

Supplementary data

Lower intensity	Equal intensity	Higher intensity
Atorvastatin 5 mg	Atorvastatin 10 mg	Atorvastatin > 10 mg
Fluvastatin any dose		Rosuvastatin > 2.5 mg
Pravastatin any dose		Simvastatin > 40 mg
Rosuvastatin 2.5 mg		
Simvastatin < 40 mg		

Supplementary Table 1 Classification of statin regimens as lower, equal or higher intensity depending on how much they lower low-density lipoprotein cholesterol levels compared to the Dutch guideline recommended 40mg simvastatin (37% lowering)

Variable	Additional sub-classifications
Sex	
Age	
Cardiovascular diagnosis at baseline	Heart failure Coronary heart disease Cardiovascular intervention Cerebrovascular Congenital
Ethnicity	
Personal income	
Height	
Weight	
Body mass index	
Systolic blood pressure	
Diastolic blood pressure	
Complaints at baseline	Chest pain Dyspnoea Fatigue Heart murmur Palpitations Collapse
Number of complaints at baseline	
Comorbidities at baseline	Diabetes mellitus Hypertension Dyslipidaemia
Current smoker	
Total cholesterol	
High-density lipoprotein cholesterol	
Low-density lipoprotein cholesterol	
Creatinine	
Estimated glomerular filtration rate	
Triglycerides	
History of cardiovascular medication	
Cardiovascular medication prescribed at baseline	Blood-pressure lowering Antiplatelet or anticoagulation Lipid-lowering other than statins

	Diabetes mellitus Nitrates Anti-arrhythmic Digoxin
Number of medication prescriptions	
Baseline appointment after 2016	

Supplementary Table 2

List of variables included in the propensity score

	Statin users (n = 17,008)	Statin non-users (n = 30,793)	Statin users after matching (n =8631)	Statin non-users after matching (n =8631)
General characteristics				
Age (years)	62 (11)	55 (13)	61 (11)	61 (13)
Women (n, %)	8171 (48.0)	17,427 (56.6)	4482 (51.9)	4499 (52.1)
Ethnicity (n, %)				
Native Dutch	13,204 (77.6)	23,740 (77.1)	6753 (78.2)	6841 (79.3)
First generation immigrant	1731 (16.1)	4563 (14.8)	1297 (15.0)	1200 (13.9)
Second generation immigrant	1073 (6.3)	2490 (8.1)	581 (6.7)	590 (6.8)
Annual personal income (€)	26,757 [14,647-46,066]	30,404 [15,679-50,823]	27,860 [14,647-48,390]	28,261 [14,956-47,613]
Current smoker (n, %)	6239 (36.7)	12,207 (39.6)	3543 (41.0)	3540 (41.0)
10-year cardiovascular mortality risk (SCORE)				
0-4%	5560 (32.7)	19,736 (64.1)	4757 (55.1)	4562 (52.9)
5-9%	3237 (19.0)	4883 (15.9)	2380 (27.6)	2175 (25.2)
≥10%	2198 (12.9)	3137 (9.9)	1493 (17.3)	1887 (21.9)
Complaints (n, %)				
Number of complaints				
0	6757 (39.7)	11,015 (35.8)	3451 (40.0)	3389 (39.3)
1	9807 (57.7)	18,809 (61.1)	4925 (57.1)	5014 (58.1)
2	416 (2.4)	906 (2.9)	235 (2.7)	216 (2.5)
≥3	28 (0.1)	63 (0.2)	20 (0.2)	12 (0.1)
Chest pain	6650 (39.1)	10,927 (35.5)	3176 (36.8)	3158 (36.6)
Dyspnoea	1562 (9.2)	2275 (7.4)	778 (9.0)	759 (8.8)
Fatigue	531 (3.1)	1060 (3.4)	277 (3.2)	273 (3.2)
Heart murmurs	158 (0.9)	353 (1.1)	77 (0.9)	75 (0.9)
Palpitations	1697 (10.0)	5924 (19.2)	1088 (12.6)	1141 (13.2)
Collapse	130 (0.8)	274 (0.9)	63 (0.7)	76 (0.9)
Co-morbidities (n, %)				
Hypertension	7888 (46.4)	7096 (23.0)	3386 (39.2)	3310 (38.4)
Diabetes mellitus	3252 (19.1)	806 (2.6)	843 (9.8)	686 (7.9)

Dyslipidaemia	6635 (39.0)	2244 (7.3)	2078 (24.1)	1957 (22.7)
Cardiovascular diagnosis at baseline	3348 (19.7)	1427 (4.6)	1061 (12.3)	939 (10.9)
Clinical characteristics				
Body mass index (kg/m ²)	27.5 (4.7)	26.3 (4.5)	27.0 (4.5)	27.0 (4.7)
Systolic blood pressure (mmHg)	148 (21)	140 (21)	146 (21)	146 (22)
Total cholesterol (mmol/L)	5.23 (1.34)	5.61 (0.86)	5.53 (1.29)	5.62 (0.86)
Low-density lipoprotein cholesterol (mmol/L)	2.90 [2.10-3.80]	3.40 [2.90-3.90]	3.30 [2.50-4.20]	3.30 [2.90-3.80]
High-density lipoprotein cholesterol (mmol/L)	1.40 [1.10-1.80]	1.40 [1.10-1.80]	1.40 [1.10-1.80]	1.40 [1.10-1.80]
Triglycerides (mmol/L)	1.60 [1.10-2.40]	1.40 [0.90-2.00]	1.50 [1.00-2.20]	1.50 [1.00-2.20]
Estimated glomerular filtration rate (mL/min/1.73m ²)	81 (27)	88 (28)	82 (27)	82 (28)
Medication prescriptions at baseline other than statins (n,%)				
History of cardiovascular medication use	1706 (10.0)	2409 (7.8)	970 (11.2)	971 (11.3)
Cardiovascular medication prescribed at baseline	13,556 (79.7)	10,418 (33.8)	5798 (67.2)	5807 (67.3)
Number of cardiovascular medications				
0	2566 (15.1)	18,620 (60.5)	2256 (26.1)	2240 (26.0)
1-3	10,488 (61.7)	11,064 (35.9)	5316 (61.6)	5457 (63.2)
4-7	3892 (22.9)	1099 (3.6)	1048 (12.1)	924 (10.7)
8-10	62 (0.4)	10 (0.0)	11 (0.1)	10 (0.1)
Blood pressure lowering medication	12,436 (73.1)	10,768 (35.0)	5388 (62.4)	5352 (62.0)
Antiplatelet or anticoagulant medication	8552 (50.3)	3432 (11.1)	3086 (35.8)	3032 (35.1)
Other lipid-lowering medication	348 (2.0)	267 (0.9)	187 (2.2)	191 (2.2)
Diabetes mellitus medication	3068 (18.0)	604 (2.0)	728 (8.4)	572 (6.6)
Nitrates	3074 (18.0)	604 (2.0)	859 (10.0)	803 (9.3)
Anti-arrhythmic medication	179 (1.1)	334 (1.1)	108 (1.3)	121 (1.4)
Digoxin	128 (0.8)	133 (0.4)	62 (0.7)	65 (0.8)
Statin prescriptions at baseline (n, %)				
Statin name				
Atorvastatin	3790 (22.3)		1859 (21.5)	
Fluvastatin	90 (0.5)		42 (0.5)	

Pravastatin	1241 (7.3)	643 (7.4)
Rosuvastatin	1735 (10.2)	889 (10.3)
Simvastatin	10,152 (59.7)	5198 (60.2)
Statin intensity		
Lower than guideline-recommended	5356 (31.5)	2805 (32.5)
Equal to guideline-recommended	6924 (40.7)	3473 (40.2)
Higher than guideline-recommended	4728 (27.8)	2353 (27.3)

Supplementary Table 3 Baseline characteristics of statin users and non-users before and after propensity score matching

	Low-intensity statin users (n = 5356)	High-intensity statin users (n = 11,652)	Low-intensity statin users after matching (n = 5344)	High intensity statin users after matching (n = 5344)
General characteristics				
Age (years)	63 (11)	62 (10)	64 (11)	63 (10)
Women (n, %)	2861 (53.4)	5310 (45.6)	2850 (53.3)	2732 (51.1)
Ethnicity (n, %)				
Native Dutch	4236 (79.1)	8968 (77.0)	4225 (79.1)	4181 (78.2)
First generation immigrant	784 (14.6)	1947 (16.7)	783 (14.7)	804 (15.0)
Second generation immigrant	336 (6.3)	737 (6.3)	336 (6.3)	359 (6.7)
Annual personal income (€)	24,943 [11,115-43,595]	27,528 [14,940-47,226]	24,968 [14,078-43,619]	25,416 [14,094-44,117]
Current smoker (n, %)	2080 (38.8)	4159 (35.7)	2223 (41.6)	2139 (40.0)
10-year cardiovascular mortality risk (SCORE)				
0-4%	1695 (31.6)	3865 (33.2)	2466 (46.1)	2544 (47.6)
5-9%	1038 (19.4)	2199 (18.9)	1611 (30.1)	1627 (30.4)
≥10%	813 (15.2)	1385 (11.9)	1267 (23.7)	1173 (21.9)
Complaints (n, %)				
Number of complaints				
0	2136 (39.9)	4621 (39.7)	2131 (39.9)	2201 (41.2)
1	3081 (57.5)	6726 (57.7)	3074 (57.5)	3006 (56.2)
2	130 (2.4)	286 (2.5)	130 (2.4)	128 (2.4)
≥3	9 (0.1)	19 (0.1)	9 (0.1)	9 (0.1)
Chest pain	1975 (36.9)	4675 (40.1)	1974 (36.9)	1969 (36.8)
Dyspnoea	554 (10.2)	1018 (8.7)	540 (10.1)	514 (9.6)
Fatigue	162 (3.0)	369 (3.2)	161 (3.0)	158 (2.9)
Heart murmurs	52 (1.0)	106 (0.9)	52 (1.0)	53 (1.0)
Palpitations	583 (10.9)	1114 (9.6)	583 (10.9)	554 (10.4)
Collapse	53 (1.0)	77 (0.7)	52 (1.0)	44 (0.8)
Co-morbidities (n, %)				
Hypertension	2544 (47.5)	5344 (45.9)	2568 (48.1)	2511 (47.0)

Diabetes mellitus	1025 (19.1)	2227 (19.1)	1036 (19.4)	1052 (19.7)
Dyslipidaemia	1952 (36.4)	4683 (40.2)	1972 (36.9)	2016 (37.7)
Cardiovascular diagnosis at baseline	861 (16.1)	2487 (21.3)	861 (16.1)	928 (17.4)
Clinical characteristics				
Body mass index (kg/m ²)	27.3 (4.7)	27.5 (4.6)	27.3 (4.7)	27.4 (4.7)
Systolic blood pressure (mmHg)	148 (21)	147 (21)	148 (21)	148 (22)
Total cholesterol (mmol/L)	5.17 (1.15)	5.26 (1.42)	5.17 (1.14)	5.16 (1.30)
Low-density lipoprotein cholesterol (mmol/L)	2.90 [2.20-3.60]	2.90 [2.00-4.00]	2.90 [2.20-3.70]	2.80 [2.00-3.80]
High-density lipoprotein cholesterol (mmol/L)	1.40 [1.10-1.80]	1.40 [1.10-1.70]	1.40 [1.10-1.80]	1.40 [1.10-1.80]
Triglycerides (mmol/L)	1.60 [1.00-2.30]	1.60 [1.10-2.40]	1.60 [1.10-2.30]	1.60 [1.10-2.30]
Estimated glomerular filtration rate (mL/min/1.73m ²)	79 (27)	83 (28)	78 (27)	79 (27)
Medication prescriptions at baseline other than statins (n,%)				
History of cardiovascular medication use	378 (8.9)	1228 (10.5)	478 (8.9)	500 (9.4)
Cardiovascular medication prescribed at baseline	4303 (80.3)	9253 (79.4)	4292 (80.3)	4268 (79.9)
Number of cardiovascular medications				
0	814 (15.2)	1752 (15.0)	813 (15.2)	820 (15.3)
1-3	3362 (62.8)	7126 (61.2)	3357 (62.8)	3314 (62.0)
4-7	1157 (21.6)	2735 (23.5)	1151 (21.5)	1198 (22.4)
8-10	23 (0.4)	39 (0.3)	23 (0.4)	12 (0.2)
Blood pressure lowering medication	3877 (72.4)	8559 (73.5)	3866 (72.3)	3847 (72.0)
Antiplatelet or anticoagulant medication	2631 (49.1)	5921 (50.8)	2624 (49.1)	2600 (48.7)
Other lipid-lowering medication	80 (1.5)	268 (2.3)	80 (1.5)	100 (1.9)
Diabetes mellitus medication	960 (17.9)	2108 (18.1)	959 (17.9)	980 (18.3)
Nitrates	810 (15.1)	2264 (19.4)	809 (15.1)	824 (15.4)
Anti-arrhythmic medication	59 (1.1)	120 (1.0)	59 (1.1)	54 (1.0)
Digoxin	51 (1.0)	76 (0.7)	47 (0.9)	40 (0.7)
Statin prescriptions at baseline (n, %)				
Statin name				
Atorvastatin	1 (0.0)	3789 (32.5)	1 (0.1)	1722 (32.2)

Fluvastatin	90 (1.7)	0 (0.0)	89 (1.7)	0 (0.0)
Pravastatin	1241 (23.2)	0 (0.0)	1239 (23.2)	0 (0.0)
Rosuvastatin	0 (0.0)	1735 (14.9)	0 (0.0)	788 (14.7)
Simvastatin	4024 (75.1)	6128 (52.6)	4015 (75.1)	2834 (53.0)
Statin intensity				
Lower than guideline-recommended	5356 (100.0)	0 (0.0)	5344 (100.0)	0 (0.0)
Equal to guideline-recommended	0 (0.0)	6924 (59.4)	0 (0.0)	3235 (60.5)
Higher than guideline-recommended	0 (0.0)	4728 (40.6)	0 (0.0)	2109 (39.5)

Supplementary Table 4 Baseline characteristics of low- and high-intensity statin users before and after propensity score matching

	Whole population (n =15,180)	Women (n =7930)	Men (n = 7250)
All-cause mortality			
No statin (ref)	1	1	1
Statin	0.78 (0.72-0.84)	0.68 (0.60-0.77)	0.89 (0.81-0.97)
Cardiovascular mortality			
No statin (ref)	1	1	1
Statin	0.78 (0.66-0.90)	0.58 (0.41-0.75)	1.02 (0.86-1.18)

Supplementary Table 5 Adjusted hazard ratios for the risk of all-cause and cardiovascular mortality associated with statin use stratified by sex in those without a cardiovascular diagnosis at baseline