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Supplementary Table 1. Patient characteristics between post-MI cohort and study cohort.

Patient Characteristics	Post-MI Cohort (N=5,989)	Study Cohort (N=4,575)	*p* value	Cohen's d (95%CI)[^]
Demographics				
Gender, Male N (%)	4,412 (73·7)	3,400 (74·3)	0·452	-
Race, N (%)				
Chinese	3,910 (65·3)	2,998 (65·5)	0·808	-
Indian	771 (12·9)	601 (13·1)		
Malay	1,053 (17·6)	774 (16·9)		
Others	255 (4·3)	202 (4·4)		
Age (years), mean (SD)	63·1 (13·1)	62·6 (12·7)	0·054	0·038 (0·038, 0·038)
Baseline biomarkers, mean (SD)				
Total cholesterol (mmol/l)	4·92 (1·33)	4·91 (1·33)	0·875	0·001 (0·001, 0·001)
LDL-C (mmol/l)	3·07 (1·14)	3·07 (1·15)	0·969	0·003 (0·003, 0·003)
Serum creatinine (μmol/l)	131·7 (155·2)	127·3 (148·8)	0·146	0·029 (0·029, 0·029)

[^]Cohen's d (95% CI) are assessed on continuous variables.

Supplementary Table 2. Inputs to the static model.

Demographics	Age
	Gender
Medical history	Diabetes
	Hypertension
	Prior heart failure
Baseline biomarkers	LDL
	VLDL + IDL
	eGFR*
	Haemoglobin
	WBC
	RDW-CV
	Troponin
Prior medication	Statin
	ACE/ARB/CCB
	Loop diuretic
	β-blocker
Index event	Index MI (STEMI/NSTEMI)
	Index procedure (PCI/CABG)
	Total number of stents
	Anti-platelet prescription at discharge

* In the scaled transformation, input data x were transformed to $\frac{x}{x+k}$ where k is optimized.

Supplementary Table 3. Inputs to the dynamic model components.

Input data	Model component and transformation (if any)		
	Ro	**Alpha**	**Gamma**
Demographics			
Age	✓ (z-scored)	✓ (z-scored)	✓ (scaled)
Gender	✓	✓	-
Medical history			
Diabetes flag	✓	✓	✓
Hypertension flag	✓	✓	-
Prior heart failure flag	✓	✓	✓
Baseline biomarkers			
LDL-c	✓ (z-scored)	-	-
VLDL-c + ILDL-c	✓ (z-scored)	-	-
eGFR	✓ (min-max)	✓ (min-max)	-
Hemoglobin	✓ (z-scored)	✓ (z-scored)	-
RDW	✓ (z-scored)	✓ (z-scored)	-
WBC counts	✓ (z-scored)	✓ (z-scored)	-
Troponin	✓ (z-scored)	✓ (z-scored)	-
Prior medications			
Statin flag	✓	-	-
ACE/ARB/CCB flag	✓	-	-
Loop diuretic flag	✓	-	-
Beta-blocker flag	✓	-	-
Index information			
STEMI flag	✓	✓	-
Baseline PCI/CABG flag	✓	✓	-
Total number of stents	✓	✓	-
Antiplatelets prescription at discharge	✓	✓	-
Follow up biomarker			
LDL-c	-	-	✓ (scaled)
VLDL-c + ILDL-c	-	-	✓ (scaled)
eGFR	-	-	✓ (scaled)
Follow up adherence			
Aspirin	-	-	✓ (scaled)
ADP inhibitor	-	-	✓ (scaled)

ACE/ARB	-	-	✓ (scaled)
β-blockers	-	-	✓ (scaled)
CCB	-	-	✓ (scaled)
Loop diuretics	-	-	✓ (scaled)

Supplementary Table 4. Sensitivity analysis of model performance (AUROC, 95% CI) of TIMI risk score with assumption of (1) smoker and (2) non-smoker as input.

Length of follow up data from index event	AUROC (95% CI)			
	Test (hold-out) dataset		Validation dataset	
	Smoker	Non-smoker	Smoker	Non-smoker
12 months	0·71 (0·64, 0·78)	0·72 (0·65, 0·79)	0·73 (0·66, 0·81)	0·72 (0·66, 0·79)
15 months	0·72 (0·64, 0·79)	0·72 (0·65, 0·80)	0·72 (0·67, 0·78)	0·72 (0·67, 0·80)
18 months	0·72 (0·67, 0·78)	0·73 (0·65, 0·79)	0·72 (0·65, 0·79)	0·72 (0·65, 0·79)
21 months	0·73 (0·68, 0·80)	0·73 (0·67, 0·79)	0·72 (0·66, 0·78)	0·72 (0·66, 0·78)
24 months	0·75 (0·69, 0·80)	0·74 (0·67, 0·79)	0·73 (0·66, 0·80)	0·72 (0·65, 0·78)

Supplementary Table 5. The patient count and proportion (N, %) on medication and their diagnosis in (a) training dataset (N=2,745); (b) test dataset (N=915); (c) validation dataset (N=915).

(a)

Medication	Prescribed	Hypertension		Heart Failure		Diabetes Mellitus	
		Absent	Present	Absent	Present	Absent	Present
Beta-blocker	No	118 (4·3)	103 (3·8)	196 (7·1)*	25 (0·9)*	148 (5·4)	73 (2·7)
	Yes	1267 (46·2)	1257 (45·8)	2103 (76·6)*	421 (15·3)*	1536 (56)	988 (36)
CCB	No	1118 (40·7)*	711 (25·9)*	1562 (56·9)*	267 (9·7)*	1213 (44·2)*	616 (22·4)*
	Yes	267 (9·7)*	649 (23·6)*	737 (26·8)*	179 (6·5)*	471 (17·2)*	445 (16·2)*
Loop Diuretics	No	1089 (39·7)*	772 (28·1)*	1800 (65·6)*	61 (2·2)*	1283 (46·7)*	578 (21·1)*
	Yes	296 (10·8)*	588 (21·4)*	499 (18·2)*	385 (14)*	401 (14·6)*	483 (17·6)*
Aspirin	No	73 (2·7)*	104 (3·8)*	134 (4·9)*	43 (1·6)*	107 (3·9)	70 (2·6)
	Yes	1312 (47·8)*	1256 (45·8)*	2165 (78·9)*	403 (14·7)*	1577 (57·4)	991 (36·1)
ADP-inhibitors	No	124 (4·5)	118 (4·3)	200 (7·3)	42 (1·5)	169 (6·2)*	73 (2·7)*
	Yes	1261 (45·9)	1242 (45·2)	2099 (76·5)	404 (14·7)	1515 (55·2)*	988 (36)*
ACEs	No	372 (13·6)*	478 (17·4)*	699 (25·5)	151 (5·5)	485 (17·7)*	365 (13·3)*
	Yes	1013 (36·9)*	882 (32·1)*	1600 (58·3)	295 (10·7)	1199 (43·7)*	696 (25·4)*
ARBs	No	1039 (37·9)*	842 (30·7)*	1600 (58·3)*	281 (10·2)*	1232 (44·9)*	649 (23·6)*
	Yes	346 (12·6)*	518 (18·9)*	699 (25·5)*	165 (6)*	452 (16·5)*	412 (15)*

(b)

Medication	Prescribed	Hypertension		Heart Failure		Diabetes Mellitus	
		Absent	Present	Absent	Present	Absent	Present
Beta-blocker	No	32 (1·2)	31 (1·1)	55 (2·0)	8 (0·3)	42 (1·5)	21 (0·8)
	Yes	415 (15·1)	437 (15·9)	702 (25·6)	150 (5·5)	517 (18·8)	335 (12·2)
CCB	No	379 (13·8)*	266 (9·7)*	548 (20)*	97 (3·5)*	433 (15·8)*	212 (7·7)*
	Yes	68 (2·5)*	202 (7·4)*	209 (7·6)*	61 (2·2)*	126 (4·6)*	144 (5·2)*
Loop Diuretics	No	358 (13)*	261 (9·5)*	598 (21·8)*	21 (0·8)*	419 (15·3)*	200 (7·3)*
	Yes	89 (3·2)*	207 (7·5)*	159 (5·8)*	137 (5)*	140 (5·1)*	156 (5·7)*
Aspirin	No	19 (0·7)*	38 (1·4)*	43 (1·6)	14 (0·5)	37 (1·3)	20 (0·7)
	Yes	428 (15·6)*	430 (15·7)*	714 (26)	144 (5·2)	522 (19·0)	336 (12·2)

ADP-inhibitors	No	30 (1·1)	44 (1·6)	56 (2·0)	18 (0·7)	49 (1·8)	25 (0·9)
	Yes	417 (15·2)	424 (15·4)	701 (25·5)	140 (5·1)	510 (18·6)	331 (12·1)
ACEs	No	104 (3·8)*	190 (6·9)*	239 (8·7)	55 (2·0)	162 (5·9)*	132 (4·8)*
	Yes	343 (12·5)*	278 (10·1)*	518 (18·9)	103 (3·8)	397 (14·5)*	224 (8·2)*
ARBs	No	337 (12·3)*	300 (10·9)*	517 (18·8)	100 (3·6)	403 (14·7)*	234 (8·5)*
	Yes	110 (4·0)*	168 (6·1)*	220 (8·0)	58 (2·1)	156 (5·7)*	122 (4·4)*

(c)

Medication	Prescribed	Hypertension		Heart Failure		Diabetes Mellitus	
		Absent	Present	Absent	Present	Absent	Present
Beta-blocker	No	34 (1·2)	37 (1·3)	62 (2·3)	9 (0·3)	44 (1·6)	27 (1)
	Yes	444 (16·2)	400 (14·6)	704 (25·6)	140 (5·1)	518 (18·9)	326 (11·9)
CCB	No	391 (14·2)*	227 (8·3)*	528 (19·2)	90 (3·3)	410 (14·9)*	208 (7·6)*
	Yes	87 (3·2)*	210 (7·7)*	238 (8·7)	59 (2·1)	152 (5·5)*	145 (5·3)*
Loop Diuretics	No	372 (13·6)*	246 (9)*	598 (21·8)*	20 (0·7)*	432 (15·7)*	186 (6·8)*
	Yes	106 (3·9)*	191 (7)*	168 (6·1)*	129 (4·7)*	130 (4·7)*	167 (6·1)*
Aspirin	No	20 (0·7)	31 (1·1)	39 (1·4)	12 (0·4)	23 (0·8)*	28 (1)*
	Yes	458 (16·7)	406 (14·8)	727 (26·5)	137 (5)	539 (19·6)*	325 (11·8)*
ADP-inhibitors	No	38 (1·4)	40 (1·5)	63 (2·3)	15 (0·5)	47 (1·7)	31 (1·1)
	Yes	440 (16)	397 (14·5)	703 (25·6)	134 (4·9)	515 (18·8)	322 (11·7)
ACEs	No	115 (4·2)*	168 (6·1)*	229 (8·3)	54 (2)	157 (5·7)*	126 (4·6)*
	Yes	363 (13·2)*	269 (9·8)*	537 (19·6)	95 (3·5)	405 (14·8)*	227 (8·3)*
ARBs	No	376 (13·7)*	275 (10)*	556 (20·3)*	95 (3·5)*	418 (15·2)*	233 (8·5)*
	Yes	102 (3·7)*	162 (5·9)*	210 (7·7)*	54 (2)*	144 (5·2)*	120 (4·4)*

* Chi-squared comparisons with a significant $p \leq 0{\cdot}05$

Supplementary Table 6. List of diagnosis codes for cohort inclusion criteria.

No	Diagnosis Code	Description
International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)		
1	I21.x	Acute myocardial infarction
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)		
1	410	Acute myocardial infarction
2	410.00	Acute myocardial infarction of anterolateral wall, episode of care unspecified
3	410.01	Acute myocardial infarction of anterolateral wall, initial episode of care
4	410.10	Acute myocardial infarction of other anterior wall, episode of care unspecified
5	410.11	Acute myocardial infarction of other anterior wall, initial episode of care
6	410.20	Acute myocardial infarction of inferolateral wall, episode of care unspecified
7	410.21	Acute myocardial infarction of inferolateral wall, initial episode of care
8	410.30	Acute myocardial infarction of inferoposterior wall, episode of care unspecified
9	410.31	Acute myocardial infarction of inferoposterior wall, initial episode of care
10	410.40	Acute myocardial infarction of other inferior wall, episode of care unspecified
11	410.41	Acute myocardial infarction of other inferior wall, initial episode of care
12	410.50	Acute myocardial infarction of other lateral wall, episode of care unspecified
13	410.51	Acute myocardial infarction of other lateral wall, initial episode of care
14	410.60	True posterior wall infarction, episode of care unspecified
15	410.61	True posterior wall infarction, initial episode of care
16	410.70	Subendocardial infarction, episode of care unspecified
17	410.71	Subendocardial infarction, initial episode of care
18	410.80	Acute myocardial infarction of other specified sites, episode of care unspecified
19	410.81	Acute myocardial infarction of other specified sites, initial episode of care
20	410.90	Acute myocardial infarction of unspecified site, episode of care unspecified
21	410.91	Acute myocardial infarction of unspecified site, initial episode of care
Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED-CT)		
1	10181000132108	ST-elevation myocardial infarction
2	129574000	Postoperative myocardial infarction
3	194802003	True posterior myocardial infarction
4	22298006	Myocardial infarction
5	233825009	Acute Q wave infarction – anteroseptal
6	233838001	Acute posterior myocardial infarction
7	233843008	Silent myocardial infarction
8	304914007	Acute Q wave myocardial infarction
9	307140009	Acute non-Q wave infarction
10	314207007	Non-Q wave myocardial infarction
11	371068009	Myocardial infarction with complication
12	394710008	First myocardial infarction
13	401303003	Acute ST segment elevation myocardial infarction
14	401314000	Acute non-ST segment elevation myocardial infarction

15	418044006	Myocardial infarction in recovery phase
16	428196007	Mixed myocardial ischemia and infarction
17	54329005	Acute myocardial infarction of anterior wall
18	57054005	Acute myocardial infarction
19	58612006	Acute myocardial infarction of lateral wall
20	62695002	Acute anteroseptal myocardial infarction
21	65547006	Acute myocardial infarction of inferolateral wall
22	70211005	Acute myocardial infarction of anterolateral wall
23	70422006	Acute subendocardial infarction
24	73795002	Acute myocardial infarction of inferior wall
25	76593002	Acute myocardial infarction of inferoposterior wall

Supplementary Table 7. List of diagnosis codes for identification of stroke due to embolism.

No	Diagnosis Code	Description
International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)		
1	I63.4x	Cerebral infarction due to embolism of cerebral arteries
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)		
1	434.11	Cerebral embolism with cerebral infarction
Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED-CT)		
1	195190007	Cerebral infarction due to embolism of cerebral arteries
2	371041009	Embolic stroke
3	413758000	Cardioembolic stroke

Supplementary Table 8. List of diagnosis codes for identification of haemorrhagic stroke.

No	Diagnosis Code	Description
International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)		
1	I62.9	Intracranial hemorrhage (nontraumatic), unspecified
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)		
1	432.9	Unspecified intracranial hemorrhage
Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED-CT)		
1	1386000	Intracranial hemorrhage

Supplementary Table 9. List of diagnosis codes for identification of diabetes-related diagnosis in SingCLOUD.

No	Diagnosis Code	Description
International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)		
1	E10.x	Type 1 diabetes mellitus
2	E11.x	Type 2 diabetes mellitus
3	E12.x	Malnutrition-related diabetes mellitus
4	E13.x	Other specified diabetes mellitus
5	E14.x	Unspecified diabetes mellitus
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)		
1	249.x	Secondary diabetes mellitus
2	250.x	Diabetes mellitus
3	357.2	Polyneuropathy in diabetes
4	362.0x	Diabetic retinopathy
5	366.41	Diabetic cataract
Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED-CT)		
1	111552007	Diabetes mellitus without complication
2	111556005	Diabetic ketoacidosis without coma
3	127013003	Diabetic renal disease
4	127014009	Diabetic peripheral angiopathy
5	170745003	Diabetic on diet only
6	170747006	Diabetic on insulin
7	190371008	Type I diabetes mellitus - poor control
8	190388001	Type II diabetes mellitus with multiple complications
9	190392008	Type II diabetes mellitus - poor control
10	190447002	Steroid-induced diabetes
11	197605007	Nephrotic syndrome in diabetes mellitus
12	200687002	Cellulitis in diabetic foot
13	201250006	Ischemic ulcer diabetic foot
14	201251005	Neuropathic diabetic ulcer - foot
15	230572002	Diabetic neuropathy
16	230575000	Diabetic chronic painful polyneuropathy
17	232020009	Diabetic maculopathy
18	232022001	Proliferative diabetic retinopathy with new vessels elsewhere than on disc
19	236500003	Proteinuric diabetic nephropathy
20	237621004	Diabetic severe hyperglycemia
21	238982009	Diabetic dermopathy
22	268519009	Diabetic - poor control
23	275918005	Unstable diabetes
24	280137006	Diabetic foot
25	310505005	Diabetic hyperosmolar non-ketotic state
26	312905005	Severe nonproliferative diabetic retinopathy

27	312912001	Diabetic macular edema
28	34140002	Diabetic gastroparesis
29	35777006	Diabetic mononeuropathy multiplex
30	371087003	Diabetic foot ulcer
31	390834004	Nonproliferative diabetic retinopathy
32	395204000	Hyperosmolar non-ketotic state in type 2 diabetes mellitus
33	399872003	Severe nonproliferative diabetic retinopathy with clinically significant macular edema
34	405749004	Newly diagnosed diabetes
35	419100001	Infection of foot associated with diabetes
36	420279001	Renal disorder associated with type 2 diabetes mellitus
37	420422005	Diabetic ketoacidosis
38	424736006	Diabetic peripheral neuropathy
39	424989000	Diabetic gastroparesis associated with type 2 diabetes mellitus
40	44054006	Type 2 diabetes mellitus
41	441656006	Hyperglycemic crisis in diabetes mellitus
42	46635009	Type 1 diabetes mellitus
43	4855003	Diabetic retinopathy
44	48951005	Bullosis diabeticorum
45	49455004	Diabetic polyneuropathy
46	50620007	Diabetic autonomic neuropathy
47	59276001	Proliferative diabetic retinopathy
48	63510008	Nodular type diabetic glomerulosclerosis
49	73211009	Diabetes mellitus
50	8801005	Secondary diabetes mellitus

Supplementary Table 10. List of drug classes used for identification of diabetes-related diagnosis in SingCLOUD.

No	Drug Class
1	Insulin
2	Metformin
3	Sulphonylurea
4	DPP-4 inhibitors
5	Thiazolidinedione
6	Meglitinide
7	SGLT2 inhibitors
8	GLP-1 receptor agonist
9	Acarbose
10	Metformin + Sulphonylurea
11	DPP-4 inhibitors + Metformin
12	Thiazolidinedione + Metformin

Supplementary Table 11. List of diagnosis codes for identification of hypertension-related diagnosis in SingCLOUD.

No	Diagnosis Code	Description
International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)		
1	I10.x	Essential (primary) hypertension
2	I11.x	Hypertensive heart disease
3	I12.x	Hypertensive kidney disease
4	I13.x	Hypertensive heart and kidney disease
5	I15.x	Secondary hypertension
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)		
1	401.x	Essential hypertension
2	402.x	Hypertensive heart disease
3	403.x	Hypertensive renal disease
4	404.x	Hypertensive heart and renal disease
5	405.x	Secondary hypertension
Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED-CT)		
1	104931000119100	Chronic kidney disease due to hypertension
2	10725009	Benign hypertension
3	1201005	Benign essential hypertension
4	123799005	Renovascular hypertension
5	129161000119100	Chronic kidney disease stage 5 due to hypertension
6	132721000119104	Hypertensive emergency
7	153851000119106	Malignant hypertensive chronic kidney disease stage 5
8	170578008	Poor hypertension control
9	193003	Benign hypertensive renal disease
10	194766005	Benign hypertensive heart disease without congestive cardiac failure
11	194767001	Benign hypertensive heart disease with congestive cardiac failure
12	194774006	Hypertensive renal disease with renal failure
13	194779001	Hypertensive heart and renal disease with (congestive) heart failure
14	194780003	Hypertensive heart and renal disease with renal failure
15	194781004	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure
16	194783001	Malignant secondary renovascular hypertension
17	194785008	Benign secondary hypertension
18	194788005	Hypertension secondary to endocrine disorder
19	276789009	Labile hypertension
20	28119000	Renal hypertension
21	285831000119108	Malignant hypertensive chronic kidney disease
22	285841000119104	Malignant hypertensive end stage renal disease
23	286371000119107	Malignant hypertensive end stage renal disease on dialysis
24	31881008	Cardiovascular renal disease
25	31992008	Secondary hypertension

26	32916005	Nephrosclerosis
27	36315003	Malignant hypertensive heart disease without congestive heart failure
28	371125006	Labile essential hypertension
29	38341003	Hypertensive disorder
30	38481006	Hypertensive renal disease
31	39018007	Renal arterial hypertension
32	426012001	Right heart failure due to pulmonary hypertension
33	427889009	Hypertension associated with transplantation
34	428163005	Hypertensive left ventricular hypertrophy
35	428575007	Hypertension secondary to kidney transplant
36	443482000	Hypertensive urgency
37	46113002	Hypertensive heart failure
38	473392002	Hypertensive nephrosclerosis
39	48146000	Diastolic hypertension
40	49220004	Hypertensive renal failure
41	5148006	Hypertensive heart disease with congestive heart failure
42	56218007	Systolic hypertension
43	59621000	Essential hypertension
44	59997006	Endocrine hypertension
45	60899001	Hypertensive heart disease without congestive heart failure
46	62275004	Hypertensive episode
47	64715009	Hypertensive heart disease
48	65443008	Malignant hypertensive renal disease
49	66052004	Benign hypertensive heart AND renal disease
50	66610008	Malignant hypertensive heart AND renal disease
51	698591006	Benign hypertensive renal disease with renal failure
52	698810000	Hypertensive renal disease with end stage renal failure
53	70272006	Malignant hypertension
54	73410007	Benign secondary renovascular hypertension
55	74451002	Secondary diastolic hypertension
56	77737007	Benign hypertensive heart disease with congestive heart failure
57	77970009	Benign hypertensive heart disease without congestive heart failure
58	78975002	Malignant essential hypertension
59	83105008	Malignant hypertensive heart disease with congestive heart failure
60	86234004	Hypertensive heart AND renal disease
61	89242004	Malignant secondary hypertension

Supplementary Table 12. List of drug classes for identification of hypertension-related diagnosis in SingCLOUD.

No	Drug Class
1	ACE inhibitors
2	ARB
3	CCB
4	Loop diuretics
5	Beta-blockers

Supplementary Table 13. List of diagnosis codes for identification of heart failure-related diagnosis in SingCLOUD.

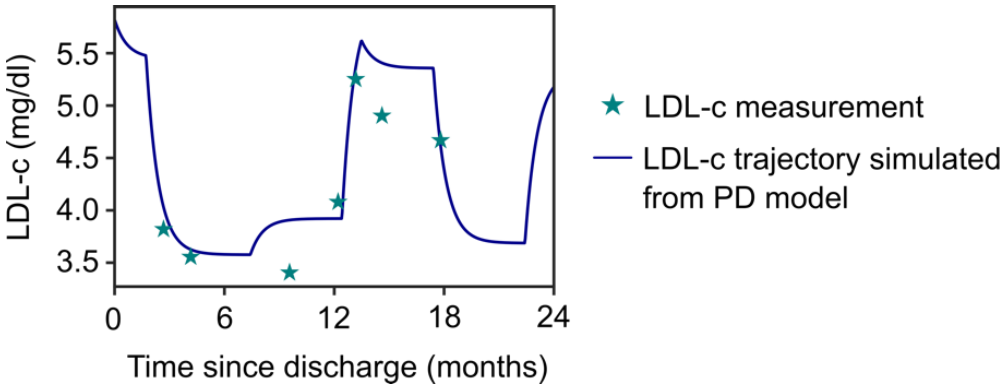
No	Diagnosis Code	Description
International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM)		
1	I11.0	Hypertensive heart disease with (congestive) heart failure
2	I13.x	Hypertensive heart and kidney disease
3	I50.x	Heart failure
International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)		
1	402.01	Malignant hypertensive heart disease with congestive heart failure
2	402.11	Benign hypertensive heart disease with congestive heart failure
3	402.91	Unspecified hypertensive heart disease with congestive heart failure
4	404.x	Hypertensive heart and renal disease
5	428.x	Heart failure
Systematized Nomenclature of Medicine -- Clinical Terms (SNOMED-CT)		
1	10335000	Chronic right-sided heart failure
2	10633002	Acute congestive heart failure
3	128404006	Right heart failure
4	195111005	Decompensated cardiac failure
5	195112003	Compensated cardiac failure
6	360371003	Acute cardiac pulmonary edema
7	364006	Acute left-sided heart failure
8	367363000	Right ventricular failure
9	417996009	Systolic heart failure
10	418304008	Diastolic heart failure
11	42343007	Congestive heart failure
12	424404003	Decompensated chronic heart failure
13	426012001	Right heart failure due to pulmonary hypertension
14	426611007	Congestive heart failure due to valvular disease
15	441530006	Chronic diastolic heart failure
16	46113002	Hypertensive heart failure
17	48447003	Chronic heart failure
18	5148006	Hypertensive heart disease with congestive heart failure
19	56675007	Acute heart failure
20	66989003	Chronic right-sided congestive heart failure
21	71892000	Cardiac asthma
22	84114007	Heart failure
23	85232009	Left heart failure
24	86234004	Hypertensive heart AND renal disease
25	88805009	Chronic congestive heart failure
26	92506005	Biventricular congestive heart failure

Supplementary Table 14. List of drug names for each drug class.

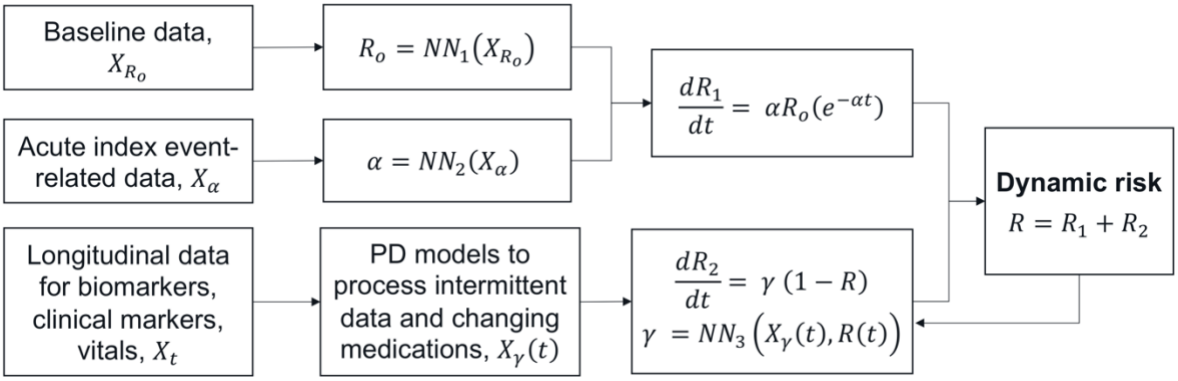
Drug class	No	Drug name
A. Statin	1	Atorvastatin
	2	Fluvastatin
	3	Lovastatin
	4	Pravastatin
	5	Rosuvastatin
	6	Simvastatin
B. Angiotensin-converting Enzyme (ACE) inhibitors	1	Accupril
	2	Aceon
	3	Captopril
	4	Coversum
	5	Coversyl
	6	Enalapril
	7	Fosinopril
	8	Imidapril
	9	Lisinopril
	10	Monopril
	11	Perindopril
	12	Quinapril
	13	Ramipril
	14	Renitec
	15	Tanatril
	16	Tert-butylamine
	17	Tritace
	18	Zestril
C. Angiotensin II Receptor Blockers (ARBs)	1	Aprovel
	2	Atacand
	3	Candesartan
	4	Cozaar
	5	Diovan
	6	Irbesartan
	7	Losartan
	8	Micardis
	9	Olmesartan
	10	Olmetec
	11	Telmisartan
	12	Valsartan
D. β-blockers	1	Atenolol
	2	Betaloc
	3	Bisohexal
	4	Bisoprolol
	5	Carvedilol
	6	Concor

	7	Coreg
	8	Dilatrend
	9	Inderal
	10	Labetalol
	11	Metoprolol
	12	Nebilet
	13	Nebivolol
	14	Propranolol
	15	Tenormin
	16	Trandate
	17	Trantalol
E. Calcium-channel blockers	1	Adalat
	2	Amlodipine
	3	Cardibloc
	4	Cardil
	5	Diltiazem
	6	Dynacirc
	7	Felodipine
	8	Herbesser
	9	Isoptin
	10	Isradipine
	11	Lacidipine
	12	Lacipil
	13	Lercanidipine
	14	Mono-tildiem
	15	Nicardipine
	16	Nifedipine
	17	Nimodipine
	18	Nimotop
	19	Norvasc
	20	Plendil
	21	Verapamil
	22	Zanidip
F. Loop diuretic	1	Bumetanide
	2	Furosemide
	3	Lasix
	4	Burinex
G. Aspirin	1	Aspirin
H. Adenosine diphosphate (ADP) receptor inhibitor	1	Clopidogrel
	2	Prasugrel
	3	Ticagrelor
	4	Ticlopidine

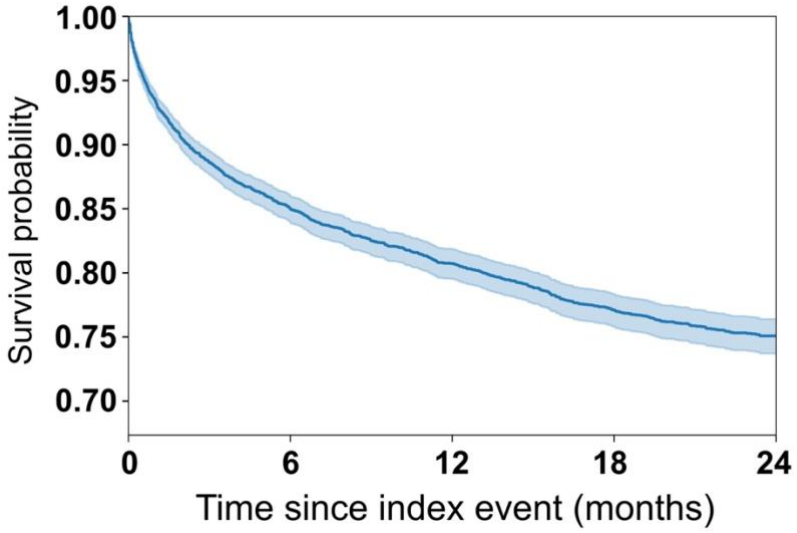
Supplementary Figure 1. An example of patient-specific lipid (LDL-c) trajectory optimization; solid line represents the continuous simulation results while asterisks represent measured values in real world.



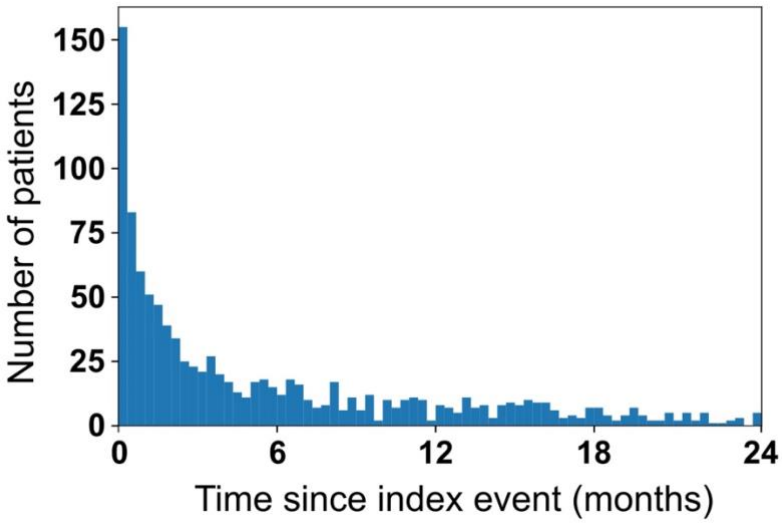
Supplementary Figure 2. Schematic of dynamic model components.



Supplementary Figure 3. Kaplan-Meier survival estimates of MACE (A) in the study cohort and the histogram of MACE distribution across time (B).

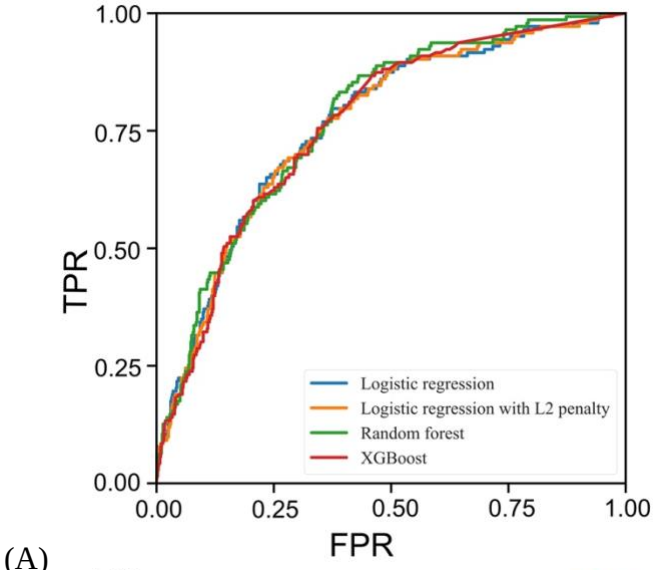


(A)

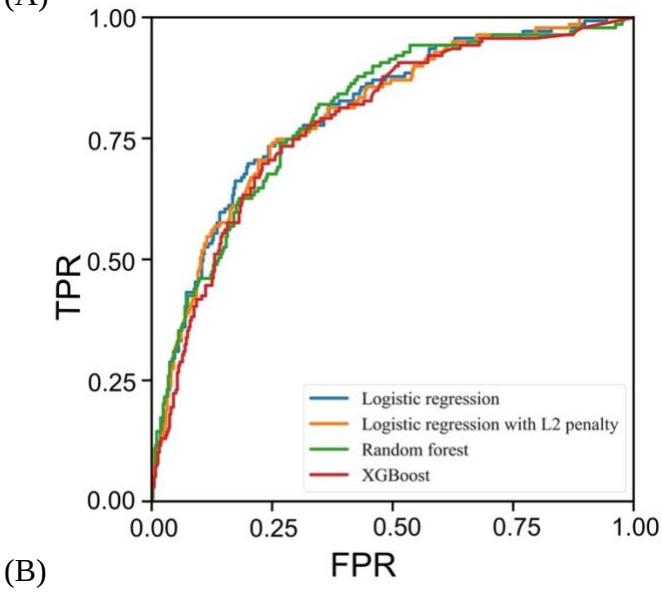


(B)

Supplementary Figure 4. AUROC of static model predicting (A) 1-year MACE events; (B) 2-year MACE events from index on hold-out dataset.

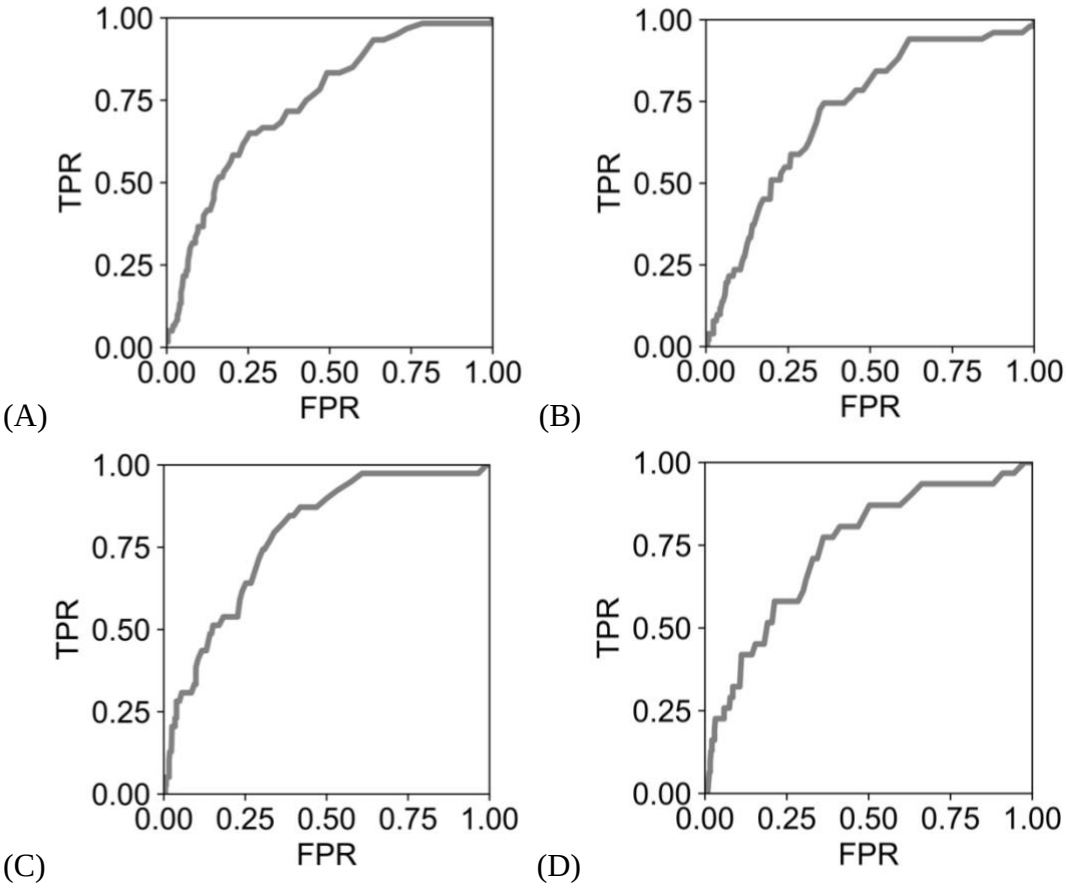


(A)

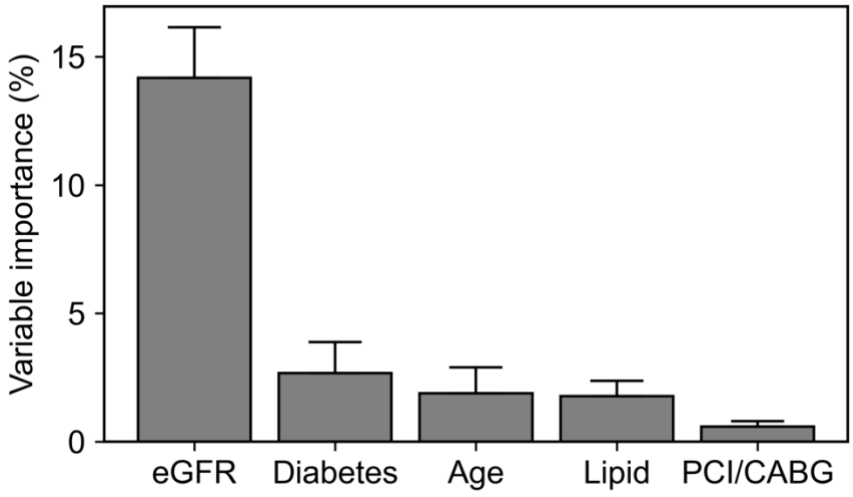


(B)

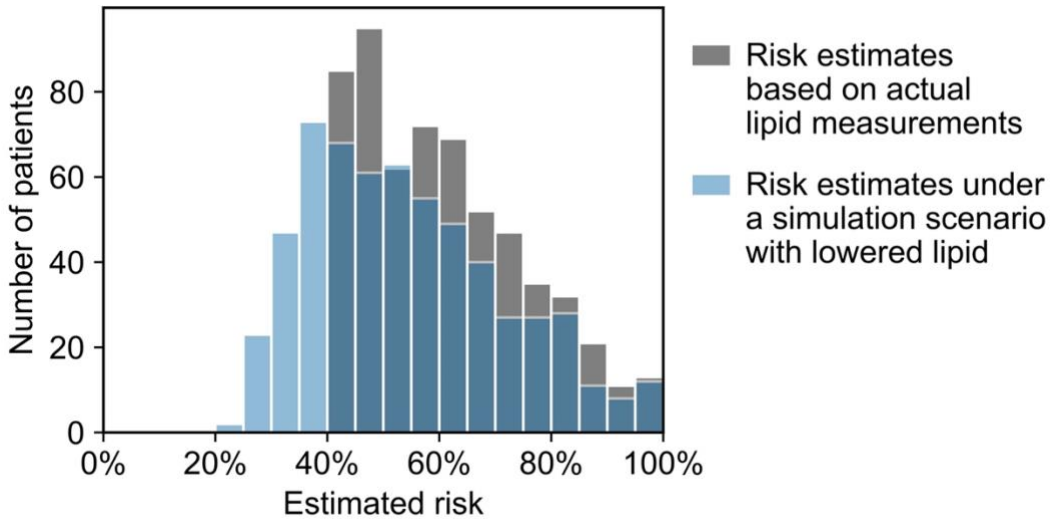
Supplementary Figure 5. AUROC of dynamic model which predicts 1-year MACE event. (A) 15th month risk prediction from 3 months post-index; (B) 18th month risk prediction from 6 months post-index; (C) 21st month risk prediction from 9 months post-index; (D) 24th month risk prediction from 12 months post-index.



Supplementary Figure 6. Top five key predictors based on permutation feature importance from dynamic model, where lipid level includes the impact of LDL, HDL and total cholesterol.



Supplementary Figure 7. Histogram of risk predictions at 1-year post index discharge for high-risk patients (N=703). The distribution of risk shifted to the left when LDL-c was lowered to 30 mg/dL, and total cholesterol was lowered to 50 mg/dL from the end of the first month post-discharge onwards.



Supplementary Method

Normalized Troponin

Cardiac troponin I and T measurements were normalized against the upper limit of normal values (0·03 ug/L for cardiac troponin T, 0·04 ug/L for cardiac troponin I) such that a normalized value of 1 represents the upper limit of normal. If troponin I is available, its normalized will be used preferentially over troponin T.

Calculation of eGFR and generation of continuous eGFR trajectory

Serum creatinine measurements were used to estimate patient's GFR using the CKD-EPI equation. This transformation was performed for all serum creatinine measurements (baseline and follow-up). The calculated follow-up eGFR values were used to generate patient's continuous eGFR trajectory by linearly interpolating eGFR values across time. This method of generating continuous curve was chosen to prevent extreme discontinuity in the trajectory given that eGFR values of a patient could vary substantially.

Model structure

Each model component was represented by a neural network as outlined in Supplementary Table 10. Potential candidates of risk factors and input covariates are informed by clinical literature and availability of reliable and consistent data capture in SingCLOUD database; however, the interaction pathways are highly complex that identifying and building precise interactions among the factors to establish a causal relationship will be challenging. Instead, neural networks, which learns complex patterns in data were used to represent these interactions. The inherent nature of opaque model interpretability and expandability amongst neural networks has been partially overcome in the current work by using (1) a causal framework to discriminate between immediate and long-term risk, (2) biologically informed variable selection and (3) use of a pharmacodynamic model for generating patient specific lipid trajectories.

Model input and variables selection

Inputs to the different model components were selected based on the model structure (Supplementary Table 10). Concretely information related to index event and baseline profile were incorporated as input to R_0 and α components, given that they are associated with immediate risk. One example is the binary flag indicating whether PCI or CABG was performed on the patient during index hospitalization and is used as an input to both R_0 and α.

Separately, the other model component R_2, which accounts for gradually progressing risk including plaque build-up, accepts inputs at each time point (*i.e.* day) of numerical integration. Follow-up information representing subsequent evolution of risk factors and their management is relevant for the component γ; examples are continuous follow up lipid trajectory and adherence to antihypertensives and DAPT. Input selection for different model components was performed based on physiological considerations instead of data-agnostic approach where all available features

were incorporated into the model. Supplementary Table 10 lists the inputs to the different model components.

Lipid trajectory simulation

Lipids play a significant role in cardiovascular disease progression. With patients on lipid-lowering therapy, the accompanying reduction in cumulative risk can be subsequently calculated through a pharmacodynamic simulation. The simulation accounts for the effect of lipids (total cholesterol (TC)) and low-density lipoproteins (LDL)) through a pharmacodynamic equation, which is solved for individual patients to generate patient-specific lipid trajectories -

$$\frac{dC_X}{dt} = S_X^o\ (1 - Hill_{Statin}) - d_X C_X$$

$$Hill_{Statin} = I_{max}\ \frac{(adherence\ \times\ dose)^n}{(IC_{50} +\ (adherence\ \times\ dose)^n)}$$

where $Hill_{Statin}$ is the Hill function accounting for the effect of statin prescription on the bare lipid synthesis term S_X^o.

There are two different cases where this term can reduce to bare synthesis – dose = 0·0 (no statin prescription/dispense) or adherence = 0·0. Lower the adherence to statins, smaller is the reduction in the bare synthesis term. Pharmacological constants, n, I_{max} and IC_{50} for different brands of statin presently used in clinical practice, were obtained from clinical literature. The second term $d_X C_X$ represents the lipid clearance term where we have used first order kinetics for the sake of simplicity. The bare synthesis term S_X^o is estimated assuming initial steady state.

Patient-specific medication adherence during each prescription period is optimized if there is at least one lipid record within that window or calculated based on prescription records if no lipid record was available within the window. Patient-specific parameters (e.g., adherence and initial value of lipids, S_X^o) were estimated using Differential Evolution optimizer by minimizing the total root mean square errors (RMSE). An example of lipid trajectories is shown in below in Supplementary Figure 6.

Differences between static and dynamic model

The notion of static model in this study refers to machine learning models which incorporate information on predictors of risk at the index date for the study. These models do not support the evolution of risk of cardiovascular events over time or how changing levels/values of the risk factors, within patients, affect risk. The model for risk of MACE over 1-yr and 2-yr are separate models and as such the predicted risk for the same patient for 1-yr and 2-yr are also independent of each other.

The alternative, the dynamic model has been developed to support the evolution of risk over time and incorporate not only information available at index date (as in the static models) but also include repeated measurements of biomarkers, risk factors over time and changing treatments post index event. Each available follow-up biomarker measurement or level of risk factor or changing

treatment, drug adherence etc. changes the rate of increase of the cumulative risk and in doing so changes the risk trajectory over time. Due to our lack of knowledge on the exact biological mechanisms through which the biomarkers, risk factors etc. affect the rate of change of the cumulative risk, we choose to represent the function as a neural network model, that is trained based on the available data in the training portion of the study cohort. As such, the cumulative risk of a MACE event predicted by the dynamic model for 2-yr is a very closely related to the risk at 1-yr as is expected from intuitive understanding of the pathophysiology of cardiovascular disease.

The dynamic model method achieves this by representing the cumulative risk over time as an ordinary differential equation:

$$\frac{dR_t}{dt} = NN(\omega, X, Z_t, R_t) \times (1 - R_t)$$

Where:

R_t represents the cumulative risk at time t

X represents the time variant inputs

Z_t represents the time varying inputs

NN represents the feedforward neural network

ω represents the parameters of the neural network to be estimated