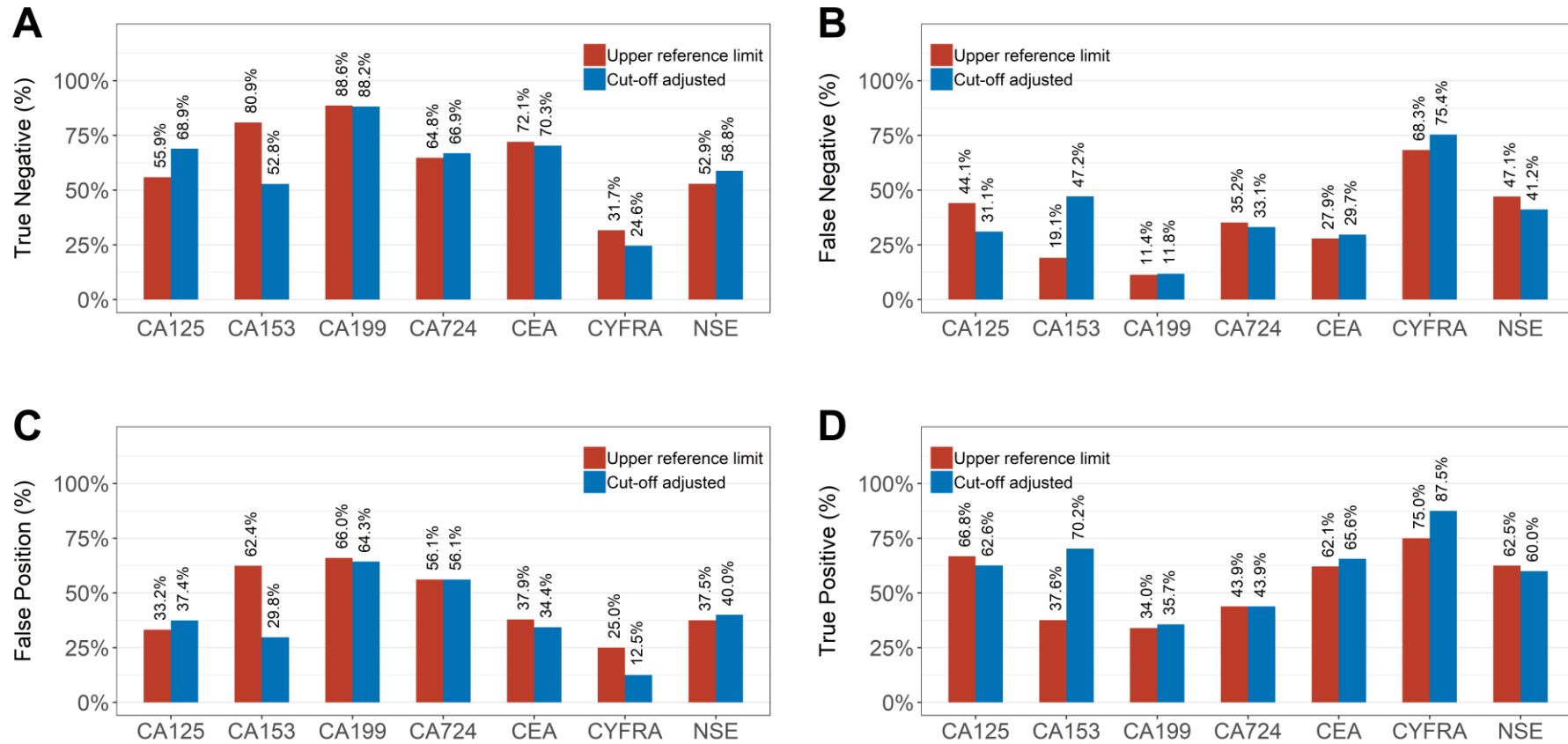
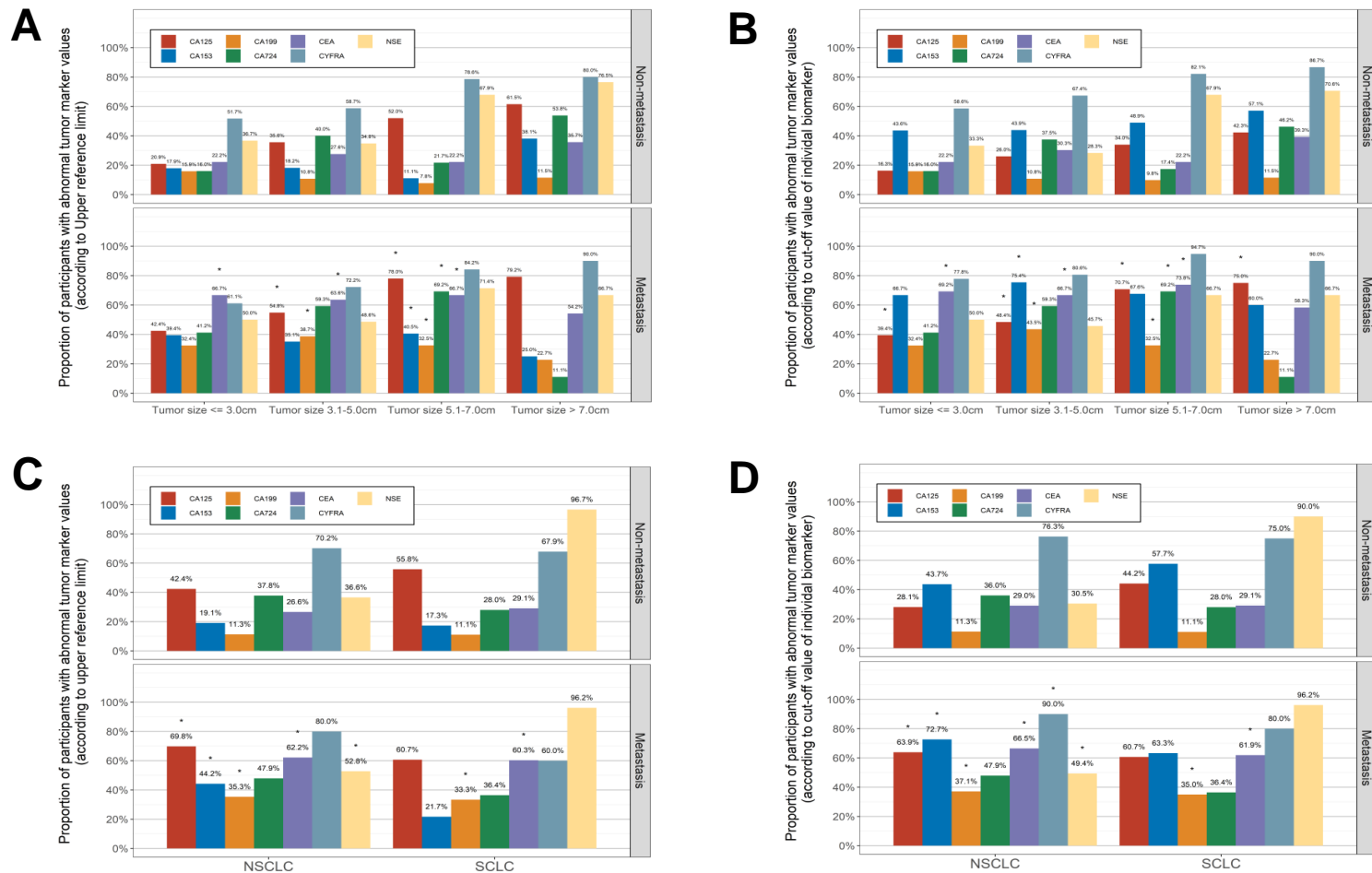


Supplementary Figure 1. Enrollment of patients.

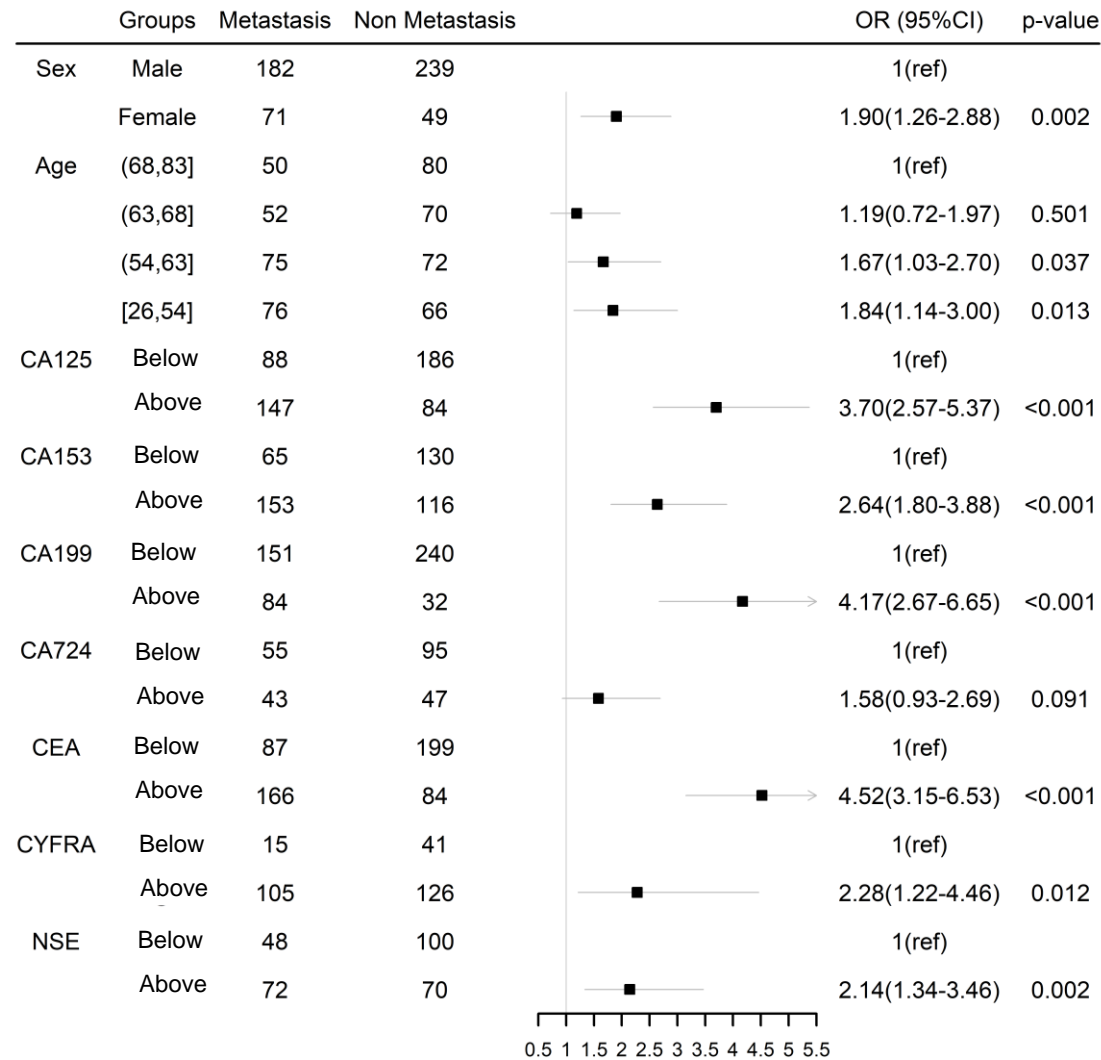


Supplementary Figure 2. TNR, FNR, FPR and TPR of each individual TM investigated assessment.

(A) Difference of TNR(True Negative Rate), (B) FNR(False Negative Rate), (C) FPR(False Positive Rate) and (D) TPR(True Negative Rate) in different grouping methods (Group by upper reference limits versus Group by cut-off value of logistic regression, single biomarker).

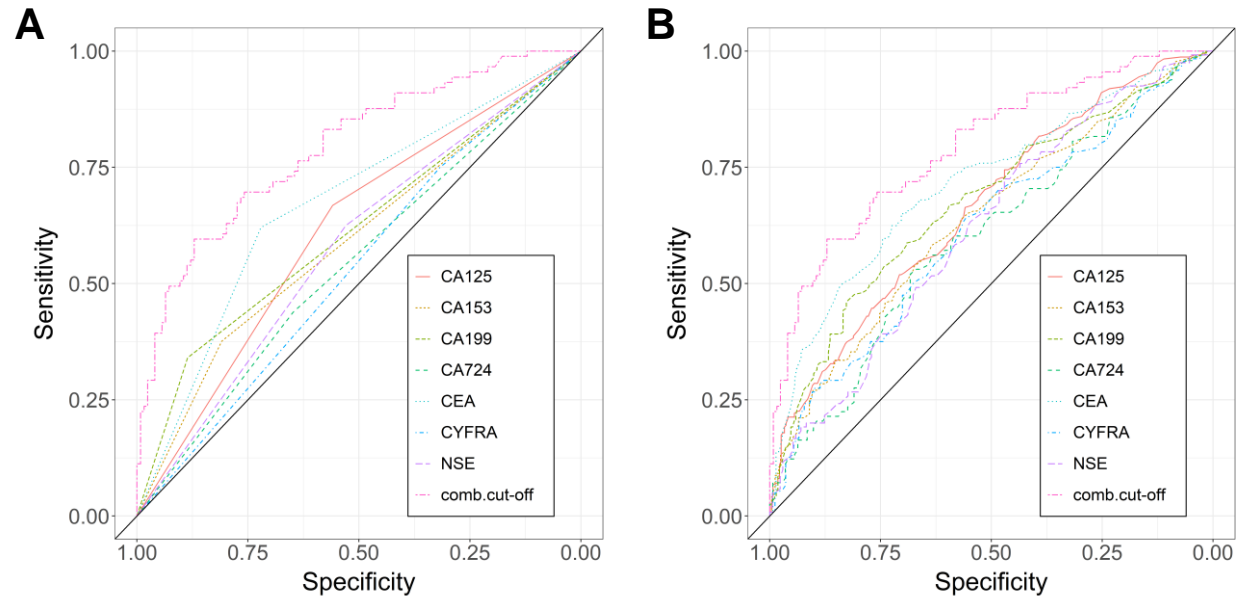


Supplementary Figure 3. Proportion of participants with abnormal tumor marker values stratified by nodule size and pathology subtype. (A) stratified by nodule size according to upper reference limit. (B) stratified by nodule size according to cut-off value. (C) stratified by pathology subtype according to upper reference limit. (D) stratified by pathology subtype according to cut-off value. Abbreviations: NSCLC, non-small cell lung cancer; SCLC, small cell lung cancer; CA125, carbohydrate antigen 125 (U/mL); CA199, carbohydrate antigen 199 (U/mL); CEA, carcinoembryonic antigen (ng/mL); NSE, neuron-specific enolase (ng/mL); CA153, carbohydrate antigen 153 (U/mL); CA724, carbohydrate antigen 724 (U/mL); CYFRA, cytokeratin-19 fragment (ng/mL). *, $p < 0.05$, Non-metastasis *versus* Metastasis.

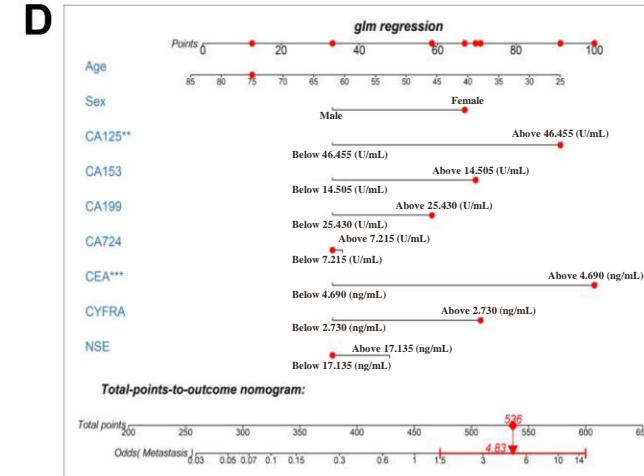
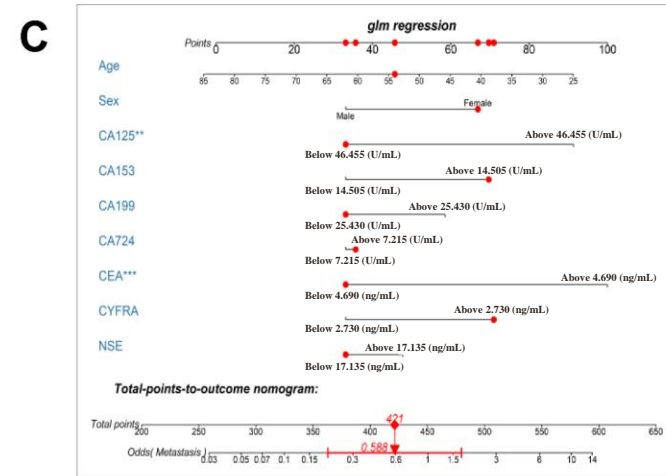
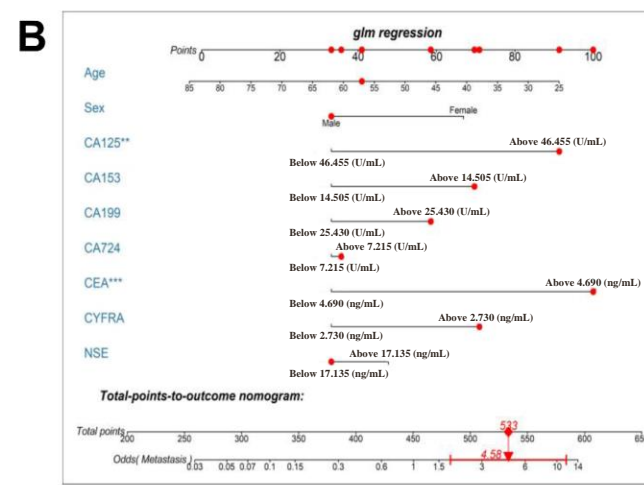
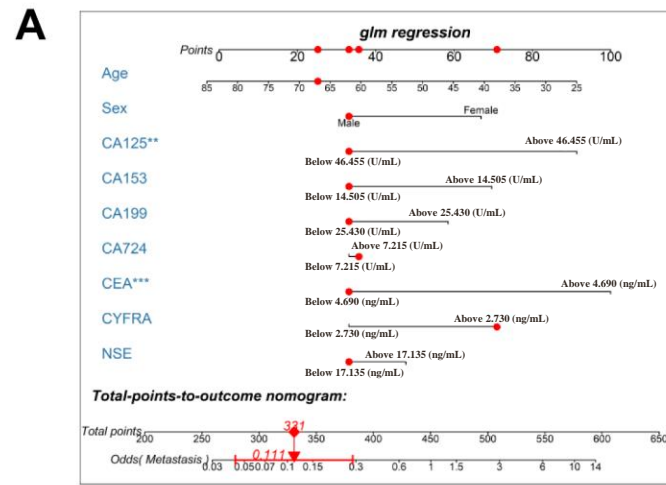


Supplementary Figure 4. Odds ratio of Age, Sex and biomarkers grouped by cut-off value. Below: below cut-off value. Above: above cut-off value.

Abbreviations: CA125, carbohydrate antigen 125 (U/mL); CA153, carbohydrate antigen 153 (U/mL); CA199, carbohydrate antigen 199 (U/mL); CA724, carbohydrate antigen 724 (U/mL); CEA, carcinoembryonic antigen (ng/mL); CYFRA, cytokeratin-19 fragment (ng/mL); NSE, neuron-specific enolase (ng/mL).



Supplementary Figure 5. Comparison alternative logistic model with models based on upper reference limit. (A) Adjusted without sex and age factors. (B) Adjusted with sex and age factors.



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Sex	Age	CA125	CA153	CA199	CA724	CEA	CYFRA	NSE	Score	Predicted status	Actual status	No. Fig
Male	67	36.97	8.36	7.62	116.50	2.43	7.63	8.85	0.11	Non-Metastasis	Non-Metastasis	A
Male	57	70.88	18.64	26.43	15.46	4.91	6.34	8.96	4.58	Metastasis	Metastasis	B
Female	54	22.51	37.75	10.62	10.85	0.59	15.44	12.51	0.59	Non-Metastasis	Non-Metastasis	C
Female	75	351.00	26.54	354.10	0.70	81.33	6.58	16.99	4.83	Metastasis	Metastasis	D

Supplementary Figure 6. Four examples for nomogram model application.