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Pertussis: diagnostic modalities and trajectory

English summary

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SUMMARY

Pertussis: diagnostic modalities and trajectory

Introduction

Pertussis is a serious and highly contagious disease caused by the bacterium *B. pertussis*. The pediatric population is the most at risk for death or complications from this disease. In Québec, it is one of the notifiable diseases (MADO) under epidemiological surveillance. Between 240 and 1,600 cases of pertussis occur annually. A number of countries with health-care systems comparable to Québec's report problems with the underdiagnosis of pertussis and the underreporting of cases to the competent public health authorities.

In Québec, a supraregional-level test performed at the Centre hospitalier universitaire Sainte-Justine is listed in the *Répertoire québécois et systèmes de mesure des procédures de biologie médicale* (hereafter the *Répertoire*). This is an "in-house" test (coded 45010) for detecting and differentiating four bacterial targets in patients who might have pertussis: *Bordetella pertussis* (*B. pertussis*), *Bordetella parapertussis* (*B. parapertussis*), *Chlamydophila pneumoniae* (*C. pneumoniae*) and *Mycoplasma pneumoniae* (*M. pneumoniae*). This test is available only through the service corridors of one of the four university health and social services networks (RUISs) in Québec's health-care system, which leads to delays in communicating the results to the requesting physician. To remedy this situation, the institutions in the regions, in particular, the CIUSSS du Saguenay-Lac-Saint-Jean, are calling for a regional option for diagnosing pertussis. This new molecular test would target *B. pertussis* and *B. parapertussis* to establish or confirm a diagnosis of pertussis. It was in this context that INESSS assessed the relevance of including or not including in the *Répertoire* a molecular approach for detecting *B. pertussis* and *B. parapertussis* at the regional level, without focusing on any specific commercial kit.

Method

The strategy for identifying relevant publications was developed in collaboration with INESSS's scientific information specialists. The initial search was conducted in March 2020, with updates in August 2020 and May 2021. The MEDLINE (PubMed), EMBASE, Evidence-Based Medicine Reviews (EBM), Cochrane, and International Network of Agencies for Health Technology Assessment (INAHTA) databases were queried. The information search was supplemented by consulting the websites of learned societies and professional and regulatory bodies in Canada, the United States, the United Kingdom, Australia, and certain European Union countries. The Google and Google Scholar search engines were used as well. A complementary selection process was used to identify articles on economic analyses of implementing the molecular detection of *B. pertussis* and *B. parapertussis.* The methodological quality of the selected publications was assessed using the AGREE II-GRS (Appraisal of Guidelines, for

Research, and Evaluation II) instrument. The aspects excluded from this review were primary prevention strategies (vaccination) and all the issues related to the treatment of pertussis. To obtain the perspectives of experts, INESSS created an advisory committee consisting of physicians specializing in medical microbiology, respirology, pediatrics and public health, and experts in laboratory tests and management. In addition, we conducted a consultation in the form of a questionnaire intended for clinicians and other health professionals in Québec who might order a molecular test to establish or confirm a diagnosis of pertussis.

The methodology was deployed for five assessment questions:

- What are the best practices recommended for establishing a diagnosis of pertussis: the population, signs and symptoms, tests, bacterial targets, and test result turnaround time?
- What is, for pertussis, the diagnostic value of a multiplex nucleic acid amplification test (NAAT) with two or more targets?
- To what extent does the turnaround time for *B. pertussis* and *B. parapertussis* tests for establishing a diagnosis of pertussis affect the patient's clinical outcome?
- What is the organizational impact of implementing, at the regional level, the molecular detection of *B. pertussis* and *B. parapertussis* for establishing a diagnosis of pertussis?
- What is the budget impact of implementing, at the regional level, the molecular detection of *B. pertussis* and *B. parapertussis* for establishing a diagnosis of pertussis?

Results

Best practices recommended for diagnosing pertussis

The guidance documents consulted from organizations of interest recommend the use of NAAT as an appropriate laboratory test for confirming a case of pertussis. Indeed, they agree in recognizing that making a diagnosis of pertussis on the basis of the patient's clinical presentation alone does not suffice. This position was endorsed by most of survey's respondents. According to the clinical practice guidelines consulted, one-third of infected infants do not present with whooping, which is known as the classic symptom of pertussis, but will instead have atypical symptoms whose interpretation will require laboratory confirmation. In this regard, the World Health Organization (WHO) recommends testing simultaneously for the bacterium *B. parapertussis* in patients suspected of having pertussis. The Laboratoire de santé publique du Québec no longer favours culturing for the purpose of diagnosing pertussis, favouring NAAT instead. However, NAAT results might not be reliable if antibiotics were administered two to five days before the test specimen is obtained.

Diagnostic performance

The 12 studies selected for the purpose of assessing the performance of NAAT in detecting and differentiating *B. pertussis* and *B. parapertussis* varied in terms of their patient inclusion criteria or when the specimens were collected, which was up to 7 to 21 days after symptom onset. In these studies, pertussis was primarily detected in children with clinical symptoms suggestive of the disease at a frequency ranging from 9% to 94%, depending on the study and clinical setting. The number of pertussis cases was generally low in patients with bronchiolitis or who presented only with a persistent cough lasting several days. In adult patients, the frequency of detection of pertussis was below 3%. In addition, an NAAT with two or more targets also detected infections caused by *B. parapertussis* and co-infections, where *B. pertussis* could be co-detected with another pathogen of bacterial or viral origin. It should be noted, however, that most of the experts consulted consider the sole detection of *B. pertussis* and *B. parapertussis* to be sufficient to establish or confirm a case of pertussis.

Turnaround time

In its standards for the surveillance of vaccine-preventable diseases, the WHO recommends, after the receipt of specimens, a two-day turnaround time for the result of a molecular test for establishing or confirming a diagnosis of pertussis. Also, treatment is generally not indicated when the patient has been sick for more than 21 days, hence the need to promptly diagnosis this disease. Furthermore, several studies have emphasized the speed of NAAT in testing for *B. pertussis* or other pathogens useful in the differential diagnosis of pertussis. According to the clinicians consulted across Québec and certain members of the advisory committee, delays in obtaining molecular test results can either discourage them from ordering a pertussis test or have a negative impact on patient management.

Organizational impact

The experts consulted endorsed the introduction of the NAAT to test for *B. pertussis* and *B. parapertussis* at the regional level. They feel that access to this test would permit prompt patient management. In addition, the resources previously assigned to transporting specimens to the supraregional laboratory would be available to be reassigned to other purposes. Moreover, the COVID-19 pandemic situation has contributed to the deployment of molecular testing equipment in the regional laboratories across the province. Some of this equipment could be used to perform molecular tests for detecting *B. pertussis* and *B. parapertussis*.

Economics

The cost-consequence analysis performed by INESSS showed that quick access to NAAT results for establishing or confirming a diagnosis of pertussis would help optimize the management of patients with suspected pertussis. The clinical data included the initiation of treatment, the length of hospital stay, and the application of isolation

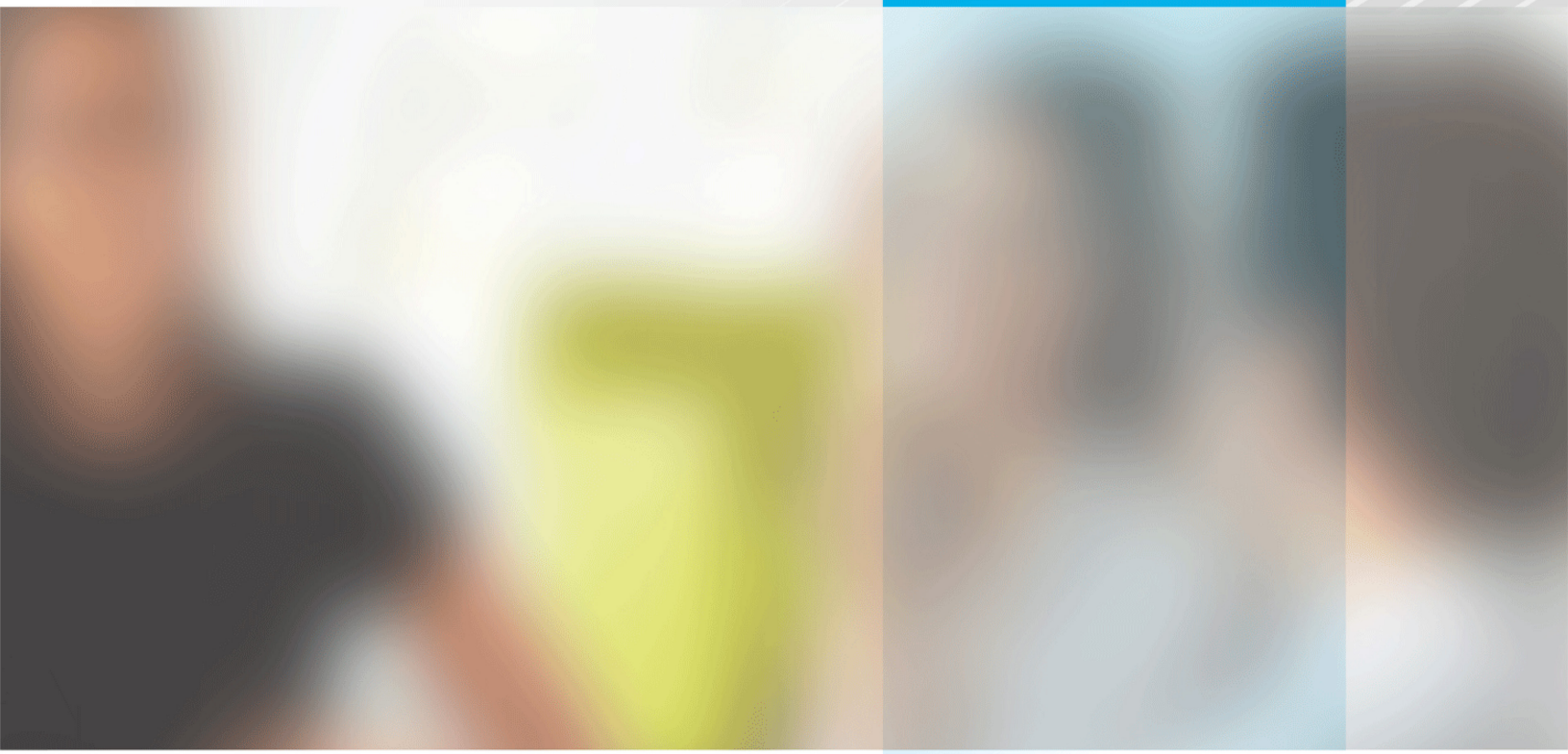
measures. The weighted value of the test with supraregional designation (36.0), however, was lower than that of the proposed regional-level test (57.4).

The budget impact analysis is divided into two parts. The first part takes into account the costs related to the number of tests estimated by the laboratory that submitted the request for an opinion, i.e., the server laboratory of the CIUSSS du Saguenay-Lac-Saint-Jean (Hôpital de Chicoutimi), to serve patients in the Saguenay-Lac-Saint-Jean (02), Côte-Nord (09) and Nord-du-Québec (10) cluster, while the second one takes into account the number of tests required to serve all Québec patients if the test were to be implemented in all the regions. Based on the assumptions made, including the regional-level NAAT test for detecting *B. pertussis* and B. *parapertussis* in the *Répertoire* could generate costs of approximately $17,000 over the first three years for the clientele of the server laboratory (Hôpital de Chicoutimi) in the Saguenay-Lac-Saint-Jean (02), Côte-Nord (09) and Nord-du-Québec (10) cluster. These costs could range from $7,000 to $26,000. Taking into account the transportation costs incurred as a result of the current pandemic situation in Québec, including the new test in the *Répertoire* could generate savings in this region of approximately $114,000 over the first three years.

For all patients in Québec, the costs generated by including this new test in the *Répertoire* could reach $361,000 for the first three years. According to INESSS's budget impact analysis, the sensitivity analyses, which considers an increase in the number of tests, show a potential variation in costs of $7,000 to $26,000 for the regional diagnosis of pertussis in patients served by the CIUSSS-SLSJ, whereas these costs could vary from $121,000 to $507,000 for the regional diagnosis of all patients in Québec.

Conclusion

The positions of the organizations of interest, the published data on the diagnostic performance of NAAT, the opinions of the experts consulted, and the information regarding the speed of NAAT support the finding that NAAT is the most appropriate laboratory test for establishing or confirming a diagnosis of pertussis. Implementing a molecular test at the regional level would help strengthen the appropriateness of clinical and preventive interventions in the fight against pertussis by permitting rapid isolation, optimizing treatment, and limiting the use of hospitalization. Implementing, at the regional level, a molecular test for confirming a case of pertussis offers several clinical advantages because of quicker access to the test results compared to the turnaround time for the currently available supraregional-level test, but at a higher cost. However, in the absence of an economic model, INESSS cannot rule on the efficiency of regional versus supraregional molecular testing. Given the significant clinical benefits identified in this assessment, INESSS recommends implementing and monitoring the new regional-level test for establishing or confirming a diagnosis of pertussis. It also recommends monitoring certain indicators concerning the number of tests performed and their turnaround time, which should be defined in conjunction with the regional public health authorities.



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