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EDITORIAL

A centralized rare disease database and whole-genome sequencing as a standard of care: two essential implementations for the future of health

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Introduction

Rare diseases affect approximately 1 in 12 Canadians and most have underlying genetic causes. Many individuals who are at risk either have yet to be diagnosed or remain unaware of their risk (Canadian Organization for Rare Disorders 2021). In Canada, research on rare diseases has been limited, as there are not enough diagnosed rare disease patients present in any one area to be able to conduct meaningful research. Data from rare disease patients need to be centralized, accessible, and shared among researchers to further research that can help diagnose and, ultimately, treat rare disease patients in Canada.

The need for greater data sharing is even more important with the advent of new technologies, such as whole-genome sequencing (WGS), which can reveal an individual's entire genetic makeup. This has the potential to increase diagnostic yield, reduce odyssey times to obtain a diagnosis, and lead to earlier treatment and intervention options. Though it is slowly entering clinical care in Canada, the clinical use of WGS is not currently the standard of care.

To advance rare disease research, Genome Canada launched the All for One initiative that seeks to implement a centralized rare disease database for the integration of rare disease research and clinical data across Canada by facilitating data sharing (Genome Canada 2018). It also seeks to ensure access to clinical WGS as the standard of care for Canadians at risk for rare diseases.

The objectives set out by the All for One initiative are innovative and ambitious, but their implementation will come with its fair share of challenges. Conversely, some drivers may facilitate the implementation of a centralized database and clinical access to WGS as a standard of care. To better understand the barriers and drivers of such a program, we surveyed stakeholders from the Canadian rare disease research community using a two-round survey. Of the 34 respondents, 12.5% were information technology (IT) managers, 12.5% clinicians, 25% directors of a genetic laboratory clinic, 19.75% policymakers, and 31.25% researchers or academics (Genome Canada 2021).

Challenges for the rare disease database

Data security and confidentiality continue to be a significant barrier to the development of a centralized database. Respondents to our survey have concerns specifically about protecting patient privacy. If the main goal of such an initiative is to facilitate data sharing, it may be accompanied by a greater risk of breaches if specific data management measures are not put in place. These concerns are especially amplified when it comes to data sharing with third parties. While enhanced consent may mitigate some of these concerns, respondents emphasized that it could act as an additional burden at the clinical level.

Another hurdle is compliance with laws, regulations, and the internal policies of some organizations. Compliance with data sharing regulations is made more difficult by the fact that legislation is subject to change, requiring an ongoing compliance process (Michaluk 2020). Not surprisingly, in terms of regulatory issues, our survey results showed that restrictive data sharing policies at clinical and hospital sites are one of the main barriers to implementing a rare disease database.

Some practical elements should also be considered, particularly at the logistical and technical level, as respondents identified the lack of IT support in hospitals needed to integrate a rare disease database.

Challenges for clinical implementation of WGS

One of the most important constraints of WGS is addressing the training needs of clinicians not specialized in genetics. Albeit less important, respondents also identified that the lack of informatics in hospitals—for example, to analyze large data sets—and privacy risks could act as a barrier to the use of WGS.

On a more structural basis, the lack of an interoperable structure for data storage and management may explain in part why respondents felt that the Canadian health system lacked the capacity to implement WGS efficiently and effectively.

Facilitating factors for the rare disease database

Many factors could facilitate the implementation of a rare disease database. Most notably, survey respondents identified securing stable long-term funding, a key challenge for the database, as necessary for its sustainability beyond initial implementation. Well-defined governance and oversight mechanisms at the national level were also identified as crucial to the implementation of the database.

Respondents also identified the need for data interoperability, that is, its ability to be shared and exchanged in a useful manner. As mentioned, data sharing in Canada operates within a complex regulatory structure with health largely a matter of provincial jurisdiction, which restricts data interoperability and sharing. Respondents highlighted leveraging existing policies, regulatory frameworks, and practices as useful mechanisms in achieving interoperability.

While greater data sharing is imperative, it should not compromise the protection of patients' rights, especially concerning privacy and the confidentiality of their personal information. Mechanisms that both respect patients' rights and facilitate data sharing will be necessary. Respondents identified sharing coded data (whereby patients' personally identifiable information is removed and replaced by an alphanumeric code) with other researchers over controlled access databases as the most common standard of care in this area.

Respondents also considered stakeholder buy-in as important in implementing the database and ensuring compliance with existing norms. The support of the decision-making bodies, at both the

national and provincial levels, and engagement with provincial health authorities were considered useful in this regard.

Facilitating factors for clinical implementation of WGS

Obtaining support from institutions and decision-makers, most notably at the provincial level, was considered by our respondents to be important for facilitating the implementation of WGS in Canada. Indeed, because of its high costs, significant resources will be required to efficiently implement WGS. Respondents also suggested harnessing existing resources, such as leveraging the expertise of trained bioinformaticians and looking to other jurisdictions where WGS has been more widely implemented for novel and efficient approaches.

Many Canadian provinces are currently repatriating WGS analyses rather than outsourcing to the United States with the goal of eventually integrating it into our health care systems (e.g., Government of Quebec 2018). In Quebec, for instance, it is estimated the province will save $25 million through repatriating WGS from laboratories in the United States (G. Rouleau, personal communication, 2021).

In anticipation of this widespread clinical implementation and to address the training needs of clinicians not specialized in genetics, our respondents viewed the incorporation of information on WGS into curricula as most effective in educating clinicians.

Conclusion

There is no doubt that the establishment of a database to facilitate the sharing of information on rare diseases will benefit the health sector in many ways. Similarly, the implementation of new technologies such as WGS as a standard of clinical care will increase the efficiency of medicine, especially at the patient level. The introduction of these innovations will certainly come with a set of challenges that may hinder the projected benefits if the right facilitators are not implemented.

Although the barriers and drivers identified in this article are presented primarily in the context of rare diseases, they could also very well occur outside of the rare disease community. Indeed, rare disease genes also play a role in the expression of common diseases. Considerations such as patient privacy and confidentiality, regulatory compliance, lack of funding, and IT infrastructure may be relevant in any data sharing context, especially when it involves sensitive genetic information as in the health sector. Perhaps, the use of WGS in the clinic will serve to "normalize" such data as part of health.

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Author contributions

JH and BMK conceived and designed the study. JH performed the experiments/collected the data. SF, DP, and JH analyzed and interpreted the data. JH and BMK contributed resources. SF and DP drafted or revised the manuscript.

Competing interests

The authors have declared that no competing interests exist.

Data availability statement

All relevant data are within the paper.

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