The Japanese Guideline for Prostate Cancer Screening

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In 2005, there were 9264 deaths from prostate cancer, accounting for 4.7% of the total number of cancer deaths in Japan. As the population continues to age, interest in prostate cancer screening has increased, and opportunistic screening for prostate cancer has been conducted worldwide. The guideline for prostate cancer screening was developed based on the established method. The efficacies of prostate-specific antigen (PSA) and digital rectal examination (DRE) were evaluated. Based on the balance of the benefits and harms, recommendations for population-based and opportunistic screening were formulated. Two methods of prostate cancer screening were evaluated. Based on the analytic framework involving key questions, 1186 articles published from January 1985 to October 2006 were selected using MEDLINE and other methods. After the systematic literature review, 28 articles were identified as providing evidence of mortality reduction from prostate cancer, including 5 observational studies for DRE screening, 1 meta-analysis, 3 randomized controlled trials and 19 observational studies for PSA screening. Although several studies showed that PSA screening had a beneficial effect, the results of the selected studies were inconsistent. Overall, the evidence that screening reduced mortality from prostate cancer was insufficient. Furthermore, prostate cancer screening is associated with serious harms, including overdiagnosis, adverse effects of needle biopsy and adverse effects of local prostatectomy. At present, the evidence for the effect of prostate cancer screening is insufficient. Both PSA and DRE were not recommended for population-based screening programs, but they could be conducted as individual-based screening if basic requirements were met.

Key words: prostate cancer – cancer screening – guideline – recommendation – prostate-specific antigen – digital rectal examination

INTRODUCTION

Prostate cancer is the seventh leading cause of death from cancer for males in Japan. The incidence of prostate cancer increased gradually until 1995 and then accelerated from the late 1990s. Between 1960 and 1998, the age-adjusted mortality increased from 1.4 to 5.4 per 100 000 in males, and it has flattened since 1999 (1). In 2005, there were 9264 deaths from prostate cancer, accounting for 4.7% of the total number of cancer deaths (1).

In 2001, the research group for cancer screening guidelines funded by the Ministry of Health and Welfare of Japan recommended the following six cancer screening programs (the Hisamichi reports) (2): gastrofluorography for gastric cancer; fecal occult blood testing for colorectal cancer; a combination of chest radiography and sputum cytology (added for current smoker only) for lung cancer; Pap smear for cervical cancer; a combination of physical examination and mammography for breast cancer; and hepatitis virus markers for hepatocellular carcinoma. These guidelines did...
not recommend prostate cancer screening using prostate-specific antigen (PSA) and digital rectal examination (DRE) because of insufficient evidence. Nevertheless, PSA screening disseminated rapidly as population-based screening nationwide after the previous guidelines were published.

Since the publication of the previous guidelines, new studies dealing with prostate cancer screening have been reported. Meanwhile, a new research group established a standardized method for developing the Japanese Guidelines for Cancer Screening (3). Based on this methodology, the effects of DRE and PSA for prostate cancer screening were evaluated, and the new guideline was developed.

**METHODS**

The target audiences for the prostate cancer screening guideline include the public, health professionals working in cancer screening programs, providers of cancer screening programs and policy makers. The members of the guideline development group for prostate cancer screening (panel) were selected from various specialties. The prostate cancer screening guideline was developed using the standardized method (3).

**Analytic Framework**

The target population for prostate cancer screening was defined to be asymptomatic males with an average risk of prostate cancer. Two methods, DRE and PSA, were evaluated. To select appropriate evidence, an analytic framework for prostate cancer screening was developed (Fig. 1). For each stage of the analytic framework, key questions based on the population, intervention, comparison and outcome (PICO) format were prepared. Direct evidence was defined as evidence provided by a study that evaluated the effect of cancer screening for reducing prostate cancer mortality (Fig. 1, arrow 1). Other studies that provided indirect evidence were selected based on key questions related to other stages of the analytic framework (Fig. 1, arrows 2–8).

![Figure 1. Analytic framework and key questions.](image-url)
A systematic literature review was conducted by the members of the review committees for prostate cancer screening, including the panel members. A search of the literature published from January 1985 to September 2006 was performed using MEDLINE, Database of Abstracts of Reviews of Effects, Health Technology Assessment Database and Japanese Medical Research Database (Igaku-Chuo-Zasshi). Key journals were searched manually, including the Journal of the Japanese Association for Urology and the Journal of the Japanese Association for Cancer Detection and Diagnosis. Further references were obtained through the ERSPC (European Randomized Study of Screening for Prostate Cancer) (4) and PLCO (Prostate, Lung, Colorectal and Ovarian Cancer Trial) (5) websites. The reference lists of the US Preventive Services Task Force (6) and the previous report (2) dealing with the evaluation of prostate cancer screening were checked, and relevant articles were included. Additional references recommended by the panel were identified and included as needed. If the result from a branch of a large-scale RCT was published during guideline development, the study was included. To select appropriate evidence, a systematic review of the retrieved articles was conducted using the checklist according to the study design (3).

FINDINGS

SYSTEMATIC LITERATURE REVIEW

Based on the literature search using MEDLINE and other databases, 1186 articles published from January 1985 to September 2006 were identified. The abstracts were reviewed, and 131 articles were selected for full-text review. After the full-text review, which included a new paper from the ERSPC study that was published after the above literature search, 28 articles were confirmed as providing direct evidence dealing with the reduction of prostate cancer mortality by screening, and 44 articles were confirmed as providing indirect evidence (Table 1).

LEVEL OF EVIDENCE

DRE (LEVEL OF EVIDENCE 2–)

Four case–control studies and one time-series study dealing with DRE were identified (7–11). Since the results of these studies were inconsistent, the evidence was insufficient to evaluate the effect of DRE screening.

CASE–CONTROL STUDIES

In one of the case–control studies, the relative risk of metastatic prostate cancer for men with a DRE screening history compared with men who had none was 0.9 (95% CI 0.5–1.7) (Table 2) (7). Richert-Boe et al. (8) reported that there was no significant mortality reduction from prostate cancer among screened men compared with controls during a 10-year interval (odds ratio = 0.84, 95% CI 0.48–1.46). Another study reported a similar result (odds ratio = 0.70, 95% CI 0.48–1.1) (9). Although the results were negative for DRE screening in three studies, positive results were reported by Jacobsen et al. (10); DRE screening was associated with a 49% mortality reduction from prostate cancer (odds ratio = 0.51, 95% CI 0.31–0.84). However, these
results must be evaluated prudently due to the possibility of misclassification of DRE performed as a diagnostic testing in symptomatic patients.

**EcoLOGICAL Study**

In the time-series study conducted in New Mexico, age-adjusted mortality from prostate cancer was decreased by 6.1%: from 23.0 per 100 000 in the period 1978 to 1982 to 21.6 per 100 000 in the period 1988 to 1991 (11). Although the age-adjusted incidence for local stage disease increased, the age-adjusted incidence for distant disease became stable.

**Test Accuracy**

Based on the meta-analysis that included 13 studies from 1996 to 1999, the sensitivity, specificity and positive predictive value of DRE were 53.2, 83.6 and 17.8%, respectively (12).

**PSA (Level of Evidence 1–/2–)**

Three RCTs and 19 observational studies were identified as providing evidence for PSA screening. Although several studies show the effect of PSA screening, the results of the selected studies were inconsistent. There was no conclusive evidence that PSA screening reduces prostate cancer mortality.

**Randomized Controlled Trials**

Although the Quebec study was the first RCT of prostate cancer screening, it could not evaluate mortality reduction from prostate cancer (13,14). In that trial, 31 133 men, aged 45–80 years, were randomly allocated to the invited group that was screened annually, whereas 15 353 men were allocated to the control group that was not to be screened. However, there was crossover within the groups; 7% of the control group was screened, and only 23% of the group allocated to screening actually participated in screening. After 11 years of follow-up, prostate cancer mortality was 62% lower in the screened group (19.8 deaths/10 000 man-years) than in the non-screened group (52.3 deaths/10 000 man-years). Mortality was calculated based on those who were screened and not screened in each group, rather than according to group allocation (invited group and not-invited group). This was a so-called per protocol analysis, which should be conducted in a cohort study, with appropriate adjustment for confounding factors in both groups. The intention-to-screen analysis, which is preferred for an RCT, showed that there was no significant difference in prostate cancer mortality (relative risk = 1.085, 95% CI 0.822–1.433) (Table 3).

The Norrkoping study was started at the same time as the Quebec study and included 15 years of follow-up (15). Since
every sixth man was randomly selected to be screened \((n=1494)\), and the remaining men \((n=7532)\) were treated as controls, the randomization method was inadequate because the result of allocation could be predicted beforehand. In addition, the screening method was changed; DRE screening was used for the first and second rounds, whereas a combination of DRE and PSA screening was used for the third and fourth rounds. Although screening led to a stage shift toward more localized cancer, there was no difference in overall and prostate cancer-specific survival between the screened and unscreened groups.

The last study reported the intermediate outcome of the Swedish branch of the ERSPC (16). After a 10-year follow-up of 9972 men in the intervention group and 9973 men in the control group, the risk of being diagnosed with metastatic prostate cancer was reduced by 48.9% in the screened group (24 advanced cancer cases) compared with the control group (41 advanced cancer cases). However, it was difficult to conclude that the beneficial effect was due to prostate cancer screening for several reasons. First, metastatic cancers included cases with a PSA increase over 100 ng/ml and cases with symptoms suggestive of bone metastasis, as well as cases diagnosed by bone scan. Second, the method for informed consent differed from that in other sections of the ERSPC group. In the Swedish section, informed consent was obtained after randomization, whereas in other sections it was obtained before randomization. Finally, a surrogate endpoint was used for evaluation of the efficacy of PSA screening.

**Systematic Review (Meta-Analysis)**

An intention-to-screen analysis of the pooled data of the Quebec and Norkoping studies showed that there was no difference in prostate cancer mortality between the randomly allocated screened group and the control group (relative risk 1.01, 95% CI 0.80–1.29) (17).

**Cohort Study**

A cohort of 6861 men, aged 60–74 years, was followed for 10 years, and the standardized mortality ratios (SMRs) of three groups (attendees, refusers and not invited) were compared (18). The SMR was defined as the ratio of observed to expected deaths, which was calculated by multiplying the age-, period- and site-specific mortality rate of the Province of Florence. The SMRs of prostate cancer were 0.48 for the attendees group (95% CI 0.26–0.83), 0.99 for the refusers (95% CI 0.69–1.37) and 2.50 for the not-invited group (95% CI 1.51–3.90). However, the SMRs for all causes excluding death from prostate cancer were similar to those of prostate cancer in all groups: 0.45 for the attendees group (95% CI 0.23–0.78), 0.85 for the refusers (95% CI 0.58–1.22) and 1.08 for the not-invited group (95% CI 0.47–2.03). Although prostate cancer mortality was reduced in the attendees group, a healthy screening effect is expected, with attendees being healthier than refusers based on the SMRs for all causes excluding death from prostate cancer. A difference in prostate cancer mortality between attendees and refusers might be ascribed to such a bias, rather than to screening.

**Case–Control Studies**

One case–control study was conducted in Japan, and two studies were conducted in Canada and the USA (Table 4). Compared with studies conducted in other countries, the sample size of the Japanese study was small (19). Although the Japanese study showed a 64% decrease in invasive cancer (odds ratio = 0.36, 95% CI 0.15–0.87) with participation in prostate cancer screening, the study was of low quality for several reasons, including a surrogate endpoint, unclear criteria for opportunity to be screened and exclusion of cases with interval cancer. The Canadian study suggested that there was a 35% reduction in metastatic cancer with PSA screening (odds ratio = 0.65, 95% CI 0.45–0.93) (20). However, for the older age group (60–84 years), which constituted the majority of this study, the odds ratio adjusted for exposure observation time and the propensity score was 0.67 (95% CI 0.41–1.09), even though more cases (40/135 = 29.6%) than controls (69/267 = 25.8%) were screened. On the other hand, a multicenter, nested, case–control study conducted at 10 Veterans Affairs facilities found no mortality reduction with PSA screening (odds ratio=1.13, 95%
Table 3. Randomized controlled trials dealing with PSA screening

<table>
<thead>
<tr>
<th>Author</th>
<th>Research area</th>
<th>Reported year</th>
<th>Numbers of target population</th>
<th>Target age (years)</th>
<th>Screening methods</th>
<th>Follow-up years</th>
<th>Endpoint/outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labrie et al.</td>
<td>Canada, Quebec</td>
<td>2004 (1999)</td>
<td>31 133</td>
<td>15 353</td>
<td>PSA + DRE</td>
<td>11</td>
<td>Disease-specific mortality, RR 1.01 (95% CI 0.76–1.33)*</td>
</tr>
<tr>
<td>Sandblom et al.</td>
<td>Sweden, Norrkoping</td>
<td>2004</td>
<td>1492</td>
<td>7532</td>
<td>DRE (1987, 1990), PSA + 1993, 1996</td>
<td>15</td>
<td>Disease-specific mortality, RR 1.04 (95% CI 0.64–1.68)*</td>
</tr>
<tr>
<td>Aus et al.</td>
<td>Sweden, Gotenberg</td>
<td>2007</td>
<td>9972</td>
<td>9973</td>
<td>PSA</td>
<td>10</td>
<td>Incidence of metastatic cancer (/1000)*, intervention group 2.4/ control 4.7 (P = 0.008)</td>
</tr>
</tbody>
</table>

*aThe results of the Quebec and Norrkoping studies were based on intention-to-screen analysis of Cochran review.

*bMetastatic cancer included both cases by following methods; bone scan and serum PSA level >100 even if it was not proven M1 at bone scan.

Table 4. Case–control studies dealing with PSA screening

<table>
<thead>
<tr>
<th>Author</th>
<th>Published year</th>
<th>Research area</th>
<th>Target age (years)</th>
<th>Source population</th>
<th>Screening method</th>
<th>Screening rate</th>
<th>Endpoint</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nakagawa et al.</td>
<td>1998</td>
<td>Japan, 34 local municipalities</td>
<td>55–89</td>
<td>Screening participants TRS, TRS + DRE, TRS + DRE + PSA, PSA</td>
<td>31/155 (23%)</td>
<td>7/31 (23%)</td>
<td>Invasive cancer (stages C and D)</td>
<td>0.36 (0.15–0.87)</td>
</tr>
<tr>
<td>Concato et al.</td>
<td>2006</td>
<td>USA, New England</td>
<td>50 and over</td>
<td>Cohorts receiving Veteran Affairs Care PSA, DRE</td>
<td>501/501 (10%)</td>
<td>70/501 (14%)</td>
<td>Prostate cancer mortality</td>
<td>1.08 (0.71–1.64)*</td>
</tr>
<tr>
<td>Kopec et al.</td>
<td>2005</td>
<td>Canada, Ontario</td>
<td>40–84</td>
<td>Residents of metropolitan Toronto and five surrounding counties PSA, DRE</td>
<td>236/462 (24.6%)</td>
<td>58/236 (24.6%)</td>
<td>Metastatic cancer</td>
<td>0.65 (0.45–0.93), all age^b</td>
</tr>
</tbody>
</table>

*TRS, transrectal sonography.

^aOdds ratio was adjusted by races and morbidity.

^bOdds ratio was adjusted by exposure observation time, age, resident area, facility, history of prostate cancer, weight, consumption of butter and doctor visits for health problems.
CI 0.63–2.06) (21). Although screening cases were distinguished from diagnostic cases based on a medical record review, information about the participants’ screening history in non-Veterans Affairs screening could not be collected and was thus not available for the analysis.

**Ecological Studies**

Of the 15 articles selected, 5 reported reduced prostate cancer mortality, whereas the others reported no reductions (22–36). In most studies, prostate cancer mortality correlated with the frequency of PSA testing (or the incidence of prostate cancer as a surrogate for PSA testing). Since PSA testing was conducted primarily in the clinical setting, it was difficult to evaluate its use solely in screening programs. However, the mortality of prostate cancer has decreased worldwide independent of the intensity of PSA screening (34). The results of ecological studies are difficult to interpret because other positive factors, including improvements in diagnostic tests and treatments, might influence the result of these studies. Although many ecological studies have been conducted in several countries, it has been difficult to distinguish between cases that were being screened and those that were being diagnosed. The studies that reported negative results may have underestimated the effect of PSA screening, since the follow-up period for mortality was short after the peak incidence of prostate cancer. The Tyrol study showed promising results compared with other regions of Austria where PSA screening was not freely available (35). Using the same data concerning the incidence and mortality of prostate cancer, Vutuc et al. (36) reported different results. Although an immediate reduction in prostate cancer mortality was observed in the 70–79 years age group in Tyrol after the introduction of PSA screening, it was difficult to consider this to be the result of screening alone. In addition, the prostate cancer mortality was stable in other age groups.

**Test Accuracy**

Sensitivity was estimated using the results of biopsies and follow-up studies as the reference (12,37–45). With a PSA screening cut-off value of 4 ng/ml, the sensitivity ranged from 72 to 93%, and the specificity ranged from 90 to 98%. A Japanese study reported that the cut-off value was changed for different age groups to increase the sensitivity, but this led to decreased specificity (41).

**Survival Analysis**

In the report from the Rotterdam section of the ERSPC, the 5-year PSA progression-free survival after radical prostatectomy was 68% in the control arm and 89% in the screening arm ($P < 0.0001$) (46). In the Japanese study, the relative survival rate was around 100% in the screening group and 40% in the non-screening group (47).

**Harms of Prostate Cancer Screening**

**Overdiagnosis**

The overdiagnosis rate and the duration of lead time were estimated based on the cohort studies and modeling (Table 5) (48–53). The overdiagnosis rate was estimated to range from 20 to 84%. The lead-time duration was reported to range from 5 to 7 years in most studies. Based on a simulation model using the results of the ERSPC study, at age 55 years, the estimated lead time was 12.3 years and the overdiagnosis rate was 27%; at age 75 years, the estimated lead time was 6.0 years and the overdiagnosis rate was 56% (52).

**Diagnostic Test**

Transrectal needle biopsy of the prostate is commonly used as the reference standard in prostate cancer screening. In Japan, other than case reports, there have been few reports dealing with complications following needle biopsy. Mild complications, such as hematuria, hematospermia and rectal bleeding, were frequently reported, with rates of 2–23.6, 29.8–54.0 and 1.7–57.0%, respectively (Table 6) (54–66). Although more severe complications occurred far less frequently, two biopsy-related deaths were reported in Japan (65,66).

**Treatment**

Both radical prostatectomy and radiation therapy have been commonly used for the treatment of clinically localized prostate cancer. Both standard treatments are associated with several complications (Table 7) (67–76). Urinary leakage and erectile dysfunction were commonly reported for both treatments. Although the complication rate following radical prostatectomy was low in a Japanese study (75,76), there has been no long-term follow-up study in Japan, such as the Prostate Cancer Outcomes Study (71,72).

**Discussion**

In the present systematic review, sufficient evidence for prostate cancer screening using both DRE and PSA could not be identified. Although many studies have addressed prostate cancer screening, especially ecological studies, the results of these studies have been inconsistent. To date, the effect of PSA screening on mortality reduction, including three RCTs, has not been properly evaluated. Recently, the Swedish section of the ERSPC reported a reduction in metastatic cancer (16). Although a decrease in metastatic cancer is a significant effect of screening, the outcomes may differ with mortality as the endpoint. Therefore, Schröder, who is chair of the scientific committee of the ERSPC, concluded that the Swedish study was not a representative of the results of the entire ERSPC study (77). Although several guidelines were published after publication of the results of the Swedish
<table>
<thead>
<tr>
<th>Author</th>
<th>Published year</th>
<th>Study design</th>
<th>Research area</th>
<th>Age (target population)</th>
<th>Number of target population</th>
<th>Result</th>
<th>Lead time</th>
<th>DCPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGregor et al.</td>
<td>1998</td>
<td>Simulation model</td>
<td>Canada</td>
<td>50–70 years</td>
<td>84%</td>
<td>Overdiagnosis Lead time DCPC</td>
<td>7 years</td>
<td></td>
</tr>
<tr>
<td>Hugosson et al.</td>
<td>2000</td>
<td>Cohort study</td>
<td>Sweden</td>
<td>Cohort of men born in 1913</td>
<td>658</td>
<td>White 29%, Black 44%</td>
<td>White 5 years, Black 7 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sweden</td>
<td>Cohort of men born in 1930 and 1931</td>
<td>710</td>
<td>White 5 years, Black 7 years</td>
<td>White 5 years, Black 7 years</td>
<td></td>
</tr>
<tr>
<td>Etzioni et al.</td>
<td>2002</td>
<td>Simulation model</td>
<td>USA</td>
<td>60–84 years</td>
<td>292</td>
<td>White 29%, Black 44%</td>
<td>White 5 years, Black 7 years</td>
<td></td>
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<tr>
<td>Auvinen et al.</td>
<td>2004</td>
<td></td>
<td>Finland</td>
<td>55, 59, 63 and 67 years</td>
<td>292</td>
<td>White 29%, Black 44%</td>
<td>White 5 years, Black 7 years</td>
<td></td>
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<tr>
<td>Draisma et al.</td>
<td>2003</td>
<td></td>
<td>The Netherlands, Rotterdam</td>
<td>55–74 years</td>
<td>292</td>
<td>White 29%, Black 44%</td>
<td>White 5 years, Black 7 years</td>
<td></td>
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<tr>
<td>Törnblom et al.</td>
<td>2004</td>
<td>Cohort study</td>
<td>Sweden</td>
<td>55–70 years screening group</td>
<td>946a</td>
<td>White 29%, Black 44%</td>
<td>White 5 years, Black 7 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Reference population (cohort of men born in 1913)</td>
<td>657</td>
<td>White 29%, Black 44%</td>
<td>White 5 years, Black 7 years</td>
<td></td>
</tr>
</tbody>
</table>

DCPC, detectable, preclinical phase; TRUS, transrectal ultrasonography.

*aBiopsies were taken in cases of abnormal finding either DRE or TRUS, irrespective of their PSA level.*
study, they did not change their previous judgments and they did not recommend PSA screening (78–80).

In developed countries, as the population has aged, interest in prostate cancer screening has increased. Opportunistic screening for prostate cancer using PSA has been conducted worldwide. Although previous guidelines did not recommend prostate cancer screening using PSA and DRE, PSA screening has rapidly disseminated as population-based screening nationwide in Japan since the late 1980s. In 2007, PSA screening was conducted as a public service in 42% of local municipalities (81). Since the government stopped the subsidies for cancer screening programs in 2001, the local government could decide the method of screening programs individually. Lacking the information of the previous guidelines, most local municipalities have chosen screening methods based on the suggestions of their local health professionals. To reduce cancer mortality, effective screening should be implemented properly. In order to accomplish this, we have to reconstruct the information delivery system for cancer screening guidelines. The guidelines are published in several forms; a full-text version, a concise version and leaflets for the public. In addition, all of the guidelines are posted on the following website: Promoting Evidence-based Cancer Screening and Research Center for Cancer Prevention and Screening, National Cancer Center (http://ganjoho.ncc.go.jp/pro/index.html).

The decrease in the prostate cancer mortality rate is impressive in countries where screening is more common, such as in the USA. In the USA, in association with the dissemination of PSA screening, prostate cancer mortality began to decline around the early 1990s, around the same time that the incidence decreased (82–84). If, based on the previous research (48–53), the lead time is estimated to be 5–7 years, a simultaneous and parallel decrease in both mortality and incidence could not be explained by a screening effect. Both the incidence and the mortality of prostate cancer have been lower in Japan than in the USA and European countries (1,85). Even if PSA screening has reduced mortality in the USA, it is difficult to apply the result of PSA screening to Japanese situation immediately.

Although prostate cancer screening has disseminated worldwide, there are no programs for population-based screening for prostate cancer. However, the American Cancer Society recommends that both DRE and PSA screening be offered annually to men aged 50 years and over who have a life expectancy of >10 years (86). The American Urological Association published similar recommendations (87). Similarly, the Japanese Association of Urology recommended population-based prostate cancer screening for men aged 50 years and over (88). On the other hand, the US Preventive Task Force judged that there was insufficient evidence to recommend for or against routine screening using PSA and DRE (78,79). In the new version revised in 2008, the recommendation was not changed for men younger than 75 years. However, for men aged 75 years or older, they did not recommend routine screening since harms outweigh the benefit of prostate cancer screening. Most guidelines and evidence reports published in European countries have not recommended prostate cancer screening (89–93). If prostate cancer screening is conducted in clinical settings, most guidelines have recommended shared decision making based on appropriate information relating to the benefits and harms.

Table 6. Complications of biopsies

<table>
<thead>
<tr>
<th>Author</th>
<th>Published year</th>
<th>Research area</th>
<th>Antibiotic prophylaxis</th>
<th>Number of patients</th>
<th>Hematuria (%)</th>
<th>Hematospermia (%)</th>
<th>Rectal bleeding (%)</th>
<th>Pain (%)</th>
<th>Fever (%)</th>
<th>Urinary retention (%)</th>
<th>Sepsis (%)</th>
<th>Patients having at least one complication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rietbergen et al.</td>
<td>1997</td>
<td>The Netherlands, Rotterdam</td>
<td>Yes</td>
<td>1687</td>
<td>23.6</td>
<td>45.3</td>
<td>1.7</td>
<td>2.5</td>
<td>4.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Mkinen et al.</td>
<td>2002</td>
<td>Finland</td>
<td>Yes</td>
<td>100</td>
<td>65</td>
<td>54</td>
<td>57</td>
<td>3</td>
<td>8</td>
<td>—</td>
<td>58</td>
<td>—</td>
</tr>
<tr>
<td>Horminger et al.</td>
<td>2005</td>
<td>Austria, Tyrol</td>
<td>Yes</td>
<td>6024</td>
<td>12.5</td>
<td>29.8</td>
<td>4.0</td>
<td>0.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
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</tr>
<tr>
<td>Kapoor et al.</td>
<td>1998</td>
<td>USA</td>
<td>Yes</td>
<td>242</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td>1.5</td>
<td>10</td>
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<td>—</td>
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<tr>
<td>Cooner et al.</td>
<td>1990</td>
<td>USA</td>
<td>No</td>
<td>206</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>0.4</td>
<td>7</td>
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</tr>
<tr>
<td>Kapoor et al.</td>
<td>1998</td>
<td>USA</td>
<td>Yes</td>
<td>629</td>
<td></td>
<td></td>
<td></td>
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<td>0.5</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rodriguez et al.</td>
<td>1998</td>
<td>USA</td>
<td>Yes</td>
<td>128</td>
<td>47.1</td>
<td>9.1</td>
<td>8.2</td>
<td>13.2</td>
<td>1.7</td>
<td>9.1</td>
<td>63.6</td>
<td>—</td>
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<tr>
<td>Djavan et al.</td>
<td>2001</td>
<td>Austria, Belgium</td>
<td>Yes</td>
<td>1051</td>
<td>15.9</td>
<td>9.8</td>
<td>2.1</td>
<td>2.1</td>
<td>0.9</td>
<td>69.7</td>
<td>—</td>
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<tr>
<td>Raaijmakers et al.</td>
<td>2002</td>
<td>The Netherlands, Rotterdam</td>
<td>Yes</td>
<td>5802</td>
<td>22.6</td>
<td>50.4</td>
<td>1.3</td>
<td>7.5</td>
<td>3.5</td>
<td>0.4</td>
<td>0.4³</td>
<td>—</td>
</tr>
</tbody>
</table>

³Including one case who was admitted in ICU for septic shock.
There are currently two large-scale, ongoing RCTs, the ERSPC and the PLCO, whose results could provide reliable evidence of the effect of prostate cancer screening. The results of both RCTs will not be available for several years, and, at present, the efficacy of prostate cancer screening remains unclear. Compared with Western countries, the mortality of prostate cancer in Japanese men is around one-third. Even if the effect of screening were to be evaluated by large-scale RCTs, introduction of population-based screening in Japan would require an original study to assess its feasibility in Japan. Given racial differences, the results obtained from studies conducted in other countries should be used cautiously. A study evaluating the efficacy of PSA screening is ongoing (88). At present, the effect of prostate cancer screening remains unclear. However, if new evidence were to be published, we are planning to revise the guideline as soon as possible.

**RECOMMENDATIONS**

Based on the balance of benefits and harms, recommendations were formulated for population-based and opportunistic screening (Table 8). Benefits were defined as evidence

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### Table 7. Complications by treatment for prostate cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Published year</th>
<th>Research area</th>
<th>Urinary retention (%)</th>
<th>Urinary leakage (%)</th>
<th>Frequent urination pads (%)</th>
<th>Erectile dysfunction (%)</th>
<th>Bowel dysfunction (%)</th>
<th>Duration (years)</th>
<th>Short-term complications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radical prostatectomy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stanford et al.</td>
<td>2000</td>
<td>USA</td>
<td>50.8</td>
<td>21.6</td>
<td>36.8</td>
<td>59.9</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schover et al.</td>
<td>2002</td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lu-Yao et al.</td>
<td>1993</td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steineck et al.</td>
<td>2002</td>
<td>Sweden</td>
<td>49</td>
<td></td>
<td></td>
<td>50</td>
<td></td>
<td></td>
<td>2% died and 8% suffered major cardiopulmonary complications(^a)</td>
</tr>
<tr>
<td>Potosky et al.</td>
<td>2004</td>
<td>USA</td>
<td>15.6</td>
<td>28.6</td>
<td>10.6</td>
<td>76.9</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potosky et al.</td>
<td>2000</td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Madalinska et al.</td>
<td>2001</td>
<td>The Netherlands</td>
<td>39</td>
<td>&gt;65 years, 79</td>
<td>2</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Talcot et al.</td>
<td>1998</td>
<td>USA</td>
<td>10</td>
<td>31.8</td>
<td></td>
<td>68.8</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arai et al.</td>
<td>2000</td>
<td>Japan</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Hisasue et al.</td>
<td>2004</td>
<td>Japan</td>
<td>13.8</td>
<td>12.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>External beam radiotherapy</strong></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Potosky et al.</td>
<td>2004</td>
<td>USA</td>
<td>4.1</td>
<td>4.2</td>
<td>8.9</td>
<td>73.1</td>
<td>5</td>
<td></td>
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<tr>
<td>Potosky et al.</td>
<td>2000</td>
<td>USA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Madalingska et al.</td>
<td>2001</td>
<td>The Netherlands</td>
<td>21</td>
<td>&gt;65 years, 43</td>
<td>16</td>
<td>1</td>
<td></td>
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<td></td>
<td>1998</td>
<td>USA</td>
<td>1.8</td>
<td>4.4</td>
<td></td>
<td>29.7</td>
<td>1</td>
<td></td>
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</tbody>
</table>

\(^{a}\)Complication within 30 days after radical prostatectomy.

\(^{b}\)Complication within 60 days after radical prostatectomy.

\(^{c}\)Decreased by improvement of operational procedure.
that mortality from a specific cancer was reduced by a cancer screening program.

Prostate cancer screening using either DRE or PSA is not recommended for population-based screening due to insufficient evidence (Recommendation grade I). With respect to opportunistic screening, if individuals request screening, they should be given appropriate information, and decision making should be made at the individual level.

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Conflict of interest statement

None declared.

References

4. ERSPC (European Randomized Study of Screening for Prostate Cancer). http://www.erspc.org/

Table 8. Recommendation for prostate cancer screening

<table>
<thead>
<tr>
<th>Screening method</th>
<th>Recommendation grade</th>
<th>Recommendations (language)</th>
<th>Population-based screening</th>
<th>Opportunistic screening</th>
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<tbody>
<tr>
<td>DRE</td>
<td>1</td>
<td>Not recommended&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Decision making at individual level&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Not recommended&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>PSA</td>
<td>1</td>
<td>Not recommended&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Decision making at individual level&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Not recommended&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>There is insufficient evidence to recommend for or against.

<sup>b</sup>If required, the health professional should explain that the evidence regarding mortality reduction by cancer screening is unclear. In addition, information about the harms is required. In such situations, the decision regarding cancer screening should be made at the individual level.


Appendix

PEER REVIEW COMMITTEE FOR THE JAPANESE PROSTATE CANCER SCREENING GUIDELINE

Nomura H (Kanazawa University), Yoshimura E (Otomai Women College), Mori S (Tokyo Metropolitan Government), Maeda O (Maeda Clinic), Arai Y (Tohoku University), Fujimoto H (National Cancer Center), Suzuku K (Gunma University), Kakei K (Kagawa University, Japanese Association of Urology), Naito S (Kyusyu University, Japanese Association of Urology).

JAPANESE RESEARCH GROUP FOR DEVELOPMENT OF CANCER SCREENING GUIDELINES

Hamashima C (Chief, National Cancer Center), Sobue T, Saito H (National Cancer Center), Nakayama T (Osaka Medical Center for Cancer and Cardiovascular Diseases), Nakayama T (Kyoto University), Ouchi N, Tsubono Y, Endo C, Osaka K (Tohoku University), Sagawa M (Kanazawa Medical University), Aoki D (Keio University), Shibuya D (Miyagi Cancer Association), Honjo S (Omuta National Hospital), Matsuda K (Fuku Health Management Association), Ikeda S (Okayama University), Simbo T (International Medical Center).