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Detection of Breast Cancer with Mammography in the First Screening Round in Relation to Expected Incidence in Different Age Groups

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The ratio (R) of prevalence of screening-detected breast cancer in the first screening round (P) was compared with the expected incidence rate (I) for different age groups in several screening programs. Published data on the first screening round from three Swedish randomized trials and six counties with service screening were used. The women invited to take part in the screening were aged 40–74 years. Not only P and I but also R increased with increasing age. With the youngest age group as reference, the increase was statistically significant for both invasive cancer and invasive cancer and carcinoma in situ together. The studied ratio (R) can be thought of as a measure of efficiency in detecting breast cancer cases in mammography screening. The reasons for the increase are probably that the breast tissue of younger women is denser, which makes the cancer more difficult to detect by mammography, and that slow-growing cancers tend to appear more frequently in older women.

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Randomized trials have shown that screening for breast cancer with mammography causes a reduction in breast cancer mortality (1,2). Today, nationwide service screening programs have been initiated in Sweden, Finland, The Netherlands, the UK, Luxembourg and Iceland.

Randomized trials on screening with mammography have shown a more pronounced relative reduction in breast cancer mortality among women aged 50–69 years than among those below 50 years of age (2). For women aged 70 or more, there is no clear evidence of a reduction in mortality.

There has been intensive discussion concerning age limits for invitation to service screening, especially the lower limit (3,4). Since the incidence of breast cancer increases with age, it naturally follows that more breast cancers should be detected among older women than among younger women. If the relative reduction in breast cancer mortality were the same for all age groups, the number of lives saved would be greater among older women. On the other hand, the number of years gained would be greater per each saved life for younger women. Besides incidence, there are several other important factors that can influence the age-specific number of screening-detected breast cancers, e.g. tumor biology and biological differences in breast tissue. Furthermore, factors depending on screening organization such as the attendance rate, skill of the radiologist, recall rate, technical equipment, single or double reading and number of views can have an impact on the result.

As a measure of the efficiency of detecting breast cancer in a screening program, the rate of screening-detected breast cancer in the first screening round (prevalence) was measured in relation to the expected incidence for different age groups. This measure has been described earlier, for example in the Two-County Study (5). The ratio has also been used to estimate lead times (6).

The aim of the present study was to investigate the ratio of the cancer detection rate in the first screening round and the expected incidence rate for different age groups in several screening programs, trials as well as service screening.

MATERIAL AND METHODS

When the first results from the Two-County Study were published (1), the National Board of Health and Welfare in Sweden issued guidelines for mammography screening (7) recommending a lower age limit of not below 40 years and not over 50 years, and an upper age limit of not below 69 years. This recommendation was reconsidered later on and the new recommendation for the lower age limit was set at

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Table 1

Time for start, age interval, number of women invited, attendance and recall rate for the first round in the randomized trials/service screening programs

Screening program	Trial/service screening	Starting month/ year	Age interval	Number invited (round 1)	Attendance rate (%)	Recall rate (%)	Number of CIS available
Stockholm	Trial	03/ 1981	40–65	40318	81	5.1	Yes
Malmö	Trial	10/ 1976	45–69	21242	65	3.4	Yes
Östergötland	Trial	05/ 1978	40–74	39034	85	5.6	Yes
Kopparberg[§]	Trial	07/ 1977	40–74	39051	91	4.9	Yes
Uppsala	Service	02/ 1988	40–74	48517	86	4.8	No
Västmanland	Service	10/ 1986	40–69	46910	90	3.9	Yes
Västernorrland	Service	01/ 1990	40–74	55158	89	1.9	Yes
Västerbotten	Service	02/ 1995	50–69*	27282	87	1.3	Yes
Norrbotten	Service	03/ 1989	40–74	52734	88	2.2	Yes
Bohuslän	Service	11/ 1986	50–74	36258	82	4.9	No

Abbreviation: CIS = carcinoma in situ.
[§] Currently Dalarna.
* Currently 40–74.

40 years (8). Consequently, the 50–69 years age group was covered in all counties where service screening was introduced. Service screening started in Sweden in 1986 and by 1997 it had been introduced in all 23 counties. Service screening in Sweden is population based. It is usually organized at county level but in four of the counties it is organized in smaller units.

We used published data from Swedish randomized trials (the group invited to screening) as well as from routinely performed service screening in different Swedish counties (Table 1). The trials/service screening programs started between 1976 and 1995. Since some of the screening programs covered only parts of the counties, we hereafter call them geographical areas. The randomized trials were the Two-County trial (9), Stockholm (10) and Malmö (11). From the service screening we have used data from the following counties: Bohuslän (12), Uppsala (13), Västmanland (14), Västenorrland (15), Västerbotten (16) and Norrbotten (17). Only data published in the 5-year age groups were used.

To obtain the aggregated number of invited women and screening-detected breast cancers in the 5-year age groups in the first screening round, we used the published data as far as possible. However, in some of the publications the data did not distinguish between invasive cancer and carcinoma in situ (CIS). For the counties of Västenorrland, Västerbotten and Norrbotten, however, for this purpose, we were able to use data derived earlier by record linkage between the screening registries and the Regional Cancer Registry in northern Sweden (combined with manual checking). For the counties of Uppsala and Bohuslän, the number of cancer cases published included both invasive cancer and CIS.

The total number of breast cancers (code = 096 in WHO/HS/CAN/24.1) during the 5-year period preceding the year of screening start for each geographical area was obtained from the National Swedish Cancer Registry. The female population data aggregated into 5-year age groups were obtained from Statistics Sweden.

As a measure of efficiency we studied the age-specific ratio (R) between the cancer detection rate per 100 000 invited women in the prevalence screening round (prevalence, P) and the estimated expected incidence rate per 100 000 person-years (incidence, I). As estimates of I the mean observed incidence rate during the 5-year calendar period preceding the screening start was used.

P and I are not the same kind of measures. P is the proportion of the population invited to screening who had a breast cancer in the clinical or preclinical phase, detected by mammography in the first screening round. I is the rate of the number of breast cancers in relation to the numbers of person-years in a population during the defined time period.

In a Poisson model the observed number of screening-detected breast cancer cases was used as the dependent variable and the logarithm of the number of women invited as offset during the first screening round. For the 5-year period preceding the start of screening, the number of breast cancers and the logarithm of the number of person-years in the female population were used as dependent variable and offset, respectively. These two measures were 'separated' by a covariate used to estimate the ratio (R). Other categorical covariates used in the model were age in 5-year groups and geographical area. Although P and I are not directly comparable measures, it is reasonable to assume a simple model in which P and I are proportional. Both I and P are assumed to be multiplicatively dependent on age and geographical area. A simple model for this is $\lambda_{ijk} = \lambda_0 a_i g_j p_k$ where

λ_{ijk} = prevalence or incidence for a certain age and geographical area
λ_0 = constant

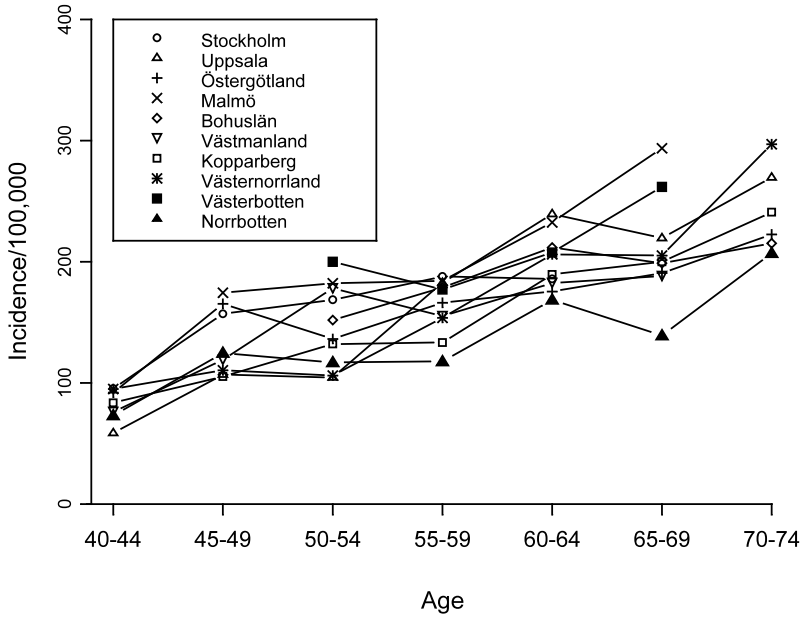

Fig. 1. Age-specific incidence (invasive breast cancer) in the 5-year period preceding the start of screening.

Table 2

Number invited, number of invasive cancer and carcinoma in situ (CIS) detected in the first screening round, proportion of CIS, prevalence, incidence and the ratio of prevalence and incidence (R) for different age groups (Bohuslän and Uppsala excluded)

Age	Number invited	Number of invasive cancers	Number of CIS	Proportion CIS of total (%)	Prevalence/100 000 invited*	Incidence/ 100 000*	R*
40–44	48755	37	16	30.2	75.9	86.3	0.88
45–49	46418	103	20	16.3	221.9	139.2	1.59
50–54	52705	152	27	15.1	288.4	152.3	1.89
55–59	53784	220	23	9.5	409.0	161.6	2.53
60–64	53404	281	28	9.1	526.2	192.6	2.73
65–69	44364	293	34	10.4	660.4	211.5	3.12
70–74	22299	188	11	5.5	843.1	241.9	3.49
Total	321729	1274	159	12.5	397.0	164.6	2.41

*Invasive cancer only.

a_i = age group i, i = 1, …, 7
g_j = geographical area j, j = 1, …, 10
p_k = incidence (k = 1), prevalence (k = 2)

In a more general model the ratio (R) is dependent on age and county. The model used was $\lambda_{ijk} = \lambda_0 a_i g_j p_k ap_{ik} gp_{jk}$ where

ap_{ik} = interaction parameters, age and prevalence
gp_{jk} = interaction parameters, geographical area and prevalence

We used the common restriction for the parameters as $a_1 = g_1 = p_1 = ap_{i1} = gp_{j1} = ap_{12} = gp_{12} = 1$.

Differences in attendance rate and screening 'quality' were adjusted by the interaction term gp_{jk}. The age-specific R relative to the age group 40–44 years was estimated by ap_{i2}.

We analyzed the data with both the number of invasive breast cancers and the total number of breast cancers in P (invasive and non-invasive cases added). For two of the geographical areas, Uppsala and Bohuslän, only the total number of breast cancers was available. Therefore these two geographical areas were not included in the analysis of the invasive cancers.

RESULTS

The age-standardized incidence in Sweden has increased almost linearly in the past 40 years, while the mean annual increase has been 1.5% in the past 20 years (18). There are also geographical differences (18–20). We compared incidence data for the included geographical areas using a Poisson model, with geographical area and age as covari-

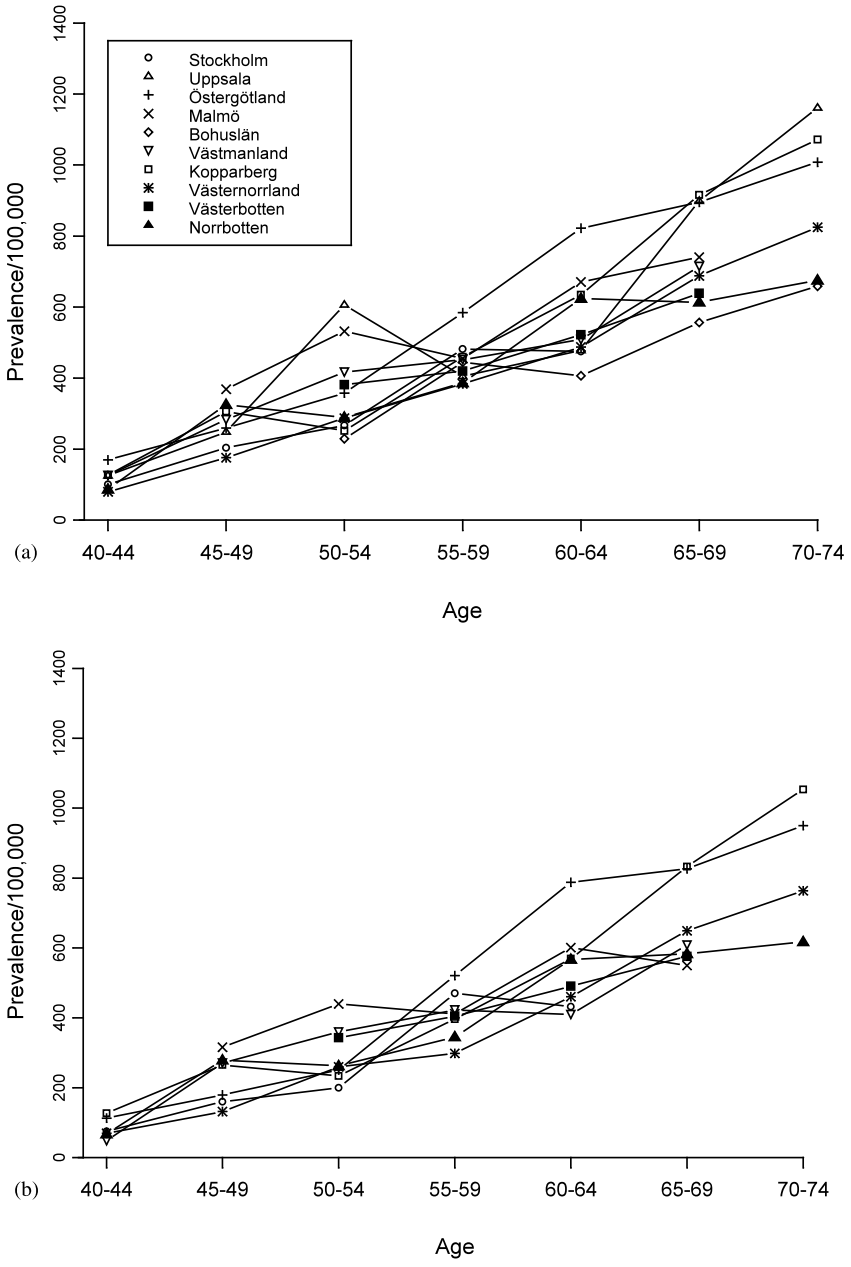

Fig. 2. (a) Prevalence of breast cancers (invasive cancer and carcinoma in situ (CIS) together). (b) Prevalence of invasive cancers.

ates. The incidence observed before the start of screening (I) differed significantly ($p < 0.001$) between the geographical areas.

The incidence rate (I) increased with age (Fig. 1, Table 2). As a consequence the cancer detection rate, by screening in the first round (P), also increased with age (Fig. 2, Table 2). The crude ratio R between P and I is shown in Fig. 3. The Poisson model was fitted for invasive cancer in P and the result is summarized in Table 3a. All parameters were significantly different from zero ($p < 0.001$) including the two-way interaction parameters. Age-specific R relative to the 40–44 years age group estimated in the model (ap_{i2}) is shown in Fig. 4 and Table 4. With both methods, a pronounced increase by age can be seen. The slope was lower than for P.

The same model was also fitted for the total number of breast cancers (invasive and CIS together) (Table 3b). Also in this case, all estimated parameters were significant ($p < 0.001$). The age-specific R, relative to age group 40–44 years (ap_{i2}) is shown in Fig. 4 and Table 4. The increase was less pronounced than for the invasive cancers only.

DISCUSSION

The main objective of mammography screening is to reduce mortality by early detection of breast cancer. Compared to

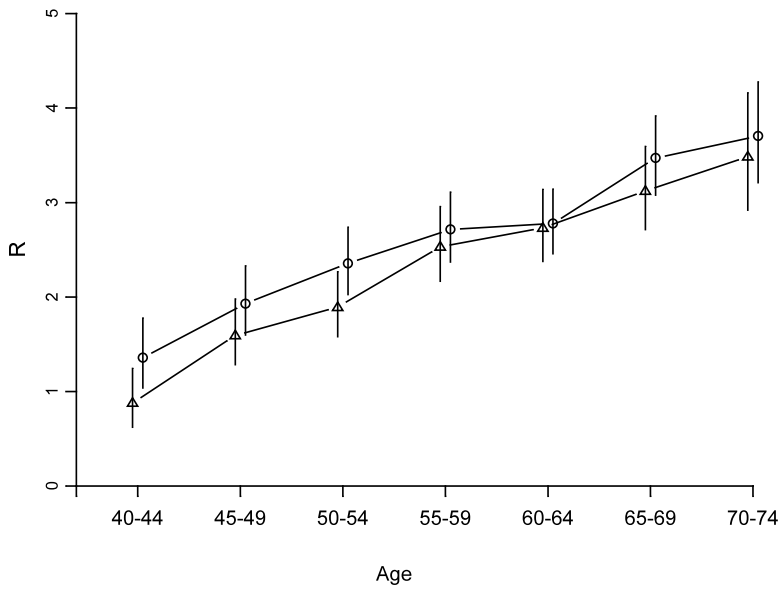

Fig. 3. Crude age-specific R. Vertical bars show the 95% confidence interval. Invasive cancer (triangles) and invasive cancer and carcinoma in situ (CIS) together (circles).

Table 3a

Summary of fitting a Poisson model for invasive breast cancer

Model	Terms included in the model	Degrees of freedom (df)	Deviance	Compared models	Difference in deviance	Difference in df	p-value
	NULL	95	1411.8	–			
1	Prevalence	94	797.1	Null-1	614.7	1	<0.001
2	Age	88	238.8	1—2	558.3	6	<0.001
3	Geographical area	81	190.4	2—3	48.4	7	<0.001
4	Prevalence*age	75	96.0	3—4	94.4	6	<0.001
5	Prevalence*geographical area	68	67.6	4—5	28.4	7	<0.001

Table 3b

Summary of fitting a Poisson model for breast cancer (invasive cancer and CIS together)

Model	Terms included in the model	Degrees of freedom (df)	Deviance	Compared models	Difference in deviance	Difference in df	p-value
	NULL	119	2090.4	–			
1	Prevalence	118	999.9	Null–1	1090.5	1	<0.001
2	Age	112	265.8	1–2	734.1	6	<0.001
3	Geographical area	103	210.7	2–3	55.0	9	<0.001
4	Prevalence*age	97	132.5	3–4	78.2	6	<0.001
5	Prevalence*geographical area	88	91.6	4–5	41.0	9	<0.001

Abbreviation: CIS = carcinoma in situ.

expected incidence before the start of screening, there were 1.9–3.6 times as many invasive breast cancers detected in women over 45 years of age compared to women aged 40–44 years (Table 4). The corresponding figures for invasive and non-invasive cancer together were 1.5–2.7. The estimated R increased monotonously over age. This is in agreement with the better possibilities to reduce mortality in older women compared to young women.

One mechanism for reduction of breast cancer mortality by mammography screening is the early detection of invasive breast cancer. However, another mechanism can be the detection of CIS that later would have developed into

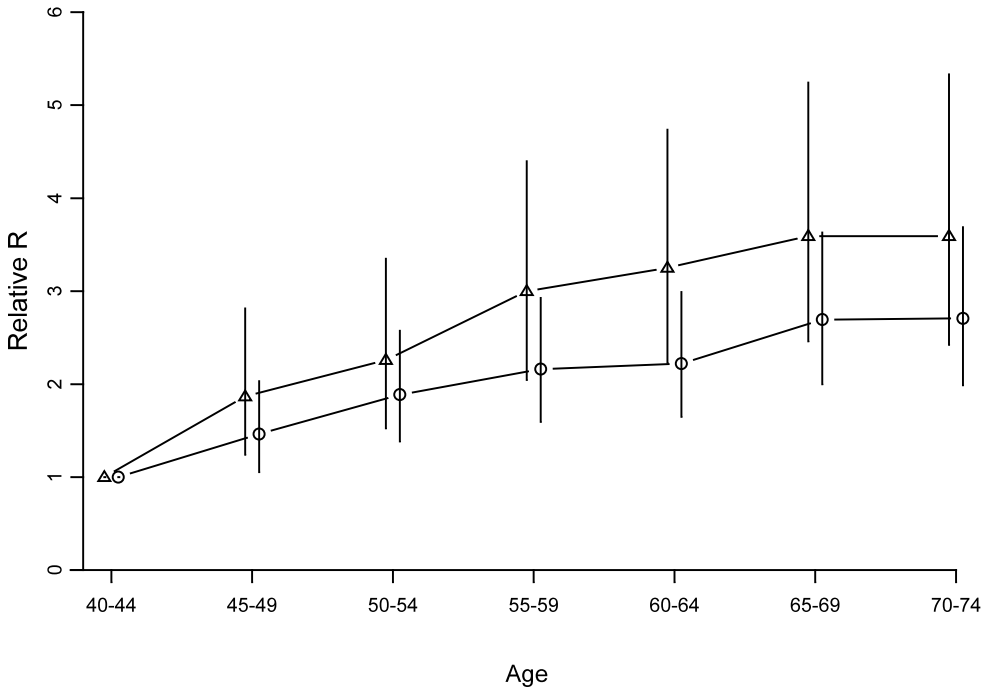

Fig. 4. Age-specific R estimated in the Poisson model relative to the 40–44 years age group adjusted for differences between geographical areas. Vertical bars show the 95% confidence interval. Invasive cancer (triangles) and invasive cancer and carcinoma in situ (CIS) together (circles).

Table 4

Ratio between prevalence and incidence (R) for different age groups relative to age 40-44 (relative R)

	Invasive breast cancer		Invasive breast cancer and CIS together	
Age	Relative R	95% CI	Relative R	95% CI
40–44	1.00	–	1.00	–
45–49	1.87	1.24–2.81	1.46	1.05–2.03
50–54	2.26	1.52–3.35	1.89	1.38–2.57
55–59	3.00	2.05–4.40	2.16	1.60–2.93
60–64	3.25	2.23–4.73	2.22	1.65–2.99
65–69	3.59	2.46–5.24	2.69	2.00–3.63
70–74	3.59	2.42–5.33	2.71	1.99–3.69

invasive cancer. Since it is not known to what extent these two factors contribute to the reduction in mortality, we have analyzed the data using both invasive cancer alone and invasive cancer and CIS together.

Several factors can affect the efficiency of a screening program. For example, attendance rate, recall rate, the skill of the radiologists, technique and routines for views and reading. In addition, the length of the first round can vary, but it is not clear if and, in that case, how it can affect efficiency. Estrogen treatment may increase the roentgenological density of the breast, which can make detection of a small cancer more difficult. Concerning these factors, it can be assumed that there are differences between the geographical areas, and R was assumed to be proportional within a given age group.

Among those factors that can affect P and hence also R, attendance rate and recall rate were the most likely to influence R differently in the various age groups. Attendance and recall rates tended to be higher in younger women (not shown) and hence could give a higher R for young women, i.e. a lower slope on age-specific R.

The expected incidence during the first screening round was based on an average over a 5-year period preceding the first round. This could have caused an underestimation of the expected incidence, because the incidence increases over time. Based on linear regression, 1965–1985 age-specific change during a 4-year period (from the mid-point in the 5-year period to the mid-point in the first round) was estimated. This analysis was based on the whole of Sweden. We found that the relative change varied between 2% and

5%. R is therefore expected to be overestimated in the same interval. The largest change was seen in women aged 50–64 years.

Another factor that could have affected the incidence is differences in diagnostic activities over age and between counties. It is probable that 'wild screening' is more common among young women. To our knowledge, this phenomenon is concentrated mostly in the big cities. Furthermore, we do not believe that such activities had started before the early 1980s, i.e. when the randomized trials were launched.

The expected incidence was based on invasive breast cancer only. CIS cases in the Cancer Registry were few in number before mammography screening activities begun. In the early 1970s the incidence of CIS was 1% and during the 1980s it increased to over 10%. Probably the increase was largely due to screening but changed routines in reporting to the Cancer Registry and coding could also have played a part. CIS was more frequent in the prevalence round among young women: 30% of the total number of breast cancers detected in the 40–44 years age group and 10% for ages 55–59 (Table 2).

There are some possible explanations for the observed differences in the ratio R between young women and old women. Young women tend to have denser breast tissue, making a cancer more difficult to detect by mammography. If this is the prevailing explanation, the conclusion would be that mammography is a method that works more effectively among older women.

Another explanation could be that slow-growing tumors tend to accumulate in the population with increasing age. Therefore a larger proportion of older women can be expected to be in the preclinical detectable phase at the time of the screening test. The phenomenon is known as length bias. The length of the detectable preclinical phase, the so-called sojourn time, has been estimated at 2.4, 3.7 and 4.2 years for women aged 40–49, 50–59 and 60–69 years, respectively (21). Consequently, the probability of detecting the slow-growing tumors by mammography screening will increase with age. If this mechanism is the principal explanation, the consequence would be to suggest shorter screening intervals for young women.

The current study cannot answer which of these hypotheses is the more plausible. However, it seems that with a screening strategy independent of age, we cannot expect the same relative mortality reduction in young women as among older women.

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REFERENCES

1. Tabár L, Fagerberg CJG, Gad A, et al. Reduction in mortality from breast cancer after mass screening with mammography. Randomised trial from the Breast Cancer Screening Working Group of the Swedish National Board of Health and Welfare. Lancet 1985; 1: 829–32.
2. Nyström L, Rutqvist L, Wall S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials. Lancet 1993; 341: 973–8.
3. Breast Cancer screening with mammography in women aged 40–49 years. Report of the Organizing Committee and Collaborators, Falun Meeting, Sweden (21 and 22 March, 1996). Int J Cancer 1996; 68: 693–9.
4. National Institutes of Health Consensus Conference on Breast Cancer Screening for Women Ages 40–49. Proceedings. Bethesda, Maryland, USA. January 21–23, 1997. J Natl Cancer Inst Monogr 1997; 22: 1–156.
5. Tabár L, Akerlund E, Gad A. Five-year experience with single-view mammography randomized controlled screening in Sweden. Recent Results Cancer Res 1984; 90: 105–13.
6. Shapiro S, Goldberg JD, Hutchison GB. Lead time in breast cancer detection and implications for periodicity of screening. Am J Epidemiol 1974; 100: 357–66.
7. General advice from the National Board of Health and Welfare. (In Swedish). Stockholm: National Board of Health and Welfare 1986.
8. Mammography screening for early detection of breast cancer. Stockholm: National Board of Health and Welfare; 1998. Report No: 17.
9. Report from mammography screening in the counties Kopparberg and Östergötland (the WE-project). Result from the first screening round (In Swedish). Stockholm: National Board of Health and Welfare 1982. Report No: 33.
10. Frisell J, Glas U, Hellstrom L, et al. Randomized mammographic screening for breast cancer in Stockholm. Design, first round results and comparisons. Breast Cancer Res Treat 1986; 8: 45–54.
11. Andersson I. Radiographic screening for breast carcinoma. I. Program and primary findings in 45–69-year-old women. Acta Radiol Diagn 1981; 22: 185–94.
12. Regnér H, Cederblom S. Screening for breast cancer with mammography in Bohuslän county. The first screening round including two years of screening: Nov 1986–Nov 1988 (in Swedish). Gothenburg: Gothenburg University; 1989.
13. Thurfjell E. Population-based mammography screening in clinical practice. Results from the prevalence round in Uppsala county. Acta Radiol 1994; 35: 487–91.
14. Murawa-Frodis E, Hedborg-Mellander C. Mammography screening. Report from the result concerning the first round October 1986–March 1989. (In Swedish). Västerås: Landstinget Västmanland; 1990.
15. Urhonen M, Berglund T. Mammography screening. Report of the result from the first round January 1990–March 1992 (In Swedish). Härnösand: Landstinget Västernorrland; 1993.
16. Carlsson S, Rydh A. Mammography in the county of Västerbotten. Report of the result concerning the first round. February 1995–March 1997. (In Swedish). Umeå: The Mammography Unit. Umeå University Hospital; 1998.
17. Mammography screening in the county of Norrbotten. Report from the result 1989–1995. (In Swedish). Luleå: Mammography Department, Luleå Hospital Norrbottens läns landsting; 1996.
18. Cancer incidence in Sweden 1998. Stockholm: The National Board of Health and Welfare 2000; Report No: 91-7201-450-4.

19. Atlas of cancer incidence in Sweden. Linköping: Swedish Oncological Centres. Linköpings tryckeri AB; 1995.
20. Cumberbatch J, Johnsson M, Larsson LG, et al. The incidence of breast cancer in northern Sweden 1959—1971. (In Swedish). Läkartidningen 1979; 76: 1413–6.
21. Duffy SW, Day NE, Tabar L, et al. Markov models of breast tumor progression: some age-specific results. J Natl Cancer Inst Monogr 1997; 22: 93–7.