CanREValue

Value-based decisions from Real World Evidence

Developing a framework for incorporating real-world evidence into drug funding decisions:

CanREValue Collaboration Policy Working Groups Interim Report 2019

Appendix

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Appendix A: RWE Planning and Drug Selection WG Surveys

Appendix A1: Survey 1

RWE Planning and Drug Selection – Survey 1

1. Does your organization have a working definition of RWE? If not, how would you define this term from your perspective and from your organization's perspective?
2. Based on your understanding of RWE, which groups of stakeholders have the most use from widespread collection of RWE? (i.e., who will be using the results from RWE studies?)
3. Based on your perspective, what clinical questions and/or policy questions does RWE have the potential to address?
4. What type/strength of evidence would be necessary for stakeholders to make informed decisions?
5. How could local/provincial priorities be used to inform a national RWE structure?
6. In your opinion, are there specific "triggers" that should initiate an RWE discussion and more detailed consideration?
7. If there are multiple RWE priorities or questions, and limited resources to conduct RWE work, what criteria could be used to prioritize work? (e.g., relevance to payers, type of evidence gap, timeliness of a result, etc.)
8. Please provide any additional informational that you think needs to be considered for incorporation of RWE into cancer decision making

Appendix A2: Survey 2

RWE Planning and Drug Selection – Survey 2

1. In general, the working definition of RWE should (please check all that apply):
   a. Take on a broad and flexible scope of non-randomized data
   b. Consider the intended application
   c. Be congruent between regulatory and HTA bodies
   d. Include any RWD collected irrespective of timing
   e. Other (please specify):

2. Based on previous discussions, the potential users of RWE can include:
   - Payers (provincial health ministries, cancer agencies): assess actual uptake, effectiveness, and cost-effectiveness; re-evaluate funding decision; re-negotiate pricing;
   - Regulators: safety and efficacy surveillance; amend approved indications; NOC/c listing conditions; supplement to RCTs
   - HTA bodies: reconsider/reassess past recommendation; submission and recommendations; optimal use; inform future submissions
   - pCPA: integrate RWE studies into pricing/listing agreements
   - PMPRB: use RWE to inform pricing
   - Physicians: effectiveness; safety
   - Patients/caregivers: effectiveness;
   - Public: effective and efficient use of resources
   - Populations: clarifying the population that benefits from the drug (expanding or narrowing compared to initial trials)
   - Industry: what is required for future studies; post-launch validation; partnerships with pCPA
   - Private organizations (consultancies, other health organization)

   Are there any other potential users or uses missing from the above list?

3. When we are thinking of planning and selection of RWE projects, who should we focus on as the main target audience (from the list above)?
   Primary User: Choose an item.
   Secondary User: Choose an item.
   Comments:

   Here is the list of answer options:
   Payers (provincial health ministries, cancer agencies)
   Regulators
   HTA Bodies
   pCPA
   PMPRB
   Physicians
   Patients/caregivers
   Public
   Populations
   Industry
   Private Organizations
   Others

4. Based on your previous answer, please select three questions you think are important for your primary and secondary users

	Primary User	Secondary User:
Question 1:	Choose an item.	Choose an item.
Question 2:	Choose an item.	Choose an item.
Question 3:	Choose an item.	Choose an item.
Comments		

   Here is the list of answer options:
   Disease burden (incidence, prevalence)
   Effectiveness (overall survival, PFS)
   Safety (toxicity, rates of discontinuations)
   Treatment patterns (drug utilization, dose adjustment)
   Quality of Care (PROs, QoL, Performance status)
   Cost (cost of care, cost effectiveness)
   Budget impact (market share, rate of uptake)
   Health systems (treatment pathway, wastage, optimal delivery)

5. Under what circumstances would evidence from non-comparative/single-arm studies be useful and relevant for decision making? Would you recommend using non-comparative/single-arm studies for questions selected above?

6. What approaches can we use to resolve or reach agreement between manufacturer and payer on the type/strength of evidence needed?

7. Below is a list of triggers to initiating a study to gather and generate RWE. Do you agree with triggers below?

	Should this be a trigger? (Yes or no)	Should this trigger always be present? (Yes or no)
Uncertainty of the magnitude of benefit: drugs thought to be effective but only with preliminary evidence and no plans for additional trials; reports of toxicity/hospitalization on treatment over and above clinical trial data;		
Trial data is insufficiently powered or has limited external validity		
Additional therapies entering the same space which alters the treatment algorithm		
pERC's Next Steps recommendations		
Agents with potentially large budget impact and health systems resources impact: originally review suggests s flags for close monitoring, risk of longer use or greater number of patients treated		
Health Canada's NOC/c conditions		
Expensive drugs for rare cancers		
Significant Unmet Need		

- Others: (please specify)

8. In some circumstances, the above triggers could potentially identify multiple RWE questions. When thinking about prioritizing multiple RWE questions, which factor would you rank most important? (Please Rank from 1 – 8; 8 = most important; 1 = least important)
   - Feasibility
   - Timeliness
   - Relevance to payers
   - Evidence gap
   - Degree of unmet need
   - Budget impact: high cost drugs with high number of patients
   - What is needed to provide access to important therapies
   - Others:

9. Below is a list of potential considerations for prioritizing RWE project selection, please provide us your thoughts on the list as well as additional considerations:
   - Would this RWE analysis change policy/funding status of a therapy/indication for use?
   - Are the outcomes for this therapy/indication appropriate to evaluate and of interest?
   - Are these outcomes currently measured/available in existing data sources (e.g. collected and mineable)? Are these measurements objective? Subjective?

- What sample size is required for this indication in order to be relevant?
- How quickly can data collection/analyses occur in order to be relevant to the treatment landscape?
- Given the sample size, outcome measures, time lines, can existing resources accommodate this request?
- Others?

10. Based on the previous survey, the suggested national RWE structure could consist of a process where local/provincial priorities will be discussed at a national forum where a national consensus can be established on overall priorities. Do you agree with this approach?
    a. Yes, I agree with the above approach
    b. No, I disagree with the above approach
        - Please specify how you envision this to developed?

11. How could a National RWE structure be budgeted/funded? (Select all that apply)
    a. Manufacturer Tax
    b. Pooled funding from provincial agencies/ministries
    c. Dedicated Federal Funding
    d. Other (please specify):

12. Should we leverage existing pan-Canadian tables/groups in the National RWE structures?
    a. Yes
    b. No
        - If yes, which existing tables/groups? If no, how should we form these groups?

13. One challenge of RWE studies is generalizability. In what context would regional or local RWE not be generalizable/useful to other jurisdictions?

14. Please provide any additional information that you think needs to be considered for incorporation of RWE into cancer decision making

Appendix A3: Survey 3

RWE Planning and Drug Selection – Survey 3

Thank you for your feedback during our last teleconference on the initial criteria for selecting and prioritizing RWE questions. Based on the discussion, we have revised the criteria for your review. The criteria below focus on priority-setting based on relevance to payers. Note that feasibility criteria must also be applied to determine final priority for RWE projects led by the public sector using administrative data.

The overall intent is to apply criteria prospectively (before funding) to a particular drug to determine high-priority questions for RWE studies. We may think of key uncertainties as they arise from a particular new drug, even if their scope reaches slightly beyond the drug itself. The more of these criteria that apply when considering a new drug, the higher priority it may be to study its uncertainties.

Please consider the criteria and the details within the sub-criteria and answer the questions below.

1. Criteria 1: Uncertainty in the clinical benefit
    - Uncertainty in the comparative effectiveness, e.g., based on indirect treatment comparison/single-arm evidence

- Uncertainty in magnitude of clinical benefit e.g., preliminary evidence, early study termination or crossover confounding OS analyses, etc.
- Uncertainty in the generalizability of the evidence e.g., based on trial with limited external validity
- Uncommon cancers – study findings based on small trials
- Uncertainty in the comparative toxicity*
- *Note: the WG commented that uncertainty about safety is rarely the primary concern, and that there are also other mechanisms in place to monitor post-market safety; while it may be included as an RWE endpoint, it is unlikely to drive the primary study question

Question: Is the criterion independently useful to refine a list of potential RWE projects?
Question: Comments?

2. Criteria 2: Uncertainty in one or more of pERC's other deliberative framework quadrants
   - Challenges related to feasibility of adoption e.g., lack of evidence for optimal sequencing, impact to treatment pathway, etc.
   - Agents with potential large or uncertain budget impact and/or health systems resources impact

   Question: Is the criterion independently useful to refine a list of potential RWE projects?
   Question: Comments?

3. Criteria 3: Uncertainty not expected to be resolved through future evidence
   - No other relevant trials or studies currently underway
   - Absence of full regulatory approval/oversight for indication
     - ✓ NOC/c: particularly when stated conditions may not fully resolve uncertainty for the indication (e.g. confirmatory study in being conducted in a different setting)
     - ✓ Absence of NOC for the stated indication (off-label use)

   Question: Is the criterion independently useful to refine a list of potential RWE projects?
   Question: Comments?

4. Criteria 4: Uncertainty cannot be managed through listing agreements
   - Uncertainty cannot be managed through pricing, expenditure caps, or clinical criteria for use

   Question: Is the criterion independently useful to refine a list of potential RWE projects?
   Question: Comments?

5. Do these criteria capture all the factors relevant to the identification and prioritization of RWE questions?

6. Is a mechanism needed to retrospectively consider emerging signals for RWE post-market?
   For example, report of toxicity/hospitalization on treatment over and above clinical trial data or a change in the treatment landscape could increase the priority for evaluation after initial funding and trigger reconsideration for an RWE study.

Appendix B: RWE Reassessment & Uptake WG Surveys

Appendix B1: Survey 1 Questions

RWE Reassessment and Uptake Working Group Survey 1

1. Who should lead and/or conduct the reassessments?
2. How should reassessments be conducted? (i.e. the same as initial drug reviews, or differently?) If differently than initial drug reviews, how would they be different?
3. What should be reassessed (i.e. clinical data only, clinical and economic, etc.)?
4. What type of data/evidence should be reassessed? How might it be different than the evidence reviewed for initial drug reviews?
5. What are the enablers and barriers to conducting reassessments? (e.g. capacity and resources to put together a submission for a reassessment)
6. What are the enablers and barriers to re-visiting funding decisions?
7. What information would be required in order to re-visit a funding decision?
8. How could/should industry be engaged in the development of this reassessment framework?
9. How could/should industry be engaged in reassessments (e.g. making submissions for reassessments, collecting data, etc.)
10. How should recommendations be made on reassessments? Do they require a different framework, different recommendation categories than for initial drug reviews?
11. How could/should patients and/or patient groups be engaged in the development of this reassessment framework?
12. How could/should patient and/or patient groups be engaged in reassessments (e.g. making submissions for reassessments, collecting data, etc.)
13. What components of the reassessment process should be transparent (e.g. topic selection, timelines, evidence reviewed, recommendations, etc.)
14. What are your expectations of the timelines for reassessments?
    1. From the decision point to collect data to the final reassessment recommendation?
    2. From the initiation of the reassessment to the final reassessment recommendation?
15. Please provide any additional information that you think needs to be considered when developing a framework for reassessment/funding decision.

Appendix B2: Survey 2 Questions

RWE Reassessment and Uptake Working Group – Survey 2

The following section includes questions where majority (or all) of us previously agree on. These are known as consensus questions, and we would like to get your final approval or identify any remaining concerns related to them.

1. Reassessment should be initiated by (please check all that apply):
    f. Provincial/jurisdictional drug plans or cancer agencies
    g. Industry
    h. Other organizations
        - If others, please specify:

2. Reassessment should be conducted by CADTH/pCODR.
    a. Yes, I agree.
    b. No, I disagree.

c. If you responded no, please indicate who should conduct reassessments

3. All types/sources of data should be considered during the reassessment, as long as the data addresses the uncertainty raised in the initial assessment (or addresses the uncertainty that triggered the reassessment)
   a. Yes, I agree.
   b. No, I disagree.
   c. If you responded no, please indicate which sources of data would be appropriate for reassessments

4. The pCODR Expert Review Committee (pERC) should make recommendations on the reassessments that would be shared with provinces/jurisdictions and cancer agencies
   a. Yes, I agree.
   b. No, I disagree.
   c. If you responded no, please indicate who should provide recommendations for reassessments

5. The recommendation framework for reassessments should be similar to the current deliberative framework for the initial assessment with adaptations to the adoption and feasibility quadrant.
   a. Yes, I agree.
   b. No, I disagree.
   c. If you responded yes, please describe the adaptations you would make to the adoption of feasibility quadrant. If you responded no, please describe what considerations should be included in a deliberative framework

6. The final recommendation categories will be 1) status quo; 2) revisit negotiation; 3) do not recommend.
   a. Yes, I agree.
   b. No, I disagree.
   c. If you responded no, what recommendations category would you add/delete?

7. A 3-6 month timeline is a reasonable timeframe for a reassessment (from the point of initiative a review new data to issuing a recommendation).
   a. Yes, I agree.
   b. No, I disagree.
   c. If you responded no, what is reasonable timeframe for the reassessment

8. Recognizing that it is likely not possible to align the duration of individual provincial Product Listing Agreements (PLAs) across the provinces, the PLAs routinely have a clause that they can renegotiate at any point during the PLA if there is a need for a join renegotiation due to a reassessment.
   - Yes, I agree.
   - No, I disagree.
   - Not applicable
   - If you responded no, please explain

9. Reassessment should not be applied routinely for all drugs
   - Yes, I agree – reassessment should be limited to certain drugs
   - No, I disagree – all drugs should be reassessed
   - If you responded no, do you have a suggestions how drugs could be prioritized for reassessment?

The following section includes questions where we have received many helpful comments which require additional clarification. These are known as clarifying questions, and we would like to get your additional feedback on.

10. It is anticipated that the majority of reassessment recommendations will be to revisit negotiations, what challenges does this pose to the negotiation process (i.e. pCPA) and the provincial drug plans and cancer agencies

11. Should there be a 'cap' on the number of reassessments conducted per year to manage the volume/capacity? If there should be a "cap", what strategies may be used ot prioritize reassessments?

12. Is it feasible to have 2 pathways for reassessment: short/tailored and comprehensive.
    a. Yes, it is feasible
    b. No, it is not feasible
    c. If you responded yes, please provide an example of a short/tailored reassessment vs a comprehensive reassessment. If you responded no, what might be more feasible

13. Would provinces (drug plans) pay more for a drug if there is rigorous evidence that the drug performs better than the evidence used to inform the initial assessment?
    a. Yes, the drug plan could pay more
    b. No, the drug plan could not pay more
    c. Not applicable
    d. If you responded no, how could this possible scenario be managed with industry?

14. Would provinces (drug plans) be able to delist a drug that is not demonstrating value compared to relevant available treatment option?
    a. Yes, the drug could be delisted
    b. No, the drug could not be delisted
    c. If you responded no, in addition to high quality evidence, is there something else that could support the ability of the drug plans to delist a drug?

15. How can industry be incentivized to participate in reassessments?

Appendix B3: Survey 3 Questions

RWE Reassessment and Uptake Working Group Survey 3

1. Reassessments would be conducted for drugs that had received a positive or conditional recommendation from pERC, there would be no reassessments for negative recommendations. If a company wanted to make a resubmission on a negative recommendation, they can do so, as per the existing resubmission procedure.

2. If CADTH were to conduct the reassessments, as per their current procedures, they would only have access to the list (public) prices for the drug undergoing reassessment. From your perspective, is this a substantial concern, and if so do you have a suggestion as to how an economic evaluation for a reassessment could be conducted using the negotiated (confidential) price?

3. There is agreement among the Working Group that 2 review streams are likely required: 1) a tailored (shorter) review; and 2) a comprehensive (longer) review. As we think about how to decide whether a drug should under a tailored vs a comprehensive review, what do you think of the following proposal:

Tailored reviews are for questions related specifically to a focused feasibility issue (dosing, administration schedule, etc.), but would not change the original recommendation. Comprehensive review for questions on the effectiveness (including outcomes of survival, safety, quality of life) and/or cost-effectiveness of a drug, and pERC would make a reassessment recommendation (status quo, revisit negotiation, do not recommend).

4. What other considerations should be included in the decision of tailored vs comprehensive?

5. In relation to question #3, do you think that a cost-effectiveness analysis will always be required for both tailored reviews and comprehensive reviews?
    - Yes for tailored reviews
    - No for tailored reviews
    - Yes for comprehensive reviews
    - No for comprehensive reviews
    - Please explain your selection

6. What information is required to revisit a funding decision in addition to the pivotal trial? For instance, would data on utilization, updated cost-effectiveness analyses, or real world data on important outcomes (survival, safety, quality of life) be required? Please provide details on what information you think would be required for a funding decision to be revisited?

7. Could CADTH's existing jurisdictional working groups (e.g., Provincial Advisory Group, PAG) be used for the purposes of selecting and prioritizing drugs for reassessment? What other mechanisms could be put in place to prioritize reassessments?

8. Should there be a cap on the number of reassessments conducted per year?