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Guidelines for Prostate Cancer Screening

Journal of Health Disparities Research and Practice

Volume 1 | Issue 3

Article 6

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2007

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Recommended Citation

Beam, C. A. (2007) "Racial Inequality in the Valuation of Health Outcomes Expressed by the 1992 ACS Guidelines for Prostate Cancer Screening," *Journal of Health Disparities Research and Practice*: Vol. 1: Iss. 3, Article 6.

Available at: <https://digitalscholarship.unlv.edu/jhdrp/vol1/iss3/6>

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Abstract

In 1992, the American Cancer Society (ACS) recommended annual screening for prostate cancer for men 50 and older using PSA. In this article, I introduce a method to use race and age-specific PSA accuracy data to evaluate differences in the valuation of outcomes by race and age that were expressed by the ACS guidelines. Using this new method, it can be concluded that the guidelines implied a 4-fold greater valuation was assigned to screening young white males with prostate cancer than the value that was assigned to young black males with cancer. Future implementation of guidelines for screening and testing should recognize and rectify any social inequities that are expressed via their implementation.

Keywords

African American men; Diagnostic technology; Health policy; Men; White; Prostate – Cancer; Prostate – Cancer – Testing; Prostate cancer; Prostate-specific antigen; PSA; ROC Curve

Cover Page Footnote

Dr. Beam would like to acknowledge the support given by the Department of Family Medicine at the Medical College of Wisconsin during the early stages of this project.



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Abstract

In 1992, the American Cancer Society (ACS) recommended annual screening for prostate cancer for men 50 and older using PSA. In this article, I introduce a method to use race and age-specific PSA accuracy data to evaluate differences in the valuation of outcomes by race and age that were expressed by the ACS guidelines. Using this new method, it can be concluded that the guidelines implied a 4-fold greater valuation was assigned to screening young white males with prostate cancer than the value that was assigned to young black males with cancer. Future implementation of guidelines for screening and testing should recognize and rectify any social inequities that are expressed via their implementation.

Key Words: diagnostic technology, health policy, ROC Curve, PSA, prostate cancer

Introduction

The aphorism ‘actions speak louder than words’ is no less true in Medicine than it is elsewhere. When actions are the result of decision-making, they then express something about the decision-maker. The action of a 17-year-old driver careening 100 mph on a highway expresses a relative valuation on life versus death and of the relative likelihood of these two outcomes in the mind of the decision-maker. In equal parts, the 1992 recommendations of the American Cancer Society¹ for prostate cancer screening beginning at age 50 using Digital Rectal Examination (DRE) and PSA with threshold 4.0 ng/ml expresses something about the relative valuation and likelihood of the outcomes of screening diseased and non-diseased individuals held by implementers of those guidelines.

A rational decision maker uses diagnostic technology in such a way so as to maximize the benefit from the technology while minimizing the cost. Whether or not the ways diagnostic technologies are actually used in medicine comes about from rational decision processes, the perspective of the rational decision-maker can always be relied upon to provide a universally acceptable referent, much as is done in Economics. This reference perspective can, among other things, provide a consistent framework for interpreting observed behavior.

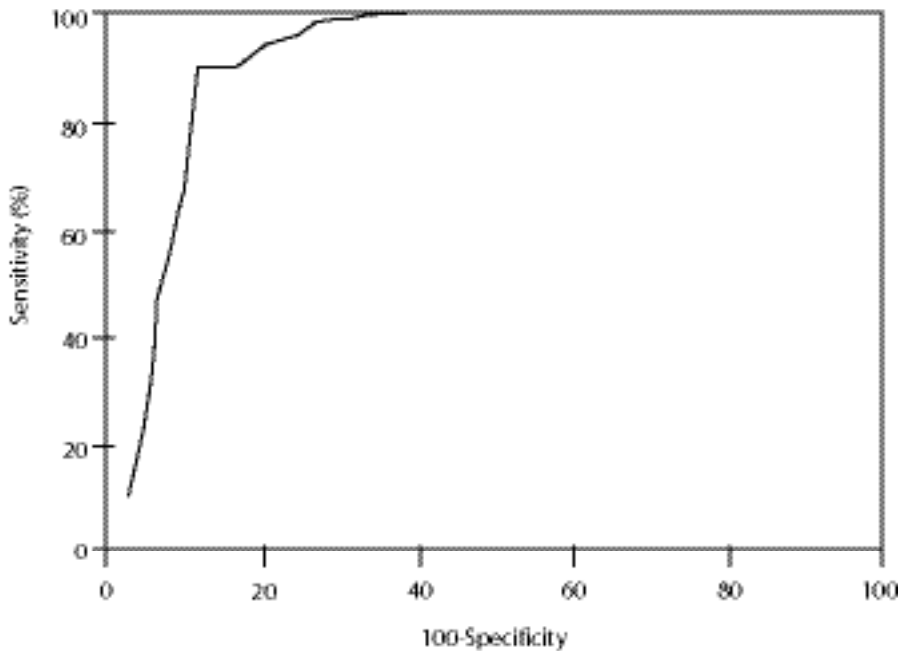
In this paper, I adopt the perspective of the rational decision-maker to derive a measure of the relative valuation of health outcomes that is expressed by the observed use of a diagnostic technology in a clinical population. The method inverts a fundamental result from Clinical Decision Analysis that is used to optimize the use of a diagnostic technology. As an example, I apply this method to then use race and age specific data published about the accuracy of PSA testing to determine the relative valuations that were expressed by 1992 ACS guidelines for the screening of prostate cancer using PSA.¹ The 1992 guidelines were selected solely to provide an example of the method and the insights the method can provide. My paper does not attempt to evaluate guidelines currently used in practice.

Methods

The choices involved in the application of a diagnostic technology in a defined clinical population are expressed in something called the "Receiver Operating Characteristic (ROC) Curve."² The ROC Curve is a graphical display of all of the Sensitivity-False Positive Probability combinations that are possible by the selection of various thresholds. For example, application of the PSA test requires selection of a threshold value to define a positive test result. Recommendations made by the ACS in 1992 were for 4.0 ng/ml¹ and this cutoff provides an estimated Sensitivity and False Positive Probability for white males 70-79 years old of 98.6% and 26.9%, respectively³. Each such threshold selection provides a different True Positive-False Positive probability combination. Selection of other thresholds yields other combinations and the entire set of such combinations can be graphically displayed in the ROC Curve. Figure 1, for example, plots the ROC curve for PSA when applied to white males 70-79 years old. The curve is estimated from data published by Morgan.³

To implement a diagnostic technology, a rational decision-maker determines the threshold value that maximizes benefit and minimizes cost. Fortunately, the solution, well known in the Clinical Decision Analysis literature, is straightforward.⁴ The rational decision maker selects the

FIGURE 1. ROC Curve of PSA for white men 70-79. Each point on the curve represents the sensitivity-false positive probability arising from the selection of a threshold for PSA testing.



threshold at which the slope of the ROC Curve equals the product of the relative probability of non-disease times the relative value of applying the test in the non-diseased versus the diseased populations.^{4,5} In short-hand, this can be expressed as:

Choose the threshold at which,

$$\text{ROC Slope} = (\text{Relative probability of Non-disease})(\text{Relative Value of Non-disease})$$

To anchor these terms, it helps to note that the “Relative Probability of Non-disease” is the odds of not having disease. That is, if “ p ” is the prevalence of disease in the population, then $(\text{Relative Probability of Non-disease}) = (1-p)/p$. Although it is not necessary to restrict the measurement of outcomes to monetary units, it is helpful to think about the term “Relative Value of Non-disease” in terms of costs. Let “ c_{TP} ,” “ c_{FN} ,” “ c_{FP} ” and “ c_{TN} ” represent the “costs” related to True Positives, False Negatives, False Positive and True Negatives (negative cost implies benefit). Then, $\text{Relative Value of Non-disease} = (c_{TN} - c_{FP}) / (c_{TP} - c_{FN})$ ⁴.

The previous relationship can be inverted. If we observe the use of a diagnostic technology, and if we have knowledge of the odds of non-dis-

ease and of the ROC Curve of the technology, we can then infer the relative valuation of outcomes by the rational decision-maker: The Relative Value (non-diseased to diseased) that is expressed by the rational use of a diagnostic technology equals the "Relative Probability of Disease" times the slope of the ROC Curve at the point observed to be used in practice.

Symbolically,

Expressed Relative Value of Non-diseased =

(Relative probability of Disease)(ROC Slope)

where "Relative Probability of Disease" is the odds of disease = $p/(1-p)$.

It is important to point out that computation of this measure requires the computation of the slope of the ROC Curve at the operating point used in practice. Hence, the analyst must have first the ROC Curve of the technology. This can be accomplished by appropriately designed and conducted technology assessment studies. Hopefully, such studies can be sourced from the literature.

Results

Table 1 presents the results of the application of this new method. In 1992, the American Cancer Society¹ recommended annual screening for prostate cancer for men 50 and older using both DRE and PSA. Here, I consider only the implications of the ACS recommendation of PSA-based screening for prostate cancer using the threshold of 4.0 ng/ml. Morgan³ estimated ROC Curves for PSA testing in the detection of prostate cancer for various age groups of white and black men. I then used this data to estimate the slope of each ROC Curve at the ACS-recommended threshold for each age-race specific ROC Curve after assuming that PSA levels are normally distributed. Estimates of age and race specific prevalence were obtained from SEER tables⁶ and were then used to estimate the odds of disease. The relative value of outcomes (no prostate cancer vs. prostate cancer) expressed by the ACS guidelines was then computed using the previous formula. This number is reported as "Relative Value of Non-diseased" in the table. To facilitate interpretation, the reciprocal also appears in the table and is denoted by "Relative Value of Diseased." This value can be interpreted as the value of outcomes in applying the screening test to the population with prostate cancer relative to the value when screening the population without prostate cancer.

Focusing on "Relative Value of Diseased," we can observe that screening young men (40-49) for prostate cancer had greater expressed relative value than screening older men in both racial groups. However, some racial disparities in this pattern do occur. For example, the relative

TABLE 1. Relative values in prostate cancer screening expressed by 1992 ACS guidelines.

Whites			Relative Value	
Age	Slope ^a	Prevalence ^b	Non-Diseased ^c	Diseased ^d
40-49	4.341	9.1	0.000395	2531.645570
50-59	5.453	146.75	0.008016	124.750499
60-69	3.211	713.8	0.023084	43.320049
70-79	1.833	1353.45	0.025149	39.763012
Blacks			Relative Value	
Age	Slope ^a	Prevalence ^b	Non-Diseased ^c	Diseased ^d
40-49	7.654	15.7	0.001202	831.946755
50-59	0.898	273.45	0.002462	406.173842
60-69	0.431	1086.5	0.004734	211.237854
70-79	0.108	1868.1	0.002056	486.381323

^aBased on cutoff of 4.0 ng/ml

^bPer 100,000/year

^cValue of outcomes from screening men without cancer relative to the value from screening men with cancer

^dValue of outcomes from screening men with cancer relative to the value from screening men without cancer

value of screening steadily declines with increasing age for white males. This is consistent with the opinion that the effectiveness of screening for and treatment of prostate cancer declines with advancing age. However, this pattern is not strictly followed for black males. The 1992 ACS guidelines suggested that the relative value of screening is less for black males in the age groups 50-59 and 60-69 than it is for males from the oldest age group (70-79).

Another salient observation from the table is that the relative value of screening young white men is at least 20 times larger than the expressed value of screening white men from any other white age group. On the other hand, the relative values for black males are much more homogeneous. The relative value of screening a young black male is at most 4 times that of screening black males from another age group.

Finally, we can observe that if the value of health outcomes in screening young healthy men were the same for both racial groups, then the guidelines express a four-fold greater valuation for screening young white males (40-49) with prostate cancer than the value assigned to young black males.

Discussion

The value of health outcomes that is expressed by the use of a diagnostic technology is the relative value implied had a rational decision

maker aware of the disease prevalence and operating characteristics of the technology in the clinical population of interest implemented the technology. What better perspective is there to understand the implications of the observed use of diagnostic technology than from the universally-accepted perspective of rationality? Is there a decision-maker not willing to affirm that it is best, when possible, to maximize benefit and minimize cost?

Had the 1992 ACS recommendations been made from a rational perspective, we would conclude that the maker of these recommendations valued outcomes quite differently for white and black men. The monotonicity of declining values for white men seems to be logical since one might anticipate the benefits from screening to decline with age. This coherent pattern does not hold for black males. Is this anomaly acceptable to modern thought in Medicine?

The ACS recommendations also express an astronomically high value for screening young white men compared to young black men. This discrepancy, although probably unintended, nonetheless expresses a substantial inequity. Is this desirable?

The utility of the measure introduced in this paper is that it provides a universally acceptable metric with which individuals having widely varying perspectives can commonly view the implications of the use of diagnostic technology. It is not important whether rational decision making processes were actually followed when the diagnostic technology was implemented. The goal is simply to provide a universal frame-of-reference for measurement, communication and discovery.

Limitations

A limitation of this paper is that it provides only the essential background required to understand and apply this new measure. The reader considering use of this measure should consult the burgeoning literature that has arisen over the past twenty years around ROC Curves in particular and the evaluation of diagnostic technologies in general. Recently, two comprehensive overviews have appeared in book form.^{7,8}

I have focused this analysis on the 1992 ACS guidelines simply in the hope that distance in time will promote objective discussion of this new methodology. Another limitation of the current paper is the focus on PSA screening and not PSA combined with DRE as was considered by the guidelines. However, this limitation points out the need for data to be collected that provides the ROC curve of PSA combined with DRE stratified by race and age. Analysis with contemporary data and contemporary guidelines should of course be conducted. If such findings replicate

the findings made in this paper, then we might seek to fashion health policy for the use of PSA in screening that is specifically directed at lessening expressed racial inequities. How would this be accomplished? The rationalist approach tells us to first establish the value of health outcomes for each age group and consider these as equal for both racial groups. Then, using updated ROC Curves, select PSA testing thresholds that are optimal for each age-race group.

In general, the methodology introduced in this paper introduces a vantage point with which the implications of the use of diagnostic technology can be quantitatively assessed. Hopefully, awareness of the implications of our actions in screening and diagnosis gained through the use of similar analyses will point the direction to improved health care by lessening unintended, yet nonetheless expressed, inequalities.

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Dr, Beam would like to acknowledge the support given by the Department of Family Medicine at the Medical College of Wisconsin during the early stages of this project.

