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Quality-of-life effects of prostate-specific antigen screening

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Abstract

Background—The European Randomized Study of Screening for Prostate Cancer (ERSPC) reported a 29% prostate cancer mortality reduction among screened men after 11 years. However, it is uncertain to what extent harms from overdiagnosis and treatment on quality of life counterbalance this benefit.

Methods—Based on ERSPC follow-up data, we used micro-simulation modeling (MISCAN) to predict the number of prostate cancers, treatments, deaths and quality-adjusted life-years (QALYs) gained following the introduction of screening. Various screening strategies, efficacies, and quality of life assumptions were modeled.

Results—Per 1,000 men of all ages followed for their entire lifespan we predicted for annual screening from age 55–69 years: 9 fewer deaths due to prostate cancer (28% reduction), 14 fewer men receiving palliative therapy (35% reduction), and 73 life-years gained (average 8.4 years per prostate cancer death avoided). QALYs gained were 56 (range: −21, 97), a reduction of 23% from unadjusted life-years gained. The number needed to screen (NNS) was 98 and number needed to detect (NND) 5. Also inviting men aged 70–74 resulted in more life-years (82) but similar QALYs (56).

Conclusions—Although NNS and NND are more favorable than previously calculated, the benefit of PSA screening is diminished by loss of QALYs, that is dependent primarily on post-diagnosis long-term effects. Longer follow-up data from both the ERSPC and quality of life are essential before making universal recommendations regarding screening.

Introduction

The initial results of the European Randomized Study of Screening for Prostate Cancer (ERSPC) showed a significant prostate cancer mortality reduction in the screening group of 20% after a median follow-up of nine years, and of 27% in screened men when adjusted for selection bias.[1] The results have recently been updated, resulting after 11 years in a prostate cancer mortality reduction of 29% in men screened when adjusted for selection bias.[2] The Gothenburg trial, one center of the ERSPC, reported a prostate cancer mortality reduction of 44% after a median follow-up of 14 years and a 56% reduction for men screened at least once.[3] The U.S. Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial found no mortality reduction in the screening group, however the rate of contamination was high and biopsy compliance low.[4]

Prostate cancer mortality reduction, life-years gained and a reduction of advanced disease are obvious benefits of screening. However, PSA screening is associated with considerable unfavorable effects. In the ERSPC screening group, the cumulative incidence of prostate cancer was 7.4%, versus 5.1% in the control group[2]. A proportion of the screen-detected tumors (10–56%) would never have led to clinical symptoms[5–8] but these overdiagnosed cancers are frequently treated nonetheless with associated risks of adverse effects.[9] Furthermore, because of a long lead-time, estimated at 5–12 years[6, 10], men have to live longer with those effects.

Reports on the harms and benefits of PSA screening are highly inconsistent due to the lack of results from randomized screening trials.[11, 12] However, as more mature data from the ERSPC are available, for the first time realistic predictions of the effects of screening can be made. Therefore, this study quantifies the effects of screening strategies on prostate cancer mortality and quality of life, using a model based on data from the ERSPC. In addition, we have determined the harms and benefits for a range of treatment, mortality reductions and screening scenarios.

Methods

ERSPC data

The ERSPC was initiated in the early 1990s to evaluate the effect of PSA screening on prostate cancer mortality[13]. In seven countries, 162,243 men were randomized. Most centers used a PSA cutoff value of 3.0 ng/mL as an indication for biopsy, others used 4.0 ng/mL, with additional tests for values between 2.5 and 4.0. The screening interval was 4 years, with the exception of Sweden (2 years). Treatment was performed according to local policies and guidelines, independent of trial arm[14]. In line with the protocol, the effect of screening in the core age group (55–69 years) was evaluated. Follow-up data on mortality until 31 December 2008 are currently available[2].

We used Microsimulation Screening Analysis (MISCAN) to extrapolate the results to alternative screening strategies and an extended follow-up.

Screening strategies

A population of men aged 0–100 years was simulated with an age distribution according to the European Standard Population.[15] The following screening strategies were simulated: annual screening in the age groups 55–69 years and 55–74 years, screening at 4-year intervals between 55–69, and single screens performed either at age 55, 60 or 65 years. An 80% participation proportion was assumed.

Quality of life

Quality-adjusted life-years (QALYs) were predicted using utility estimates for various health states. The utility estimates were obtained from the CEA Registry[16] and literature (Table 1) and ranged from 0 (death or worst imaginable health) to 1 (full health). In addition, data from ERSPC on treatment-related complications as urinary incontinence, bowel dysfunction and erectile dysfunction were analyzed. Favorable and unfavorable values were assigned according to the minimum and maximum values in the cited references. A utility estimate of 0.99 was used for the screening phase, because prostate cancer screening has little effect on short-term health status and anxiety.[17] The health states of men receiving treatment were divided into 2 months of treatment, an intermediate period (10 months of recovery from treatment), and a post-recovery period (1–10 years after treatment). Utility estimates for this post-recovery period were obtained by combining the percentage of men with side-effects from the treatment[18] with the utility estimates for those side-effects.[19] This led to a utility estimate of 0.95 for all men during the period 1–10 years after diagnosis and after receiving radical prostatectomy or radiation therapy. The loss in quality of life was calculated by multiplying the loss in utility by the duration of the health state and the number of men in that state as predicted by MISCAN.

The MISCAN model

MISCAN was used to model prostate cancer screening.[5, 6] This model simulates individual life histories stochastically. The natural history of prostate cancer starts with a transition from ‘no prostate cancer’ to preclinical screen-detectable prostate cancer in a subset of the population. From each preclinical stage, the tumor may become screen detected, clinically diagnosed, or progress into a more advanced preclinical stage.

In the model, prostate cancers were characterized according to their clinical T-stage (T1 impalpable, T2 palpable, confined to the prostate and T3+ palpable, with extension beyond the prostatic capsule), differentiation grade (Gleason score ≤7, 7, or ≥7) and metastatic stage (locoregional or distant). The parameters for the natural history of the disease and for stage-specific test sensitivities (0.82–0.98 depending on clinical T-stage and Gleason score) were first estimated using incidence in the Dutch population during 1992–2002 (a period with limited opportunistic screening)[20] and using age and stage distributions from the Rotterdam and Gothenburg sections of the ERSPC, being the largest centers, that varied in randomization, recruitment and screening interval. In a second phase, this model was

validated using screen data from all centers. The model and calibration methods and results are described in the Appendix.

Treatment assignment for locoregional cases in MISCAN was based on the age-, stage- and Gleason score-specific primary treatments (radiation therapy, radical prostatectomy and active surveillance) assigned in both arms of the ERSPC. All men with metastases and all men dying of prostate cancer were assumed to receive palliative treatment. The proportion of men receiving treatment within 7 years after having started using active surveillance was based on recent data.[21]

Survival of unscreened men diagnosed with locoregional prostate cancer was modeled using Gleason score-specific survival curves.[22] These data are from a large unscreened cohort, followed for a median period of 24 years, and the data are available by age, stage and grade. For distant disease, survival curves were based on SEER data. The effects of treatment were modeled by assuming a relative risk of dying from prostate cancer of 0.65 for radical prostatectomy[23] compared with watchful waiting. This effect was also assumed for radiation therapy.

A proportion of the screen-detected men with a locoregional cancer will be cured. In the base model, this stage-dependent cure proportion was estimated by calibrating to a prostate cancer mortality reduction of 29% after 11 years follow-up of screening at 4-year intervals for men who attended at least one screen, corresponding to the ERSPC[2]. This estimated cure proportion was used as an input to the model. Cure proportions were also estimated for hypothetical prostate cancer mortality reductions of 31% (estimated reduction adjusted for noncompliance and contamination),[24] 35% and 39% (the intended reduction to reach of the trial in the Gothenburg center) after nine years follow-up, and of 56% after 14 years follow-up (the Gothenburg trial)[3]. In the model, all screened men with prostate cancer who are cured will die from other causes at the time they would have died had they not had prostate cancer. The screened men who are not cured from prostate cancer will die at the same moment as they would have if they had not been screened. The effects of screening were calculated from 2010 until 2110, when all men will have died.

This study was designed by Heijnsdijk and de Koning. ERSPC data were gathered by each individual center and analyzed by the epidemiology committee led by Moss. Modeling was performed by Heijnsdijk, Wever, Draisma and de Koning. Quality of life data were provided by Carlsson and Korfage. The first draft was written by Heijnsdijk, with all co-authors participating in several revisions and the decision to publish the manuscript. There were no agreements concerning confidentiality of the data between the sponsors and the authors or the institutions.

Results

Quality of life following treatment

Two specific studies on quality of life after prostate cancer treatment have been performed for men participating in Rotterdam and Sweden[9, 25]. Pre-operatively 1–2% of the men were incontinent and 31–40% were impotent. After 18–52 months 6–16% of the radical

prostatectomy patients and 3% of the radiation therapy patients were incontinent (Table 2). Six to 52 months after a radical prostatectomy, 83–88% of pre-operatively potent men became impotent, compared with 42–66% of the men receiving radiation therapy. In general, screen detected men had fewer complaints postoperatively than clinically detected men (Appendix Table S4). This difference could be a result of aging, due to later diagnosis in the unscreened group. These ERSPC data are consistent with data from a large international cohort (Appendix Figure S7).

Predicted effects of annual screening at 55–69 years (base model)

The number of men experiencing each of the various health states in both the absence and presence of annual screening was modeled over the lifetime of 1,000 men (Table 3). The number of life-years and QALYs gained or lost as a result of the differences between the numbers of men experiencing each health state were also calculated. The model predicted that a total of 73 life-years would be gained through the introduction of annual screening. The number of prostate cancer diagnoses was predicted to increase by screening from 112 cases to 157 cases (40% increase). The number of prostate cancer deaths was predicted to decrease from 31 to 22 (28% decrease), and the number of men receiving palliative care was predicted to decrease from 40 to 26 (35% reduction). The total number of life-years gained per prostate cancer death avoided was 8.4 years (73/9). Among screened men, there was a 37% prostate cancer mortality reduction over the entire lifetime (Table 4).

The predicted adverse effects of screening were 247 additional negative biopsies and 41 additional men receiving radical prostatectomy or radiation therapy. The model predicted a gain of 56 QALYs (range: −21, 97), which means that (73–56)/73 = 23% of the unadjusted life-years gained would be counterbalanced by loss in quality of life. This loss was primarily attributable to the short and long-term effects of primary treatment and a longer post-recovery period with side effects.

The number of QALYs predicted to be gained in the base model was also calculated in sensitivity analyses considering various assumptions for overdiagnosis, screening attendance, and utility estimates (Figure 1). A hypothetical situation without overdiagnosis was predicted to yield a gain of 79 QALYs. Screening attendance ranging from 50–100% was predicted to produce a gain of 30–60 QALYs (23% adjusted of 39 and 78 life-years gained, respectively). The most favorable utility estimates resulted in 97 QALYs gained, and the least favorable in 21 QALYs lost. The utility estimate for the post-recovery period had a considerable impact. If no loss in utility in this period was assumed, screening resulted in 72 QALYs gained, whereas a utility estimate of 0.93 instead of 0.95 for the remaining life-time resulted in 6 QALYs gained. A utility estimate of 0.95 during the first 5, 7, or 15 years after diagnosis in combination with no loss in utility after that period resulted in a gain of 66, 62 and 47 QALYs, respectively (results not shown in graph). Other utility estimates besides those for the post-recovery period and for palliative therapy had minor impact on the results.

In the base model, 104 cancers were screen detected, and 45 (43%) of these were overdiagnosed (Table 4). Overdiagnosed cancers are screen-detected cancers that would not have become clinically diagnosed during a person’s lifetime in the absence of screening. The prostate cancer mortality reduction in a steady state (20 years after the start of screening) for

men who attended at least one screening was estimated at 37%. The predicted number of men needed to screen (NNS) to prevent one prostate cancer death was 98 (845/9), and the number of men needed to detect (NND) to prevent one prostate cancer death was 5 (45/9).

The predicted effects of various cure rates, based on various mortality reductions are described in the Appendix.

Predicted effects of screen strategies

Extending the screening age to 74 years resulted in an overall gain of 82 life-years and an increase in the number of prostate cancer deaths prevented from 9 to 11 (Table 4). However, the model predicts that only 56 QALYs (range: −47, 111) would be gained, representing a 32% reduction in unadjusted life-years. This reduction in quality of life is mainly due to the large number of overdiagnosed cases (48% of the screen detected cancers) and the 372 additional negative biopsies that would occur. On the other hand, the NNS was more favorable (84) compared with screening up to age 69.

Screening at 4-year intervals at age 55–69 years led to a gain of 52 life-years and 41 QALYs (range: −10, 69). There was a steady-state prostate cancer mortality reduction of 21% and the NNS was 129.

A single screen at age 55, 60, or 65 resulted in the detection of fewer cancers but also in less overdiagnosis. The steady-state prostate cancer mortality reduction was 27–31% and the life-years gained ranged from 12–25. The NNS for a single screen at 55, 60, or 65 years of age were 490, 249, and 186, respectively.

Discussion

Weighing the balance between the benefits and harms of prostate cancer screening is essential for decision-making regarding screening at both individual and policy level. Our model predicts that there would be 9 fewer prostate cancer deaths and 73 life-years gained over the lifetime of 1,000 men using annual screening between the ages of 55–69 years. The harms caused by the introduction of such screening would be the overdiagnosis and overtreatment of 45 cases, and the loss of 1,134 prostate cancer–free life-years (lead time years). Adjusting the number of life-years gained from screening by consideration of quality of life effects showed that 56 QALYs would be gained, which is a 23% reduction from the predicted number of life-years gained.

We used a one-year screening interval in the base runs to comply with existing practice in the USA, however, the conclusions are comparable with a 4-year interval.

The NNS (98) and NND (5) predicted in the base model are more favorable than reported in the earlier results of the ERSPC (1068 and 48, respectively).[1] The Gothenburg trial reported a NNS of 293 and a NND of 12 at 14 years follow-up.[3] Our model predicts long-term effects after a much longer period. After eleven years, the cumulative incidence of prostate cancer in the ERSPC screening group far exceeded that in the control group (9.7 versus 6.0 per 1000 person-years); however, the control group will partly catch-up because of the lead-time, and therefore the absolute difference between the groups will decrease. In addition, the

absolute difference in prostate cancer deaths is likely to increase over time, reducing the NNS and the NND.

A substantial part of the predicted difference between life-years and QALYs gained is caused by overdiagnosed cancers. The proportion of overdiagnosed cases (42% of the screen-detected cancers) predicted in the base model is comparable to previous studies.[6] Strategies to reduce overdiagnosis would seem to be necessary before screening can be generally advocated. Distinguishing indolent cancers from aggressive cancers, will be crucial.[26, 27] More active surveillance, and deferring treatment until early signs of disease progression may also increase the QALYs gained.[28, 29]

The optimal screening strategy can also depend on co-morbidity status. In our model we used general life tables for other cause mortality and therefore the distribution of co-morbidity was that of a general population. We can roughly estimate the effect of co-morbidity by adjusting the life tables. For example for men of 65 having the life expectancy of men of 62 (low co-morbidity), annual screening from age 55–69 resulted in 93 life years gained and 80 QALYs gained (an adjustment of 14%) and annual screening until age 75 resulted in 108 life years gained and 86 QALYs gained (an adjustment of 20%). Therefore, screening until age 75 in men with low co-morbidity has approximately the same adjustment for quality of life as screening until age 69 in the general population.

The 23% predicted reduction in life-years gained due to quality of life effects is higher than the 8% estimated for breast cancer screening.[30] In addition to cancer deaths avoided, screening for breast cancer allows the use of less radical treatment (e.g. lumpectomy vs. mastectomy) in early detected cancers, whereas screening for prostate cancer leads to a substantial increase in treatments, especially when active surveillance strategy for indolent disease is not embraced. Also, an average of 15 life-years are gained per breast cancer death prevented while (due to older age at diagnosis and shorter life expectancy among men) only 8.4 life-years are gained per prostate cancer death prevented.

The predicted adjustment for quality of life is due to the long-term side-effects from treatment. Both over-diagnosed and non-overdiagnosed men will live many years with adverse effects of treatment. For example, in the post-recovery period, 5 life-years were adjusted for the non-overdiagnosed men and 11 life-years for the overdiagnosed men. How these side-effects influence the long-term quality of life is not well studied. Most side-effects affecting the urinary tract and bowel will improve after some years, but significant symptoms persist in many patients up to 5 years after treatment.[18, 31, 32] Although patients can adapt to these effects,[33, 34] partly because they consider themselves cured from a life-threatening disease (though they could be overdiagnosed), they still report lower physical functioning 5–10 years after treatment than a control group of similar age[31, 35, 36]. The results from a study of the urinary, bowel and sexual function over time after radical prostatectomy and radiation therapy, measured within the ERSPC have been compared with one of the largest studies outside the ERSPC[37] (Appendix). General patterns are similar: there is an improvement in function over time until a level slightly lower than baseline is reached (Appendix Figure S7). A published analysis used a decremented post-treatment

utility for life-time[38]. In our base model we used a utility estimate of 1 for the time period more than ten years after diagnosis, assuming improvement of symptoms.

One limitations of our model is that some of the utility estimates used in the present analysis are based on studies performed in the USA and these may not be representative for Europe. Also, no corrections in utility estimates were made for the detection mode (screen or clinically detected),[34] for the individual baseline quality of life level[39], or for improvements in treatments, due to lack of detailed data. It is obvious that decreasing long-term morbidity from treatment is another important goal. However, the perceived effect of treatment on quality of life is subjective. Therefore general recommendations regarding screening do not necessarily apply to the individual.

Another limitation is that we used different datasets to develop the model. We used data from the ERSPC to estimate the parameters that are directly related with screening, or that can only be estimated from such data. For other parameters other sources were more appropriate, because of more extensive populations, more recent data or longer follow-up. We mostly used data from Rotterdam and Gothenburg, because these two large centers have different screening intervals and recruitment and therefore this variation is reflected in the model. Also, the stage distributions match well those of the entire ERSPC and they cover the entire age range. No important differences were found when PSA test sensitivities in Finland, Sweden, and the Netherlands were compared.[40]

We assumed similar effects of radiation treatment as of radical prostatectomy. No clinical trials have directly compared radical prostatectomy with radiation therapy, although some studies have shown a mortality benefit for radical prostatectomy over radiation therapy[41, 42]. Assuming a relative risk of dying of 0.7 for radiation treatment would lead to an increase in the number of QALYs of a few percent.

In the Netherlands, men have a lifetime risk of prostate cancer death of 3.5%. When screening reduces this probability with 30%, this means that 1 per 100 men would die less. This difference is too small to become statistically significant in all-cause mortality in the trial, but indeed would have an impact when screening nationwide.

The next step should be calculating the cost-effectiveness of screening. However, to find the optimal screening strategy, more screening scenarios than the ones presented in this paper should be simulated, including various intervals, starting and stopping ages, and intervals varying by age.

In conclusion, this study quantifies how much of the benefit with the currently reported overall prostate cancer mortality reduction within ERSPC must be adjusted when the harms are taken into consideration. It is essential to await longer follow-up data from the ERSPC, as well as longer-term data on how treatment and active surveillance effects long-term quality of life before more general recommendations could be made regarding mass screening with PSA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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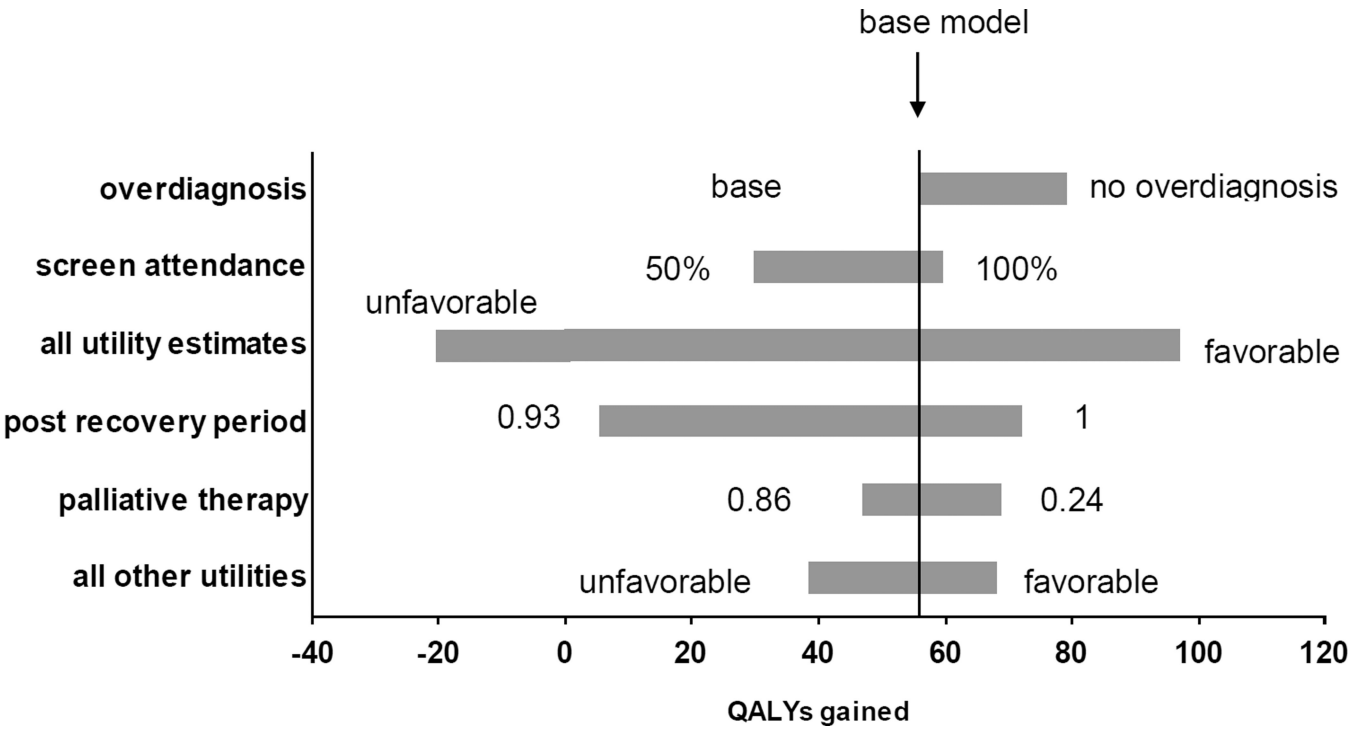

Figure 1. Effect of various modeling assumptions on QALYs gained in comparison with the base model (56 QALYs gained)

The assumptions are: 1) no overdiagnosis, 2) screen attendance of 50% and 100%, 3) all unfavorable and favorable utility estimates, 4) utility estimate of 0.93 and 1 for the life-time post-recovery period, 5) utility estimate of 0.86 and 0.24 for palliative therapy, and 6) the utility estimates for the post-recovery period (0.95) and palliative therapy (0.6) as used in the base model combined with the unfavorable and favorable utility estimates of all other health states.

Table 1

Base, favorable (fav.) and unfavorable (unfav.) utility estimates and durations for each health state.

Health state	Utility estimate			Source of utility estimate	Duration	Source of duration
	base	fav.	unfav.			
Screening attendance	0.99	1	0.99	[17, 30]	1 week	Assumption
Biopsy	0.90	0.94	0.87	[30]	3 weeks	Assumption
Diagnosis	0.80	0.85	0.75	based on[43]	1 month	Assumption
Radiation therapy (RT)	0.73	0.91	0.71	[19]	2 months	[19]
Radical prostatectomy (RP)	0.67	0.9	0.56	[19]	2 months	[19]
Active surveillance	0.97	1	0.85	[44–46]	7 years	[47]
2 months – 1 year RT	0.78	0.88	0.61	[48]	10 months	[18]
2 months – 1 year RP	0.77	0.91	0.70	[49]	10 months	[18]
Post-recovery period	0.95	1	0.93	[18, 19]	9 years *	Assumption
Palliative therapy	0.60	0.24	0.86	[50–53]	30 months	[54]
Terminal illness	0.40	0.24	0.40	[50, 52, 53]	6 months	[52, 53]

*The duration of the post-recovery period used for the sensitivity analysis was the residual life-time[38]

Table 2

Frequencies of incontinence and erectile dysfunction in prostate cancer patients at two ERSPC centers at different time points

	Treatment	Pre-operatively	6 months	12 months	18 months	52 months
Incontinence						
Regular daytime use of pads (Gothenburg[25])	Radical Prostatectomy n = 294	1%			16%	
Every day urinary leakage and use of 3 or more pads per day (Rotterdam[9])	Radical Prostatectomy n = 127	2%	16%	7%		6%
	Radiation Therapy n = 187	1%	1%	1%		3%
Erectile dysfunction *						
No sexual activity or impotent (Gothenburg[25])	Radical Prostatectomy n = 294	32%			83%	
Sexually active and erectile dysfunction or sexually inactive because of erectile dysfunction (Rotterdam[9])	Radical Prostatectomy n = 127	31%	88%	88%		88%
	Radiation Therapy n = 187	40%	42%	43%		66%

* The post-operative scores for erectile dysfunction represent men having normal pre-operative erectile function.

Table 3

Predicted number of men and life-years per health state comparing annual screening in men aged 55–69 years with no screening. Numbers presented are per 1,000 men aged 0–100 years, over their entire lifetime. The attendance at screening is assumed to be 80%.

Absolute number of life-years gained due to screening (output of the model, not adjusted for quality of life)						**72.7**
Health state	**Utility loss**	**No Screening**	**Screening**	**Difference**		**Quality adjustment**
		Number	**Number**	**Number**	**Life-years** *	**Life-years (range)**‡
Screening attendance	− 0.01	0	8,242	8,242	158	−1.6 (−1.9, −0.3)
Biopsy	− 0.10	313	605	292	17	−1.7 (−2.2, −1.0)
Diagnosis	− 0.20	112	157	45	4	−0.7 (−0.9, −0.6)
Radiation therapy (RT)	− 0.27	43	48	5	1	−0.2 (−0.2, −0.1)
Radical prostatectomy (RP)	− 0.33	32	68	35	6	−2.0 (−2.7, −0.6)
Active surveillance	− 0.03	28	48	20	106	−3.2 (−15.8, 0)
2 months – 1 year post RT	− 0.22	43	48	5	4	−0.9 (−1.6, −0.5)
2 months – 1 year post RP	− 0.23	32	68	35	30	−6.9 (−9.1, −2.7)
Post-recovery period:	− 0.05	75	116	41		
- non-overdiagnosed	−0.05	75	71	−4	109	−5.5 (−36.4, 0)
- overdiagnosed	−0.05	0	45	45	215	−10.8 (−30.3, 0)
Palliative therapy	− 0.40	40	26	−14	−35	14.1 (5.1, 26.9)
Terminal illness	− 0.60	31	22	−9	−4	2.6 (2.6, 3.3) +
Total life-years adjustment due to quality of life effects (sum of all health states)						**−16.7 (−93.8, 24.4)**
Percentage adjustment to total life-years gained due to quality of life effects						−23% (−128%, +34%)
QALYs gained due to screening						**56.0 (−20.7, 97.1)**

* The difference in the number of men in the screened and unscreened scrnario is multiplied by the duration of the health states (Table 1).

‡ The difference in life-years for each health state is multiplied by the utility loss to calculate the adjustment for quality of life.

Table 4

Predicted effects of various screening strategies compared with no screening[†]. A prostate cancer mortality reduction of 29% after 11 years using a 4 year screening interval was assumed.[2] Numbers presented are per 1,000 men aged 0–100 years, over their entire lifetime. The attendance at screening was assumed to be 80%.

Screening age (years)	**55–69 base model**	**55–74**	**55–69**	**55**	**60**	**65**
Interval (years)	1	1	4	-	-	-
Screening tests	8,242	10,577	2,250	548	584	588
Population invited[*]	853	891	833	685	730	735
Population screened[*]	845	883	777	548	584	588
Effects						
Cancers diagnosed	+ 45	+ 73	+ 29	+ 3	+ 9	+ 19
Screen detected cancers	104	150	70	8	23	42
Overdiagnosed cancers	45	72	29	2	8	19
% overdiagnosed of screen-detected	43%	48%	41%	30%	35%	45%
Negative biopsies	+ 247	+ 372	+ 166	+ 18	+ 52	+ 102
Prostate cancer deaths	− 9	− 11	− 6	− 1	− 2	− 3
Prostate cancer mortality reduction[≠]	37%	41%	32%	27%	29%	31%
Lead-time years	1,134	1,508	750	106	262	419
Life-years (LY) gained	73	82	52	12	22	25
QALYs gained	56	56	41	12	19	17
% LY gained adjusted for quality	23%	32%	21%	6%	15%	33%
Number needed to screen	98	84	129	490	249	186
Number needed to detect	5	7	5	2	4	6

[†] In the unscreened scenario, there would be 112 cancers diagnosed, 201 negative biopsies and 31 prostate cancer deaths.

[*] The number of men invited or screened at least once

[≠] The steady-state prostate cancer mortality reduction (after 20 years screening) for men who have attended at least one screen.