

## Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

**eMethod. Imputation method for replacing missing Grade Group values**

The cancer case with a missing Grade Group among the participating men in the screening group was assigned a Grade Group 2, as this was the most common observation in this group (63/160).

Of the seven cases with missing Grade Group in men who were allocated to screening but did not participate, one was assigned to Grade Group 1, one GG 2, two GG 3 and three GG 4, following the distribution of the observed values (8/49 GG1, 10/49 GG2, 11/49 GG3 and 20/49 GG4-5)

In the control arm, of the eight cases with missing Grade Group, two were assigned to Grade Group 1, three GG 2, one GG 3 and two GG 4-5, as 65/347 (19%) of the cases in the control group with known Grade Group were GG1 and 121/347 (35%) GG2, 62 (18%) GG3 and 99 (29%) GG 4-5.

eTable 1. Previous PSA test and prostate biopsies among men in the control group. Results from a mail survey to a random sample of 2009 men with 574 participants

Previous PSA (571 responses)	<b>N (%)</b>
Past 12 months	99 (17)
Past 12–24 months	90 (16)
Past 3–5 years	67 (12)
More than 5 years ago	24 (4)
Never	291 (51)
Previous prostate biopsy (569 responses)	
Yes	19 (3)

eTable 2. Numbers of prostate cancer detected at screening by Grade Group, age group, PSA, kallikrein panel risk score, and MRI PI-RADS score

	Grade Group 1, N (%)	Grade Group 2–5, N (%)	Number of men
<b>Age at entry (years)</b>			
50–54	4 (0.1)	17 (0.3)	4998
55–59	10 (0.2)	50 (0.9)	5541
60–64	18 (0.4)	61 (1.4)	4308
<b>Previous PSA</b>			
Past 12 months	4 (0.5)	17 (2.0)	855
Past 12-24	3 (0.4)	14 (1.7)	832
Past 2-5 years	5 (0.6)	15 (1.9)	791
>5 years ago	1 (0.2)	10 (2.5)	406
No	16 (0.4)	56 (1.5)	3629
Missing	3 (0.2)	16 (1.3)	1231
<b>Previous prostate biopsy</b>			
Yes	1 (0.5)	10 (5.1)	195
No	26 (0.5)	102 (1.6)	6318
Missing	5 (0.4)	16 (1.3)	1231
<b>Family history</b>			
Yes	5 (0.5)	23 (2.5)	927
No	23 (0.4)	89 (1.6)	5550
Missing	4 (0.3)	16 (1.3)	1267
<b>PSA (ng/mL)</b>			
3.0–4.9	20 (4.0)	52 (10.4)	499
5.0–10.0	10 (5.3)	45 (23.8)	189
>10	2 (3.1)	31 (48.4)	64
<b>Kallikrein panel risk score</b>			
7.5–14.9	14 (5.9)	24 (10.0)	239
15–24.9	8 (6.2)	31 (24.0)	129
≥25	10 (6.3)	73 (46.2)	158
<b>MRI PI-RADS score</b>			
<3*	11 (3.6)	16 (5.3)	303
3	8 (13.1)	16 (26.2)	61
4	10 (10.4)	53 (55.2)	96
5	3 (6.0)	43 (86.0)	50

\*Fifty-three men biopsied for PSA density  $\geq 0.15$  ng/mL<sup>2</sup>

eTable 3. Detailed Grade Group classification of cases detected at screening by biopsy type (targeted or systematic)

Type of biopsy	Grade group					Missing	Total
	1	2	3	4	5		
Targeted biopsy <sup>a</sup>	22	52	42	10	9	1	136
Systematic biopsy <sup>b</sup>	10	11	3	-	1	-	25
TOTAL	32	63	45	10	10	1	161

<sup>a</sup>Indication: PI-RADS score 3-5 with PSA  $\geq 3.0$  ng/mL and kallikrein panel score  $\geq 7.5\%$ .

<sup>b</sup>Indication: Negative MRI (PI-RADS $<3$ ) with PSA density  $>0.15$  ng/mL<sup>2</sup> with PSA  $\geq 3$  ng/mL and kallikrein panel risk score  $\geq 7.5\%$ .

eTable 4. Age, PSA and kallikrein panel risk score (median with interquartile range) for men with screen-detected Grade Group 1 cancer, Grade Group 2–5 cancer and benign biopsy result (excluding one case with a missing Gleason score)

	Grade Group 1	Grade Group 2–5	Benign biopsy <sup>a</sup>
Age at entry <sup>b</sup>	60 (56.5–62)	59 (57–62)	60 (56–62)
Screening PSA (ng/mL) <sup>b</sup>	4.8 (3.8–7.0)	5.8 (4.1–10.0)	4.8 (3.6–7.7)
Kallikrein panel risk score <sup>b</sup>	17.8 (10.4–29.8)	27.8 (19.2–52.7)	16.7 (11.1–28.9)
Number of men	32	128	101

<sup>a</sup>Men with PSA  $\geq 3$  ng/mL, kallikrein panel risk score  $\geq 7.5\%$  and PI-RADS score 3–5 but no cancer at biopsy <sup>b</sup>Median and interquartile range

eTable 5. Analysis of cancer detection by trial group with imputation of missing Grade Group based on the stratum-specific observed relative frequencies\* (by trial group and screening attendance)

	Screening group		Control group (N=45,544)	Risk difference in screened men vs. control arm (per protocol analysis)	Risk difference in screening arm vs. control arm (intention to screen analysis)
	Screened men (N=7744)	All men (N=15,201)			
Grade Group 1	32 (0.41%)	40 (0.26%)	67 (0.15%)	0.27% (95% CI 0.12–0.41)	0.12% (95% CI 0.03–0.20)
Grade Group 2–5	129 (1.67%)	179 (1.18%)	288 (0.63%)	1.03% (95% CI 0.74–1.33)	0.55% (95% CI 0.36–0.73)
All cancers	161 (2.08%)	219 (1.44%)	355 (0.78%)	1.30% (95% CI 0.97–1.63)	0.66% (95% CI 0.45–0.87)
Detailed Grade Group classification					
1	32 (0.41%)	40 (0.26%)	67 (0.15%)	0.27% (95% CI 0.12–0.41)	0.12% (95% CI 0.03–0.20)
2	64 (0.83%)	78 (0.51%)	124 (0.27%)	0.56% (95% CI 0.35–0.76)	0.24% (95% CI 0.12–0.37)
3	45 (0.58%)	59 (0.39%)	63 (0.14%)	0.44% (95% CI 0.27–0.61)	0.25% (95% CI 0.14–0.35)
4–5	20 (0.26%)	42 (0.28%)	101 (0.22%)	0.04% (95% CI -0.08, 0.16)	0.05% (95% CI -0.04, 0.15)
Total	161	219	355		

\*One missing case in screening participants was assigned GG 2; seven missing cases among men assigned to screening who did not participate were assigned to GG 1 (one case), GG 2 (one), GG 3 (two cases) and GG 4–5 (three cases) to 4+4; in the control arm, of the eight cases with missing Grade Group two cases were assigned to GG 1, three GG 2, one GG 3, and two cases GG 4–5. See also Appendix 1.

eTable 6. Clinical TNM stage in cancers detected at screening, among men invited to screening who did not participate, and in the control group. Incident cases in the non-screened groups include those detected in surgery for benign prostatic hyperplasia (one in men invited to screening who did not participate and fourteen in the control group)

TNM stage	Screened men in the intervention group, N (%)	Men invited who did not participate, N (%)	Screening group total, N (%)	Control group, N (%)
T1–2 <sup>a</sup>	142 (88)	31 (53)	173 (79)	276 (78)
T3–4/N1 <sup>b</sup>	13 (8)	11 (19)	24 (11)	30 (8)
M1 <sup>c</sup>	4 (2)	10 (17)	14 (6)	34 (10)
Missing	2 (1)	6 (10)	8 (4)	15 (4)
Total	161	58	219	355

<sup>a</sup>N0/Nx and M0/Mx <sup>b</sup>M0/Mx <sup>c</sup>Any T and N



eTable 7. Primary treatment of prostate cancers by trial group, number of cases (%)

Treatment modality	Screened men in the intervention group, N (%)	Men invited to screening who did not participate	Entire screening group, N (%)	Control group, N (%)
Active surveillance	62 (39)	8 (14)	70 (32)	85 (24)
Prostatectomy alone	46 (29)	15 (26)	61 (28)	116 (33)
Prostatectomy with adjuvant treatment	8 (5)	2 (3)	10 (5)	9 (3)
Radiotherapy alone	11 (7)	4 (7)	15 (7)	28 (8)
Radiotherapy with adjuvant treatment	32 (20)	19 (33)	51 (23)	75 (21)
Androgen deprivation therapy	–	6 (10)	6 (3)	26 (7)
None, other or unknown	2 (1)	4 (7)	6 (3)	16 (5)
Total	161	58	219	355