Washington State Health Care Authority

Gene Expression Profiling for Cancer

Evidence Update

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Health Technology Assessment Program (HTA)

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This evidence update report is based on research conducted by the Center for Evidence-based Policy (Center) under contract to the Washington State Health Care Authority (HCA). This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the authors, who are responsible for the content. These findings and conclusions do not necessarily represent the views of the Washington HCA, and thus no statement in this report shall be construed as an official position or policy of the HCA.

The information in this assessment is intended to assist health care decision makers, clinicians, patients, and policymakers in making evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

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Bottom Line

This evidence update includes studies published since the original evidence review[1] conducted in 2018 that informed the coverage policy for gene expression profiling (GEP) for cancer, as adopted by the Washington State Health Technology Clinical Committee (HTCC) in May 2018. After summarizing the effectiveness, harms, and economic outcomes from eligible studies in this evidence update, we have determined that these outcomes may change the conclusions of the 2018 evidence report in specific cancers (namely colon and colorectal cancer, lung cancer, and skin cancer).

Background

GEP uses the differential multigenic patterns of messenger RNA (mRNA) levels transcribed in diverse cell types to identify cellular changes, such as those in diseased cells with cancer-causing mutations. Those mRNA expression patterns respond to the environmental and internal status of the cells, as various genes are transcriptionally up- or down-regulated in response to the cell circumstances. Thus, GEP can be used to help diagnose a disease or condition, such as cancer.[2] It can also be used to help plan treatment, assess how well treatment is working, or determine disease prognosis.[2]

The use of GEP tests for cancer tissue is increasing, with the potential for better patient outcomes and more appropriate treatment decisions, including avoidance of unnecessary treatments and subsequent treatment-related side effects and costs.[3]

The current coverage determination, made in 2018, states GEP testing is[4]:

- A covered benefit with conditions for breast or prostate cancer
- Not a covered benefit for multiple myeloma or colon cancer

Limitations of coverage include the use of 1 test per 12 months and only when test results will impact treatment decisions, along with additional conditions specified for each individual test (Oncotype DX, EndoPredict, Prosigna, MammaPrint, Mammostrat, and Breast Cancer Index (BCI) for breast cancer; Oncotype Dx, Polaris, and Decipher for prostate cancer).[4]

Policy Context

Due to recent legislative changes in Washington state, topics subject to certain coverage conditions need to be assessed for new evidence (i.e., via a signal search) on an annual basis. Therefore, to meet the new legal requirements, this signal search will focus on GEP testing of solid tumor cancer tissues.

Objectives

The primary aim of this assessment is to determine whether there is new evidence that would likely change the conclusions of the most recent health technology assessment (HTA) report in 2018.[1]

Methods

To identify studies published since the 2018 evidence update,[1] we conducted updated searches of Ovid MEDLINE All, Cochrane Database of Systematic Reviews, and the Cochrane Controlled Trials Register database (from December 2017 through June 2024). We updated the search

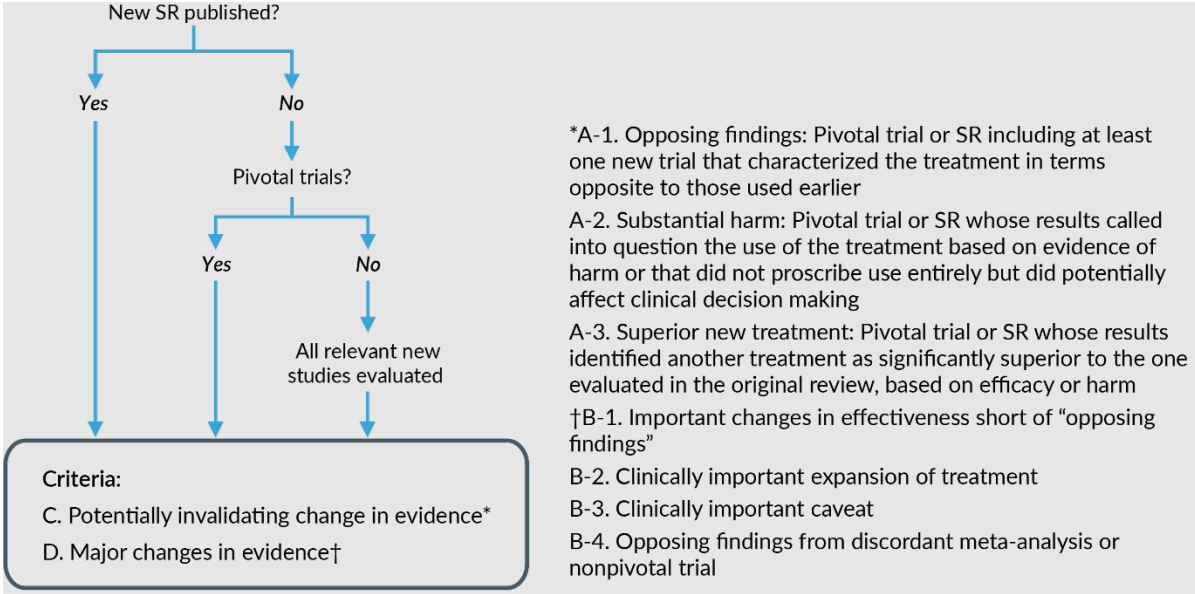
strategies used in previous reports to reflect newer searching methods and improve the efficiency of the strategies (Appendix A). We also searched ClinicalTrials.gov and ScanMedicine registries for upcoming and ongoing studies that would likely be included in an updated evidence review. Further, we searched the reference lists of all identified systematic reviews, meta-analyses, and guidelines for relevant studies. Additionally, we searched the Agency for Healthcare Research and Quality, National Institute for Health and Care Excellence, and Veterans Affairs Evidence Synthesis Program websites and the websites of commercial GEP test providers for relevant studies.

To determine if a signal exists (i.e., there is new evidence that may change the current coverage determination), we followed a modified Ottawa method (Figure 1) and examined full texts of new systematic reviews published in the past 5 years. If a treatment or technology was not covered, the signal search centered on efficacy and looked at peer-reviewed abstracts of trials for newly identified randomized controlled trials (RCTs) or comparative nonrandomized studies (NRS) published since any relevant systematic reviews. Conversely, if a treatment or technology was already covered based on a previous HTCC decision, the signal search was on harms as reported in systematic reviews only.

To assess whether the conclusions might need updating, we used an algorithm based on a modification of the Ottawa method (Figure 1). Our approach to screening and reviewing eligible studies was as follows:

- We screened the retrieved references and ongoing study records against the inclusion criteria (Appendix B).
- We assessed the likelihood, by indication, of recent evidence triggering an update to the 2018 coverage determination for GEP testing in cancer.

Figure 1. Algorithm of the Modified Ottawa Method of Identifying Signals for Update



We summarized the findings of any eligible published systematic reviews and health technology assessments in the following manner:

- If there were 2 or more comparable reviews identified and 1 is more recent or more comprehensive, then the other review(s) was not summarized, and the rationale for selection was documented.

We did not assess the risk of bias of the eligible reviews or primary studies.

We reported a narrative description of the search results along with the following key study characteristics of the included reviews and primary studies:

- The number of studies (for systematic reviews) and number of participants (for all study designs)
- The intervention studied
- Comparators to the intervention
- Relevant outcomes reported in the publication

We also highlighted any discrepancies and differences across systematic reviews and individual primary studies.

For each indication, we assessed the evidence of effectiveness and harms, depending on coverage status, and the potential impact on the 2018 coverage decision.[4] The summary assessment aims to give the Washington State HTA Team and their Agency Medical Directors' Group information on whether there is new evidence that may warrant a reconsideration of the existing coverage policy.

PICO

Appendix B provides detailed inclusion and exclusion criteria used to guide the selection of eligible studies.

Populations

- Adults with cancer (specifically solid tumors)

Interventions

- Multigene commercially or clinically available GEP tests of cancer tumor tissue

Comparators

- Another GEP test
- Other clinicopathological forms of testing to guide treatment decisions
- No tumor tissue GEP testing
- Usual care

Outcomes

- Patient management decisions
- Clinical outcomes
- Harms of testing
- Cost and cost-effectiveness

Key Questions

KQ1. What is the clinical utility of GEP testing of cancer tissue to inform treatment decisions for patients with cancer?

a. Is there evidence that test results affect treatment decisions?

b. Do treatment decisions guided by GEP testing of cancer tissue result in clinically meaningful improvements in patient outcomes?

KQ2. What harms are associated with GEP testing of cancer tissue?

KQ3. Compared with usual care, do treatment decisions, patient outcomes, or harms after GEP testing of cancer tissue vary by:

a. Patient demographics (e.g., age, sex, race/ethnicity)?

b. Clinical history (e.g., means of diagnosis, stage or grade of cancer, results of other testing, previous treatments, chronicity)?

c. Medical comorbidities?

d. Provider type or care setting?

KQ4. What are the cost-effectiveness and other economic outcomes of GEP testing used to inform treatment management decisions?

Findings

We identified 2,335 unique publications in our updated searches, with 239 articles screened at the full-text stage. Of these, 21 publications, including systematic reviews, guidelines and primary studies, were eligible for inclusion in this signal search report.[5-25] The list of studies excluded at the full-text level, with exclusion reasons, is in Appendix C. Although studies of effectiveness in covered tests was not the focus of this report, we have provided a list of studies of interest evaluating the use of GEP testing in breast and prostate cancers in Appendices D and E.{Barni, 2022 #73;Berdunov, 2023 #28;Canfield, 2017 #43;Carbunaru, 2023 #27;Chang, 2019 #59;Chin-Lenn, 2018 #75;Cognetti, 2021 #74;Curtit, 2019 #76;Dannehl, 2022 #47;Dieci, 2018 #86;Dieci, 2019 #77;Dinan, 2019 #57;Eichler, 2019 #40;Ettl, 2017 #44;Fallowfield, 2018 #78;Gaffney, 2019 #68;Gore, 2020 #71;Gustavsen, 2020 #55;Hassan, 2022 #52;Hu, 2018 #65;LeVasseur, 2022 #79;Licata, 2023 #26;Lynch, 2018 #69;Marascio, 2020 #66;Mariotto, 2020 #49;Mokbel, 2018 #60;Murphy, 2021 #33;Perez Ramirez, 2020 #35;Picado, 2022 #48;Retel, 2020 #36;Sanft, 2019 #80;Seiden, 2022 #67;Thangarajah, 2019 #39;Thibodeau, 2019 #84;Torres, 2018 #81;Tsai, 2018 #87;Viale, 2018 #50;Voelker, 2018 #90;Wang, 2019 #58;Wuerstlein, 2019 #38;Zambelli, 2020 #56;Zhang, 2020 #85}

Breast Cancer

GEP testing of breast cancer tissue is a covered benefit at a rate of 1 test per 12 months per index cancer and when test results will impact treatment decisions.[4] The 2018 HTCC decision was limited to the particular named tests with specific conditions for coverage.[4] Additional conditions are as follows[4]:

- Oncotype Dx, EndoPredict, Prosigna, and MammaPrint tests are covered for stage I or II cancer when the tumor tissue is:

    - Estrogen receptor positive and human epidermal growth factor receptor 2 (HER2-NEU) negative.
    - Lymph node negative or 1 to 3 lymph nodes positive.
- Mammostrat and BCI are covered only for patients with stage I or II cancer who are deciding about hormone therapy.

For this evidence update, we therefore focused on harms only for the covered tests and both effectiveness and harms for tests currently not covered.

Since the evidence review in 2018,[1] we identified 1 systematic review and 1 newly published eligible study evaluating GEP testing in breast cancer (specifically, ductal carcinoma in situ [DCIS] breast cancer).[18,20] We also identified 3 guidelines on the harms of GEP testing for breast cancer.[6,7,14]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in breast cancer.[18] The review by Parker and colleagues identified 87 studies in 11 cancer types, including breast cancer.[18] Overall, the 87 studies evaluated the use of 18 proprietary and 1 generic assay for multiple measures of clinical decision making on breast, lung, prostate, colon, pancreaticobiliary, melanoma, sarcoma, glioma, and unknown cancers.[18] The tests included GEP testing along with other DNA-based tests, and the majority of the studies were conducted in Europe and North America.[18] The authors identified 22 discrete measures of clinical decision making related to the impact of testing on the diagnostic process, clinical management, patient benefit, and societal outcomes, such as cost-effectiveness and societal acceptability.[18]

The majority of studies (63 of 87; 72%) evaluated the use of GEP testing in breast cancer.[18] Of these 63 studies, of which only 5 were conducted in the United States, the specific tests were as follows[18]:

- Oncotype Dx (Genomic Health/Exact Sciences)
    - 44 studies
- Prosigna (Veracyte)
    - 9 studies
- BCI (Biotheranostics)
    - 3 studies
- EndoPredict (Myriad Genetics)
    - 2 studies
- MammaPrint (Agendia)
    - 2 studies
- CanAssist Breast (OncoStem)
    - 1 study
- DCISionRT Test (PreludeDx)
    - 1 study
- FoundationOne (Foundation Medicine)
    - 1 study

Of these 8 different GEP tests, Oncotype Dx, Prosigna, BCI, EndoPredict, and MammaPrint are currently covered with conditions. Of the remaining 3 tests—CanAssist Breast (OncoStem), DCISionRT Test (PreludeDx), and FoundationOne (Foundation Medicine)—only DCISionRT Test and FoundationOne are available in the United States.

The 2 studies evaluating FoundationOne and DCISionRT Test were both conference abstracts and, without the availability of peer-reviewed full publications, would therefore not provide a sufficient signal for an updated evidence review.[66,67] We did not identify any other new primary studies evaluating tests currently not covered for breast cancer. Additionally, FoundationOne is a DNA-based test, so it does not meet our inclusion criteria.

We did identify 1 new nonrandomized study (NRS) in 217 patients with DCIS (a noninvasive breast cancer) treated with breast-conserving surgery.[20] Rakovitch and colleagues found that the addition of the Oncotype Breast DCIS 12-gene score led to a change in treatment recommendations in 35.2% of patients.[20] Radiotherapy recommendations decreased significantly from 79% pre-assay to 50% post-assay, due to a significant increase in the proportion of patients with a predicted low local recurrence rate (less than 10% over 10 years) post-assay and the subsequent recommendation to omit radiotherapy for these patients.[20] Additionally, the score led to a change in patient-treatment preferences in 28.2% of cases, with 22.1% of those being a change from preferring radiotherapy to no radiotherapy.[20] Decisional conflict scores measure personal perceptions of uncertainty when choosing options, modifiable factors contributing to uncertainty (such as feeling uninformed, unclear about personal values, or unsupported in decision making) and effective decision making (such as feeling the choice is informed, values-based, and likely to be implemented and expressing satisfaction with the choice).[68] In this study, the use of GEP testing decreased decisional conflict scores post-assay from 26.4 to 13.1; a change in 5 points is generally considered to be a meaningful change.[20,69]

Harms

We did not identify any eligible systematic reviews or primary studies on the harms of GEP testing in breast cancer. We did identify 1 long-term follow-up publication for the MINDACT RCT on the use of MammaPrint to determine genomic risk in patients with histologically confirmed unilateral primary nonmetastatic (M0) invasive breast cancer (clinical stage T1 or T2 or operable T3) with 0 to 3 positive axillary lymph nodes, an RCT previously included in the 2018 evidence report.[70] The 2021 publication focused on overall survival and other clinical outcomes; harms were not reported.[70]

We identified a further 33 studies on the utility or cost-effectiveness of currently covered GEP tests for breast cancer; however, none reported on harms associated with the various tests (Appendix D).

In the guideline recommendations from the European Commission Initiative on Breast Cancer regarding the use of multigene testing to guide the use of adjuvant chemotherapy in patients with early breast cancer, Giorgi Rossi and colleagues state that the undesirable effects of using the 21-gene recurrence score (Oncotype Dx) were trivial and the undesirable effects of using the 70-gene signature assay (MammaPrint) were trivial in patients with low clinical risk and small in patients with high clinical risk.[14] However, no definition of trivial or small was provided.[14] They

considered these data to have a very low certainty of evidence and to be conditional, as the downstream effects of avoiding chemotherapy were not quantified.[14] Meanwhile, the guidelines on GEP for early-stage invasive breast cancer, developed by Ontario Health (Cancer Care Ontario)'s Program in Evidence-Based Care (PEBC), reported that patients in the consultation rated adverse events as critical outcomes when considering the recommendations; however, no details of adverse events were provided in the guideline or in the underpinning systematic review.[7] The 2022 ASCO guideline on biomarkers for early breast cancer reported the same lack of studies reporting adverse events for GEP testing as the Ontario guideline.[6]

Costs and Cost-Effectiveness

We did not identify any eligible cost or cost-effectiveness studies for GEP tests currently not covered.

Bottom Line

Based on the lack of newly identified evidence, we conclude that at this time the conclusions of the 2018 evidence review are unlikely to change.

Prostate Cancer

GEP testing of prostate cancer tissue is a covered benefit at a rate of 1 test per 12 months per index cancer and when test results will impact treatment decisions.[4] The 2018 HTCC decision was limited to the particular named tests with specific conditions for coverage.[4] Additional conditions are as follows[4]:

- Oncotype Dx and Prolaris are covered only for low-risk or favorable intermediate-risk disease.
- Decipher is covered for patients deciding between active surveillance and adjuvant radiotherapy after radical prostatectomy.

For this evidence update, we therefore focused on harms only for the covered tests and both effectiveness and harms for tests currently not covered.

Since the evidence review in 2018, we identified 1 systematic review evaluating GEP testing in prostate cancer and no newly published eligible studies.[18]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in prostate cancer.[18] None of the other identified systematic reviews evaluated the effectiveness of GEP tests for prostate cancer available in the United States, other than the 3 tests already covered with conditions.[71-77]

Of the 87 included studies in the review by Parker and colleagues, 4 (5%) were in prostate cancer and all were conducted in the United States.[18] The following tests were evaluated[18]:

- Decipher (Veractye) in 3 studies[78-80]
- ExoDx Prostate (Exosome Diagnostics) in 1 study[81]

The 1 new study published since the 2018 evidence review is evaluating ExoDx; while this test is available in the United States, this publication is a conference abstract and, without a full peer-reviewed publication, would therefore not provide a sufficient signal for an updated evidence

review.[81] We did not identify any other new primary studies evaluating tests currently not covered for prostate cancer.

Harms

We did not identify any eligible systematic reviews or primary studies on the harms of GEP testing in prostate cancer. We did identify 11 studies on the utility or cost-effectiveness of currently covered GEP tests for prostate cancer; however, none reported on harms associated with the various tests (Appendix E).

Costs and Cost-Effectiveness

We did not identify any eligible cost or cost-effectiveness studies for GEP tests currently not covered.

Bottom Line

Based on the lack of newly identified evidence, we conclude that at this time the conclusions of the 2018 evidence review are unlikely to change.

Colon and Colorectal Cancer

GEP is currently not a covered benefit for colon or colorectal cancer.[4]

For this evidence update, we therefore focused on both effectiveness and harms for GEP testing in colon or colorectal cancer.

Since the evidence review in 2018, we identified 2 systematic reviews and 2 newly published eligible primary studies evaluating GEP testing in colon or colorectal cancer.[9,10,17,18]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in colon and colorectal cancer.[18]

Of the 87 included studies, 3 (3%) were in colon or colorectal cancer, and none of the studies were conducted in the United States.[18] The following tests were evaluated[18]:

- Oncotype Dx Colon Cancer Assay (Genomic Health/Exact Sciences) in 2 studies in colon cancer[82,83]
- A nonspecific next generation sequencing (NGS) test in 1 study in colorectal cancer (23%), lung cancer (56%), or melanoma (21%)[9]

Of the 2 studies in Oncotype Dx, 1 was included in the 2018 evidence report,[82] leaving only 1 new publication evaluating the use of Oncotype Dx in people with colon cancer.[83] This new publication is a conference abstract and would therefore not provide a sufficient signal for an updated evidence review.[83]

The study by Coquerelle and colleagues[9] evaluated how the use of NGS could modify care pathways in an observational retrospective impact study conducted in France.[9] While NGS is primarily a DNA-based technique, it can be used for RNA-based cDNA sequencing. We have therefore included for this report given the authors' comprehensive coverage by multiple cancer types.[9] In people with colorectal cancer, there were[9]:

- Missing data or no results for 0.8% of people
- A genetic alteration identified in 92.8% of people, with 72.0% of alterations being actionable (see Table 1)

Table 1. Genotype-Matched and Nonmatched Treatments Before and After NGS Analyses in Colorectal Cancer[9]

Matched and Nonmatched Treatment for Colorectal Cancer	N (%)	
	Before	After[a]
Genotype-matched	21 (11.4)	60 (32.8)
Targeted therapies prescribed	10 (5.5)	9 (4.9)
Clinical trials proposed	11 (6.0)	51 (27.9)
Non-genotype matched	119 (65.0)	109 (59.6)
Chemotherapy	21 (11.5)	10 (5.4)
Radiotherapy	2 (1.0)	2 (1.0)
Chemotherapy 1 (radiotherapy or surgery)	6 (3.3)	0
Surgery	20 (10.9)	0
Clinical surveillance	6 (3.3)	2 (1.0)
Palliative care	0	0
Complementary test or examination	0	1 (0.5)
Other treatment	0	5 (2.7)
No treatment or no modification of treatment	11 (6.0)	6 (3.3)
Unknown treatment	53 (28.9)	83 (45.3)
Missing data	43 (23.5)	14 (7.6)

Note. [a] No statistical testing was reported between groups.

Davey and colleagues conducted a systematic review and meta-analysis of the impact of the Oncotype Dx 12-gene recurrence score (12-gene RS) on decision making regarding adjuvant chemotherapy in stage II or III colon cancer.[10] In total, the following 4 NRSs with a total of 855 patients were selected and included in the meta-analysis[10]:

- A retrospective analysis in 269 people with stage II colon cancer who underwent the 12-gene RS testing[82]
- A survey of 346 oncologists asking about the use of the 12-gene RS in their most recent patient with stage II colon cancer and the impact on treatment recommendations[84]
- A prospective study evaluating the impact of the 12-gene RS on physician recommendations before and after testing for 275 people with stage IIIA/IIIB or stage II colon cancer[17]
- A prospective study evaluating the impact of the 12-gene RS before and after testing on physician recommendations for 141 people with stage IIA colon cancer[85]

Study results indicate the following:

- Overall, 79.2% of patients had stage II disease and 20.8% had stage III disease.[10]
- For patients with any stage of disease:
  - Concordant results between the 12-gene RS and the tumor board were significantly more likely than discordant (odds ratio [OR], 0.38; 95% confidence interval [CI], 0.25 to 0.56).
  - Patients were significantly more likely to have chemotherapy omitted than escalated when using the test findings (OR, 9.76; 95% CI, 6.72 to 14.18).
- For patients with stage II disease:

- Concordant results between the 12-gene RS and the tumor board were significantly more likely than discordant (OR, 0.30; 95% CI, 0.17 to 0.53).
- Patients were significantly more likely to have chemotherapy omitted than escalated when using the test findings (OR, 7.39; 95% CI, 4.85 to 11.26).

The authors concluded the use of the Oncotype Dx 12-gene RS decreased the use of adjuvant chemotherapy in colon cancer patients, thus reducing overtreatment in some people when relying on tumor board decisions alone.[10]

Of the 4 studies included in the review by Davey and colleagues,[10] 2 were included in the 2018 evidence report.[82,85] The newly eligible NRS by Oki and colleagues[17] included 275 people with stage IIIA/IIIB or stage II colon cancer and evaluated whether treatment recommendations changed after receipt of the test results.[17] Overall, the findings were as follows[17]:

- Treatment recommendations changed in 40% of all patients with colon cancer.
- Patients with stage IIIA/B cancer had significantly more change than those with stage II cancer after receipt of the test results (45% vs. 30%; $P = .01$).
- The percentage of patients whose physicians reported being confident in their treatment recommendations significantly increased from 54% to 81% in stage IIIA/B and from 65% to 83% in stage II (both $P < .001$).

Harms

We did not identify any eligible systematic reviews or primary studies on the harms of GEP testing in colon cancer.

Cost and Cost-effectiveness

We identified 1 eligible cost-effectiveness modeling study comparing 3 GEP tests (Oncotype Dx, ColoPrint, and ColDx) with a non-GEP assay (Immunoscore).[8] The analysis was based on a hypothetical cohort of 1,000 people aged older than 50 years diagnosed with stage II colorectal cancer, who underwent tumor resection, and who were waiting for treatment decisions based on marketed genomic tests.[8] In total, the following 4 strategies were compared[8]:

- Strategy 1:
  - 12-gene assay (Oncotype Dx) followed by either adjuvant chemotherapy if patients were classified into the high-risk category or no chemotherapy if patients were classified into the low-risk category
- Strategy 2:
  - 18-gene expression assay (ColoPrint) followed by either adjuvant chemotherapy if patients were classified into the high-risk category or no chemotherapy if patients were classified into the low-risk category.
- Strategy 3:
  - 482-gene signature (ColDx) followed by either adjuvant chemotherapy if patients were classified into the high-risk category or no chemotherapy if patients were classified into the low-risk category
- Strategy 4:
  - Immunoscore assay followed by either adjuvant chemotherapy if patients were classified into the high-risk category or no chemotherapy if patients were classified into the low-risk category

Based on a 5-year Markov model, use of the Immunoscore assay was found to be a more cost-effective strategy than the other 3 GEP tests at a threshold willingness-to-pay of $50,000 per quality-adjusted life-year (QALY).[8] When the 12-gene assay (Oncotype Dx) and the 18-gene expression assay (ColoPrint) were compared, Oncotype Dx was found to be less costly than the ColoPrint test (with a cost saving of $3,829) but was less effective (with a reduction of 0.054 fewer QALYs).[8]

Bottom Line

Based on limited newly identified evidence (2 NRSs and 1 cost-effectiveness analysis), we conclude that at this time the conclusions of the 2018 evidence review may change; there is some signal that the use of the 12-gene recurrence score (Oncotype DX Recurrence Score) may change treatment plans in people with colon and colorectal cancer. However, the use of the test may not be cost-effective when compared with other testing options.

Lung Cancer

GEP is currently not a covered benefit for lung cancer.[4] For this evidence update, we therefore focused on both effectiveness and harms for GEP testing in lung cancer. Since the evidence review in 2018, we identified 1 systematic review evaluating GEP testing in lung cancer and 5 newly published eligible NRSs.[5,9,13,18,21,23]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in lung cancer.[18] Of the 87 included studies, 8 (9%) were in lung cancer, and the following tests were evaluated[18]:

- Percepta (Veracyte)
  - 5 studies[13,23,86-88]
- FoundationOne (Foundation Medicine)
  - 1 study[21]
- VeriStrat (Biodesix)
  - 1 study[5]
- A nonspecific NGS test
  - 1 study[9]

Of these 8 studies, 3 were conference abstracts and would not provide a sufficient signal for any updated evidence review.[86-88] Additionally, one paper reviewed FoundationOne which is a DNA test not eligible for this signal search. Thus, 4 NRS may be eligible for an evidence review of GEP testing in lung cancer (Table 2).[5,9,13,21,23]

Table 2. Summary Characteristics of Eligible Primary Studies of GEP for Lung Cancer

Author and Year NCT Identifier or Name Country	Population	Aim	Study Design
Percepta (Veracyte)			
Ferguson et al., 2016[13]	202 pulmonologists providing 1,523 case	To determine if a negative genomic classifier result that	Randomized, prospective

Author and Year NCT Identifier or Name Country	Population	Aim	Study Design
PIONEER (based on patient cases from NCT01309087 and NCT00746759) United States	evaluations on 36 patients undergoing workup for lung cancer who had an inconclusive bronchoscopy	down-classifies a patient from intermediate risk to low risk (< 10%) for lung cancer would reduce the rate that physicians recommend more invasive testing among patients with an inconclusive bronchoscopy	decision impact survey study
Sethi et al., 2022[23] NR (based on patient cases from NCT01309087 and NCT00746759 and the Percepta registry) United States	101 pulmonologists providing 1,341 case evaluations on 37 patients undergoing workup for lung cancer who had an inconclusive bronchoscopy and the pre-bronchoscopy risk was high	To determine if an up-classification of risk of malignancy from high to very high will increase the rate of referral for surgical or ablative therapy without additional intervening procedures while increasing physician confidence	Randomized, prospective decision impact survey study
VeriStrat (Biodesix)			
Akerley et al., 2013[5] NR United States	226 physicians who ordered 403 tests for people with NSCLC	To assess the impact of a serum-based proteomic test for NSCLC on physician treatment recommendations	Prospective, nonrandomized decision impact study (before and after receipt of GEP results)
Nonspecific NGS Test			
Coquerelle et al., 2020[9] NR France	683 patients with lung cancer	To evaluated how NGS can modify care pathways	Retrospective, nonrandomized decision impact study (before and after receipt of GEP results)

Abbreviations. ALK: anaplastic kinase lymphoma gene; GEP: gene expression profiling; NCT: National Clinical Trial; NGS: next generation sequencing; NR: not reported; NSCLC: nonsmall cell lung cancer; TKI: tyrosine kinase inhibitor.

Percepta

The study by Ferguson and colleagues found the following[13]:

- Invasive procedure recommendations:
  - Reduced from 57% without Percepta to 18% with a negative (low risk) GEP result ($P < .001$).
  - Increased from 50% to 65% with a positive (intermediate risk) Percepta result ($P < .001$).
- When stratified by ultimate disease diagnosis:
  - Invasive procedure recommendations reduced significantly in patients with benign disease when Percepta results were reported (54% to 41 %; $P < .001$).[13]
- For patients ultimately diagnosed with malignant disease:

- Invasive procedure recommendations increased significantly when Percepta results were reported (50% to 64%; *P* = .003).

The study by Sethi and colleagues found the following[23]:

- In the independent arm, recommendation for surgical resection was significantly higher in patients with a Percepta result compared to patients without a Percepta result (45% vs. 17%, *P* < .001).
- In the pre-post cross-over cohort, recommendation for surgical resection increased from 17%to 56% (*P* < .001) following the review of the Percepta result.
- Up-classification from high to very high risk of malignancy with Percepta increased pulmonologists' confidence in decision making following a nondiagnostic bronchoscopy.

VeriStrat

In the single study evaluating VeriStrat (a multivariate, serum-based proteomic test), pre- and post-test treatment recommendations were prospectively collected from ordering physicians on a voluntary basis.[5] After receiving the test results, 90% of patients who tested as having a significantly better prognosis received erlotinib treatment recommendations compared with 10% of patients who tested as having a poorer prognosis (P < .001).[5] Overall, 90% of post-test treatment recommendations positively correlated with test results, with 40% showing a change from pre-test considerations.[5]

Nonspecific Next Generation Sequencing Test

Coquerelle and colleagues[9] evaluated how the use of NGS could modify care pathways in an observational, retrospective impact study conducted in France.[9] While NGS is primarily a DNA-based technique, it can be used for RNA-based cDNA sequencing. Therefore, we are considering NGS for this study, given the authors' comprehensive coverage of the effect of this procedure for multiple cancer types.[9]In people with lung cancer, there were[9]:

- Missing data or no results in 0.3% of people
- An alteration identified in 82.7% of people, with 56.5% of alterations being actionable (see Table 3)

Table 3. Genotype-Matched and Nonmatched Treatments Before and After NGS Analyses in Lung Cancer[9]

Matched and Nonmatched Treatment for Lung Cancer	N (%)	
	Before	After[a]
Genotype-matched	37 (10.1)	133 (36.2)
Targeted therapies prescribed	18 (5.0)	33 (8.9)
Clinical trials proposed	19 (5.1)	100 (27.2)
Non-genotype matched	191 (52.0)	199 (54.2)
Chemotherapy	50 (13.6)	31 (8.4)
Radiotherapy	7 (1.9)	11 (2.9)
Chemotherapy plus radiotherapy or surgery	19 (5.2)	4 (1.1)
Surgery	21 (5.7)	4 (1.1)
Clinical surveillance	3 (0.8)	9 (2.4)
Palliative care	1 (0.2)	5 (1.3)
Complementary test or examination	0	0
Other treatment	0	0

Matched and Nonmatched Treatment for Lung Cancer	N (%)	
	Before	After[a]
No treatment or no modification of treatment	52 (14.2)	5 (1.1)
Unknown treatment	38 (10.3)	130 (35.4)
Missing data	139 (37.8)	35 (9.5)

Note. [a] No statistical testing was reported between groups.

Harms

We identified 1 study reporting on harms.[23] Overall, there were 44 individual instances where confidence in the treatment plan decreased following a Percepta result compared with 297 instances where confidence remained the same or increased.[23] No significant demographic differences were observed, and the decrease in confidence in was not specific to any case or any individual physician.[23]

Cost and Cost-effectiveness

We did not identify any eligible cost or cost-effectiveness studies for GEP testing in lung cancer.

Bottom Line

Based on some newly identified evidence (5 NRSs), we conclude that at this time the conclusions of the 2018 evidence review may change; GEP testing in lung cancer was not considered in the prior evidence review.

Pancreatobiliary Cancer

GEP is currently not a covered benefit for pancreatobiliary cancer.[4] For this evidence update, we therefore focused on both effectiveness and harms for GEP testing in pancreatobiliary cancer. Since the evidence review in 2018, we identified 1 systematic review evaluating GEP testing in pancreatobiliary cancer and 1 newly published eligible study.[12,18]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in pancreatobiliary cancer.[18]

Of the 87 included studies, 2 (2%) were in pancreatobiliary cancer; both were conducted in the Israel and evaluated the use of Target Now (Caris Life Sciences).[18] Of the 2 studies, 1 is a conference abstract[89] and would therefore not provide a sufficient signal for an updated evidence review.

The other study by the same research team evaluated the use of impact of molecular profiling using Target Now in 30 people with advanced pancreaticobiliary cancer.[12] The retrospective study found that in the 27 patients for whom treatment decisions were available before testing, 20 (74.1%) experienced a treatment decision change in the first line after testing.[12] The changes were as follows[12]:

- Omitting, replacing, or adding agents to the specific regimen that was recommended before testing in 12 patients
- Changing a specific regimen where the physician had been unsure prior to testing in 2 patients

- Changing from recommended best supportive care to treatment with an anticancer therapy after testing in 6 patients

Harms

We did not identify any eligible systematic reviews or primary studies on the harms of GEP testing in pancreaticobiliary cancer.

Costs and Cost-Effectiveness

We did not identify any eligible cost or cost-effectiveness studies for GEP testing in pancreaticobiliary cancer.

Bottom Line

Based on the very limited newly identified evidence (1 NRS), we conclude that at this time the conclusions of the 2018 evidence review are unlikely to change.

Sarcoma

GEP is currently not a covered benefit for sarcoma.[4] For this evidence update, we therefore focused on both effectiveness and harms for GEP testing in sarcoma. Since the evidence review in 2018, we identified 1 systematic review.[15,18]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in sarcoma.[18] Of the 87 included studies, 1 (1%) involved sarcoma, but evaluated the DNA-based FoundationOne test which is not an eligible test for this signal search.

Harms

We did not identify any eligible systematic reviews or primary studies on the harms of GEP testing in sarcoma.

Costs and Cost-Effectiveness

We did not identify any eligible cost or cost-effectiveness studies for GEP testing in sarcoma.

Bottom Line

Based on the lack of identified evidence, we conclude that at this time, the conclusions of the 2018 evidence review are unlikely to change.

Skin Cancer

GEP is currently not a covered benefit for skin cancer. For this evidence update, we therefore focused on both effectiveness and harms for GEP testing in skin cancers. Since the evidence review in 2018, we identified 1 systematic review and 6 newly eligible primary studies evaluating GEP testing in skin cancer.[9,11,16,18,19,22,24] We also identified 1 recently published guideline on the use of GEP in the management of cutaneous squamous cell carcinoma (cSCC).[25]

Effectiveness

We identified 1 scoping review identifying and characterizing decision impact studies in genomic medicine in cancer, including in skin cancer.[18] Of the 87 included studies, 3 (3%) were in skin cancer; 2 studies were conducted in the United States and 1 in France.[18] The following tests were evaluated[18]:

- DecisionDx-UM (Castle Biosciences)in 2 studies[19,90]
- A nonspecific NGS test in 1 study in melanoma (21%), lung cancer (56%), or colorectal cancer (23%)[9]

Only 1 of the 2 studies evaluating DecisionDx-UM is a peer-reviewed journal publication[19]; the other study is a conference abstract and would therefore not provide a sufficient signal for an updated evidence review.[90]

Plasseraud and colleagues evaluated the use of DecisionDx-UM in 70 people with uveal melanoma (melanoma in the eye).[19] The NRS was prospective and multicenter and aimed to assess patient management differences associated with low-risk class 1 and high-risk class 2 results, as indicated by DecisionDx-UM testing.[19] Patients with high-risk results received significantly higher-intensity monitoring and more oncology or clinical trial referrals compared to patients who had low-risk results.[19] However, no analysis of how the testing results changed or not after the test results was reported.[19]

Coquerelle and colleagues[9] evaluated how the use of NGS could modify care pathways in an observational, retrospective impact study conducted in France.[9] While NGS is primarily a DNA-based technique, it can be used for RNA-based cDNA sequencing. Therefore, we are considering NGS for this study, given the authors' comprehensive coverage of the effect of this procedure for multiple cancer types.[9] In people with melanoma (no further details on the specific type), there were[9]:

- Missing data or no results in 52.3% of people
- An alteration identified in 38.3% of people, with 25.0% of alterations being actionable (see Table 4)

Table 4. Genotype-Matched and Nonmatched Treatments Before and After NGS Analyses in Melanoma[9]

Matched and Nonmatched Treatment for Melanoma	N (%)	
	Before	After[a]
Genotype-matched	6 (9.4)	39 (60.9)
Targeted therapies prescribed	5 (7.8)	12 (18.7)
Clinical trials proposed	1 (1.5)	27 (42.2)
Non-genotype matched	58 (90.6)	23 (35.9)
Chemotherapy	0	0
Radiotherapy	1 (1.5)	0
Chemotherapy plus radiotherapy or surgery	0	0
Surgery	34 (53.1)	9 (14.0)
Clinical surveillance	2 (3.1)	6 (9.4)
Palliative care	0	2 (3.1)
Complementary test or examination	0	1 (1.5)
Other treatment	0	0

Matched and Nonmatched Treatment for Melanoma	N (%)	
	Before	After[a]
No treatment or no modification of treatment	21 (32.8)	5 (7.8)
Unknown treatment	0	NR
Missing data	0	2 (3.1)

Note. [a] No statistical testing was reported between groups.
Abbreviation. NR: not reported.

We also identified 2 primary studies evaluating GEP testing in skin cancer (Table 5).[11,22]

Table 5. Summary Characteristics of Eligible Primary Studies of GEP for Skin Cancer

Author and Year NCT Identifier or Name Country	Population	Aim	Study Design
DecisionDx-Melanoma (Castle Biosciences Inc.)			
Dillon et al., 2018[11] NR US	247 patients with melanoma	To evaluate the test impact on clinical management of melanoma	Prospective decision impact study (before and after receipt of GEP results)
DecisionDx-SCC (Castle Biosciences Inc.)			
Saleeby et al., 2022[22] NR US	59 people aged 65 and older with cSCC	To demonstrate patterns of test utilization, including the impact on clinician recommendations for clinical management of high-risk cSCC	Prospective decision impact study (before and after receipt of GEP results)

Abbreviations. cSCC: cutaneous squamous cell carcinoma; GEP: gene expression profiling; NCT: National Clinical Trial; NR: not reported.

In 247 patients with primary melanoma, Dillon and colleagues found that management recommendations changed in 122 people (49%) with the addition of the DecisionDx-Melanoma test results (36% of low-risk melanoma cases and 85% of high-risk melanoma cases).[11] In addition, GEP class was a significant factor for change in care ($P < .001$), with low-risk status accounting for 91% of people with decreased management intensity and high-risk status accounting for 72% of people with increased management intensity.[11]

In the study by Saleeby and colleagues, 24% of clinicians made changes to their treatment plan for cutaneous squamous cell carcinoma (cSCC) with the addition of the DecisionDx-SC test results, and 59% reported an increased confidence in their original treatment plan.[22] Overall, 42% of clinicians reported the DecisionDx-SC test results as being the most influential factor in deciding the management plan.[22] By risk status, 64.7% of clinicians reported increased confidence in their pre-test treatment plan and 17.6% reported a direct impact on treatment decisions for their patients receiving a low-risk status result; for clinicians whose patients received a moderate-risk status result, 14.3% of clinicians reported increased confidence in their pre-test treatment plan and 71.4% reported a direct impact on treatment plans.[22]

In the 2024 guidelines, developed by 8 dermatologists with expertise in the diagnosis and management of cSCC, published studies and consensus were used to draft the following recommendations[25]:

- There is data to support that specific genes influence cSCC clinical behavior (Level A, defined as being based on consistent and good quality patient-oriented evidence)
- The data supports the 40-GEP test's ability to identify a subset of cSCCs that are at high risk for metastasis (Level A)
- The 40-GEP test provides clinically useful data for cSCC prognosis independent of the AJCC8 and BWH staging systems (Level A)
- Adding 40-GEP data to the AJCC8 and BWH staging systems enhances the prognostic assessment of cSCC (SOT Level A)
- The 40-GEP test results can increase the precision and confidence in cSCC management decisions (Level A)
- The 40-GEP test should be considered for use on cSCC tumors with at least 1 high-risk feature per AJCC8 and/or BWH and/or NCCN guidelines (Level A)
- The 40-GEP test is not recommended to be used on cSCC in situ or invasive cSCC without high-risk features, or for patients that are not candidates for additional procedures or therapies (Level C, defined as being based on consensus, usual practice, opinion, disease-oriented evidence, or case series)

Each of the recommendations were unanimously approved for adoption into clinical practice.[25]

Harms

We did not identify any eligible systematic reviews or primary studies on the harms of GEP testing in skin cancer.

Costs and Cost-Effectiveness

We identified 1 cost-benefit analysis and 1 claims-based analysis on GEP testing in skin cancer.[16,24]

Hu and colleagues used a Markov model to model the clinical impact and cost of implementing a GEP test, using DecisionDx-Melanoma, to guide adjuvant therapy for people with resected stage IIIA melanoma.[16] The 3 treatment options were as follows[16]:

- Observation
- Adjuvant pembrolizumab for all patients
- Selective adjuvant therapy, where only high-risk patients based on GEP stratification were treated with pembrolizumab

The primary outcome was cost per death avoided at 10 years.[16] Based on this analysis (Table 6), Hu and colleagues concluded routine adjuvant pembrolizumab was costly, and risk stratification by GEP testing only marginally improved the value of this therapy in stage IIIA melanoma.[16]

Table 6. Incremental Cost and Effect by Treatment Strategy Over 10 Years[16]

Strategy	Overall Survival	Cost per Patient	Cost per Death Avoided	Cost per Life-Year
Observation	0.68	$77.2K	Reference	Reference

Strategy	Overall Survival	Cost per Patient	Cost per Death Avoided	Cost per Life-Year
Selective pembrolizumab	0.73	$182.1K	$2.10M	$583.0K
Routine pembrolizumab	0.76	$272.4K	$2.44M	$697.1K

Abbreviations. K: thousand; M: million.

Somani and colleagues analyzed Medicare claims data for new diagnoses of cSCC for 12 months (ending June 2022).[24] The total direct annual cost for radiation therapy for Medicare patients was estimated at approximately $1.4 billion, with the cost of GEP testing being approximately $195 million.[24] Using the distribution of GEP results, specifically DecisionDx-SCC, from published studies, the analysis estimated that avoidance of adjuvant radiation therapy based on risk status could save up to $972 million in the Medicare-eligible population per year.[24] Sensitivity analysis showed for every additional 10% of moderate-risk test results, an extra $38 million to $66 million in annual savings could be expected through avoiding adjuvant radiation therapy.[24]

Bottom Line

Based on some newly identified evidence (4 NRSs and 2 cost analyses), we conclude that at this time the conclusions of the 2018 evidence review may change; GEP testing in skin cancer was not considered in the prior evidence review.

Ongoing Studies

We identified 6 ongoing clinical studies (Table 7). There are 5 cohort studies and one quasi-experimental pre-post-test study (PROMMIS). In total, 4 studies include patients with prostate cancer and 1 study includes patients with bladder and urothelial cancer. We have been inclusive when selecting these ongoing studies, and some of these may not meet our strict inclusion criteria once published.

Table 7. Summary Characteristics of Ongoing Studies of GEP for Cancer

Study Test Evaluated Estimated Completion Date	Title	Relevant Outcomes
Prostate Cancer		
NCT04396808[91] G-MAJOR Decipher, Prolaris or Oncotype Dx Genomic Prostate Score July 2025	Genomics in Michigan to Adjust Outcomes in Prostate Cancer (G-MAJOR) for Men With Newly Diagnosed Favorable Risk Prostate Cancer	• Impact of GEP testing on rate of potentially unnecessary surgery, predicting adverse pathology and predicting biochemical recurrence
NCT05424783[92] MAGIC Oncotype Dx Genomic Prostate Score December 2025	MRI and GPS Informing Choices for Prostate Cancer Treatment (MAGIC)	• Proportion with active surveillance prostate biopsy by 18 months • Proportion with reclassification within 18 months

Study Test Evaluated Estimated Completion Date	Title	Relevant Outcomes
NCT02783950[93] G-MINOR Decipher Prostate Cancer Classifier August 2024	Genomics in Michigan Impacting Observation or Radiation (G-MINOR)	• Number receiving adjuvant therapy • Time to treatments • Time to biochemical recurrence or metastasis • Patient-reported outcomes
NCT04476537[94] HIPPOCRATES OncoTreat August 2024	RNA Precision Oncology in Advanced Pancreatic Cancer (HIPPOCRATES)	• Number assigned therapy with OncoTreat compared to usual care
Bladder or Urothelial Cancer		
ISRCTN17378733[95] GUSTO Decipher Bladder September 2027	GUSTO: Gene Expression Subtypes of Urothelial Cancer: Stratified Treatment and Oncological Outcomes	• Pathological complete response rate by gene expression subtype in the gene expression subtype-guided arm post-cystectomy and in standard care arm

Abbreviations. GEP: gene expression profiling; NCT: National Clinical Trial identifier; RNA: ribonucleic acid.

Summary

In this evidence review, we identified studies on the use of GEP for adults with cancer. After summarizing the effectiveness, harms, and economic outcomes from eligible studies in this evidence update, we have determined that these outcomes may change the conclusions of the 2018 evidence report in specific cancers—namely, colon and colorectal cancer, lung cancer, and skin cancer.

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93. ClinicalTrials.gov. Genomics in Michigan Impacting Observation or Radiation (G-MINOR). 2023; https://clinicaltrials.gov/study/NCT02783950. Accessed June 27, 2024.

94. ClinicalTrials.gov. RNA precision oncology in advanced pancreatic cancer (HIPPOCRATES). 2024; https://clinicaltrials.gov/study/NCT04476537. Accessed June 27, 2024.

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Appendix A. Search Strategies

Systematic Reviews and Meta-Analyses

Search run May 29, 2024.

Ovid MEDLINE(R) ALL <1946 to May 28, 2024>

1 exp Gene Expression Profiling/ 166007

2 (((gene-expression or gene expression) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)) or GEP).ti,ab,kf. 104814

3 (multi-gene* adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 1051

4 ((genom* or multi-genom*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 170691

5 ((mRNA* or messenger RNA or RNA-seq* or single-cell gene or single-cell RNA or sc-RNA*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 111878

6 ((cDNA* or copy DNA) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 19842

7 Exome Sequencing/ 8602

8 ((exome* or exomic*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 32120

9 Transcriptomes/ 69636

10 transcriptom*.ti,ab,kf. 162974

11 exp "Transcription, Genetic"/ 245173

12 or/1-11 757785

13 (Oncotype* or “21-gene” or EndoPredict* or “12-gene” or MammaPrint* or “70-gene” or Mammostrat* or Breast Cancer Ind* or Prosigna* or PAM50* or “50-gene” or “46-Gene” or “17-gene” or “40-gene” or Prolaris* or Oncogram* or DecisionDX* or Decision DX*).mp. 7014

14 (decipher* adj3 (assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 495

15 (PanCancer adj3 (Pathway* or assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 160

16 or/13-15 7637

17 exp *neoplasms/ 3544669

18 (cancer* or neoplas* or tumo?r* or carcinom* or adenocarcinom* or malig* or metasta*).ti,kf,kw. 2832438

19 or/17-18 4165973

20 exp Decision Support Techniques/ 82937

21 Decision Support Systems, Clinical/ 9833

22 exp Clinical Decision-Making/ 17187

23 exp Decision Making/ 238974

24 (Decision-making or decision making).mp. 297543

25 (decision* adj3 (aid$1 or aiding or assist* or guide or guides or guiding or guidance or impact* or implication* or influenc* or manage* or managing or tailor* or support*)).mp. 136374

26 ((adjust* or approach$2 or influenc* or path$4) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 377320

27 ((choice or choose* or optim* or recommend* or select* or tailor*) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 412814

28 (decision* adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 69831

29 ((effect* or efficac* or impact* or implication*) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 4338256

30 ((guidance or guide or guides or guiding) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 50339

31 ((individual* or person-cent* or personal* or precision) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 211435

32 ((manage* or managing) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 186509

33 (decision* adj3 (clinical* or clinician* or physician* or oncologist* or practitioner*)).mp. 88228

34 ((clinical* or medical*) adj3 (action* or benefit* or impact* or significan* or utility or utili?ation)).mp. 387803

35 or/20-34 5984258

36 (12 and 19 and 35) or (16 and 35) 48361

37 (exp Animals/ not Humans/) or (baboon$1 or bovine$1 or canine$1 or cat$1 or chimpanzee$1 or cow$1 or dog$1 or feline$1 or fish or goat$1 or hens or macque$1 or mice or monkey$1 or mouse or murine$1 or ovine or pig$1 or porcine or primate$1 or sheep or rabbit$1 or rat or rats or rattus or rhesus or rodent$1 or zebrafish).ti.5712562

38 36 not 37 44617

39 limit 38 to (english language and yr="2019 -Current") 20963

40 (systematic review or meta-analysis).pt. 350975

41 systematic reviews as topic/ or meta-analysis as topic/ or network meta-analysis/ or technology assessment, biomedical/ 49456

42 ((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab,kf. 366494

43 ((quantitative adj3 (review* or overview* or synthes*)) or (research adj3 (integrati* or overview*))).ti,ab,kf. 17550

44 ((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*)).ti,ab,kf. 42736

45 (data adj3 (synthes* or extract* or abstracted or abstracting or abstraction*)).ti,ab,kf. 133087

46 (handsearch* or hand search*).ti,ab,kf. 11626

47 (mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab,kf. 38585

48 (met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab,kf. 13138

49 (meta-regression* or meta regression*).ti,ab,kf. 15540

50 (meta-analy* or meta analy* or systematic review*).ti,ab,kf. 474753

51 ((indirect or indirect treatment or mixed-treatment or bayesian) adj3 comparison*).ti,ab,kf. 4652

52 umbrella review*.ti,ab,kf. 2058

53 (("review of" or "overview of") adj2 reviews).ti,ab,kf. 1780

54 (evidence adj2 (synthes* or review*)).ti,ab,kf. 56342

55 (research adj2 synthes*).ti,ab,kf. 3675

56 ((bibliographic or electronic or digital) adj2 database*).ab. 55465

57 cinahl.ab. 50537

58 cochrane.ab. 151224

59 ebsco.ab. 6591

60 embase.ab. 174982

61 medline.ab. 179433

62 ovid.ab. 22344

63 proquest.ab. 7564

64 (psychinfo or psyclit or (psycinfo not "psycinfo database")).ab. 37846

65 pubmed.ab. 239916

66 scopus.ab. 69214

67 "sociological abstracts".ab. 860

68 "web of science".ab. 93221

69 systematic reviews.jw.20966

70 technology assessment*.jw. 5201

71 cochrane.jw. 16766

72 JBI.jw. 2808

73 evidence synthes?s.jw. 918

74 or/40-73 816448

75 39 and 74 583

Randomized Controlled Trials and Nonrandomized Studies

Searches run June 3, 2024.

Ovid MEDLINE(R) ALL <1946 to May 30, 2024>

1 exp Gene Expression Profiling/ 165682

2 (((gene-expression or gene expression) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)) or GEP).ti,ab,kf. 104581

3 (multi-gene* adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 1046

4 ((genom* or multi-genom*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 170190

5 ((mRNA* or messenger RNA or RNA-seq* or single-cell gene or single-cell RNA or sc-RNA*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 111348

6 ((cDNA* or copy DNA) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 19840

7 Exome Sequencing/ 8546

8 ((exome* or exomic*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 31971

9 Transcriptomes/ 69278

10 transcriptom*.ti,ab,kf. 162143

11 exp "Transcription, Genetic"/ 244753

12 or/1-11 755797

13 (Oncotype* or 21-gene or EndoPredict* or 12-gene or MammaPrint* or 70-gene or Mammostrat* or Breast Cancer Ind* or Prosigna* or PAM50* or 50-gene or 46-Gene or 17-gene or 40-gene or Prolaris* or Oncogram* or DecisionDX* or Decision DX*).mp. 7004

14 (decipher* adj3 (assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 494

15 (PanCancer adj3 (Pathway* or assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 159

16 or/13-15 7626

17 exp *neoplasms/ 3539990

18 (cancer* or neoplas* or tumo?r* or carcinom* or adenocarcinom* or malig* or metasta*).ti,kf,kw. 2827645

19 or/17-18 4160007

20 exp Decision Support Techniques/ 82878

21 Decision Support Systems, Clinical/ 9804

22 exp Clinical Decision-Making/ 17103

23 exp Decision Making/ 238639

24 (Decision-making or decision making).mp. 296704

25 (decision* adj3 (aid$1 or aiding or assist* or guide or guides or guiding or guidance or impact* or implication* or influenc* or manage* or managing or tailor* or support*)).mp. 135933

26 ((adjust* or approach$2 or influenc* or path$4) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 376124

27 ((choice or choose* or optim* or recommend* or select* or tailor*) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 411890

28 (decision* adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 69625

29 ((effect* or efficac* or impact* or implication*) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 4332278

30 ((guidance or guide or guides or guiding) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 50146

31 ((individual* or person-cent* or personal* or precision) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 210559

32 ((manage* or managing) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 186066

33 (decision* adj3 (clinical* or clinician* or physician* or oncologist* or practitioner*)).mp. 87879

34 ((clinical* or medical*) adj3 (action* or benefit* or impact* or significan* or utility or utili?ation)).mp. 386737

35 or/20-34 5974170

36 (12 and 19 and 35) or (16 and 35) 48177

37 (exp Animals/ not Humans/) or (baboon$1 or bovine$1 or canine$1 or cat$1 or chimpanzee$1 or cow$1 or dog$1 or feline$1 or fish or goat$1 or hens or macque$1 or mice or monkey$1 or mouse or murine$1 or ovine or pig$1 or porcine or primate$1 or sheep or rabbit$1 or rat or rats or rattus or rhesus or rodent$1 or zebrafish).ti.5708056

38 36 not 37 44440

39 (201709* or 201710* or 201711* or 201712* or 2018* or 2019* or 2020* or 2021* or 2022* or 2023* or 2024* or 2025*).dp,dt,ep.9887662

40 38 and 39 24113

41 limit 40 to english language 23886

42 Randomized Controlled Trial/ 614044

43 Random Allocation/ 107235

44 Control Groups/ 2130

45 Placebos/ 35960

46 (random* or sham or placebo* or head-to-head).ti,ab,kf. 1694501

47 Single-Blind Method/ 33533

48 Double-Blind Method/ 178721

49 ((singl* or doubl*) adj (blind* or dumm* or mask*)).ti,ab,kf. 204020

50 ((tripl* or trebl*) adj (blind* or dumm* or mask*)).ti,ab,kf. 1839

51 Controlled Clinical Trial/ 95541

52 exp "Controlled Clinical Trials as Topic"/ 180301

53 (control* adj3 (study or studies or trial* or group*)).ti,ab,kf. 1301567

54 (non random* or non-random* or quasi-random*).ti,ab,kf. 33675

55 allocated.ti,ab,kf. 89307

56 ((open label or open-label) adj5 (study or studies or trial*)).ti,ab,kf. 47987

57 ((equivalence or superiority or non-inferiority or noninferiority) adj3 (study or studies or trial*)).ti,ab,kf. 12736

58 (pragmatic study or pragmatic studies).ti,ab,kf. 653

59 ((pragmatic or practical) adj3 trial*).ti,ab,kf. 6667

60 (quasi-experimental adj3 (study or studies or trial*)).ti,ab,kf. 13332

61 "Clinical Trials, Phase II as Topic"/ 9426

62 ((phase adj3 (II or "2") adj3 (study or studies or trial*)) or phase2).ti,ab,kf. 67471

63 "Clinical Trials, Phase III as Topic"/ 11445

64 ((phase adj3 (III or "3") adj3 (study or studies or trial*)) or phase3).ti,ab,kf. 54080

65 "Clinical Trials, Phase IV as Topic"/ 397

66 ((phase adj3 (IV or "4") adj3 (study or studies or trial*)) or phase4).ti,ab,kf. 3059

67 Comparative Effectiveness Research/ 4030

68 (compar* adj3 (effectiveness or efficacy)).ti,ab,kf. 107213

69 (active adj1 (comparator* or control$1 or treatment* or intervention*)).ti,ab,kf. 25238

70 (Randomized Controlled Trial or Controlled Clinical Trial or Pragmatic Clinical Trial or Equivalence Trial or clinical trial, phase ii or Clinical Trial, Phase III or clinical trial, phase iv).pt. 736635

71 or/42-70 2848966

72 41 and 71 1515

EBM Reviews - Cochrane Central Register of Controlled Trials <April 2024>

1 exp Gene Expression Profiling/ 885

2 (((gene-expression or gene expression) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)) or GEP).ti,ab,kf. 2386

3 (multi-gene* adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 39

4 ((genom* or multi-genom*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 2025

5 ((mRNA* or messenger RNA or RNA-seq* or single-cell gene or single-cell RNA or sc-RNA*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 1425

6 ((cDNA* or copy DNA) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 62

7 Exome Sequencing/ 56

8 ((exome* or exomic*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 427

9 Transcriptomes/ 461

10 transcriptom*.ti,ab,kf. 1698

11 exp "Transcription, Genetic"/ 609

12 or/1-11 7240

13 (Oncotype* or 21-gene or EndoPredict* or 12-gene or MammaPrint* or 70-gene or Mammostrat* or Breast Cancer Ind* or Prosigna* or PAM50* or 50-gene or 46-Gene or 17-gene or 40-gene or Prolaris* or Oncogram* or DecisionDX* or Decision DX*).mp. 778

14 (decipher* adj3 (assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 40

15 (PanCancer adj3 (Pathway* or assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 21

16 or/13-15 832

17 exp *neoplasms/ 75572

18 (cancer* or neoplas* or tumo?r* or carcinom* or adenocarcinom* or malig* or metasta*).ti,kf,kw. 209360

19 or/17-18 228316

20 exp Decision Support Techniques/ 4478

21 Decision Support Systems, Clinical/ 646

22 exp Clinical Decision-Making/ 685

23 exp Decision Making/ 6437

24 (Decision-making or decision making).mp. 19227

25 (decision* adj3 (aid$1 or aiding or assist* or guide or guides or guiding or guidance or impact* or implication* or influenc* or manage* or managing or tailor* or support*)).mp. 10686

26 ((adjust* or approach$2 or influenc* or path$4) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 32984

27 ((choice or choose* or optim* or recommend* or select* or tailor*) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 51801

28 (decision* adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 8484

29 ((effect* or efficac* or impact* or implication*) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 440680

30 ((guidance or guide or guides or guiding) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 4584

31 ((individual* or person-cent* or personal* or precision) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 24636

32 ((manage* or managing) adj3 (adjuvant or care or chemoradi* or chemotherap* or drug$1 or immunotherap* or medicine or neoadjuvant or pharmacotherap* or radiation* or radiotherap* or therap* or treatment*)).mp. 27999

33 (decision* adj3 (clinical* or clinician* or physician* or oncologist* or practitioner*)).mp. 8725

34 ((clinical* or medical*) adj3 (action* or benefit* or impact* or significan* or utility or utili?ation)).mp. 65746

35 or/20-34 587542

36 (12 and 19 and 35) or (16 and 35) 1859

37 (exp Animals/ not Humans/) or (baboon$1 or bovine$1 or canine$1 or cat$1 or chimpanzee$1 or cow$1 or dog$1 or feline$1 or fish or goat$1 or hens or macque$1 or mice or monkey$1 or mouse or murine$1 or ovine or pig$1 or porcine or primate$1 or sheep or rabbit$1 or rat or rats or rattus or rhesus or rodent$1 or zebrafish).ti.11905

38 36 not 37 1853

39 limit 38 to (yr="2017 -Current" and english language) 1373

40 limit 39 to (trial registry record or conference proceeding or dissertation thesis) 866

41 38 not 40 508

Economic Evaluations

Searches run June 3, 2024.

Ovid MEDLINE(R) ALL <1946 to May 30, 2024>

1 exp Gene Expression Profiling/ 165682

2 (((gene-expression or gene expression) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)) or GEP).ti,ab,kf. 104581

3 (multi-gene* adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 1046

4 ((genom* or multi-genom*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 170190

5 ((mRNA* or messenger RNA or RNA-seq* or single-cell gene or single-cell RNA or sc-RNA*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 111348

6 ((cDNA* or copy DNA) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 19840

7 Exome Sequencing/ 8546

8 ((exome* or exomic*) adj3 (analys?s or assay* or classifi* or differential display* or microarray* or panel* or profil* or sequencing or signature* or test*)).ti,ab,kf. 31971

9 Transcriptomes/ 69278

10 transcriptom*.ti,ab,kf. 162143

11 exp "Transcription, Genetic"/ 244753

12 or/1-11 755797

13 (Oncotype* or 21-gene or EndoPredict* or 12-gene or MammaPrint* or 70-gene or Mammostrat* or Breast Cancer Ind* or Prosigna* or PAM50* or 50-gene or 46-Gene or 17-gene or 40-gene or Prolaris* or Oncogram* or DecisionDX* or Decision DX*).mp. 7004

14 (decipher* adj3 (assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 494

15 (PanCancer adj3 (Pathway* or assay* or classifier* or panel* or profil* or prostate or signature* or test*)).mp. 159

16 or/13-15 7626

17 exp *neoplasms/ 3539990

18 (cancer* or neoplas* or tumo?r* or carcinom* or adenocarcinom* or malig* or metasta*).ti,kf,kw. 2827645

19 or/17-18 4160007

20 Economics/ 27534

21 exp "Costs and Cost Analysis"/ 270815

22 Economics, Nursing/ 4013

23 Economics, Medical/ 9280

24 Economics, Pharmaceutical/ 3137

25 exp Economics, Hospital/ 25856

26 Economics, Dental/ 1922

27 exp "Fees and Charges"/ 31454

28 exp Budgets/ 14217

29 budget*.ti,kf. 9436

30 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. 296589

31 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ti,kf. 59612

32 (value adj2 (money or monetary)).ti,kf. 465

33 exp models, economic/ 16345

34 economic model*.ti,ab,kf. 4873

35 markov chains/ 16186

36 markov.ti,ab,kf. 30865

37 monte carlo method/ 32904

38 monte carlo.ti,ab,kf. 63260

39 exp Decision Theory/ 13673

40 or/20-39 601855

41 ((12 and 19) or 16) and 40 670

Appendix B. Detailed Inclusion and Exclusion Criteria

Table B1. Detailed Inclusion and Exclusion Criteria

Study Component	Inclusion	Exclusion
Populations	• Adults with cancer	• Studies in children with cancer • Studies in adults without cancer
Interventions	• Multigene commercially or clinically available GEP testing of cancer tumor tissue	• Genetic testing other than that stated • Genetic testing of nonsolid tumor tissues (liquid biopsy, saliva, urine, bronchoalveolar lavage) • Molecular testing of other types (DNA, protein, noncoding RNAs) • Radiomics • Mixed/multi "omics" • Molecular tumor typing (cancer type identification)
Comparators	• Another GEP test • Other clinicopathological forms of testing to guide treatment decisions, without GEP • No tumor tissue GEP testing • Usual care	• Comparators other than those stated • No comparator
Outcomes	• Patient management decisions • Clinical outcomes • Harms of testing • Cost and cost-effectiveness	• Studies that do not report outcomes of interest • Risk of cancer in patients not diagnosed with cancer • Outcomes in cancer survivors • Economic outcomes from studies performed in non-United States countries • Economic outcomes from studies performed in the United States that were published more than 5 years ago
Timing	• Post-cancer diagnosis	• None stated • Pre-cancer diagnosis • Long term survivors
Setting	• Any outpatient or inpatient clinical setting in countries categorized as very high on the UN Human Development Index	• Emergency settings • Nonclinical settings (e.g., studies in healthy volunteers, animal models of disease, cell culture, xenografts, organoids) • Countries categorized other than very high on the UN Human Development Index

Study Component	Inclusion	Exclusion
Study Design	• Systematic reviews and meta-analyses • Comparative primary studies	• Abstracts, conference proceedings, posters, editorials, letters • Studies without a comparator • Noncomparative association or correlation studies • Development of novel GEPs • Proof-of-principle studies (e.g., device development or surgical technique modification)
Sample Size	• None specified	• Studies that do not meet the minimum sample size
Publication	• Publication	• Published, peer-reviewed, English-language articles

Abbreviations. DNA: Deoxyribonucleic Acid; GEP: gene expression profiling; KQ: key question; RNA: Ribonucleic Acid; UN: United Nations.

Appendix C. Excluded Studies With Reasons

Reference	Exclusion Criteria
Precision medicine improves outcomes in metastatic breast cancer. *Nature.* 2022. #volume#:#pages# 10.1038/d41586-022-02276-9	Publication Type
Abdelhakam, D. A., Hanna, H., & Nassar, A. **Oncotype DX and Prosigna in breast cancer patients: A comparison study.** *Cancer Treatment and Research Communications. 2021, 26*, 100306.	Outcomes
Adamo, B., Bellet, M., Pare, L., Pascual, T., Vidal, M., Perez Fidalgo, J. A., Blanch, S., Martinez, N., Murillo, L., Gomez-Pardo, P., Lopez-Gonzalez, A., Amillano, K., Canes, J., Galvan, P., Gonzalez-Farre, B., Gonzalez, X., Villagrasa, P., Ciruelos, E., Prat, A. **Oral metronomic vinorelbine combined with endocrine therapy in hormone receptor-positive HER2-negative breast cancer: SOLTI-1501 VENTANA window of opportunity trial.** *Breast Cancer Res.* 2019. 21:108 10.1186/s13058-019-1195-z	Aim
Afonso, S., Vieira, A. C. L., Pereira, C., Oliveira, M. D. **Advancing hospital-based health technology assessment: evaluating genomic panel contracting strategies for blood tumors through a multimethodology.** *Int J Technol Assess Health Care.* 2023. 39:e76 10.1017/S0266462323002751	Intervention
Alaeikhanehshir, S., Ajayi, T., Duijnhoven, F. H., Poncet, C., Olaniran, R. O., Lips, E. H., van 't Veer, L. J., Delaloge, S., Rubio, I. T., Thompson, A. M., Cardoso, F., Piccart, M., Rutgers, E. J. T. **Locoregional Breast Cancer Recurrence in the European Organisation for Research and Treatment of Cancer 10041/BIG 03-04 MINDACT Trial: Analysis of Risk Factors Including the 70-Gene Signature.** *J Clin Oncol.* 2024. 42:1124-1134 10.1200/JCO.22.02690	Study Design
Alarcon-Zendejas, A. P., Scavuzzo, A., Jimenez-Rios, M. A., Alvarez-Gomez, R. M., Montiel-Manriquez, R., Castro-Hernandez, C., Jimenez-Davila, M. A., Perez-Montiel, D., Gonzalez-Barrios, R., Jimenez-Trejo, F., Arriaga-Canon, C., Herrera, L. A. **The promising role of new molecular biomarkers in prostate cancer: from coding and non-coding genes to artificial intelligence approaches.** *Prostate Cancer Prostatic Dis.* 2022. 25:431-443 10.1038/s41391-022-00537-2	Study Design
Alderdice, M., Richman, S. D., Gollins, S., Stewart, J. P., Hurt, C., Adams, R., McCorry, A. M., Roddy, A. C., Vimalachandran, D., Isella, C., Medico, E., Maughan, T., McArt, D. G., Lawler, M., Dunne, P. D. **Prospective patient stratification into robust cancer-cell intrinsic subtypes from colorectal cancer biopsies.** *J Pathol.* 2018. 245:19-28 10.1002/path.5051	Aim
Alexandre M, Maran-Gonzalez A, Viala M, et al. **Decision of Adjuvant Systemic Treatment in HR+ HER2- Early Invasive Breast Cancer: Which Biomarkers Could Help?** *Cancer Manag Res.* 2019;11:10353-10373. doi: 10.2147/CMAR.S221676.	Newer Systematic Review Available
Aragaki, A. K., Jing, Y., Hoffman-Censits, J., Choi, W., Hahn, N. M., Trock, B. J., McConkey, D. J., Johnson, B. A., 3rd. **Gender-specific Stratification of Survival Following Immune Checkpoint Inhibitor Therapy Based on Intratumoral Expression of a B cell Gene Signature.** *Eur Urol Oncol.* 2022. 5:338-346 10.1016/j.euo.2021.07.003	Outcomes
Banerjee, Punnen, S. **A review on the role of tissue-based molecular biomarkers for active surveillance.** *World J Urol.* 2022. 40:27-34 10.1007/s00345-021-03610-y	Study Design

Reference	Exclusion Criteria
Bao, X., Shi, R., Zhao, T., Wang, Y. **Mast cell-based molecular subtypes and signature associated with clinical outcome in early-stage lung adenocarcinoma.** *Mol Oncol.* 2020. 14:917-932 10.1002/1878-0261.12670	Aim
Barlesi, F., Tomasini, P., Karimi, M., Michiels, S., Raimbourg, J., Daniel, C., Janicot, H., Madroszyk, A., Audigier-Valette, C., Quoix, E., Mazieres, J., Moro-Sibilot, D., Dansin, E., Molinier, O., Morel, H., Pichon, E., Cortot, A., Otto, J., Chomy, F., Souquet, P. J., Cloarec, N., Giroux-Leprieur, E., Bieche, I., Lacroix, L., Boyault, S., Attignon, V., Soubeyran, I., Morel, A., Tran-Dien, A., Jacquet, A., Dall'Olio, F. G., Jimenez, M., Soria, J. C., Besse, B. **Comprehensive Genome Profiling in Patients With Metastatic Non-Small Cell Lung Cancer: The Precision Medicine Phase II Randomized SAFIR02-Lung/IFCT 1301 Trial.** *Clin Cancer Res.* 2022. 28:4018-4026 10.1158/1078-0432.CCR-22-0371	Comparator
Bartlett, J. M. S., Sgroi, D. C., Treuner, K., Zhang, Y., Ahmed, I., Piper, T., Salunga, R., Brachtel, E. F., Pirrie, S. J., Schnabel, C. A., Rea, D. W. **Breast Cancer Index and prediction of benefit from extended endocrine therapy in breast cancer patients treated in the Adjuvant Tamoxifen-To Offer More? (aTTom) trial.** *Ann Oncol.* 2019. 30:1776-1783 10.1093/annonc/mdz289	Study Design
Battisti NML, De Glas N, Soto-Perez-de-Celis E, et al. **Chemotherapy and gene expression profiling in older early luminal breast cancer patients: An International Society of Geriatric Oncology systematic review**. *Eur J Cancer.* 2022;172:158-170. doi: 10.1016/j.ejca.2022.05.039.	Newer Systematic Review Available
Berdunov, V., Millen, S., Paramore, A., Griffin, J., Reynia, S., Fryer, N., Brown, R., Longworth, L. **Cost-Effectiveness Analysis of the Oncotype DX Breast Recurrence Score((R)) Test in Node-Negative Early Breast Cancer.** *Clinicoecon Outcomes Res.* 2022. 14:619-633 10.2147/CEOR.S360049	Setting
Berdunov, V., Millen, S., Paramore, A., Hall, P., Perren, T., Brown, R., Griffin, J., Reynia, S., Fryer, N., Longworth, L. **Cost-effectiveness analysis of the Oncotype DX Breast Recurrence Score test in node-positive early breast cancer.** *J Med Econ.* 2022. 25:591-604 10.1080/13696998.2022.2066399	Setting
Berlin, A., Murgic, J., Hosni, A., Pintilie, M., Salcedo, A., Fraser, M., ... & Chua, M. L. **Genomic classifier for guiding treatment of intermediate-risk prostate cancers to dose-escalated image guided radiation therapy without hormone therapy**. International Journal of Radiation Oncology* Biology* Physics. 2019. 103(1), 84-91.	Aim
Bestvina, C. M., Waters, D., Morrison, L., Emond, B., Lafeuille, M. H., Hilts, A., Lefebvre, P., He, A., Vanderpoel, J. **Cost of genetic testing, delayed care, and suboptimal treatment associated with polymerase chain reaction versus next-generation sequencing biomarker testing for genomic alterations in metastatic non-small cell lung cancer.** *J Med Econ.* 2024. 27:292-303 10.1080/13696998.2024.2314430	Intervention
Biran, N., Dhakal, B., Lentzsch, S., Siegel, D., Usmani, S. Z., Rossi, A., ... & Niesvizky, R**. Gene expression profiling impacts treatment decision making in newly diagnosed multiple myeloma patients in the prospective PROMMIS trial.** EJHaem. 2021. 2(3), 375-384.	Population
Bottosso, M., Miglietta, F., Vernaci, G. M., Giarratano, T., Dieci, M. V., Guarneri, V., Griguolo, G. **Gene-expression assays to tailor adjuvant endocrine therapy for HR+/HER2- breast cancer.** *Clin Cancer Res.* 2024. 24:24 10.1158/1078-0432.CCR-23-4020	Study Design

Reference	Exclusion Criteria
Boyer MJ, Carpenter D, Gingrich JR, et al. **Prognostic Value of Genomic Classifier Testing for Prostate Cancer: A Systematic Review.** *Department of Veterans Affairs (US).* 2023;03:03.	Outcomes
Boyer MJ, Carpenter DJ, Gingrich JR, et al. **Genomic classifiers and prognosis of localized prostate cancer: a systematic review.** *Prostate Cancer Prostatic Dis.* 2024;10:10. doi: 10.1038/s41391-023-00766-z.	Outcomes
Burd, A., Levine, R. L., Ruppert, A. S., Mims, A. S., Borate, U., Stein, E. M., Patel, P., Baer, M. R., Stock, W., Deininger, M., Blum, W., Schiller, G., Olin, R., Litzow, M., Foran, J., Lin, T. L., Ball, B., Boyiadzis, M., Traer, E., Odenike, O., Arellano, M., Walker, A., Duong, V. H., Kovacsovics, T., Collins, R., Shoben, A. B., Heerema, N. A., Foster, M. C., Vergilio, J. A., Brennan, T., Vietz, C., Severson, E., Miller, M., Rosenberg, L., Marcus, S., Yocum, A., Chen, T., Stefanos, M., Druker, B., Byrd, J. C. **Precision medicine treatment in acute myeloid leukemia using prospective genomic profiling: feasibility and preliminary efficacy of the Beat AML Master Trial.** *Nat Med.* 2020. 26:1852-1858 10.1038/s41591-020-1089-8	Intervention
Canino, F., Piacentini, F., Omarini, C., Toss, A., Barbolini, M., Vici, P., Dominici, M., Moscetti, L. **Role of Intrinsic Subtype Analysis with PAM50 in Hormone Receptors Positive HER2 Negative Metastatic Breast Cancer: A Systematic Review.** *Int J Mol Sci.* 2022. 23:25 10.3390/ijms23137079	Aim
Canter, D. J., Freedland, S., Rajamani, S., Latsis, M., Variano, M., Halat, S., Tward, J., Cohen, T., Stone, S., Schlomm, T., Bishoff, J., Bardot, S. **Analysis of the prognostic utility of the cell cycle progression (CCP) score generated from needle biopsy in men treated with definitive therapy.** *Prostate Cancer Prostatic Dis.* 2020. 23:102-107 10.1038/s41391-019-0159-9	Study Design
Caparica, R., Brandao, M., Piccart, M. **Systemic treatment of patients with early breast cancer: recent updates and state of the art.** *Breast.* 2019. 48 Suppl 1:S7-S20 10.1016/S0960-9776(19)31115-4	Aim
Chandler, Y., Jayasekera, J. C., Schechter, C. B., Isaacs, C., Cadham, C. J., Mandelblatt, J. S. **Simulation of Chemotherapy Effects in Older Breast Cancer Patients With High Recurrence Scores.** *J Natl Cancer Inst.* 2020. 112:574-581 10.1093/jnci/djz189	Study Design
Chaudhari, V. S., Hole, K. C., Issa, A. M. **Evaluating the quality of the economic evidence in colorectal cancer genomics studies.** *Per Med.* 2022. 19:361-375 10.2217/pme-2021-0006	Intervention
Chen, J., Shen, S., Li, Y., Fan, J., Xiong, S., Xu, J., Zhu, C., Lin, L., Dong, X., Duan, W., Zhao, Y., Qian, X., Liu, Z., Wei, Y., Christiani, D. C., Zhang, R., Chen, F. **APOLLO: An accurate and independently validated prediction model of lower-grade gliomas overall survival and a comparative study of model performance.** *EBioMedicine.* 2022. 79:104007 10.1016/j.ebiom.2022.104007	Aim
Chung, C., Yeung, V. T. Y., Wong, K. C. W. **Prognostic and predictive biomarkers with therapeutic targets in breast cancer: A 2022 update on current developments, evidence, and recommendations.** *J Oncol Pharm Pract.* 2023. 29:1343-1360 10.1177/10781552221119797	Study Design
Davey, M. G., Davey, M. S., Boland, M. R., Ryan, E. J., Lowery, A. J., Kerin, M. J. **Radiomic differentiation of breast cancer molecular subtypes using pre-operative breast imaging - A systematic review and meta-analysis.** *Eur J Radiol.* 2021. 144:109996 10.1016/j.ejrad.2021.109996	Intervention

Reference	Exclusion Criteria
Davey, M. G., Davey, M. S., Ryan, E. J., Boland, M. R., McAnena, P. F., Lowery, A. J., Kerin, M. J. **Is radiomic MRI a feasible alternative to OncotypeDX(R) recurrence score testing? A systematic review and meta-analysis.** *BJS Open.* 2021. 5:06 10.1093/bjsopen/zrab081	Comparator
Davey, M. G., Richard, V., Lowery, A. J., Kerin, M. J. **OncotypeDX(c) Recurrence Score in BRCA mutation carriers: a systematic review and meta-analysis.** *Eur J Cancer.* 2021. 154:209-216 10.1016/j.ejca.2021.06.032	Comparator
Davey MG, Cleere EF, O'Donnell JP, Gaisor S, Lowery AJ, Kerin MJ. **Value of the 21-gene expression assay in predicting locoregional recurrence rates in estrogen receptor-positive breast cancer: a systematic review and network meta-analysis.** *Breast Cancer Res Treat.* 2022;193(3):535-544. doi: 10.1007/s10549-022-06580-w.	Outcomes
Davey MG, Davey CM, Bouz L, et al. **Relevance of the 21-gene expression assay in male breast cancer: A systematic review and meta-analysis.** *Breast.* 2022;64:41-46. doi: 10.1016/j.breast.2022.04.009.	Outcomes
Davey MG, Ryan EJ, Boland MR, Barry MK, Lowery AJ, Kerin MJ. **Clinical utility of the 21-gene assay in predicting response to neoadjuvant endocrine therapy in breast cancer: A systematic review and meta-analysis.** *Breast.* 2021;58:113-120. doi: 10.1016/j.breast.2021.04.010.	Outcomes
Davies, A., Cummin, T. E., Barrans, S., Maishman, T., Mamot, C., Novak, U., Caddy, J., Stanton, L., Kazmi-Stokes, S., McMillan, A., Fields, P., Pocock, C., Collins, G. P., Stephens, R., Cucco, F., Clipson, A., Sha, C., Tooze, R., Care, M. A., Griffiths, G., Du, M. Q., Westhead, D. R., Burton, C., Johnson, P. W. M. **Gene-expression profiling of bortezomib added to standard chemoimmunotherapy for diffuse large B-cell lymphoma (REMoDL-B): an open-label, randomised, phase 3 trial.** *Lancet Oncol.* 2019. 20:649-662 10.1016/S1470-2045(18)30935-5	Comparator
DiGennaro, C., Vahdatzad, V., Jalali, M. S., Toumi, A., Watson, T., Gazelle, G. S., Mercaldo, N., Lubitz, C. C. **Assessing Bias and Limitations of Clinical Validation Studies of Molecular Diagnostic Tests for Indeterminate Thyroid Nodules: Systematic Review and Meta-Analysis.** *Thyroid.* 2022. 32:1144-1157 10.1089/thy.2022.0269	Intervention
Dong, O. M., Poonnen, P. J., Winski, D., Reed, S. D., Vashistha, V., Bates, J., Kelley, M. J., Voora, D. **Cost-Effectiveness of Tumor Genomic Profiling to Guide First-Line Targeted Therapy Selection in Patients With Metastatic Lung Adenocarcinoma.** *Value Health.* 2022. 25:582-594 10.1016/j.jval.2021.09.017	Intervention
Dubin, D. P., Dinehart, S. M., Farberg, A. S. **Level of Evidence Review for a Gene Expression Profile Test for Cutaneous Melanoma.** *Am J Clin Dermatol.* 2019. 20:763-770 10.1007/s40257-019-00464-4	Study Design
Ebell, M. H. **Prolaris Test for Prostate Cancer Risk Assessment.** *Am Fam Physician.* 2019. 100:311-312 #DOI#	Publication Type
Faraj, K. S., Kaufman, S. R., Herrel, L. A., Maganty, A., Oerline, M., Caram, M. E. V., Shahinian, V. B., Hollenbeck, B. K. **The immediate effects of private equity acquisition of urology practices on the management of newly diagnosed prostate cancer.** *Cancer Med.* 2023. 12:22325-22332 10.1002/cam4.6788	Comparator
Faraj, K. S., Kaufman, S. R., Herrel, L. A., Oerline, M. K., Maganty, A., Shahinian, V. B., Hollenbeck, B. K. **Association between urology practice use of multiparametric MRI and genomic testing and treatment of men with newly diagnosed prostate cancer.** *Urol Oncol.* 2023. 41:430 e17-430 e23 10.1016/j.urolonc.2023.08.002	Aim

Reference	Exclusion Criteria
Farberg AS, Marson JW, Glazer A, et al. **Expert Consensus on the Use of Prognostic Gene Expression Profiling Tests for the Management of Cutaneous Melanoma: Consensus from the Skin Cancer Prevention Working Group.** *Dermatol Ther (Heidelb).* 2022;12(4):807-823. doi: 10.1007/s13555-022-00709-x.	Publication Type
Fastner, S., Shen, N., Hartman, R. I., Chu, E. Y., Kim, C. C., Kirkwood, J. M., Grossman, D. **Prognostic gene expression profile testing to inform use of adjuvant therapy: A survey of melanoma experts.** *Cancer Med.* 2023. 12:22103-22108 10.1002/cam4.6819	Study Design
Feng, X., Wang, E., Cui, Q. **Gene Expression-Based Predictive Markers for Paclitaxel Treatment in ER+ and ER- Breast Cancer.** *Front Genet.* 2019. 10:156 10.3389/fgene.2019.00156	Aim
Fine ND, LaPolla F, Epstein M, Loeb S, Dani H. **Genomic classifiers for treatment selection in newly diagnosed prostate cancer.** *BJU Int*. 2019;124(4):578-586. doi: 10.1111/bju.14799	Outcomes
Fu, Y., Sun, S., Bi, J., Kong, C., Yin, L. **A novel immune-related gene pair prognostic signature for predicting overall survival in bladder cancer.** *BMC Cancer.* 2021. 21:810 10.1186/s12885-021-08486-0	Setting
Gluz, O., Kuemmel, S., Nitz, U., Braun, M., Ludtke-Heckenkamp, K., von Schumann, R., Darsow, M., Forstbauer, H., Potenberg, J., Uleer, C., Grischke, E. M., Aktas, B., Schumacher, C., Zu Eulenburg, C., Kates, R., Jozwiak, K., Graeser, M., Wuerstlein, R., Baehner, R., Christgen, M., Kreipe, H. H., Harbeck, N. **Nab-paclitaxel weekly versus dose-dense solvent-based paclitaxel followed by dose-dense epirubicin plus cyclophosphamide in high-risk HR+/HER2- early breast cancer: results from the neoadjuvant part of the WSG-ADAPT-HR+/HER2- trial.** *Ann Oncol.* 2023. 34:531-542 10.1016/j.annonc.2023.04.002	Comparator
Green, N., Al-Allak, A., Fowler, C. **Benefits of introduction of Oncotype DX((R)) testing.** *Ann R Coll Surg Engl.* 2019. 101:55-59 10.1308/rcsann.2018.0173	Study Design
Griffin, Jon, Down, Jenny, Quayle, Lewis A., Heath, Paul R., Gibb, Ewan A., Davicioni, Elai, Liu, Yang, Zhao, Xin, Swain, Jayne, Wang, Dennis, Hussain, Syed, Crabb, Simon, Catto, James W. F. **Verification of molecular subtyping of bladder cancer in the GUSTO clinical trial.** *The Journal of Pathology: Clinical Research.* 2024. 10:#pages# 10.1002/2056-4538.12363	Study Design
Hall, P. S., Smith, A., Hulme, C., Vargas-Palacios, A., Makris, A., Hughes-Davies, L., Dunn, J. A., Bartlett, J. M. S., Cameron, D. A., Marshall, A., Campbell, A., Macpherson, I. R., Dan, Rea, Francis, A., Earl, H., Morgan, A., Stein, R. C., McCabe, C., Group, Optima Trial Management. **Value of Information Analysis of Multiparameter Tests for Chemotherapy in Early Breast Cancer: The OPTIMA Prelim Trial.** *Value Health.* 2017. 20:1311-1318 10.1016/j.jval.2017.04.021	Setting
Hannouf, M. B., Zaric, G. S., Blanchette, P., Brezden-Masley, C., Paulden, M., McCabe, C., Raphael, J., Brackstone, M. **Cost-effectiveness analysis of multigene expression profiling assays to guide adjuvant therapy decisions in women with invasive early-stage breast cancer.** *Pharmacogenomics J.* 2020. 20:27-46 10.1038/s41397-019-0089-x	Setting
Harnan S, Tappenden P, Cooper K, et al. **Tumour profiling tests to guide adjuvant chemotherapy decisions in early breast cancer: a systematic review and economic analysis**. *Health Technol Assess.* 2019;23(30):1-328. doi: 10.3310/hta23300.	Newer Systematic Review Available

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Harvey, M. J., Cunningham, R., Sawchyn, B., Montesion, M., Reddy, P., McBride, A., Chawla, A. J. **Budget Impact Analysis of Comprehensive Genomic Profiling in Patients With Advanced Non-Small-Cell Lung Cancer.** *JCO Precis Oncol.* 2021. 5:1611-1624 10.1200/PO.20.00540	Intervention
Haslem, D. S., Chakravarty, I., Fulde, G., Gilbert, H., Tudor, B. P., Lin, K., Ford, J. M., Nadauld, L. D. **Precision oncology in advanced cancer patients improves overall survival with lower weekly healthcare costs.** *Oncotarget.* 2018. 9:12316-12322 10.18632/oncotarget.24384	Study Design
Hayashi, H., Kurata, T., Takiguchi, Y., Arai, M., Takeda, K., Akiyoshi, K., Matsumoto, K., Onoe, T., Mukai, H., Matsubara, N., Minami, H., Toyoda, M., Onozawa, Y., Ono, A., Fujita, Y., Sakai, K., Koh, Y., Takeuchi, A., Ohashi, Y., Nishio, K., Nakagawa, K. **Randomized Phase II Trial Comparing Site-Specific Treatment Based on Gene Expression Profiling With Carboplatin and Paclitaxel for Patients With Cancer of Unknown Primary Site.** *J Clin Oncol.* 2019. 37:570-579 10.1200/JCO.18.00771	Intervention
Helland, A., Russnes, H. G., Fagereng, G. L., Al-Shibli, K., Andersson, Y., Berg, T., Bjorge, L., Blix, E., Bjerkehagen, B., Brabrand, S., Cameron, M. G., Dalhaug, A., Dietzel, D., Donnem, T., Enerly, E., Flobak, A., Fluge, S., Gilje, B., Gjertsen, B. T., Gronberg, B. H., Gronas, K., Guren, T., Hamre, H., Haug, A., Heinrich, D., Hjortland, G. O., Hovig, E., Hovland, R., Iversen, A. C., Janssen, E., Kyte, J. A., von der Lippe Gythfeldt, H., Lothe, R., Lund, J. A., Meza-Zepeda, L., Munthe-Kaas, M. C., Nguyen, O. T. D., Niehusmann, P., Nilsen, H., Puco, K., Ree, A. H., Riste, T. B., Semb, K., Steinskog, E. S. S., Stensvold, A., Suhrke, P., Tennoe, O., Tjonnfjord, G. E., Vassbotn, L. J., Aas, E., Aasebo, K., Tasken, K., Smeland, S. **Improving public cancer care by implementing precision medicine in Norway: IMPRESS-Norway.** *J Transl Med.* 2022. 20:225 10.1186/s12967-022-03432-5	Intervention
Henderson, R., French, D., Sullivan, R., Maughan, T., Clarke, M., Lawler, M. **Molecular biomarkers and precision medicine in colorectal cancer: a systematic review of health economic analyses.** *Oncotarget.* 2019. 10:3408-3423 10.18632/oncotarget.26909	Setting
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Hochheiser L, Hornberger J, Turner M, Lyman GH. **Multi-gene assays: effect on chemotherapy use, toxicity and cost in estrogen receptor-positive early stage breast cancer.** *J Comp Eff Res*. 2019;8(5):289-304. doi: 10.2217/cer-2018-0137.	Newer Systematic Review Available
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Hu, T. X., Nguyen, D. T., Patel, M., Beckett, K., Douek, M., Masamed, R., Rhyu, J., Kim, J., Tseng, C. H., Yeh, M. W., Livhits, M. J. **The Effect Modification of Ultrasound Risk Classification on Molecular Testing in Predicting the Risk of Malignancy in Cytologically Indeterminate Thyroid Nodules.** *Thyroid.* 2022. 32:905-916 10.1089/thy.2021.0659	Intervention
Ishimaru, S., Shimoi, T., Sunami, K., Nakajima, M., Ando, Y., Okita, N., Nakamura, K., Shibata, T., Fujiwara, Y., Yamamoto, N. **Platform trial for off-label oncology drugs using comprehensive genomic profiling under the universal public healthcare system: the BELIEVE trial.** *Int J Clin Oncol*. 2024. 29:89-95 10.1007/s10147-023-02439-2	Intervention
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Italiano, A., Dinart, D., Soubeyran, I., Bellera, C., Esperou, H., Delmas, C., Mercier, N., Albert, S., Poignie, L., Boland, A., Bourdon, A., Geneste, D., Cavaille, Q., Laizet, Y., Khalifa, E., Auzanneau, C., Squiban, B., Truffaux, N., Olaso, R., Gerber, Z., Wallet, C., Benard, A., Blay, J. Y., Laurent-Puig, P., Deleuze, J. F., Lucchesi, C., Mathoulin-Pelissier, S., group, Multisarc study. **Molecular profiling of advanced soft-tissue sarcomas: the MULTISARC randomized trial.** *BMC Cancer*. 2021. 21:1180 10.1186/s12885-021-08878-2	Intervention
Jagsi, R., Barlow, W. E., Woodward, W. A., Connolly, E., Mahtani, R., Shumway, D., Speers, C., Stecklein, S. R., Zeidan, Y., Zhang, H., Sharma, P., Pusztai, L., Hortobagyi, G. N., Kalinsky, K. **Radiotherapy Use and Incidence of Locoregional Recurrence in Patients With Favorable-Risk, Node-Positive Breast Cancer Enrolled in the SWOG S1007 Trial.** *JAMA Oncol*. 2023. 9:1083-1089 10.1001/jamaoncol.2023.1984	Aim
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Johnston, K. M., Sheffield, B. S., Yip, S., Lakzadeh, P., Qian, C., Nam, J. **Costs of in-house genomic profiling and implications for economic evaluation: a case example of non-small cell lung cancer (NSCLC).** *J Med Econ.* 2020. 23:1123-1129 10.1080/13696998.2020.1789152	Setting
Kagawa, H., Hatakeyama, K., Shiomi, A., Hino, H., Manabe, S., Yamaoka, Y., Nagashima, T., Ohshima, K., Urakami, K., Yamaguchi, K. **Consensus molecular subtyping improves the clinical usefulness of canonical tumor markers for colorectal cancer.** *Biomed Res.* 2022. 43:201-209 10.2220/biomedres.43.201	Aim
Kantor, O., King, T. A., Freedman, R. A., Mayer, E. L., Chavez-MacGregor, M., Korde, L. A., Sparano, J. A., Mittendorf, E. A. **Racial and Ethnic Disparities in Locoregional Recurrence Among Patients With Hormone Receptor-Positive, Node-Negative Breast Cancer: A Post Hoc Analysis of the TAILORx Randomized Clinical Trial.** *JAMA Surg.* 2023. 158:583-591 10.1001/jamasurg.2023.0297	Study Design
Katipally, R. R., Martinez, C. A., Pugh, S. A., Bridgewater, J. A., Primrose, J. N., Domingo, E., Maughan, T. S., Talamonti, M. S., Posner, M. C., Weichselbaum, R. R., Pitroda, S. P., with the S. Cort Consortium. **Integrated Clinical-Molecular Classification of Colorectal Liver Metastases: A Biomarker Analysis of the Phase 3 New EPOC Randomized Clinical Trial.** *JAMA Oncol.* 2023. 9:1245-1254 10.1001/jamaoncol.2023.2535	Study Design
Kim, H. L., Li, P., Huang, H. C., Deheshi, S., Marti, T., Knudsen, B., ... & Bismar, T. A. **Validation of the Decipher Test for predicting adverse pathology in candidates for prostate cancer active surveillance**. Prostate cancer and prostatic diseases. 2019. 22(3), 399-405.	Outcomes
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Kreuz, M., Otto, D. J., Fuessel, S., Blumert, C., Bertram, C., Bartsch, S., Loeffler, D., Puppel, S. H., Rade, M., Buschmann, T., Christ, S., Erdmann, K., Friedrich, M., Froehner, M., Muders, M. H., Schreiber, S., Specht, M., Toma, M. I., Benigni, F., Freschi, M., Gandaglia, G., Briganti, A., Baretton, G. B., Loeffler, M., Hackermuller, J., Reiche, K., Wirth, M., Horn, F. **ProstaTrend-A Multivariable Prognostic RNA Expression Score for Aggressive Prostate Cancer.** *Eur Urol.* 2020. 78:452-459 10.1016/j.eururo.2020.06.001	Aim
Kringelbach, T., Hojgaard, M., Rohrberg, K., Spanggaard, I., Laursen, B. E., Ladekarl, M., Haslund, C. A., Harslof, L., Belcaid, L., Gehl, J., Sondergaard, L., Eefsen, R. L., Hansen, K. H., Kodahl, A. R., Jensen, L. H., Holt, M. I., Oellegaard, T. H., Yde, C. W., Ahlborn, L. B., Lassen, U. **ProTarget: a Danish Nationwide Clinical Trial on Targeted Cancer Treatment based on genomic profiling - a national, phase 2, prospective, multi-drug, non-randomized, open-label basket trial.** *BMC Cancer.* 2023. 23:182 10.1186/s12885-023-10632-9	Intervention
Kunst NR, Alarid-Escudero F, Paltiel AD, Wang SY. **A Value of Information Analysis of Research on the 21-Gene Assay for Breast Cancer Management.** *Value Health.* 2019;22(10):1102-1110. doi: 10.1016/j.jval.2019.05.004.	Aim

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Lambert, T., Pobel, C., Colmet-Daage, L., Bigorgne, A., Rauby, Y. B., Aladro, N. S., Ter-Minassian, N. L., Kerisit, M., Marabelle, A., Besse, B., Hollebecque, A., Champiat, S., Massard, C., Morel, D., Verlingue, L., Scoazec, J. Y. **Prognostic value of tumor immune biomarkers in biopsies from patients with refractory solid cancers.** *Cancer Treat Res Commun.* 2022. 32:100611 10.1016/j.ctarc.2022.100611	Intervention
Leapman, M. S., Nguyen, H. G., Cowan, J. E., Xue, L., Stohr, B., Simko, J., ... & Carroll, P. R. **Comparing prognostic utility of a single-marker immunohistochemistry approach with commercial gene expression profiling following radical prostatectomy.** European urology, 2018. 74(5), 668-675.	Outcomes
Lehto, T. K., Sturenberg, C., Malen, A., Erickson, A. M., Koistinen, H., Mills, I. G., Rannikko, A., Mirtti, T. **Transcript analysis of commercial prostate cancer risk stratification panels in hard-to-predict grade group 2-4 prostate cancers.** *Prostate.* 2021. 81:368-376 10.1002/pros.24108	Comparator
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Léon, P., Cancel-Tassin, G., Drouin, S., Audouin, M., Varinot, J., Comperat, E., ... & Cussenot, O. **Comparison of cell cycle progression score with two immunohistochemical markers (PTEN and Ki-67) for predicting outcome in prostate cancer after radical prostatectomy.** World journal of urology. 2018. 36, 1495-1500.	Outcomes
Lin, S. H., Chien, C. H., Chang, K. P., Lu, M. F., Chen, Y. T., Chu, Y. W. **SaBrcada: Survival Intervals Prediction for Breast Cancer Patients by Dimension Raising and Age Stratification.** *Cancers (Basel).* 2023. 15:20 10.3390/cancers15143690	Study Design
Lin X, Kapoor A, Gu Y, et al. **Assessment of biochemical recurrence of prostate cancer (Review).** *Int J Oncol.* 2019;55(6):1194-1212. doi: 10.3892/ijo.2019.4893.	Outcomes
Liu, Y., Zhu, X. Z., Xiao, Y., Wu, S. Y., Zuo, W. J., Yu, Q., Cao, A. Y., Li, J. J., Yu, K. D., Liu, G. Y., Wu, J., Sun, T., Cui, J. W., Lv, Z., Li, H. P., Zhu, X. Y., Jiang, Y. Z., Wang, Z. H., Shao, Z. M. **Subtyping-based platform guides precision medicine for heavily pretreated metastatic triple-negative breast cancer: The FUTURE phase II umbrella clinical trial.** *Cell Res.* 2023. 33:389-402 10.1038/s41422-023-00795-2	Setting
Lopes Cardozo, J. M. N., Drukker, C. A., Rutgers, E. J. T., Schmidt, M. K., Glas, A. M., Witteveen, A., Cardoso, F., Piccart, M., Esserman, L. J., Poncet, C., van 't Veer, L. J. **Outcome of Patients With an Ultralow-Risk 70-Gene Signature in the MINDACT Trial.** *J Clin Oncol.* 2022. 40:1335-1345 10.1200/JCO.21.02019	Study Design
LoRusso, P. M., Sekulic, A., Sosman, J. A., Liang, W. S., Carpten, J., Craig, D. W., Solit, D. B., Bryce, A. H., Kiefer, J. A., Aldrich, J., Nasser, S., Halperin, R., Byron, S. A., Pilat, M. J., Boerner, S. A., Durecki, D., Hendricks, W. P. D., Enriquez, D., Izatt, T., Keats, J., Legendre, C., Markovic, S. N., Weise, A., Naveed, F., Schmidt, J., Basu, G. D., Sekar, S., Adkins, J., Tassone, E., Sivaprakasam, K., Zismann, V., Calvert, V. S., Petricoin, E. F., Fecher, L. A., Lao, C., Eder, J. P., Vogelzang, N. J., Perlmutter, J., Gorman, M., Manica, B., Fox, L., Schork, N., Zelterman, D., DeVeaux, M., Joseph, R. W., Cowey, C. L., Trent, J. M. **Identifying treatment options for BRAFV600 wild-type metastatic melanoma: A SU2C/MRA genomics-enabled clinical trial.** *PLoS One.* 2021. 16:e0248097 10.1371/journal.pone.0248097	Intervention

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Lundgren C, Tutzauer J, Church SE, et al. **Tamoxifen-predictive value of gene expression signatures in premenopausal breast cancer: data from the randomized SBII:2 tria**l. *Breast Cancer Res.* 2023;25(1):110. doi: 10.1186/s13058-023-01719-z.	Outcomes
Lux, M. P., Minartz, C., Muller-Huesmann, H., Sandor, M. F., Herrmann, K. H., Radeck-Knorre, S., Neubauer, A. S. **Budget impact of the Oncotype DX(R) test compared to other gene expression tests in patients with early breast cancer in Germany.** *Cancer Treat Res Commun.* 2022. 31:100519 10.1016/j.ctarc.2022.100519	Setting
Lux, M. P., Minartz, C., Muller-Huesmann, H., Sandor, M. F., Radeck-Knorre, S., Neubauer, A. S. **Budget Impact of the Oncotype DX Breast Recurrence Score((R)) Test in Patients with Early Primary Hormone-Receptor-Positive, HER2-Negative, Node-Positive Breast Cancer in Germany.** *Breast Care (Basel).* 2024. 19:27-33 10.1159/000534096	Setting
Luyendijk, M., Jager, A., Buijs, S. M., Siesling, S., Groot, C. A. U., Blommestein, H. M. **Cost-Effectiveness Analysis of MammaPrint((R)) to Guide the Use of Endocrine Therapy in Patients with Early-Stage Breast Cancer.** *Pharmacoeconomics.* 2023. 41:981-997 10.1007/s40273-023-01277-4	Setting
Madeo, G., Bonetti, G., Maltese, P. E., Tanzi, B., Tezzele, S., Mareso, C., Agostini, F., Generali, D., Donofrio, C. A., Cominetti, M., Fioravanti, A., Riccio, L., Beccari, T., Ceccarini, M. R., Calogero, A. E., Cannarella, R., Stuppia, L., Stuppia, L., Gatta, V., Nughman, M., Cecchin, S., Marceddu, G., Bertelli, M. **Omics sciences and precision medicine in testicular cancer.** *Clin Ter.* 2023. 174:21-28 10.7417/CT.2023.2468	Intervention
Mangat, P. K., Garrett-Mayer, E., Perez, J. K., Schilsky, R. L. **The Targeted Agent and Profiling Utilization Registry Study: A pragmatic clinical trial.** *Clin Trials.* 2023. 20:699-707 10.1177/17407745231182013	Aim
Mangat, P. K., Halabi, S., Bruinooge, S. S., Garrett-Mayer, E., Alva, A., Janeway, K. A., Stella, P. J., Voest, E., Yost, K. J., Perlmutter, J., Pinto, N., Kim, E. S., Schilsky, R. L. **Rationale and Design of the Targeted Agent and Profiling Utilization Registry (TAPUR) Study.** *JCO Precis Oncol.* 2018. 2018:#pages# 10.1200/PO.18.00122	Aim
Mansani, F. P., Soares, L. R., Freitas Junior, R. **Impact of the genomic signature of 70-genes for breast cancer in the public system and in supplementary health care in a country of medium socioeconomic development.** *Breast.* 2024. 76:103752 10.1016/j.breast.2024.103752	Setting
Marchetti, M. A., Coit, D. G., Dusza, S. W., Yu, A., McLean, L., Hu, Y., Nanda, J. K., Matsoukas, K., Mancebo, S. E., Bartlett, E. K. **Performance of Gene Expression Profile Tests for Prognosis in Patients With Localized Cutaneous Melanoma: A Systematic Review and Meta-analysis.** *JAMA Dermatol.* 2020. 156:953-962 10.1001/jamadermatol.2020.1731	Outcomes
Martin, J. C. **Genetic Biomarkers: Implications of Increased Understanding and Identification in Lung Cancer Management.** *Clin J Oncol Nurs.* 2020. 24:648-656 10.1188/20.CJON.648-656	Intervention
Masarwy, R., Shilo, S., Carmel Neiderman, N. N., Kampel, L., Horowitz, G., Muhanna, N., Mansour, J. **The Prognostic Value and Clinical Utility of the 40-Gene Expression Profile (40-GEP) Test in Cutaneous Squamous Cell Carcinoma: Systematic Review and Meta-Analysis.** *Cancers (Basel).* 2023. 15:25 10.3390/cancers15092456	Comparator

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Matsuyama, T., Kandimalla, R., Ishikawa, T., Takahashi, N., Yamada, Y., Yasuno, M., Kinugasa, Y., Hansen, T. F., Fakih, M., Uetake, H., Gyorffy, B., Goel, A. **A novel mesenchymal-associated transcriptomic signature for risk-stratification and therapeutic response prediction in colorectal cancer.** *Int J Cancer.* 2020. 147:3250-3261 10.1002/ijc.33129	Study Design
Mayer, M., Selig, K., Tuttelmann, F., Dinkel, A., Gschwend, J. E., Herkommer, K. **Interest in, willingness-to-pay for and willingness-to-recommend genetic testing for prostate cancer among affected men after radical prostatectomy.** *Fam Cancer.* 2019. 18:221-230 10.1007/s10689-018-0101-7	Study Design
Mayhew, G. M., Uronis, J. M., Hayes, D. N., Zevallos, J. P. **Mesenchymal gene expression subtyping analysis for early-stage human papillomavirus-negative head and neck squamous cell carcinoma reveals prognostic and predictive applications.** *Front Oncol.* 2022. 12:954037 10.3389/fonc.2022.954037	Study Design
McSorley, L. M., Tharmabala, M., Al Rahbi, F., Keane, F., Evoy, D., Geraghty, J. G., Rothwell, J., McCartan, D. P., Greally, M., O'Connor, M., O'Mahony, D., Keane, M., Kennedy, M. J., O'Reilly, S., Millen, S. J., Crown, J. P., Kelly, C. M., Prichard, R. S., Quinn, C. M., Walshe, J. M. **Real-World Analysis of the Clinical and Economic Impact of the 21-Gene Recurrence Score (RS) in Invasive Lobular Early-Stage Breast Carcinoma in Ireland.** *Curr Oncol.* 2024. 31:1302-1310 10.3390/curroncol31030098	Setting
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Merseburger, A. S., Waldron, N., Ribal, M. J., Heidenreich, A., Perner, S., Fizazi, K., Sternberg, C. N., Mateo, J., Wirth, M. P., Castro, E., Olmos, D., Petrylak, D. P., Chowdhury, S. **Genomic Testing in Patients with Metastatic Castration-resistant Prostate Cancer: A Pragmatic Guide for Clinicians.** *Eur Urol.* 2021. 79:519-529 10.1016/j.eururo.2020.12.039	Intervention
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Mizuno, T., Yoshida, T., Sunami, K., Koyama, T., Okita, N., Kubo, T., Sudo, K., Shimoi, T., Ueno, H., Saito, E., Katanoda, K., Shibata, T., Yonemori, K., Okusaka, T., Boku, N., Ohe, Y., Hiroshima, Y., Ueno, M., Kuboki, Y., Doi, T., Nakamura, K., Kohno, T., Yatabe, Y., Yamamoto, N. **Study protocol for NCCH1908 (UPFRONT-trial): a prospective clinical trial to evaluate the feasibility and utility of comprehensive genomic profiling prior to the initial systemic treatment in advanced solid tumour patients.** *Jpn J Clin Oncol.* 2021. 51:1757-1760 10.1093/jjco/hyab159	Intervention
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Mooi, J. K., Wirapati, P., Asher, R., Lee, C. K., Savas, P., Price, T. J., Townsend, A., Hardingham, J., Buchanan, D., Williams, D., Tejpar, S., Mariadason, J. M., Tebbutt, N. C. **The prognostic impact of consensus molecular subtypes (CMS) and its predictive effects for bevacizumab benefit in metastatic colorectal cancer: molecular analysis of the AGITG MAX clinical trial.** *Ann Oncol.* 2018. 29:2240-2246 10.1093/annonc/mdy410	Study Design
Morgan, A. J., Giannoudis, A., Palmieri, C. **The genomic landscape of breast cancer brain metastases: a systematic review.** *Lancet Oncol.* 2021. 22:e7-e17 10.1016/S1470-2045(20)30556-8	Intervention
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Pennarun, N., Chiu, J. Y., Chang, H. C., Huang, S. L., Cheng, S. H. **Cost-Effectiveness Analysis from a Societal Perspective of Recurrence Index for Distant Recurrence (RecurIndex) in Women with Hormone Receptor-Positive and HER2-Negative Early-Stage Breast Cancer.** *Cancer Manag Res.* 2022. 14:761-773 10.2147/CMAR.S339549	Setting
Pennell, N. A., Mutebi, A., Zhou, Z. Y., Ricculli, M. L., Tang, W., Wang, H., Guerin, A., Arnhart, T., Dalal, A., Sasane, M., Wu, K. Y., Culver, K. W., Otterson, G. A. **Economic Impact of Next-Generation Sequencing Versus Single-Gene Testing to Detect Genomic Alterations in Metastatic Non-Small-Cell Lung Cancer Using a Decision Analytic Model.** *JCO Precis Oncol.* 2019. 3:1-9 10.1200/PO.18.00356	Intervention
Peters, A. L., Hall, P. S., Jordan, L. B., Soh, F. Y., Hannington, L., Makaranka, S., Urquhart, G., Vallet, M., Cartwright, D., Marashi, H., Elsberger, B. **Enhancing clinical decision support with genomic tools in breast cancer: A Scottish perspective.** *Breast.* 2024. 75:103728 10.1016/j.breast.2024.103728	Study Design
Piccart M, van 't Veer LJ, Poncet C, et al. **70-gene signature as an aid for treatment decisions in early breast cancer: updated results of the phase 3 randomised MINDACT trial with an exploratory analysis by age.** *Lancet Oncol.* 2021;22(4):476-488. doi: 10.1016/S1470-2045(21)00007-3	Outcomes
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Proudman, D., DeVito, N. C., Belinson, S., Allo, M. A., Morris, E. D., Signorovitch, J., Patel, A. K. **Comprehensive genomic profiling in advanced/metastatic colorectal cancer: number needed to test and budget impact of expanded first line use.** *J Med Econ.* 2022. 25:817-825 10.1080/13696998.2022.2080463	Intervention
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Qadir, F., Lalli, A., Dar, H. H., Hwang, S., Aldehlawi, H., Ma, H., Dai, H., Waseem, A., Teh, M. T. **Clinical correlation of opposing molecular signatures in head and neck squamous cell carcinoma.** *BMC Cancer.* 2019. 19:830 10.1186/s12885-019-6059-5	Aim
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Ronen, O., Oichman, M. **National differences in cost analysis of Afirma Genomic sequencing classifier.** *Clin Endocrinol (Oxf).* 2021. 94:717-724 10.1111/cen.14400	Intervention
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Schanne, D. H., Koch, A., Elicin, O., Giger, R., Medova, M., Zimmer, Y., Aebersold, D. M. **Prognostic and Predictive Biomarkers in Head and Neck Squamous Cell Carcinoma Treated with Radiotherapy-A Systematic Review.** *Biomedicines.* 2022. 10:19 10.3390/biomedicines10123288	Aim
Sestak, I., Martin, M., Dubsky, P., Kronenwett, R., Rojo, F., Cuzick, J., Filipits, M., Ruiz, A., Gradishar, W., Soliman, H., Schwartzberg, L., Buus, R., Hlauschek, D., Rodriguez-Lescure, A., Gnant, M. **Prediction of chemotherapy benefit by EndoPredict in patients with breast cancer who received adjuvant endocrine therapy plus chemotherapy or endocrine therapy alone.** *Breast Cancer Res Treat.* 2019. 176:377-386 10.1007/s10549-019-05226-8	Comparator
Sestak I, Buus R, Cuzick J, et al. **Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor-Positive Breast Cancer: A Secondary Analysis of a Randomized Clinical Trial**. *JAMA Oncol.* 2018;4(4):545-553. doi: 10.1001/jamaoncol.2017.5524.	Outcomes
Shaw, V. R., Amos, C. I., Cheng, C. **Predicting Chemotherapy Benefit across Different Races in Early-Stage Breast Cancer Patients Using the Oncotype DX Score.** *Cancers (Basel).* 2023. 15:16 10.3390/cancers15123217	Comparator

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Signorovitch, J., Zhou, Z., Ryan, J., Anhorn, R., Chawla, A. **Budget impact analysis of comprehensive genomic profiling in patients with advanced non-small cell lung cancer.** *J Med Econ.* 2019. 22:140-150 10.1080/13696998.2018.1549056	Intervention
Soliman, H., Flake, D. D., 2nd, Magliocco, A., Robson, M., Schwartzberg, L., Sharma, P., Brown, K., Wehnelt, S., Kronenwett, R., Gutin, A., Lancaster, J., Cuzick, J., Gradishar, W. **Predicting Expected Absolute Chemotherapy Treatment Benefit in Women With Early-Stage Breast Cancer Using EndoPredict, an Integrated 12-Gene Clinicomolecular Assay.** *JCO Precis Oncol.* 2019. 3:#pages# 10.1200/PO.18.00361	Study Design
Sood A, Kishan AU, Evans CP, et al. **The Impact of Positron Emission Tomography Imaging and Tumor Molecular Profiling on Risk Stratification, Treatment Choice, and Oncological Outcomes of Patients with Primary or Relapsed Prostate Cancer: An International Collaborative Review of the Existing Literature.** *Eur Urol Oncol.* 2024;7(1):27-43. doi: 10.1016/j.euo.2023.06.002.	Outcomes
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Spratt, D. E., Liu, V. Y. T., Michalski, J., Davicioni, E., Berlin, A., Simko, J. P., Efstathiou, J. A., Tran, P. T., Sandler, H. M., Hall, W. A., Thompson, D. J. S., Parliament, M. B., Dayes, I. S., Correa, R. J. M., Robertson, J. M., Gore, E. M., Doncals, D. E., Vigneault, E., Souhami, L., Karrison, T. G., Feng, F. Y. **Genomic Classifier Performance in Intermediate-Risk Prostate Cancer: Results From NRG Oncology/RTOG 0126 Randomized Phase 3 Trial.** *Int J Radiat Oncol Biol Phys.* 2023. 117:370-377 10.1016/j.ijrobp.2023.04.010	Study Design
Stemmer, S. M., Steiner, M., Rizel, S., Ben-Baruch, N., Uziely, B., Jakubowski, D. M., Baron, J., Shak, S., Soussan-Gutman, L., Bareket-Samish, A., Fried, G., Rosengarten, O., Itay, A., Nisenbaum, B., Katz, D., Leviov, M., Tokar, M., Liebermann, N., Geffen, D. B. **Ten-year clinical outcomes in N0 ER+ breast cancer patients with Recurrence Score-guided therapy.** *NPJ Breast Cancer.* 2019. 5:41 10.1038/s41523-019-0137-3	Study Design
Stemmer, S. M., Steiner, M., Rizel, S., Soussan-Gutman, L., Ben-Baruch, N., Bareket-Samish, A., Geffen, D. B., Nisenbaum, B., Isaacs, K., Fried, G., Rosengarten, O., Uziely, B., Svedman, C., McCullough, D., Maddala, T., Klang, S. H., Zidan, J., Ryvo, L., Kaufman, B., Evron, E., Karminsky, N., Goldberg, H., Shak, S., Liebermann, N. **Clinical outcomes in patients with node-negative breast cancer treated based on the recurrence score results: evidence from a large prospectively designed registry.** *NPJ Breast Cancer.* 2017. 3:33 10.1038/s41523-017-0034-6	Study Design
Svoboda, M., Lohajova Behulova, R., Slamka, T., Sebest, L., Repiska, V. **Comprehensive Genomic Profiling in Predictive Testing of Cancer.** *Physiol Res.* 2023. 72:S267-S275 10.33549/physiolres.935154	Intervention
Tan, T. Z., Rouanne, M., Tan, K. T., Huang, R. Y., Thiery, J. P. **Molecular Subtypes of Urothelial Bladder Cancer: Results from a Meta-cohort Analysis of 2411 Tumors.** *Eur Urol.* 2019. 75:423-432 10.1016/j.eururo.2018.08.027	Study Design

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Tsimberidou, A. M., Hong, D. S., Ye, Y., Cartwright, C., Wheler, J. J., Falchook, G. S., Naing, A., Fu, S., Piha-Paul, S., Janku, F., Meric-Bernstam, F., Hwu, P., Kee, B., Kies, M. S., Broaddus, R., Mendelsohn, J., Hess, K. R., Kurzrock, R. **Initiative for Molecular Profiling and Advanced Cancer Therapy (IMPACT): An MD Anderson Precision Medicine Study.** *JCO Precis Oncol.* 2017. 2017:#pages# 10.1200/PO.17.00002	Intervention
Tward, J. D., Lenz, L., Gutin, A., Clegg, W., Kasten, C. R., Finch, R., Cohen, T., Michalski, J., Kishan, A. U. **Using the Cell-Cycle Risk Score to Predict the Benefit of Androgen-Deprivation Therapy Added to Radiation Therapy in Patients With Newly Diagnosed Prostate Cancer.** *JCO Precis Oncol.* 2024. 8:e2300722 10.1200/PO.23.00722	Study Design
Tyson, M. D., Abouassaly, R., Durant, A., Smith, A. B., Seemann, K., Shoskes, D. A. **Budgetary Impact of Including the Urinary Genomic Marker Cxbladder Detect in the Evaluation of Microhematuria Patients.** *Urol Pract.* 2024. 11:54-60 10.1097/UPJ.0000000000000489	Population
Unal, C., Ozmen, T., Ordu, C., Uras, C., Kara, H., Gokmen, E., Ozdogan, M., Demircan, O., Pilanci, K. N., Duymaz, T., Ozmen, V. **Assessment High-Risk Breast Cancer in Older Patients: A Comparative Analysis of PREDICT Scores and TAILORx Risk Categorization.** *Eur J Breast Health.* 2023. 19:325-330 10.4274/ejbh.galenos.2023.2023-8-5	Aim
Uppal, N., Collins, R., James, B. **Thyroid nodules: Global, economic, and personal burdens.** *Front Endocrinol (Lausanne).* 2023. 14:1113977 10.3389/fendo.2023.1113977	Study Design
Vano, Y. A., Elaidi, R., Bennamoun, M., Chevreau, C., Borchiellini, D., Pannier, D., Maillet, D., Gross-Goupil, M., Tournigand, C., Laguerre, B., Barthelemy, P., Coquan, E., Gravis, G., Houede, N., Cancel, M., Huillard, O., Beuzeboc, P., Fournier, L., Mejean, A., Cathelineau, X., Doumerc, N., Paparel, P., Bernhard, J. C., de la Taille, A., Bensalah, K., Tricard, T., Waeckel, T., Pignot, G., Braychenko, E., Caruso, S., Sun, C. M., Verkarre, V., Lacroix, G., Moreira, M., Meylan, M., Bougouin, A., Phan, L., Thibault-Carpentier, C., Zucman-Rossi, J., Fridman, W. H., Sautes-Fridman, C., Oudard, S. **Nivolumab, nivolumab-ipilimumab, and VEGFR-tyrosine kinase inhibitors as first-line treatment for metastatic clear-cell renal cell carcinoma (BIONIKK): a biomarker-driven, open-label, non-comparative, randomised, phase 2 trial.** *Lancet Oncol.* 2022. 23:612-624 10.1016/S1470-2045(22)00128-0	Comparator
Varga, Z., Sinn, P., Seidman, A. D. **Summary of head-to-head comparisons of patient risk classifications by the 21-gene Recurrence Score(R) (RS) assay and other genomic assays for early breast cancer.** *Int J Cancer.* 2019. 145:882-893 10.1002/ijc.32139	Study Design

Reference	Exclusion Criteria
Villarreal-Garza, C., Ferrigno, A. S., De la Garza-Ramos, C., Barragan-Carrillo, R., Lambertini, M., Azim, H. A., Jr. **Clinical utility of genomic signatures in young breast cancer patients: a systematic review.** *NPJ Breast Cancer.* 2020. 6:46 10.1038/s41523-020-00188-3	Comparator
Vince, R. A., Jr., Jiang, R., Qi, J., Tosoian, J. J., Takele, R., Feng, F. Y., Linsell, S., Johnson, A., Shetty, S., Hurley, P., Miller, D. C., George, A., Ghani, K., Sun, F., Seymore, M., Dess, R. T., Jackson, W. C., Schipper, M., Spratt, D. E., Morgan, T. M. **Impact of Decipher Biopsy testing on clinical outcomes in localized prostate cancer in a prospective statewide collaborative.** *Prostate Cancer Prostatic Dis.* 2022. 25:677-683 10.1038/s41391-021-00428-y	Study Design
Visser, W. C. H., de Jong, H., Melchers, W. J. G., Mulders, P. F. A., Schalken, J. A. **Commercialized Blood-, Urinary- and Tissue-Based Biomarker Tests for Prostate Cancer Diagnosis and Prognosis.** *Cancers (Basel).* 2020. 12:16 10.3390/cancers12123790	Intervention
Vuong, H. G., Nguyen, T. P. X., Hassell, L. A., Jung, C. K. **Diagnostic performances of the Afirma Gene Sequencing Classifier in comparison with the Gene Expression Classifier: A meta-analysis.** *Cancer Cytopathol.* 2021. 129:182-189 10.1002/cncy.22332	Outcomes
Waks, A. G., Ogayo, E. R., Pare, L., Marin-Aguilera, M., Braso-Maristany, F., Galvan, P., Castillo, O., Martinez-Saez, O., Vivancos, A., Villagrasa, P., Villacampa, G., Tarantino, P., Desai, N., Guerriero, J., Metzger, O., Tung, N. M., Krop, I. E., Parker, J. S., Perou, C. M., Prat, A., Winer, E. P., Tolaney, S. M., Mittendorf, E. A. **Assessment of the HER2DX Assay in Patients With ERBB2-Positive Breast Cancer Treated With Neoadjuvant Paclitaxel, Trastuzumab, and Pertuzumab.** *JAMA Oncol.* 2023. 9:835-840 10.1001/jamaoncol.2023.0181	Study Design
Wallerstedt SM, Nilsson Ek A, Olofsson Bagge R, Kovacs A, Strandell A, Linderholm B. **Personalised medicine and the decision to withhold chemotherapy in early breast cancer with intermediate risk of recurrence - a systematic review and meta-analysis.** *Eur J Clin Pharmacol.* 2020;76(9):1199-1211. doi: 10.1007/s00228-020-02914-z.	Outcomes
Wang, K., Li, Y., Wang, J., Chen, R., Li, J. **A novel 12-gene signature as independent prognostic model in stage IA and IB lung squamous cell carcinoma patients.** *Clin Transl Oncol.* 2021. 23:2368-2381 10.1007/s12094-021-02638-1	Study Design
Weymann, D., Pollard, S., Chan, B., Titmuss, E., Bohm, A., Laskin, J., Jones, S. J. M., Pleasance, E., Nelson, J., Fok, A., Lim, H., Karsan, A., Renouf, D. J., Schrader, K. A., Sun, S., Yip, S., Schaeffer, D. F., Marra, M. A., Regier, D. A. **Clinical and cost outcomes following genomics-informed treatment for advanced cancers.** *Cancer Med.* 2021. 10:5131-5140 10.1002/cam4.4076	Intervention
Williams, A. D., McGreevy, C. M., Tchou, J. C., De La Cruz, L. M. **Utility of Oncotype DX in Male Breast Cancer Patients and Impact on Chemotherapy Administration: A Comparative Study with Female Patients.** *Ann Surg Oncol.* 2020. 27:3605-3611 10.1245/s10434-020-08473-y	Comparator
Wong, K. M., Ding, K., Li, S., Bradbury, P., Tsao, M. S., Der, S. D., Shepherd, F. A., Chung, C., Ng, R., Seymour, L., Leighl, N. B. **A Cost-Effectiveness Analysis of Using the JBR.10-Based 15-Gene Expression Signature to Guide Adjuvant Chemotherapy in Early Stage Non-Small-Cell Lung Cancer.** *Clin Lung Cancer.* 2017. 18:e41-e47 10.1016/j.cllc.2016.06.009	Intervention

Reference	Exclusion Criteria
Yabroff, K. R., Sylvia Shi, K., Zhao, J., Freedman, A. N., Zheng, Z., Nogueira, L., Han, X., Klabunde, C. N., de Moor, J. S. **Importance of Patient Health Insurance Coverage and Out-of-Pocket Costs for Genomic Testing in Oncologists' Treatment Decisions.** *JCO Oncol Pract*. 2024. 20:429-437 10.1200/OP.23.00153	Study Design
Yang, B., Fu, L., Xu, S., Xiao, J., Li, Z., Liu, Y. **A nomogram based on a gene signature for predicting the prognosis of patients with head and neck squamous cell carcinoma.** *Int J Biol Markers.* 2019. 34:309-317 10.1177/1724600819865745	Study Design
Yordanova, M., Hassan, S. **The Role of the 21-Gene Recurrence Score((R)) Assay in Hormone Receptor-Positive, Node-Positive Breast Cancer: The Canadian Experience.** *Curr Oncol.* 2022. 29:2008-2020 10.3390/curroncol29030163	Study Design
Yothers, G., Venook, A. P., Oki, E., Niedzwiecki, D., Lin, Y., Crager, M. R., Chao, C., Baehner, F. L., Wolmark, N., Yoshino, T. **Patient-specific meta-analysis of 12-gene colon cancer recurrence score validation studies for recurrence risk assessment after surgery with or without 5FU and oxaliplatin.** *J Gastrointest Oncol.* 2022. 13:126-136 10.21037/jgo-21-620	Aim
Zambelli A, Simoncini E, Giordano M, et al. **Prospective observational study on the impact of the 21-gene assay on treatment decisions and resources optimization in breast cancer patients in Lombardy: The BONDX study.** *Breast.* 2020;52:1-7. doi: 10.1016/j.breast.2020.04.003.	Outcomes

Appendix D. Other Studies in Breast Cancer

Studies Evaluating Utility

EndoPredict

Ettl J, Klein E, Hapfelmeier A, et al. Decision impact and feasibility of different ASCO-recommended biomarkers in early breast cancer: Prospective comparison of molecular marker EndoPredict and protein marker uPA/PAI-1. *PLoS One.* 2017;12(9):e0183917. doi: 10.1371/journal.pone.0183917.

Fallowfield L, Matthews L, May S, Jenkins V, Bloomfield D. Enhancing decision-making about adjuvant chemotherapy in early breast cancer following EndoPredict testing. *Psychooncology.* 2018;27(4):1264-1269. doi: 10.1002/pon.4664.

Mokbel K, Wazir U, Wazir A, Kasem A, Mokbel K. The impact of EndoPredict Clinical Score on chemotherapy recommendations in women with invasive ER(+)/HER2(-) breast cancer stratified as having moderate or poor prognosis by Nottingham Prognostic Index. *Anticancer Res.* 2018;38(8):4747-4752. doi: 10.21873/anticanres.12782.

Thibodeau S, Voutsadakis IA. The Oncotype Dx assay in ER-positive, HER2-negative breast cancer patients: a real life experience from a single cancer center. *Eur J Breast Health.* 2019;15(3):163-170. doi: 10.5152/ejbh.2019.4901.

MammaPrint and BluePrint

Viale G, de Snoo FA, Slaets L, et al. Immunohistochemical versus molecular (BluePrint and MammaPrint) subtyping of breast carcinoma. Outcome results from the EORTC 10041/BIG 3-04 MINDACT trial. *Breast Cancer Res Treat.* 2018;167(1):123-131. doi: 10.1007/s10549-017-4509-9.

Wuerstlein R, Kates R, Gluz O, et al. Strong impact of MammaPrint and BluePrint on treatment decisions in luminal early breast cancer: results of the WSG-PRIMe study. *Breast Cancer Res Treat.* 2019;175(2):389-399. doi: 10.1007/s10549-018-05075-x.

Oncotype Dx

Barni S, Cognetti F, Petrelli F. Is the oncotype DX test useful in elderly breast cancer patients: a subgroup analysis of real-life Italian PONDx study. *Breast Cancer Res Treat.* 2022;191(2):477-480. doi: 10.1007/s10549-021-06464-5.

Berdunov V, Laws E, Cuyun Carter G, et al. The budget impact of utilizing the Oncotype DX Breast Recurrence Score test from a US healthcare payer perspective. *J Med Econ.* 2023;26(1):973-990. doi: 10.1080/13696998.2023.2235943.

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Cognetti F, Masetti R, Fabi A, et al. PONDx: real-life utilization and decision impact of the 21-gene assay on clinical practice in Italy. *NPJ Breast Cancer.* 2021;7(1):47. doi: 10.1038/s41523-021-00246-4.

Curtit E, Vannetzel JM, Darmon JC, et al. Results of PONDx, a prospective multicenter study of the Oncotype DX((R)) breast cancer assay: real-life utilization and decision impact in French clinical practice. *Breast.* 2019;44:39-45. doi: 10.1016/j.breast.2018.12.015.

Dannehl D, Engler T, Volmer LL, et al. Recurrence Score result impacts treatment decisions in hormone receptor-positive, HER2-negative patients with early breast cancer in a real-world setting-results of the IRMA trial. *Cancers (Basel).* 2022;14(21). doi: 10.3390/cancers14215365.

Dieci MV, Guarneri V, Giarratano T, et al. First prospective multicenter Italian study on the impact of the 21-gene recurrence score in adjuvant clinical decisions for patients with ER positive/HER2 negative breast cancer. *Oncologist.* 2018;23(3):297-305. doi: 10.1634/theoncologist.2017-0322.

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Eichler C, Fromme J, Thangarajah F, et al. Gene-expression Profiling - A Decision Impact Analysis: Decision Dependency on Oncotype DX(R) as a Function of Oncological Work Experience in 117 Cases. *Anticancer Res.* 2019;39(1):297-303. doi: 10.21873/anticanres.13111.

Hassan S, Younan R, Patocskai E, et al. Impact of the 21-gene recurrence score assay on treatment decisions and cost in patients with node-positive breast cancer: a multicenter study in Quebec. *Oncologist.* 2022;27(10):822-831. doi: 10.1093/oncolo/oyac123.

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Torres S, Trudeau M, Gandhi S, et al. Prospective evaluation of the impact of the 21-gene recurrence score assay on adjuvant treatment decisions for women with node-positive breast cancer in Ontario, Canada. *Oncologist.* 2018;23(7):768-775. doi: 10.1634/theoncologist.2017-0346.

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Oncotype Dx and MammaPrint

Perez Ramirez S, Del Monte-Millan M, Lopez-Tarruella S, et al. Prospective, multicenter study on the economic and clinical impact of gene-expression assays in early-stage breast cancer from a single region: the PREGECAM registry experience. *Clin Transl Oncol*. 2020;22(5):717-724. doi: 10.1007/s12094-019-02176-x.

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Cost and Cost-Effectiveness Studies

Breast Cancer Index

Sanft T, Berkowitz A, Schroeder B, et al. A prospective decision-impact study incorporating breast cancer index into extended endocrine therapy decision-making. *Breast Cancer Manag*. 2019;8(1):BMT22. doi: 10.2217/bmt-2019-0001.

MammaPrint

Retel VP, Byng D, Linn SC, et al. Cost-effectiveness analysis of the 70-gene signature compared with clinical assessment in breast cancer based on a randomised controlled trial. *Eur J Cancer*. 2020;137:193-203. doi: 10.1016/j.ejca.2020.07.002.

Oncotype Dx

Berdunov V, Laws E, Cuyun Carter G, et al. The budget impact of utilizing the Oncotype DX Breast Recurrence Score test from a US healthcare payer perspective. *J Med Econ*. 2023;26(1):973-990. doi: 10.1080/13696998.2023.2235943.

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Appendix E. Other Studies in Prostate Cancer

Studies Evaluating Utility

Decipher

Gore JL, du Plessis M, Zhang J, et al. Clinical utility of a genomic classifier in men undergoing radical prostatectomy: the PRO-IMPACT trial. *Pract Radiat Oncol.* 2020;10(2):e82-e90. doi: 10.1016/j.prro.2019.09.016.

Marascio J, Spratt DE, Zhang J, et al. Prospective study to define the clinical utility and benefit of Decipher testing in men following prostatectomy. *Prostate Cancer Prostatic Dis.* 2020;23(2):295-302. doi: 10.1038/s41391-019-0185-7.

Genomic Prostate Score (Previously Known as Oncotype Dx)

Canfield S, Kemeter MJ, Hornberger J, Febbo PG. Active surveillance use among a low-risk prostate cancer population in a large US payer system: 17-gene genomic prostate score versus other risk stratification methods. *Rev.* 2017;19(4):203-212. doi: 10.3909/riu0786.

Carbunaru S, Sun Z, McCall C, et al. Impact of genomic testing on urologists' treatment preference in favorable risk prostate cancer: a randomized trial. *Cancer Med.* 2023;12(19):19690-19700. doi: 10.1002/cam4.6615.

Gaffney C, Golan R, Cantu MD, et al. The clinical utility of the Genomic Prostate Score in men with very low to intermediate risk prostate cancer. *J Urol.* 2019;202(1):96-101. doi: 10.1097/JU.0000000000000170.

Lynch JA, Rothney MP, Salup RR, et al. Improving risk stratification among veterans diagnosed with prostate cancer: impact of the 17-gene prostate score assay. *Am J Manag Care.* 2018;24(1 Suppl):S4-S10.

Murphy AB, Abern MR, Liu L, et al. Impact of a genomic test on treatment decision in a predominantly African American population with favorable-risk prostate cancer: a randomized trial. *J Clin Oncol.* 2021;39(15):1660-1670. doi: 10.1200/JCO.20.02997.

Seiden B, Weng S, Sun N, et al. NCCN risk reclassification in black men with low and intermediate risk prostate cancer after genomic testing. *Urology.* 2022;163:81-89. doi: 10.1016/j.urology.2021.08.055.

Decipher, Genomic Prostate Score, and Prolaris

Hu JC, Tosoian JJ, Qi J, et al. Clinical utility of gene expression classifiers in men with newly diagnosed prostate cancer. *JCO Precis Oncol.* 2018;2(2):1-15. doi: 10.1200/po.18.00163.

Cost and Cost-Effectiveness Studies

Genomic Prostate Score (Previously Known as Oncotype Dx

Chang EM, Punglia RS, Steinberg ML, Raldow AC. Cost effectiveness of the Oncotype Dx genomic prostate score for guiding treatment decisions in patients with early stage prostate cancer. *Urology.* 2019;126:89-95. doi: 10.1016/j.urology.2018.12.016.

Prolaris

Gustavsen G, Taylor K, Cole D, Gullet L, Lewine N. Health economic impact of a biopsy-based cell cycle gene expression assay in localized prostate cancer. *Fut Oncol.* 2020;16(36):3061-3074. doi: 10.2217/fon-2020-0648.

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