Commentary: Which Principles Should Apply for a National Strategy on Rare Diseases?

Commentaire : Quels principes devraient s'appliquer à une stratégie nationale pour les maladies rares?

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Abstract

Lexchin and Sirrs (2024) proposed five relevant principles to guide the use of federal funding for expensive drugs for rare diseases, including funding of outcomes-based risk-sharing agreements (OBRSAs) and proactive commitment and participation in the generation of high-quality evidence in a transparent way. This rejoinder, however, questions whether the federal funding should be used only to buy new drugs or whether it could be used to develop new drugs as well. It also examines what OBRSAs would require in terms of institutional capacities to allow the collection of real-world evidence.

Résumé

Lexchin et Sirrs (2024) proposent cinq principes pertinents pour guider l'utilisation du financement fédéral pour les médicaments onéreux pour les maladies rares, dont le financement des ententes de partage des risques axées sur les résultats ainsi qu'une participation proactive à la production de données de qualité de manière transparente. Cette réplique pose toutefois la question à savoir si le financement fédéral devrait être utilisé uniquement pour acheter de nouveaux médicaments ou s'il pourrait également être employé pour développer de nouveaux médicaments. Il examine également ce dont les ententes de partage des risques auraient besoin en matière de capacités institutionnelles afin de permettre la collecte de données probantes concrètes.

Overview

Lexchin and Sirrs (2024) have identified a serious problem with the Canadian government's announcement (Health Canada 2023) of a national strategy for high-cost drugs for rare diseases (DRDs): money is being provided without any guidelines on how it should be used. Lexchin and Sirrs (2024) propose five principles that they assert should guide the use of federal funding for expensive drugs for rare diseases (EDRDs), including funding of outcomes-based risk-sharing agreements (OBRSAs) and proactive commitment and participation in the generation of high-quality evidence in a transparent way. While the proposed principles are sound, some additional nuance seems necessary.

Should a national strategy for rare diseases be limited to drugs?

Patients with rare diseases (and their families) have important needs beyond pharmaceuticals that must also be taken into account. Key issues for families dealing with a rare disease go beyond accessing medication: they may need to obtain appropriate medical equipment, adapt the house or the car or cope with lost income because of constant hospital visits or because one parent needs to stay at home with a sick child (Awada 2023). It is odd that governments are willing to pay $300,000 per year for a drug that will slow the progress of a rare disease by 15%, yet ensuring that even a small fraction of that amount is available to pay for adequate social support apparently remains unviable. A national strategy should focus on how to best help patients with rare diseases in all areas of their lives, not only on costly pharmaceutical provision.

Should we only buy drugs or also develop them?

In March 2023, the federal government announced a three-year plan to spend $1.5 billion over three years on high-cost rare disease drugs, but most of the money ($1.43 billion) was meant to boost the ability of public drug plans to purchase EDRDs (Health Canada 2023). Another $36 million of the $1.5 billion will be spent to help the Canadian Drug Agency, the Canadian Institute for Health Information and Health Canada to support the implementation of the strategy and improve the collection of information. Lastly, only $32 million of the $1.5 billion will go to the Canadian Institutes of Health Research to advance rare disease research and establish a rare disease clinical trials network. In many ways, this focus on buying drugs marketed by corporations instead of advancing institutional capacity to develop drugs ourselves is baffling. The market system is not well adapted for DRDs; the term "orphan drugs" describes drugs that lack market incentives for their development (Mikami 2019: 609). Why then are efforts so focused on buying drugs marketed by private interests?

The stories of two DRDs developed in Canada – Strensiq and Glybera – help illustrate the point. Strensiq is a drug for an ultra-rare bone disease called hypophosphatasia and was developed in Montreal's universities and by a start-up company, Enobia. The drug was then acquired by the company Alexion, as Enobia did not have the capacity to bring the drug to market (Gagnon 2021). At the time, Alexion was selling only one drug, Soliris, considered

the world's most expensive drug. Alexion marketed Strensiq in 2014 at a prohibitive price; consequently, most Canadians who stood to benefit from the drug could not access it. Following the acquisition and the successful marketing of Strensiq, in 2014, Alexion's chief executive officer, Leonard Bell, became the world's highest paid pharmaceutical executive ever with a total compensation of $217 million (Lazonick et al. 2017), an amount larger than the total payroll for all non-executive employees at the company. If we only make policy decisions that encourage paying more for EDRDs instead of developing alternative ways to bring these drugs to the market, are we really incentivizing relevant research or are we simply fattening shareholders?

Glybera is a gene therapy that treats a genetic condition called lipoprotein lipase deficiency. It was the first-ever gene therapy, developed by academics at the University of British Columbia in partnership with a small European drug company called Amsterdam Molecular Therapeutics (AMT). The company went bankrupt during the drug's regulatory approval process time and was acquired by the company uniQure. uniQure attempted to market the drug at $1 million per treatment, the highest price ever seen at the time. No drug plan was willing to reimburse the drug and, instead of selling the drug at a lower price, the company shelved the drug entirely (Crowe 2018). In 2019, the National Research Council (NRC) announced that they would start producing the drug themselves through their public labs (Crowe 2019) and would sell the drug at a portion of its initial price (NRC 2020). This example makes the case that the national strategy for DRDs should also support alternative ways to bring drugs to the market, such as the public production of DRDs by the NRC. As it currently stands, however, we only have significant additional funding for buying DRDs, not developing them ourselves.

Which principles should apply for the purchase of DRDs?

Because of the lack of guidelines on how this money should be spent, the principles proposed by Lexchin and Sirrs (2024) are relevant and deserve a closer look. According to the authors, no additional funding should be used for drugs that already have high-quality evidence, meaning that the purpose of the funding ought to be associated with securing OBRSAs for new DRDs entering the market without high-quality evidence of risks and benefits, under the condition of a commitment by the manufacturer to transparently generate the missing evidence. This approach provides sound principles for the national strategy based on existing literature about OBRSAs (Dabbous et al. 2020; Facey et al. 2021; Kim et al. 2020; Mendell et al. 2023; Thanimalai et al. 2021). However, some challenges remain for the implementation of such principles.

While some DRDs are offered only in hospital settings, which is a suitable environment for the generation of real-world evidence (RWE), many DRDs are only offered as prescription drugs taken outside hospital settings. This requires additional institutional capacity to collect real-world evidence (Gonçalves et al. 2018). While this work would normally fall on the shoulders of the prescribing physician, it is worth noting that community pharmacists

in Quebec showed considerable capacity to collect RWE for Paxlovid in the context of the COVID-19 pandemic, based on a provincial not-for-profit patient-support program (Accessa 2022). Such capacity could be of interest for the implementation of OBRSAs for DRDs.

Moreover, OBRSAs are agreements between the payer (the drug plan) and the manufacturer in which the funding of the drug can be withdrawn if post-market trials fail to provide clear evidence of the drug's therapeutic value (Thanimalai et al. 2021). OBRSAs are easier to achieve when the whole population is covered through one national drug plan. However, in Canada, there are more than 100 public drug plans and more than 100,000 private drug plans (Advisory Council on the Implementation of National Pharmacare 2019). While public drug plans collaborate in negotiating financial risk-sharing agreements (confidential rebates) through the pan-Canadian Pharmaceutical Alliance and could develop better capacity to negotiate OBRSAs, most private plans have no capacity to negotiate such OBRSAs. Do the principles proposed by the authors imply full public coverage for DRDs without high-quality evidence? If this is the case, this assumption should be explicit.

These caveats should not be interpreted as obstacles to implementing the suggested principles. On the contrary, by setting down clear principles regarding how this new federal funding for DRDs should be used, Lexchin and Sirrs (2024) have started an important discussion on how to make this funding work in the best interest of patients.

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