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 result in long turnaround times and healthcare 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’s growing availability and applicability (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. 2022-11-24, Search: FDA

Purpose of this research

The purpose of the 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 when relevant.

Results

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

- Comparison of direct testing costs (n=17)
  - These studies only include the costs of the test and consumables in their cost comparisons, 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 limited insight into holistic testing cost analyses present a more complete picture of the economic value of genetic testing strategy. For example, these analyses often account for personnel-related costs, reagent needs, and turnaround time, which impact overall healthcare expenditure and patient care. These 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 holistic testing costs (n=4)
  - These papers expand on the direct testing cost approach by including other parameters such as turnaround time, reagent 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 for each oncology population, allowing for a given number of genes.

- Comparison of long-term patient outcomes and costs associated with treatment and diagnosis (n=13)
  - These papers expand on the direct testing cost approach by including other parameters such as turnaround time, reagent 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 for each oncology population, allowing for a given number of genes.

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. Factors influencing the cost-effectiveness of NGS biomarker testing include:

- Type of NGS technology evaluated
  - TPP is currently the most commonly used technology, with sufficient capacity to test all relevant genes with low testing expense or CGP or WGS.

- Number of genes being tested
  - NGS is generally more cost-effective than single-gene tests, if it provides savings when multiple genes require testing.

- Prevalence of actionable mutations
  - NGS is more cost-effective in cancers with actionable 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 testing cost of NGS and the time horizon of targeted treatments suggest NGS will become increasingly cost-effective in the future.

Consider a holistic cost for NGS and ideally include an assessment of benefits. Consider both direct and indirect costs as well as patient benefits should be considered when assessing the value of NGS.

Policy recommendations

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

- Targeted panel testing should be fully reimbursed by 1%, or 2%, 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. To encourage long-term planning and commitment to genetic testing, we recommend a framework for how to maximize the potential of genetic testing. A strong underlining testing infrastructure with collaborative and ethical guidelines required to effectively apply NGS. Furthermore, hospital cost savings and lower resource requirements can offset high investment costs.

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” in similar terms. We performed a supplementary manual search to ensure all relevant studies were captured. All geographies and tumour types were included. Relevant articles were reserved for validation.

Validation

1. Validation with reviews and industry reports

Review articles, position papers, and industry reports from both the academic and policy-making field were collected (see Table 1, Figure 1). These were validated against the studies identified through systematic and hand searches were included with grey literature to validate our evidence on the cost-effectiveness of NGS.

2. Paper/polymerase research

We conducted five blinded, 60-minute paper/polymerase interviews across the US, Germany, Spain, and Poland to validate our findings and inform policy recommendations.