

Supplementary Online Content

Johnson RH, Chien FL, Bleyer A. Incidence of breast cancer with distant involvement among women in the United States, 1976 to 2009. *JAMA*. doi:10.1001/jama.2013.776.

eTable 1. Evaluating Historic Stage A Subtypes for Stage Migration into Distant Disease, SEER9, Women, Breast Cancer

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Evaluating Historic Stage A Subtypes for Stage Migration into Distant Disease, SEER9, Women, Breast Cancer

SEER9 Population	No. of Women					Incidence*					
	In situ	Localized	Regional	Distant	Unstaged	In situ	Localized	Regional	Distant	Unstaged	
1976	2,231,725	32	303	228	29	36 (5.7%)	1.79	16.37	12.19	1.53	1.97
1977	2,313,414	45	340	268	26	28 (4.0%)	2.47	17.65	13.65	1.31	1.32
1978	2,398,860	29	338	284	29	29 (4.1%)	1.48	16.91	13.84	1.41	1.43
1979	2,489,286	27	335	283	28	28 (4.0%)	1.34	15.73	13.17	1.22	1.38
1980	2,584,156	45	369	334	30	26 (3.2%)	2.09	16.59	15.27	1.41	1.26
1981	2,661,993	50	423	345	30	32 (3.6%)	2.21	18.69	15.36	1.41	1.40
1982	2,735,388	34	430	379	36	52 (5.6%)	1.47	18.06	16.02	1.41	2.15
1983	2,793,620	44	418	377	52	23 (2.5%)	1.86	17.11	15.58	2.08	0.94
1984	2,863,858	69	455	404	49	37 (3.6%)	2.81	18.36	16.13	2.00	1.46
1985	2,933,735	73	488	388	57	45 (4.3%)	2.85	18.81	15.02	2.28	1.74
1986	3,012,610	110	480	441	45	32 (2.9%)	4.17	17.60	16.37	1.60	1.13
1987	3,036,123	95	483	423	43	40 (3.7%)	3.61	17.73	15.41	1.61	1.42
1988	3,068,807	127	486	393	45	30 (2.8%)	4.66	17.43	14.20	1.59	1.11
1989	3,092,215	102	461	396	50	33 (3.2%)	3.67	16.33	13.87	1.76	1.12
1990	3,113,077	131	506	416	52	39 (3.4%)	4.66	17.68	14.37	1.77	1.34
1991	3,142,771	136	535	454	58	37 (3.0%)	4.71	18.30	15.38	1.97	1.30
1992	3,162,320	124	530	389	51	40 (3.5%)	4.22	17.73	12.98	1.70	1.31
1993	3,169,482	124	541	389	56	27 (2.4%)	4.15	17.88	12.72	1.83	0.89
1994	3,170,211	131	447	407	42	29 (2.7%)	4.31	14.57	13.25	1.36	0.94
1995	3,171,944	146	512	408	56	42 (3.6%)	4.76	16.57	13.21	1.80	1.35
1996	3,173,568	141	519	402	61	30 (2.6%)	4.59	16.81	13.02	1.97	0.96
1997	3,158,118	162	541	396	63	43 (3.6%)	5.28	17.54	12.83	2.04	1.38
1998	3,131,353	169	542	417	73	28 (2.3%)	5.55	17.68	13.58	2.37	0.92
1999	3,094,677	171	517	439	54	14 (1.2%)	5.67	17.07	14.48	1.78	0.47
2000	3,063,466	169	480	466	57	24 (2.0%)	5.68	16.06	15.53	1.91	0.79
2001	3,037,410	152	518	469	71	28 (2.3%)	5.16	17.45	15.77	2.38	0.96
2002	3,002,078	152	453	420	60	24 (2.2%)	5.26	15.57	14.39	2.05	0.81
2003	2,969,836	131	480	435	70	13 (1.2%)	4.61	16.74	15.20	2.46	0.45
2004	2,946,534	153	502	441	75	16 (1.3%)	5.51	17.87	15.57	2.64	0.57
2005	2,946,183	178	474	379	70	16 (1.4%)	6.44	16.97	13.55	2.50	0.57
2006	2,967,909	164	455	396	79	11 (1.0%)	5.87	16.13	14.03	2.81	0.38
2007	2,988,879	167	468	416	74	19 (1.7%)	5.96	16.54	14.70	2.60	0.67
2008	3,005,421	170	491	437	79	13 (1.1%)	6.09	17.31	15.46	2.78	0.46
2009	3,014,208	148	489	413	84	12 (1.0%)	5.34	17.44	14.61	2.90	0.41

*Rate per 100,000 and age-adjusted to 2000 US Std Pop (19 age groups - Census P25-1130) standard.

Estimates of Stage Migration from Unstaged to Other Categories by Weighted Distribution

	In situ	Localized	Regional	Distant	Unstaged	In situ	Localized	Regional	Distant	Unstaged	
1976-1995 Mean					34.3 (3.6%)					1.35	
2003-2009 Mean					14.3 (1.2%)					0.50	
2003-2009 Mean minus 1976-1995 Mean					20.0					0.84	
Proportionate Distribution:	2.80	8.47	7.35	1.34	←	0.12	0.36	0.31	0.06	←	
	Unstaged contributes 7% of Distant						Unstaged contributes 7% of Distant				

eTable 2: 5-Year Survival, Women, Breast Cancer*

Extent of Disease	SEER18, 2000-2004				
	Number	Observed	Relative	Observed 95% CI	Relative 95% CI
Locoregional	12,387	86.8%	87.3%	86.2-87.4%	86.7-87.9%
Distant	925	31.4%	31.6%	28.4-34.5%	28.6-34.7%
Difference		55.4%			

*Malignant behavior

Actuarial method. Ederer II method used for cumulative expected.

Confidence interval: Log(-Log()) Transformation. The level is 95%.

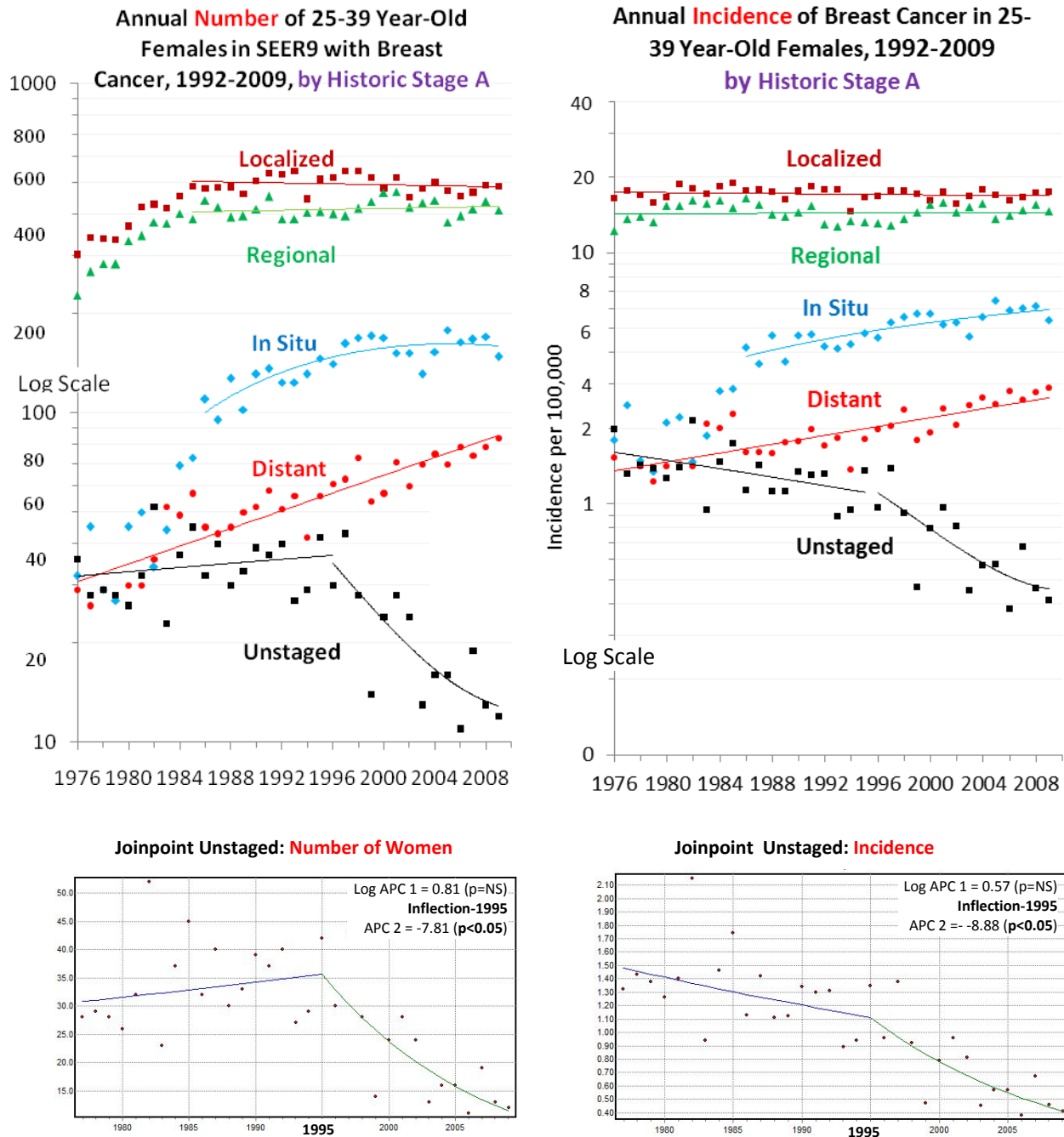
eTable 3: Person-Years of Life Affected (PYLA), 2009

Women Diagnosed with Distant-Disease Breast Cancer	Age 25-39	Age 40+	
	2009	2009	
	Due to Incidence Increase from 1976 to 2009		
Annual Number*	838	545	12,801
% of All Women with Distant Disease	6.1%	4.1%	93.9%
% of 25-39 Year-Old Women Due to Incidence Increase		66.5%	
Mean Age at Diagnosis (Years)	34.3	34.3	63.5
Expected Survival (Years)**	81.1	81.1	81.1
Person-Years of Life Affected (PYLA)	39,218	25,506	225,298
% of PYLA in All Women with Distant Disease	14.8%	10.2%	85.2%
% of PYLA in 25-39 Year-Olds Due to Incidence Increase		68.6%	

Louisiana Cases, Nov 2011 Sub (2000-2009) <Single Ages to 85+, Katrina/Rita Population Adjustment> - Linked To County Attributes - Total U.S., 1969-2009 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2011 (updated 10/28/2011), based on the November 2010 submission. Accessed December 25, 2012, and the U.S. Census <http://www.census.gov/popest/data/intercensal/state/state2010.html>

**<https://www.cia.gov/library/publications/the-world-factbook/geos/us.html>

eFigure: Evaluating Historic Stage A Subtypes for Stage Migration into Distant Disease



SUMMARY Stage Migration Does Not Explain the Increasing Incidence of Distant-Disease in <40 Year-Old Women

1. Stage migration almost always occurs from an adjacent category (e.g., regional ⇔ distant) and usually from a lower to (next) higher stage category (e.g. regional ⇒ distant).
2. There is no evidence for migration from *regional* (green) or *localized* (brown); both categories have had a stable incidence rate and number of affected women during the past decade or longer. The *in situ* has had a steady increase and thus also is not a source for migration of patients from this category.
3. Only *unstaged* disease (black) declined and only since 1995 per Joinpoint analysis (of both incidence and number).
 - a. The increasing incidence of *distant* disease **preceded the unstaged decline by at 2+ decades** (1976 or earlier)
 - b. The **number of unstaged patients is also too small to account for the increase** in *distant* disease even if the entire reduction moved to distant disease. On a statistical basis 7% of the increase in *distant* disease can be attributed to transfer from the unstaged group and If stage migration were responsible, probably <3%.
 - c. A long-time SEER veteran (Lynn Ries) advised us on 3b and a poll of breast cancer medical oncologists and surgeons at MD Anderson, Dana Farber, and the University of North Carolina agree with this interpretation.