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Prostate Cancer Screening Using Prostate-Specific Antigen Tests in a High-Risk Population in China: A Cost-Utility Analysis ☆,☆☆

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ABSTRACT

Background: Both National Comprehensive Cancer Network and Chinese guidelines recommend beginning prostate-specific antigen (PSA) screening for men aged 50 years or 45 years with a family history because they were at a higher risk of developing prostate cancer. Several model-based economic evaluations of PSA screening studies have been conducted, but with little evidence from China.

Objective: The aim of this study was to conduct an economic evaluation of the cost-utility of PSA-based prostate cancer screening in Chinese men.

Methods: We developed a decision-tree and Markov model in Excel (Microsoft Corp, Redmond, Washington) to compare 2 strategies that can be used to detect prostate cancer: PSA-based screening followed by a biopsy, and non-PSA screening. We assumed that the patients would repeat screening in subsequent years if their first-year PSA value was higher than 4.0 ng/mL. The model adopted health care system perspective and lifetime horizon. Screening efficacy, cost, utility, and long-term survival of prostate cancer were retrieved from published literature and physician surveys. Both quality-adjusted life year and costs were discounted at an annual rate of 3.5%. Uncertainty was assessed by 1-way and probabilistic sensitivity analyses. Our model also calculated the risk-to-benefit ratio as the ratio of overdiagnosis (biopsy without diagnosed) to prostate cancer-related deaths prevented in different age groups.

Results: The results suggested that PSA-based screening was cost-effective compared with no PSA screening, with an incremental cost-utility ratio of ¥11,381 ($1821/€1480) per quality-adjusted life year. This value was less than the threshold of 1-time gross domestic product per capita in China (ie, ¥70,892 [$11,343/€9216]). Sensitivity analyses confirmed the robustness of the results. The risk-to-benefit ratios of the 50 to 65 years and the 65 to 80 years age groups were 1.3 and 2.8, respectively.

Conclusions: PSA-based prostate cancer screening appears to be cost-effective in some high-risk Chinese men. PSA screening (PSA testing followed by magnetic resonance imaging and biopsy if positive) can be recommended for Chinese men aged 50 to 65 years because this approach had the lowest risk-to-benefit ratio. The approach should be further adapted based on future updated data. (*Curr Ther Res Clin Exp.* 2022; 83:XXX–XXX)

Introduction

Prostate cancer (PCa) is the most frequently diagnosed cancer among men, and the fifth leading cause of cancer death in men.[1] A previous study showed that the incidence and mortality rate of PCa increased with age, and the annual disease burden of PCa increased significantly in China.[2]

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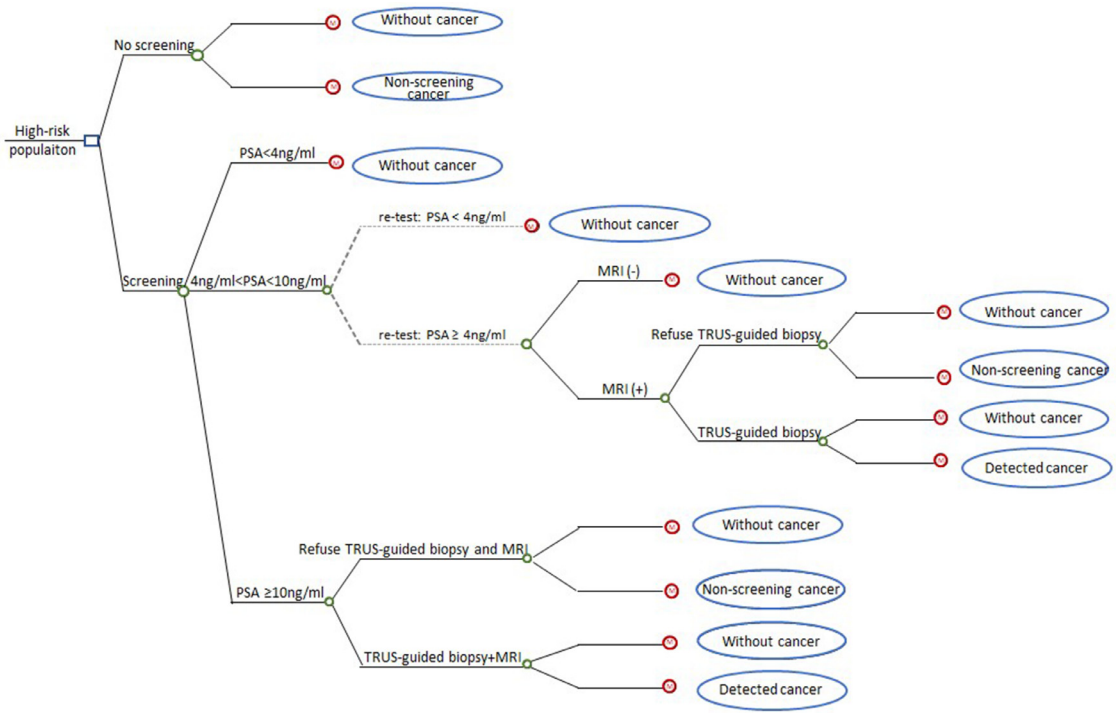

Figure 1. Decision tree model structure

Approximately 70% of PCa diagnosed in China was metastatic.[3,4] This percentage was much higher than in other Asian countries. In Korea, newly diagnosed local advanced and metastatic PCa rates were 22% and 4%, respectively.[5]

Once PCa metastasizes, it becomes much harder to treat with a worse prognosis. The age-standardized 5-year survival rate in Chinese men was 69.2% during 2012 to 2015,[6] whereas the 5-year survival rate for patients with PCa in Korea and the United States was 90.2% and 99.2%, respectively, during the past decade.[7]

The prostate-specific antigen (PSA) blood test followed by magnetic resonance imaging (MRI) and biopsy can be used to detect PCa when asymptomatic and localized within the prostate gland. The PSA test includes radioimmunoassay and chemiluminescence immunoassay. Many clinical guidelines recommend PSA-test-based PCa screening for high-risk populations; that is, men older than age 50 years or men older than age 45 years with a family history.[4,8,9] In China, PSA screening rate is low, resulting in diagnoses of PCa at a later stage. According to the screening results of the 2 observational studies in China, the cancer detection rates were 1.28% and 0.68%, respectively, which is much lower compared with other countries.[10,11]

Several model-based economic evaluations of PSA screening studies have been conducted[5,12–13], but there is less evidence in China. Thus, our study aimed to conduct an economic evaluation of PSA-based screening in high-risk men (ie, aged 50 years or older or aged 45 years with a positive family history) in China. The results of our study can be used to advocate for investment in PCa screening programs to improve the diagnosis rate, the prognosis, and the quality of life of patients with PCa. It can also provide evidence for health care decision makers to develop guidelines and support policy making.

Methods

Model structure

A decision-analytic model was established in Excel (Microsoft Corp, Redmond, Washington) to estimate the cost-utility of PSA-based screening compared with no screening for PCa (Figures 1 and 2). Two different strategies were compared: PSA screening arm and nonscreening arm. In the screening arm, all asymptomatic men could be healthy (no cancer) or not healthy (had a detected cancer via screening). In the nonscreening strategy, nonscreening population could also advance to a healthy state (no cancer), or a state with a nonscreening-detected cancer. In the scenario analysis, as the false-positive screening rate is much higher in the group older than age 65 years, we further divided populations into 2 age groups: 50 to 65 years and 65 to 80 years.[14]

The model was constructed in 2 parts: a decision tree model simulating the PCa diagnosis processes with or without PSA screening, and a Markov model simulating the PCa progression until death. This combined structure was selected because the decision tree model consists of pathways representing different sequences of events over a short time (eg, PSA screening), whereas the Markov model represents a set of possible transitions between different disease states that are suitable for handling the progression of disease over a long period of time (eg, PCa progression).

In the decision tree model (Figure 1), each person underwent a PSA test and was assigned to 1 of 3 different groups based on the levels of the PSA detected ($\leq$4 ng/mL, $>$ 4 and $<$ 10 ng/mL, or $\geq$ 10 ng/mL). Individuals with a PSA value $<$ 4 ng/mL were considered at low risk of developing PCa and thus did not receive the follow-up examinations and repeated screening. MRI was conducted in those individuals with a PSA value $>$ 4 ng/mL and $<$ 10 mg/mL. If the result was positive, a biopsy was then suggested. Some individuals may refuse MRI and biopsy.

We used different Markov models for the screening and nonscreening arms (Figure 2). Five health states (without cancer, screening-detected cancer, nonscreened cancer, non–PCa-specific death, and PCa-specific death) were included in the PSA screening arm, whereas 4 health states (without cancer, nonscreened cancer, non–PCa-specific death, and PCa-specific death) were included in the nonscreening arm. The transition probabilities were estimated based on the survival curve we derived from a previous screening study for the Chinese population.[15] Background mortality for the

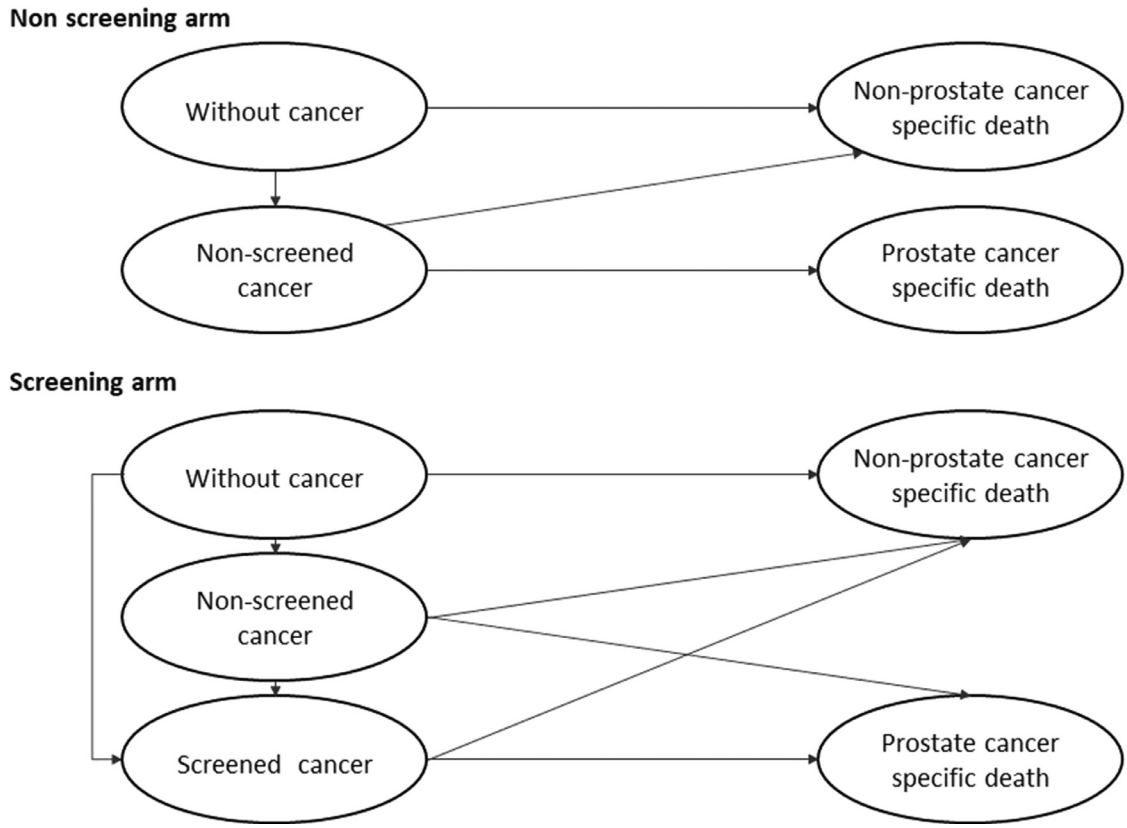

Figure 2. Markov model structure

entire population was derived from the 2010 China census data.[16] This study took the perspective of the public health care payer. The discount rate was 3.5% and the time horizon was lifetime.

Clinical input

Transition probabilities in the decision tree model were based on a real-world PSA screening study of Chinese population in Nanjing.[11] The data we used were further adjusted by physicians through interviews (Table 1). The physicians we interviewed were from 6 representative cities in China, including Beijing, Shanghai, Guangzhou, Chengdu, Wuhan, and Shenyang. Transition probabilities in the Markov model were derived from Xu et al,[16] a respective study that compared the survival characteristics between patients whose PCa was detected via PSA-based screening versus clinical diagnosis in China.

Health utilities were derived from publications based on the Asian population (Table 1).[17] The utility values of palliative therapy and terminal illness were adjusted by physicians. The end-of-life treatment would not improve the quality of life for patients with metastatic disease, so the utility could not be higher than the value of later metastatic patients.

Cost inputs

Costs included test costs, PCa treatment costs, and end-of-life treatment costs (Table 2).[19–21] PCa treatment costs were calculated based on different treatment patterns, including radical prostatectomy, radiotherapy, or hormone therapy, through matching different treatments with patient percentage. The treatment costs of PCa can be different every year, so we split the costs of the first year from the remaining years. All the costs were inflated to 2020.

Table 1
Clinical input.

Parameter	Value	Source
Proportion of PSA level*, ng/mL		
PSA ≤ 4	86	Adjusted by physician
PSA > 4 and < 10	9	Adjusted by physician
PSA ≥ 10	5	Adjusted by physician
MRI results for PSA 4–10 population*		
MRI positive	34	Interview
Go-through biopsy*		
Accept biopsy	88	Interview
Positive biopsies*, ng/mL		
PSA > 4 and < 10	21	Hua et al, 2011[11]
PSA ≥ 10	39	Hua et al, 2011[11]
Population in no-screening arm*		
Local PCa	43	Interview
Local advanced PCa	25	Interview
Metastatic PCa	32	Interview
Population in screening arm*		
Local PCa	82	Shin et al, 2014[5]
Local advanced PCa	16	Shin et al, 2014[5]
Metastatic PCa	2	Shin et al, 2014[5]
Utility†		
PSA screening attendance	0.99	Heijnsdijk et al, 2012[18]
Biopsy	0.9	Heijnsdijk et al, 2012[18]
Local PCa (first year)	0.727	Shin et al, 2014[5]
Local PCa (second year)	0.653	Shin et al, 2014[5]
Local advanced PCa (first year)	0.545	Shin et al, 2014[5]
Local advanced PCa (second year)	0.485	Shin et al, 2014[5]
Metastatic PCa (first year)	0.321	Shin et al, 2014[5]
Metastatic PCa (second year)	0.149	Shin et al, 2014[5]
Palliative therapy	0.149	Adjusted by physician
Terminal illness	0.149	Adjusted by physician

MRI = magnetic resonance imaging; PCa = prostate cancer; PSA = prostate-specific antigen.
* Values are presented as %.
† Values are presented as xxxxxx.

Table 2
Costs inputs.

Cost inputs	Cost, ¥	Source
Test costs		
PSA testing	145.5	Interview
MRI	1,230	Interview
TRUS-guided biopsy	1,650	Interview
First-year PCa treatment costs		
Local PCa	42,351	Adjusted by physician
Local advanced PCa	53,623	Adjusted by physician
Metastatic PCa	64,514	Adjusted by physician
Second-year PCa treatment costs		
Local PCa	3,042	Adjusted by physician
Local advanced PCa	67,123	Adjusted by physician
Metastatic PCa	64,514	Adjusted by physician
End-of-life treatment cost		
Terminal care for PCa	21,093	Interview
Non-PCa death	21,093	Interview

MRI = magnetic resonance imaging; PCa = prostate cancer; PSA = prostate-specific antigen; TRUS = transrectal ultrasound.

Sensitivity and Scenario Analyses

One-way sensitivity analysis (OWSA) was conducted for all the parameters 1 at a time. As suggested and confirmed by the panel of local clinical experts, the range of values for the variables in the OWSA was determined by ±20% of the base case estimate. The result of OWSA was displayed with a tornado diagram. Probabilistic sensitivity analysis was performed to test the effect of parameter uncertainty on the study results. It was assumed that the transition probability and utility values obey beta distribution, and the costs data obey gamma distribution. We calculated the incremental cost-utility ratio (ICUR) by running 1000 Monte Carlo simulations to determine the proportions of simulations that were under predefined willingness-to-pay (WTP) thresholds of 3 times the gross domestic product per capita in 2020. Then, a cost-utility acceptability curve was generated to summarize the uncertainty of the cost-utility analysis and to determine the proportions of simulations that were under the WTP thresholds. We also tested scenarios of screening different age groups (50–65 years vs 65–80 years).

Results

Base case results

In the base case analysis, the cumulative cost of 1000 cohort in the PSA screening arm was ¥4,550,283 ($728,045/€591,537), with 2414.62 quality-adjusted life years (QALYs); the cumulative cost of 1000 cohort members in the nonscreening arm was ¥3,857,937 ($617270/€501532), and 2353.78 QALYs were gained. Besides this, the screening arm had a higher PCa-related treatment cost and a lower end-of-life cost compared with the nonscreening arm (details in Table 3). The ICUR was ¥11,381 ($1821/1480 EUR) per QALY. This value was less than the willingness-to-pay threshold of 1-time gross domestic product per capita in China in 2020, which was ¥70,892 ($11,343/€9216). PSA-based screening in the high-risk population was cost-effective compared with nonscreening of all populations.

Sensitivity analyses results

The results of the OWSA were shown in Figure 3. The utility of screening attendance, proportion of local advanced PC in the PSA screening arm and the treatment cost of local advanced PC after the first year were the most relevant factors to the results. As for the results of probabilistic sensitivity analyses, the cost-utility acceptability curve was shown in Figure 4. When the WTP was higher than ¥40,000 ($6400/€5200), the acceptability of PSA screening was 100%. The sensitivity analyses confirmed the robustness of the results.

Scenario analysis results

In the scenario analysis, we divided the population into 2 age groups: 50 to 65 years and 65 to 80 years. The ICUR result was better in the 50 to 65 years age group, indicating that PSA screening may be launched in the early stage for men, and was able to lower the costs due to early diagnosis and treatment.

Discussion

This study explored the cost-utility of PSA-based PCa screening in China. The results suggested that PSA screening can be a promising tool to identify PCa with an ICUR of ¥11,381 ($1821/€1480)/QALY. The sensitivity analyses suggested that the main drivers of uncertainty included utility of screening attendance, proportion of local advanced PCa in the PSA screening arm, and the treatment cost of local advanced PCa after the first year. We also tested scenarios by age groups. Scenario analyses suggested that PSA screening was recommended to the younger population.

PSA screening has always been controversial. That is because PSA tests often alert doctors to the presence of cancer, but whether or not the cancers detected would have ever influenced quality of life remains uncertain. Two large randomized controlled trials of PSA-based screening, the Prostate, Lung, Colorectal, and Ovarian (PLCO) and the European Randomized Study of Screening for Prostate Cancer (ERSPC) study, came to the opposite conclusion.[8,9] The ERSPC study found that screening reduced PCa mortality, whereas the PLCO found no difference. A critique of the PLCO study stated that participants in the control arm, both before and during the study, were contaminated.[18] Studies reanalyzed the existing data of the ERSPC and the PLCO and found that screening reduced PCa mortality.[19,20] A third study that included younger men (median age 56 years at baseline) receiving PSA-based screening indicated that PCa mortality was reduced almost by half over

Table 3
Base case results.

Variable	PSA screening	No screening	Difference
Cost for screening, ¥	512,993	0	512,993
End-of-life cost, ¥	1,339,855	1,400,047	−60,193
PCa-related treatment cost, ¥	2,697,435	2,457,889	239,546
Total cost, ¥	4,550,283	3,857,937	692,346
Total QALY	2,414.62	2,353.78	60.84
ICER	–	–	11,381/QALY

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; PCa = prostate cancer; PSA = prostate-specific antigen.

Table 4
Scenario analysis results.

Scenario	PSA screening	No screening	Difference
Scenario 1: 50–65 y age group			
Total cost, ¥	4,225,770	3,805,204	420,567
Total QALY	4856.11	4805.75	50.35
ICER, ¥	–	–	8,352/QALY
Scenario 2: 65–80 y age group			
Total cost, ¥	5,627,908	4,717,643	910,265
Total QALY	1711.74	1634.75	76.99
ICER, ¥	–	–	11,823/QALY

ICER = incremental cost-effectiveness ratio; QALY = quality-adjusted life year; PSA = prostate-specific antigen.

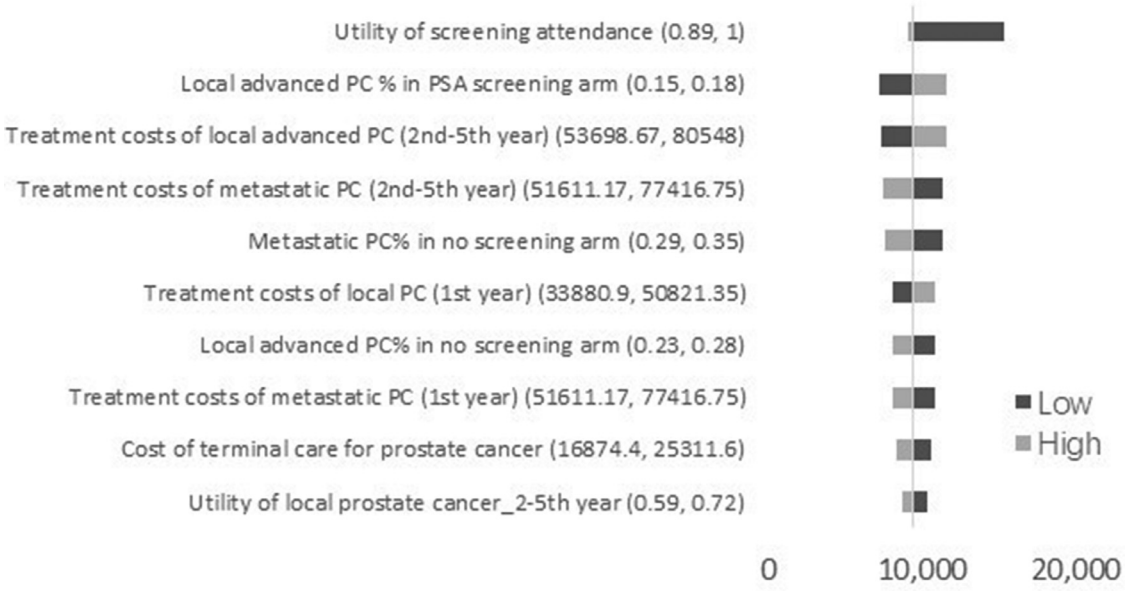

Figure 3. Tornado diagram for one-way sensitivity analysis results
Tornado diagram is a common tool used in illustrating the sensitivity of a result on key model parameters changes with the expected ICERs (Cost/QALY).
Abbreviations: PSA: prostate-specific antigen; ICER: incremental cost-effectiveness Ratio; QALY, quality-adjusted life-year.

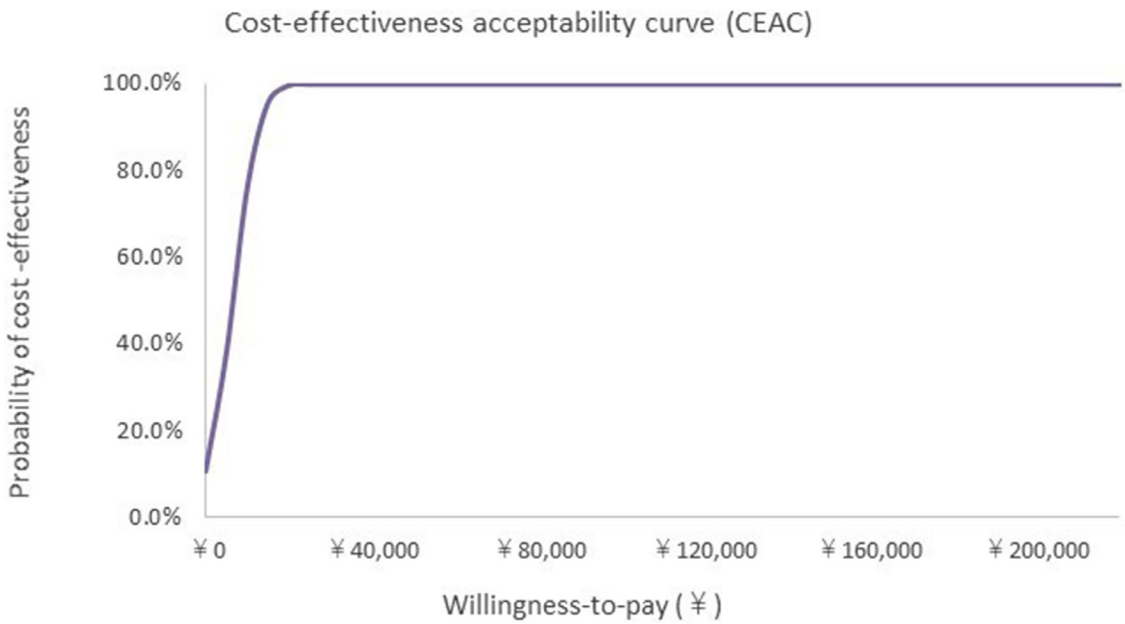

Figure 4. Cost-utility acceptability curve for PSA screening
The cost-effectiveness acceptability curve (CEAC) is an intuitive graphical method of summarizing information on uncertainty in cost-effectiveness estimates.

14 years,[21] which compared favorably with other cancer screening programs.

Guideline recommendations for PSA screening have also been reversed in the past decade. In 2012, the US Preventive Services Task Force recommended against PSA screening due to concerns about overdiagnosis and treatments for screen-detected indolent tumors combined with misinterpretation of clinical trial data.[22] Years later, PCa screenings were found to have significantly declined among men older than age 50 years,[23] resulting in a reversion to more high-grade, advanced disease at diagnosis.[24] So, after reanalysis and reevaluation of previous trials, the US Preventive Services Task Force has recently worn down its opposition to routine PCa screening in favor of a shared decision-making process between men ages 55 and 69 years and their physicians.[24]

We utilized local data to make the model results more applicable to the Chinese population. The values of parameters in the base case were assumed to best represent practical clinical settings. The probability parameters of health states of PSA screening in our decision tree were based on a real-world study conducted in Nanjing, China.[11] The specific survival probabilities were based on a respective study in which the survival characteristics were compared between patients with PCa in China. Local cost data and treatment patterns were collected from local literature or local clinical expert interviews.

There were a few economic evaluations to compare the cost-utility of PSA screening in China and other countries. We referred to the model structures in other published PSA screening Cost-effectiveness analysis (CEA) studies.[5,12] Only one research had been searched when this study was conducted by using key words such as *cost-effectiveness* and *economic*. The only related research was conducted by Zhao et al.[21] Zhao et al[21] conducted an economic evaluation for PSA screening in China. Their result (ICUR = ¥14,747 [$2360/€1,917]/QALY) is very similar to our study. However, there were some differences in model settings and data source. First and most importantly, local cost data from Zhao et al[21] were based on literature published in 2016.[24] Because the treatment pattern for PCa changed rapidly in recent years, including a novel hormone-based chemotherapy using abiraterone acetate and a novel prostate surgery using da Vinci robot (Intuitive Surgical, Sunnyvale, California), the local cost data used in their model might be out of date. Second, our study filled an evidence gap of age-specific information by conducting the scenario analysis to evaluate the cost-utility of PSA screening programs in different age groups. Third, our model considered the possibility that patients may refuse to undergo MRI and biopsy. Fourth, our model is more flexible because it can be refined by adapting up-to-date, real-world data.

Similar to other model-based cost-utility analyses, this study had inherent limitations. We used those utility scores reported in the studies where the populations of interest were Korean due to a lack of specific data in China. Sensitivity analyses suggested that the variation of input parameters only had a small influence on the ICURs. In addition, the cost data used in this study were mainly from clinical expert interviews due to the inaccessibility of updated and relevant data.

Conclusions

PSA-based PCa screening appears to be cost-effective in some high-risk Chinese men. PSA screening (PSA testing followed by MRI and biopsy if positive) can be recommended for 50- to 65-year-old Chinese men because this approach had the lowest risk-to-benefit ratio. The approach should be further adapted based on future updated data.

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All authors contributed extensively to the work presented in this article. Xiaojian Qin, Dingwei Ye, and Shuli Qu led the study design. Shuli Qu and Han Yang conducted the literature review, designed, and implemented local data collection and analysis. Xiaojian Qin, Chengyuan Gu, Yongqiang Huang, Weijie Gu, Bo Dai, Hailiang Zhang, Yao Zhu, and Dingwei Ye reviewed data and model simulation analysis. All authors jointly contributed to manuscript writing. All authors read and approved the final manuscript.

Conflicts of Interest

The authors have indicated that they have no conflicts of interest regarding the content of this article.

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