

Breast density & the diagnosis of breast cancer at screening

Aim: To assess the association between breast density and the likelihood of diagnosis of invasive breast cancer in a screening mammography program

A pilot study

An amendment to the original Ethics application was required to allow the investigation of the association between breast density and the diagnosis of breast cancer

Cancer diagnosed at screening & breast density

4 th ed	No lesion	Invasive cancer	DCIS or other	total	5 th ed	No lesion	Invasive cancer	DCIS or other	total
1	4020 29.0%	24 30.0%	9 31.0%	4053 29.0%	a	1487 10.7%	6 7.5%	3 10.4%	1496 10.7%
2	4249 30.7%	22 27.5%	9 31.0%	4280 30.7%	b	6390 46.2%	38 47.5%	15 51.7%	6443 46.2%
3	4091 29.6%	33 41.3%	7 24.2%	4131 29.6%	c	4266 30.8%	33 41.3%	7 24.1%	4306 30.9%
4	1484 10.7%	1 1.2%	4 13.8%	1489 10.7%	d	1701 12.3%	3 3.7%	4 13.8%	1708 12.2%
	13844	80	29	13953		13844	80	29	13953

Analysis restricted to women who were not high risk at screening and were of either Caucasian or Asian ethnicity

Logistic regression: factors associated with being diagnosed with invasive cancer - univariate (4th edition)

4 th edition	Odds Ratio	95% CI for Odds ratio	P value
Density			
Cat 2	0.867	0.486 to 1.550	0.631
Cat 3	1.311	0.771 to 2.229	0.318
Cat 4	0.113	0.015 to 0.836	0.033
Age	1.022	0.995-1.050	0.104
Ethnicity	0.275	0.068-1.122	0.072
HT	1.169	0.697-1.962	0.554

Multivariable regression for invasive cancer (4th edition)

4 th edition	Odds Ratio	95% CI for Odds ratio	P value
Density only			
Cat 2	0.867	0.486 to 1.550	0.631
Cat 3	1.311	0.771 to 2.229	0.318
Cat 4	0.113	0.015 to 0.836	0.033
Density+age			
Cat 2	0.875	0.490 to 1.563	0.652
Cat 3	1.397	0.816 to 2.394	0.223
Cat 4	0.127	0.017 to 0.949	0.044
age	1.020	0.992 to 1.049	0.154
Density+age+ ethnicity			
Cat 2	0.908	0.508 to 1.622	0.743
Cat 3	1.514	0.883 to 2.598	0.132
Cat 4	0.141	0.019 to 1.050	0.141
age	1.019	0.992 to 1.047	0.170
ethnicity	0.283	0.069 to 1.160	0.080
Density + age+ ethnicity + HT			
Cat 2	0.906	0.506 to 1.619	0.738
Cat 3	1.510	0.880 to 2.593	0.135
Cat 4	0.140	0.019 to 1.047	0.055
age	1.019	0.991 to 1.047	0.185
ethnicity	0.284	0.069 to 1.169	0.081
HT	1.049	0.620 to 1.774	0.859

Logistic regression: factors associated with being diagnosed with invasive cancer - univariate (5th edition)

5th edition	Odds ratio	95% CI for Odds Ratio	P value
Density only			
Cat b	1.474	0.622 to 3.493	0.378
Cat c	1.859	0.776 to 4.456	0.164
Cat d	0.437	0.109 to 1.752	0.243
Age	1.022	0.995-1.050	0.104
Ethnicity	0.275	0.068-1.122	0.072
HT	1.169	0.697-1.962	0.554

Multivariable regression for invasive cancer (5th edition)

5th edition	Odds ratio	95% CI for Odds Ratio	P value
Density only			
Cat 2	1.474	0.622 to 3.493	0.378
Cat 3	1.859	0.776 to 4.456	0.164
Cat 4	0.437	0.109 to 1.752	0.243
Density+age			
Cat 2	1.452	0.613 to 3.442	0.397
Cat 3	1.941	0.808 to 4.659	0.138
Cat 4	0.483	0.120 to 1.947	0.306
age	1.020	0.992 to 1.048	0.155
Density+age+ ethnicity			
Cat 2	1.500	0.633 to 3.557	0.357
Cat 3	2.115	0.880 to 5.084	0.094
Cat 4	0.539	0.134 to 2.176	0.385
age	1.019	0.992 to 1.047	0.176
ethnicity	0.277	0.068 to 1.136	0.075
Density + age+ ethnicity + HT			
Cat 2	1.498	0.631 to 3.553	0.359
Cat 3	2.110	0.887 to 5.075	0.096
Cat 4	0.537	0.133 to 2.171	0.383
age	1.019	0.991 to 1.047	0.188
ethnicity	0.278	0.068 to 1.143	0.076
HT	1.036	0.613 to 1.751	0.895

Summary - cancer diagnosis at screening

4th edition only

Compared with being in the lowest density category, being in the highest density category was associated with a trend towards a reduced likelihood of being diagnosed with invasive cancer (masking) adjusted OR 0.14 (95%CI 0.02 to 1.05)

The OR for HT was diminished when breast density was taken into account ?the impact of HT on BC risk is mediated by density

Both 4th and 5th editions

Once density, age and HT were taken into account, ethnicity remained “protective” (odds ratio <1, $p \sim 0.08$) ?confounding by body mass index

Cancer diagnosed at screening & breast density % by column

4 th ed	No lesion	Invasive cancer	DCIS or other	total	5 th ed	No lesion	Invasive cancer	DCIS or other	total
1	4020 29.0%	24 30.0%	9 31.0%	4053 29.0%	a	1487 10.7%	6 7.5%	3 10.4%	1496 10.7%
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	13844	80	29	13953		13844	80	29	13953

Analysis restricted to women who were not high risk at screening and were of either Caucasian or Asian ethnicity

Cancer diagnosed at screening & breast density

Retrospective data set only (n=7723) % by column

4 th ed	No lesion	Invasive cancer	DCIS / other	total	5 th ed	No lesion	Invasive cancer	DCIS/ other	total
1	2057 26.9%	17 30.9%	5 26.3%	2079 26.9%	a	785 10.3%	5 9.1%	2 10.5%	792 10.3%
2	2242 29.3%	14 25.5%	6 31.5%	2262 29.3%	b	3292 43.0%	24 43.6%	9 47.3%	3325 43.0%
3	2392 31.3%	23 41.8%	4 21.1%	2419 31.3	c	2482 32.4%	23 41.8%	4 21.1%	2509 32.5%
4	958 12.5%	1 1.8%	4 21.1%	963 12.5%	d	1090 14.3%	3 5.5%	4 21.1%	1097 14.2%
	7649	55	19	7723		7649	55	19	7723

Retrospective data set only (10 interval cancers) % by column

4 th ed	No lesion	Invasive cancer	DCIS / other	total	5 th ed	No lesion	Invasive cancer	DCIS/ other	total
1	2057 (2) 26.9%	17 30.9%	5 26.3%	2079 26.9%	a	785 10.3%	5 9.1%	2 10.5%	792 10.3%
2	2242 (1) 29.3%	14 25.5%	6 31.5%	2262 29.3%	b	3292(3) 43.0%	24 43.6%	9 47.3%	3325 43.0%
3	2392 (3) 31.3%	23 41.8%	4 21.1%	2419 31.3	c	2482 (3) 32.4%	23 41.8%	4 21.1%	2509 32.5%
4	958 (3) 12.5%	1 1.8%	4 21.1%	963 12.5%	d	1090 (3) 14.3%	3 5.5%	4 21.1%	1097 14.2%
	7649	55	19	7723		7649	55	19	7723

Breast cancer and breast density

This was a pilot study of the association between breast density and the identification of invasive cancer at the time of screening and subsequently

Interval cancers diagnosed in women in the highest density category provided some “catch up” in terms of the total number of invasive cancers diagnosed in this group

There is a relative “under-representation” of interval cancers diagnosed in the two lowest categories of density

Breast cancer and breast density

- Depending on how you define “high”, a relatively large proportion of women have “high” breast density
- The relative increase in breast cancer risk in women with high breast density, but no other risk factors, is relatively small, compared with women with average breast density (from the literature, ORs of 1.2-2.2)
- The proportion of variation in total breast cancer risk attributable to breast density is also modest, <20% (age-dependent)
- These considerations are important when counselling women about the implications of their breast density, especially considering the episodic media attention given to breast density
- The future: a reliable automated assessment of breast density may play a role in the stratification of risk for “tailored screening” analogous to the current BreastScreen system of stratifying women on the basis of family history