

Surgery for Men with Breast Cancer: Do the same data still apply?

Plichta JK*, Ren Y, Marks CE, Thomas SM, Greenup RA, Rosenberger LH, Fayanju OM, Hwang ES, Force J
*Corresponding Author: Jennifer Plichta (Jennifer.Plichta@duke.edu)

Introduction

- Men with breast cancer = 1% of breast cancer population^{1,2}
- Men often excluded from clinical trials
- Treatment for men extrapolated from evidence in women³
 - NSABP B-06: lumpectomy+radiation (BCT) = mastectomy
 - CALGB 9343: lumpectomy+tamoxifen = lumpectomy+radiation+tamoxifen
 - ACOSOG Z0011: SLNB = ALND

Objective

To compare contemporary practice patterns between men and women with breast cancer after publication of several landmark clinical trials in surgery (NSABP B-06, CALGB 9343, ACOSOG Z0011).

Methods

- Patients, stages 0-IV breast cancer from 2004-2015 in the National Cancer Database
- Stratified by gender
- Sub-cohorts based on trial eligibility
 - NSABP B-06
 - CALGB 9343
 - ACOSOG Z0011
- Patient, tumor, and treatment characteristics compared by gender
 - Chi-square and t-tests, as appropriate
- Practice patterns stratified by gender, compared over time
- Survival analyses
 - Kaplan-Meier curves to visualize unadjusted overall survival
 - Cox proportional hazards model to estimate the effect of gender, after adjustment

Results

Table 1. Patient, disease, & treatment characteristics, and trial eligibility.

	Female N=1,648,070 99.0%	Male N=16,676 1.0%	P-Value
Follow-up (months)			
Median (IQR)	68.1 (40.0-100.4)	67.0 (38.8-98.7)	
Age			<0.0001
Median (IQR)	61 (51 - 71)	66 (56 - 75)	
Race/Ethnicity			<0.0001
Non-Hispanic White	1228247 (79.5%)	12,635 (81.2%)	
Non-Hispanic Black	174,093 (11.3%)	1,923 (12.4%)	
Non-Hispanic Other	59,660 (3.9%)	401 (2.6%)	
Hispanic	82,969 (5.4%)	597 (3.8%)	
Charlson/Deyo Comorbidity Score			<0.0001
0	1393146 (85.1%)	13,164 (79.9%)	
1	206,106 (12.6%)	2,662 (16.2%)	
≥ 2	37,868 (2.3%)	640 (3.9%)	
Histology			<0.0001
Ductal	1449381 (87.9%)	15,899 (95.3%)	
Lobular	173,464 (10.5%)	582 (3.5%)	
Other	25,225 (1.5%)	195 (1.2%)	
Tumor Size (mm)			<0.0001
Median (IQR)	16 (10 - 27)	20 (14 - 30)	
Positive LNs			<0.0001
Median (IQR)	2 (1 - 4)	2 (1 - 5)	
Oncotype Dx Recurrence Score			0.02
Median (IQR)	16 (11-22)	15 (9-24)	
Grade			<0.0001
1	341,769 (22.3%)	2,233 (14.3%)	
2	661,283 (43.1%)	7,789 (50%)	
3	531,751 (34.6%)	5,566 (35.7%)	
ER Status			<0.0001
ER+	1278261 (79.9%)	14,686 (92.1%)	
ER-	321,042 (20.1%)	1,257 (7.9%)	
PR Status			<0.0001
PR+	1105028 (69.5%)	13,189 (83.3%)	
PR-	485,883 (30.5%)	2,637 (16.7%)	
HER2 Status			<0.0001
HER2+	129,119 (14.8%)	1,104 (12.5%)	
HER2-	742,419 (85.2%)	7,742 (87.5%)	
Molecular Subtypes by Receptors			<0.0001
HR+/HER2-	631,178 (72.5%)	7,312 (82.8%)	
HER2+	128,822 (14.8%)	1,098 (12.4%)	
TNBC	110,403 (12.7%)	419 (4.7%)	
Anatomic Stage Groups			<0.0001
I	686,273 (56.4%)	5,081 (42.8%)	
II	357,125 (29.4%)	4,487 (37.8%)	
III	94,445 (7.8%)	1,199 (10.1%)	
IV	78,715 (6.5%)	1,103 (9.3%)	
Prognostic Stage Group			<0.0001
I	774,586 (74.7%)	6,501 (66.9%)	
II	128,478 (12.4%)	1,519 (15.6%)	
III	55,167 (5.3%)	589 (6.1%)	
IV	78,715 (7.6%)	1,103 (11.4%)	
Extent of Axillary Surgery			<0.0001
[1-5] LNs removed	893,665 (63.3%)	7,062 (50.2%)	
[6-9] LNs removed	166,600 (11.8%)	1,897 (13.5%)	
≥ 10 LNs removed	351,818 (24.9%)	5,115 (36.3%)	
Local-Regional Therapy			<0.0001
Lumpectomy alone	151,553 (10%)	1,127 (7.5%)	
Mastectomy alone	462,519 (30.6%)	8,265 (55.2%)	
Lumpectomy+Radiation	713,079 (47.2%)	2,327 (15.5%)	
Mastectomy+Radiation	184,704 (12.2%)	3,265 (21.8%)	
Received Any Chemotherapy			<0.0001
No	879,526 (55%)	9,214 (57.5%)	
Yes	718,775 (45%)	6,818 (42.5%)	
Received Endocrine Therapy based on HR status			<0.0001
Endocrine if HR+	829,361 (51.9%)	7,778 (48.8%)	
No Endocrine if HR+	467,577 (29.3%)	7,011 (44%)	
Endocrine if HR-	8,726 (0.5%)	42 (0.3%)	
No Endocrine if HR-	292,679 (18.3%)	1,108 (7%)	
NSABP-B06 Eligible			0.2606
No	938,252 (56.9%)	9,566 (57.4%)	
Yes	709,818 (43.1%)	7,110 (42.6%)	
CALGB9343 Eligible			<0.0001
No	1561943 (94.8%)	16,412 (98.4%)	
Yes	86,127 (5.2%)	264 (1.6%)	
ACOSOG Z0011 Eligible			<0.0001
No	1601474 (97.2%)	16,503 (99%)	
Yes	46,596 (2.8%)	173 (1%)	

ER: estrogen receptor, PR: progesterone receptor, HER2: human-epidermal-growth-factor-receptor-2, HR: hormone receptor, TNBC: triple negative breast cancer, LN: lymph nodes.

Figure 1. Uptake of landmark clinical trials in surgery and comparison of practice patterns over time between men and women with breast cancer.

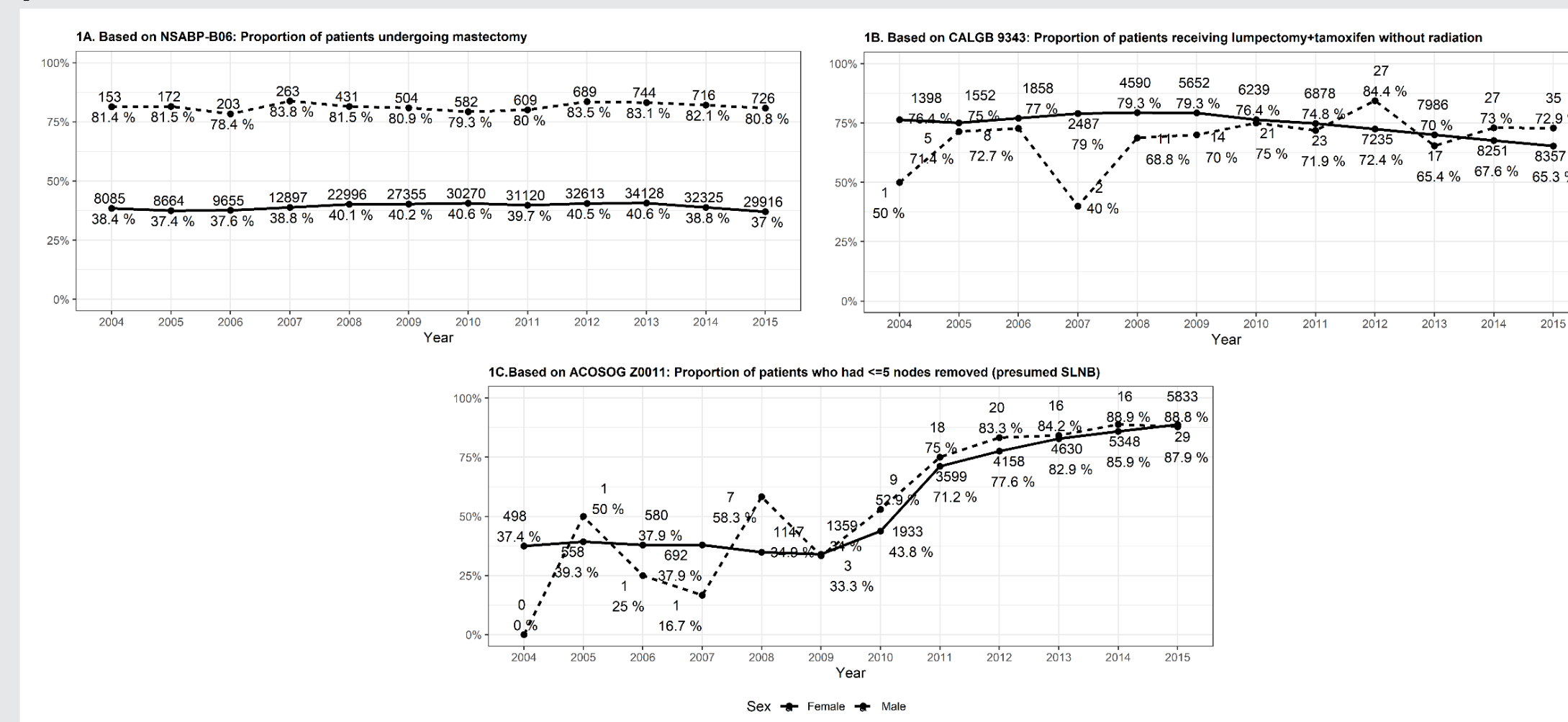


Figure 2. Overall survival for men and women eligible for (A) NSABP B-06; (B) NSABP B-06 stratified by local-regional treatment; (C) CALGB 9343; (D) ACOSOG Z0011.

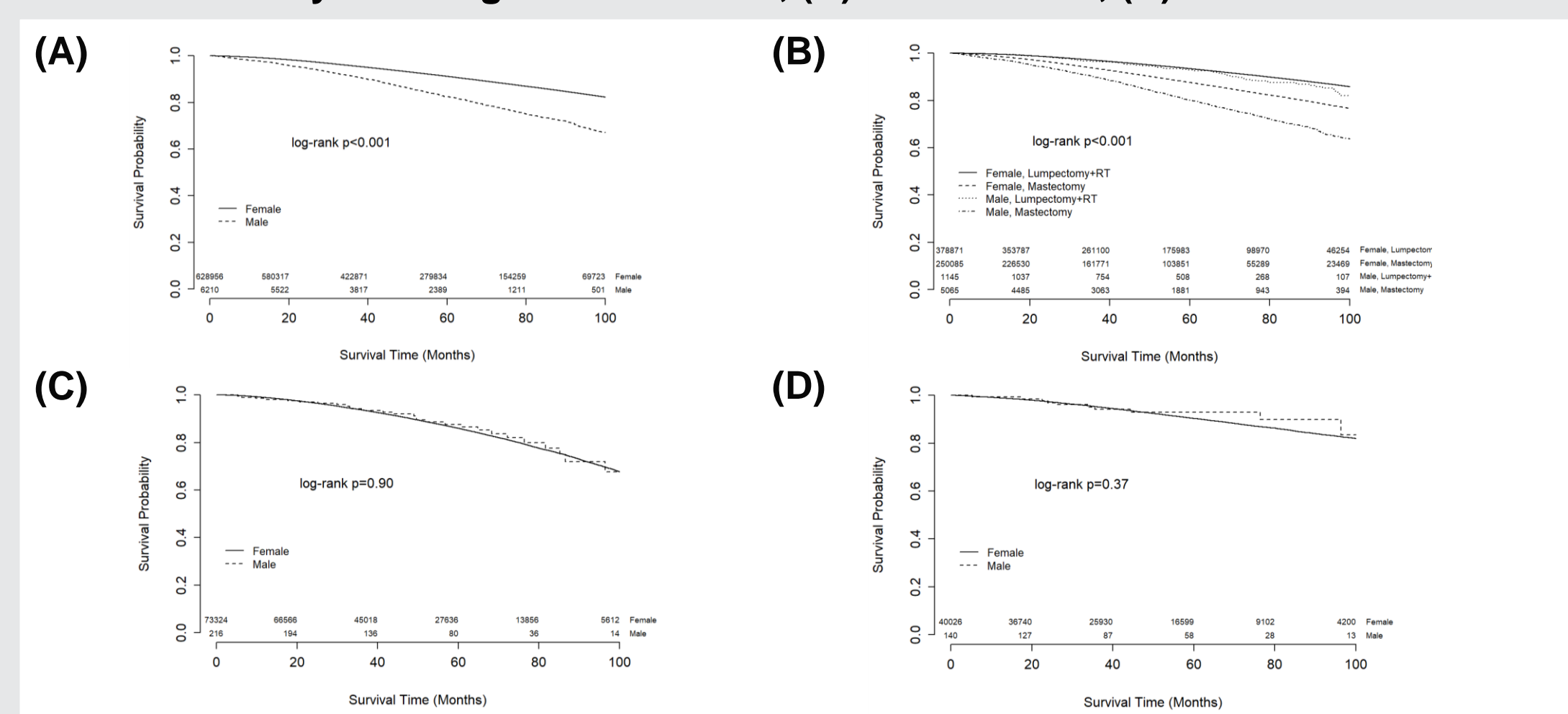


Table 2. Adjusted overall survival by trial eligibility.*

	Hazard Ratio (95% CI)	P-Value	Overall P-Value
NSABP-B06 eligible patients			
Female	-REF-		<0.001
Male	1.192 (1.106 - 1.284)	<0.001	
CALGB 9343 eligible patients			
Female	-REF-		0.721
Male	0.922 (0.589 - 1.441)	0.721	
ACOSOG Z011 eligible patients			
Female	-REF-		0.327
Male	0.692 (0.331 - 1.446)	0.327	

*All models adjusted for year of diagnosis (2004-2009 or 2010-2014), facility type/location, patient age, insurance status, race/ethnicity, Charlson/Deyo comorbidity score, tumor histology, size, grade, number of positive lymph nodes, estrogen receptor (ER) status, progesterone receptor (PR) status, human-epidermal-growth-factor-receptor-2 (HER2) status, type of breast surgery, chemotherapy receipt, radiation receipt, and endocrine therapy receipt.

Data Highlights

1,664,746 patients → 1% men, 99% women

Characteristics of Men with Breast Cancer

- Older age, more comorbidities
- Higher T/N stage, tumor grade
- Worse overall survival

NSABP B-06 Eligible Patients

- More men still undergoing mastectomy
- Similar survival for men and women undergoing BCT
- After adjustment, slightly worse survival for men

CALGB 9343 Eligible Patients

- Similar omission of radiation after lumpectomy
- No difference in overall survival (unadjusted and adjusted)

ACOSOG Z0011 Eligible Patients

- Similar omission of ALND for limited +SLN
- No difference in overall survival (unadjusted and adjusted)

Conclusions

- Uptake of landmark clinical trial results for men with breast cancer often mirrors that for women, despite exclusion from these studies.
- Using the same eligibility criteria, survival outcomes are similar for men and women.
- Observational studies may be useful for this small, unique population.

References

- Greif JM, Pezzi CM, Klimberg VS, Bailey L, Zuraek M. Gender differences in breast cancer: analysis of 13,000 breast cancers in men from the National Cancer Data Base. *Ann Surg Oncol.* 2012;19(10):3199-3204.
- Giordano SH. Breast Cancer in Men. *N Engl J Med.* 2018;378(24):2311-2320.
- Hassett MJ, Somerfield MR, Baker ER, et al. Management of Male Breast Cancer: ASCO Guideline. *J Clin Oncol.* 2020;Jco1903120.