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From the Past to the Present: Insurer Coverage Frameworks for Next-Generation Tumor Sequencing

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ABSTRACT

Next-generation sequencing promises major advancements in precision medicine but faces considerable challenges with insurance coverage. These challenges are especially important to address in oncology in which next-generation tumor sequencing (NGTS) holds a particular promise, guiding the use of life-saving or life-prolonging therapies. Payers' coverage decision making on NGTS is challenging because this revolutionary technology pushes the very boundaries of the underlying framework used in coverage decisions. Some experts have called for the adaptation of the coverage framework to make it better equipped for assessing NGTS. Medicare's recent decision to cover NGTS makes this topic particularly urgent to examine. In this article, we discussed the previously proposed approaches for adaptation of the NGTS coverage framework, highlighted their innovations, and outlined remaining gaps in their ability to assess the features of NGTS. We then compared the three approaches with Medicare's national coverage determination for NGTS and discussed its implications for US private payers as well as for other technologies and clinical areas. We focused on US payers because analyses of coverage approaches and policies in the large and complex US health care system may inform similar efforts in other countries. We concluded that further adaptation of the coverage framework will facilitate a better suited assessment of NGTS and future genomics innovations.

Keywords: insurance coverage, next-generation sequencing, precision medicine, precision oncology, reimbursement, tumor sequencing.

Introduction

Precision medicine—the use of genomics to guide health care decisions—is permeating many areas of health care [1]. The advent of massively parallel next-generation sequencing to simultaneously identify large numbers of genetic mutations promises even more significant advancements of precision medicine [2,3]. Nevertheless, this revolutionary technology has been faced with challenges in insurance coverage [4–7]. Although next-generation sequencing is increasingly used in clinical practice [8–10] and may be reimbursed by US payers [11], the lack of explicit insurance coverage from payers causes payment uncertainty and variable access [12–14], and thus should be understood and addressed.

One of the challenges of insurance coverage for next-generation sequencing is that it pushes the very boundaries of the underlined framework used by insurers in coverage decisions [15–17]. For example, to receive insurance coverage, a medical technology must be determined "medically necessary" and not "experimental/investigational." Next-generation sequencing blurs the boundaries between these two concepts, making coverage decisions difficult [16–18]. Hence, a number of experts have called for adaptation of coverage framework for next-generation sequencing [6,16,17,19].

In oncology, with more than 8,200,000 annual cancer deaths worldwide and more than 609,000 annual US cancer deaths [20,21], next-generation sequencing holds a particular promise that interrogating multiple genes in one's tumor (or next-generation tumor sequencing [NGTS]) will lead to identification of genetic targets for life-saving or life-prolonging treatments and optimization of an overall therapeutic strategy. Although a growing number of US cancer centers offer NGTS in clinical settings, public and many private payers have not been formally covering it—a position congruent with that of some experts who consider clinical adoption of NGTS premature [20,21]. The recent announcement by the Centers for Medicare & Medicaid Services (CMS) of a new national coverage policy for NGTS in advanced solid cancers [22] made the topic of NGTS coverage even more controversial and urgent, as evidenced by immediate debate [23–26] and 315 public comments on the previous draft policy of CMS [27].

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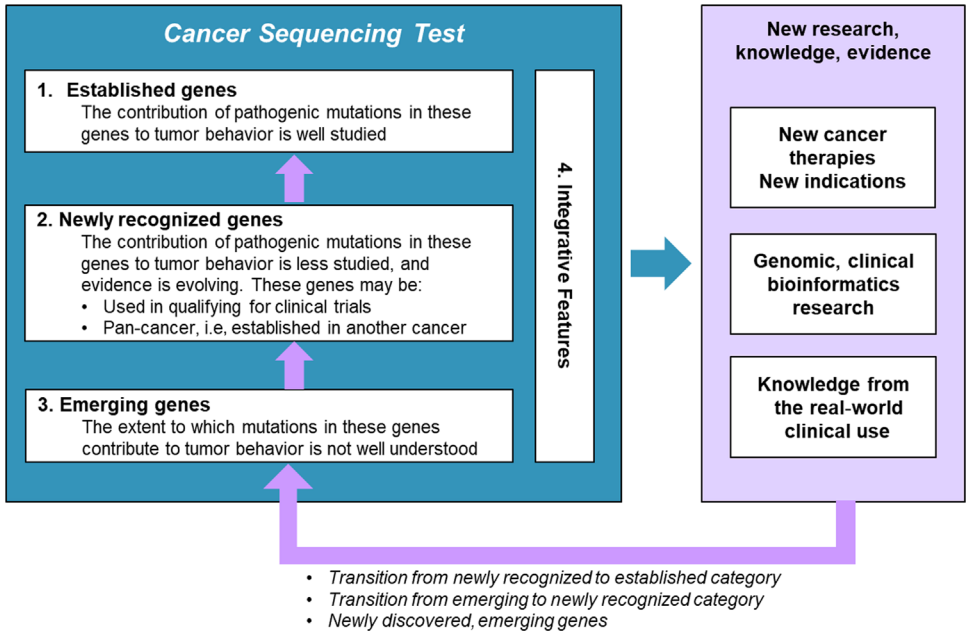

Fig. 1 – Inherent evolutionary nature of cancer sequencing. *Source*: **Authors' analysis.**

Our objective is to describe the previous proposals to adapt the insurance coverage framework for NGTS and discuss the new CMS coverage policy in the context of these proposals. We reviewed literature to identify the adaptation approaches relevant to coverage for NGTS and assessed these approaches on the basis of a specific illustrative proposal for each. We then assessed the CMS policy against the previously proposed adaptation approaches and identified areas of alignment and misalignment, as well as opportunities for further development of the coverage framework. We focused on US payers because analyses of insurance coverage approaches and policies in the large and complex US health care system may inform similar efforts in other countries.

Importantly, we did not advocate for or against clinical adoption or insurance coverage of NGTS. Instead, we aimed to highlight the challenges of evaluating it for insurance coverage and to discuss potential opportunities for addressing these challenges.

NGTS Explained

NGTS refers to simultaneously interrogating multiple genes in one's tumor using next-generation sequencing technology. Knowing tumor genetic mutations can inform the understanding of one's cancer (e.g., prognosis) and guide selection of therapy either targeting an alteration (targeted therapy) or mobilizing one's immune system to fight cancer (immunotherapy). In the past, single-gene tests were used to identify relevant mutations one at a time, often requiring numerous tests, multiple invasive biopsies, prolonged time, and significant cost [28,29]. NGTS produces the needed information in one test, potentially resolving these issues, and possibly offering other benefits not feasible in the single-gene test era. These benefits result from profiling not only established (well-studied) genes, but also newly recognized (less studied) and emerging (not well-understood) genes concurrently in one test (Fig. 1). Table 1 presents the unique features of NGTS, compared with single-gene testing, and we describe several key aspects herein.

By including all three categories of genes (established, newly recognized, and emerging), NGTS can provide information that supports both clinical and research purposes, such as qualifying patients for a clinical trial of targeted therapy or immunotherapy and collecting data for further genetic research. Testing the same set of genes across different cancers (pan-cancer testing) allows identification of targeted therapy effective in one cancer and using it for a patient with a different cancer, but with the same mutation. This use of therapies across cancers based on a common cancer genetic mutation may potentially extend survival for patients with advanced cancer with no other therapeutic options.

Another unique feature of NGTS is its integrative utility—cumulative analysis of interrogated genes—informing anticipation of tumor behavior, such as resistance to therapy, as well as the calculation of a tumor mutational burden that may predict response to immunotherapy, the newest class of cancer drugs [30]. Tumors, especially in advanced stages, often mutate, developing resistance to therapy and requiring repeat sequencing to identify genetic targets for other therapies. This serial sequencing pathway allows tailoring one's treatment strategy to tumor development and creates a full picture of temporal tumor behavior.

Rationale for Adapting the Insurance Coverage Framework for Evaluating NGTS

US payers typically cover a medical technology if they determine it medically necessary and not experimental/investigational. The concepts of "medically necessary" and "experimental/investigational" are the cornerstone of insurance coverage framework and are typically considered mutually exclusive (Table 2). Accordingly, payers do not cover technologies that are under research. Payers have been applying this framework to coverage decisions on conventional genetic tests, which typically generate a single result (e.g., a cancer recurrence score, or whether a tumor is HER2/neu-positive or -negative). For genetic tests that guide treatment decisions, payers have based determination of medical necessity on how well the test predicts benefit from the related