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**Title**: CDX2 biomarker testing and adjuvant therapy for stage II colon cancer: A cost-effectiveness analysis

**Purpose:** Adjuvant chemotherapy is not recommended for patients with average risk stage II colon cancer (P3N0). However, lacking CDX2 biomarker expression predicts responsiveness to adjuvant chemotherapy. We determined the cost-effectiveness of testing for the absence of CDX2 biomarker followed by adjuvant chemotherapy for average risk stage II colon cancer patients.

**Methods:** We developed a state-transition model to simulate a hypothetical cohort of 65-year-old average risk stage II (P3N0) colon cancer patients under three different strategies: (1) test for CDX2 biomarker expression followed by adjuvant chemotherapy (leucovorin and fluorouracil, LV5FU) for patients lacking CDX2 expression and (2) no adjuvant chemotherapy for any patient. CDX2-negative patients (i.e., those without biomarker expression, representing 4.1% of all patients) face a higher rate of developing recurrence (hazard ratio [HR] = 2.73) compared to CDX2-positive patients (0.0042 per month; calibrated). However, adjuvant chemotherapy only benefits patients who lack CDX2 expression (HR = 0.163). Most patients who develop recurrence will advance to distant metastasis and face an additional risk of dying from colon cancer. We derived the parameters that describe disease progression and adjuvant chemotherapy effectiveness from a recently published analysis, the costs of cancer care from SEER-Medicare and the utility losses associated with cancer care from published literature. Outcomes were quality-adjusted life-years (QALYs), lifetime cost, and incremental cost-effectiveness ratio (ICER).

**Results:** For the base case analysis, we considered a test cost of $500. Testing for the absence of CDX2 expression followed by adjuvant chemotherapy on those without the biomarker (strategy 1) resulted on a cost-saving strategy with 5.9 QALYs and lifetime costs of $132,566 compared strategy 2 where no adjuvant chemotherapy is provided to any patient with 5.3 QALYs and $132,722 lifetime costs. Strategy 1 remains cost-saving under a range of assumptions, and only changes if the cost of the test is higher than $660 USD. A test cost of $1,000 USD yields an ICER of $622 USD/QALY.

**Conclusions:**  We found that identifying a small subgroup of average risk stage II colon cancer patients that lack CDX2 biomarker expression for targeted chemotherapy is effective and potentially cost-saving.