Why orphan drug coverage reimbursement decision-making needs patient and public involvement

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A B S T R A C T

Recently there has been an increase in the active involvement of publics and patients in healthcare and research, which is extending their roles beyond the passive recipients of medicines. However, there has been noticeably less work engaging them into decision-making for healthcare rationing exercises, priority setting, health technology assessment, and coverage decision-making. This is particularly evident in reimbursement decision-making for ‘orphan drugs’ or drugs for rare diseases. Medicinal products for rare disease offer particular challenges in coverage decision-making because they often lack the ‘evidence of efficacy’ profiles of common drugs that have been trialed on larger populations. Furthermore, many of these drugs are priced in the high range, and with limited health care budgets the prospective opportunity costs of funding them means that those resources cannot be allocated elsewhere. Here we outline why decision-making for drugs for rare diseases could benefit from increased levels of publics and patients involvement, suggest some possible forms that involvement could take, and advocate for empirical experimentation in this area to evaluate the effects of such involvement. Focus is given to the Canadian context in which we are based; however, potentialities and challenges relating to involvement in this area are likely to be similar elsewhere.

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1. Introduction: The rise of publics and patients involvement in healthcare and research

Over the past twenty years there has been a considerable increase in the active involvement of publics and patients (Ps&Ps) in healthcare and research, extending their roles beyond those of passive recipients of medicines [1,2]. Patients’ views on their treatment preferences are now routinely gathered in the process of evaluating health interventions and prioritizing medical research [3], and publics are regularly engaged on emerging health technologies [4] in which their participation is being structured as a form of governance [5,6]. These developments have been mirrored in diverse areas of healthcare decision-making in which Ps&Ps have been involved in rationing exercises, priority setting, health technology assessment (HTA), and coverage decision-making. For instance, a recent survey of members of the International Network of Agencies for Health Technology Assessment (INAHTA) found that 22 agencies involved “consumers” in some aspects of their HTA programs, which ranged from seeking comments for refining the scope and nature of HTA projects, to considering suggestions of health technology topics, or even deeper involvement such as committee participation in the development of HTA protocols [7].
the area of healthcare rationing and resource allocation studies have explored various methods through which publics could be included through techniques such as discrete choice experiments [8], citizens’ panels and citizens’ juries [9,10]; however, there is noticeably less work reporting on actual experiences of integrating the outcomes of Ps&P involvement in decision-making.

In the face of these developments, there has yet to be research exploring how Ps&P involvement could be involved in reimbursement decision-making for “orphan drugs” or drugs for rare diseases (DRDs), and what role they might play in that process – some exceptions notwithstanding [11,12]. As we detail below, reimbursement decision-making for DRDs poses supplementary challenges to the ones already facing decision-making for common drugs or other areas of research and care. To be sure, all allocation decisions have implications for the kind of health care that will be available, and therefore benefit from involvement of Ps&P. In the absence of involvement activities, and in light of the supplementary challenges outlined below, we suggest here some possible forms that Ps&P involvement could take in the area of DRDs, and advocate for empirical experimentation to assess the effects of such involvement.

There is now a tremendous body of scholarship on public involvement in a broad set of topics ranging from environmental issues, civic planning, and other various forms of scientific practice and technological development. In fact the work is developing so fast that we cannot review it within the constraints of this paper; instead, we will focus on recent research concerning the involvement of publics in coverage decision-making and HTA in the Canadian context [13], drawing on authoritative reviews of the different approaches and their assessments [14]. As we show here, many of the dynamics surrounding the potentialities and challenges relating to DRDs are international. We draw on European and American legislation and use international research to help to frame some of the challenges of DRDs. However, jurisdictional forces require that coverage decision-making takes place at the level of the healthcare payer, requiring a focus on a specific (and in our case Canadian) context in which those decisions are based and where Ps&P involvement could practically be located. Furthermore, Canada stands at a particular historical moment in which orphan drug legislation may soon be introduced; providing a kind of research agenda—as we do here—for Ps&P involvement in DRD coverage decision-making is therefore both timely and important for the development of health policy. While the importance of fair representation of diverse interests and reasonableness of decision-making in the determination of what drugs are funded is of international relevance, the particular form that Ps&P involvement takes will inevitably depend on jurisdictional diversity of regulation and assessment that together define what will constitute trustworthy governance in its implementation [15].

2. Challenges and specificities surrounding drugs for rare diseases

One of the challenges facing DRDs is the absence of a consistent definition of what currently constitutes a rare disease both internationally and across Canada. Without a definition of what constitutes a rare disease, it is nearly impossible to be consistent in what drugs are designated as DRDs. The United States of America (USA) define a rare disease as “any disease or condition that affects less than 200,000 people in the United States,” [16] or about 1 in 1500 people. The province of Alberta states that a rare disease is a condition that affects fewer than 1 in 50,000, whereas in Ontario it ranges from 1 in 100,000 to 1 in 150,000, and the Canadian Organization for Rare Disorders uses 1 in 2000, which is also the case for the European Union and World Health Organization [17]. Alongside this variation in definitions there exists a wide range of rare conditions from those that are severe and life threatening (e.g. Paroxysmal nocturnal hemoglobinuria [PNH], Tyrosinemia) to others that do not immediately express themselves phenotypically (e.g. late onset Pompe, Gaucher), or may not be totally incapacitating (e.g. Phenylketonuria [PKU]).

There are a number of other challenges facing coverage decision-making in this area that relate to the growing number of DRDs, their associated high costs, and technological developments in disease stratification that are common across countries. The medicinal products used to treat such conditions have been labelled ‘orphan’ because of their applicability to very small populations, which historically represented a considerable disincentive to investment in research and development (R&D) by pharmaceutical companies. The implementation of the of the Orphan Drug Act in 1983 in the USA has worked to reverse these dynamics by offering pharmaceutical companies tax incentives, enhanced patent protection and market exclusivity, and clinical research subsidies to incentivise drug development for rare diseases [18]. Since then in the USA “more than 2800 orphan designations have been assigned and more than 400 products have received market authorization” [19], and there is considerable future growth anticipated with an estimated 1800 new DRDs in the development pipeline [20].

What is more, developments in genomic sequencing technologies and the emergence of “personalised medicine” are facilitating the identification of previously unknown rare diseases, as well as the stratification of more common diseases like cancer into increasingly rare subtypes. This means that there will be an increasing number of rare disease patients and an increasing number of DRDs, which can often – but not always – be costly. A recent European study authored by GlaxoSmithKline employees found that 30% of all approved DRDs are “first-to-market non-oncology rare disease treatments [that] are in the high range with the average price per patient per year of 200,000 Euros” [21]. DRDs are not the only high-cost drugs on the market, but the fact that they are often first-in-class, responding to an unmet medical need, differentiates them from other expensive medicinal products since they offer new hope to patients where often there has been none. Yet in the absence of alternative treatment there is an obvious reluctance on the part of decision-makers to refuse coverage of a DRD for cost reasons alone. Other high-cost drugs can be evaluated against comparator treatments in the coverage decision-making process, and can therefore be more justifiably refused coverage if they fail to meet cost-effectiveness criteria.
Organizations such as the Canadian Agency for Drugs and Technologies in Health (CADTH) and the pan-Canadian Oncology Drug Review (pCODR) are national bodies responsible for cost-effectiveness assessments; despite these institutions Canada is one of a few advanced industrialized countries that lacks of a national orphan drug program. This may change with a Canadian Orphan Drug Framework currently being developed and soon to be debated in the legislature to address that policy gap [22,23]. If actualized the framework would seek to “set the criteria for orphan drug designation… and outline the requirements for market authorization and mandate post-market oversight of the use of the orphan drug”, as well as allowing “for flexibility in the design of trials and in the evaluation of those results in order to accommodate smaller patient populations” thereby placing “a greater emphasis on post-market activities for orphan drugs” [22,23]. The existence of legislative frameworks and regulations in a number of different countries around the world to address issues relating to DRDs [24] works to differentiate these kinds of medicinal products from other high-cost drugs. What will not be addressed by the proposed Canadian framework is the jurisdictional conundrum relating to the regulation and delivery of pharmaceuticals. Individual provinces and territories are themselves responsible for the delivery of healthcare to their residents, and consequently make their own final decisions regarding all drug coverage on their individual formularies – not just DRDs – despite a drug market authorization process that takes place at the national level. Hypothetically, a DRD could pass through Health Canada and be issued market authorization (i.e. Notice of Compliance) allowing it to be sold anywhere in Canada; yet, the Common Drug Review undertaken by CADTH could find that it fails to meet cost-effectiveness criteria and therefore not recommend it to the provinces for coverage. In the face of these federal adjudications, individual provinces and territories still make their own decisions on listing and reimbursement of drugs. This leads to discrepancies across the country with regards to the availability of medicinal products, invoking rhetoric of ‘healthcare by postal code’.

There is no uniformity in the coverage decision-making process across provinces, and decision-making authorities in only a few provinces – British Columbia (BC) and Ontario – have developed specialized structures for coverage decision-making for DRDs. These specialized structures are separate from the review of more common drugs where it is more straightforward to insist upon and utilize clinical trial data. In 2007 the province of Ontario “established a working group of clinical experts (including genetic medicine) and health economists to develop a new evaluation framework to review and evaluate DRDs for funding by the province” [25]. Ontario’s Drugs for Rare Diseases Working Group is distinct from the province’s Committee to Evaluate Drugs, and has since established and published a seven steps “policy framework that attempts to address the policy challenges of funding drugs for rare diseases” that is summarized in Fig. 1 and described in full detail elsewhere [26].

Ontario also established Canada’s first Citizens’ Council in 2009. This ‘advisory body to the Executive Officer of Ontario’s Public Drug Programs and the Minister of Health and Long-Term Care… [which] provides advice on the values that reflect the needs, culture and attitudes of Ontario’s citizens about government drug policy” [27]. Discussed in further detail below, this council met in 2010 to consider questions related to DRDs. Meanwhile, there are currently no public or patient members sitting on Ontario’s Drugs for Rare Diseases Working Group, and two patient members on the Committee to Evaluate Drugs. Acknowledging the challenge of representing the diversity of views across public and patient groups through two patient members on the Committee to Evaluate Drugs “the Ontario government has now established a formal process for patients or caregivers, through an advocacy group, to submit evidence for new drugs undergoing funding review, including DRDs” [25]. The situation in BC is similar. Their Drug Benefit Council that provides coverage advice to the Ministry of Health for common pharmaceuticals has three public members, and the Ministry has “implemented a process that lets British Columbia patients, care givers and patient advocacy groups submit input on specific drug reviews” [28] that is called Your Voice [29]. The make-up of BC’s specialized structure for DRD coverage advice is not explicitly described in public documents or through their website, nor is the process through which their advisory decisions are made. It is therefore unknown what role – if any – Ps&Ps play in the provision of coverage advice for DRDs in BC. What weight or value that patient evidence is given – particularly in relation to cost-effectiveness criteria – is not clear in BC’s Drug Benefit Council nor Ontario’s Committee to Evaluate Drugs and their Drugs for Rare Diseases Working Group. Furthermore, while these systems for patient input may relieve pressure from organized patient groups, it is inadequate as a response to the challenge of wider representation of Ps&Ps. More innovative approaches (e.g. NICE’s Ps&Ps involvement) are still nascent and their assessment is not well developed [30,31].

Similar coverage decision-making dynamics are at work with cancer drugs, some of which could eventually be designated as DRDs with oncolgical conditions acting as a primary example of disease stratification dynamics described above. The pCODR is a process “designed to bring consistency and clarity to the assessment of cancer drugs by reviewing clinical evidence, cost-effectiveness, and patient perspectives, and using this information to make recommendations to Canada’s provinces and territories (except Quebec) in guiding their drug funding decisions” [32]. As of April 1st, 2014 pCODR has been brought under the auspices of CADTH, which provides similar funding guidance on all drugs to the provinces and territories. It is true that in oncology drugs can come with a comparably high financial costs and can serve relatively few patients when targeting a specific (genetic) sub-type of a more common condition; however, those treatment regimens are often relatively short courses, whereas DRDs can have treatment courses that can be more comparable to those associated with chronic conditions. For example, enzyme replacement therapy for Fabry’s disease is administered every few weeks for as long as the patient is responsive, which can continue for years.

Small patient populations also mean that generating statistically significant evidence of efficacy for DRDs is
almost impossible. Therefore, while there can be large price tags attached to some of these drugs, it is not always known if those high costs will translate into transformative health outcomes. If the conventional criteria used in decision-making for other medicinal products were deployed in the case of DRDs, many patients with rare conditions would go untreated. However, the rarity of a disease in-and-of itself is of course an insufficient basis upon which coverage decision-making would proceed. Not only has it been argued elsewhere that “valuing health outcome more highly for rare conditions is incompatible with other equity principles and theories of justice” [33], it might also be argued that valuing/prioritizing rarity in-and-of itself could signal an infinite willingness to pay to drug manufacturers thereby skewing the price for DRDs and (artificially) shifting the drug development pipeline from “blockbusters to niche busters” [34–36]. Recent research within our group has found strong values amongst Canadians concerning equal access to healthcare, but found a lack of evidence for coverage decision-making on the basis of rarity alone [37]. The so-called rule of rescue is sometimes invoked by media and stakeholders as a justification of coverage (i.e., the appeal to a felt imperative to act on behalf of identifiable individuals in great peril) [38], but the often unclear benefits, risks and extent of opportunity costs undermine any simple application of the rule of rescue to justify funding independent of assessing these features of each coverage decision.

As a result of these dynamics, decision-makers are facing increasingly difficult judgments about the amount of resources they dedicate to DRDs, and which ones specifically to cover. Since DRDs serve small patient populations, they represent a disproportionate use of resources compared with many of the expenditures for other patients. Therefore with limited healthcare budgets, the prospective opportunity costs of funding DRDs means that those resources cannot be allocated elsewhere, which raises questions about how best to spend public funds. Reimbursement decision-making related to DRDs could therefore benefit from Ps&Ps involvement so that adjudications are not solely reliant on conventional criteria of decision-makers and/or bureaucrats (i.e. cost effectiveness and evidence based on double blind randomized controlled trials) as is the case with other drugs and high cost interventions, but also take into consideration broadly held values of the Ps&Ps that sustain and use health products and services. Decisions about which medicinal products and services to fund shape what will be available in the future, and therefore what kind of society we will become and how we will support healthy and sick people. This is a political discussion about the kind of society we wish to become, and requires wide participation.

3. Existing research on patients and publics involvement in decision-making for drugs for rare diseases in Canada

As noted above, in 2010 Ontario’s Citizens’ Council met on the issue of DRDs, and was asked to consider “under what situations and/or conditions should the Ontario Government (i.e. taxpayers) pay for drugs for rare diseases?” [39]. This process resulted in sixteen recommendations (see Appendix 1) and garnered a direct response from Ontario’s Assistant Deputy Minister of Health [40]. This activity and its concurrent recommendations are a first step in opening the policy discussion on DRDs to a wider
Table 1
Possibilities for Patient and Public involvement in decision making for drugs for rare diseases.

<table>
<thead>
<tr>
<th>Goal of involvement</th>
<th>Group of tasks</th>
<th>Form of involvement</th>
<th>Accountability mechanism</th>
<th>Example in orphan drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Instrumental</td>
<td>Technology assessment</td>
<td>Institutionalized involvement</td>
<td>Answerability, citizen engagement</td>
<td>Citizens’ Council on Orphan Drugs Patient Task Force for Criteria Development</td>
</tr>
<tr>
<td>Democratic</td>
<td>Priority setting</td>
<td>Direct involvement</td>
<td>Answerability, citizen engagement, sanction, and appeals</td>
<td>Deliberative event that produces member(s) to sit on decision-making body (i.e. adaptive governance)</td>
</tr>
<tr>
<td>Developmental</td>
<td>Priority setting, criteria development</td>
<td>Ad hoc involvement</td>
<td>Answerability, citizen engagement, sanction, and appeals</td>
<td>Town hall meeting or national televised debate</td>
</tr>
</tbody>
</table>

A group of Ontarians. However, what this engagement activity failed to explore was the prospective trade-offs involved in funding DRDs vis-à-vis other health care interventions, and the processes through which agreement was reached on the diverse values underpinning their recommendations. Without being able to identify how decisions and preferences are come to by Ps&Ps it is nearly impossible to build on this kind of engagement and actually apply it to coverage decision-making.

Work appearing recently in Health Policy has examined stakeholder involvement in expensive drug recommendation decisions in Canada, Israel, England and Wales, Australia, and the USA [41] where “stakeholder involvement” included industry representatives and other actors alongside Ps&Ps. They concluded that a “central component of a legitimate and fair priority setting process is to make priority setting explicit and to involve both pertinent values and stakeholders in decision-making” [41]. However, given the study’s focus on the Canadian Drug Expert Committee (CDEC) an explicit role for Ps&Ps in coverage decision-making could not be explored in detail because of the lack public members on CDEC until 2007, and therefore fell outside the scope of that study.

Finally it should be noted that in 2013 a “Consultation on Drugs for Rare Diseases” was opened by CADTH, which houses the Common Drug Review (CDR) [42]. As it stands now it is unclear what the results of this consultation were, and what role they have played in influencing CADTH’s evolving position on DRDs [43]. As previously mentioned, centralized authorities like CADTH only provide recommendations through the CDR regarding whether or not to cover a medicine on a provincial formulary to the provinces, based heavily on cost effectiveness ratios, and decisions are made at the provincial and territorial level.

4. How patients and publics could be involved in decision-making around drugs for rare diseases

When deciding how Ps&Ps might be involved in decision-making processes it is crucial to first make the objectives of the involvement activity explicit. Abelson and colleagues stress this point, by stating that “only when the purpose and goals for public involvement and accountability are clearly articulated can the questions of by whom, for what and how, be addressed” [13]. Herein, we draw on the work of Abelson and her colleagues relating to involvement in HTA and coverage policy in Canada and apply it to the issue of DRDs in the same national context. We explore the three different goals of Ps&Ps involvement (instrumental, democratic, and developmental), and sketch out what involvement might entail in the area of DRDs, which are summarized in Table 1. We recognise the diversity of language and terms that have been used to describe these goals since Arnstein’s early characterization of a “ladder of citizen participation” [44]. To avoid confusion in the use of this terminology we link the discussion of goals with the direction of the flow of information as discussed by Rowe and Frewer and as exemplified in their Fig. 2 represented below [45]. It is important to underline that these different goals are not mutually exclusive, and the various involvement activities stand to embody a combination of these goals through the process. Crucial to the prospective involvement activities outlined below is the need for their formal evaluation. Involvement frameworks that are advanced by Abelson et al. and activities such as we describe below in the context of DRDs therefore require a synthesis with the kinds of frameworks provided in Rowe and Frewer’s earlier work and captured in Table 2 [14]. Not only are evaluations necessary to assess the outcomes and planning for future undertakings, but are also critical to be kept in mind during the design phases of involvement activities – a point we return to later.

In their framework for involvement in HTA and coverage policy decisions Abelson and colleagues distinguish “specific roles for the public, and relate them to several layers of policy analysis and policy making where ‘the public’ may engage in different tasks” [13]. A primary component of that framework is the identification of particular types of involvement (i.e. direct public representation, ad hoc public involvement, and institutionalized public involvement), and the summary of specific tasks that stand to facilitate decision-making in health arenas (i.e. priority setting, criteria development, and technology assessment). They also describe public accountability mechanisms that could be deployed across these tasks (i.e. answerability, citizen engagement, sanction, and appeals) [13]. To be clear, their framework does not directly link the above-mentioned tasks to specific models of Ps&Ps involvement, whereas our work below does attempt to make such linkages and provide examples of possible involvement in the space of DRDs.

Instrumental goals of an involvement activity are directed at improving the quality of decision-making. They “emphasize finding the most meaningful ways to gather input from relevant patient groups and publics to make
better quality decisions that reflect these groups’ preferences and values” [13]. With instrumental goals, the flow of information is one-way, from Ps&Ps to decision-makers, or what Rowe and Frewer describe as “public consultation” [45]. When such goals are made explicit involvement could be developed to undertake technology assessment tasks associated with evaluating specific technologies. Keeping in mind the work of Ontario Citizens’ Council noted above, consideration might be given here to experimenting with an institutionalized form of involvement such as a national Citizens’ Council that meets exclusively for the technology assessment of orphan medicinal products. The National Institute of Health and Care Excellence (NICE) in the UK has a Citizens’ Council that conducts assessments for all kinds of health interventions [46] – including “ultra orphan drugs” [47]. Patient involvement could also play an instrumental role in coverage criteria development tasks since the experience of living with a rare condition could aid in developing and operationalizing general and specific criteria, and in applying specific eligibility criteria, especially cut-offs and standards. This experiential expertise could be capitalized on either through the direct integration of patients in the coverage decision-making process, or through an institutionalized form in which patients meet to develop their own generic criteria that is then fed into the coverage process across all diseases.

Involvement activities can also be designed around democratic or political goals, which aim to increase the level of accessibility to decision-making processes and make them accountable to a greater number of citizens. Key to these goals is the bi-directional flow of information in which participatory or engagement activity facilitates the co-production of a coverage policy or HTA task between decision-makers and Ps&Ps. In such cases it might make sense to include Ps&Ps in priority setting tasks that help to define the scope of public funding for DRDs. Priority setting tasks can also include allocating budgets for health care services among competing social welfare needs, setting priorities for assessment among specific services, and setting priorities for public funding within a budget among specific services [12]. In the scope of such activities, Ps&Ps could be involved directly in the process through which decisions are made on the DRDs that are covered. However, the goal of democratic involvement is undermined by merely privileging a few individuals from the wider community or patients/patient groups. Such representatives are usually outnumbered, tend to take on or defer to the perspectives of the experts, and can only reflect their own personal perspective rather than recognize and reflect the diversity in the community. The result is usually a reinforcement of informed consent and few decisions about what is appropriate to approve and fund. To avoid this kind of tokenism deliberative public events [48] can first be held on DRDs that can yield members who understand the technical issues and the diversity of perspectives across communities. The Ps&Ps members then form an advisory body, some or all of which are

![Fig. 2. Flow of information as discussed by Rowe and Frewer.](image)

### Table 2
Criteria for the Evaluation of Public Participation in Science and Technology Policy.

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptance criteria</td>
<td>Criterion of representativeness</td>
<td>The public participants should comprise a broadly representative sample of the population of the affected public.</td>
</tr>
<tr>
<td></td>
<td>Criterion of independence</td>
<td>The participation process should be conducted in an independent, unbiased way.</td>
</tr>
<tr>
<td></td>
<td>Criterion of early involvement</td>
<td>The public should be involved as early as possible in the process as soon as value judgments become salient.</td>
</tr>
<tr>
<td></td>
<td>Criterion of influence</td>
<td>The output of the procedure should have a genuine impact on policy.</td>
</tr>
<tr>
<td></td>
<td>Criterion of transparency</td>
<td>The process should be transparent so that the public can see what is going on and how decisions are being made.</td>
</tr>
<tr>
<td>Process criteria</td>
<td>Criterion of resource availability</td>
<td>Public participants should have access to the appropriate resources to enable them to successfully fulfill their brief.</td>
</tr>
<tr>
<td></td>
<td>Criterion of task definition</td>
<td>The nature and scope of the participation task should be clearly defined.</td>
</tr>
<tr>
<td></td>
<td>Criterion of structured decision making</td>
<td>The participation exercise should use/provide appropriate mechanisms for structuring and displaying the decision-making process.</td>
</tr>
<tr>
<td></td>
<td>Criterion of cost-effectiveness</td>
<td>The procedure should in some sense be cost-effective.</td>
</tr>
</tbody>
</table>

(Adapted from Rowe and Frewer, [14])
involved in the HTA or coverage decision-making body. While involving Ps&Ps stakeholders in this way has been described as “adaptive governance” [6], it is important to stress that such participation needs to be supported by sufficient resources (financial and administrative) to enable them to engage the wider community again in the future.

According to Abelson and colleagues involvement can also be undertaken with developmental goals in mind, in which the activity seeks to increase the knowledge, capacity and competency of participants. Elsewhere, these goals have been described as “educative” [49], and in these situations the flow of information is one-way from decision-makers to Ps&Ps. In such circumstances an ad-hoc public involvement such as a town hall meeting or televised debate would reach a large number of people, and could potentially be used for criteria development or priority setting tasks. Involvement activities with developmental goals need not close down discussion on this issue of DRDs, and we are not advancing a “deficit model” argument whereby the purpose of involving publics is to increase their knowledge in anticipation that they will be more trusting and their concerns will be alleviated [50]. The point, rather, of these kinds of involvement activities would be provide balanced information so that publics and patients in Canada could have a broader and increasingly informed discussion about the challenges – and prospective solutions – facing DRDs.

As we have noted, there is a wide body of work on the evaluation, which couples the scholarship on public involvement in science, technology and policy. The framework offered by Rowe and Frewer has been very influential in this area suggesting that “evaluation criteria may be divided into acceptance criteria, which are related to the effective construction and implementation of a procedure, and process criteria, which are related to the potential public acceptance of a procedure” [14]. These criteria are summarized in Table 2.

In a hopeful future in which experimentation are made with a diversity of involvement activities outlined here it is imperative that they are coupled with evaluative criteria to inform the development and deployment of future Ps&Ps involvement activities for DRDs. While Rowe and Frewer offer a framework for evaluation of involvement activities they themselves remark that “future research needs to develop instruments to measure these criteria more precisely and identify the contextual and environmental factors that will mediate the effectiveness of the different participation methods” [14]. To be sure, there may currently be a lack of validated instruments to evaluate involvement activities; however, it does not follow that such activities are without value or merit. Experimentation with the kinds of activities outlined here is therefore required not only to fill the void of Ps&Ps involvement with DRDs, but also to further sharpen existing evaluative frameworks.

It is important to note that the examples provided above and summarized in Table 1 do not represent an exhaustive list of ways through which Ps&Ps could be involved in decision making for DRDs, nor does it present a prescriptive framework for which Ps&Ps should necessarily be involved in diverse health policy tasks. As has been discussed in relation to Ps&Ps involvement for the governance of biobanks, the scale and structure of the involvement must be tailored to the decisions to be made [6]. Such a determination requires experimentation with – and evaluation of – different forms of P&P involvement and governance. Once these kinds of experiments of involvement have been conducted and evaluated we will be in a better position to refine the involvement process, sharpen their assessment and answer questions pertaining to their operations and evaluations (e.g. which kind of institution would be able to support – in terms of finance and capacity – the involvement activity in question? Would each province require involvement activities, or could a national body undertake some tasks on behalf of the provinces?)

5. Conclusion–A call for implementation and evaluation of Ps&Ps involvement in decision-making for drugs for rare diseases

Considerable scholarship exists that has described the benefits and drawbacks of Ps&Ps involvement in a diversity of areas of science, technology and policy, whereas another body of work has identified the challenging issues facing DRDs. What is needed now is concrete action to link these two areas of scholarship by conducting experiments with meaningful forms of Ps&Ps involvement in the space of DRD coverage decision-making. To be sure, difficult decisions constantly have to be made in medicine and healthcare, and while there are many areas—such as the organization and delivery of services, or medical R&D—that have seen an increase in active Ps&Ps involvement, this has been lacking in the area of DRDs. The high costs of many DRDs for small patient populations pose significant opportunity costs to tightening health care budgets, which represent just the tip of the iceberg when it comes to the host of challenges that are both common internationally, and in some cases specific to Canada. Decision-making on DRD coverage is therefore especially difficult, making it suitable for Ps&Ps involvement. While we have outlined some forms in which involvement in orphan drugs could take, a dearth of empirical research in this area means that we do not know how they might be executed and what effect they might have in either helping or hindering decision-making processes. Here we have extended an existing framework for bringing publics into HTA and coverage policy decisions that has been offered by Abelson et al., suggested a synthesis with evaluative frameworks provided by Rowe and Frewer, and applied it to the specific area of DRDs. Considerable work still needs to be done so that Ps&Ps are meaningfully involved in decision-making spaces for DRDs, and further refinement of evaluative frameworks is also still necessary to ensure that involvement is carried out in a robust and meaningful way. Such work requires careful experimentation with a range of different Ps&Ps involvement activities, which can then be further refined and ultimately linked to particular health policy tasks and broader instrumental, democratic, and developmental goals as they pertain to DRDs.
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Appendix 1. Ontario Citizen’s Council Recommendations for Funding Drugs for Rare Diseases

1. Drugs for rare diseases should have their own set of funding criteria.
2. There must be different standards for the approval of drugs for rare diseases.
3. The common good of the majority of the population must take into consideration the minority of citizens suffering from rare diseases.
4. The competing needs for health care dollars mean that there should be an attitude fostering prudent fiscal management for drugs for rare diseases.
5. Decisions regarding funding for rare diseases need to be transparent, as does the rationale for them.
6. The medical community must document the progression of the disease when a drug is administered to sufferers of rare diseases. Sharing national and international research is essential, particularly for rare diseases.
7. It is the responsibility of experts to evaluate the evidence for the effectiveness of drugs for rare diseases. This evaluation must not be determined by politics or economics.
8. Beneficiaries of drugs for rare diseases, their families and their caregivers and their health care professionals share the responsibility to use the drugs properly, to monitor and to report on its effectiveness.
9. Quality of life and potential lifespan must underpin all consideration of funding for drugs for rare diseases.
10. The Ministry should raise awareness of its policies and procedures for approving and adding new drugs to the Formulary and removing old ones; these explanations should not only be focused on those suffering from rare diseases, but also directed to the public at large.
11. A definition of rare diseases must be established by experts and publicized. A national standard would be desirable.
12. The treatment must be monitored throughout to assess continued effectiveness and to add to medical knowledge. Patients must follow the prescribed regimen.
13. The patient, his or her caregivers and health care professionals share the responsibility to make data collection possible. The patient must agree – in a contractual arrangement- to participate in monitoring studies.
14. Funding for an individual patient can start if the patient has been diagnosed, is likely to benefit, and agrees to abide by conditions set by the Ministry experts even though the process for adding an approved critically-needed drug to the Formulary may not be completed.
15. Funding for an individual patient should be stopped if the drug is no longer effective or if, even with appropriate support, the patient does not comply with the contractual conditions of monitoring and of following the prescribed regimen.
16. The Ministry should develop a transparent plan for removing drugs from the Formulary that are found to be no longer effective.

References
