

Measuring and Overcoming Health Delivery Barriers to Optimal Breast Cancer Outcomes

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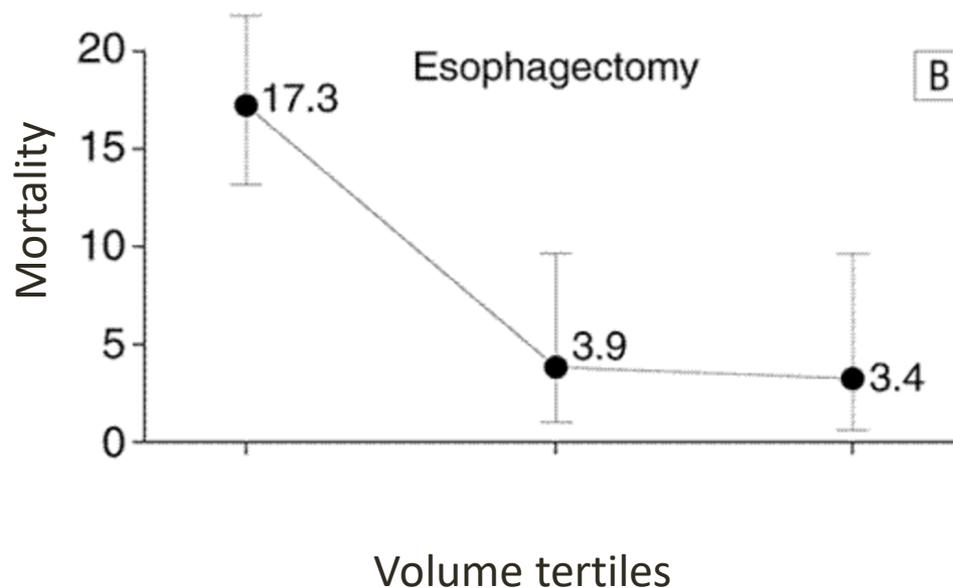
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Overview

- Surgical volume and outcomes in breast cancer
- Fractures, lymphedema and quality of life in survivorship
- Adherence: Remediable factors?
 - Health system/health delivery
 - Cost
 - Pharmacy access
- Future research directions

Surgical Volume and Cancer

- Strong association between surgical volume for high-surgical risk cancers
- Esophageal, pancreas
- Have led to volume-based referral initiatives (eg Leapfrog Group)
- Evidence less clear for cancers where mortality is more delayed
 - Breast cancer 30-day mortality <0.2%



Begg, JAMA1998
Birkmeyer, NEJM 2002

Volume and Breast Cancer Outcomes in Europe

- In several European breast cancer studies, about half of patients were taken care of by "high volume" physicians
- In UK, half of patients cared for by physicians performing at least 30 surgeries, and mortality 15% lower.
- Mechanisms were unknown
- US general surgeons are all trained to perform mastectomy and lumpectomy (or breast conserving surgery)
- Surgical care has on average been less centralized than in other countries, driving distances are much higher, so we began by first examining volumes and processes of care here



The Challenge of Achieving High US Volumes

Table 2. Volume Distribution of Surveillance, Epidemiology, and End Results Breast Cancer Surgeons and Their Patients: 1994–1995 ^a

Two-yr surgeon volume	Surgeons (%) (<i>n</i> = 987)	Patients (%) (<i>n</i> = 8105)
1–2	26	4
3–6	27	15
7–12	26	29
13–29	18	41
≥ 30	2	10

a Volume was defined as the number of breast cancer operations performed by individual physicians during 1994–1995 on cohort patients.

Physician Factors Associated with Breast Cancer Volume

Characteristic	Mean 2-yr volume	P value (adjusted)
Age		
< 45 yrs	7.5	< 0.001
45-54 yrs	9.1	< 0.001
> 54 yrs	8.1	—
Gender		
Male	8.2	< 0.001
Female	10.3	—
Specialty and board certification		
Surgical oncology	9.4	0.90
Board-certified general surgery	9.0	—
Cardiothoracic or vascular surgery	9.5	0.34
General surgery, not board certified	5.0	< 0.001
Other	4.7	< 0.001
Academic ^b		
Yes	9.9	< 0.001
No	7.7	—
Type of practice		
Solo	7.9	—
Two-physician	9.4	< 0.001

Physician volume and Processes of Care

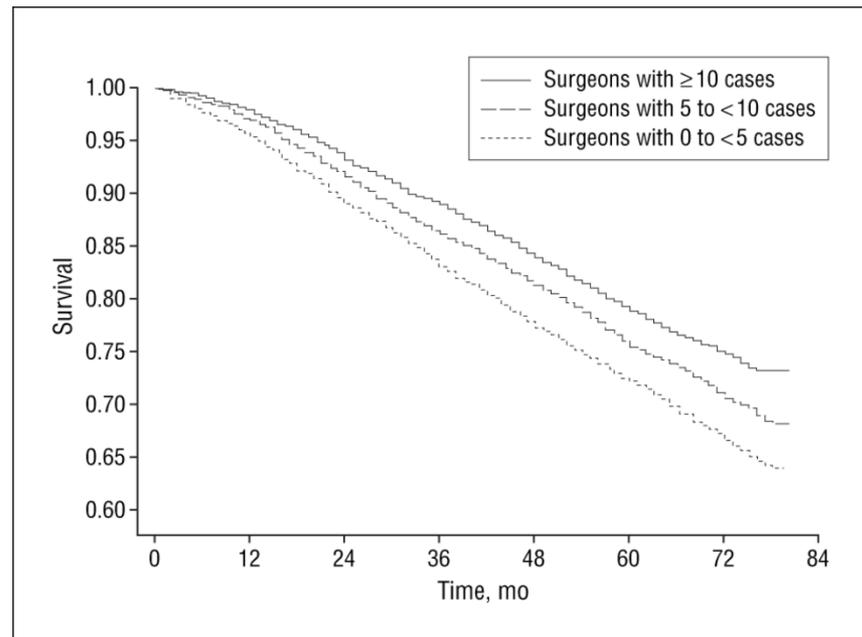
Variable	Surgeon volume					P value
	1-2	3-6	7-12	13-29	≥ 30	
ER/PR testing performed (%)	77	82	81	84	85	0.044
Breast-conserving surgery (%)	39	38	41	42	55	< 0.001
Axillary lymph node dissection (%)						
Breast-conserving surgery (<i>n</i> = 2557)	50	55	60	60	56	0.079
Mastectomy (<i>n</i> = 3484)	86	86	92	93	91	0.001

ER/PR: estrogen receptor/progesterone receptor.

a From a regression model of the effect of the log of physician volume (with a physician random effect to account for clustering) on patient receipt of surgical care practices developed from the National Institutes of Health consensus statement on the management of early-stage breast cancer.¹⁰

Also Gilligan AJPH 2007,
Gilligan Cancer

Kaplan-Meier (unadjusted) survival estimates for a cohort of 12 216 Medicare patients with stage I or II breast cancer, by average annual surgeon volume of Medicare breast cancer cases



Nattinger et al, Arch Intern Med. 2007;167

Table 3. Relationship of Surgeon Volume to Disease-Specific Mortality^a

Patient Characteristic	Breast Cancer Mortality	Non-Breast Cancer Mortality
Surgeon volume		
Low	1 [Reference]	1 [Reference]
Medium	1.00 (0.84-1.20)	0.91 (0.81-1.02)
High	0.94 (0.76-1.16)	0.86 (0.75-0.98)
Tumor size, cm		
< 2	1 [Reference]	1 [Reference]
2-5	2.38 (2.03-2.79)	1.39 (1.26-1.54)
> 5	4.38 (2.90-6.63)	1.22 (0.86-1.74)
Lymph node status		
Negative	1 [Reference]	1 [Reference]
Positive	2.81 (2.39-3.31)	1.08 (0.95-1.22)
Hormone receptor status		
Negative	1 [Reference]	1 [Reference]
Positive for ER and/or PR	0.43 (0.36-0.51)	0.88 (0.76-1.03)
Tumor grade		
Well or moderately differentiated	1 [Reference]	1 [Reference]
Poorly differentiated or undifferentiated	2.31 (1.94-2.74)	1.12 (1.01-1.26)
Comorbidity index		
0	1 [Reference]	1 [Reference]
1	1.23 (1.01-1.48)	1.73 (1.54-1.95)
≥ 2	1.44 (1.11-1.86)	3.58 (3.11-4.11)
Hospital volume, cases		
< 20	1 [Reference]	1 [Reference]
20 to < 40	0.83 (0.68-1.01)	0.99 (0.88-1.12)
≥ 40	0.84 (0.68-1.03)	0.89 (0.78-1.02)

Abbreviations: See Table 1.

^aData are given as relative risk (95% confidence interval). Results from Cox proportional hazards models including 12 216 Medicare patients undergoing surgery for stage I or II breast cancer. Each model also adjusts for patient age; race; Surveillance, Epidemiology, and End Results site; zip code per capita income; propensity for care by a medium- or high-volume surgeon; and surgeon clustering.

Nattinger et al, Arch Intern Med. 2007

Survey Methods

- Selection bias vs real mechanisms for volume and mortality, morbidity/quality of life
- Population-based, longitudinal survey of community-dwelling elderly women with incident breast cancer.
- Women >65 in 4 geographic and racially diverse states—California, Florida, Illinois, and New York—identified from Medicare claims (Nattinger, HSR 2003) as having had surgery for incident, early-stage (<3) breast cancer 2003
- Potentially eligible participants were contacted by phone in 4 annual structured interviews early 2005-2008
 - Response rate 70%, n=3,083

Table 1.

Characteristics	Distribution
Patient Demographic & Economic Characteristics	
Age (in years, mean/standard deviation)	72.9 (5.5)
<i>Race/Ethnicity (%)</i>	
African American/Black	3.6
Hispanic	2.9
Other race/ethnicity (mostly Caucasian)	93.4
<i>Marital Status: Married (%)</i>	48.4
<i>Education (%)</i>	
Less than High School	8.3
High School Graduate	35.3
Some College	54.0
<i>Annual Household Income (%)</i>	
< \$15,000	16.6
\$15,000–\$29,999	27.5
>\$30,000	34.7
Missing Information	21.2
<i>Social Support: Low (%)</i>	24.4
Health Status (%)	
<i>No Comorbidities</i>	62.0
<i>1+ Comorbid Conditions</i>	38.0
Disease Stage (%)	
0 (in situ)	15.4
1 (localized)	56.7
2 (regional by direct extension only)	16.2
3 (ipsilateral regional lymph node)	1.5
4-7 (advanced or distant disease)	0.3

Pezzin, Liliana E.; Laud, Purushottam; Yen, Tina W.F.; Neuner, Joan; Nattinger, Ann B. Medical Care 53(12):1033-1039, December 2015.

Table 1 Continued....Distance Information for Instrumental Variable and Hospital Volume

Distance to Providers	
<i>Distance to Nearest Hospital</i> (in miles, mean/standard deviation)	4.7 (4.7)
<i>Distance to Nearest Moderately High Volume Hospital</i> (top tertile of incident Medicare cases, in miles)	31.9 (48.0)
<i>Distance to Nearest High Volume Hospital</i> (top decile of incident Medicare cases, in miles)	96.5 (99.7)
Hospital Volume where Treated (mean/standard deviation) [range]	37.2 (31.1) [1.5–160.5]

Hospital Volume, Surgeon Volume, and 5-Year Mortality Among Older Breast Cancer Patients

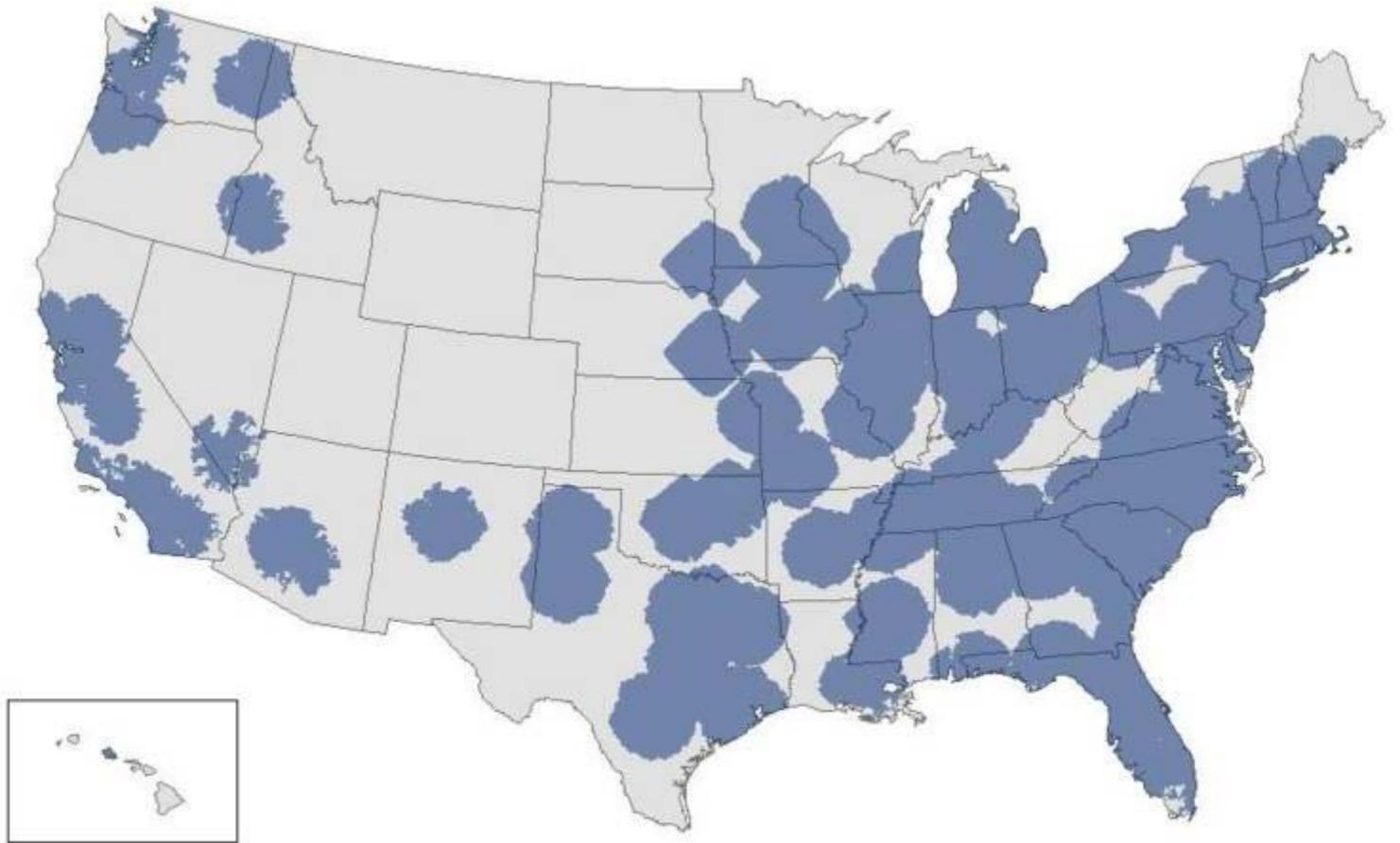
	All-cause Mortality [Coefficient (P)]		Breast Cancer–specific Mortality [Coefficient (P)]	
	Moderately High Volume	High Volume	Moderately High Volume	High Volume
Hospital	−0.08 (0.79)	−0.98* (0.04)	−0.11 (0.76)	−1.80* (0.01)
Surgeon	1.31 (0.33)	0.53 (0.63)	0.89 (0.39)	0.11 (0.94)

*Statistically significant coefficients at the $P < 0.05$ level. Hospitals were classified as moderately high volume if they ranked at the top tertile of annual Medicare cases (hospitals performing >40 Medicare incident breast cancer cases per year) during the 24 months preceding the subjects' incident surgery. Hospitals were classified as high-volume hospitals, the subset of the moderately high hospitals that rank in the top decile of annual Medicare cases (> 81 Medicare cases per year) during the 24 months preceding the subject's incident surgery. For surgeon volume, the thresholds for top tertile and top decile were ≥ 12 and ≥ 28 annual incident breast cancer surgeries during the 12-month period preceding the woman's surgery, respectively. Models also control for sociodemographic, economic, extent of disease factors, and first-stage residuals. See Supplemental Digital Appendix for the full set of coefficient estimates (Supplemental Digital Content 1, <http://links.lww.com/MLR/B28>).

MEDICAL CARE

Pezzin, Liliana E.; Laud, Purushottam; Yen, Tina W.F.; Neuner, Joan; Nattinger, Ann B.
 Medical Care 53(12):1033-1039, December 2015.
 doi: 10.1097/MLR.0000000000000439

US high-volume areas

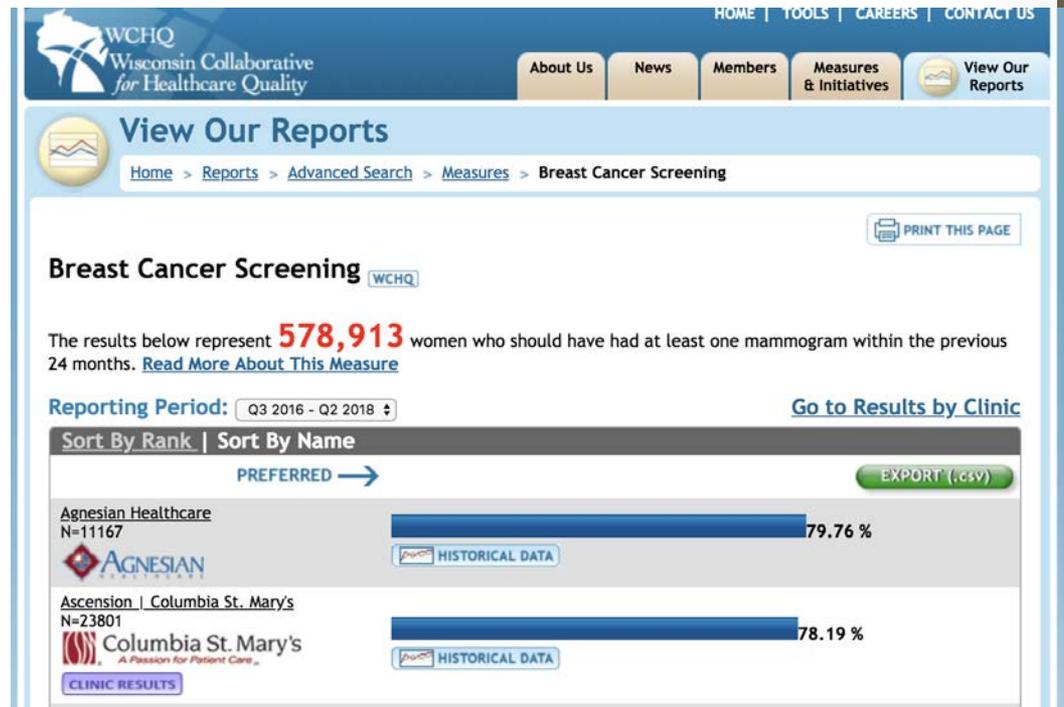


*No 80+ volume hospitals in Alaska; state not shown.

100 mile driving distance service area

Next steps

- Work to examine how high-volume hospitals achieve outcomes
- “Provocative Questions” grant from NCI (Nattinger, Pezzin PIs) of a public reporting intervention
- Added practice-level breast cancer process information to Wisconsin Collaborative for Healthcare Quality, mobile app to support communication



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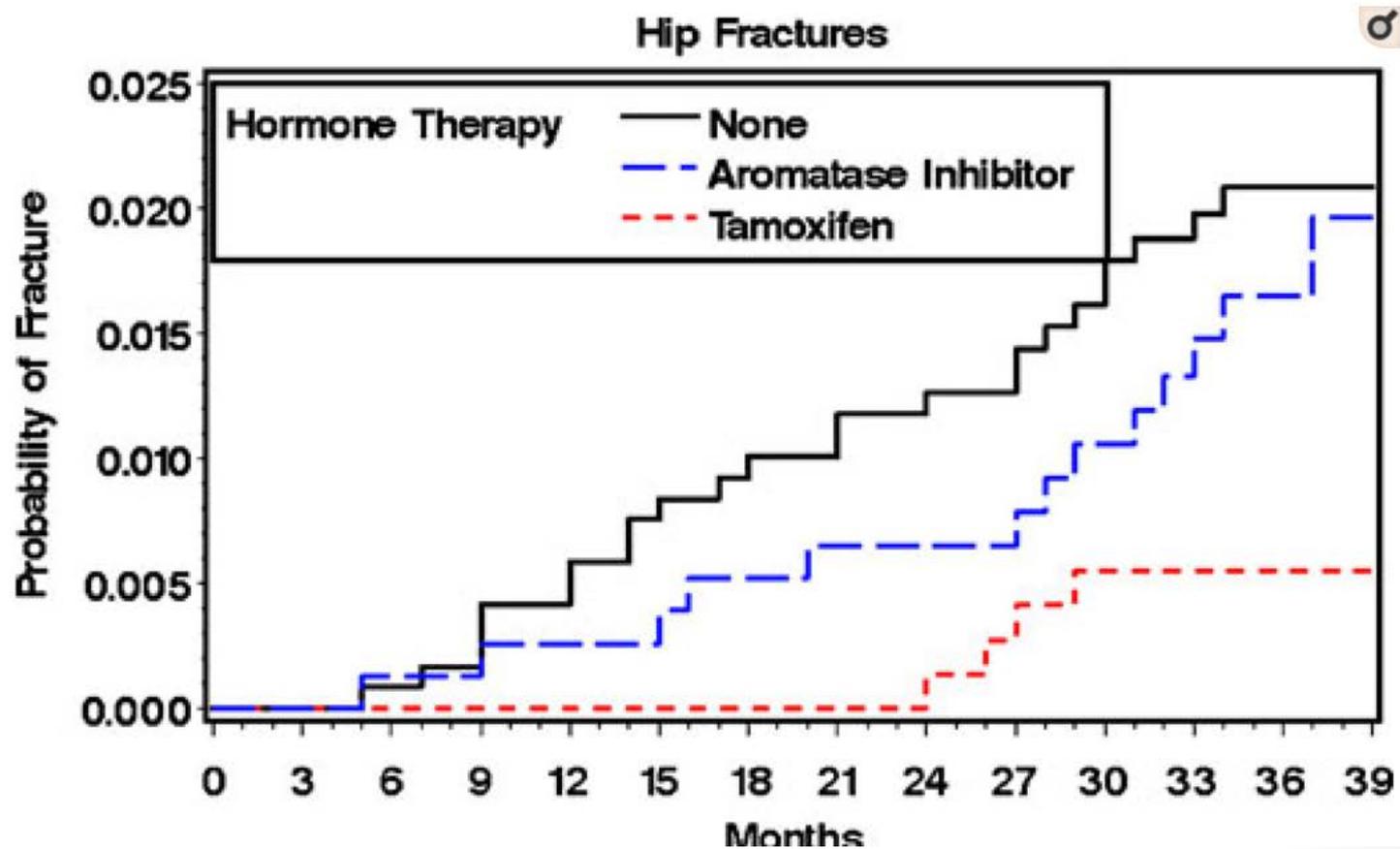
Survivorship

Prevalence of factors associated with hip fractures in a breast cancer cohort

	Aromatase inhibitor. (n = 775)	Tamoxifen (n = 764)	Neither (n = 1,209)	p value for difference
Mean body mass index (SD) ^a	27.6 (5.6)	26.8 (4.9)	26.8 (5.3)	0.003
History of nonvertebral fracture in prior year (%) ^a	1.7	2.1	2.1	0.790
Family history of fracture (%) ^a	25.3	24.8	23.9	0.761
No comorbidity (%) ^a	62.3	66.9	62.2	0.141
Cytotoxic chemotherapy use (%)	14.1	9.4	29.8	<.001
Oral bisphosphonate use	35.2	27.8	25.7	<.001

Survivorship

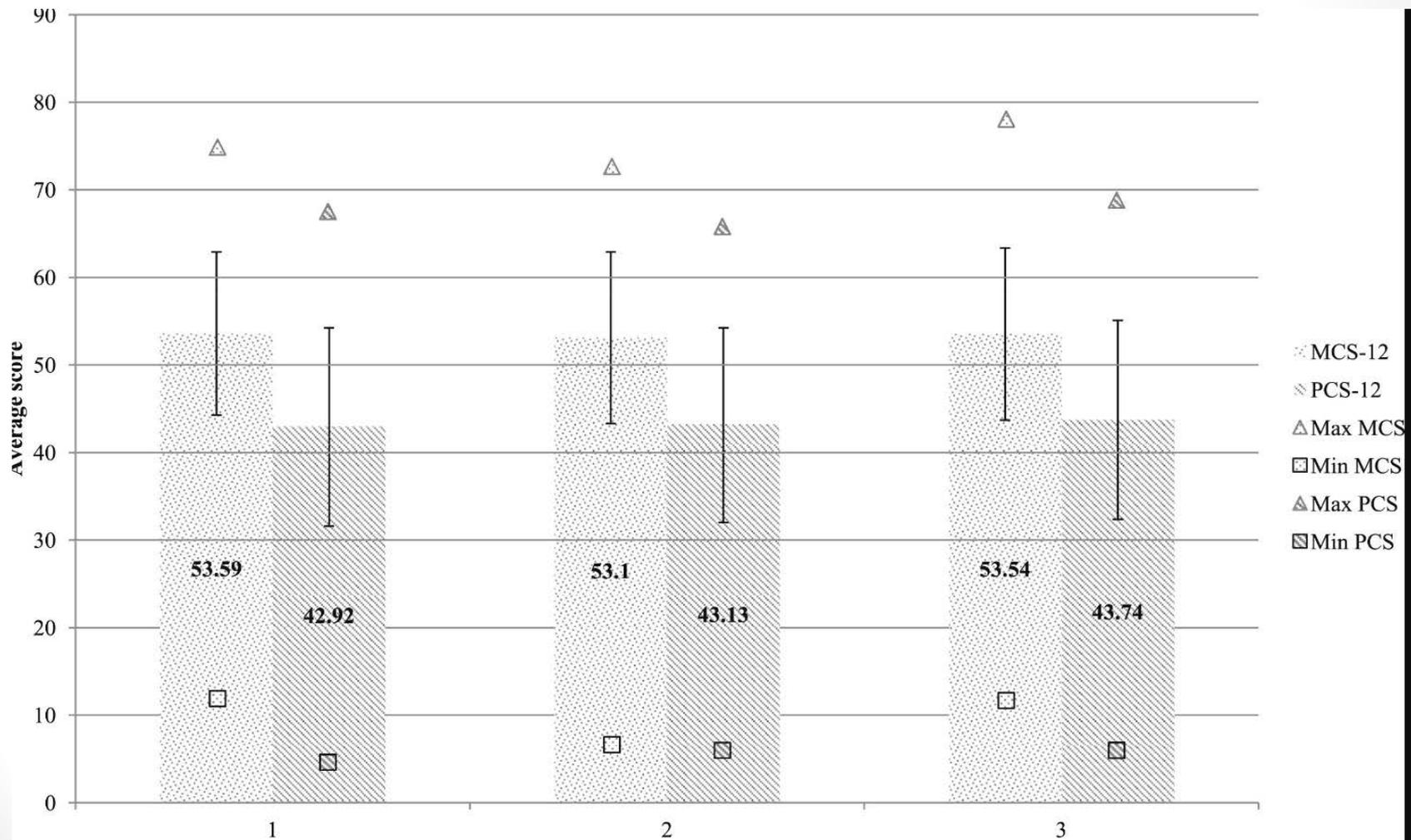
Hip Fracture Risk among Older Breast Cancer Patients



Quality of Life in Older Breast Cancer Patients

- Randomized trials suggest that treatment-related reductions in QOL are rare, but only 5% of patients enroll in randomized trials
- RCT enrollees are younger, with less comorbidity and higher functional status
- Many trials do not follow patients long enough to assess potential longer-term effects on QOL from neuropathy, CHF
- Upper arm dysfunction may play a larger role in QOL than previously suspected

Quality of Life among Breast Cancer Survivors



Lymphedema and Quality of Life among Breast Cancer Survivors

Effects of age, comorbidity and lymphedema upon multivariate-adjusted general and breast cancer related quality of life.

	General health-related quality of life						%Breast cancer-related quality of life		
	Summary physical (PCS-12)			Summary mental (MCS-12) scores			Yes	No	%Difference
	Yes	No	%Difference	Yes	No	%Difference			
Age > 75	43.1	45.1	-4.4%	53.70	54.0	-0.6%	16.4	16.3	0.6%
Comorbid illness ^a	41.4	45.2.0	-8.4%	52.6	54.0	-2.6%	17.0	15.8	7.6%
Lymphedema	40.0	43.8	-9.5%	51.0	53.8	-5.2%	18.8	16.4	14.6%

^a Compared with none.

Even Bigger Data? PCORNet and Cancer Research



Even Bigger Data?

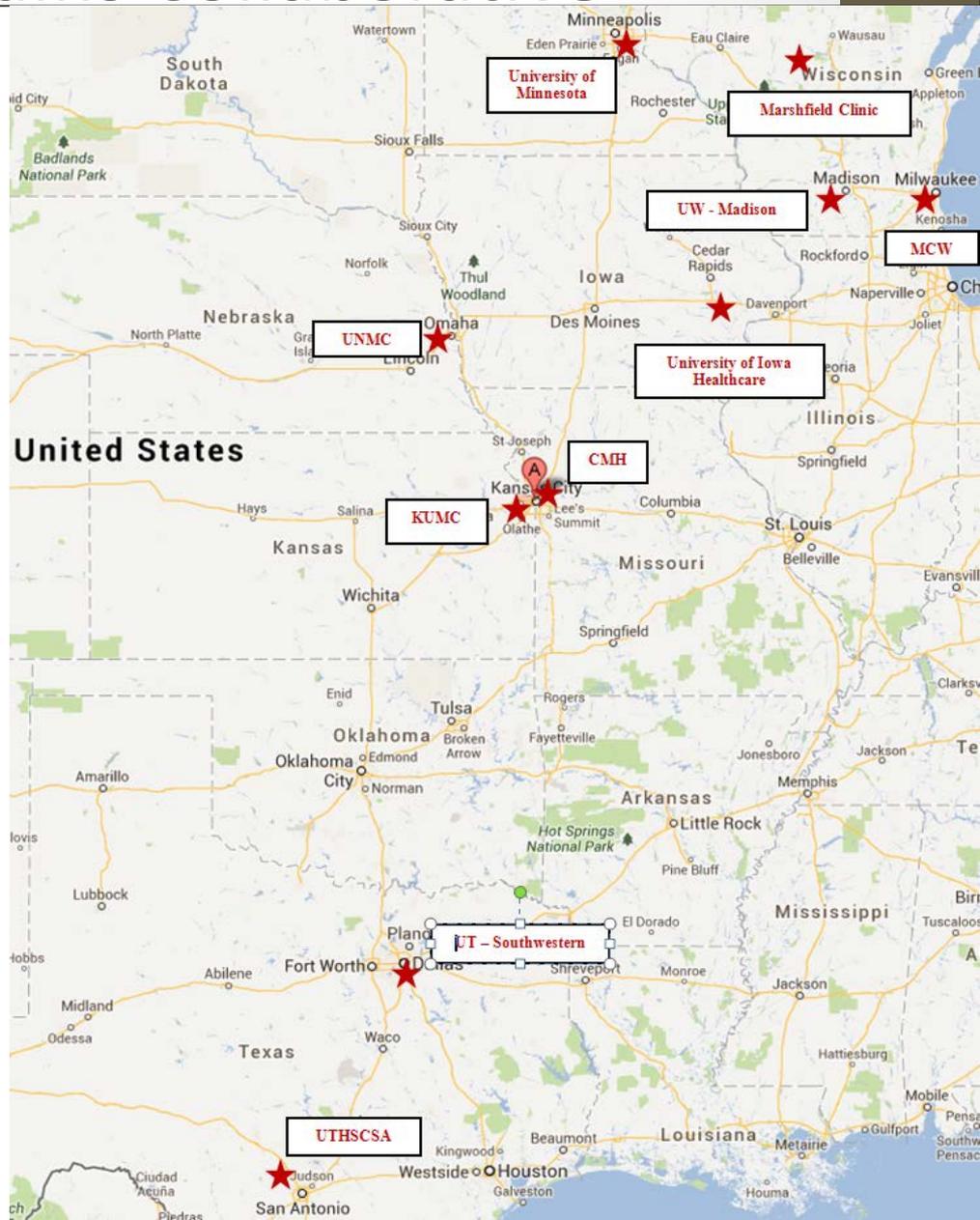
PCORNet and Cancer Research

- Patient-centered comparative effectiveness studies nested in rich data systems also are needed to answer questions that patients and their physicians need to know but which are not the typical questions addressed in phase 1-3 cooperative group trials.
- Cancer registry, Medicare (5 states) and Medicaid (3 states)
- When mature, should enhance and complement existing cooperative group trial mechanisms, e.g. for efficient recruitment

- Compare the effectiveness of strategies (rapid access to information vs usual care) for informing patients about personalized medicine tests for breast cancer care. (UK DUET database of uncertainties, topic brief submitted for PCORNet large trial topic generation exercise)
- Are there markers, serum or histologic that predict pathologic complete response to chemotherapy, radiologic and clinical outcomes?
- Are there serum markers or radiologic findings (breast density) in high risk patients that predict for development of disease? (IOM, 2009)
- Compare the effectiveness of using Magnetic Resonance Imaging (MRI) or mammography in young patients and women who have dense breasts to improve health outcomes (i.e., survival, local recurrence, mortality) (IOM, 2009)
- Compare the safety and effectiveness of therapies for reducing risk of breast cancer among high risk patients
- Compare the disease-free survival and health-related quality of life for patients receiving molecularly-guided therapy vs usual care (IOM, 2009)
- Prevalence of polymorphisms and abnormalities in typical clinical populations
- Compare the adherence, overall survival, and health-related quality for patients receiving various diet/exercise interventions
- Compare effects of survivorship care planning models on cancer follow-up care, preventive services, health promotion behaviors, and patient-reported outcomes

Electronic Medical Record Data -PCORNet and the Greater Plains Collaborative

- 11.8 Million Covered Lives
- 13 hospitals, 430 clinics, 1800 primary care providers, 7600 specialists
- \$7 million total costs over 18 months
- **Sites by state:**
 - **KS**, the **University of Kansas Medical Center (KUMC)**
 - **MO**, **Children's Mercy Hospital**
 - **IA**, **University of Iowa Healthcare**
 - **WI**, the **University of Wisconsin-Madison**, the **Medical College of Wisconsin**, and **Marshfield Clinic**
 - **MN**, **U of Minnesota Medical Center**
 - **NE**, **University of Nebraska Medical Center**
 - **TX**, the **University of Texas Health Sciences Center at San Antonio** and the **University of Texas Southwestern Medical Center**.



GPC Breast Cancer Survey

- Each participating medical center North American Association of Central Cancer Registries (NAACCR)-formatted data extracted, transformed, and loaded from their institution's tumor registry into its i2b2 (Informatics for Integrating Biology and the Bedside) research warehouse.
- GPC i2b2 research warehouse is fully de-identified with re-identification possible when accompanied by an approved IRB protocol
- A cohort of all patients aged 18 or older diagnosed with first Stage 0-III breast cancer between 2013-14
- De-identified data files were submitted to the GPC Honest Broker who selected a random sample of 250 eligible patients from each center's file.

Survey Methods

- Cover letter from the participating medical center, a 21-page questionnaire, medical record consent, and \$10 incentive.
- One re-mailing to non-respondents was conducted four weeks after the initial mailing.
- A total of 1,986 patients were invited and 1,235 (62.2%) responded to a mailed questionnaire. Signed consent to obtain information from medical records was obtained for 852 (69%).
- Study data were collected and managed using REDCap electronic data capture tools hosted at informatics lead site.

Upper Extremity Symptoms and Outcomes in SLNB era

- Patients with worse UED reported significantly worse QOL.
- Income, and health literacy were independently associated with QOL after adjustment for UED but treatment and prior conditions were not, indicating mediation by UED.
- UED mediated 52-79% of the effect of mastectomy-based treatments on QoL

Survivorship Future Directions

- Cancer registry data linked at all GPC sites, 3 other networks
- Linkage made to Medicare (7 states) and Medicaid (2 states) through RESDAC, allowing better ascertainment of complications (eg outside hospitalizations)
- PCORI rapid cycle research project to expand the common data model to capture chemotherapy administration, dosing
 - Mixed evidence on ascertainment of biomarkers
- Two KL2 (MCW, KU) training grants to use linked data (Winn, Roberts)

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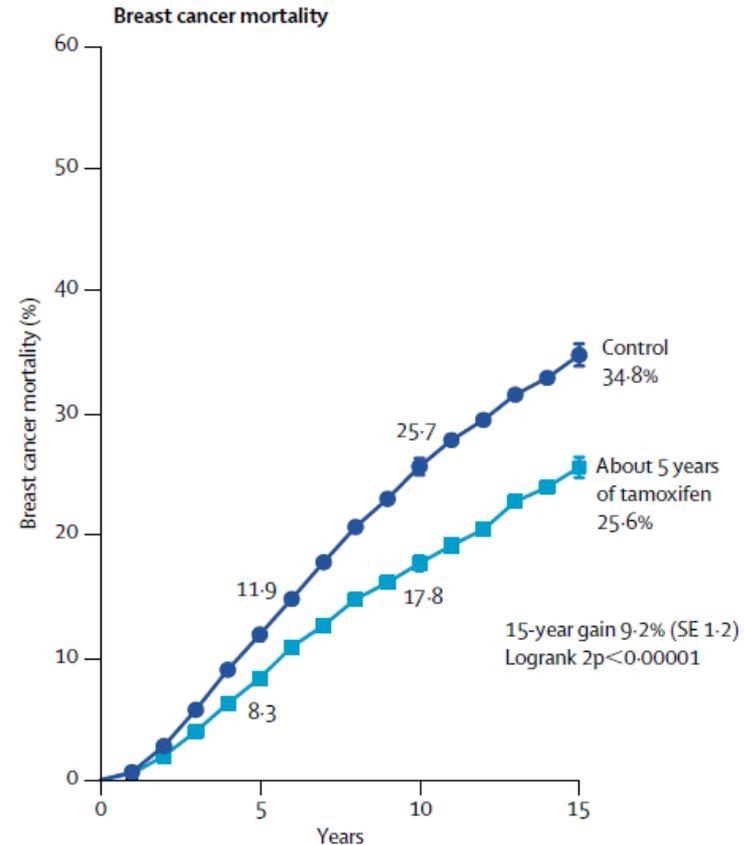
Medication Nonadherence

- Patient adherence to chronic medications averages only 50% across a number of chronic conditions
- World Health Organization considers discontinuation of and nonadherence to medications as a leading cause of preventable death



Efficacy of breast cancer hormonal therapy

- 72% of black and 81-87% of women of other races/ethnicities have ER/PR+ breast cancers
- Tamoxifen reduced 15-year breast cancer mortality from 35% to 26%, and recurrence from 45% to 33%
- Aromatase inhibitors (AIs) for postmenopausal women reduce the relative risk of cancer recurrence by an additional 50%

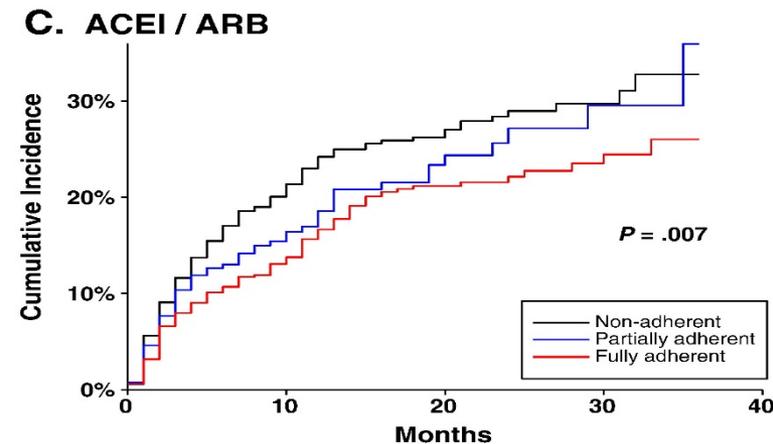
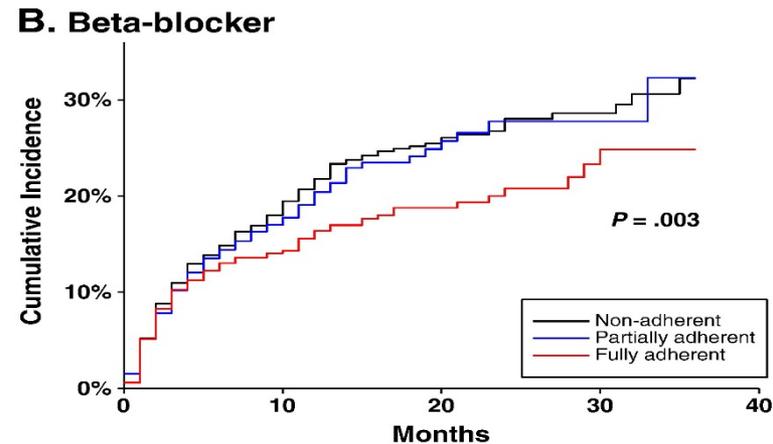
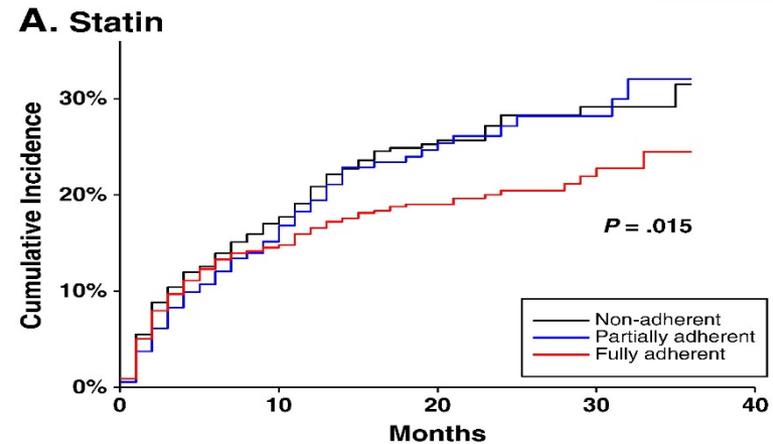


About 5 years of tamoxifen versus not in ER-positive (or ER-unknown) disease: 15-year probabilities of breast cancer mortality. 10, 386 women: 20% ER-unknown, 30% node-positive. Error bars are (+/-) 1 SE

What is the evidence for bad outcomes with nonadherence?

- One-third to one-half of patients either take less than 80% of their doses or discontinue it altogether
- Discontinuation and nonadherence (<80%) is associated with absolute survival reductions of 4-8%.
- Post-MI results from MI-free similar

Choudhry NK . Am Heart J . 2014,
Sackett 1979, Naderi 2012



Remediable mechanisms of nonadherence: Ability to pay

- Medicare Part D out-of-pocket costs for breast cancer patients increased between 58-112% for the three aromatase inhibitors between 2007-2010 (Table 2).

**Table 2. Patient Out-of-pocket Costs during initial Benefit Period of Medicare Part D for Aromatase Inhibitors
Comparison of brand costs over time, 2007 vs 2010**

	Mean Monthly Costs (State-level Medians) \$, (Range of mean costs)		
	2007	2010	Change (%)
Arimidex	40(38-48)	63 (60-75)	+58
Aromasin	44 (41-51)	87 (82-101)	+103
Femara	42 (39-51)	89 (81-103)	+112

Ability to pay #1

Natural experiment in out of pocket cost reductions

- Initial objective: Examine trends in adherence to breast cancer therapy with aromatase inhibitors before and after generic anastrozole release

Natural experiment in out of pocket cost reductions

Cohort

- Nationwide cohort of non-HMO Medicare women aged ≥ 65 with a 2006- 2007 surgery for incident breast cancer (Nattinger, HSR 2004)
- Continuous enrollment in Medicare for at least one year prior to surgery, and enrollment in a Medicare D prescription drug plan.
- At least one Medicare D prescription (claim) for endocrine therapy with either an aromatase inhibitor (anastrozole, letrozole, or exemestane) or tamoxifen between 7/1-12/31/2008.

Outcome

- Adherence as calculated by number of days of medication prescription fills [tamoxifen or an aromatase inhibitor (anastrozole, letrozole, and/or exemestane)] or medication possession ratio (MPR).
 - Adherence to therapy was defined as an $MPR \geq 80\%$.

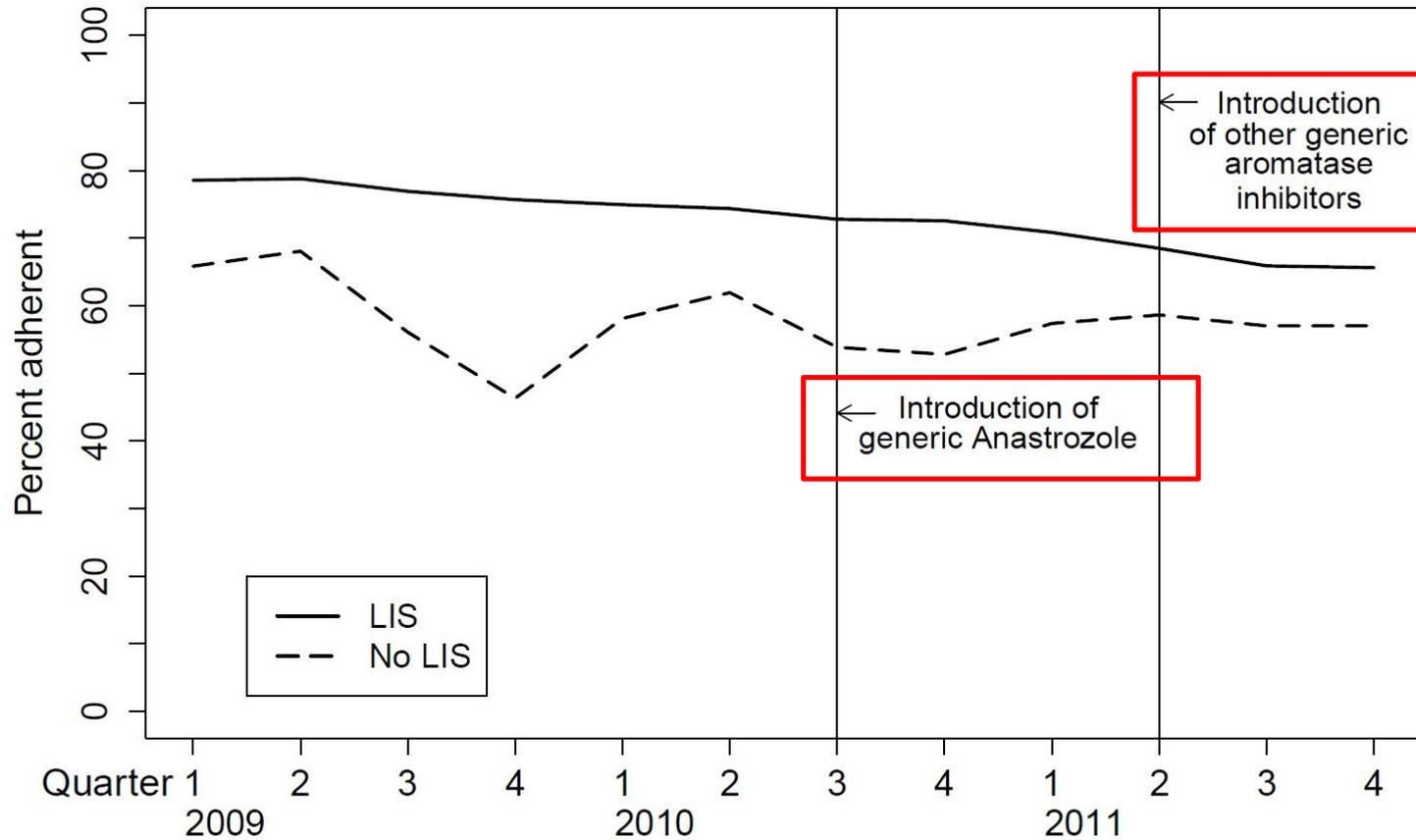
Baseline Characteristics of 2006-2007 US Breast Cancer Patients Age ≥ 65 Years Who Received Aromatase Inhibitors*

	Total (Percent) (N=16,462)
Age	
65-74	8,827 (53.6%)
75-84	6,424 (39.0%)
85+	1,211 (7.4%)
Race/Ethnicity	
White	13,830 (84.0%)
Non-White	2,632 (16.0%)
Receipt of low-income subsidy (1/1 – 3/31/2009)	
Yes	5568 (33.8%)
No	10894 (66.2%)
Comorbidity score (2008)	
Low (zero comorbidity)	7760 (47.1%)
Moderate (0 – 0.7)	4342 (26.4%)
High (≥ 0.7)	3762 (22.9%)
Missing	598 (3.6%)
Aromatase inhibitor	
Anastrozole	10,647 (65.0%)
Letrozole or Exemestane	5,815 (35.0%)
Years since endocrine therapy initiation	
Mean (SD)	1.77 (0.63)
(IQR)	(1.27, 2.26)
Number of medications (1/1-3/31/2009)	
Mean (SD)	4.31 (3.17)
(IQR)	(2.00, 6.00)

*All variables are at time of surgery, unless noted.

Results

Aromatase Inhibitor adherence by subsidy status



% non-LIS patients
in donut hole

3.9 36.0 73.1 82.8 5.5 38.2 62.3 72.1 3.8 19.9 31.4 40.1

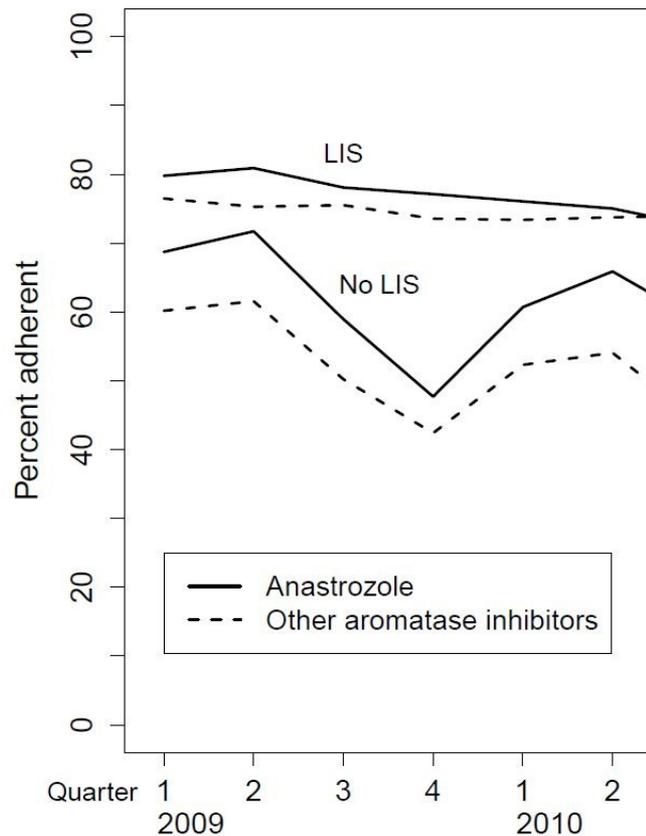
Medicare D and its Low Income Subsidy Benefit (2006)

- High cost estimates led to “cap” on the total cost to the government (at approx. \$3000 total drug costs), with catastrophic coverage for those who spent over \$5100 (The gap, which is slowly being closed by the ACA)
- All Medicare drug plans required to cover all oncology medications (along with 5 other essential medicine categories such as antipsychotics), relatively wide latitude for benefit design (copays, quantity limits)

Medicare prescription drug benefit subsidies for low-income beneficiaries, 2006			
Low-Income Subsidy Level	Premium	Monthly Deductible	Annual Copayments
Full-benefit dual eligibles Income <100% of poverty (\$9,750 individual; \$12,830/couple)	\$0	\$0	\$1/generic, \$3/brand-name; no copays after total drug spending reaches \$5,100
Full-benefit dual eligibles Income ≥100% poverty	\$0	\$0	\$2/generic, \$5/brand-name

Source: Kaiser Family Foundation summary of Medicare prescription drug benefit low-income subsidies in 2006.

Aromatase Inhibitor adherence by subsidy status and medication type: pre-generic



Median out-of-pocket costs

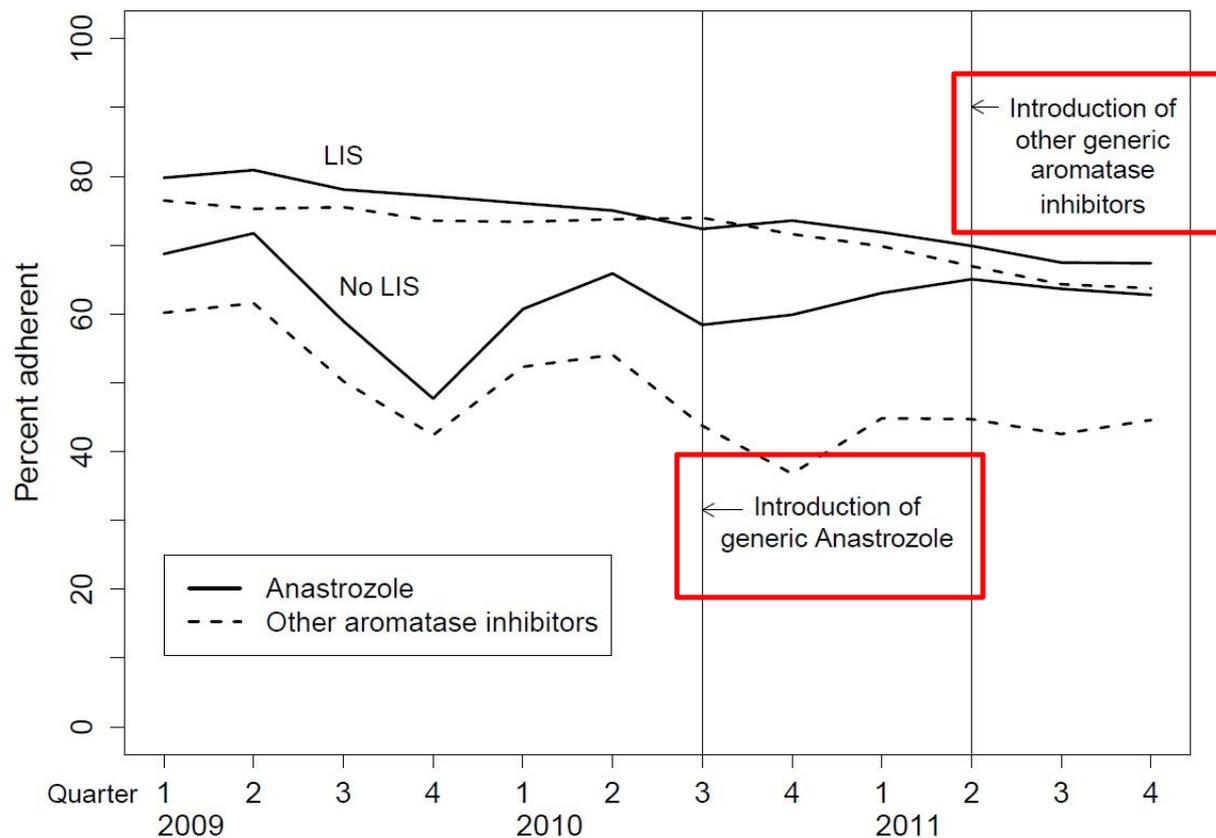
Anastrozole

LIS	\$8	\$9	\$7	\$4	\$7	\$8
No LIS	\$106	\$104	\$200	\$183	\$121	\$125

Other Aromatase Inhibitors

LIS	\$8	\$9	\$7	\$4	\$8	\$9
No LIS	\$104	\$105	\$174	\$116	\$105	\$105

Aromatase Inhibitor adherence by subsidy status and medication type



Median out-of-pocket costs

Anastrozole

LIS	\$8	\$9	\$7	\$4	\$7	\$8	\$4	\$2	\$3	\$3	\$2	\$2
No LIS	\$106	\$104	\$200	\$183	\$121	\$125	\$97	\$32	\$21	\$16	\$16	\$15

Other Aromatase Inhibitors

LIS	\$8	\$9	\$7	\$4	\$8	\$9	\$7	\$3	\$7	\$6	\$2	\$1
No LIS	\$104	\$105	\$174	\$116	\$105	\$105	\$112	\$68	\$81	\$62	\$22	\$16

Adjusted results-Difference in Difference and Model-Predicted

- Patterns of improved adherence (reduced decline) among non-LIS recipients persisted in models adjusted for age, comorbidities, years since AI initiation, and other possible confounders (OR ranging from 1.08 (1.02-1.14) to 1.51 (1.44-1.58) by calendar quarter examined)
- Regression-adjusted average predicted probabilities of adherence (non-LIS):
 - 5.4% more patients adherent in the nine-month period after generic anastrozole was introduced than if no generic had been available
 - 11% more patients in the subsequent nine months after generic letrozole and exemestane were introduced.

Do Subsidies Improve Disparities?

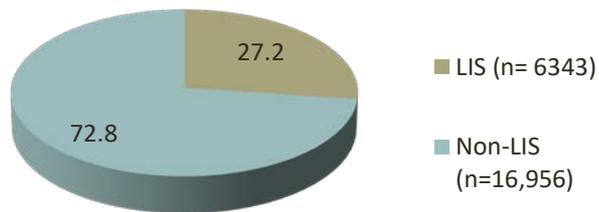
- To evaluate the effect of the Medicare Part D Low-Income Subsidy (also known as the Extra Help program) by racial/ethnic group on adherence to hormonal therapy

Methods

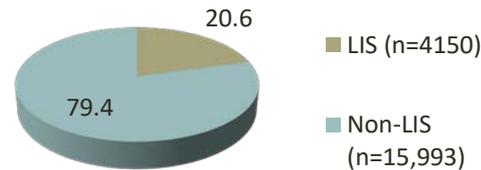
- Nationwide cohort of all female Medicare D enrollees
 - aged ≥ 65
 - breast cancer operation between 2006-2007
 - at least one prescription filled for oral breast cancer hormonal therapy (HT)
- A logistic regression model applied to annual data from 2009 to 2011, using generalized estimation equations to examine the effect of LIS on overall hormonal therapy adherence

LIS Enrollment by Race/Ethnicity

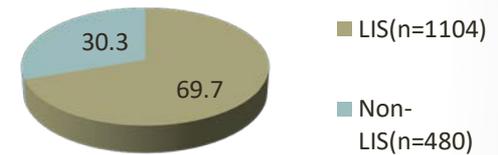
Total (n=23,299)



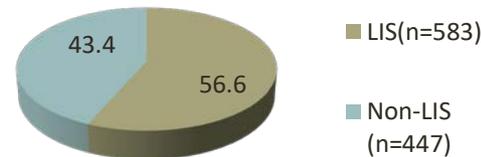
White (n=20,143)



Black (n=1,584)

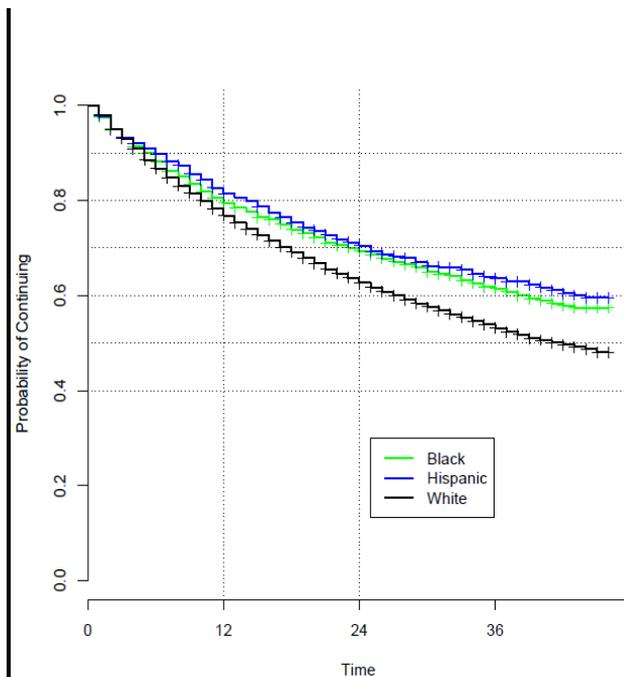


Hispanic (n=1,030)

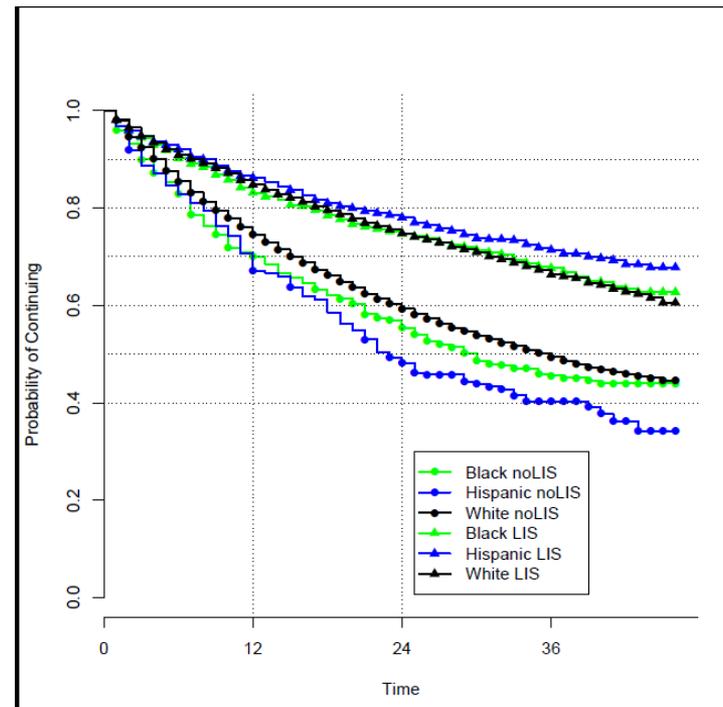


Results

Unadjusted continuation
(persistence) by race/ethnicity



Unadjusted persistence by six groups based
on subsidy and race/ethnicity



Subsidized black women were still **23% less likely** (OR 0.77 (0.70-0.84)) than subsidized white women to be adherent (taking 80% or more of their medications)

Conclusions and Implications

- Women enrolled in the Low Income Subsidy program had substantially higher adherence, a finding that held for each racial/ethnic group.
- Black and Hispanic women had overall better adherence than White women, due to the greater likelihood of minority women being enrolled in the Low Income Subsidy program.
- Extended findings of Hershman group to show policy may reduce disparities
 - Questions remain about threshold, costs

Pharmacy Complexity

Pharmacy visit number

- High frequency of medication-related encounters with the health system can negatively impact adherence
 - Users of antihypertensive and lipid-lowering medications, filled a mean of 11.4 prescriptions at a retail pharmacy over 90 days,
 - Mean of **five** pharmacy visits
 - Over 10% of the patients made **11 or more** pharmacy refill visits in 90 days.



Choudhry, *Arch Int Med* 2011

Brancati, *Ann Epidemiol* 2006

Bangalore, *Curr Hypertens Rep* 2007

Pharmacy Complexity

Pharmacy visit number

- Even with adjustment for medication regimen complexity, poor “synchronization” of prescription refills visits resulted in 10% lower adherence

Table 2. Relationship Between Adherence and Complexity Measures for Statin and ACEI/ARB Users^a

Predictors (Referent)	All Statin Users		All ACEI/ARB Users	
	Unadjusted ^b	Adjusted ^b	Unadjusted ^b	Adjusted ^b
Patient demographics				
Age ≥65 y (vs <65 y)	6.57	5.35	4.61	3.39
Male (vs female)	-1.71	-2.44	-0.07	-0.60
Income per quintile	1.38	1.72	0.76	0.98
Copayments				
Mean monthly copayments for index class, per tertile ^c	-2.77	-1.52	-1.56	-0.89
Mean monthly copayments for all other drugs, per tertile	-2.11	-0.82	-1.35	-0.59
Morbidity score	-0.62	-1.32	-0.43	-0.97
Complexity measures				
Daily dose, per additional dose	NA	NA	-0.01	-0.25
Unique medications, per additional medication	0.57	0.89	0.46	0.69
Prescriber, per additional practitioner	0.11	-0.25	-0.07	-0.31
Unique retail pharmacies, per additional pharmacy	-2.43	-1.60	-2.82	-2.02
Refill consolidation, full (vs none) ^d	13.35	8.42	12.60	8.12
Intercept	NA	58.86	NA	63.60

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; NA, not applicable.

^aData are given as percentage change in adherence.

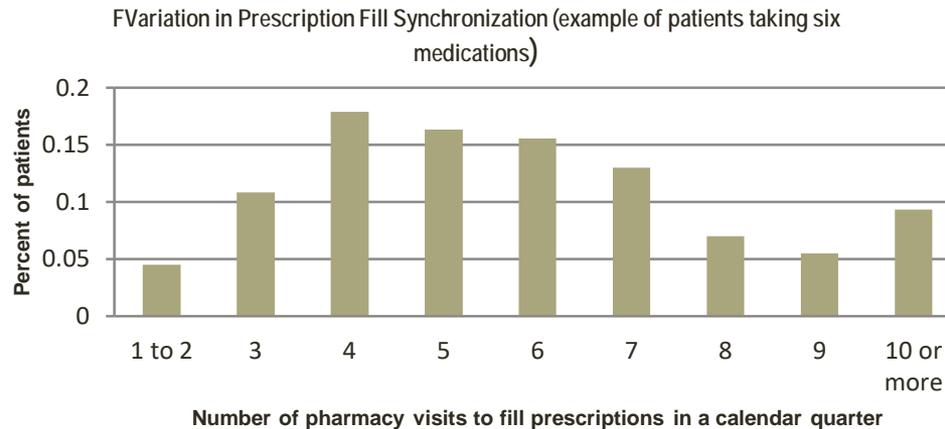
^b $P < .001$ for all parameters.

^cStatins or ACEI/ARB as appropriate.

^dHigher values represent greater refill consolidation.

Pharmacy Complexity

Pharmacy visit number



- 15% of patients on the median number of unique quarterly medications (six) visited a pharmacy for prescription refill three or fewer times in a quarter, and 9.3% ten or more times

Synchronization Measure

- Synchronization = $1 - (\# \text{ Pharmacy Visits} / \# \text{ Prescriptions Filled})$
- Values 0-1 with higher values representing fewer visits/fill

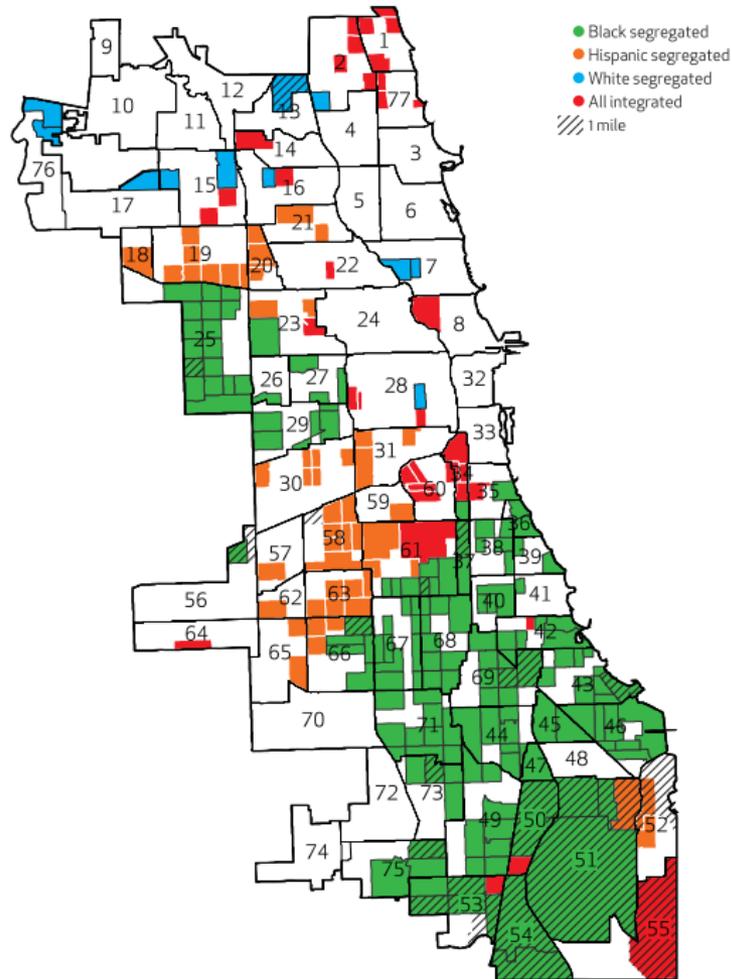
Number of Medications	# Pharmacy Visits	# Medication Fills	Synchronization
4	4	16	0.75
	6	16	0.63
	8	16	0.5
	16	16	0
6	4	24	0.83
	6	24	0.75
	8	24	0.67
	16	24	0.33

		Odds Ratio	95% Confidence Interval	
Medication-Stratified Synchronization Quantiles	Quartile 1	- (reference)		
	Quartile 2	1.21	0.97	1.52
	Quartile 3	1.29	1.04	1.59
	Quartile 4	1.49	1.19	1.86
Race	White	- (reference)		
	African-American	1.00	0.71	1.41
	Other	1.88	1.19	2.98
	Unknown	0.77	0.28	2.09
Low Income Subsidy		1.06	0.87	1.28
Comorbidity (one or more)		0.80	0.68	0.94
Rural-Urban county category	Big Metropolitan	- (reference)		
	Metropolitan	0.76	0.62	0.94
	Micropolitan	1.08	0.75	1.58
	Rural	1.14	0.84	1.54
Cancer Stage	0	- (reference)		
	I	0.96	0.70	1.34
	II	1.16	0.82	1.64
	III	0.92	0.60	1.39
	Unknown	0.72	0.40	1.28
Tamoxifen Use (vs Aromatase Inhibitor)		0.86	0.69	1.08

Mechanisms for adherence disparities: Pharmacy Access

EXHIBIT 3

Pharmacy Deserts In Chicago, By Community Type, 2012





Future plans

- Recently completed dataset of distance from pharmacy at census tract level
- PCORnet Cancer Research Group to link cancer registry, electronic medical record and Medicare/Medicaid claims
- Processes that allow high-volume hospitals to improve care, including reducing unnecessary care
- Multicenter observational and SCTs using PCORnet, other sites?