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PSA levels and cancer detection rate by centre in the European Randomized Study of Screening for Prostate Cancer

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ABSTRACT

Background: To describe the variation in PSA level by age group and screening round in the ERSPC centres and the variation in cancer detection rates in relation to the underlying prostate cancer incidence.

Methods: Individual data on men invited for the first and second screening rounds according to protocol (excluding early recalls and interval cancers) were obtained from the central database of the ERSPC (cut-off date 31st December 2006). Data were compared between and within centres for the core age group (55–69 at entry). The cancer detection rate (CDR) was compared with the expected background prostate cancer incidence rate in the absence of screening adjusted for the incidence rate in non-attenders and the control arm (IRS).

Results: Mean PSA values in the age groups 55–59 years and 65–69 years showed little variation by centre, except for the Dutch centre, where an increase from 1.6 to 1.8 ng/ml and a decline from 2.9 to 2.5 ng/ml was observed, respectively. Most tumours were detected at the PSA range 4.0–9.9 ng/ml, with a shift to more cancer detection at 3.0–3.9 ng/ml in the second screening round. There was high variability in the CDR between the centres in both the first (16–46 per 1000) and the second screening rounds (14–50 per 1000). Although the ratio CDR/IRS was less variable, it is somewhat lower in Italy and Switzerland (12 and 14,respectively) and higher in the Netherlands (28), than in most other centres and in Belgium the ratio increased markedly, from 20 to 44 between the first and second rounds.

Conclusion: There was no clear evidence of a relationship between the underlying incidence and mean PSA levels at screening or the cancer detection rate.

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1. Introduction

The large-scale randomised trial of screening for prostate cancer in Europe (European Randomized Study of Screening for Prostate Cancer, ERSPC) to assess the effectiveness of screening for prostate cancer by Prostate Specific Antigen (PSA) testing, recently demonstrated a 20% reduction in mortality from prostate cancer in men invited to be screened after a median follow-up of 9 years.[1] An analysis correcting for non-compliance in the screening arm and contamination in the control arm yielded a benefit of screening of up to 31% attributable to attending the screening.[2]

The ERSPC trial has been conducted in eight countries: Belgium, Finland, France, Italy, the Netherlands, Spain, Sweden and Switzerland. Amongst the participating countries, there is considerable difference in the underlying incidence of prostate cancer,[3] both in the pre-PSA era (1983–1987) and in the PSA-era (1993–1997). This difference in the underlying incidence could possibly be reflected in the differences between countries in PSA levels and cancer detection rates. In breast cancer screening, it has been pointed out that the cancer detection rate at initial screening is highly dependent on the underlying incidence.[4,5]

In this paper we describe the variation in PSA level by age group, centre and screening round and the variation in cancer detection rates in relation to the underlying prostate cancer incidence in the eight centres.

2. Materials and methods

2.1. ERSPC

The design and planned evaluations of the ERSPC have been previously described.[1,6,7] Briefly, the ERSPC trial has been conducted in eight countries. Over 200,000 men were enrolled and randomised to the screening and control arms in a ratio of 1 to 1 (1 to 1.5 in the Finnish centre). Randomisation differed amongst the participating centres; in some centres men gave written informed consent before randomisation (Belgium, Netherlands, Spain and Switzerland) whilst in the other centres consent was asked after randomisation, only for men in the screening arm (Finland, France, Italy and Sweden).[6] Each centre followed a common core protocol, with slight differences between centres in age groups and screening procedures.[6] The trial included men aged 50–74 years. The age group at randomisation varied amongst the centres (Table 1), however, the core age group for evaluation is 55–69 years at entry. The screening interval was 4 years, except for the Swedish with a 2-year interval. In the Belgian centre, the interval between the first and second screening rounds was 7 years. A PSA value of 3.0 ng/ml was used in most centres as the threshold for biopsy indication. In Italy and Finland, the threshold was set at 4.0 ng/ml, but in Italy men with PSA values between 2.5 and 3.9 ng/ml underwent digital rectal examination (DRE) and transrectal ultrasound (TRUS) and in Finland men with PSA values between 3.0 and 3.9 ng/ml underwent DRE until 1998, whereafter the ratio of free PSA to total PSA was used as a criteria for referral. From February 1997 in the Dutch and Belgian centres, a PSA value of 3.0 ng/ml or higher was the only modality for referral, replacing either an abnormal DRE, abnormal TRUS or PSA of 4.0 ng/ml or higher. In the Swiss centre a side study was conducted in which prostate biopsy was offered to men with a PSA outcome between 1 and 3 ng/ml with a free-to-total PSA ratio below 20%.[7,8]

2.2. Data collection

For this study, individual data for each screening round, including centre, age, PSA value and cancer detection were obtained from the central database of the ERSPC. This paper reports on the first round visits, i.e. screens in response to the first invitation, and the second round visits, i.e. those screens in men re-invited at an interval after the first screen according to normal protocol. Data on early recall screens and interval cancers are not included in the analyses. The cut-off date for follow-up is 31st December 2006.

Age specific data on the underlying background cancer incidence of prostate cancer in Italy, France, Spain, Switzerland and Finland for the age groups 55–59, 60–64 and 65–69 years were obtained from the original database of Cancer Incidence in Five Continents I–VIII (CI5).[9] This provided regional data for the Italian centre (Florence) and the French centre (Tarn). For the Spanish and the Swiss centres regional

Table 1 – Number of men randomised in the screening arm in the different centres (cut-off date 2006).

	Age group invited	Number of men randomised								
		N	45–49[a] %	50–54 %	55–59 %	60–64 %	65–69 %	70–74 %	75–79[a] %	Mean age (median) Years
Belgium	55–74	5188	0	1	18	36	28	15	0	63.8 (64)
Finland	55/59/63/67	31,970	0	0	58	23	20	0	0	60.3 (59)
France	55–69	42,558	0	1	36	32	27	4	0	61.8 (61)
Italy	55–70	7496	0	0	37	31	29	2	0	61.8 (61)
Netherlands	55–74	21,206	0	1	32	27	24	16	0	63.1 (63)
Spain	50–70	2416	6	31	30	20	12	1	0	56.6 (56)
Sweden	51–66	9957	0	38	32	30	0	0	0	56.1 (56)
Switzerland	55–70	5158	0	3	40	31	24	1	0	60.0 (60)
Total	50–74	125,949	0	4	39	28	23	6	0	61.24 (61)

[a] Age group 45–49: Sweden $n = 4$, mean age 49.0, Spain $n = 153$, mean age 47.8 years; age group 75–79: Netherlands $n = 51$ and Belgium $n = 1$, mean age 75 years.

data of the region nearest to the municipalities where the trial was conducted were used (Zaragoza for the Madrid centre, Spain, and Basel for the Aarau centre, Switzerland). As the regional age-specific data for the Finnish centre were not available either in CI5 or from the Finnish cancer registry for the required period, national data were used instead. A comparison of the age adjusted rates for Helsinki and Tampere in the period 1992–1996 with the national age adjusted incidence rate of prostate cancer shows the rates to be similar. For the Dutch and Swedish centres, regional data were obtained from the web sites of the respective cancer registries, (Comprehensive Cancer Centres, www.ikcnet.nl, and Health and Welfare Statistical Database, www.socialstyrelsen.se) and for the Belgian centre; cancer registry data for the Antwerp region were used.[6] The incidence rate for the core age group in the 3 years preceding the start of the trial was used for all centres; 1989–1991 for Belgian, 1990–1992 for the Netherlands, 1991–1993 for Sweden, 1993–1995 for Finland, Italy and Spain and 1995–1997 for Switzerland. However the years 1995–1997 were also used for French centres as these were the latest available regional data in CI5. These prostate cancer incidence rates were used to estimate the underlying background incidence in the absence of screening in each centre.

2.3. *Data analysis*

Mean and median PSA values were calculated within each centre by age group at entry (55–59, 60–64 and 65–69) and by screening round, and for men with cancer detected in the first and second screening rounds (according to protocol) for the core age group, 55–69 years. Univariate analysis of variance adjusted for age at screening visit was used for comparisons within centres (between screening rounds) and between centres (within age groups at screening round).

Cancer detection rate (CDR, the ratio of the number of prostate cancers detected by screening to the number of men screened) was calculated for each screening round and analysed using the Chi-square test. In each centre the cancer detection rate was compared with the estimated background prostate cancer incidence rate in the absence of screening (IR), which was obtained by applying the crude age specific incidence rate for each age group to the number of men randomised in that age group. However, because the incidence rates in both the non-responders and the control arm were considerably higher than the underlying incidence based on pre-trial data, we calculated a correction factor according to the method of Cuzick and colleagues[10] using the trial data,

$$c = [(pc - (1 - ar) * p_{nres})/ar]/pc$$

where c is the correction factor; p_c is the incidence rate in control arm; ar is the attendance rate; p_{nres} is the incidence rate in non-responders; and then calculated the adjusted IR is IRS = IR * c. The IRS is shown in Table 2. For the prostate cancer incidence amongst the control arm and non-responders at first and second round visit, the rate in the first 5 years of follow-up and that from year five of follow-up onwards was used, respectively.

3. Results

Table 1 shows the number of men randomised into the screening arm per centre and age category. A total of 125,949 men were randomised. As the Swedish and Spanish centres included men in the age group 50–54 years (31% and 38% of men randomised, respectively), the mean ages at entry in these centres were accordingly significantly lower.

Table 2 presents the attendance rates in the screening arm and the expected incidence rates (IRS) in the absence of screening corrected for the difference between prostate cancer incidence in the non-attenders and the control arm. The attendance rate varied between 100%, in the Spanish centre, and 28%, in the French centre. Overall attendance was 60% or 76%, if the French centre is excluded. The differences in the attendance rate in the first screening round reflected the method of randomisation; high attendance rates were observed in the centres with consent prior to randomisation (Belgium, Netherlands, Spain and Switzerland), whilst the opposite applied for the second round, with the low rate in the Belgian centre possibly being a result of the long interval between the rounds. The IRS for round 1 was in most centres slightly higher than the uncorrected underlying incidence, the largest difference being in Sweden (185.6 versus 146.3

Table 2 – The attendance and expected underlying prostate cancer incidence rate by centre for the age group 55–69 years.

	Background incidence rate[a] per 100,000	Attendance rate			Expected incidence rate (IRS) per 100,000	
		Round 1	Round 2	Round 3	Round 1	Round 2
Belgium	108.2	88	61		111.6	114.7
Finland	147.9	68	87		159.4	154.1
France	311.7	28			332.0	
Italy	126.4	68	84		136.3	125.6
Netherlands	162.3	95	78		162.3	175.8
Spain	110.4	100	69		110.4	160.0
Sweden	146.3	62	84	85	185.6	158.9
Switzerland	249.9	96	83		250.7	228.0

[a] Estimated incidence rate in the trial based on the trial population and the age-specific incidence rate of cancer registries (Netherlands, 90–92, Sweden, 91–93 and Belgium, 89–91) or Cancer Incidence in five continents, www-dep.iarc.fr (Finland, 93–95; Italy, Florence, 93–95; Spain, Zaragoza, 93–95; Switzerland, Basel, 95–97; and France, Tarn, 95–97).

Table 3 – Mean and median PSA levels (ng/ml) by 5-year age category at entry in the eight centres.

Centre	55–59 years at entry Mean PSA ng/ml (median)				60–64 years at entry mean PSA ng/ml (median)				65–69 years at entry mean PSA ng/ml (median)		
	Round 1[a]	Round 2	Round 3[b]	*P-value* [c]	Round 1	Round 2	Round 3 [b]	*P-value*	Round 1	Round 2	*P-value* [c]
Belgium	1.6 (1.0) *n* = 840	1.6 (1.1) *n* = 494		0.049	2.1 (1.3) *n* = 1641	2.5 (1.6) [d] *n* = 917		0.007	2.9 (1.5) [e] *n* = 1262	2.9 (1.9) *n* = 434	0.098
Finland	1.5 (1.0) *n* = 12,005	1.7 (1.2) *n* = 9595		0.067	2.2 (1.2) *n* = 4728	2.2 (1.5) *n* = 3639		0.747	2.7 (1.4) *n* = 4056	2.5 (1.7) *n* = 3011	0.321
France	1.5 (1.1) *n* = 4193				1.9 (1.3) *n* = 3752				2.2 (1.4) *n* = 3224		
Italy	1.6 (1.0) *n* = 1904	1.7 (1.1) *n* = 1574		0.067	1.8 (1.1) *n* = 1577	1.9 (1.2) *n* = 1210		0.522	2.5 (1.3) *n* = 1480	2.2 (1.4) *n* = 1021	0.752
Netherlands	1.6 (1.0) *n* = 6438	1.8 (1.1) *n* = 5009		0.000	2.1 (1.3) *n* = 5315	2.2 (1.5) *n* = 3921		0.000	2.9 (1.6) *n* = 4749	2.5 (1.7) *n* = 3102	0.000
Spain	1.7 (1.0) *n* = 550	1.6 (1.1) *n* = 418		0.038	2.0 (1.1) *n* = 326	1.9 (1.4) *n* = 225		0.016	2.2 (1.4) *n* = 180	2.0 (1.7) *n* = 88	0.242
Sweden [e]	1.6 (1.0) *n* = 1867	1.6 (1.0) *n* = 1485	2.7 (2.1) *n* = 681	0.000	2.6 (1.3) *n* = 1782	2.0 (1.3) *n* = 1439	2.7 (2.0) *n* = 931	0.001			
Switzerland	1.5 (1.0) *n* = 1994	1.8 (1.2) *n* = 1772		0.055	1.8 (1.1) *n* = 1529	2.1 (1.4) *n* = 1328		0.000	2.1 (1.4) *n* = 1208	2.4 (1.6) *n* = 995	0.452
P-value [b]	0.449	0.002			0.000	0.018			0.000	0.010	

[a] Only first screen visits in response to invitation in first screening round; hence, total number of first screens are not complete for Sweden.
[b] Visit 3 in Sweden (2-year interval; other centres 4-year screening interval).
[c] Univariate analysis of variance with correction for age at screening visit.
[d] Excluding outlier of PSA 1500 ng/ml.
[e] Excluding outlier of PSA 706 ng/ml.

per 100,000 men). The IRS at round 1 varied considerably between centres, ranging from 110.4 per 100,000 in Spain to 332.0 in France.

Mean and median values of PSA by centre, screening round and age group at entry are shown in Table 3. The mean PSA value increases with age, in all centres, however, the mean PSA value within age groups was similar at the first and second rounds, regardless of the screening interval, particularly for the youngest and the oldest age groups, 55–59 years and 65–69 years. In the Dutch centre the mean PSA value of men aged 55–59 years at entry increased in the second screening round (from 1.6 to 1.8 ng/ml), whilst in the age group 65–69 years a decline from 2.9 to 2.5 ng/ml was observed.

Fig. 1 shows the proportion of tumours detected by PSA category (0–2.9, 3.0–3.9, 4.0–9.9 and $\geqslant$10.0) in the two screening rounds. Cancer detection at PSA categories lower than 4.0 ng/ml in the first screening round reflected the different centre specific ancillary studies conducted at low PSA values. This pattern remained observable to a large extent in the second (incidence) screening round. Overall, in all centres, the majority of the tumours detected in the first screening round were at the PSA range 4.0–9.9 ng/ml (37% in Switzerland to 73% in Spain). Except for the French and Swiss centres, over 20% of the tumours was detected at a PSA value higher than 10 ng/ml. In the second screening round, there was a shift to more cancer detection in the PSA range 3.0–3.9 ng/ml. Nevertheless, in most centres the majority of tumours were still detected in the range 4.0–9.9 ng/ml. In contrast, cancer detection at PSA level $\geqslant$10 ng/ml became modest at the second screening round.

The cancer detection rate (CDR) in the first and second round for each centre is also presented in Table 4. There is high variability in the CDR between the centres. In the Dutch centre, the prevalent screening round yielded a detection rate of 46 per 1000 men screened, whilst in the Italian centre the rate was 16 per 1000 men screened. This difference reflects the intensity of the screening protocol in the Dutch centre in the early years. At the second screening round, the variability in the CDR amongst countries remained, and in most countries the rate was comparable to that observed in the first, except for the Belgian centre, possibly due to the long screening interval of 7 years, and the Finnish centre, possibly due to changes in the biopsy technique, where the CDR in the second round was significantly higher than that of the prevalent screening round (22 versus 50 per 1000 men screened and 26 versus 32 per 1000 men screened, respectively).

Fig. 2 presents the cancer detection rate in men with PSA values 4.0 ng/ml or higher, to allow comparison amongst the centres at a common threshold, thus excluding tumours detected in the ancillary studies described above. As expected, in the second screening round cancer detection is considerably lower amongst the men who were screened in the first round according to protocol (no early recall or delay visits) in the Dutch and Spanish centres (34 versus 21 per 1000 and 22 versus 8 per 1000 men screened, respectively) and to a lesser extent in the Italian and Swedish centres (14 versus 12 per 1000 and 24 versus 18 per 1000 men screened, respectively). For the Belgian, Finnish and Swiss centres the opposite is observed, with a doubling of the cancer detection rate in the second round in the Belgian centre (16 versus 35 per 1000 men screened).

As shown in Table 4, the proportion of men screened who subsequently underwent a biopsy after referral differed between centres within the same screening round. High biopsy rates were observed, except for the French and Italian centre,

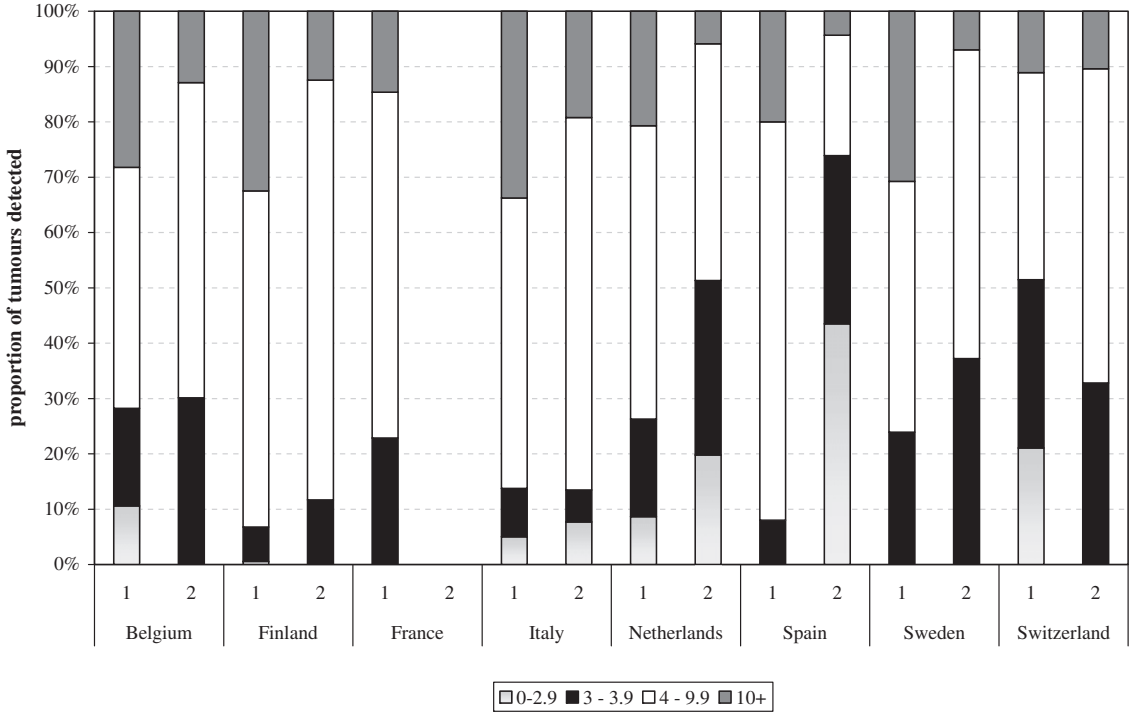

Fig. 1 – The proportion of prostate cancer detected in the core age group (age 55–69 at entry) by PSA categories (0–2.9, 3.0–3.9, 4.0–9.9 and $\geqslant$10.0) in the first and second screening round.

Table 4 – Screening outcome at the first and second screening round and the ratio of cancer detection rate to expected incidence in men screened in the core age group (55–69 years at entry).

	Men screened N		Proportion of men biopsied[a] %			Cancers detected N		Cancer detection rate (CDR) per 1000			CDR/IRS[b]		
	Round 1	Round 2	Round 1	Round 2	*P-value* [c]	Round 1	Round 2	Round 1	Round 2	*P-value* [c]	Round 1	Round 2	Round 1[d]	Round 2[d]
Belgium	3795	1846	67.9	77.6	0.001	85	93	22	50	0.000	20	44	15	31
Finland	20,789	16,245	94.2	90.6	0.000	545	514	26	32	0.002	16	21	15	18
France	11,169		39.8			280		25			8		6	
Italy	4961	3805	43.8	31.8	0.000	80	52	16	14	0.349	12	11	10	9
Netherlands	16,502	12,032	91.4	89.3	0.006	753	526	46	44	0.440	28	25	21	12
Spain	1056	731	86.2	68.7	0.000	25	23	24	31	0.317	22	19	20	5
Sweden	3649	2924	91.2	81.7	0.000	117	86	32	29	0.537	17	18	13	12
Switzerland	4731	4095	86.4	76.1	0.000	171	125	36	31	0.144	14	14	7	9

[a] i.e. the proportion of men that had undergone biopsy after referral upon positive screening testing
[b] CDR, cancer detection rate, IRS, expected incidence rate in men screened; calculated based on the underlying incidence.
[c] Chi-square test.
[d] Calculated with the rate of cancer detected at the PSA threshold 4.0 ng/ml or higher.

which remained considerably low in the second screening round (39% in France centre and 43.8% versus 31.8% in Italy), despite an overall tendency to lower rates in this round. The ratio of the CDR to the expected underlying prostate cancer incidence in attenders (IRS) was calculated for each centre (Table 4), which is comparable with the widely known prevalent to incidence (P/I) ratio for the prevalent screening round. Despite the previously observed variability in the CDR amongst the centres, the ratio of CDR/IRS in the first screening rounds was close in four centres (16–22), with somewhat lower values in Italy and Switzerland and a higher value in the Netherlands. For the French centre the ratio was only 8, possibly due to the low biopsy rate. In the second round, this ratio hardly changed in several centres, but increased markedly in Belgium. When only cancers detected at a PSA value of 4 ng/ml or higher are considered, the ratio in the first round remains high and comparable to when cancers detected at all PSA levels are included. However, this no longer applied for the second round, where the ratio is much lower.

4. Discussion

In this study we described the mean PSA value by age group at entry and the CDR relative to the underlying prostate cancer incidence in the centres participating in the ERSPC trial. Given the difference in the underlying cancer incidence between the countries, it is assumed that this could lead to variability between countries with respect to PSA levels and the cancer detection rate. In the present study, variations were indeed observed in the mean PSA values at screening and cancer detection rates; however, this variation could not appear to be related to the underlying incidence in absence of screening, but rather reflected the differences in study protocols. In all centres, the majority of prostate cancers detected were in the PSA range 4.0–9.9 ng/ml. Cancer detection at lower PSA values reflected the different ancillary studies conducted in the centres and the changes in protocol with respect to the PSA threshold, from $\geqslant$4.0 to $\geqslant$3.0 ng/ml,[11] particularly in the second round screening.

In the prevalent round of cancer screening, the detection rate is expected to be dependent on the underlying incidence of the disease, given the sensitivity of the screening test.[4,5] In the current study cancer detection rates in the first screening round were between 12 and 28 times higher than the expected background underlying incidence in the absence of screening, with the exception of the French centre. There is no clear evidence of a relationship between the underlying incidence and cancer detection, as the latter appeared to be affected by the local study protocol allowing ancillary studies, and the compliance with biopsy amongst those with a positive screening test, as apparent from the data for the French and the Italian centres. The estimated underlying incidence was highest for the French cohort and lowest for the Spanish, but this was not reflected in the cancer detection rate, with CDR/IRS ratios of 8 and 22, respectively.

The re-screening interval of 4-year between the first and the second round was applied in most centres, except for Sweden, 2-year period, and Belgium, 7-year period because of an interruption in funding.[1] In Belgium, the effect of the

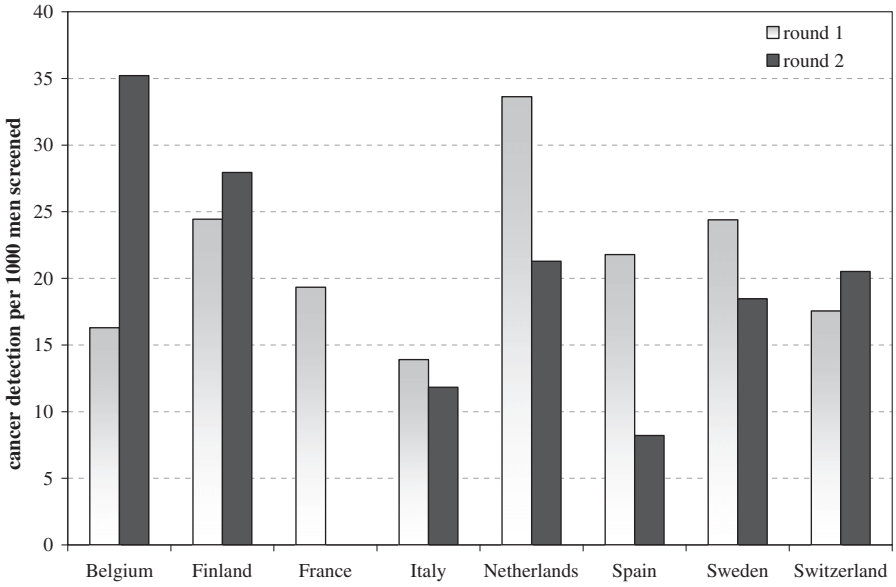

Fig. 2 – Cancer detection at PSA threshold 4 ng/ml or higher in the core age group (age 55–69 at entry).

long re-screening interval was evident on the cancer detection rate in the second screening round. In contrast, the short screening interval in the Swedish centre did not lead to a significantly lower CDR at the second screening round, neither did the 4-year interval in the Dutch centre, where no differences were observed in the CDR. However, at the third screening round in the Swedish centre, a CDR of 48 per 100 men screened is observed, for men who attended the regular screenings, compared to 32 and 29 per 1000 men screened in the two previous rounds (2-year interval). It could be argued that in the Swedish centre cancers are detected that would have arisen as interval cancers in the longer re-screening interval; however Roobol and colleagues[12] recently showed that the 10-year cumulative incidence of interval cancer in the Dutch centre was 0.43% and Swedish centre 0.74%, although not statistically and significantly different. The difference in background incidence of prostate cancer amongst the two centres was raised as a possible explanation.[12] On the other hand, the method of randomisation, before (Sweden) and after (Netherlands) informed consent, may also partly explain this bias, as people consenting to be randomised might be different to the general population with respect to prostate cancer risk.[13]

In breast cancer screening the ratio CDR to the background underlying incidence is one of the performance indicators of the breast cancer screening programmes reported in the European guidelines for quality assurance,[14] stipulated at minimum 3 (CDR is 3 × the IRS) at prevalent screens and 1.5 at subsequent screens. The findings of the current study show that in prostate cancer screening cancer detection rates are higher and the CDR/IR ratio is 12–28 times the incidence of prostate cancer expected amongst men (aged 55–69 years at randomisation) in the absence of screening. In the second screening round, incident screens, values of the ratio CDR to IRS were only slightly lower (11–25, excluding the Belgian centre, ratio of 44). A possible explanation for the difference in this indicator between breast cancer screening and prostate cancer screening is the very high age dependency of prostate cancer, with incidence doubling for each 5-year category. It might also lie in the differences in lead time. The estimated lead time in prostate is about two to five times longer than the estimated lead time for breast cancer (5–12 years[15,16] versus approximately 2.2 years[17]).

The high figures for the CDR/IRS ratio might suggests a high rate of overdiagnosis in the ERSPC centres. Assuming that the mean sojourn time of prostate cancer is 10 years[15] to 12.7 years[16] and the test sensitivity of PSA is about 85%,[18] the cancer detection in the prevalent screening round is expected to be about 8–11 times the underlying prostate cancer incidence rate.[19] As mentioned above, the CDR in all centres is at least 11 times the IRS, in both screening rounds. However, when only tumours detected at PSA 4 ng/ml or higher are considered, in the majority of the centres the second round ratios approximate the expected values.

In this study we used historical data to estimate the underlying incidence of prostate cancer because of the marked increase in rates in the trial period; this and the high rates observed in the control arm are likely to reflect contamination due to ad hoc PSA screening.[20] Nevertheless there may be underlying trends in incidence which we have not been able to take account of. As shown by Bray and colleagues in this Special Issue,[21] for all centres, the prostate cancer incidence increased by 4–7% since 1980s (in the Southern countries) and 1990s (in the Northern and Western countries) up to 2005, except the Netherlands where the rates tended to decline between 1995 and 2001, about –0.8%. The latter particularly applied to men aged 65–74 as demonstrated by Cremers and colleagues.[22] Our adjustment for selection bias had to use data from the control arm of the trial, and may also have been influenced by contamination. Furthermore, the variability in the compliance with biopsy referrals, as indicated by the biopsy rate, amongst the different centres might affect a true relationship between underlying risk and cancer detection, as seen for the Dutch and the Italian centre.

In conclusion, comparable patterns are seen within countries for the mean PSA values at screening and high variation is observed in the cancer detection rates amongst the countries, which likely reflect the differences in protocol rather than a true relationship between the underlying incidence and cancer detection rate. However, compliance with biopsy after referral plays an important role. Within the margins of these differences, the anticipated 20% mortality difference between the screening arm and the control arm in the ERSPC trial has been demonstrated, although current levels of overdiagnosis would make population screening less viable. Hence, we must await the outcome of the longer-follow-up period in the ERSPC trial and the sestimates of cost-effectiveness.

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Conflict of interest statement

None declared.

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