# Cost-benefit analysis of total, free/total, and complexed prostate-specific antigen for prostate cancer screening

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## Record Status

This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

## Health technology

The use of prostate-specific antigen (PSA) for population-based prostate cancer screening. Five strategies were identified. These were total PSA (tPSA) 4.0 ng/mg, free PSA/tPSA (f/tPSA), and complexed PSA (cPSA) 3.8, 3.4, and 3.0 ng/mg.

## Type of intervention

Screening.

## Economic study type

Cost-utility analysis.

## Study population

The study population comprised men aged between 40 and 75 years who were undergoing prostate biopsy, as suggested by their physician, according to established local practice. Patients were excluded from the study if they had a history of prostate cancer or of a transurethral prostatic resection. They were also excluded if they were taking any medication that could decrease levels of serum PSA, such as estrogen or finasteride, or a course of quinolone antibiotic therapy (minimum 7 days) within 30 days of biopsy. Also excluded were those patients taking any medication or food supplement that could increase serum PSA levels, for example dehydroepiandrosterone or testosterone.

## Setting

The setting was a hospital. The economic study was carried out in the USA.

## Dates to which data relate

The dates for the effectiveness and resource use data were not reported. The price year was 2001 (fiscal year).

## Source of effectiveness data

The effectiveness data were derived from a single study. The utility values were derived from two published studies.

## Link between effectiveness and cost data

The costing was not performed on the same sample of patients as that used in the single effectiveness study.

## Study sample

Power calculations to determine the sample size were not performed. A total sample of 3,757 eligible patients was identified using two merged contemporary databases (UroCor Labs and Bayer Diagnostics), of which a final sample of 2,138 men was used in the effectiveness study. The were 1,519 patients with a mean age of 64.2 (+/- 0.19) years in the

group of those without cancer. The remaining 619 patients, who had a mean age of 66.6 (+/- 0.29) years, were in the group of those with cancer.

## Study design

This appears to have been a retrospective cohort study based on the merger of two contemporary databases. The evidence came from several study centres. Details on the methodology, such as follow-up and assessment, were not reported.

## Analysis of effectiveness

The basis for the analysis of effectiveness (intention to treat or treatment completers only) was not stated. However, all the patients included in the initial study sample were taken into account when estimating the effectiveness. The health outcomes used in the analysis were test characteristics (specificity and sensitivity) and the distribution of Gleason scores for the cases detected by the test strategy. Receiver operating curves (ROC) were also constructed to evaluate the performance of the tests. The authors commented that the age was significantly higher among those who developed cancer. In addition, men with a diagnosis of cancer had significantly higher mean tPSA and cPSA values and lower f/tPSA values.

## Effectiveness results

The specificity and sensitivity values were:

for tPSA greater than 4.0 ng/mL, 16.3% and 92.4%;

for f/tPSA less than 25 ng/mL, 29% and 81.2%;

for cPSA greater than 3.8 ng/mL, 32.6% and 81.1%;

for cPSA greater than 3.6%, 28.2% and 84.3%;

for cPSA greater than 3.4 ng/mL, 22.8% and 88.5%;

for cPSA greater than 3.2 ng/mL, 18.6% and 91.3%; and

for cPSA greater than 3.0 ng/mL, 16.9% and 92.6%.

The Gleason scores were:

for tPSA greater than 4.0 ng/mL, 5 in 5 patients, 6 in 226 patients, 7 in 111 patients, 8 in 25 patients, and 9 in 1 patient (368 total cases);

for f/tPSA less than 25 ng/mL, 5 in 4 patients, 6 in 183 patients, 7 in 89 patients, 8 in 25 patients, and 9 in 1 patient (302 total cases);

for cPSA greater than 3.8 ng/mL, 5 in 5 patients, 6 in 194 patients, 7 in 101 patients, 8 in 25 patients, and 9 in 1 patient (326 total cases);

for cPSA greater than 3.6%, 5 in 5 patients, 6 in 201 patients, 7 in 104 patients, 8 in 25 patients, and 9 in 1 patient (336 total cases);

for cPSA greater than 3.4 ng/mL, 5 in 5 patients, 6 in 216 patients, 7 in 109 patients, 8 in 25 patients, and 9 in 1 patient (356 total cases);

for cPSA greater than 3.2 ng/mL, 5 in 5 patients, 6 in 225 patients, 7 in 112 patients, 8 in 25 patients, and 9 in 1 patient (368 total cases); and

for cPSA greater than 3.0 ng/mL, 5 in 5 patients, 6 in 228 patients, 7 in 112 patients, 8 in 25 patients, and 9 in 1 patient (371 total cases).

The ROC analysis showed that the curves obtained were significantly different. cPSA and tPSA had better performance in minimising false-negatives, while f/tPSA had better performance in minimising false-positives.

### Clinical conclusions
The test characteristic values derived from the effectiveness study were used as inputs in the decision model.

### Modelling
The authors stated that a decision analytic model was constructed to identify the most cost-effective strategy for prostate cancer screening. However, no details on the decision model were reported.

### Measure of benefits used in the economic analysis
The utility values associated with biomarker-defined false-positive and false-negative status were used as benefit measures. These were derived from two published studies, although the details were not reported.

### Direct costs
Discounting was, appropriately, not applied since the time horizon of the study was one year. The unit costs were not reported separately from the quantities of resources used. The health service costs included in the analysis were the screening costs associated with office and staffing, running the various assays, TRUS biopsy, and pathological review. The cost/resource boundary adopted in the analysis of the direct costs was not stated. The costs and resource use were estimated using data derived from published studies and from the clinical chemistry department of the study hospital. All the costs were inflated to the fiscal year (2001).

### Statistical analysis of costs
The costs were treated deterministically.

### Indirect Costs
The authors stated that the indirect costs were included in the analysis. However, it was unclear whether such costs referred to costs not strictly related to the screening procedure or to productivity losses.

### Currency
US dollars ($).

### Sensitivity analysis
Sensitivity analyses were performed on all variables used in the decision model, in order to assess the impact of variations in these variables on the result of the analysis. Threshold analyses were performed to identify the critical values that may change the indications obtained in the base-case analysis.

### Estimated benefits used in the economic analysis
The disutility values used as model inputs in the analysis were 0.99 (range: 0.95 - 1) for false-positives and 0.93 (range: 0.85 - 1) for false-negatives. The benefit (utility) was 0.9908 for cPSA 3.8 ng/mL, 0.9922 for tPSA 4.0 ng/mL, and 0.9923 for cPSA 3.0 ng/mL. The utility values of the remaining strategies were not reported since they were dominated strategies, as shown when the costs and benefits were combined.

## Cost results

The estimated costs were $139.9 for cPSA 3.8 ng/mL, $154.9 for tPSA 4.0 ng/mL, and $164.3 for cPSA 3.0 ng/mL. The costs of the remaining strategies were not reported since they were dominated strategies, as shown when the costs and benefits were combined.

## Synthesis of costs and benefits

An incremental analysis was performed to combine the costs and the benefits of the five screening strategies. The cPSA strategy dominated the remaining strategies, as it was associated with more benefits and less costs. The sensitivity analyses showed that the strategy of tPSA became dominant when the cost of cPSA was greater than $35 (a 75% increase over the rate used in the base-case). It also became dominant when the cost of a prostate biopsy was smaller than $67.3 (60% reduction in comparison with the costs used in the base-case). Variations in the remaining variables used in the decision model did not affect the conclusions of the analysis.

## Authors' conclusions

A complexed prostate-specific antigen (cPSA) test with a threshold of 3.8 ng/mL was the most cost-effective population-based screening for prostate cancer. The sensitivity of the test represented the most critical parameter of the analysis.

## CRD COMMENTARY - Selection of comparators

The rationale for the choice of the comparators was clear. All of the screening strategies selected represented various molecular forms of the same approach (PSA test). You should decide whether they are widely used in your own setting.

## Validity of estimate of measure of effectiveness

The analysis of the effectiveness used information extracted from two merged databases. Overall, there were few details on the methodology used in the effectiveness study. Thus, a comprehensive comment on this part of the study is not possible. The authors defined the study sample, which appears to have been representative of the study population. The method used to select the sample was not stated. It was not possible to evaluate the impact of bias and confounding.

## Validity of estimate of measure of benefit

Utility values, considered to be associated with biomarker-defined false-positive and false-negative status, were used as the benefit measure in the economic analysis. These values were derived from the literature.

## Validity of estimate of costs

It was unclear whether the societal perspective adopted in the study was the most appropriate, given the categories of costs actually included. The unit costs were not reported separately from the quantities of resources. Also, a detailed breakdown of the costs was not given. The price year was reported. Data on the costs and resource use were derived from studies that were published more than 10 years before the present study, but the authors stated that, after the actualisation process, the estimated costs were similar to those observed at their institution. However, the lifetime costs were not calculated as the time horizon of the study was one year.

## Other issues

The authors compared their findings with those from other studies, but did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were performed but the results were not presented, as the authors stated that none of the model input variations performed affected the conclusions of the base-case analysis. Consequently, the external validity of the analysis may be low. The authors commented on some limitations of their analysis. For example, a simple decision model was used rather than more sophisticated models used in other studies. Also, the results may not be generalisable, as the probability values used in the model were derived from specific studies (although the authors were quite confident that their dataset was representative of the general population).

## Implications of the study

The main implication of the study is that cPSA with a threshold of 3.8 ng/mL represented the most effective and less expensive approach for population-based screening for prostate cancer. However, this finding should be interpreted with caution given the limitations of the analysis (reported above), as acknowledged by the authors. Further research should be based on Markov modelling considering the changes of the PSA tests over time.

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## Bibliographic details

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