ΣΤΑΤΙΝΕΣ ΚΑΙ ΚΙΝΔΥΝΟΣ ΕΜΦΑΝΙΣΗΣ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ-ΝΕΟΤΕΡΑ ΕΠΙΣΤΗΜΟΝΙΝΑ ΔΕΔΟΜΕΝΑ

ΜΩΥΣΗΣ ΕΛΙΣΑΦ,
ΚΑΘΗΓΗΤΗΣ ΠΑΘΟΛΟΓΙΑΣ ΙΑΤΡΙΚΗΣ ΣΧΟΛΗΣ ΠΑΝΕΠΙΣΤΗΜΙΟΥ ΙΩΑΝΝΙΝΩΝ

FDA, 2012

STATINS AND DIABETES MELLITUS

GLYCEMIC CONTROL vs LIPID LOWERING THERAPY IN DIABETES

GLYCEMIC CONTROL: 2.9 ΛΙΓΟΤΕΡΑ ΣΥΜΒΑΜΑΤΑ ΓΙΑ 200 ΑΣΘΕΝΕΙΣ ΥΠΟ ΑΓΩΓΗ ΓΙΑ 5 ΕΤΗ

ΣΤΑΤΙΝΕΣ: 8.2 ΛΙΓΟΤΕΡΑ ΣΥΜΒΑΜΑΤΑ ΓΙΑ ΚΑΘΕ ΜΕΙΩΣΗ ΤΗΣ LDL CHOL ΚΑΤΑ 40mg/dl

ΑΝΤΙΥΠΕΡΤΑΣΙΚΗ ΑΓΩΓΗ: 12.5 ΛΙΓΟΤΕΡΑ ΣΥΜΒΑΜΑΤΑ ΓΙΑ ΚΑΘΕ ΜΕΙΩΣΗ ΤΗΣ ΣΑΠ ΚΑΤΑ 4mmHg

LANCET 2009;373:1765-70

Rosuvastatin 20mg Is Associated With a 25% Increased Risk of Diabetes in Patients Without Evident CVD

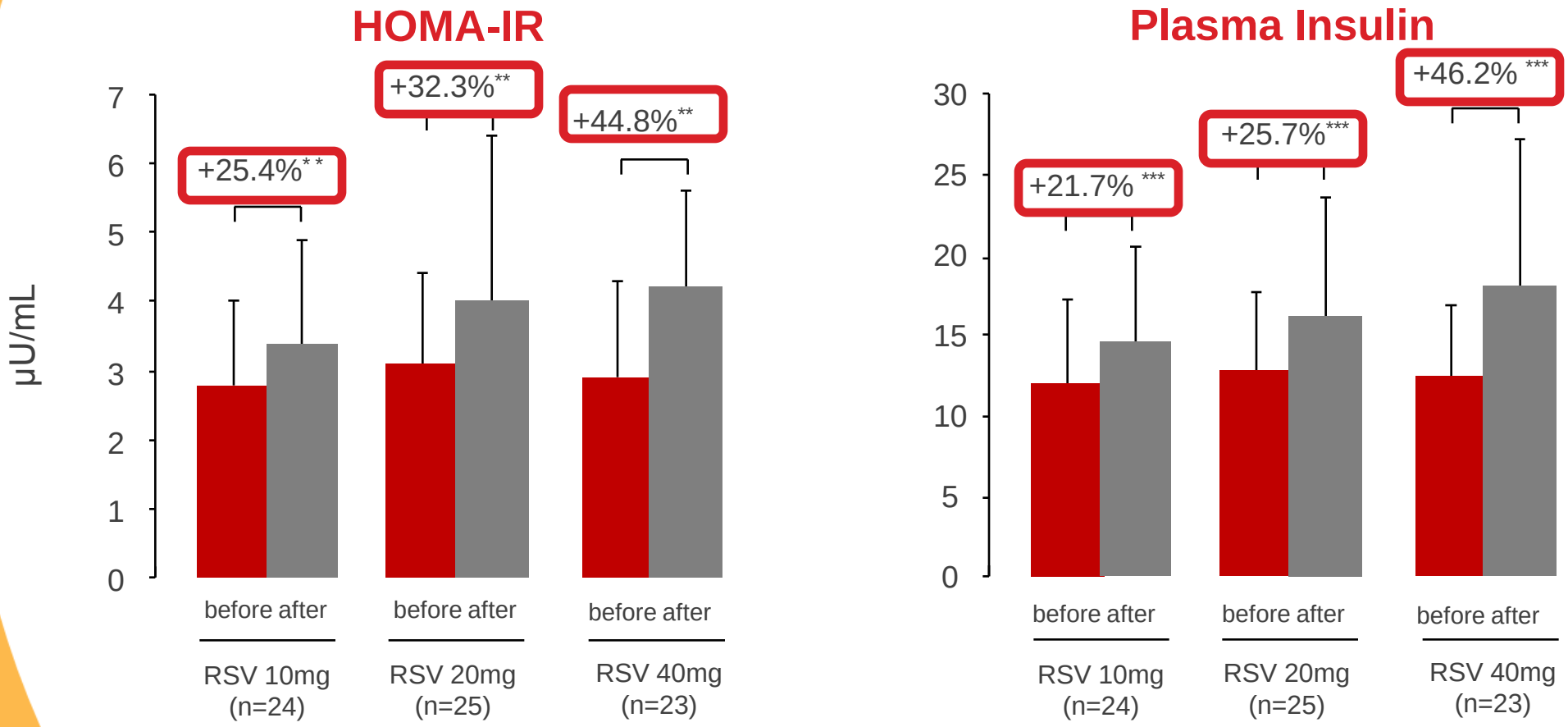
Analysis from JUPITER* (n=17,802)

Event	Rosuvastatin (N=8901)	Placebo (N=8901)	*P* Value
Monitored adverse events			
Any serious event – no. (%)	1352 (15.2)	1377 (15.5)	0.60
Muscular weakness, stiffness or pain – no. (%)	1421 (16.0)	1375 (15.4)	0.34
Myopathy – no. (%)	10 (0.1)	9 (0.1)	0.82
Rhabdomyolysis – no. (%)	1 (<0.1)	0	–
Newly diagnosed cancer – no. (%)	298 (3.4)	314 (3.5)	0.51
Death from cancer – no. (%)	35 (0.4)	58 (0.7)	0.02
Gastrointestinal disorder – no. (%)	1753 (19.7)	1711 (19.2)	0.43
Renal disorder – no. (%)	535 (6.0)	480 (5.4)	0.08
Bleeding – no. (%)	258 (2.9)	275 (3.1)	0.45
Hepatic disorder – no. (%)	216 (2.4)	186 (2.1)	0.13
Laboratory values			
Creatinine, >100% increase from baseline – no. (%)	16 (0.2)	10 (0.1)	0.24
Glomerular filtration rate at 12 mo – ml/min/1.73m^2			0.02
Median	66.8	66.6	
Interquartile range	59.1-76.5	58.8-76.2	
Alanine aminotransferase >3xULN on consecutive visits – no. (%)	23 (0.3)	17 (0.2)	0.34
Glycated haemoglobin at 24 mo - %			0.001
Median	5.9	5.8	
Interquartile range	5.7-6.1	5.6-6.1	
Fasting glucose at 24 mo – mg/dl			0.12
Median	98	98	
Interquartile range	91-107	90-106	
> Trace of glucose in urine at 12 mo – no. (%)	36 (0.5)	32 (0.4)	0.64
Other events			
Newly diagnosed diabetes (physician-reported) – no. (%)	270 (3.0)	216 (2.4)	0.01
Haemorrhagic stroke – no. (%)	6 (0.1)	9 (.01)	0.44

Ridker *et al. NEJM* 2008;359(21):2195-2207

*JUPITER: Justification for Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin

Rosuvastatin Causes Dose Dependent Insulin Resistance After 12 Weeks in Hyperlipidaemic Patients with Impaired Fasting Glucose

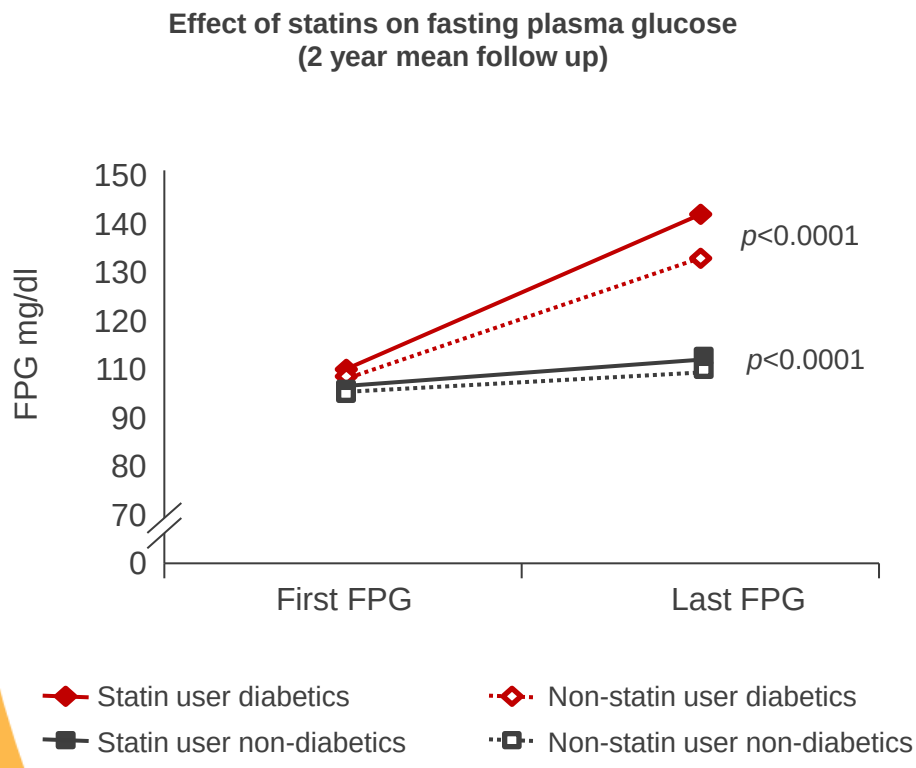


RSV: rosuvastatin; *** p<0.001; ** p<0.01 (*vs*. before)

HOMA-IR: Homeostatic Model of Insulin Resistance

Kostapanos *et al. Int J Clin Pract* 2009;63:1308-1313.

Statins Increase Fasting Plasma Glucose Among Those With and Without Diabetes After 2 Years



- Veterans base analysis (n=69,083) of the effect of statins on fasting plasma glucose (FPG)
- Patients taking statins experienced a significantly greater rise of FPG compared to those not taking statins ($p<0.0001$)
- This was independent of age and use of aspirin, beta-blockers, and angiotensin-converting enzyme inhibitors
- Statin use: simvastatin (69%), lovastatin (23%), atorvastatin (7%), others (1%)

Sukhija *et al. J Investig Med*. 2009 Mar;57(3):495-9.

ΣΤΑΤΙΝΕΣ ΚΑΙ ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ

ΜΕΤΑ-ΑΝΑΛΥΣΗ 13 ΜΕΛΕΤΩΝ, n=91.140

↑ ΚΙΝΔΥΝΟΥ ΕΜΦΑΝΙΣΗΣ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ ΚΑΤΑ 9%

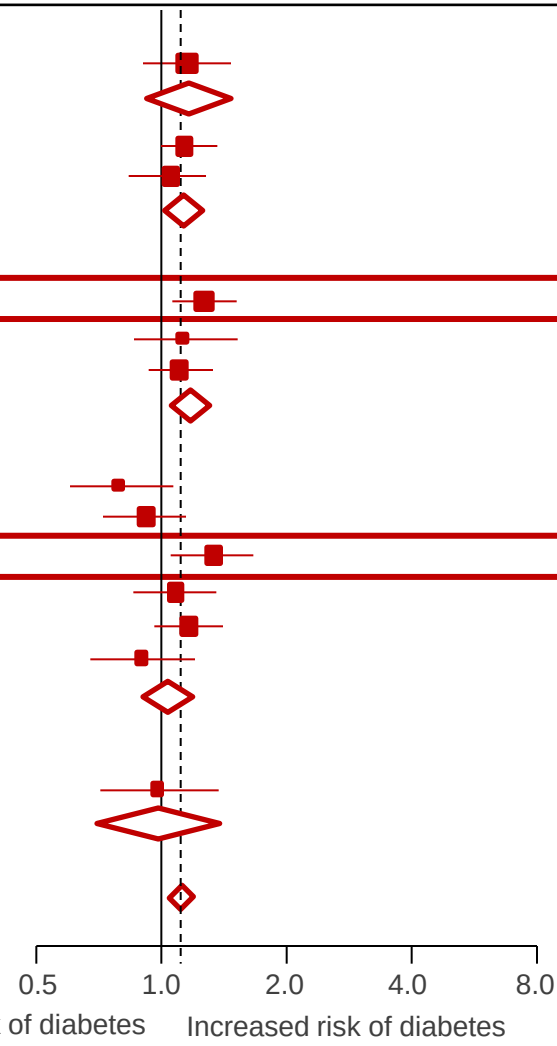
1.09[1.02-1.17]

LANCET 2010;375:735-742

Statins Increase the Risk of New Onset T2DM

9% risk of diabetes over 4 years (n=91,140)

	n	Statin	Placebo or control	OR (95% CI)	Weight (%)
Atorvastatin					
ASCOT-LLA	7773	154	134	1.14 (0.89-1.46)	7.07%
Simvastatin					
HPS	14573	335	293	1.15 (0.98-1.35)	13.91%
4S	4242	198	193	1.03 (0.84-1.28)	8.88%
Subtotal (I^2=0.0%, p=0.445)				1.11 (0.97-1.26)	22.80%
Rosuvastatin					
JUPITER	17802	270	216	1.26 (1.04-1.51)	11.32%
CORONA	3534	100	88	1.14 (0.84-1.55)	4.65%
GISSI HF	3378	225	215	1.10 (0.89-1.35)	9.50%
Subtotal (I^2=0.0%, p=0.607)				1.18 (1.04-1.33)	25.46%
Pravastatin					
WOSCOPS	5974	75	93	0.79 (0.58-1.10)	4.24%
LIPID	6997	126	138	0.91 (0.71-1.17)	6.53%
PROSPER	5023	165	127	1.32 (1.03-1.69)	6.94%
MEGA	6086	172	164	1.07 (0.86-1.35)	8.03%
ALLHAT-LLT	6087	238	212	1.15 (0.95-1.41)	10.23%
GISSI PREVENZIONE	3460	96	105	0.89 (0.67-1.20)	4.94%
Subtotal (I^2=47.5%, p=0.090)				1.03 (0.90-1.19)	40.91%
Lovastatin					
AFCAPS/TexCAPS	6211	72	74	0.98 (0.70-1.38)	3.76%
Overall (I^2=11.2%)				**1.09 (1.02-1.17)**	**100%**



Sattar *et al. Lancet* 2010; 375: 735-42

POST-HOC ANALYSIS OF THE SPARCL

ATORVA 80mg/d: ΣΧΕΤΙΚΟΣ ΚΙΝΔΥΝΟΣ ΓΙΑ ΤΗΝ ΕΜΦΑΝΙΣΗ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ 1.37[1.08-1.75], p=0.011

JACC 2011;57:1135

ΔΟΣΟΕΞΑΡΤΩΜΕΝΗ ΔΙΑΒΗΤΟΓΟΝΟΣ ΔΡΑΣΗ ΤΩΝ ΣΤΑΤΙΝΩΝ

ΜΕΤΑ-ΑΝΑΛΥΣΗ 5 ΜΕΛΕΤΩΝ, n=32.752 ΑΤΟΜΑ

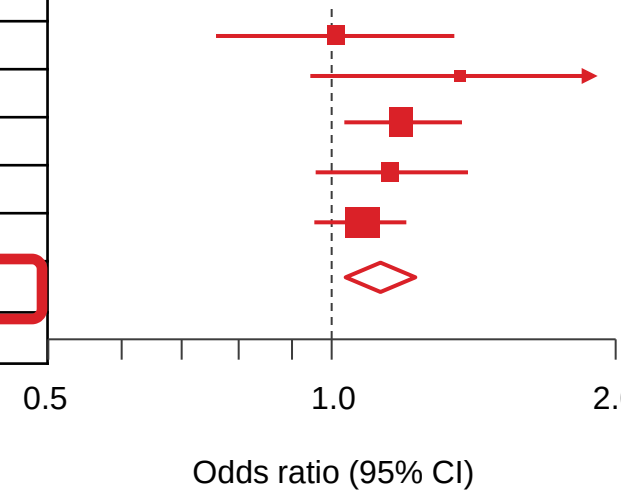
INTENSIVE vs STANDARD-DOSE STATINS / ΣΧΕΤΙΚΟΣ ΚΙΝΔΥΝΟΣ ΕΜΦΑΝΙΣΗΣ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ: 1.12

JAMA 2011;305:2556-2564

Intensive Statin Doses Increase the Risk of Diabetes Development

Pooled analysis of 5 statin trials (n=32,752)

	Cases/Total, No (%)		
Incident diabetes	**Intensive dose**	**Moderate dose**	**OR (95% CI)**
PROVE IT-TIMI 22	101/1707 (5.9)	99/1688 (5.9)	1.01 (0.76-1.34)
A to Z	65/1768 (3.7)	47/1736 (2.7)	1.37 (0.94-2.01)
TNT	418/3798 (11.0)	358/3797 (9.4)	1.19 (1.02-1.38)
IDEAL	240/3737 (6.4)	209/3724 (5.6)	1.15 (0.95-1.40)
SEARCH	625/5398 (11.6)	587/5399 (10.9)	1.07 (0.95-1.21)
Pooled odds ratio	1449/16,408 (8.8)	1300/16,344 (8.0)	1.12 (1.04-1.22)
Heterogeneity: I^2=0%; p=0.60			



PROVE-IT: atorvastatin 80mg *vs.* Pravastatin 40mg; A to Z: simvastatin 40/80mg *vs*. 20mg;
TNT: Atorvastatin 80mg *vs.* 10mg; IDEAL: atorvastatin 80mg *vs.* simvastatin 20mg;
SEARCH: Simvastatin 80mg *vs.* 20mg

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

A Positive Correlation Exists Between the Risk of New-onset Diabetes and Atorvastatin Dose

SPARCL (Stroke Prevention by Aggressive Reduction in Cholesterol Levels)

Group	New onset diabetes		Adjusted HR(95% CI)
Atorvastatin 80 mg	166 / 1,905	8.71%	1.37 (1.08-1.75), p=0.011
Placebo	115 / 1,898	6.06%	

TNT (Treat to New Targets)

Group	New onset diabetes		Adjusted HR(95% CI)
Atorvastatin 80 mg	351 / 3,798	9.24%	1.10 (0.94-1.29), p=0.226
Atorvastatin 10 mg	308 / 3,797	8.11%	

IDEAL (Incremental Decrease in End Points Through Aggressive Lipid Lowering)

Group	New onset diabetes		Adjusted HR(95% CI)
Atorvastatin 80 mg	239 / 3,737	6.40%	1.19 (0.98-1.43), p=0.075
Simvastatin 20 mg	208 / 3,724	5.59%	

Waters *et al. J Am Coll Cardiol* 2011; 57:1535-1545.

ΠΡΟΓΝΩΣΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ ΓΙΑ ΤΗΝ ΕΜΦΑΝΙΣΗ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ ΣΕ ΑΣΘΕΝΕΙΣ ΥΠΟ ΑΓΩΓΗ ΜΕ ΣΤΑΤΙΝΗ (1)

ΑΝΑΛΥΣΗ ΤΩΝ ΔΕΔΟΜΕΝΩΝ ΤΗΣ TNT(n=7.595) ΚΑΙ ΤΗΣ IDEAL(n=7.461)

- ΓΛΥΚΟΖΗ ΟΡΟΥ > 100mg/dl
- ΠΑΡΟΥΣΙΑ ΤΩΝ ΧΑΡΑΚΤΗΡΙΣΤΙΚΩΝ ΤΟΥ ΜΕΤΑΒΟΛΙΚΟΥ ΣΥΝΔΡΟΜΟΥ

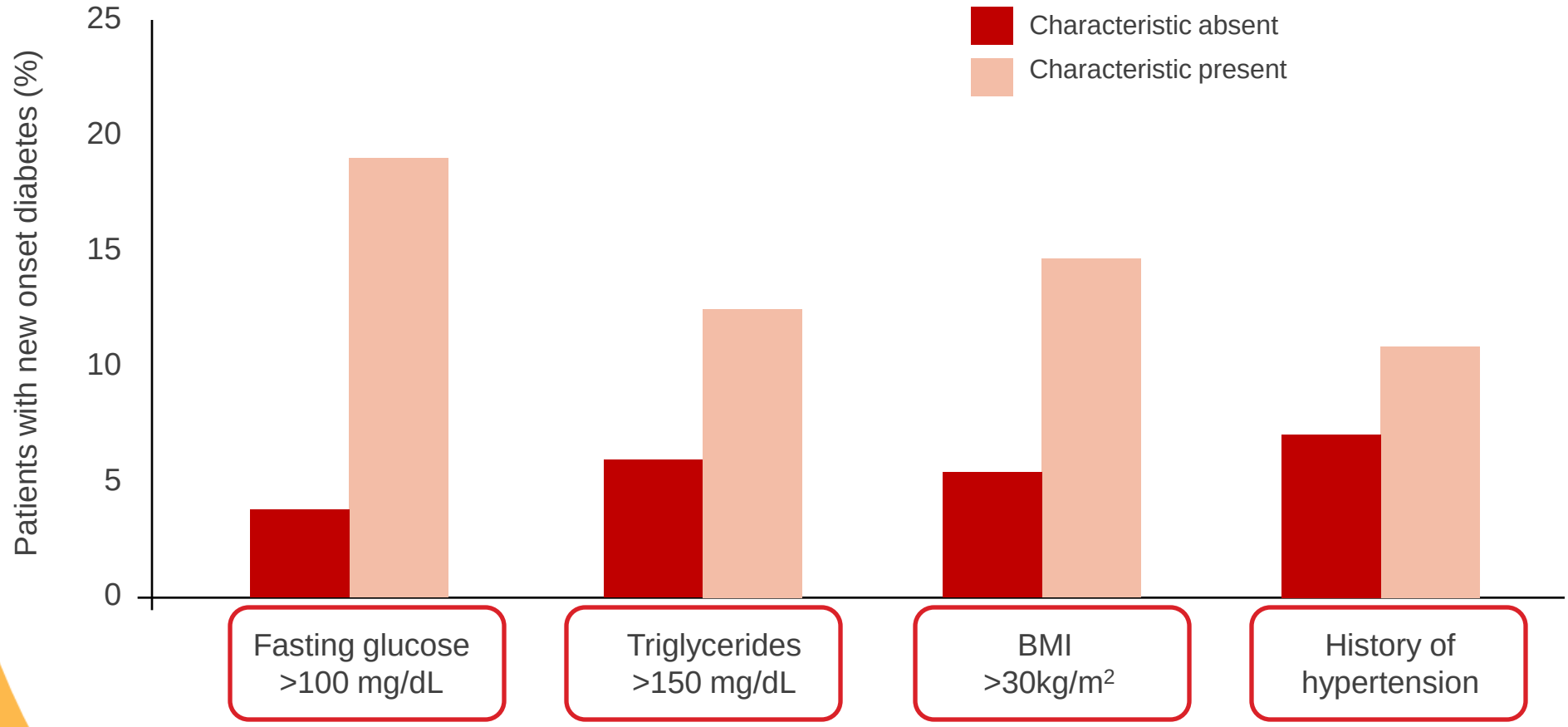
[TRG>150mg/dl, BMI>30Kg/m^2 ΚΑΙ ΥΠΕΡΤΑΣΗ]

Η ΔΟΣΟΕΞΑΡΤΩΜΕΝΗ ΑΥΞΗΣΗ ΤΟΥ ΚΙΝΔΥΝΟΥ ΕΜΦΑΝΙΣΗΣ ΣΔ ΠΑΡΑΤΗΡΕΙΤΑΙ ΚΥΡΙΩΣ ΣΕ ΠΡΟΔΙΑΒΗΤΙΚΑ ΑΤΟΜΑ

JACC 2011;57:1535 , JACC 2013;61:148

Independent Risk Factors for the Development of Diabetes with High Dose Atorvastatin

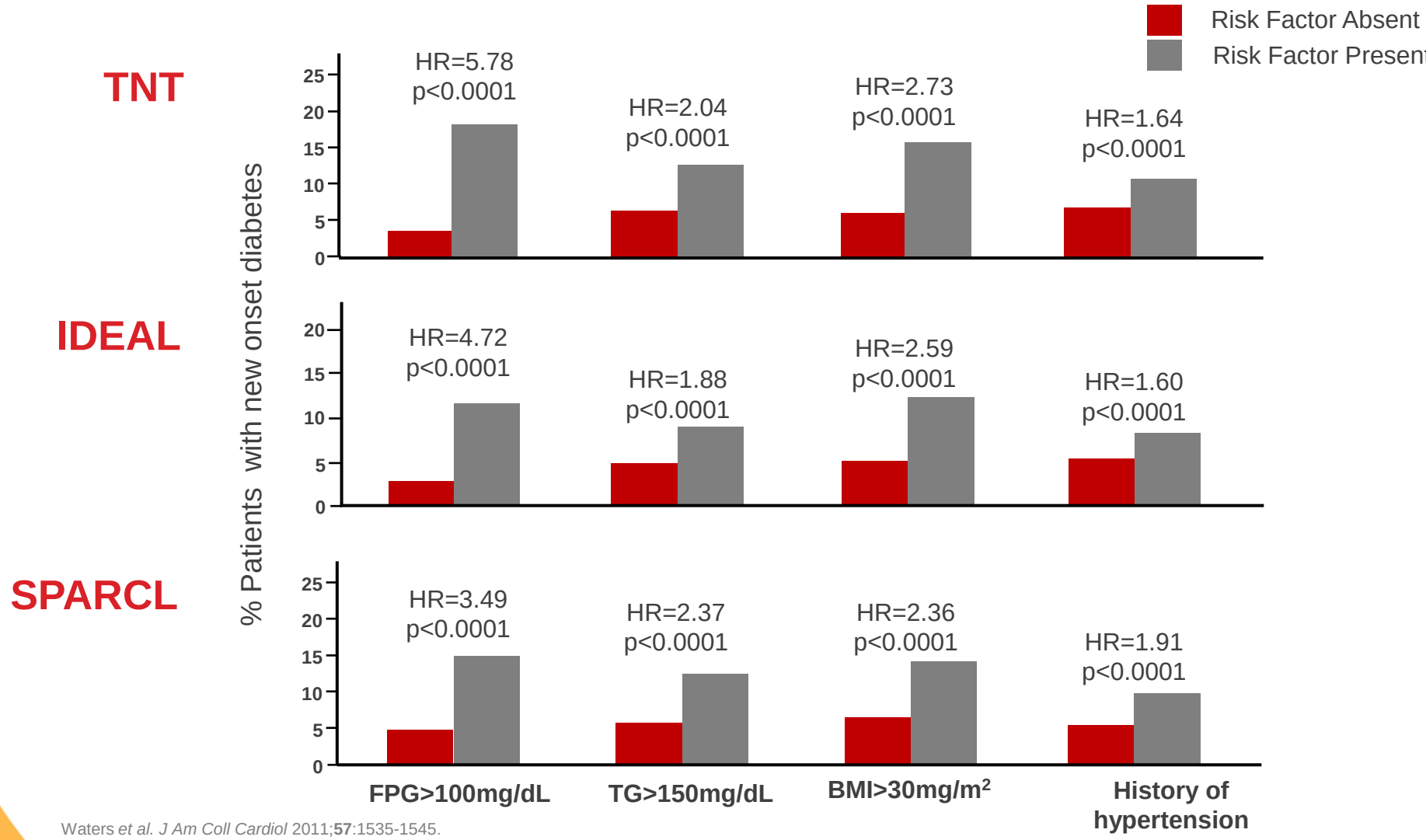
Analysis from TNT* (n=7,595)



Waters *et al. JACC.* 2011;57(14):1535-1545

*TNT: Treat to New Targets

Risk of T2DM with Atorvastatin is Strongly Correlated to the Presence of Risk Factors



Waters *et al. J Am Coll Cardiol* 2011;**57**:1535-1545.

The Risk of New-Onset Diabetes is Affected by the Number of Metabolic Risk Factors in Patients with Established CVD

	TNT *Trial (n=7,595)			IDEAL* Trial (n=7,595)			SPARCL* Trial (n=3,803)		
Risk factors	**Incidence %**	**HR (95% CI)**	***P* value**	**Incidence %**	**HR (95% CI)**	***P* value**	**Incidence %**	**HR (95% CI)**	***P* value**
0	1.46	1.00		1.55	1.00		2.06	1.00	
1	4.54	3.19	<0.0001	4.37	2.89	<0.0001	4.51	2.23	0.0034
2	9.89	7.15	<0.0001	8.10	5.48	<0.0001	8.39	4.28	<0.0001
3	19.6	14.91	<0.0001	14.9	10.54	<0.0001	15.8	8.58	<0.0001
4	30.0	25.40	<0.0001	24.8	18.78	<0.0001	34.3	20.16	<0.0001
Total	**8.68**			**5.99**			**7.39**		

Waters *et al. JACC* 2011;57:1535
*TNT: Treat to New Targets; SPARCL: Stroke Prevention by Aggressive Reduction in Cholesterol Levels; IDEAL: Incremental Decrease in End Points Through Aggressive Lipid Lowering

ΠΡΟΓΝΩΣΤΙΚΟΙ ΠΑΡΑΓΟΝΤΕΣ ΓΙΑ ΤΗΝ ΕΜΦΑΝΙΣΗ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ ΣΕ ΑΣΘΕΝΕΙΣ ΥΠΟ ΑΓΩΓΗ ΜΕ ΣΤΑΤΙΝΗ (2)

ΑΝΑΛΥΣΗ ΤΩΝ ΔΕΔΟΜΕΝΩΝ ΤΗΣ ΜΕΛΕΤΗΣ JUPITER

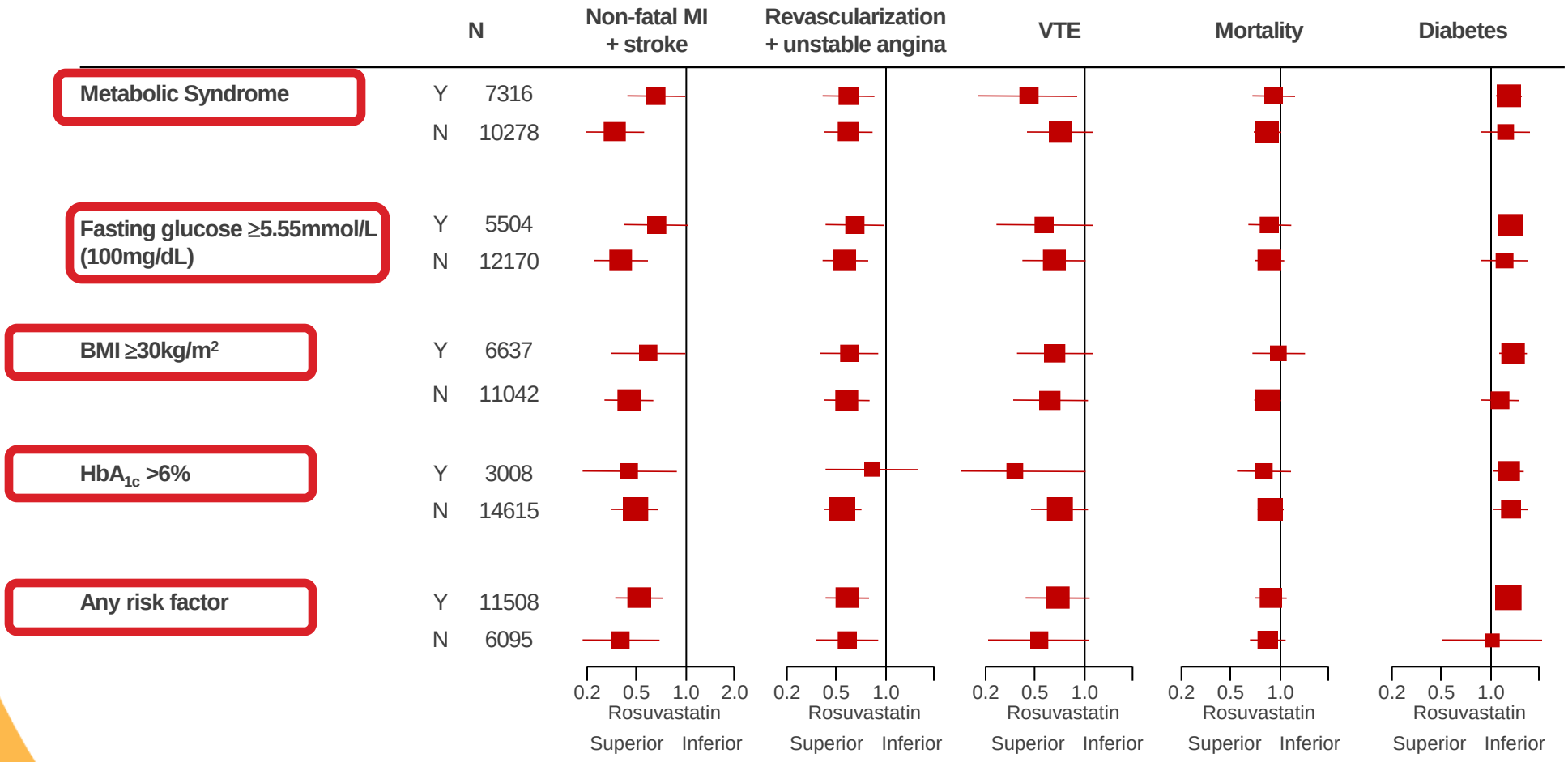
ΠΑΡΟΥΣΙΑ ≥ 1 ΠΑΡΑΓΟΝΤΩΝ ΚΙΝΔΥΝΟΥ ΓΙΑ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ

[ΜΕΤΑΒΟΛΙΚΟ ΣΥΝΔΡΟΜΟ - IFG-BMI>36Kg/m^2-HbA1c>6%]

↑ ΚΙΝΔΥΝΟΥ ΕΜΦΑΝΙΣΗΣ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ ΚΑΤΑ 28%, p=0.01

LANCET 2012;380:565-571 LANCET 2012;380:541-543

Risk Factors for the Development of Diabetes in Patients Receiving Rosuvastatin 20mg in the JUPITER* Trial (n=17,603)

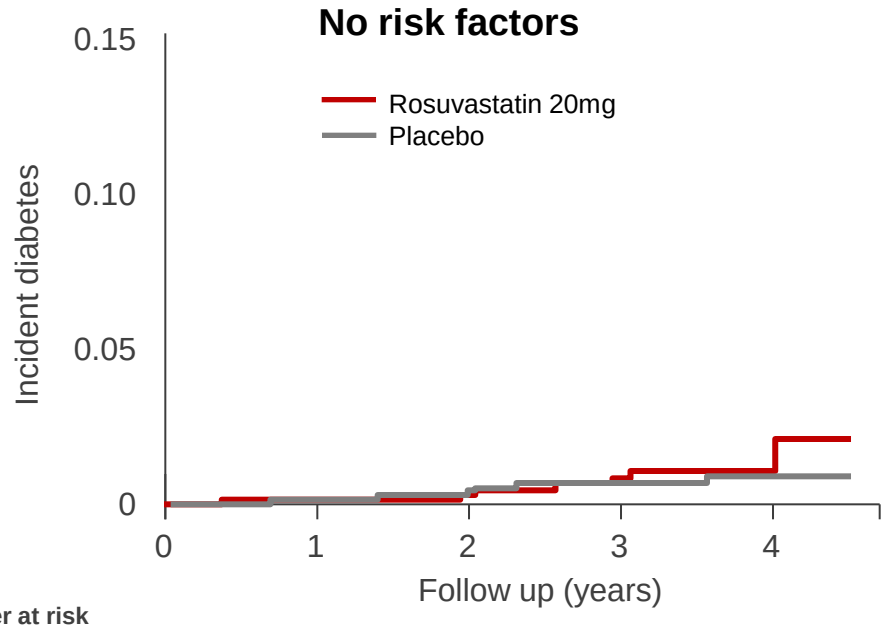


Ridker *et al. Lancet* 2012;380:565-71

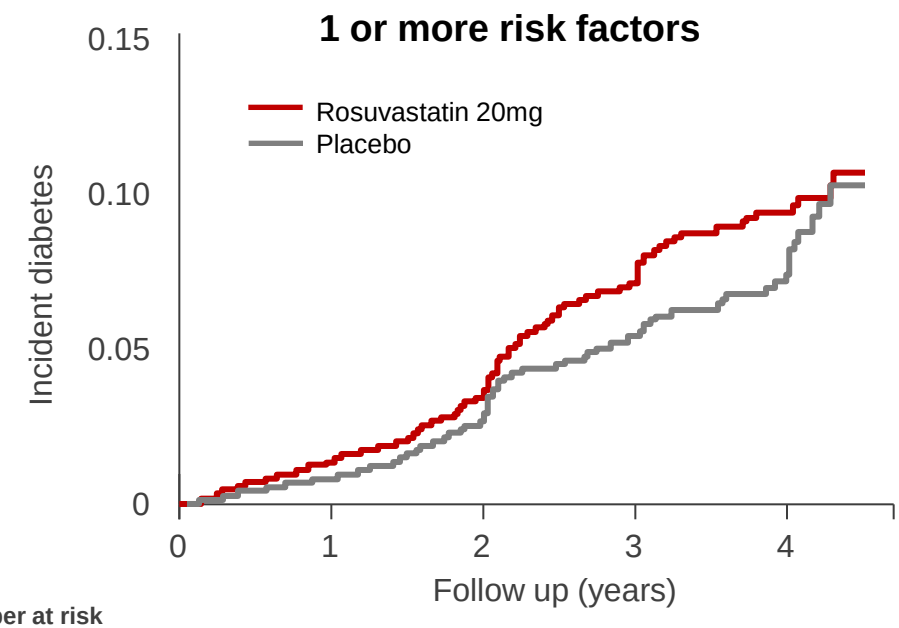
*JUPITER: Justification for Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin

The Increased Risk of Diabetes Largely Occurs in Patients With 1 or More Risk Factor Analysis from JUPITER* (n=17,603)

Cumulative incidence of diabetes in those with or without 1 or more risk factors



Number at risk										
Rosuvastatin	3065	2969	2902	2477	1555	725	473	343	189	48
Placebo	3030	2944	2856	2448	1521	739	488	348	195	69



Number at risk										
Rosuvastatin	5743	5564	5394	4515	2639	1330	870	624	365	126
Placebo	5765	5600	5442	4580	2685	1386	909	644	368	178

Population	Deaths/CV events avoided	New diabetes cases
Those with no diabetes risk factors at baseline	86	0
Those with 1 or more diabetes risk factors at baseline	134	54

Ridker *et al. Lancet* 2012;380:565-71

*JUPITER: Justification for Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin

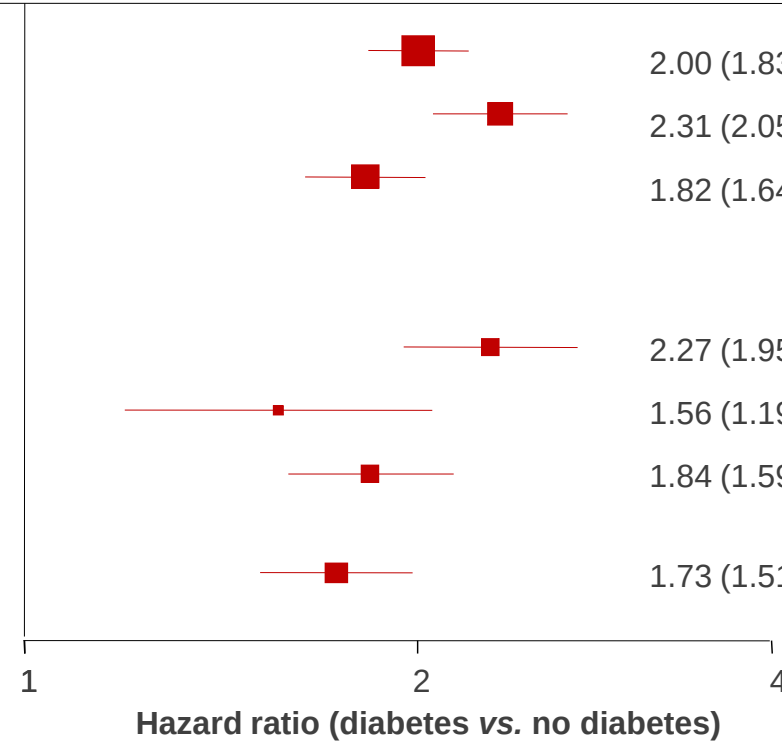
THE SHORT TERM RISK OF DEVELOPING DM IN PATIENTS WITHOUT T_2DM RISK FACTOR IS NEGLIGIBLE

Diabetes Doubles the Risk of CV Disease

Data from 102 prospective studies, n=530,083

Adjusted for age, sex, SBP, smoking, BMI

Outcome	Number of cases	HR (95% CI)	I^2 (95% CI)
Coronary heart disease	26,505	2.00 (1.83 - 2.19)	64 (54-71)
Coronary death	11,556	2.31 (2.05 - 2.60)	41 (24-54)
Non-fatal myocardial infarction	14,741	1.82 (1.64 - 2.03)	37 (19-51)
Stroke subtypes			
Ischaemic stroke	3799	2.27 (1.95 - 2.65)	1 (0-20)
Haemorrhagic stroke	1183	1.56 (1.19 - 2.05)	0 (0-26)
Unclassified stroke	4973	1.84 (1.59 - 2.13)	33 (12-48)
Other vascular deaths	3826	1.73 (1.51 - 1.98)	0 (0-26)



The risk of vascular death for adults with diabetes is increased by a factor of 2.32 compared to adults without diabetes

ERFC. *Lancet.* 2010 ;375(9733):2215-22

ΡΟΣΟΥΒΑΣΤΑΤΙΝΗ ΚΑΙ ΜΕΙΩΣΗ ΤΩΝ ΚΑΡΔΙΑΓΓΕΙΑΚΩΝ ΣΥΜΒΑΜΑΤΩΝ

Η ΜΕΛΕΤΗ JUPITER

ΣΕ ΑΣΘΕΝΕΙΣ ΠΟΥ ΕΜΦΑΝΙΣΑΝ ΔΙΑΒΗΤΗ: ↓ ΣΥΜΒΑΜΑΤΩΝ ΚΑΤΑ 37%

ΣΤΟ ΣΥΝΟΛΙΚΟ ΠΛΗΘΥΣΜΟ ΤΗΣ ΜΕΛΕΤΗΣ: ↓ ΣΥΜΒΑΜΑΤΩΝ ΚΑΤΑ 44%

ΑΓΓΕΙΑΚΑ ΣΥΜΒΑΜΑΤΑ ΚΑΙ ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ

Η ΜΕΛΕΤΗ JUPITER

ROSUVA: HIGH-RISK PATIENTS FOR T2DM

134 ΛΙΓΟΤΕΡΑ ΣΥΜΒΑΜΑΤΑ (16 ΛΙΓΟΤΕΡΟΙ ΘΑΝΑΤΟΙ)

54 ΝΕΑ ΠΕΡΙΣΤΑΤΙΚΑ ΔΙΑΒΗΤΗ

ROSUVA: LOW-RISK PATIENTS FOR T2DM

86 ΛΙΓΟΤΕΡΑ ΣΥΜΒΑΜΑΤΑ

ΟΧΙ ΝΕΑ ΠΕΡΙΣΤΑΤΙΚΑ ΔΙΑΒΗΤΗ

LANCET 2012;380:565-571

MORE INTENSIVE vs LESS INTENSIVE STATIN THERAPY

NNT: 155 ΓΙΑ ΚΑΡΔΙΑΓΓΕΙΑΚΑ ΣΥΜΒΑΜΑΤΑ

NNH: 498 ΓΙΑ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ

3 ΝΕΑ ΠΕΡΙΣΤΑΤΙΚΑ T2DM

6.5 ΛΙΓΟΤΕΡΑ ΜΕΙΖΟΝΑ ΑΓΓΕΙΑΚΑ ΣΥΜΒΑΜΑΤΑ

} 1000 ΑΤΟΜΑ/ΕΤΟΣ

ΣΤΑΤΙΝΕΣ ΚΑΙ ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ: ΥΠΟΚΕΙΜΕΝΟΙ ΜΗΧΑΝΙΣΜΟΙ

Α. CONFOUNDING FACTORS: ΚΑΛΥΤΕΡΗ ΕΠΙΒΙΩΣΗ/ ΜΕΓΑΛΥΤΕΡΕΣ ΠΙΘΑΝΟΤΗΤΕΣ ΑΝΙΧΝΕΥΣΗΣ ΔΙΑΒΗΤΗ

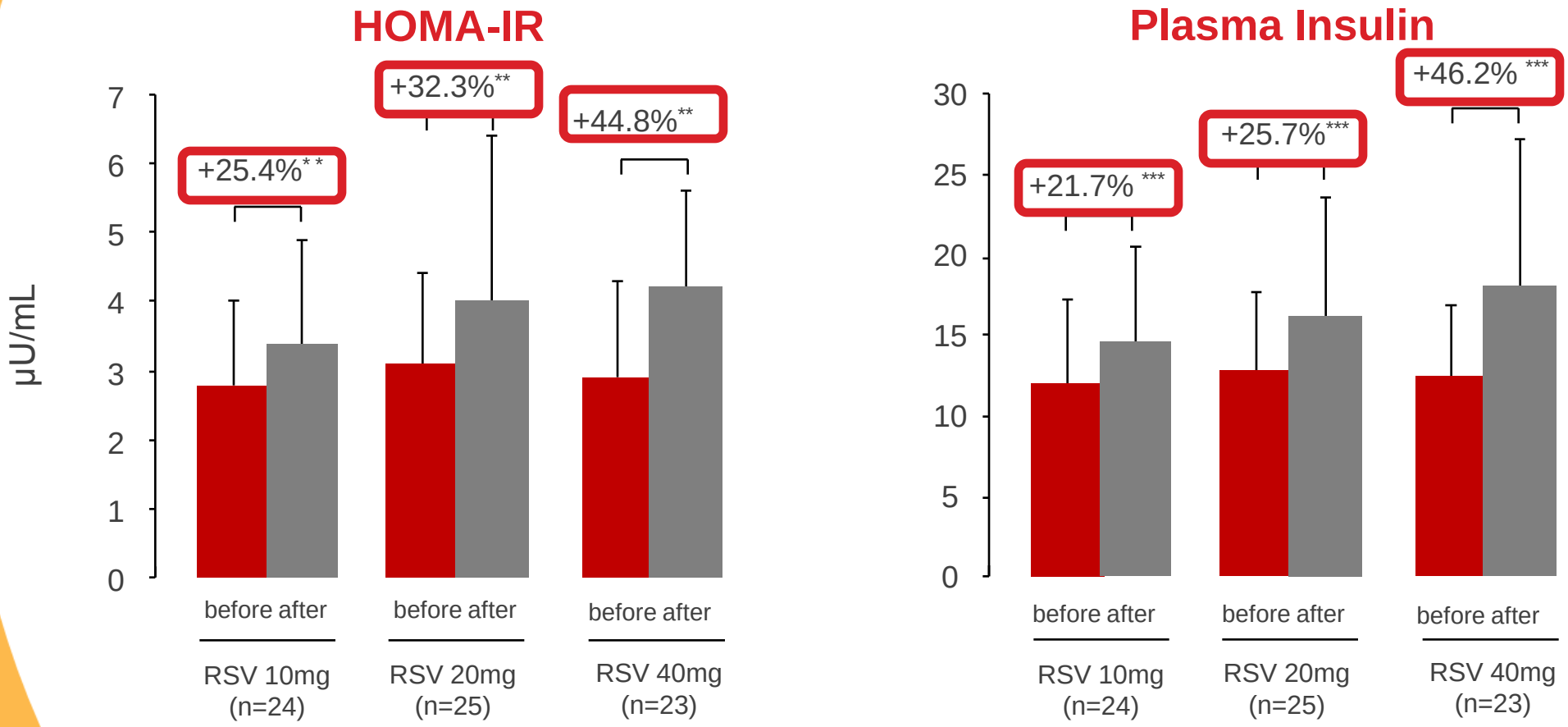
Β. ΕΠΙΤΑΧΥΝΣΗ ΤΗΣ ΕΞΕΛΙΞΗΣ ΤΟΥ ΠΡΟΔΙΑΒΗΤΗ ΣΕ ΔΙΑΒΗΤΗ

C. ΠΡΟΚΛΗΣΗ ΣΑΚΧΑΡΩΔΗ ΔΙΑΒΗΤΗ

ΣΤΑΤΙΝΕΣ → ΕΚΚΡΙΣΗΣ ΙΝΣΟΥΛΙΝΗΣ

ΣΤΑΤΙΝΕΣ → ΑΝΤΙΣΤΑΣΗ ΣΤΗ ΔΡΑΣΗ ΤΗΣ ΙΝΣΟΥΛΙΝΗΣ

Rosuvastatin Causes Dose Dependent Insulin Resistance After 12 Weeks in Hyperlipidaemic Patients with Impaired Fasting Glucose



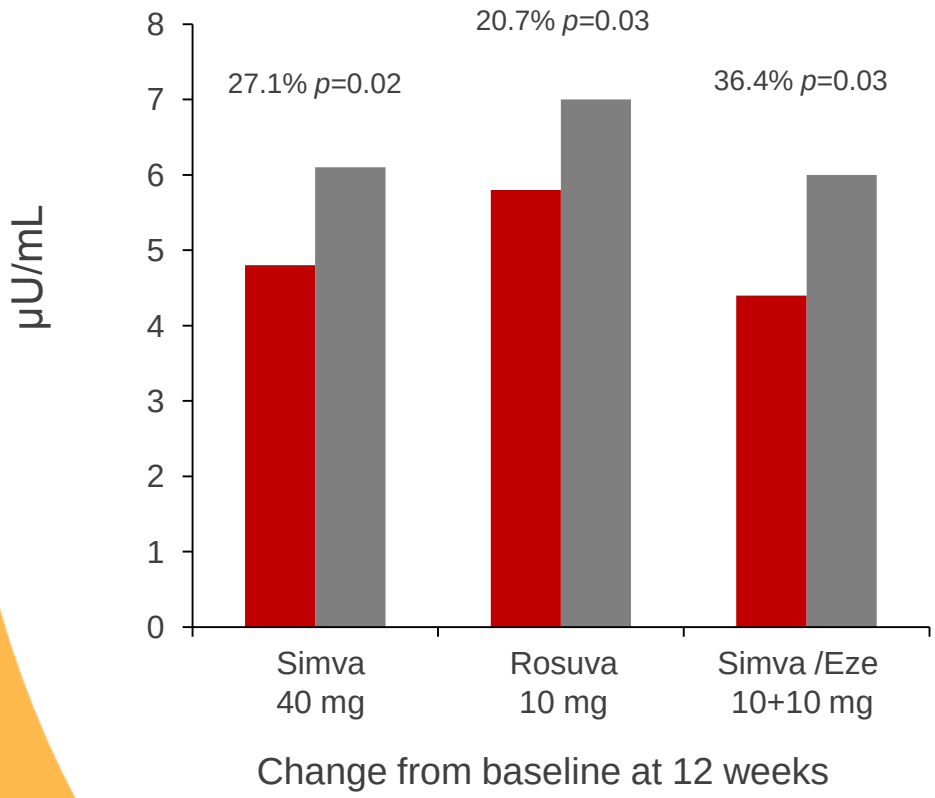
RSV: rosuvastatin; *** p<0.001; ** p<0.01 (*vs*. before)

HOMA-IR: Homeostatic Model of Insulin Resistance

Kostapanos *et al. Int J Clin Pract* 2009;63:1308-1313.

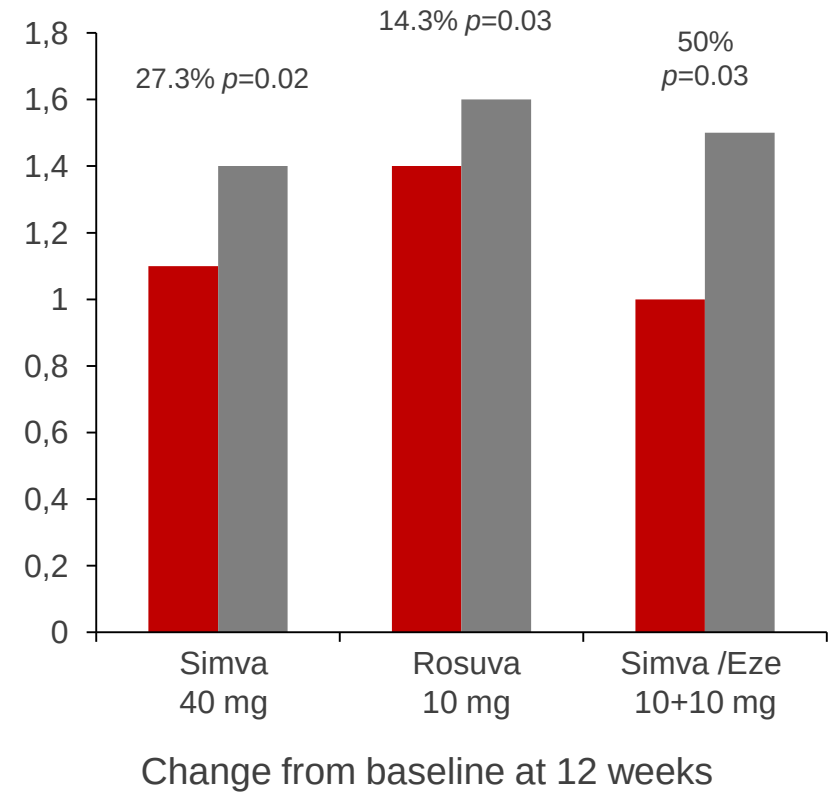
Rosuvastatin, Simvastatin and Simva + EZE Increase Fasting Insulin and HOMA in Primary Hypercholesterolaemic Adults

Fasting insulin



Change from baseline at 12 weeks

HOMA-IR

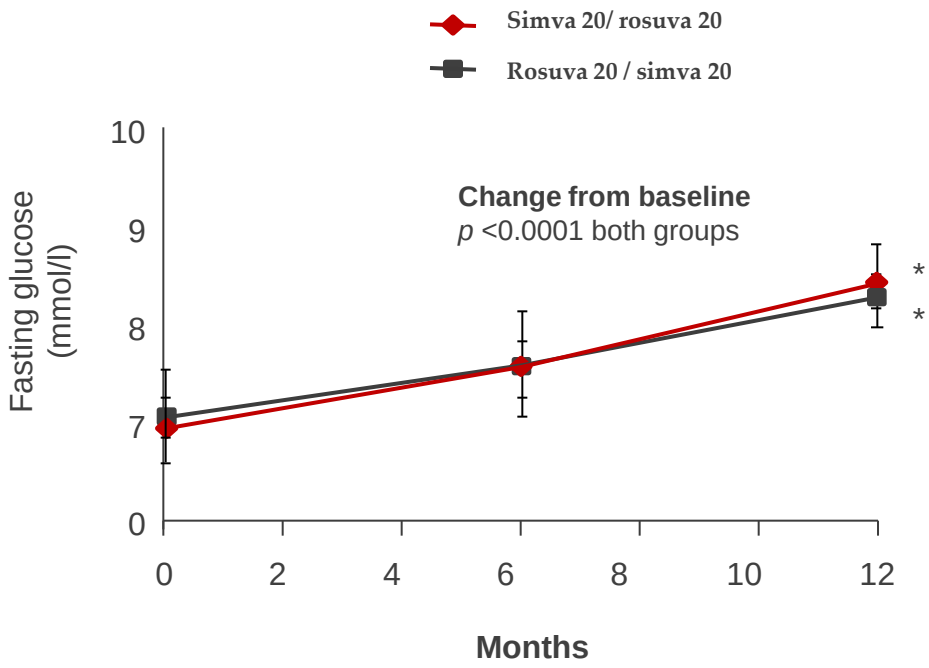


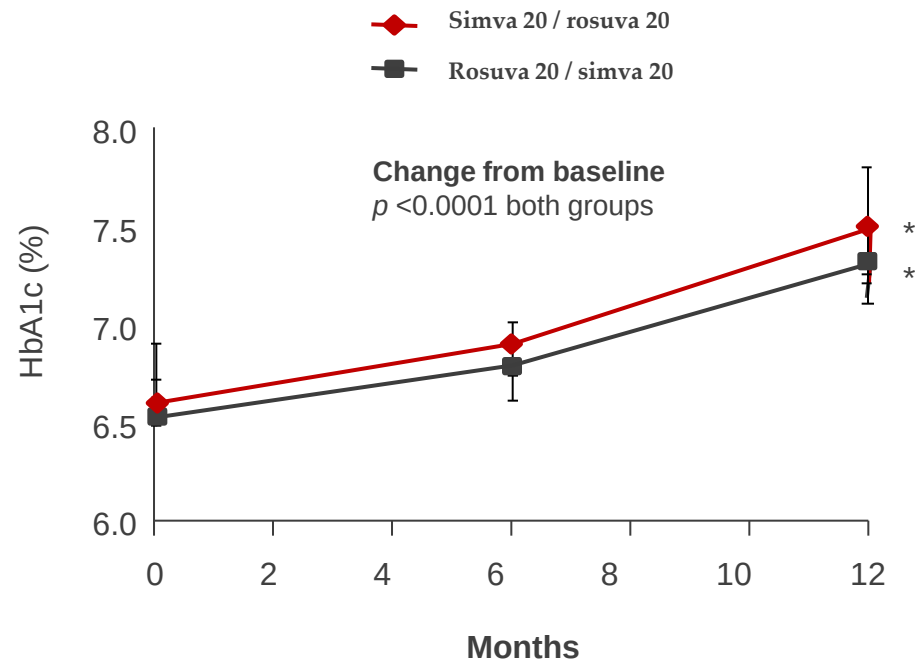
Change from baseline at 12 weeks

HOMA-IR: Homeostatic Model of Insulin Resistance

Mitzouri *et al. Int J Clin Pract* 2011;65(11):1141–1148

In Patients with Well-controlled T2DM both Rosuvastatin and Simvastatin Significantly Impaired Glycaemic Control and Insulin Secretion, Without Affecting Insulin Sensitivity





27 patients with well controlled diabetes
Cross over design; 12 months treatment with rosuvastatin (6 months) and simvastatin (6 months)

HOMA-ß levels significantly decreased from months 6-12 in both groups
No effects on insulin sensitivity

Bellia *et al. Atherosclerosis* 2012; 223:197-203

ARE THE DIABETOGENIC EFFECTS SIMILAR FOR ALL STATINS (1)

ΑΝΑΛΥΣΗ ΤΩΝ ΔΕΔΟΜΕΝΩΝ ΤΗΣ ΜΕΛΕΤΗΣ PROVE-IT

	ΑΥΞΗΣΗ ΤΗΣ HbA1c%
PRAVA 40mg/d	0.12%
ATORVA 80mg/d	0.30%

CIRCULATION 2004

ARE THE DIABETOGENIC EFFECTS SIMILAR FOR ALL STATINS (2)

ΜΕΤΑ-ΑΝΑΛΥΣΗ 16 ΜΕΛΕΤΩΝ

Η ΠΡΑΒΑΣΤΑΤΙΝΗ ΒΕΛΤΙΩΣΕ ΤΗΝ ΑΝΤΙΣΤΑΣΗ ΣΤΗΝ ΙΝΣΟΥΛΙΝΗ (p=0.03 vs PLACEBO)

ΜΙΚΡΗ ΕΠΙΔΕΙΝΩΣΗ ΤΗΣ ΑΝΤΙΣΤΑΣΗΣ ΜΕ ROSUVA/ATORVA

Η SIMVA ΕΠΙΔΕΙΝΩΣΕ ΤΗΝ ΑΝΤΙΣΤΑΣΗ ΣΤΗΝ ΙΝΣΟΥΛΙΝΗ (p=0.03)

DIABETES RES CLIN PRACT 2010;87:98-107

A RETROSPECTIVE COHORT STUDY, n=239628

ΣΧΕΤΙΚΟΣ ΚΙΝΔΥΝΟΣ ΓΙΑ ΤΗΝ ΕΜΦΑΝΙΣΗ T_2DM

ATORVA	1.25
SIMVA	1.14
PRAVA	1.02
FLUVA	1.04

BR J CLIN PHARMACOL 2013;75:1118-1124

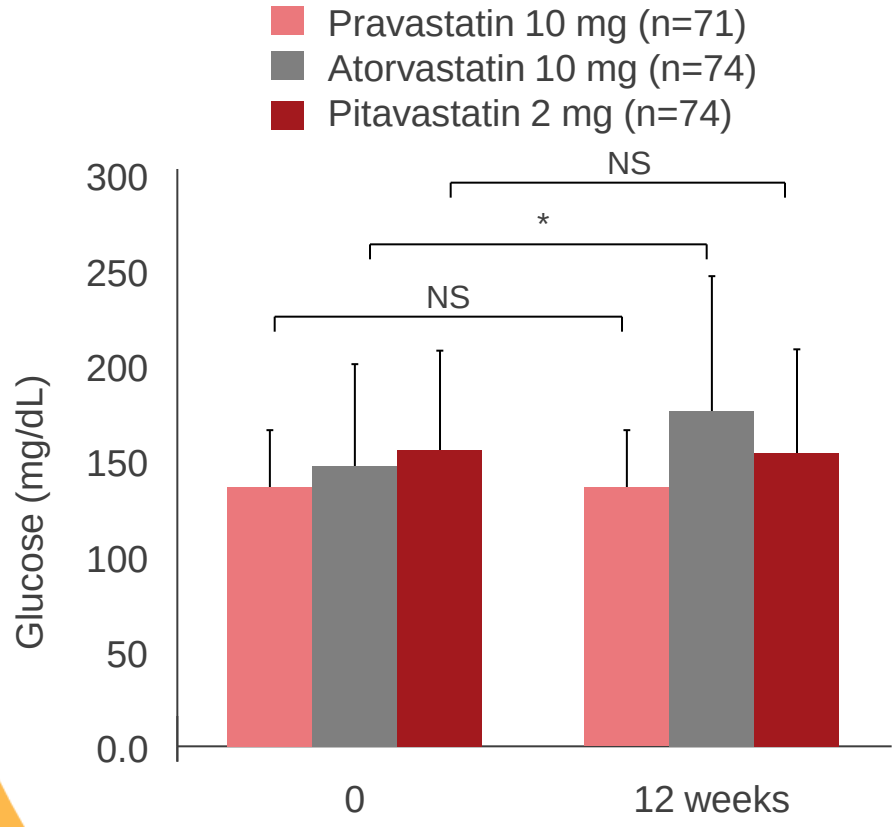
Summary

- Few prospective studies have been performed to evaluate the effects of statins on glucose or insulin resistance on adults with diabetes, those at risk of diabetes or adults without diabetes
- The majority of clinical data are derived from retrospective post hoc analyses
- From the available data it would appear that statins exert different effects on glucose and insulin resistance
  - Pravastatin appears to have neutral or positive effects on blood glucose / insulin sensitivity[1,2] while high-dose atorvastatin and rosuvastatin appear to have deleterious effects[1,3,4]

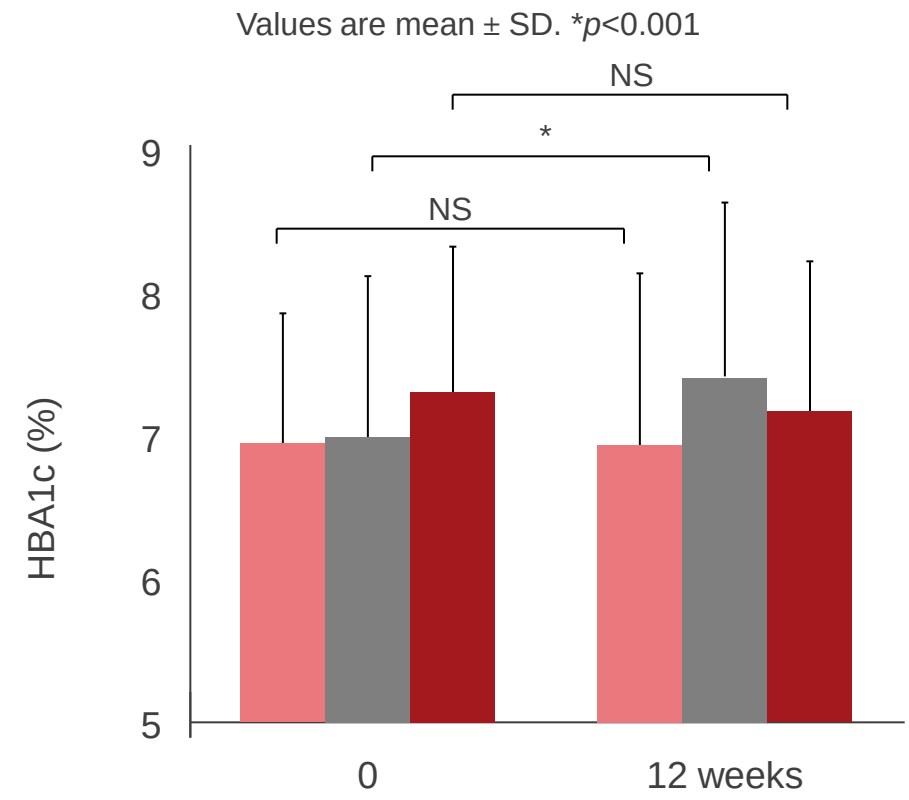
Baker *et al. Diabetes Res Clin Pract*. 2010 Jan;87(1):98-107
Gannagé-Yared *et al. Metabolism*. 2005 Jul;54(7):947-51
Waters *et al. J Am Coll Cardiol* 2011; 57:1535-1545.
Ridker *et al. NEJM* 2008;359(21):2195-2207

Pitavastatin and Pravastatin Have Neutral Effects on Glycaemic Control in Japanese Adults with T2DM

Changes in fasting plasma glucose levels after 12 weeks from baseline

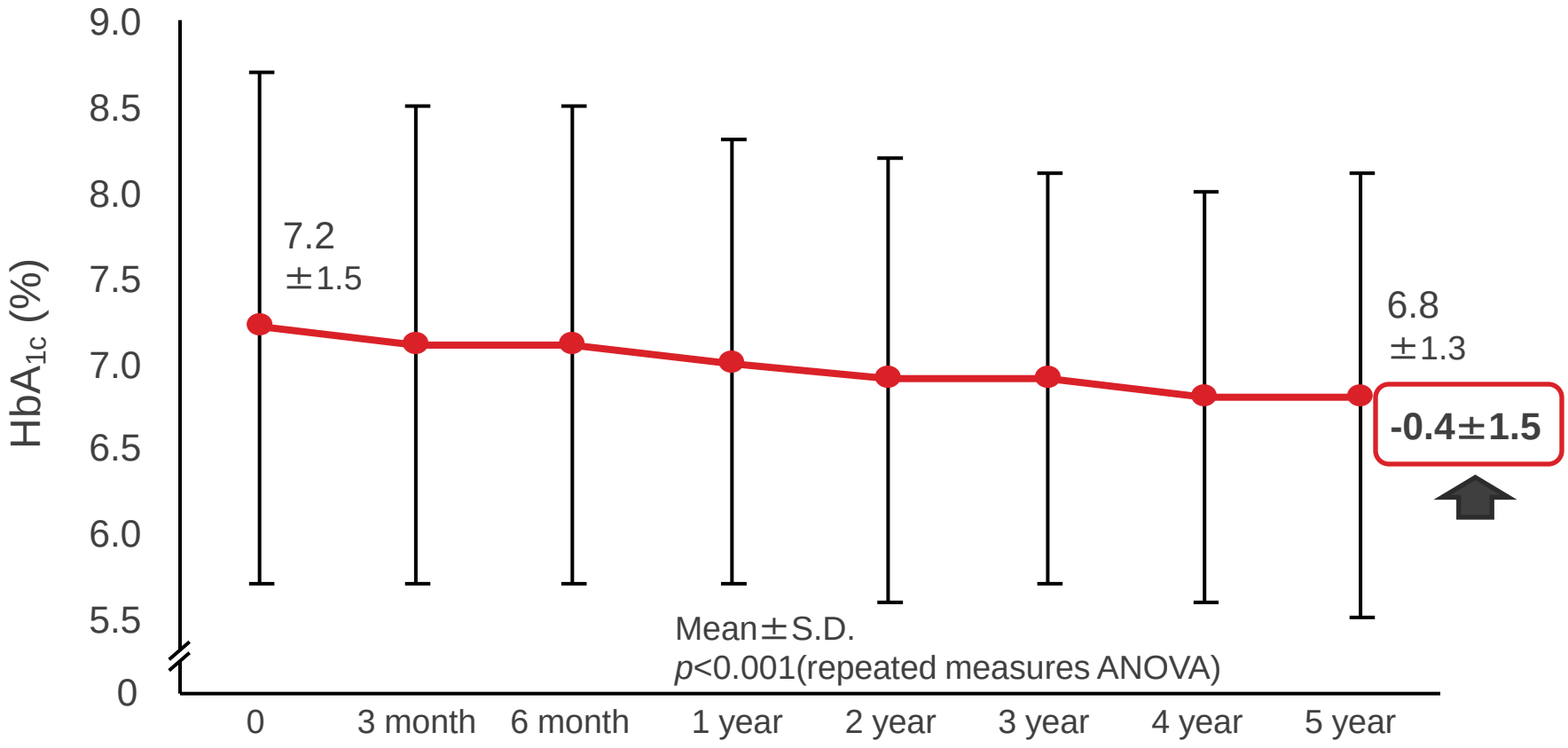


Change in HbA1c after 12 weeks from baseline



Yamakawa T *et al. J Atheroscler Thromb* 2008;**15**:269–275.

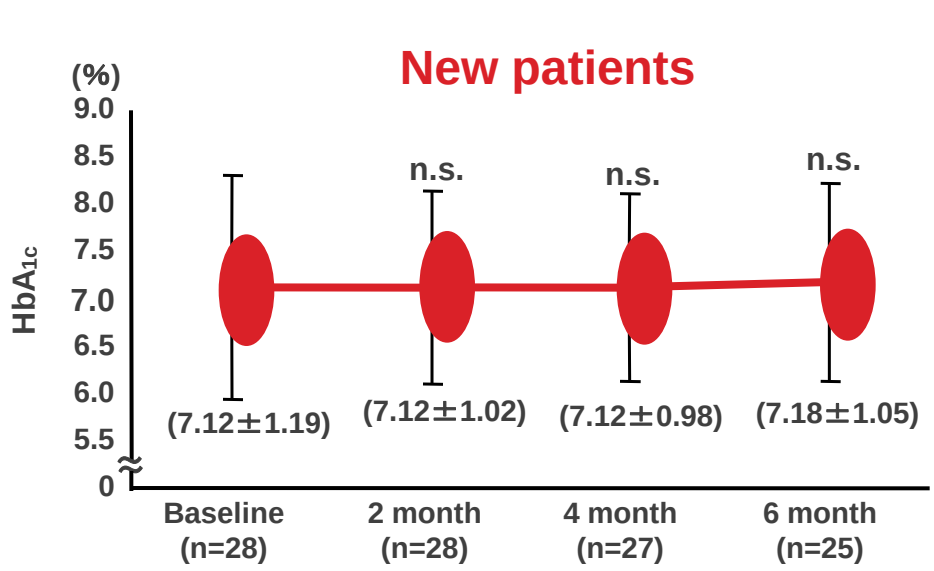
HbA1c Levels Significantly Decrease Over Time with Pitavastatin in Japanese Patients with T2DM Post marketing survey (n=1,843)

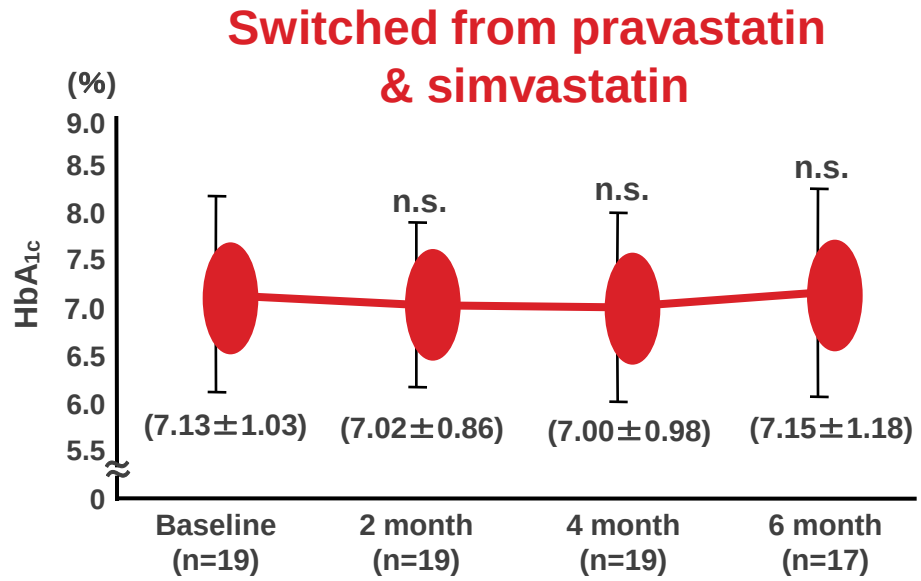


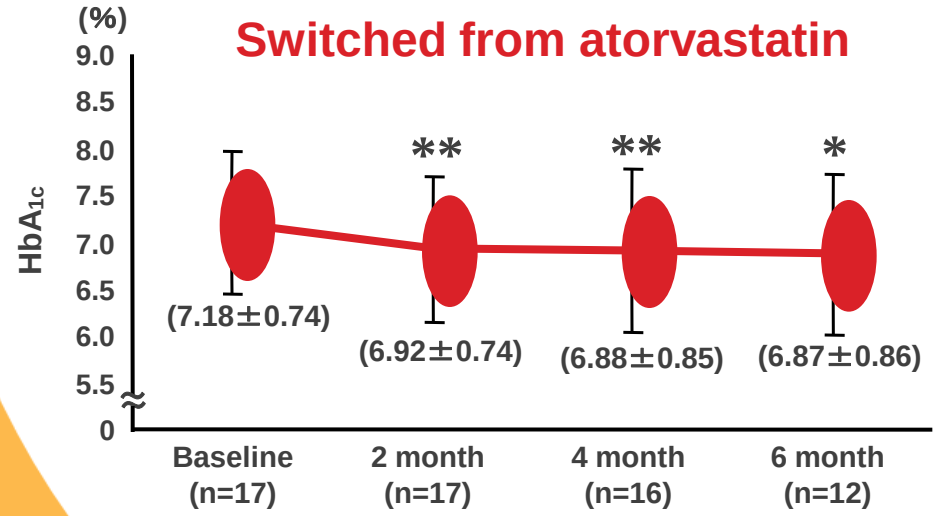
No. of patients	1,544	1,274	1,339	1,519	1,691	1,703	1,713	1,663

Teramoto T *et al. Jn Pharmacol Ther* 2011;**39**:789-803.

HbA1c levels Significantly Decrease in Japanese Patients with T2DM and HC When Switched from Atorvastatin to Pitavastatin for 6 months







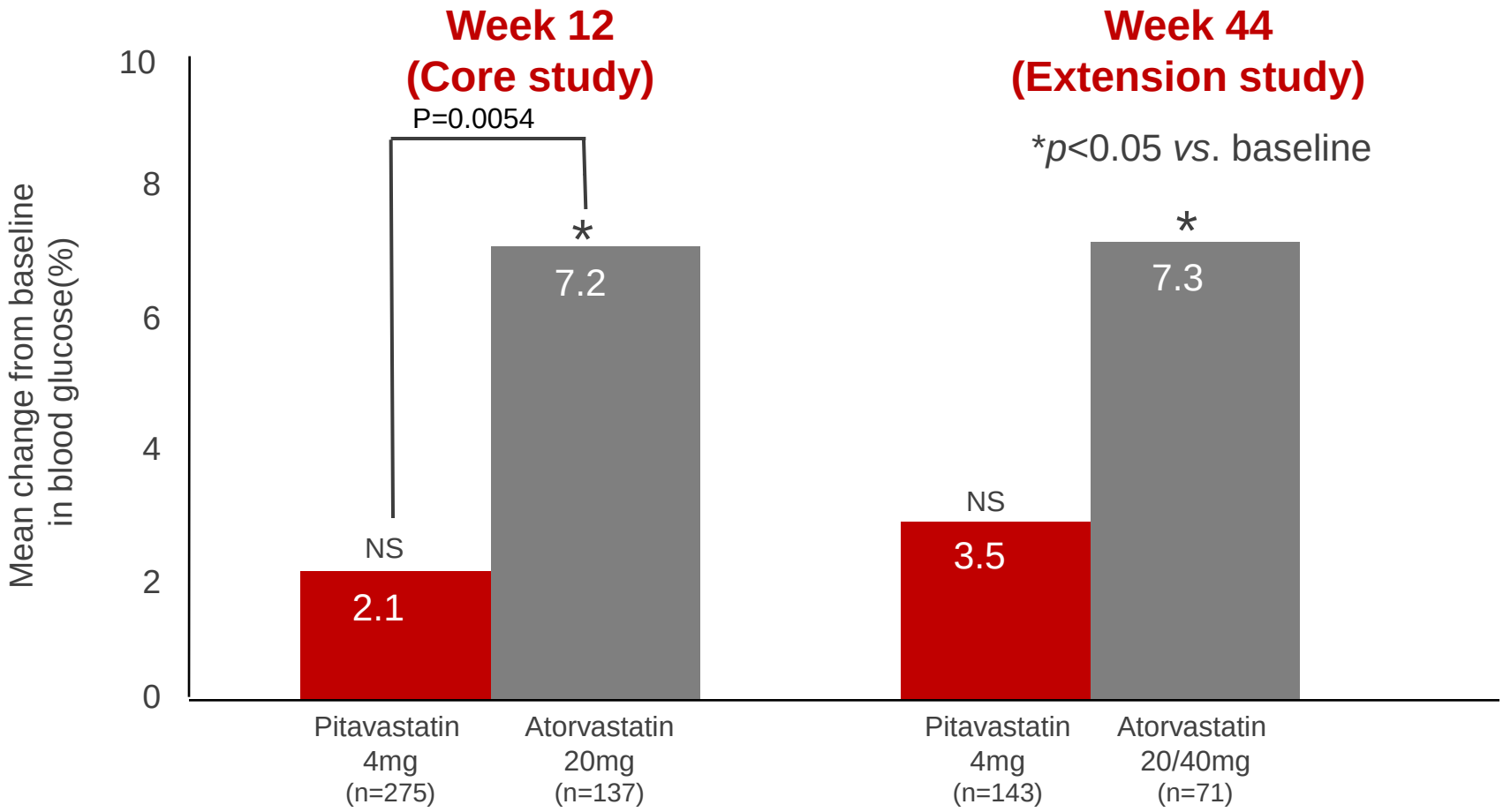
* $p<0.05$ ** $p<0.01$ (vs. before)
n.s.: not significant (paired-t)

T2DM with hypercholesterolaemia
(new=29, switched=39)
Pitavastatin 2mg/day for 6 months

Kotani *et al. Prog Med* 2006;26(10): 2537.

Pitavastatin has No Effect on Blood Glucose After 12 or 44 Weeks Among Patients with T2DM and Mixed Dyslipidaemia

Prospective randomised trial

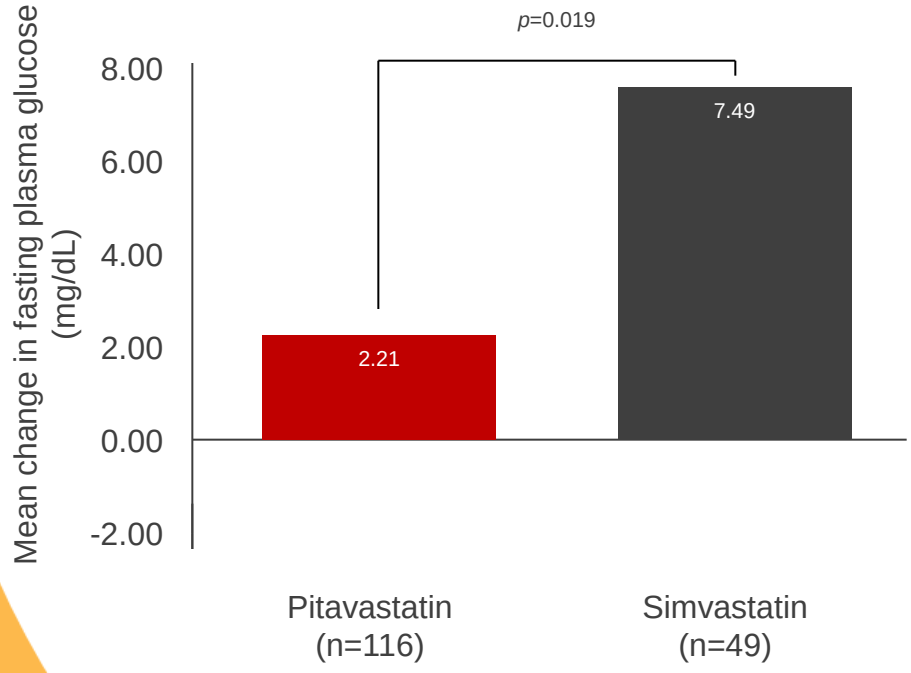


Gumprecht *et al. Diabetes Obes Metab* 2011;**13**(11):1047-1055

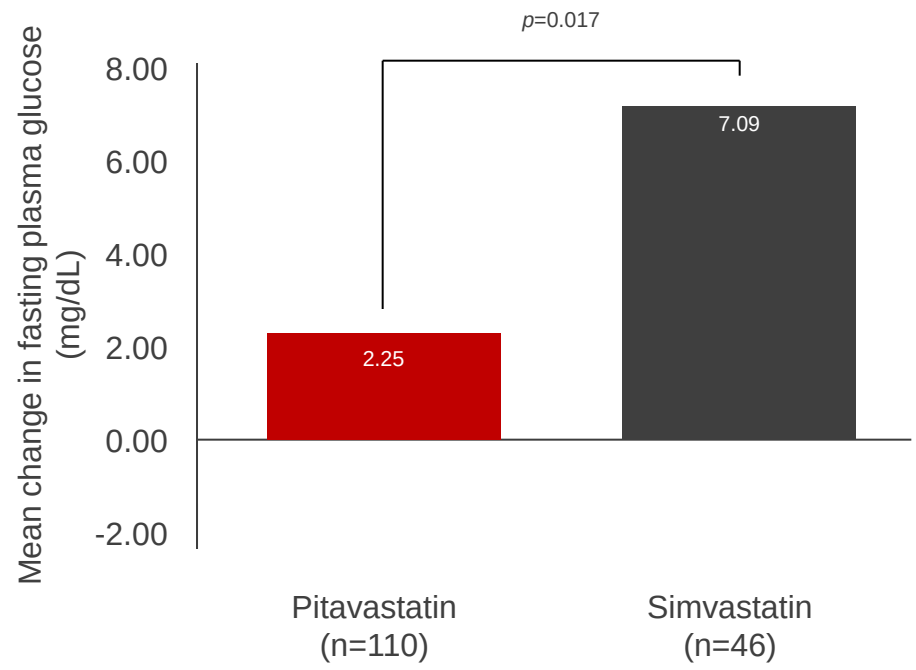
After 56 weeks Pitavastatin Has Minimal Effects on Fasting Plasma Glucose Among Dyslipidaemic Adults with 2 or More CV Risk Factors

Prospective randomised study comparing pitavastatin 4mg to simvastatin 40mg over 56 weeks (n=173)

Mean change from baseline to week 56 in fasting plasma glucose (all patients)

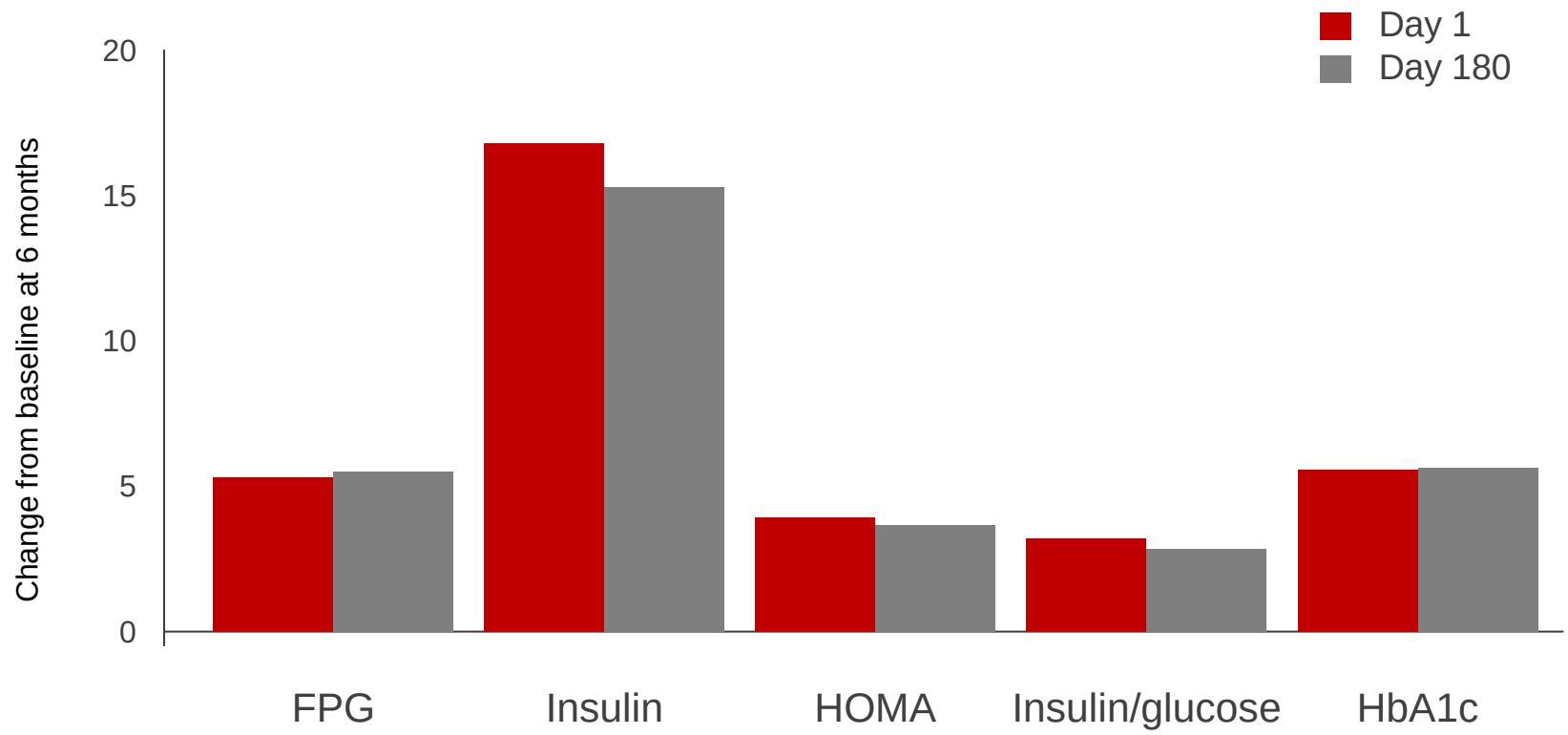


Mean change from baseline to week 56 in fasting plasma glucose after excluding patients with type 2 diabetes mellitus



Kryzhanovski, *et al. ACC* 2012 Poster 288.

Pitavastatin 4mg Has No Effect on Glycaemic Parameters in Patients with Metabolic Syndrome After 6 Months (n=13)



FPG: mmol/L; Insulin: mU/L; HbA1c: %

Hounslow, *et al.* WCPD 2012 abstract 7161542

COMPARISON OF PITA vs ATORVA ON GLUCOSE METABOLISM IN TYPE 2 DM WITH HYPERCHOLESTEROLEMIA

PITA 2mg vs ATORVA 10mg

ΔHbA1c%: -0.18%, p=0.03

ΠΑΡΟΜΟΙΑ ΜΕΙΩΣΗ ΤΗΣ LDL CHOL

J DIABETES INVEST 2013;4:297

J-PREDICT

Overview

Japan PREvention trial of Diabetes by pItavastatin in patients with impaired gluCose Tolerance

Population	IGT
Primary endpoint	Cumulative incidence of diabetes (75g OGTT test)
Study drug	Pitavastatin 1–2 mg/day *vs.* control
Target No. of patients	1,240 (620 in each group)
Duration	5 year follow up
Principal investigator	Prof. Takashi Kadowaki (Tokyo University)

ClinicalTrials. gov ID: NCT00301392
UMIN ID: UMIN000000394
Yamazaki *et al. Diabetol Int* 2011. Published online August 03 2011.

J-PREDICT: First Prospective Trial to Evaluate Statin-induced T2DM in an At-Risk Population

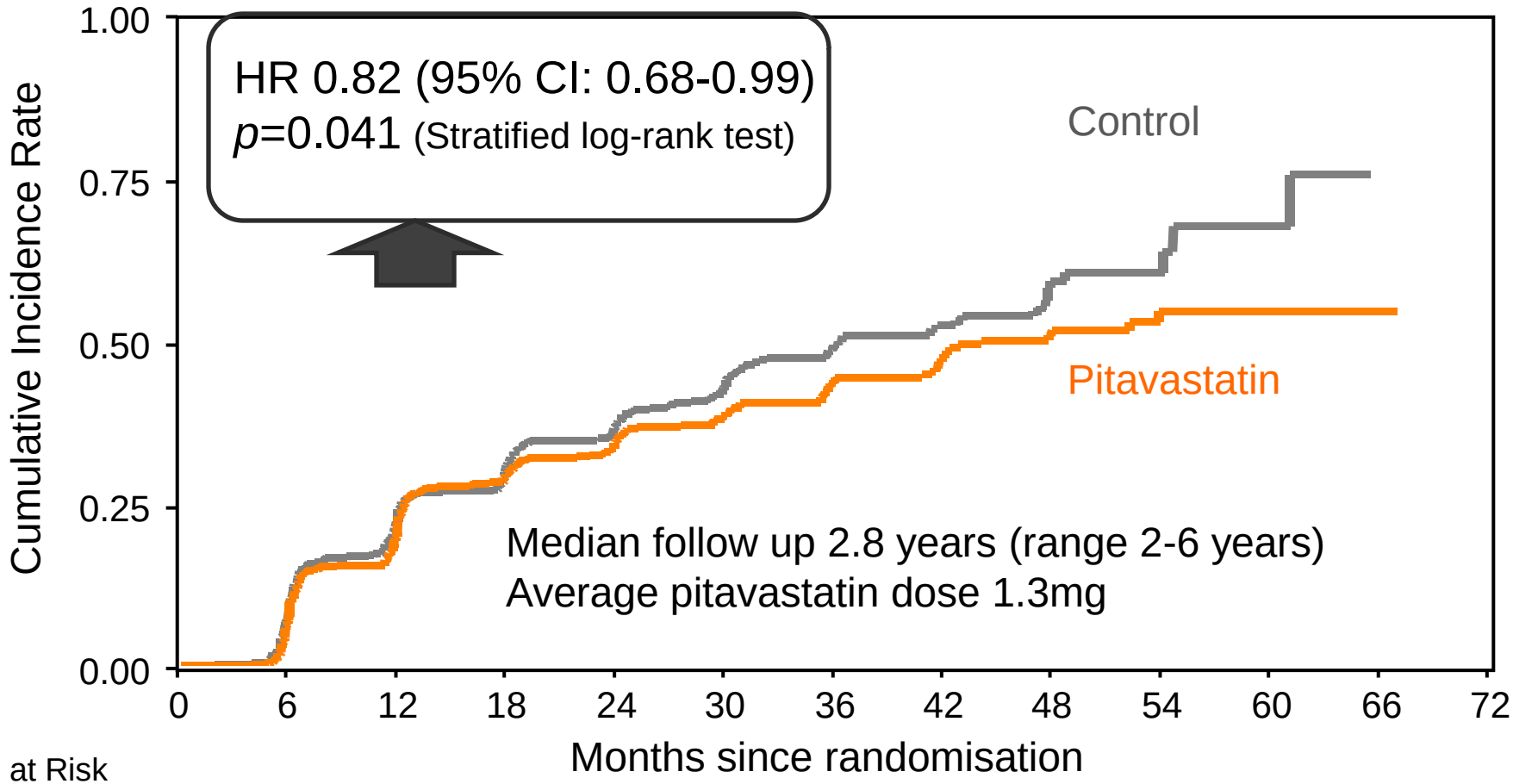
An open-label randomised controlled study to evaluate the effect of pitavastatin on new onset of diabetes in a population with impaired glucose tolerance (IGT)

Study hypothesis:

"The treatment group receiving pitavastatin 1–2 mg/day will show a lower incidence of new-onset diabetes compared with the control group receiving lifestyle modification alone"

Yamazaki *et al. Diabetol Int* 2011. Published online August 03 2011.

Pitavastatin reduced the incidence of diabetes by 18% after a median of 2.8 years



No. at Risk											
Control	556	500	405	350	277	190	123	77	42	15	5
Pitavastatin	534	475	385	320	263	178	124	101	68	30	23

http://www.easdvirtualmeeting.org/resources/3645
http://mtpro.medical-tribune.co.jp/mtpronews/nct/nct130701.html
73rd ADA 2013, Chicago, IL, USA: Late Breaking Studies 61-LB

UNDERSTANDING THE LINK BETWEEN DYSGLYCEMIA AND CVD RISK

ΑΛΓΟΡΙΘΜΟΣ ΠΡΟΣΕΓΓΙΣΗΣ ΤΩΝ ΑΣΘΕΝΩΝ

ΥΠΟΛΟΓΙΣΜΟΣ ΤΟΥ SCORE

ΥΠΟΛΟΓΙΣΜΟΣ ΤΟΥ ΚΙΝΔΥΝΟΥ ΕΜΦΑΝΙΣΗΣ T2DM

ΣΕ ΑΤΟΜΑ ΥΨΗΛΟΥ ΚΙΝΔΥΝΟΥ: ΠΡΟΣΔΙΟΡΙΣΜΟΣ, ΓΛΥΚΟΖΗΣ, HbA1c

ΣΕ ΑΤΟΜΑ ΧΑΜΗΛΟΥ ΚΙΝΔΥΝΟΥ ΕΠΑΝΕΛΕΓΧΟΣ ΜΕΤΑ ΕΤΗ

ΓΛΥΚΟΖΗ 100-124mg/dl, HbA1c 6-6.4% ➡ ΥΓΙΕΙΝΟΔΙΑΙΤΗΤΙΚΗ ΑΓΩΓΗ

ΕΠΑΝΕΛΕΓΧΟΣ ΓΛΥΚΟΖΗΣ ΚΑΙ HbA1c% 3 ΜΗΝΕΣ ΜΕΤΑ ΑΓΩΓΗ ΜΕ ΣΤΑΤΙΝΗ