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ORIGINAL RESEARCH

Early diagnostic potential of *APC* hypermethylation in esophageal cancer

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Background: The hypermethylation of APC gene is observed in various cancers, including esophageal cancer (EC). However, the association between APC methylation and the initiation and progression of EC is poorly understood.

Purpose and methods: The current study systematically reviewed studies on abnormal methylation of APC in EC and quantitatively synthesized 18 studies by meta-analysis involving 1008 ECs, 570 Barrett's esophagus (BE), and 782 controls.

Results: Our results showed higher methylation of APC in EC (OR = 23.33, $P < 0.001$) and BE (OR = 9.34, $P < 0.001$) than in normal controls. Whereas APC methylation in EC was similar to that in BE ($P = 0.052$), it was not associated with tumor stage ($P = 0.204$). Additionally, APC methylation was not significantly associated with overall survival (OS) and relapse-free survival (RFS) in patients with EC. The performance of APC methylation for the detection of EC and BE achieved areas under the receiver operating characteristic curves of 0.94 and 0.88, respectively.

Conclusion: Our results imply that APC methylation detection is a potential diagnostic biomarker for EC and BE.

Keywords: esophageal cancer, Barrett's esophagus, methylation, *APC*

Introduction

Cancer poses a major public health burden after cardiovascular diseases, as its global incidence and mortality continue to increase.[1] Esophageal cancer (EC) is the leading cause of cancer death; about 16,940 new cases and 15,690 deaths were estimated in the 2017 US statistics.[2] Due to a lack of specific symptoms and preventive measures, many EC patients are diagnosed at an advanced stage. Multimodality therapy, consisting of surgery combined with chemotherapy, is the standard treatment for resectable advanced EC.[3] In spite of improvements in surgery and chemotherapy, the prognosis for EC patients presenting with advanced stage disease is poor, with the most recent statistics showing 5-year survival rates <50%.[4] EC arises from Barrett's esophagus (BE), which is metaplastic change of the normal squamous mucosa to specialized columnar epithelium. BE ultimately progresses to dysplasia (low-grade dysplasia to high-grade dysplasia) and subsequently to EC. Therefore, early diagnosis of EC and proper endoscopic therapies for BE are key strategies for improving the survival of EC patients.

The etiology of EC is multifactorial, including interactions between various environmental, epigenetic, and genetic changes involved in inflammation.[5] The relevant environmental factors have been elucidated by several large-scale and well-designed epidemiological studies and include obesity, *Helicobacter pylori* infection, and tobacco

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smoking.[6–8] Genetic changes such as single-nucleotide polymorphisms involved in multiple cellular pathways may be biomarkers of EC risk.[9,10] Recent studies have identified the important role of DNA methylation in esophageal carcinogenesis.[11] DNA methylation is one of the important epigenetic modifications involved in the inactivation of numerous tumor suppressor genes (TSGs).[12] It is well established that hypermethylation of multiple TSGs in association with the dysfunction of cellular biological pathways characterize human cancers. Additionally, DNA methylation biomarkers are of clinical value for early cancer diagnosis.

Adenomatous polyposis coli (*APC*) is a classical TSG located on chromosomal band 5q21-q22.[13] *APC* was initially uncovered through genetic linkage analysis in colorectal cancer (CRC).[13,14] APC protein serves as a negative regulator of the Wnt/beta-catenin pathway.[15] Loss of APC expression leads to the stabilization and nuclear accumulation of beta-catenin that could result in the activation of downstream target genes involved in the initiation of tumorigenesis.[16,17] In the past decades, the downregulation of *APC* through promoter hypermethylation has frequently been observed in many cancers, including EC.[18–21] However, the diagnostic strength and association of *APC* methylation with EC progression has been less consistent. The present study aimed at summarizing recent studies on aberrant methylation of *APC* in EC progression.

Materials and methods

Identification of relevant studies

All relevant studies were systematically searched from PubMed, Google Scholar, Web of Science, China National Knowledge Infrastructure, and Wanfang literature databases and updated until June 11, 2017. The search strategies for potential studies applied different combinations of the following terms: adenomatous polyposis coli, *APC*, methylation, esophagus cancer, and esophagus carcinomas.

In addition, a manual search was performed to seek potential studies in the references of retrieved publications. All eligible studies had to have measured *APC* methylation status in EC patients rather than cancer cell lines. Neither reviews nor abstracts were included in our analysis. Studies without detailed information on *APC* methylation were excluded.

Data extraction

For the eligible studies, we extracted the first author's name, year of publication, country of study subjects, methylation assessment methods, and frequency of gene methylation (Table S1). In addition, DNA methylation data of *APC* in EC were obtained from The Cancer Genome Atlas (TCGA) online database (https://cancergenome.nih.gov/). The methylation status of 186 ECs was analyzed using the human methylation 450K array (HM450). More than 450,000 CpG sites in the human genome were included in the HM450 platform. A total of 20 CpG sites (cg08636638, cg19115695, cg27062904, cg07661636, cg00190738, cg16110711, cg16451027, cg27379240, cg11057897, cg07003745, cg04011030, cg16481008, cg18315896, cg01528425, cg08934600, cg18536802, cg26660754, cg08512345, cg25922032, and cg04226363) in the promoter region of *APC* were included (Figure S1). We also downloaded clinical stage, gender, age, overall survival (OS), and relapse-free survival (RFS) data of the EC patients (Table S1).

Statistical analysis

The Stata-12.0 software (StataCorp LP, College Station, TX, USA) was used to calculate the pooled odds ratios (ORs) and the corresponding 95% confidence intervals (CIs). The heterogeneity across studies was represented as the I^2 statistic with corresponding *P*-value.[22] When there was remarkable heterogeneity (I^2>50%, χ^2 test with P<0.05) in the meta-analysis, a Dersimonian–Laird (D + L) model was applied to calculate the pooled OR; otherwise, a Mantel–Haenszel (M–H) model was used.[23] Besides, the potential source of heterogeneity was identified by meta-regression. For the pooled ORs of studies with unknown heterogeneity source, sensitivity analysis was applied to assess the robustness of the results. The sensitivity analysis estimated the stability of results by excluding single study to estimate the effect of the individual study on the overall pooled OR. Publication bias was estimated by Begg's and Egger's linear regression tests. Diagnostic meta-analyses were also performed. The pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic OR (DOR), and their corresponding 95% CIs were calculated. Summary receiver operating characteristic (SROC) curves with the areas under the receiver operating characteristic curve (AUC) were then generated. Additionally, the failsafe number (N_{fs}) test was performed using the R software (version 3.3.0) to identify the robustness of our results when significant publication bias among the studies was observed. Cox regression models were used to calculate the adjusted hazard ratios to estimate the relationship between OS and RFS with other covariates (*APC* methylation level, clinical stage, age, and gender). The survival analysis was performed by SPSS. All *P*-values are two-sided, and a *P*-value of <0.05 was deemed statistically significant.

Results

Study characteristics

In order to analyze the relationship between *APC* methylation and EC progression, we quantitatively synthesized 18 studies including 1008 ECs, 570 BEs, and 782 controls.[18,19,24–39] A total of 260 studies were identified using the search strategy described earlier, and 204 studies were excluded after careful filtration, of which 38 were duplicates, 21 were without methylation data, 55 were abstracts or reviews, and 94 were irrelevant. Finally, 18 studies (17 published in English and in Chinese) were included in the meta-analysis. The basic characteristics of all the included studies are shown in Table 1, and the selection process is illustrated in Figure 1.

Association of APC methylation with EC progression

First, we performed a meta-analysis of 17 studies including 948 EC patients and 757 normal controls to ascertain if there were any *APC* methylation differences between the two groups. Considering the presence of significant heterogeneity across the studies (I^2=68.3%, P<0.01, Table 2), a meta-regression was performed to assess the potential resource of heterogeneity. The results showed that the two studies from Japan might be responsible for the significant heterogeneity. Other parameters such as year of publication, methylation detection method, and normal controls contributed little to the heterogeneity (Table 3). Therefore, we compared the pooled ORs as well as the heterogeneity value before and after removal of these two studies. Our results showed a significant decrease in heterogeneity with exclusion of the two studies (I^2=45.1%, P=0.03, Table 2). The pooled ORs therefore showed that *APC* methylation was associated with an increased risk of EC (OR = 23.33; range, 12.72-42.78; Table 2; Figure S2). The Begg's test showed an absence of publication bias (P=0.175; Figure 2A), whereas the Egger's test implied the presence of publication bias (P<0.001; Figure 2B). Therefore, we applied the N_{fs} test and sensitivity analysis to assess the efficacy of the meta-analysis. Both the N_{fs} test ($N_{fs0.05}$=1127 and $N_{fs0.01}$=878) and sensitivity analysis supported the robustness of our results (Table 4).

Second, a meta-analysis was performed on eight studies involving 377 EC and 482 BE patients. The difference in *APC* methylation level between the two groups was slight with no statistical significance (OR = 2.58; range, 0.99–6.70; Table 2; Figure S2). The D + L model was used to compute OR because of the presence of significant heterogeneity (I^2=81.2%, P<0.001, Table 2). However, meta-regression failed to identify any potential resource of heterogeneity (Table 5). The Begg's and Egger's tests for publication bias were not statistically significant (P=0.174 and 0.204, respectively; Figure 2C and D).

Third, the association between methylated *APC* and progression of BE was analyzed in nine studies, including 442 BEs and 288 controls. The pooled OR was computed by the D + L model, as significant heterogeneity was observed (I^2=76.5%, P<0.001, Table 2). Our results demonstrated that methylation of *APC* was associated with an increased risk for developing BE (OR =9.34; range, 2.92–29.82). The pooled OR was not significantly transformed by the M–H model (Table 2), indicating that our results were robust. The sensitivity analysis also confirmed the stability and credibility of our results (Table 6). No potential source of heterogeneity was identified by meta-regression (Table 7). No publication bias was observed by Begg's test (P=0.917; Figure 2E) and Egger's test (P=0.222; Figure 2F).

Finally, in order to examine the association between *APC* methylation and the progression of EC, we quantitatively analyzed the association between *APC* methylation and tumor stage. A total of three studies including 76 patients classified as stage T1 or T2 and 164 patients classified as stage T3 or T4 were analyzed. Due to remarkable heterogeneity across the studies, a D + L model was applied and results showed no statistical significance (OR = 2.25; range, 0.64-7.87;Table 2; Figure S2). The results of Begg's (P=0.734) and Egger's (P=0.686) tests illustrated no publication bias among these three studies (Figure 2G and H).

The diagnostic accuracy of methylated APC for EC and BE

The diagnostic accuracy of methylated *APC* for EC was analyzed from 17 studies involving 948 EC patients and 757 controls. The summary specificity and sensitivity of methylated *APC* for distinguishing EC from controls were 0.96 (95% CI: 0.92–0.98) and 0.55 (95% CI: 0.39–0.69), respectively (Figure 3). The SROC based on the specificity and sensitivity is shown in Figure 3, and the AUC was 0.94 (95% CI: 0.91–0.95). The summary diagnostic OR was 30 (95% CI: 10–88). The PLR and NLR were 14.0 (95% CI: 5.9–32.8) and 0.47 (95% CI: 0.33–0.67), respectively. As indicated by the PLR, EC patients had a ~14 times higher chance of having methylated *APC* than normal controls. Also, as indicated by the NLR, normal controls had a twofold greater chance (the reciprocal of the value of NLR) of having unmethylated *APC* than EC patients. As shown in Figure 4, the Fagan plot analyses based on the PLR and NLR demonstrated that the probability of a patient being diagnosed with EC was,

Table 1 Main characteristics of studies included in the current analyses

First author (reference)	Year	Country	Normal source	Method	EC		BE		Control		$T_{1/2}$		$T_{3/4}$		Stage I/II		Stage III/IV		N+		N-	
					M+	Total	M+	Total	M+	Total	M+	Total	M+	Total	M+	Total	M+	Total	M+	Total	M+	Total
Moriichi et al [33]	2009	Japan	H	MSP	–	–	63	88	10	25	–	–	–	–	–	–	–	–	–	–	–	–
Kawakami et al [24]	2000	USA	H	qMSP	64	84	17	43	0	20	–	–	–	–	–	–	–	–	–	–	–	–
Eads et al [25]	2001	USA	A	qMSP	15	22	16	19	1	31	8	11	7	11	–	–	–	–	–	–	–	–
Brock et al [26]	2003	USA	A	MSP	27	41	–	–	3	41	–	–	–	–	–	–	–	–	–	–	–	–
Brock et al [26]	2003	USA	H	MSP	–	–	–	–	0	17	–	–	–	–	–	–	–	–	–	–	–	–
Sarbia et al [27]	2004	Germany	A	qMSP	39	50	–	–	1	50	–	–	–	–	–	–	–	–	–	–	–	–
Schulmann et al [28]	2005	USA	A	qMSP	54	77	75	92	9	64	–	–	–	–	–	–	–	–	–	–	–	–
Clement et al [29]	2006	Switzerland	H	MS-DBA	25	27	15	25	0	16	–	–	–	–	–	–	–	–	–	–	–	–
Guo et al [30]	2006	China	H	MSP	9	69	1	60	0	17	–	–	–	–	–	–	–	–	–	–	–	–
Ishii et al [31]	2007	Japan	A	MSP	15	56	4	21	10	56	–	–	–	–	–	–	–	–	–	–	–	–
Ishii et al [31]	2007	Japan	H	MSP	–	–	–	–	4	42	–	–	–	–	–	–	–	–	–	–	–	–
Kim et al [32]	2009	Korea	H	MSP	23	50	–	–	–	–	7	15	16	35	–	–	–	–	8	26	15	24
Zare et al [34]	2009	Iran	A	MSP	20	45	–	–	0	45	–	–	–	–	–	–	–	–	–	–	–	–
Wang et al [18]	2009	USA	H	MSP	20	32	52	94	0	17	–	–	–	–	–	–	–	–	–	–	–	–
Li et al [35]	2011	China	A	MSP	6	47	–	–	2	47	–	–	–	–	–	–	–	–	–	–	–	–
Wang et al [36]	2011	China	A	MSP	34	76	–	–	5	76	1	16	33	60	3	35	31	41	31	48	3	28
Hoshimoto et al [37]	2015	USA	A	MSP	21	114	–	–	0	28	4	45	17	69	9	68	12	46	–	–	–	–
Fukui et al [38]	2016	Japan	H	MS-HRM	9	10	18	128	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Guilleret et al [19]	2016	Switzerland	H	MLM	25	26	–	–	0	8	–	–	–	–	–	–	–	–	–	–	–	–
Lei et al [39]	2011	China	A	qMSP	99	182	–	–	18	182	–	–	–	–	–	–	–	–	–	–	–	–

Notes: A, autologous (control sample from the same patients); H, heterogeneous (control samples from other individuals); M+, positive for *APC* methylation; N+, positive for lymph node metastasis; N-, negative for lymph node metastasis.
Abbreviations: BE, Barrett's esophagus; EC, esophageal cancer; MLM, methylation ligation-dependent macroarray; MSP, methylation-specific polymerase chain reaction; MD-DBA, methylation-sensitive dot-blot assay; MS-HRM, methylation-sensitive high-resolution melting; qMSP, quantitative methylation-specific polymerase chain reaction.

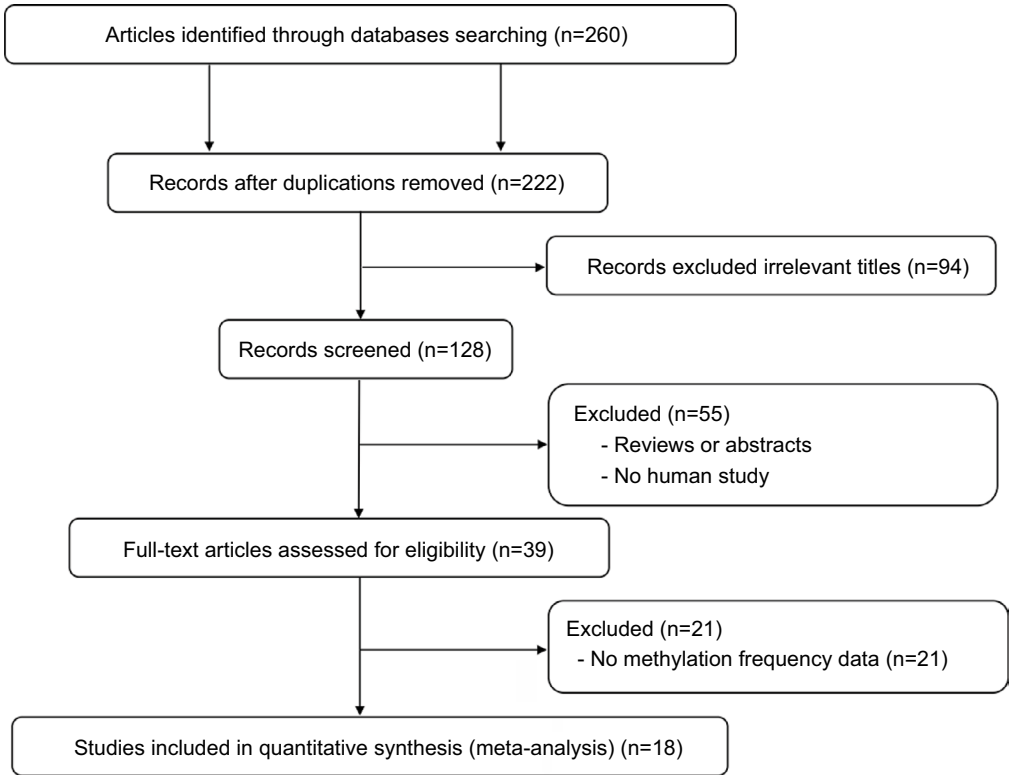

Figure 1 Flow diagram of the search strategy for this meta-analysis.

Table 2 Summary of pooled OR of *APC* methylation during the carcinogenesis of EC

Characteristics	N	M–H model			D + L model			Test of heterogeneity	
		OR	95% CI	*P*	OR	95% CI	*P*	I^2	*P*
EC vs control	17	12.95	9.57–17.52	<0.001	17.64	8.90–34.95	<0.001	68.30%	<0.001
EC vs control[a]	15	18.79	13.24–26.67	0.03	23.33	12.72–42.78	<0.001	45.10%	0.03
EC vs BE	8	1.91	1.36–2.70	<0.001	2.58	0.99–6.70	0.052	81.20%	<0.001
BE vs control	9	9.3	6.04–14.34	<0.001	9.34	2.92–29.83	<0.001	76.50%	<0.001
$T_{3/4}$ vs $T_{1/2}$	4	2.56	1.35–4.89	0.04	2.25	0.64–7.87	0.204	63.90%	0.04

Note: [a]The pooled OR of *APC* methylation was computed after removal of two studies from Japan, which might be responsible for the significant heterogeneity in EC vs control.

Abbreviations: BE, Barrett's esophagus; CI, confidence interval; EC, esophageal cancer; OR, odds ratio.

respectively, 82% and 93% following a positive methylated *APC* result, whereas the pretest probability of being diagnosed with EC was 25% and 50%, respectively. However, the probability of an exclusion diagnosis of EC was 14 and 32% following a negative methylated *APC* result. Besides, the Deek's funnel plot test indicated no publication bias across the studies included in the diagnostic analysis (Figure 5).

The diagnostic accuracy of *APC* methylation for BE was analyzed in nine studies involving 442 BEs and 288 controls. The pooled specificity and sensitivity were 0.96 (95% CI: 0.79–0.99) and 0.48 (95% CI: 0.22–0.74), respectively (Figure 3). The area under the SROC was 0.88 (95% CI: 0.85–0.91). The summary diagnostic OR was 24 (95% CI: 3–163). The PLR and NLR were 12.8 (95% CI: 2.2–74.7) and 0.54 (95% CI: 0.32–0.93), respectively. As indicated by the PLR, BE patients had a ~13 times higher chance of having methylated *APC* than normal controls. Similarly, as indicated by the NLR, normal controls had a 1.9-fold greater chance (the reciprocal of the value of NLR) of having unmethylated *APC* than BE patients. The Fagan plot analyses based on the PLR and NLR demonstrated that the probability of a patient being diagnosed with BE was, respectively, 81 and 93% following a positive methylated *APC* result, whereas the pretest probability of being diagnosed with BE was 25% and 50%, respectively (Figure 4). However, the probability of an exclusion diagnosis of BE was 15% and 35%, following a

Table 3 Meta-regression analysis of *APC* promoter methylation in EC vs control

Characteristics	Coefficient	*P*	95% CI	
			Lower	Upper
Year	–0.094	0.333	–0.296	0.107
Country				
China	–2.01	0.2	–5.25	1.231
Germany	0.865	0.641	–3.101	4.831
Japan	–3.507	0.039	–6.804	–0.208
Switzerland	1.455	0.449	–2.625	5.534
USA	–1.162	0.451	–4.434	2.109
Iran	Dropped			
Method				
MLM	–0.152	0.956	–5.979	5.675
MSP	–3.613	0.082	–7.75	0.523
qMSP	–2.399	0.241	–6.612	1.815
MS–DBA	Dropped			
Normal source				
Autologous	–0.894	0.303	–2.681	0.892
Heterogeneous	Dropped			

Abbreviations: CI, confidence interval; EC, esophageal cancer; MLM, methylation ligation-dependent macroarray; MSP, methylation-specific polymerase chain reaction; qMSP, quantitative methylation-specific polymerase chain reaction; MD-DBA, methylation-sensitive dot-blot assay; MS-HRM, methylation-sensitive high-resolution melting.

Table 4 Sensitivity analysis of *APC* methylation in EC vs control

Study omitted	Estimate	95% CI	
		Lower	Upper
Kawakami et al (2000)[24]	21.509	11.769	39.309
Eads et al (2001)[25]	21.959	11.784	40.922
Brock et al (2003)[26]	24.022	12.334	46.784
Brock et al (2003)[26]	22.514	12.103	41.883
Sarbia et al (2004)[27]	19.232	10.945	33.794
Schulmann et al (2005)[28]	26.945	13.249	54.801
Clement et al (2006)[29]	20.521	11.509	36.590
Guo et al (2006)[30]	24.966	13.317	46.804
Zare et al (2009)[34]	22.336	12.041	41.434
Wang et al (2009)[18]	22.720	12.178	42.387
Li et al (2011)[35]	26.488	14.505	48.373
Wang et al (2011)[36]	27.021	13.588	53.736
Hoshimoto et al (2015)[37]	24.373	12.908	46.021
Guilleret et al (2016)[19]	21.081	11.683	38.041
Lei et al (2011)[39]	28.045	13.984	56.244
Combined	23.328	12.722	42.776

Abbreviations: CI, confidence interval; EC, esophageal cancer.

negative methylated *APC* result. There was no publication bias observed by the Deek's funnel plot test (Figure 5).

Association between methylation of APC and prognosis of EC

In the current study, we analyzed 11 different probes located in the promoter region of *APC* including the transcription start site (chr 5:112043265-112043265) and CpG island (chr 5:112043080-112043917). The association between *APC* methylation and RFS was analyzed using 144 EC patients from TCGA. Analysis of the relationship between *APC* methylation and OS was conducted using data from 186 patients.

Table 5 Meta-regression analysis of *APC* promoter methylation in EC vs BE

Characteristics	Coefficient	*P*	95% CI	
			Lower	Upper
Year	0.136	0.258	–0.126	0.398
Country				
China	0.060	0.981	–5.969	6.089
USA	–1.786	0.348	–6.220	2.647
Japan	–0.174	0.932	–5.180	4.832
Switzerland	Dropped			
Method				
MS–DBA	–1.887	0.389	–7.029	3.254
MSP	–3.221	0.110	–7.482	1.040
qMSP	–3.687	0.072	–7.851	0.477
MLM	Dropped			

Abbreviations: BE, Barrett's esophagus; CI, confidence interval; EC, esophageal cancer; MLM, methylation ligation-dependent macroarray; MSP, methylation-specific polymerase chain reaction; qMSP, quantitative methylation-specific polymerase chain reaction; MD-DBA, methylation-sensitive dot-blot assay; MS-HRM, methylation-sensitive high-resolution melting.

Table 6 Sensitivity analysis of *APC* methylation in BE vs control

Study omitted	Estimate	95% CI	
		Lower	Upper
Moriichi et al (2009)[33]	11.255	2.784	45.504
Kawakami et al (2000)[24]	8.518	2.476	29.298
Eads et al (2001)[25]	6.714	2.132	21.142
Schulmann et al (2005)[28]	7.686	2.184	27.048
Clement et al (2006)[29]	8.073	2.385	27.320
Guo et al (2006)[30]	11.250	3.360	37.672
Ishii et al (2007)[31]	13.016	4.093	41.395
Ishii et al (2007)[31]	11.698	3.243	42.193
Wang et al (2009)[18]	8.126	2.395	27.565
Combined	9.339	2.923	29.834

Abbreviations: BE, Barrett's esophagus; CI, confidence interval.

Table 7 Meta-regression analysis of *APC* promoter methylation in BE vs control

Characteristics	Coefficient	*P*	95% CI	
			Lower	Upper
Year	–0.391	0.091	–0.866	0.084
Country				
China	–4.011	0.165	–10.572	2.550
Japan	–3.080	0.142	–7.761	1.601
USA	–0.068	0.970	–4.739	4.603
Switzerland	Dropped			
Method				
qMSP	–0.057	0.977	–4.928	4.814
MSP	–2.873	0.130	–5.322	0.424
MS-DBA	Dropped			

Abbreviations: BE, Barrett's esophagus; CI, confidence interval; MSP, methylationspecific polymerase chain reaction; qMSP, quantitative methylation-specific polymerase chain reaction; MD-DBA, methylation-sensitive dot-blot assay; MS-HRM, methylation-sensitive high-resolution melting.

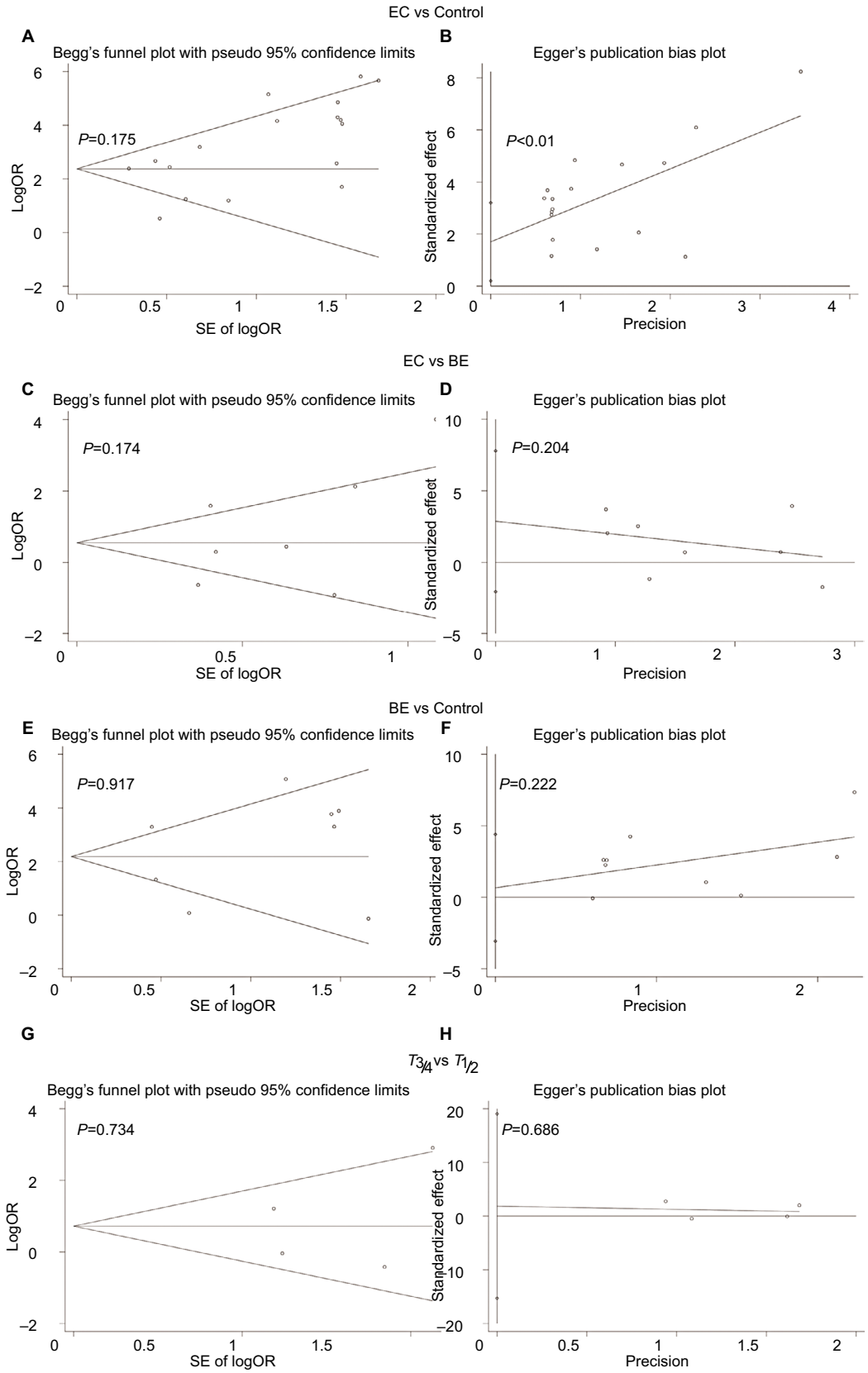

Figure 2 Begg's funnel and Egger's plots of publication bias for *APC* methylation during esophageal carcinogenesis.
Notes: (**A** and **B**) Cancer vs controls. (**C** and **D**) Cancer vs BE. (**E** and **F**) BE lesions vs control. (**G** and **H**) $T_{3/4}$ vs $T_{1/2}$.
Abbreviations: BE, Barrett's esophagus; EC, esophageal cancer; OR, odds ratio; SE, standard error.

Cox proportional-hazards regression models were applied to adjust multiple variables to estimate the OS and RFS. As we speculated, no statistically significant difference was found between *APC* methylation and the examined clinical parameters (Table 8).

Discussion

Esophageal carcinoma is thought to develop from BE following accumulation of genetic and epigenetic abnormalities leading to the activation of oncogenes and/or inactivation of TSGs.[40–42] These aberrant genetic and epigenetic changes result in the failure to maintain the equilibrium of multiple biological pathways. The Wnt/beta-catenin pathway is a main regulator of development through impacting the cell cycle at various points.[43] Dysfunction of the Wnt/beta-catenin pathway components underlies multiple growth-related pathologies and human cancers.[43] Genomic studies have identified various epigenetically silenced genes such as *SFRP5*, *SOX17*, *WIF1*, and *APC* involved in the Wnt/beta-catenin pathway.[43] The APC protein is the core constituent of the Wnt pathway that was first identified in CRC.[44] A direct correlation between *APC* methylation and loss of expression has been

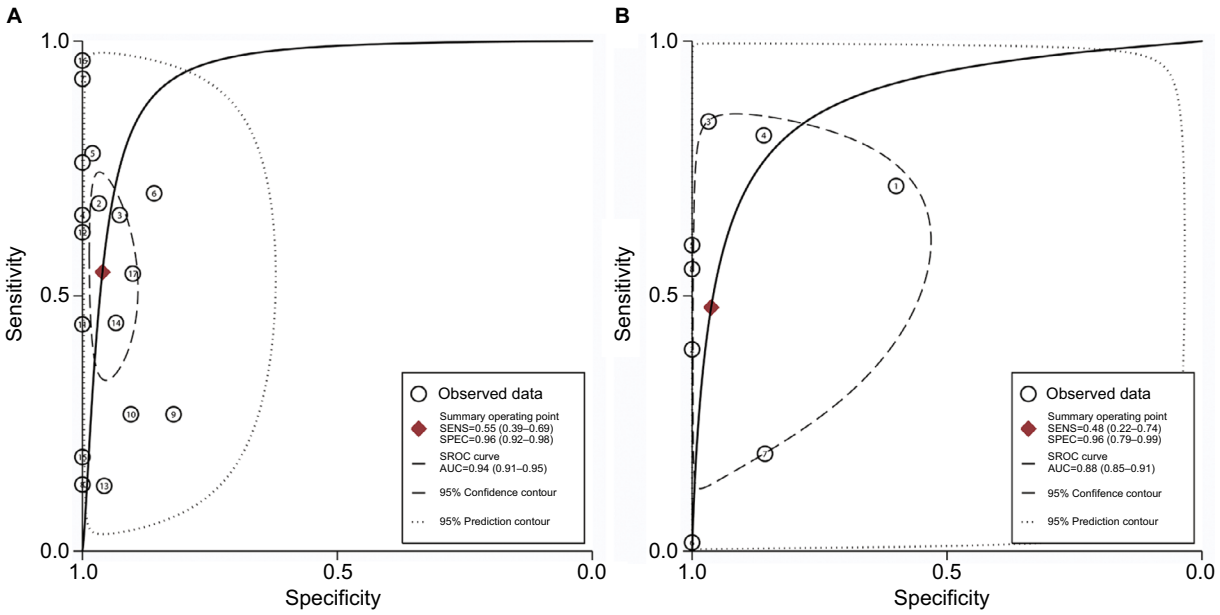

Figure 3 SROC plots of methylated *APC* for the diagnosis of EC and BE.
Notes: (A) Cancer vs control: specificity, 0.96 (95% CI: 0.92–0.98); sensitivity, 0.55 (95% CI: 0.39–0.69); AUC, 0.94 (95% CI: 0.91–0.95). (**B**) BE vs control: specificity, 0.96 (95% CI: 0.79–0.99); sensitivity, 0.48 (95% CI: 0.22–0.74); AUC, 0.88 (95% CI: 0.85–0.91).
Abbreviations: AUC, area under the receiver operating characteristic curve; BE, Barrett's esophagus; CI, confidence interval; EC, esophageal cancer; SROC, summary of receiver operating characteristic; SENS, sensitivity; SPEC, specificity.

Table 8 Survival analysis of 11 CpG island probes located in the promoter region of *APC* applying TCGA cohort

ID	RFS				OS			
	HR	95% CI		*P*	HR	95% CI		*P*
		Lower	Upper			Lower	Upper	
cg11057897	0.0111	0.000073	1.684989	0.079	0.101	0.004315	2.373252	0.16
cg04011030	0.000000498	3.71E-19	691,601.878	0.31	0.00876	1.47E-10	529,992.6672	0.6
cg16481008	1,900,000	7.62E-14	4.43E+25	0.53	3,380,000,000	0.000341	3.29935E+22	0.15
cg18315896	5.04E-18	1.94E-38	1410.265256	0.097	0.145	5.12E-14	3.89619E+11	0.89
cg01528425	2.54E-16	3.84E-36	18,725.35578	0.12	14,050.57	1.04E-09	1.87534E+17	0.54
cg08934600	38.87	8.27E-08	1,856,960,942	0.72	0.0167	1.38E-11	20,103,936.74	0.7
cg18536802	9608.5	5.82E-10	1.57E+17	0.55	27,382.19	0.000507	1.43E+12	0.26
cg26660754	9.43E-08	6.74E-17	129.948781	0.13	4229.44	0.000458	36,992,750,139	0.31
cg08512345	8.73E-27	1.48E-61	547,656,291.1	0.14	1.79E-08	4.69E-32	7.28E+15	0.52
cg25922032	6.64E-40	3.12E-85	1,424,872.33	0.09	4.29E-20	3.05E-49	5,826,722,563	0.19
cg04226363	2.83E-24	1.16E-56	801,341,200.2	0.15	4.09E-15	3.49E-35	456,874.5593	0.16

Abbreviations: CI, confidence interval; HR, hazard ratio; OS, overall survival; RFS, relapse-free survival.

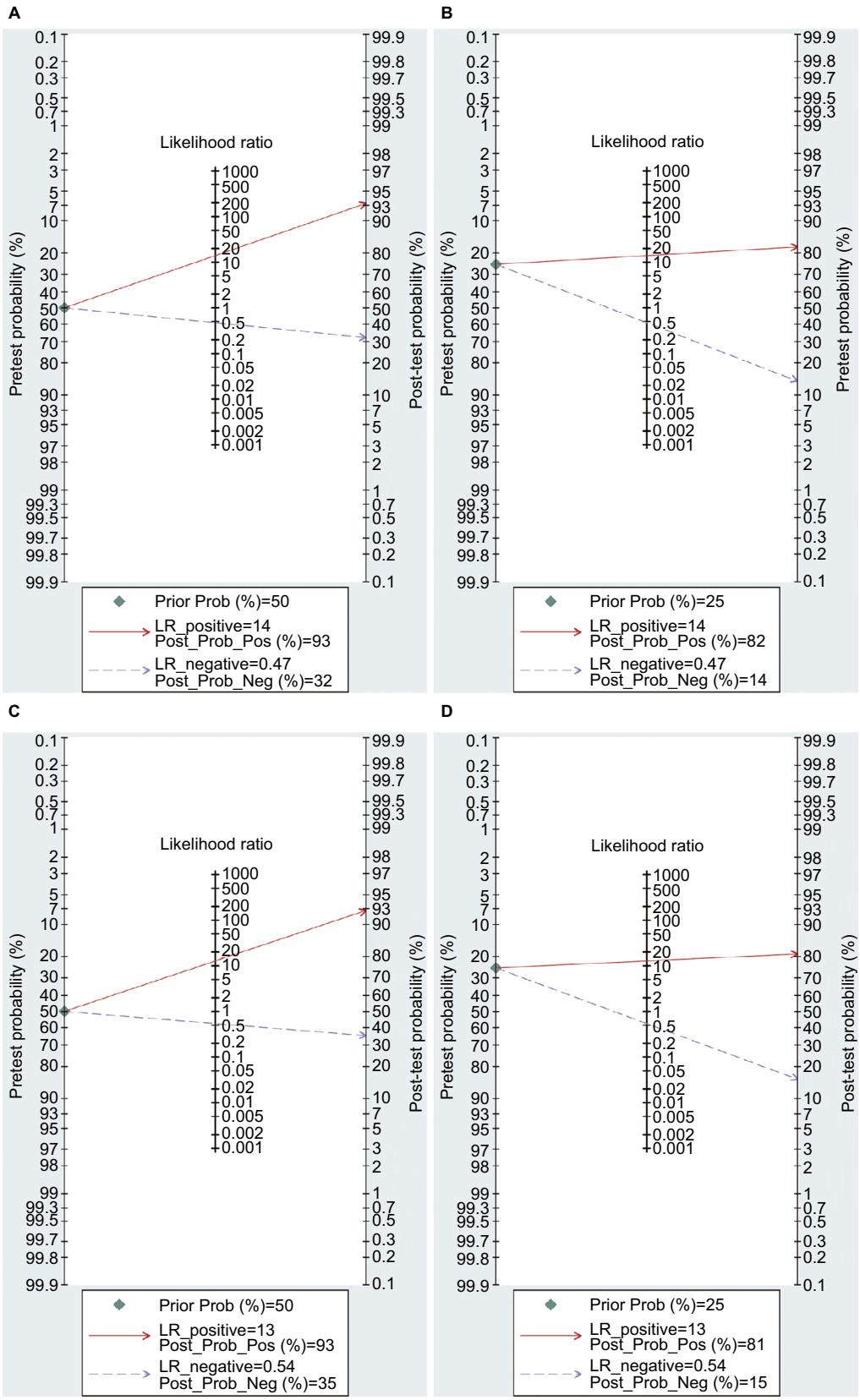

Figure 4 Fagan plot analysis to evaluate the clinical applicability of screening for methylated *APC* in EC diagnosis.

Notes: (**A**) The post-test probability of EC was 93% at a pretest probability of 50%. (**B**) The post-test probability of EC was 82% at a pretest probability of 25%. (**C**) The post-test probability of BE was 93% at a pretest probability of 50%. (**D**) The post-test probability of BE was 81% at a pretest probability of 25%.

Abbreviations: BE, Barrett's esophagus; EC, esophageal cancer; LR, likelihood ratio.

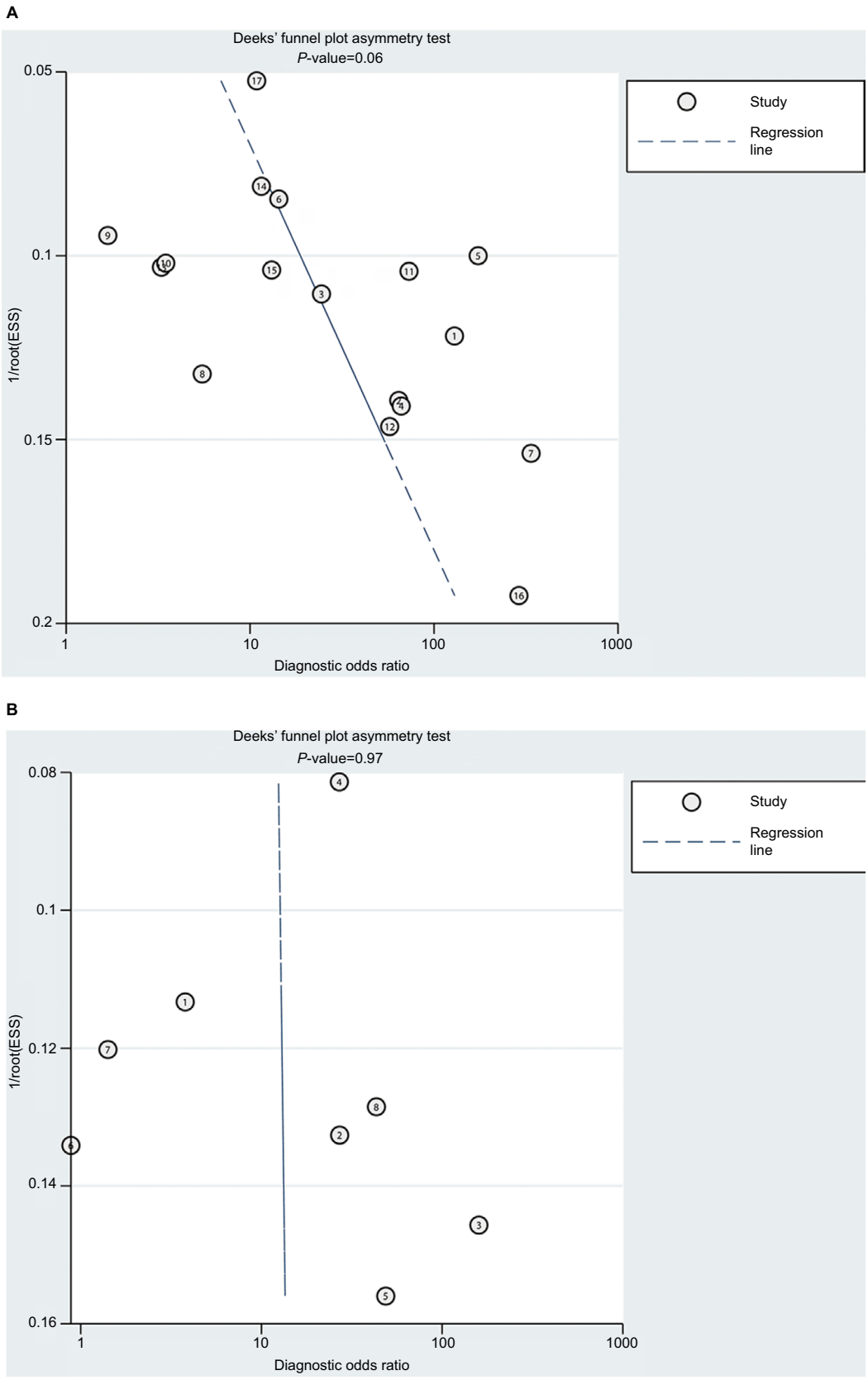

Figure 5 Deek's funnel plot test of publication bias across studies included in the diagnostic analysis.
Notes: (**A**) Cancer vs control. (**B**) BE vs control.
Abbreviations: BE, Barrett's esophagus; ESS, effective sample size.

observed in ~70–80% of CRC.[44–46] As the third deadly malignancy of the digestive system, the effect of *APC* hypermethylation on the progression of EC remains inconsistent and inconclusive. The study by Kawakami et al[24] identified *APC* methylation in ~40% of BE and 80% of EC patients compared with normal controls. However, other study[30] reported that 3% of their patients with low-grade esophageal dysplasia harbored high frequency of *APC* methylation, with none observed in patients with high-grade dysplasia and healthy normal controls. Considering the distribution of subjects in the study by Guo et al[30] (39 patients with low-grade dysplasia and only nine patients with high-grade dysplasia), it is necessary to analyze the association between *APC* methylation and esophageal carcinogenesis using a large sample.

The current study systematically reviewed all relevant evidences and synthesized data from 18 studies inclusive of 1008 ECs, 570 BEs, and 782 normal controls using meta-analysis. The main finding of this study was the significant association between *APC* promoter methylation and increased risk of BE and EC. In particular, the *APC* methylation was 23 and 10 times more likely to predict EC and BE, respectively, although the effects came from heterogeneous sources. Whereas the frequency of *APC* hypermethylation was similar between EC and BE, and these results are consistent with previous studies.[25,28] Besides, our analysis of tumor stage appears consistent with a previous study[32] in terms of the slight effect of *APC* methylation on EC progression. These findings suggest that *APC* promoter hypermethylation is an early event in esophageal carcinogenesis.

Field cancerization was first proposed for oral cancer with the description of occult multifocal precancerous lesions in the epithelium of normal appearing oral mucosa.[47] These lesions can now be detected by molecular analyses for genetic or epigenetic alterations associated with tumorigenesis and could precede morphological tumor formation.[48] An emerging indication that alterations in epigenetic marks could be used as biomarkers (especially DNA methylation) was provided by analyses of hypermethylation of O-6-methylguanine-DNA methyltransferase (*MGMT*)[49] in gliomas and glutathione S-transferase pi 1 (*GSTP1*) in prostate cancer.[50] These hypermethylation events have been shown to be effective in the diagnosis of cancers. The detection of epigenetic alterations is therefore a promising auxiliary cancer diagnostic tool. *APC* promoter methylation seems an ideal cancer biomarker because previous study demonstrates this to be an early event in a number of different malignancies.[51] However, the diagnostic power of *APC* hypermethylation in EC has been less investigated. Therefore, we performed a pooled analysis of 18 studies, including 2360 samples. Our results showed that the pooled AUC of *APC* methylation in distinguishing EC from normal control was 0.94, with 96% specificity and 55% sensitivity, and the pooled AUC for differentiating BE from normal controls was 0.88, with 96% specificity and 48% sensitivity. Besides, we mapped Fagan plots to analyze the clinical utility of *APC* methylation as an auxiliary diagnostic biomarker of EC and BE. The Fagan plot indicated that the probability of EC or BE diagnosis was remarkably increased with the detection of significant *APC* hypermethylation frequency even in people with low risks of developing EC or BE based on other clinical parameters. These findings suggest that the hypermethylation of *APC* has a potential in the diagnosis of EC and BE.

Conclusion

The notable findings of the current study are the significant association between *APC* methylation and increased risk of EC and BE and its potential role as an early diagnostic biomarker of EC. However, further studies regarding the role of *APC* methylation in EC progression are required.

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Author contributions

BW, HS, XD, and CZ contributed to the conception, design, and final approval of the submitted version. BW, HS, YF, HJ, and CZ contributed to the meta-analysis, interpretation of data, and preparation of figures and tables. All authors are responsible for the content and writing of the paper. All the authors read and approved the final manuscript. All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work

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Supplementary materials

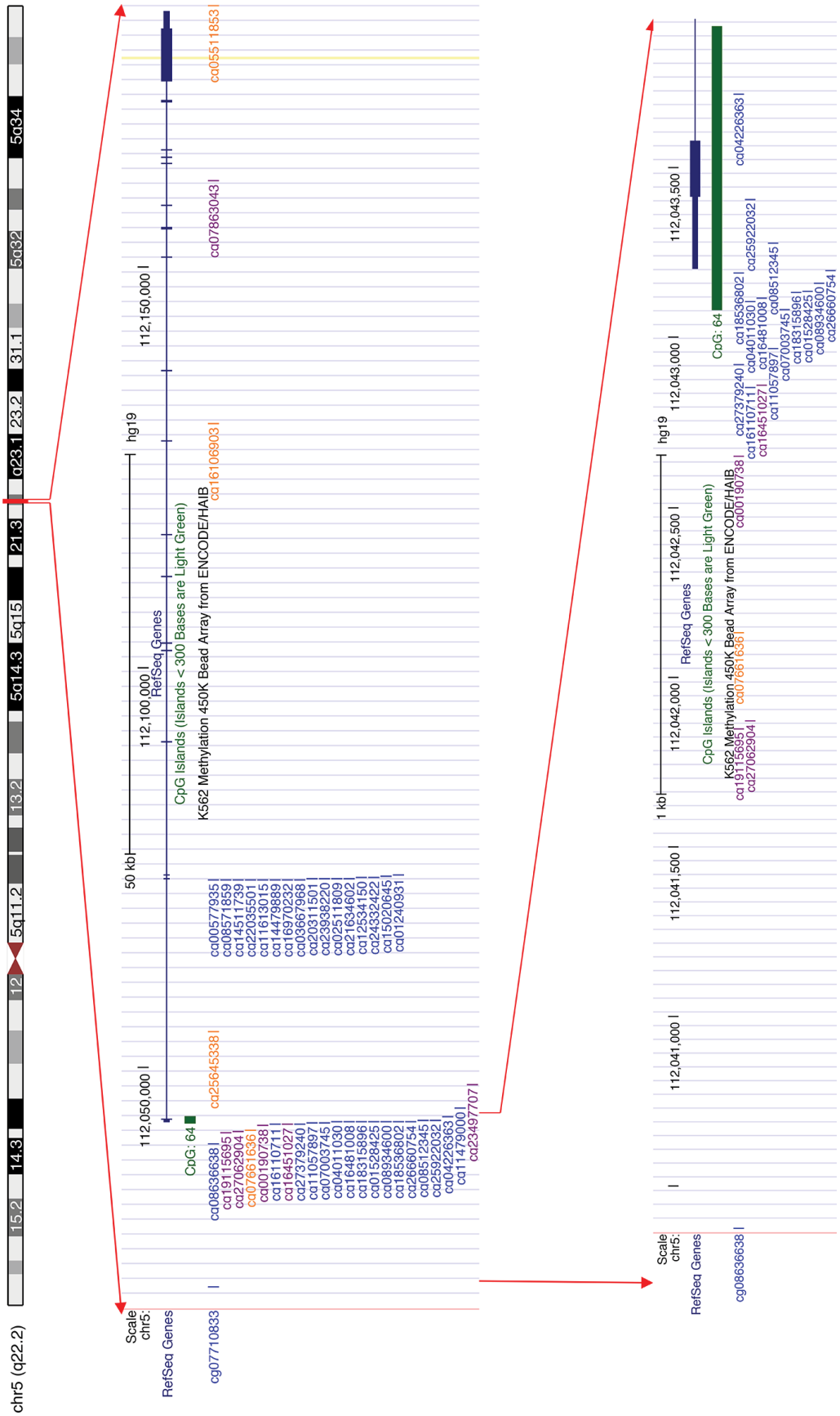

Figure S1 All the CpG island probes located in the APC.

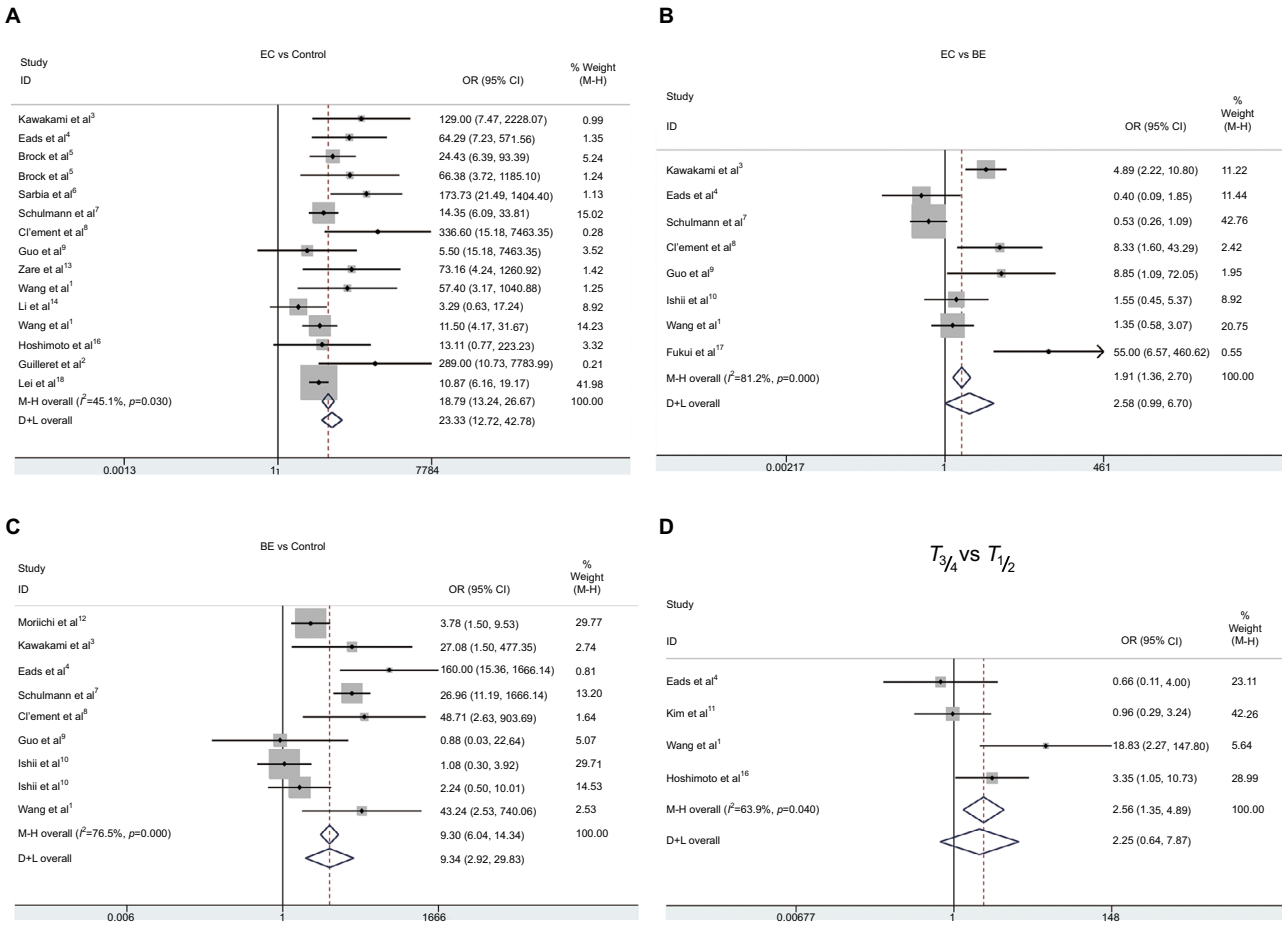

Figure S2 Pooled forest plot of *APC* methylation status during the carcinogenesis of EC.
Note: (**A**) Cancer vs. control: OR = 23.33; 95% CI, 12.72 – 42.78. (**B**) Cancer vs. BE: OR = 2.58; 95% CI,0.99– 6.70. (**C**) BE vs. control: OR = 9.34; 95% CI, 2.92 – 29.82. (**D**) $T_{3/4}$ vs. $T_{1/2}$: OR = 2.25; 95% CI, 0.64 – 7.87.
Abbreviations: BE, Barrett's esophagus; EC, esophageal cancer.

Table S1 Methylation data of *APC* and survival data of all EC patients from TCGA

sample	RFS days	RFS status	OS days	OS status	cg25673075	cg07710833	cg08636638	cg19115695	cg27062904	cg07661636	cg00190738	cg16110711	cg16451027	cg27379240	cg11057897	cg07003745	cg04011030	cg16481008	cg18315896	cg01528425	cg08934600	cg18536802	cg26640754	cg08512345	cg25922032	cg04226363	cg11479000	cg23497707	cg25645338	cg00577935	cg08571859	cg14511739	cg22035501	cg11613015	cg14479889	cg16970232	cg03667968	cg20311501	cg23938220	cg02511809	cg21634602	cg12534150	cg24332422	cg15020645	cg01240931	cg16106903	cg07863043
TCGA-R6-A6L6-01	214	other wise	214	death	/	0.7396	/	/	/	/	/	/	/	/	0.1803	/	0.062	0.0558	0.0282	0.0501	0.0282	0.0557	0.0819	0.0226	0.0254	0.0286	0.427	0.803	/	0.1577	0.2072	0.1807	0.187	0.1121	0.2465	0.2591	0.1433	0.3341	0.2776	0.4332	0.3162	0.0639	0.2024	0.162	0.4214	/	/
TCGA-R6-A6DN-01	199	other wise	243	death	/	0.5852	/	/	/	/	/	/	/	/	0.1083	/	0.0464	0.0443	0.0348	0.0467	0.0382	0.0437	0.0514	0.016	0.015	0.0191	0.3513	0.8433	/	0.815	0.7797	0.8708	0.8792	0.7379	0.831	0.874	0.9216	0.8257	0.7381	0.772	0.9297	0.8709	0.6476	0.7684	0.8194	/	/
TCGA-R6-A6KZ-01	154	other wise	154	death	/	0.7996	/	/	/	/	/	/	/	/	0.1571	/	0.0568	0.0375	0.0463	0.0427	0.0267	0.0459	0.0626	0.0164	0.0157	0.0256	0.2268	0.6776	/	0.4881	0.439	0.529	0.6249	0.4388	0.6202	0.6203	0.7034	0.6288	0.6213	0.7133	0.8064	0.5363	0.5093	0.4953	0.5162	/	/
TCGA-V5-A7RC-06	104	other wise	104	death	/	0.861	/	/	/	/	/	/	/	/	0.2098	/	0.0466	0.0408	0.0455	0.0526	0.0337	0.0961	0.1517	0.0128	0.0147	0.0311	0.429	0.6627	/	0.0324	0.0488	0.032	0.0393	0.0481	0.0356	0.0446	0.0301	0.0779	0.0374	0.1817	0.059	0.027	0.0638	0.0293	0.2265	/	/
TCGA-V5-A7RC-01	104	other wise	104	death	/	0.8414	/	/	/	/	/	/	/	/	0.257	/	0.0472	0.0499	0.0457	0.0471	0.0301	0.0382	0.0708	0.0164	0.0181	0.0225	0.2508	0.7325	/	0.0359	0.0371	0.0358	0.049	0.0483	0.0254	0.0396	0.0347	0.0658	0.0178	0.1127	0.0574	0.0316	0.0354	0.0193	0.1523	/	/
TCGA-IG-A51D-01	518	other wise	518	censor	/	0.8635	/	/	/	/	/	/	/	/	0.2247	/	0.0502	0.0406	0.0431	0.0442	0.0264	0.0492	0.0792	0.0187	0.0166	0.0261	0.6547	0.8295	/	0.0267	0.024	0.0257	0.0296	0.0337	0.0384	0.0289	0.0216	0.0619	0.0143	0.0887	0.0449	0.0192	0.0381	0.0199	0.2311	/	/
TCGA-VR-AA7D-01	/	/	279	death	/	0.8072	/	/	/	/	/	/	/	/	0.4361	/	0.052	0.0496	0.042	0.049	0.0367	0.0536	0.0852	0.0182	0.0152	0.0323	0.7353	0.8351	/	0.0312	0.0343	0.0279	0.035	0.0418	0.0246	0.034	0.0224	0.0579	0.0166	0.1616	0.0407	0.0278	0.0387	0.024	0.4049	/	/
TCGA-VR-AA7B-01	/	/	342	censor	/	0.8886	/	/	/	/	/	/	/	/	0.1536	/	0.0512	0.0437	0.0436	0.0611	0.0384	0.0652	0.0847	0.0202	0.0199	0.0293	0.2892	0.752	/	0.0283	0.026	0.0245	0.0408	0.0321	0.0318	0.0326	0.0227	0.0545	0.0144	0.1454	0.0559	0.0269	0.0545	0.0181	0.2923	/	/
TCGA-VR-A8EP-01	824	other wise	824	censor	/	0.8387	/	/	/	/	/	/	/	/	0.2289	/	0.0466	0.033	0.0462	0.0497	0.0314	0.0406	0.0898	0.0272	0.0212	0.0275	0.6123	0.5997	/	0.0284	0.0307	0.0314	0.0382	0.0335	0.0294	0.0369	0.0257	0.072	0.0158	0.1347	0.0516	0.0243	0.0525	0.0272	0.2925	/	/
TCGA-VR-A8EZ-01	/	/	553	death	/	0.8628	/	/	/	/	/	/	/	/	0.1594	/	0.0715	0.0384	0.0426	0.0495	0.0328	0.0603	0.0567	0.0184	0.0186	0.0339	0.428	0.7159	/	0.0399	0.0538	0.0463	0.0553	0.0613	0.04	0.0594	0.0498	0.1198	0.0202	0.1257	0.1108	0.0349	0.0751	0.0471	0.3249	/	/
TCGA-VR-A8EY-01	1025	other wise	1025	censor	/	0.7792	/	/	/	/	/	/	/	/	0.4462	/	0.0589	0.0346	0.0285	0.0513	0.0332	0.0487	0.0521	0.0158	0.0184	0.0312	0.4783	0.8577	/	0.0337	0.0317	0.0346	0.0784	0.0457	0.0381	0.0493	0.0324	0.1032	0.0138	0.0616	0.1098	0.0252	0.0416	0.0304	0.0947	/	/
TCGA-VR-A8ET-01	47	other wise	47	death	/	0.7944	/	/	/	/	/	/	/	/	0.2608	/	0.055	0.0453	0.0452	0.0538	0.0336	0.0547	0.0818	0.016	0.0169	0.0266	0.6508	0.7627	/	0.2437	0.2867	0.3169	0.3625	0.3186	0.3675	0.3851	0.3505	0.421	0.4174	0.5245	0.3591	0.2055	0.283	0.2558	0.4088	/	/
TCGA-L7-A56G-01	270	new tumor	330	death	/	0.8841	/	/	/	/	/	/	/	/	0.1561	/	0.044	0.0357	0.0357	0.0343	0.0361	0.0393	0.0553	0.0178	0.0148	0.0227	0.7135	0.7817	/	0.0208	0.0263	0.0208	0.0284	0.0446	0.0389	0.0325	0.0221	0.0648	0.0102	0.0596	0.0574	0.019	0.0279	0.0178	0.5353	/	/
TCGA-VR-AA4D-01	1405	other wise	1405	death	/	0.6214	/	/	/	/	/	/	/	/	0.1291	/	0.0532	0.0449	0.0477	0.0557	0.0391	0.036	0.0664	0.0156	0.0151	0.0314	0.7403	0.855	/	0.5287	0.7325	0.8108	0.8794	0.7128	0.8197	0.8293	0.8853	0.7681	0.7126	0.752	0.9229	0.8147	0.6501	0.7042	0.7819	/	/
TCGA-V5-AASX-01	273	new tumor	273	censor	/	0.6749	/	/	/	/	/	/	/	/	0.2309	/	0.0499	0.0361	0.0363	0.0465	0.0374	0.0441	0.0552	0.015	0.016	0.0273	0.5005	0.8457	/	0.0646	0.0494	0.037	0.0677	0.0735	0.0515	0.0759	0.0587	0.125	0.0108	0.0818	0.5328	0.0309	0.0507	0.0635	0.6175	/	/
TCGA-VR-A8EW-01	/	/	247	death	/	0.9043	/	/	/	/	/	/	/	/	0.1747	/	0.037	0.0347	0.0307	0.0381	0.0335	0.0466	0.0603	0.0154	0.0203	0.028	0.6847	0.6238	/	0.0416	0.0366	0.0308	0.0444	0.0473	0.0395	0.0396	0.0362	0.0824	0.0131	0.0791	0.0943	0.0262	0.0357	0.0296	0.3308	/	/
TCGA-VR-AA4G-01	549	other wise	549	censor	/	0.7497	/	/	/	/	/	/	/	/	0.2446	/	0.0548	0.0441	0.0487	0.0552	0.0303	0.0686	0.0762	0.0141	0.0158	0.0315	0.5819	0.819	/	0.0294	0.0351	0.0279	0.0383	0.053	0.0272	0.0463	0.0344	0.1071	0.0136	0.1507	0.2	0.0256	0.0578	0.0294	0.3756	/	/
TCGA-L5-A43C-01	96	other wise	96	censor	/	0.807	/	/	/	/	/	/	/	/	0.321	/	0.093	0.0458	0.0506	0.054	0.0489	0.0539	0.087	0.0178	0.0201	0.0339	0.593	0.8634	/	0.4494	0.4635	0.5079	0.512	0.5026	0.4999	0.5453	0.5461	0.5861	0.5355	0.6065	0.6166	0.4213	0.4222	0.4349	0.4707	/	/
TCGA-V5-A7RB-01	161	other wise	161	death	/	0.904	/	/	/	/	/	/	/	/	0.222	/	0.0632	0.0376	0.045	0.0617	0.0403	0.0568	0.087	0.0206	0.0238	0.0283	0.3535	0.5852	/	0.6194	0.5894	0.6311	0.6861	0.4848	0.6256	0.679	0.663	0.703	0.6066	0.6687	0.6907	0.5636	0.4905	0.564	0.6099	/	/
TCGA-R6-A6XQ-01	193	other wise	193	death	/	0.2666	/	/	/	/	/	/	/	/	0.0967	/	0.057	0.0461	0.0424	0.0475	0.0468	0.0596	0.0785	0.0184	0.0211	0.0335	0.1181	0.5982	/	0.7268	0.7406	0.8232	0.8794	0.7805	0.717	0.7218	0.8406	0.8467	0.7421	0.7933	0.8391	0.7685	0.6379	0.7225	0.5055	/	/
TCGA-R6-A6Y0-01	1641	other wise	1641	censor	/	0.8703	/	/	/	/	/	/	/	/	0.2433	/	0.0567	0.0395	0.0394	0.0531	0.044	0.052	0.0733	0.0194	0.0195	0.0265	0.5568	0.795	/	0.2865	0.3212	0.2619	0.2452	0.1744	0.3595	0.3882	0.376	0.4692	0.4244	0.5175	0.5429	0.2092	0.2797	0.292	0.4837	/	/
TCGA-VR-A8EX-01	/	/	855	death	/	0.8593	/	/	/	/	/	/	/	/	0.2905	/	0.0385	0.0432	0.0352	0.044	0.0309	0.0471	0.0646	0.0165	0.0202	0.0248	0.566	0.6864	/	0.3259	0.3802	0.2512	0.3316	0.1593	0.4329	0.4545	0.3947	0.485	0.3992	0.498	0.4992	0.2274	0.2791	0.2433	0.503	/	/
TCGA-VR-A8EU-01	557	other wise	557	death	/	0.902	/	/	/	/	/	/	/	/	0.1889	/	0.0472	0.0351	0.0397	0.0517	0.0398	0.0648	0.0673	0.0175	0.0193	0.0288	0.8683	0.8899	/	0.0441	0.0337	0.0385	0.0406	0.0529	0.0495	0.041	0.0255	0.1011	0.0146	0.0592	0.0955	0.024	0.0364	0.0479	0.3012	/	/
TCGA-VR-A8ER-01	/	/	378	death	/	0.8998	/	/	/	/	/	/	/	/	0.2219	/	0.0427	0.0389	0.0431	0.0352	0.0285	0.0369	0.0679	0.0237	0.0208	0.0248	0.7936	0.5685	/	0.0328	0.0389	0.0264	0.0452	0.0518	0.035	0.0424	0.0286	0.0884	0.0148	0.0947	0.0859	0.0262	0.0402	0.0309	0.156	/	/
TCGA-R6-A6DQ-01	231	other wise	231	death	/	0.8252	/	/	/	/	/	/	/	/	0.2241	/	0.0678	0.0387	0.0417	0.0375	0.0385	0.0541	0.0615	0.0147	0.0139	0.0312	0.4649	0.7839	/	0.5803	0.5827	0.7051	0.6342	0.5544	0.6027	0.686	0.7202	0.6785	0.6137	0.6614	0.8463	0.528	0.463	0.4774	0.5964	/	/
TCGA-V5-AASW-01	282	new tumor	282	censor	/	0.8693	/	/	/	/	/	/	/	/	0.1363	/	0.0458	0.0296	0.043	0.0485	0.0562	0.052	0.0852	0.0126	0.0162	0.0233	0.2762	0.8175	/	0.68	0.6666	0.7575	0.7191	0.6758	0.7181	0.7271	0.7638	0.7398	0.6428	0.7032	0.7774	0.638	0.5976	0.6432	0.7069	/	/
TCGA-R6-A8W8-01	88	other wise	88	death	/	0.824	/	/	/	/	/	/	/	/	0.1677	/	0.0536	0.046	0.0545	0.0397	0.0406	0.0531	0.0658	0.0133	0.0155	0.031	0.2715	0.7296	/	0.7636	0.7438	0.7198	0.7691	0.5219	0.7769	0.837	0.8611	0.788	0.7092	0.7353	0.8921	0.7099	0.6352	0.6208	0.763	/	/
TCGA-R6-A6XG-01	572	new tumor	1168	censor	/	0.8773	/	/	/	/	/	/	/	/	0.1475	/	0.0559	0.0417	0.0407	0.0561	0.0419	0.0396	0.0815	0.0236	0.0241	0.027	0.353	0.8976	/	0.801	0.74	0.8302	0.87	0.8095	0.7805	0.7955	0.8832	0.8208	0.7196	0.8091	0.8784	0.7579	0.6843	0.6813	0.7307	/	/
TCGA-VR-A8Q7-01	1590	other wise	1590	censor	/	0.6443	/	/	/	/	/	/	/	/	0.2905	/	0.0468	0.0447	0.0366	0.0463	0.0215	0.0504	0.0852	0.0184	0.0145	0.03	0.5783	0.7695	/	0.4124	0.4485	0.4483	0.4324	0.3395	0.5284	0.5369	0.5472	0.5923	0.4973	0.5743	0.8889	0.4043	0.3462	0.4061	0.557	/	/
TCGA-IG-A50L-01	/	/	16	censor	/	0.8959	/	/	/	/	/	/	/	/	0.2536	/	0.0457	0.035	0.0378	0.0406	0.0342	0.0395	0.0552	0.0203	0.0159	0.0225	0.8131	0.8491	/	0.0269	0.0238	0.0263	0.033	0.0467	0.0297	0.0477	0.0217	0.0909	0.0135	0.078	0.0619	0.0214	0.0435	0.0221	0.3322	/	/
TCGA-Z6-A8JE-01	64	other wise	64	censor	/	0.6096	/	/	/	/	/	/	/	/	0.226	/	0.0593	0.047	0.0762	0.0491	0.035	0.0649	0.0774	0.0166	0.0209	0.0289	0.6648	0.4568	/	0.0496	0.0421	0.057	0.09	0.0795	0.0381	0.0655	0.0645	0.1334	0.02	0.1269	0.3344	0.0453	0.0629	0.0386	0.5918	/	/
TCGA-V5-A7RE-01	294	new tumor	500	censor	/	0.4425	/	/	/	/	/	/	/	/	0.1425	/	0.0674	0.0429	0.0414	0.0465	0.0348	0.0341	0.0691	0.0152	0.0201	0.031	0.1838	0.8798	/	0.7584	0.7095	0.8124	0.791	0.6872	0.7394	0.7717	0.8189	0.7541	0.6823	0.7546	0.852	0.7339	0.6568	0.6964	0.7828	/	/
TCGA-R6-A6L4-01	167	new tumor	496	death	/	0.8563	/	/	/	/	/	/	/	/	0.1335	/	0.0539	0.0344	0.0417	0.0434	0.0273	0.0436	0.0638	0.0176	0.0184	0.0214	0.3477	0.7953	/	0.4844	0.4493	0.5138	0.5755	0.5006	0.5565	0.5658	0.6162	0.5907	0.5186	0.6192	0.8059	0.4443	0.4043	0.4572	0.5734	/	/
TCGA-VR-A8EQ-01	694	other wise	694	death	/	0.7624	/	/	/	/	/	/	/	/	0.3162	/	0.0498	0.0534	0.0369	0.0396	0.033	0.0557	0.0779	0.0199	0.0302	0.0265	0.7316	0.7784	/	0.4606	0.469	0.494	0.5303	0.4024	0.545	0.5858	0.5636	0.6445	0.4482	0.6052	0.6496	0.4481	0.3843	0.4316	0.5362	/	/
TCGA-LN-A49W-01	403	other wise	403	censor	/	0.8949	/	/	/	/	/	/	/	/	0.2354	/	0.0623	0.0382	0.0442	0.053	0.0416	0.0461	0.0811	0.0203	0.016	0.0262	0.8196	0.8843	/	0.0343	0.0294	0.0238	0.0332	0.0375	0.0313	0.0289	0.0204	0.0852	0.0149	0.0948	0.0496	0.0224	0.0647	0.0241	0.3446	/	/
TCGA-LN-A4A3-01	388	other wise	388	censor	/	0.8062	/	/	/	/	/	/	/	/	0.2333	/	0.054	0.0469	0.0392	0.0614	0.0298	0.0428	0.0783	0.0197	0.019	0.0333	0.7745	0.6627	/	0.0239	0.0342	0.0266	0.0334	0.0324	0.035	0.0325	0.0209	0.0841	0.0114	0.1057	0.0655	0.0212	0.0417	0.0259	0.3168	/	/
TCGA-LN-A49R-01	407	other wise	407	censor	/	0.9024	/	/	/	/	/	/	/	/	0.2537	/	0.0685	0.0387	0.0402	0.0442	0.0439	0.0451	0.0785	0.0136	0.0163	0.034	0.2959	0.8653	/	0.0245	0.0259	0.0236	0.0269	0.0395	0.036	0.0402	0.0257	0.0706	0.0148	0.1096	0.0672	0.0199	0.0782	0.0323	0.2606	/	/
TCGA-LN-A4MQ-01	25	new tumor	375	censor	/	0.877	/	/	/	/	/	/	/	/	0.4409	/	0.0394	0.047	0.0337	0.0477	0.0541	0.062	0.0743	0.0229	0.0233	0.0277	0.7124	0.8032	/	0.0325	0.0383	0.0341	0.0355	0.0478	0.0254	0.0361	0.0265	0.1034	0.0167	0.1191	0.0605	0.0296	0.0576	0.0231	0.234	/	/
TCGA-LN-A4A4-01	383	other wise	383	censor	/	0.8943	/	/	/	/	/	/	/	/	0.1645	/	0.0415	0.0387	0.0526	0.0489	0.0317	0.0352	0.0731	0.0266	0.019	0.0249	0.7001	0.6699	/	0.6337	0.5255	0.6751	0.7148	0.6627	0.6487	0.6431	0.7561	0.7424	0.6291	0.6939	0.7204	0.6254	0.5026	0.5872	0.5413	/	/
TCGA-R6-A6Y2-01	/	/	283	death	/	0.8226	/	/	/	/	/	/	/	/	0.2512	/	0.0625	0.0447	0.0607	0.0414	0.0348	0.059	0.0671	0.0184	0.0273	0.0435	0.5082	0.8535	/	0.5088	0.5324	0.4714	0.5485	0.4419	0.5422	0.5828	0.5808	0.6637	0.5309	0.647	0.6903	0.4682	0.4786	0.4733	0.5486	/	/
TCGA-LN-A49N-01	378	other wise	378	censor	/	0.8837	/	/	/	/	/	/	/	/	0.28	/	0.0729	0.038	0.0437	0.0491	0.0408	0.0567	0.0683	0.0179	0.02	0.0285	0.5309	0.7917	/	0.0276	0.0445	0.0342	0.0444	0.0567	0.0284	0.0538	0.0261	0.1087	0.0137	0.1409	0.063	0.0284	0.0627	0.0266	0.2421	/	/
TCGA-IC-A6RF-01	293	new tumor	477	censor	/	0.8957	/	/	/	/	/	/	/	/	0.2438	/	0.0302	0.0365	0.0467	0.0469	0.0385	0.0549	0.0739	0.0245	0.0223	0.0224	0.3839	0.7189	/	0.5219	0.6114	0.6403	0.6813	0.5927	0.5862	0.6463	0.669	0.6523	0.587	0.6726	0.6606	0.5235	0.4918	0.5051	0.5811	/	/
TCGA-XP-A8T8-01	437	other wise	437	censor	/	0.9055	/	/	/	/	/	/	/	/	0.1986	/	0.0603	0.0558	0.0462	0.0602	0.0345	0.0526	0.0611	0.0198	0.0225	0.0255	0.6179	0.7323	/	0.0308	0.0383	0.0312	0.046	0.0581	0.029	0.0421	0.032	0.0806	0.0151	0.1089	0.0826	0.0212	0.0519	0.0618	0.5387	/	/
TCGA-S8-A6BV-01	267	new tumor	609	censor	/	0.8899	/	/	/	/	/	/	/	/	0.2078	/	0.0499	0.043	0.0332	0.0343	0.0298	0.0505	0.0649	0.0181	0.0173	0.0238	0.5982	0.8659	/	0.4824	0.4858	0.5239	0.5181	0.4364	0.494	0.6083	0.5912	0.605	0.5531	0.6061	0.7895	0.403	0.3948	0.4147	0.5159	/	/
TCGA-VR-AA7I-01	/	/	484	death	/	0.8391	/	/	/	/	/	/	/	/	0.2089	/	0.0542	0.0366	0.0474	0.0538	0.0414	0.063	0.0835	0.0226	0.021	0.0279	0.4418	0.7658	/	0.0279	0.0312	0.029	0.0416	0.063	0.0396	0.0325	0.0241	0.065	0.0158	0.1529	0.05	0.0318	0.0565	0.0256	0.277	/	/
TCGA-LN-A49Y-01	90	new tumor	379	censor	/	0.1139	/	/	/	/	/	/	/	/	0.1228	/	0.0458	0.0493	0.0376	0.042	0.0452	0.0463	0.067	0.0141	0.0166	0.0226	0.1144	0.2491	/	0.6267	0.567	0.8386	0.9569	0.8866	0.7727	0.7103	0.9272	0.8887	0.8452	0.8651	0.8453	0.9058	0.7515	0.7649	0.7302	/	/
TCGA-LN-A49P-01	320	new tumor	375	censor	/	0.9109	/	/	/	/	/	/	/	/	0.2819	/	0.0896	0.0639	0.0418	0.0463	0.0366	0.0581	0.0617	0.0201	0.0205	0.0341	0.6664	0.7074	/	0.0372	0.0304	0.0261	0.0362	0.0405	0.0306	0.0415	0.0288	0.0637	0.0142	0.1358	0.0639	0.0269	0.0774	0.0415	0.4178	/	/
TCGA-LN-A49K-01	180	other wise	180	death	/	0.8929	/	/	/	/	/	/	/	/	0.2661	/	0.0594	0.0408	0.043	0.0503	0.0457	0.0426	0.06	0.0175	0.0201	0.0309	0.6186	0.8136	/	0.0349	0.0303	0.0361	0.04	0.0553	0.0332	0.04	0.0257	0.0686	0.0149	0.1298	0.0681	0.0286	0.0941	0.0436	0.3822	/	/
TCGA-LN-A49U-01	467	other wise	467	censor	/	0.8512	/	/	/	/	/	/	/	/	0.1913	/	0.0481	0.0401	0.0373	0.0402	0.0219	0.0296	0.0556	0.0317	0.022	0.0245	0.3969	0.7316	/	0.0332	0.028	0.0337	0.0424	0.0534	0.05	0.0304	0.0321	0.0546	0.013	0.0766	0.0559	0.0287	0.0345	0.0257	0.1633	/	/
TCGA-LN-A4A1-01	205	new tumor	383	censor	/	0.6696	/	/	/	/	/	/	/	/	0.1681	/	0.0319	0.0414	0.0352	0.0485	0.0323	0.0459	0.0762	0.0184	0.0167	0.0277	0.8739	0.8268	/	0.0247	0.0228	0.0261	0.0369	0.0391	0.0229	0.0398	0.0245	0.0532	0.0128	0.0564	0.0592	0.0207	0.0368	0.0265	0.3236	/	/
TCGA-R6-A8WG-01	/	/	386	death	/	0.4056	/	/	/	/	/	/	/	/	0.1882	/	0.0514	0.0441	0.048	0.0334	0.0219	0.045	0.0861	0.0157	0.0165	0.0317	0.3673	0.6375	/	0.6122	0.6079	0.6888	0.6384	0.4315	0.6685	0.7089	0.6791	0.6526	0.5965	0.6719	0.8515	0.4558	0.4487	0.5074	0.6509	/	/
TCGA-LN-A49S-01	49	new tumor	400	censor	/	0.8629	/	/	/	/	/	/	/	/	0.2653	/	0.0492	0.0276	0.029	0.0451	0.0475	0.0426	0.0569	0.0148	0.0174	0.0289	0.4297	0.543	/	0.032	0.0438	0.0226	0.0402	0.0557	0.034	0.0384	0.0212	0.0528	0.015	0.1275	0.0553	0.0238	0.0773	0.0258	0.3319	/	/
TCGA-LN-A4A2-01	380	other wise	380	censor	/	0.9061	/	/	/	/	/	/	/	/	0.3182	/	0.0449	0.0348	0.0329	0.0401	0.025	0.0356	0.0607	0.0193	0.0191	0.0229	0.4528	0.8448	/	0.025	0.0212	0.0241	0.0332	0.04	0.0238	0.0319	0.0176	0.039	0.0129	0.0784	0.0519	0.0226	0.05	0.0196	0.4797	/	/
TCGA-R6-A8WC-01	70	other wise	70	censor	/	0.1862	/	/	/	/	/	/	/	/	0.078	/	0.0518	0.0461	0.0575	0.0552	0.0273	0.0551	0.0734	0.0153	0.0191	0.0391	0.2363	0.8405	/	0.8908	0.8466	0.9529	0.9472	0.7559	0.9242	0.9141	0.9585	0.8606	0.8726	0.8578	0.8956	0.949	0.8081	0.886	0.8356	/	/
TCGA-VR-A8EO-01	785	other wise	785	censor	/	0.8574	/	/	/	/	/	/	/	/	0.4058	/	0.0541	0.0383	0.0378	0.0437	0.04	0.0406	0.0528	0.0259	0.0247	0.0358	0.7981	0.8747	/	0.0589	0.0399	0.0413	0.0535	0.0716	0.046	0.0578	0.0424	0.0906	0.0192	0.0632	0.0996	0.0323	0.0422	0.04	0.5191	/	/
TCGA-LN-A49V-01	383	other wise	383	censor	/	0.9257	/	/	/	/	/	/	/	/	0.3911	/	0.062	0.0511	0.0545	0.0623	0.039	0.0512	0.0749	0.0194	0.017	0.0262	0.6584	0.9173	/	0.5386	0.5323	0.618	0.5869	0.5862	0.5505	0.6395	0.6447	0.6651	0.5921	0.6492	0.6974	0.5432	0.4756	0.502	0.6771	/	/
TCGA-LN-A49O-01	193	new tumor	408	censor	/	0.8392	/	/	/	/	/	/	/	/	0.2169	/	0.0617	0.0579	0.0384	0.0555	0.0336	0.0406	0.0463	0.0158	0.0157	0.025	0.7271	0.9017	/	0.028	0.0351	0.0273	0.0316	0.0448	0.0419	0.0418	0.0295	0.0958	0.0134	0.1315	0.0611	0.0257	0.0772	0.0364	0.2519	/	/
TCGA-LN-A49X-01	384	other wise	384	censor	/	0.8963	/	/	/	/	/	/	/	/	0.3129	/	0.0528	0.0405	0.0427	0.0411	0.0362	0.0541	0.0804	0.0174	0.0203	0.0304	0.7548	0.861	/	0.0268	0.0388	0.0214	0.0313	0.0438	0.0299	0.0316	0.0225	0.0855	0.0109	0.0813	0.054	0.0186	0.0716	0.0292	0.3866	/	/
TCGA-LN-A49M-01	385	other wise	385	censor	/	0.6217	/	/	/	/	/	/	/	/	0.293	/	0.0357	0.0351	0.0257	0.045	0.0265	0.0339	0.0512	0.0217	0.0183	0.0231	0.489	0.7971	/	0.0266	0.0214	0.022	0.0327	0.0536	0.0246	0.0335	0.0278	0.0652	0.0148	0.0747	0.0472	0.023	0.0328	0.0214	0.2337	/	/
TCGA-LN-A4A9-01	274	new tumor	351	death	/	0.8559	/	/	/	/	/	/	/	/	0.1811	/	0.0637	0.0426	0.0452	0.0469	0.0621	0.0746	0.0788	0.0164	0.0198	0.0306	0.2277	0.8781	/	0.0237	0.0353	0.0317	0.0407	0.0387	0.033	0.0358	0.0265	0.0835	0.0172	0.1821	0.0581	0.0244	0.0557	0.025	0.2188	/	/
TCGA-LN-A4MR-01	226	new tumor	402	censor	/	0.9066	/	/	/	/	/	/	/	/	0.2224	/	0.0799	0.0497	0.0535	0.0463	0.0463	0.0583	0.0781	0.0263	0.0183	0.0227	0.5113	0.7986	/	0.0303	0.0289	0.0242	0.0415	0.0356	0.0271	0.034	0.0254	0.076	0.0122	0.1457	0.0479	0.0273	0.0716	0.0297	0.2467	/	/
TCGA-LN-A4A8-01	250	new tumor	472	censor	/	0.5523	/	/	/	/	/	/	/	/	0.2296	/	0.0439	0.0343	0.028	0.0399	0.0345	0.0334	0.0601	0.0152	0.0179	0.0248	0.5319	0.7719	/	0.0261	0.023	0.0312	0.0425	0.0437	0.028	0.0391	0.0236	0.078	0.0132	0.107	0.0552	0.0238	0.0496	0.0399	0.5333	/	/
TCGA-LN-A4A5-01	224	new tumor	681	death	/	0.8679	/	/	/	/	/	/	/	/	0.2395	/	0.0388	0.034	0.0393	0.0477	0.0348	0.0448	0.0488	0.0198	0.0153	0.0207	0.6905	0.8777	/	0.0198	0.0229	0.025	0.0336	0.0404	0.025	0.0311	0.0239	0.0537	0.014	0.0888	0.0437	0.0234	0.0508	0.0303	0.3385	/	/
TCGA-LN-A49L-01	318	other wise	318	death	/	0.9206	/	/	/	/	/	/	/	/	0.2305	/	0.0779	0.0536	0.0453	0.0497	0.0439	0.0448	0.0796	0.0156	0.0207	0.0315	0.433	0.6468	/	0.042	0.0346	0.0297	0.0419	0.0551	0.0354	0.0577	0.0281	0.0816	0.014	0.1583	0.0537	0.0269	0.0883	0.0604	0.411	/	/
TCGA-LN-A4A6-01	158	new tumor	391	censor	/	0.8501	/	/	/	/	/	/	/	/	0.2577	/	0.0482	0.0509	0.0589	0.0496	0.0349	0.0369	0.0617	0.0149	0.0171	0.0217	0.4464	0.5069	/	0.0215	0.0279	0.0213	0.0251	0.0365	0.0376	0.0341	0.0193	0.0536	0.0116	0.1137	0.0451	0.0166	0.0474	0.0208	0.3249	/	/
TCGA-KH-A6WC-01	191	other wise	191	censor	/	0.887	/	/	/	/	/	/	/	/	0.2766	/	0.0501	0.0508	0.0486	0.0542	0.0402	0.0495	0.0866	0.023	0.0217	0.0234	0.6006	0.6789	/	0.0343	0.0302	0.026	0.0374	0.0405	0.0383	0.0481	0.0241	0.0947	0.0159	0.1052	0.0647	0.0262	0.0583	0.0385	0.3406	/	/
TCGA-L5-A43J-01	98	new tumor	131	death	/	0.923	/	/	/	/	/	/	/	/	0.1947	/	0.0399	0.0643	0.0459	0.0486	0.0395	0.0494	0.0718	0.0317	0.0169	0.0306	0.3059	0.8773	/	0.0254	0.0301	0.0303	0.0413	0.0576	0.0317	0.0426	0.0257	0.0723	0.0134	0.1091	0.0726	0.0249	0.0862	0.0248	0.5433	/	/
TCGA-L5-A88T-01	694	other wise	694	censor	/	0.8861	/	/	/	/	/	/	/	/	0.2464	/	0.0466	0.0495	0.0313	0.0327	0.0302	0.0491	0.0789	0.0165	0.0215	0.0275	0.3889	0.6071	/	0.041	0.0441	0.027	0.0367	0.0517	0.0421	0.0604	0.0274	0.0986	0.0269	0.1033	0.083	0.0238	0.0575	0.0352	0.3332	/	/
TCGA-L5-A4OS-01	1782	other wise	1782	censor	/	0.8398	/	/	/	/	/	/	/	/	0.3159	/	0.0596	0.0506	0.0491	0.0493	0.0452	0.059	0.1004	0.0202	0.0217	0.04	0.7576	0.7289	/	0.3001	0.3394	0.3446	0.3286	0.2921	0.4048	0.4547	0.4193	0.4604	0.4872	0.5208	0.448	0.2401	0.3119	0.3039	0.4146	/	/
TCGA-L5-A88S-01	471	other wise	471	censor	/	0.826	/	/	/	/	/	/	/	/	0.2272	/	0.0649	0.0426	0.039	0.0509	0.0384	0.05	0.0658	0.0183	0.0177	0.0331	0.5073	0.6858	/	0.0406	0.0391	0.0263	0.0347	0.0391	0.0337	0.0443	0.0284	0.0959	0.0166	0.0968	0.1074	0.0268	0.0485	0.0253	0.2093	/	/
TCGA-L5-A8NU-01	/	/	2532	death	/	0.8547	/	/	/	/	/	/	/	/	0.3081	/	0.0698	0.0386	0.0452	0.0414	0.0461	0.0496	0.0754	0.0201	0.0208	0.0351	0.654	0.716	/	0.3883	0.4204	0.3793	0.3493	0.2462	0.4561	0.4836	0.4225	0.5486	0.4414	0.5573	0.5539	0.2835	0.3417	0.3469	0.4856	/	/
TCGA-L5-A43M-01	272	other wise	272	censor	/	0.9364	/	/	/	/	/	/	/	/	0.2172	/	0.08	0.0415	0.0377	0.0527	0.0551	0.0483	0.0709	0.0174	0.0166	0.0386	0.3832	0.8809	/	0.2218	0.2093	0.1991	0.1932	0.1194	0.3343	0.384	0.2835	0.4491	0.4137	0.4874	0.4614	0.1938	0.2707	0.2612	0.6197	/	/
TCGA-L5-A8NM-01	236	other wise	236	death	/	0.8598	/	/	/	/	/	/	/	/	0.369	/	0.0393	0.0352	0.0408	0.0497	0.0266	0.053	0.0845	0.0114	0.019	0.0222	0.3475	0.8286	/	0.6249	0.6064	0.6779	0.6748	0.5869	0.6873	0.6213	0.7224	0.6659	0.6217	0.6496	0.8893	0.5051	0.5254	0.503	0.5597	/	/
TCGA-L5-A8NK-01	/	/	412	censor	/	0.8736	/	/	/	/	/	/	/	/	0.2036	/	0.0342	0.032	0.0277	0.0375	0.0155	0.0314	0.0569	0.0111	0.0117	0.0187	0.4798	0.6888	/	0.0273	0.0209	0.0212	0.0368	0.0671	0.0239	0.0332	0.0341	0.0942	0.0115	0.0506	0.3161	0.0201	0.0399	0.0174	0.271	/	/
TCGA-L5-A4OR-01	96	other wise	96	death	/	0.6327	/	/	/	/	/	/	/	/	0.1964	/	0.0574	0.0468	0.0432	0.0269	0.0327	0.0438	0.0599	0.0201	0.0192	0.03	0.4204	0.6206	/	0.6281	0.532	0.6906	0.7238	0.6637	0.6865	0.7151	0.7805	0.7195	0.6548	0.7161	0.7052	0.5407	0.5701	0.5898	0.6234	/	/
TCGA-L5-A4OU-01	882	other wise	882	censor	/	0.8842	/	/	/	/	/	/	/	/	0.2806	/	0.0609	0.0444	0.0492	0.0481	0.0409	0.0539	0.0811	0.0276	0.0212	0.0268	0.5924	0.8831	/	0.2221	0.2452	0.2262	0.1736	0.1159	0.2634	0.2945	0.2334	0.3723	0.3478	0.4287	0.2664	0.1184	0.2122	0.1969	0.3636	/	/
TCGA-L5-A4OE-01	730	other wise	730	death	/	0.8447	/	/	/	/	/	/	/	/	0.3586	/	0.0596	0.0364	0.0365	0.0576	0.0435	0.0554	0.0496	0.0172	0.0178	0.0253	0.4521	0.8975	/	0.5645	0.567	0.6306	0.6597	0.6671	0.6054	0.6169	0.6528	0.6573	0.5583	0.6468	0.6507	0.5433	0.4484	0.4837	0.5701	/	/
TCGA-L5-A8NN-01	/	/	167	censor	/	0.9158	/	/	/	/	/	/	/	/	0.1455	/	0.0521	0.0422	0.0522	0.0439	0.0422	0.0557	0.0771	0.0117	0.0143	0.0224	0.4092	0.8107	/	0.7585	0.7253	0.8402	0.835	0.7857	0.7656	0.7912	0.879	0.807	0.6974	0.779	0.8997	0.7488	0.6332	0.6603	0.7043	/	/
TCGA-L5-A8NR-01	/	/	265	censor	/	0.7968	/	/	/	/	/	/	/	/	0.1531	/	0.0651	0.0475	0.0505	0.0601	0.026	0.0911	0.0747	0.0144	0.0176	0.0328	0.2779	0.7783	/	0.6781	0.7195	0.7416	0.7873	0.5472	0.7434	0.7459	0.83	0.714	0.6416	0.6972	0.8707	0.6677	0.58	0.6241	0.6632	/	/
TCGA-2H-A9GR-01	/	/	987	death	/	0.749	/	/	/	/	/	/	/	/	0.2552	/	0.0572	0.054	0.0508	0.0478	0.018	0.0583	0.0686	0.0152	0.0174	0.03	0.567	0.7744	/	0.6504	0.561	0.4916	0.5517	0.377	0.6698	0.6446	0.6821	0.6314	0.5841	0.6124	0.8665	0.3696	0.4474	0.4903	0.5564	/	/
TCGA-2H-A9GQ-01	/	/	128	death	/	0.7412	/	/	/	/	/	/	/	/	0.1159	/	0.0477	0.0298	0.042	0.0537	0.0235	0.0465	0.0756	0.0143	0.0156	0.026	0.7489	0.8427	/	0.7986	0.7656	0.8939	0.8592	0.8065	0.8375	0.8383	0.928	0.8578	0.7697	0.7953	0.9154	0.8176	0.6763	0.7758	0.7295	/	/
TCGA-L5-A4OI-01	267	new tumor	608	censor	/	0.8627	/	/	/	/	/	/	/	/	0.1253	/	0.0468	0.0522	0.042	0.0486	0.0341	0.0536	0.0771	0.0149	0.0186	0.0242	0.1765	0.8974	/	0.754	0.7354	0.8454	0.8418	0.8097	0.7366	0.7604	0.8574	0.776	0.699	0.7853	0.8018	0.7457	0.632	0.6788	0.6954	/	/
TCGA-L5-A8NI-01	/	/	410	death	/	0.8213	/	/	/	/	/	/	/	/	0.1204	/	0.0614	0.0377	0.0412	0.056	0.0279	0.0365	0.0729	0.015	0.0154	0.0359	0.2214	0.7292	/	0.5445	0.5653	0.5977	0.6609	0.4072	0.6321	0.6889	0.6851	0.6687	0.5785	0.6007	0.862	0.4482	0.4687	0.4675	0.5084	/	/
TCGA-L5-A4OG-01	143	other wise	143	censor	/	0.8704	/	/	/	/	/	/	/	/	0.3013	/	0.0718	0.0442	0.0462	0.0547	0.0287	0.0379	0.0537	0.0197	0.0175	0.0268	0.594	0.8368	/	0.0271	0.0358	0.0294	0.0373	0.049	0.0322	0.0406	0.0271	0.0804	0.0118	0.0399	0.052	0.0215	0.0559	0.025	0.2667	/	/
TCGA-JY-A6FB-01	1837	other wise	1837	censor	/	0.4896	/	/	/	/	/	/	/	/	0.1741	/	0.05	0.0351	0.0342	0.0417	0.032	0.0564	0.0717	0.0178	0.0184	0.0332	0.5027	0.8682	/	0.6549	0.6566	0.7418	0.7598	0.7954	0.7148	0.7238	0.7631	0.7895	0.6289	0.7306	0.7626	0.6588	0.5829	0.6019	0.6337	/	/
TCGA-L5-A8NE-01	1688	other wise	1688	censor	/	0.8198	/	/	/	/	/	/	/	/	0.2029	/	0.0542	0.0371	0.0606	0.0562	0.0338	0.0619	0.0923	0.0181	0.02	0.0386	0.2669	0.7485	/	0.7032	0.7515	0.7769	0.7929	0.6096	0.8118	0.6436	0.8266	0.7313	0.7103	0.7511	0.8827	0.6574	0.6266	0.6732	0.5896	/	/
TCGA-L5-A8NG-01	1094	other wise	1094	censor	/	0.7933	/	/	/	/	/	/	/	/	0.2696	/	0.0595	0.0332	0.0467	0.042	0.0247	0.0594	0.0691	0.0156	0.0157	0.0288	0.4959	0.8473	/	0.2466	0.2709	0.1984	0.2433	0.1495	0.3474	0.4001	0.2787	0.391	0.3898	0.4717	0.6309	0.1446	0.2518	0.2433	0.5254	/	/
TCGA-JY-A939-01	660	other wise	660	censor	/	0.8512	/	/	/	/	/	/	/	/	0.2929	/	0.0694	0.0287	0.0348	0.0474	0.0318	0.062	0.0831	0.0124	0.0135	0.0302	0.5994	0.8568	/	0.3472	0.4018	0.3661	0.405	0.3218	0.4936	0.5241	0.4836	0.5775	0.4963	0.562	0.8171	0.378	0.3775	0.4217	0.5607	/	/
TCGA-L5-A43I-01	556	other wise	556	death	/	0.7916	/	/	/	/	/	/	/	/	0.131	/	0.0657	0.0626	0.0412	0.0654	0.0503	0.0593	0.0885	0.0241	0.0193	0.0285	0.2163	0.6709	/	0.791	0.7498	0.8647	0.8885	0.8729	0.7796	0.7725	0.9004	0.8343	0.7839	0.8286	0.8551	0.832	0.7207	0.7241	0.7098	/	/
TCGA-L5-A4OT-01	149	other wise	149	death	/	0.8021	/	/	/	/	/	/	/	/	0.2046	/	0.0728	0.0464	0.0498	0.0642	0.0444	0.0507	0.0823	0.0259	0.0181	0.0355	0.4626	0.7335	/	0.4154	0.4259	0.4917	0.4309	0.348	0.4654	0.5022	0.5269	0.5547	0.4847	0.5787	0.4908	0.3179	0.32	0.3684	0.4947	/	/
TCGA-L5-A8NJ-01	/	/	501	censor	/	0.8252	/	/	/	/	/	/	/	/	0.1088	/	0.0715	0.0419	0.0289	0.0435	0.0444	0.0467	0.0579	0.0157	0.0175	0.0335	0.257	0.8807	/	0.9046	0.8534	0.9386	0.941	0.8991	0.8981	0.8643	0.9557	0.8852	0.8458	0.8728	0.8976	0.9375	0.7564	0.8328	0.8376	/	/
TCGA-L5-A8NS-01	/	/	408	censor	/	0.734	/	/	/	/	/	/	/	/	0.2302	/	0.0878	0.059	0.068	0.0555	0.0436	0.0785	0.0641	0.0221	0.0226	0.0444	/	0.6412	/	0.505	0.6042	0.6019	0.5208	0.4031	0.6284	0.6625	0.6127	0.7438	0.5646	0.6614	0.8004	0.4	0.5303	0.4993	0.5813	/	/
TCGA-L5-A88Y-01	/	/	11	censor	/	0.5087	/	/	/	/	/	/	/	/	0.2127	/	0.0629	0.0401	0.0464	0.0647	0.0389	0.0572	0.0714	0.0156	0.0165	0.0357	0.3658	0.79	/	0.6419	0.6313	0.7015	0.7255	0.6231	0.6488	0.6916	0.7362	0.7029	0.5984	0.6828	0.7196	0.6197	0.5553	0.5654	0.6524	/	/
TCGA-JY-A938-01	493	new tumor	1060	censor	/	0.8299	/	/	/	/	/	/	/	/	0.2015	/	0.061	0.0429	0.0477	0.0494	0.0338	0.0586	0.0734	0.013	0.0147	0.0324	0.7981	0.8251	/	0.4938	0.5382	0.5752	0.621	0.4981	0.5624	0.6052	0.6406	0.6293	0.5501	0.603	0.8081	0.4505	0.3881	0.4628	0.5174	/	/
TCGA-L5-A43H-01	9	other wise	9	death	/	0.9217	/	/	/	/	/	/	/	/	0.1971	/	0.0875	0.0595	0.0412	0.0675	0.0439	0.0602	0.0869	0.0253	0.0212	0.0253	0.5333	0.6801	/	0.0284	0.0324	0.0326	0.0401	0.0445	0.0369	0.0507	0.0274	0.0632	0.0152	0.1505	0.0477	0.0385	0.0752	0.0338	0.3179	/	/
TCGA-L5-A8NV-01	/	/	1599	death	/	0.8792	/	/	/	/	/	/	/	/	0.2639	/	0.0314	0.0242	0.0393	0.046	0.0209	0.0395	0.0587	0.0141	0.0155	0.023	0.4294	0.793	/	0.3673	0.3898	0.3112	0.3492	0.2993	0.4578	0.449	0.4293	0.5229	0.4212	0.5271	0.7735	0.2201	0.3025	0.297	0.4102	/	/
TCGA-L5-A4OO-01	/	/	101	censor	/	0.8859	/	/	/	/	/	/	/	/	0.2936	/	0.0537	0.0466	0.046	0.0733	0.0445	0.0465	0.0802	0.018	0.018	0.0232	0.4071	0.8668	/	0.2825	0.3294	0.2734	0.3097	0.2949	0.395	0.4063	0.3462	0.4523	0.409	0.5187	0.4129	0.1788	0.2884	0.2684	0.4557	/	/
TCGA-L5-A4OQ-01	/	/	42	death	/	0.8526	/	/	/	/	/	/	/	/	0.2521	/	0.0414	0.0452	0.04	0.0485	0.0672	0.0525	0.0604	0.0167	0.0157	0.0238	0.4263	0.8038	/	0.5229	0.5491	0.5906	0.6258	0.5805	0.5804	0.593	0.6424	0.6783	0.5776	0.66	0.6419	0.417	0.4524	0.4976	0.5609	/	/
TCGA-L5-A43E-01	885	new tumor	920	censor	/	0.6557	/	/	/	/	/	/	/	/	0.1905	/	0.0777	0.0467	0.0426	0.0501	0.0266	0.0566	0.0844	0.0273	0.022	0.0291	0.4993	0.875	/	0.6889	0.5974	0.7098	0.7581	0.7592	0.6942	0.7368	0.8004	0.7554	0.6885	0.7382	0.7627	0.7277	0.5827	0.6447	0.654	/	/
TCGA-2H-A9GL-01	/	/	180	death	/	0.6227	/	/	/	/	/	/	/	/	0.1695	/	0.0471	0.0499	0.052	0.06	0.0279	0.0675	0.0606	0.0153	0.0155	0.0296	0.3593	0.8212	/	0.8549	0.7663	0.8457	0.8389	0.7141	0.8434	0.8455	0.8714	0.7913	0.6931	0.8012	0.882	0.7886	0.6868	0.7135	0.7846	/	/
TCGA-LN-A7HX-01	372	other wise	372	censor	/	0.3937	/	/	/	/	/	/	/	/	0.1615	/	0.0561	0.0302	0.0468	0.0461	0.0422	0.0487	0.0738	0.0231	0.0202	0.0285	0.4614	0.7574	/	0.0336	0.0309	0.0257	0.0324	0.0508	0.1171	0.0602	0.033	0.1645	0.0336	0.2198	0.2319	0.0395	0.3755	0.2978	0.6036	/	/
TCGA-IG-A3Y9-01	26	other wise	26	death	/	0.9145	/	/	/	/	/	/	/	/	0.2336	/	0.0574	0.0431	0.0407	0.0529	0.0595	0.0548	0.0791	0.0216	0.0196	0.0318	0.5833	0.7594	/	0.0317	0.0366	0.0258	0.0314	0.0458	0.0356	0.0506	0.0302	0.0725	0.0139	0.1223	0.0651	0.0223	0.0825	0.0447	0.405	/	/
TCGA-IG-A5B8-01	24	other wise	24	death	/	0.8608	/	/	/	/	/	/	/	/	0.2409	/	0.0582	0.0514	0.0549	0.0625	0.0447	0.0749	0.0923	0.017	0.0222	0.0346	0.5056	0.7203	/	0.0311	0.0345	0.033	0.0447	0.0407	0.0409	0.0336	0.0263	0.069	0.0159	0.1446	0.0591	0.0254	0.0534	0.0268	0.2378	/	/

TCGA-RE-A7BO-01	213	other wise	213	death	/	0.4844	/	/	/	/	/	/	/	/	0.2105	/	0.0612	0.0345	0.0398	0.0495	0.0425	0.0529	0.0756	0.024	0.0222	0.0256	0.3273	0.8506	/	0.5354	0.5899	0.6447	0.6399	0.6615	0.6265	0.6563	0.7043	0.6744	0.6115	0.6851	0.6906	0.5962	0.4988	0.5254	0.5133	/	/
TCGA-L5-A4OH-01	992	other wise	992	censor	/	0.8436	/	/	/	/	/	/	/	/	0.2075	/	0.0463	0.0376	0.0589	0.0462	0.032	0.0428	0.0551	0.0211	0.0207	0.0283	0.3215	0.8709	/	0.643	0.5999	0.7225	0.7081	0.7232	0.6665	0.6298	0.7313	0.7329	0.5849	0.6882	0.7375	0.5367	0.5085	0.5788	0.5793	/	/
TCGA-IG-A4QS-01	118	other wise	118	death	/	0.5874	/	/	/	/	/	/	/	/	0.1657	/	0.0556	0.0374	0.0439	0.0499	0.034	0.044	0.0617	0.0254	0.0199	0.0249	0.3447	0.6991	/	0.7712	0.692	0.7336	0.7938	0.7874	0.6668	0.701	0.7539	0.7539	0.6966	0.7646	0.7802	0.6232	0.5639	0.617	0.6756	/	/
TCGA-L5-A8NQ-01	/	/	650	death	/	0.8532	/	/	/	/	/	/	/	/	0.281	/	0.0589	0.0429	0.0507	0.0615	0.0299	0.0651	0.061	0.0221	0.024	0.0266	0.7231	0.8615	/	0.0426	0.0348	0.0329	0.0398	0.0626	0.0424	0.0428	0.0432	0.0695	0.0156	0.0533	0.0919	0.0321	0.0478	0.044	0.5103	/	/
TCGA-L5-A893-01	92	other wise	92	censor	/	0.8638	/	/	/	/	/	/	/	/	0.2245	/	0.0441	0.0464	0.0448	0.0507	0.0241	0.052	0.0772	0.0181	0.0236	0.0287	0.5367	0.8397	/	0.5788	0.5894	0.6418	0.6413	0.6062	0.652	0.6852	0.731	0.7148	0.5766	0.6655	0.7064	0.607	0.4627	0.541	0.6512	/	/
TCGA-LN-A9FR-01	373	other wise	373	censor	/	0.8665	/	/	/	/	/	/	/	/	0.2462	/	0.0451	0.0347	0.0461	0.0434	0.0268	0.0471	0.0605	0.0139	0.0131	0.021	0.692	0.8575	/	0.061	0.0645	0.05	0.0751	0.0887	0.0498	0.0625	0.0613	0.1395	0.0202	0.1204	0.4795	0.0449	0.0784	0.04	0.3573	/	/
TCGA-2H-A9GN-01	/	/	272	death	/	0.8413	/	/	/	/	/	/	/	/	0.1271	/	0.0462	0.0396	0.032	0.03	0.0221	0.034	0.0702	0.0144	0.0149	0.0212	0.2521	0.8065	/	0.0336	0.0387	0.0371	0.0511	0.057	0.0403	0.0529	0.0402	0.1025	0.0126	0.0932	0.3822	0.0285	0.0377	0.026	0.3537	/	/
TCGA-L5-A4OJ-01	639	other wise	639	censor	/	0.3929	/	/	/	/	/	/	/	/	0.1999	/	0.0348	0.0381	0.0323	0.0465	0.0266	0.0278	0.0436	0.0201	0.0175	0.0221	0.473	0.8448	/	0.0264	0.0289	0.0298	0.0426	0.0492	0.0285	0.0392	0.0281	0.0669	0.0115	0.052	0.0615	0.0272	0.0407	0.0225	0.2069	/	/
TCGA-L5-A88Z-01	225	other wise	225	censor	/	0.8947	/	/	/	/	/	/	/	/	0.2051	/	0.0475	0.0435	0.0627	0.0591	0.0251	0.0445	0.0563	0.0159	0.0215	0.0235	0.3147	0.6396	/	0.0306	0.0298	0.0341	0.0358	0.0567	0.0332	0.053	0.0276	0.1136	0.0159	0.0425	0.0703	0.0307	0.024	0.0272	0.3572	/	/
TCGA-X8-AAAR-01	554	other wise	554	censor	/	0.8284	/	/	/	/	/	/	/	/	0.2293	/	0.0774	0.0297	0.0533	0.0475	0.0386	0.0523	0.0824	0.0119	0.0265	0.0311	0.4701	0.8172	/	0.6216	0.6213	0.7096	0.672	0.5741	0.6034	0.6508	0.7252	0.6895	0.5867	0.6504	0.6352	0.4801	0.4787	0.5455	0.6319	/	/
TCGA-L5-A8NT-01	/	/	825	censor	/	0.8825	/	/	/	/	/	/	/	/	0.1788	/	0.0523	0.0354	0.0368	0.0468	0.0316	0.0452	0.0633	0.0133	0.0158	0.0273	0.4001	0.706	/	0.5709	0.5556	0.5606	0.6949	0.4723	0.6275	0.6784	0.6419	0.7004	0.5782	0.669	0.827	0.5194	0.4517	0.4577	0.6385	/	/
TCGA-IG-A5S3-01	712	other wise	712	censor	/	0.8973	/	/	/	/	/	/	/	/	0.1757	/	0.0726	0.0547	0.0568	0.0558	0.0457	0.0742	0.1006	0.0303	0.0218	0.0264	0.4722	0.8463	/	0.0897	0.115	0.0579	0.0733	0.0626	0.1614	0.1843	0.0706	0.2323	0.2638	0.3753	0.1775	0.0781	0.1683	0.2458	0.5941	/	/
TCGA-2H-A9GI-01	/	/	435	death	/	0.7672	/	/	/	/	/	/	/	/	0.2072	/	0.0595	0.0391	0.0495	0.0511	0.0233	0.0535	0.0689	0.0136	0.0132	0.0522	0.4526	0.8012	/	0.6412	0.6949	0.6494	0.6416	0.5665	0.6603	0.6923	0.74	0.785	0.6346	0.6874	0.8948	0.5388	0.4896	0.5785	0.6768	/	/
TCGA-V5-AASV-01	322	new tumor	467	censor	/	0.26	/	/	/	/	/	/	/	/	0.1995	/	0.0587	0.0365	0.048	0.0521	0.0451	0.0448	0.0655	0.0115	0.014	0.0323	0.8354	0.8545	/	0.7205	0.8073	0.8004	0.8719	0.6466	0.8166	0.8497	0.8816	0.8476	0.7452	0.7608	0.8971	0.7795	0.701	0.7316	0.829	/	/
TCGA-2H-A9GF-01	/	/	784	death	/	0.8907	/	/	/	/	/	/	/	/	0.1222	/	0.0546	0.0457	0.0567	0.0623	0.0257	0.0475	0.087	0.0145	0.0164	0.0307	0.2628	0.8388	/	0.7364	0.7264	0.7617	0.8233	0.7669	0.774	0.819	0.8543	0.8407	0.685	0.7283	0.8948	0.6463	0.6129	0.6573	0.716	/	/
TCGA-L5-A88W-01	/	/	764	death	/	0.5977	/	/	/	/	/	/	/	/	0.1997	/	0.046	0.0399	0.0463	0.0471	0.0421	0.0532	0.0662	0.0186	0.0221	0.0298	0.2925	0.6497	/	0.6266	0.6232	0.7122	0.7569	0.6921	0.66	0.7116	0.7406	0.6991	0.6464	0.7272	0.7405	0.6507	0.5271	0.6113	0.5412	/	/
TCGA-LN-A8I1-01	401	other wise	401	censor	/	0.8666	/	/	/	/	/	/	/	/	0.2903	/	0.0561	0.0452	0.0364	0.0455	0.0315	0.0278	0.0459	0.0262	0.0224	0.025	0.4745	0.8809	/	0.0413	0.049	0.0416	0.0716	0.0814	0.0498	0.071	0.0461	0.1276	0.0152	0.0463	0.1015	0.0363	0.0562	0.025	0.2366	/	/
TCGA-L5-A4OP-01	218	other wise	218	censor	/	0.8911	/	/	/	/	/	/	/	/	0.2771	/	0.0566	0.0309	0.0395	0.0472	0.029	0.0445	0.0709	0.0193	0.022	0.0296	0.42	0.8625	/	0.3433	0.5065	0.489	0.6175	0.5596	0.6252	0.6147	0.6566	0.6517	0.599	0.6894	0.6868	0.5183	0.4791	0.4996	0.5793	/	/
TCGA-2H-A9GG-01	/	/	610	death	/	0.8233	/	/	/	/	/	/	/	/	0.1325	/	0.0393	0.0242	0.0324	0.0391	0.0254	0.0698	0.06	0.0145	0.0171	0.0248	0.3711	0.7585	/	0.8302	0.8007	0.8247	0.8854	0.7955	0.8313	0.8575	0.8673	0.7695	0.6684	0.7446	0.8733	0.7412	0.6136	0.6584	0.7351	/	/
TCGA-L5-A4ON-01	558	other wise	558	death	/	0.8388	/	/	/	/	/	/	/	/	0.1452	/	0.0469	0.0425	0.0497	0.0477	0.0269	0.027	0.0658	0.0168	0.02	0.0245	0.2294	0.7921	/	0.6901	0.7095	0.8037	0.8406	0.7772	0.6776	0.6943	0.7964	0.7613	0.6553	0.7476	0.7656	0.6877	0.5895	0.6217	0.5561	/	/
TCGA-ZR-A9CJ-01	163	new tumor	600	death	/	0.8458	/	/	/	/	/	/	/	/	0.2371	/	0.0681	0.0369	0.0321	0.0445	0.0243	0.0404	0.0439	0.0115	0.0149	0.0244	0.5499	0.7597	/	0.4867	0.5518	0.4937	0.5464	0.3383	0.6345	0.6923	0.5964	0.6582	0.5408	0.5866	0.8954	0.4451	0.4388	0.5	0.5767	/	/
TCGA-L5-A4OF-01	801	other wise	801	death	/	0.7798	/	/	/	/	/	/	/	/	0.1488	/	0.0396	0.0555	0.0452	0.0546	0.0305	0.0376	0.086	0.0238	0.0169	0.0226	0.5425	0.8377	/	0.0345	0.0496	0.0374	0.0385	0.0512	0.057	0.0552	0.0312	0.1014	0.0703	0.1783	0.0964	0.0264	0.0828	0.0357	0.277	/	/
TCGA-XP-A8T7-01	1254	other wise	1254	censor	/	0.8914	/	/	/	/	/	/	/	/	0.1954	/	0.0837	0.0378	0.0551	0.0493	0.0298	0.0514	0.0549	0.0189	0.0223	0.0324	0.7303	0.7604	/	0.0423	0.0391	0.0297	0.0433	0.0605	0.0401	0.0383	0.035	0.0866	0.0186	0.0769	0.0623	0.0318	0.0385	0.0304	0.1596	/	/
TCGA-IG-A3YC-01	542	new tumor	612	censor	/	0.8016	/	/	/	/	/	/	/	/	0.2532	/	0.0599	0.0366	0.0539	0.0457	0.0449	0.0464	0.0638	0.0185	0.0167	0.0308	0.6454	0.7865	/	0.033	0.0314	0.0265	0.0308	0.0458	0.037	0.0311	0.0241	0.055	0.0155	0.1283	0.0527	0.0239	0.0777	0.0334	0.3839	/	/
TCGA-L7-A6VZ-01	315	other wise	315	censor	/	0.8697	/	/	/	/	/	/	/	/	0.1825	/	0.0451	0.0397	0.0383	0.0408	0.0313	0.0535	0.0722	0.0208	0.0163	0.0239	0.2529	0.7942	/	0.7758	0.7372	0.8177	0.882	0.8604	0.7364	0.7379	0.8445	0.8025	0.703	0.7817	0.873	0.7416	0.6645	0.6714	0.7368	/	/
TCGA-IG-A8O2-01	142	other wise	142	death	/	0.7048	/	/	/	/	/	/	/	/	0.2851	/	0.0566	0.0382	0.0427	0.0423	0.0282	0.0447	0.0464	0.0201	0.0223	0.0356	0.5714	0.6395	/	0.0353	0.0499	0.0263	0.0461	0.0443	0.0297	0.048	0.0333	0.0721	0.0159	0.1084	0.091	0.0331	0.0447	0.0278	0.2267	/	/
TCGA-LN-A9FQ-01	82	new tumor	391	censor	/	0.8838	/	/	/	/	/	/	/	/	0.186	/	0.0575	0.0374	0.0319	0.0462	0.0336	0.0736	0.0466	0.0161	0.0159	0.0329	0.7601	0.8003	/	0.0861	0.0401	0.0448	0.0598	0.0928	0.0583	0.109	0.0516	0.15	0.0113	0.0887	0.5268	0.0374	0.0584	0.0397	0.3026	/	/
TCGA-JY-A93E-01	767	other wise	767	censor	/	0.5534	/	/	/	/	/	/	/	/	0.274	/	0.0379	0.0349	0.0503	0.0467	0.0345	0.0453	0.067	0.0144	0.0148	0.0231	0.5967	0.8526	/	0.5039	0.5273	0.5287	0.5224	0.3854	0.5668	0.6023	0.5926	0.5819	0.5405	0.5992	0.8801	0.397	0.4494	0.4657	0.6228	/	/
TCGA-Q9-A6FW-01	238	other wise	238	censor	/	0.8805	/	/	/	/	/	/	/	/	0.1447	/	0.0471	0.041	0.0517	0.0469	0.0382	0.0457	0.0571	0.0209	0.0187	0.0377	0.4321	0.8145	/	0.5651	0.5867	0.6135	0.6805	0.4954	0.6091	0.6711	0.6728	0.6982	0.5742	0.6875	0.8468	0.4898	0.5025	0.527	0.5698	/	/
TCGA-IG-A3YB-01	80	other wise	80	censor	/	0.9283	/	/	/	/	/	/	/	/	0.2097	/	0.0698	0.0496	0.0444	0.0552	0.0452	0.061	0.0741	0.0231	0.0222	0.0388	0.8657	0.9041	/	0.6413	0.6302	0.7177	0.7278	0.7074	0.6846	0.7127	0.7421	0.7379	0.6476	0.7089	0.7586	0.6498	0.567	0.6046	0.6566	/	/
TCGA-IG-A625-01	390	other wise	390	death	/	0.8469	/	/	/	/	/	/	/	/	0.1696	/	0.0705	0.0454	0.0399	0.041	0.0312	0.0571	0.0477	0.018	0.0163	0.018	0.3926	0.7074	/	0.03	0.0256	0.0237	0.0302	0.0399	0.0286	0.0337	0.0227	0.0443	0.0162	0.0778	0.2251	0.0219	0.0443	0.0213	0.1768	/	/
TCGA-L5-A4OX-01	226	other wise	226	death	/	0.7188	/	/	/	/	/	/	/	/	0.1614	/	0.0885	0.0489	0.0476	0.0513	0.0439	0.0571	0.0788	0.0299	0.0208	0.0312	0.3526	0.8601	/	0.4086	0.4614	0.5047	0.4699	0.3952	0.4678	0.5305	0.5404	0.532	0.4744	0.59	0.4669	0.3678	0.3355	0.3843	0.6044	/	/
TCGA-L5-A88V-01	79	other wise	79	censor	/	0.9184	/	/	/	/	/	/	/	/	0.1319	/	0.0489	0.036	0.0454	0.0343	0.0266	0.0469	0.0607	0.0189	0.0201	0.0311	0.1515	0.742	/	0.7885	0.7697	0.7992	0.831	0.6729	0.7708	0.8067	0.8332	0.8291	0.714	0.7777	0.8382	0.7387	0.641	0.7344	0.7472	/	/
TCGA-R6-A8W5-01	/	/	480	death	/	0.7575	/	/	/	/	/	/	/	/	0.2145	/	0.0575	0.0439	0.0375	0.041	0.0461	0.0689	0.0872	0.0135	0.0144	0.0327	0.5851	0.7077	/	0.0385	0.0544	0.0288	0.0409	0.0489	0.0602	0.054	0.031	0.0782	0.0511	0.1814	0.1914	0.0253	0.0641	0.0427	0.3135	/	/
TCGA-LN-A9FP-01	290	new tumor	366	censor	/	0.8697	/	/	/	/	/	/	/	/	0.3261	/	0.0579	0.0434	0.0504	0.0565	0.0332	0.0522	0.0537	0.015	0.0218	0.0396	0.6163	0.7822	/	0.1018	0.1385	0.093	0.0915	0.0714	0.1477	0.172	0.0735	0.2284	0.221	0.3176	0.3164	0.051	0.1338	0.1342	0.3723	/	/
TCGA-IC-A6RE-01	234	other wise	234	censor	/	0.5999	/	/	/	/	/	/	/	/	0.1757	/	0.0352	0.0361	0.0367	0.0423	0.0239	0.0448	0.0794	0.0175	0.02	0.0215	0.287	0.7999	/	0.6276	0.5843	0.676	0.7108	0.6038	0.5871	0.6761	0.7138	0.7055	0.6057	0.6452	0.7092	0.5723	0.5065	0.5816	0.6103	/	/
TCGA-LN-A7HW-01	97	new tumor	365	censor	/	0.9306	/	/	/	/	/	/	/	/	0.1705	/	0.0522	0.0372	0.0493	0.0511	0.0325	0.0446	0.0738	0.0211	0.024	0.0401	0.8582	0.8945	/	0.0356	0.0418	0.033	0.0387	0.0377	0.0363	0.0507	0.0248	0.0894	0.0168	0.0861	0.0869	0.0218	0.0458	0.0273	0.196	/	/
TCGA-M9-A5M8-01	1007	other wise	1007	censor	/	0.8723	/	/	/	/	/	/	/	/	0.2155	/	0.0612	0.0428	0.0535	0.0585	0.0535	0.0512	0.0722	0.0177	0.0262	0.0345	0.4302	0.5826	/	0.0306	0.0394	0.0319	0.0575	0.049	0.0362	0.0414	0.0335	0.1662	0.0195	0.1451	0.0737	0.0336	0.0609	0.0291	0.2713	/	/
TCGA-IG-A97I-01	370	other wise	370	censor	/	0.916	/	/	/	/	/	/	/	/	0.1503	/	0.0526	0.0405	0.0375	0.0626	0.0332	0.0421	0.0667	0.0118	0.0137	0.0271	0.3086	0.785	/	0.0365	0.033	0.0252	0.0497	0.0491	0.0449	0.049	0.0352	0.0812	0.0159	0.0976	0.4794	0.0266	0.0568	0.0345	0.1899	/	/
TCGA-LN-A7HV-01	320	other wise	320	censor	/	0.8584	/	/	/	/	/	/	/	/	0.2688	/	0.0579	0.0373	0.0375	0.0578	0.0414	0.0592	0.0506	0.0161	0.0225	0.0316	0.6132	0.779	/	0.0314	0.0369	0.0359	0.0415	0.0529	0.0331	0.0476	0.0376	0.0913	0.0187	0.0869	0.1129	0.0314	0.0387	0.028	0.3198	/	/
TCGA-2H-A9GO-01	/	/	494	death	/	0.7083	/	/	/	/	/	/	/	/	0.2928	/	0.0343	0.0524	0.0432	0.0396	0.026	0.027	0.0711	0.018	0.0154	0.0262	0.6478	0.6114	/	0.2893	0.3191	0.1912	0.2274	0.1446	0.4457	0.4367	0.3814	0.5032	0.4093	0.5061	0.7285	0.1774	0.302	0.2236	0.4044	/	/
TCGA-JY-A93F-01	731	other wise	731	censor	/	0.4008	/	/	/	/	/	/	/	/	0.1608	/	0.064	0.0466	0.0414	0.0637	0.0268	0.06	0.0849	0.0169	0.0183	0.0285	0.7121	0.8441	/	0.6606	0.7235	0.8415	0.825	0.7349	0.7665	0.8085	0.8584	0.7322	0.6904	0.7583	0.8872	0.7383	0.6158	0.6656	0.7167	/	/
TCGA-LN-A5U5-01	136	other wise	136	death	/	0.8911	/	/	/	/	/	/	/	/	0.166	/	0.0758	0.0478	0.0393	0.0471	0.0414	0.0497	0.0627	0.0326	0.0185	0.0251	0.4469	0.7303	/	0.0285	0.0298	0.0226	0.036	0.0327	0.0335	0.0306	0.0214	0.1173	0.0156	0.1325	0.0561	0.0249	0.0686	0.0229	0.3662	/	/
TCGA-L5-A8NF-01	81	other wise	81	death	/	0.8484	/	/	/	/	/	/	/	/	0.1383	/	0.0588	0.0374	0.0517	0.042	0.0254	0.057	0.0859	0.0183	0.0178	0.0329	0.202	0.8219	/	0.8405	0.8363	0.9058	0.9291	0.8239	0.8426	0.8468	0.9426	0.8514	0.7818	0.8119	0.9514	0.8411	0.6939	0.7534	0.7628	/	/
TCGA-Z6-AAPN-01	81	other wise	81	censor	/	0.8631	/	/	/	/	/	/	/	/	0.2825	/	0.0561	0.0379	0.0497	0.053	0.0322	0.0523	0.0977	0.02	0.0192	0.0335	0.6239	0.8405	/	0.3385	0.3902	0.4449	0.3873	0.3022	0.4224	0.4512	0.4326	0.4868	0.4782	0.5352	0.4258	0.2795	0.2969	0.3354	0.5342	/	/
TCGA-2H-A9GJ-01	/	/	1781	death	/	0.8132	/	/	/	/	/	/	/	/	0.1379	/	0.06	0.0548	0.0586	0.0448	0.0434	0.0627	0.0768	0.0129	0.0135	0.0332	0.1755	0.764	/	0.0286	0.0286	0.028	0.04	0.048	0.0343	0.0465	0.033	0.1055	0.0153	0.1407	0.3465	0.0313	0.0517	0.0247	0.1591	/	/
TCGA-Q9-A6FU-01	/	/	157	death	/	0.8272	/	/	/	/	/	/	/	/	0.1775	/	0.047	0.038	0.0352	0.0457	0.0278	0.0431	0.0541	0.0206	0.0189	0.0237	0.5164	0.6797	/	0.0426	0.0355	0.0389	0.0433	0.0603	0.0385	0.047	0.0296	0.0421	0.0119	0.1161	0.2321	0.0299	0.0436	0.0228	0.2322	/	/
TCGA-JY-A6F8-01	3714	other wise	3714	censor	/	0.2822	/	/	/	/	/	/	/	/	0.1506	/	0.0364	0.0339	0.0388	0.0385	0.0283	0.0395	0.0733	0.021	0.0254	0.0283	0.1959	0.6397	/	0.738	0.7245	0.8434	0.8634	0.7939	0.7308	0.7926	0.8593	0.8161	0.721	0.79	0.8166	0.7366	0.6529	0.6768	0.7192	/	/
TCGA-L5-A8NL-01	402	other wise	402	censor	/	0.735	/	/	/	/	/	/	/	/	0.2404	/	0.0616	0.0427	0.0531	0.0629	0.0308	0.087	0.1082	0.0189	0.0198	0.0308	0.4076	0.6824	/	0.4034	0.5323	0.4785	0.5275	0.3625	0.5657	0.5313	0.5364	0.574	0.4753	0.5758	0.8079	0.317	0.4047	0.3899	0.5072	/	/
TCGA-LN-A8HZ-01	375	other wise	375	censor	/	0.8952	/	/	/	/	/	/	/	/	0.2229	/	0.0638	0.0358	0.0394	0.0424	0.0381	0.0457	0.0555	0.0174	0.0191	0.0261	0.498	0.7764	/	0.0328	0.0335	0.029	0.0509	0.0487	0.0358	0.0438	0.0333	0.0841	0.0134	0.0767	0.0655	0.0259	0.0348	0.0334	0.2433	/	/
TCGA-IG-A4QT-01	283	other wise	283	death	/	0.7519	/	/	/	/	/	/	/	/	0.3922	/	0.0434	0.0395	0.0436	0.0497	0.0458	0.0403	0.0679	0.0164	0.0204	0.0285	0.8783	0.8889	/	0.0288	0.0306	0.0195	0.0313	0.0517	0.0324	0.0363	0.0207	0.0935	0.0145	0.1187	0.0587	0.0224	0.0729	0.0318	0.3716	/	/
TCGA-L5-A4OW-01	217	other wise	217	death	/	0.8368	/	/	/	/	/	/	/	/	0.2207	/	0.0647	0.052	0.0547	0.0503	0.0433	0.0466	0.0973	0.0195	0.0241	0.0246	0.4492	0.8052	/	0.5026	0.5426	0.5752	0.6231	0.5254	0.5639	0.5883	0.631	0.6443	0.5255	0.6342	0.5682	0.475	0.4018	0.4296	0.5599	/	/
TCGA-L5-A8NW-01	/	/	1402	death	/	0.6781	/	/	/	/	/	/	/	/	0.1687	/	0.0262	0.0352	0.0408	0.0429	0.0218	0.0284	0.064	0.0135	0.0149	0.024	0.3127	0.775	/	0.6221	0.6783	0.6799	0.7289	0.5344	0.6571	0.7112	0.7422	0.7172	0.5736	0.6435	0.8903	0.6222	0.5191	0.537	0.664	/	/
TCGA-IG-A3QL-01	1071	other wise	1071	censor	/	0.9184	/	/	/	/	/	/	/	/	0.1271	/	0.0759	0.0434	0.0448	0.0416	0.0413	0.0599	0.0831	0.0215	0.0189	0.0314	0.1446	0.9014	/	0.0343	0.0444	0.0323	0.0428	0.049	0.0325	0.0587	0.0315	0.1289	0.0188	0.1284	0.0721	0.0343	0.0791	0.0287	0.3125	/	/
TCGA-XP-A8T6-01	763	other wise	763	death	/	0.8417	/	/	/	/	/	/	/	/	0.2556	/	0.0584	0.0462	0.0389	0.0472	0.0227	0.0391	0.0438	0.0144	0.0183	0.0282	0.484	0.6421	/	0.0344	0.0241	0.0298	0.0409	0.0544	0.0371	0.0402	0.0331	0.0942	0.014	0.0841	0.1064	0.0247	0.0387	0.0312	0.2282	/	/
TCGA-LN-A5U6-01	375	other wise	375	censor	/	0.8736	/	/	/	/	/	/	/	/	0.1644	/	0.0656	0.0471	0.0533	0.0357	0.033	0.0512	0.0694	0.0286	0.0191	0.0346	0.5049	0.8889	/	0.0354	0.0381	0.0317	0.0454	0.0582	0.0262	0.0405	0.0298	0.0485	0.0182	0.1384	0.0713	0.027	0.0523	0.0297	0.3829	/	/
TCGA-IG-A6QS-01	303	other wise	303	death	/	0.8958	/	/	/	/	/	/	/	/	0.1963	/	0.0512	0.0447	0.0413	0.0574	0.0347	0.0589	0.0813	0.0188	0.0208	0.0256	0.486	0.8554	/	0.0317	0.0329	0.0258	0.0324	0.0396	0.0314	0.0385	0.0221	0.101	0.029	0.1372	0.0613	0.0267	0.0624	0.0414	0.3143	/	/
TCGA-L5-A8NH-01	/	/	393	death	/	0.4814	/	/	/	/	/	/	/	/	0.2113	/	0.0452	0.0311	0.0362	0.0402	0.0234	0.0339	0.065	0.0136	0.0123	0.0255	0.4944	0.8452	/	0.5898	0.5769	0.6233	0.7284	0.5411	0.6192	0.6736	0.7544	0.6672	0.5749	0.6777	0.8681	0.4661	0.4946	0.5679	0.6543	/	/
TCGA-L5-A4OM-01	1458	other wise	1458	death	/	0.8686	/	/	/	/	/	/	/	/	0.4697	/	0.0326	0.0478	0.0394	0.0321	0.0349	0.0556	0.0426	0.0215	0.0205	0.031	0.5105	0.7954	/	0.0294	0.0289	0.0256	0.0343	0.0542	0.0281	0.0351	0.024	0.0743	0.0133	0.0864	0.0602	0.0241	0.0456	0.0323	0.3977	/	/
TCGA-JY-A6FH-01	1441	other wise	1441	censor	/	0.8326	/	/	/	/	/	/	/	/	0.1736	/	0.0511	0.0458	0.0446	0.0461	0.0445	0.0439	0.0613	0.0258	0.024	0.0317	0.2507	0.7376	/	0.766	0.7384	0.837	0.8465	0.9016	0.794	0.7855	0.8455	0.7872	0.7309	0.7854	0.8638	0.7343	0.6446	0.6805	0.6909	/	/
TCGA-IG-A3YA-01	632	other wise	632	censor	/	0.9167	/	/	/	/	/	/	/	/	0.2965	/	0.0773	0.0549	0.0533	0.0461	0.0534	0.0545	0.0661	0.0222	0.0189	0.032	0.6562	0.7658	/	0.0338	0.0343	0.034	0.0276	0.0442	0.0343	0.0485	0.0194	0.058	0.0143	0.1436	0.0558	0.0267	0.0816	0.0403	0.4062	/	/
TCGA-Z6-A8JD-01	104	other wise	104	censor	/	0.8024	/	/	/	/	/	/	/	/	0.3156	/	0.0537	0.043	0.0469	0.0568	0.0342	0.0522	0.0739	0.0201	0.0263	0.0325	0.7406	0.875	/	0.0438	0.0415	0.0284	0.0452	0.0478	0.0369	0.0467	0.0321	0.0935	0.0131	0.0693	0.0966	0.0266	0.0388	0.0435	0.2948	/	/
TCGA-Z6-A9VB-01	40	other wise	40	censor	/	0.8549	/	/	/	/	/	/	/	/	0.2196	/	0.0343	0.0428	0.0333	0.0418	0.0242	0.0256	0.0585	0.0164	0.0173	0.031	0.5023	0.6962	/	0.0394	0.0334	0.037	0.0468	0.0645	0.0445	0.0536	0.0393	0.1073	0.0111	0.056	0.3231	0.023	0.0303	0.035	0.2797	/	/
TCGA-2H-A9GM-01	/	/	424	death	/	0.3129	/	/	/	/	/	/	/	/	0.1586	/	0.0611	0.0352	0.0407	0.0485	0.0492	0.0883	0.0913	0.0138	0.0153	0.0476	0.2611	0.7994	/	0.6581	0.653	0.6866	0.7817	0.5932	0.7283	0.7198	0.804	0.689	0.6655	0.7187	0.899	0.5959	0.5164	0.578	0.6098	/	/
TCGA-LN-A8I0-01	57	new tumor	407	censor	/	0.8984	/	/	/	/	/	/	/	/	0.1972	/	0.0559	0.0405	0.037	0.0328	0.0399	0.0626	0.0567	0.0219	0.0255	0.0346	0.6463	0.8536	/	0.0506	0.0458	0.0426	0.0706	0.0698	0.0452	0.0627	0.0458	0.0962	0.0166	0.0864	0.1143	0.0433	0.0373	0.0384	0.3699	/	/
TCGA-JY-A93D-01	732	new tumor	960	death	/	0.7641	/	/	/	/	/	/	/	/	0.274	/	0.0557	0.04	0.0447	0.0487	0.0262	0.0703	0.0635	0.0126	0.0137	0.0223	0.7035	0.8798	/	0.3545	0.3682	0.2561	0.3307	0.1729	0.463	0.4406	0.4457	0.6159	0.4525	0.5431	0.8367	0.2116	0.2897	0.3348	0.5404	/	/
TCGA-S8-A6BW-01	620	other wise	620	censor	/	0.8793	/	/	/	/	/	/	/	/	0.1312	/	0.0566	0.0329	0.0399	0.0485	0.0289	0.0415	0.0516	0.0171	0.0167	0.0283	0.5475	0.6918	/	0.0319	0.0312	0.0311	0.0426	0.0558	0.0343	0.039	0.0276	0.0756	0.0117	0.1371	0.1931	0.0286	0.0437	0.0225	0.1137	/	/
TCGA-L5-A891-01	114	other wise	114	censor	/	0.3617	/	/	/	/	/	/	/	/	0.175	/	0.0521	0.0387	0.0443	0.0498	0.0434	0.0512	0.0671	0.027	0.0226	0.0396	0.2315	0.8835	/	0.8295	0.7482	0.7957	0.8979	0.8271	0.8106	0.7877	0.8652	0.8073	0.7556	0.8269	0.8617	0.8219	0.7024	0.7563	0.7507	/	/
TCGA-JY-A6FA-01	/	/	1361	death	/	0.5798	/	/	/	/	/	/	/	/	0.136	/	0.0672	0.0448	0.0535	0.0546	0.0333	0.0418	0.0711	0.022	0.0204	0.0245	0.6116	0.5032	/	0.0293	0.0369	0.0204	0.0241	0.0341	0.0371	0.0343	0.019	0.121	0.0187	0.1551	0.0692	0.0249	0.0923	0.1457	0.587	/	/
TCGA-JY-A6FD-01	2069	other wise	2069	censor	/	0.5468	/	/	/	/	/	/	/	/	0.212	/	0.0698	0.0432	0.0383	0.04	0.0437	0.0443	0.0648	0.0205	0.0187	0.0304	0.3967	0.7515	/	0.0313	0.0243	0.0205	0.0269	0.0344	0.0406	0.0333	0.0237	0.0794	0.0133	0.0643	0.037	0.0231	0.0441	0.0428	0.2895	/	/
TCGA-IG-A3I8-01	1012	other wise	1012	censor	/	0.9076	/	/	/	/	/	/	/	/	0.2628	/	0.0591	0.0445	0.0465	0.04	0.0441	0.0368	0.0454	0.0195	0.0179	0.0364	0.4828	0.9054	/	0.0384	0.0261	0.0291	0.0447	0.0585	0.0358	0.0438	0.0227	0.0864	0.0112	0.1233	0.0712	0.0347	0.0512	0.0219	0.3402	/	/
TCGA-JY-A6FG-01	1263	other wise	1263	death	/	0.7197	/	/	/	/	/	/	/	/	0.1426	/	0.0503	0.047	0.0456	0.063	0.0343	0.0452	0.0625	0.0152	0.0168	0.0217	0.1733	0.704	/	0.0296	0.0256	0.023	0.0315	0.0525	0.0272	0.0402	0.0302	0.0763	0.019	0.0822	0.0576	0.0189	0.0915	0.0266	0.5591	/	/
TCGA-LN-A7HY-01	88	new tumor	366	censor	/	0.8792	/	/	/	/	/	/	/	/	0.3061	/	0.0699	0.0468	0.0442	0.0508	0.0321	0.0767	0.0791	0.0221	0.0235	0.0353	0.584	0.8667	/	0.0354	0.0331	0.0312	0.0427	0.0448	0.033	0.0539	0.0296	0.0896	0.0207	0.12	0.0972	0.0257	0.0428	0.0293	0.3916	/	/
TCGA-IG-A7DP-01	452	other wise	452	censor	/	0.7932	/	/	/	/	/	/	/	/	0.3751	/	0.0564	0.0338	0.0448	0.0498	0.0419	0.0498	0.068	0.0198	0.0214	0.0337	0.8218	0.8398	/	0.1334	0.1817	0.1318	0.1187	0.0818	0.2028	0.1937	0.1544	0.2564	0.2755	0.3877	0.2897	0.0802	0.1624	0.1598	0.5019	/	/
TCGA-LN-A7HZ-01	117	new tumor	401	censor	/	0.7621	/	/	/	/	/	/	/	/	0.2136	/	0.0519	0.0367	0.0474	0.0513	0.0377	0.0379	0.0665	0.0215	0.0206	0.03	0.8719	0.8397	/	0.0344	0.0371	0.0294	0.0372	0.0507	0.0457	0.042	0.0281	0.0818	0.0158	0.066	0.0546	0.0265	0.0508	0.0291	0.2136	/	/
TCGA-JY-A6FE-01	/	/	112	death	/	0.7778	/	/	/	/	/	/	/	/	0.1559	/	0.0451	0.0444	0.0509	0.0376	0.0327	0.037	0.0674	0.0255	0.0198	0.0281	0.3422	0.8666	/	0.0397	0.0315	0.0223	0.0332	0.0426	0.0302	0.0402	0.0304	0.101	0.0132	0.0932	0.042	0.0237	0.0222	0.0318	0.1795	/	/
TCGA-IG-A4P3-01	567	other wise	567	death	/	0.8767	/	/	/	/	/	/	/	/	0.2577	/	0.0516	0.0343	0.037	0.0438	0.0301	0.0397	0.072	0.0181	0.0203	0.0212	0.7524	0.7789	/	0.0288	0.0259	0.0213	0.0268	0.0338	0.0361	0.0286	0.019	0.0718	0.015	0.0782	0.0466	0.0205	0.0498	0.0343	0.3536	/	/
TCGA-JY-A93C-01	652	new tumor	705	censor	/	0.8509	/	/	/	/	/	/	/	/	0.1435	/	0.0572	0.0494	0.0394	0.0358	0.0318	0.0522	0.0527	0.0116	0.0141	0.0245	0.1736	0.8486	/	0.822	0.7743	0.8198	0.8645	0.6115	0.8328	0.8439	0.874	0.8109	0.728	0.7288	0.9149	0.7832	0.7047	0.7513	0.7527	/	/
TCGA-LN-A5U7-01	535	new tumor	768	censor	/	0.7093	/	/	/	/	/	/	/	/	0.1208	/	0.057	0.0492	0.0429	0.041	0.0428	0.0575	0.0627	0.0178	0.0149	0.024	0.8777	0.8544	/	0.0251	0.0275	0.0294	0.027	0.0424	0.0282	0.0328	0.0236	0.0663	0.0144	0.142	0.1808	0.0276	0.0525	0.0195	0.2918	/	/
TCGA-2H-A9GH-01	/	/	951	death	/	0.8552	/	/	/	/	/	/	/	/	0.1451	/	0.0611	0.0427	0.0561	0.063	0.0382	0.092	0.0686	0.0136	0.017	0.0331	0.1708	0.7794	/	0.0411	0.0395	0.0329	0.0415	0.0467	0.0504	0.0578	0.0419	0.1059	0.0279	0.1862	0.3024	0.0304	0.0641	0.0701	0.4104	/	/
TCGA-2H-A9GK-01	/	/	232	death	/	0.8695	/	/	/	/	/	/	/	/	0.2078	/	0.0479	0.0407	0.0459	0.0536	0.0431	0.0753	0.0829	0.013	0.0124	0.0267	0.4622	0.8046	/	0.4626	0.5475	0.6005	0.6072	0.4144	0.5915	0.6038	0.6273	0.6292	0.5641	0.6049	0.8567	0.43	0.427	0.4272	0.5642	/	/
TCGA-LN-A9FO-01	4	other wise	4	censor	/	0.7838	/	/	/	/	/	/	/	/	0.1952	/	0.0564	0.0458	0.0447	0.0471	0.0359	0.0552	0.0771	0.0137	0.0204	0.0255	0.4614	0.8033	/	0.0307	0.027	0.0235	0.0346	0.0409	0.0331	0.0444	0.027	0.0771	0.0155	0.1061	0.0482	0.0242	0.066	0.0287	0.3175	/	/
TCGA-IG-A97H-01	441	other wise	441	censor	/	0.8513	/	/	/	/	/	/	/	/	0.2449	/	0.0652	0.0407	0.047	0.0549	0.1621	0.0373	0.0145	0.014	0.0128	0.0256	0.7599	0.8235	/	0.0598	0.0696	0.0463	0.068	0.0628	0.0356	0.0757	0.049	0.1054	0.0145	0.0842	0.5338	0.037	0.0475	0.044	0.5701	/	/

Abbreviations: EC, esophageal cancer; TCGA, The Cancer Genome Atlas.

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