Supplementary material:

Statin adherence and risk of acute cardiovascular events among women: a cohort study accounting for time-dependent confounding affected by previous adherence

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Table S1. Definitions of exclusion criteria.

Definition	ATC codes	Reimbursement code	ICD-10 code in primary or secondary diagnosis	Other code	Data Source	Time of measurement
Treatment initiation with cerivastatin	C10AA06				SII	t_0
Evidence of atherosclerotic cardiovascular disease						
Coronary heart disease			I20–I25		FCR	t_{-3} - t_0
		206, 213, 280			SII	$\leq t_0$
CABG/PTCA				FNA, FNB, FNC, FND, FNE, FN1AT, FN1BT, FN1YT, TFN40, TFN50	FCR	t_{-3} - t_0
Clopidogrel		315			SII	$\leq t_0$
Nitrates	C01DA				SII	t_{-3} - t_0
Cerebrovascular diseases and TIA			I60–I66, I68–I69, G45–G46		FCR	t_{-3} - t_0
Carotid endarterectomy or thrombolytic therapy				PAF, AAL120	FCR	t_{-3} - t_0
Atherosclerosis			I70		FCR	t_{-3} - t_0
Peripheral arterial disease				PFH, PDQ, PEQ, PFQ, PF1AT, PF1BT, PE1AT, PE1BT	FCR	t_{-3} - t_0
Aneurysm			I71			
Use of other lipid lowering medications	C10A (excl. C10AA)				SII	t_{-3} - t_0
Long-term institutionalization				date of decision	SII	$\leq t_1$
Death					SII	t_0 - t_1
Acute cardiovascular event						
Acute coronary syndrome			I20.0, I21, I22 as a primary diagnosis		FCR	t_0 - t_1
Acute ischemic stroke			I63 as a primary diagnosis		FCR	t_0 - t_1

Abbreviations: ATC, Anatomical Therapeutic Chemical; CABG, coronary artery bypass graft; FCR, Finnish Care Register; ICD, International Classification of Diseases; PTCA, percutaneous transluminal coronary angioplasty; SII, Social Insurance Institution; TIA, transient ischemic attack.

t_0 = date of the cohort entry = date of the first statin dispensation, t_{-3}= three years prior to statin initiation, t_1 = one year since statin initiation

Table S2. Definitions of outcomes.

Definition	ICD-10 code/Medical procedure code	Data Source
MAIN OUTCOME		
Acute cardiovascular event	As a primary diagnosis:	
Acute coronary syndrome	I20.0, I21, I22	FCR
Acute ischemic stroke	I63	FCR
OUTCOMES IN SENSITIVITY ANALYSES		
Composite outcome		
Acute coronary syndrome	I20.0, I21, I22	FCR
Acute ischemic stroke	I63	FCR
CABG/PTCA	FNA, FNB, FNC, FND, FNE, FN1AT, FN1BT, FN1YT, TFN40, TFN50	FCR
Death from any cause		SII
Low-energy fracture	As a primary or secondary diagnosis:	FCR
Hip fracture	S32.1−S32.4, S72.0−S72.8	FCR
Wrist fracture	S52.0, S62.4	FCR
Ankle fracture	S82.1−S82.7, S92.0, S92.3	FCR
Forearm fracture	S42.2−S42.4	FCR

Abbreviations: CABG, coronary artery bypass graft; FCR, Finnish Care Register; ICD, International Classification of Diseases; PTCA, percutaneous transluminal coronary angioplasty; SII, Social Insurance Institution.

Table S3. Definitions and classifications of baseline characteristics.

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
SOCIO-DEMOGRAPHIC FACTORS						
Age, years 45–49 50–54 55–59 60–64					SII	t_0
University hospital catchment area Helsinki Turku Tampere Kuopio Oulu					SF	t_0
Marital status Married, partner in a registered partnership, separated Divorced or widowed Unmarried					SF	t_0
SOCIO-ECONOMIC FACTORS						
Quartiles of income, euros ≤11,200 11,300–18,700 18,800–25,400 ≥25,500					SF	t_0
Educational level Basic level Secondary level Higher-degree level					SF	t_0
Labor market status Employed labor force Unemployed Pensioner or unemployment pensioner Others outside the labor force					SF	t_0

Table continues

Table S3. Continued

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
FACTORS DESCRIBING STATIN THERAPY						
Statin at baseline						t_0
Simvastatin	C10AA01				SII	
Lovastatin	C10AA02				SII	
Pravastatin	C10AA03				SII	
Fluvastatin	C10AA04				SII	
Atrovastatin	C10AA05				SII	
Rosuvastatin	C10AA07				SII	
Year of statin initiation	C10AA				SII	t_0
2001						
2002						
2003						
2004						
Intensity of statin therapy[a]				Strength and type of statin	SII	t_0
Low						
Moderate						
High						
CARDIAC COMORBIDITY FACTORS						
Diabetes (yes/no)						
			E10– E14		FCR	$t_{-3} – t_0$
		103			SII	$\leq t_0$
	A10A or A10B				SII	$t_{-1} – t_0$
Insulin (yes/no)	A10A				SII	$t_{-1} – t_0$
Hypertensive diseases (yes/no)			I10– I15		FCR	$t_{-3} – t_0$
		205			SII	$\leq t_0$
Heart failure or chronic cardiac insufficiency (yes/no)			I50		FCR	$t_{-3} – t_0$
		201			SII	$\leq t_0$
Cardiac arrhythmia (yes/no)			I46–I49		FCR	$t_{-3} – t_0$
		207			SII	$\leq t_0$
Dysfunctions of lipid metabolism (yes/no)			E78		FCR	$t_{-3} – t_0$
		211			SII	$\leq t_0$

Table continues

Table S3. Continued

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
Number of concurrent CVD medications 0 1 2 3–6	Total number of different ATC codes related to CVD (B01, C01, C02, C03, C07, C08, C09)				SII	$t_{-1} - t_0$
Charlson Comorbidity Index 0 ≥1					FCR	$t_{-1} - t_0$
NON-CARDIAC COMORBIDITY FACTORS						
Rheumatoid arthritis (yes/no)			M05, M06 or M45		FCR	$t_{-3} - t_0$
		202			SII	$\leq t_0$
Cancer (yes/no)			C00–C99 or D00–D09		FCR	$t_{-3} - t_0$
		115–117, 128, 130, 180, 184, 185, 189, 311, 312, 316			SII	$\leq t_0$
	L01				SII	$t_{-1} - t_0$
Mental disorders (yes/no)			F20–F31		FCR	$t_{-3} - t_0$
		112, 188			SII	$\leq t_0$
	N05A				SII	$t_{-1} - t_0$
Depression (yes/no)			F32–F34		FCR	$t_{-3} - t_0$
	N06A				SII	$t_{-1} - t_0$
Respiratory diseases (yes/no)			J44–J46		FCR	$t_{-3} - t_0$
		203			SII	$\leq t_0$
	R03				SII	$t_{-1} - t_0$
Alcohol-related diseases (yes/no)			F10, Z50.2, Z71.4, G31.2, G40.51, G62.1, G72.1, K29.2, K85.2, K86.0, K86.01, K86.08, I42.6, R78.0, T51.0, Y91.1, Y91.2, Y91.3, Y91.9, E24.4, K70.4, K70		FCR	$t_{-3} - t_0$

Table continues

Table S3. Continued

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
NSAID (yes/no)	M01A excluding M01AX05				SII	$t_{-1} - t_0$
Anxiolytics, hypnotics and sedatives (yes/no)	N05B or N05C				SII	$t_{-1} - t_0$
Corticosteroids for systemic use (yes/no)	H02A				SII	$t_{-1} - t_0$
Hormone therapy (yes/no)	G03C or G03F				SII	$t_{-1} - t_0$
Total number of concurrent medications 1–2 3–5 6–31	Total number of different ATC codes				SII	120 days before $t_0 - t_0$
Number of in-hospital days 0 1–2 3–7 8–321					FCR	$t_{-1} - t_0$

Abbreviations: ATC, Anatomical Therapeutic Chemical; CHD, coronary heart disease; CVD, cardiovascular diseases; FCR, Finnish Care Register; ICD, International Classification of Diseases; NSAID, nonsteroidal anti-inflammatory medications; SII, Social Insurance Institution; SF, Statistics Finland.

t_{-3} = three years prior to statin initiation
t_{-1} = one year prior to statin initiation
t_0 = date of statin initiation

[a] Intensity of statin therapy:
Low: Fluvastatin 20–40mg, lovastatin 20mg, pravastatin 10–20mg, simvastatin 5–10mg.
Moderate: Atorvastatin 10–20mg, fluvastatin 80mg, lovastatin 40mg, pravastatin 40mg, rosuvastatin 10mg, simvastatin 20–40mg.
High: Atorvastatin 40–80mg, rosuvastatin 20–40mg, simvastatin 80mg.

Table S4. Definitions and classifications of potential time-dependent confounders at time t_i, i=1,2,3.

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
SOCIO-DEMOGRAPHIC FACTORS						
Marital status Married, partner in a registered partnership, separated Divorced or widowed Unmarried					SF	t_i
SOCIO-ECONOMIC FACTORS						
Quartiles of income					SF	t_i
Labor market status Employed labor force Unemployed Pensioner or unemployment pensioner Others outside the labor force					SF	t_i
FACTORS DESCRIBING STATIN THERAPY						
Increase in intensity of statin therapy[a] (yes/no)				Strength and type of statin	SII	latest prescription in $t_{i-1} - t_i$ vs. latest prescription in $t_{i-2} - t_{i-1}$
CARDIAC COMORBIDITY FACTORS						
Diabetes (yes/no)			E10–E14		FCR	$\leq t_i$
		103			SII	$\leq t_i$
	A10A or A10B				SII	$\leq t_i$
Insulin (yes/no)	A10A				SII	$t_{i-1} - t_i$
Hypertensive diseases (yes/no)			I10–I15		FCR	$\leq t_i$
		205			SII	$\leq t_i$
Heart failure or chronic cardiac insufficiency (yes/no)			I50		FCR	$t_{i-1} - t_i$
		201			SII	$\leq t_i$

Table continues

Table S4. Continued

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
Cardiac arrhythmia (yes/no)			I46–I49		FCR	$t_{i-1} - t_i$
		207			SII	$t_{i-1} - t_i$
Dysfunctions of lipid metabolism (yes/no)			E78		FCR	$\leq t_i$
		211			SII	$\leq t_i$
Number of concurrent CVD medications 0 1 2 ≥3	Total number of different ATC codes related to CVD (B01, C01, C02, C03, C07, C08, C09)				SII	$t_{i-1} - t_i$
Charlson comorbidity index 0 ≥1					FCR	$t_{i-1} - t_i$
Chronic CHD (yes/no)		206, 213, 280			SII	$\leq t_i$
Chronic CHD hospitalization (yes/no) Note: I20.0, I21–I22 in secondary diagnoses only			I20–I25		FCR	$t_0 - t_i$
Medical procedure related to CHD (CABG/PTCA) (yes/no)				FNA, FNB, FNC, FND, FNE, FN1AT, FN1BT, FN1YT, TFN40, TFN50	FCR	$t_{i-1} - t_i$
Chronic cerebrovascular diseases and TIA (yes/no) Note: I63 in secondary diagnoses only			I60–I66, I68, I69, G45–G46		FCR	$t_0 - t_i$
Atherosclerosis (yes/no)			I70, I71		FCR	$t_0 - t_i$
(including peripheral arterial diseases & aneurysm)				PFH, PDQ, PEQ, PFQ, PF1AT, PF1BT, PE1AT, PE1BT	FCR	$\leq t_i$
Nitrates (yes/no)	C01DA				SII	$t_{i-1} - t_i$

Table continues

Table S4. Continued

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
NON-CARDIAC COMORBIDITY FACTORS						
Rheumatoid arthritis (yes/no)			M05, M06 or M45		FCR	$t_{-3} - t_i$
		202			SII	$\leq t_i$
Cancer (yes/no)			C00–C99 or D00–D09		FCR	$t_{-3} - t_i$
		115–117, 128, 130, 180, 184, 185, 189, 311, 312, 316			SII	$\leq t_i$
	L01				SII	$t_{-1} - t_i$
Mental disorders (yes/no)			F20–F31		FCR	$t_{i-1} - t_i$
		112, 188			SII	$t_{i-1} - t_i$
	N05A				SII	$t_{i-1} - t_i$
Depression (yes/no)			F32–F34		FCR	$t_{i-1} - t_i$
Respiratory diseases (yes/no)			J44–J46		FCR	$t_{i-1} - t_i$
		203			SII	$t_{i-1} - t_i$
	R03				SII	$t_{i-1} - t_i$
Alcohol-related diseases (yes/no)			F10, Z50.2, Z71.4, G31.2, G40.51, G62.1, G72.1, K29.2, K85.2, K86.0, K86.01, K86.08, I42.6, R78.0, T51.0, Y91.1, Y91.2, Y91.3, Y91.9, E24.4, K70.4, K70		FCR	$t_{-3} - t_i$
NSAID (yes/no)	M01A excluding M01AX05				SII	$t_{i-1} - t_i$

Table continues

Table S4. Continued

Definition	ATC code	Special reimbursement code	ICD-10 code in primary or secondary diagnoses	Other specifications	Data source	Time of measurement
Anxiolytics, hypnotics and sedatives (yes/no)	N05B or N05C				SII	$t_{i-1} - t_i$
Corticosteroids for systemic use (yes/no)	H02A				SII	$t_{i-1} - t_i$
Hormone therapy (yes/no)	G03C or G03F				SII	$t_{i-1} - t_i$
Total number of concurrent medications	Total number of different ATC codes				SII	$t_{i-1} - t_i$
0–4						
5–9						
≥10						
Number of in-hospital days					FCR	$t_{i-1} - t_i$
0						
1–2						
3–7						
≥8						

Abbreviations: ATC, Anatomical Therapeutic Chemical; CABG, coronary artery bypass graft; CHD, coronary heart disease; CVD, cardiovascular diseases; FCR, Finnish Care Register; ICD, International Classification of Diseases; NSAID, nonsteroidal anti-inflammatory medications; PTCA, percutaneous transluminal coronary angioplasty; SII, Social Insurance Institution; SF, Statistics Finland; TIA, transient ischemic attack.

t_{-3} = three years prior to statin initiation
t_{-1} = one year prior to statin initiation
t_0 = date of statin initiation
t_1 = one year since statin initiation
t_2 = two years since statin initiation
t_3 = three years since statin initiation

[a] Intensity of statin therapy:
Low: Fluvastatin 20–40mg, lovastatin 20mg, pravastatin 10–20mg, simvastatin 5–10mg.
Moderate: Atorvastatin 10–20mg, fluvastatin 80mg, lovastatin 40mg, pravastatin 40mg, rosuvastatin 10mg, simvastatin 20–40mg.
High: Atorvastatin 40–80mg, rosuvastatin 20–40mg, simvastatin 80mg.

Table S5. Distributions of baseline characteristics according to adherence level during the first adherence ascertainment year.

	Non-adherers (PDC <80%) (*n* = 20,120)		**Adherers (PDC ≥80%)** (*n* = 22,687)		**SD**
	n	***%***	***n***	***%***	
Age, years					
45–49	2,423	12.0	2,238	9.9	0.070
50–54	5,286	26.3	5,409	23.8	0.056
55–59	6,621	32.9	7,949	35.0	0.045
60–64	5,790	28.8	7,091	31.3	0.054
University hospital catchment area					
Helsinki	6,450	32.1	7,452	32.9	0.017
Turku	2,657	13.2	2,865	12.6	0.017
Tampere	4,352	21.6	5,058	22.3	0.016
Kuopio	3,716	18.5	4,532	20.0	0.038
Oulu	2,945	14.6	2,780	12.3	0.070
Marital status					
Married, partner in a registered partnership, separated	13,087	65.0	15,347	67.6	0.055
Divorced or widowed	5,282	26.3	5,084	22.4	0.090
Unmarried	1,751	8.7	2,256	9.9	0.043
Quartiles of income, €					
≤11,200	5,070	25.2	5,704	25.1	0.001
11,300–18,700	4,996	24.8	5,694	25.1	0.006
18,800–25,400	5,047	25.1	5,635	24.8	0.006
≥25,500	5,007	24.9	5,654	24.9	0.001
Educational level					
Basic level	7,861	39.1	9,222	40.7	0.032
Secondary level	7,357	36.6	8,008	35.3	0.026
Higher-degree level	4,902	24.4	5,457	24.1	0.007
Labor market status					
Employed labor force	11,562	57.5	12,447	54.9	0.052
Unemployed	2,029	10.1	2,277	10.0	0.002
Pensioner or unemployment pensioner	5,705	28.4	7,124	31.4	0.067
Others outside the labor force	824	4.1	839	3.7	0.021
Statin at baseline					
Simvastatin	7,801	38.8	8,768	38.7	0.003
Lovastatin	373	1.9	337	1.5	0.029
Pravastatin	1,421	7.1	1,046	4.6	0.105
Fluvastatin	1,485	7.4	1,818	8.0	0.024
Atorvastatin	7,147	35.5	8,095	35.7	0.003
Rosuvastatin	1,893	9.4	2,623	11.6	0.070
Year of statin initiation					
2001	4,566	22.7	4,459	19.7	0.074
2002	4,695	23.3	4,858	21.4	0.046
2003	4,925	24.5	5,610	24.7	0.006
2004	5,934	29.5	7,760	34.2	0.101

Table continues

Table S5. Continued

	Non-adherers (PDC <80%) (*n* = 20,120)		Adherers (PDC ≥80%) (*n* = 22,687)		SD
	n	***%***	***n***	***%***	
Intensity of statin therapy					
Low[a]	5,954	29.6	7,114	31.4	0.038
Moderate[b]	14,057	69.9	15,512	68.4	0.032
High[c]	109	0.5	61	0.3	0.043
Diabetes	2,040	10.1	2,732	12.0	0.061
Use of insulin	605	3.0	765	3.4	0.021
Hypertensive diseases	5,246	26.1	6,485	28.6	0.056
Heart failure or chronic cardiac insufficiency	99	0.5	112	0.5	0.000
Cardiac arrhythmia	468	2.3	509	2.2	0.006
Dysfunctions of lipid metabolism	226	1.1	222	1.0	0.014
Number of concurrent CVD medications					
0	10,443	51.9	10,812	47.7	0.085
1	5,470	27.2	6,682	29.5	0.050
2	3,078	15.3	3,781	16.7	0.037
3–6	1,129	5.6	1,412	6.2	0.026
Charlson Comorbidity Index ≥1	1,307	6.5	1,583	7.0	0.019
Rheumatoid arthritis	536	2.7	614	2.7	0.003
Cancer	706	3.5	911	4.0	0.026
Mental disorders	478	2.4	727	3.2	0.050
Depression	2,624	13.0	3,089	13.6	0.017
Respiratory diseases	3,418	17.0	3,502	15.4	0.042
Alcohol-related diseases	143	0.7	101	0.5	0.035
NSAID	6,780	33.7	7,456	32.9	0.018
Anxiolytics, hypnotics and sedatives	427	2.1	485	2.1	0.001
Corticosteroids for systemic use	909	4.5	964	4.3	0.013
Hormone therapy	7,654	38.0	9,398	41.4	0.069
Total number of concurrent medications					
1–2	7,085	35.2	7,289	32.1	0.065
3–5	7,202	35.8	8,037	35.4	0.001
6–31	5,833	29.0	7,361	32.5	0.077
Number of in-hospital days					
0	12,193	60.6	14,222	62.7	0.043
1–2	3,902	19.4	4,099	18.1	0.034
3–7	2,656	13.2	2,825	12.5	0.022
8–321	1,369	6.8	1,541	6.8	0.000

Abbreviations: CVD, cardiovascular disease; NSAID, nonsteroidal anti-inflammatory medications; PDC, proportion of days covered; SD, standardized difference.

[a] Fluvastatin 20–40mg, lovastatin 20mg, pravastatin 10–20mg, simvastatin 5–10mg.

[b] Atorvastatin 10–20mg, fluvastatin 80mg, lovastatin 40mg, pravastatin 40mg, rosuvastatin 10mg, simvastatin 20–40mg.

[c] Atorvastatin 40–80mg, rosuvastatin 20–40mg, simvastatin 80mg.

Table S6. Follow-up year specific un-weighted and stabilized inverse probability of treatment weighted (model 3) standardized differences comparing distributions of baseline characteristics and time-dependent confounders between the adherers and the non-adherers.

	At the beginning of the 1st follow-up year (t_1)		**At the beginning of the 2nd follow-up year (t_2)**		**At the beginning of the 3rd follow-up year (t_3)**	
	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD
BASELINE CHARACTERISTICS						
Socio-demographic factors						
Age, years						
45–49	0.070	0.000	0.076	0.002	0.080	0.003
50–54	0.056	0.000	0.052	0.001	0.061	0.003
55–59	0.045	0.000	0.035	0.000	0.037	0.001
60–64	0.054	0.000	0.065	0.000	0.073	0.001
University hospital catchment area						
Helsinki	0.017	0.000	0.029	0.000	0.020	0.000
Turku	0.017	0.000	0.031	0.000	0.025	0.003
Tampere	0.016	0.000	0.003	0.000	0.018	0.002
Kuopio	0.038	0.001	0.037	0.001	0.051	0.000
Oulu	0.070	0.001	0.057	0.001	0.041	0.001
Marital status						
Married, partner in a registered partnership, separated	0.055	0.000	0.044	0.001	0.046	0.000
Divorced or widowed	0.090	0.000	0.081	0.001	0.075	0.002
Unmarried	0.043	0.000	0.048	0.001	0.035	0.003
Socio-economic factors						
Quartiles of income, €						
≤11,300	0.001	0.000	0.005	0.001	0.007	0.001
11,400–18,700	0.006	0.001	0.018	0.002	0.035	0.000
18,800–25,400	0.006	0.001	0.008	0.000	0.012	0.001
≥25,500	0.001	0.000	0.015	0.001	0.031	0.000
Educational level						
Basic level	0.032	0.000	0.033	0.001	0.035	0.001
Secondary level	0.026	0.000	0.020	0.000	0.018	0.001
Higher-degree level	0.007	0.001	0.016	0.001	0.020	0.000
Labor market status						
Employed labor force	0.052	0.000	0.062	0.001	0.072	0.001
Unemployed	0.002	0.000	0.012	0.001	0.001	0.000
Pensioner or unemployment pensioner	0.067	0.000	0.083	0.000	0.090	0.000
Others outside the labor force	0.021	0.000	0.020	0.000	0.030	0.001

Table continues

Table S6. Continued

	At the beginning of the 1st follow-up year (t_1)		At the beginning of the 2nd follow-up year (t_2)		At the beginning of the 3rd follow-up year (t_3)	
	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD
Factors describing statin therapy						
Statin at baseline						
Simvastatin	0.003	0.000	0.002	0.001	0.038	0.001
Lovastatin	0.029	0.001	0.023	0.001	0.017	0.000
Pravastatin	0.105	0.000	0.078	0.004	0.060	0.006
Fluvastatin	0.024	0.001	0.028	0.000	0.024	0.001
Atorvastatin	0.003	0.000	0.006	0.001	0.031	0.004
Rosuvastatin	0.070	0.001	0.050	0.000	0.019	0.001
Year of statin initiation						
2001	0.074	0.000	0.061	0.001	0.061	0.002
2002	0.046	0.000	0.046	0.001	0.017	0.000
2003	0.006	0.000	0.041	0.001	0.018	0.003
2004	0.101	0.000	0.057	0.001	0.021	0.004
Intensity of statin therapy						
Low	0.038	0.000	0.048	0.001	0.060	0.004
Moderate	0.032	0.000	0.044	0.000	0.057	0.004
High	0.043	0.001	0.027	0.003	0.022	0.002
Cardiac comorbidity factors						
Diabetes	0.061	0.000	0.068	0.001	0.078	0.001
Insulin	0.021	0.000	0.029	0.000	0.032	0.001
Hypertensive diseases	0.056	0.000	0.073	0.002	0.093	0.002
Heart failure or chronic cardiac insufficiency	0.000	0.000	0.011	0.004	0.007	0.004
Cardiac arrhythmia	0.006	0.001	0.013	0.001	0.002	0.002
Dysfunctions of lipid metabolism	0.014	0.000	0.014	0.001	0.020	0.001
Number of concurrent CVD medications						
0	0.085	0.000	0.092	0.002	0.097	0.000
1	0.050	0.000	0.048	0.002	0.040	0.003
2	0.037	0.000	0.041	0.002	0.056	0.000
3–6	0.027	0.000	0.039	0.002	0.044	0.005
Charlson Comorbidity Index ≥1	0.019	0.000	0.031	0.000	0.022	0.005

Table continues

Table S6. Continued

	At the beginning of the 1st follow-up year (t_1)		At the beginning of the 2nd follow-up year (t_2)		At the beginning of the 3rd follow-up year (t_3)	
	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD
Non-cardiac comorbidity factors						
Rheumatoid arthritis	0.003	0.001	0.011	0.001	0.000	0.005
Cancer	0.026	0.000	0.023	0.001	0.012	0.007
Mental disorders	0.050	0.001	0.050	0.001	0.051	0.004
Depression	0.017	0.001	0.003	0.001	0.002	0.000
Respiratory diseases	0.042	0.000	0.024	0.002	0.024	0.001
Alcohol-related diseases	0.035	0.001	0.032	0.003	0.036	0.006
NSAID	0.018	0.000	0.021	0.000	0.008	0.001
Anxiolytics, hypnotics and sedatives	0.001	0.001	0.001	0.001	0.005	0.001
Corticosteroids for systematic use	0.013	0.000	0.006	0.002	0.007	0.000
Hormone therapy	0.069	0.001	0.059	0.002	0.056	0.002
Total number of concurrent medications						
1–2	0.065	0.000	0.070	0.000	0.066	0.000
3–5	0.001	0.000	0.008	0.001	0.005	0.001
6–31	0.077	0.000	0.093	0.001	0.084	0.002
Number of in-hospital days						
0	0.043	0.000	0.027	0.001	0.036	0.001
1–2	0.034	0.000	0.010	0.003	0.028	0.003
3–7	0.022	0.000	0.021	0.000	0.015	0.000
8–321	0.000	0.000	0.008	0.002	0.006	0.006
LAGGED TIME-DEPENDENT CONFOUNDERS						
Socio-demographic factors						
Marital status						
Married, partner in a registered partnership, separated			0.048	0.001	0.034	0.000
Divorced or widowed			0.046	0.002	0.053	0.001
Unmarried			0.083	0.003	0.080	0.001
Socio-economic factors						
Quartiles of income						
1st quartile			0.003	0.001	0.000	0.008
2nd quartile			0.018	0.003	0.032	0.004
3rd quartile			0.012	0.002	0.001	0.016
4th quartile			0.009	0.000	0.033	0.004

Table continues

Table S6. Continued

	At the beginning of the 1st follow-up year (t_1)		At the beginning of the 2nd follow-up year (t_2)		At the beginning of the 3rd follow-up year (t_3)	
	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD
Labor market status						
Employed labor force			0.061	0.001	0.070	0.001
Unemployed			0.018	0.002	0.021	0.007
Pensioner or unemployment pensioner			0.081	0.002	0.098	0.008
Others outside the labor force			0.016	0.008	0.040	0.010
Factors describing statin therapy						
Increase in intensity of statin therapy			0.045	0.009	0.025	0.109
Cardiac comorbidity factors						
Diabetes			0.081	0.009	0.106	0.017
Insulin			0.029	0.000	0.035	0.002
Hypertensive diseases			0.087	0.013	0.109	0.015
Heart failure or chronic cardiac insufficiency			0.019	0.007	0.004	0.006
Cardiac arrhythmia			0.009	0.007	0.000	0.009
Dysfunctions of lipid metabolism			0.009	0.002	0.008	0.002
Number of concurrent CVD medications						
0			0.092	0.000	0.097	0.000
1			0.048	0.002	0.040	0.003
2			0.041	0.002	0.056	0.000
≥3			0.039	0.002	0.044	0.005
Charlson Comorbidity Index ≥1			0.017	0.007	0.011	0.015
Chronic CHD			0.066	0.006	0.064	0.003
Chronic CHD hospitalization			0.040	0.021	0.034	0.008
CABG/PTCA			0.052	0.003	0.038	0.005
Chronic cerebrovascular diseases and TIA			0.007	0.002	0.025	0.004
Atherosclerosis			0.005	0.007	0.018	0.010
Nitrates			0.027	0.000	0.026	0.005
Non-cardiac comorbidity factors						
Rheumatoid arthritis			0.006	0.003	0.003	0.007
Cancer			0.019	0.004	0.006	0.002
Mental disorders			0.058	0.017	0.052	0.017
Depression			0.007	0.005	0.017	0.010

Table continues

Table S6. Continued

	At the beginning of the 1st follow-up year (t_1)		At the beginning of the 2nd follow-up year (t_2)		At the beginning of the 3rd follow-up year (t_3)	
	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD	Un-weighted SD	Stab IPTW weighted SD
Respiratory diseases			0.003	0.006	0.009	0.024
Alcohol-related diseases			0.035	0.007	0.050	0.015
NSAID			0.005	0.007	0.019	0.027
Anxiolytics, hypnotics and sedatives			0.007	0.008	0.006	0.014
Corticosteroids for systemic use			0.013	0.005	0.034	0.014
Hormone therapy			0.067	0.028	0.076	0.033
Total number of concurrent medications						
0–4			0.103	0.031	0.177	0.086
5–9			0.056	0.019	0.115	0.056
≥10			0.073	0.019	0.095	0.047
Number of in-hospital days						
0			0.035	0.025	0.028	0.033
1–2			0.008	0.003	0.004	0.008
3–7			0.019	0.019	0.011	0.015
≥8			0.029	0.027	0.031	0.031

Abbreviations: CABG, coronary artery bypass graft; CHD, coronary heart disease; CVD, cardiovascular diseases; IPTW, inverse probability of treatment weight; NSAID, nonsteroidal anti-inflammatory medications; PTCA, percutaneous transluminal coronary angioplasty; SD, standardized difference; TIA, transient ischemic attack.

Appendix 1. Inverse probability weights and marginal structural model.

Stabilized inverse probability of treatment weights (IPTWs) were specified as follows at 12, 24 and 36 months after statin initiation:

$IPTW_{12} = [P(A_{12}=a_{12})]/[P(A_{12}=a_{12}|\boldsymbol{B}=\boldsymbol{b})]$

$IPTW_{24} = [P(A_{24}=a_{24}|A_{12}=a_{12})\times P(A_{12}=a_{12})] / [P(A_{24}=a_{24}|A_{12}=a_{12},\boldsymbol{L}_{12}=\boldsymbol{l}_{12},\boldsymbol{B}=\boldsymbol{b})\times P(A_{12}=a_{12}|\boldsymbol{B}=\boldsymbol{b})]$

$IPTW_{36}= [P(A_{36}=a_{36}|A_{24}=a_{24},A_{12}=a_{12})\times P(A_{24}=a_{24}|A_{12}=a_{12})\times P(A_{12}=a_{12})] /$

$[P(A_{36}=a_{36}|A_{24}=a_{24},A_{12}=a_{12},\boldsymbol{L}_{24}=\boldsymbol{l}_{24},\boldsymbol{L}_{12}=\boldsymbol{l}_{12},\boldsymbol{B}=\boldsymbol{b})\times P(A_{24}=a_{24}|A_{12}=a_{12},\boldsymbol{L}_{12}=\boldsymbol{l}_{12},\boldsymbol{B}=\boldsymbol{b})\times P(A_{12}=a_{12}|\boldsymbol{B}=\boldsymbol{b})]$.

In the equations, capitalized letters denote random variables and lowercase letters observations (values) of random variables. Bolded letters denote vectors. A_{12}–A_{36} refer to adherence level (adherence or non-adherence) at 12, 24 and 36 months after statin initiation. $\boldsymbol{B}$ is a vector of baseline characteristics measured prior to or at statin initiation, and $\boldsymbol{L}_{12}$–$\boldsymbol{L}_{24}$ vectors of time-dependent confounders measured at 12 and 24 months after statin initiation. Time-specific probabilities were estimated using logistic regression models with the observed adherences over the previous 12 months as dependent variables.

Marginal structural model was specified using pooled log-binomial regression model with person-month level observations weighted by stabilized IPTWs as follows:

$$log\,[P(Y_t=1 \mid Y_{t-1}=0, A_{t-1}=a_{t-1})] = \beta_0 + \beta_1 * a_{t-1},\ t=13,14,\ldots,48.$$

In the above, Y_t refers to outcome measured between months t_{13} and t_{48} and β_0 represents intercept. Here, A_{t-1} refers to the adherence level measured at the preceding adherence assessment period prior to the month t. Exponential function of coefficient β_1, $exp(\beta_1)$, can be interpreted as an average (pooled over the follow-up months) causal effect of adherence on the hazard of an acute cardiovascular event when everybody remains adherent during the previous adherence ascertainment year compared with remaining non-adherent. We used SAS PROC GENMOD (SAS Institute, Cary, NC) to derive the MSMs and obtained robust standard errors for coefficients.

Following SAS syntax was used to construct the primary analysis:

```
/*
Inverse probability of treatment weights at 12 months after statin initiation
*/
*Numerator calculation;
proc logistic data=data;
where year=2;
model dipdc12(event='1')= ;
output out=mo2a p=pa_0;
run;

*Denominator calculation. Predictors include baseline confounders.;
proc logistic data=data;
where year=2;
class age_cat hosparea marital incomeqrt educ labor statin startyr
          intensity diabetesbl insulinbl hypertenbl hefaibl dyslipbl cararrbl
          nofCVDmedbl charlsonbl rheumabl cancerbl mentaldisbl depressionbl
          asthmabl alcodisbl NSAIDbl AnxHypnSedbl corticostbl hormonebl
          nofmedcatbl inhospdays_catbl /param=ref ref=first;
model dipdc12(event='1')= age_cat hosparea marital incomeqrt educ labor
          statin startyear intensity diabetesbl insulinbl hypertenbl hefaibl
          dyslipbl cararrbl nofCVDmedbl charlsonbl rheumabl cancerbl mentaldisbl
          depressionbl asthmabl alcodisbl NSAIDbl AnxHypnSedbl corticostbl
          hormonebl nofmedcatbl inhospdays_catbl /link=logit;
output out=mo2b p=pa_N;
run;
```

```
data we2; merge mo2a mo2b; by id;
if dipdc12=1 then sw= pa_O / pa_N;
else if dipdc12=0 then sw= (1-pa_O) / (1-pa_N);
run;

/*
Inverse probability of treatment weights at 24 months after statin initiation.
*/
*Numerator calculation;
proc logistic data=data;
where year =3;
class dipdc12 /param=ref ref=first;
model dipdc24(event='1')= dipdc12 /link=logit;
output out=mo3a p=pa_O;
run;

/*Denominator calculation. Predictors include baseline confounders and potential
time-dependent confounders measured at 12 months since statin initiation.*/
proc logistic data=data;
where year= 3;
class dipdc12 marstal12 incomeqrt12 labor12 incrintensity12 diabetes12
           insulin12 hyperten12 hefai12 cararr12 dyslip12 nofCVDmed12 charlson12
           chronCHD12 chronCHDhosp12 proced12 cerebro12 athero12 nitrates12
           rheuma12 cancer12 mentaldis12 depression12 asthma12 alcodis12 NSAID12
           AnxHypnSed12 corticost12 hormone12 nofmedcat12 inhospdays_cat12 age_cat
           hosparea marital incomeqrt educ labor statin startyear intensity
           diabetesbl insulinbl hypertenbl hefaibl dyslipbl cararrbl nofCVDmedbl
           charlsonbl rheumabl cancerbl mentaldisbl depressionbl asthmabl
           alcodisbl NSAIDbl AnxHypnSedbl corticostbl hormonebl nofmedcatbl
           inhospdays_catbl /param=ref ref=first;
model dipdc24(event='1')= dipdc12 marital12 incomeqrt12 labor12
           incrintensity12 diabetes12 insulin12 hyperten12 hefai12 cararr12
           dyslip12 nofCVDmed12 charlson12 chronCHD12 chronCHDhosp12 proced12
           cerebro12 athero12 nitrates12 rheuma12 cancer12 mentaldis12
           depression12 asthma12 alcodis12 NSAID12 AnxHypnSed12 corticost12
           hormone12 nofmedcat12 inhospdays_cat12 age_cat hosparea marital
           incomeqrt educ labor statin startyear intensity diabetesbl insulinbl
           hypertenbl hefaibl dyslipbl cararrbl nofCVDmedbl charlsonbl rheumabl
           cancerbl mentaldisbl depressionbl asthmabl alcodisbl NSAIDbl
           AnxHypnSedbl corticostbl hormonebl nofmedcatbl inhospdays_catbl
           /link=logit;
output out=mo3b p=pa_N;
run;

data we3; merge mo3a mo3b; by id year;
if dipdc2=1 then sw= pa_O / pa_N;
else if dipdc2=0 then sw= (1-pa_O) / (1-pa_N);
run;

/*
Inverse probability of treatment weights at 36 months after statin initiation.
*/
*Numerator calculation;
proc logistic data=data;
where year=4;
class dipdc12 dipdc24 /param=ref ref=first;
model dipdc36(event='1')= dipdc12 dipdc24 /link=logit;
output out=mo4a p=pa_O;
run;
```

```
/* Denominator calculation. Predictors include baseline confounders and potential
time-dependent confounders measured at 24 and 12 months since statin initiation.
*/
proc logistic data=data;
where year= 4;
class dipdc24 dipdc12 marital24 income_cat24 labor24 incrintensity24
           diabetes24 insulin24 hyperten24 hefai24 cararr24 dyslip24 nofCVDmed24
           charlson24 chronCHD24 chronCHDhosp24 proced24 cerebro24 athero24
           nitrates24 rheuma24 cancer24 mentaldis24 depression24 asthma24
           alcodis24 NSAID24 AnxHypnSed24 corticost24 hormone24 nofmedcat24
           inhospdays_cat24 marital12 incomeqrt12 labor12 incrintensity12
           diabetes12 insulin12 hyperten12 hefai12 cararr12 dyslip12 nofCVDmed12
           charlson12 chronCHD12 chronCHDhosp12 proced12 cerebro12 athero12
           nitrates12 rheuma12 cancer12 mentaldis12 depression12 asthma12
           alcodis12 NSAID12 AnxHypnSed12 corticost12 hormone12 nofmedcat12
           inhospdays_cat12 age_cat hosparea marital incomeqrt educ labor statin
           startyear intensity diabetesbl insulinbl hypertenbl hefaibl dyslipbl
           cararrbl nofCVDmedbl charlsonbl rheumabl cancerbl mentaldisbl
           depressionbl asthmabl alcodisbl NSAIDbl AnxHypnSedbl corticostbl
           hormonebl nofmedcatbl inhospdays_catbl /param=ref ref=first;
model dipdc36(event='1')= dipdc24 dipdc12 marital24 incomeqrt24 labor24
           incrintensity24 diabetes24 insulin24 hyperten24 hefai24 cararr24
           dyslip24 nofCVDmed24 charlson24 chronCHD24 chronCHDhosp24 proced24
           cerebro24 athero24 nitrates24 rheuma24 cancer24 mentaldis24
           depression24 asthma24 alcodis24 NSAID24 AnxHypnSed24 corticost24
           hormone24 nofmedcat24 inhospdays_cat24 marital12 incomeqrt12 labor12
           incrintensity12 diabetes12 insulin12 hyperten12 hefai12 cararr12
           dyslip12 nofCVDmed12 charlson12 chronCHD12 chronCHDhosp12 proced12
           cerebro12 athero12 nitrates12 rheuma12 cancer12 mentaldis12
           depression12 asthma12 alcodis12 NSAID12 AnxHypnSed12 corticost12
           hormonether12 nofmedcat12 inhospdays_cat12 age_cat hosparea marital
           incomeqrt educ labor statin startyear intensity diabetesbl insulinbl
           hypertenbl hefaibl dyslipbl cararrbl nofCVDmedbl charlsonbl rheumabl
           cancerbl mentaldisbl depressionbl asthmabl alcodisbl NSAIDbl
           AnxHypnSedbl corticostbl hormonebl nofmedcatbl inhospdays_catbl
           /link=logit;
output out=mo4b p=pa_N;
run;

data we4; merge mo4a mo4b; by id year;
if dipdc3=1 then sw= pa_O / pa_N;
else if dipdc3=0 then sw= (1-pa_O) / (1-pa_N);
run;

data weights (keep=id sw year dipdc_tvl pa_N pa_O); set we2 we3 we4; run;

proc sort data=weights; by id year; run;

/*Stabilized inverse probability of treatment weights at 24 and 36 months after
statin initiation are calculated cumulatively by multiplying the stabilized
inverse probabilities from previous time points up to the specific time point. */
DATA weights2; set weights; by id;
  if first.id then stabwt=sw;
                else stabwt=sw*dum;
  retain dum;
  drop dum;
  dum=stabwt;
run;

data main; merge data weights2; by id year; run;
```

```
*Marginal structural model. Below, dipdc_tvl denotes lagged time-dependent
variable of statin adherence;
proc genmod data=main desc;
class id dipdc_tvl(ref='0') /param=ref;
model event=dipdc_tvl /link=log dist=bin;
scwgt stabwt;
repeated subject=id /type=ind;
run; quit;
```

Appendix 2. Sensitivity analyses.

Statin adherence and acute cardiovascular events

To examine the magnitude of potential bias introduced to effect estimate when using time-dependent confounders assessed simultaneously with adherence, we replaced time-dependent confounders in adherence models with those measured concurrently with adherence, i.e. intermediate variables, and examined its effect on the effect estimate (model 1) (see Figure S1). We observed a slightly larger reduction in the hazard of acute cardiovascular events (hazard ratio: 0.74, 95% confidence interval: 0.61, 0.89) when compared with our primary analyses for adherers versus non-adherers (model 1, Table S7).

In an alternative MSM we added medical procedures (coronary artery bypass graft, CABG/percutaneous transluminal coronary angioplasty PTCA) and deaths from any cause to the composite outcome (model 2) as these events can be viewed as competing risks that alter the probability of having the primary outcome and, thus, censoring because of them can cause selection bias. For this, we excluded patients with medical procedures during the first year (n=48). During the follow-up, 464 patients had an acute cardiovascular event, 345 died from any cause, and 88 had CABG/PTCA. Further, 171 patients were censored because of long-term institutionalization and the rest were followed up to the end of the study. Being adherent (proportion of days covered, PDC, ≥80%) resulted in 21% reduction in the hazard of composite outcome (hazard ratio: 0.79, 95% confidence interval: 0.69, 0.90) compared with being non-adherent (PDC <80%) (model 2, Table S7). The estimate is close to the one of our primary analysis (hazard ratio: 0.77, 95% confidence interval: 0.64, 0.93) indicating minor effect of selection bias due to competing risks towards our main results.

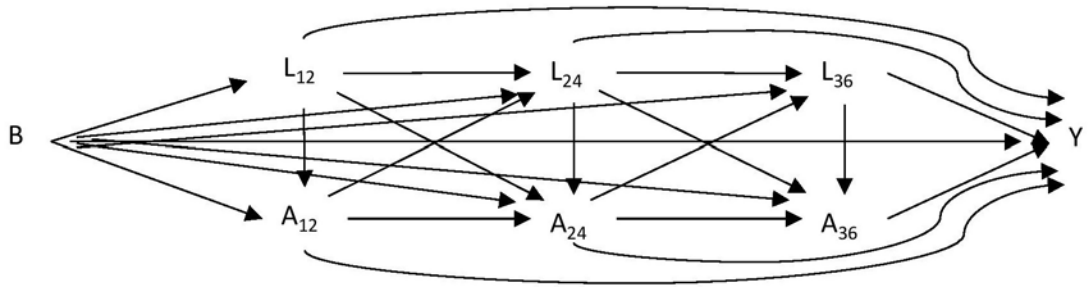

Figure S1. Directed acyclic graph for time-dependent adherence and confounding structures. B, baseline characteristics; A_{12}–A_{36}, time-dependent adherences; L_{12}–L_{36}, time-dependent confounders measured at times 12, 24 and 36; Y outcome.

Table S7. Effect of statin adherence on acute cardiovascular events.

Model	Exposure definition	Outcome definition	Variables in adherence model	HR	95% CI
1	Adherent vs. non-adherent	Acute cardiovascular events	Baseline[a], lagged[b] and current[c] time-dependent confounders	0.74	0.61, 0.89
2	Adherent vs. non-adherent	Composite of acute cardiovascular events, deaths from any cause and CABG/PTCA	Baseline[a] and lagged[b] time-dependent confounders	0.79	0.69, 0.90

Abbreviations: CABG, coronary artery bypass graft ; CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; PTCA, percutaneous transluminal coronary angioplasty.

[a] **Baseline confounders** as presented in Table S5.

[b] **Lagged time-dependent confounders**: Marital status, income, labor market status, increase in intensity of statin therapy, diabetes, use of insulin, hypertensive diseases, heart failure or chronic cardiac insufficiency, cardiac arrhythmia, dysfunctions of lipid metabolism, number of concurrent cardiovascular medications, Charlson Comorbidity Index, chronic CHD, chronic CHD hospitalization, medical procedure related to CHD, chronic cerebrovascular diseases and transient ischemic attack, atherosclerosis, use of nitrates, rheumatoid arthritis, cancer, mental disorders, depression, respiratory diseases, alcohol-related diseases, use of non-steroidal anti-inflammatory medications, anxiolytics, hypnotics and sedatives, corticosteroids for systemic use, and hormone therapy, total number of concurrent medications, number of in-hospital days.

[c] **Current time-dependent confounders**: Marital status, income, labor market status, increase in intensity of statin therapy, diabetes, use of insulin, hypertensive diseases, heart failure or chronic cardiac insufficiency, cardiac arrhythmia, dysfunctions of lipid metabolism, number of concurrent cardiovascular medications, Charlson Comorbidity Index, chronic CHD, chronic CHD hospitalization, medical procedure related to CHD, chronic cerebrovascular diseases and transient ischemic attack, atherosclerosis, use of nitrates, rheumatoid arthritis, cancer, mental disorders, depression, respiratory diseases, alcohol-related diseases, use of non-steroidal anti-inflammatory medications, anxiolytics, hypnotics and sedatives, corticosteroids for systemic use, and hormone therapy, total number of concurrent medications, number of in-hospital days.

Statin refills and acute cardiovascular events

In addition, we compared at least slightly adherent women to extremely non-adherent women in order to mimic exposure in randomized controlled trials by assuming that patients with only the initial dispensation during the follow-up could reflect those with a similar indication but without statin exposure. More specifically, time-dependent exposure was measured as a number of statin refills after statin initiation within time periods (0–12], (0–24] and (0–36] months and categorized as no refills and at least one refill during the time period (Figure S2). After a refill patient was considered to continue in the group with at least one refill. The association of additional statin refill with acute cardiovascular events was investigated with i) discrete-time hazards model with time-varying adherence and baseline confounders (model 3) and ii) MSM (model 4). Estimation results from conventional model indicated potential effect of adherence (hazard ratio: 0.81, 95% confidence interval: 0.60, 1.11) on the hazard of an acute cardiovascular event when compared with extreme non-adherence (model 3, Table S8). Weighting the model 3 with IPTWs resulted in hazard ratio of 0.85 (95% confidence interval: 0.62, 1.16) (model 4, Table S8).

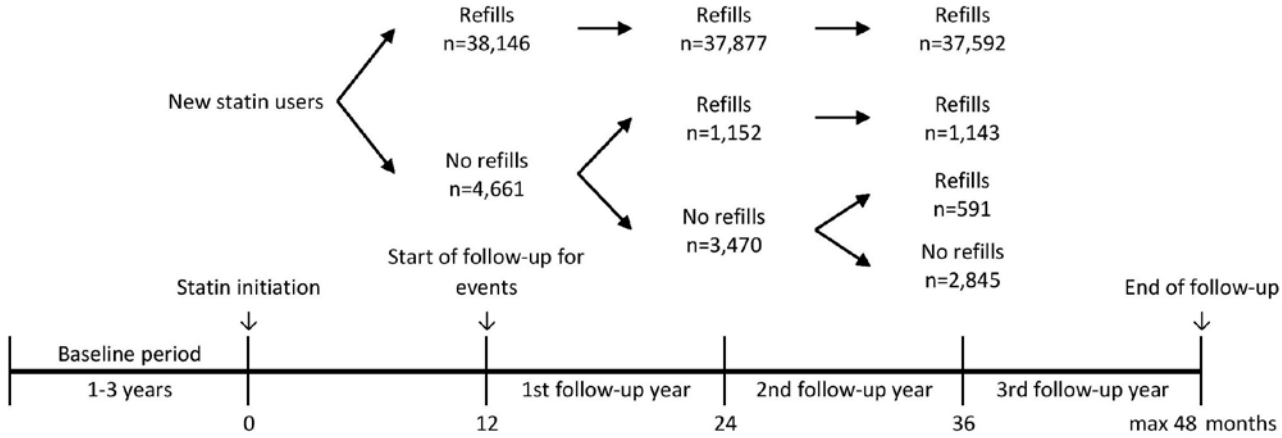

Figure S2. Flow of patients according to statin refills.

Table S8. Effect of statin refill on acute cardiovascular events.

Model	Type of model	Exposure definition	Variables in adherence model	Variables in outcome model	HR	95% CI
3	Discrete-time hazards model	At least slightly adherents vs. extreme non-adherents	Not applicable	Time-dependent adherence and baseline confounders[a]	0.81	0.60, 1.11
4	MSM	At least slightly adherents vs. extreme non-adherents	Baseline[a] and lagged time-dependent[b] confounders	Adherence during the previous assessment year	0.85	0.62, 1.16

Abbreviations: CHD, coronary heart disease; CI, confidence interval; HR, hazard ratio; MSM, marginal structural model.

[a] **Baseline confounders** as presented in Table S5.

[b] **Lagged time-dependent confounders**: Marital status, income, labor market status, diabetes, use of insulin, hypertensive diseases, heart failure or chronic cardiac insufficiency, cardiac arrhythmia, dysfunctions of lipid metabolism, number of concurrent cardiovascular medications, Charlson Comorbidity Index, chronic CHD, chronic CHD hospitalization, medical procedure related to CHD, chronic cerebrovascular diseases and transient ischemic attack, atherosclerosis, use of nitrates, rheumatoid arthritis, cancer, mental disorders, depression, respiratory diseases, alcohol-related diseases, use of non-steroidal anti-inflammatory medications, anxiolytics, hypnotics and sedatives, corticosteroids for systemic use, or hormone therapy, total number of concurrent medications, number of in-hospital days.