Decision-making impact on adjuvant chemotherapy allocation in early node negative breast cancer with a 21-gene assay: Systematic review and Meta-Analysis

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PURPOSE
To perform a systematic review and meta-analysis of decision impact and net change in CT use before and after a 21-gene assay

BACKGROUND
Risk stratification based on results provided by a 21-gene assay (Oncotype DX®) in early stage breast cancer can help to optimize hormone therapy (HT) +/- chemotherapy (CT) decisions, by stratifying women according to recurrence risk and benefit-risk balance of treatments. HTA bodies as NICE recommends it for intermediate risk women. Previous reviews of decision impact did not provide data on both overall and net decision impact regarding use of CT in this group.

METHODS
Systematic Review
• PRISMA reporting guidelines were followed (1).
• Eligible studies were those with prospective data collection that reported physician’s decision on allocation of hormone-therapy (HT) plus CT or HT alone in women with early stage node negative, estrogen receptor-positive breast cancer before and after assay results. Searches were conducted in Medline and Embase (detailed strategy is available upon request). Prospective collection of data was defined as availability of data on pre-test decisions recorded before test results in the context of real clinical settings. Studies with less than 80% of lymph node-negative (ND) patients, or that did not report on patient’s lymph-node status were excluded.
• Outcomes of interest were decision impact (DI), defined as the proportion of patients whose treatment decision was altered after the test, and net change (NC) in CT use, defined as the difference between the proportion of all patients receiving chemotherapy before and after the test.
• We evaluate both global impact as well as impact by risk score (RS) group.
• Study quality assessment was based on the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group (2). In addition, we considered two quality strata: (1) universal enrollment, and (2) selective enrollment. Conflict of interests was also assessed.

RESULTS

Table 1: Results of Meta-Analyses of Decision Impact for each assay-defined group of patients
| RS | N Studies | N subjects | Decision Impact (95% CI) | Evidence results
|----|-----------|------------|--------------------------|------------------|
| Low RS | 7 | 377 | 30.41% (24.65% to 36.50%) |#### 33.70%
| Int RS | 7 | 278 | 28.82% (23.40% to 34.56%) |#### 8.50%
| High RS | 7 | 72 | 26.88% (17.74% to 37.14%) |#### 0.00%

Table 2: Results of Meta-Analyses of Net-Change for each assay-defined group of patients
| RS | N studies | N subjects | Net change (95% CI) |#### Evidence results
|----|-----------|------------|---------------------|------------------|
| Low RS | 12 | 1419 | 16.00% (12.00% to 19.00%) |#### 62.00%
| Int RS | 13 | 1419 | 0.00% (-3.00% to 3.00%) |#### 80.00%
| High RS | 13 | 1419 | -2.00% (-3.00% to -1.00%) |#### 60.00%

RS: Risk score strata
• Summary results did not change in the subgroup analysis by study quality/risk of bias, though heterogeneity in decision impact was smaller in the universal enrollment studies.
• In decision change, results were similar for the global population as well as those derived from analyses according to risk score.
• Qualitative and quantitative analyses of funnel plots showed no evidence of publication bias. Most of the studies were sponsored by the assay producer.

CONCLUSIONS
• In the era of personalized medicine, it is increasingly common to have companion tests for specific treatments. In early breast cancer, available tools estimate probability of recurrence.
• The 21-gene assay showed that it can have a significant impact on optimizing treatment decisions. Its main effects consist of better tailoring treatment according to patient risk, changing decisions in 30 out of 100 women, sparing CT in low risk patients, and increasing its use in the high risk category.
• These results represent decision impact in studies where all eligible patients were included. This may underestimate the impact on populations where the decision of CT remains unclear.
• Further research should further clarify issues such as how this decision impact translates to patient relevant outcomes, globally and by risk groups, and especially in patients with intermediate risk scores; as well as the comparative effectiveness of the several existing risk stratification tools.

SELECTED REFERENCES

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