Statin Benefit and Risk ; Recent Evidence on New-onset Diabetes Mellitus

- From the Single Center All Comer Registry -

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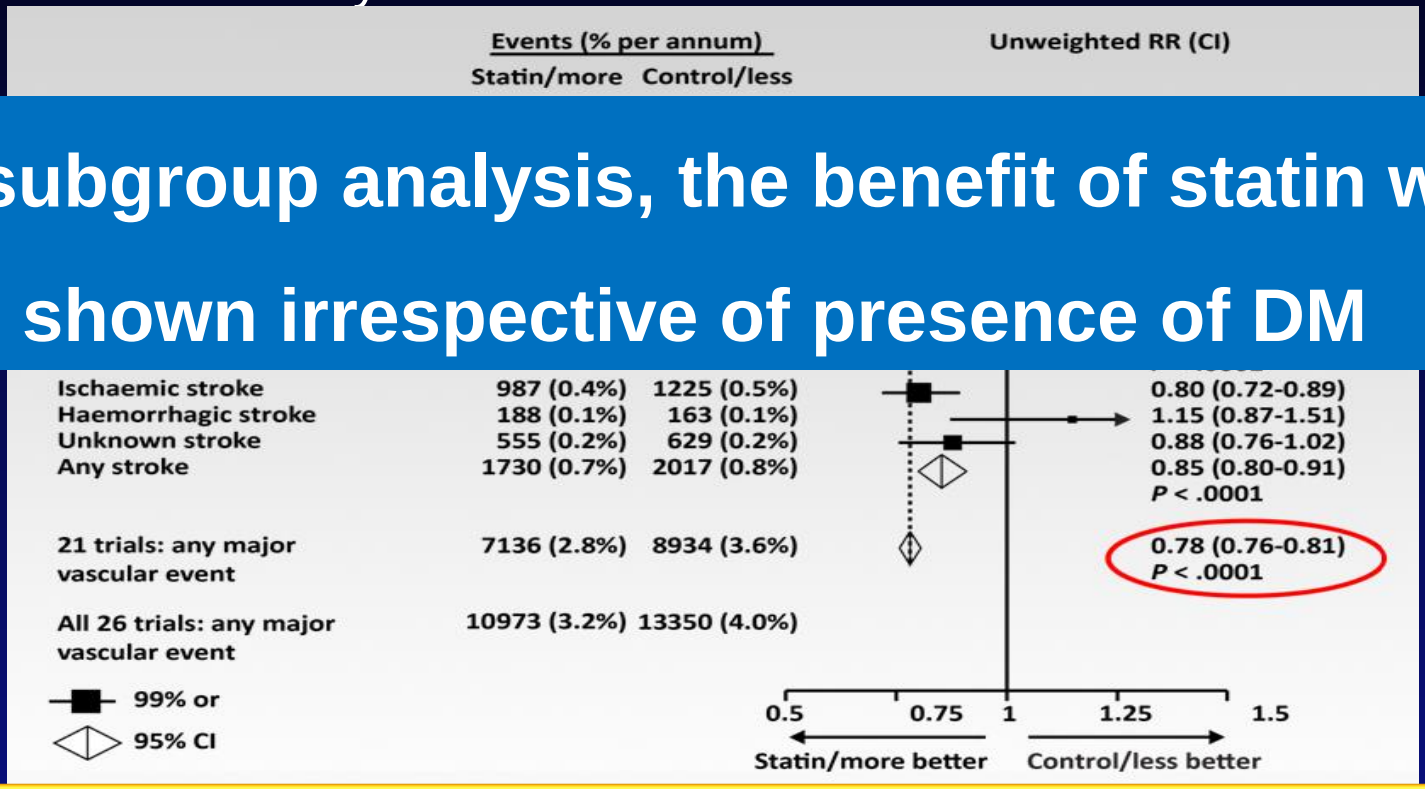
Which is more important for patients?
- CV prevention vs. DM risks

Benefits of statin therapy on major vascular events

Statins reduce the risk of major vascular events

- Lowering LDL-C by 1 mmol/L reduces the incidence of major vascular events by 21%

By subgroup analysis, the benefit of statin was shown irrespective of presence of DM



Risk reduction is proportional to statin dose; more intense the dose, greater the reduction.

1. Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet. 2010;376(9753):1670–1681.

Statins significantly reduce the first major vascular events

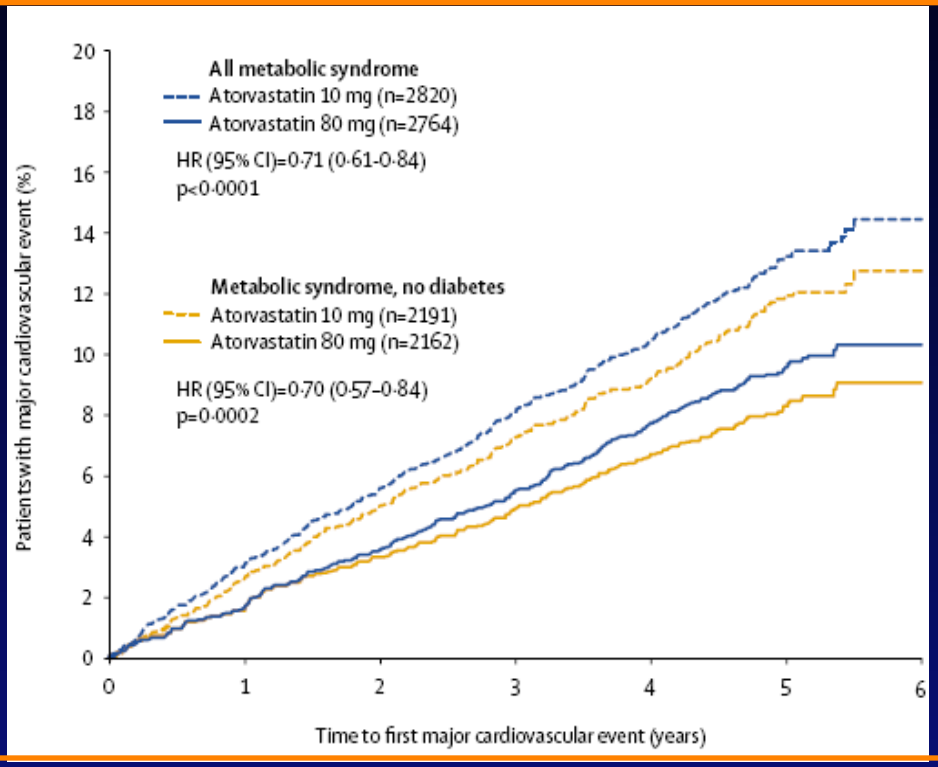
- First major vascular events reduced by one-fifth per 1 mmol/L (18 mg/dl) LDL-C reduction

Patient group	Reduction
No previous history of vascular disease	25%
Women	17%
Patients aged >75 years	16%

1. Cholesterol Treatment Trialists' (CTT) Collaborators. Lancet. 2010;376(9753):1670–1681.

Diabetes and CHD derive benefit from lower LDL-C levels achieved

- Significantly better reductions in CV events are associated with high-dose statin therapy

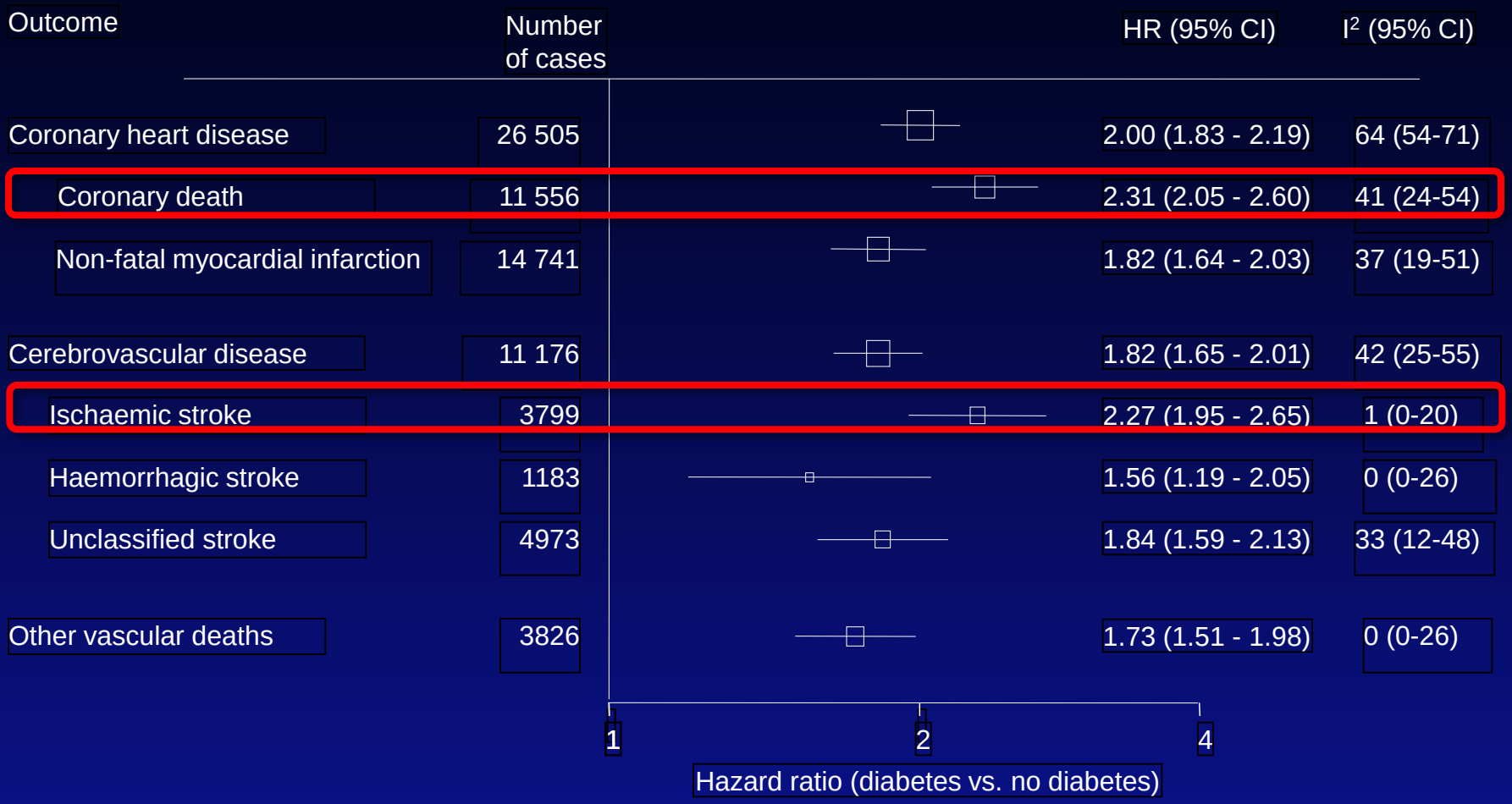


Irrespective of the presence of diabetes, patients with CHD and metabolic syndrome benefit from intensive statin therapy.

1. Breuer HWM. *Business Briefing Eur Cardiol*. 2005;18–20.
2. Deedwania P, *et al. Lancet*. 2006;368(9539):919–928.

Diabetes doubles the risk of vascular disease

Data from 528,877 participants
(adjusted for age, sex, cohort, SBP, smoking, BMI)



Seshasai et al. Lancet. 2010 Jun 26;375(9733):2215-22

Effects of statins on glucose homeostasis

Hydrophilic statins are preferred over lipophilic statins

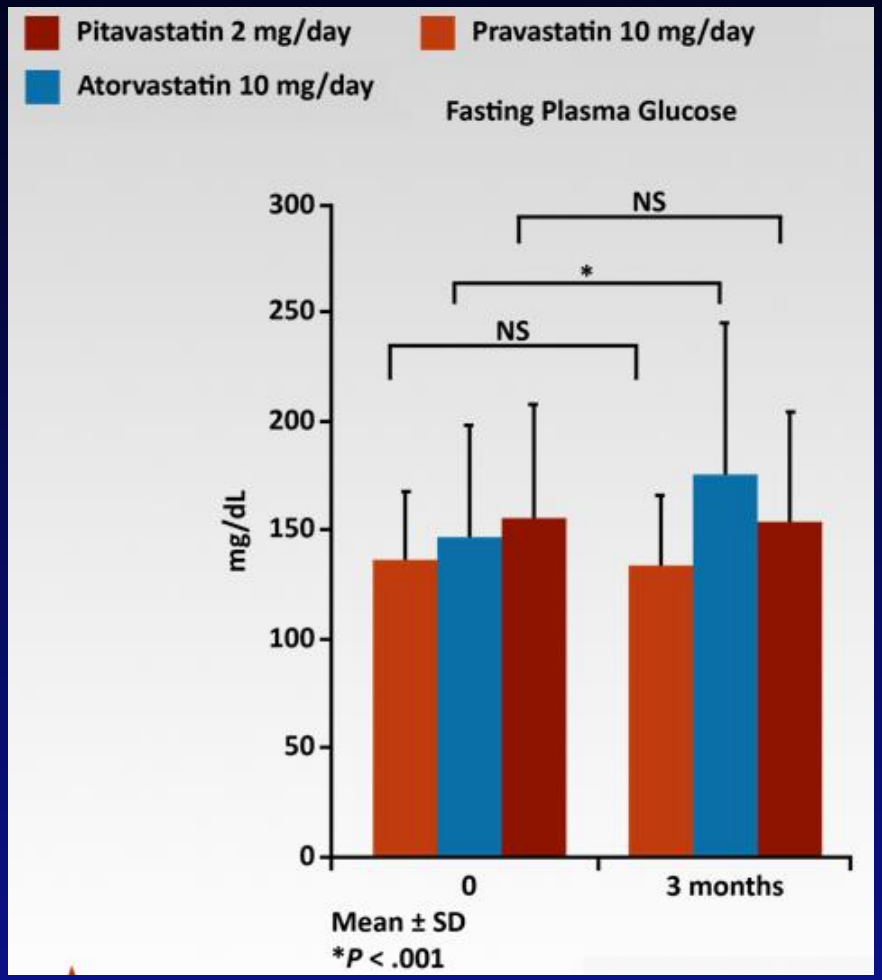
- Hypotriglyceridemic capacity
- Endothelial-dependent increase in pancreatic islet blood flow
- Anti-inflammatory properties
- Capacity to alter circulating levels of adipokines

Hydrophilic statins (such as rosuvastatin, pravastatin and pitavastatin) have preferable effect over lipophilic statins (such as atorvastatin and simvastatin).

1. Kostapanos MS, et al. Curr Vasc Pharmacol. 2010;8(5):612–631.

Baseline fasting glucose levels to be assessed before using statins

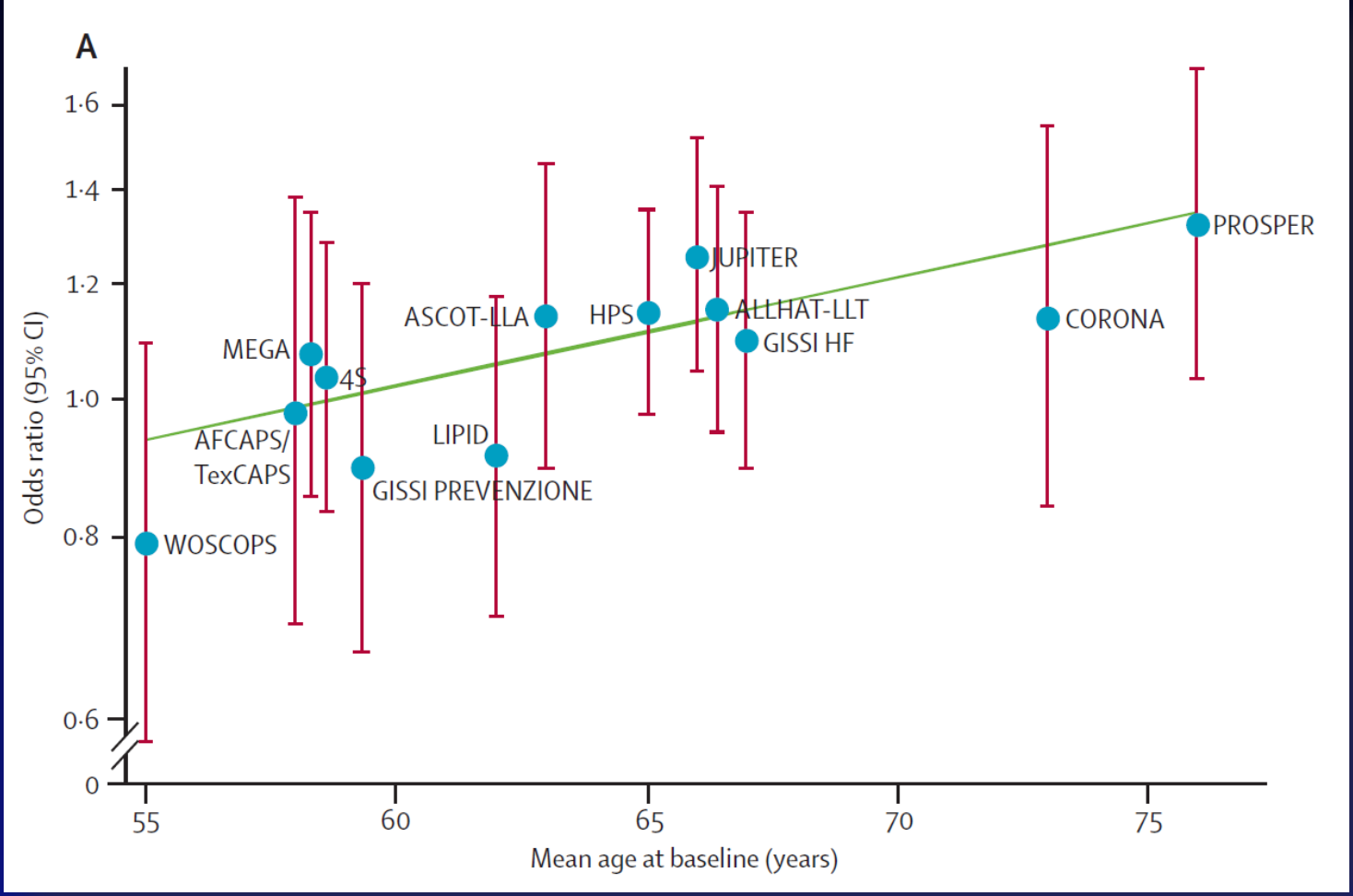
- Statins have individual effects on glycemic control[1]
- Statins can increase FPG in both diabetes and non-diabetes patients[2]
- Only atorvastatin and not pravastatin or pitavastatin have negative effect on glycemic control[1]
- Baseline fasting glucose levels are to be assessed before using statins[2]



1. Yamakawa T, et al. J Atheroscler Thromb. 2008;15:269–275.
2. Sukhija R, et al. J Investigative Med. 2009;57(3):495–499.

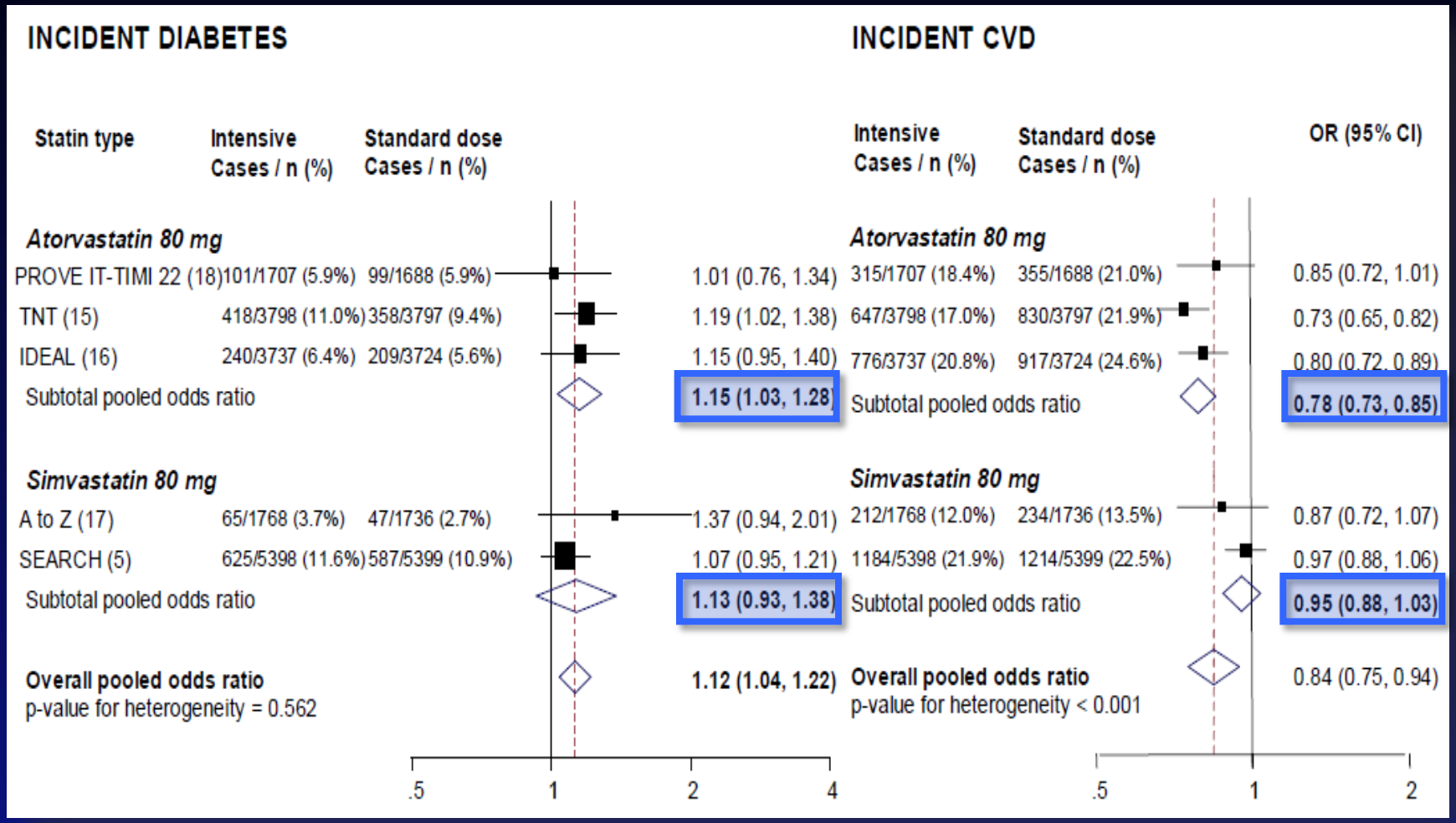
Association between statin therapy and incident diabetes

DM incidence risk greater at increasing age



Sattar et al. Lancet feb17th 2010 375

Intensive-dose vs. moderate-dose statin Tx



Preiss et al. JAMA 2011;305:2556-64

High-risk subgroups are more prone to new-onset T2DM

High-risk group of patients

- Old age
- Baseline fasting glucose >100 mg/dL
- Fasting triglycerides >150 mg/dL
- BMI >30 kg/m^2
- History of hypertension

Number of risk factors=risk severity

1. Waters DD, et al. JACC. 2011;57:1535–1545.

Safety profile of statins

Generally well-tolerated[1]

Low incidence of side-effects, such as muscle aches and increase in liver enzymes[1]

Linked to the development of incident diabetes[1], but the risk is small and of no clear practical evidence[2]

1. Bhatia L, et al. *Evidence-Based Med.* 2010;15(3):84–85.
2. Sampson UK, et al. *Curr Opin Cardiol*. 2011;26(4):342–347.

Risks versus benefits

Overall risks vs benefits of statins

- *CV risk associated with statin-induced diabetes is not equivalent to diabetes-induced CV risk*[1]
- If 255 patients were treated with statins for 4 years, it results in[2]
  - Only one case of new-onset diabetes
  - Prevention of 5.4 coronary deaths or MIs for each mmol/L LDL-C reduction

Statin-induced CV risk reduction outweighs the risk of statin-induced new-onset diabetes[2]

1. Waters *et al*. *JACC*. 2011;57:1535–1545.
2. Sattar *et al*. *Lancet*. 2010;375(9716):735–742

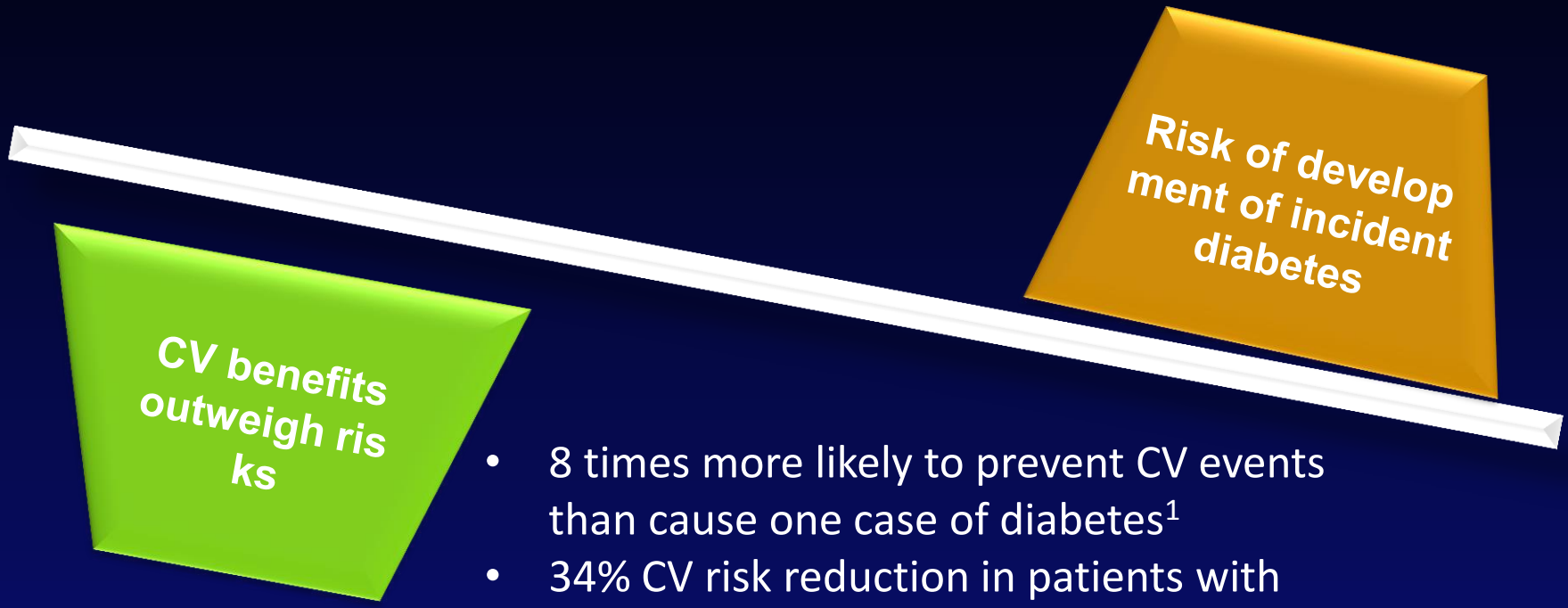
Dose-dependent risks vs benefits of statins

- Dose-dependent risk of new-onset diabetes
  - 2 additional cases of new-onset diabetes/1000 patient-years were observed with intensive therapy compared to moderate therapy
- Dose-dependent benefit in terms of CV events
  - 6.5 fewer first major CV events/1000 patient-years were observed with intensive therapy compared to moderate therapy

Risk vs benefit with intensive-dose therapy should hence be weighed before treatment initiation/discontinuation.

1. Preiss D, et al. *JAMA.* 2011;305(24):2556–2564.

Statin risk summary
: CV benefits outweigh risk



- 8 times more likely to prevent CV events than cause one case of diabetes[1]
- 34% CV risk reduction in patients with IFG[2]

Statin use is encouraged but with vigilance, particularly in high-risk patients

1. Bhatia L, et al. *Evidence-Based Med.* 2010;15(3):84–85.
2. Sampson UK, et al. *Curr Opin Cardiol.* 2011;26(4):342–347.

Rosuvastatin and risk of diabetes

Rosuvastatin is associated with low risk of new-onset diabetes

- Not all statins are associated with new-onset diabetes

Cox univariate analysis of incidence of hazard ratios (HRs) with 95% CIs for patients with new-onset diabetes (NOD) according to prescriptions for statins compared with non-NOD subjects.

Drug class	HR	95% CI	p	HR*	95% CI*	p†
Pravastatin	1.40	1.20–1.62	<0.0001	1.34	1.15–1.55	0.0001
Fluvastatin	0.45	0.34–0.60	<0.0001	0.45	0.34–0.60	<0.0001
Lovastatin	0.66	0.57–0.78	<0.0001	0.71	0.61–0.84	<0.0001
Simvastatin	1.12	0.94–1.34	0.2068	1.10	0.92–1.31	0.3034
Atorvastatin	1.32	1.19–1.47	<0.0001	1.29	1.16–1.44	<0.0001
Rosuvastatin	0.53	0.38–0.74	0.0002	0.54	0.39–0.77	0.0005

*All variables were adjusted for age and sex. †P values between NOD and non-NOD subjects.

The risk estimate of new-onset diabetes for fluvastatin, lovastatin and rosuvastatin was lower than nonusers.

1. Ma T, et al. *Clin Therap.* 2012;34(9):1977–1983.

Rosuvastatin provides cardiovascular and mortality benefits in patients at high risk of developing diabetes

- JUPITER trial assessed the cardiovascular benefits and risk of diabetes in patients without previous cardiovascular disease or diabetes

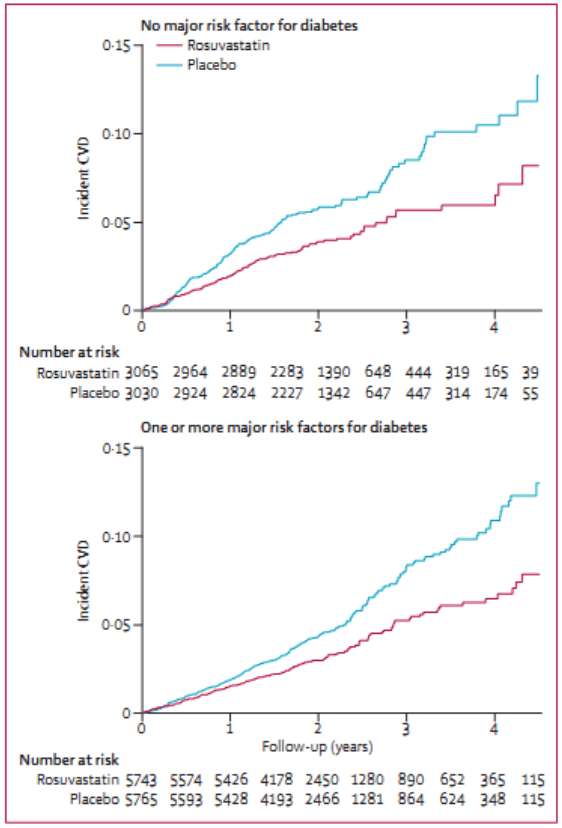


Figure 2: Cumulative incidence of cardiovascular events and total mortality in participants with and without major risk factors for diabetes
CVD=cardiovascular disease.

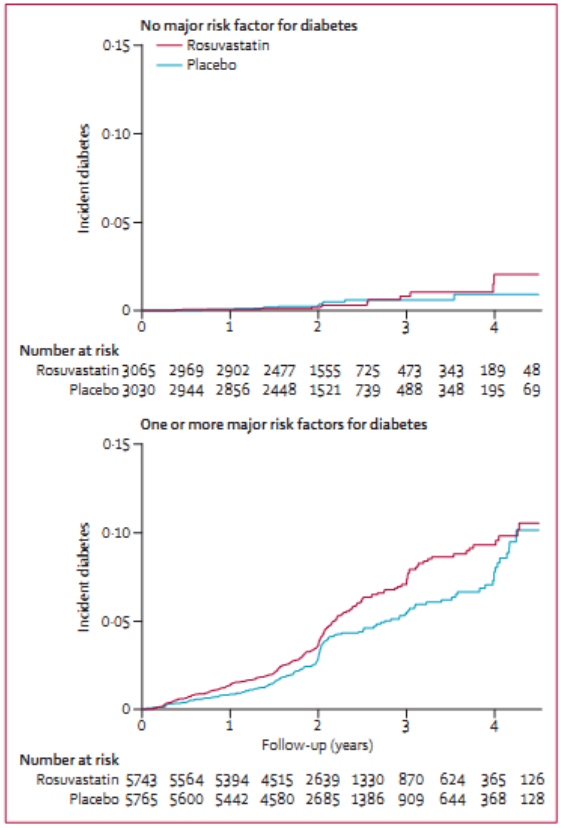


Figure 3: Cumulative incidence of diabetes in participants with and without major risk factors for diabetes

The cardiovascular and mortality benefits of rosuvastatin exceed the hazard ratio of diabetes, even in patients who are at high risk of developing diabetes.

1. Ridker DM, et al. *Lancet.* 2012;380:565–571.

Taiwan Data

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Statins, Risk of Diabetes, and Implications on Outcomes in the General Population

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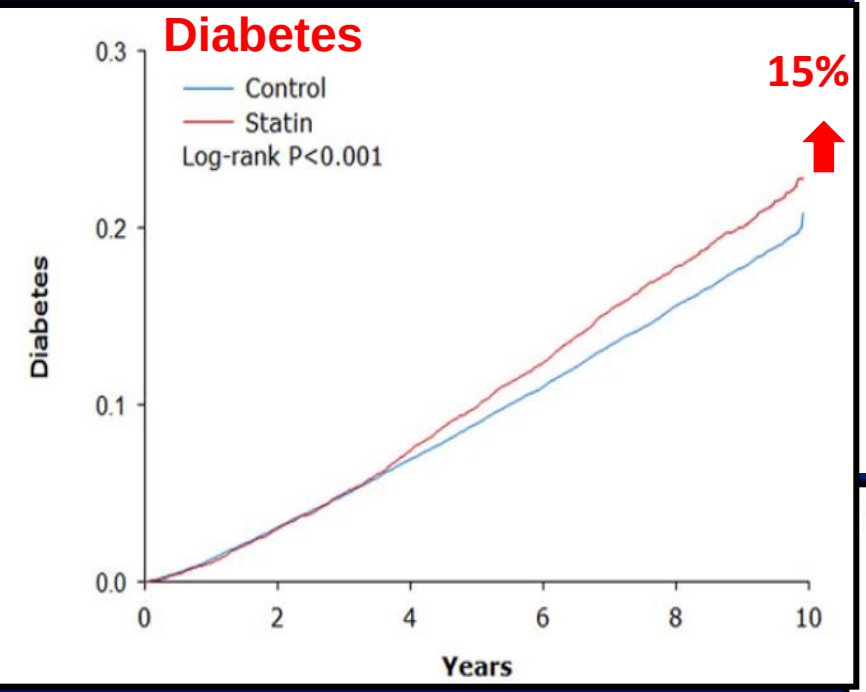
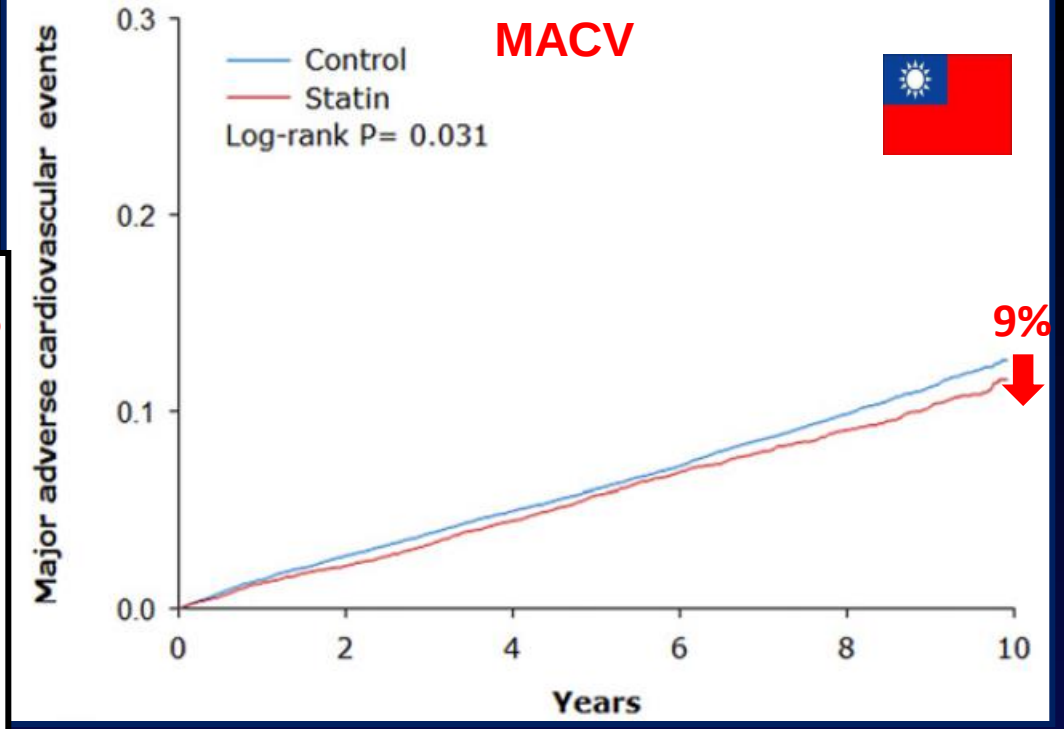
J Am Coll Cardiol 2012; 60:1231-1238





Risk of diabetes was increased after statins, but outcomes were favorable

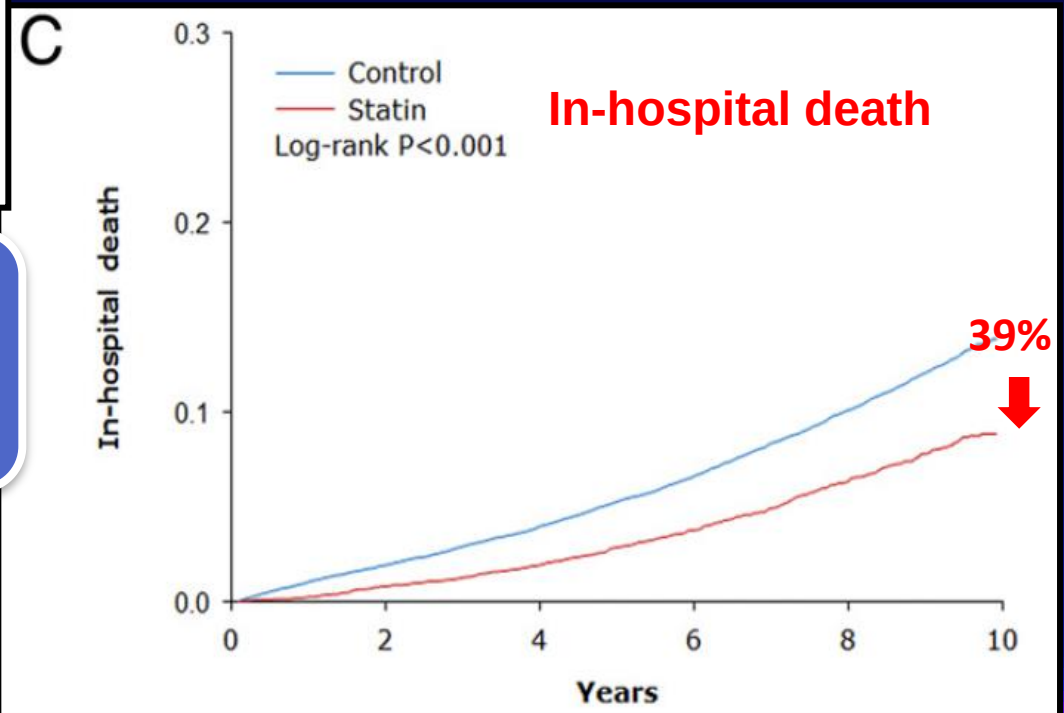


Table 2 Univariate and Multivariate Analyses of In-Hospital Deaths According to Status of Diabetes and Prior Exposure of Statins

nonDM nonStatin > DM nonStatin > DM Statin > nonDM Statin

Overall cohort				
N	29,332	4,316	1,387	7,025
Crude	Reference	1.70 (1.51–1.91)	1.38 (1.10–1.73)	0.59 (0.54–0.66)
Adjusted*	Reference	1.91 (1.70–2.15)	1.54 (1.23–1.92)	0.58 (0.53–0.64)
High-risk cohort†				
N	15,481	2,206	728	3,720
Crude	Reference	1.45 (1.25–1.69)	1.11 (0.83–1.49)	0.61 (0.54–0.68)
Adjusted*	Reference	1.69 (1.45–1.96)	1.31 (0.98–1.75)	0.62 (0.55–0.70)
Secondary prevention cohort				
N	13,733	1,986	652	3,266
Crude	Reference	1.43 (1.22–1.67)	1.08 (0.79–1.47)	0.61 (0.53–0.69)
Adjusted*	Reference	1.68 (1.44–1.98)	1.28 (0.94–1.73)	0.62 (0.55–0.71)

High risk

Secondary p revention

Statins and New-onset DM ; Korean Data

Published Abstracts (1)

A. Coronary Artery Spasm and NODM

1. Rha SW, Choi BG, Choi SY, Park Y, Goud Akkala R, Lee S, Kim JB, Im SI, Na Jo, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Coronary Artery Spasm on Development of New-onset Diabetes Mellitus in Asian Population. Journal of the American College of Cardiology. 2013;62:B99.

2. Rha SW, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Coronary Artery Spasm on Development of New-onset Diabetes Mellitus in Asian Population. The American Journal of Cardiology. 2013;111:92B-93B.

3. Rha SW, Choi BG, Choi SY, Park Y, Akkala RG, Lee Sk, Lee Sk, Kim JB, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Coronary Artery Spasm on Development of New-onset Diabetes Mellitus in Asian Population. Circulation. 2013;128:A10707.

B. Drugs and NODM

1. Rha SW, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Chronic Calcium Channel Blocker Therapy on Development of New-onset Diabetes Mellitus in Asian Population. The American Journal of Cardiology. 2013;111:93B.

2. Rha SW, Choi BG, Choi SY, Im SI, Kim S, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo H-S and Oh DJ. IMPACT OF CHRONIC CALCIUM CHANNEL BLOCKER THERAPY ON DEVELOPMENT OF NEW-ONSET DIABETES MELLITUS IN ASIAN POPULATION. Journal of the American College of Cardiology. 2013;61:E1180.

Published Abstracts (2)

3. Rha SW, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Chronic Diuretics Therapy on Development of New-onset Diabetes Mellitus in Asian Population. The American Journal of Cardiology. 2013;111:93B-94B.

4. Rha SW, Choi BG, Choi SY, Park Y, Akkala RG, Lee Sk, Kim JB, Im SI, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Chronic Diuretics Therapy on Development of New-onset Diabetes Mellitus in Asian Population. Circulation. 2013;128:A12814.

5. Rha SW, Choi BG, Choi SY, Im SI, Kim S, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo H-S and Oh DJ. Impact of Chronic Beta-Blocker Therapy on Development of New-Onset Diabetes Mellitus in Asian Population. Journal of the American College of Cardiology. 2013;61:E1456.

6. Rha SW, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Chronic Beta Blocker Therapy on Development of New-onset Diabetes Mellitus in Asian Population. The American Journal of Cardiology. 2013;111:88B-89B.

7. Park JY, Rha SW, Choi JW, Ryu SK, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Han SW, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Angiotensin Receptor Blocker on Development of Glucose Intolerance and New-onset Diabetes Mellitus in Asian Population. Circulation. 2012;126:A19071.

8. Park JY, Rha SW, Choi JW, Choi BG, Choi SY, Choi CU, Kim EJ, Park CG, Seo HS and Oh DJ. Angiotensin converting enzyme inhibitor versus angiotensin receptor blocker on the incidence of new-onset diabetes mellitus in Asian population. European Heart Journal. 2013;34.

Published Abstracts (3)

C. Disease/Risk Factors and NODM

1. Park SH, Rha SW, Shin WY, Choi BG, Choi SY, Choi CU, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of hyperlipidemia on development of new-onset diabetes mellitus in Asian population: 5-year clinical outcomes. European Heart Journal. 2013;34.

2. Park YJ, Rha SW, Choi BG, Choi SY, Choi CU, Kim EJ, Park CG, Seo HS, Oh DJ and Park SH. Impact of hypertension on development of new-onset diabetes mellitus in Asian population: five-year clinical follow up results. European Heart Journal. 2013;34.

3. Choi BG, Rha S-W, Choi SY, Park Y, Akkala RG, Lee Sk, Kim JB, Im SI, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Hyperuricemia on Development of New-onset Diabetes Mellitus in Asian Population: Five-year Clinical Outcomes. Circulation. 2013;128:A13336.

Published Abstracts (4)

D. Statins and NODM

1. Park S-H, Rha S-W, Jun U, Lee S-W, Shin W-Y, Lee SJ, Jin D-K, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Han SW, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Chronic Statin Therapy on Development of Glucose Intolerance and New-onset Diabetes Mellitus in Asian Population. Journal of the American College of Cardiology. 2012;60:B97.

2. Park S-H, Rha SW, Jun U, Lee S-W, Shin W-Y, Lee S-J, Jin D-K, Choi BG, Choi SY, Im SI, Kim SW, Na JO, Han SW, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Chronic Statin Therapy on Development of Glucose Intolerance and New-onset Diabetes Mellitus in Asian Population. Circulation. 2012;126:A18170.

3. Park Y, Rha S-W, Choi BG, Choi SY, Akkala RG, Lee Sk, Kim JB, Im SI, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Atorvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical Follow up Results. Circulation. 2013;128:A13414.

4. Park Y, Rha S-W, Choi BG, Choi SY, Akkala RG, Lee Sk, Kim JB, Im SI, Na JO, Choi CU, Lim HE, Kim JW, Kim EJ, Park CG, Seo HS and Oh DJ. Impact of Rosuvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical follow up Results. Circulation. 2013;128:A13425.

5. Park JY, Rha S-W, Choi BG, Choi JW, Ryu SK, Choi CU and Oh DJ. Impact of Low Dose Atorvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Five-year Clinical Outcomes. Circulation. 2013;128:A13485.

Statins and IGT/NODM

1. Atorvastatin (Lipitor)
2. Rosuvastatin (Crestor)
3. Simvastatin (Zocor)
4. Pitavastatin (Livalo)
5. Fluvastatin (Lescol)
6. Pravastatin (Mevalotin)
7. Overall Statins

Impact of Atorvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical Follow up Results

Seung-Woon Rha, Byoung Geol Choi, Yunjee Park,
Se Yeon Choi, Sung Il Im, Jin Oh Na, Cheol Ung Choi,
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AHA 2013

Background

Although statin therapy is beneficial for vascular diseases, the relationship between statin therapy and incidence of new-onset diabetes mellitus (DM) remains limited data.

Carter AA et al, British Medical Journal 2013;346.

Waters DD et al. J Am Coll Cardiol 2013;61:148-52.

Purpose

The aim of this study was to evaluate the impact of chronic atorvastatin therapy on the development of new-onset DM from 5-year clinical follow up database in a series of Asian population.

Methods

1. Study Population

We investigated total 3,566 patients (pts) who had baseline hemoglobin A1c level < 6.0% and fasting glucose level < 100 mg/dL from January 2004 to February 2007.

2. Definition

New-onset DM was defined as having a fasting blood glucose ≥126mg/dL or HbA1c ≥6.5%.

American Diabetes A. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36 Suppl 1:S67-74

Methods

3. Study Groups

Atorvastatin = 566 pts

No Atorvastatin = 3,000 pts

4. Study Endpoint

The primary end-point was the cumulative incidence of new-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL)

Statistics

1. All statistical analyses were performed using SPSS 20.0.
2. Continuous variables were expressed as means ± standard deviation and were compared using Student's t-test.
3. Categorical data were expressed as percentages and were compared using chi-square statistics or Fisher's exact test.
4. A *P*-value of 0.05 was considered statistically significant.

Statistics

5. Multivariate logistics analysis were performed.

1) After univariate analyses, baseline confounding factors and medical treatment history were entered into the multivariable Cox regression analysis to determine the impact of atorvastatin on development of new-onset diabetes mellitus

2) Following factors were co-analyzed in multivariable analysis: gender, age, hypertension, angina, stable angina, unstable angina, coronary spasm, heart failure, prior PTCA, prior CABG, hyperlipidemia, chronic kidney disease, cerebrovascular accident, peripheral vascular disease, AF, cancer, thyroid disease, ARB, ACEI, diuretics and statins.

Statistics

6. We calculated propensity score predicting probability for atorvastatin in each patient.

1) The covariates that were adjusted for atorvastatin included gender, age, hypertension, angina, stable angina, unstable angina, coronary spasm, heart failure, prior PTCA, prior CABG, hyperlipidemia, chronic kidney disease, cerebrovascular accident, peripheral vascular disease, AF, cancer, thyroid disease, ARB, ACEI, Diuretics and Statins.

2) The C-statistic for the logistic regression model that was used to calculate the propensity score matching for the 2 groups was 0.851.

3) Patients with atorvastatin were then 1-to-1 matched to the patients without atorvastatin on the propensity scores with the nearest available pair matching method. Subjects were matched with a caliper width equal to 0.05. The procedure yielded 409 well-matched pairs.

4) After propensity score matching, the baseline covariates were compared between the 2 groups.

Baseline Clinical Characteristics

	Entire Patients				Propensity score matching			
Variables, n(%)	Total (n=3,566)	Atorva (n=566)	Control (n=3,000)	P-Value	Total (n=818)	Atorva (n=409)	Control (n=409)	P-Value
Gender (Male)	1804 (50.5)	316 (55.8)	1488 (49.6)	0.007	416 (50.8)	208 (50.8)	208 (50.8)	-
Age	55.3 ± 12.9	60.7 ± 10.5	54.3 ± 13.4	< 0.001	61.0 ± 10.9	60.3 ± 10.5	61.6 ± 11.3	0.083
Body mass index	24.4 ± 3.3	24.6 ± 3.14	24.4 ± 3.42	0.129	24.6 ± 3.6	24.6 ± 3.14	24.7 ± 4.23	0.951
Hypertension	2011 (56.3)	305 (53.8)	1706 (56.8)	0.190	441 (53.9)	222 (54.2)	219 (53.5)	0.833
Dyslipidemia	584 (16.3)	124 (21.9)	460 (15.3)	< 0.001	159 (19.4)	80 (19.5)	79 (19.3)	0.930
Coronary artery disease	340 (9.5)	102 (18.0)	238 (7.9)	< 0.001	120 (14.6)	57 (13.9)	63 (15.4)	0.553
Cerebrovascular accident	267 (7.4)	48 (8.4)	219 (7.3)	0.328	59 (7.2)	29 (7.0)	30 (7.3)	0.892
Heart failure	147 (4.1)	19 (3.3)	128 (4.2)	0.318	31 (3.7)	15 (3.6)	16 (3.9)	0.855
Coronary artery spasm	213 (5.9)	37 (6.5)	176 (5.8)	0.537	58 (7.0)	29 (7.0)	29 (7.0)	-
Angina pactoris	1029 (28.8)	181 (31.9)	848 (28.2)	0.074	272 (33.2)	131 (32)	141 (34.4)	0.458
Chest pain	218 (6.1)	36 (6.3)	182 (6.0)	0.789	44 (5.3)	24 (5.8)	20 (4.8)	0.535
Cardiac arrhythmia	261 (7.3)	41 (7.2)	220 (7.3)	0.940	51 (6.2)	29 (7.0)	22 (5.3)	0.311
A-fib	158 (4.4)	28 (4.9)	130 (4.3)	0.515	32 (3.9)	19 (4.6)	13 (3.1)	0.279
Smoking history	813 (22.7)	237 (41.8)	576 (19.2)	< 0.001	297 (36.3)	145 (35.4)	152 (37.1)	0.611
Alcoholic history	1175 (32.9)	268 (47.3)	907 (30.2)	< 0.001	359 (43.8)	188 (45.9)	171 (41.8)	0.231

Baseline Laboratory Findings

Variables, n(%)	Entire Patients				Propensity score matching			
	Total (n=3,566)	Atorva (n=566)	Control (n=3,000)	P-Value	Total (n=818)	Atorva (n=409)	Control (n=409)	P-Value
HbA1c	5.5 ± 0.2	5.6 ± 0.2	5.5 ± 0.3	< 0.001	5.6 ± 0.2	5.6 ± 0.2	5.6 ± 0.2	0.824
Fasting glucose	93.6 ± 8.0	93.6 ± 8.1	93.6 ± 8.0	0.982	93.5 ± 8.0	93.7 ± 7.9	93.3 ± 8.2	0.547
Insulin (base)	7.1 ± 5.1	7.8 ± 5.4	7.0 ± 5.1	0.090	7.5 ± 5.1	7.9 ± 5.7	7.2 ± 4.7	0.248
HOMA-IR	1.6 ± 1.2	1.8 ± 1.3	1.6 ± 1.2	0.119	1.7 ± 1.2	1.8 ± 1.4	1.7 ± 1.1	0.304
Total cholesterol	175.1 ± 32.6	175.3 ± 43.9	175.1 ± 30.4	0.906	175.6 ± 37.0	175.7 ± 43.0	175.4 ± 30.9	0.884
Triglyceride	128.3 ± 91.3	131.4 ± 79.6	127.8 ± 93.54	0.334	134.8 ± 94.2	131.9 ± 84.2	137.6 ± 104.3	0.385
HDL-C	52.1 ± 13.8	50.4 ± 13.8	52.4 ± 13.8	0.002	51.1 ± 13.5	51.3 ± 13.5	50.8 ± 13.5	0.665
LDL-C	98.1 ± 28.5	99.0 ± 40.4	97.9 ± 26.3	0.540	98.21 ± 32.7	98.6 ± 39.3	97.7 ± 26.2	0.707
Hemoglobin	13.8 ± 1.6	13.6 ± 1.5	13.8 ± 1.6	0.058	13.6 ± 1.6	13.7 ± 1.5	13.6 ± 1.6	0.714
Hematocrit	40.8 ± 4.62	40.4 ± 4.4	40.8 ± 4.6	0.091	40.4 ± 4.48	40.5 ± 4.3	40.4 ± 4.5	0.725
Platelet count	238.3 ± 59.9	235.2 ± 56.8	238.8 ± 60.4	0.228	236.9 ± 59.6	236.5 ± 57.7	237.3 ± 61.3	0.856
hs CRP	2.4 ± 7.5	3.7 ± 13.1	2.2 ± 6.5	0.016	3.0 ± 9.8	3.1 ± 12.0	2.8 ± 7.9	0.714
Uric acid	5.0 ± 1.5	5.2 ± 1.6	5.0 ± 1.5	0.028	5.1 ± 1.6	5.2 ± 1.6	5.1 ± 1.6	0.535
Protein	7.1 ± 0.5	6.8 ± 0.6	7.2 ± 0.5	< 0.001	7.0 ± 0.5	6.9 ± 0.6	7.1 ± 0.5	0.007
Albumin	4.3 ± 0.3	4.2 ± 0.4	4.3 ± 0.3	< 0.001	4.2 ± 0.3	4.2 ± 0.3	4.2 ± 0.3	0.346

Current medication treatments

Variables, n (%)	Entire Patients				Propensity score matching			
	Total (n=3,566)	Atorva (n=566)	Control (n=3,000)	P-Value	Total (n=818)	Atorva (n=409)	Control (n=409)	P-Value
Current medication treatments								
Anti-hypertensive drug	2546 (71.3)	490 (86.5)	2056 (68.5)	< 0.001	683 (83.4)	341 (83.3)	342 (83.6)	0.925
Beta blocker	729 (20.4)	189 (33.3)	540 (18)	< 0.001	235 (28.7)	116 (28.3)	119 (29.0)	0.817
Calcium channel blocker	1512 (42.4)	269 (47.5)	1243 (41.4)	0.007	393 (48.0)	196 (47.9)	197 (48.1)	0.944
ARB	1016 (28.4)	193 (34.0)	823 (27.4)	0.001	283 (34.5)	147 (35.9)	136 (33.2)	0.419
ACEI	299 (8.3)	103 (18.1)	196 (6.5)	< 0.001	96 (11.7)	47 (11.4)	49 (11.9)	0.828
Diuretics	759 (21.2)	136 (24)	623 (20.7)	0.082	214 (26.1)	105 (25.6)	109 (26.6)	0.750

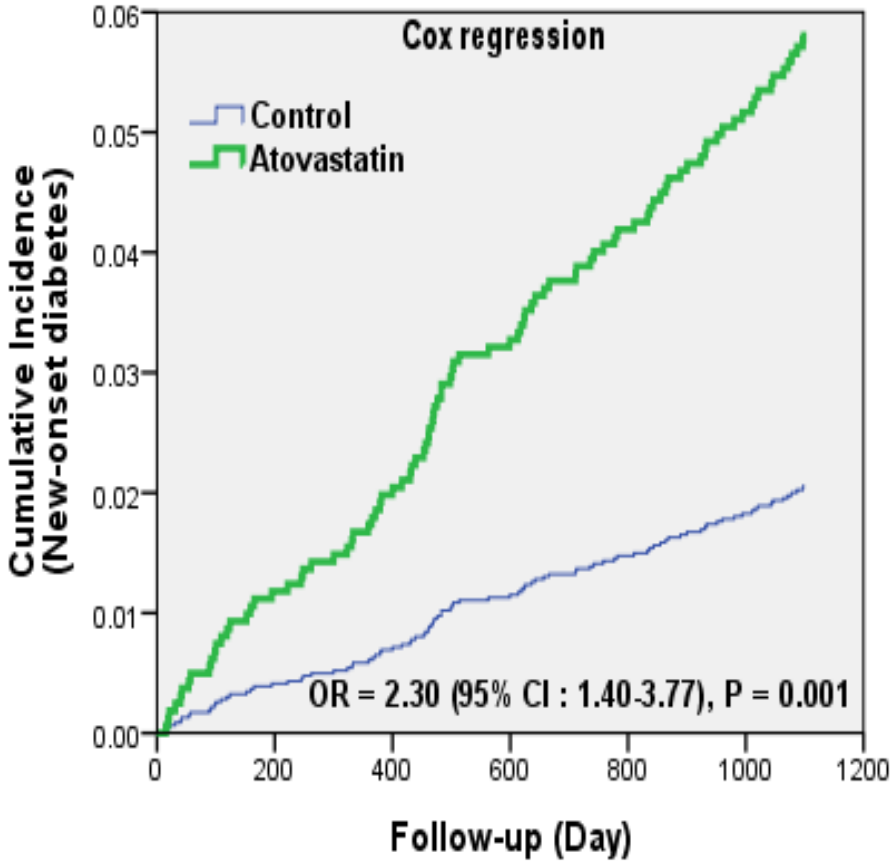
Three-year Clinical Outcomes

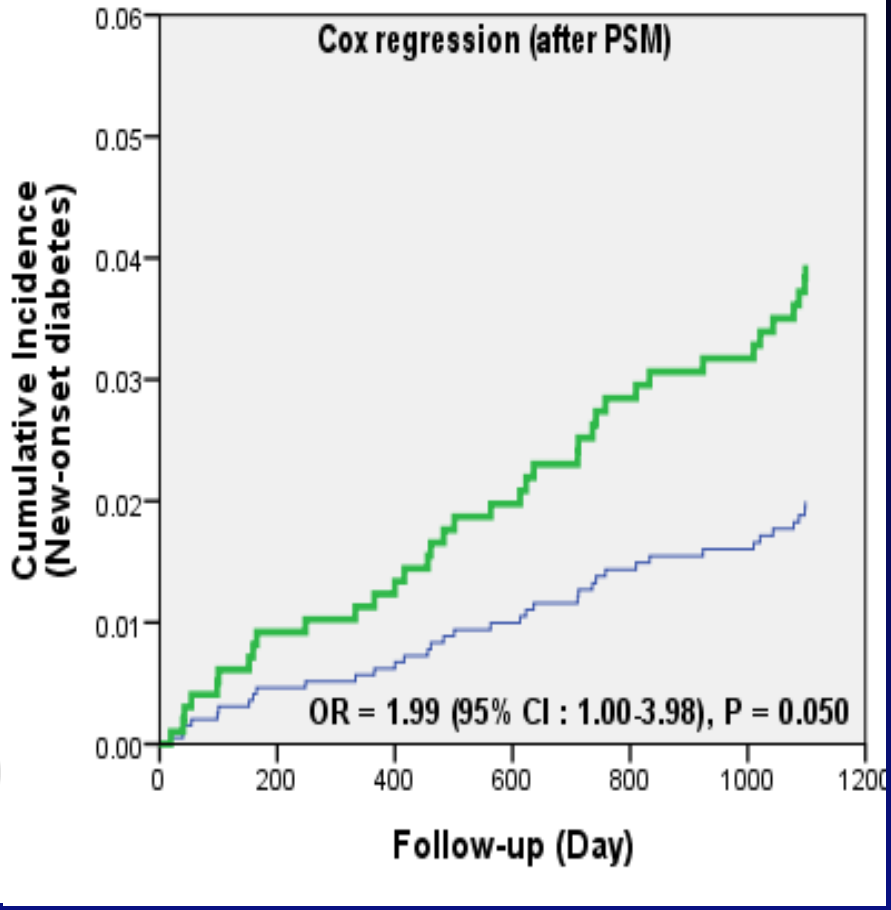
Variables, n (%)	Entire Patients				Propensity score matching			
	Total (n=3,566)	Atorva (n=566)	Control (n=3,000)	P-Value	Total (n=818)	Atorva (n=409)	Control (n=409)	P-Value
Five-year Clinical Outcomes								
New onset diabetes	95 (2.7)	33 (5.8)	62 (2.1)	< 0.001	37 (4.5)	24 (5.9)	13 (3.2)	0.064
Follow-up day	836.3 ± 385.6	976.4 ± 278.1	809.8 ± 405.9	< 0.001	959.5 ± 293.2	962 ± 291	956 ± 295	0.802

Predictors of New-onset diabetes at 3-years

	Entire Patients		Propensity score matching	
Variables, n (%)	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Atorvastatin*	**2.30 (1.40-3.77)**	**0.001**	**1.99 (1.00-3.98)**	**0.050**
Gender (Male)	1.30 (0.85-1.97)	0.211	1.44 (0.73-2.84)	0.287
Age	1.03 (1.01-1.05)	< 0.01	1.02 (0.99-1.05)	0.125
BMI	1.01 (0.95-1.07)	0.741	0.94 (0.83-1.06)	0.360
HbA1c	3.32 (1.42-7.78)	0.006	2.02 (0.51-8.00)	0.315
Fasting glucose	1.01 (0.99-1.04)	0.222	1.00 (0.96-1.04)	0.770
Smoking history	0.75 (0.43-1.30)	0.312	0.61 (0.26-1.41)	0.255
Alcoholic history	1.17 (0.74-1.86)	0.489	1.48 (0.70-3.13)	0.300
Coronary artery disease	0.75 (0.36-1.55)	0.442	0.75 (0.26-2.15)	0.602
Hypertension	1.42 (0.89-2.25)	0.133	2.72 (1.26-5.90)	0.011
Dyslipidemia	1.16 (0.70-1.92)	0.564	0.96 (0.40-2.30)	0.936
Heart failure	0.89 (0.32-2.48)	0.833	1.03 (0.22-4.75)	0.961
Cerebrovascular accident	1.20 (0.57-2.51)	0.622	0.38 (0.05-2.90)	0.357
Coronary artery spasm	1.34 (0.56-3.25)	0.504	3.72 (1.27-10.9)	0.016
Angina pectoris	1.22 (0.74-2.02)	0.420	1.61 (0.68-3.81)	0.273
Chest pain	0.96 (0.37-2.46)	0.940	2.07 (0.43-9.76)	0.357
A-Fib	1.02 (0.37-2.85)	0.955	2.39 (0.51-11.1)	0.265
Beta blocker	1.33 (0.84-2.10)	0.212	2.15 (1.07-4.28)	0.030
Calcium channel blocker	0.56 (0.36-0.88)	0.012	0.64 (0.31-1.31)	0.228
ARB	1.07 (0.68-1.69)	0.748	1.27 (0.62-2.63)	0.505
ACEI	0.53 (0.22-1.26)	0.155	0.51 (0.11-2.25)	0.377
Diuretics	1.84 (1.14-2.97)	0.012	1.67 (0.77-3.62)	0.187
Nitrate	1.12 (0.67-1.88)	0.639	1.50 (0.72-3.09)	0.271
Aspirin	0.87 (0.52-1.44)	0.596	0.83 (0.41-1.69)	0.620

Cumulative Incidence of New-onset Diabetes





Results (1)

1. At baseline, patients in the Atorvastatin group had higher prevalence of elderly, male gender, dyslipidemia, coronary artery disease, smoking history, alcoholic history, higher levels of HbA1c and lower levels of HDL-C.

2. Higher incidence of new-onset DM in the Atorvastatin group (5.8% vs. 2.1%, $p<0.001$) was observed up to 3 years before baseline adjustment.

Results (2)

3. Adjusted with cox-regression analysis, atorvastatin use remained as an independent predictor of new-onset DM (OR=2.30, 95% CI 1.40 – 3.77, p=0.001) at 3 years.

Conclusion

In our study, chronic atorvastatin therapy was associated with increased incidence of new-onset DM at 3 years cumulative clinical follow up.

Impact of Rosuvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical follow up Results

Seung-Woon Rha, Byoung Geol Choi, Yunjee Park,
Se Yeon Choi, Sung Il Im, Jin Oh Na, Cheol Ung Choi,
Hong Euy Lim, Jin Won Kim, Eung Ju Kim, Chang Gyu Park,
Hong Seog Seo, Dong Joo Oh

Cardiovascular Center,
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AHA 2013

Methods

3. Study Groups

Rosuvastatin = 260 pts

No Rosuvastatin = 3,000 pts

4. Study Endpoint

The primary end-point was the cumulative incidence of new-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL)

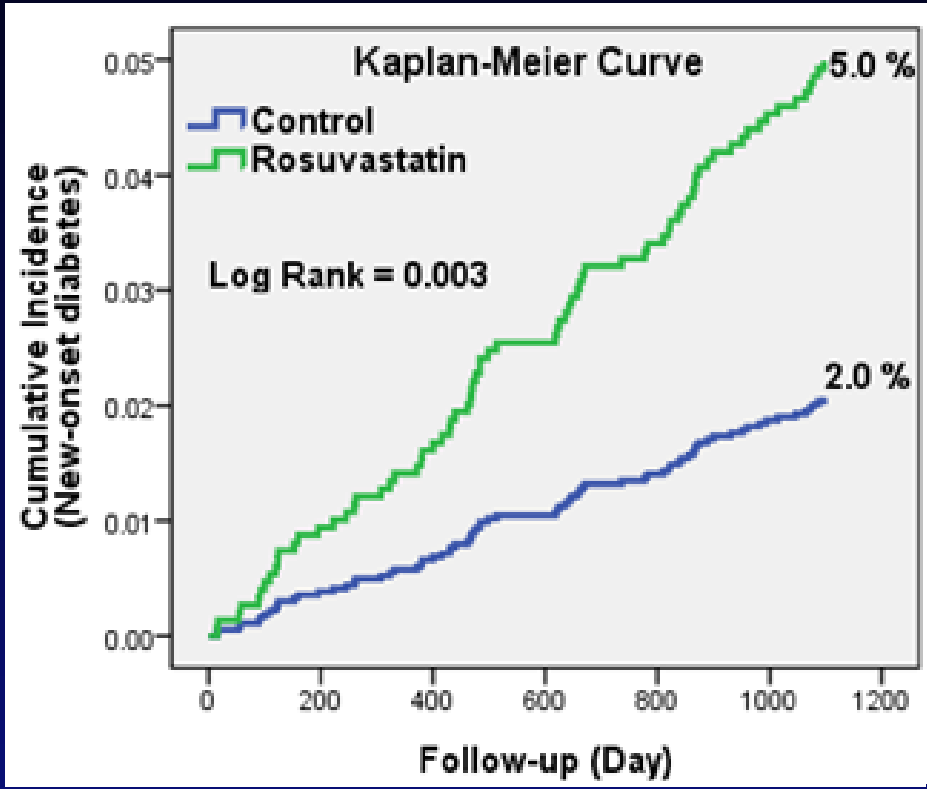
Current medication treatments

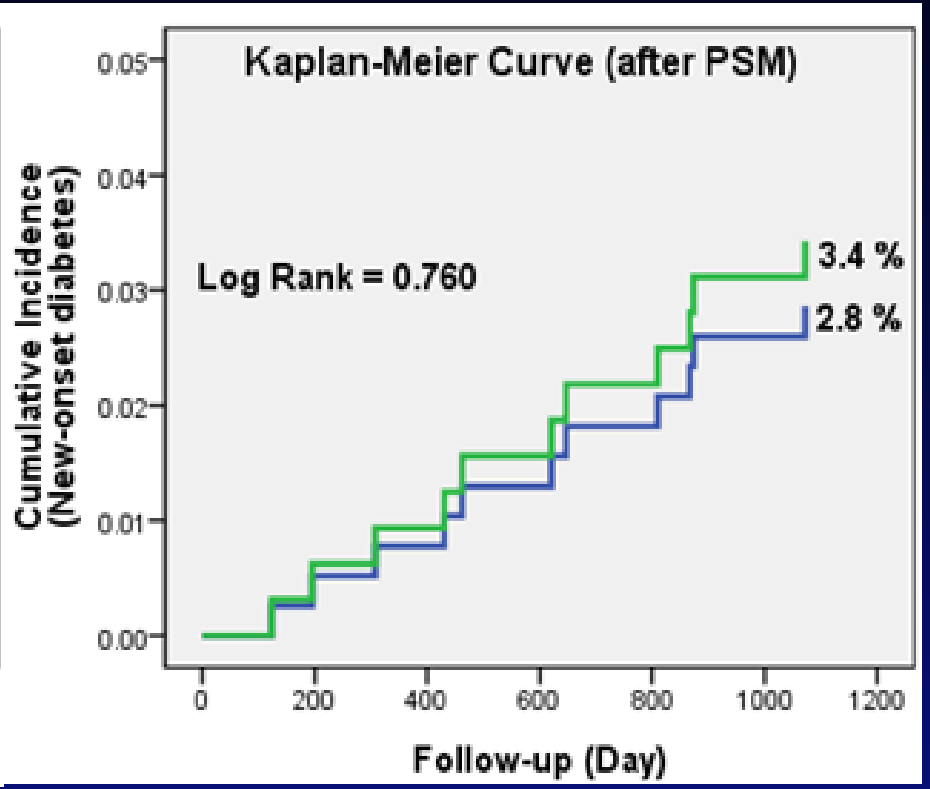
Variable.n	Entire Patients				Propensity score matching			
	Total (n=3,260)	Rosuva (n=260)	Control (n=3,000)	P-Value	Total (n=350)	Rosuva (n=175)	Control (n=175)	P-Value
Current medication treatments								
Anti-hypertensive drug	2277 (69.8)	221 (85)	2056 (68.5)	< 0.001	284 (81.1)	145 (82.8)	139 (79.4)	0.412
Beta blocker	629 (19.2)	89 (34.2)	540 (18.0)	< 0.001	88 (25.1)	44 (25.1)	44 (25.1)	-
Calcium channel blocker	1360 (41.7)	117 (45)	1243 (41.4)	0.263	169 (48.2)	85 (48.5)	84 (48.0)	0.915
ARB	906 (27.7)	83 (31.9)	823 (27.4)	0.121	100 (28.5)	58 (33.1)	42 (24.0)	0.058
ACEI	245 (7.5)	49 (18.8)	196 (6.5)	< 0.001	46 (13.1)	24 (13.7)	22 (12.5)	0.752
Diuretics	669 (20.5)	46 (17.6)	623 (20.7)	0.239	72 (20.5)	34 (19.4)	38 (21.7)	0.597
STATIN	260 (7.9)	260 (100)	-	-	175 (50.0)	175 (100.0)	-	-

Three-year Clinical Outcomes

Variable.n	Entire Patients				Propensity score matching			
	Total (n=3,260)	Rosuva (n=260)	Control (n=3,000)	P-Value	Total (n=350)	Rosuva (n=175)	Control (n=175)	P-Value
Five-year Clinical Outcomes								
New onset diabetes	75 (2.3)	13 (5.0)	62 (2.0)	0.002	11 (3.1)	6 (3.4)	5 (2.8)	0.759
Follow-up day	823.9 ± 395.4	986.3 ± 274.6	809.8 ± 405.9	< 0.001	955.7 ± 299.5	955.1 ± 309.0	956.4 ± 290.1	0.969

Impact of Rosuvastatin on New-onset Diabetes





Conclusion

1. In our study, the relationship between the use of Rosuvastatin and the incidence of new-onset DM remains unclear.

2. Long-term follow up with larger study population will be necessary for final conclusion.

Impact of Simvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical Follow up Results

Seung-Woon Rha, Byoung Geol Choi, Yunjee Park,
Se Yeon Choi, Sung Il Im, Jin Oh Na, Cheol Ung Choi,
Hong Euy Lim, Jin Won Kim, Eung Ju Kim, Chang Gyu Park,
Hong Seog Seo, Dong Joo Oh

Cardiovascular Center,
Korea University Guro Hospital

Methods

3. Study Groups

Simvastatin = 436 pts

No Simvastatin = 3,000 pts

4. Study Endpoint

The primary end-point was the cumulative incidence of new-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL)

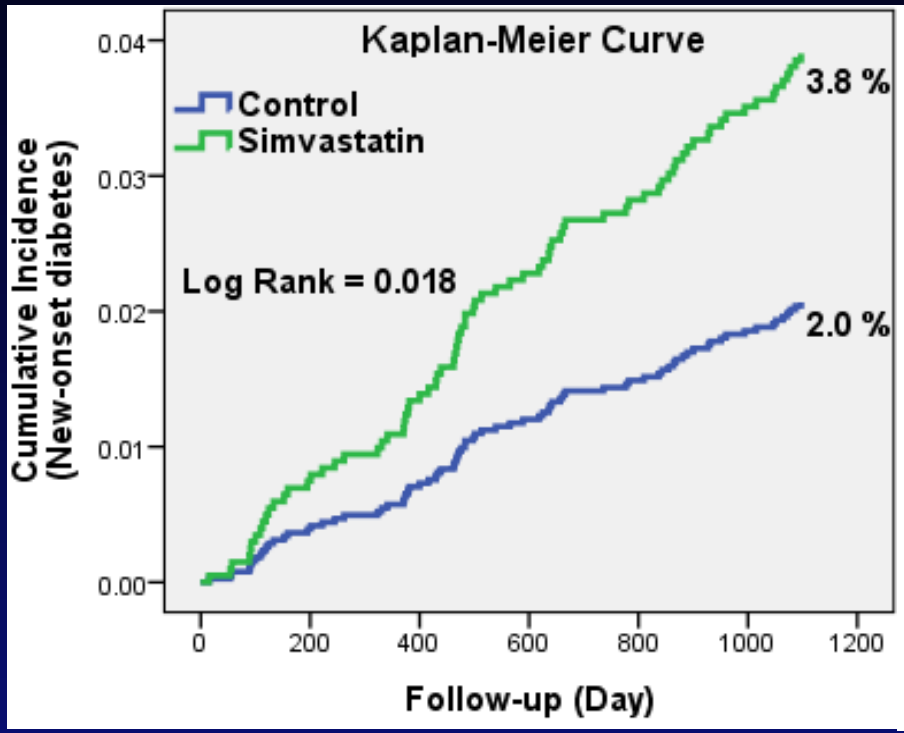
Current medication treatments

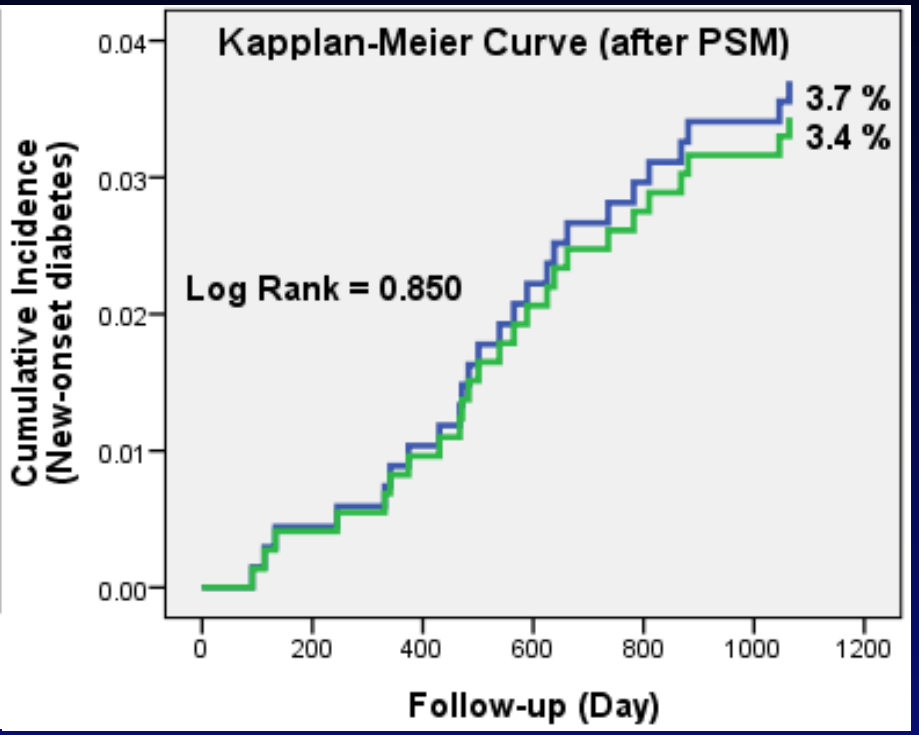
Variables, n(%)	Entire Patients				Propensity score matching			
	Total (n=3,436)	Simva (n=436)	Control (n=3,000)	P-Value	Total (n=700)	Simva (n=350)	Control (n=350)	P-Value
Current medication treatments								
Anti-hypertensive drug	2388 (69.4)	332 (76.1)	2056 (68.5)	0.001	529 (75.5)	263 (75.1)	266 (76)	0.792
Beta blocker	662 (19.2)	122 (27.9)	540 (18.0)	< 0.001	175 (25.0)	87 (24.8)	88 (25.1)	0.930
Calcium channel blocker	1442 (41.9)	199 (45.6)	1243 (41.4)	0.096	309 (44.1)	157 (44.8)	152 (43.4)	0.704
ARB	962 (27.9)	139 (31.8)	823 (27.4)	0.053	218 (31.1)	114 (32.5)	104 (29.7)	0.414
ACEI	237 (6.8)	41 (9.4)	196 (6.5)	0.027	54 (7.7)	28 (8.0)	26 (7.4)	0.777
Diuretics	716 (20.8)	93 (21.3)	623 (20.7)	0.787	152 (21.7)	80 (22.8)	72 (20.5)	0.463
STATIN	436 (12.6)	436 (100.0)	-	-	350 (50.0)	350 (100.0)	-	-

Three-year Clinical Outcomes

Variables, n(%)	Entire Patients				Propensity score matching			
	Total (n=3,436)	Simva (n=436)	Control (n=3,000)	P-Value	Total (n=700)	Simva (n=350)	Control (n=350)	P-Value
Five-year Clinical Outcomes								
New onset diabetes	79 (2.2)	17 (3.8)	62 (2.0)	0.017	25 (3.5)	12 (3.4)	13 (3.7)	0.839
Follow-up day	831.5 ± 390.6	981.0 ± 285.3	809.8 ± 405.9	< 0.001	972.0 ± 286.8	961.4 ± 307.3	982.5 ± 266.4	0.332

Impact of Simvastatin on New-onset Diabetes





Conclusion

1. In our study, the relationship between the use of Simvastatin and the incidence of new-onset DM remains unclear.

2. Long-term follow up with larger study population will be necessary for further information.

Impact of Pitavastatin on the Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical Follow up Results

Yoonjee Park, Seung-Woon Rha, Byoung Geol Choi, Se Yeon Choi, Raghu Akkala, Sunki Lee, Ji Bak Kim, Sung Il Im, Jin Oh Na, Cheol Ung Choi, Hong Euy Lim, Jin Won Kim, Eung Ju Kim, Chang Gyu Park, Hong Seog Seo, Dong Joo Oh

Cardiovascular Center,

Korean University Guro Hospital

KSC 2013

Methods

3. Study Groups

1) Pitavastatin = 147 pts
2) No Pitavastatin = 3,000 pts

4. Study Endpoint

The primary end-point was the cumulative incidence of new-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL)

American Diabetes A. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36 Suppl. 1:S67-74.

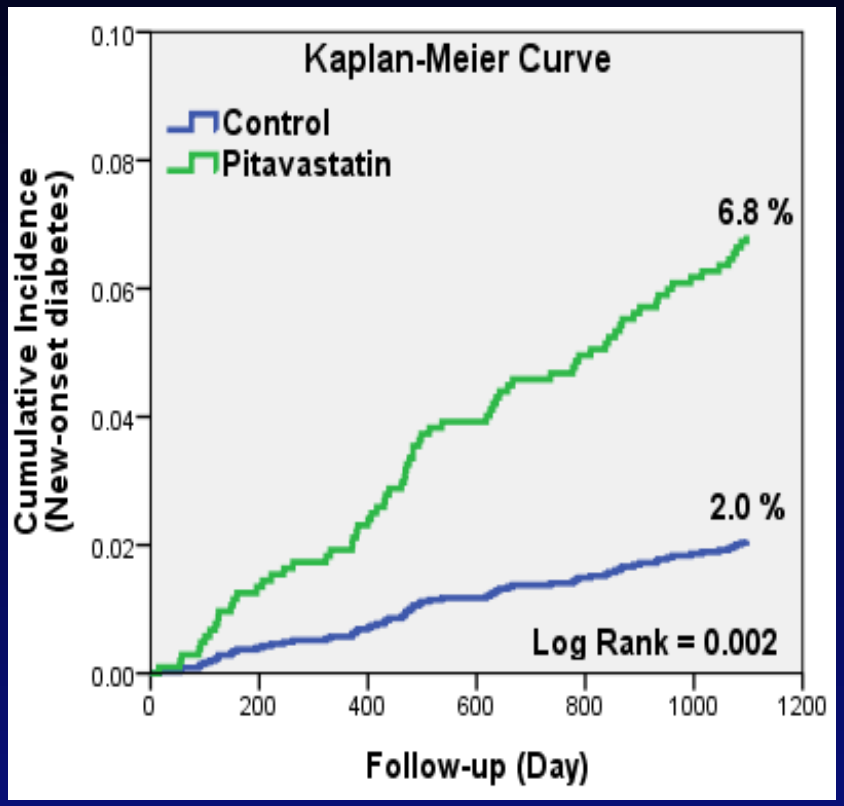
Current medication treatments

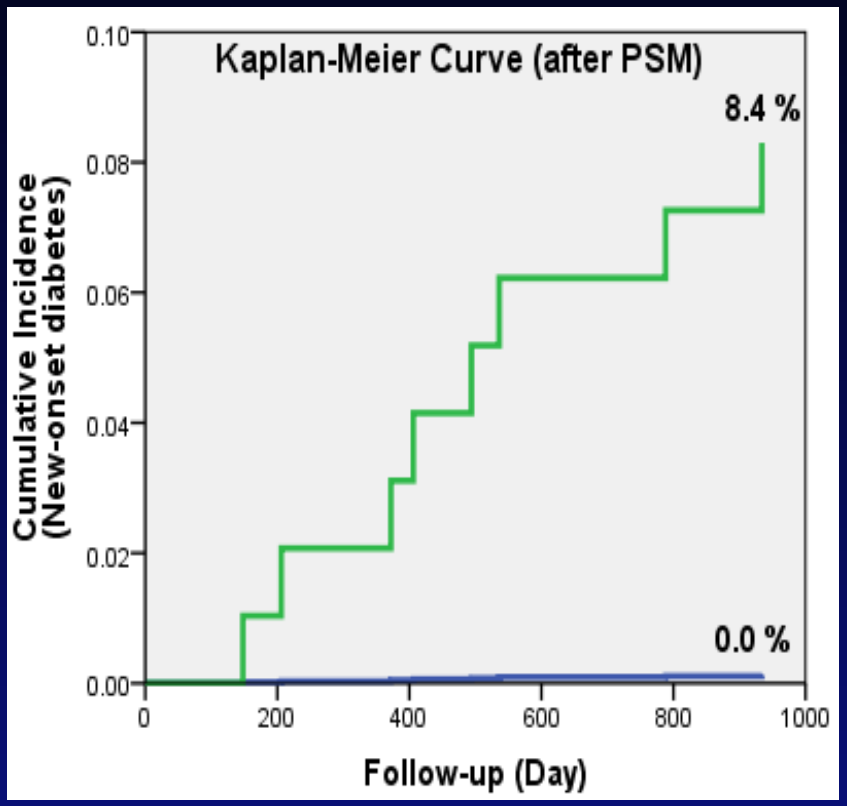
Variables, n (%)	Entire Patients				Propensity score matching			
	Total (n=3,147)	Pitava (n=147)	Control (n=3,000)	P-Value	Total (n=190)	Pitava (n=95)	Control (n=95)	P-Value
Current medication treatments								
Anti-hypertensive drug	2178 (69.2)	122 (82.9)	2056 (68.5)	< 0.001	144 (75.7)	74 (77.8)	70 (73.6)	0.498
Beta blocker	603 (19.1)	63 (42.8)	540 (18.0)	< 0.001	66 (34.7)	34 (35.7)	32 (33.6)	0.761
Calcium channel blocker	1302 (41.3)	59 (40.1)	1243 (41.4)	0.755	81 (42.6)	41 (43.1)	40 (42.1)	0.883
ARB	863 (27.4)	40 (27.2)	823 (27.4)	0.953	45 (23.6)	26 (27.3)	19 (20.0)	0.232
ACEI	222 (7)	26 (17.6)	196 (6.5)	< 0.001	17 (8.9)	9 (9.4)	8 (8.4)	0.799
Diuretics	649 (20.6)	26 (17.6)	623 (20.7)	0.368	40 (21.0)	21 (22.1)	19 (20.0)	0.722
STATIN	147 (4.6)	147 (100)	-	-	95 (50.0)	95 (100.0)	-	-

Three-year Clinical Outcomes

Variables, n (%)	Entire Patients				Propensity score matching			
	Total (n=3,147)	Pitava (n=147)	Control (n=3,000)	P-Value	Total (n=190)	Pitava (n=95)	Control (n=95)	P-Value
Five-year Clinical Outcomes								
New onset diabetes	72 (2.2)	10 (6.8)	62 (2.0)	< 0.001	8 (4.2)	8 (8.4)	0 (0.0)	0.004
Follow-up day	818 ± 399	997 ± 270	809 ± 405	< 0.001	962 ± 299	974 ± 295	949 ± 303	0.567

Impact of Pitavastatin on New-onset Diabetes





Conclusion

In our study, the chronic use of pitavastatin was associated with an increased incidence of new-onset DM at 3 years.

Impact of Fluvastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Follow up Results

Seung-Woon Rha, Byoung Geol Choi, Yunjee Park,
Se Yeon Choi, Sung Il Im, Jin Oh Na, Cheol Ung Choi,
Hong Euy Lim, Jin Won Kim, Eung Ju Kim, Chang Gyu Park,
Hong Seog Seo, Dong Joo Oh

Cardiovascular Center,
Korea University Guro Hospital

Methods

3. Study Groups

Fluvastatin = 119 pts

No Fluvastatin = 3,000 pts

4. Study Endpoint

The primary end-point was the cumulative incidence of new-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL)

Current medication treatments

Variable.n	Entire Patients				Propensity score matching			
	Total (n=3,119)	Fluva (n=119)	Control (n=3,000)	P-Value	Total (n=164)	Fluva (n=82)	Control (n=82)	P-Value
Current medication treatments								
Anti-hypertensive drug	2148 (68.8)	92 (77.3)	2056 (68.5)	0.043	119 (72.5)	59 (71.9)	60 (73.1)	0.861
Beta blocker	561 (17.9)	21 (17.6)	540 (18.0)	0.922	31 (18.9)	16 (19.5)	15 (18.2)	0.842
Calcium channel blocker	1298 (41.6)	55 (46.2)	1243 (41.4)	0.299	73 (44.5)	41 (50.0)	32 (39.0)	0.157
ARB	861 (27.6)	38 (31.9)	823 (27.4)	0.282	44 (26.8)	22 (26.8)	22 (26.8)	-
ACEI	215 (6.8)	19 (15.9)	196 (6.5)	< 0.001	20 (12.1)	8 (9.7)	12 (14.6)	0.340
Diuretics	642 (20.5)	19 (15.9)	623 (20.7)	0.204	31 (18.9)	18 (21.9)	13 (15.8)	0.319

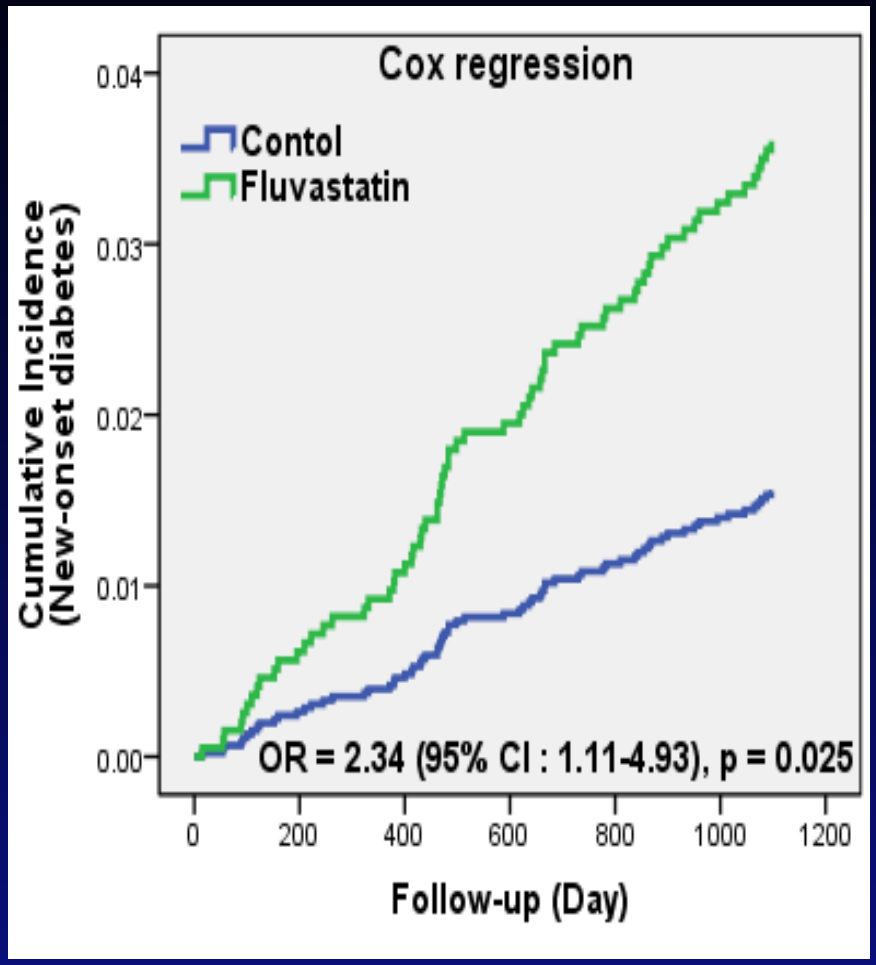
Three-year Clinical Outcomes

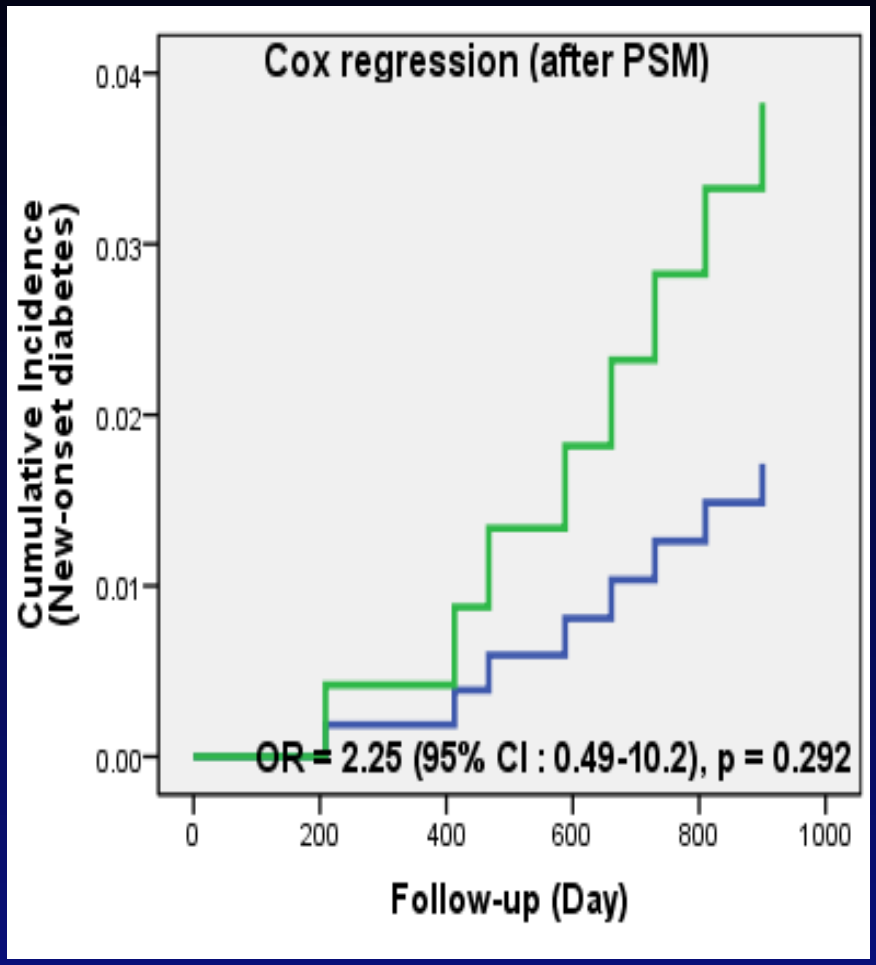
Variable.n	Entire Patients				Propensity score matching			
	Total (n=3,119)	Fluva (n=119)	Control (n=3,000)	P-Value	Total (n=164)	Fluva (n=82)	Control (n=82)	P-Value
Five-year Clinical Outcomes								
New onset diabetes	70 (2.2)	8 (6.7)	62 (2.1)	0.001	8 (4.9)	5 (6.1)	6 (3.7)	0.386
Follow-up day	815.3 ± 402.0	954.3 ± 304.5	809.8 ± 405.9	< 0.001	895.4 ± 354.1	901.5 ± 347.4	889.3 ± 360.8	0.826

Predictors of New-onset Diabetes on 3-years Clinical Outcomes

	Entire Patients		Propensity score matching	
Variables,n	OR (95% CI)	P-Value	OR (95% CI)	P-Value
Gender (Male)	1.23 (0.76-1.99)	0.380	1.69 (0.37-7.56)	0.490
Age	1.03 (1.01-1.06)	< 0.001	0.99 (0.92-1.05)	0.791
Hypertension	1.00 (0.93-1.07)	0.854	1.65 (0.32-8.50)	0.547
Dyslipidemia	0.89 (0.55-1.45)	0.666	0.56 (0.09-3.27)	0.524
Coronary artery spasm	1.11 (0.60-2.04)	0.736	5.60 (0.99-31.5)	0.051
Alcoholic history	1.23 (0.48-3.10)	0.659	1.01 (0.80-1.28)	0.911
HbA1c	4.74 (1.75-12.8)	0.002	30.2 (0.38-2392)	0.126
Fasting glucose	1.01 (0.98-1.05)	0.232	1.04 (0.94-1.16)	0.388
Fluvastatin*	2.34 (1.11-4.93)	0.025	2.25 (0.49-10.2)	0.292

Cumulative Incidence of New-onset Diabetes





Conclusion

1. In our study, the impact of chronic fluvastatin use on the incidence of new-onset DM remains unclear.

2. Long-term follow up with a larger study population will be necessary for final conclusion.

Impact of Pravastatin on Development of New-onset Diabetes Mellitus in Asian Population: Three-year Clinical Follow up Results

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KSC 2013

Methods

3. Study Groups

Pravastatin = 179 pts

No Pravastatin = 3,000 pts

4. Study Endpoint

The primary end-point was the cumulative incidence of new-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL)

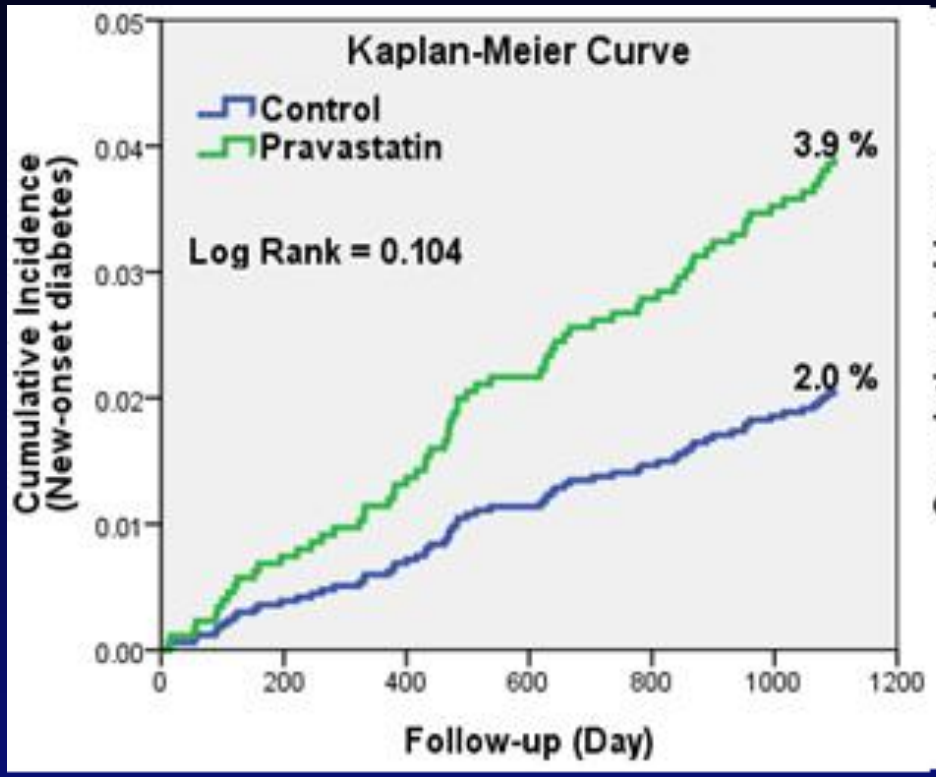
Current medication treatments

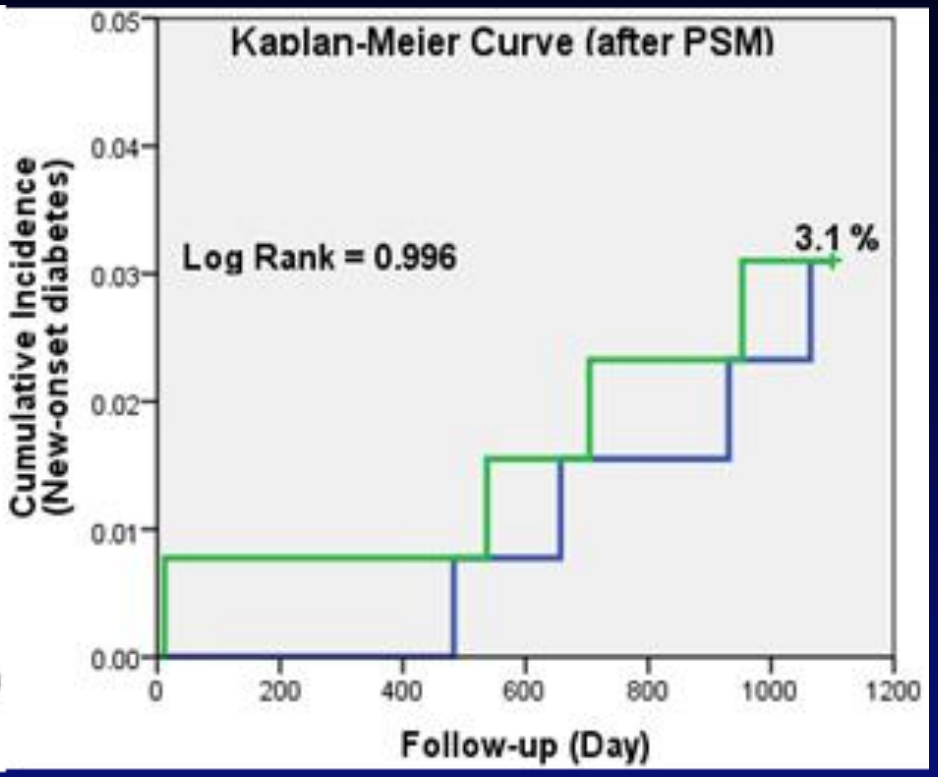
Variable.n	Entire Patients				Propensity score matching			
	Total (n=3,179)	Prava (n=179)	Control (n=3,000)	P-Value	Total (n=258)	Prava (n=129)	Control (n=129)	P-Value
Current medication treatments								
Anti-hypertensive drug	2196 (69)	140 (78.2)	2056 (68.5)	0.006	205 (79.4)	102 (79)	103 (79.8)	0.878
Beta blocker	583 (18.3)	43 (24.0)	540 (18.0)	0.043	60 (23.2)	32 (24.8)	28 (21.7)	0.556
Calcium channel blocker	1329 (41.8)	86 (48.0)	1243 (41.4)	0.081	130 (50.3)	66 (51.1)	64 (49.6)	0.803
ARB	885 (27.8)	62 (34.6)	823 (27.4)	0.037	89 (34.4)	47 (36.4)	42 (32.5)	0.513
ACEI	216 (6.7)	20 (11.1)	196 (6.5)	0.017	16 (6.2)	11 (8.5)	5 (3.8)	0.121
Diuretics	657 (20.6)	34 (18.9)	623 (20.7)	0.569	52 (20.1)	27 (20.9)	25 (19.3)	0.756
STATIN	179 (5.6)	179 (100.0)	-	-	129 (50.0)	129 (100.0)	-	-

Three-year Clinical Outcomes

Variable.n	Entire Patients				Propensity score matching			
	Total (n=3,179)	Prava (n=179)	Control (n=3,000)	P-Value	Total (n=258)	Prava (n=129)	Control (n=129)	P-Value
Five-year Clinical Outcomes								
New onset diabetes	69 (2.1)	7 (3.9)	62 (2.0)	0.100	8 (3.1)	4 (3.1)	4 (3.1)	NS
Follow-up day	819.6 ± 398.7	984.1 ± 278.0	809.8 ± 405.9	< 0.001	957.4 ± 306.7	972.5 ± 295.2	942.2 ± 318.3	0.428

Impact of Pravastatin on New-onset Diabetes





Conclusion

In our study, the use of Pravastatin seems to have no significant impact on the development of new-onset DM, at least up to 3 years.

Impact of Chronic Statin Therapy on Development of Glucose Intolerance and New-onset Diabetes Mellitus in Asian Population

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AHA 2013

Methods

1. Study Population

We investigated total 13,561 pts who showed hemoglobin A1C level ≤ 5.7% and fasting glucose level < 100 mg/dL from January 2004 to February 2010.

American Diabetes A. Diagnosis and classification of diabetes mellitus. Diabetes Care 2013;36 Suppl 1:S67-74.

2. Study Groups

Statin therapy group (n=2,324 pts)

Control group (n=8,670 pts)

Methods

3. Study Endpoint

The primary end-point was the cumulative incidence of IGT or New-onset DM (HbA1C level > 6.5% or fasting glucose level > 126 mg/dL) up to 2 years.

Three-year Clinical Outcomes

Variable	All Patients (n=10994)	Statin Use (n=2324)	No Use (n=8670)	P-value
Clinical outcomes at 3yrs				
New-onset diabetes	227 (2.0)	116 (4.9)	111 (1.2)	< 0.001
Mortarity	66 (0.6)	18 (0.7)	48 (0.5)	0.221
Cardiac death	21 (0.1)	10 (0.4)	11 (0.1)	0.006
Myocardial infarction	22 (0.3)	14 (1.0)	8 (0.1)	< 0.001
Cerebrovascular accidents	37 (0.3)	11 (0.4)	26 (0.2)	0.200
MACCE	98 (0.8)	34 (1.4)	64 (0.7)	0.001

Three-year Clinical Outcomes After Propensity Score Matching

Variable	All Patients (n=3398)	Statin Use (n=1699)	No Use (n=1699)	P-value
Clinical outcomes at 3yrs				
New-onset diabetes	121 (3.5)	80 (4.7)	41 (2.4)	< 0.001
Mortarity	31 (0.9)	8 (0.4)	23 (1.3)	0.007
Cardiac death	10 (0.2)	3 (0.1)	7 (0.4)	0.205
Myocardial infarction	10 (0.5)	4 (0.4)	6 (0.6)	0.755
Cerebrovascular accidents	21 (0.6)	6 (0.3)	15 (0.8)	0.049
MACCE	46 (1.3)	15 (0.8)	31 (1.8)	0.018

Risk of Diabetes Mellitus (DM) and MACCE by Statin Use

		Risk of Diabetes Mellitus (DM) and MACCE by Statin Use			
		Type 2 DM		MACCE	
Description	Patients. No.	OR (95% CI)	P Value	OR (95% CI)	P Value
Unadjusted OR	10 994	4.05 (3.10-5.27)	< 0.001	1.99 (1.31-3.03)	0.001
Adjusted OR (95% CI)					
Multivariate	10 994	2.70 (1.99-3.67)	< 0.001	0.70 (0.42-1.18)	0.191
Propensity score	10 994	2.71 (1.94-3.79)	< 0.001	0.50 (0.29-0.87)	0.015
Multivariate including propensity score	10 994	2.55 (1.86-3.49)	< 0.001	0.58 (0.33-1.00)	0.052
Propensity score matched	3398	1.99 (1.36-2.92)	< 0.001	0.47 (0.25-0.89)	0.020

*Adjusted by propensity score includind Age gender, hypertension, myocardial infarction, PTCA, Coronary artery spasm, dyslipidemia, heart failure, angina pectoris, chest pain, artrial filbriation, cardiac arrhythmia, A1c, fasting glucose total cholesterol, triglyceride, HDL c holesterol, LDL cholesterol, ARB, ACEI, CCB, BB, Diuretics, Statins

Risk of Diabetes Mellitus (DM) and MACCE by Statin Use

		Risk of Diabetes Mellitus (DM) and MACCE by Statin Use			
		Type 2 DM		MACCE	
Subanalysis Description	Patients. No.	OR (95% CI)	P Value	OR (95% CI)	P Value
Gender					
Male	**5351**	3.15 (2.06-4.81)	< 0.001	0.56 (0.27-1.15)	0.119
Female	**5643**	1.93 (1.19-3.13)	0.007	0.57 (0.24-1.35)	0.202
Age					
< 60	**7313**	2.62 (1.58-4.35)	< 0.001	0.76 (0.22-2.59)	0.667
60-70	**2293**	2.48 (1.42-4.32)	0.001	0.40 (0.14-1.13)	0.086
>70	**1387**	2.45 (1.34-4.48)	0.004	0.61 (0.28-1.32)	0.217
Hypertension					
Yes	**4422**	2.50 (1.66-3.77)	< 0.001	0.53 (0.24-1.18)	0.123
No	**6572**	2.55 (1.55-4.18)	< 0.001	0.64 (0.30-1.40)	0.272
Dyslipidemia					
Yes	**1722**	3.05 (1.47-6.33)	0.003	0.13 (0.03-0.56)	0.006
No	**9272**	2.48 (1.74-3.53)	< 0.001	0.81 (0.45-1.47)	0.505
Coronary artery disease					
Yes	**1079**	4.19 (1.44-12.2)	0.008	0.29 (0.12-0.72)	0.008
No	**9915**	2.43 (1.74-3.39)	< 0.001	0.82 (0.44-1.53)	0.539
Coronary spasm					
Yes	**381**	1.83 (0.47-7.12)	0.378	18.2 (0.21-1518)	0.198
No	**10613**	2.62 (1.89-3.62)	< 0.001	0.51 (0.29-0.90)	0.021
Cerebrovascular accident					
Yes	**1108**	2.64 (1.44-4.84)	0.002	0.65 (0.25-1.65)	0.368
No	**9886**	2.22 (1.53-3.21)	< 0.001	0.55 (0.28-1.06)	0.078

*** Adjusted by Gender (Male), Age, Hypertension, Cardiovascular disease, Coronary spasm, Dyslipidemia, ARBs, ACEIs, CCBs, Beta -blockers, Diuretics, nitrates, Statins, Propensity score**

Multivariate analysis for predicting New onset DM or MACCE

		Risk of Diabetes Mellitus (DM) and MACCE by Statin Use			
		Type 2 DM		MACCE	
Subanalysis Description	Patients. No.	OR (95% CI)	P Value	OR (95% CI)	P Value
Gender (Male)	5351 (48.6)	1.52 (1.15-2.01)	0.003	1.35 (0.87-2.08)	0.171
Age, [median, IQR]	53.6 [44.3-63.5]	1.02 (1.01-1.04)	< 0.001	1.06 (1.04-1.08)	< 0.001
Hypertension	4422 (40.2)	1.33 (1.01-1.76)	0.041	0.67 (0.43-1.02)	0.066
Cardiovascular disease	1079 (9.8)	0.61 (0.37-1.00)	0.054	1.91 (1.01-3.61)	0.044
Coronary spasm	381 (3.4)	1.38 (0.75-2.54)	0.286	1.02 (0.36-2.87)	0.960
Dyslipidemia	1722 (15.6)	0.91 (0.63-1.32)	0.636	0.95 (0.55-1.64)	0.864
ARBs	1974 (17.9)	1.20 (0.84-1.71)	0.310	0.86 (0.48-1.53)	0.617
ACEIs	614 (5.5)	0.56 (0.31-1.02)	0.059	1.58 (0.81-3.07)	0.176
CCBs	1448 (13.1)	0.71 (0.52-0.98)	0.038	0.73 (0.45-1.18)	0.205
Beta blockers	2976 (27.0)	1.25 (0.88-1.77)	0.196	0.93 (0.54-1.59)	0.792
Diuretics	1573 (14.3)	1.74 (1.23-2.45)	0.001	1.52 (0.89-2.58)	0.122
Nitrates	1772 (16.1)	0.85 (0.55-1.31)	0.483	0.72 (0.38-1.36)	0.320
Statins	2324 (21.1)	2.55 (1.86-3.49)	< 0.001	0.54 (0.31-0.94)	0.032
Type 2 DM	227 (2.0)	-	-	3.40 (1.68-6.89)	0.001
Statin Use	116 (4.9)	-	-	4.40 (1.71-11.2)	0.002
No Use	111 (1.2)	-	-	2.55 (0.86-7.55)	0.089

* Adjusted by Gender (Male), Age, Hypertension, Cardiovascular disease, Coronary spasm, Dyslipidemia, ARBs, ACEIs, CCBs, Beta blockers, Diuretics, Nitrates, Statins, Propensity score
* IQR; Interquartile range, * NA;Not applicable

Statins and NODM-Summary

1. Atorvastatin (Lipitor)-Yes (566)
2. Rosuvastatin (Crestor)-No (260)
3. Simvastatin (Zocor)-No (436)
4. Pitavastatin (Livalo)-Yes (147,?)
5. Fluvastatin (Lescol)-No (117, ?)
6. Pravastatin (Mevalotin)-No (179,?)
7. Overall Statins-Yes (2,324)

*4,5,6; limited N number for final conclusion

Conclusion

Despite of higher risk of new-onset DM following chronic statin use, net benefit for risk reduction of overall clinical events should be considered, particularly in higher risk patients.

Take home messages (1)

1. Clinical studies have linked statins with the development of new-onset and incident diabetes
2. Statin-induced diabetes can be predicted by:
   - Baseline fasting glucose >100 mg/dL
   - Components of metabolic syndrome: Higher triglycerides (>150 mg/dL), higher BMI (>30 kg/m^2), age and hypertension.
3. Statin therapy has a dose-dependent risk of development of new-onset diabetes, but also a dose-dependent benefit in terms of CV events

Take home messagesm (2)

4. The benefits of statin therapy outweigh the risks
   - The absolute risk of developing diabetes is one case per 1000 patient-years of treatment
   - Statins are eight times more likely to prevent CV even ts than cause 1 case of diabetes

5. The cardiovascular and mortality benefits of rosuvastatin exceed the hazard of diabetes, even in patients who are at high risk of developing diabetes

Thank you for your attention