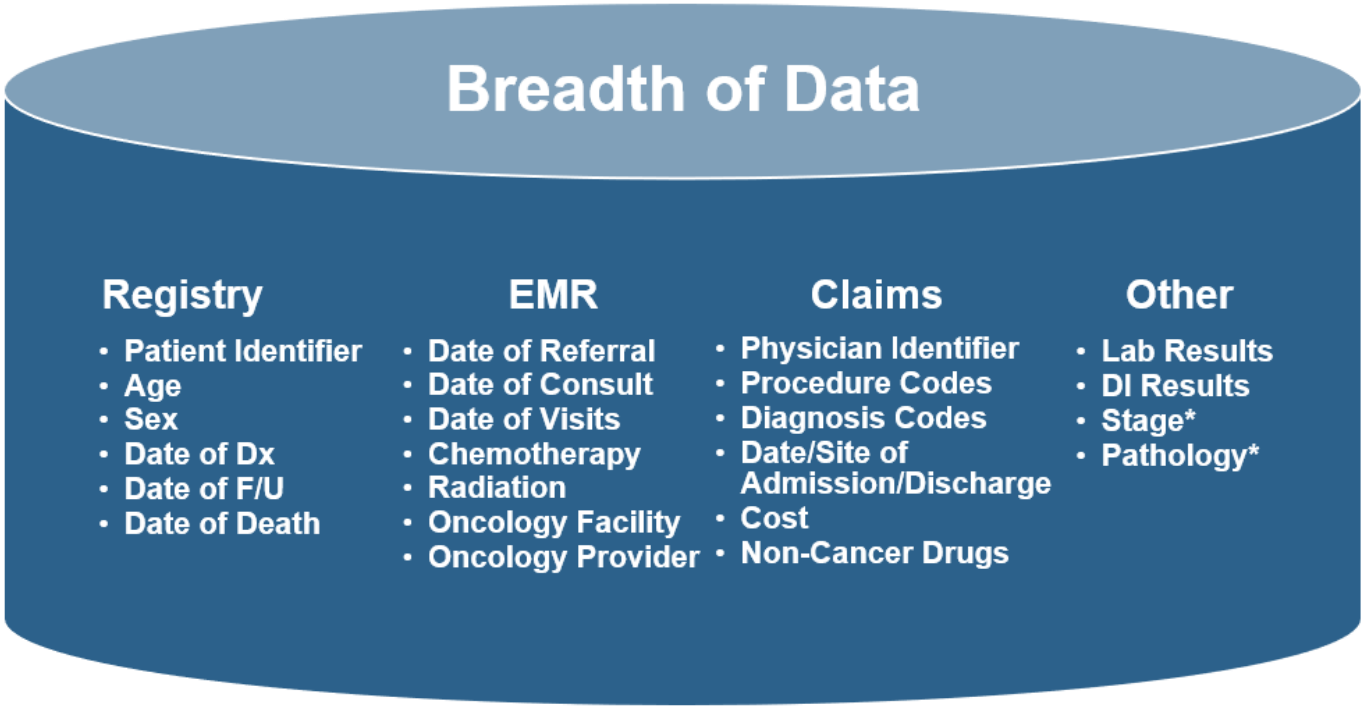
Measurement Challenges

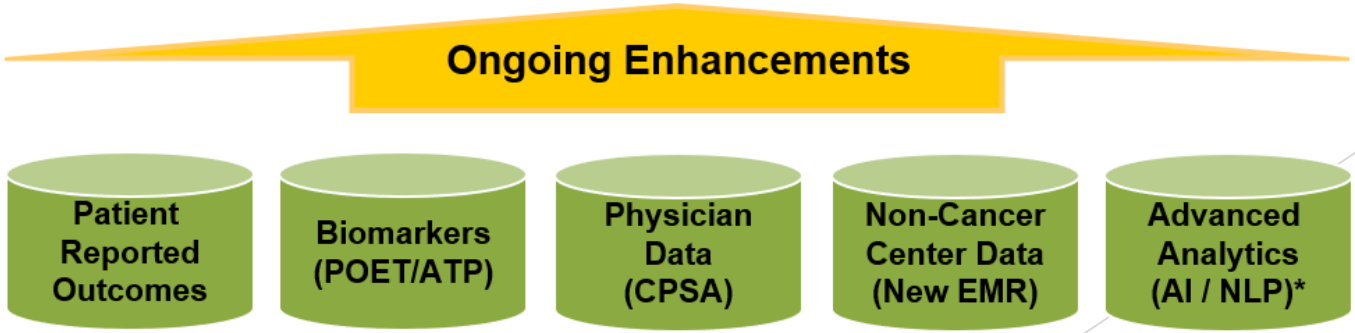
- Metrics
- Timeline
- Data collection method
- Quality assurance
- Validation mechanism
- Stakeholder/manufacturer participation

Additional Barriers

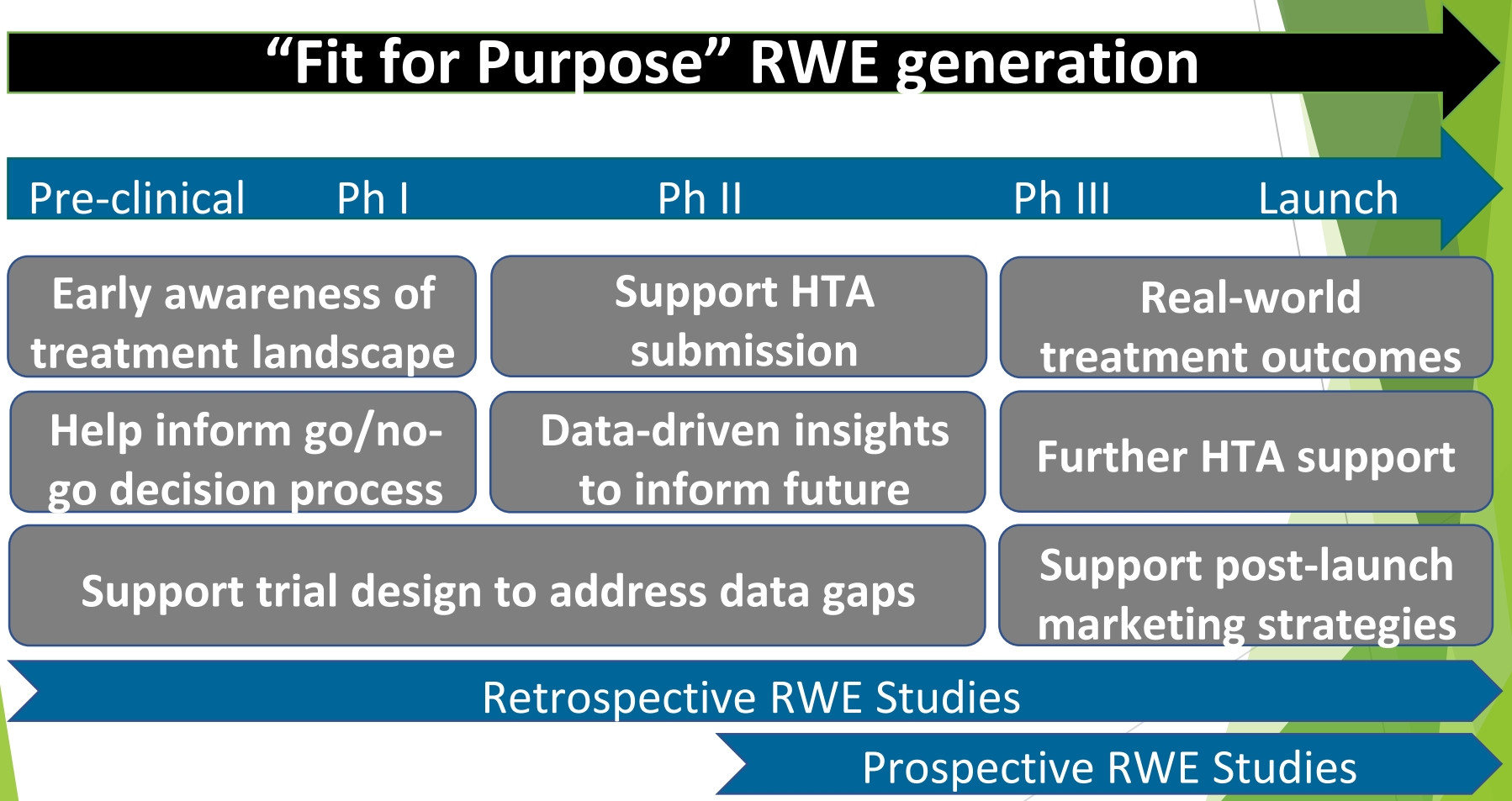
- Limitations with IT (NLP of free text)
- Timeliness of outcome measures
- Insufficient patients on drug (rare)
- Administrative burden and costs
- Lack of adherence to measurement
- Regulatory infrastructure/process

Oncology Outcomes (O2) Group





RWE across product lifecycle



O2/RWE Ecosystem for VBA

Precision Medicines and Value Based Frameworks in Canada

The Patient Perspective

Barry D. Stein

Colorectal Cancer Canada

CAPT 2020 Conference

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Precision Medicines and Immunotherapies

Precision medicines and immunotherapies, are tumour-agnostic treatments for cancer focus on genetic and molecular mutations regardless of the cancer type or location in the body.

They do not always fit into the traditional approach of our HTA agencies in Canada for funding recommendations and implementation decisions.

We are lagging behind other developed countries in terms of patient access to personalized medicines.

Integrating precision medicine into existing value assessment frameworks **is a priority for Canadian cancer patients.**

Canadian HTA agencies have not recommended public access to personalized healthcare innovations

pCODR and INESSS issued negative recommendations for a tumour-agnostic cancer treatment largely because they were unable to accept a novel trial design. (Larotrectinib)

If Canadian patients are to benefit from these new technologies, health system stakeholders need to adapt their assessment and decision-making methods for funding and implementation recommendations including frameworks for the collection of RWD and value-based agreements.

Solutions are needed to manage the entry and to monitor approved medicines that may not fit the traditional approach.

- **We need to build consensus among the various stakeholders to build a precision medicine value assessment framework.**

Stakeholder Perspectives[1]

PATIENTS (Heterogeneous population)

SYSTEM LEVEL

Clinicians, F/P/T Health Systems, Life Science Industry

(Variations between: Best evidence-based practice, quality patient care, ability to identify certain patients as better responders to certain therapeutic applications based on biomarker status)

REGULATOR

Health Canada (Safety and efficacy of health technologies)

HTA

CADTH, INESSS (Clinical and cost effectiveness) [Patient values, adoption feasibility (and societal values)]

PAYERS

Federal, Provincial, Territorial (Value for Money, fiscal certainty, budget impact) (Funding of diagnostic tests and the ability to tie access to reimbursement of the biomarker)

SOCIETAL

Policy makers (safe, effective health policies, fiscal responsibility and protect patient rights)

PATIENT PERSPECTIVES

Drivers for precision medicine and immunotherapies:

Patients want a timely and accurate diagnosis to make decisions with increased confidence.
Ability to select the most appropriate and effective treatments to improve our outcomes – (right treatment for right patient at the right time)
Shared decision making and ability to evaluate benefits and risks
To incorporate our preferences and values throughout the precision medicine lifecycle (personal treatment goals – risk /benefits /tradeoffs)
Improved QoL
Value in Knowing (e.g. rare disease)
Access to Clinical trials
Q. Will AI in combination with NGS be able to chart clinical pathways in the future and if so, how will it affect patient preferences? Q. Will patients accept being ruled out if criteria for reimbursement is not met?

PATIENT PERSPECTIVES GAPS & CHALLENGES

INCOMPLETE OR LACK OF:

Timely access to biomarker testing & precision medicines – equitable access to reimbursed testing (NGS?) (Monitoring – ctDNA)
Knowledge of the implications of biomarkers impact on family members
Knowledge of potential harm from data sharing or lapse in data security
Knowledge and understanding of differences in treatment options
Timely access to treatment (if reimbursed at all)
Understanding of risk prediction e.g. of a rare disease without a cure
Preparedness for prognostic features and future insurance coverage (Ability to provide true informed consent)
Patient preferences input not systematically taken into account (at all stages in the precision medicine lifecycle)

PATIENT PERSPECTIVES

OTHER FACTORS TO EXAMINE:

Evaluate the performance of diagnostic tests and precision medicines (RWE)
Alignment of evidence and reimbursement of the diagnostic test and subsequent treatment management
Examine Treatment Algorithms
Ensure transparent evidence collection
Study designs for the smaller group of patients to whom it is intended
Agree in advance on what will and won't be reimbursed in accordance with the diagnostic test and further evidence

CPHIN – The Canadian Personalized Healthcare Innovation Network[2]

Aims to create Canada's first digitized interconnected and patient centered health data network.

Make health data findable and accessible, ultimately helping patients tailor their own health decisions in partnership with physicians.

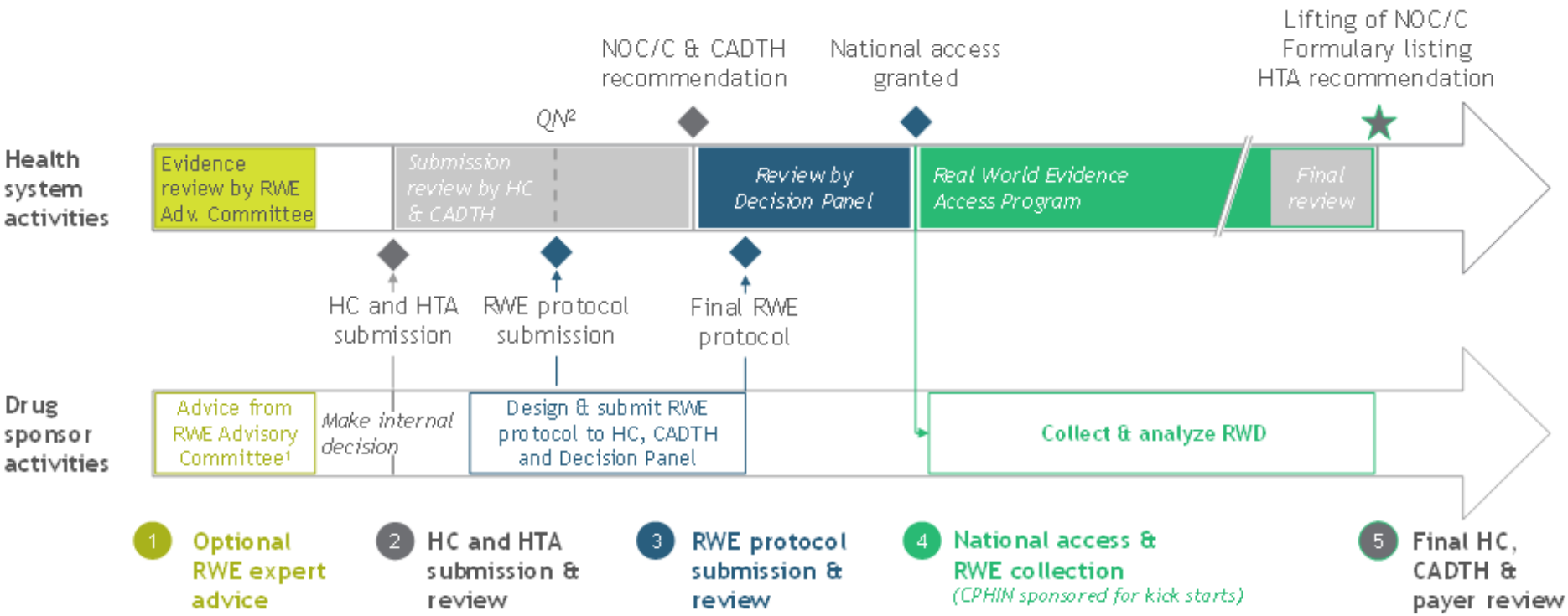
Use RWE in regulatory and reimbursement decision-making for life-cycle management of health technologies to help enable and/or accelerate the access of innovative drugs for patients.

CPHIN developed, the Real-World Evidence & Access in Canadian Healthcare (REACH) Program to enable the generation of RWE to support decisions for regulatory approval and reimbursement of new therapies where non- RCTs are critical.

The REACH Program is divided in 5 steps

1. An optional RWE expert advice
2. Health Canada (HC) & Health technology assessment (HTA) submission and review,
3. RWE protocol submission & review,
4. National access & RWE Collection,
5. Final HC, Canadian Agency for Drugs and Technologies in Health (CADTH) & Payer Review

Proposal: Introduction of a Real World Evidence Access Program, allowing conditional access to new drugs where non-RCT data is critical



1. Optional, fee based service 2. Qualifying Notice

Thank You!

The promise of precision medicine is the ability to leverage known heterogeneity in a population of patients to improve patient management and outcomes

Sources:

1. Being Precise About Precision Medicine: What Should Value Frameworks Incorporate to Address Precision Medicine? A Report of the Personalized Precision Medicine Special Interest Group Eric Faulkner et al VALUE HEALTH. 2020; 23(5):529–539 https://doi.org/10.1016/j.jval.2019.11.010

2. Canadian Personalized Healthcare Innovation Network : www.cphin.ca

RWE and VBAs – A Clinician Perspective

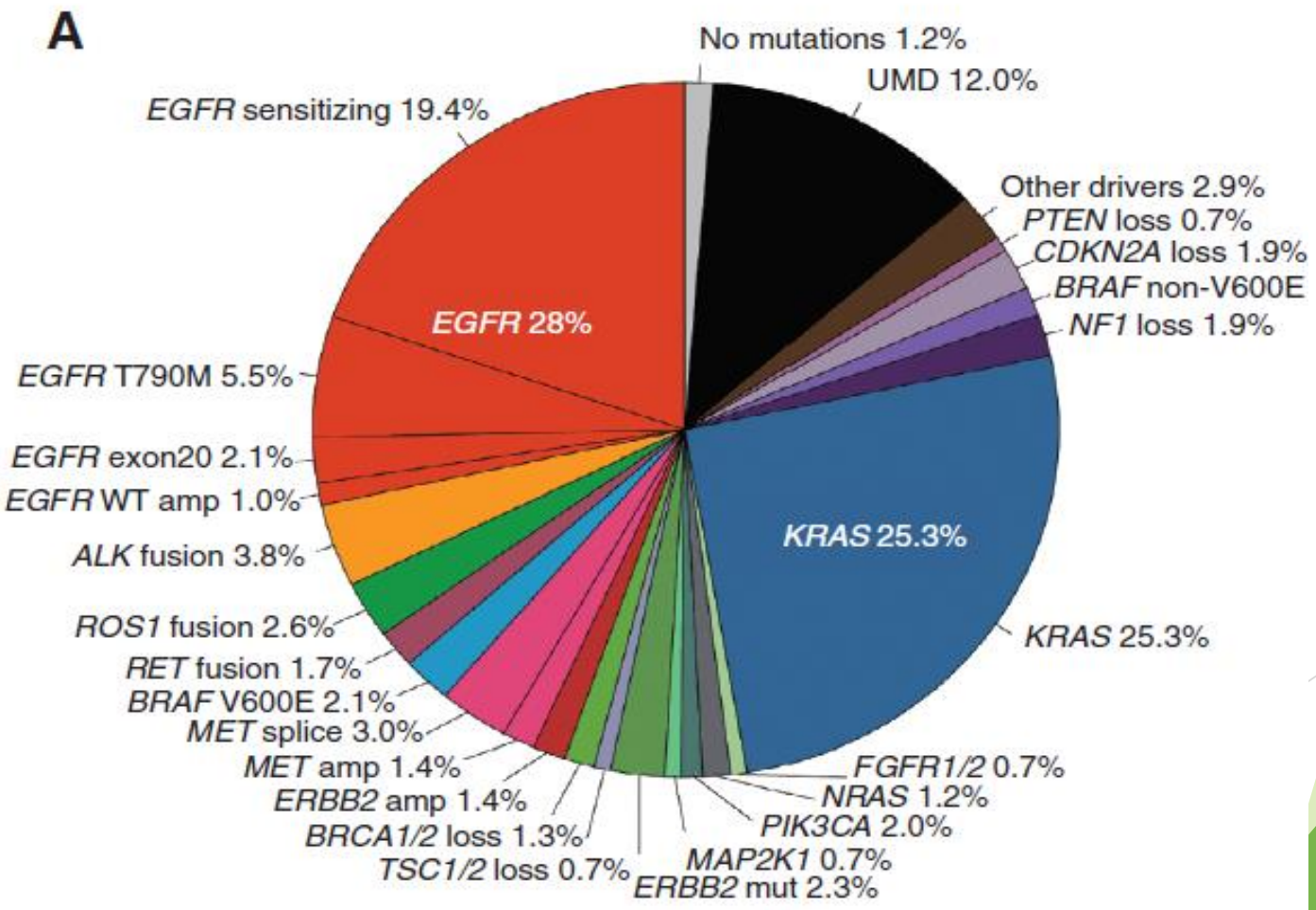
Dr. Parneet Cheema

RWE and VBAs - A clinician perspective

- To create a system of VBAs that incorporate RWE, we first and foremost need to create a system of robust generation of high-quality RWE
- Databases that have provided hypothesis generating evidence in oncology have not always panned out in Phase 3 trials
  - Generally retrospective data collection
  - Perception of clinicians: the data is full of bias and missing data
  - Leading to skepticism of RWE to treating oncologists
- The role of RWE in VBAs would be to supplement clinical trial data

Let's take the example of Non small cell lung cancer (NSCLC)

Each patient with NSCLC is not treated the same – it's based on genomic information

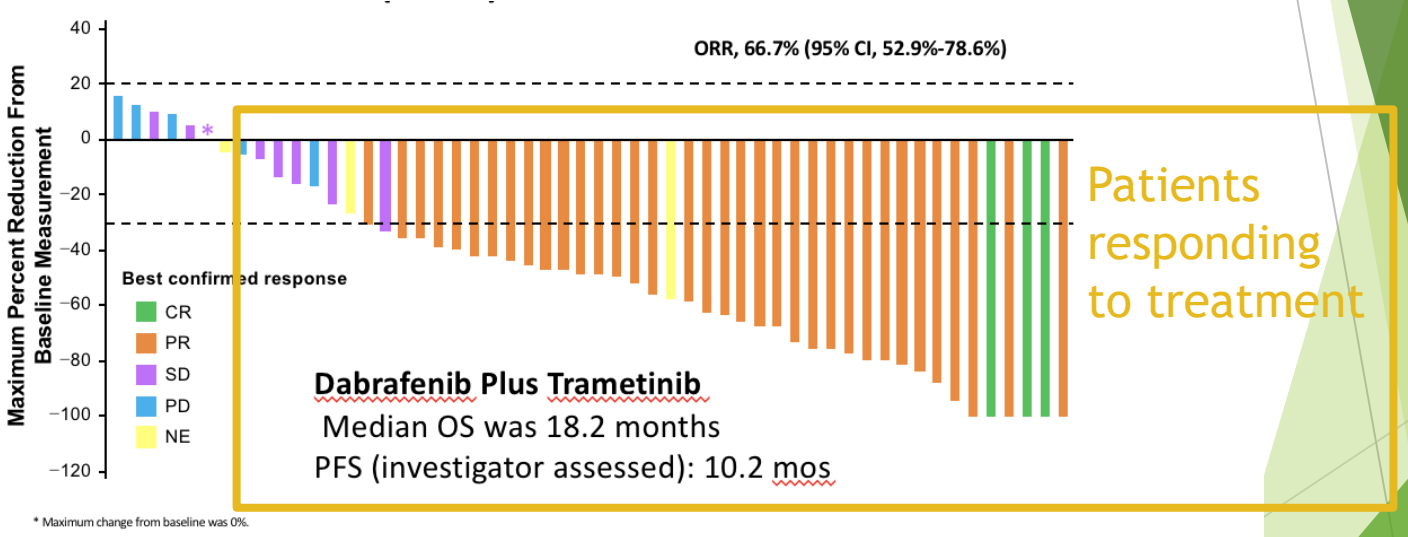


A case of targeted therapy for a subset of lung cancer patients

Phase 2 data
Single arm

Dabrafenib/Trametinib for BRAF V600E NSCLC

>1 line (N=57)[2]



14 months to enroll 59 patients from 30 centres, 9 countries!

Kris MG, et al. *JAMA*. 2014;311:1998-2006

pCODR Decision - Dabrafenib/Trametinib

A step backwards for precision medicine

CADTH | pCODR

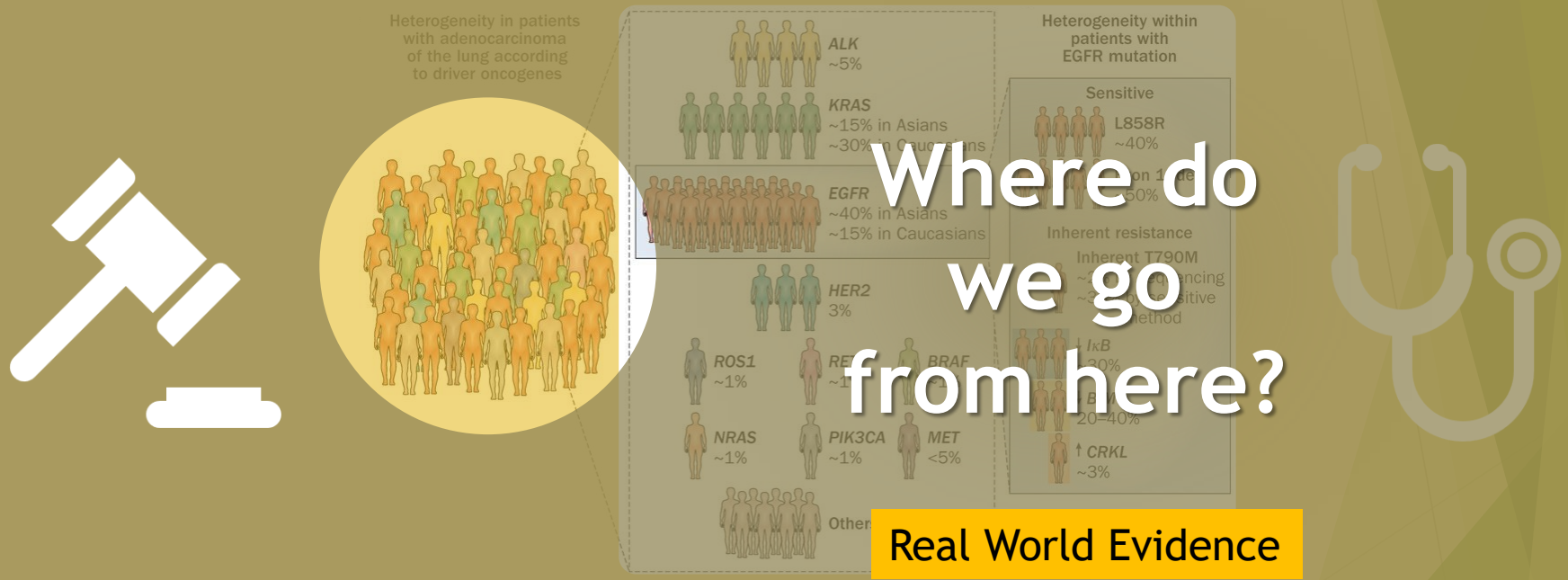
pCODR Expert Review Committee (pERC): Nov 2017

- pERC made this recommendation because the Committee **was not confident of the net clinical benefit** of dabrafenib plus trametinib due to limitations in the evidence from available clinical trials.
- **Did not meet an unmet need as had other treatment options such as immunotherapy**

LUNG CANCER CANADA

LCC Medical Advisory Committee

- **Lumping all patients** by saying *we **have immunotherapy*** **discredits** the approach of **personalized** approach



Mitsudomi et al. Nat Rev Clin Oncol (2013)

Almost saw the same fate for targeted therapy for ROS1-NSCLC

Rare population - 250 cases/year in Canada
Randomized phase 3 trial not possible

CADTH | pCODR

pCODR Expert Review Committee (pERC): May 2019

Committee considered that there **is a net clinical benefit of crizotinib**

pERC also considered that there is a significant unmet need for patients

pERC **considered input from registered clinicians** and **discussed clinicians' real-world experience** in treating patients with ROS1-positive NSCLC with crizotinib.

pERC considered that the registered clinicians observed durable responses similar to those reported in the trials, as well as improved QoL and well-being in patients who had been treated with crizotinib

Data are with the patient!

Most patients with cancer are treated in the community - need this data!

Current state of RWE collection by clinicians

Plea to government / pharma

→ Invest in RWE Generation!

Invest in long term solutions over one off real world studies that are:

- $$$
- In large part have not been well received by payers or clinicians
  - Data often filled with bias of retrospective analysis
- Lack of continuity of staff for data entry

Invest to support infrastracture

- Clinical coordinators – often rate limiting cost
- Prospective data collection is critical for buy in of RWE
- Database for electronic data capture and ease of data transfer between sites
- Support and integrate AI

Need patient buy-in to support development of RWE

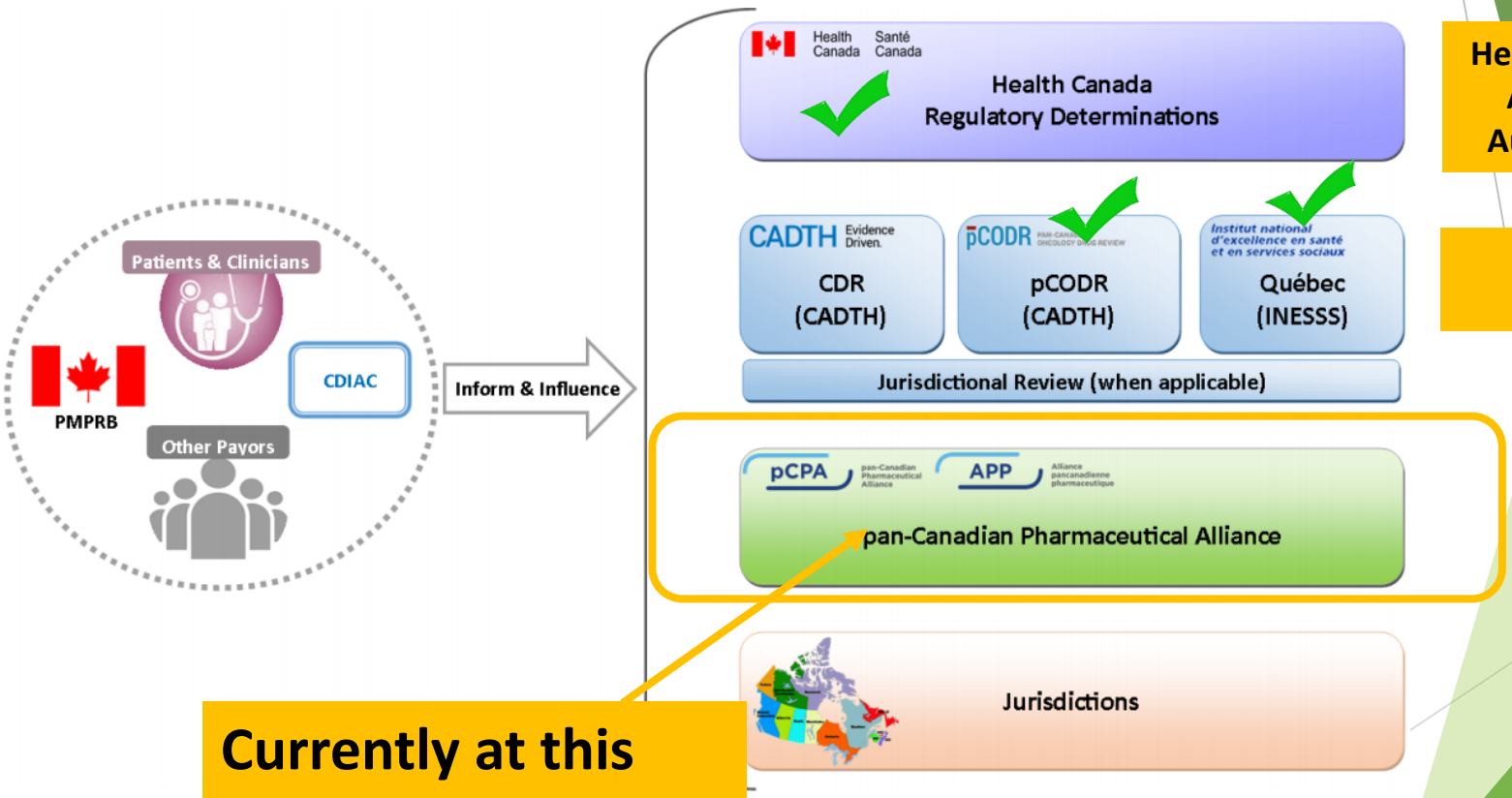
- Campaign to inform patients of value of participating in registries/databases
- Patients may be worried about how their data is being used – need for education
- Simplify consenting
  - Opt-out registries
  - Web-based/electronic data capture

PALEOS – Pan Canadian Lung Cancer Observational Study

Steering Committee: Drs. P. Cheema, S. Kuruvilla, G. Liu, P. Wheatly-Price

- Prospective generation of RWE for lung cancer patients
- Infrastructure support provided by Pulse Infoframe/multiple pharmaceutical companies – electronic database, funding for clinical coordinator, data analysis support
- Standardized variables that can be used by HTAs
- All sites entering prospective data in identical manner
  - Centralized education of coordinators for data entry
  - Continuity of hired clinical coordinator
- Ability to scale with incorporation of AI

The Reimbursement Pathway of crizotinib for ROS1-NSCLC



Health Canada Approved August 2017

Jun 2019
Sep 2019

Currently at this step >3 years after HC approval!

What should an RWE-based VBA framework look like from a clinician perspective?

- For a drug that pCODR will likely conclude has unknown clinical benefit and unmet clinical need, e.g. Phase 2 single arm trials
- Provisional funding of the drug to patients with the stipulation to provide RWE for each patient receiving the drug
  - Companies to submit their RWE generation plan along with pCODR submission
- Allows clinicians/patients to generate RWE that is needed to address uncertainty and will include community centres in addition to academic
- Established timeframe to evaluate the data

Accelerates access to patients as the RWE is generated

RWE and VBAs – A Decision-Maker Perspective

Sylvie Bouchard

Reaction to Panelists

- Researchers
  - RWE : Where and how in the lifecycle?
  - For what purpose(s)?
- Patients
  - Integrating precision medicine
    - Not a reality for a distant future: we already are in the future
    - How the methodologies are used to produce quality data
    - Drug and test assessment : we do
- Clinicians
  - Allowing access while RWE is generated : positive recommendation with conditions
  - RWD not always the answer… we still need RCTs
  - Delays between NOC and reimbursement : manufacturer?

HTA's Perspective

- In the files now
  - Phase I/II without comparators
  - Dose finding trials
  - A lot of uncertainties
  - Secondary outcomes : no data on survival, QOL
  - High costs
  - Doubtful cost effectiveness
  - Huge budget impact
  - …

RWE IN OUR PROCESS
SLIDE FROM 2018 CAPT PRESENTATION

- More than economic concern
  - exposure to « bad drugs »
  - more harm than asset in accordance with patient preferences
- Not always a regulator's concern

✓ efficacy

 innocuity

uncertainty on long term outcomes… OS

Must we deny the patients of treatments potentially safe and effective during the time the evidence is coming?

Institut national d'excellence en santé et en services sociaux Québec

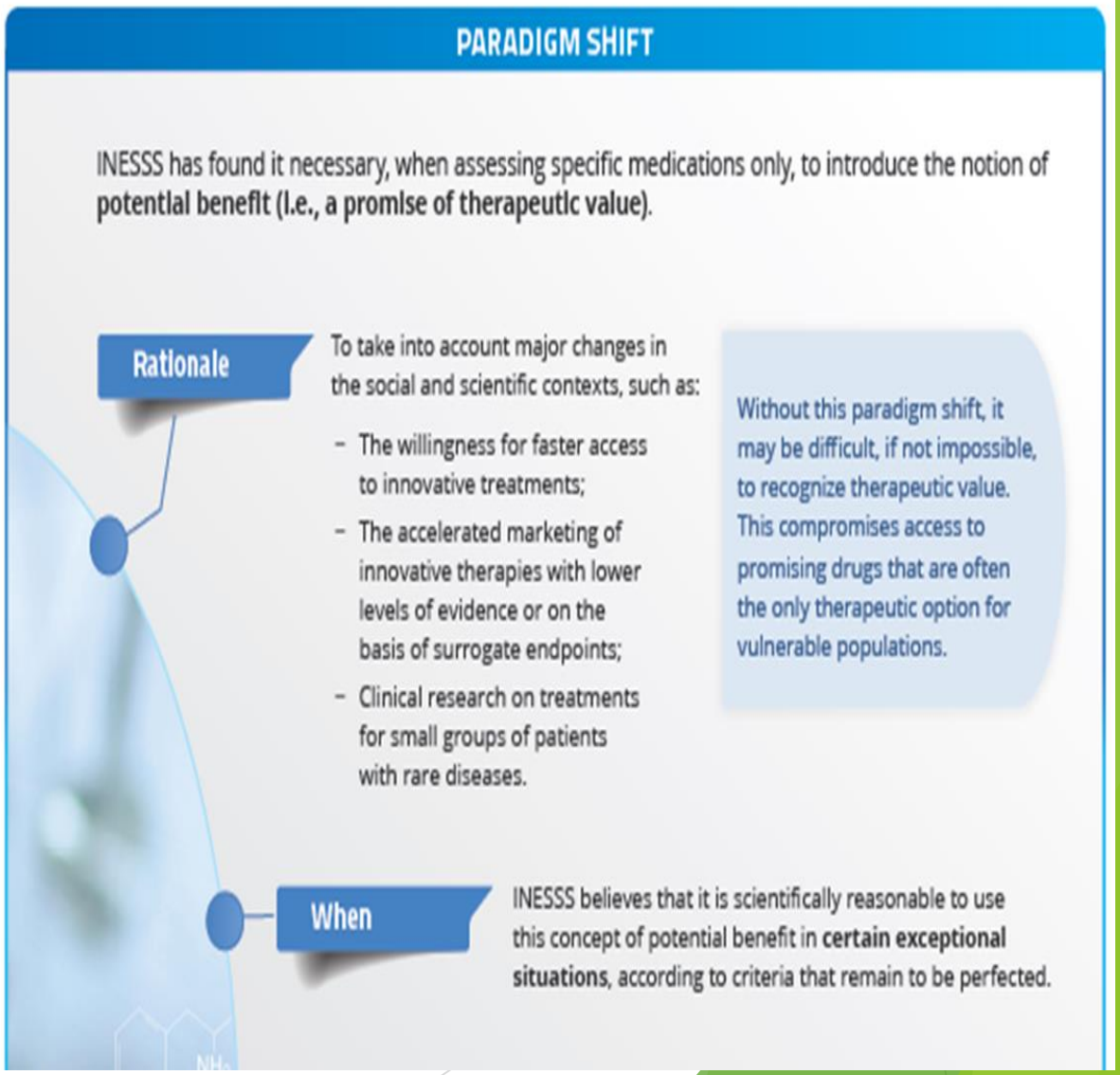
INESSS Framework

- Adapted
  - Unmet need…. How the drug fulfill that need
  - In constant updating
  - Frequent subject of discussion with industry
  - Introduction in 2018 … promise of therapeutic value…

Promise of Therapeutic Value

After a complex deliberative process, has been used twice to date:

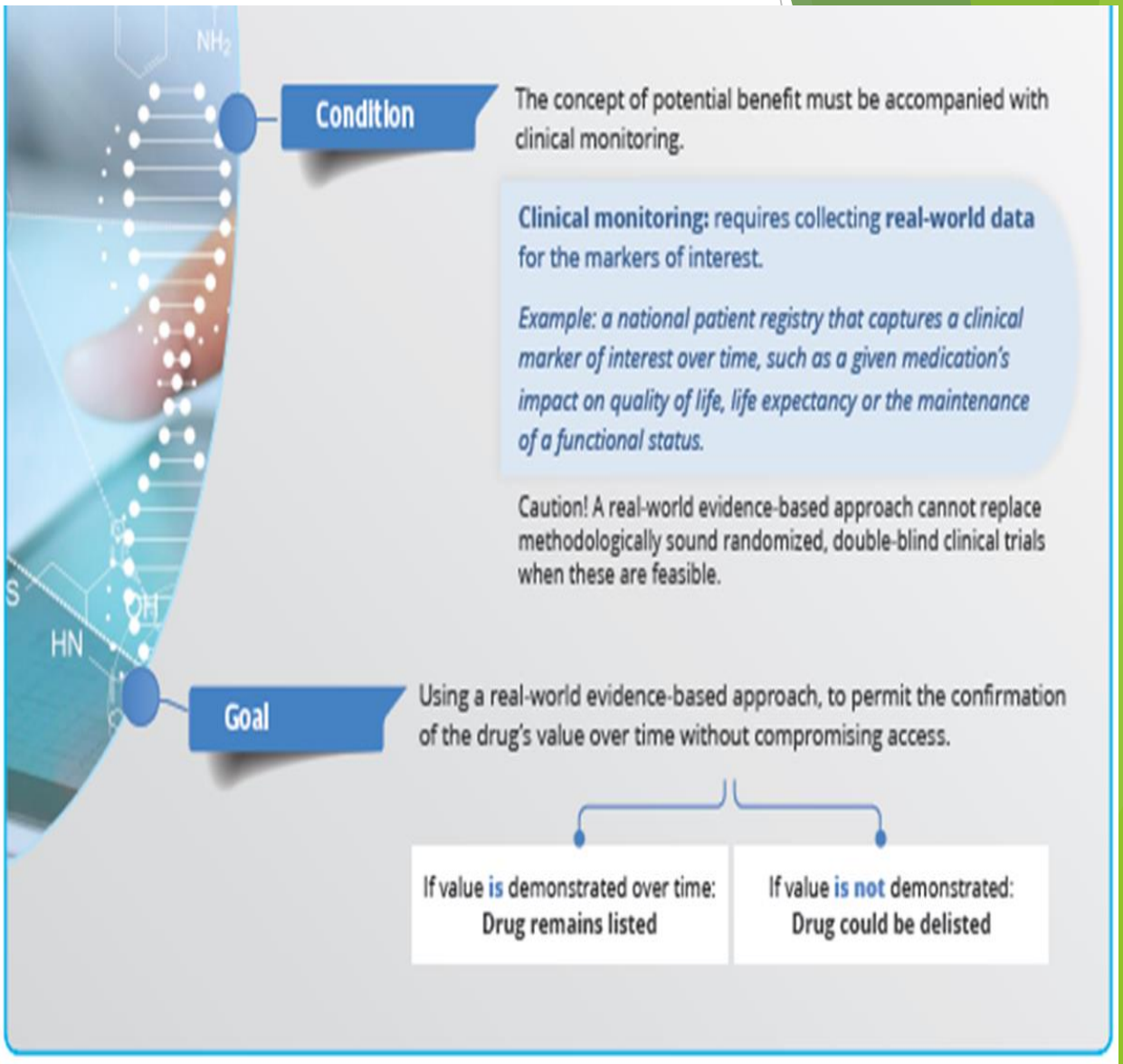
- Galafold (migalastat): Fabry disease, INESSS 2018
- Spinraza (nusinersen): spinal muscular atrophy type II or III, INESSS 2019



Promise of Therapeutic Value

Context :

- Rare or ultra-rare disease
- Poor vital and functional prognosis
- Limited clinical data and hard to obtain
- Significant unmet need



Conditional implementation for innovative technologies (1)

- Roughly speaking:
  - coverage with evidence development : providing access to a technology while evidence is being developed
  - performance-linked reimbursement : managing the use of the technology in order to control its cost-effectiveness in real-world conditions

- Agreements
  - The assessment of the technology's expected value from the available evidence, which is generally the starting point.

Conditional implementation for innovative technologies (2)

- Agreements
  - The gaps in the available evidence can be established, along with the corresponding uncertainty, which has an impact on coverage decision-making;
  - Estimating the value of reducing this uncertainty by generating additional evidence. In other words, seek to weigh the potential benefits of new data against the associated costs;
  - Investment costs and unrecoverable costs can be considered when making a coverage with evidence development decision;
  - Lastly, in certain situations, the possibility of obtaining a price reduction on the technology is examined, since it can have an impact on the assessment of the technology's expected value and the uncertainty.

Conditional implementation for innovative technologies (3)

- Complicated… guiding principles needed
- Sharing the risk associated with uncertainty… embedded in the agreements
  - What will happen if RWD is negatively conclusive?
- Issues about governance and funding… must be clear

Audience Q&A

Please enter your question into the chat room.

Leigh will select questions from the chat.

Wrap-up

Housekeeping - Reminders

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  - Feedback on this session and the whole event would be greatly appreciated.

Thank You!

- Thank you to our panelists!
- Thank you to our audience!
- Thank you to CAPT for this opportunity!

Thank You!