Journal of Cancer Policy 9 (2016) 14–17

Contents lists available at ScienceDirect

Journal of Cancer Policy

journal homepage: www.elsevier.com/locate/jcpo

Reviews

The cost-effectiveness and value of gynecological cancer biomarker screening in financially vulnerable female populations

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ARTICLE INFO

Article history:
Received 2 April 2016
Accepted 23 July 2016
Available online 2 August 2016

Keywords:
Gynecological cancer
Biomarker
Cancer prevention
Genetic testing
Value-based healthcare

ABSTRACT

Biomarkers are currently being developed and used to assess a female patient's risk of gynecological cancer such as ovarian cancer, which is one of the most lethal forms of gynecological cancer. Certain biomarkers can be measured in blood samples of female patients, and the results can be used to analyze, predict, and manage those patients' cancer outcomes. Financially vulnerable populations of women who could benefit from biomarker screening that either assesses cancer risk or detects early stage cancer face relatively higher mortality rates as a result of delayed and/or inefficient cancer screening. Delayed and/or inefficient cancer screening is largely due to their inability to afford such biomarker screenings. Given the financial hardship faced by this population of women, it is important to understand exactly what biomarkers are and the value they currently or could provide in clinical settings. It is also important to understand how biomarker screening contributes directly to our nation's goal of achieving a value-based healthcare system that emphasizes disease prevention and personalized medicine. This article explores the "value-added" portfolio of biomarker screening, and provides a written analysis of current literature. This article then describes how biomarkers can be used to achieve affordable gynecological cancer prevention and/or early-stage cancer detection and management in financially vulnerable populations of women.

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1. Introduction

Biomarkers are measurable characteristics of a biological component or state, and are typically present in bio-specimens as cellular proteins or genetic molecules. Biomarkers can help assess risk factors accompanying a particular disease, such as gynecological cancer. Biomarker screening however, has been deemed a relatively expensive endeavor for those who either lack health insurance or are underinsured, and has yet to be widely accepted for coverage by insurance payers such Medicare and Medicaid.

Overall, insurance coverage for biomarker screening is a challenge in most cases and coverage is particularly dependent upon the following: the screening technique and type and the level and type of insurance coverage. For instance, insurance claims are often denied when a biomarker screening is determined as "purely investigational" versus "medically necessary." Together, these hurdles place financially vulnerable populations of women at higher risk of mortality. As our nation's healthcare industry begins to adopt preventative and cost-effective healthcare models, it is important to address this current gap in our healthcare system. This gap merely

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http://dx.doi.org/10.1016/j.jcpo.2016.07.001
2213-5383/

illustrates our nation's reluctance to embrace innovative forms of preventative gynecological cancer care.

Our nation's healthcare system has recently made great strides toward emphasizing and building an affordable, preventative healthcare system through overhauling healthcare policy and practice. By virtue of this national effort, health-oriented government agencies such as the National Institutes of Health (NIH) have created and funded various research programs that serve to bridge basic research discovery and clinical care [19]. A clinical care example is where investigators take blood samples from female patients at risk of various forms of gynecological cancer, such as ovarian cancer, to analyze, predict, and manage health outcomes. This effort is accompanied however by wide-spread inquiries on the cost-efficacy and market-influence associated with biomarker screenings.

The article discusses the importance of providing affordable cancer biomarker screening to financially vulnerable populations of women at risk of or faced with forms of gynecological cancer. This article also provides a cross-sectional overview of both current and promising biomarkers and biomarker screening techniques that are used and tested in clinical settings, and reviews published literature evaluating the cost-effectiveness of certain cancer biomarker screenings in comparison to late-stage treatment. The overall aim of this article is to provide a written analysis of current literature, retrieved using PubMedCentral.gov and various scholarly web sources, describing the use of biomarkers to achieve affordable gynecological cancer prevention and/or early-stage cancer management in financially vulnerable populations of women.

2. Overcoming financial barriers to preventative biomarker screening

Lack of proper insurance coverage combined with what may be expensive biomarker screening results in significant out-of-pocket medical expenses for patients considering preventive health measures via molecular screening. Research shows that financially vulnerable populations of women, being those who are either underinsured or uninsured, face relatively higher mortality rates as a result of delayed and/or inefficient cancer screening [8,22,23]. Also, fully insured women are also at risk of acquiring significant financial burdens when their insurance provides only partial to no coverage for such screenings. For example, it is often the case that insurance payers deny coverage for biomarker screenings, such as genetic testing, claiming that such testing is purely investigational and not medically necessary. The combined lack of both biomarker screening affordability and insurance coverage exacerbates the financial vulnerability and mortality risk in a large portion of women in the United States. Therefore, it is important to understand and address the affordability factor associated with innovative and preventative biomarker screenings that have the potential to provide a higher quality of life in women at risk of various forms of gynecological cancer.

In general, higher quality of life that is achieved through the implementation of innovative forms of technology is often accompanied by a hefty price tag that may be unaffordable to patients, insurance companies, and charitable foundations alike. In order to emphasize the societal benefits associated with personalized and preventative biomarker screening, it is imperative that its associated costs also be addressed. Academics specializing in this area have discussed the potential costs and impacts of such (expensive) innovation to both society and the marketplace. To illustrate, Barbara J. Culliton, contributing editor of *Health Affairs* journal, conducted a recent interview on the issue with Thomas G. Roberts, hedge fund manager for Noonday Global Management, attending oncologist at Massachusetts General Hospital, visiting scientist at the Massachusetts Institute of Technology, and instructor of medicine at Harvard Medical School [5]. In the interview, Culliton and Roberts discuss the fact that revolutionary biomarker innovation would result in an expensive product cost to society, which only exacerbates the ongoing issue of patients being unable to afford their out-of-pocket insurance costs. The costs of biomarker innovation would be an obstacle for other payers as well, such as cancer-related charities and Medicare, as they may also be unable to properly assist patients with these costs. Roberts also provided his perspective on whether innovative diagnostic tests, such as cost-efficient, personalized biomarker screenings that match drugs to patients based on tumor types, could also result in less profitable niche markets for pharmaceutical companies.

Despite the aforementioned hurdles, Roberts emphasizes that it is better to move forward with and invest in innovative cancer patient-centered care rather than worry about its high prices; "It would be smarter for us to actually concentrate on using these drugs for those patients who are most likely to receive a benefit and to spend money learning how to use the agents in a more rational way," Roberts quotes. Additional field experts have built upon Roberts' idea. For example, Susan Delaney from the Coriell Institute for Medical Research in Camden, NJ, along with several co-authors provide an expert review on the matter in their article discussing the idea of using genomic biomarker testing as a clinical decision-making guide, versus as clear diagnostic indicators, that can be used in combination with other patient-specific, non-genetic information to provide preventive or targeted care that is more specialized [6]. This form of approach is a step toward ensuring that preventative cancer biomarker screenings are implemented in rational, patient-centered ways that balance the scales between upfront costs, and the costs of late-stage treatment and/or mortality.

3. Novel biomarkers screening techniques currently used in clinical settings

There are currently thousands of cancer biomarker candidates, however the FDA has approved only a handful of biomarkers for clinical use, such as cancer antigen 125 (CA125) and human epididymis protein 4 (HE4). Cancer antigen 125 (CA125) is currently used to detect various forms of gynecological cancer. CA125 is well-studied among many scientists for early-stage cancer detection [12,20]. For example, blood serum analysis shows that a significant percentage (nearly 80%) of epithelial ovarian cancers, a lethal form of gynecological cancer, express quantifiable amounts of CA125 [1].

Limitations to diagnosing early stage epithelial ovarian cancer using CA125 biomarker screening have also been identified; sole reliance on CA125 to predict epithelial ovarian cancer alone in clinical settings. For instance, some studies show that roughly 20% of ovarian cancers express little to no CA125, while many other forms of gynecological malignancies and benign tumors demonstrate elevated blood serum CA125 levels [15]. One way to achieve keener specificity for CA125 is to observe trend measures of CA125 over time in annual screenings of stratified populations of women (cancer-specific) under and over the age of 50 [9]. It is important to consider however is that elevated levels of CA125 alone indicate the presence of myriad gynecological malignancies and benign tumors, therefore this limitation is also advantageous.

HE4 is a protein encoded by the *WFDC2* gene and has an equivalent sensitivity for detecting cancer in women with pelvic masses or epithelial ovarian cancer, and also elevated CA125 [7,14]. Cellular transcription of the *WFDC2* gene is heightened in ovarian malignancies when compared to normal tissues, and HE4 is subsequently found in circulating epithelial ovarian cancer patient serum [7,11]. Studies have demonstrated HE4's ability to yield greater sensitivity at set specificities than CA125 alone [13].