

Supplemental online content for:

A Study of Novel Febrile Neutropenia Risk Factors Related to Bone Marrow or Immune Suppression, Barrier Function, and Bacterial Flora

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eTable 1. Proposed Risk Factors for FN and Associated Hypothesized Biological Pathways		
Potential Biological Pathway	Known Risk Factors	Newly Proposed Risk Factors
Bone marrow suppression	Preexisting anemia Preexisting neutropenia HIV infection	Recent/Concurrent RT
Impaired neutrophil function	Congestive heart failure Diabetes Renal disease Thyroid disease Osteoarthritis Rheumatoid disease Autoimmune disease HIV infection	Recent antibiotic use Recent corticosteroid use
Disturbance of barrier function	Peptic ulcer disease COPD	Dermatologic disease Mucosal disease Recent surgery Recent/concurrent RT
Altered bacterial flora	Peptic ulcer disease COPD	Prior antibiotic use

Abbreviations: COPD, chronic obstructive pulmonary disease; FN, febrile neutropenia; RT, radiation therapy.

eTable 2. Methods and Time Window for Identifying Potential New Risk Factors		
Potential Risk Factors for FN	Time Window for Assessment	Methods for Identifying Potential Risk Factors
Prior surgery	Within 6 months before chemotherapy	ICD-9 V codes and CPT-4 procedure codes: 0.31, 0.39, 17.33, 17.34, 17.35, 17.36, 17.39, 32.2, 32.28, 32.29, 32.3, 32.4, 32.41, 32.49, 32.5, 40.21, 40.23, 40.24, 40.29, 40.3, 40.4, 40.41, 40.51, 40.52, 40.53, 40.54, 40.59, 43.42, 43.6, 43.7, 43.81, 43.89, 43.91, 43.99, 45.41, 45.71, 45.72, 45.73, 45.74, 45.75, 45.76, 45.79, 45.8, 48.35, 48.5, 48.51, 48.62, 48.63, 48.69, 65.25, 65.29, 65.39, 65.49, 65.51, 65.61, 65.62, 68.8, 85.2, 85.21, 85.22, 85.23, 85.24, 85.34, 85.36, 85.41, 85.42, 85.43, 85.44, 85.45, 85.47, 19020, 19120, 19125, 19162, 19301, 19302, 19303, 19304, 19305, 19306, 19307, 32095, 32100, 32141, 32150, 32215, 32225, 32440, 32650, 32652, 32657, 32663, 38100, 38101, 38102, 38300, 38542, 38570, 38571, 38572, 38724, 38740, 38745, 38746, 38747, 38760, 38780, 43621, 43632, 43633, 43830, 44020, 44025, 44110, 44111, 44120, 44130, 44140, 44141, 44143, 44144, 44145, 44160, 44300, 44310, 44320, 45110, 45111, 45114, 45116, 45170, 45395, 58210, 58661, 58662, 58720, 58940, 58943, 58950, 58951, 58952, 58953, 58954
Prior RT	Within 2 months before chemotherapy	Cancer registry, KPSC Internal Radiation Therapy database, Radiation Oncology department visits, ICD-9 V codes, and CPT-4 procedure codes: 58.0, 77400, 77401, 77402, 77403, 77404, 77406, 77407, 77408, 77409, 77411, 77412, 77413, 77414, 77415, 77416, 77417, 77418, 77421, 77422, 77423, 77427, 77431, 77432, 77435, 77470, 77499
Concurrent RT	Within 5 days after chemotherapy	
Oral corticosteroid use	Within 3 months before chemotherapy	KPSC pharmacy dispensing database
Oral and intravenous antibiotic use	Within 3 months before chemotherapy	KPSC pharmacy dispensing database and infusion database
Selected dermatologic conditions	Within 1 month before chemotherapy	ICD-9 codes: 690, erythematous squamous dermatosis 691, atopic dermatitis and related conditions 692, contact dermatitis and other eczema 693, dermatitis due to substances taken internally 694, bullous dermatoses 696, psoriasis and similar disorders 698, pruritus and related conditions 698, other hypertrophic and atrophic conditions of skin 707, chronic ulcer of skin 708, urticarial
Selected mucosal conditions	Within 1 month before chemotherapy	ICD-9 codes: 528.0, stomatitis and mucositis (ulcerative) 530.10, esophagitis 535, gastritis and duodenitis 616.81, mucositis of cervix, vagina, and vulva 538, gastrointestinal mucositis (ulcerative) 478.11, nasal mucositis

Abbreviations: FN, febrile neutropenia; KPSC, Kaiser Permanente Southern California; RT, radiation therapy.

eTable 3. Distribution of Covariates by Propensity Score Quintiles and Prior Surgery Status

Propensity Score Quintile	1 (N=3,191)		2 (N=3,192)		3 (N=3,192)		4 (N=3,193)		5 (N=3,191)	
Prior surgery status	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Number	2,696	495	1,967	1,225	987	2,205	390	2,803	308	2,883
Mean age at diagnosis (SD), y	67.0 (10.66)	67.6 (10.71)	60.7 (11.48)	61.0 (12.19)	65.3 (11.17)	64.3 (10.58)	57.9 (9.95)	57.5 (9.86)	49.9 (8.97)	50.5 (8.35)
Female sex	604 (22.4%)	120 (24.24%)	1,535 (78.04%)	886 (72.33%)	487 (49.34%)	1,153 (52.29%)	384 (98.46%)	2,753 (98.22%)	308 (100%)	2,883 (100%)
Race/Ethnicity										
Non-Hispanic white	1,915 (71.03%)	363 (73.33%)	1,254 (63.75%)	742 (60.57%)	680 (68.9%)	1,446 (65.58%)	227 (58.21%)	1,878 (67%)	135 (43.83%)	1,213 (42.07%)
Non-Hispanic black	328 (12.17%)	56 (11.31%)	265 (13.47%)	170 (13.88%)	132 (13.37%)	321 (14.56%)	63 (16.15%)	420 (14.98%)	43 (13.96%)	375 (13.01%)
Asian	174 (6.45%)	32 (6.46%)	172 (8.74%)	112 (9.14%)	66 (6.69%)	167 (7.57%)	48 (12.31%)	221 (7.88%)	46 (14.94%)	498 (17.27%)
Hispanic	252 (9.35%)	39 (7.88%)	270 (13.73%)	193 (15.76%)	92 (9.32%)	234 (10.61%)	52 (13.33%)	274 (9.78%)	84 (27.27%)	797 (27.64%)
Other/Unknown	27 (1%)	5 (1.01%)	6 (0.31%)	8 (0.65%)	17 (1.72%)	37 (1.68%)	0 (0%)	10 (0.36%)		
Mean length of membership (SD), y	18.1 (12.42)	17.4 (11.36)	17.6 (12.20)	16.9 (11.42)	17.3 (11.85)	18.1 (12.40)	16.2 (11.73)	16.5 (11.33)	15.9 (14.00)	15.8 (11.79)
Medicare enrollees	1,495 (55.45%)	283 (57.17%)	710 (36.1%)	456 (37.22%)	509 (51.57%)	1,066 (48.34%)	97 (24.87%)	659 (23.51%)	10 (3.25%)	99 (3.43%)
Medicaid enrollees	22 (0.82%)	2 (0.4%)	13 (0.66%)	14 (1.14%)	8 (0.81%)	24 (1.09%)	4 (1.03%)	26 (0.93%)	3 (0.97%)	39 (1.35%)
Stage at diagnosis										
Localized	114 (4.23%)	9 (1.82%)	95 (4.83%)	77 (6.29%)	364 (36.88%)	563 (25.53%)	182 (46.67%)	1,774 (63.29%)	80 (25.97%)	921 (31.95%)
Regional	499 (18.51%)	72 (14.55%)	202 (10.27%)	238 (19.43%)	623 (63.12%)	1,642 (74.47%)	208 (53.33%)	1,029 (36.71%)	228 (74.03%)	1,962 (68.05%)
Distant	2,083 (77.26%)	414 (83.64%)	1,670 (84.9%)	910 (74.29%)						
Chemotherapy regimen FN risk group										
High	9 (0.33%)	3 (0.61%)	40 (2.03%)	12 (0.98%)	16 (1.62%)	15 (0.68%)	20 (5.13%)	42 (1.5%)	35 (11.36%)	100 (3.47%)
Medium	2,043 (75.78%)	324 (65.45%)	1,560 (79.31%)	894 (72.98%)	795 (80.55%)	1,250 (56.69%)	315 (80.77%)	2,121 (75.67%)	246 (79.87%)	2,162 (74.99%)
Unclassified	644 (23.89%)	168 (33.94%)	367 (18.66%)	319 (26.04%)	176 (17.83%)	940 (42.63%)	55 (14.1%)	640 (22.83%)	27 (8.77%)	621 (21.54%)
Dose reduction, yes (any agent)	750 (27.82%)	122 (24.65%)	507 (25.78%)	251 (20.49%)	279 (28.27%)	460 (20.86%)	77 (19.74%)	421 (15.02%)	63 (20.45%)	410 (14.22%)
Myelosuppressive agents, mean (SD)	1.7 (0.53)	1.4 (0.53)	1.7 (0.53)	1.5 (0.56)	1.7 (0.56)	1.4 (0.64)	1.7 (0.59)	2.0 (0.71)	1.6 (0.61)	1.8 (0.75)
Number dose reduced, mean (SD)	0.3 (0.56)	0.3 (0.51)	0.3 (0.53)	0.2 (0.46)	0.3 (0.59)	0.2 (0.51)	0.2 (0.49)	0.2 (0.50)	0.2 (0.48)	0.2 (0.45)
Number not dose reduced, mean (SD)	1.4 (0.72)	1.1 (0.70)	1.4 (0.71)	1.3 (0.72)	1.4 (0.75)	1.2 (0.76)	1.4 (0.75)	1.8 (0.88)	1.3 (0.70)	1.6 (0.88)
Mean neutrophil (SD), 1,000/mcL	6.8 (3.83)	5.6 (2.77)	6.8 (4.15)	5.5 (3.44)	5.8 (3.06)	4.8 (2.12)	5.4 (3.84)	4.5 (2.12)	4.7 (2.31)	4.6 (2.20)
Prior infection	667 (24.74%)	112 (22.63%)	303 (15.4%)	197 (16.08%)	132 (13.37%)	332 (15.06%)	42 (10.77%)	149 (5.32%)	3 (0.97%)	29 (1.01%)
Census level household income, median	\$55,106	\$53,684	\$56,039	\$56,037	\$52,738	\$53,322	\$51,091.5	\$54,123	\$57,213	\$58,318
Mean (SD)	55.4 (19.94)	55.5 (18.47)	56.6 (19.56)	56.5 (19.82)	55.4 (19.73)	54.8 (19.61)	55.8 (19.56)	55.4 (19.10)	55.7 (20.36)	57.3 (20.27)
Median census level education, % with high school degree	56.8	56.1	57.7	58.7	56.6	56.7	57.3	56.6	57.7	59.8
Total number of comorbidities, mean (SD)	1.9 (1.85)	1.9 (1.79)	1.3 (1.51)	1.3 (1.54)	1.5 (1.69)	1.5 (1.55)	1.0 (1.24)	0.9 (1.21)	0.4 (0.77)	0.5 (0.84)
Previous cancer	45 (1.67%)	4 (0.81%)	11 (0.56%)	15 (1.22%)	12 (1.22%)	29 (1.32%)	3 (0.77%)	9 (0.32%)	–	–

Abbreviation: FN, febrile neutropenia.

eTable 4. Distribution of Covariates by Propensity Score Quintiles and Prior Radiation Status

Propensity Score Quintile	1 (N=3,191)		2 (N=3,193)		3 (N=3,192)		4 (N=3,192)		5 (N=3,191)	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Prior radiation status										
Number	3,135	56	3,127	66	3,062	130	2,928	264	2,647	544
Mean age at diagnosis (SD), y	57.3 (15.47)	60.7 (14.92)	57.2 (10.60)	60.9 (10.77)	59.7 (10.22)	60.8 (11.40)	62.5 (10.85)	62.7 (10.58)	63.9 (9.90)	62.4 (9.73)
Female sex	2,955 (94.26%)	55 (98.21%)	3,037 (97.12%)	64 (96.97%)	2,374 (77.53%)	79 (60.77%)	1,474 (50.34%)	143 (54.17%)	801 (30.26%)	131 (24.08%)
Race/Ethnicity										
Non-Hispanic white	1,338 (42.68%)	28 (50%)	1,974 (63.13%)	42 (63.64%)	2,020 (65.97%)	80 (61.54%)	1,932 (65.98%)	186 (70.45%)	1,871 (70.68%)	382 (70.22%)
Non-Hispanic black	467 (14.9%)	13 (23.21%)	385 (12.31%)	7 (10.61%)	423 (13.81%)	17 (13.08%)	436 (14.89%)	29 (10.98%)	322 (12.16%)	74 (13.6%)
Asian	417 (13.3%)	7 (12.5%)	258 (8.25%)	6 (9.09%)	317 (10.35%)	11 (8.46%)	256 (8.74%)	28 (10.61%)	200 (7.56%)	36 (6.62%)
Hispanic	884 (28.2%)	8 (14.29%)	487 (15.57%)	11 (16.67%)	289 (9.44%)	20 (15.38%)	282 (9.63%)	19 (7.2%)	237 (8.95%)	50 (9.19%)
Other/Unknown	29 (0.93%)	0 (0%)	23 (0.74%)	0 (0%)	13 (0.42%)	2 (1.54%)	22 (0.75%)	2 (0.76%)	17 (0.64%)	2 (0.37%)
Mean length of membership (SD), y	17.2 (12.68)	16.3 (12.14)	16.3 (11.41)	17.0 (10.72)	17.6 (12.00)	18.2 (12.59)	17.4 (12.13)	17.0 (10.65)	16.8 (11.74)	16.6 (12.03)
Medicare enrollees	912 (29.09%)	24 (42.86%)	746 (23.86%)	21 (31.82%)	883 (28.84%)	46 (35.38%)	1,207 (41.22%)	110 (41.67%)	1,217 (45.98%)	218 (40.07%)
Medicaid enrollees	25 (0.8%)	0 (0%)	30 (0.96%)	0 (0%)	36 (1.18%)	4 (3.08%)	23 (0.79%)	1 (0.38%)	26 (0.98%)	10 (1.84%)
Stage at diagnosis										
Localized	248 (7.91%)	2 (3.57%)	983 (31.44%)	25 (37.88%)	1,984 (64.79%)	61 (46.92%)	339 (11.58%)	43 (16.29%)	390 (14.73%)	104 (19.12%)
Regional	2,023 (64.53%)	24 (42.86%)	1,669 (53.37%)	24 (36.36%)	631 (20.61%)	32 (24.62%)	1,172 (40.03%)	86 (32.58%)	829 (31.32%)	213 (39.15%)
Distant	864 (27.56%)	30 (53.57%)	475 (15.19%)	17 (25.76%)	447 (14.6%)	37 (28.46%)	1,417 (48.39%)	135 (51.14%)	1,428 (53.95%)	227 (41.73%)
Chemotherapy regimen FN risk group										
High	86 (2.74%)	2 (3.57%)	70 (2.24%)	1 (1.52%)	36 (1.18%)	0 (0%)	51 (1.74%)	0 (0%)	46 (1.74%)	0 (0%)
Medium	2,313 (73.78%)	35 (62.5%)	2,367 (75.7%)	39 (59.09%)	2,209 (72.14%)	78 (60%)	2,058 (70.29%)	162 (61.36%)	2,123 (80.2%)	326 (59.93%)
Unclassified	736 (23.48%)	19 (33.93%)	690 (22.07%)	26 (39.39%)	817 (26.68%)	52 (40%)	819 (27.97%)	102 (38.64%)	478 (18.06%)	218 (40.07%)
Dose reduction, yes (any agent)	620 (19.78%)	10 (17.86%)	562 (17.97%)	11 (16.67%)	543 (17.73%)	26 (20%)	711 (24.28%)	42 (15.91%)	722 (27.28%)	93 (17.1%)
Myelosuppressive agents, mean (SD)	1.7 (0.68)	1.6 (0.57)	1.8 (0.72)	1.6 (0.67)	1.9 (0.69)	1.6 (0.63)	1.5 (0.56)	1.5 (0.50)	1.7 (0.54)	1.5 (0.51)
Number dose reduced, mean (SD)	0.2 (0.51)	0.2 (0.44)	0.2 (0.51)	0.2 (0.47)	0.2 (0.50)	0.2 (0.47)	0.3 (0.52)	0.2 (0.39)	0.3 (0.54)	0.2 (0.43)
Number not dose reduced, mean (SD)	1.5 (0.83)	1.4 (0.62)	1.6 (0.87)	1.4 (0.80)	1.7 (0.87)	1.4 (0.80)	1.2 (0.71)	1.4 (0.61)	1.4 (0.71)	1.3 (0.60)
Mean neutrophil count (SD), 1,000/mcL	5.1 (3.20)	5.5 (2.97)	4.9 (2.50)	5.2 (2.63)	4.7 (2.34)	5.4 (3.09)	5.8 (3.39)	6.2 (3.54)	6.5 (3.67)	6.7 (4.07)
Prior infection	397 (12.66%)	14 (25%)	228 (7.29%)	2 (3.03%)	263 (8.59%)	18 (13.85%)	463 (15.81%)	49 (18.56%)	459 (17.34%)	73 (13.42%)
Census level household income, median	\$55,114	\$57,389.50	\$56,190	\$59,786.50	\$55,894.50	\$56,089	\$54,758.50	\$55,469.50	\$53,750	\$55,941
Median census level education, % with high school degree	56.1	62.7	58.0	59.3	58.6	57.8	57.1	57.8	57.2	56.4
Total number of comorbidities, mean (SD)	1.0 (1.39)	1.3 (1.58)	1.0 (1.37)	1.0 (1.30)	1.1 (1.41)	1.4 (1.50)	1.5 (1.64)	1.5 (1.67)	1.5 (1.70)	1.4 (1.59)
Previous cancer	33 (1.05%)	0 (0%)	17 (0.54%)	2 (3.03%)		0 (0%)	22 (0.75%)	0 (0%)	25 (0.94%)	6 (1.1%)

Abbreviation: FN, febrile neutropenia.

eTable 5. Distribution of Covariates by Propensity Score Quintiles and Concurrent Radiation Status

Propensity Score Quintile	1 (N=3,192)		2 (N=3,192)		3 (N=3,192)		4 (N=3,191)		5 (N=3,192)	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Concurrent radiation status										
Number	3,189	3	3,181	11	3,184	8	3,180	11	2,803	389
Mean age at diagnosis (SD), y	57.7 (15.62)	67.0 (7.55)	58.1 (11.92)	61.8 (11.49)	60.1 (10.52)	67.4 (6.46)	61.2 (10.06)	66.1 (7.92)	63.5 (9.21)	62.1 (10.21)
Female sex	2,535 (79.49%)	3 (100%)	2,622 (82.43%)	7 (63.64%)	2,434 (76.44%)	2 (25%)	2,175 (68.4%)	6 (54.55%)	1,187 (42.35%)	142 (36.5%)
Race/Ethnicity										
Non-Hispanic white	2,073 (65%)	3 (100%)	2,048 (64.38%)	8 (72.73%)	1,981 (62.22%)	6 (75%)	1,852 (58.24%)	8 (72.73%)	1,622 (57.87%)	252 (64.78%)
Non-Hispanic black	166 (5.21%)	0 (0%)	265 (8.33%)	1 (9.09%)	427 (13.41%)	1 (12.5%)	608 (19.12%)	1 (9.09%)	640 (22.83%)	64 (16.45%)
Asian	295 (9.25%)	0 (0%)	336 (10.56%)	2 (18.18%)	329 (10.33%)	0 (0%)	309 (9.72%)	2 (18.18%)	235 (8.38%)	28 (7.2%)
Hispanic	566 (17.75%)	0 (0%)	519 (16.32%)	0 (0%)	446 (14.01%)	1 (12.5%)	410 (12.89%)	0 (0%)	301 (10.74%)	44 (11.31%)
Other/Unknown	89 (2.79%)	0 (0%)	13 (0.41%)	0 (0%)	1 (0.03%)	0 (0%)	1 (0.03%)	0 (0%)	5 (0.18%)	1 (0.26%)
Mean length of membership (SD), y	15.6 (11.56)	11.6 (5.99)	15.8 (11.24)	11.3 (9.10)	17.7 (12.32)	21.2 (8.77)	17.7 (12.14)	15.5 (8.74)	18.7 (12.39)	17.9 (12.48)
Medicare enrollees	1,064 (33.36%)	2 (66.67%)	872 (27.41%)	3 (27.27%)	989 (31.06%)	5 (62.5%)	1,088 (34.21%)	4 (36.36%)	1,200 (42.81%)	157 (40.36%)
Medicaid enrollees	33 (1.03%)	0 (0%)	24 (0.75%)	1 (9.09%)	22 (0.69%)	0 (0%)	41 (1.29%)	0 (0%)	32 (1.14%)	2 (0.51%)
Stage at diagnosis										
Localized	498 (15.62%)	0 (0%)	1,095 (34.42%)	0 (0%)	965 (30.31%)	1 (12.5%)	892 (28.05%)	1 (9.09%)	607 (21.66%)	120 (30.85%)
Regional	708 (22.2%)	0 (0%)	973 (30.59%)	1 (9.09%)	1,422 (44.66%)	1 (12.5%)	1,730 (54.4%)	7 (63.64%)	1,663 (59.33%)	198 (50.9%)
Distant	1,983 (62.18%)	3 (100%)	1,113 (34.99%)	10 (90.91%)	797 (25.03%)	6 (75%)	558 (17.55%)	3 (27.27%)	533 (19.02%)	71 (18.25%)
Chemotherapy regimen FN risk group										
High	30 (0.94%)	0 (0%)	43 (1.35%)	1 (9.09%)	70 (2.2%)	0 (0%)	97 (3.05%)	0 (0%)	50 (1.78%)	1 (0.26%)
Medium	2,991 (93.79%)	3 (100%)	2,902 (91.23%)	10 (90.91%)	2,642 (82.98%)	8 (100%)	1,875 (58.96%)	7 (63.64%)	1,120 (39.96%)	152 (39.07%)
Unclassified	168 (5.27%)	0 (0%)	236 (7.42%)	0 (0%)	472 (14.82%)	0 (0%)	1,208 (37.99%)	4 (36.36%)	1,633 (58.26%)	236 (60.67%)
Dose reduction, yes (any agent)	707 (22.17%)	2 (66.67%)	622 (19.55%)	2 (18.18%)	676 (21.23%)	2 (25%)	680 (21.38%)	2 (18.18%)	587 (20.94%)	60 (15.42%)
Myelosuppressive agents, mean (SD)	1.8 (0.55)	2.0 (0)	1.8 (0.62)	1.7 (0.47)	1.7 (0.65)	2.0 (0.53)	1.7 (0.75)	1.8 (0.40)	1.4 (0.61)	1.4 (0.49)
Number dose reduced, mean (SD)	0.3 (0.55)	1.0 (1.00)	0.2 (0.51)	0.2 (0.40)	0.2 (0.52)	0.3 (0.46)	0.2 (0.52)	0.2 (0.40)	0.2 (0.48)	0.2 (0.39)
Number not dose reduced, mean (SD)	1.5 (0.75)	1.0 (1.00)	1.6 (0.80)	1.5 (0.69)	1.5 (0.82)	1.8 (0.89)	1.5 (0.91)	1.6 (0.50)	1.2 (0.74)	1.2 (0.57)
Mean neutrophil count (SD), 1,000/mcL	5.8 (3.63)	7.2 (1.90)	5.5 (3.33)	8.5 (3.58)	5.3 (2.94)	6.3 (2.23)	5.1 (2.73)	7.8 (3.03)	5.5 (3.02)	5.6 (3.31)
Prior infection	605 (18.97%)	0 (0%)	358 (11.25%)	2 (18.18%)	325 (10.21%)	1 (12.5%)	304 (9.56%)	3 (27.27%)	329 (11.74%)	39 (10.03%)
Census level household income, median	\$53,632	\$38,549	\$54,841	\$70,100	\$56,832.5	\$67,858.5	\$55,255	\$69,790	\$55,455	\$55,390
Median census level education, % with high school degree	60.2	69.3	59.2	68.3	57.0	65.3	55.5	65.9	55.1	54.1
Total number of comorbidities, mean (SD)	1.0 (1.33)	4.3 (1.15)	0.8 (1.23)	0.7 (1.10)	1.2 (1.43)	1.8 (1.58)	1.5 (1.59)	1.6 (1.21)	1.8 (1.82)	1.5 (1.56)
Previous cancer	16 (0.5%)	0 (0%)	24 (0.75%)	0 (0%)	22 (0.69%)	0 (0%)	33 (1.04%)	0 (0%)	30 (1.07%)	3 (0.77%)

Abbreviation: FN, febrile neutropenia.

eTable 6. Distribution of Covariates by Propensity Score Quintiles and Oral Corticosteroid Use Status

Propensity Score Quintile	1 (N=3,191)		2 (N=3,192)		3 (N=3,193)		4 (N=3,191)		5 (N=3,192)	
Oral corticosteroid use status	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Number	3,134	57	3,143	49	3,092	101	2,962	229	2,744	448
Mean age at diagnosis (SD), y	56.7 (14.49)	58.5 (14.76)	57.8 (9.75)	56.7 (11.20)	60.3 (11.87)	63.3 (11.34)	61.8 (11.23)	62.1 (10.51)	63.8 (10.09)	62.9 (10.24)
Female sex	2,674 (85.32%)	46 (80.7%)	2,517 (80.08%)	38 (77.55%)	2,231 (72.15%)	72 (71.29%)	1,726 (58.27%)	136 (59.39%)	1,425 (51.93%)	248 (55.36%)
Race/Ethnicity										
Non-Hispanic white	1,236 (39.44%)	23 (40.35%)	2,672 (85.01%)	39 (79.59%)	1,564 (50.58%)	53 (52.48%)	2,010 (67.86%)	161 (70.31%)	1,797 (65.49%)	298 (66.52%)
Non-Hispanic black	29 (0.93%)	3 (5.26%)	136 (4.33%)	4 (8.16%)	893 (28.88%)	29 (28.71%)	309 (10.43%)	25 (10.92%)	646 (23.54%)	99 (22.1%)
Asian	815 (26.01%)	12 (21.05%)	90 (2.86%)	1 (2.04%)	255 (8.25%)	5 (4.95%)	238 (8.04%)	18 (7.86%)	87 (3.17%)	15 (3.35%)
Hispanic	1,052 (33.57%)	19 (33.33%)	212 (6.75%)	3 (6.12%)	355 (11.48%)	12 (11.88%)	391 (13.2%)	24 (10.48%)	185 (6.74%)	34 (7.59%)
Other/Unknown	2 (0.06%)	0 (0%)	33 (1.05%)	2 (4.08%)	25 (0.81%)	2 (1.98%)	14 (0.47%)	1 (0.44%)	29 (1.06%)	2 (0.45%)
Mean length of membership (SD), y	17.1 (13.19)	18.3 (12.39)	15.6 (11.31)	14.7 (11.96)	18.0 (11.90)	19.3 (12.46)	17.2 (11.69)	18.1 (12.62)	17.5 (11.56)	16.8 (11.54)
Medicare enrollees	828 (26.42%)	15 (26.32%)	728 (23.16%)	11 (22.45%)	1,024 (33.12%)	46 (45.54%)	1,165 (39.33%)	90 (39.3%)	1,279 (46.61%)	198 (44.2%)
Medicaid enrollees	22 (0.7%)	0 (0%)	28 (0.89%)	3 (6.12%)	33 (1.07%)	0 (0%)	39 (1.32%)	0 (0%)	26 (0.95%)	4 (0.89%)
Stage at diagnosis										
Localized	1,597 (50.96%)	35 (61.4%)	1,256 (39.96%)	23 (46.94%)	888 (28.72%)	29 (28.71%)	214 (7.22%)	14 (6.11%)	105 (3.83%)	18 (4.02%)
Regional	1,520 (48.5%)	21 (36.84%)	1,858 (59.12%)	26 (53.06%)	1,950 (63.07%)	65 (64.36%)	773 (26.1%)	60 (26.2%)	360 (13.12%)	70 (15.63%)
Distant	17 (0.54%)	1 (1.75%)	29 (0.92%)	0 (0%)	254 (8.21%)	7 (6.93%)	1,975 (66.68%)	155 (67.69%)	2,279 (83.05%)	360 (80.36%)
Chemotherapy regimen FN risk group										
High	68 (2.17%)	4 (7.02%)	80 (2.55%)	1 (2.04%)	62 (2.01%)	2 (1.98%)	45 (1.52%)	2 (0.87%)	20 (0.73%)	8 (1.79%)
Medium	2,160 (68.92%)	43 (75.44%)	2,185 (69.52%)	38 (77.55%)	2,119 (68.53%)	83 (82.18%)	2,269 (76.6%)	192 (83.84%)	2,251 (82.03%)	370 (82.59%)
Unclassified	906 (28.91%)	10 (17.54%)	878 (27.94%)	10 (20.41%)	911 (29.46%)	16 (15.84%)	648 (21.88%)	35 (15.28%)	473 (17.24%)	70 (15.63%)
Dose reduction, yes (any agent)	534 (17.04%)	9 (15.79%)	542 (17.24%)	10 (20.41%)	602 (19.47%)	24 (23.76%)	684 (23.09%)	63 (27.51%)	757 (27.59%)	115 (25.67%)
Myelosuppressive agents, mean (SD)	1.8 (0.74)	1.8 (0.64)	1.7 (0.72)	1.8 (0.61)	1.7 (0.67)	1.8 (0.63)	1.6 (0.56)	1.8 (0.53)	1.7 (0.53)	1.8 (0.50)
Number dose reduced, mean (SD)	0.2 (0.51)	0.2 (0.61)	0.2 (0.49)	0.3 (0.60)	0.2 (0.51)	0.3 (0.48)	0.3 (0.50)	0.3 (0.57)	0.3 (0.54)	0.3 (0.53)
Number not dose reduced, mean (SD)	1.6 (0.88)	1.6 (0.87)	1.5 (0.86)	1.5 (0.87)	1.4 (0.83)	1.5 (0.78)	1.4 (0.73)	1.4 (0.73)	1.3 (0.72)	1.5 (0.70)
Mean neutrophil count (SD), 1,000/mcL	4.7 (2.22)	6.2 (3.43)	4.7 (2.20)	7.0 (8.43)	4.8 (2.37)	6.0 (4.28)	5.9 (3.47)	7.3 (3.99)	6.6 (3.81)	8.4 (5.16)
Number of patients who developed FN in the first cycle of chemotherapy	119 (3.8%)	4 (7.02%)	98 (3.12%)	6 (12.24%)	139 (4.5%)	6 (5.94%)	116 (3.92%)	17 (7.42%)	151 (5.5%)	36 (8.04%)
Prior infection	16 (0.51%)	1 (1.75%)	14 (0.45%)	0 (0%)	337 (10.9%)	8 (7.92%)	277 (9.35%)	17 (7.42%)	1,083 (39.47%)	213 (47.54%)
Census level household income, median	\$55,473	\$61,974	\$57,870	\$61,286	\$52,876.5	\$51,923	\$55,606	\$58,333	\$54,364	\$52,802.5
Mean census level education, % with high school degree (SD)	55.4 (20.14)	57.2 (23.94)	58.6 (19.19)	59.0 (21.64)	54.4 (19.52)	54.5 (20.16)	56.5 (19.76)	57.5 (19.27)	54.7 (19.61)	53.8 (19.07)
Total number of comorbidities, mean (SD)	0.9 (1.26)	1.1 (1.13)	0.7 (1.11)	0.7 (1.24)	1.3 (1.42)	1.5 (1.35)	1.3 (1.52)	1.4 (1.49)	2.0 (1.85)	2.2 (1.82)
Previous cancer	29 (0.93%)	0 (0%)	17 (0.54%)	0 (0%)	29 (0.94%)	0 (0%)	26 (0.88%)	2 (0.87%)	22 (0.8%)	3 (0.67%)

Abbreviation: FN, febrile neutropenia.

eTable 7. Distribution of Covariates by Propensity Score Quintiles and Antibiotic Use Status

Propensity Score Quintile	1 (N=3,191)		2 (N=3,192)		3 (N=3,193)		4 (N=3,192)		5 (N=3,191)	
Antibiotic use status	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Number	2,295	896	2,017	1,175	1,846	1,347	1,686	1,506	1,094	2,097
Mean age at diagnosis (SD), y	60.6 (12.71)	61.0 (12.61)	57.3 (11.86)	57.8 (11.83)	60.2 (11.82)	59.5 (12.23)	59.9 (11.15)	59.2 (11.38)	62.3 (11.10)	63.1 (10.81)
Female sex	1,588 (69.19%)	629 (70.2%)	1,595 (79.08%)	932 (79.32%)	1,426 (77.25%)	1,028 (76.32%)	1,130 (67.02%)	1,015 (67.4%)	587 (53.66%)	1,183 (56.41%)
Race/Ethnicity										
Non-Hispanic white	1,234 (53.77%)	470 (52.46%)	1,306 (64.75%)	749 (63.74%)	1,106 (59.91%)	755 (56.05%)	1,095 (64.95%)	993 (65.94%)	698 (63.8%)	1,447 (69%)
Non-Hispanic black	439 (19.13%)	186 (20.76%)	233 (11.55%)	128 (10.89%)	316 (17.12%)	252 (18.71%)	158 (9.37%)	144 (9.56%)	120 (10.97%)	197 (9.39%)
Asian	435 (18.95%)	185 (20.65%)	149 (7.39%)	88 (7.49%)	228 (12.35%)	157 (11.66%)	75 (4.45%)	62 (4.12%)	50 (4.57%)	107 (5.1%)
Hispanic	162 (7.06%)	50 (5.58%)	317 (15.72%)	201 (17.11%)	183 (9.91%)	170 (12.62%)	350 (20.76%)	300 (19.92%)	220 (20.11%)	334 (15.93%)
Other/Unknown	25 (1.09%)	5 (0.56%)	12 (0.59%)	9 (0.77%)	13 (0.7%)	13 (0.97%)	8 (0.47%)	7 (0.46%)	6 (0.55%)	12 (0.57%)
Mean length of membership (SD), y	18.4 (13.12)	18.5 (13.22)	16.1 (11.10)	16.2 (11.16)	17.9 (12.01)	18.2 (12.98)	16.0 (11.64)	16.0 (10.94)	16.9 (11.44)	16.7 (11.74)
Medicare enrollees	792 (34.51%)	316 (35.27%)	513 (25.43%)	302 (25.7%)	602 (32.61%)	419 (31.11%)	558 (33.1%)	470 (31.21%)	468 (42.78%)	944 (45.02%)
Medicaid enrollees	15 (0.65%)	5 (0.56%)	14 (0.69%)	13 (1.11%)	16 (0.87%)	14 (1.04%)	17 (1.01%)	19 (1.26%)	13 (1.19%)	29 (1.38%)
Stage at diagnosis										
Localized	906 (39.48%)	333 (37.17%)	1,226 (60.78%)	723 (61.53%)	301 (16.31%)	249 (18.49%)	83 (4.92%)	75 (4.98%)	89 (8.14%)	194 (9.25%)
Regional	454 (19.78%)	163 (18.19%)	365 (18.1%)	187 (15.91%)	967 (52.38%)	678 (50.33%)	1,196 (70.94%)	1,099 (72.97%)	576 (52.65%)	1,018 (48.55%)
Distant	935 (40.74%)	400 (44.64%)	426 (21.12%)	265 (22.55%)	578 (31.31%)	420 (31.18%)	407 (24.14%)	332 (22.05%)	429 (39.21%)	885 (42.2%)
Chemotherapy regimen FN risk group										
High	49 (2.14%)	17 (1.9%)	47 (2.33%)	17 (1.45%)	44 (2.38%)	15 (1.11%)	35 (2.08%)	30 (1.99%)	14 (1.28%)	24 (1.14%)
Medium	1,659 (72.29%)	712 (79.46%)	1,575 (78.09%)	902 (76.77%)	1,398 (75.73%)	955 (70.9%)	1,174 (69.63%)	1,016 (67.46%)	808 (73.86%)	1,511 (72.06%)
Unclassified	587 (25.58%)	167 (18.64%)	395 (19.58%)	256 (21.79%)	404 (21.89%)	377 (27.99%)	477 (28.29%)	460 (30.54%)	272 (24.86%)	562 (26.8%)
Dose reduction, yes (any agent)	469 (20.44%)	218 (24.33%)	383 (18.99%)	235 (20%)	368 (19.93%)	243 (18.04%)	336 (19.93%)	282 (18.73%)	282 (25.78%)	524 (24.99%)
Myelosuppressive agents, mean (SD)	1.7 (0.61)	1.8 (0.61)	1.9 (0.65)	1.9 (0.67)	1.7 (0.65)	1.6 (0.67)	1.6 (0.67)	1.5 (0.67)	1.6 (0.62)	1.6 (0.59)
Number dose reduced, mean (SD)	0.2 (0.51)	0.3 (0.57)	0.2 (0.52)	0.2 (0.53)	0.2 (0.49)	0.2 (0.47)	0.2 (0.50)	0.2 (0.46)	0.3 (0.55)	0.3 (0.54)
Number not dose reduced, mean (SD)	1.5 (0.76)	1.5 (0.80)	1.7 (0.84)	1.7 (0.87)	1.5 (0.81)	1.4 (0.81)	1.4 (0.80)	1.3 (0.81)	1.3 (0.77)	1.3 (0.74)
Mean neutrophil count (SD), 1,000/mcL	5.5 (3.22)	6.1 (3.69)	5.2 (3.02)	5.2 (2.60)	5.1 (2.88)	5.0 (3.09)	5.1 (2.48)	5.0 (2.44)	6.0 (3.54)	6.3 (3.92)
Prior infection	–	–	–	–	1 (0.05%)	1 (0.07%)	10 (0.59%)	11 (0.73%)	542 (49.54%)	1401 (66.81%)
Census level household income, median	\$60,987	\$61,102.5	\$55,303	\$55,141	\$60,536	\$59,091	\$50,212	\$50,602	\$50,579.5	\$51,944
Median census level education, % with high school degree	62.2	63.6	58	57.3	61.2	59.7	53.1	54.2	51.7	53.4
Total number of comorbidities, mean (SD)	0.9 (1.24)	1.0 (1.30)	0.8 (1.26)	0.9 (1.26)	1.2 (1.42)	1.2 (1.44)	1.2 (1.44)	1.2 (1.48)	2.2 (1.84)	2.0 (1.80)
Previous cancer	24 (1.05%)	13 (1.45%)	15 (0.74%)	11 (0.94%)	15 (0.81%)	8 (0.59%)	11 (0.65%)	10 (0.66%)	11 (1.01%)	10 (0.48%)

Abbreviation: FN, febrile neutropenia.

eTable 8. Distribution of Covariates by Propensity Score Quintiles and Dermatologic and/or Mucosal Condition Status										
Propensity Score Quintile	1 (N=3,191)		2 (N=3,192)		3 (N=3,193)		4 (N=3,191)		5 (N=3,192)	
Dermatologic and/or mucosal conditions	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Number	3,146	45	3,133	59	3,119	74	3,082	109	3,002	190
Mean age at diagnosis (SD), y	52.3 (13.38)	57.2 (16.07)	57.0 (10.59)	54.8 (8.55)	60.9 (10.27)	60.5 (11.06)	63.7 (10.18)	64.7 (10.50)	66.5 (8.98)	66.1 (8.78)
Female sex	2,632 (83.66%)	41 (91.11%)	2,508 (80.05%)	46 (77.97%)	2,211 (70.89%)	57 (77.03%)	1,899 (61.62%)	62 (56.88%)	1,562 (52.03%)	95 (50%)
Race/Ethnicity										
Non-Hispanic white	1,659 (52.73%)	27 (60%)	1,830 (58.41%)	35 (59.32%)	1,940 (62.2%)	45 (60.81%)	2,002 (64.96%)	76 (69.72%)	2,112 (70.35%)	127 (66.84%)
Non-Hispanic black	678 (21.55%)	8 (17.78%)	439 (14.01%)	9 (15.25%)	376 (12.06%)	7 (9.46%)	372 (12.07%)	8 (7.34%)	253 (8.43%)	23 (12.11%)
Asian	322 (10.24%)	6 (13.33%)	349 (11.14%)	6 (10.17%)	339 (10.87%)	8 (10.81%)	283 (9.18%)	7 (6.42%)	201 (6.7%)	15 (7.89%)
Hispanic	482 (15.32%)	4 (8.89%)	503 (16.05%)	8 (13.56%)	437 (14.01%)	14 (18.92%)	391 (12.69%)	17 (15.6%)	408 (13.59%)	23 (12.11%)
Other/Unknown	5 (0.16%)	0 (0%)	12 (0.38%)	1 (1.69%)	27 (0.87%)	0 (0%)	34 (1.1%)	1 (0.92%)	28 (0.93%)	2 (1.05%)
Mean length of membership (SD), y	12.2 (9.03)	13.2 (9.53)	15.3 (9.96)	15.0 (9.56)	17.5 (11.45)	19.1 (12.35)	19.0 (12.51)	18.8 (12.13)	21.4 (14.05)	21.4 (16.55)
Medicare enrollees	327 (10.39%)	9 (20%)	486 (15.51%)	6 (10.17%)	957 (30.68%)	24 (32.43%)	1,464 (47.5%)	53 (48.62%)	1,932 (64.36%)	126 (66.32%)
Medicaid enrollees	8 (0.25%)	0 (0%)	18 (0.57%)	0 (0%)	38 (1.22%)	0 (0%)	42 (1.36%)	1 (0.92%)	45 (1.5%)	3 (1.58%)
Stage at diagnosis										
Localized	785 (24.95%)	14 (31.11%)	1,291 (41.21%)	29 (49.15%)	1,081 (34.66%)	21 (28.38%)	642 (20.83%)	19 (17.43%)	280 (9.33%)	17 (8.95%)
Regional	2,291 (72.82%)	31 (68.89%)	1,597 (50.97%)	24 (40.68%)	1,214 (38.92%)	34 (45.95%)	837 (27.16%)	33 (30.28%)	606 (20.19%)	36 (18.95%)
Distant	70 (2.23%)	0 (0%)	245 (7.82%)	6 (10.17%)	824 (26.42%)	19 (25.68%)	1,603 (52.01%)	57 (52.29%)	2,116 (70.49%)	137 (72.11%)
Chemotherapy regimen FN risk group										
High	114 (3.62%)	0 (0%)	74 (2.36%)	2 (3.39%)	45 (1.44%)	3 (4.05%)	32 (1.04%)	1 (0.92%)	17 (0.57%)	4 (2.11%)
Medium	2,138 (67.96%)	28 (62.22%)	2,260 (72.14%)	46 (77.97%)	2,269 (72.75%)	55 (74.32%)	2,362 (76.64%)	84 (77.06%)	2,319 (77.25%)	149 (78.42%)
Unclassified	894 (28.42%)	17 (37.78%)	799 (25.5%)	11 (18.64%)	805 (25.81%)	16 (21.62%)	688 (22.32%)	24 (22.02%)	666 (22.19%)	37 (19.47%)
Dose reduction, yes (any agent)	544 (17.29%)	7 (15.56%)	559 (17.84%)	16 (27.12%)	612 (19.62%)	15 (20.27%)	694 (22.52%)	21 (19.27%)	813 (27.08%)	59 (31.05%)
Myelosuppressive agents, mean (SD)	1.6 (0.72)	1.7 (0.75)	1.8 (0.71)	1.7 (0.60)	1.7 (0.67)	1.7 (0.64)	1.7 (0.60)	1.6 (0.56)	1.7 (0.55)	1.8 (0.57)
Number dose reduced, mean (SD)	0.2 (0.47)	0.2 (0.44)	0.2 (0.49)	0.3 (0.57)	0.2 (0.50)	0.2 (0.45)	0.3 (0.53)	0.2 (0.45)	0.3 (0.56)	0.4 (0.59)
Number not dose reduced, mean (SD)	1.4 (0.84)	1.6 (0.89)	1.6 (0.86)	1.4 (0.78)	1.5 (0.82)	1.5 (0.76)	1.4 (0.76)	1.4 (0.71)	1.4 (0.74)	1.4 (0.77)
Mean neutrophil count (SD), 1,000/mcL	4.8 (2.45)	5.5 (2.19)	4.9 (2.91)	4.5 (2.80)	5.2 (2.72)	5.1 (2.46)	5.8 (3.18)	5.6 (2.93)	6.5 (3.94)	7.6 (4.63)
Number of patients who developed FN in the first cycle of chemotherapy	94 (2.99%)	4 (8.89%)	121 (3.86%)	5 (8.47%)	114 (3.66%)	3 (4.05%)	129 (4.19%)	3 (2.75%)	197 (6.56%)	22 (11.58%)
Prior infection	8 (0.25%)	0 (0%)	59 (1.88%)	0 (0%)	164 (5.26%)	4 (5.41%)	399 (12.95%)	13 (11.93%)	1,228 (40.91%)	91 (47.89%)
Census level household income, median	\$47,500	\$50,224	\$55,033	\$51,222	\$56,343	\$55,835	\$57,528	\$58,421	\$60,068.5	\$60,443
Median census level education, % with high school degree	49.9	54.2	57.0	52.2	58.9	53.2	60.1	60.3	60.6	63.6
Total number of comorbidities, mean (SD)	0.3 (0.66)	0.4 (0.75)	0.6 (0.89)	0.7 (0.90)	1.0 (1.09)	1.1 (1.01)	1.5 (1.33)	1.6 (1.47)	2.7 (1.96)	3.0 (2.06)
Previous cancer	81 (2.57%)	1 (2.22%)	20 (0.64%)	1 (1.69%)	15 (0.48%)	0 (0%)	8 (0.26%)	0 (0%)	2 (0.07%)	0 (0%)

Abbreviation: FN, febrile neutropenia.