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Original Research

Body weight and sensitivity of screening mammography

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Abstract ***Aim:*** Obese women tend to participate less in breast cancer screening than normal weight women. However, obese women have fattier breast than normal weight women, and screening mammography works better in fatty than in dense breasts. One might, therefore, hypothesise that obese women would actually benefit more from screening than other women.
Methods: We combined data from the Danish Diet, Cancer and Health study and the organised population-based screening mammography programme in Copenhagen, Denmark. Women were categorised according to body mass index (BMI) (<20; 20 to <25; 25 to <30; 30 to <35, and 35+). We measured recall rate, sensitivity and specificity for subsequent screens with a 2-year follow-up period.
Results: The study included 6787 women. The recall rate varied from 1.4% for women with BMI <20 to 1.9% for women with BMI 35+, test for trend p = 0.86. Sensitivity varied from 42% (95% confidence interval [CI] 20–64%) for women with BMI <20 to 100% (95% CI 69–100%) for women with BMI 35+, test for trend p = 0.015. Specificity was fairly constant across BMI levels, being on average 98.8%, test for trend p = 0.79.
Conclusion: This study showed that obese women were the ones with the highest sensitivity of screening mammography, while the specificity of screening remained stable across weight groups. Screening programmes should be organized to encourage these women to overcome obstacles for participation.

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1. Introduction

The incidence of breast cancer in post-menopausal women is increasing in most European countries [1], and after menopause, women with a high body mass index (BMI) have a higher risk of breast cancer than women with a normal BMI [2–4]. Despite their higher risk of breast cancer, women with a high BMI tend to participate less in screening mammography than normal weight women [5]. This has in particular been found for women with a BMI 35+; a group that constituted 10% of women in a study from the US Breast Cancer Surveillance Consortium [6] and 5% of women in a Danish study [7]. However, it is easier at mammography to detect a tumour in fatty breast tissue than in dense breast tissue [8]. It is furthermore known that overweight and obese women have on average fattier breasts than women with normal BMI [9,10].

It is, therefore, reasonable to hypothesise that overweight and obese women would—provided other factors being equal—benefit more from screening mammography than normal weight women. Previous studies have indicated somewhat conflicting results [11,12], but it should be taken into account that these studies relied on self-reported height and weight data.

It was the purpose of the present study to determine sensitivity and specificity of screening mammography based on individually linked data from a population survey with measured height and weight and outcome from an organised screening mammography program.

2. Materials and methods

The sensitivity is the proportion of women with breast cancer found at screening. The specificity is the proportion of women without breast cancer declared normal at screening. If the sensitivity of screening is higher and the specificity is not lower among overweight/obese women than in normal weight women, then overweight/obese women would potentially benefit more from screening than normal weight women. The benefit of screening might also be influenced by breast cancer incidence, tumour type, screening lead time and available treatment; all factors not investigated in the present study.

The Danish Diet, Cancer and Health study [13] that forms part of the European Prospective Investigation into Cancer and Nutrition, took place in December 1993 to May 1997. In total 79,729 women free of cancer, aged 50–64 years, and residents of greater Copenhagen or Aarhus were invited to participate. Of these, 29,875 (37%) participated. At recruitment, height and weight were measured by trained professionals. BMI was calculated as (weight [kg]/[height {m}]^2) and divided into underweight and lower end of normal weight (BMI < 20), normal weight (BMI 20 to <25), overweight (BMI 25 to <30), obese class I (BMI 30 to <35), and obese classes II and III (BMI 35+). All participants were registered by their unique Danish personal identification number, which permitted linkage with other data sources.

In the Copenhagen municipality, an organised, population-based screening mammography program started in April 1991. Women aged 50–69 years were personally invited for screening every second year. Screening took place in a specialised clinic. At first screen, all women had two projections. At subsequent screens up until 2004, women with fatty breast tissue had one projection, while women with mixed/dense breast tissue had two. From 2004 and onwards, all women had two projections. Independent, double reading was performed, and where available, mammograms from up to three previous rounds were used for comparison, and disagreements were resolved by senior radiologists [14]. We distinguished between initial screens representing the first screen in the program for a given women and subsequent screens. A comprehensive survey of all mammography activity in Denmark in 2000 showed use of opportunistic screening to be very limited [15], thus indicating that for by far the majority of women the first screen in the program was in fact the first screen ever. By far the majority of screens included in the present study was film based. Breast density data were available from only the early part of our study period and were not included in our analysis.

Women with screening mammograms classified as positive were referred for assessment, and women with screening mammography classified as negative were invited again in 2 years. If breast cancer and/or ductal carcinoma *in situ* (DCIS) were diagnosed at assessment, the woman was counted as a screen-detected cancer or a true positive. Otherwise, she was classified as having a false-positive screen. Women with negative screens were referred back to the screening program. An interval cancer was defined as breast cancer/DCIS within the next 2 years of a negative or a false-positive screen, excluding the very few cases detected at the next screen, if this took place less than 2 years since last screen.

Our study population included women who participated in the Danish Cancer and Health study and had at least one screen in the Copenhagen organised screening program after the date of their enrolment in the Danish Cancer and Health study. They were followed up for screening participation and screen-detected breast cancer/DCIS until 12 July 2012 and for interval cancers until 2 years later. Incident breast cancer/DCIS cases were identified by linkage to the Danish Cancer Register [16] and for DCIS to data from the Danish Breast Cancer Cooperative Group [17].

We checked for similarity across BMI groups in the distribution of number of screens by age. Screen detection rate was defined as the number of screen-detected cases divided by the number of screens. Recall rate was defined as the number of positive screens divided by the number of screens. Sensitivity was calculated as the

proportion of screen-detected cancers out of all screen-detected and interval breast cancer/DCIS (true positive/[true positive + false negative]). Specificity was calculated as the proportion of women with a true negative screen out of all women not diagnosed with screen-detected or interval breast cancer/DCIS (true negative/[true negative + false positive]); 95% confidence intervals for sensitivity and specificity were calculated as exact binomial confidence intervals. We have calculated the sensitivity and specificity over a 2-year period because this is the reality for women offered screening in Denmark.

We tested for trend in recall rate, sensitivity and specificity across BMI groups using a binomial model including also age group and screening round, and taking into account that screens from a given woman are correlated. Calculation without taking this correlation into account did not change the results.

Data were processed using SAS (version 9.4). According to Danish legislation approval from the Danish Data Inspection Agency serves as ethical approval of register-based research with no contact to the patients, their relatives and/or their treating physician. Our project has notification number 2008-41-2191.

3. Results

In total, 6787 women had at least one screen after their enrolment in the Danish Diet, Cancer and Health study (Fig. 1). Of these, 206 had only an initial screen, 5040 had only subsequent screens, and 1541 had both an initial and subsequent screens.

Our data set included 1740 initial screens in which only 8 screen-detected cancers and 3 interval cancers occurred, and therefore, we did not analyse initial screens by BMI. In total, 31,196 subsequent screens were included. The distribution by age at screen was fairly similar across BMI group with the average age being 62.4 years for women with BMI ≥25 and 62.0 years for women with BMI <25 (Table 1).

At subsequent screens, the recall rate was 1.4% for underweight (BMI < 20) women; 1.8% for normal weight (BMI 20 to <25) and overweight (BMI 25 to <30) women; 1.7% for obese class I (BMI 30 to <35);

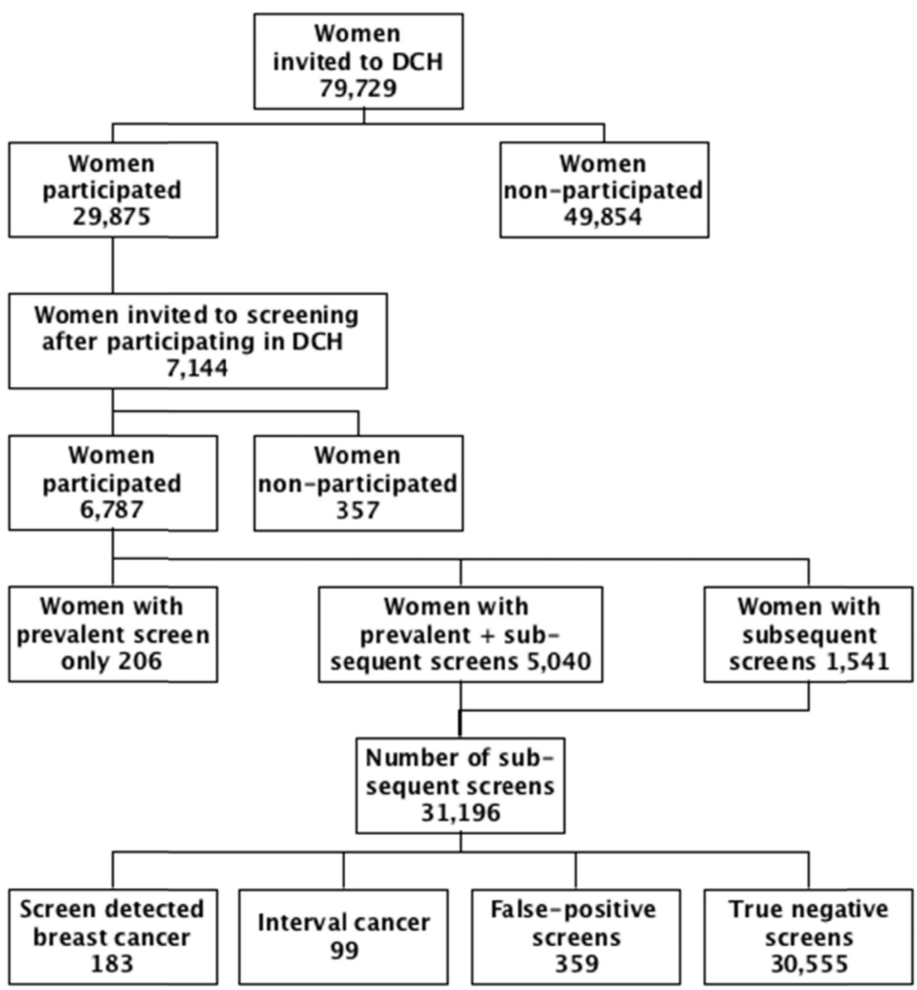

Fig. 1. Women invited to the Danish Diet, Cancer and Health (DCH) study in 1993–1997 and participating in the screening mammography program in Copenhagen, Denmark 1993–2012.

Table 1
Number of subsequent screens by age at screen and BMI in the combined Danish Diet, Cancer and Health study and in the Copenhagen screening mammography program 1993–2012.

Age, years	BMI <20	BMI 20 to <25	BMI 25 to <30	BMI 30 to <35	BMI 35+	Total
50–54	132 (7%)	837 (6%)	567 (5%)	201 (5%)	83 (6%)	1820
55–50	481 (26%)	3457 (26%)	2489 (23%)	865 (23%)	322 (23%)	7614
60–64	590 (32%)	4502 (33%)	3620 (34%)	1281 (34%)	464 (33%)	10,457
65–69	587 (32%)	4454 (33%)	3694 (35%)	1318 (35%)	474 (34%)	10,527
70–74	39 (2.1%)	285 (2.1%)	297 (2.8%)	111 (2.9%)	46 (3.3%)	778
Total	1829 (100%)	13,535 (100%)	10,667 (100%)	3776 (100%)	1389 (100%)	31,196 (100%)
Average age (years)	61.8	62.0	62.4	62.4	62.4	62.2
Number of screens per woman	4.1	4.2	4.2	3.9	4.1	4.2

BMI, body mass index.

and 1.9% for obese classes II and III (BMI 35+) women (Table 2). Test for trend, p = 0.86. In total, 183 cancers were detected at subsequent screens, and 99 interval cancers were observed (Table 2). There was no trend in the crude overall breast cancer risk (screen detected + interval cancers) by BMI, p = 0.90. The sensitivity of subsequent screens increased with increasing BMI. In underweight women, the sensitivity was 42% (95% CI 20–64%); in normal weight women, it was 62% (95% CI 53–71%); in overweight women, 65% (95% CI 56–75%); in obese class I women 76% (95% CI 62–91%); and in obese classes II and III women 100% (95% CI 69–100%). Taking age and screening round into account, this represented a statistically significantly increasing trend, p = 0.015. The specificity of subsequent screens remained stable with increasing BMI as the point estimates for the specificity varied only from 98.8% to 99.1%, test for trend, p = 0.79.

4. Discussion

4.1. Main finding

This study based on combined, personal measurement data from a population survey and an organised screening program showed increasing sensitivity of screening mammography with increasing BMI from a level of 42% (95% CI 20–64%) in underweight women to a level of 100% (95% CI 69–100%) in severely obese women. The specificity of screening remained stable across weight groups.

4.2. Other studies

In the present study, with 2 years of follow-up of subsequent screens, the overall recall rate was 1.7%, and the sensitivity over 2 years was 65%. In order to compare with other studies, it is useful to know also the recall rate for initial screens and the sensitivity over one year in the Copenhagen program. For all screened women in Copenhagen during the same period, the recall rates were 4.4% and 1.8% for initial and subsequent screens, respectively. With a 1-year follow-up, the sensitivity was 90% and 89% for initial and subsequent screens, respectively [18] (Table 3).

Based on the Million Women Study from the United Kingdom (UK) and including both initial and subsequent screens, Banks et al. [11] found the recall rate for women with a BMI <25 to be 3.9% and for women with a BMI ≥25 to be 3.5%. With a 1-year follow-up, the sensitivity was 85.7% (95% CI 81.2–89.3) and 91.0 (95% CI 87.5–93.6), respectively, and the specificity was 97.2% (95% CI 97.0–97.3) and 97.4% (95% CI 97.3–97.6), respectively (Table 3). These estimated were adjusted for age, likelihood of previous National Health Service breast screening, screening center, pervious breast surgery, menopausal status, and use of hormone therapy. Although the UK recall rates were higher for normal weight than for overweight + women, the sensitivity and specificity patterns were as see in Copenhagen.

Our data were only in part in agreement with those of Elmore et al. [12]. They analysed data from the Group Health Cooperative in the Northwestern United States and included both initial and subsequent screens. In this study, the crude recall rate was fairly similar across BMI groups varying between 11.5% and 12.3%. The crude sensitivity increased from 84.6% (95% CI 79.8–88.6) for underweight and normal weight women to 91.3% (95% CI 82.8–96.4) for obesity classes II–III women, though with overlapping confidence intervals. The crude specificity was fairly similar across BMI groups varying between 88.3% and 89.0% (Table 3).

The US estimates [12] changed when they were adjusted for age, breast density, menopausal and hormone therapy status, breast symptoms, family history of breast cancer, history of breast biopsy, and time since last mammogram. The adjusted odds ratio of recall was 1.31 (95% CI 1.22–1.41) for obesity classes II–III women compared to that of underweight and normal weight women. The adjusted odds ratio for sensitivity was 0.89 (95% CI 0.52–1.55) for overweight, 0.88 (95% CI 0.44–1.82) for obesity class I, and 1.13 (95% CI 0.47–3.02) for obesity classes II–III women compared to that of underweight and normal weight women. The adjusted odds ratios for specificity were 0.86 (95% CI

Table 2
Number of subsequent screens, screen-detected cancers, interval cancers, false-positive screens, sensitivity and specificity by BMI.

	BMI <20	BMI 20 to <25	BMI 25 to <30	BMI 30 to <35	BMI 35+	Total	Test for trend
Subsequent screens	1829	13535	10667	3776	1389	31,196	NR
Screen detected cancers	8	71	68	26	10	183	NR
Screen detection per 1000 screens	4	5	6	7	7	6	NR
Interval cancers	11	44	36	8	0	99	NR
False-positive screens	17	166	122	38	16	359	NR
Screen detected + interval cancers per 1000 screens	10	9	10	9	7	9	p = 0.90
Recall rate (%)	1.4	1.8	1.8	1.7	1.9	1.7	p = 0.856
Sensitivity	42% (20–64%)	62% (53–71%)	65% (56–75%)	76% (62–91%)	100% (69–100%)	65% (59–70%)	p = 0.015
Specificity	99.1% (98.6–99.5%)	98.8% (98.6–99.0%)	98.8% (98.6–99.0%)	99.0% (98.7–99.3%)	98.8% (98.3–99.4%)	98.8% (98.7–99.0%)	p = 0.790

BMI, body mass index; NR, not relevant.

0.81–.0.90), 0.79 (95% CI 0.74–0.84), and 0.77 (95% CI 0.71–0.82), respectively. The authors concluded that 'obese women had a more than 20% increased risk of having a false-positive mammogram result compared with underweight and normal weight women', and the authors found the 'finding that obese women have less accurate mammograms … surprising'. These conclusions from the authors will be discussed below.

With a purpose somewhat different from ours, Kerlikowske et al. [7] examined whether extent of mammography use and accuracy of mammography modified the association between BMI and rate of breast cancer. They included only post-menopausal women not currently using hormone therapy and found that the odds ratio of breast cancer, controlled for a number of potential confounders, increased with increasing BMI. The purpose of our study was exclusively to assess the association between BMI and screening sensitivity. Our study population was more heterogeneous (including both pre- and post-menopausal women and both users and non-users of hormone therapy) than at the one studied by Kerlikowske et al., and we found no trend in breast cancer risk by BMI. Anyhow, Kerlikowske et al. also found a higher sensitivity for women with a BMI ≥25 (89.0%; 95% CI 85.9–91.2), than for women with a BMI <25 (84.0%; 95% CI 79.3–87.6; Table 3).

An Australian study found slightly improved sensitivity of screening mammography in women aged 50–69 years with larger sized breasts, 94.51%, compared to women with average sized breasts (91.13% [19], Table 3).

4.3. Strength and weakness

It was a strength of our study that all data derived from objective measurements thus avoiding any recall bias. It was furthermore a strength that the study population had very limited use of opportunistic screening. Is was a weakness of our study that we could only include women participating in the Danish Diet, Cancer and Health study, as these women health wise constituted a somewhat selected group with an overall mortality below that of the general population [20]. Participants in the Diet, Cancer and Health cohort were on average healthier than non-participants. The overall mortality rate ratio for non-participants compared with participants was 2.29 (95% CI 2.19–2.40) compared with participants. Anyhow, this selection affected all women in our study as we relayed only on internal comparisons.

The overall 2-year sensitivity in our study was 65%, which was slightly lower than the 71% for the Copenhagen program overall (unpublished data). The difference might be due to the fact that participants in the Diet, Cancer and Health cohort were healthier than the average of Copenhagen women, and the proportion of obese women was, therefore, expected to be lower in our cohort than in the Copenhagen population at large.

Table 3
Overview of sensitivity and specificity, including 95% confidence intervals, of screening mammography by BMI.

Study	Screen type	Follow-up time	BMI					Total
			BMI <20	BMI 20 to <25	BMI 25 to <30	BMI 30 to <35	BMI 35+	
Sensitivity								
Present study	S 2 years since last	2 Years	42% (20–64)	62% (53–71)	65% (56–75)	76% (62–91)	100% (69–100)	65% (59–100)
Kemp Jacobsen et al, 2015 [18]		1 Year	NA	NA	NA	NA	NA	88.9% (86.5–90.9)
Banks et al, 2004 [11]	I + S	1 Year	83.8% Crude 85.7% Adj[a] (81.2–89.3)		89.8% Crude 91.0% Adj[a] (87.5–93.6)			86.6% Crude NA
Elmore et al, 2004 [12]	I + S	1 Year	84.6% Crude (79.8–88.6) OR 1 (baseline)		85.9% Crude (80.7–90.2) OR 0.89 Adj[b] (0.52–1.55)	86.2% Crude (78.6–91.9) OR 0.88 Adj[b] (0.44–1.82)	91.3% Crude (82.8–96.4) OR 1.13 Adj[b] (0.47–3.02)	86.0% Crude (83.3–88.5) NR
Kerlikowske et al, 2008 [7]	S 1 year since last	1 Year	79.9% (76.3–82.7) Adj[c]		86.1% (83.5–88.1) Adj[c]			NA
Kerlikowske et al, 2008 [7]	S 2 years since last	1 Year	84.0% (79.3–87.6) Adj[c]		89.0% (85.9–91.2) Adj[c]			NA
Gayde et al, 2012 [19]	I + S	1 year	Average size breasts, 50–59 years: 86.77%[d]		Larger size breasts, 50–59 years: 94.01%[d]			NA
Gayde et al, 2012 [19]	I + S	1 Year	Average size breasts, 60–69 years: 91.13%[e]		Larger size breasts, 60–69 years: 94.51%[e]			NA
Specificity								
Present study	S 2 years since last	2 Years	99.1% (98.6–99.5)	98.8% (98.6–99.0)	98.8% (98.6–99.0)	99.0% (98.7–99.3)	98.8% (98.3–99.4)	98.8% (98.7–99.0)
Kemp Jacobsen et al, 2015 [18]		1 Year	NA	NA	NA	NA	NA	98.8% (98.8–98.9)
Banks et al, 2004 [11]	1 + 2	1 year	96.6% Crude 97.2% Adj[a] (97.0–97.3)		97.0% Crude 97.4% Adj[a] (97.3–97.6)			96.8% Crude NA
Elmore et al, 2004 [12]	I + S	1 Year	89.0% Crude (88.7–89.3) OR 1 (baseline)		88.3% Crude (88.0–88.7) OR 0.86 Adj[b] (0.81–0.90)	88.3% Crude (87.8–88.8) OR 0.79 Adj[b] (0.74–0.84)	88.5% Crude (87.9–89.0) OR 0.77 Adj[b] (0.71–0.82)	88.6% Crude (88.4–88.8) NR
Kerlikowske et al, 2008 [7]	S 1 year since last	1 Year	Non-screen detected per 1000 examinations: 0.8 (0.7–1.0)		Non-screen detected per 1000 examinations: 0.6 (0.6–0.8)			NA
Kerlikowske et al, 2008 [7]	S 2 years since last	1 Year	Non-screen detected per 1000 examinations: 0.8 (0.6–1.1)		Non-screen detected per 1000 examinations: 0.7 (0.6–0.9)			NA
Gayde et al, 2012 [19]	I + S	1 Year	Average size breasts, 50–59 years[d]: 95.54%[e]		Larger size breasts, 50–59 years[d]: 96.41%[e]			NA
Gayde et al, 2012 [19]	I + S	1 Year	Average size breasts, 60–69 years[d]: 96.91%[e]		Larger size breasts, 60–69 years[d]: 97.35%[e]			NA

BMI, body mass index; NA, not available; NR, not relevant; OR, odds ratio; I, initial; S, subsequent.

[a] Adjusted for age, likelihood of previous NHS breast screening programme screening, screening center, previous breast surgery, menopausal status, and use of hormone replacement therapy.

[b] Adjusted for age, breast density, menopausal or hormone therapy status, breast symptoms, family history of breast cancer, history of breast biopsy or surgery, and time since last mammogram.

[c] Adjusted for age, race, and mammography registry.

[d] Categorized only according to breast size and not according to BMI.

[e] Difference not statistically significant at the 0.05 level.

The Diet, Cancer and Health cohort has been followed for only a short time period after the women stopped to be invited to screening. Due to the lead time bias, it would, therefore, not make sense to compare the breast cancer incidence between screened and non-screened obese women. It is a weakness in the study that BMI was measured only at time of recruitment. However, the largest possible age span between recruitment and screening was from age 50 to age 67 years, a period in life with limited changes in female BMI [21].

Although the Diet, Cancer and Health study had information on a number of breast cancer risk factors, we did not include these factors in the analysis. The reason being that the purpose of our study was to determine the sensitivity and specificity of screening mammography for obese women. All women know the size and shape of their body, while few women know their breast cancer risk factors. It was not the purpose of our study to clarify whether BMI was a determinant of sensitivity and specificity independently of other breast cancer risk factors.

4.4. Clinical implications

Although the European data from the UK and Denmark at surface seem to differ from the data from the Northwestern United States, this might derive from differences in the analysis. In the study from the Group Health Cooperative, breast density was included in the list of variable adjusted for in the analysis [12]. However, BMI and breast density correlated in this as in other studies as overweight and obese women had more fatty breasts than normal weight women [9,10,12]. Adjustment for breast density in the measurement of the association between obesity and mammography sensitivity will, therefore, tend to eliminate any sensitivity advantage that obese women might have in screening. Furthermore, the crude US data showed no difference in specificity across BMI groups. The '20% increased risk of having a false-positive mammogram result' [12] appeared only after adjustment in the analysis for breast density and other variables. Overall, the available data, therefore, show the unadjusted sensitivity of screening mammography to be higher in obese than in normal weight women, while the unadjusted specificity remains fairly constant over weight groups of women.

In the United States, 24 states have now implemented breast density notification laws requiring physicians to notify women who have undergone mammography and were found to have dense breast tissue [22]. Although this information will allow women to include the density information in their decision on screening participation, density information is not available for all women and not for potential first-time users. In contrast, all women know the shape of their body. In terms of the public health advice to be derived from these screening studies, it is, therefore, more relevant for obese women to be informed about the crude than the adjusted screening sensitivity and specificity. Unadjusted, both data from the UK, the United States, and from Denmark indicated a higher sensitivity and a constant specificity for obese women compared with that of normal weight women.

It is, therefore, important to encourage obese women to overcome obstacles and to participate in screening. There are two ways in which this message can be conveyed. First, information material in text should include the positive message to obese women about their expected benefit from screening. Second, photos illustrating screening should include images—or drawings—of obese women stressing that this is also a preventive measure available for them and not only for the normal weight women most often shown in information material.

In conclusion, based on linkage of objective height and weight measures with the outcome from an organised population-based screening program, we found the sensitivity of mammography to increase with increasing BMI and the specificity to remain constant across BMI levels.

Conflict of interest statement

Ilse Vejborg, My von Euler-Chelpin and Elsebeth Lynge collaborate on imaging analysis with the private company Biomediq. They do not own stocks in the company nor do they receive any payment from the company. Sisse Njor and Anne Tjønneland have no conflict of interest.

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