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Reduced mortality for women with mammography-detected breast cancer in east Denmark and south Sweden

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ABSTRACT

The 5-year relative survival from breast cancer in Denmark is 10 percentage points lower than in Sweden. This difference has been demonstrated previously as being caused partly by more involved lymph nodes and larger tumours in Denmark. Sweden has had nationwide mammography-screening coverage since 1991, whereas this is still in its infancy in Denmark. In the search for an explanation for the remaining survival difference, patient delay was a likely candidate. This study compared patient delay and mammography-detection between two national regions. Data on patient delay and mammography were obtained from hospital records from 1989 and 1994, and analysed using Cox proportional hazard analysis of death within the first 5 years, with the factors age, country, delay/mammography detection and established patho-anatomic variables. A comparison of patient delay and mammography detection in 1989 and 1994 showed more mammography-detected tumours in south Sweden and more women with long delay in east Denmark. Mammography detection, but not long patient delay, had a significant effect on the death hazard when adjusting for patho-anatomic risk factors. The hazard ratio was not eliminated in 1989, but in 1994, the hazard ratio between east Denmark and south Sweden was reduced from 1.3 to 1.1. In conclusion, patient delay did not appear to have any effect on 5-year survival when adjusting for patho-anatomic factors, but tumour detection by mammography affected survival favourably and partly explained the survival difference between east Denmark and south Sweden.

1. Introduction

The importance of diagnostic (or patient) delay for breast cancer survival is controversial. A delayed diagnosis of breast cancer (i.e. a prolonged time from first symptom noticed by the patient until first presentation of the tumour to a health professional) is commonly believed to result in decreased survival, because the tumour presents itself at a more advanced stage, and patient delay of more than 12 weeks has been found to be associated with increased tumour size, more advanced stage of disease[1–4] and reduced long-term survival.[5–9] However, the correlation is not that clear-cut, and other studies have failed to link delayed diagnosis to inferior survival,[10–14] possibly because of biological characteristics of the tumour,

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i.e. delayed diagnosis being associated with slow tumour growth.[15–20]

A more recent large systematic review of 87 observational studies worldwide on 101,954 patients has shown that any type of delay of 3–6 months between onset of symptoms and treatment is associated with a 5-year survival deficit, which exceeds what could be attributed to the 3–6 months delay, and which therefore cannot be accounted for by lead-time bias alone.[21]

Population-based mammography screening programs have been initiated in many countries in order to ensure early diagnosis and reduce mortality.[22]

In a large Finnish study,[23] and in a North American/Canadian analysis of 3 randomised screening trials,[24] mode of tumour detection (i.e. +/− detection by mammography screening) was demonstrated as an important prognostic factor, even after adjustment had been made for tumour size, lymph node status and disease stage. A large population-based Swedish analysis has further concluded, that screened women have a 39% reduction in breast cancer mortality, after adjustment for contemporaneous changes and self-selection bias.[25,26]

In comparison with Sweden, Denmark has experienced a 10 percentage point reduction in 5-year relative survival from breast cancer for the last 35 years.[27] In our previous study the results suggested that this reduced survival could be explained partly by a different distribution of patho-anatomic factors, with larger tumours and a higher fraction of involved lymph nodes in east Denmark,[28] but an increased hazard rate ratio of RR = 1.7 in 1989 and of RR = 1.3 in 1994 for east Denmark compared with south Sweden still existed within the first 5 years after diagnosis.

Table 1 – Cox proportional hazard analysis in the first 5 years after diagnosis: women with breast cancer diagnosis at age 50–79 years in 1989 in east Denmark and south Sweden

1989 cohorts	DK (623) SE (481)		Model 1			Model 2			Model3		
			Including patient delay			Excluding patient delay			Including patient delay		
Risk factors	%	%	RR	(95% CI)	P	RR	(95% CI)	P	RR	(95% CI)	P
Country					0.0002			0.0002			0.001
South Sweden			1			1			1		
East Denmark			1.7	(1.3–2.2)		1.7	(1.3–2.2)		1.6	(1.2–2.1)	
Age at diagnosis (years)					<0.0001			0.0003			0.0005
50–59	38	29	1			1			1		
60–69	40	44	1.0	(0.8–1.4)		1.2	(0.9–1.6)		1.2	(0.9–1.6)	
70–79	23	27	1.8	(1.4–2.5)		1.8	(1.3–2.4)		1.7	(1.3–2.4)	
Lymph nodes examined								0.01			0.01
1–4	27	14				1.6	(1.2–2.2)		1.6	(1.2–2.1)	
5–9	50	42				1			1		
10+	23	44				1.1	(0.8–1.4)		1.1	(0.8–1.4)	
Nodal status								<0.0001			< 0.0001
No. nodes examined	57	58				1			1		
Node-positive 1–3	28	26				1.7	(1.3–2.3)		1.7	(1.3–2.3)	
Node-positive 4–6	7	10				4.6	(3.2–6.6)		4.6	(3.2–6.6)	
Node-positive 7+	8	6				5.0	(3.3–7.3)		4.9	(3.3–7.3)	
Tumour size (mm)								0.0006			0.001
1–10	14	19				0.8	(0.5–1.3)		0.8	(0.5–1.4)	
11–20	42	44				1			1		
21–30	24	22				1.4	(1.0–1.9)		1.4	(1.0–1.9)	
31–50	15	10				1.7	(1.2–2.4)		1.7	(1.2–2.4)	
51+	6	5				2.2	(1.4–3.3)		2.2	(1.4–3.4)	
Histology								0.01			0.01
Well-differentiated	28	37				0.7	(0.5–0.9)		0.7	(0.5–0.9)	
Poorly differentiated	72	63				1			1		
Oestrogen receptor status											0.0008
Positive	51	63				1		0.0005	1		
Negative	12	12				1.8	(1.3–2.5)		1.8	(1.3–2.4)	
Unknown	37	26				1.5	(1.2–1.9)		1.5	(1.1–2.0)	
Patient delay					0.18						0.89
Mammography	2	33	0.6	(0.4–0.9)					0.8	(0.5–1.4)	
<3 months	73	59	1						1		
3–6 months	8	3	1.0	(0.6–1.6)					0.9	(0.5–1.4)	
>6 months	12	3	1.2	(0.8–1.8)					1.0	(0.7–1.5)	
Unknown	5	1	0.8	(0.4–1.7)					0.8	(0.4–1.6)	

RR, hazard rate ratio.

Mammography screening was initiated in the city of Malmo, Sweden, in 1976 and covered the whole of south Sweden by 1991.[29] Screening was not initiated in east Denmark until 1991 and then only in the municipality of Copenhagen.[30]

The present study considers differences in patient delay and mammography-detection practice between the 2 regions. Its purpose is to describe the effect on survival and to determine whether these factors contribute to the remaining difference in breast cancer survival between countries.

2. Patients and methods

2.1. Patient selection

Women with a diagnosis of invasive carcinoma of the breast in 1989 and 1994 in east Denmark and south Sweden were identified in the Danish Cancer Register and the Regional Tumour Register of Southern Sweden and followed-up for death or emigration through the year 2000 in the national population registers. For more specific details regarding patient selection, see Christensen.[28]

The female populations were 1.1 million in east Denmark and 0.7 million in south Sweden in both 1989 and 1994. The two regions are comparable with regard to socio-economic factors, such as education, employment and income. Age-adjusted (world) incidence rates of breast cancer in 1989 and 1994 for east Denmark were 77.1 and 73.9 per 100,000 inhabitants (in Denmark 71.5 and 75.2 per 100,000, respectively) and for south Sweden 69.5 and 77.2 per 100,000 inhabitants (in Sweden 66.5 and 73.5 per 100,000, respectively). The cohorts to be compared consisted of 1139 and 1150 Danish patients and 815 and 900 Swedish patients in 1989 and 1994, respectively.

Table 2 – Cox proportional hazard analysis in the first 5 years after diagnosis: women with breast cancer diagnosis at age 50–79 years in 1994 in East Denmark and South Sweden

1994 cohorts	DK (718)	SE (519)	Model 1			Model 2			Model 3		
			Including patient delay			Excluding patient delay			Including patient delay		
Risk factors	%	%	RR	(95% CI)	P	RR	(95% CI)	P	RR	(95% CI)	P
Country					0.28			0.05			0.48
South Sweden			1			1			1		
East Denmark			1.2	(0.9–1.6)		1.3	(1.0–1.8)		1.1	(0.8–1.5)	
Age at diagnosis (years)					0.006			<0.0001			0.0002
50–59	36	34	1			1			1		
60–69	38	34	1.4	(1.0–1.9)		1.3	(0.9–1.8)		1.3	(1.0–1.8)	
70–79	26	31	1.7	(1.2–2.3)		2.0	(1.4–2.8)		2.0	(1.4–2.7)	
Lymph nodes examined								0.04			0.04
1–4	4	9				1.3	(0.7–2.1)		1.3	(0.8–2.3)	
5–9	35	43				1			1		
10+	61	48				0.7	(0.6–1.0)		0.8	(0.6–1.0)	
Nodal status								<0.0001			<0.0001
No nodes examined	55	66				1			1		
Node-pos 1–3	25	22				2.5	(1.7–3.5)		2.4	(1.7–3.4)	
Node-pos 4–6	9	5				4.3	(2.8–6.5)		4.4	(2.9–6.9)	
Node-pos 7+	12	7				8.7	(6.0–12.8)		8.4	(5.7–12.4)	
Tumour size (mm)								0.02			0.04
1–10	14	25				0.8	(0.5–1.4)		0.8	(0.5–1.4)	
11–20	42	43				1			1		
21–30	24	23				1.3	(0.9–1.8)		1.2	(0.9–1.7)	
31–50	15	8				1.4	(1.0–2.1)		1.4	(1.0–2.0)	
51+	4	2				2.0	(1.3–3.2)		2.0	(1.2–3.1)	
Histology								0.001			0.003
Well-differentiated	30	40				0.6	(0.4–0.8)		0.6	(0.4–0.8)	
Poorly differentiated	70	60				1			1		
Oestrogen receptor status								<0.0001			<0.0001
Positive	70	53				1			1		
Negative	27	18				2.0	(1.5–2.6)		2.0	(1.5–2.6)	
Unknown	3	29				0.8	(0.5–1.5)		0.9	(0.5–1.6)	
Patient delay					<0.0001						0.02
Mammography	6	51	0.3	(0.2–0.5)					0.6	(0.4–0.9)	
<3 months	70	42	1						1		
3–6 months	6	4	1.2	(0.7–2.0)					0.9	(0.5–1.5)	
>6 months	8	2	1.5	(1.0–2.4)					1.0	(0.6–1.5)	
Unknown	7	1	1.3	(0.8–2.2)					1.8	(1.0–3.0)	

RR, hazard rate ratio.

2.2. Data collection and management

Information on patient delay and mammography-screening detection was obtained from hospital records, supplemented with written information from general practitioners and private surgeons. Information on classical patho-anatomic variables was obtained from hospital records.[28]

2.3. Definitions

Patient delay was defined as time from first detection of the tumour (mainly by the patient) until first contact with the health authorities (i.e. general practitioner, private specialist, mammography clinic). Mammography-detected tumours, i.e. tumours detected by population based mammography screening, or by mammography control on own initiative, might be considered as having a 'negative' patient delay by diagnosing the tumour before it gave clinical symptoms. These tumours were therefore kept as a separate group in the analysis. Women with interval tumours, i.e. self-detection of the tumour between screening rounds, were not included in the group of mammography-detected tumours.

Patient delay and mammography-detection was analysed as a categorical factor with five levels: mammography-detected, delay <3 months, 3–5 months, 6+ months, and unknown delay information.

System delay was defined as the interval from first contact to the health authorities (e.g. a screening clinic or a general practitioner (GP)) until first treatment or, in case of no treatment, until date of diagnosis.

2.4. Statistical methods

Logistic regression with modelling of the dependency between the patho-anatomic variables and delay was performed.

Cox proportional hazard analysis from all causes of death in the first 5 years following diagnosis was performed firstly with the factors age, country and delay/mammography (model 1 in Tables 1 and 2), and secondly supplemented with the established patho-anatomic factors (models 2 and 3). For the models in Tables 1 and 2 the age group was restricted to age 50–79 years, as we have previously shown that the survival difference between countries was restricted to this age group.

Modelling of relative survival by excess risk models was attempted, but appeared to be unstable with this large amount of explaining factors, and is not presented.

2.5. Ethics

The study was approved by the scientific ethics committee of greater Copenhagen and the Danish Register Council, as well as the research ethics committee of Lund University, Sweden.

3. Results

3.1. Distribution of delay and mammography detection

Tables 3 and 4 show the distribution of patient delay and mammography detection for all age groups in relation to age and established prognostic factors for each of the four cohorts defined by country and year.

For all ages a larger share of mammography-detected tumours was seen in south Sweden, especially in 1994, and a larger share of women with long patient delay was seen in east Denmark. High age and large tumour size were both associated with longer delay. Logistic regression of patient delay demonstrated that tumour size was the most important factor for long delay (analyses not shown).

For the age group 50–79 years the mammography-detected tumours were those detected by national screening programs (0% in east Denmark and 30.6% in south Sweden in 1989, 5.8% in east Denmark and 48.5% in south Sweden in 1994) – and those detected by mammography on own initiative (2.1% in east Denmark and 1.1% in south Sweden in 1989; 2.7% in east Denmark and 0.3% in south Sweden in 1994) (not shown in tables). Median system delay for mammography-detected tumours was 16 d (east Denmark, 1994) and 18 and 20 d (south Sweden, 1989 and 1994). For tumours detected by mammography on own initiative the corresponding figures were 40 and 33 d (east Denmark, 1989 and 1994) and 20 and 22 d (south Sweden, 1989 and 1994), respectively. The same pattern was seen for all ages.

Median patient delay for clinically detected tumours was for all age groups 14 d in east Denmark in 1989 and 1994 and in south Sweden in 1989, and only 11 d in south Sweden in 1994.

3.2. Survival analyses

Tables 1 and 2 show Cox proportional hazard analysis within the first 5 years after tumour detection for patients age 50–79 years. The models include a factor of patient delay with mammography detection as an extra category along with the previously used variables.[28]

If age, national region, and delay/mammography were the only factors standardised for, delay of more than 6 months had a statistically significant elevated death hazard in 1994, but not in 1989 (model 1 in Tables 1 and 2). Patients with mammography-detected tumours had a significantly lower death hazard than patients with tumours detected within the first 3 months after first symptom (hazard rate ratio, RR = 0.6, 95% confidence interval (CI) 0.4–0.9 in 1989 and RR = 0.3, 95% CI 0.2–0.5 in 1994).

The impact on the death hazard of classical patho-anatomic variables has been described previously[28] and is shown in model 2. The number of positive lymph nodes had the highest influence on death hazard in all analyses.

Adding the factor of patient delay/mammography detection in model 3 in Tables 1 and 2 showed that it had no importance in 1989 ($P = 0.5$), while it was significant in 1994 ($P = 0.02$) with no difference between the four delay categories, but with a reduced risk for mammography detection of 0.6 (95% CI 0.4–0.9). RR for east Denmark compared with south Sweden was reduced from 1.3 (95% CI 1.0–1.7) to a non-significant 1.1 (95% CI 0.8–1.5) (model 3 compared with model 2, Table 2). If analyses were made for patients of all ages, the corresponding RR for east Denmark was reduced from 1.2 (95% CI 1.0–1.5) to 1.1 (95% CI 0.9–1.4) (analyses not shown). Patient delay on its own had no direct effect on survival, but mammogra-

Table 3 – Distribution of patient delay and mammography detection among breast cancer patients in east Denmark and south Sweden in 1989

	East Denmark 1989						South Sweden 1989					
	n	Unknown	Mammography	Delay in months			*n*	Unknown	Mammography	Delay in months		
		n = 68 %	*n* = 25 %	<3 *n* = 806 %	3–5 *n* = 99 %	6+ *n* = 141 %		*n* = 25 %	*n* = 193 %	<3 *n* = 523 %	3–5 *n* = 32 %	6+ *n* = 42 %
All	1139	6	2	71	9	12	815	3	24	64	4	5
Age at diagnosis (years)												
40–49	230	7	3	70	9	10	142	1	15	69	7	8
50–59	273	5	3	73	8	10	145	1	33	60	2	4
60–69	285	5	2	72	7	14	232	1	47	47	3	2
70–79	224	6	1	71	8	14	162	5	9	75	5	6
80+	127	7	1	65	13	15	134	10	1	80	1	8
Distant metastases												
Present	51	4	0	57	12	27	26	4	0	77	4	15
Absent	1088	6	2	71	9	12	789	3	24	64	4	5
Lymph nodes examined												
No. nodes examined	181	8	0	65	6	20	131	11	7	69	4	10
1–4	259	4	2	70	10	14	96	5	23	69	2	1
5–9	470	7	3	72	9	10	282	1	33	56	4	6
10+	229	5	3	72	8	10	306	1	23	69	4	3
Nodal status												
No. nodes examined	181	8	0	65	6	20	132	11	7	69	4	10
Node-negative	526	5	4	74	7	11	386	1	34	56	4	4
Node-positive 1–3	275	5	2	71	11	11	175	2	22	71	2	2
Node-positive 4–6	74	8	0	62	19	11	73	1	14	67	8	10
Node-positive 7+	83	7	0	71	10	12	49	2	6	84	4	4
Tumour size (mm)												
0–10	153	9	7	70	7	8	135	2	48	48	0	2
11–20	432	4	2	76	9	9	308	2	26	66	3	4
21–30	274	7	1	70	10	12	190	2	15	72	5	6
31–50	162	4	1	76	7	12	96	2	10	75	5	7
51+	90	8	0	48	9	36	53	4	9	62	13	11
Multiple/unknown	28	21	4	46	0	29	33	27	18	42	0	12
Histology												
Well-differentiated	285	6	2	71	8	12	268	2	28	63	3	5
Poorly differentiated	788	5	2	71	9	12	546	4	22	65	4	5
Unknown	66	12	0	65	8	15	1			100		
Oestrogen receptor status												
Positive	518	5	2	70	11	12	459	1	22	68	4	5
Negative	144	4	1	81	7	7	101	1	13	72	6	8
Unknown	477	7	3	69	6	14	255	8	30	55	2	5

Table 4 – Distribution of patient delay and mammography detection among breast cancer patients in east Denmark and south Sweden in 1994

	East Denmark 1994						South Sweden 1994					
	n	Unknown	Mammography	Delay in months			*n*	Unknown	Mammography	Delay in months		
		n = 80 %	*n* = 73 %	<3 *n* = 798 %	3–5 *n* = 81 %	6+ *n* = 118 %		*n* = 16 %	*n* = 343 %	<3 *n* = 457 %	3–5 *n* = 38 %	6+ *n* = 46 %
All	1150	7	7	69	7	10	900	2	38	51	4	5
Age at diagnosis (years)												
40–49	215	7	2	76	6	8	178	1	31	53	6	8
50–59	276	7	7	70	7	9	193	2	56	36	4	2
60–69	298	8	12	67	4	8	198	1	59	36	1	4
70–79	243	7	5	67	9	12	195	1	31	58	6	5
80+	118	5	0	65	12	18	136	7	1	79	5	9
Distant metastases												
Present	37	8	3	57	5	27	40	0	3	70	5	23
Absent	1113	7	6	70	7	10	860	2	40	50	4	4
Lymph nodes examined												
No. nodes examined	139	6	1	64	7	22	141	9	13	64	5	9
1–4	63	3	3	78	10	6	60	0	50	42	7	2
5–9	354	7	4	70	8	11	318	0	42	48	4	6
10+	594	8	9	69	6	8	381	1	42	50	4	4
Nodal status												
No. nodes examined	139	6	1	64	7	22	142	8	14	63	5	9
Node-negative	533	7	10	70	6	7	473	1	52	42	3	2
Node-positive 1–3	268	7	5	73	7	7	175	1	33	57	5	5
Node-positive 4–6	92	5	3	62	9	21	49	0	27	49	10	14
Node-positive 7+	118	7	2	70	10	11	61	0	13	69	8	10
Tumour size (mm)												
0–10	156	8	15	67	4	5	187	1	67	30	1	1
11–20	434	6	7	74	7	6	352	1	43	47	5	4
21–30	268	8	4	71	7	10	189	2	22	69	3	3
31–50	181	6	4	67	7	17	98	0	12	68	9	10
51+	81	4	0	56	10	31	39	3	10	46	15	26
Multiple/unknown	30	20	3	47	13	17	35	11	23	54	0	11
Histology												
Well-differentiated	317	6	10	71	5	8	329	2	48	43	4	3
Poorly differentiated	810	7	5	70	7	11	570	2	33	55	5	6
Unknown	23	13	4	43	30	9	1			100		
Oestrogen receptor status												
Positive	776	6	7	69	8	11	449	2	35	53	4	6
Negative	312	8	5	71	7	10	171	0	28	60	8	5
Unknown	62	11	2	73	7	6	280	3	50	41	2	4

phy-detection had, with a non-significant RR = 0.7 (95% CI 0.5–1.2) in 1989 and RR = 0.6 (95% CI 0.4–0.9) in 1994.

Restriction of mammography-detected tumours to screen-detected tumours only did not change the results. Only confidence intervals were wider, due to a reduced number of patients in the effect group. Interestingly, however, tumours detected by mammography on own initiative had a lower death hazard than clinically detected tumours and were thus comparable to screening detected tumours (data not shown).

System delay did not appear to have any influence on breast cancer survival. In both east Denmark and south Sweden system delay was reduced for tumours with a poor prognostic potential (data not shown).

4. Discussion

From a biological point of view it will take approximately 8 years from the first appearance of a cancer cell in the breast until a tumour is detectable, even at its earliest presentation,[12] and for the individual patient it must be assumed that the earlier the tumour is diagnosed, irrespective of growth rate, the better the likelihood of finding confined disease.[9,21,31] Survival from breast cancer may, however, also rely on predetermined tumour biology,[1,10–14] and this is believed to differ from one patient to the other, depending not only on growth rate but also on inherent characteristics of the patient and the tumour.[31]

We have concentrated on the age group 50–79 years, because we have previously found that breast cancer survival did not differ between east Denmark and south Sweden in the young (40–49 years) and the old age groups (80 years or more).[28]

We have also concentrated on patient delay and detection by mammography screening and not doctor's or treatment delay, as we could confirm the findings of others[6] that this factor had no influence on breast cancer survival.

Apart from finding a larger share of mammography-detected tumours in south Sweden in 1994, we also found that these tumours were associated with a higher share of negative lymph nodes, or, if positive, a lower number of these (Tables 3 and 4).

Mammography screening was introduced in Malmo in 1976 on a trial basis. In 1989, the regular screening started in a few hospital districts and was by 1991 covering the whole southern part of Sweden.[25] It is therefore not surprising that as many as 24% and 38% of Swedish women in 1989 and 1994, respectively, had their tumour detected by mammography. The only Swedish women with long patient delay were those too young or too old to be invited to participate in a mammography screening program, those who had declined to participate in the program, and those who presented with an interval cancer. Among Danish women, only 2% and 7% in 1989 and 1994, respectively, presented with mammography-detected tumours. In 1989 this could only happen by mammography screening on own initiative, but in 1994 contribution from the limited mammography screening in the municipality of Copenhagen, starting in 1991,[30] added to the higher mammography detection rate of these tumours. We found, like others,[23–26] that mode of detection (i.e. mammography versus conventional detection) was a major independent prognostic factor of survival. It had the effect that the difference in death hazard between east Denmark and south Sweden was reduced in 1989 and disappeared in 1994, if tumours detected by mammography were kept as a separate group in the Cox analysis (Table 1). One reason for this effect of mammography detection on the death hazard may be due to a higher social status among mammography-users. Another may be due to biological factors, specific for mammography-detected tumours.

Differences in the hazard between patients with tumours detected by mammography screening and tumours detected by mammography control on own initiative might have been suspected, but was not confirmed by the Cox analyses. Only the confidence intervals were wider due to the reduced number of patients in the effect group. Interestingly, however, the hazard for those detected by self-initiated mammography appeared to be more comparable to that for patients with tumours detected by mammography screening and better than that for patients with clinically detected tumours (data not shown).

Some subtypes of breast cancer with a more favourable course (e.g. mucinous and lobular type carcinomas) are difficult to diagnose by mammography and may pose a bias in the calculations, but their share were similar between east Denmark and south Sweden and between tumours detected by and not detected by mammography (data not shown).

Studies on patient delay have shown that if this exceeds 3 months, it affects survival adversely.[6,9] Our Cox analysis with age, region and patient delay as the only risk factors showed that delay longer than 6 months was connected with an increased hazard rate, but the effect disappeared in the multivariate analysis, if the previously shown influential pathoanatomic factors were included in the model (Tables 1 and 2).[28]

We were not able to explain why the category 'unknown delay' appeared to carry a high RR in the Cox analysis for 1994 (Table 2).

Unfortunately, modelling of relative survival with excess risk models did not give stable results. If such an analysis had been possible we would have expected a further reduction in the survival difference between countries, because population mortality is lower in Sweden than in Denmark.[28]

Opponents of mammography screening argue that the reason that groups of women survive longer if diagnosed at an earlier stage is partially a reflection of lead-time bias, but the fact that the risk of regional and distant spread is increased with increasing tumour size must be considered as well. Our results have shown that although long delay is most closely correlated with large tumour size, it is to a minor degree also correlated with positive lymph node status, which is the more important factor for survival. The difference in mammography screening between east Denmark and south Sweden in 1994 contributed significantly to the explanation of the difference in survival between countries. This effect was not found in 1989, where mammography screening was still in its infancy in Sweden and non-existent in Denmark. However, the fact that our modelling only showed some reduction in the survival differences between countries in 1989, suggests that other explaining factors should be considered. One may be the educating effect of implementation of mammography screening programs, which emphasise the early detection of breast cancer in general with their organisation and treatment consequences.[20,32] Other explaining factors may be differences between the two national regions in co-morbidity and lifestyle (tobacco and alcohol consumption and obesity)[33] as well as differences in treatment.

Conflict of interest statement

None declared.

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