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Hereditary Cardiovascular diseases NGS Panel

Evaluation report on the repatriation of an analysis carried out outside of the province of Québec

English summary

Une production de l'Institut national d'excellence en santé et en services sociaux (INESSS)

Québec

SUMMARY

Hereditary Cardiovascular diseases NGS Panel

Evaluation report on the repatriation of an analysis carried out outside of the province of Québec

Background and mandate

Requests for authorization of medical laboratory services that are not available in Québec are mainly for high-throughput simultaneous sequencing of multiple genes using the so-called next-generation approach. The province's laboratories have the technology and expertise to perform these tests. With a view to achieving economies of scale and promoting more judicious use of these services, the Ministère de la Santé et des Services sociaux (MSSS) has undertaken to quickly repatriate several tests performed using next-generation sequencing (NGS), under the governance of the Réseau québécois de diagnostic moléculaire (RQDM). The rollout of this vast project undoubtedly entails opportunities and risks with respect to the overall offer of service and requires reflection in this regard.

At the MSSS's request, the Institut national d'excellence en santé et en services sociaux (INESSS) is conducting a rapid assessment of the relevance of, the issues surrounding and, when appropriate, the optimal implementation mechanisms for the repatriation of these tests, from the overall perspective of Québec's healthcare system. The present report deals specifically with NGS gene panels for the molecular diagnosis of hereditary cardiovascular diseases: cardiomyopathies, arrythmias and aortopathies.

Method

The process included a rapid review of the scientific and grey literature regarding the clinical and economic aspects, a budget impact analysis, and consultations with Québec experts. Only documents containing synthesis data or recommendations concerning the use of an NGS test to diagnose hereditary cardiovascular diseases were retained. INESSS set up an advisory committee, whose members were invited to express their views on the different issues associated with the repatriation of the proposed tests. The final findings are based on the triangulation of the scientific data, the positions of the main learned societies consulted, and the contextual data and experiential knowledge gathered.

Clinical contexts and proposed tests

Cardiovascular diseases are a very heterogeneous group of disorders that can be acquired or inherited. The hereditary forms include the familial cardiomyopathies, arrhythmias and aortopathies. The mode of transmission and penetrance vary according to the phenotypic group and the gene involved. Therefore, to identify or confirm the genetic etiology of a hereditary cardiovascular disease (genotype/phenotype correlation), the requester is proposing the rollout of an offer of service that includes 17 virtual panels

of genes associated with the different phenotypic groups of hereditary arrhythmias, cardiomyopathies and aortopathies. These panels will be analyzed using the sequencing data on 445 genes, of which a maximum of 97 will be reported on in the context of the current knowledge.

Validity and clinical utility

The genes for the provincial offer of molecular diagnosis of hereditary cardiovascular diseases were chosen mainly on the basis of the scientific literature and widely recognized resources, such as PanelApp (Genomics England, UK) and ClinGen (National Institutes of Health, USA).

Based on preliminary local data, the diagnostic performance of the proposed tests is approximately 14% for hereditary arrhythmias and 22% for hereditary cardiomyopathies. Data for the aortopathies were not available at the time of writing.

In addition to confirming a genetic etiology, identifying a pathological or likely pathological variant enables one to assess the prognosis, target family screening and tailor the medical management of the patients concerned. In individuals with significant cardiomyopathy or arrhythmia or at known risk of arrhythmia, an implantable automatic defibrillator might be considered.

Fifteen learned society publications support the clinical utility of these molecular tests. It is recognized that gene panels and whole-exome sequencing play an important role in the diagnosis, management and monitoring of hereditary cardiovascular diseases. This type of testing has, in fact, received favourable public coverage recommendations in Australia, France and the United Kingdom.

Implementation considerations

The experts consulted and the literature agree that genetic testing should be prioritized on the basis of a combination of clinical presentation and family history information. In this regard, to support the rollout of this offer of service and the optimal use of these tests, a clinical algorithm is presented. A prior medical genetics or cardiogenetics consultation is recommended in order to assess the presence of clinical and paraclinical criteria and guide the choice of molecular tests accordingly. Given that this service is already offered to patients at the Institut de cardiologie de Montréal and that procedures for sending specimens outside Québec are used for patients at other institutions, an impact on their continuum of care or a significant increase in demand is not anticipated. In light of the consultations held, the offer of service appears to be generally in line with the needs.

Nevertheless, certain suggestions regarding the clinical criteria, the wording used in the algorithms, and the thoroughness of the testing for certain cardiovascular conditions were offered by the experts consulted. In addition, some experts felt that it would be useful to consider adding genes previously identified as being potentially associated with a hereditary cardiovascular condition by outside laboratories, in order to ensure an offer of service tailored to the needs of the local populations.

Also, concerns of a more generic nature that do not specifically pertain to cardiovascular disease panels were raised during the consultations. Some of these concerns were about the procedures for ordering tests, the validation of their appropriateness, the training of prescribers, reporting procedures, access to the patient's medical records, the lack of clear policies on the management and disclosure of variants of uncertain significance, retesting for these variants, and the dissemination of modified reports.

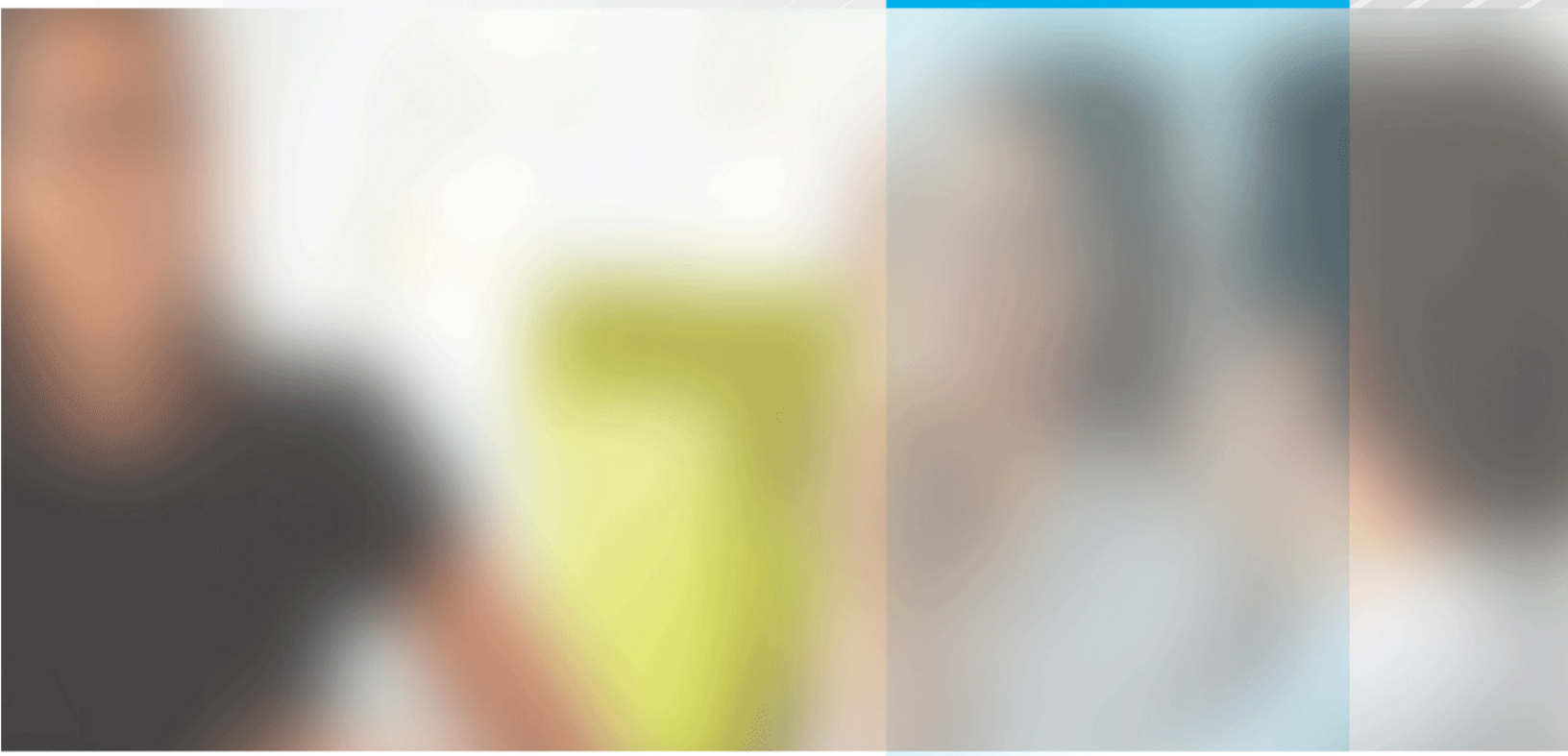
Economic analysis

Two health technology assessment reports were identified whose conclusions regarding the cost-effectiveness analysis seem to be transferable to the Québec context. According to their authors, hereditary arrhythmia and cardiomyopathy NGS panels are more cost-effective than the usual care, but they mention the significant level of uncertainty in these results.

As for the budget impact analysis, depending on the assumptions made, repatriating all of the NGS molecular tests for the diagnosis of hereditary cardiovascular diseases could generate savings of close to $1.2 million over 3 years for serving patients throughout Québec. These savings could range from around $750,000 to $1.8 million.

Conclusion

This report is based on a rapid review of the scientific and grey literature and on the expert perspective. It is intended to assist the MSSS in its decision to repatriate the gene panels for the molecular diagnosis of hereditary cardiovascular diseases. In this exercise, no major issues were identified, and the information gathered supports the appropriateness of repatriating these tests. However, certain concerns pertaining to the needs of local populations and the organization of the services surrounding the execution of these tests in Québec were raised and should be explored to ensure optimal implementation. Also, the conclusions regarding the stated potential savings should be viewed with caution.



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