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Supplementary Material

Title: Comparison of quadrant-specific breast cancer incidence trends in the United States and England between 1975-2013

Journal: Cancer Epidemiology

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Online Table 1 Distribution of quadrant-specific breast cancers (malignant) in SEER registries for all and specific years.

Quadrant of the Breast	Number of Cases (%)			
	1975	1996	2013	1975-2013
<i>Nipple</i>	102 (1.1)	160 (0.9)	103 (0.5)	5538 (0.9)
<i>Central Portion</i>	632 (6.5)	1,091 (6.3)	1,024 (4.6)	35386 (5.6)
<i>UIQ</i>	658 (6.8)	1,481 (8.5)	2,703 (12.0)	59549 (9.5)
<i>LIQ</i>	296 (3.1)	940 (5.4)	1,313 (5.8)	31038 (4.9)
<i>UOQ</i>	2,635 (27.2)	5,803 (33.4)	7,313 (32.5)	209633 (33.3)
<i>LOQ</i>	611 (6.3)	1,119 (6.4)	1,646 (7.3)	41055 (6.5)
<i>Axillary Tail</i>	71 (0.7)	148 (0.9)	132 (0.6)	4910 (0.8)
<i>Overlapping Lesions</i>	1,189 (12.3)	3,142 (18.1)	5,226 (23.2)	128515 (20.4)
<i>NOS</i>	3,476 (35.9)	3,494 (20.1)	3,044 (13.5)	114383 (18.2)
Total	9,670	17,378	22,504	630007

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant, NOS= not otherwise specified

Online Table 2 Distribution of quadrant-specific breast cancers (malignant) in England for all and specific years.

Quadrant of the Breast	Number of Cases (%)			
	1979	1996	2013	1979-2013
<i>Nipple</i>	300 (1.5)	420 (1.3)	451 (1.0)	12995 (1.2)
<i>Central Portion</i>	723 (3.6)	1485 (4.7)	2211 (4.9)	45437 (4.1)
<i>UIQ</i>	836 (4.1)	1819 (5.8)	3950 (8.8)	65351 (5.8)
<i>LIQ</i>	334 (1.7)	791 (2.5)	2096 (4.7)	31467 (2.8)
<i>UOQ</i>	2668 (13.2)	6409 (20.4)	12542 (28.1)	228473 (20.4)
<i>LOQ</i>	573 (2.8)	1202 (3.8)	2395 (5.4)	43851 (3.9)
<i>Axillary Tail</i>	133 (0.7)	171 (0.5)	246 (0.6)	5418 (0.5)
<i>Overlapping Lesions</i>	1178 (5.8)	1904 (6.0)	2274 (5.1)	62450 (5.6)
<i>NOS</i>	13489 (66.7)	17285 (54.9)	18514 (41.4)	625692 (55.8)
Total	20234	31486	44679	1121134

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant, NOS= not otherwise specified

Online Table 3: Sensitivity Analysis investigating the effect of improvement in site-coding accuracy over time on the distribution of breast cancer in the SEER registry.

Quadrant of the Breast	Number of Cases (%)		
	1975	1996	2013
<i>Nipple</i>	197 (2.0)	256 (1.5)	163 (0.7)
<i>Central Portion</i>	1221 (12.6)	1765 (10.2)	1619 (7.2)
<i>UIQ</i>	1271 (13.1)	2396 (13.8)	4273 (19.0)
<i>LIQ</i>	572 (5.9)	1521 (8.8)	2076 (9.2)
<i>UOQ</i>	5091 (52.6)	9388 (54.0)	11562 (51.4)
<i>LOQ</i>	1180 (12.2)	1810 (10.4)	2602 (11.6)
<i>Axillary Tail</i>	137 (1.4)	239 (1.4)	209 (0.9)
<i>Non-Site-Specific*</i>	-	-	-
Total	9,670	17,378	22,504

*Non-Site-Specific includes overlapping lesions and tumours not otherwise specified (NOS)

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant

Online Table 4: Sensitivity Analysis investigating the effect of improvement in site-coding accuracy over time on the distribution of breast cancer in England.

Quadrant of the Breast	Number of Cases (%)		
	1979	1996	2013
<i>Nipple</i>	1090 (5.4)	1075 (3.4)	843 (1.9)
<i>Central Portion</i>	2628 (13.0)	3802 (12.1)	4135 (9.3)
<i>UIQ</i>	3039 (15.0)	4657 (14.8)	7387 (16.5)
<i>LIQ</i>	1214 (6.0)	2025 (6.4)	3920 (8.8)
<i>UOQ</i>	9697 (47.9)	16410 (52.1)	23455 (52.5)
<i>LOQ</i>	2083 (10.3)	3078 (9.8)	4479 (10.0)
<i>Axillary Tail</i>	483 (2.4)	438 (1.4)	460 (1.0)
<i>Non-Site-Specific</i>	-	-	-
Total	20234	31486	44679

*Non-Site-Specific includes overlapping lesions and tumours not otherwise specified (NOS)

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant

Online Table 5: Sensitivity Analysis investigating the effect of improvement in site-coding accuracy over time on the distribution of breast cancer in the SEER registry, using the proportion of tumours with missing site information in 2013 as the standard level of missingness.

Quadrant of the Breast	Number of Cases (%)		
	1975	1996	2013
<i>Nipple</i>	125 (1.3)	164 (0.9)	103 (0.5)
<i>Central Portion</i>	773 (8.0)	1117 (6.4)	1,024 (4.6)
<i>UIQ</i>	805 (8.3)	1517 (8.7)	2,703 (12.0)
<i>LIQ</i>	362 (3.7)	963 (5.5)	1,313 (5.8)
<i>UOQ</i>	3223 (33.3)	5942 (34.2)	7,313 (32.5)
<i>LOQ</i>	474 (7.7)	1146 (6.6)	1,646 (7.3)
<i>Axillary Tail</i>	87 (0.9)	152 (0.9)	132 (0.6)
<i>Non-Site-Specific</i>	3549 (36.7)	6378 (36.7)	8270 (36.7)
Total	9,670	17,378	22,504

*Non-Site-Specific includes overlapping lesions and tumours not otherwise specified (NOS)

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant

Online Table 6: Sensitivity Analysis investigating the effect of improvement in site-coding accuracy over time on the distribution of breast cancer in England, using the proportion of tumours with missing site information in 2013 as the standard level of missingness.

Quadrant of the Breast	Number of Cases (%)		
	1979	1996	2013
<i>Nipple</i>	583 (2.9)	575 (1.8)	451 (1.0)
<i>Central Portion</i>	1406 (6.9)	2034 (6.5)	2211 (4.9)
<i>UIQ</i>	1626 (8.0)	2492 (7.9)	3950 (8.8)
<i>LIQ</i>	649 (3.2)	1084 (3.4)	2096 (4.7)
<i>UOQ</i>	5188 (25.6)	8779 (27.9)	12542 (28.1)
<i>LOQ</i>	114 (5.5)	1647 (5.2)	2395 (5.4)
<i>Axillary Tail</i>	259 (1.3)	234 (0.7)	246 (0.6)
<i>Non-Site-Specific</i>	9409 (46.5)	14641 (46.5)	20788 (46.5)
Total	20234	31486	44679

*Non-Site-Specific includes overlapping lesions and tumours not otherwise specified (NOS)

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant

Online Table 7 Multivariable negative binomial regression for breast cancer incidence with respect: year of diagnosis, age at diagnosis and breast quadrant (categorised into 3 categories- UOQ, site-specific excluding UOQ, non-site-specific) for SEER and England.

Variable	SEER		England	
	IRR (95% CI)	P-value	IRR (95% CI)	P-value
Year of diagnosis (per decade)†				
Year	1.04 (0.95-1.14)	0.360	1.33 (1.19-1.48)	<0.001
Year ²	-*	-	-*	-
Age Group				
0-39 (reference)	1 (ref)			
40-44	9.79 (8.40-11.42)	<0.001	9.65 (8.11-11.47)	<0.001
45-49	415.44 (13.25-18.00)	<0.001	15.25 (12.83-18.13)	<0.001
50-54	18.78 (16.12-21.90)	<0.001	19.68 (16.56-23.39)	<0.001
55-59	23.08 (19.80-26.90)	<0.001	21.46 (18.06-25.51)	<0.001
60-64	28.20 (24.20-32.88)	<0.001	25.02 (21.05-29.74)	<0.001
65-69	32.76 (28.11-38.19)	<0.001	25.14 (21.15-29.89)	<0.001
70-74	35.23 (30.22-41.07)	<0.001	25.34 (21.32-30.12)	<0.001
75-79	37.11 (31.84-43.26)	<0.001	26.72 (22.47-31.76)	<0.001
80-84	36.00 (30.88-41.97)	<0.001	27.17 (22.85-32.30)	<0.001
≥85	31.56 (27.07-36.81)	<0.001	18.25 (15.34-21.70)	<0.001
Quadrant of diagnosis				
UOQ (reference)	1 (ref)		1 (ref)	
Site-specific excluding UOQ‡	0.16 (0.14-0.17)	<0.001	0.16 (0.15-0.19)	<0.001
Non-site-specific**	0.59 (0.52-0.66)	<0.001	1.50 (1.31-1.71)	<0.001
Interaction of Year and Quadrant of diagnosis (per decade)				
UOQ (reference)	1 (ref)		1 (ref)	
Site-specific excluding UOQ‡	1.04 (0.94-1.15)	0.423	0.99 (0.88-1.12)	0.896
Non-site-specific**	0.97 (0.87-1.08)	0.617	0.78 (0.68-0.89)	<0.001

† Year was centred and provided per decade to enable easier interpretation.

*model fit better without year², therefore year² not included in model

‡ includes: upper inner quadrant, lower inner quadrant, lower outer quadrant, nipple, axillary tail and central portion

** includes: overlapping lesions and tumour not otherwise specified

Definitions: UOQ = Upper Outer Quadrant

Online Table 8 Multivariable negative binomial regression for breast cancer incidence in SEER 9 registries with respect to: year of diagnosis, age at diagnosis and breast quadrant. IARC rules for multiple primary neoplasms were applied [10].

Variable	IRR (95% CI)	P-value
Year of diagnosis (per decade)†		
Year	1.04 (0.96-1.11)	0.356
Year ²	0.95 (0.93-0.98)	<0.001
Age Group		
0-39 (reference)	1 (Ref)	
40-44	9.53 (8.41-10.81)	<0.001
45-49	14.82 (13.08-16.80)	<0.001
50-54	17.73 (15.65-20.09)	<0.001
55-59	21.76 (19.20-24.66)	<0.001
60-64	26.58 (23.45-30.12)	<0.001
65-69	30.65 (27.04-34.73)	<0.001
70-74	32.99 (29.11-37.40)	<0.001
75-79	35.63 (31.43-40.40)	<0.001
80-84	35.17 (31.00-39.90)	<0.001
≥85	31.75 (27.97-36.04)	<0.001
Quadrant of diagnosis		
UOQ (reference)	1 (Ref)	
Nipple	0.02 (0.02-0.03)	<0.001
Central portion	0.15 (0.14-0.17)	<0.001
UIQ	0.27 (0.24-0.31)	<0.001
LIQ	0.14 (0.12-0.15)	<0.001
LOQ	0.20 (0.17-0.22)	<0.001
Axillary tail	0.03 (0.02-0.03)	<0.001
Overlapping lesions	0.61 (0.54-0.69)	<0.001
NOS	0.55 (0.49-0.62)	<0.001
Interaction of Year and Quadrant of diagnosis (per decade)		
UOQ (reference)	1 (Ref)	
Nipple	0.79 (0.70-0.89)	<0.001
Central portion	0.95 (0.86-1.06)	0.367
UIQ	1.08 (0.97-1.20)	0.158
LIQ	1.10 (0.99-1.22)	0.079
LOQ	1.03 (0.93-1.14)	0.595
Axillary tail	0.86 (0.76-0.96)	0.008
Overlapping lesions	1.00 (0.91-1.11)	0.942
NOS	0.93 (0.84-1.03)	0.158

† Year was centred and provided per decade to enable easier interpretation.

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant, NOS= not otherwise specified

Online Table 9 IRR and percentage change in incidence over time (per decade) for SEER 9 registries (p-value corresponds to Figure 1). IARC rules for multiple primary neoplasms were applied [10].

Quadrant of Diagnosis	IRR	%change	P-value
<i>UOQ</i>	1.04	4%	0.356
<i>Nipple</i>	0.82	-18%	<0.001
<i>Central Portion</i>	0.99	-1%	0.719
<i>UIQ</i>	1.12	12%	0.003
<i>LIQ</i>	1.14	14%	0.001
<i>LOQ</i>	1.06	6%	0.090
<i>Axillary Tail</i>	0.89	-11%	0.007
<i>Overlapping Lesions</i>	1.04	4%	0.297
<i>NOS</i>	0.96	-4%	0.282

Definitions: UIQ= Upper Inner Quadrant, LIQ= Lower Inner Quadrant, UOQ= Upper Outer Quadrant, LOQ= Lower Outer Quadrant, NOS= not otherwise specified

Online Figure 1: Trends in the annual incidence of female breast cancer in SEER 9 registries from 1975 to 2013 for each quadrant. Incidence rate has been standardized to the WHO std population 2000-2025 [18]. (A P-value<0.5 corresponds to significant change in incidence over time [corresponds to Table 2]). IARC rules for multiple primary neoplasms were applied [10].



