

Supplementary Methods

Search cancer trials for supporting evidence: The determination of intent was ascertained from the ClinicalTrials.gov XML field(s) <primary_outcome>; if a trial record did not contain this field, the narrative in <brief_summary> and <detailed_description> was also examined. The distinct drugs used in the final candidate trials (category A or B) were defined as the ground truth for our evaluation here. We compared signals detected from EHRs with the ground truth and calculated the numbers of True Positives (TP) – drugs in both detected signals and the ground truth, False Positives (FP) – drugs in detected signals but not in the ground truth, and False Negatives (FN) – drugs in the ground truth but not in our detected signals. Then we reported precision ($TP/TP+FP$) and recall ($TP/TP+FN$). Furthermore, to test whether our signal detection method is significantly different from the random method, we designed a permutation analysis to compare our method with random sampling, which randomly selects the same number of drugs from the 146 drugs as positives and calculates precision and recall according to the ground truth. We repeated the random sampling for 100,000 times and compared our results with random sampling results to generate the permutation *p-value*, which was used to determine whether our method is significantly better than random sampling.

Variables collected for multivariable Cox model

VUMC: We collected a total number of 2,630 variables for each individual, including 3 patient demographics (age, biological sex, race), 2 tumor information (tumor type and stage), 1,279 diagnoses and 1,346 medications

Mayo: We collected a total number of 5,725 variables for each individual, including 3 patient demographics (age, biological sex, race), 2 tumor information (tumor type and stage), 1,279 diagnoses and 4,441 medications.

Supplementary eTable 1. All 146 candidate drugs.

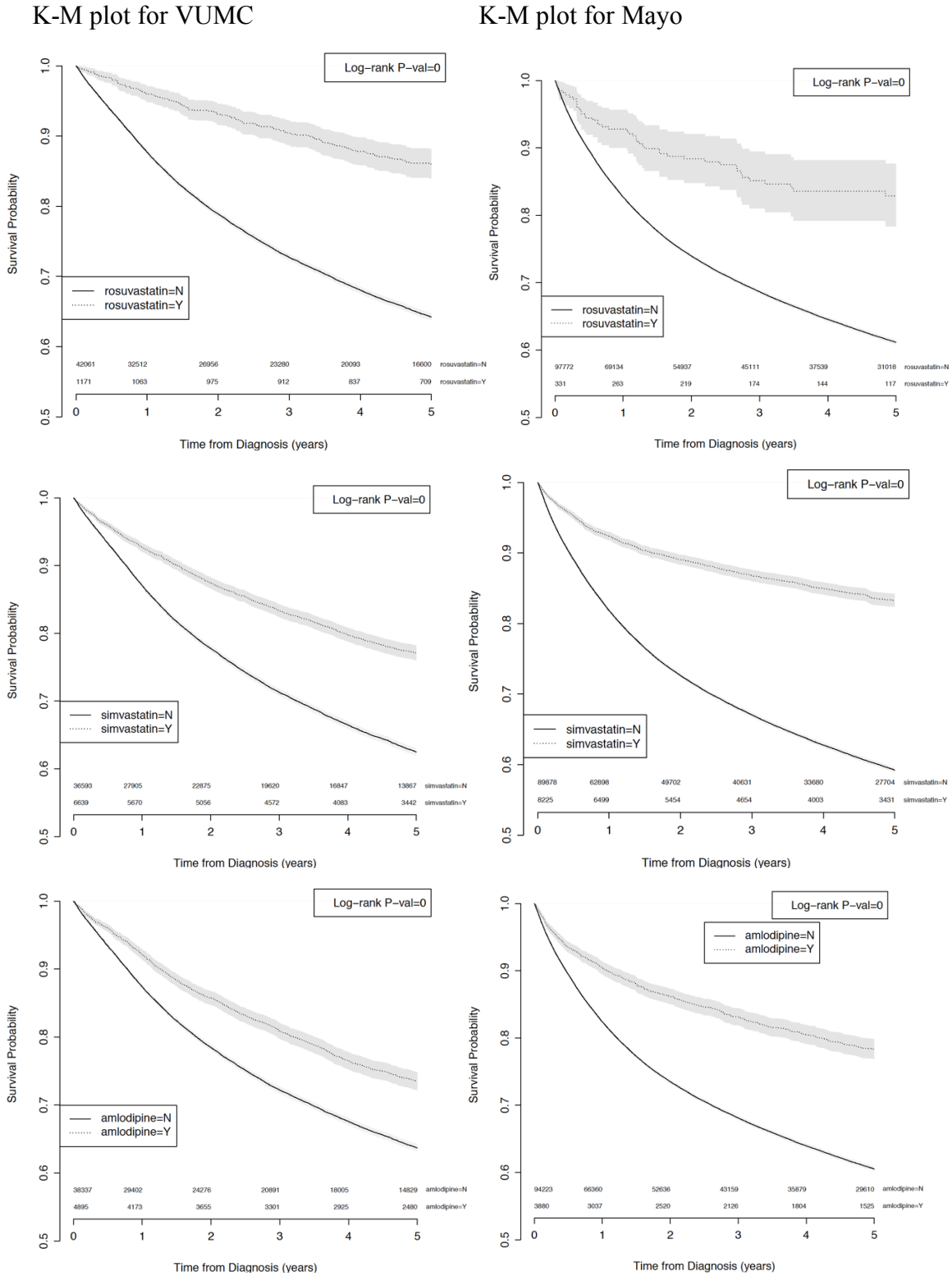
	Drug
1	albuterol
2	allopurinol
3	aluminum hydroxide
4	amiodarone
5	amitriptyline
6	amlodipine
7	amylase
8	aripiprazole
9	atenolol
10	atorvastatin
11	azathioprine
12	azelastine
13	baclofen
14	benazepril
15	bupropion
16	bupirone
17	captopril
18	carbamazepine
19	carbidopa
20	carisoprodol
21	carvedilol
22	celecoxib
23	citalopram
24	clonidine
25	clopidogrel
26	colchicine
27	cyclobenzaprine
28	desloratadine
29	diclofenac
30	dicyclomine
31	digoxin
32	diltiazem
33	donepezil
34	doxazosin
35	doxepin
36	duloxetine
37	enalapril
38	enoxaparin

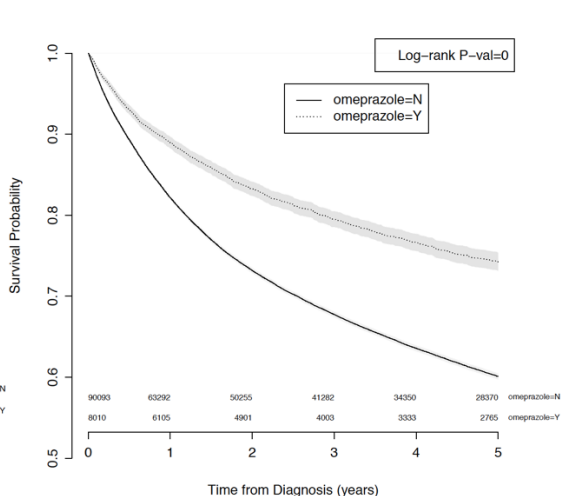
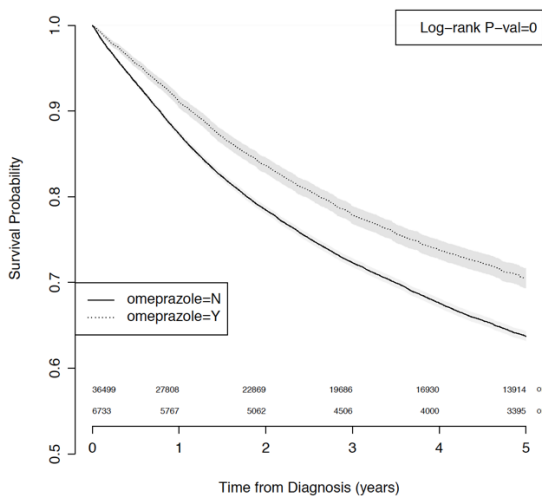
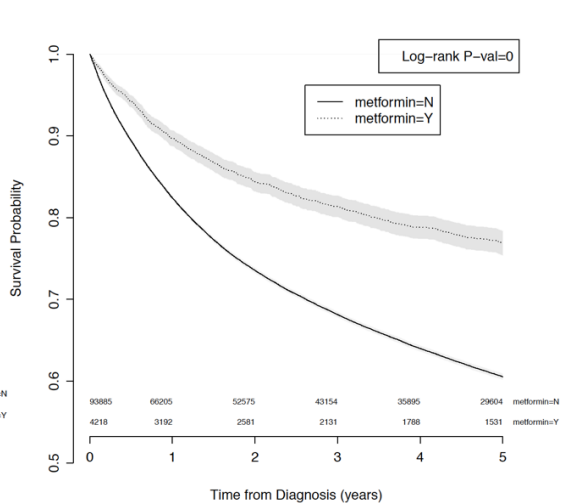
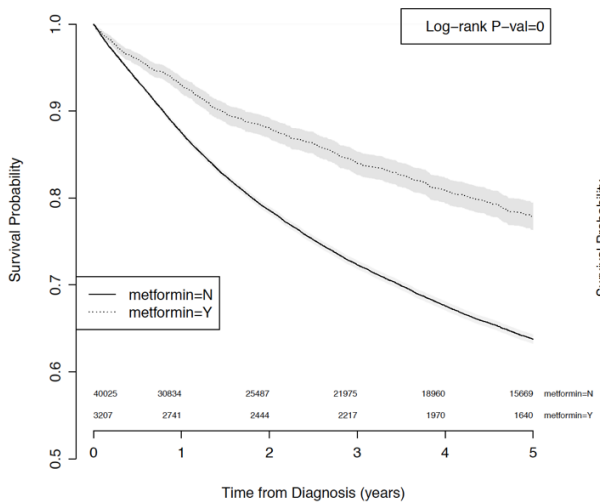
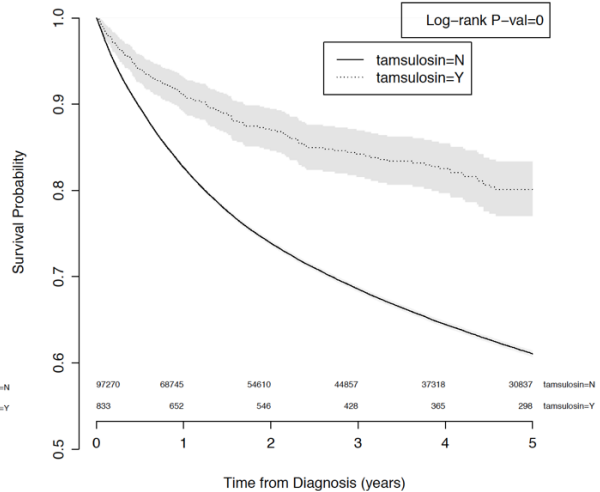
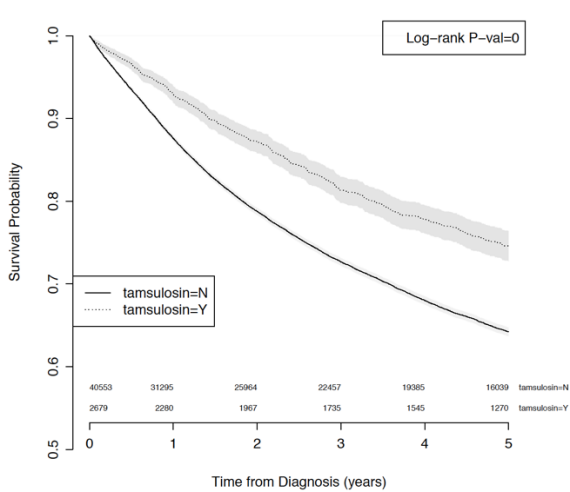
39	epoetin
40	ergocalciferol
41	escitalopram
42	esomeprazole
43	estradiol
44	estrogens
45	eszopiclone
46	ethinyl estradiol
47	etodolac
48	ezetimibe
49	fenofibrate
50	finasteride
51	fluconazole
52	fluoxetine
53	furosemide
54	gabapentin
55	gemfibrozil
56	glimepiride
57	glipizide
58	glyburide
59	haloperidol
60	hydralazine
61	hydrochlorothiazide
62	hydroxychloroquine
63	hydroxyzine
64	ibandronate
65	indomethacin
66	insulin
67	insulin glargine
68	insulin lispro
69	ipratropium
70	irbesartan
71	isosorbide
72	isosorbide dinitrate
73	ketorolac
74	labetalol
75	lamotrigine
76	lansoprazole
77	levalbuterol
78	levetiracetam
79	lipase

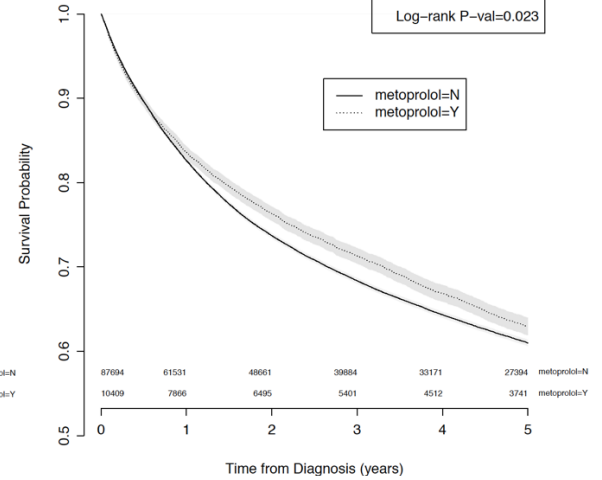
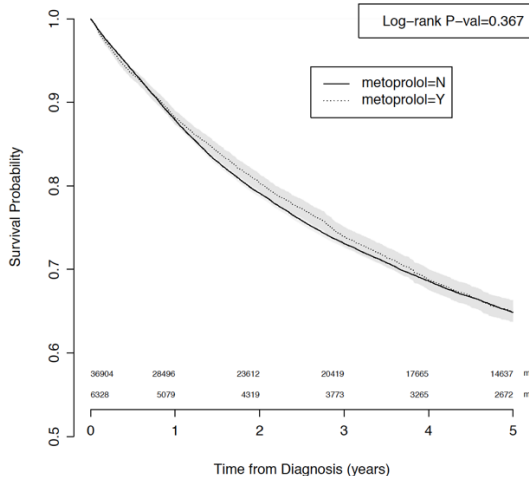
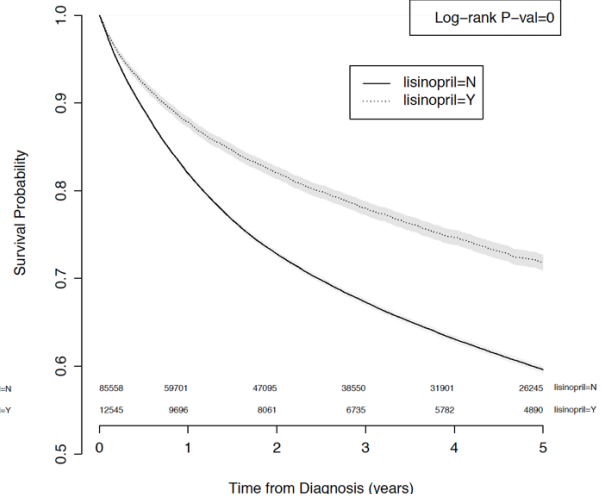
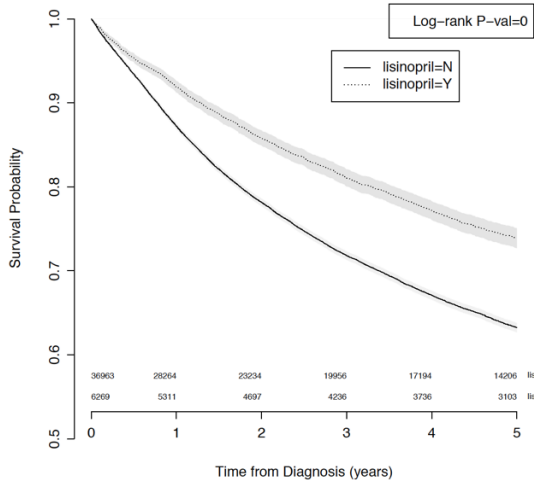
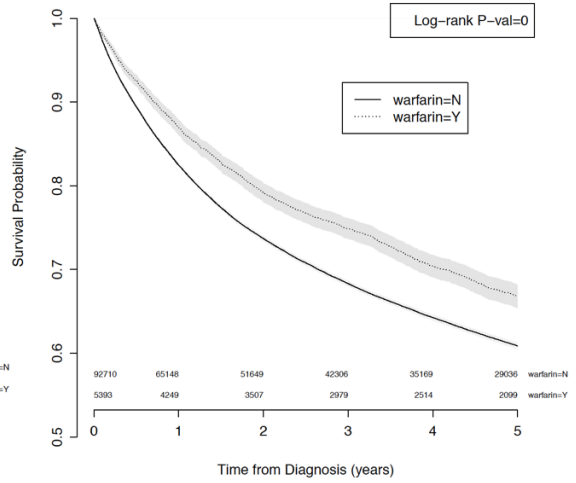
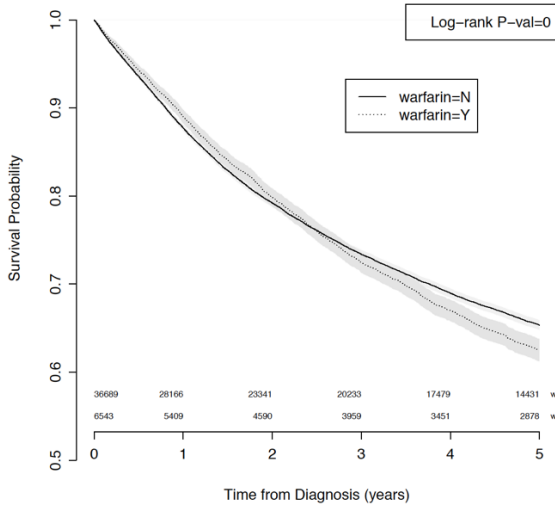
80	lisinopril
81	losartan
82	lovastatin
83	mesalamine
84	metaxalone
85	metformin
86	methocarbamol
87	metoprolol
88	metronidazole
89	midazolam
90	minocycline
91	mirtazapine
92	montelukast
93	mycophenolate mofetil
94	nabumetone
95	niacin
96	nifedipine
97	nitrofurantoin
98	nizatidine
99	nortriptyline
100	olanzapine
101	olmesartan
102	omeprazole
103	oxcarbazepine
104	oxybutynin
105	oxymetazoline
106	pantoprazole
107	paroxetine
108	phenobarbital
109	phenytoin
110	pioglitazone
111	pravastatin
112	pregabalin
113	progesterone
114	propranolol
115	quetiapine
116	quinapril
117	rabeprazole
118	ramipril
119	risperidone

120	rofecoxib
121	ropinirole
122	rosiglitazone
123	rosuvastatin
124	sertraline
125	sildenafil
126	simvastatin
127	spironolactone
128	sulfamethoxazole
129	sumatriptan
130	tacrolimus
131	tamsulosin
132	testosterone
133	timolol
134	tiotropium
135	tizanidine
136	topiramate
137	tramadol
138	trazodone
139	valdecoxib
140	valproate
141	valsartan
142	varenicline
143	venlafaxine
144	verapamil
145	warfarin
146	zolpidem

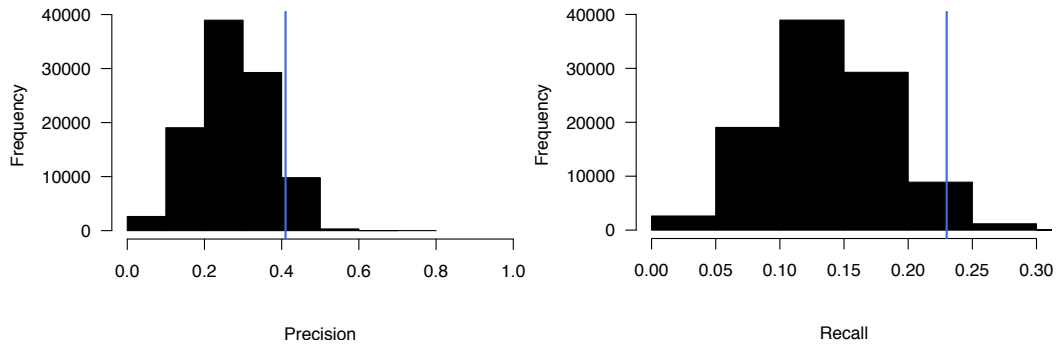
Supplementary eFigure 1. Kaplan–Meier (K–M) plot of overall cancer survival for the 9 drugs detected from VUMC and replicated by Mayo. (K-M Plots without adjusting for other covariates)







Supplementary eFigure 2. Permutation analysis between our method and random sampling. We compared our method with 100,000 times of random sampling. Our method outperformed random sampling with significant *p-value* of 0.04. (The vertical line represents the scores for our large-scale mining method)



Permutation results