Fractional Exhaled Nitric Oxide Testing for the Diagnosis and Management of Asthma

Recommendation

JULY 2024

Ontario Health

Final Recommendations

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding fractional exhaled nitric oxide (FeNO) testing as an adjunct to standard testing to support the diagnosis of asthma in children and adults.

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends against publicly funding FeNO testing to monitor and manage asthma in children and adults.

Rationale for the Recommendations

The Ontario Health Technology Advisory Committee made the above recommendations after considering the clinical, economic, and patient preferences and values evidence reported in the health technology assessment.[1]

The committee members noted that FeNO testing may benefit Ontarians if included as an additional test in the current asthma diagnostic pathway in both children and adults. Despite variable sensitivity, FeNO testing has good diagnostic specificity and was found to be cost-effective in children, as well as in adults when a higher FeNO cut-off threshold is applied. The total 5-year cost of publicly funding FeNO testing for diagnosis is estimated to range from $0.1 million to $0.2 million for children and $1.2 million to $1.6 million for adults, which is considered reasonable given the potential to reduce the number of bronchial provocation tests. Committee members noted that FeNO testing evaluates airway inflammation and is not meant to be used in isolation, but should be used as an adjunct to standard diagnostic testing with spirometry to support a diagnosis of asthma and predict responsiveness to treatment.

The committee noted that FeNO testing when used to monitor and manage asthma likely reduces exacerbations and oral corticosteroid use in children and adults; however, the evidence showed little to no impact on system level outcomes such as hospitalization and emergency department rates. The committee concluded that the addition of FeNO testing was unlikely to be cost-effective to monitor and manage asthma in either population. Additionally, the total cost to the province to publicly fund FeNO testing to monitor and manage asthma over 5 years was large ($22.4 million for children and $196.0 million for adults).

Committee members considered the lived experience of patients with asthma and parents of children with asthma who described barriers to receiving a timely diagnosis. These barriers included long wait times to see specialists and access to standard testing, as well as difficulties in performing the standard tests. The committee also acknowledged the potential for FeNO testing to improve over- and undertreatment, and people's preferences for accurate asthma medication dosages, which can lead to increased confidence in people self-managing asthma symptoms.

The committee noted that it was important that clinicians with appropriate expertise in asthma care administer and interpret the results of FeNO testing in addition to standard testing and that accessibility to standard spirometry testing across the province be improved.

Decision Determinants for Fractional Exhaled Nitric Oxide Testing for the Diagnosis and Management of Asthma

Overall Clinical Benefit

Effectiveness

How effective is the health technology/intervention likely to be (taking into account any variability)?

Asthma Diagnosis

Children and Adults

Studies on the use of FeNO testing compared with a reference standard for the diagnosis of asthma reported low and variable (~30%–90%) sensitivities (GRADE: Very low) and consistently high (~70%–100%) specificities (GRADE: Low) in children and adults. The test specificity values reported across studies may support the use of FeNO testing as an additional test to help rule-in the diagnosis of asthma.

Asthma Management

Children

Based on an overview of reviews on children with diagnosed asthma, compared with standard testing alone, including FeNO testing to monitor and manage asthma likely results in fewer patients with exacerbations (asthma attacks or other sudden worsening of symptoms; GRADE: Moderate) and decreased use of oral corticosteroids (GRADE: Moderate), and may result in little to no difference in asthma symptom control scores on the asthma control test or questionnaire (GRADE: Low), inhaled corticosteroid dose (GRADE: Moderate), emergency department visits (GRADE: Low), hospitalizations due to asthma (GRADE not reported in the systematic reviews), and asthma-related quality of life (GRADE not reported in the systematic reviews).

Adults

Based on an overview of reviews on adults with diagnosed asthma, compared with standard testing alone, including FeNO testing to monitor and manage asthma likely results in fewer patients with exacerbations (asthma attack or sudden worsening of symptoms; GRADE: Moderate) and decreased exacerbation rate (GRADE: Moderate), and may result in little to no difference in asthma symptom control scores (GRADE: Moderate), inhaled corticosteroid dose (GRADE: Very low), use of oral corticosteroids (GRADE not reported in the systematic reviews), hospitalizations due to asthma (GRADE not reported in the systematic reviews), and asthma-related quality of life (GRADE not reported in the systematic reviews),

Studies With Combined Results for Children and Adults

Based on an overview of reviews that combined children and adults with diagnosed adults, compared with standard testing alone, including FeNO test to monitor and manage asthma likely results in a small improvement in lung function (GRADE: Moderate) and may result in little to no difference in blood eosinophil count (GRADE: Low), days missed from school or work (GRADE: Low), and frequency of symptom-free days (GRADE not reported in the systematic reviews).

Safety

How safe is the health technology/intervention likely to be?

There are no safety concerns with using FeNO testing for the diagnosis or management of asthma in children or adults.

Burden of Illness

What is the likely size of the burden of illness pertaining to this health technology/intervention?

Asthma is the third most common chronic condition in Canada and the most common respiratory condition, affecting 3.8 million people, of which 850,000 are children under the age of 14. On average, 317 Canadians are newly diagnosed with asthma every day and 250 lose their lives to asthma each year.[2] As of 2020 in Ontario, 1,073,600 people over 12 years of age reported being diagnosed by a health professional as having asthma.[3]

Need

How large is the need for this health technology/intervention?

Although asthma care in Ontario is improving, concerns remain around misdiagnosis and poor control of the health condition. In a 2017 study,[4] 33% of people with physician-diagnosed asthma were found to not have asthma when objective testing (e.g., spirometry, bronchial challenge tests) was administered and medication tapered off, highlighting the importance of objective testing to prevent unnecessary treatment and health care spending. In addition, a study from 2011[5] suggests that over 50% of people with asthma in Canada do not have good control of their health condition. Poor asthma control contributes to lowered quality of life and increases asthma's burden on the health care system in terms of health human resources and costs.

Patient Preferences and Privacy

Patient Preferences and Values

Do patients have specific preferences, values, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment?

Patient participants value FeNO testing and its perceived use to support the diagnosis and to monitor and manage their asthma. They reported that the use of FeNO testing would provide their health care provider with an additional level of information to address concerns about misdiagnosis and over- and undertreatment of asthma.

Autonomy, Privacy, Confidentiality, and/or Other Relevant Ethical Principles as Applicable

Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment?

Patient participants strongly valued the autonomy to self-manage their asthma with the guidance of their care provider.

No ethical or legal concerns or issues related to privacy or confidentiality were identified when using FeNO testing as an adjunct to standard testing for the diagnosis of asthma or to monitor and manage asthma.

Equity and Patient Care

Equity of Access or Outcomes

Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?

Timely access to specialists and/or asthma testing facilities and spirometry testing to diagnose and manage asthma can be a challenge in certain geographical areas of Ontario. Spirometry and the methacholine challenge test can be difficult to administer in children. Access to objective tests such as spirometry is hampered by long wait times, despite clinical guidelines that say diagnosis ought to be supported with objective testing. Because of this, the diagnosis and management of asthma may be based on clinical symptoms alone, which can result in over- and underdiagnosis of asthma.

Patient Care

Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?

Objective testing is recommended for the diagnosis of asthma; however, the wait time for a publicly funded lung function test like spirometry or bronchoprovocation can be months in certain parts of the province (if available at all), which can make it challenging to effectively diagnose and manage asthma symptoms. Publicly funding FeNO testing would make another objective test available to Ontarians and will potentially improve the accuracy of diagnoses.

Cost-Effectiveness

Economic Evaluation

How efficient is the health technology/intervention likely to be?

To diagnose asthma with children, using either a sequential (spirometry testing is done first and FeNO testing second if spirometry results are negative) or combined (spirometry testing and FeNO testing are done at the same time) testing strategy, using FeNO testing and spirometry is likely cost-effective

compared with standard testing (ICERs of $6,192 and $8,972 per QALY for sequential and combined testing, respectively). To diagnose asthma in adults, neither the sequential nor the combined testing strategy is likely to be cost-effective (both are more costly and with fewer QALYs compared to standard testing). However, they may be cost-effective when a higher FeNO testing diagnostic cut-off value is applied (cost-effective at the higher cut-off value of > 50 parts per billion). For the monitoring and management of children diagnosed with asthma, it is uncertain if FeNO testing with standard testing is cost-effective (ICER of $103,893 per QALY). For the monitoring and management of adults diagnosed with asthma, FeNO testing with standard testing is unlikely to be cost-effective (ICER of $200,135 per QALY).

Feasibility of Adoption Into Health System

Economic Feasibility

How economically feasible is the health technology/intervention?

For asthma diagnosis, the total 5-year budget impact of publicly funding FeNO testing in addition to standard testing ranged between $0.1 million and $0.2 million for children and between $1.2 million and $1.6 million for adults. For monitoring and managing asthma, the total 5-year budget impact of publicly funding FeNO testing was $22.4 million for children and $196.0 million for adults.

Organizational Feasibility

How organizationally feasible is it to implement the health technology/intervention?

FeNO testing may fit within the current asthma diagnostic pathway. The cost of physician services and FeNO test administration in Ontario may be included in an existing insured service or may require its own fee code. Changes to the schedule of benefits are jointly negotiated between the Ministry of Health and the Ontario Medical Association. FeNO testing devices are easy-to-use and are not expected to require extensive training.

References

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