Disparities in Use of HER2-targeted Therapy for Early Stage Breast Cancer

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APPENDIX A: CODES FOR TREATMENTS

For defined regimens, ACTH was defined as a pattern of claims including a first claim for doxorubicin occurring before or on the same date as a first claim for trastuzumab, with the first claim for trastuzumab appearing within 120 days after the first doxorubicin claim, at least 2 doxorubicin claims within 60 days and at least one claim for either docetaxel or paclitaxel within +/- 7 days of the first trastuzumab claim. TCH was defined as a first carboplatin claim and a first docetaxel claim appearing within +/- 7 days of the first trastuzumab claim and at least 2 carboplatin claims within 60 days.

1. **Table of codes used to identify the drug categories:**

Drug Category	HCPCS/CPT codes searched
Trastuzumab	J9355
Doxorubicin	C9415, J9000
Taxanes (docetaxel/paclitaxel)	C9127, C9431, J9170, J9171, J9264, J9265
Carboplatin	J9045
Other chemotherapy drugs	C9004, C9012, C9020, C9110, C9120, C9129, C9131, C9205, C9207, C9214, C9218, C9233, C9235, C9239, C9240, C9253, C9257, C9259, C9260, C9262, C9265, C9273, C9276, C9280, C9284, C9287, C9292, C9295, C9296, C9298, C9414, C9417, C9418, C9420, C9421, C9422, C9423, C9424, C9425, C9426, C9427, C9428, C9429, C9432, C9433, C9436, C9437, C9440, J8510, J8520, J8521, J8530, J8560, J8561, J8562, J8565, J8600, J8610, J8700, J8705, J8999, J9001, J9002, J9010, J9015, J9017, J9020, J9025, J9027, J9033, J9035, J9040, J9041, J9042, J9043, J9050, J9055, J9060, J9062, J9065, J9070, J9080, J9090, J9091, J9092, J9093, J9094, J9095, J9096, J9097, J9098, J9100, J9110, J9130, J9140, J9150, J9151, J9155, J9178, J9179, J9180, J9181, J9182, J9185, J9190, J9200, J9201, J9206, J9207, J9208, J9211, J9212, J9213, J9214, J9215, J9216, J9228, J9230, J9245, J9250, J9260, J9261, J9263, J9266, J9268, J9270, J9280, J9290, J9291, J9293, J9300, J9302, J9303, J9305, J9310, J9315, J9320, J9328, J9330, J9340, J9350, J9351, J9357, J9360, J9370, J9375, J9380, J9390

2: **Table of codes used to identify breast surgeries**

Procedure	ICD-9-CM	HCPCS/CPT
Mastectomy	PROCEDURE: 85.4x	19180, 19182, 19200, 19220, 19240, 19303, 19304, 19305, 19306, 19307
Breast Conserving Surgery	PROCEDURE: 85.2x	19101, 19110, 19120, 19125, 19126, 19160, 19162, 19300, 19301, 19302

3: Table of codes used to identify radiation therapy

ICD-9-CM	REVENUE CENTER	HCPCS/CPT
DIAGNOSIS: V58.0, V66.1, V67.1 PROCEDURE: 92.2x	0330, 0333, 0339	772xx, 773xx, 774xx, 775xx, 7775x, 7776x, 7777x, 7778x, 7779x

Chemotherapy Drug HCPCS Codes

CODE	DESCRIPTION
J9355	Trastuzumab [**Herceptin**] injection
J9045	**Carboplatin** injection
C9415	**Doxorubic** HCl chemo, brand
J9000	**Doxorubicin** HCl injection
J9170	**Docetaxel** injection
J9171	**Docetaxel** injection
C9127	**Paclitaxel** protein pr
C9431	**Paclitaxel** inj, brand
J9264	**Paclitaxel** protein bound
J9265	**Paclitaxel** injection
C9420	**Cyclophosphamide** inj, brand
C9421	**Cyclophosphamide** lyo, brand
J8530	**Cyclophosphamide** oral 25 mg
J9070	**Cyclophosphamide** 100 mg inj
J9080	**Cyclophosphamide** 200 mg inj
J9090	**Cyclophosphamide** 500 mg inj
J9091	**Cyclophosphamide** 1.0 grm inj
J9092	**Cyclophosphamide** 2.0 grm inj
J9093	**Cyclophosphamide** lyophilized
J9094	**Cyclophosphamide** lyophilized
J9095	**Cyclophosphamide** lyophilized
J9096	**Cyclophosphamide** lyophilized
J9097	**Cyclophosphamide** lyophilized
J9190	Fluorouracil injection
J8610	Methotrexate oral 2.5 mg
J9250	Methotrexate sodium inj
J9260	Methotrexate sodium inj
C9004	Gemtuzumab ozogamicin inj,5m
C9012	Injection, arsenic trioxide
C9020	Sirolimus tablet, 1 mg
C9110	Alemtuzumab, per 10mg/ml
C9120	Injection, fulvestrant
C9129	Inj clofarabine
C9205	Oxaliplatin
C9207	Injection, bortezomib
C9214	Injection, bevacizumab
C9218	Injection, azacitidine
C9233	Injection, ranibizumab

CODE	DESCRIPTION
C9235	Injection, panitumumab
C9239	Inj, temsirolimus
C9240	Injection ixabepilone
C9253	Injection, temozolomide
C9257	Bevacizumab injection
C9260	Ofatumumab injection
C9262	Fludarabine phosphate, oral
C9265	Romidepsin injection
C9273	Sipuleucel-T, per infusion
C9276	Cabazitaxel injection
C9280	Injection, eribulin mesylate
C9284	Injection, ipilimumab
C9287	Inj, brentuximab vedotin
C9292	Injection, pertuzumab
C9414	Etoposide oral, brand
C9417	Bleomycin sulfate inj, brand
C9418	Cisplatin inj, brand
C9422	Cytarabine HCl inj, brand
C9423	Dacarbazine inj, brand
C9424	Daunorubicin, brand
C9425	Etoposide inj, brand
C9426	Floxuridine inj, brand
C9427	Ifosfamide inj, brand
C9428	Mesna injection, brand
C9429	Idarubicin HCl inj, brand
C9432	Mitomycin inj, brand
C9433	Thiotepa inj, brand
C9436	Azathioprine, parenteral, br
C9437	Carmustine, brand name, per
C9440	Vinorelbine tar, brand
J8510	Oral busulfan
J8520	Capecitabine, oral, 150 mg
J8521	Capecitabine, oral, 500 mg
J8560	Etoposide oral 50 mg
J8561	Oral everolimus
J8562	Oral fludarabine phosphate
J8565	Gefitinib oral
J8600	Melphalan oral 2 mg

CODE	DESCRIPTION	CODE	DESCRIPTION
J8700	Temozolomide	J9211	Idarubicin HCl injection
J8705	Topotecan oral	J9212	Interferon alfacon-1inj
J8999	Oral prescription drug chemo	J9213	Interferon alfa-2a inj
J9001	Doxorubicin HCl liposome inj	J9214	Interferon alfa-2b inj
J9010	Alemtuzumab injection	J9215	Interferon alfa-n3 inj
J9015	Aldesleukin injection	J9216	Interferon gamma 1-b inj
J9017	Arsenic trioxide injection	J9228	Ipilimumab injection
J9020	Asparaginase injection	J9230	Mechlorethamine HCl inj
J9025	Azacitidine injection	J9245	Inj melphalan hydrochl 50 mg
J9027	Clofarabine injection	J9261	Nelarabine injection
J9033	Bendamustine injection	J9263	Oxaliplatin
J9035	Bevacizumab injection	J9266	Pegaspargase injection
J9040	Bleomycin sulfate injection	J9268	Pentostatin injection
J9041	Bortezomib injection	J9270	Plicamycin (mithramycin) inj
J9043	Cabazitaxel injection	J9280	Mitomycin 5 mg inj
J9050	Carmustine injection	J9290	Mitomycin 20 mg inj
J9055	Cetuximab injection	J9291	Mitomycin 40 mg inj
J9060	Cisplatin 10 mg injection	J9293	Mitoxantrone hydrochl / 5 mg
J9062	Cisplatin 50 mg injection	J9300	Gemtuzumab ozogamicin inj
J9065	Inj cladribine per 1 mg	J9302	Ofatumumab injection
J9098	Cytarabine liposome inj	J9303	Panitumumab injection
J9100	Cytarabine HCl 100 mg inj	J9305	Pemetrexed injection
J9110	Cytarabine HCl 500 mg inj	J9310	Rituximab injection
J9130	Dacarbazine 100 mg inj	J9315	Romidepsin injection
J9140	Dacarbazine 200 mg inj	J9320	Streptozocin injection
J9150	Daunorubicin injection	J9328	Temozolomide injection
J9151	Daunorubicin citrate inj	J9330	Temsirolimus injection
J9155	Degarelix injection	J9340	Thiotepa injection
J9178	Inj, epirubicin HCl, 2 mg	J9350	Topotecan injection
J9179	Eribulin mesylate injection	J9351	Topotecan injection
J9180	Epirubicin HCl injection	J9357	Valrubicin injection
J9181	Etoposide injection	J9360	Vinblastine sulfate inj
J9182	Etoposide 100 mg inj	J9370	Vincristine sulfate 1 mg inj
J9185	Fludarabine phosphate inj	J9375	Vincristine sulfate 2 mg inj
J9200	Floxuridine injection	J9380	Vincristine sulfate 5 mg inj
J9201	Gemcitabine HCl injection	J9390	Vinorelbine tartrate inj
J9206	Irinotecan injection	C9131	Injection, ado-trastuzumab emtansin
J9207	Ixabepilone injection	C9259	Injection, pralatrexate, 1 mg
J9208	Ifosfamide injection		

CODE	DESCRIPTION
C9295	Injection, carfilzomib, 1 mg
C9296	Injection, ziv-aflibercept, 1 mg
C9298	Injection, ocriplasmin, 0.125 mg
J9002	Injection, doxorubicin hydrochloride, liposomal, doxil, 10 mg
J9042	Injection, brentuximab vedotin, 1 mg

Appendix B. Modified Poisson Parameter Estimates for models using alternative measures of cardiac co-morbidity

Parameter	level	Primary Model	Conditions 12 months prior to 3 months post diagnosis (excluding those with 1st Herceptin up to 90 days after diagnosis)				
			A: Primary model covariates	B: CCW Heart-related conditions	C: CCW Heart-related conditions, excluding Charlson	D: CCW Heart failure	E: CCW Heart failure, excluding Charlson
Age Groups	65 to 69~						
	70 to 74	0.98 (0.88, 1.09)	1.02 (0.87, 1.21)	1.02 (0.86, 1.21)	1.02 (0.86, 1.21)	1.03 (0.87, 1.22)	1.03 (0.87, 1.22)
	75 to 84	**0.74 (0.65, 0.83)**	**0.70 (0.57, 0.85)**	**0.68 (0.56, 0.83)**	**0.68 (0.56, 0.83)**	**0.69 (0.57, 0.84)**	**0.69 (0.57, 0.84)**
	85 plus	**0.25 (0.17, 0.37)**	**0.20 (0.11, 0.34)**	**0.19 (0.11, 0.33)**	**0.19 (0.11, 0.33)**	**0.20 (0.11, 0.34)**	**0.20 (0.11, 0.34)**
Race	Black	**0.75 (0.60, 0.93)**	**0.67 (0.49, 0.90)**	**0.67 (0.50, 0.91)**	**0.67 (0.49, 0.90)**	**0.66 (0.49, 0.89)**	**0.66 (0.49, 0.89)**
	Other	1.01 (0.86, 1.20)	0.93 (0.71, 1.20)	0.93 (0.72, 1.22)	0.93 (0.71, 1.21)	0.92 (0.70, 1.21)	0.92 (0.70, 1.20)
	White~						
Marital Status	Married~						
	Unmarried	0.93 (0.84, 1.03)	0.98 (0.83, 1.14)	0.99 (0.84, 1.15)	0.99 (0.84, 1.15)	1.01 (0.86, 1.18)	1.01 (0.87, 1.19)
SEER Region	North Central	0.90 (0.77, 1.06)	0.98 (0.77, 1.24)	0.98 (0.77, 1.24)	0.98 (0.77, 1.24)	0.99 (0.78, 1.25)	0.98 (0.78, 1.24)
	Northeast	1.03 (0.91, 1.17)	1.16 (0.96, 1.41)	1.18 (0.97, 1.42)	1.17 (0.97, 1.42)	1.12 (0.93, 1.36)	1.12 (0.93, 1.36)
	South	0.98 (0.87, 1.11)	0.95 (0.77, 1.16)	0.95 (0.77, 1.16)	0.95 (0.77, 1.16)	0.94 (0.77, 1.15)	0.94 (0.77, 1.15)
	West~						
% below poverty	< 5.0%~						
	5.0 - 9.9%	**0.85 (0.75, 0.97)**	0.81 (0.66, 1.00)	0.82 (0.66, 1.01)	0.82 (0.66, 1.01)	0.81 (0.66, 0.99)	0.81 (0.66, 1.00)
	10.0-19.9%	**0.87 (0.77, 0.99)**	**0.78 (0.63, 0.96)**	**0.78 (0.63, 0.96)**	**0.78 (0.63, 0.96)**	**0.78 (0.63, 0.96)**	**0.78 (0.63, 0.95)**
	>= 20.0%	0.88 (0.76, 1.02)	0.83 (0.65, 1.06)	0.83 (0.65, 1.06)	0.83 (0.65, 1.06)	0.80 (0.63, 1.02)	0.81 (0.63, 1.02)
Charlson score for 1yr prior	0~						

Parameter	level	Primary Model	Conditions 12 months prior to 3 months post diagnosis (excluding those with 1st Herceptin up to 90 days after diagnosis)				
			A: Primary model covariates	B: CCW Heart-related conditions	C: CCW Heart-related conditions, excluding Charlson	D: CCW Heart failure	E: CCW Heart failure, excluding Charlson
	1	0.90 (0.80, 1.02)	0.90 (0.75, 1.09)	0.94 (0.77, 1.16)		0.92 (0.77, 1.11)	
	2+	**0.84 (0.73, 0.97)**	0.90 (0.72, 1.12)	0.96 (0.75, 1.24)		1.06 (0.85, 1.32)	
Diagnosis Year	2010~						
	2011	**1.12 (1.02, 1.23)**	1.06 (0.91, 1.23)	1.06 (0.92, 1.23)	1.06 (0.92, 1.23)	1.08 (0.93, 1.25)	1.08 (0.94, 1.25)
ER/PR Status	HR+~						
	HR-	1.04 (0.94, 1.15)	1.09 (0.93, 1.27)	1.10 (0.94, 1.29)	1.11 (0.94, 1.30)	1.11 (0.95, 1.30)	1.11 (0.95, 1.30)
AJCC Tumor Size	T1a~						
	T1b	**1.72 (1.18, 2.51)**	1.64 (0.97, 2.78)	1.66 (0.98, 2.81)	1.67 (0.99, 2.83)	1.67 (0.98, 2.83)	1.68 (0.99, 2.85)
	T1c	**2.19 (1.54, 3.12)**	**2.08 (1.28, 3.38)**	**2.11 (1.30, 3.44)**	**2.13 (1.31, 3.45)**	**2.09 (1.28, 3.42)**	**2.10 (1.28, 3.43)**
	T2	**2.30 (1.61, 3.28)**	**2.20 (1.35, 3.58)**	**2.23 (1.37, 3.64)**	**2.26 (1.39, 3.67)**	**2.20 (1.34, 3.60)**	**2.22 (1.36, 3.63)**
	T3	**2.04 (1.36, 3.05)**	**1.94 (1.09, 3.43)**	**1.99 (1.12, 3.54)**	**2.00 (1.13, 3.55)**	**2.00 (1.12, 3.56)**	**1.97 (1.11, 3.51)**
	T4	**2.58 (1.75, 3.81)**	**2.15 (1.21, 3.83)**	**2.16 (1.22, 3.83)**	**2.18 (1.23, 3.86)**	**2.36 (1.34, 4.17)**	**2.35 (1.33, 4.17)**
AJCC Nodes Involved	N0~						
	N1	**1.26 (1.14, 1.41)**	**1.53 (1.29, 1.82)**	**1.54 (1.29, 1.82)**	**1.54 (1.30, 1.83)**	**1.59 (1.34, 1.89)**	**1.58 (1.33, 1.88)**
	N2/N3	**1.36 (1.19, 1.55)**	**1.75 (1.40, 2.19)**	**1.74 (1.39, 2.17)**	**1.74 (1.39, 2.17)**	**1.71 (1.37, 2.13)**	**1.72 (1.37, 2.15)**
Tumor Grade	Well~						
	Moderately	**1.68 (1.19, 2.38)**	1.61 (1.00, 2.57)	**1.63 (1.02, 2.61)**	**1.64 (1.03, 2.61)**	**1.62 (1.02, 2.58)**	**1.63 (1.02, 2.59)**
	Poorly	**2.29 (1.63, 3.23)**	**2.41 (1.52, 3.82)**	**2.43 (1.54, 3.85)**	**2.44 (1.54, 3.85)**	**2.48 (1.57, 3.91)**	**2.48 (1.58, 3.91)**
	Unknown	1.48 (0.90, 2.44)	1.18 (0.56, 2.51)	1.23 (0.58, 2.64)	1.25 (0.58, 2.66)	1.21 (0.57, 2.56)	1.21 (0.57, 2.55)
Surgery Type	Mast only~						

Parameter	level	Primary Model	A: Primary model covariates	B: CCW Heart-related conditions	C: CCW Heart-related conditions, excluding Charlson	D: CCW Heart failure	E: CCW Heart failure, excluding Charlson
			Conditions 12 months prior to 3 months post diagnosis (excluding those with 1st Herceptin up to 90 days after diagnosis)				
	BCS only	**1.15 (1.04, 1.28)**	**1.31 (1.11, 1.55)**	**1.30 (1.10, 1.53)**	**1.31 (1.11, 1.54)**	**1.28 (1.09, 1.51)**	**1.29 (1.10, 1.52)**
	BCS & Rad	**0.73 (0.63, 0.86)**	**0.56 (0.43, 0.73)**	**0.57 (0.44, 0.74)**	**0.57 (0.44, 0.74)**	**0.57 (0.44, 0.74)**	**0.57 (0.44, 0.74)**
	Mast & Rad	1.02 (0.83, 1.25)	0.86 (0.58, 1.28)	0.87 (0.58, 1.29)	0.87 (0.58, 1.29)	0.85 (0.57, 1.27)	0.86 (0.57, 1.29)
Heart-related chronic conditions (CCW)	0~						
	1			1.04 (0.82, 1.32)	1.04 (0.82, 1.32)		
	2			1.17 (0.93, 1.47)	1.16 (0.93, 1.46)		
	3+			0.94 (0.72, 1.23)	0.92 (0.72, 1.16)		
Heart failure (CCW)	Absent~						
	Present					**0.41 (0.26, 0.64)**	**0.42 (0.27, 0.66)**

Table legend: Alternative models above display the results of sensitivity analyses testing two cardiac-specific measures of co-morbidity, one using all heart-related conditions listed in the Medicare Chronic Conditions Warehouse (*CCW Heart-related conditions*), the second using only heart failure diagnoses *(CCW Heart Failure)*. Sensitivity analyses were limited to the subset of patients untreated with herceptin until at least 3 months after diagnosis, in order to capture pre-treatment prevalent heart conditions (n=1042). The primary model was re-run on this subset (Model A) with results generally similar to the full cohort primary model. Models B and C include a control variable for CCW Heart related conditions with and without a separate variable for the overall Charlson co-morbidity score, while Models D and E include a control variable for CCW-defined heart failure with and without a separate variable for the Charlson score. Significant findings are indicated in bold text. The overall CCW heart-related conditions count was not a significant predictor of trastuzumab receipt; the CCW heart failure variable was significantly associated with lower likelihood of receiving trastuzumab. There did not appear to be significant attenuation of the effect of race or age on the likelihood of trastuzumab receipt regardless of which combination of co-morbidity variables was included in the model.