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Initial statin dose after myocardial infarction and long-term cardiovascular outcomes

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Aims Effective statin therapy is a cornerstone of secondary prevention after myocardial infarction (MI). Real-life statin dosing is nevertheless suboptimal and largely determined early after MI. We studied long-term outcome impact of initial statin dose after MI.

Methods and results Consecutive MI patients treated in Finland who used statins early after index event were retrospectively studied (N = 72 401; 67% men; mean age 68 years) using national registries. High-dose statin therapy was used by 26.3%, moderate dose by 69.2%, and low dose by 4.5%. Differences in baseline features, comorbidities, revascularisation, and usage of other evidence-based medications were adjusted for with multivariable regression. The primary outcome was major adverse cardiovascular or cerebrovascular event (MACCE) within 10 years. Median follow-up was 4.9 years. MACCE was less frequent in high-dose group compared with moderate dose [adjusted hazard ratio (HR) 0.92; $P < 0.0001$; number needed to treat (NNT) 34.1] and to low dose [adj.HR 0.81; $P < 0.001$; NNT 13.4] as well as in moderate-dose group compared with low dose (adj.HR 0.88; $P < 0.0001$; NNT 23.4). Death (adj.HR 0.87; $P < 0.0001$; NNT 23.6), recurrent MI (adj.sHR 0.91; $P = 0.0001$), and stroke (adj.sHR 0.86; $P < 0.0001$) were less frequent with a high- vs. moderate-dose statin. Higher initial statin dose after MI was associated with better long-term outcomes in subgroups by age, sex, atrial fibrillation, dementia, diabetes, heart failure, revascularisation, prior statin usage, or usage of other evidence-based medications.

Conclusion Higher initial statin dose after MI is dose-dependently associated with better long-term cardiovascular outcomes. These results underline the importance of using a high statin dose early after MI.

Keywords Coronary artery disease • Myocardial infarction • Statin • Outcomes

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Table 1 **Classification of statin intensity and Anatomical Therapeutic Classification codes used for statin detection.**

	Intensity			
	High	**Moderate**	**Low**	**ATC codes**
Atorvastatin	40–80 mg	10–20 mg	-	C10AA05, C10BA05, C10BX03, C10BX08, C10BX11, C10BX12, C10BX15
Fluvastatin	-	80 mg	20–40 mg	C10AA04
Lovastatin	-	40 mg	20 mg	C10AA02, C10BA01
Pitavastatin*				C10AA08
Pravastatin	-	40–80 mg	10–20 mg	C10AA03, C10BA03, C10BX02
Cerivastatin*				C10AA06
Simvastatin	80 mg	20–60 mg	10 mg	C10AA01, C10BA02, C10BA04, C10BX01, C10BX04
Rosuvastatin	20–40 mg	10 mg	-	C10AA07, C10BA06, C10BX05, C10BX07, C10BX09, C10BX10, C10BX13, C10BX14

* Not used by study patients

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Table 2 **Baseline features of myocardial infarction patients by intensity of statin therapy after myocardial infarction.**

Variable	Statin dose N = 19 078 High	 N = 50 082 Moderate	 N = 3241 Low	*P*-value Between group
Age, years (SD)	64.8 (11.6)	68.9 (12.1)	76.2 (10.5)	<0.0001
Women	26.6%	34.4%	48.8%	<0.0001
Medical history				
Alcohol abuse	3.6%	2.8%	1.9%	<0.0001
Anaemia	2.2%	2.9%	4.9%	<0.0001
Atrial fibrillation	9.8%	13.2%	22.4%	<0.0001
Cerebrovascular disease	9.4%	10.1%	15.8%	<0.0001
Chronic pulmonary disease	11.4%	12.9%	14.6%	<0.0001
Coagulopathy	0.4%	0.4%	0.7%	0.005
Dementia	2.0%	3.4%	7.4%	<0.0001
Depression	9.4%	8.6%	11.0%	<0.0001
Diabetes	24.7%	24.3%	34.6%	<0.0001
Insulin dependent	8.2%	8.2%	12.9%	<0.0001
Non-insulin dependent	16.5%	16.1%	21.6%	<0.0001
Heart failure	12.2%	17.9%	31.1%	<0.0001
Hypertension	47.6%	49.8%	61.3%	<0.0001
Liver disease	1.0%	0.8%	1.1%	0.026
Malignancy	11.1%	11.3%	14.0%	<0.0001
Paralysis	0.5%	0.3%	0.3%	0.045
Peripheral vascular disease	6.4%	6.8%	9.9%	<0.0001
Prior CABG	3.7%	3.1%	5.2%	<0.0001
Prior myocardial infarction	12.6%	13.5%	20.4%	<0.0001
Psychotic disorder	2.7%	3.0%	3.2%	0.027
Rheumatic disease	5.3%	7.4%	6.1%	<0.0001
Renal failure	2.1%	2.7%	5.5%	<0.0001
Valvular disease	4.0%	4.7%	8.7%	<0.0001
Revascularization	79.7%	62.7%	38.9%	<0.0001
PCI	72.7%	54.9%	33.6%	<0.0001
CABG	7.9%	8.5%	6.1%	<0.0001
ST-elevation MI	45.8%	38.4%	24.6%	<0.0001
Pharmacotherapy after MI				
ADP-inhibitor	85.8%	71.5%	51.9%	<0.0001
ACEi or ARB	78.0%	70.8%	64.5%	<0.0001
Aldosterone antagonist	4.4%	3.7%	4.7%	<0.0001
Antiarrhythmic	1.2%	1.2%	1.6%	0.075
Beta-blocker	86.5%	88.2%	85.5%	<0.0001
Digoxin	1.0%	2.9%	6.1%	<0.0001
Ezetimibe	5.0%	2.4%	3.2%	<0.0001
Oral anticoagulant	11.2%	14.3%	18.1%	<0.0001
Treatment in university hospital	60.6%	49.6%	41.8%	<0.0001
Admission > 30 days	2.0%	3.7%	6.9%	<0.0001

ADP, adenosine diphosphate; ACEi, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; PCI, percutanous coronary intervention; CABG, coronary artery bypass grafting; MI, myocardial infarction.

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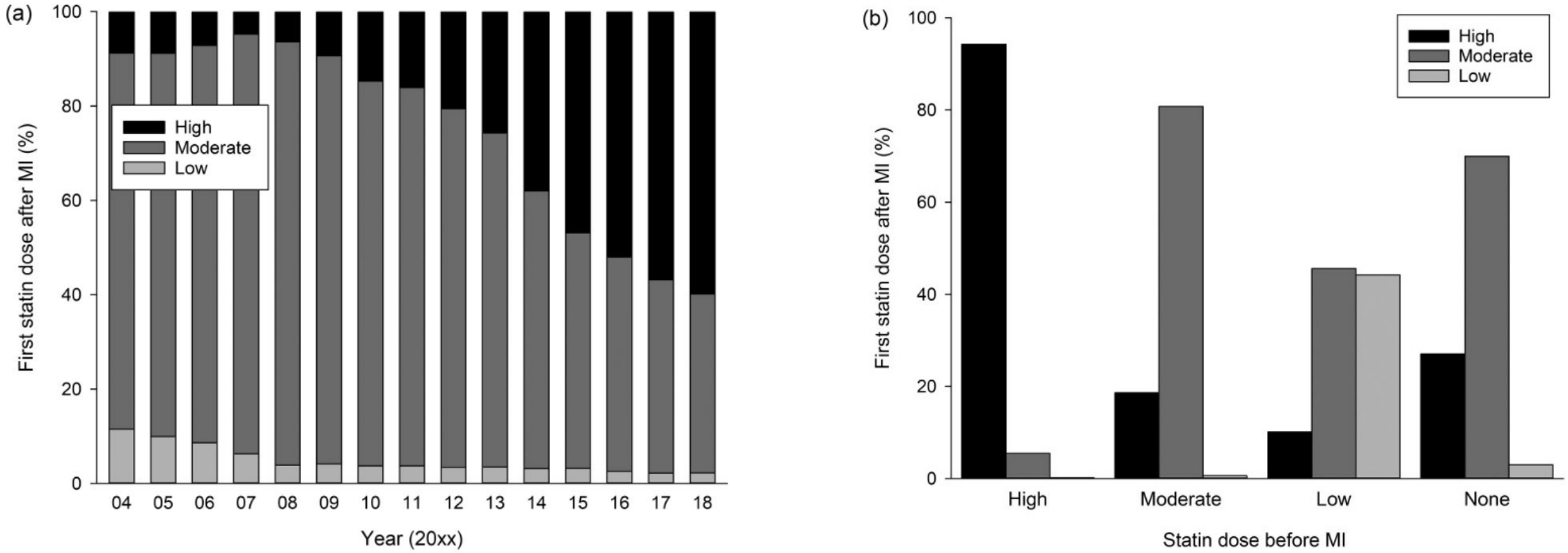

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Figure 1 (a) Trends for first statin dose after myocardial infarction during the study period. (b) Association of statin dose used before and after myocardial infarction.

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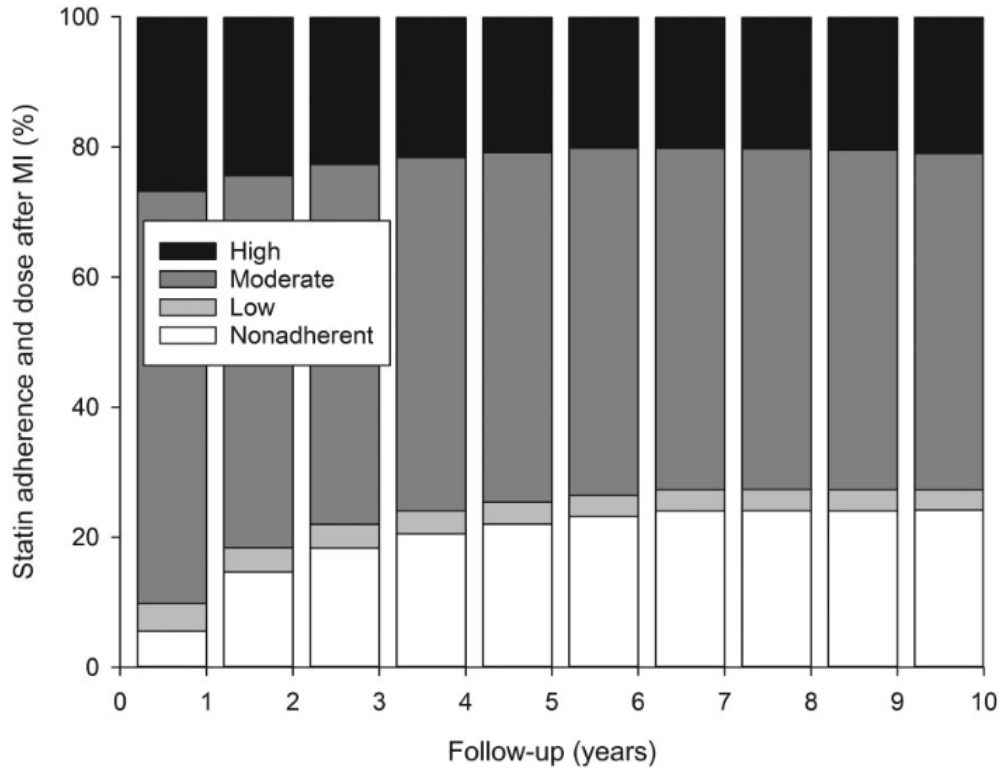

Figure 2 Adherence to statin use and used dose during the follow-up after index myocardial infarction.

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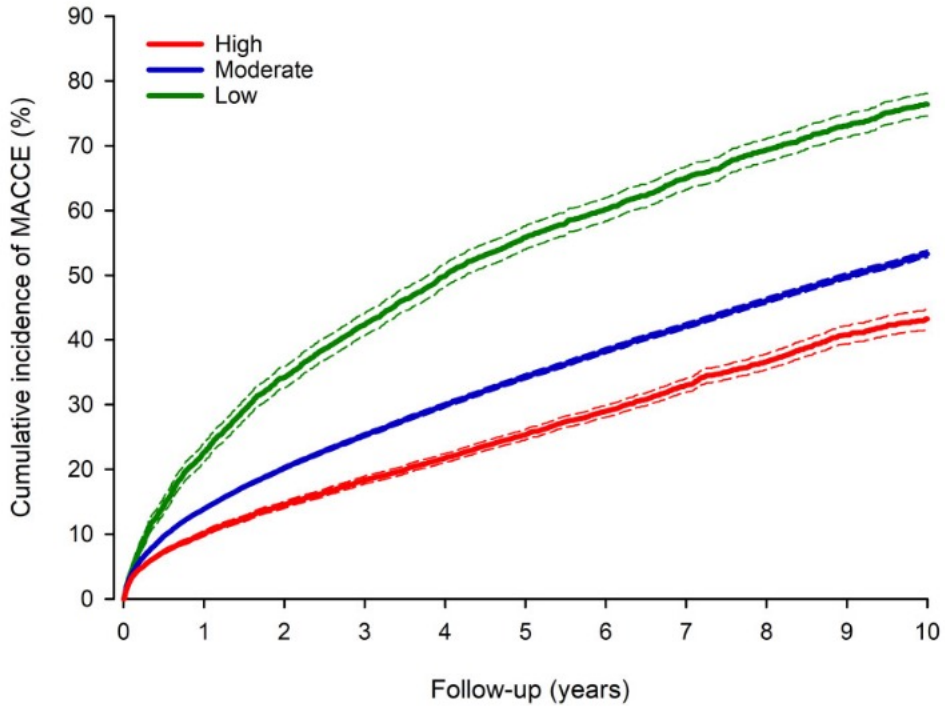

Figure 3 Cumulative incidence of major adverse cardiovascular or cerebrovascular event after myocardial infarction by first statin dose after index event. Dashed lines represent 95% confidence intervals.

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Table 3 **Results of multivariable adjusted regression models comparing 10-year outcomes between patients with different initial statin dose after myocardial infarction. Models are adjusted for age, sex, comorbidities (listed in Table 2), revascularization (PCI or CABG), ST-elevation, pharmacotherapy after MI (listed in Table 1), treating hospital, and index admission duration of > 30 days.**

	High vs. Moderate		High vs. Low		Moderate vs. Low	
Outcome	**adj.HR (95%CI)**	***P*-value**	**adj.HR (95%CI)**	***P*-value**	**adj.HR (95%CI)**	***P*-value**
MACCE	0.92 (0.89–0.95)	<0.0001	0.81 (0.77–0.86)	<0.0001	0.88 (0.85–0.92)	<0.0001
Death	0.87 (0.83–0.91)	<0.0001	0.76 (0.71–0.81)	<0.0001	0.88 (0.83–0.92)	<0.0001
Outcome	**adj.sHR (95%CI)**	***P*-value**	**adj.sHR (95%CI)**	***P*-value**	**adj.sHR (95%CI)**	***P*-value**
Recurrent MI	0.91 (0.87–0.96)	0.0001	0.79 (0.73–0.85)	<0.0001	0.86 (0.81–0.92)	<0.0001
Stroke	0.86 (0.80–0.92)	<0.0001	0.88 (0.78–1.00)	0.049	1.03 (0.93–1.15)	0.570

MACCE = Major adverse cardiovascular or cerebrovascular event. MI = myocardial infarction. sHR = Subdistribution HR.

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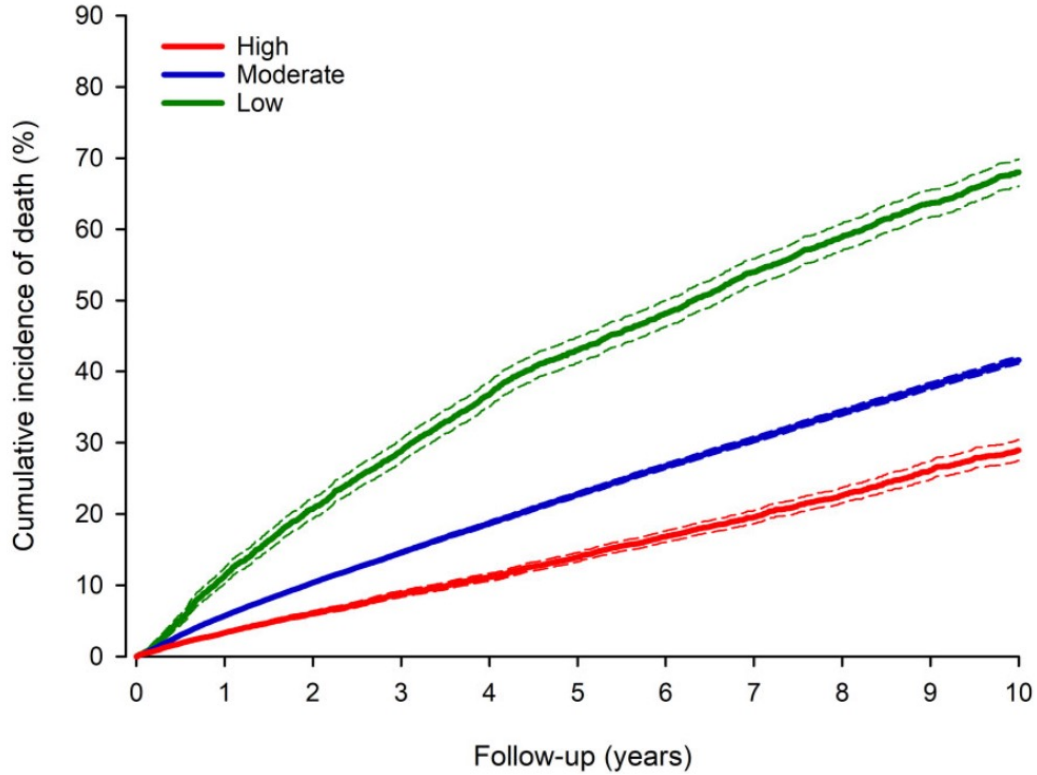

Figure 4 All-cause mortality after myocardial infarction by first statin dose after index event. Dashed lines represent 95% confidence intervals.

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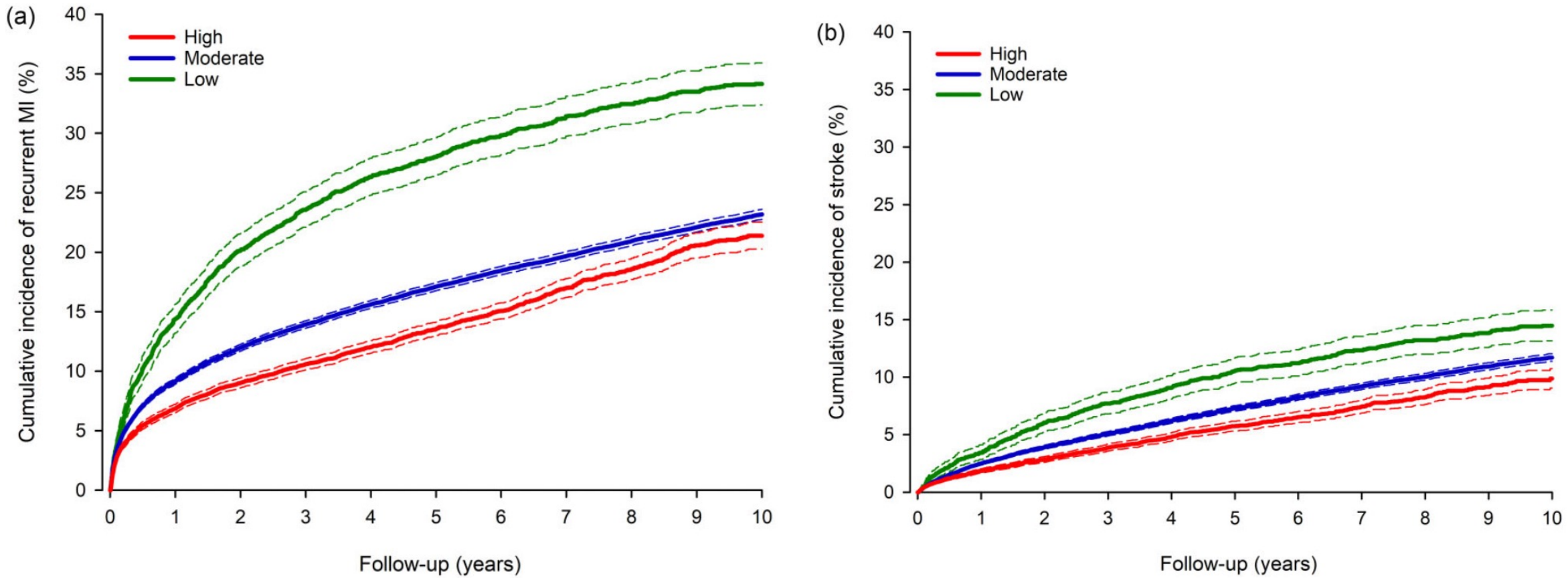

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Figure 5 Cumulative incidence of (a) recurrent myocardial infarction and (b) stroke after MI by first statin dose after index event. Competing risk curves. Dashed lines represent 95% confidence intervals.