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The excess burden of side-effects from treatment in men allocated to screening for prostate cancer. The Göteborg randomised population-based prostate cancer screening trial

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ABSTRACT

Background: The number of men needed to treat to prevent one death is rather high in prostate cancer screening. How this affects the burden of treatment-related side-effects is unclear. The aim of this study was to evaluate the treatment related morbidity following radical prostatectomy in men participating in the Göteborg randomised population-based prostate cancer screening trial.

Methods: In 1995, 20,000 men aged 50–64 years were randomly allocated (1:1) to biennial PSA-screening or to a control group not invited. A subset of prostate cancer patients undergoing radical prostatectomy between 2001 and 2008 responded to questionnaires preoperatively and at 18 months postoperatively. The primary endpoint was patient-reported frequencies of erectile dysfunction as measured by the validated International Index of Erectile Function-5 questionnaire and urinary incontinence as assessed by use of pads. Analyses were made according to intention to screen.

Findings: After 14 years of follow-up, a total of 1849 men were detected with prostate cancer (1138 screened versus 711 controls, excluding 7 cancers detected at autopsy in the control group). Overall, 1047 received treatment with curative intent and radical prostatectomy was performed in 829 cases (79.2%). In this study, 294 of these men participated (205 screened and 89 controls). Of preoperatively potent men 79.1% (91/115) in the screening-group and 90.7% (49/54) in the control-group became impotent or sexually inactive 18 months postoperatively, whereas 14.3% (29/203) of screened men and 20.5% (18/88) of controls were considered postoperatively incontinent (regular use of pads). Extrapolated data yields that 120/10,000 more men become impotent and 25/10,000 more men will have the need of pads among men invited to regular PSA screening. The 'cost' per life saved at the same follow-up of screening is four men impotent and less than one man incontinent.

Interpretation: Despite the relatively high risk of erectile dysfunction and incontinence following radical prostatectomy for prostate cancer, the excess burden of permanent side-effects after population-based screening can be regarded as relatively low, when related to the number of men saved from prostate cancer death. These data can be useful when calculating the harms and benefits of screening. However, the outcome on a population-level may differ from the benefit for the individual.

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1. Introduction

Large-scaled randomised trials have reported about the effectiveness of prostate cancer screening in terms of decreased disease-specific mortality. The first report from the European Randomised Study of Screening for Prostate Cancer (ERSPC) in Europe showed a 20% reduction in prostate cancer mortality after a median follow-up of 9 years.[1] The smaller prostate, lung, colorectal and ovary (PLCO) trial in the United States that included many previously screened men could not corroborate this finding.[2] With longer follow-up (median 14 years) in the Göteborg randomised population-based prostate cancer screening trial, we recently reported that prostate cancer mortality was reduced almost by half.[3]

Although PSA screening seems to prevent prostate cancer deaths it is still questioned whether this outweighs the large risk for over-diagnosis and subsequent over-treatment. In the ERSPC study, the number needed to treat (NNT) to save one prostate cancer death was estimated to 48.[1] In the Göteborg screening trial, we now estimate NNT to 12. This number, though considerably lower, still implies a significant risk for over-diagnosis. In prostate cancer screening, most cancers are detected at early stages and even if many of these cancers are subjected to active monitoring there is a lack of reliable prognostic factors resulting in a considerable risk of over-treatment of indolent cancers. A high frequency of over-treatment could be accepted if the treatment is associated with few side-effects, as for example in cervical cancer. In Sweden, radical prostatectomy is the most common treatment option for localised disease.[4] The most bothersome permanent side-effects after prostatectomy are urinary incontinence and erectile dysfunction.[5] In reviews, the incidence of post prostatectomy potency rates has varied between 11% and 87%[6,7] and post prostatectomy incontinence between 0.3% and 87%.[6,8]

In order to get a balanced picture of screening for prostate cancer, there is an urgent need to quantify the potentially negative side-effects following treatment in screening trials. The Göteborg randomised population-based prostate cancer screening trial is a prospective, randomised trial evaluating the effects of biennial PSA-based screening.

The present study aims at investigating the side-effects of the most common therapy for early stage prostate cancer – radical prostatectomy – and to compare the outcome between the screening and control arm. As the study is truly population-based with up-front randomization, it should be possible to calculate reliable estimates on how much more surgically induced morbidity screening will cause on a population level if a screening program is to be introduced.

2. Materials and methods

The Göteborg randomised population-based prostate cancer screening trial was established in 1995. The study design has been described in detail previously.[3] The study protocol of the Göteborg trial was approved by the Ethical Review Committee at Göteborg University in 1994. The present study is based on men detected within this screening trial. The frequencies of side-effects in a subset of these men are extrapolated to the total number of men treated within the trial. Fig. 1a depicts the study design.

Beginning in 1st January 2001 all men operated upon with radical prostatectomy at the Sahlgrenska University Hospital were entered into a quality assurance database including pre-operative and 18-month postoperative evaluation of erectile and urinary function. Men belonging to the screening trial (screened men and controls) and operated upon between 2001 and 2008 form the study population. Erectile function was assessed using the validated and internationally well-established International Index of Erectile Function (IIEF)-5 questionnaire as described by Rosen et. al.[9] The five items on the score range from 0 or 1 to 5 (depending on the item), yielding a total score ranging from 1 to 25, where a higher score indicates a better sexual health. The version used in this study included the answer 'X', meaning 'No sexual activity' or 'Did not attempt intercourse' (instead of '0' in the original version). For men who reported one or more 'X', no total IIEF-5 score was calculated. Similarly, men who failed to answer all of the five questions were reported as 'Missing answer'. For men who were sexually active, erectile function was classified into three categories based on the total IIEF-5 score as follows: '1' = 'severe to moderate ED' (ED = 'Erectile dysfunction') = IIEF-5 score 5–11, '2' = 'moderate to mild ED' = IIEF-5 score 12–21 and '3' = 'fully potent' = IIEF-5 score 22–25.[9] Results were reported as group '2' and '3' together and compared with group '1' and 'X' together. In the literature, there is inconsistency in how to define and report erectile function after radical prostatectomy, however, many authors have used the definition 'erection sufficient for intercourse either with or without phosphodiesterase type 5 (PDE-5) inhibitors (as used in the treatment of ED)'.[10] Therefore, men in our study who reported use of PDE-5 inhibitors were included with their reported scores, whereas those who reported use of alprostadil (intraurethral or intracavernosal treatment for ED) were incorporated into group '1' (impotency group), regardless of which IIEF-5-score they reported with this use.

In addition to the IIEF-5 questionnaire, a questionnaire regarding urinary incontinence was also included, which measured sporadic or regular use of pads or diapers. The answers were measured on a five point scale ranging from 0 to 4, where a score $\geqslant 2$ was supportive of urinary incontinence. This questionnaire has previously been used by Carlsson et al. when measuring postoperative urinary continence after robot-assisted laparoscopic radical prostatectomy.[11]

Hospital records were reviewed for all men who underwent surgery after 2001 and who were sent questionnaires preoperatively and at 18 months and reached this follow-up, but for whom one or both questionnaires were missing (non-responders, $n = 120$).

3. Statistics

Descriptive statistics was calculated by conventional methods and tables created using SPSS® 17.0 statistical software. Analyses were made according to intention to screen and compared screened men with controls (i.e. standard clinical care). Missing answers were reported but excluded from analyses. Data were extrapolated from our results (patients operated upon from 2001 to 2008) to the full screening setting with 14 years of follow-up. Extrapolated numbers of pre-operatively

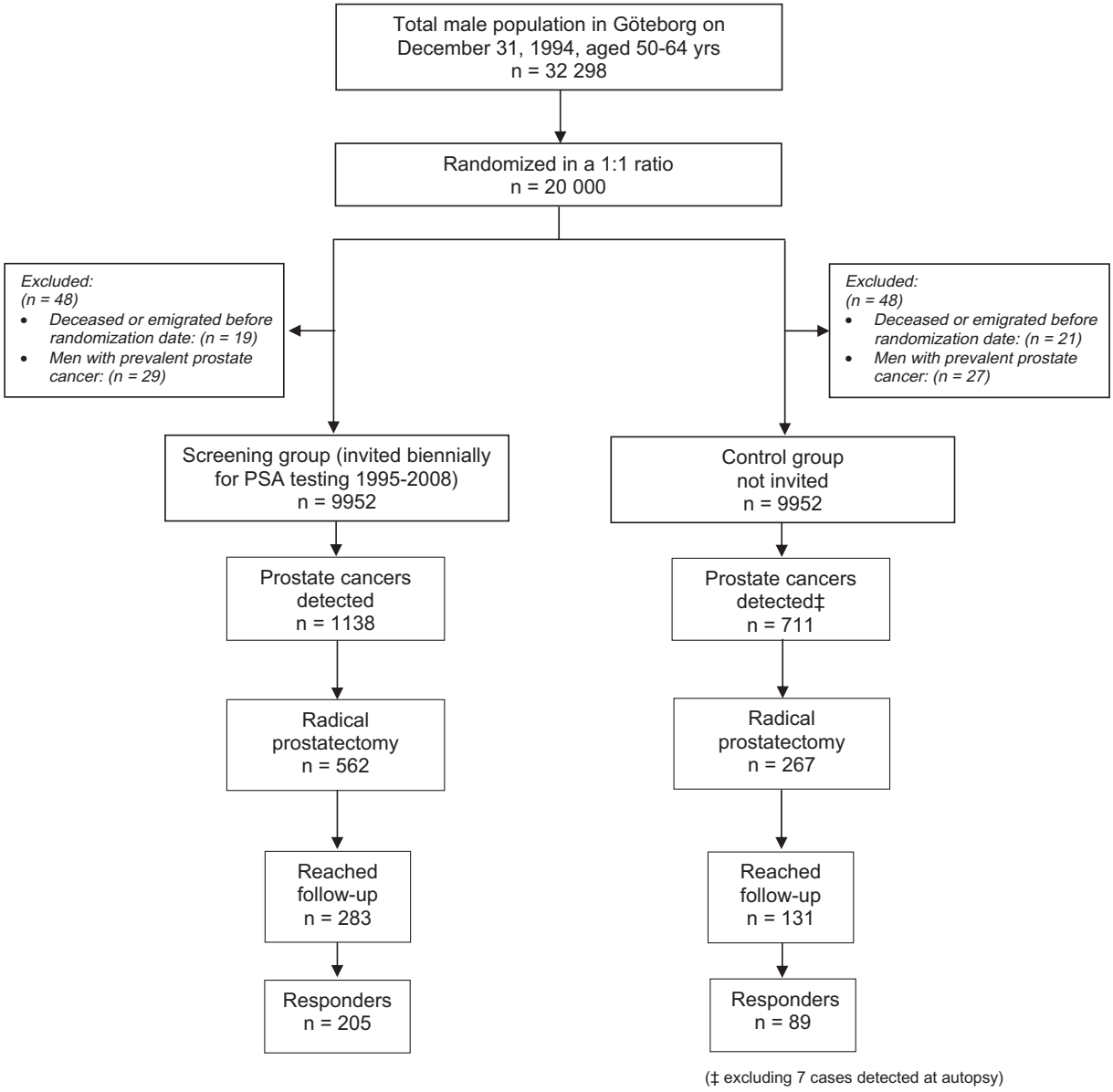

Fig. 1a – Consort diagram.

partially or fully potent and sexually active men were derived from the proportion of men in category '2' and '3' of all men with eligible questionnaires, for screened versus controls, respectively. Extrapolated numbers of post-operatively impotent or sexually inactive men were derived from the proportion of men in category 'X' and '1' at 18 months out of preoperatively potent men. Extrapolated numbers of post-operatively incontinent men, among all men who underwent surgery, were derived from proportions of men reporting urinary incontinence grade '2–4' at 18 months of follow-up.

4. Results

With 14 years of PSA-screening in the Göteborg randomised population-based prostate cancer screening trial 1849 men were detected with prostate cancer (1138 screened, 711 controls, excluding 7 cancers detected at autopsy in the control group). Overall, 1047 received treatment with curative intent (radical prostatectomy, radiation therapy and cryosurgery), out of which 829/1047 (79.2%) were radical prostatectomies. The different types of treatments are presented in Table 1. Of these, 414 men were included in the quality assurance program (underwent surgery between 2001 and 2008) and were sent questionnaires preoperatively and at 18 months of follow-up. Of these, a total of 294/414 (71.0%) men had complete questionnaires at both occasions (205/283 screened or 72.4% of eligible men and 89/131 controls or 67.9% of eligible men) (Fig. 1a). The characteristics of the prostate cancers operated are presented in Table 2. The study group is representative for all radical prostatectomies performed during this time period.

Erectile function according to IIEF-5 questionnaires preoperatively and at 18 months is presented in Table 3. Preoperatively, 123/188 (65.4%) of sexually active men in the screening group and 60/85 (70.6%) of sexually active men in the control group belonged to group '2' or '3' (potent men with mild to moderate ED or no ED). Of these men, 91/115 (79.1%) of

Table 1 – Treatments for prostate cancer in the Göteborg randomised population-based prostate cancer screening trial.

Treatment no. (%)	Screening group (n = 1138)	Control group (n = 711[a])
Primary radical prostatectomy	455 (40.0)	239 (33.6)
Primary surveillance followed by radical prostatectomy	107 (9.4)	28 (3.9)
Primary radiation therapy	93 (8.2)	75 (10.5)
Primary surveillance followed by radiation therapy	34 (3.0)	7 (1.0)
Cryosurgery	8 (0.7)	1 (0.1)
Surveillance at last follow-up	314 (27.6)	152 (21.4)
Primary surveillance followed by endocrine treatment	23 (2.0)	20 (2.8)
Primary endocrine treatment	80 (7.0)	162 (22.8)
Cystoprostatectomy	6 (0.5)	2 (0.3)
Not treated	18 (1.6)	25 (3.5)

[a] Excluding 7 cases detected at autopsy.

Table 2 – Characteristics.

	All operations (1995–2008)		Questionnaire responders (2001–2008)	
	Screened (n = 562)	Controls (n = 267)	Screened (n = 205)	Controls (n = 89)
Age at surgery				
Md (Q1; Q3), years	64.1 (61.2; 66.7)	64.9 (62.3; 67.4)	65.2 (62.9; 67.6)	65.8 (63.3; 67.7)
Missing	0	0	0	0
PSA at diagnosis				
Md (Q1; Q3), ng/ml	4.7 (3.6; 7.1)	7.6 (4.9; 12.0)	4.5 (3.5; 6.2)	7.5 (4.8; 11.0)
Missing	1	0	1	1
Gleason (RP) score no. (%)				
5	40 (7.2)	12 (4.7)	10 (5.0)	2 (2.3)
6	308 (55.6)	103 (40.6)	103 (51.0)	34 (39.1)
7	183 (33.0)	116 (45.7)	79 (39.1)	45 (51.7)
8	10 (1.8)	7 (2.8)	8 (4.0)	3 (3.4)
9	8 (1.4)	13 (5.1)	2(1.0)	3 (3.4)
Other	5 (0.9)	3 (1.2)	0	0
Missing	8	13	3	2
cT stage no. (%)				
T1c	407 (72.5)	159 (59.6)	158 (77.5)	51 (57.3)
T2	134 (23.9)	94 (35.2)	38 (18.6)	32 (36.0)
T3	12 (2.1)	5 (1.9)	5 (2.5)	1 (1.1)
Other (T1a, T1b, TX)	8 (1.4)	9 (3.4)	3 (1.5)	5 (5.6)
Missing	1	0	1	0
NSRP no. (%)				
Bilat.	129 (48.0)	32 (24.2)	99 (50.0)	25 (28.4)
NSRP Unilat.	48 (17.8)	18 (13.6)	33 (16.7)	8 (9.1)
Non-NSRP	92 (34.2)	82 (62.1)	66 (33.3)	55 (62.5)
Missing	293	135	7	1
Capsule penetration no. (%)				
Yes	131 (23.8)	82 (32.2)	42 (21.0)	37 (42.0)
No	420 (76.2)	173 (67.8)	158 (79.0)	51 (58.0)
Missing or uncertain	11	12	5	1
Positive margins no. (%)				
Yes	151 (27.3)	77 (29.5)	53 (26.2)	30 (33.7)
No	403 (72.7)	184 (70.5)	149 (73.8)	59 (66.3)
Missing or uncertain	8	6	3	0

Data are presented as n (%) if otherwise not given. T2, T2a or T2b were classified as 'T2'. T3, T3a, b, or c were classified as 'T3'. 'T1' = the primary tumour is not palpable through digital rectal examination. T1a < 5% of cancer in specimen from trans-urethral resection of the prostate, TURP, T1b > 5% of cancer in specimen from TURP, 'T1c' – cancer diagnosed by biopsy, 'T2' – the tumour is palpable as intra capsular, 'T3' – the tumour is spread outside the prostate capsule, but no growth to other organs (except the seminal vesicles). 'Capsule penetration yes' = extra capsular growth with or without involving the seminal vesicles). 'Capsule penetration no' = organ confined tumour in prostatectomy specimen.

screened and 49/54 (90.7%) of controls reported either no sexual activity, an ED score $\leqslant$ 11 or use of alprostadil for impotency at 18 months after surgery. Applying the patient selection as used by Parsons and colleagues[12] (age $\leqslant$ 60 years,

Table 3 – Erectile function before and 18 months after radical prostatectomy, presented as categorised IIEF-5 scores.

Potency no. (%)	Preoperative erectile function (all men)		Postoperative erectile function (18 months) (for men in category '2' and '3' pre-op.)	
	Screened (n = 205)	Controls (n = 89)	Screened (n = 123)	Controls (n = 60)
'X', No sexual activity	51 (27.1)	18 (21.2)	56 (48.7)	28 (51.9)
'1', Impotent (IIEF-5-score 5–11 + *alprostadil users*)	14 (7.4)	7 (8.2)	35 (30.4)	21 (38.9)
'2', Potent (IIEF-5-score 12–21)	49 (26.1)	21 (24.7)	12 (10.4)	4 (7.4)
'3', Potent (IIEF-5-score 22–25)	74 (39.4)	39 (45.9)	12 (10.4)	1 (1.9)
Questionnaire filled out incorrectly, excluded	17	4	8	6

preoperative IIEF-5-score $\geqslant$ 21 and who had a bilateral nerve-sparing procedure) yielded only 10/294 (3.4%) patients of our study population (data not shown). In this small subgroup, 7/10 (70%, data not shown) were potent (IIEF-5-score $\geqslant$ 16) at 18 months according to the criteria suggested by Parsons and colleagues.

As regards urinary continence, preoperative and postoperative rates are reported in Table 4. Preoperatively, only three men in total reported mild incontinence and none severe incontinence. At 18 months, 29/203 men (14.3% of operated men) in the screening group and 18/88 men (20.5% of operated men) in the control group reported some degree of incontinence (regular use of any pads; category '2', '3' or '4') (Table 4).

The analysis of postoperative erectile function from hospital records (doctors' reported) for non-responders to one or both questionnaires (both screened and controls) indicated a slightly more favourable picture than that obtained from responders to the questionnaires. Based on hospital record reviewing for the 120 non-responders, 68/81 men (84.0%) were reported to be preoperatively potent (comparable to group '2' and '3', with information missing in 39 hospital records or records unavailable). Postoperative potency at 18 months was reported in 18/55 (32.7%) men (information unavailable for 13 of the 68 preoperatively potent men) to be compared with 29/169 (17.2%) for questionnaire responders. The hospital records reviewing for incontinence gave an almost identical picture as that from the patient-reported questionnaires. Postoperative severe urinary incontinence (corresponding to group '3' and '4') was reported in 7/115 (6.1%) men (hospital records unavailable for 5 out of 120 non-responders) to be compared with 18/291 (6.2%) for questionnaire responders. The corresponding figures for incontinence corresponding to all of groups '2', '3' and '4' was 18/115 (15.7%) versus 47/291 (16.2%), respectively.

Extrapolating data from patients responding to the questionnaires to the full screening setting yields that, with 14 years of organised PSA-screening, the frequency of post prostatectomy impotence and sexual inactivity is increased by 120/10,000 men for men subjected to screening as compared to the control population (representing the current clin-

Table 4 – Urinary continence before and after radical prostatectomy.

Degree of urinary leakage	Status no. (%)	Preoperative status		Postoperative status (18 months)	
		Screened (n = 205)	Controls (n = 89)	Screened (n = 205)	Controls (n = 89)
0 = Never	Continent	191 (93.6)	75 (85.2)	76 (37.4)	32 (36.4)
1 = Sometimes urinary leakage when coughing or sneezing/ sporadic use of pads associated with physical exertion such as sports, gardening et cetera	Continent	12 (5.9)	11 (12.5)	98 (48.3)	38 (43.2)
2 = Regular use of pads (except sometimes at night), but they are not always wet	Incontinent	1 (0.5)	2 (2.3)	18 (8.9)	11 (12.5)
3 = Regular use of pads that need to be changed because they are wet	Incontinent	0 (0)	0 (0)	6 (3.0)	5 (5.7)
4 = Constant urinary leakage that requires diapers to be changed continuously	Incontinent	0 (0)	0 (0)	5 (2.5)	2 (2.3)
Missing answer		1	1	2	1

Preoperative, two screened men reported '4'. Checking the hospital files for these men yielded that the date of completion of the questionnaire exceeded the date of surgery (after which they had severe urinary leakage). Hence, the answers were considered to be postoperative, not preoperative.

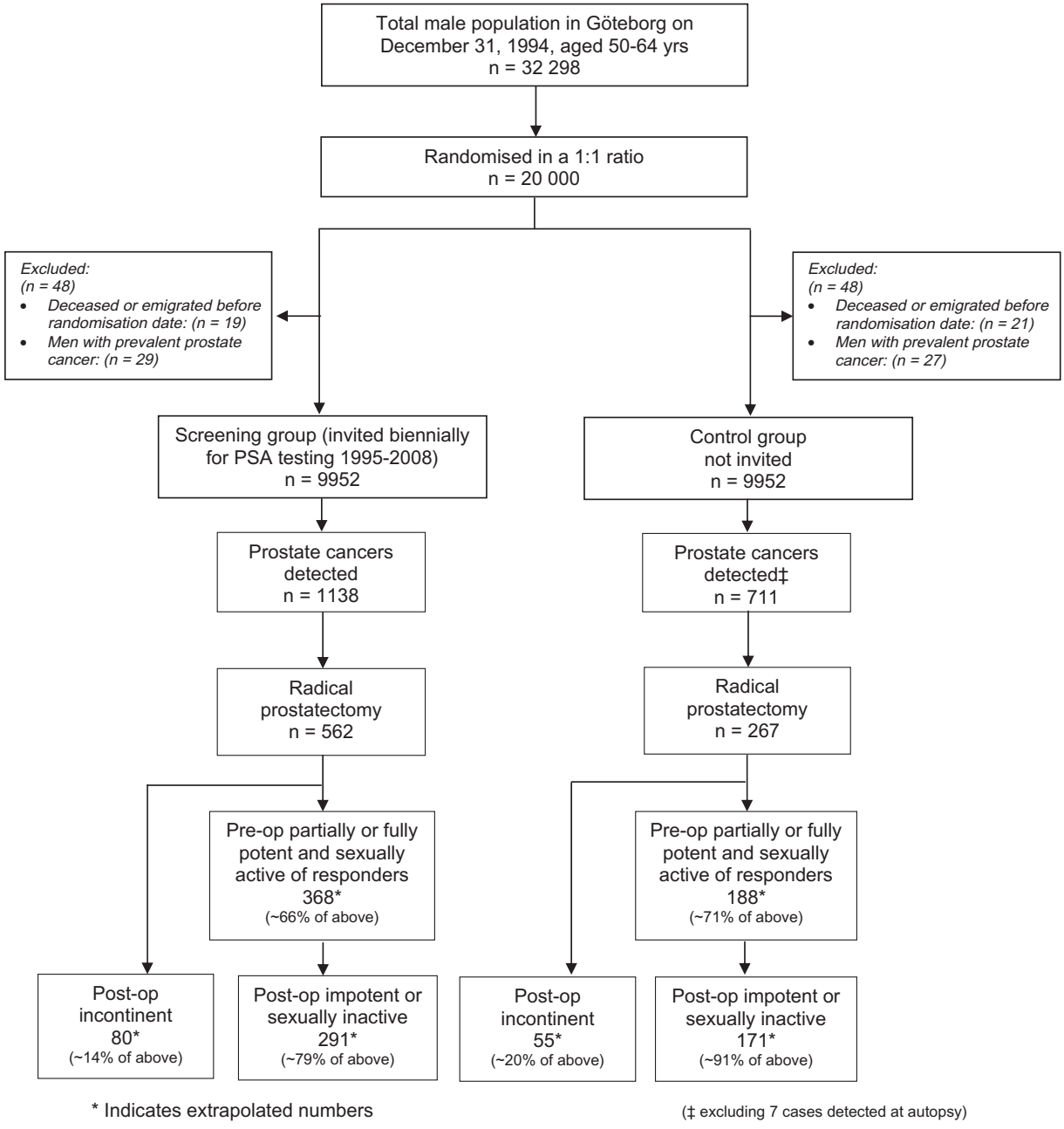

Fig. 1b – Flow chart, 14 years of screening.

ical practice in Sweden). The corresponding figure for post prostatectomy urinary incontinence (defined as daily use of pads) is an increase of 25/10,000 screened men (Fig. 1b).

5. Comment

The men included in the present study represent a truly population-based sample of men aged 50–64 years (at randomization), randomised between a PSA-based, biennial screening program and common clinical practice (including PSA-testing when needed) in Sweden. The present report focus on self-reported side-effects of the most commonly used curative therapy for men with localised prostate cancer – radical prostatectomy – and a comparison between men randomised to screening and the control group.

5.1. *Erectile function*

Of preoperatively partially or fully potent men, 79% in the screening group and 91% in the control group were sexually inactive or impotent at 18 months postoperative. A review by Alivizatos and colleagues revealed potency rates varying from 11% to 87% after radical prostatectomy.[6] In 2007, Burnett and colleagues for the American Urological Association Prostate Cancer Guideline Update Panel reported on this great variability that exists among clinical studies in reporting erectile function outcomes after localised prostate cancer treatment.[13] Based on 436 articles in the medical literature, Burnett and colleagues demonstrated diverse and inconsistent manners of assessment of erectile function, together with widely disparate outcome rates. Their results show the difficulties in

interpreting studies on erectile function, which also hinder meaningful conclusions and comparative analyses to be made. For further studies, the authors stressed the need to apply erection specific instruments, such as the validated self-reported IIEF-5-questionnaire used in this study. Presenting frequencies for men reporting several 'X' on the IIEF-5 score as 'No sexual activity/Did not attempt intercourse', instead of calculating a total IIEF-5 score where an 'X' contributes with 0, is an accurate way of presenting data, since it is not possible to judge whether a man did not attempt intercourse because of erectile dysfunction or any other cause, such as psychological distress due to cancer diagnosis, co-existing urinary leakage or having no partner et cetera. Using these presumptions, results in lower potency figures compared to if these men are excluded from analysis. Other explanation to the low reported potency rates is the fact that only half of the men in the screening group and one quarter in the control group had a bilateral nerve sparing procedure. Nor were any patient excluded from analysis due to second-line treatment with radiation and/or hormone therapy. Only 3% of men in this population based study fit into the patient selection published by Parsons and colleagues in which they reported 71% postoperative potency after 12 months.[12] However, in this small subgroup a higher potency rate was recorded, in complete harmony with Parsons (70%). The low postoperative potency rate is in line with other studies on unselected patients found in the literature.[5,13–17] It is worth to point out that in the present study, erectile function was evaluated at 18 months postoperatively. However, it has been shown that the sexual function can continue to improve even beyond 2 years postoperatively.[18,19]

It should be noted that already before surgery, the prevalence of erectile dysfunction was high for both screened and controls in this population that emerges from a randomised sample from the population. This could probably, at least in part, be explained by the age of the participants. This finding is in line with Long and colleagues who showed that erectile dysfunction, also as measured by the IIEF-5, was present in a large proportion of men before radical prostatectomy: 64% suffered from erectile dysfunction overall; 43% of patients younger than 65% and 84% of patients over 65.[20] Also, Salonia and colleagues showed that only 43% of men with localised prostate cancer candidates for bilateral nerve-sparing radical prostatectomy had a normal erectile function preoperatively.[21]

5.2. *Continence*

Similar to frequencies of post prostatectomy erectile function, there is inconsistency in the literature as regards urinary continence. The incidence of post prostatectomy incontinence ranges from 0% to 87%,[6,8,22] with an average incidence of no more than 5% for total incontinence.[22] In a review by Grise and colleagues, post prostatectomy urinary continence rates, when defined as any leakage, varied between 25% and 70%.[23]

In the present study, 14.3% of screened men and 20.5% of controls reported some degree of daily urinary incontinence at 18 months post prostatectomy. Most of these men belonged to group '2' which means they use pads daytime but not necessary wet. More severe incontinence (group '4') was more uncommon but still reported by 2.5% in the screening group and 2.3% in the control group. The reported continence rate was lower compared to that reported by Catalona et al. who found that 92% were continent (no pads) at 18 months of follow-up.[24] However, very similar rates of incontinence were reported by Stanford and colleagues in the Prostate Cancer Outcomes Study.[17] They reported use of 1–2 pads a day in 18% of men at 24 months postoperatively and more severe incontinence in 3.3% of men. From the Netherlands branch of the ERSPC, Madalinska et al. showed that 3% reported no urinary control. In their study, there was no statistically significant difference between the groups with screen-detected and with clinically diagnosed prostate cancer.[14] The difference observed between the groups in this study could be explained by the difference in the frequency of nerve-sparing operations. It has been reported that men who undergo a non-nerve-sparing procedure have a lower chance[25] or at least need longer time to regain continence.

5.3. *Increase in complications in relation to effects of PSA-based screening programs*

The now concomitant first outcome report from the Göteborg randomised population-based prostate cancer screening trial shows that a PSA based screening program with a median of 14 years of follow-up may decrease prostate cancer mortality with an RR of 0.56.[3] This corresponded to an absolute number of 34 prostate cancer deaths averted/10,000 screened men.

The present study describes the side-effects from treatment induced in the population during the same time-period (14 years) as a result of the screening program. To the best of our knowledge, the present study provides the first data available that has made an effort to quantify these side-effects of screening based on a truly population-based randomised controlled trial. We extrapolated this increased frequency of impotence or sexual inactivity as 120/10,000 invited men and for incontinence 25/10,000 men with screening as compared to the control group. This can be interpreted as for each prostate cancer death averted with screening (34/10,000), the surgically induced morbidity because of screen-detected prostate cancer will render four (120/34) more men impotent or sexually inactive and less than one (25/34) more man incontinent. Thus, in relation to a reduced prostate cancer mortality, the side-effects from radical prostatectomy can be regarded as relatively low. However, the outcome on a population level may differ from the benefit for the individual. Further studies from patient views are warranted.

5.4. *Limitations of the study*

The main limitation of the present study is the relatively small number of evaluable men and that not all men operated upon provided full and complete answers to all questionnaires. The present study only included men who provided complete answers at both pre- and post treatment assessments. However, we have no reason to believe that this has resulted in a skewed sample of men, thus introducing a potential bias in the results presented. According to hospital records, non-responders to the questionnaires did not report more unfavourable outcomes. This is further supported by the fact that the actual complications reported by the patients are well in line with the published literature. If anything, the rate of

side-effects in the present study was higher than reported in many other studies. In another unselected population-based cohort, the Prostate Cancer Outcomes Study, 21.6% used $\geqslant 1$ pad per day at $\geqslant 18$ or more months of follow-up after radical prostatectomy and of the 72.7% of men who were potent at baseline, 72.4% reported that their erections were not firm enough for intercourse at follow-up.[17] If we apply these proportions to the patients operated upon in our study, under the assumption that the outcomes do not differ for men with screen-detected tumours (screened) and clinically diagnosed (controls), the extrapolation leads to 155/10,000 more men impotent and 63/10,000 more men incontinent corresponding to five more men impotent (155/34) and two more men incontinent (63/34) per prostate cancer death averted (34/10,000).

Furthermore, we are aware of the fact that these side-effects are not the total population-induced effect of screening, but from the most common treatment option used with curative intent (80% of cases in the present study). The absolute number of men who received radiation therapy was only slightly higher in the screening compared to the control group in the whole study population (127 versus 82). Radiation therapy will therefore in this study only marginally contribute to the increased burden of long-term side-effects associated with screening. On the other hand, there were significantly more men in the control group who received primary endocrine treatment (162 controls versus 80 screened) which will act in the opposite direction, i.e. increase long-term side effects in the control group. Another limitation is that we have not adjusted for the number of years the men will have to live with these side-effects relative to the life-years gained for each prostate cancer death averted.

6. Conclusions

In conclusion, pre-operative erectile dysfunction is common in men with prostate cancer subjected to radical prostatectomy even if diagnosed by screening. The vast majority of men suffer from erectile dysfunction post prostatectomy. Even with advances in surgical technique and despite the best efforts of experienced surgeons, side-effects are sometimes inevitable.

The present study provides one of the first reports of how an organised, population-based prostate cancer screening program will affect the number of men who will have to live with complications if such a program is introduced. Data such as the ones obtained in the present study are useful when evaluating the benefits and harms of prostate cancer screening, and also for future comparison between different screening algorithms.

Role of funding sources

None of the funding sources have had access to the data or been involved in the data collection, data management or writing of this paper.

Conflict of interest statement

None declared.

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