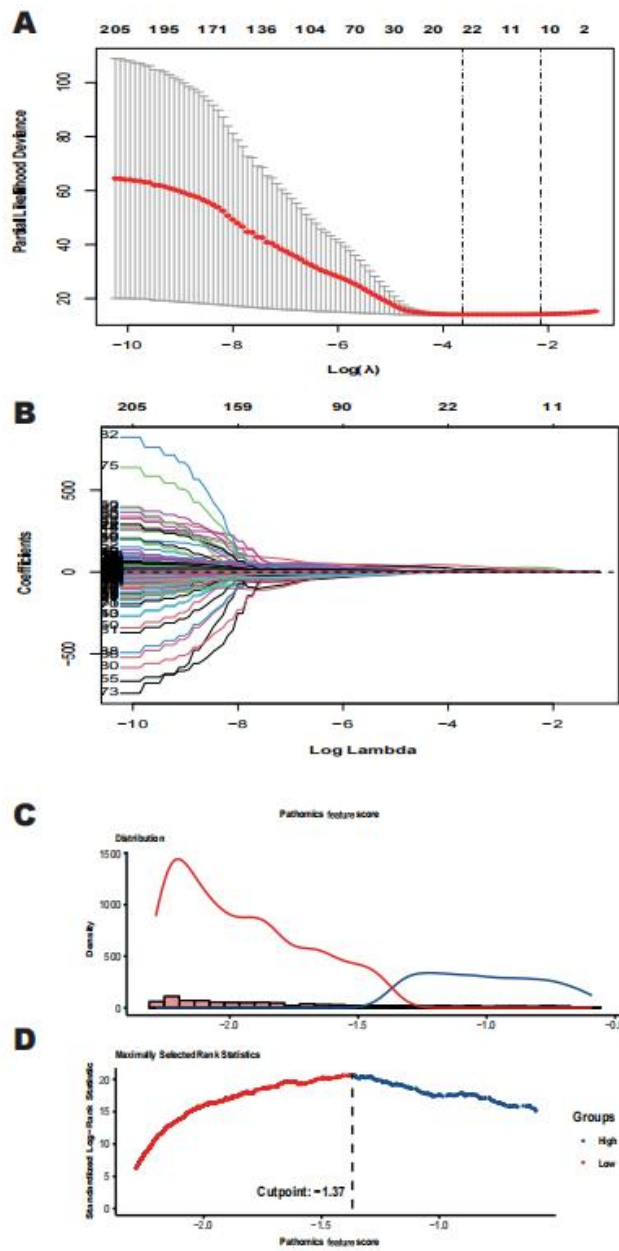
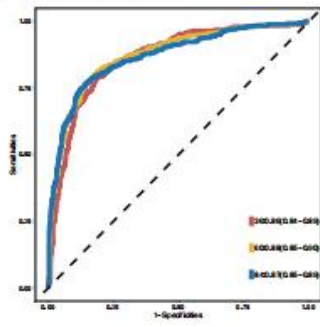
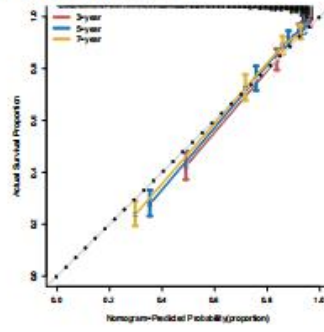
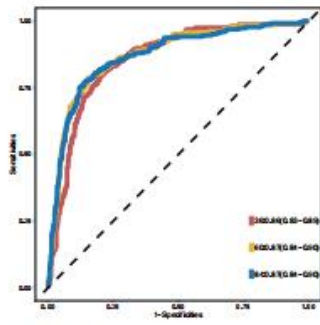




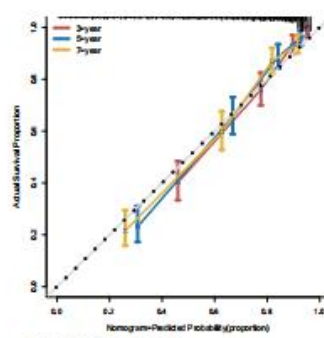
Supplementary Figure 1. Pathomics signature construction. (A) Tuning parameter (λ) selection for the LASSO-Cox regression model *via* 10-fold cross-validation. (B) Profiles of coefficients from the LASSO-Cox regression model of the extracted pathomics features. (C) Histogram showing the density distribution for high- and low-PS_{GC} groups divided by the optimum cutoff value. (D) Scatter plot showing the standardized log-rank statistic value for each PS_{GC} cutoff value. The cutoff value was determined *via* the two-sided maximally selected rank statistics. LASSO, least absolute shrinkage, and selection operator. **Abbreviations:** PS_{GC}, pathomics signature of gastric cancer.

A HMUCH cohort**B** HMUCH cohort

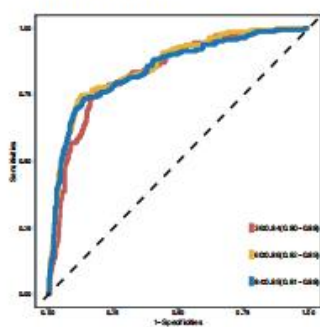
HMUSH cohort



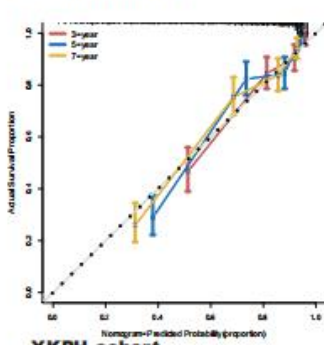
HMUSH cohort



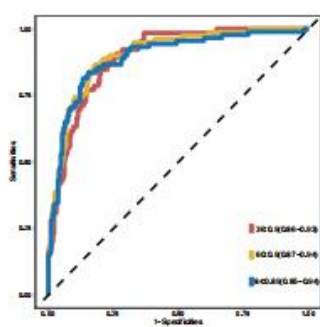
QMUSH cohort



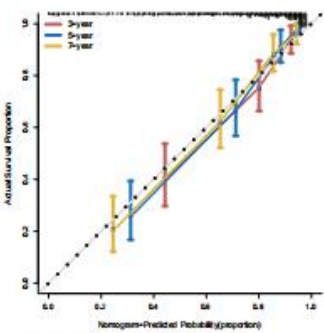
QMUSH cohort



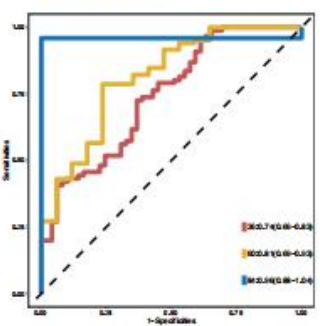
YKPH cohort



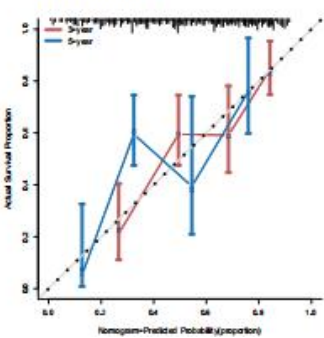
YKPH cohort



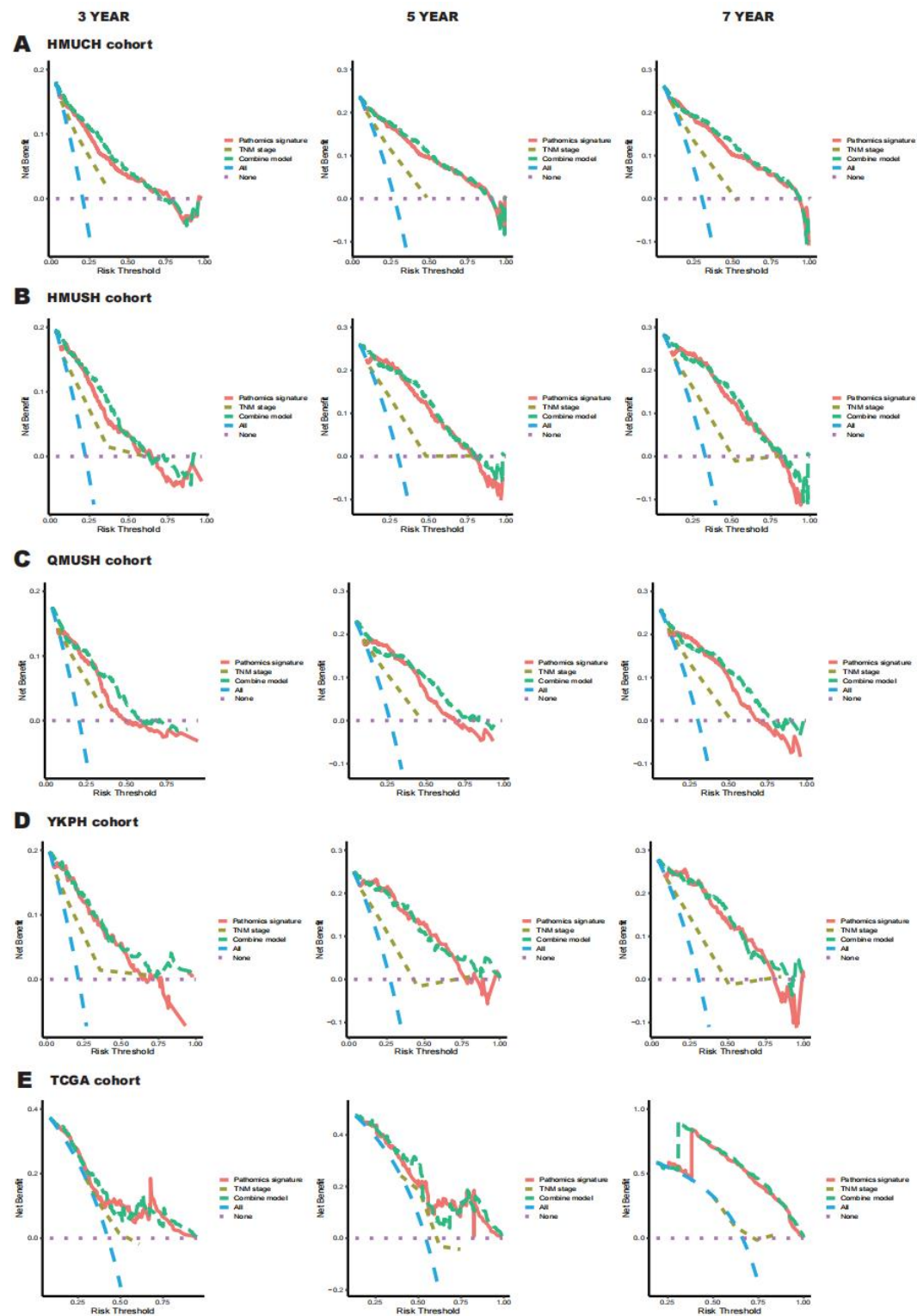
TCGA cohort



TCGA cohort

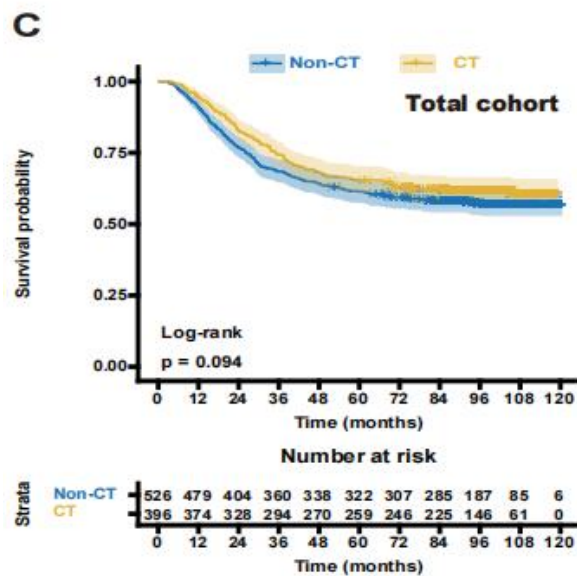
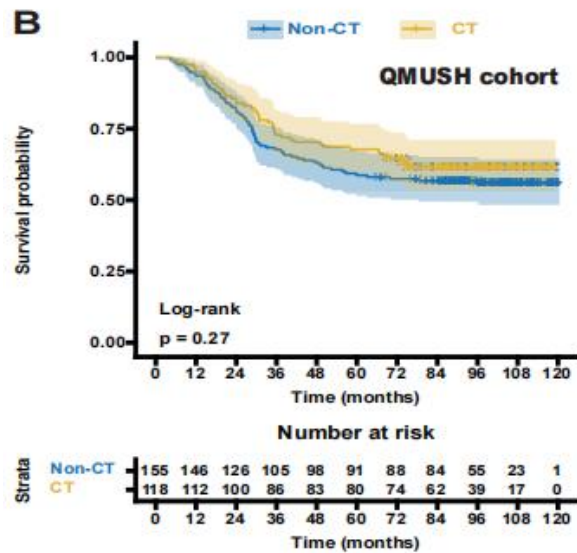
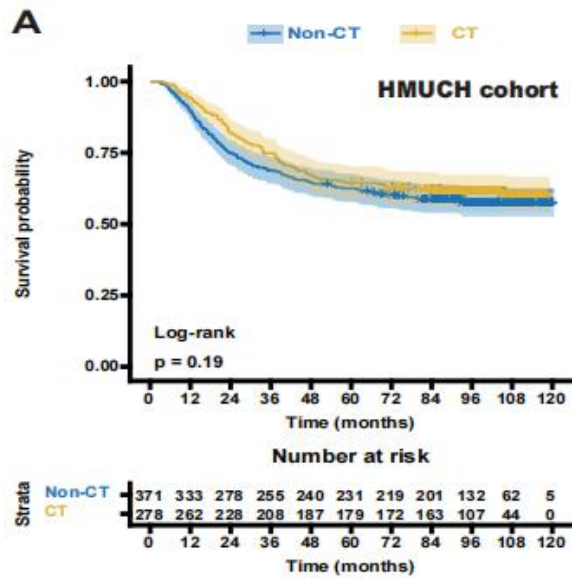


Supplementary Figure 2. Time-dependent ROC curves and decision curve analysis of the pathomics signature. (A) 3-, 5- and 7-year time-dependent ROC curves of the pathomics signature for OS in the training and validation cohorts. **(B)** 3-, 5- and 7-year decision curve analysis of OS in the training and validation cohorts. **Abbreviations:** OS, overall survival; TNM, tumor-node-metastasis.

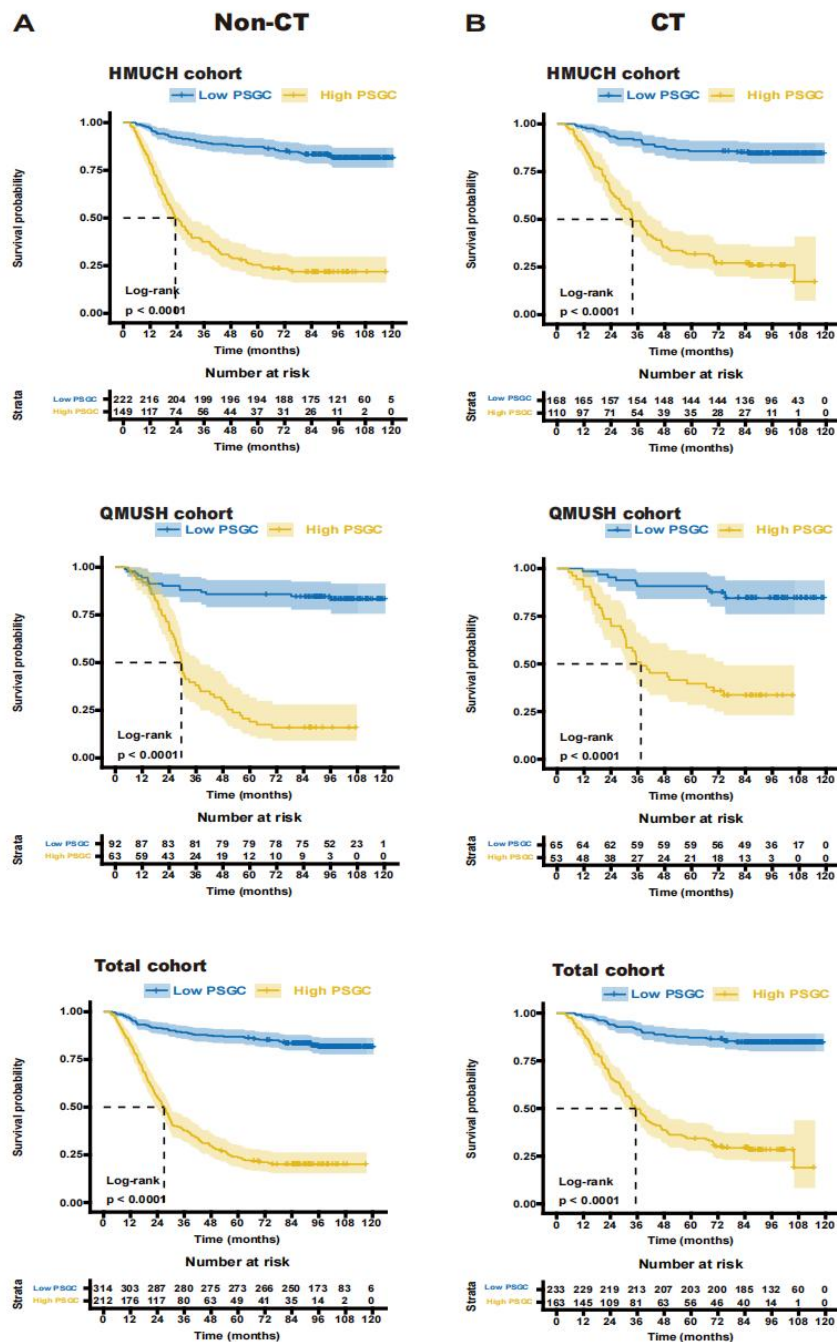


Supplementary Figure 3. Calibration curves of the pathomics signature. (A) Calibration curves of the pathomics signature for 3-, 5- and 7-year OS in the H MUCH cohort. **(B)** Calibration curves of the pathomics signature for 3-, 5- and 7-year OS in the HMUSH cohort. **(C)** Calibration curves of the pathomics signature for 3-, 5- and 7-year OS in the QMUSH

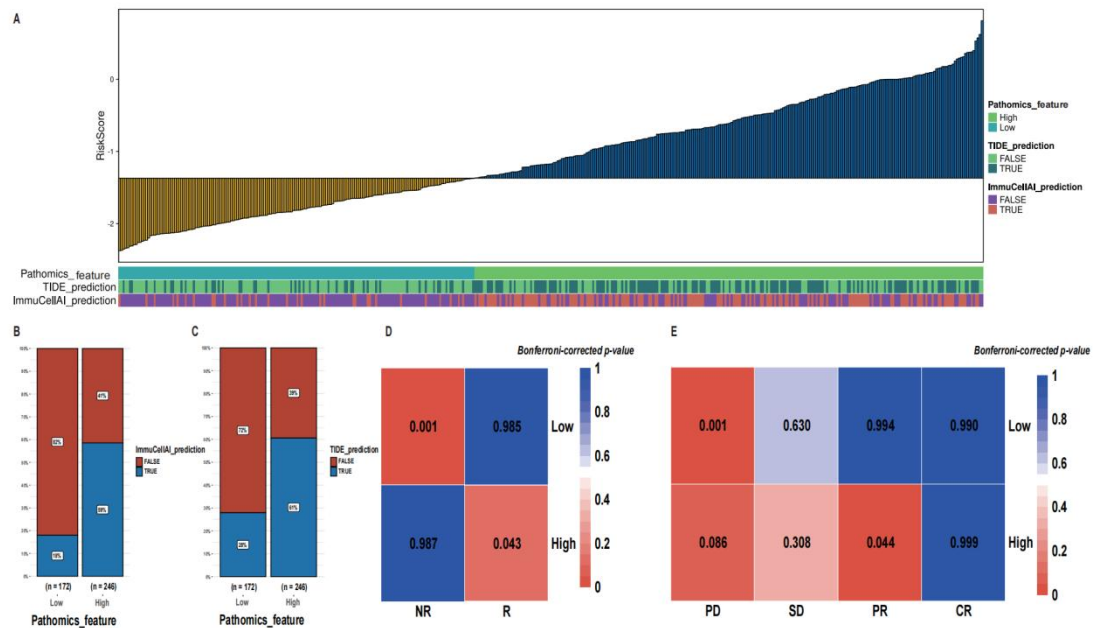
cohort. **(D)** Calibration curves of the pathomics signature for 3-, 5- and 7-year OS in the YKPH cohort. **(E)** Calibration curves of the pathomics signature for 3- and 5-year OS in the TCGA cohort.



Supplementary Figure 4. Kaplan–Meier analyses of OS in stage II and stage III gastric cancer based on adjuvant chemotherapy. (A) The OS rate difference between the CT and non-CT patients in the H MUCH cohort. (B) The OS rate difference between the CT and non-CT patients in the QMUSH cohort. (C) The OS rate difference between the CT and non-CT patients in the total cohort. Abbreviations: CT, chemotherapy, OS, overall survival.



Supplementary Figure 5. Kaplan-Meier analysis of OS in stage II and stage III gastric cancer with or without adjuvant chemotherapy according to the pathomics signature. (A) The OS rate difference between the high- and low-PS_{GC} patients with adjuvant chemotherapy. **(B)** The OS rate difference between the high- and low-PS_{GC} patients without adjuvant chemotherapy. **Abbreviations:** OS overall survival, PS_{GC}, pathomics signature of gastric cancer.



Supplementary Figure 6. Identification of potential response to immunotherapy for the pathomics signature. (A) The heatmap shows the association between the pathomics signature and the predicted response outcomes. (B) The bar plot shows the distribution of the pathomics signature and ImmuCellAI prediction groups. (C) The bar plot shows the distribution of the pathomics signature and TIDE prediction groups. (D, E) The heatmap shows the potential response to the anti-PD-1 therapy for the different PS_{GC} subgroups. **Abbreviations:** PS_{GC}, pathomics signature of gastric cancer.

Supplementary Table 1. Characteristics of the patients according to the PS_{GC} across the training and validation cohorts

Variables	HMUCH cohort (n = 1,257)			HMUSH cohort (n = 752)			QMUSH cohort (n = 540)			YKPH cohort (n = 319)			TCGA-STAD cohort (n = 270)		
	Low	High	P	Low	High	P	Low	High	P	Low	High	P	Low	High	P
	(n = 894)	(n = 363)	value	(n = 470)	(n = 282)	value	(n = 370)	(n = 170)	value	(n = 212)	(n = 107)	value	(n = 72)	(n = 198)	value
Age, years			0.001			<0.001			0.826			0.002			0.811
Mean	58.20	59.83		58.96	60.82		57.65	57.45		57.59	60.45		65.39	64.93	
(SD)	(9.73)	(9.98)		(9.90)	(10.92)		(9.55)	(10.55)		(10.09)	(10.67)		(11.60)	(10.71)	
Median	59.00	61.00		59.00	61.00		59.00	58.50		58.50	60.00		67.00	67.00	
(Q1-Q3)	(52.00-64.00)	(53.00-66.00)		(52.25-65.00)	(53.25-68.00)		(51.25-64.00)	(50.25-65.00)		(50.00-65.00)	(55.50-67.00)		(57.50-73.50)	(58.00-72.00)	
Age, years			0.006			<0.001			0.246			0.188			0.502
≤ 65	707 (79.08%)	261 (71.90%)		366 (77.87%)	183 (64.89%)		299 (80.81%)	130 (76.47%)		163 (76.89%)	75 (70.09%)		35 (49.30%)	88 (44.67%)	
> 65	187 (20.92%)	102 (28.10%)		104 (22.13%)	99 (35.11%)		71 (19.19%)	40 (23.53%)		49 (23.11%)	32 (29.91%)		36 (50.70%)	109 (55.33%)	
Early-onset			0.125			0.455			0.466			0.050			0.521
Yes	184 (20.58%)	61 (16.80%)		85 (18.09%)	45 (15.96%)		83 (22.43%)	43 (25.29%)		54 (25.47%)	17 (15.89%)		6 (8.45%)	22 (11.17%)	
No	710 (79.42%)	302 (83.20%)		385 (81.91%)	237 (84.04%)		287 (77.57%)	127 (74.71%)		158 (74.53%)	90 (84.11%)		65 (91.55%)	175 (88.83%)	
Sex			0.981			0.205			0.751			0.706			0.877
Male	657 (73.49%)	267 (73.55%)		342 (72.77%)	193 (68.44%)		265 (71.62%)	124 (72.94%)		149 (70.28%)	73 (68.22%)		48 (66.67%)	130 (65.66%)	
Female	237 (26.51%)	96 (26.45%)		128 (27.23%)	89 (31.56%)		105 (28.38%)	46 (27.06%)		63 (29.72%)	34 (31.78%)		24 (33.33%)	68 (34.34%)	

	(26.51 %)	(26.45 %)	(27.23 %)	(31.56 %)	(28.38 %)	(27.06 %)	(29.72 %)	(31.78 %)	(33.33 %)	(34.34 %)
Lymph			<0	0.		0.		0.		0.
node			.0	61		04		06		83
harvest			01	4		5		2		4
Mean	26.57	29.12	26.62	26.16	28.65	30.20	29.28	26.39	25.00	20.51
(SD)	(11.01)	(11.38)	(11.77)	(12.65)	(12.33)	(10.57)	(13.22)	(12.50)	(22.90)	(15.26)
Median	26.00	27.00	26.00	28.00	27.00	29.00	28.00	25.00	17.00	15.50
(Q1-Q3)	(19.00- 33.00)	(21.00- 36.00)	(18.00- 33.00)	(18.00- 34.00)	(20.00- 36.00)	(22.00- 38.00)	(19.75- 37.00)	(18.00- 32.50)	(7.00-3 5.00)	(10.00- 27.25)
Lymph			<0	0.		0.		0.		0.
node			.0	15		02		09		91
harvest			01	8		1		5		8
	133	27	74	55	40	8	25	20	34	94
≤ 15	(14.88 %)	(7.44%)	(15.74 %)	(19.78 %)	(10.81 %)	(4.71%)	(11.79 %)	(18.69 %)	(49.28 %)	(50.00 %)
	761	336	396	223	330	162	187	87	35	94
> 15	(85.12 %)	(92.56 %)	(84.26 %)	(80.22 %)	(89.19 %)	(95.29 %)	(88.21 %)	(81.31 %)	(50.72 %)	(50.00 %)
Depth of			<0	<0		<0		<0		0.
invasion			.0	.0		.0		.0		20
			01	01		01		01		9
	310	16	150	17	140	18	62	5	6	8
T1	(34.68 %)	(4.41%)	(31.91 %)	(6.03%)	(37.84 %)	(10.59 %)	(29.25 %)	(4.67%)	(8.33%)	(4.04%)
	167	29	88	32	60	5	42	7	17	35
T2	(18.68 %)	(7.99%)	(18.72 %)	(11.35 %)	(16.22 %)	(2.94%)	(19.81 %)	(6.54%)	(23.61 %)	(17.68 %)
	327	217	175	163	136	111	82	66	28	101
T3	(36.58 %)	(59.78 %)	(37.23 %)	(57.80 %)	(36.76 %)	(65.29 %)	(38.68 %)	(61.68 %)	(38.89 %)	(51.01 %)
	90	101	57	70	34	36	26	29	21	54
T4	(10.07 %)	(27.82 %)	(12.13 %)	(24.82 %)	(9.19%)	(21.18 %)	(12.26 %)	(27.10 %)	(29.17 %)	(27.27 %)
Lymph			<0	<0		<0		<0		0.
node			.0	.0		.0		.0		02
metasta			01	01		01		01		7
sis										
	491	68	254	67	197	38	108	26	27	64
N0	(54.92 %)	(18.73 %)	(54.04 %)	(23.76 %)	(53.24 %)	(22.35 %)	(50.94 %)	(24.30 %)	(37.50 %)	(32.32 %)
	164	74	84	53	70	23	30	22	24	55
N1	(18.34 %)	(20.39 %)	(17.87 %)	(18.79 %)	(18.92 %)	(13.53 %)	(14.15 %)	(20.56 %)	(33.33 %)	(27.78 %)

	124	86	66	72	47	35	39	24	17	37
N2	(13.87	(23.69	(14.04	(25.53	(12.70	(20.59	(18.40	(22.43	(23.61	(18.69
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)
	115	135	66	90	56	74	35	35	4	42
N3	(12.86	(37.19	(14.04	(31.91	(15.14	(43.53	(16.51	(32.71	(5.56%	(21.21
	%)	%)	%)	%)	%)	%)	%)	%)	)	%)
Distant metastasis					0.				0.	0.
			N		19		N		62	91
			A		6		A		1	4
	894	363	470	281	370	170	211	106	70	192
M0	(100%	(100%	(100.0	(99.65	(100%	(100%	(99.53	(99.07	(97.22	(96.97
	)	)	0%)	%)	)	)	%)	%)	%)	%)
			0	1			1	1	2	6
M1	0 (0%)	0 (0%)	(0.00%	(0.35%	0 (0%)	0 (0%)	(0.47%	(0.93%	(2.78%	(3.03%
			)	)			)	)	)	)
TNM stage			<0.01		<0.01		<0.01		<0.01	0.41
	387	25	204	26	171	19	80	6	14	25
Stage I	(43.29	(6.89%	(43.40	(9.22%	(46.22	(11.18	(37.74	(5.61%	(19.44	(12.63
	%)	)	%)	)	%)	%)	%)	)	%)	%)
	276	99	130	86	95	36	66	35	32	83
Stage II	(30.87	(27.27	(27.66	(30.50	(25.68	(21.18	(31.13	(32.71	(44.44	(41.92
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)
	231	239	136	169	104	115	65	65	24	84
Stage III	(25.84	(65.84	(28.94	(59.93	(28.11	(67.65	(30.66	(60.75	(33.33	(42.42
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)
			0	1			1	1	2	6
Stage IV	0 (0%)	0 (0%)	(0.00%	(0.35%	0 (0%)	0 (0%)	(0.47%	(0.93%	(2.78%	(3.03%
			)	)			)	)	)	)
Tumour grade			<0.01		0.001		0.12		0.17	0.04
	40	2	21	4	9	2	7	0	4	1
G1	(4.54%	(0.56%	(4.48%	(1.45%	(2.44%	(1.23%	(3.38%	(0.00%	(5.71%	(0.52%
	)	)	)	)	)	)	)	)	)	)
	273	74	158	67	116	39	48	25	24	71
G2	(30.95	(20.85	(33.69	(24.36	(31.44	(23.93	(23.19	(24.51	(34.29	(36.79
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)
	569	279	290	204	244	122	152	77	42	121
G3	(64.51	(78.59	(61.83	(74.18	(66.12	(74.85	(73.43	(75.49	(60.00	(62.69
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)
Lauren type			0.18		0.10		0.46		0.98	0.62

	8		8		8		4			
Intestina I	361	153	205	122	163	74	77	45	37	104
	(62.13	(55.64	(67.88	(61.31	(65.46	(59.20	(57.04	(58.44	(72.55	(72.73
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)
Diffuse	138	75	61	40	53	30	36	20	1	7
	(23.75	(27.27	(20.20	(20.10	(21.29	(24.00	(26.67	(25.97	(1.96%	(4.90%
	%)	%)	%)	%)	%)	%)	%)	%)	)	)
Mixed	82	47	36	37	33	21	22	12	13	32
	(14.11	(17.09	(11.92	(18.59	(13.25	(16.80	(16.30	(15.58	(25.49	(22.38
	%)	%)	%)	%)	%)	%)	%)	%)	%)	%)

PS_{GC}, pathomics signature of gastric cancer; TNM, tumor-node-metastasis

Supplementary Table 2. Univariate and multivariate Cox regression analyses of the PS_{GC} and clinicopathological characteristics for overall survival across the training and validation cohorts

Variables	HMUCH cohort (n = 1,257)				HMUSH cohort (n = 752)				QMUSH cohort (n = 540)				YKPH cohort (n = 319)				TCGA-STAD cohort (n = 270)			
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis	
	HR	P	HR	P	HR	P	HR	P	HR	P	HR	P	HR	P	HR	P	HR	P	HR	P
	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value	(95% CI)	value
Age, years		<0.001		0.006		<0.001		0.001		0.001		0.008		0.000		0.002		0.015		0.094
Continuous variable	1.03 (1.02, 1.04)		1.03 (1.01, 1.05)		1.04 (1.02, 1.05)		1.03 (1.02, 1.05)		1.02 (1.01, 1.04)		1.02 (1.00, 1.05)		1.03 (1.01, 1.05)		1.02 (1.00, 1.05)		1.01 (0.99, 1.03)			
Early-onset		0.009		0.997		0.035		0.097		0.088		0.033		0.013				0.005		
No	Reference		Reference		Reference		Reference		Reference		Reference		Reference		Reference		Reference		Reference	
Yes	0.62 (0.46, 0.82)		1.00 (0.63, 1.60)		0.55 (0.37, 0.82)		1.00 (0.60, 1.69)		0.66 (0.44, 0.98)		0.78 (0.43, 1.41)		0.58 (0.33, 1.00)				0.93 (0.48, 1.79)			
Sex		0.871				0.246				0.316				0.066				0.346		
Female	Reference		Reference		Reference		Reference		Reference		Reference		Reference		Reference		Reference		Reference	
Male	1.02 (0.81, 1.28)				0.85 (0.64, 1.12)				1.19 (0.84, 1.69)				0.67 (0.44, 1.02)				1.23 (0.80, 1.91)			
Lymph node harvest		0.0054		0.0938		0.466				0.0034		0.6802		0.013				0.0314		0.6435

Continuous variable	1.00				1.02				1.00				0.99				0.98				1.00
	(0.99				(1.01				(0.99,				(0.97,				(0.97,				(0.98
	,				,				1.02)				1.00)				1.00)				,
	1.02)				1.03)				1.02)				1.00)				1.00)				1.02)
Depth of invasion																					
T1	Refer		Refer		Refer		Refer		Refer		Refer		Refere		Refere		Refer				
	ence		ence		ence		ence		ence		ence		nce		nce		ence				
					2.03		1.22		1.06								5.35				
T2	1.37	0.	0.80	0.	(1.12	0.	(0.57	0.	(0.48	0.	1.24	0.	0.90	0.	0.47	0.	(0.71,	0.			
	(0.85,	19	(0.38,	55	01	60		88	(0.48,	65	(0.26,	86	(0.10,	34		40.25	10				
	2.22)	35	1.67)	41	,	9	,	27	,	71	3.16)	48	3.07)	28	2.27)	44		35			
					3.68)		2.60)		2.31)								)				
					4.36		<0		1.37		<0						6.82				
T3	4.14		0.84	0.	(2.72	0.	(0.52	0.	(2.41	0.	2.10	0.	5.06		0.78	0.	(0.94,	0.			
	(2.93,		(0.34,	71	00	52			(0.55,	27	(2.31,		00	(0.14,	78	49.42	05				
	5.85)		2.08)	36	,	00	,	11	,	00	7.96)	7	11.09)	00	4.54)	67		74			
					6.98)		1		3.60)		6.18)		1				)				
					5.88		<0		1.55		5.27		<0				6.32				
T4	6.88		0.81	0.	(3.54	0.	(0.54	0.	(3.07	0.	2.68		0.	6.71	<0	0.86	0.	6.32			
	(4.75,		(0.30,	68	00	41			(0.63,	0.	0.63,		0.	6.71	0.	0.86	0.	(0.86,			
	9.97)		2.19)	45	,	00	,	45	,	00	11.32	17	(2.87,	00	(0.12,	87	46.63	07			
					9.78)		1		4.42)		9.06)		1				)				
Lymph node metastasis																					
N0	Refer		Refer		Refer		Refer		Refer		Refer		Refere		Refere		Refer				
	ence		ence		ence		ence		ence		ence		nce		nce		ence				
					3.00		<0		2.20		1.49						0.90				
N1	2.08		1.50	0.	(1.99	0.	(1.36	0.	(0.87	0.	1.14	0.	1.95	0.	1.19	0.	1.58	0.			
	(1.51,		(0.97,	06	,	00	,	00	,	14	(0.62,	67	(1.00,	05	(0.56,	64	(0.89,	11			
	2.87)		2.31)	94	4.52)	1	3.57)	13	2.55)	22	2.10)	16	3.81)	1	2.52)	88	2.80)	57			
					4.04		<0		2.43		2.32						1.28				
	3.66		1.80	0.	(2.73	0.	(1.20	0.	(1.40	0.	1.78	0.	2.94	0.	1.70	0.	2.28	0.			
N2	(2.72,		(0.97,	06	,	00	,	01	,	00	(0.70,	22	(1.65,	00	(0.59,	32	(1.26,	00			
	4.93)		3.33)	38	5.97)	1	4.93)	41	3.82)	1	4.51)	7	5.24)	03	4.86)	36	4.12)	66			
					5.62		<0		3.35		6.40		<0				1.64				
	5.81		2.56	0.	(3.90	0.	(1.64	0.	(4.33	0.	1.68,	0.	3.98	0.	1.91	0.	2.98	0.			
N3	(4.44,		(1.35,	00	,	00	,	00	,	00	10.09		00	(2.33,	00	(0.71,	19	(1.65,			
	7.62)		4.84)	4	8.09)	1	6.84)	09	9.45)	1	)	2	6.82)	00	5.15)	89	5.37)	03			
					8.09)		1		6.84)		9.45)		1				5.57)				
TNM stage																					
Stage I	Refer		Refer		Refer		Refer		Refer		Refer		Refere		Refere		Refer				
	ence		ence		ence		ence		ence		ence		nce		nce		ence				

		<0		2.92	<0	1.01		1.82										1.88
	2.68		1.37	0.			0.		0.	0.69	0.	3.63	0.	1.88	0.	1.93	0.	0.
Stage II	(1.87,	.0	(0.60,	45	(1.85	.0	(0.40	(1.06	0.	0.18,	57	(1.56,	00	(0.32,	48	(0.90,	09	(0.69
	3.84)	00	3.13)	83	,	00	,	,	87	2.55)	43	8.44)	27	11.11)	64	4.16)	1	,
		1			4.60)	1	2.51)	3.10)										5.11)
		<0			5.92	<0	0.96	5.48	<0				<0					1.76
	7.20		1.50	0.			0.			0.53	0.	8.54		2.36	0.	2.61	0.	0.
Stage III	(5.21,	.0	(0.48,	48	(3.92	.0	(0.27	3.55	.0	(0.09,	48	(3.91,	.0	(0.24,	46	(1.22,	01	(0.47
	9.96)	00	4.65)	09	,	00	,	,	00	3.15)	19	18.69)	00	23.74)	51	5.58)	3	,
		1			8.92)	1	3.46)	8.46)	1				1					6.56)
												18.45		7.08				0.90
Stage					0.		0.					(2.25,	0.	(0.31,	0.	2.09	0.	(0.14
IV	NA		NA		NA ⁵	99	NA ⁵	99	NA	NA		151.22	00	161.2	21	(0.55,	27	,
					33		2					)	66	7)	97	7.90)	75	5.57)
Tumou																		
r grade																		
G1	Refer		Refer		Refer			Refer				Refere				Refer		
	ence		ence		ence			ence				nce				ence		
	3.85		2.52															
	(1.22,	0.	(0.35,	0.		0.			0.			1.47	0.				0.	
G2	02		36	NA ⁵	99		NA ⁵	99		(0.19,	71			NA ⁵	99			
	12.16	18	18.32	15		17		15		11.24)	05				39			
	)		)															
	5.74		2.75															
	(1.84,	0.	(0.38,	0.		0.		0.		2.84	0.					0.		
G3	00		31	NA ⁵	99		NA ⁵	99		(0.39,	30			NA ⁵	99			
	17.89	26	19.84	57		16		14		20.41)	01				38			
	)		)															
Lauren																		
type																		
Intestina	Refer		Refer		Refer			Refer				Refere				Refer		Refer
l	ence		ence		ence			ence				nce				ence		ence
					1.14			1.18										1.75
	1.37	0.	1.01	0.	(0.79	0.		(0.71	0.			1.23	0.		3.11	0.	(0.58	0.
Diffuse	(1.00,	05	(0.71,	96	47			52		(0.70,	47			(1.10,	03	,		32
	1.89)	27	1.42)	86	9			01		2.15)	29			8.79)	23		5.23)	
					1.66)			1.95)										
	1.38	0.	0.96	0.	1.37	0.		1.10	0.			1.04	0.		1.36	0.	1.54	0.
	(1.06,	01	(0.72,	80	(0.90	14		(0.72	67			(0.50,	91		(0.78,	27	(0.83	16
Mixed	1.81)	86	1.29)	09	,	7		,	15			2.17)	06		2.35)	52	,	88
					2.09)			1.68)								2.86)		
		<0		<0		<0		<0		<0		<0		<0		<0		<0
		.0		.0		.0		.0		.0		.0		.0		.0		.0
PS _{Gc}	00		00		00		00	00		00		00		00		00		00
	1		1		1		1	1		1		1		1		1		1
					3.24		2.88	3.05										3.14
Continu	4.28		3.82		(2.81		(2.45	(2.58		2.71		4.53		3.98		2.74		(2.07
ous	(3.78,		(3.23,		,		,	,		(2.22,		(3.49,		(2.96,		(1.99,		,
variable	4.85)		4.52)		3.74)		3.39)	3.61)		3.32)		5.88)		5.35)		3.78)		4.74)

PS_{GC}, pathomics signature of gastric cancer; HR, hazard ratio; CI, confidence interval; TNM, tumor-node-metastasis; NA, not available; \$, Due to the limited sample size of the reference group, the outcome was excessively large, resulting in an infinite confidence interval, which was thus not shown in the table.

Supplementary Table 3. E-Values for the PS_{GC} for overall survival across the training and validation cohorts

Pathomics signature	Sample size	Adjusted hazard ratio	E-value	
		HR (95% CI)	For point estimate	For confidence interval
HMUCH cohort	1257	3.82 (3.23, 4.52)	4.41	3.88
HMUSH cohort	752	2.88 (2.45, 3.39)	3.54	3.11
QMUSH cohort	540	2.71 (2.22, 3.32)	3.37	2.86
YKPH cohort	319	3.98 (2.96, 5.35)	4.54	3.62
TCGA-STAD cohort	270	3.14 (2.07, 4.74)	3.79	2.69

PS_{GC}, pathomics signature of gastric cancer; HR, hazard ratio; CI, confidence interval

Supplementary Table 4. Subgroup analysis for the PS_{GC} among different clinical features across the training and validation cohorts

Variables	HMMCH cohort (n = 1,257)		HMMSH cohort (n = 752)		QMUSH cohort (n = 540)		YKPH cohort (n = 319)		TCGA-STAD cohort (n = 270)	
	Sam ples	HR (95% CI)	Sa mpl es	HR (95% CI)	Sa mpl es	HR (95% CI)	Sa mpl es	HR (95% CI)	Sam ples	HR (95% CI)
Age, years										
≤ 65	968	4.53		3.36		3.03		5.74		2.56
		(3.91,	549	(2.81,	429	(2.50,	238	(4.09,	123	(1.50,
		5.24)		4.01)		3.67)		8.07)		4.38)
> 65	289	3.70		2.80		3.15		2.95		2.73
		(2.95,	203	(2.16,	111	(2.26,	81	(1.87,	145	(1.85,
		4.65)		3.61)		4.40)		4.65)		4.04)
Sex										
Male	924	4.36		3.49		3.03		4.78		2.85
		(3.78,	535	(2.94,	389	(2.49,	222	(3.43,	178	(1.95,
		5.03)		4.14)		3.68)		6.66)		4.15)
Female	333	4.06		2.75		3.17		4.45		2.46
		(3.21,	217	(2.12,	151	(2.29,	97	(2.86,	92	(1.37,
		5.15)		3.57)		4.37)		6.93)		4.42)
Lymph node harvest										
≤ 15	160	5.05		2.66		2.54		4.70		2.39
		(3.40,	129	(1.80,	48	(1.34,	45	(2.18,	128	(1.59,
		7.50)		3.92)		4.78)		10.17)		3.58)
> 15	109 7	4.18		3.32		3.09		4.48		3.38
		(3.67,	619	(2.84,	492	(2.59,	274	(3.39,	129	(1.98,
		4.77)		3.88)		3.68)		5.93)		5.75)
Serosal invasion										
Yes	191	2.50		2.31		2.16		2.72		2.91
		(1.97,	127	(1.64,	70	(1.42,	55	(1.51,	75	(1.64,
		3.18)		3.24)		3.31)		4.90)		5.17)
Not	106 6	4.87		3.43		3.17		4.90		2.67
		(4.21,	625	(2.92,	470	(2.64,	264	(3.65,	195	(1.82,
		5.65)		4.02)		3.81)		6.56)		3.91)
Lymph node metastasis										

		3.57		2.94		3.30		4.66		2.83
Yes	698	(3.09, 4.12)	431	(2.45, 3.52)	305	(2.64, 4.13)	185	(3.28, 6.62)	179	(1.95, 4.10)
		4.88		3.13		2.38		3.99		2.75
No	559	(3.69, 6.45)	321	(2.34, 4.19)	235	(1.71, 3.31)	134	(2.53, 6.31)	91	(1.43, 5.31)
TNM stage										
Early (Stage I and II)	787	(5.40, 6.72)	446	(3.37, 4.16)	321	(2.62, 3.44)	187	(4.55, 6.78)	154	(2.72, 4.19)
Advance (Stage III and IV)	470	(2.94, 3.45)	306	(2.70, 3.34)	219	(2.92, 3.79)	132	(3.82, 5.60)	116	(2.84, 4.60)
Differentiation status										
Well and moderate	389	(4.29, 5.48)	250	(2.85, 3.67)	166	(2.44, 3.24)	80	(4.98, 9.91)	100	(2.49, 4.44)
Poor and undifferentiated	848	(4.24, 4.91)	494	(3.50, 4.21)	366	(3.77, 4.72)	229	(4.73, 6.36)	163	(2.84, 4.19)
Lauren type										
Intestinal	514	(4.78, 5.79)	327	(3.69, 4.63)	237	(3.88, 5.08)	122	(5.26, 8.22)	141	(2.85, 4.69)
Diffuse and mixed	342	(4.07, 5.02)	174	(3.02, 4.03)	137	(2.86, 3.98)	90	(4.65, 7.56)	53	(3.44, 6.58)

PS_{GC}, pathomics signature of gastric cancer; TNM, tumor-node-metastasis; HR, hazard ratio; CI, confidence interval

Supplementary Table 5. Concordance-index comparison of the different models for overall survival

Variables	C-index (95% CI)	Change of C-index (95% CI)	P value
<i>HMUCH cohort (n = 1,257)</i>			
TNM stage	0.7002 (0.6781, 0.7223)	<i>Reference</i>	
PS _{GC}	0.806 (0.7859, 0.8261)	0.1059 (0.0821, 0.1316)	<0.0001
Combined model	0.8118 (0.7924, 0.8312)	0.1117 (0.0927, 0.1306)	<0.0001
<i>HMUSH cohort (n = 752)</i>			
TNM stage	0.6812 (0.6530, 0.7095)	<i>Reference</i>	
PS _{GC}	0.7914 (0.7657, 0.8171)	0.1102 (0.0772, 0.1423)	<0.0001
Combined model	0.795 (0.7697, 0.8203)	0.1137 (0.0861, 0.139)	<0.0001
<i>QMUHSH cohort (n = 540)</i>			
TNM stage	0.6924 (0.6588, 0.7260)	<i>Reference</i>	
PS _{GC}	0.7761 (0.7405, 0.8117)	0.0837 (0.0426, 0.1233)	<0.0001
Combined model	0.7861 (0.7544, 0.8179)	0.0938 (0.0633, 0.1187)	<0.0001
<i>YKPH cohort (n = 319)</i>			
TNM stage	0.6947 (0.6512, 0.7383)	<i>Reference</i>	
PS _{GC}	0.8253 (0.7908, 0.8598)	0.1305 (0.0837, 0.1793)	<0.0001
Combined model	0.8209 (0.7860, 0.8558)	0.1262 (0.0818, 0.1653)	<0.0001
<i>TCGA-STAD cohort (n = 270)</i>			
TNM stage	0.5604 (0.5051, 0.6158)	<i>Reference</i>	
PS _{GC}	0.6876 (0.6307, 0.7444)	0.1271 (0.0563, 0.2139)	0.0016
Combined model	0.6981 (0.6430, 0.7533)	0.1377 (0.0767, 0.2061)	<0.0001

PS_{GC}, pathomics signature of gastric cancer; C-index, Concordance-index; TNM, tumour -node-metastasis; CI, confidence interval