Gene Expression Profiling Tests for Early-Stage Invasive Breast Cancer: Recommendation

FINAL RECOMMENDATION

- The Quality business unit at Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding gene expression profiling tests for people with early-stage invasive breast cancer whose tumours have all of the following characteristics:
    - Estrogen receptor (ER) positive
    - Human epidermal growth factor receptor 2 (HER2) negative
    - Lymph-node negative or micrometastasis

RATIONALE FOR THE RECOMMENDATION

The Ontario Health Technology Advisory Committee has reviewed the findings of the health technology assessment[1] and the recommendation of a subcommittee, the Ontario Genetics Advisory Committee. Ontario Health Technology Advisory Committee members determined that several gene expression profiling tests (EndoPredict, Oncotype DX, Prosigna, and MammaPrint) demonstrated clinical effectiveness (e.g., can predict the risk of cancer recurrence and allow for less aggressive treatment for cancers at relatively low risk of recurrence) in patients with ER positive, HER2 negative, and lymph-node negative early-stage invasive breast cancer.

Ontario Health Technology Advisory Committee members recognized that gene expression profiling tests are a valuable decision-making tool and facilitate shared decision-making for treatment decisions. Gene expression profiling tests are likely cost-effective for patients with ER positive, HER2 negative, and lymph-node negative early-stage invasive breast cancer.

Ontario Health Technology Advisory Committee members noted that publicly funding gene expression profiling tests in Ontario may reduce geographical inequities and administrative burden for providers. Members also noted that opportunities for cost savings should be explored given the variation in price among different gene expression profiling tests. Implementation considerations also ought to be considered, such as laboratory licensing and capacity, as well as educational support for patients and health care providers.

Consideration for using gene expression profiling tests in a lymph-node positive population (specifically 1–3 positive nodes) will be revisited when further evidence of clinical utility becomes available.

Decision Determinants for Gene Expression Profiling Tests for Early-Stage Invasive Breast Cancer

Decision Criteria	Subcriteria	Decision Determinants Considerations
Overall clinical benefit How likely is the health technology/intervention to result in high, moderate, or low overall benefit?	**Effectiveness** How effective is the health technology/ intervention likely to be (taking into account any variability)?	In the LN negative patient population, GEP tests are likely prognostic for freedom from distant recurrence (GRADE: Moderate) and may be prognostic for disease-free and overall survival (GRADE: Low). In the LN positive patient population, GEP tests may be prognostic for freedom from distant recurrence (GRADE: Low). GEP tests may be prognostic for disease-free and overall survival (GRADE: Very low), but this is very uncertain. Some GEP tests may predict chemotherapy benefit in the LN negative population (GRADE: Low). GEP tests may predict chemotherapy benefit in the LN positive population (GRADE: Very low), but this is very uncertain. GEP tests may lead to changes in treatment recommendations (GRADE: Low). The tests may increase physician confidence in treatment recommendations (GRADE: Very low), but this is very uncertain.
	Safety How safe is the health technology/ intervention likely to be?	GEP tests use tumour samples obtained from surgery for analysis, so direct safety concerns are not an issue.
	Burden of illness What is the likely size of the burden of illness pertaining to this health technology/intervention?	In Ontario in 2018, about 12,000 cases of breast cancer were expected to be diagnosed.
	Need How large is the need for this health technology/intervention?	Most breast cancer cases in Ontario are diagnosed at stage 1 or stage 2. Standard tests do not consider the genetic profile of a person's tumour. GEP tests can provide additional personalized information about a tumour's characteristics and the likelihood of cancer recurrence.
Patient preferences and values How likely is adoption of the health technology/intervention to be congruent with patient preferences and values, and ethical or legal standards?	**Patient preferences and values** Do patients have specific values, preferences, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment? (Note: The values and preferences of family and informal caregivers are to be considered as appropriate.)	Patients value the information that GEP tests provide and test results impact their chemotherapy decision-making. Patients value the reduced uncertainty and anxiety about whether they ought to receive chemotherapy that GEP test results provide.
	Autonomy, privacy, and confidentiality and/or other relevant ethical principles if applicable Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles or values that are relevant to this assessment? (Note: The values and preferences of the public are to be considered as appropriate.)	Patients make chemotherapy treatment decisions in consultation with their physicians and choose whether to accept chemotherapy. GEP testing may support the autonomy of patients in the decision-making process about which treatments to receive.

Decision Criteria	Subcriteria	Decision Determinants Considerations
Equity and patient care How could the health technology/ intervention affect equity of access and coordination of 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?	Some GEP tests can predict chemotherapy benefit and may lead to decisions by patients to forgo chemotherapy. Funding GEP tests in Ontario may reduce geographical inequities and administrative burden for providers.
	Patient care Are there challenges in the coordination of care for patients and other system-level aspects of patient care (i.e., timeliness of care, setting of care etc.) that might be improved or worsened that are relevant to this assessment?	GEP tests are currently funded through the out-of-country program. Local testing may improve patient access and timeliness of GEP testing and treatment.
Cost-effectiveness How efficient is the health technology/ intervention likely to be?	**Economic evaluation** How efficient is the health technology/ intervention likely to be?	GEP tests may be cost-effective in people with early-stage invasive, ER positive, LN negative, HER2 negative breast cancer. Incorporating uncertainty in various model parameters, it was estimated that the probability of GEP tests being cost-effective versus usual care ranges from 63% to 100% at a willingness-to-pay of $50,000 per QALY gained.
Feasibility of adoption into health system How feasible is it to adopt the health technology/intervention into the Ontario health care system?	**Economic feasibility** How economically feasible is the health technology/intervention?	The cost of a GEP test is approximately $2,500 to $5,000 per test. In addition, costs related to adjuvant chemotherapy and ongoing treatment are expected to be incurred over time. It was estimated that, compared with publicly funding through the out-of-country program, the annual budget impact of publicly funding GEP tests to be conducted in Ontario over the next 5 years will range from $1.29 million in year 1 to $2.22 million in year 5, assuming increased uptake when the tests are available in Ontario. Compared with no funding for GEP tests (neither in province nor through the out-of-country program), the annual budget impact of publicly funding GEP tests to be conducted in Ontario over the next 5 years will range from $4.61 million to $5.77 million.
	Organizational feasibility How organizationally feasible is it to implement the health technology/ intervention?	EndoPredict and Prosigna tests can be performed in Ontario laboratories. MammaPrint and Oncotype DX currently do not have local testing options and all tests must be sent to a centralized laboratory, which is out of country, for analysis. Both test manufacturers are considering a local testing model.

Abbreviations: ER, estrogen receptor; GEP, gene expression profiling; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HER2, human epidermal growth factor receptor 2; LN−, lymph-node–negative; LN+, lymph-node–positive; HR, hormone receptor; QALY, quality-adjusted life-year.

REFERENCE

(1) Ontario Health (Quality). Gene expression profiling tests for early-stage invasive breast cancer: a health technology assessment. Ont Health Technol Assess Ser [Internet]. 2020 Mar;20(10):1–234. Available from: https://www.hqontario.ca/evidence-to-improve-care/health-technology-assessment/reviews-and-recommendations/gene-expression-profiling-tests-for-early-stage-invasive-breast-cancer

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