Regulation and reimbursement of paediatric medicines: A comparative analysis of health system approaches in Canada and Europe

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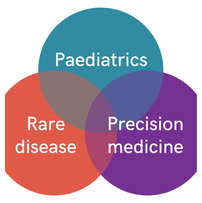
RESEARCH CONTEXT

Policies for paediatric drug regulation and reimbursement lag dramatically behind the adult context. In fact, up to 80% of drugs given to children are off-label (by age or indication). Additionally, public policies for paediatric drug regulation and reimbursement in Canada and most countries are sparse, resulting in limited access to therapies.
This reality stems from many research and development barriers in paediatrics, including:

- Small sample sizes and small benefitting populations
- Few clinical trials
- Complicated research ethics
- Limited incentives and weak regulatory obligations

The effect is that fewer therapies are approved and available for children, and where there is access, it is variable and inequitable across jurisdictions.



As a result of their rarified populations, paediatrics, rare disease and precision medicine face an overlapping set of challenges. These three populations typically face a high degree of uncertainty coupled with high costs. Additionally, there is a paradox in paediatrics that drug needs are rare, yet rare disease in paediatrics is common. Precision medicine is contributing to even greater rarity, compounding existing problems.

STUDY AIMS & METHODS

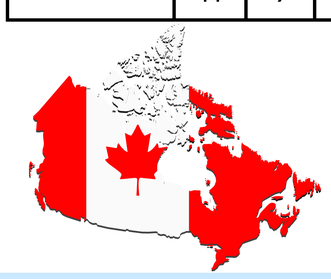
Question: ***What challenges & opportunities exist in access to precision therapies for children & young adults?***

Aims:
1. Explore how current regulations, policies and system realities impact the implementation of paediatric therapies
2. Compare findings across similar health systems
3. Generate lessons and recommendations for Canadian policymakers for the design and implementation of policies that **improve access** and reduce inequities

Approach:
Qualitative methods involving in-depth interviews with experts, and document analysis to identify:

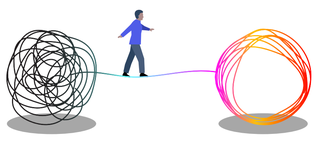
- Policy, legislative and regulatory environments across Canada and comparator jurisdictions
- Structures and processes of decision-making and the dynamics between stakeholders
- Mechanisms to integrate paediatric and precision medicine into drug regulation, pricing and reimbursement processes

KEY INFORMANTS TO DATE	JURISDICTION			
Primary role	**CAN**	**EU**	**UK**	
Regulator	3	4		7
HTA	6	2	1	9
Payer	1			1
Industry		1		1
Advocacy	1		1	2
Clinical	4	2	2	8
	14	**9**	**4**	**28**



NEXT STEPS

1. Expand comparison into the UK and Australia
2. Deeper examination of:
   - Differences in funding allocation and reimbursement of paediatric drugs
   - Impacts of various policy levers and governance structures on access (e.g., whether carrot vs stick approaches produce different results)
   - Tensions and opportunities for resolution, between evidentiary needs of distinct stakeholder groups
3. Develop set of considerations and recommendations for Canadian and international policymakers
   - In tandem with the refinement of a child-focused value framework [6]



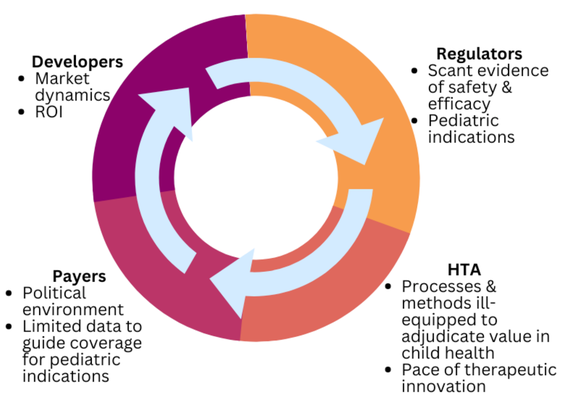
FINDINGS

1. Paediatric drugs fit into three archetypes:
a. Developed in adults, and often later for paediatrics for the same indication
b. Developed in adults and children for a different indication
c. Developed only in paediatrics
These three types of drugs face overlapping and distinct regulatory and evidence development hurdles, and may require different policy strategies.

2. Policymaking is complex and nuanced:

- The drug development and implementation pathway involves multiple stages and sets of decision-makers
- Decisions about which therapies are funded is a complex, value-laden process, and not only a technical exercise of evidence adjudication
- Each jurisdiction has distinct governance structures and processes that create a unique architecture to support or constrain policy choices

3. Stakeholders across the drug development pathway face a shared set of challenges:

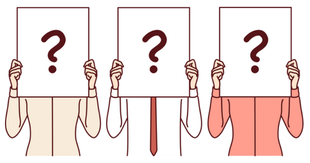


4. A number of ongoing tensions merit further exploration:

a) ***Who makes decisions***
What is the composition of voices at decision-making tables?
What is the appropriate remit and political authority of stakeholders?

- between types of stakeholders
- between levels of government
- between health and social care systems

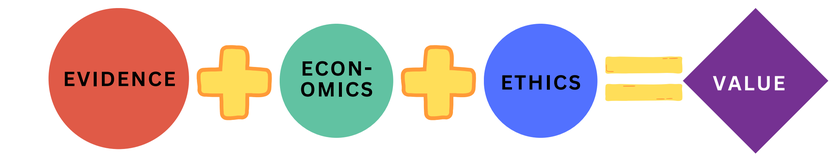
b) ***How decisions are made***
How can we manage and meet the needs of different ***evidentiary standards*** of various stakeholders?



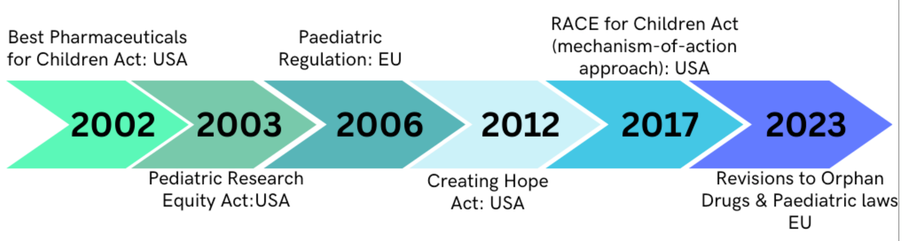
5. Comparative policy analysis offers possible solutions for paediatric-tailored policy improvements:

PROPOSED OPTIONS FOR POLICY REFORM

1. **Upstream and repeated multi-stakeholder engagement** and advice (e.g. EU offers lesson that there is value in engaging paediatric committee from start; regulators can set the tone [2])
2. **Coordinated review processes** at regulatory (e.g., FDA-EMA joint submissions for marketing authorization [3]; Project Orbis for regulation of oncology drugs) and HTA stages (e.g., EU joint clinical assessments; CADTH-NICE parallel scientific advice)
3. **Harmonization of standards and principles** across regions (e.g. consensus on how to treat different forms of paediatric data; paediatric extrapolation [4]) and principles (e.g. EUnetHTA)
4. **Amplifying the patient voice** and expanding the set of decision-making tables that include patient and public representation (e.g., the UK's NICE has 20+ years of formal patient involvement [5])



Legal frameworks for paediatric drug development



Incentives to submission of paediatric data:
- Market exclusivity
  - EU & UK: 6-mos if paediatric investigative plan (PIP) is completed + 2yr extension for orphan designation
  - CAN: 6-mos paediatric extension for innovative drugs
- Reduced fees and review time

Conditions:
- EU & US: Paediatric data submitted within specific timelines (e.g. end of adult phase 1 trial)
- US: If molecular target is relevant to paediatric cancer, trials in children are required

Impact: dramatic increase in % of submissions including paediatric data

Policy Approaches to Innovative Paediatric Therapies

	CANADA	EU
Paediatric Legislation	✗	✓
Framing of Priorities	• Rare disease • Equity of access to paediatric drugs • Regulatory reform	• Rare disease • Availability & accessibility of paediatric medicines • Innovation
Assessment by expert informants	• Need for greater collaboration & transparency of processes • Targeted paediatric policy under consideration • Federal-provincial division of powers restricts policy evolution • In state of planning & piloting	• Existing paediatric and orphan drug policies are improving access yet impacts are insufficient [1] • Need for policy iteration including stronger mandates • In state of reflection & refinement

REGULATORY REFORM:

We have to somehow start to anticipate needs at a very early stage. *Ideally, we would want to agree on a PIP [pediatric investigative plan] that actually takes into consideration HTA needs, whether it's through PROs, or other quality of life measures, which we might already request to satisfy the HTA decision making.*
-Regulator

REDESIGNED HTA:

HTA has to encompass more than just the patient as an adult […] ***Kids are dependent on their surroundings and their support system, and those people are impacted,*** *and their quality of life is impacted."*
-Pharmacist

EVIDENCE GENERATION:

There are uncertainties, and you're never going to really align regulatory and payer requirements, because they are different decisions. So the only resolution is to reward data, and that needs very early engagement, and we need to be all agreeing what the key outcomes are.
-HTA

POLICY IMPLICATIONS

1. More attention to paediatrics is required
   - Comparison can be inspiring and instructive
2. Paediatrics offers an opportunity to pilot innovative reform
3. This work exists within an evolving policy landscape
   - (e.g., Health Canada's Pediatric Drug Action Plan, 2020; National list of priority drugs; forthcoming pilot of paediatric study submission policy) signalling additional opportunity for new ways of thinking and action and growth

"The problem is small enough and the problem is big enough"
[8]

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