Evaluating the Cost-Effectiveness of Next-Generation Sequencing as a Biomarker Testing Strategy in Oncology and Implications for Policy: A literature review

Charles River Associates

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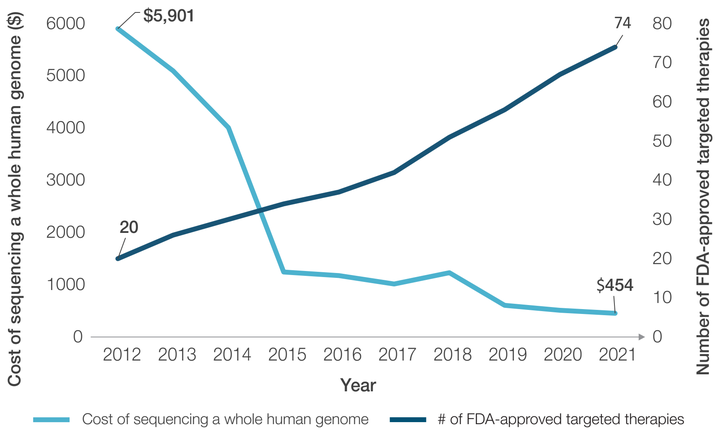
Myriam Mirza[1]* (CRAI, Munich, DE), Lutz Goerke[1] (CRAI, Munich, DE), Tim Wilsdon[2] (CRAI, London, UK)
[1]Charles River Associates (CRA), Munich, DE; [2]Charles River Associated (CRA), London, UK; *mmirza@crai.com

Introduction

Given the growing availability of targeted oncology therapies, genetic biomarker testing is becoming increasingly important. Currently, clinical oncology practices primarily use inexpensive but limited single-gene tests to detect actionable mutations, which can result in long turnaround times and treatment delays in cases where multiple genes need to be tested sequentially. Next-generation sequencing (NGS) is a technology that enables the simultaneous detection of multiple genetic biomarkers. NGS panels applied to oncology vary in size, with targeted panels consisting of 2-200 genes. Despite NGS' growing availability and affordability (figure 1), wide implementation has been limited due to cost concerns and other barriers. Specifically, there are questions regarding the cost-effectiveness of NGS.

Figure 1: Number of FDA-approved targeted therapies versus cost of whole human genome sequencing, 2012-2021, Source: CRA analysis



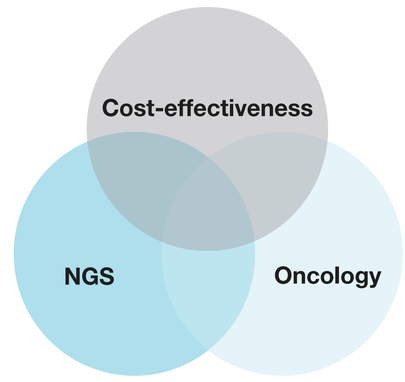
Purpose of this research

The purpose of this research was to assess the current evidence base on the cost-effectiveness of NGS as a biomarker testing strategy in oncology. Based on the evidence evaluated, we also aimed to develop policy recommendations to inform ongoing discussions on the merits of wider NGS adoption in oncology from a cost-effectiveness perspective and the need for targeted policy strategies to support access to NGS now and in the future where relevant.

Methodology

We performed a systematic literature review of existing evidence on the cost-effectiveness of NGS biomarker testing in oncology.

In October 2022, we searched PubMed for recent studies using a combination of search terms, including "NGS", "cost-effectiveness", and "oncology" or similar terms. We performed a supplementary manual search to ensure all relevant studies were captured. All geographies and tumour types were included. Review articles were reserved for validation.



Limits

2017-present, English language, human studies

Abstract inclusion criteria

1. Analysis or comparison of the cost or cost-effectiveness of NGS biomarker testing in oncology
2. Comparative analysis of biomarker testing strategies (comparing the cost or cost-effectiveness of NGS to either no testing, single-gene testing, or another NGS testing strategy)

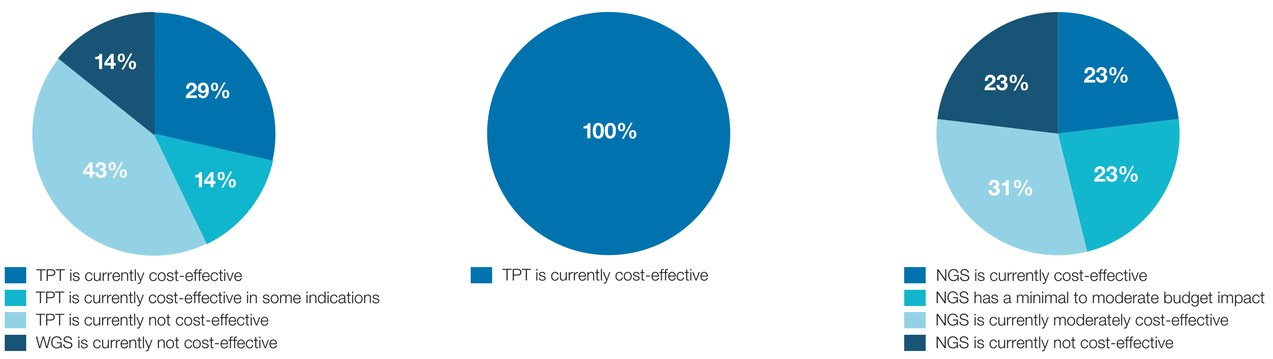
Validation

1. **Validation with reviews and industry reports**
   Review articles, position papers, and industry reports from both the systematic search and additional hand-searches were included with grey literature to validate the findings from the targeted literature review.
2. **Payer/policymaker research**
   We conducted five blinded, 60-minute payer/policymaker interviews across the US, UK, Germany, Spain, and Poland to validate our findings and inform policy recommendations.

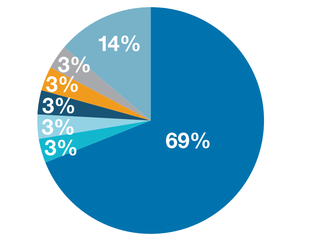
Results

Summary of Literature Search Results

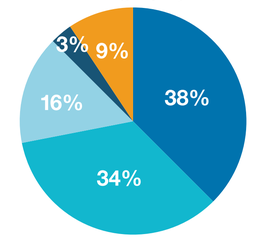
Analysis of the studies revealed cost-analysis to be assessed using three different methodologies:



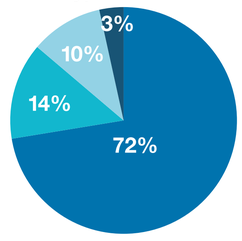
Indications studied



Geography



Type of NGS



NGS Taxonomy

Single gene testing (SGT) 1 gene	Targeted Panel Testing (TPT) 2-200 genes	Comprehensive Genomic Profiling (CGP) 200-1000 genes	Whole Exome Sequencing (WES) 1k-30k genes	Whole Genome Sequencing (WGS) 30k+ genes

Comparison of direct testing costs (n=7)

These studies only include the cost of the test and consumables in their cost comparison, allowing for a simple but incomplete assessment of costs. They assume a given number of tests is performed per patient and assess the most inexpensive way to reach a diagnosis. These analyses provide a quick impression of testing costs but do not capture several important factors contributing to the overall cost-effectiveness of a testing strategy.

Comparison of holistic testing costs (n=9)

These papers expand on the direct testing cost approach by including other parameters such as turnaround time, rebiopsy costs, hospital resource utilization, and additional patient visits. Similar to direct testing cost comparisons, cost-effectiveness is determined by identifying the most affordable testing strategy when testing an average population for a given number of genes.

Comparison of long-term patient outcomes and costs associated with treatment and diagnosis (n=13)

In contrast to the previous two analysis methodologies, these studies evaluate the long-term costs and benefits of testing strategies, including the costs of both genetic testing and the treatment as well as long-term patient benefits. The results are often reported as the cost per life years (LY) or quality-adjusted life years (QALY) gained, and are typically compared against a predefined threshold to determine whether a testing strategy is considered cost-effective.

Discussion

15 out of 29 papers concluded NGS was cost-effective today, with four studies demonstrating moderate cost-effectiveness and another three considering the budget impact of NGS to be minimal to moderate. Only 7 studies found NGS not to be cost-effective. A variety of factors influence the cost-effectiveness of NGS biomarker testing.

The analysis methodology is a key factor influencing the cost-effectiveness of NGS biomarker testing

Comparison of direct testing costs

These analyses provide a rough estimate of comparative testing costs and can be consistently conducted across a variety of scenarios, providing comparable data. However, they are limited in their ability to capture patient benefits and the full costs of each testing strategy. For example hospital staff time and patient outcomes are not considered in these analyses. Thus, while they provide a simple overview of costs, they do not adequately capture the full economic value of different genetic testing strategies.

Comparison of holistic testing costs

By incorporating broader costs and benefits, these holistic testing cost analyses present a more complete picture of the economic value of genetic testing strategies. For example, these analyses often account for personnel-related costs, rebiopsy needs, and turnaround time, which impact overall healthcare expenditure and patient care.

These 9 studies provide strong evidence that NGS testing can reduce overall costs. However, they do not incorporate long-term patient benefits in their analysis.

Comparison of long-term patient outcomes and costs associated with treatment and diagnosis

By assessing QALYs and LYs, these studies capture the full long-term patient benefits and cost impacts of genetic testing. Mixed cost-effectiveness outcomes for NGS demonstrate several key challenges when performing a comprehensive cost-effectiveness analysis, the most important of which is the separation of the costs and benefits of the testing strategy vs the therapies genetic testing may provide access to. Given the proportionately high cost of targeted therapies, a combined cost-effectiveness measure does not effectively assess the cost-effectiveness of the testing approach.

Other factors influencing the cost-effectiveness of NGS biomarker testing factors

Type of NGS technology evaluated

TPT is currently the most cost-effective NGS technology, with sufficient capacity to test all relevant genes while being less expensive vs CGP or WGS

Number of genes being tested

NGS is cost-effective when 4+ genes are tested – while NGS is generally more costly than single-gene tests, it provides savings when multiple genes require testing

Prevalence of actionable mutations

NGS is more cost-effective in cancers with multiple targetable mutations (e.g., NSCLC) and in populations without one or two highly prevalent mutations

NGS-testing infrastructure

Robust testing infrastructure reduces testing costs through economies of scale and can reduce turnaround time and hospital staff requirements

Time horizon

The decreasing cost of NGS and the rising number of targeted therapies suggest NGS will become increasingly cost-effective within 3-5 years

Policy recommendations

A forward-looking approach to ensuring equitable reimbursement and access is required

- → Targeted panel testing should be fully reimbursed in 1L or 2L today, depending on indication and mutation prevalence
- → Frameworks to ensure future expansion of NGS reimbursement and access need to be put in place now

Invest in expanding NGS-supporting infrastructure today

- → Testing infrastructure should be developed and supported/ encouraged by policy frameworks such as long-term plans and commitments to genetic testing and detailed guidance on how to maximize the potential of genetic testing. A strong underlying testing infrastructure with certified laboratories is required to effectively apply NGS testing. Furthermore, hospital cost-savings and lower resource requirements can offset high investment costs.

Consider a holistic cost for NGS and ideally include an assessment of benefits

- → Both direct and indirect costs as well as patient benefits should be considered when assessing the value of NGS testing
- → The assessment of the testing method should include only the costs and benefits of the test, not those associated with treatment

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Funding: This research was funded by Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945). The views expressed in this work are those of the author(s) and do not necessarily reflect those of the funder. **Publication:** This research has been submitted for publication in a peer-reviewed journal.