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Review Article

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

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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).

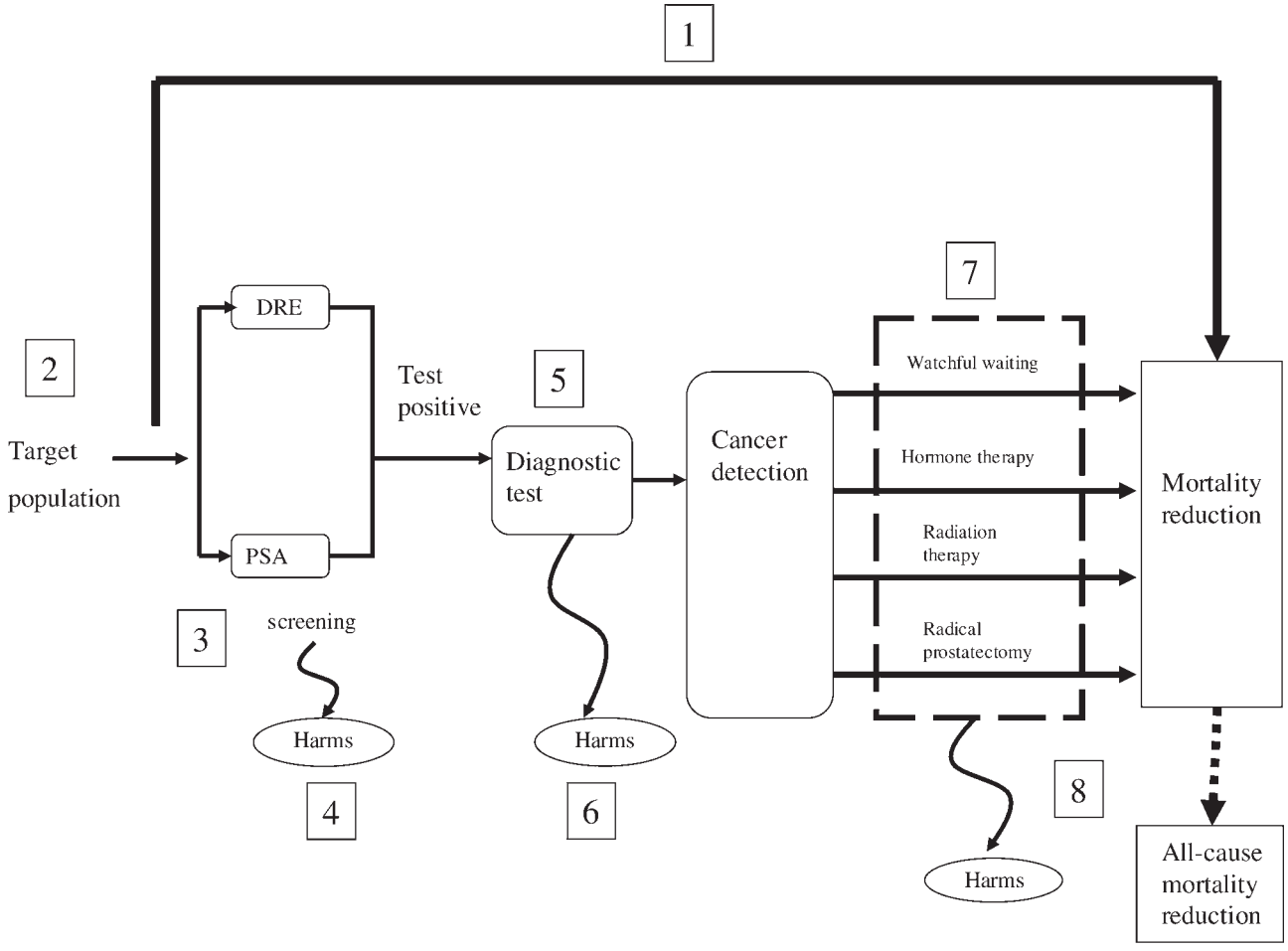

Figure 1. Analytic framework and key questions.

Systematic Literature Review

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).

Translation into Recommendations

Considering the balance of the benefits and harms, five grades of recommendations were determined for population-based and opportunistic screening (3). The recommendations were assessed in conjunction with the board members of the Japanese Research Group for Cancer Screening Guidelines. The body of evidence for each screening method was summarized in an evidence table based on the analytic framework's key questions. The benefit of each screening modality was determined based on the level of evidence (3). The evidence was divided into eight levels based on study design, quality and consistency. The harms, including overdiagnosis and complications of diagnostic tests and treatment, were assessed.

Since they are supported by sufficient evidence, both grades A and B recommendations could be conducted as both population-based and opportunistic screening programs. However, a method with a grade D recommendation should not be used for either population-based or opportunistic screening programs. A grade C recommendation implies that the method should not be used for population-based screening. However, a grade C recommendation implies that the method could be used in clinical settings if both adequate risk management and informed consent with respect to the harms were assured. Screening methods for which there is insufficient evidence are graded as I; they are not recommended for routine population-based screening or as screening methods in clinical settings, although the decision to undergo screening could be made at the individual level based on proper information provided by health professionals in clinical settings.

Formulating the Guideline

The guideline was reviewed in draft form by nine independent referees from two expert groups: an expert group for prostate cancer and another specialty group. Major issues identified during the review of the draft were discussed at a national open meeting. Taking into account the comments received, the appropriateness of the recommendation was again discussed, and the guideline was refined. After the consultations were completed, the guideline was published and posted on the Promoting Evidence-based Cancer Screening website (http://canscreen.ncc.go.jp/).

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

Table 1. Evidence for prostate cancer screening

Methods	Level of evidence	References (total numbers)	Direct evidence (AF1): disease-specific mortality reduction										Indirect evidence					
			Systematic review (meta-analysis)		RCT		Cohort study		Case–control study		Time series and ecological study		AF2	AF3	AF4		AF5, 6	AF7, 8
			Numbers of reference	Effective (significant)	Numbers of reference	Effective (significant)	Numbers of reference	Effective (significant)	Numbers of reference	Effective (significant)	Numbers of reference	Effective (significant)	Target population (high-risk group)	Test accuracy	Overdiagnosis		Needle biopsy	Treatment
DRE	2–	6	0	0	0	0	0	0	4	1	1	1	0	1				
PSA	1–/2–	67	1	0	3	1	1	0[a]	3	2	15	5	2	12[b]	6		13	10

AF, analytic framework (see Fig. 1); RCT, randomized control trial; DRE, digital rectal examination; PSA, prostate-specific antigen.
[a]Although reduction of prostate cancer mortality was shown, all-causes morality was reduced, too. Based on the results, authors concluded that the finding might suggest a screening effect, but might also be ascribed to an healthy screening effect.
[b]Reference including duplication of one reference for DRE screening.

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

Table 2. Case–control studies dealing with DRE screening

Author	Published year	Numbers (case/control)	Target age (years)	Effect of mortality reduction for prostate cancer, odds ratio (95% CI)
Friedman et al.	1991	139/139	Case: 39–95, control: 40–93	0.9 (0.5–1.7)[a]
Richert-Boe et al.	1998	150/299	40–84	0.84 (0.48–1.46)
Weinmann et al.	2004	171/342	45–84	0.70 (0.46–1.1)
Jacobsen et al.	1998	173/364	73–85[b]	0.51 (0.31–0.84)

[a]Reduction of metastatic prostate cancer relative risk (95% CI).
[b]25th–75th percentile.

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

Author	Reseach area	Reported year	Numbers of target population		Target age (years)	Screening methods	Follow-up years	Endpoint/outcomes
			Intervention group	Control group				
Labrie et al.	Canada, Quebec	2004 (1999)	31 133	15 353	45–80	PSA+DRE	11	Disease-specific mortality, RR 1.01 (95% CI 0.76–1.33)[a]
Sandblom et al.	Sweden, Norrkoping	2004	1492	7532	50–69	DRE (1987, 1990), PSA+1993, 1996)	15	Disease-specific mortality, RR 1.04 (95% CI 0.64–1.68)[a]
Aus et al.	Sweden, Gotenberg	2007	9972	9973	50–66	PSA	10	Incidence of metastatic cancer (/1000)[b], intervention group 2.4/ control 4.7 ($P = 0.008$)

[a]The results of the Quebec and Norrkoping studies were based on intention-to-screen analysis of Cochran review.
[b]Metastatic 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

Author	Published year	Research area	Target age (years)	Source population	Screening method	Definition/ numbers		Screening rate		Endpoint	Odds ratio (95% CI)
						Case	Control	Case	Control		
Nakagawa et al.	1998	Japan, 34 local municipalities	55–89	Screening participants	TRS, TRS+DRE, TRS+DRE+PSA, PSA	31	155	7/31 (23%)	69/155 (45%)	Invasive cancer (stages C and D)	0.36 (0.15–0.87)
Concato et al.	2006	USA, New England	50 and over	Cohorts receiving Veteran Affairs Care	PSA, DRE	501	501	70/501 (14%)	65/501 (13%)	Prostate cancer mortality	1.08 (0.71–1.64)[a]
Kopec et al.	2005	Canada, Ontario	40–84	Residents of metropolitan Toronto and five surrounding counties	PSA, DRE	236	462	58/236 (24.6%)	126/462 (27.3%)	Metastatic cancer	0.65 (0.45–0.93), all age[b]
								18/101 (17.8%)	57/195 (29.2%)		0.52 (0.28–0.98), 45–59 years[b]
								40/135 (29.6%)	69/267 (25.8%)		0.67 (0.41–1.09), 60–84 years[b]

TRS, transrectal sonography.
[a]Odds ratio was adjusted by races and morbidity.
[b]Odds 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 5. Overdiagnosis by prostate cancer screening

Author	Published year	Study design	Reseach area	Age (target population)	Number of target population	Result		
						Overdiagnosis	Lead time	DCPC
McGregor et al.	1998	Simulation model	Canada	50–70 years		84%		
Hugosson et al.	2000	Cohort study	Sweden	Cohort of men born in 1913	658		7 years	
				Cohort of men born in 1930 and 1931	710			
Etzioni et al.	2002	Simulation model	USA	60–84 years		White 29%, Black 44%	White 5 years, Black 7 years	
Auvinen et al.	2004		Finland	55, 59, 63 and 67 years	292		5–7 years	10–14 years
Draisma et al.	2003		The Netherlands, Rotterdam	55–74 years		55 years, 27(24–37)%	12.3 (11.6–14.1) years	
						75 years, 56 (53–61)%	6.0 (5.8–6.3) years	
						Annual screening for age 55–67 years, 50%		
Törnblom et al.	2004	Cohort study	Sweden	55–70 years screening group	946[a]		PSA >3; 4.5 years	
							PSA 3–9.9; 5.3 years	
							PSA ≤10; 3.5 years	
				Reference population (cohort of men born in 1913)	657		PSA >3; 10.7 years	
							PSA 3 – 9.9; 11.2 years	
							PSA ≤10; 3.6 years	

DCPC, detectable, preclinical phase; TRUS, transrectal ultrasonography.
[a]Biopsies were taken in cases of abnormal finding either DRE or TRUS, irrespective of their PSA level.

Table 6. Complications of biopsies

Author	Published year	Research area	Antibiotic prophylaxis	Number of patients	Complication (%)							
					Hematuria	Hematospermia	Rectal bleeding	Pain	Fever	Urinary retention	Sepsis	Patients having at least one complication
Rietbergen et al.	1997	The Netherlands, Rotterdam	Yes	1687	23.6	45.3	1.7	2.5	4.2			—
Mkinen et al.	2002	Finland	Yes	100	65	54	57	3	8			58
Horninger et al.	2005	Austria, Tyrol	Yes	6024	12.5	29.8		4.0	0.8			—
Kapoor et al.	1998	USA	Yes	242				6			1.5	10
			Yes	241				2			0.4	7
Cooner et al.	1990	USA	No	206							1	
			Yes	629							0.5	
Rodríguez et al.	1998	USA	Yes	128	47.1	9.1	8.2	13.2	1.7	9.1		63.6
Djavan et al.	2001	Austria, Belgium	Yes	1051	15.9	9.8	2.1		2.1	0.9		69.7
Raaijmakers et al.	2002	The Netherlands, Rotterdam	Yes	5802	22.6	50.4	1.3	7.5	3.5	0.4	0.4[a]	

[a]Including one case who was admitted in ICU for septic shock.

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 pubic 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 7. Complications by treatment for prostate cancer

Author	Published year	Research area	Complication (%)							
			Urinary retention	Urinary leakage	Use of pads	Frequent urination	Erectile dysfunction	Bowel dysfunction	Duration (years)	Short-term complications
Radical protectomy										
Stanford et al.	2000	USA		50.8	21.6	36.8	59.9		2	
Schover et al.	2002	USA					85		4.3	
Lu-Yao et al.	1993	USA								2% died and 8% suffered major cardiopulmonary complications[a]
Steineck et al.	2002	Sweden		49			50			
Potosky et al.	2004	USA		15.6	28.6	10.6	76.9		5	
Potosky et al.	2000	USA							5	Cardiopulmonary complications 5.5%, wound infection and/or hemorrhage 3.9%, urinary tract infection or prostatitis 5.5%, treated for urinary strictures 17.4%[b]
Madalinska et al.	2001	The Netherlands		39			>65 years, 79 ≤65 years, 86	2	1	
Talcot et al.	1998	USA		10	31.8		68.8		1	
Arai et al.	2000	Japan								Infection 7.5%, cardiopulmonary complications 2.3%, death 0.2%
Hisasue et al.	2004	Japan	13.8	12.7						Infection 25.5–8.4%[c]
External beam radiotherapy										
Potosky et al.	2004	USA		4.1	4.2	8.9	73.1		5	
Potosky et al.	2000	USA							5	Cardiopulmonary complications 1.9%, radiation proctitis 18.7%, wound infection and/or hemorrhage 0.4%, urinary tract infection or prostatitis 7.5%, treated for urinary strictures 7.2%[b]
Madalingska et al.	2001	The Netherlands		21			>65 years, 43 ≤65 years, 61	16	1	
	1998	USA		1.8	4.4		29.7		1	

[a]Complication within 30 days after radical proctectomy.
[b]Complication within 60 days after radical proctectomy.
[c]Decreased by improvement of operational procedure.

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

Table 8. Recommendation for prostate cancer screening

Screening method	Recommendation grade	Recommendations (language)	
		Population-based screening	Opportunistic screening
DRE	I	Not recommended[a]	Decision making at individual level[b]
PSA	I	Not recommended[a]	Decision making at individual level[b]

[a]There is insufficient evidence to recommend for or against.
[b]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.

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

1. Center for Cancer Control and Information Services, National Cancer Center, Japan. Cancer mortality (1959–2005). http://ganjoho.ncc.go.jp/professional/statistics/
2. Hisamichi S. Guidelines for cancer screening programs. Tokyo: Japan Public Health Association 2001 (in Japanese).
3. Hamashima C, Saito H, Nakayama T, Nakayama T, Sobue T. The standardized development method of the Japanese Guidelines for Cancer Screening. *Japan J Clinical Oncol* 2008;38:288–95.
4. ERSPC (European Randomized Study of Screening for Prostate Cancer). http://www.erspc.org/
5. PLCO?Prostate, Lung, Colorectal and Ovarian)Publications. http://prevention.cancer.gov/programs-resources/groups/ed/programs/plco
6. Harris R, Lohr KN. Screening for prostate cancer: an update of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med* 2002;137:917–29.
7. Friedman GD, Hiatt RA, Quesenberry CP, Jr, Selby JV. Case–control study of screening for prostatic cancer by digital rectal examinations. *Lancet* 1991;337:1526–9.
8. Richert-Boe KE, Humphrey LL, Glass AG, Weiss NS. Screening digital rectal examination and prostate cancer mortality: a case–control study. *J Med Screen* 1998;5:99–103.
9. Weinmann S, Richert-Boe K, Glass AG, Weiss NS. Prostate cancer screening and mortality: a case–control study (United States). *Cancer Causes Control* 2004;15:133–8.
10. Jacobsen SJ, Bergstralh EJ, Katusic SK, Guess HA, Darby CH, Silverstein MD, et al. Screening digital rectal examination and prostate cancer mortality: a population-based case–control study. *Urology* 1998;52:173–9.
11. Gilliland F, Becker TM, Smith A, Key CR, Samet JM. Trends in prostate cancer incidence and mortality in New Mexico are consistent with an increase in effective screening. *Cancer Epidemiol Biomarkers Prev* 1994;3:105–11.
12. Mistry K, Cable G. Meta-analysis of prostate-specific antigen and digital rectal examination as screening tests for prostate carcinoma. *J Am Board Fam Prac* 2003;16:95–101.
13. Labrie F, Candas B, Cusan L, Gomez JL, Belanger A, Brousseau G, et al. Screening decreases prostate cancer mortality: 11-year follow-up of the 1988 Quebec prospective randomized controlled trial. *Prostate* 2004;59:311–8.
14. Labrie F, Candas B, Dupont A, Cusan L, Gomez JL, Suburu RE, et al. Screening decreases prostate cancer death: first analysis of the 1988 Quebec prospective randomized controlled trial. *Prostate* 1999;38:83–91.
15. Sandblom G, Varenhorst E, Lofman O, Rosell J, Carlsson P. Clinical consequences of screening for prostate cancer: 15 years follow-up of a randomized controlled trial in Sweden. *Eur Urol* 2004;46:717–24.
16. Aus G, Bergdahl S, Lodding P, Lilja H, Hugosson J. Prostate cancer screening decreases the absolute risk of being diagnosed with advanced prostate cancer—results from a prospective, population-based randomized controlled trial. *Eur Urol* 2007;51:659–64.
17. Ilic D, O'Connor D, Green S, Wilt T. Screening for prostate cancer. A Cochrane database of systematic review. *Cancer Causes Control* 2007;18:279–85.
18. Ciatto S, Gervasi G, Gorini G, Lombardi C, Zappa M, Crocetti E. Prostate cancer specific mortality in the Florence screening pilot study cohort 1992–1993. *Eur J Cancer* 2006;42:1858–62.
19. Nakagawa S, Nakamura A, Watanabe H. A case–control study on the interval of mass screening for prostate cancer. *Japan J Urol* 1998;89:894–8.
20. Kopec JA, Goel V, Bunting PS, Neuman J, Sayre EC, Warde P, et al. Screening with prostate specific antigen and metastatic prostate cancer risk: a population based case–control study. *J Urol* 2005;174:495–9.
21. Concato J, Wells CK, Horwitz RI, Penson D, Fincke G, Berlowitz DR, et al. The effectiveness of screening for prostate cancer: a nested case–control study. *Arch Intern Med* 2006;166:38–43.
22. Lu-Yao G, Albertsen PC, Stanford JL, Stukel TA, Walker-Corkery ES, Barry MJ. Natural experiment examining impact of aggressive screening and treatment on prostate cancer mortality in two fixed cohorts from Seattle area and Connecticut. *BMJ* 2002;325:740.
23. Perron L, Moore L, Bairati I, Bernard PM, Meyer F. PSA screening and prostate cancer mortality. *CMAJ* 2002;166:586–91.
24. Coldman AJ, Phillips N, Pickles TA. Trends in prostate cancer incidence and mortality: an analysis of mortality change by screening intensity. *CMAJ* 2003;168:31–5.
25. La Rosa F, Stracci F, Minelli L, Mastrandrea V. Epidemiology of prostate cancer in the Umbria region of Italy: evidence of opportunistic screening effects. *Urology* 2003;62:1040–4.
26. Threlfall TJ, English DR, Rouse IL. Prostate cancer in West Australia: trends in incidence and mortality from 1985 to 1996. *Med J Aus* 1998;169:21–4.
27. Skarsgard D, Tonita J. Prostate cancer in Saskatchewan Canada, before and during the PSA era. *Cancer Cause Control* 2000;11:79–88.
28. Majeed A, Babb P, Jones J, Quinn M. Trends in prostate cancer incidence, mortality and survival in England and Wales 1971–1998. *BJU Int* 2000;85:1058–62.
29. Post PN, Kil PJ, Crommelin MA, Schapers RF, Coebergh JW. Trends in incidence and mortality rates for prostate cancer before and after prostate-specific antigen introduction. A registry-based study in Southeastern Netherlands, 1971–1995. *Eur J Cancer* 1998;34:705–9.

30. Brewster DH, Fraser LA, Harris V, Black RJ. Rising incidence of prostate cancer in Scotland: increased risk or increased detection? *BJU Int* 2000;85:463–73.
31. Roberts RO, Bergstralh EJ, Katusic SK, Lieber MM, Jacobsen SJ. Decline in prostate cancer mortality from 1980 to 1997, and an update on incidence trends in Olmsted Country. *Minn J Urol* 1999;161:529–33.
32. Shaw PA, Etzioni R, Zeliadt SB, Mariotto A, Karnofski K, Penson DF, et al. An ecologic study of prostate-specific antigen screening and prostate cancer mortality in nine geographic areas of the United States. *Am J Epidemiol* 2004;160:1059–69.
33. Jemal A, Ward E, Wu X, Martin HJ, McLaughlin CC, Thun MJ. Geographic patterns of prostate cancer mortality and variations in access to medical care in the United States. *Cancer Epidemiol Biomarkers Prev* 2005;14:590–5.
34. Baade PD, Coory MD, Aitken JF. International trends in prostate-cancer mortality: the decrease is continuing and spreading. *Cancer Causes Control* 2004;15:237–41.
35. Oberaigner W, Horninger W, Klocker H, Schonitzer D, Stuhlinger W, Bartsch G. Reduction of prostate cancer mortality in Tyrol, Austria, after introduction of prostate-specific antigen testing. *Am J Epidemiol* 2006;164:376–84.
36. Vutuc C, Schernhammer ES, Haidinger G, Waldhor T. Prostate cancer and prostate-specific antigen (PSA) screening in Austria. *Wien Klin Wochenschr* 2005;117:457–61.
37. Labrie F, Dupont A, Suburu R, Cusan L, Tremblay M, Gomez JL, et al. Serum prostate specific antigen as pre-screening test for prostate cancer. *J Urol* 1992;147:846–52.
38. Stenman UH, Hakama M, Knekt P, Aromaa A, Teppo L, Leinonen J. Serum concentrations of prostate specific antigen and its complex with alpha 1-antichymotrypsin before diagnosis of prostate cancer. *Lancet* 1994;344:1594–8.
39. Imai K, Ichinose Y, Kubota Y, Yamanaka H, Sato J. Diagnostic significance of prostate specific antigen and the development of a mass screening system for prostate cancer. *J Urol* 1995;154:1085–9.
40. Jacobsen SJ, Bergstralh EJ, Guess HA, Katusic SK, Klee GG, Oesterling JE, et al. Predictive properties of serum-prostate-specific antigen testing in a community-based setting. *Arch Intern Med* 1996;156:2462–8.
41. Ito K, Yamamoto T, Kubota Y, Suzuki K, Fukabori Y, Kurokawa K, et al. Usefulness of age-specific reference range of prostate-specific antigen for Japanese men older than 60 years in mass screening for prostate cancer. *Urology* 2000;56:278–82.
42. Hakama M, Stenman UH, Aromaa A, Leinonen J, Hakulinen T, Knekt P. Validity of the prostate specific antigen test for prostate cancer screening: follow up study with a bank of 21,000 sera in Finland. *J Urol* 2001;166:2189–92.
43. van der Cruijsen-Koeter IW, van der Kwast TH, Schroder FH. Interval carcinomas in the European Randomized Study of Screening for Prostate Cancer (ERSPC)—Rotterdam. *J Natl Cancer Inst* 2003;95:1462–6.
44. Auvinen A, Maattanen L, Finne P, Stenman UH, Aro J, Juusela H, et al. Test sensitivity of prostate-specific antigen in the Finnish randomized prostate cancer screening trial. *Int J Cancer* 2004;111:940–3.
45. McLernon DJ, Donnan PT, Gray M, Weller D, Sullivan F. Receiver operating characteristics of the prostate specific antigen test in an unselected population. *J Med Screen* 2006;13:102–7.
46. Postma R, van Leenders AG, Roobol MJ, Schroder FH, van der Kwast TH. Tumor features in the control and screening arm of a randomized trial of prostate cancer. *Eur Urol* 2006;50:70–5.
47. Kubota Y, Ito K, Imai K, Yamanaka H. Effectiveness of mass screening for the prognosis of prostate cancer patients in Japanese communities. *Prostate* 2002;50:262–9.
48. McGregor M, Hanley JA, Boivin JF, McLean RG. Screening for prostate cancer: estimating the magnitude of overdetection. *CMAJ* 1998;159:1368–72.
49. Hugosson J, Aus G, Becker C, Carlsson S, Eriksson H, Lilja H, et al. Would prostate cancer detected by screening with prostate-specific antigen develop into clinical cancer if left undiagnosed? A comparison of two population-based studies in Sweden. *BJU Int* 2000;85:1078–84.
50. Etzioni R, Penson DF, Legler JM, di Tommaso D, Boer R, Gann PH, et al. Overdiagnosis due to prostate-specific antigen screening: lessons from U.S. prostate cancer incidence trends. *J Natl Cancer Inst* 2002;94:981–90.
51. Auvin A, Maattanen L, Stenman UH, Tammela T, Rannikko S, Aro J, et al. Lead-time in prostate cancer screening (Finland). *Cancer Causes Control* 2002;13:279–85.
52. Draisma G, Boer R, Otto SJ, van der Cruijsen IW, Damhuis RA, Schroder FH, et al. Lead times and overdetection due to prostate-specific antigen screening: estimates from the European Randomized Study of Screening for Prostate Cancer. *J Natl Cancer Inst* 2003;95:868–78.
53. Törnblom M, Eriksson H, Franzen S, Gustafsson O, Lilja H, Norming U, et al. Lead time associated with screening for prostate cancer. *Int J Cancer* 2004;108:122–9.
54. Rietbergen JB, Kruger AE, Kranse R, Schröder FH. Complications of transrectal ultrasound-guided systematic sextant biopsies of the prostate: evaluation of complication rates and risk factors within a population-based screening program. *Urology* 1997;49:875–80.
55. Mkinen T, Auvinen A, Hakama M, Stenman UH, Tammela TL. Acceptability and complications of prostate biopsy in population-based PSA screening versus routine clinical practice: a prospective, controlled study. *Urology* 2002;60:846–50.
56. Horninger W, Berger A, Pelzer A, Klocker H, Oberaigner W, Schonitzer D, et al. Screening for prostate cancer: updated experience from the Tyrol study. *Can J Urol* 2005;12(Suppl 1):7–13.
57. Kapoor DA, Klimberg IW, Malek GH, Wegenke JD, Cox CE, Patterson AL, et al. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. *Urology* 1998;52:552–8.
58. Cooner WH, Mosley BR, Rutherford CL, Jr, Beard JH, Pond HS, Terry WJ, et al. Prostate cancer detection in a clinical urological practice by ultrasonography, digital rectal examination and prostate specific antigen. *J Urol* 1990;167:966–75.
59. Rodríguez LV, Terris MK. Risks and complications of transrectal ultrasound guided prostate needle biopsy: a prospective study and review of the literature. *J Urol* 1998;160:2115–20.
60. Djavan B, Waldert M, Zlotta A, Dobronski P, Seitz C, Remzi M, et al. Safety and morbidity of first and repeat transrectal ultrasound guided prostate needle biopsies: results of a prospective European prostate cancer detection study. *J Urol* 2001;166:856–60.
61. Raaijmakers R, Kirkels WJ, Roobol MJ, Wildhagen MF, Schrder FH. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based screening program. *Urology* 2002;60:826–30.
62. Crawford ED, Haynes AL, Jr, Story MW, Borden TA. Prevention of urinary tract infection and sepsis following transrectal prostatic biopsy. *J Urol* 1982;127:449–51.
63. Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study. *BJU Int* 2000;85:682–5.
64. Norberg M, Holmberg L, Häggman M, Magnusson A. Determinants of complications after multiple transrectal core biopsies of the prostate. *Eur Radiol* 1996;6:457–61.
65. Kumagai A, Ogawa D, Koyama T, Takeuchi I, Ohama I. A case report of fournier's gangrene in a diabetic patient induced by transrectal prostate biopsy (TRPB). *Jpn J Urol* 2002;93:648–51.
66. Hasegawa T, Siomura T, Yamada H, Ito H, Katao N, Hasegawa M, et al. Fatal septic shock caused by transrectal needle biopsy of the prostate; a case report. *Jn J Inf* 2002;76:893–7.
67. Stanford JL, Feng Z, Hamilton AS, Gilliland FD, Stephenson RA, Eley JW, et al. Urinary and sexual function after radical prostatectomy for clinically localized prostate cancer: the Prostate Cancer Outcomes Study. *JAMA* 2000;283:354–60.
68. Schover LR, Fouladi RT, Warneke CL, Neese L, Klein EA, Zippe C, et al. The use of treatments for erectile dysfunction among survivors of prostate carcinoma. *Cancer* 2002;95:2397–407.
69. Lu-Yao GL, McLerran D, Wasson J, Wennberg JE. An assessment of radical prostatectomy. Time trends, geographic variation, and outcomes. The Prostate Patient Outcomes Research Team. *JAMA* 1993;269:2633–6.
70. Steineck G, Helgesen F, Adolfsson J, Dickman PW, Johansson JE, Norlén BJ, et al. Quality of life after radical prostatectomy or watchful waiting. *N Engl J Med* 2002;347:790–6.
71. Potosky AL, Davis WW, Hoffman RM, Stanford JL, Stephenson RA, Penson DF, et al. Five-year outcomes after prostatectomy or radiotherapy for prostate cancer: the Prostate Cancer Outcomes Study. *J Natl Cancer Inst* 2004;96:1358–67.

72. Potosky AL, Legler J, Albertsen PC, Stanford JL, Gilliland FD, Hamilton AS, et al. Health outcomes after prostatectomy or radiotherapy for prostate cancer: results from the Prostate Cancer Outcomes Study. *J Natl Cancer Inst* 2000;92:1582–92.
73. Madalinska JB, Essink-Bot ML, de Koning HJ, Kirkels WJ, van der Maas PJ, Schröder FH. Health-related quality-of-life effects of radical prostatectomy and primary radiotherapy for screen-detected or clinically diagnosed localized prostate cancer. *J Clin Oncol* 2001;19: 1619–28.
74. Talcott JA, Rieker P, Clark JA, Propert KJ, Weeks JC, Beard CJ, et al. Patient-reported symptoms after primary therapy for early prostate cancer: results of a prospective cohort study. *J Clin Oncol* 1998;16:275–83.
75. Arai Y, Egawa S, Tobisu K, Sagiyama K, Sumiyoshi Y, Hashine K, et al. Radical retropubic prostatectomy: time trends, morbidity and mortality in Japan. *BJU Int* 2000;85:287–94.
76. Hisasue S, Takahashi A, Kato R, Shimizu T, Masumori N, Itoh N, et al. Early and late complications of radical retropubic prostatectomy: experience in a single institution. *Jpn J Clin Oncol* 2004;34:274–9.
77. Schröder FH, Habbema DF, Roobol MJ, Bangma CH. Prostate cancer in the Swedish section of ERSPC—evidence for less metastases at diagnosis but not for mortality reduction. *Eur Urol.* 2007;51:588–90.
78. US Preventive Services Task Force. Screening for prostate cancer: U.S. Preventive Services Task Force. *Ann Intern Med* 2002;137:917–29.
79. Lin K, Lipsitz R, Miller T, Janakiraman S. Benefits and harms of prostate-specific antigen screening for prostate cancer: an evidence update for the U.S. Preventive Services Task Force. *Ann Intern Med* 2008;149:192–9.
80. Lim LS, Sherin K, the ACPM Prevention Practice Committee. Screening for prostate cancer in U.S. men ACPM position statement on preventive practice. *Am J Prev Med.* 2008;34:164.
81. Ministry of Labour and Health. Cancer Screening Committee. Report for implementations and fund for cancer screening programs in local municipalities; 2007 (in Japanese).
82. Mettlin C. Impact of screening on prostate cancer rates and trends. *Microsc Res Tech* 2000;51:415–8.
83. Legler JM, Feuer EJ, Potosky AL, Merrill RM, Kramer BS. The role of prostate-specific antigen (PSA) testing patterns in the recent prostate cancer incidence decline in the United States. *Cancer Causes Control* 1998;9:519–27.
84. Potosky AL, Feuer EJ, Levin DL. Impact of screening on incidence and mortality of prostate cancer in the United States. *Epidemiol Rev* 2001;23:181–6.
85. Matsuda T, Saika K. Comparison of time trends in prostate cancer incidence (1973–1997) in East Asia, Europe and USA, from cancer incidence in five continents. *Jpn J Clin Oncol* 2007;37:556–7.
86. Smith RA, Cokkinides V, Eyre HJ. Cancer screening in the United States, 2007: a review of current guidelines, practices, and prospects. *CA Cancer J Clin* 2007;57:90–104.
87. American Urological Association. Prostate-specific antigen (PSA) best practice policy. *Oncology* 2000;14:267–86.
88. Ito K, Kakehi Y, Naito S, Okuyama A. Japanese Urological Association guidelines on prostate-specific antigen-based screening for prostate cancer and the ongoing cluster cohort study in Japan. *Int J Urol* 2008;15:763–8.
89. Heidenreich A, Aus G, Michel Bolla M, Joniau S, Matveev VB, Schmid HS, et al. EAU Guidelines on Prostate Cancer. *Eur Urol* 2008;53:68–80.
90. Selley S, Donovan J, Faulkner A, Coast J, Gillatt D. Diagnosis, management and screening of early localized prostate cancer. *Health Technol Assess* 1997;1:19–23.
91. NHS National Cancer Screening Programmes. Prostate Cancer Risk Management. http://www.cancerscreening.nhs.uk/prostate/index.html.
92. European Code Against Cancer third edition. http://www.cancercode.org/add_items.htm
93. Schersten T, Baile A, Asua J, Jonsson E. *Prostate Cancer Screening: Evidence Synthesis and Update Statements of Findings*. INAHTA: International Network of Agencies for Health Technology Assessment. http://inahta.episerverhotell.net/Publications/Joint-Synthesis/2314/ 1999.

Appendix

Peer Review Committee for the Japanese Prostate Cancer Screening Guideline

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