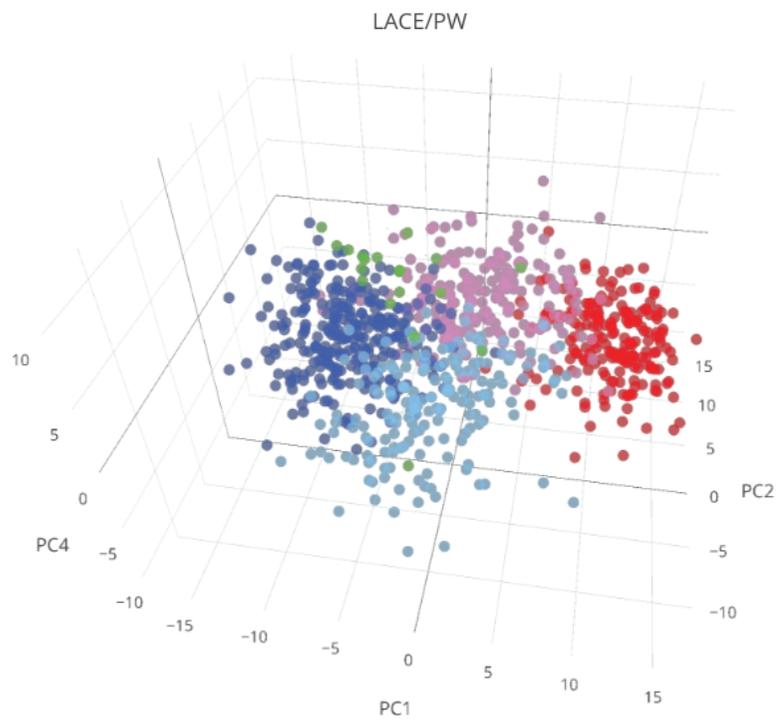
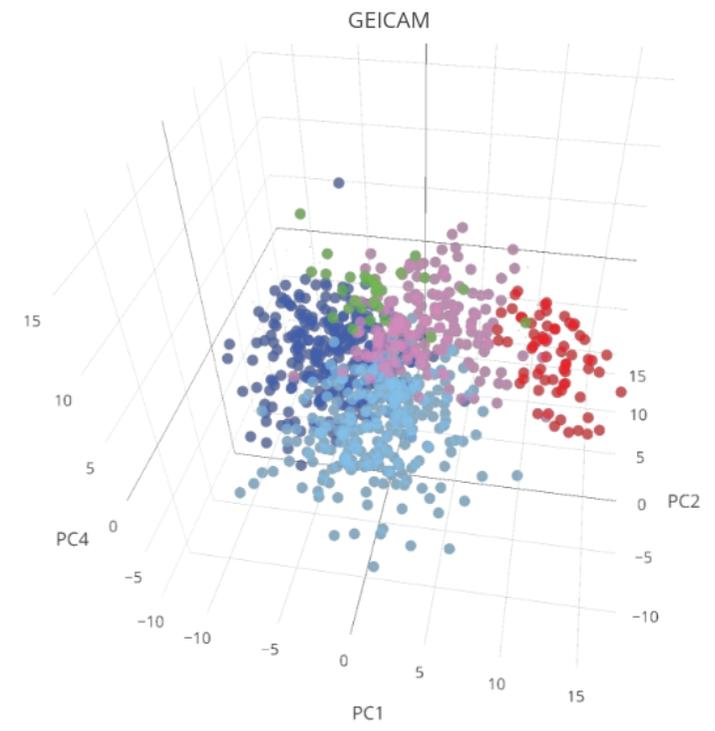


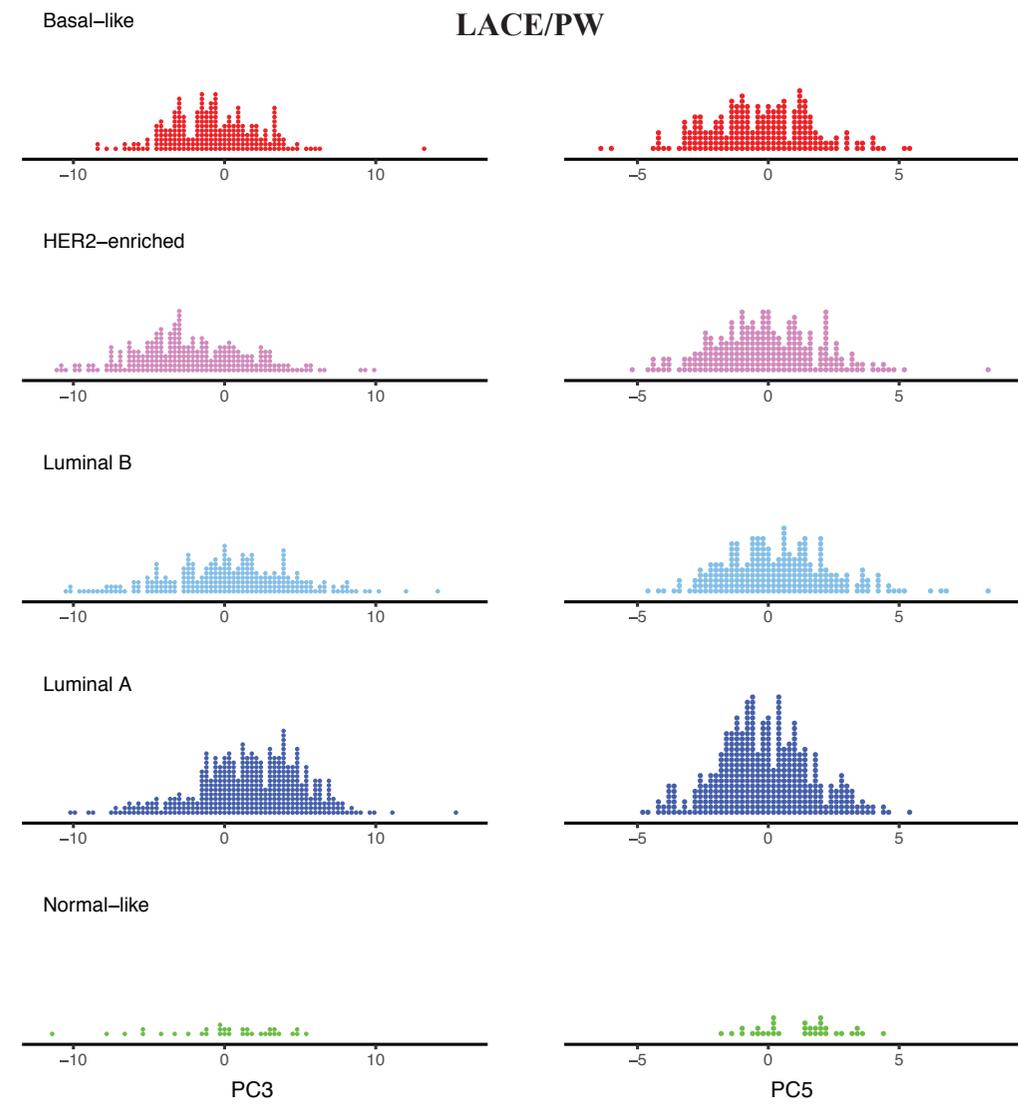
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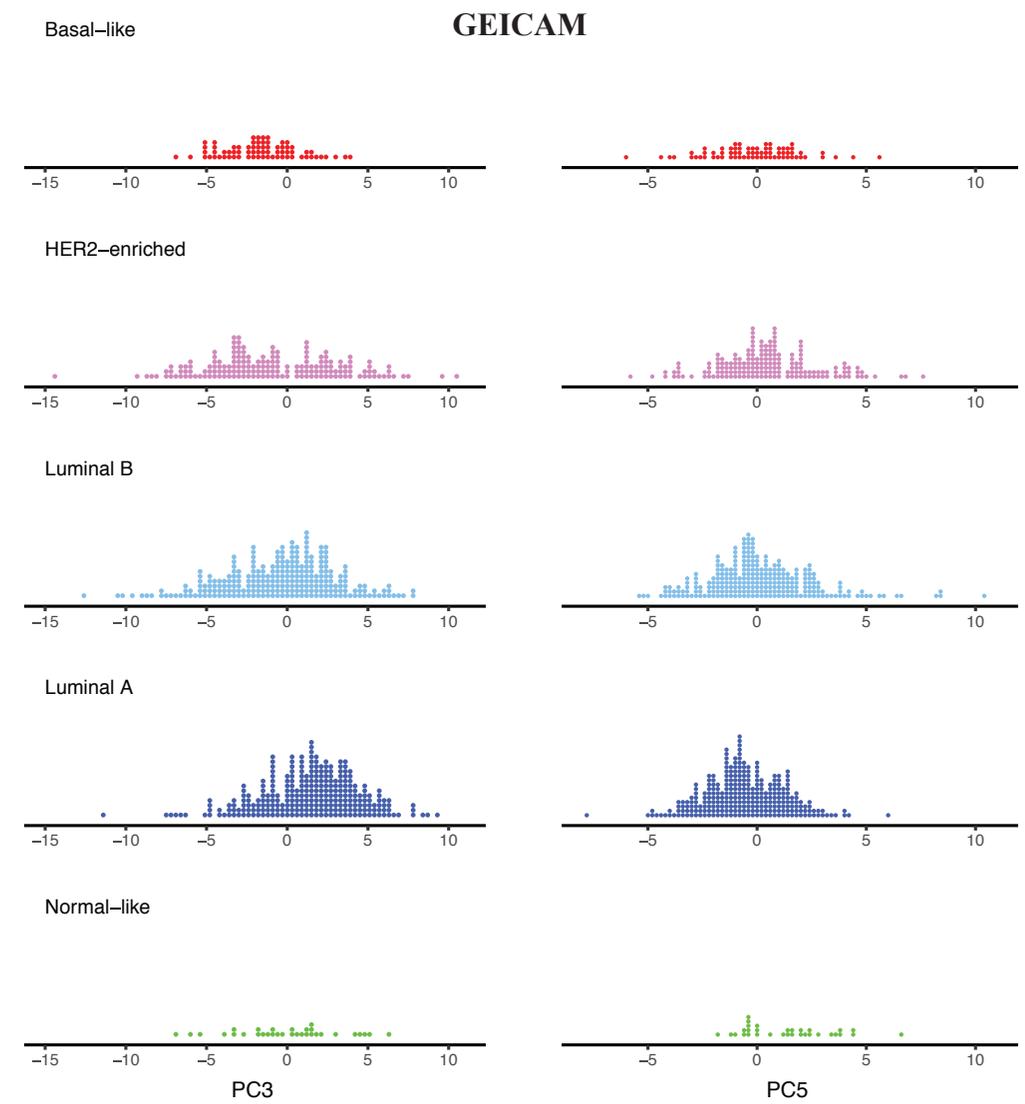
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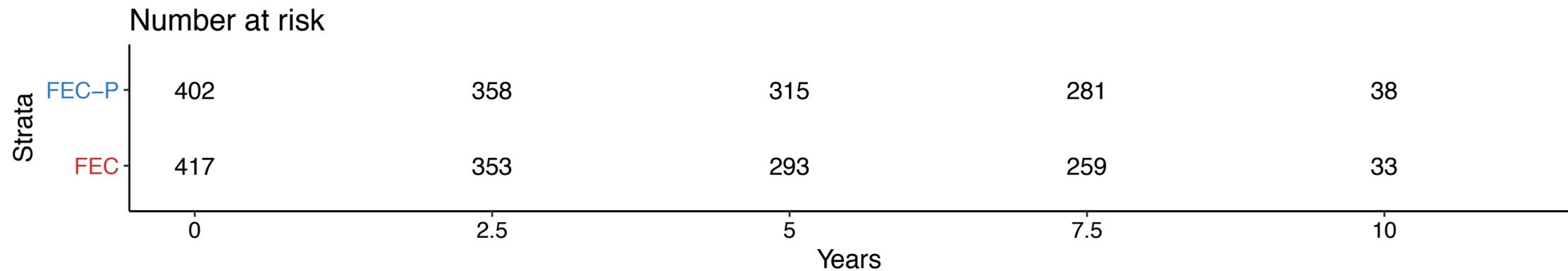
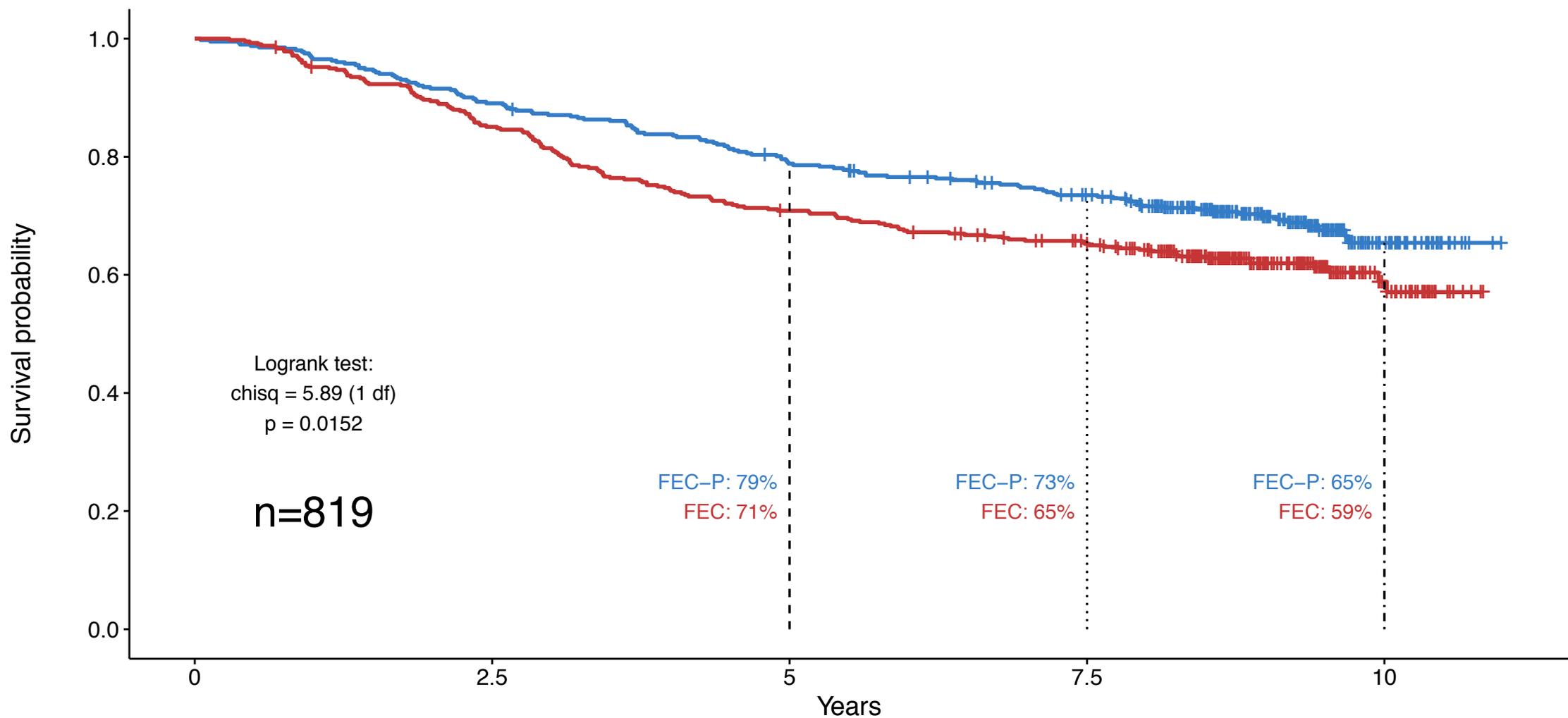
C

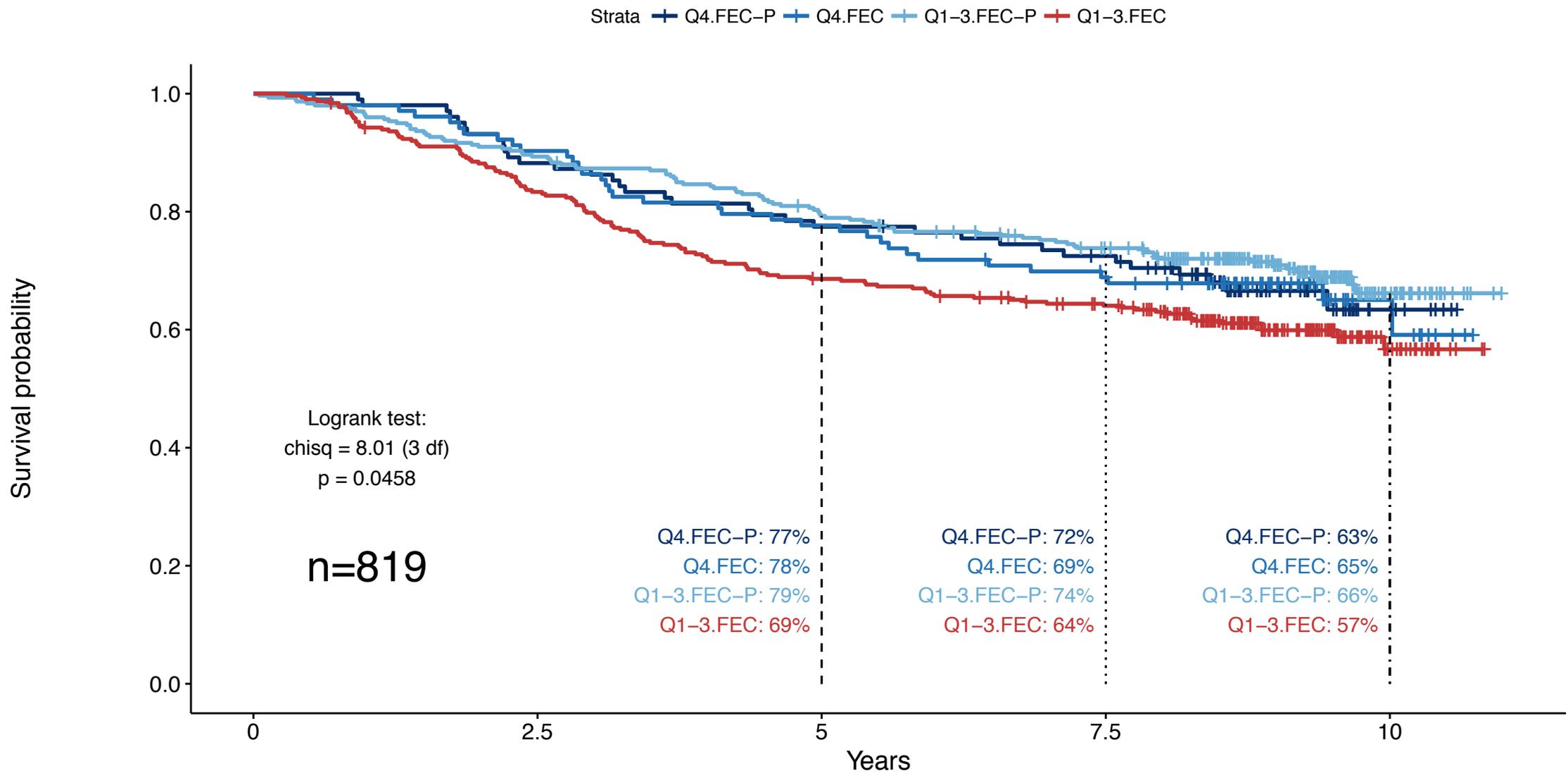


D



Strata + FEC-P + FEC



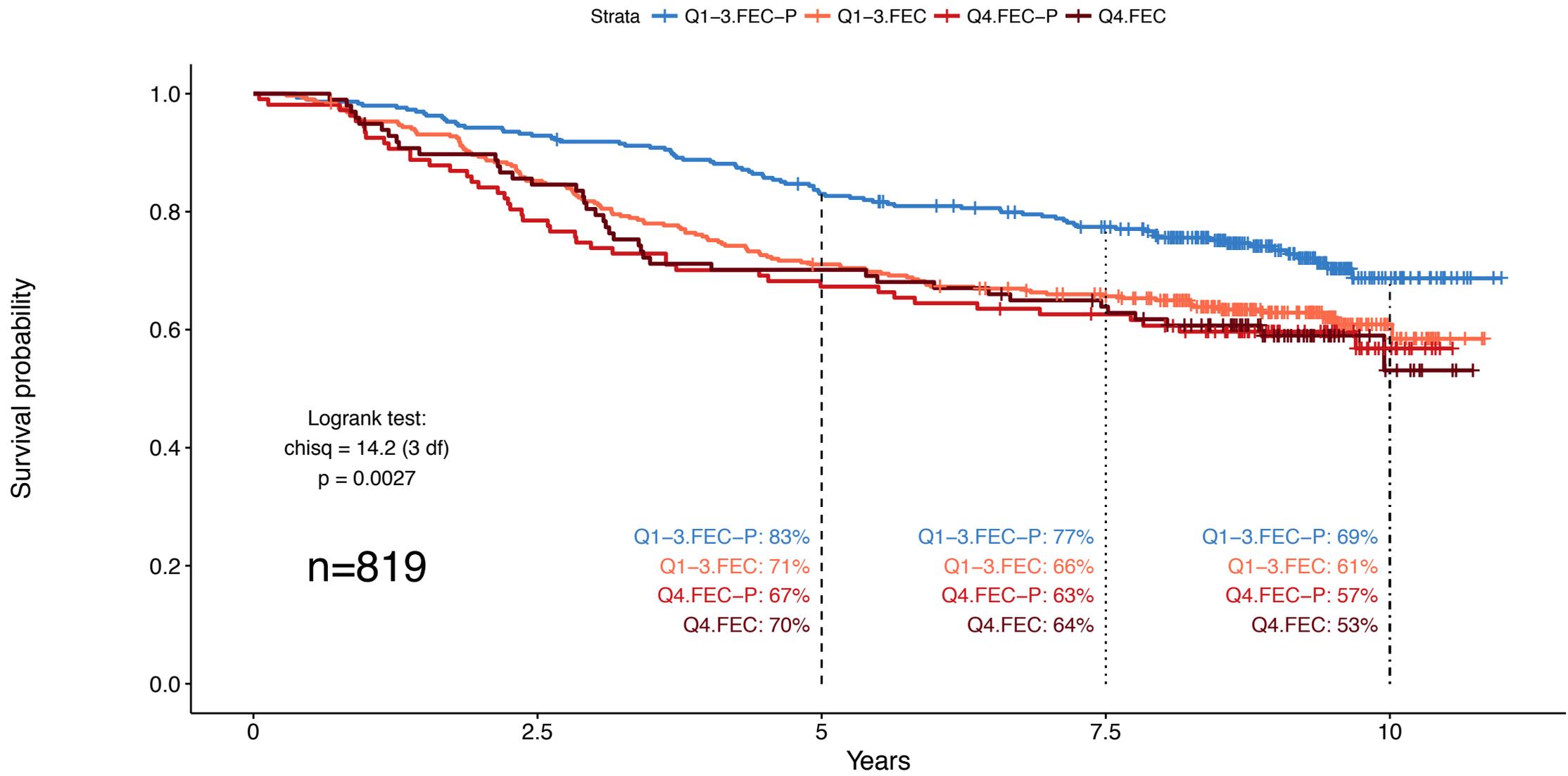


Number at risk

Strata	0	2.5	5	7.5	10
Q4.FEC-P	102	90	79	72	8
Q4.FEC	103	93	80	69	11
Q1-3.FEC-P	300	268	236	209	30
Q1-3.FEC	314	260	213	190	22

DFS by treatment arm, high PC4

FIGURE S4

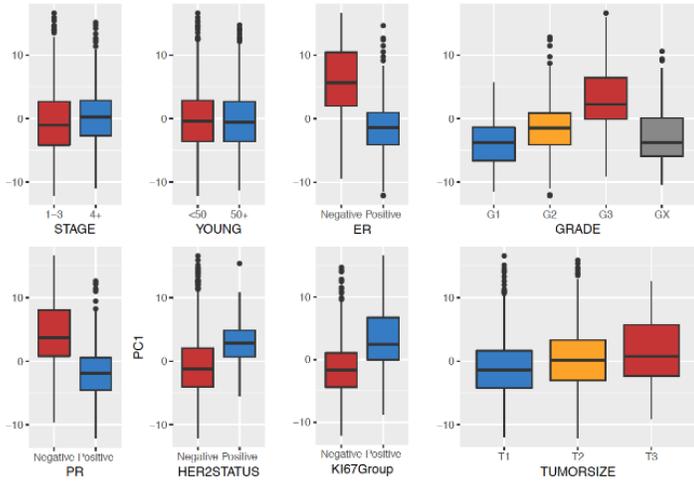


Number at risk

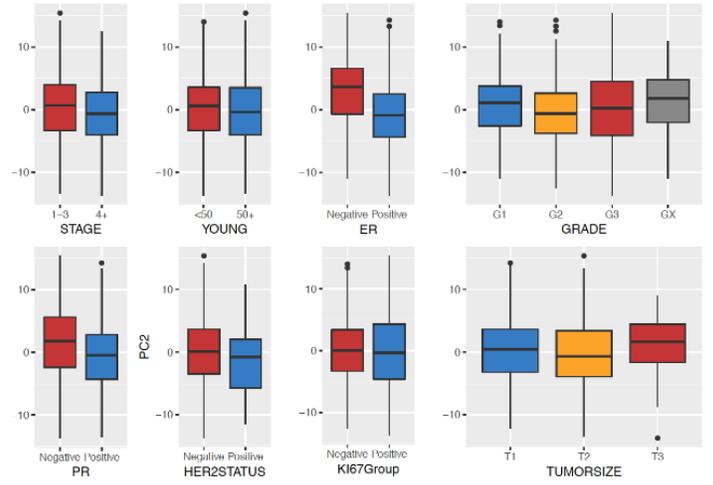
Strata	0	2.5	5	7.5	10
Q1-3.FEC-P	295	274	243	216	26
Q1-3.FEC	319	271	225	199	25
Q4.FEC-P	107	84	72	65	12
Q4.FEC	98	82	68	60	8

FIGURE S5

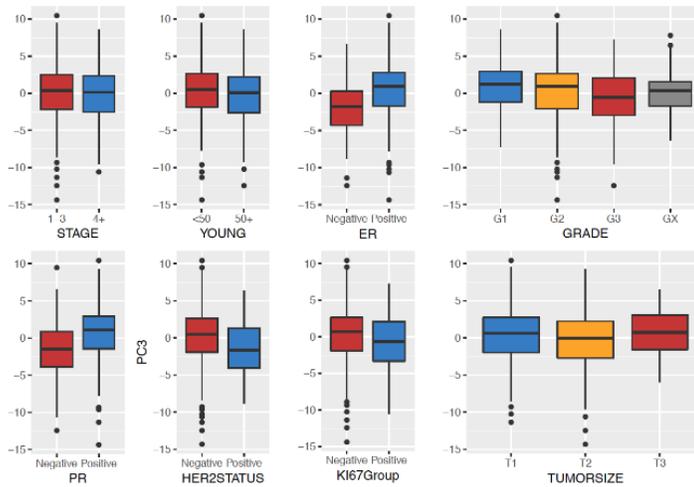
PC1



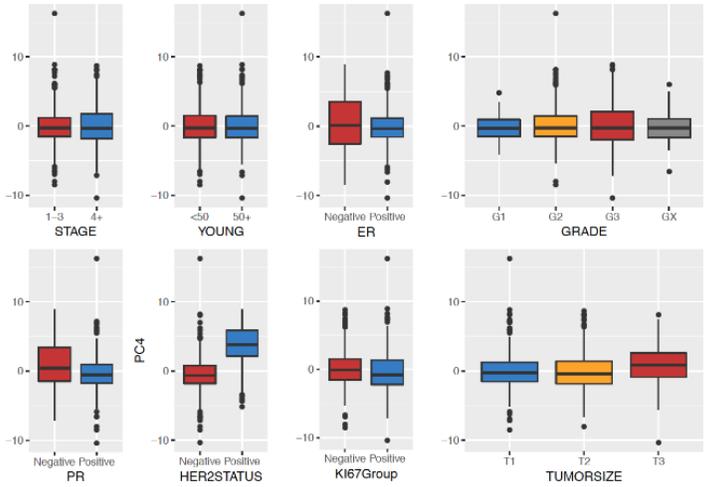
PC2



PC3



PC4



PC5

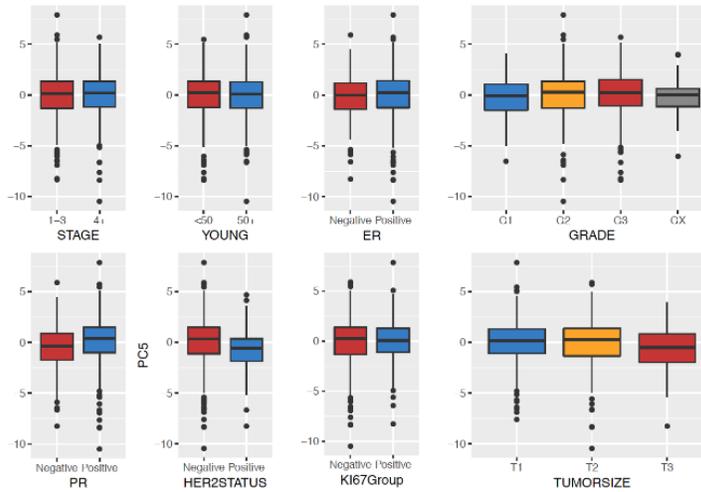


TABLE S1

	PC1	PC2	PC3	PC4	PC5
Eigenvalues (variance)	40.4616	25.1278	13.509	7.0587	4.2068
%Cumul. Variance	0.3046	0.1892	0.1017	0.0531	0.0317
PGR	-0.2811	-0.0954	0.335	-0.1923	0.2781
ESR1	-0.2514	-0.1858	0.2487	-0.1292	-0.0375
NAT1	-0.2342	-0.1189	0.2959	-0.0573	0.0444
FOXA1	-0.2186	-0.1888	0.1518	0.2437	-0.0639
MLPH	-0.1986	-0.1045	0.1694	0.1239	-0.2245
MAPT	-0.1752	-0.0928	0.1625	-0.0845	0.12
MYBL2	0.2323	-0.1256	0.0742	0.021	0.0861
EXO1	0.2025	-0.1507	0.1142	0.0118	-0.0671
CDC20	0.195	-0.0991	0.1046	-0.0051	-0.0022
BIRC5	0.1943	-0.1465	0.1389	-0.0002	-0.0306
CEP55	0.1816	-0.119	0.1292	-0.0005	0.0399
ORC6L	0.1807	-0.0569	0.0583	0.0231	0.0075
RRM2	0.1801	-0.1337	0.0978	0.014	0.0383
MELK	0.1754	-0.0643	0.0594	-0.0195	0.0805
CCNE1	0.1698	-0.0223	0.0008	0.022	0.0489
KIF2C	0.1682	-0.0867	0.0883	0.0214	-0.0355
KNTC2	0.1679	-0.0914	0.0903	-0.0444	0.069
MKI67	0.1589	-0.1065	0.1228	-0.0181	0.0556
CDC6	0.1579	-0.1392	0.0976	0.0774	-0.1266
CDCA1	0.1501	-0.1115	0.1506	-0.0239	0.0265
KRT14	-0.0235	0.393	0.3526	0.0603	-0.0022
KRT5	0.0528	0.3944	0.3062	0.1079	0.0518
KRT17	0.0888	0.3665	0.2469	0.1816	0.2391
SFRP1	0.0332	0.2693	0.0674	-0.1137	-0.26
MIA	0.0986	0.2368	0.1781	-0.1115	-0.1924
SLC39A6	-0.1161	-0.1015	0.2166	-0.0663	-0.133
BCL2	-0.0945	-0.0287	0.1505	-0.0457	-0.1773
TMEM45B	-0.1462	-0.042	-0.0488	0.5837	0.1404
GRB7	0.0522	-0.0671	0.0133	0.3506	-0.152
ERBB2	-0.0026	-0.0561	0.0216	0.3424	-0.0871
FGFR4	0.0301	-0.0458	0.0152	0.2116	-0.3159
EGFR	0.0342	0.1035	-0.0002	0.1595	-0.115
GPR160	-0.0852	-0.0756	0.0782	0.1564	-0.0929
FOXC1	0.0977	0.1095	0.0576	-0.0637	-0.224
MMP11	-0.0083	-0.0639	0.0137	0.1293	0.4308
CDH3	0.1146	0.1449	0.0801	0.1431	0.1431
CXXC5	-0.0536	-0.0893	0.1373	0.0164	-0.0827
ANLN	0.1341	-0.0563	0.0793	0.0291	0.07
PHGDH	0.1302	0.063	-0.0188	0.0031	0.0542
MYC	0.0401	0.0179	0.0254	-0.1238	-0.1296
UBE2C	0.1247	-0.1102	0.1111	-0.0192	-0.0298
TYMS	0.1238	-0.0691	0.0774	-0.0649	0.0554
PTTG1	0.1237	-0.0849	0.0731	-0.0183	-0.0199
CCNB1	0.1234	-0.0932	0.1055	0.0156	0.036
MDM2	-0.0249	-0.0192	0.0676	0.0141	-0.1066
UBE2T	0.0982	-0.0732	0.0963	0.0309	-0.0094
CENPF	0.071	-0.0268	0.091	0.0175	-0.0526
BAG1	-0.0241	-0.0154	0.0893	0.0118	-0.0329
BLVRA	-0.0189	-0.0435	0.0763	0.0704	-0.016
ACTR3B	-0.0132	-0.0063	0.0332	-0.0302	-0.0416

TABLE S2

INTRINSIC DIMENSIONS, DESCRIPTIVES												
Variable	Arm								Total sub-study (N=819, 100%)			
	FEC (N=417, 50.9%)				FEC-P (N=402, 49.1%)							
	Mean	s.d.	min.	max.	Mean	s.d.	min.	max.	Mean	s.d.	min.	max.
PC1	0.5	5.5	-12.0	16.6	-0.6	5.1	-12.1	15.2	0.0	5.4	-12.1	16.6
PC2	-0.1	5.3	-13.7	13.4	0.1	5.2	-13.5	15.4	0.0	5.3	-13.7	15.4
PC3	0.0	3.7	-14.4	10.4	0.0	3.5	-11.4	9.2	0.0	3.6	-14.4	10.4
PC4	-0.1	2.9	-10.4	16.3	0.1	2.8	-8.5	8.9	0.0	2.8	-10.4	16.3
PC5	0.0	2.3	-7.9	10.4	0.0	2.1	-5.5	8.4	0.0	2.2	-7.9	10.4

TABLE S3

MULTIVARIABLE COX PROPORTIONAL HAZARDS for DISEASE FREE SURVIVAL										
Model	Variables	Type	Reference	Tested	n	HR	95% CI		p	Wald p
PC5 + Age at dx										
	PC5	quantitative	na		819	0.88	0.78	0.99	0.037	0.070
	Age at dx	categorical	onset ≥50	onset<50		1.12	0.89	1.42	0.34	
PC5 + Nodal status										
	PC5	quantitative	na		819	0.88	0.78	0.99	0.030	2.9E-06
	Nodal status	categorical	1 - 3	4+		1.73	1.37	2.18	4.3E-06	
PC5 + Grade										
	PC5	quantitative	na		819	0.89	0.79	1.00	0.057	5.5E-04
	Histologic Grade	categorical	G1	G2		1.94	1.23	3.06	4.4E-03	
				G3		2.35	1.50	3.70	2.2E-04	
				GX		1.48	0.79	2.79	0.22	
PC5 + Tumor Size										
	PC5	quantitative	na		819	0.87	0.77	0.98	0.021	2.2E-06
	Tumor size	categorical	T1	T2		1.67	1.29	2.16	8.4E-05	
				T3		2.69	1.71	4.22	1.8E-05	
PC5 + ER status										
	PC5	quantitative	ER		815	0.88	0.78	0.99	0.031	0.013
	ER status	categorical	positive	negative		1.34	1.02	1.76	0.036	
PC5 + PR status										
	PC5	quantitative	na		814	0.85	0.75	0.96	7.1E-03	1.6E-04
	PR status	categorical	positive	negative		1.58	1.23	2.02	2.9E-04	
PC5 + Her2-status										
	PC5	quantitative	na		812	0.85	0.76	0.96	0.011	5.7E-04
	Her2 status	categorical	negative	positive		1.67	1.23	2.26	1.0E-03	
PC5 + Ki-67 status										
	PC5	quantitative	na		799	0.89	0.79	1.00	0.055	2.7E-03
	Ki-67 status	categorical	<14%	≥14%		1.42	1.11	1.81	5.1E-03	
PC5, adjusted for all clinical-pathologic characteristics										
	PC5	quantitative	na		819	0.84	0.74	0.95	5.9E-03	4.5E-08
	Age at dx	categorical	onset ≥50	onset<50		1.07	0.84	1.36	0.58	
	Nodal status	categorical	1 - 3	4+		1.43	1.12	1.83	4.4E-03	
	Histologic Grade	categorical	G1	G2		1.60	1.00	2.54	0.050	
				G3		1.59	0.98	2.58	0.059	
				GX		1.08	0.57	2.05	0.82	
	Tumor size	categorical	T1	T2		1.38	1.06	1.80	0.017	
				T3		2.24	1.39	3.64	1.0E-03	
	ER status	categorical	positive	negative		0.90	0.63	1.29	0.57	
	PR status	categorical	positive	negative		1.42	1.03	1.98	0.035	
	Her2 status	categorical	negative	positive		1.32	0.95	1.83	0.093	
	Ki-67 status	categorical	<14%	≥14%	1.11	0.85	1.45	0.45		

TABLE S4

MULTIVARIABLE COX PROPORTIONAL HAZARDS FOR INTERACTION OF CLASSIC RISK FACTORS WITH TREATMENT									
Model	Variables	Type	Reference	Tested	n	HR	95% CI	p	Interaction p
CLINICAL-PATHOLOGICAL CHARACTERISTICS									
TREATMENT ARM + Age at dx									
	Treatment Arm * Age at dx	INTERACTION					1.29 0.81 2.07		0.29
	Treatment Arm	categorical	FEC	FEC-P	819	1.01	0.74 1.37	0.015	
	Age at dx	categorical	onset ≥50	onset<50		1.29	0.81 2.07	0.97	
TREATMENT ARM + Nodal status									
	Treatment Arm * Nodal status	INTERACTION				0.68	0.43 1.09		0.11
	Treatment Arm	categorical	FEC	FEC-P	819	0.89	0.64 1.23	0.48	
	Nodal status	categorical	1 - 3	4+		2.05	1.50 2.80	6.3E-06	
TREATMENT ARM + Histologic Grade									
	Treatment Arm * G2	INTERACTION				2.30	0.84 6.30		0.104
	Treatment Arm * G3	INTERACTION				2.40	0.88 6.54		0.087
	Treatment Arm * GX	INTERACTION				1.72	0.45 6.63		0.428
	Treatment Arm	categorical	FEC	FEC-P	819	0.35	0.14 0.89	0.027	
	Histologic Grade	categorical	G1	G2		1.45	0.84 2.50	0.187	
				G3		1.72	1.00 2.97	0.050	
				GX		1.25	0.57 2.75	0.581	
TREATMENT ARM + Tumor Size									
	Treatment Arm * T2	INTERACTION				0.92	0.55 1.53		0.74
	Treatment Arm * T3	INTERACTION				2.33	0.94 5.80		0.07
	Treatment Arm	categorical	FEC	FEC-P	819	0.76	0.50 1.15	0.20	
	Tumor size	categorical	T1	T2		1.70	1.20 2.40	0.0027	
				T3		1.68	0.85 3.33	0.14	
TREATMENT ARM + ER status									
	Treatment Arm * ER status	INTERACTION				1.15	0.66 2.00		0.61
	Treatment Arm	categorical	FEC	FEC-P	815	0.74	0.56 0.96	0.026	
	ER status	categorical	positive	negative		1.23	0.86 1.77	0.26	
TREATMENT ARM + PR status									
	Treatment Arm * PR status	INTERACTION				0.98	0.59 1.60		0.92
	Treatment Arm	categorical	FEC	FEC-P	814	0.78	0.59 1.05	0.10	
	PR status	categorical	positive	negative		1.46	1.06 2.01	0.019	
TREATMENT ARM + Her2 status									
	Treatment Arm * Her2 status	INTERACTION				0.74	0.41 1.36		0.34
	Treatment Arm	categorical	FEC	FEC-P	812	0.77	0.59 1.00	0.047	
	Her2 status	categorical	negative	positive		1.93	1.26 2.96	0.0026	
TREATMENT ARM + Ki-67 status									
	Treatment Arm * Ki-67 status	INTERACTION				1.23	0.75 2.02		0.41
	Treatment Arm	categorical	FEC	FEC-P	799	0.71	0.53 0.96	0.025	
	Ki-67 status	categorical	<14%	≥14%		1.29	0.93 1.78	0.13	
INTRINSIC SUBTYPES									
TREATMENT ARM + Intrinsic Subtype									
	Treatment Arm * Luminal B	Subtype				0.98	0.53 1.81		0.94
	Treatment Arm * Her2-enriched	Subtype				1.08	0.56 2.07		0.82
	Treatment Arm * Basal-like	Subtype				0.82	0.33 2.07		0.68
	Treatment Arm * Normal-like	Subtype				0.48	0.11 2.15		0.33
	Treatment Arm	categorical	FEC	FEC-P	819	0.79	0.49 1.28	0.34	
	Subtype	categorical	Luminal A	Luminal B		1.80	1.19 2.73	0.0055	
				Her2-enriched		2.12	1.34 3.35	0.0014	
				Basal-like		2.15	1.24 3.73	0.006	
				Normal-like		1.47	0.58 3.76	0.42	

TABLE S5

CLINICAL-PATHOLOGICAL CHARACTERISTICS BY QUARTILES OF PC3 & PC4										
Variable	All		PC3				PC4			
	n	%	Q1-Q3		Q4		Q1-Q3		Q4	
			n	%	n	%	n	%	n	%
All	819		614		205		614		205	
Age (years)										
<50	394	48.1%	281	45.8%	113	55.1%	294	47.9%	100	48.8%
≥ 50	425	51.9%	333	54.2%	92	44.9%	320	52.1%	105	51.2%
Nodal Status										
1-3	506	61.8%	375	61.1%	131	63.9%	393	64.0%	113	55.1%
>3	313	38.2%	239	38.9%	74	36.1%	221	36.0%	92	44.9%
Histologic Grade										
G1	108	13.2%	74	12.1%	34	16.6%	92	15.0%	16	7.8%
G2	337	41.1%	236	38.4%	101	49.3%	253	41.2%	84	41.0%
G3	315	38.5%	256	41.7%	59	28.8%	221	36.0%	94	45.9%
GX	59	7.2%	48	7.8%	11	5.4%	48	7.8%	11	5.4%
Primary Tumor Size										
T1	342	41.8%	246	40.1%	96	46.8%	262	42.7%	80	39.0%
T2	431	52.6%	337	54.9%	94	45.9%	324	52.8%	107	52.2%
T3	46	5.6%	31	5.0%	15	7.3%	28	4.6%	18	8.8%
Estrogen receptor (IHC)										
Negative	172	21.0%	156	25.4%	16	7.8%	108	17.6%	64	31.2%
Positive	643	78.5%	455	74.1%	188	91.7%	503	81.9%	140	68.3%
Progesterone receptor (IHC)										
Negative	246	30.0%	216	35.2%	30	14.6%	152	24.8%	94	45.9%
Positive	568	69.4%	394	64.2%	174	84.9%	458	74.6%	110	53.7%
Her2 status (CISH)										
Negative	696	85.0%	511	83.2%	185	90.2%	586	95.4%	110	53.7%
Positive	116	14.2%	98	16.0%	18	8.8%	22	3.6%	94	45.9%
Ki-67 (IHC)										
Low (<14%)	557	68.0%	407	66.3%	150	73.2%	413	67.3%	144	70.2%
High (≥14%)	242	29.5%	192	31.3%	50	24.4%	183	29.8%	59	28.8%
PAM50 Intrinsic subtypes										
Luminal A	280	34.2%	175	28.5%	105	51.2%	253	41.2%	27	13.2%
Luminal B	261	31.9%	213	34.7%	48	23.4%	206	33.6%	55	26.8%
Her2-enriched	175	21.4%	132	21.5%	43	21.0%	54	8.8%	121	59.0%
Basal-like	71	8.7%	68	11.1%	3	1.5%	71	11.6%	0	0.0%
Normal-like	32	3.9%	26	4.2%	6	2.9%	30	4.9%	2	1.0%

Color key

	≥5% absolute difference compared to percentage in the overall dataset
--	---

	<5% absolute difference compared to percentage in the overall dataset
--	---

TABLE S6

INTRINSIC DIMENSIONS, DESCRIPTIVES by OTHER TUMOR CHARACTERISTICS										
Variable	PC1		PC2		PC3		PC4		PC5	
	mean	sd								
All	0.0	5.4	0.0	5.3	0.0	3.6	0.0	2.8	0.0	2.2
Age at dx										
<50	0.1	5.4	0.3	5.2	0.3	3.5	0.1	2.9	0.0	2.2
≥ 50	0.0	5.3	-0.3	5.3	-0.2	3.6	0.0	2.8	0.1	2.2
Nodal Status										
1-3	-0.3	5.7	0.4	5.4	0.1	3.6	-0.1	2.7	0.0	2.2
>3	0.5	4.8	-0.6	4.9	0.0	3.5	0.2	3.1	0.1	2.2
Histologic grade										
G1	-3.8	3.6	0.9	5.1	0.9	3.0	-0.3	1.7	0.2	1.9
G2	-1.5	4.2	-0.6	4.9	0.4	3.8	0.1	2.7	0.0	2.3
G3	3.3	5.2	0.1	5.7	-0.7	3.5	0.1	3.3	-0.1	2.2
GX	-2.3	5.4	1.1	5.0	0.3	2.9	-0.1	2.3	0.2	1.8
Tumor Size										
T1	-1.0	5.1	0.3	5.1	0.3	3.6	0.0	2.8	0.0	2.2
T2	0.6	5.4	-0.4	5.4	-0.2	3.6	-0.1	2.8	0.0	2.2
T3	1.5	5.8	0.9	5.0	0.6	3.1	0.6	3.3	0.7	2.4
Estrogen receptor status (IHC)										
Negative	5.5	5.9	2.9	5.2	-2.0	3.5	0.6	4.1	0.1	2.2
Positive	-1.5	4.1	-0.8	5.0	0.6	3.4	-0.1	2.4	0.0	2.2
Progesterone receptor status (IHC)										
Negative	4.4	5.3	1.3	5.7	-1.5	3.6	0.9	3.5	0.5	2.2
Positive	-1.9	4.1	-0.6	5.0	0.7	3.4	-0.3	2.4	-0.2	2.2
Her2 status (FISH)										
Negative	-0.5	5.5	0.2	5.3	0.3	3.5	-0.6	2.3	-0.1	2.2
Positive	2.9	3.3	-1.2	5.0	-1.6	3.6	3.6	3.0	0.7	2.0
Ki-67 status (IHC)										
Low (<14%)	-1.4	4.7	0.0	4.9	0.4	3.5	0.2	2.7	0.1	2.2
High (≥14%)	3.4	5.3	-0.1	5.9	-0.7	3.6	-0.3	3.3	-0.2	2.2
Subtype Prediction										
Luminal A	-4.3	3.1	1.2	3.3	1.4	3.1	-0.5	1.9	-0.5	1.9
Luminal B	0.3	3.0	-5.3	3.1	-0.4	3.5	-0.5	2.4	0.1	2.4
Her2-enriched	2.4	3.2	1.5	3.3	-0.8	4.1	2.8	2.9	0.5	2.3
Basal-like	11.4	2.2	6.6	3.0	-1.6	2.3	-2.8	2.3	-0.1	2.0
Normal-like	-3.7	4.1	10.0	2.6	0.0	3.2	-0.6	1.8	1.4	2.0

Color key

	mean value >2.0
	mean value <-2.0