

The Economic Impact of Prostate Cancer Screening and Treatment

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Prostate cancer is a significant public health concern. Because of its high incidence and mortality and a lack of consensus on the recommended frequency of screening and the most appropriate treatments, prostate cancer is also characterized by high costs and uncertainty. As a result, there is perhaps no bigger debate in medicine today as far as whether or not there should be widespread screening for prostate cancer and if and/or how to treat early-detected cases.

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The corresponding economic costs of screening, diagnosis, treatment, and follow-up for prostate cancer are not trivial and are expected to increase with the aging of the population and a larger volume of screening. In 1990, the total annual costs to treat prostate cancer were estimated to range from \$1.72 billion to \$4.75 billion.¹ With the advent of prostate-specific antigen (PSA) screening in the early 1990s, the costs of treating prostate cancer in the United States likely far exceeded this amount, based on trends toward earlier detection and more aggressive treatment. Based on early estimates, the cost of

screening increases prostate cancer expenditures by three-to-ten times.¹ The costs of treating prostate cancer in Sweden have been observed to fall within this range, increasing three-fold between 1991 and 2002 (20 million to 65 million euros).²

The exponential increase in the volume of prostate cancer screening adds to healthcare costs via the cost of the screening test, follow-up biopsies for positive tests, and treatment (or long-term monitoring) for confirmed prostate cancers. For

example, the use of PSA tests increased seven fold, and radical prostatectomies increased six fold between 1991 and 2002 in Sweden.² Radiation therapy increased ten fold from 1997-2002.² In the United States, similar trends were likely. Between 1989 and 2002, there was a 234% increase in radical prostatectomy in the United States.¹ In 2003,

there were 90,328 hospital discharges with the diagnosis of prostate cancer and associated costs of \$673 million.³ While treatment for prostate cancer is expensive, the overuse and/or inappropriate use of diagnostic tests in a manner inconsistent with treatment guidelines significantly inflates costs for disease management.² According to the Medicare Current Beneficiary Survey (2002), nearly two thirds of the 17.6 million Medicare beneficiaries received prostate cancer screening.⁴ If all Medicare beneficiaries or all men older than 50 (34.7 million in 2000) sought screening, annual costs for the PSA screening test for

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one year would approach ~\$2 billion assuming Medicare reimbursement (~\$50 per test).⁵ With costs in the range of a few billion dollars per year (screening, treatment, disease management, monitoring, etc.), costs of a population-based screening program, including disease management, could easily exceed \$20 billion within five-to-seven years.

The biggest controversy in prostate cancer research is in the lack of consensus on the value of prostate cancer screening given the test's performance at diagnosing cancer and the inconsistent demonstration of effectiveness of early intervention at improving patient outcomes, including reductions in mortality. Although the existing evidence of effectiveness has improved in recent years, and cost-effectiveness analyses have been increasingly performed, uncertainty about the benefits of treatments in improving patient outcomes remains. A recent systematic review demonstrated that it was difficult to draw conclusions without uncertainty on the benefits of treatment alternatives due to lack of randomized clinical trials. Newer technologies, in particular, were hardest to evaluate given a lack of evidence of effectiveness and a lack of comparison with standard treatment alternatives.⁶ Although radical prostatectomy and radiation rapidly replaced watchful waiting for early disease detection with the advent of PSA, there was weak and inconsistent evidence regarding any benefits in terms of improved patient outcomes (including mortality) during this period.² One recent study demonstrated lower mortality using radical prostatectomy versus watchful waiting in early-stage disease,⁷ but evidence is otherwise weak or inconsistent from other trials, including those with long follow-up.

The lack of consistent or compelling evidence about early detection of prostate cancer showing an improvement in survivorship has not stopped numerous treatments from being rapidly diffused, including aggressive treatments in relatively young men. This is problematic in that aggressive treatments themselves have consequences. For example, after 18 months of follow-up, patients receiving radical prostatectomy in one study experienced significant erectile dysfunction (59.9%) and urinary incontinence (8.4%).⁸ Other treatment alternatives result in co-morbidities affecting sexual and urinary function. If these patients experience a long survival period, they must face the psychosocial consequences of treatment-related adverse effects that might not have been necessary if their underlying disease was latent or extremely slow in progressing.

Whereas the increase in screening detects cancer early and at a *potentially* curable stage with aggressive treatment, it has also resulted in the overdiagnosis of latent disease and unnecessary biopsies for men with false-negative screening tests.⁹ False positive screening has financial and psychological costs, with about half of men with suspicious screening test results and subsequent negative biopsies reporting worrying "a lot" or "some of the

time" about prostate cancer.¹⁰ For men with confirmed prostate cancer, those choosing either watchful waiting or aggressive intervention for early-stage disease must address the implications of their choices, which can result in anxiety, decreased activity level, decreased quality-of-life, adverse effects of treatment, etc.¹¹

From an economic perspective, the value of a screening test can be determined by estimating the relative costs and benefits, where benefits of screening can be measured in terms of test performance, unnecessary biopsies, and/or formal cost-effectiveness analyses. Studies that evaluate prostate cancer screening focus primarily on the PSA test. One recent study found that complexed PSA (cPSA)^a (threshold 2.2 ng/ml) was a better test than total PSA (tPSA) (2.5 ng/ml), with higher sensitivity and specificity and fewer unnecessary biopsies.¹² A cost-benefit study looking at five screening strategies found that cPSA (3.8 ng/ml) was dominant (more costly and less effective), with a threshold of 3.0 ng/ml identifying a similar number of cancers with fewer biopsies than tPSA (4.0 ng/ml).¹³

Using simulations including Markov modeling that simulate the progression of disease to determine the most efficient PSA screening algorithm, the benefits of prostate screening vary by age and were not recommended above age 70, where the competing risk of mortality outweighs the benefit.^{14,15} In their Markov model, Ross and colleagues conclude that annual PSA screening (4.0 ng/ml threshold) starting at 50 years of age is dominant (i.e., more costly and less effective) by a biennial screening strategy after tests at 40 and 45 years of age.¹⁶ Screening beyond age 70 required more treatments (and significant additional costs) per person-year of life saved.¹⁴ A second computer model supports screening every two years (4.0 ng/ml threshold), which reduces false-positive and overdiagnosis rates sharply, while catching most cases relative to the more traditional annual screening without any age-specific thresholds.¹⁷ Clearly, additional research to determine the best thresholds for PSA measures (tPSA, cPSA, PSA velocity,^b etc.) and to determine the utility of other biomarkers in detecting aggressive prostate cancer is critical. If future screening tests can better distinguish latent disease from aggressive disease and minimize false positives, they offer great potential to lower unnecessary expenditures for prostate cancer.

The utility of prostate cancer screening and treatment will be debated for the foreseeable future, especially with the advent of new treatments and the absence of randomized clinical trials. The most common treatments, radiation and radical prostatectomy, might never be compared in a randomized trial for a variety of reasons. PSA is the only real biomarker available today to detect prostate cancer, and it is imperfect. Based on the current economic evidence, routine prostate cancer screening using PSA and subsequent treatment for early-stage disease do not appear to be cost-effective until improvement in patient outcomes, including

a Complexed PSA is a test measuring the level of PSA that has been complexed or bound with a certain protein (alpha-1-antichymotrypsin) in a patient's blood sample.

b PSA velocity is the rate of change in the PSA level over time.

mortality, have been demonstrated. Methods calculating the expected value of perfect information (EPVI is a measure of the cost of making an incorrect decision due to uncertainty) should also be factored into decisions about prostate cancer screening.¹⁸

Despite its shortcomings, PSA will continue to be used to detect prostate cancer in the absence of a more accurate biomarker. Furthermore, we will continue to treat early-stage

prostate cancer aggressively if a patient prefers this to watchful waiting. However, healthcare administrators might give more scrutiny to screening and treatment programs as costs continue to escalate with the aging of the population. With this increased scrutiny, cost containment might include a prostate cancer screening schedule tailored to individuals based on prognostic factors that are still being identified. **NCMedJ**

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