

## SUPPLEMENTAL PUBLICATION MATERIAL

## Supplementary figure

**Fig. S1.** The proportion of patients who received statins before and after diagnosis with moyamoya disease (MMD)

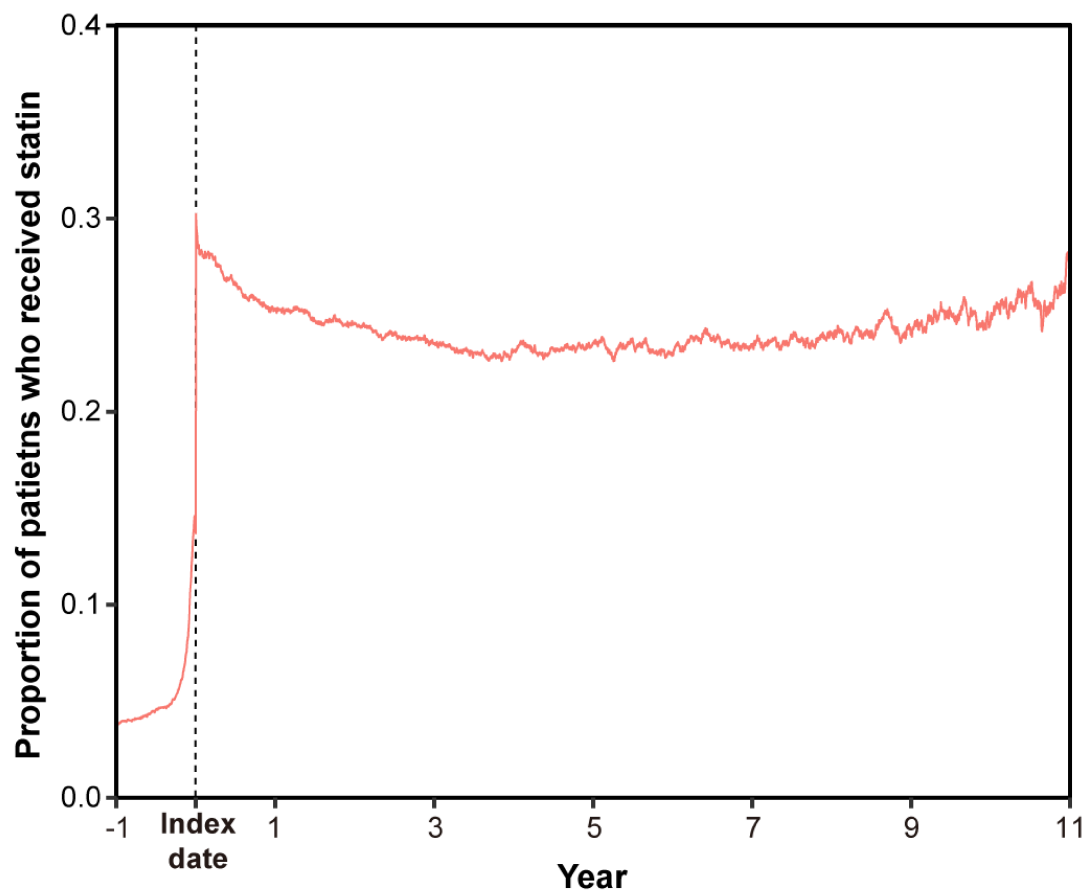
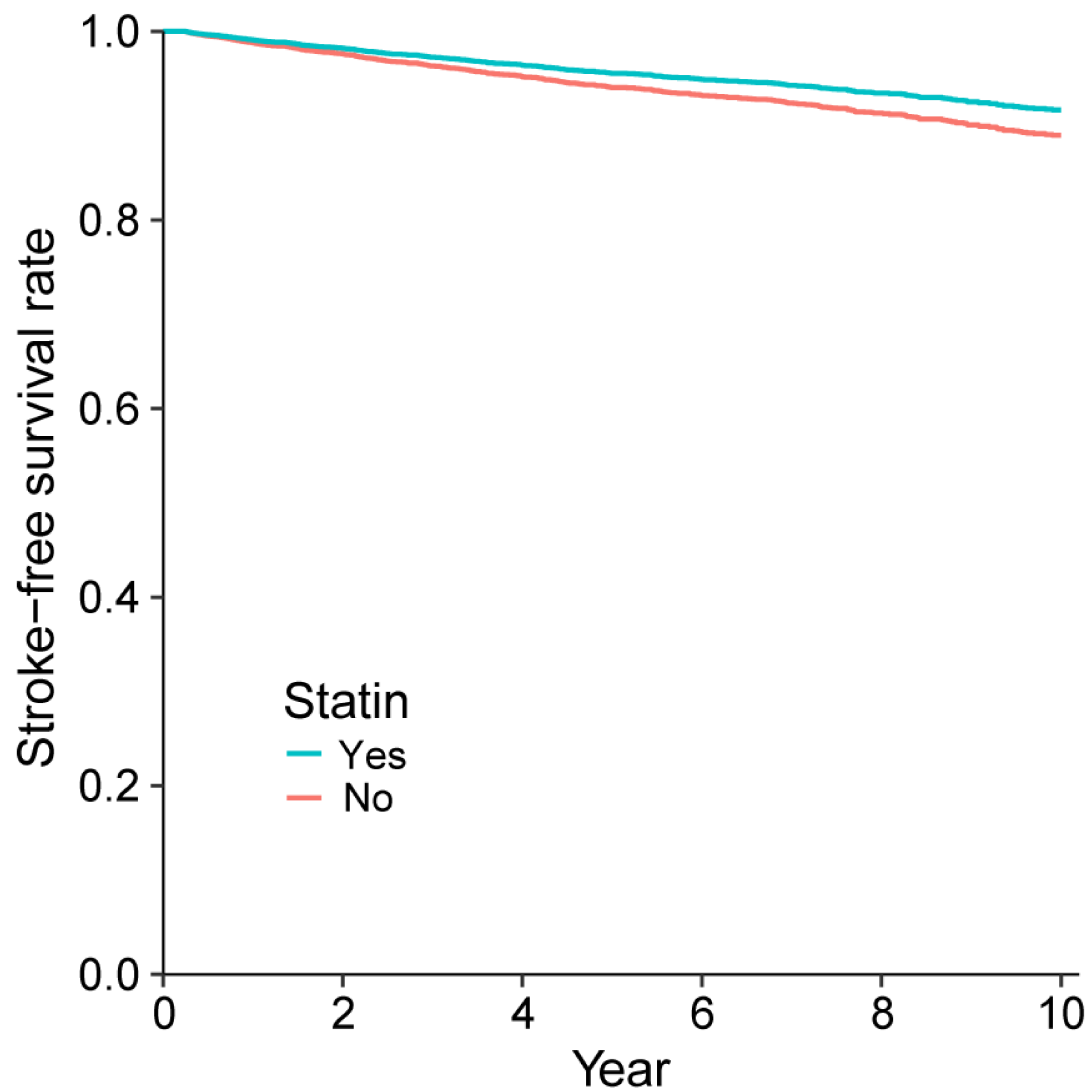


Fig. S2. Estimated stroke-free survival curve according to the use of statins



The X-axis indicates the time (year) from the diagnosis of moyamoya disease (index date). The plot indicates estimated stroke-free survival curves according to the use of statins based on the multivariate time-dependent Cox regression model (Table 2).

**Supplementary tables****Supplementary table S1.** Baseline characteristics of the included and excluded patients in the study

Variable	Total (N=23,310)	Included (N=13,373)	Excluded (N=9,937)	P value
Sex, male	8,210 (35.2)	4,657 (34.8)	3,553 (35.8)	0.141
Age, year	40.1 ±18.7	38.7 ± 18.2	41.9 ± 19.1	<0.001
Concurrent stroke	7,472 (32.1)	5,454 (40.8)	2,018 (20.3)	<0.001
Revascularization surgery	5,199 (22.3)	3,877 (29.0)	1322 (13.3)	<0.001
<b>Comorbidity</b>				
Hypertension	9,375 (40.2)	4,800 (35.9)	4,575 (46.0)	<0.001
Diabetes mellitus	2,616 (11.2)	1,377 (10.3)	1,239 (12.5)	<0.001
Atrial fibrillation	677 (2.9)	340 (2.5)	337 (3.4)	<0.001
Renal disease	1,005 (4.3)	439 (3.3)	566 (5.7)	<0.001
Malignancy	662 (2.8)	372 (2.8)	290 (2.9)	0.535

The data are represented as numbers (%) or mean ± standard deviation. P value is derived from chi-square test for categorical variables and independent t-test for continuous variable.

**Supplementary table S2.** Type and daily dose of statin in the patients at 90 days after the index date

Type of statin	Dose per day, mg									
	1	2	2.5	4	5	10	20	40	60	80
Atorvastatin	0	0	0	0	24	1036	661	285	53	0
Fluvastatin	0	0	0	0	0	0	0	2	0	17
Lovastatin	0	0	0	0	0	0	1	0	1	0
Pitavastatin	7	101	0	52	0	0	0	0	0	0
Pravastatin	0	0	0	0	3	21	22	49	0	0
Rosuvastatin	0	0	3	0	231	597	182	1	0	0
Simvastatin	0	0	0	0	1	77	142	16	0	0

Data are number of patients taking the statin at 90 days from the diagnosis of moyamoya disease.

**Supplementary table S3.** Characteristics of the patients at 90 days after the index date

Variable	Total (n = 13,373)	No statin (n=9,788)	Statin (n=3,585)	P value
Sex, male	4,657 (34.8)	3,376 (34.5)	1,281 (35.7)	0.182
Age, year	38.7 ± 18.2	34.9 ± 18.7	49.0 ± 11.7	<0.001
Concurrent stroke	5,454 (40.8)	3,645 (37.2)	1,809 (50.5)	<0.001
Revascularization surgery	3,877 (29.0)	3,272 (33.4)	605 (16.9)	
Comorbidity				
Hypertension	4,800 (35.9)	2,773 (28.3)	2,027 (56.5)	<0.001
Diabetes mellitus	1,377 (10.3)	602 (6.2)	775 (21.6)	<0.001
Atrial fibrillation	340 (2.5)	208 (2.1)	132 (3.7)	<0.001
Renal disease	439 (3.3)	248 (2.5)	191 (5.3)	<0.001
Malignancy	372 (2.8)	251 (2.6)	121 (3.4)	0.535

The data are represented as numbers (%) or mean ± standard deviation. P value is derived from chi-square test for categorical variables and independent t-test for continuous variable.

**Supplementary table S4.** Risk factors for the primary outcome regarding the statin intensity in MMD patients

Variable	Adjusted HR (95% CI)*	P value
Sex, male	0.89 (0.75–1.06)	0.198
Age, years	1.02 (1.02–1.03)	<0.001
Concurrent stroke <sup>†</sup>	1.28 (1.08–1.50)	0.004
Revascularization surgery	0.67 (0.54–0.85)	<0.001
Comorbidities		
Hypertension	0.85 (0.71–1.02)	0.086
Diabetes mellitus	1.03 (0.80–1.34)	0.803
Atrial fibrillation	0.79 (0.44–1.40)	0.415
Renal disease	1.31 (0.90–1.92)	0.163
Malignancy	1.25 (0.82–1.93)	0.302
Medication		
Antiplatelet		
No antiplatelet	1 (ref)	
Single antiplatelet	1.00 (0.83–1.19)	0.974
Dual antiplatelet	1.24 (0.90–1.69)	0.184
Statin intensity <sup>‡</sup>		
No statin	1 (ref)	
Low	0.63 (0.28–1.41)	0.263
High	0.75 (0.61–0.92)	0.006

Data were obtained from the multivariable time-dependent Cox proportional hazards regression model for the development of stroke.

MMD, moyamoya disease; HR, hazard ratio; CI, confidence interval

\*Adjusted for the covariates listed in this table.

<sup>†</sup>Stroke within 3 months before or after the diagnosis of moyamoya disease

<sup>‡</sup>'Low intensity statin' was determined according to the 2013 American Heart

Association/American College of Cardiology guidelines on the management of blood cholesterol.<sup>1</sup> Statins above the dosage of 'low intensity' was determined as 'high-intensity'.

## References

- 1 Stone NJ, Robinson JG, Lichtenstein AH, *et al.* 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;**129**:S1-45. doi:10.1161/01.cir.0000437738.63853.7a