Budget Impact Analysis of Sentinel® Prostate Cancer Test versus Current Diagnostic Strategy for Men with Suspicion of Prostate Cancer in the United States

Yang Meng[1], Martin Tenniswood[2], David Elsea[1], Jonathan Kowalski[1]

1. Lumanity Inc, Bethesda, United Sates of America, 2. miR Scientific LLC, Research and Development, New York, United Sates of America.

Introduction

Prostate cancer (PCa) is the second most common cancer and the second leading cause of cancer death in US men.[1]

In the US, the National Comprehensive Cancer Network (NCCN) recommends men aged 45–75 years have a serum prostate-specific antigen (PSA) test as part of their annual wellness visit. Men aged 45–75 years with a PSA >3 ng/mL are regarded as having a suspicion of PCa and should be recommended for further evaluation, including a core needle biopsy (CNB).[2] In current standards of care (SOC) in the US, CNB is most commonly guided by transrectal ultrasound (TRUS), but it may also be targeted by multi-parametric magnetic resonance imaging (mpMRI).

The serum PSA test has low accuracy, with sensitivity of 32% and specificity of 87% with a 3 ng/mL cutoff[3], resulting high false-positive (FP) and false-negative (FN) rates. Thus, men without PCa but who have elevated PSA levels are subjected to unnecessary CNBs (and mpMRIs), which are both costly and associated with complications.

The miR Sentinel® Prostate Cancer Test (Sentinel Test) is a non-invasive urine test designed to detect and risk-classify PCa with predictive accuracy over 90%.[4] The Sentinel Test classifies patients into one of four categories: no molecular evidence of prostate cancer (NMEPC), Low-Risk PCa (nominally corresponding to Grade Group 1 [GG1]), Intermediate-Risk PCa (nominally corresponding to Grade Group 2 [GG2]), and High-Risk PCa (nominally corresponding to [GG3–5]).

The objective of this analysis is to develop a budget impact model to estimate the clinical and economic impacts of using the Sentinel Test for men over 45 with suspicion of PCa as compared with the current SOC from a US commercial payer perspective.

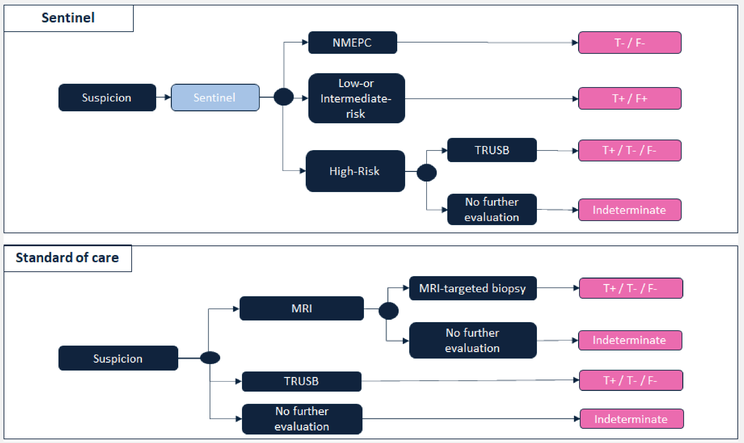
Methods

Population

The model assesses the clinical and budget impacts for introducing the Sentinel Test to a 1-million-member commercial administrative services only (ASO) plan in the US. The eligible population for the Sentinel Test is men aged 45 years and older who have no prior diagnosis of PCa and no prior biopsy for PCa but who also have annual PSA tests and elevated serum PSA levels (>3 ng/mL).

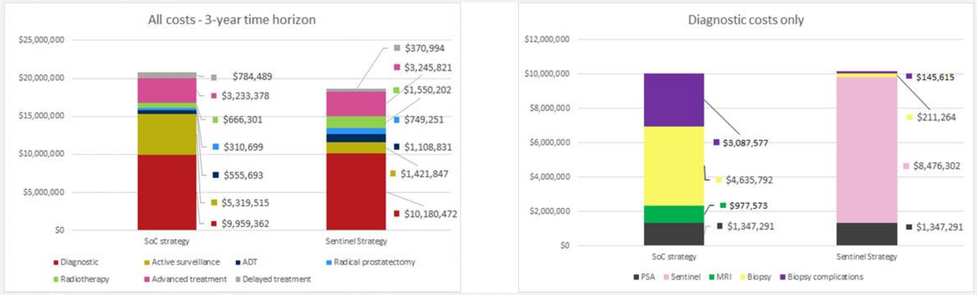
We also performed a de novo US claims analysis using Optum data to inform model inputs.[5]

Figure 1: Intervention and comparator strategies



Key: F, false; NMEPC, no molecular evidence of prostate cancer; MRI, magnetic resonance imaging; T, true; TRUSB, transrectal ultrasound biopsy.

Figure 3: Budget impact outcomes



Key: ADT, androgen deprivation therapy; MRI, magnetic resonance imaging; PSA, prostate-specific antigen.

Intervention and comparator strategies

Figure 1 presents the intervention and comparator strategies.

For the intervention Sentinel Test strategy, the model assumes that the Sentinel Test is performed for all men with PSA >3 ng/mL. All men with a Sentinel Test classification of High-Risk should be referred for a TRUS-guided CNB.

The modeled comparator SOC strategy was informed by the NCCN guidelines (version 1.2022).[2] It is assumed that a proportion of men with elevated PSA levels will receive CNB and that a proportion may have a diagnostic mpMRI and subsequently undergo a TRUS-guided and/or mpMRI-targeted CNB.

Model structure

The model follows the eligible population over 3 years and estimates the clinical and economic outcomes of the Sentinel and SOC strategies. The clinical and economic impacts of the Sentinel Test are the differences between these two strategies.

True PCa status is assumed to be known in the model so that, together with test accuracy inputs, the diagnostic outcomes, i.e., true-positive (TP), FP, true-negative (TN), FN and indeterminate, could be established. Five underlying disease status groups are modeled: no PCa, low-risk PCa (GG1), intermediate-risk PCa (GG2), high-risk PCa (GG3–5, excluding advanced/metastatic PCa), and advanced PCa. The follow-on management and treatment options depend on the final diagnostic outcomes of each strategy.

Clinical inputs

Sentinel accuracy is implemented as a set of probabilities of having test results as NMEPC, Low- or Intermediate-Risk PCa (GG1–2), or High-Risk PCa (GG3–5) conditional on the true disease status.[6]

True disease status of the eligible population is based on the Optum analysis, literature[7] and accuracy of the PSA test with a 3 ng/mL cutoff.

For the SOC strategy, it is assumed that 41% of men with elevated PSA levels receive biopsy.[8, 9] Based on Optum analysis and assumption, it is assumed that 25% of biopsies are mpMRI-targeted, 57.7% are TRUS-guided, and the rest (17.3%) are other types of biopsies. It is further assumed that an additional 10% of mpMRIs are performed without a subsequent CNB.

For both SOC and Sentinel strategies, the probability of complication related to biopsy is 21.1%.[5] The model also assumes that the average number of biopsies performed is 1.09[5], which is used to adjust the accuracy and costs for biopsies and the rate and costs for biopsy-related complications.

The distribution of active surveillance (AS) and treatment options for men with TP results are based on the literature and depend on the PCa risk category.[7] For men with FN results, the time to delayed diagnosis and treatments is 1.9 years[5], and it is assumed that 2.8% of intermediate- and high-risk PCa cases with a FN diagnosis will progress to advanced PCa when delayed treatments are received.[10]

Resource use and cost inputs

The Sentinel Test price is set at $1,200 per test.

Men under AS in the SOC strategy are assumed to receive an annual PSA test and a biopsy every 2 years.[11] Men under AS in the Sentinel strategy are assumed to receive an annual Sentinel test. It was also assumed that 10% of patients in AS would initiate active treatments due to worsening of PCa each year.

All costs were sourced as or inflation-adjusted to 2020 US dollars.

Results

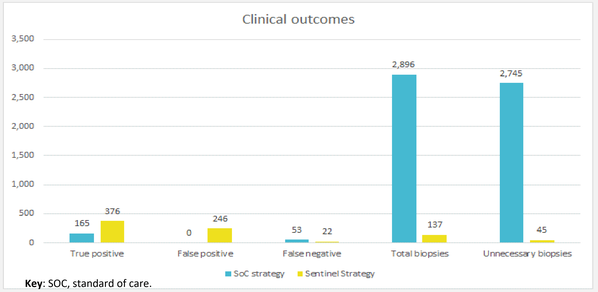
For a 1-million-member commercial ASO plan, 50,763 men over 45 are estimated to be biopsy-naïve and would receive an annual PSA test based on the current SOC. Using the sensitivity and specificity of PSA tests and the true disease status distribution, the model estimated 7,064 men with PSA levels (>3 ng/mL) are eligible for the Sentinel Test.

Following the 7,064 eligible men, the model estimates that the Sentinel strategy reduces unnecessary biopsies by 98% (from 2,745 in the SOC strategy to 45 in the Sentinel strategy), reduces missed PCa cases, i.e., FNs, by 59% (53 to 22), and increases correct diagnoses, i.e., TPs, by 128% (165 to 376) compared with the SOC strategy. The Sentinel strategy is estimated to produce 246 FP results; however, this only represents 3.5% of all Sentinel Tests performed. Clinical and budget outcomes are presented in Figure 2 and Figure 3, respectively.

The model estimates that the Sentinel strategy yields an overall budget savings of $2.3 million and a per-member-per-month savings of $0.06. The $8.5 million cost of the Sentinel Tests is estimated to be offset by savings in MRI and biopsy costs ($5.4 million), costs of biopsy-related complications ($2.9 million), and costs in delayed treatment ($0.4 million).

The economically justified price (EJP) for Sentinel, defined as the breakeven price at which the overall budget impact is zero, is estimated to be $1,478.

Figure 2: Clincial impact outcomes



Key: SOC, standard of care.

Discussion and Conclusions

In conclusion, the Sentinel Test identifies and risk-classifies PCa non-invasively, substantially reduces unnecessary biopsies, provides overall budget savings over a 3-year period, and resolves the uncertainty from suspicious PSA more effectively than the current SOC.

Further, the Sentinel Test can help minimize overtreatment of indolent cancers by accurate characterizations of the biology of the cancer. The Sentinel Test can also help to accurately identify high-risk cancers in select patients for directing to treatment. In sum, the Sentinel Test has great potential to help to improve outcomes for patients and to enhance the efficiency of the health care system.

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Contact information

Contact the author at martin.tenniswood@mirscientific.com for questions or comments

Presented at the 2022 ISPOR conference; May 15-18, 2022; National Harbor, MD, United States