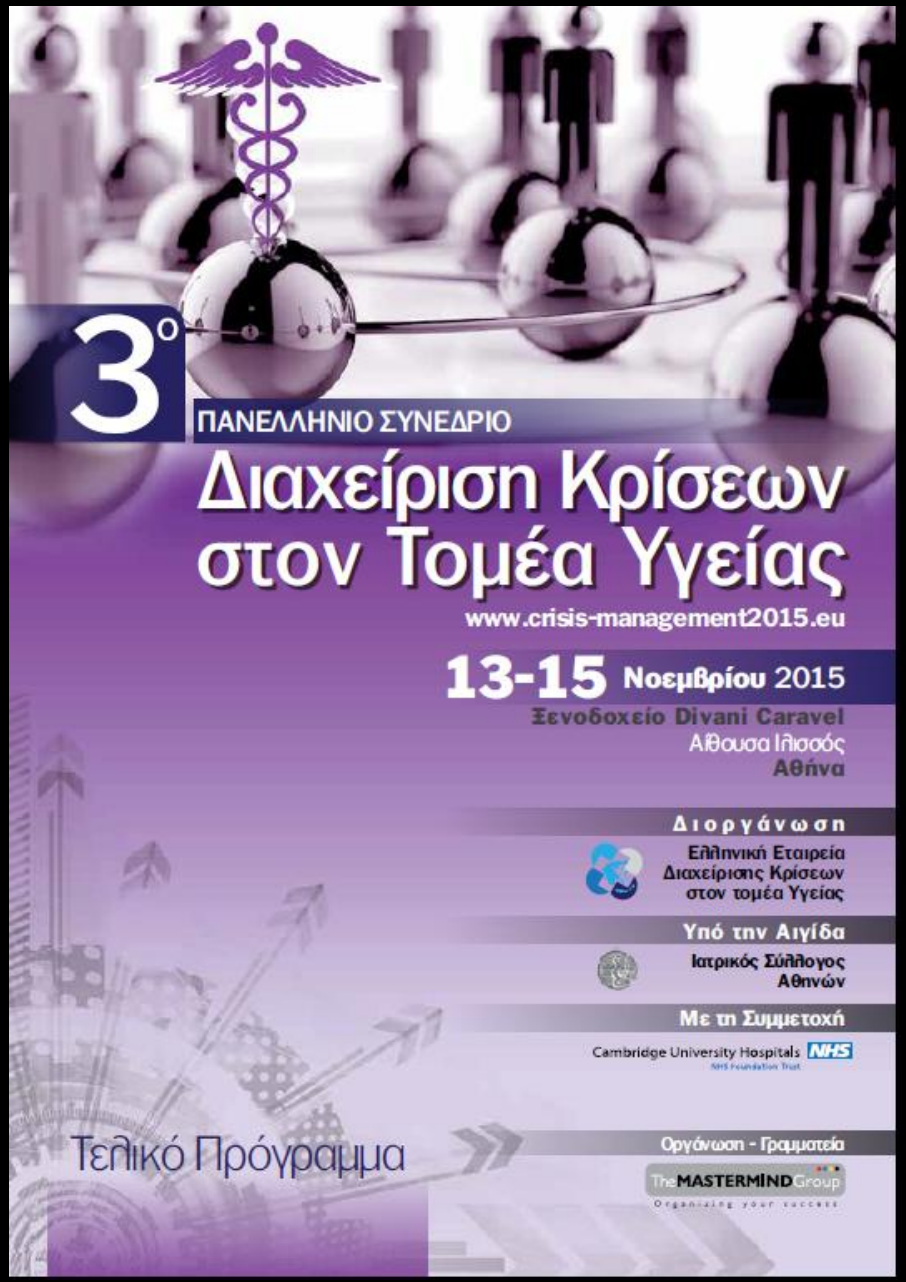


Σακχαρώδης διαβήτης: πρόληψη και αντιμετώπιση στην σημερινή Ελληνικη πραγματικότητα

Θεραπευτική αντιμετώπιση ΣΔ

Δρ Αντώνης Αλαβέρας
Διευθυντής Παθολόγος
Γ' Παθολογικό Τμήμα
Νοσοκομείο ΕΕΣ
Κοργιαλλένειο-Μπενάκιο

Ο επιπλοκές του σακχαρώδους διαβήτη

- Σακχαρώδης διαβήτης
  - Μικροαγγειοπάθεια
    - Αμφιβληστροειδοπάθεια
    - Νεφροπάθεια
    - Νευροπάθεια
  - Μακροαγγειοπάθεια
    - Στεφανιαία νόσος
    - Περιφερική αγγειοπάθεια
    - ΑΕΕ
  - Άλλα
    - ΓΕΣ (πάρεση, διάρροια)
    - Δέρμα
    - Λοιμώξεις
    - Καταρράκτη
    - Αρθροπάθεια

HEALTH

Study: Economic Crisis Improved Cuba's Health

During the devastating downturn of the 1990s, a new report shows, the average Cuban lost 11 pounds and was far less likely to be diagnosed with diabetes.

By Ollie John | April 12, 2013 | 4 Comments

The devastating economic crisis that gripped Cuba in the 1990s led to a marked improvement in the nation's health, researchers have found.

After the collapse of the Soviet Union — and the subsequent termination of Soviet aid — and amid the tightening of the U.S. embargo, Cuba's government was forced to implement tight rationing of food and fuel. But it also introduced policies like commercial neighborhood gardens and the use of animals in farming in place of machinery. Cuba imported 1.5

Economic Crisis Provides Insight into Obesity, Diabetes, and Heart Disease

In the early 1990s, shortages of food and gasoline forced Cubans to eat less and do more walking and cycling. Adults lost, on average, nine to 11 pounds, and type 2 diabetes and cardiovascular disease dropped sharply.

TOULA VASILOPOULOS
HEALTH SCIENCES DIVISION
TVASILOPOULOS@LUC.EDU

In the early 1990s, shortages of food and gasoline forced Cubans to eat less and do more walking and cycling. Adults lost, on average, nine to 11 pounds, and type 2 diabetes and cardiovascular disease dropped sharply.

But after the economy began a slow but steady recovery, adults gradually gained back the weight they had lost, and then some. This weight gain was accompanied by a 116 percent increase in the prevalence of type 2 diabetes. And while heart disease

TOULA VASILOPOULOS
HEALTH SCIENCES DIVISION
TVASILOPOULOS@LUC.EDU

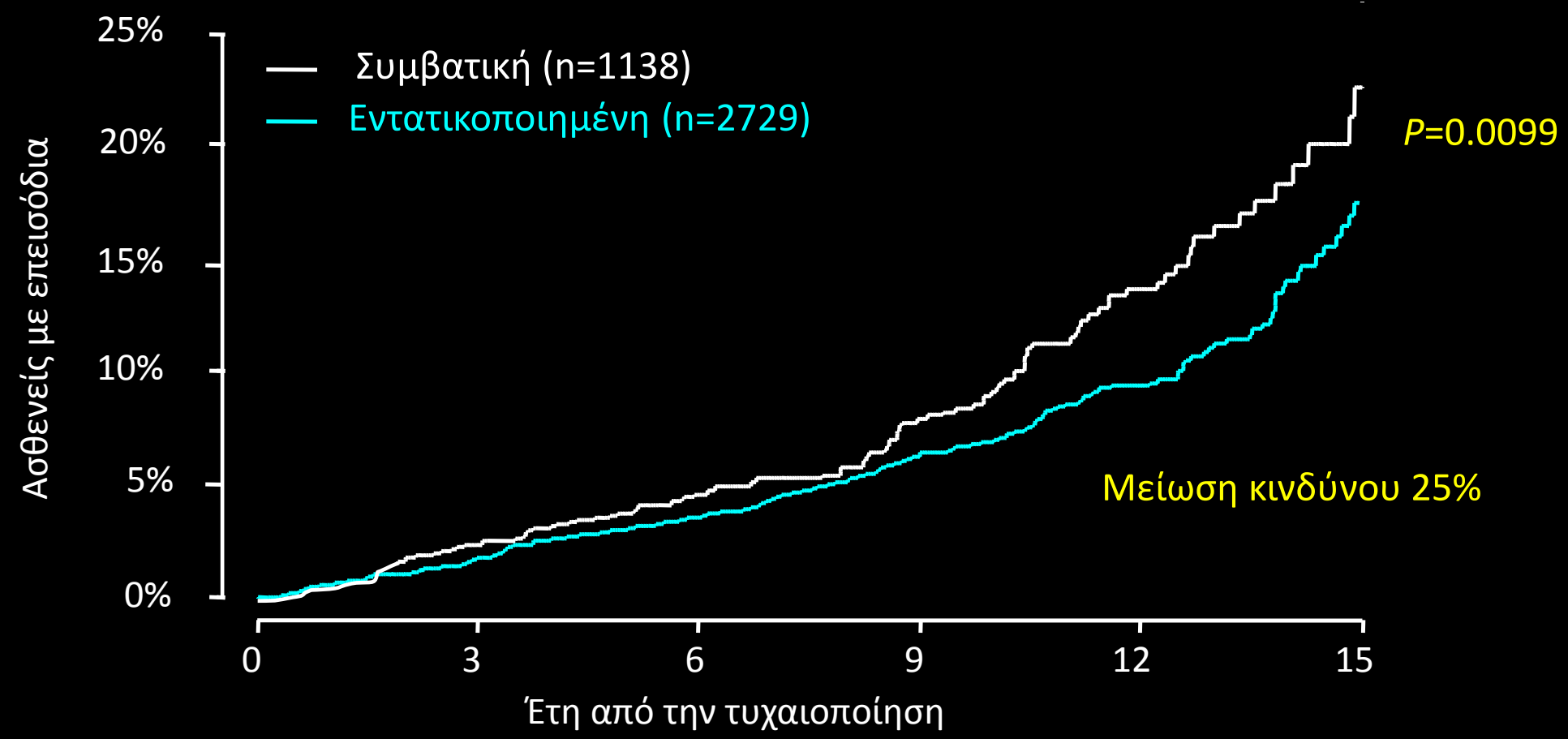
MORE NEWS

JOIN US ON FACEBOOK

United Kingdom Prospective Diabetes Study

Μικροαγγειακές επιπλοκές και μεταβολική ρύθμιση

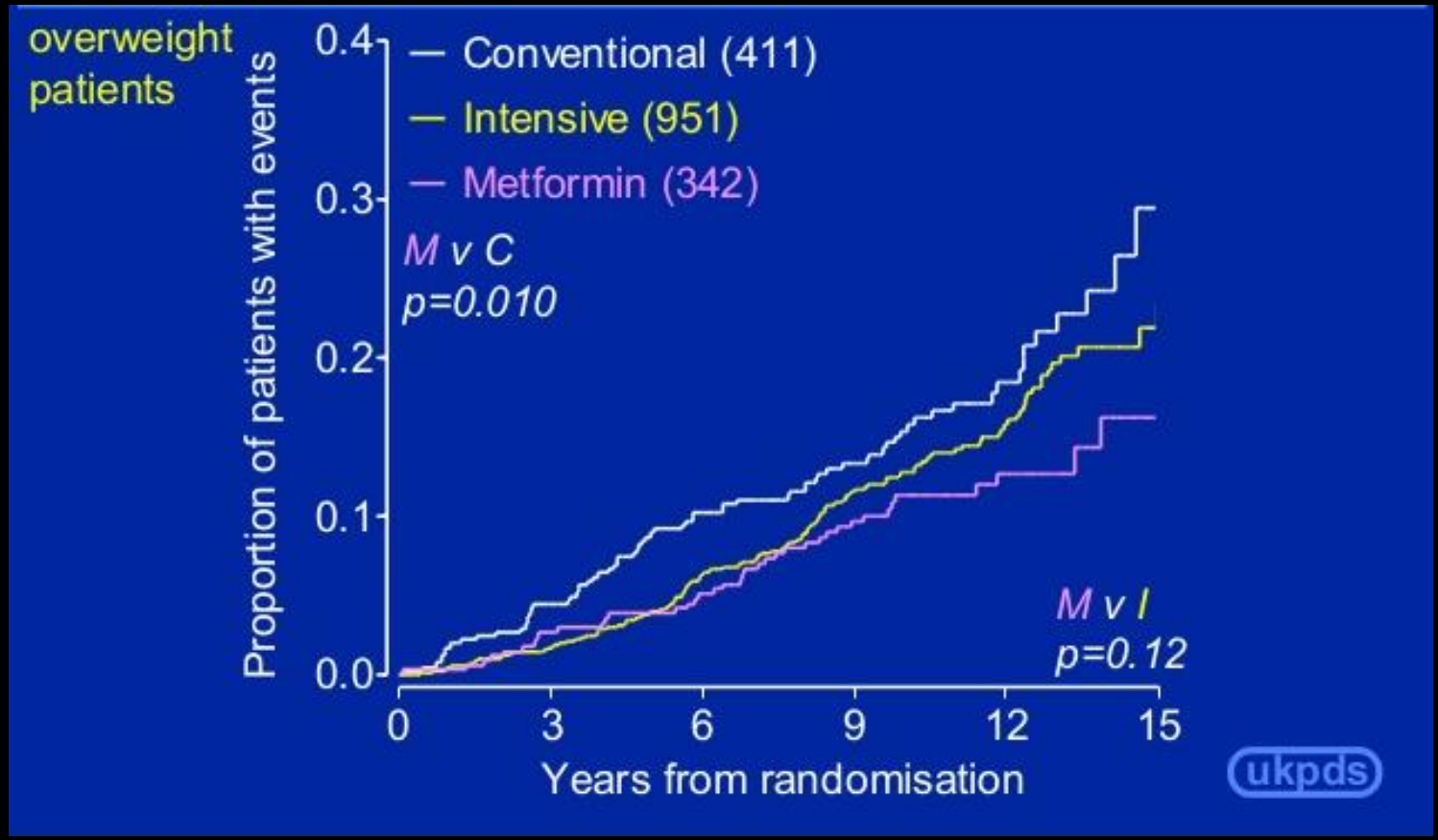
Intensive (SU/Ins) *vs.* Conventional glucose control



UKPDS Group. *Lancet*. 1998;352:837-853.

United Kingdom Prospective Diabetes Study

Έμφραγμα μυοκαρδίου και **μετφορμίνη**



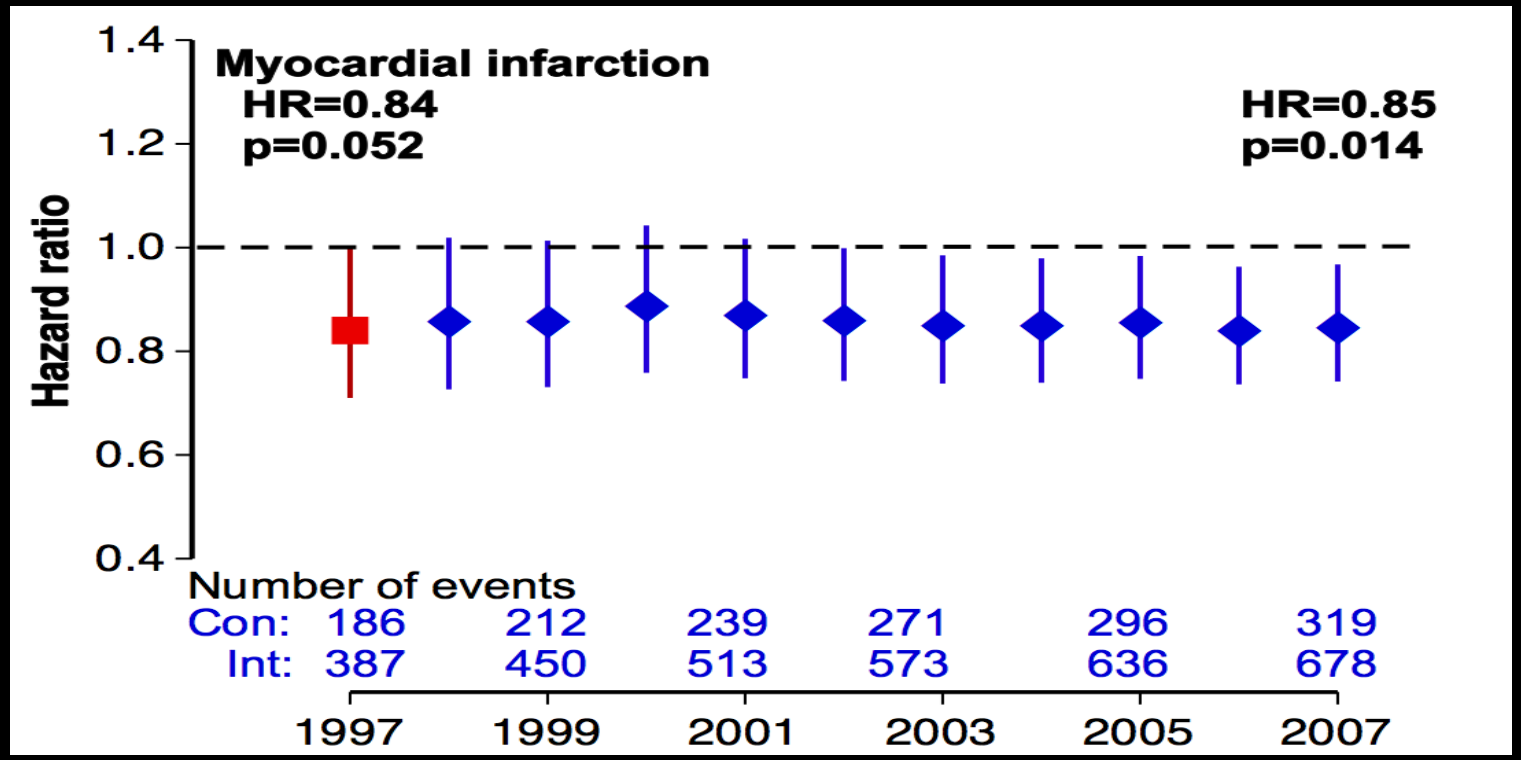
UKPDS Group. *Lancet*. 1998

United Kingdom Prospective Diabetes Study

(fatal or non-fatal myocardial infarction or sudden death)

Έμφραγμα μυοκαρδίου και **μεταβολική ρύθμιση**

Intensive (**SU/Ins**) *vs.* Conventional glucose control



HR (95%CI)

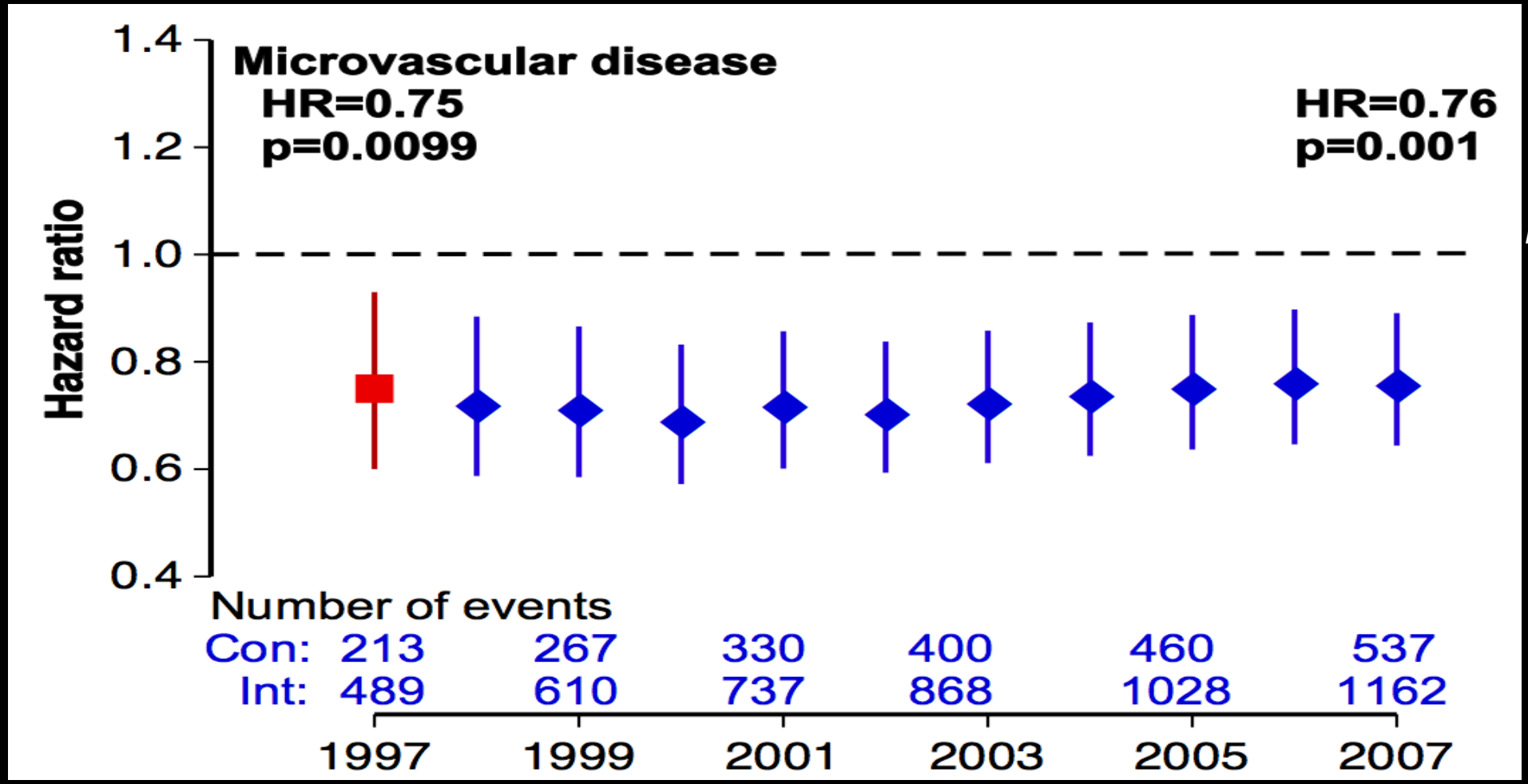
UKPDS N Eng J Med 2008

United Kingdom Prospective Diabetes Study

Μικροαγγειοπάθεια Hazard Ratio

(photocoagulation, vitreous haemorrhage, renal failure)

Intensive (**SU/Ins**) *vs.* Conventional glucose control



UKPDS N Eng J Med 2008

United Kingdom Prospective Diabetes Study

UKPDS
N Eng J Med 2008

Table 2. Aggregate Outcomes for Patients during Follow-up.*

Aggregate Outcome	Patients with Clinical Outcome		Absolute Risk†		P Value‡	Risk Ratio for Intensive-Therapy Regimen (95% CI)
	Intensive Therapy	Conventional Therapy	Intensive Therapy	Conventional Therapy		
	no. of patients					
Sulfonyurea–insulin group	2729	1138				
Any diabetes-related end point	1571	686	48.1	52.2	0.04	0.91 (0.83–0.99)
Diabetes-related death	618	297	14.5	17.0	0.01	0.83 (0.73–0.96)
Death from any cause	1162	537	26.8	30.3	0.007	0.87 (0.79–0.96)
Myocardial infarction	678	319	16.8	19.6	0.01	0.85 (0.74–0.97)
Stroke	260	116	6.3	6.9	0.39	0.91 (0.73–1.13)
Peripheral vascular disease	83	40	2.0	2.4	0.29	0.82 (0.56–1.19)
Microvascular disease	429	222	11.0	14.2	0.001	0.76 (0.64–0.89)
Metformin group	342	411				
Any diabetes-related end point	209	262	45.7	53.9	0.01	0.79 (0.66–0.95)
Diabetes-related death	81	120	14.0	18.7	0.01	0.70 (0.53–0.92)
Death from any cause	152	217	25.9	33.1	0.002	0.73 (0.59–0.89)
Myocardial infarction	81	126	14.8	21.1	0.005	0.67 (0.51–0.89)
Stroke	34	42	6.0	6.8	0.35	0.80 (0.50–1.27)
Peripheral vascular disease	13	21	2.3	3.4	0.19	0.63 (0.32–1.27)
Microvascular disease	66	78	12.4	13.4	0.31	0.84 (0.60–1.17)

Action in **D**iabetes and **V**ascular Disease: PreterA**x** and DiamicroN Modified Release **C**ontrolled **E**valuation ObservatioN**a**l Study (**ADVANCE-ON**)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes

S. Zoungas, J. Chalmers, B. Neal, L. Billot, Q. Li, Y. Hirakawa, H. Arima, H. Monaghan, R. Joshi, S. Colagiuri, M.E. Cooper, P. Glasziou, D. Grobbee, P. Hamet, S. Harrap, S. Heller, L. Lisheng, G. Mancia, M. Marre, D.R. Matthews, C.E. Mogensen, V. Perkovic, N. Poulter, A. Rodgers, B. Williams, S. MacMahon, A. Patel, and M. Woodward, for the ADVANCE-ON Collaborative Group*

N Engl J Med 2014;371:1392-406.

THE NEW ENGLAND JOURNAL of MEDICINE

Follow-up of Blood-Pressure Lowering and Glucose Control in Type 2 Diabetes

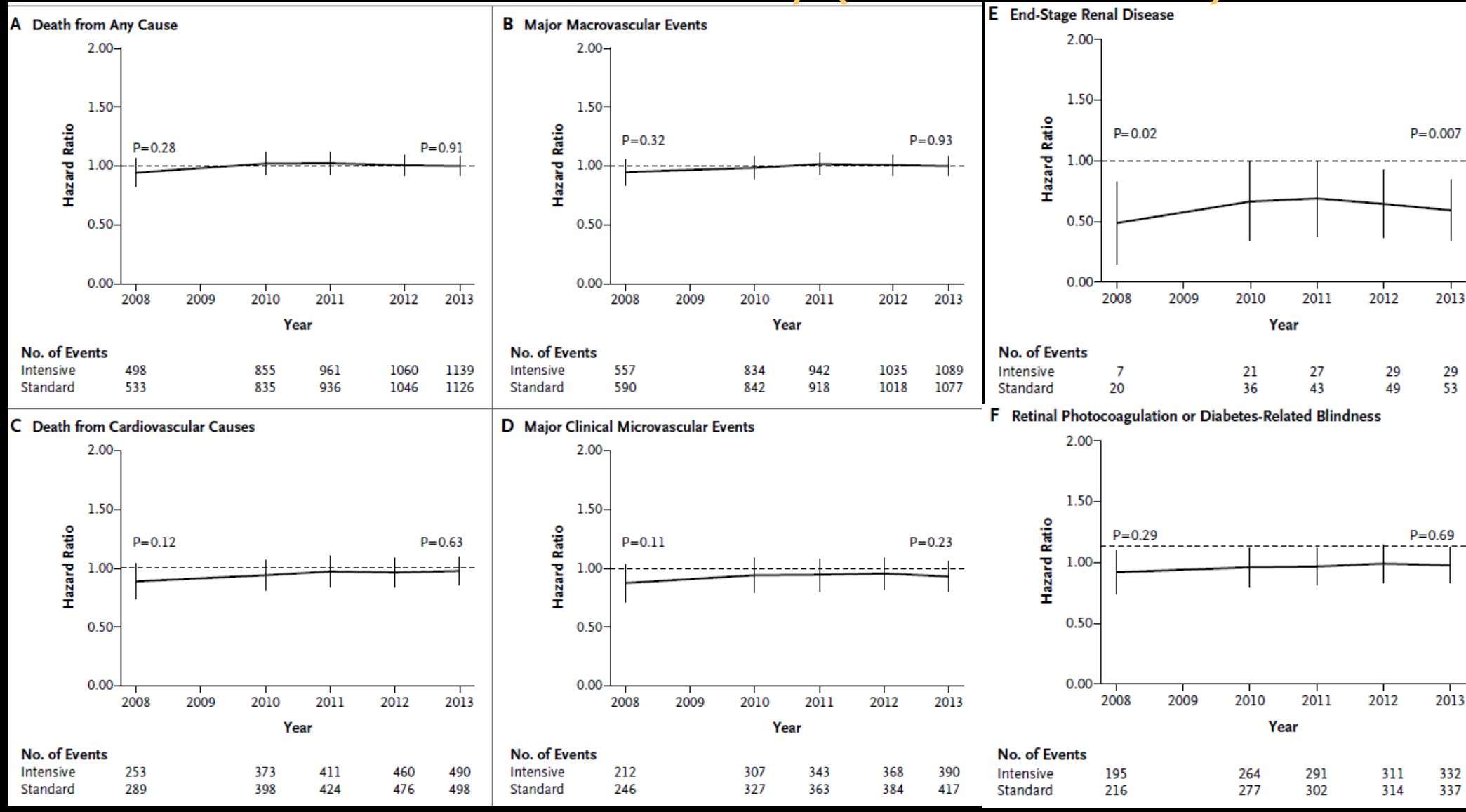
S. Zoungas, J. Chalmers, B. Neal, L. Billot, Q. Li, Y. Hirakawa, H. Arima,

Table 1. Baseline Characteristics of All Participa ost-Trial Follow-up, According to Assignment in the Randomized Trial.*

Variable	Glucose-Control Comparison			
	Clinical Trial		Post-Trial Follow-up	
	Intensive Control (N=5571)	Standard Control (N=5569)	Intensive Control (N=4283)	Standard Control (N=4211)
Age — yr	66±6	66±6	65±6	66±6
Female sex — no. (%)	2376 (42.6)	2357 (42.3)	1867 (43.6)	1781 (42.3)
Age at diagnosis of diabetes — yr	58±9	58±9	58±9	58±9
Previous vascular disease — no. (%)				
Major macrovascular disease	1794 (32.2)	1796 (32.2)	1274 (29.7)	1301 (30.9)
Major microvascular disease	571 (10.2)	584 (10.5)	385 (9.0)	415 (9.9)
Blood glucose assessment				
Glycated hemoglobin — %†				
Mean	7.5±1.6	7.5±1.5	7.5±1.5	7.5±1.5
Median (interquartile range)	7.2 (6.5–8.2)	7.2 (6.5–8.2)	7.2 (6.5–8.2)	7.2 (6.5–8.2)
Fasting blood glucose — mmol/liter	8.5±2.8	8.5±2.8	8.4±2.7	8.5±2.7
Serum creatinine — μmol/liter	0.9	0.9.8	1.00	0.96
Body-mass index§	28±5	28±5	28±5	28±5

New Engl J Med 2014

Action in Diabetes and Vascular Disease: PreterAx and DiamicroN Modified Release Controlled Evaluation ObservatioNal Study (ADVANCE-ON)



N Engl J Med 2014;371:1392-406.

Επίδραση εντατικοποιημένης αγωγής επί των επιπλοκών του διαβήτη: περίληψη κύριων μελετών

	Μικροαγγειοπάθεια	CVD	Θνησιμότητα
DCCT/EDIC[1,2] (T1DM)	↓ / ↓	↔ / ↓	↔ / ↔
UKPDS[3,4] (T2DM)	↓ / ↓	↔ / ↓	↔ / ↓
ACCORD[5] (T2DM)	↓	↔	↑
ADVANCE[6] (T2DM)	↓	↔	↔
VADT[7] (T2DM)	↓	↔	↔

Αρχική μελέτη
Παράταση -follow-up

[1]DCCT. *N Engl J Med* 1993;329:977–986. [2]DCCT/EDIC study. *N Engl J Med* 2005;353:2643–2653. [3]UKPDS Group. *Lancet* 1998;352:837–853. [4]Holman R, *et al. N Engl J Med* 2008;359:1577–1589. [5]ACCORD Study Group. *N Engl J Med* 2008;358:2545–2559. [6]ADVANCE Collaborative Group. *N Engl J Med* 2008;358:2560–2572. [7]Duckworth W, *et al. N Engl J Med* 2009;360:129–139.

	φάρμακο	Περιεχόμενο σε	Τιμή	Δόση	Τιμή μήνα
TZD	Actos	28	19.85	1 ημέρα	21
	Competact	56	27.71	2 ημέρα	29
GLP1	Bydureon	4	107	1 εβδ	107
	Victoza	2	114.21	1 ημέρα	114
	Lyxymia 20	2	88	1 ημέρα	88
Σουλφονυλουρίες	Soloza 3mg	30	7.88	1 ημέρα	7.88
	Diamicron 60	30	10,01	1-2 ημέρα	15
	Starlix 180	60	31.64	2-3 ημέρα	32
	Glucophage 850	30	1.96	2 ημέρα	3.92
α-DPP4	Galvus	28	22.67	2 ημέρα	45
	Eucreas	60	49.96	3 ημέρα	50
	Januvia 100μγ	28	42.17	1 ημέρα	42
	Janumet	56	48.60	2 ημέρα	49
	Onglyza 5mg	28	43.53	1 ημέρα	47
	Komboglyza	56	75.48	2 ημέρα	81
	Trajenta	28	46.21	1 ημέρα	50
	Jentadueto	60	48.49	2 ημέρα	49
A-SGLT2	Forxiga	28	49.96	1 ημέρα	54
	Xiduo	30-60	51.33	1 ημέρα	??
	Jardiance	30	58.99	1 ημέρα	59

	φάρμακο	Περιεχόμενο σε	Τιμή	Δόση	Τιμή μήνα
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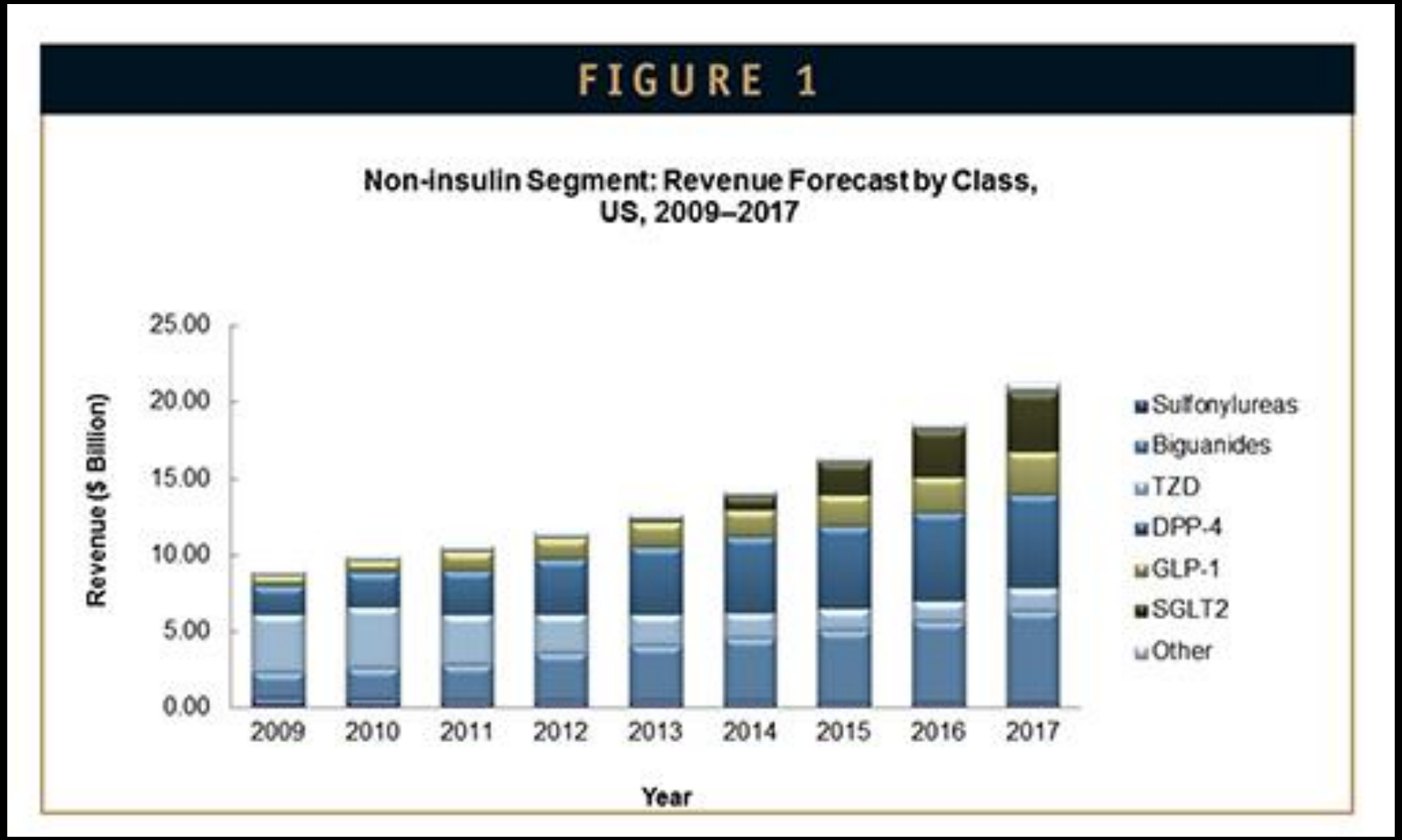
	Jardiance	30	58.99	1 ημέρα	59

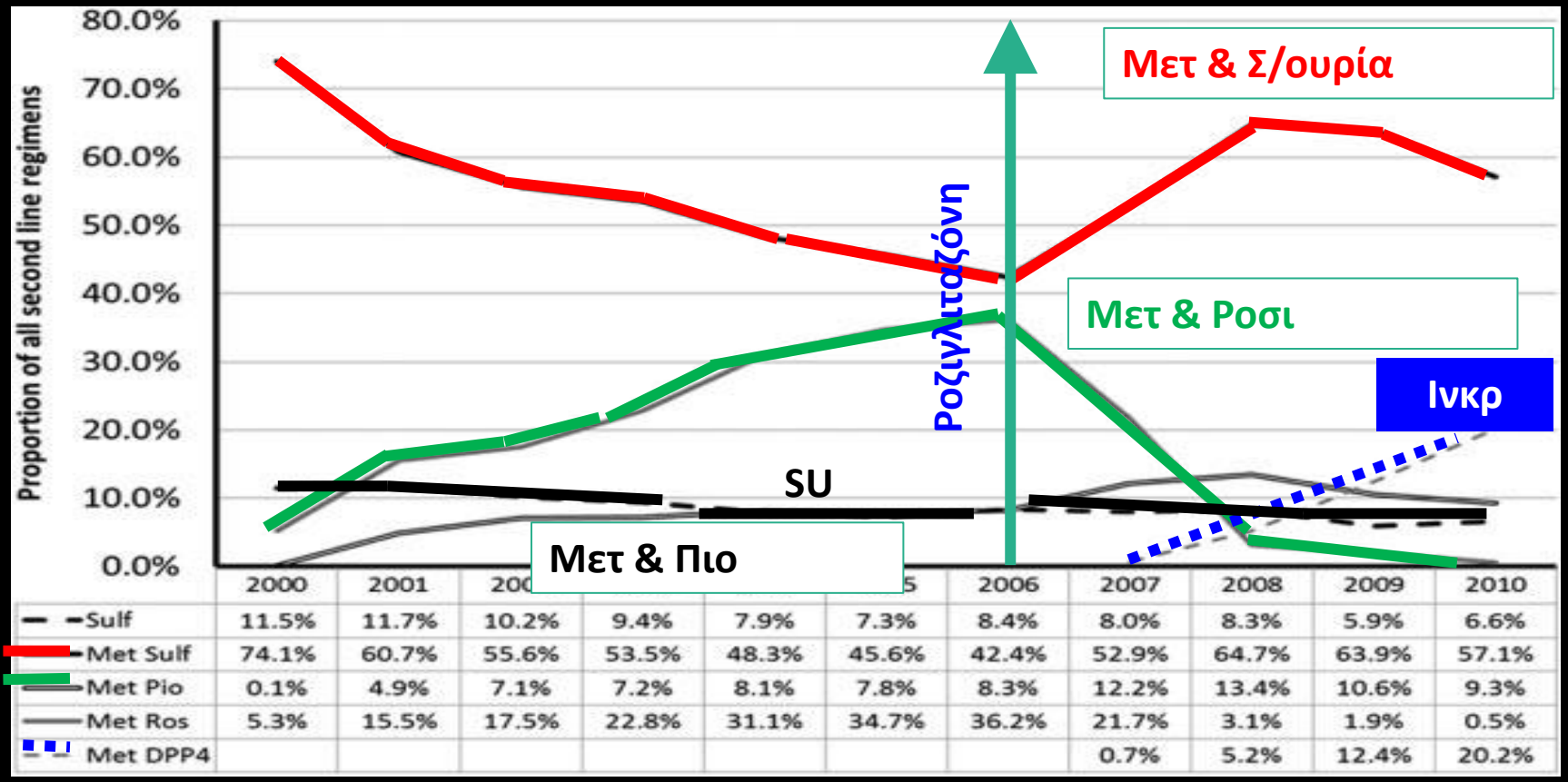
Η ADVANCE στο πλαίσιο των άλλων μεγάλων μελετών στο ΣΔΤ2

	ADVANCE	ACCORD	UKPDS
Αριθμός ασθενών	11.400	10.251	3.867
Μείωση Πρωτεύοντος Τελικού σημείου	-10%*	-10% (ns)	-12%*
Θάνατος κάθε αιτίας	-7% (ns)	+22%*	-6% (ns)
Καρδ/κός Θάνατος	-12% (ns)	+35%*	-7% (ns)
Νέα ή Επιδεινούμενη Νεφροπάθεια	-21%*	-	ns
Μακροαλβουμινουρία	-30%*	-	ns
HbA_{1c}	6,5%	6,4%	7,0%
Σοβαρή Υπογλυκαιμία/Ετος	0,7%	3,1%	1,4%
Αύξηση Σωμ. Βάρους	0,7kg	3,5kg *>10kg (28%)*	3,1kg
Βασική Αγωγή	γλικλαζίδη MR μετφορμίνη	ροσιγλιταζόνη γλιμεπιρίδη μετφορμίνη	γλιβενκλαμίδη ινσουλίνη μετφορμίνη

Market Brief
The market for DMT2 Therapeutics (Dec 2013)



What Next after Metformin? A Retrospective Evaluation of the Outcome of Second-Line, Glucose-Lowering Therapies in People with Type 2 Diabetes



	2000	2001	200			5	2006	2007	2008	2009	2010
Sulf	11.5%	11.7%	10.2%	9.4%	7.9%	7.3%	8.4%	8.0%	8.3%	5.9%	6.6%
Met Sulf	74.1%	60.7%	55.6%	53.5%	48.3%	45.6%	42.4%	52.9%	64.7%	63.9%	57.1%
Met Pio	0.1%	4.9%	7.1%	7.2%	8.1%	7.8%	8.3%	12.2%	13.4%	10.6%	9.3%
Met Ros	5.3%	15.5%	17.5%	22.8%	31.1%	34.7%	36.2%	21.7%	3.1%	1.9%	0.5%
Met DPP4								0.7%	5.2%	12.4%	20.2%

Morgan CLI et al, J Clin Endocrinol Metab, December 2012: 4605–4612

Liatis et al. BMC Endocrine Disorders 2014, 14:23
http://www.biomedcentral.com/1472-6823/14/23

BMC Endocrine Disorders

RESEARCH ARTICLE Open Access

Management of type 2 diabetes and its prescription drug cost before and during the economic crisis in Greece: an observational study

Stavros Liatis[1*], Stavroula Papaoikonomou[1], Asimina Ganotopoulou[3], Athanasia Papazafiropoulou[2], Constantinos Dinos[1], Marios Michail[1], Apostolos Xilomenos[1], Andreas Melidonis[3] and Stavros Pappas[2]

- Conclusions: During the economic crisis, the **cardiovascular risk indices** of Greek patients with type 2 diabetes being followed in public outpatient diabetes clinics **did not deteriorate** and in the case of lipid profile improved. However, the total prescription **cost increased**, mainly due to the higher cost of **glucose-lowering prescriptions**

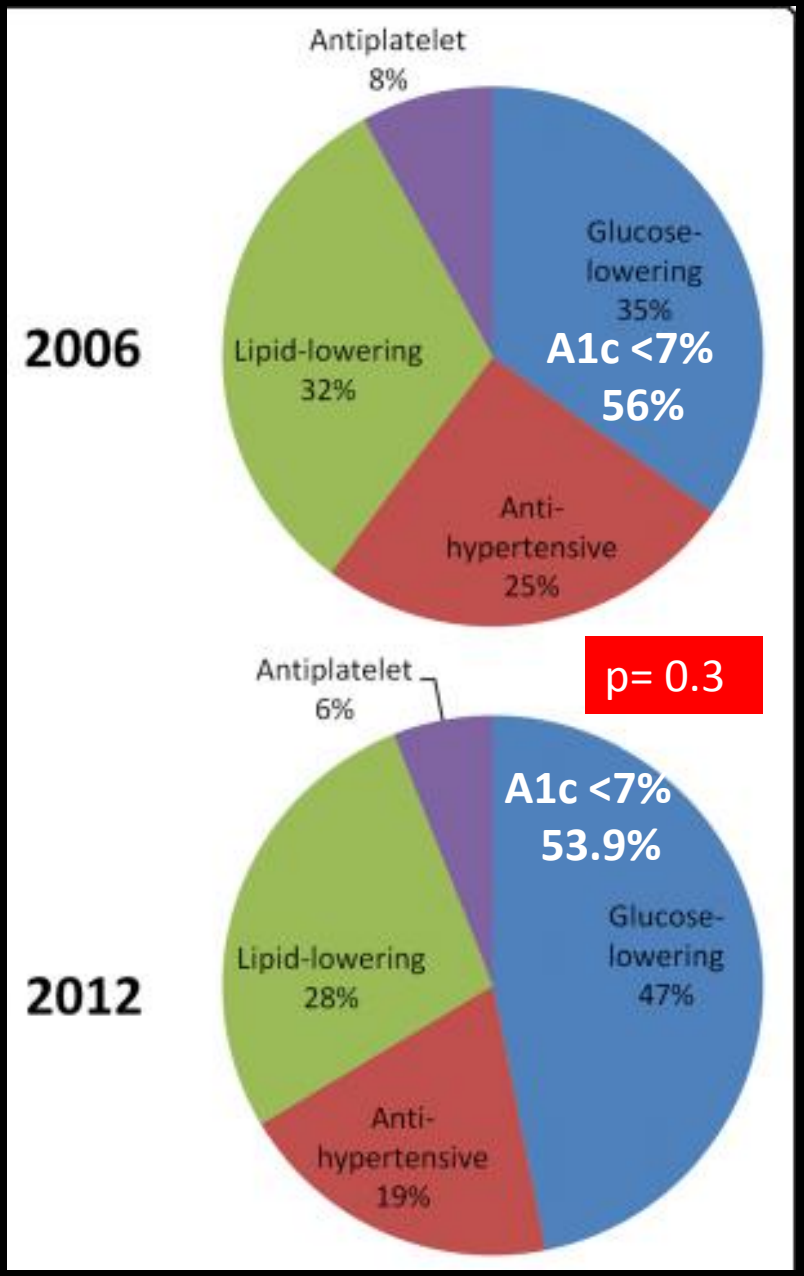


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Table 4 Prescription cost per patient-year for all diabetes-related medications (€PY)

	2006	2012	p
Glucose-lowering (all patients)	390.7 [363.5-418.0]	612.4 [586.5-638.2]	< 0.001
Glucose-lowering (only treated patients)	405.3 [377.6-433.1]	621.1 [595.1-647.1]	< 0.001
OAD only	324.9 [297.0-352.9]	504.5 [476.3-532.7]	< 0.001
Insulin	553.8 [501.6-606.0]	763.8 [720.6-807.0]	< 0.001
Excluding incretins	405.3 [501.6-606.0]	508.0 [474.7-541.3]	< 0.001
Excluding incretins & adjusting for insulin analog use	442.4 [415.2-469.6]	463.2 [431.5-495.0]	0.34
Antihypertensive (all patients)	285.3 [270.6-300.1]	255.2 [241.1-269.2]	0.004
Antihypertensive (only treated patients)	371.5 [356.0-387.1]	318.7 [304.7-332.7]	< 0.001
Lipid-lowering (all patients)	357.3 [335.0-379.5]	361.0 [339.9-382.1]	0.81
Lipid-lowering (only treated patients)	571.8 [547.2-596.4]	449.9 [429.5-450.3]	< 0.001
Antiplatelet (all patients)	89.0 [75.8-102.1]	78.1 [65.6-90.7]	0.25
Antiplatelet (only treated patients)	169.8 [146.2-193.4]	146.4 [124.2-168.5]	0.16
Total	1122.3 [1078.1-1166.5]	1306.7 [1264.6-1348.7]	< 0.001

Data are shown as mean [95% CI]. Treated patients are considered as those receiving the respective class of medication. All comparisons have been adjusted for age and duration of diabetes

Συμπέρασμα

Μήπως θα πρέπει να χρησιμοποιούμε περισσότερο ορισμένες σουλφονυλουρίες παρά τον κίνδυνο πιθανής υπογλυκαιμίας και το οικονομικό κόστος που αυτη επιφέρει;

EMPA-REG OUTCOME: Design and Baseline Characteristics

- CVOT for the SGLT2 inhibitor, empagliflozin
- 7,020 subjects with type 2 diabetes at high CV risk on standard care randomized to:

  Empagliflozin 10 mg • Empagliflozin 25 mg • Placebo
- Primary composite endpoint: CV mortality, nonfatal MI, nonfatal stroke
- Key secondary composite outcome: Primary plus hospitalization for UA
- Median 3.1-yr follow-up

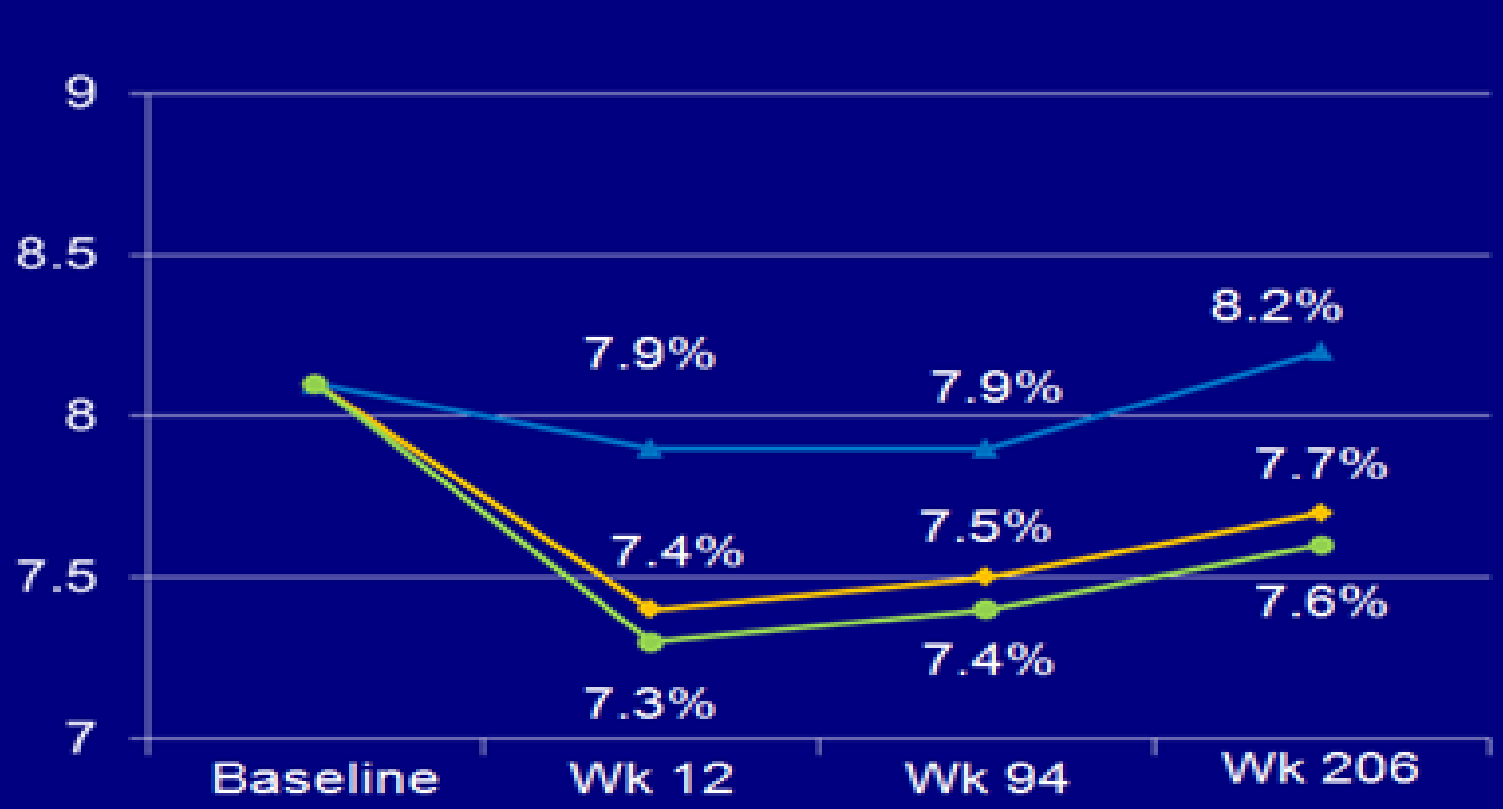
Select baseline characteristics		
	Placebo (n=2,333)	Empagliflozin (n=4,687)
Age, yrs	63.2	63.1
CV history	2,307 (98.9%)	4,657 (99.4%)
A1C	8.08%	8.07%
Dual glucose-lowering therapy	1,148 (49.2%)	1,380 (29.4%)

CVOT=cardiovascular outcome trial;
UA=unstable angina

Zinman B, et al; for the EMPA-REG OUTCOME Investigators. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1504720.

A1C Lowering With Empagliflozin Vs Placebo in High-Risk Patients With Type 2 Diabetes

EMPA-REG OUTCOM



Mean A1C change vs placebo		
	Empa 10 mg	Empa 25 mg
Wk 12	-0.54% (-0.58, -0.49)	-0.60% (-0.64, -0.55)
Wk 94	-0.42% (-0.48, -0.36)	-0.47% (-0.54, -0.41)
Wk 206	-0.24% (-0.40, -0.08)	-0.36% (-0.51, -0.20)

Empagliflozin Reduces CV Events & Mortality in High-Risk Type 2 Diabetes

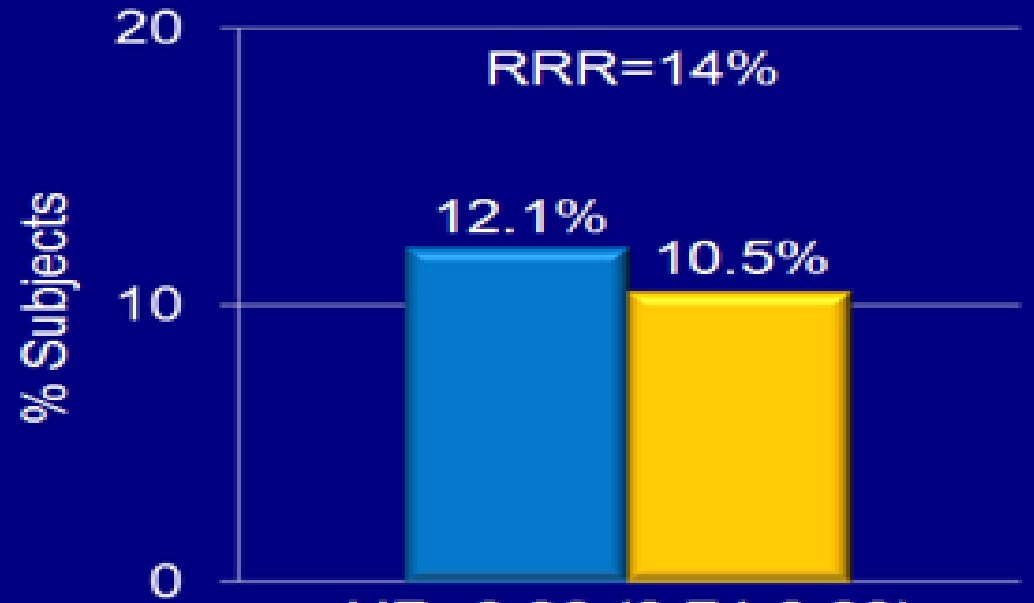
EASD 2015

EMPA-REG OUTCOME

Placebo (n=2,333)

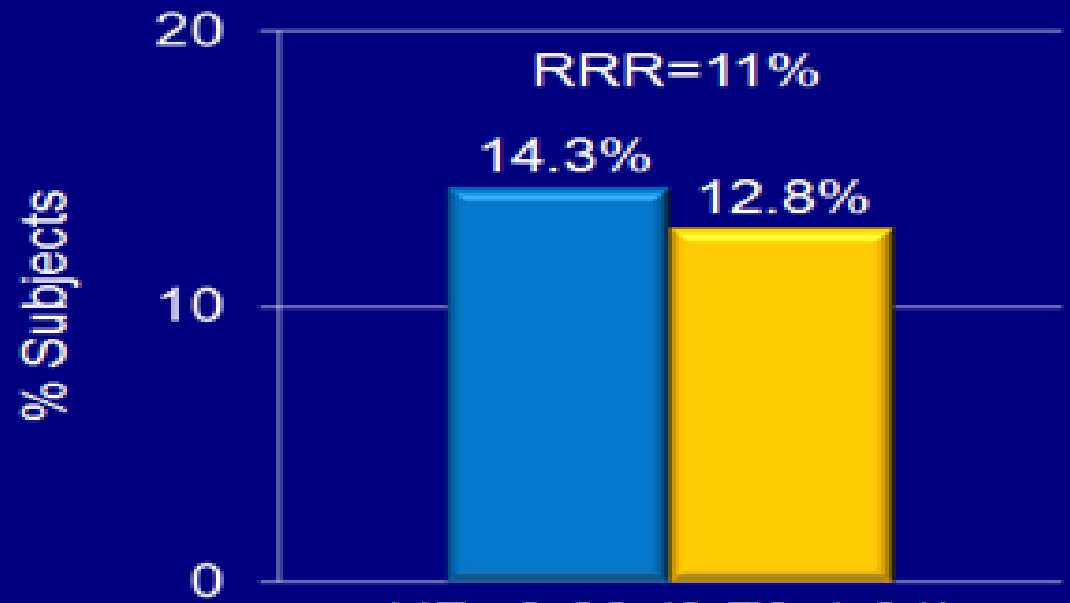
Empagliflozin (n=4,687)

Primary composite endpoint: Death from CV causes, nonfatal MI, or nonfatal stroke



HR=0.86 (0.74-0.99)
P<0.001 for noninferiority
P=0.04 for superiority

Key secondary endpoint: Death from CV causes, nonfatal MI, nonfatal stroke, or UA hospitalization



HR=0.89 (0.78-1.01)
P<0.001 for noninferiority
P=0.08 for superiority

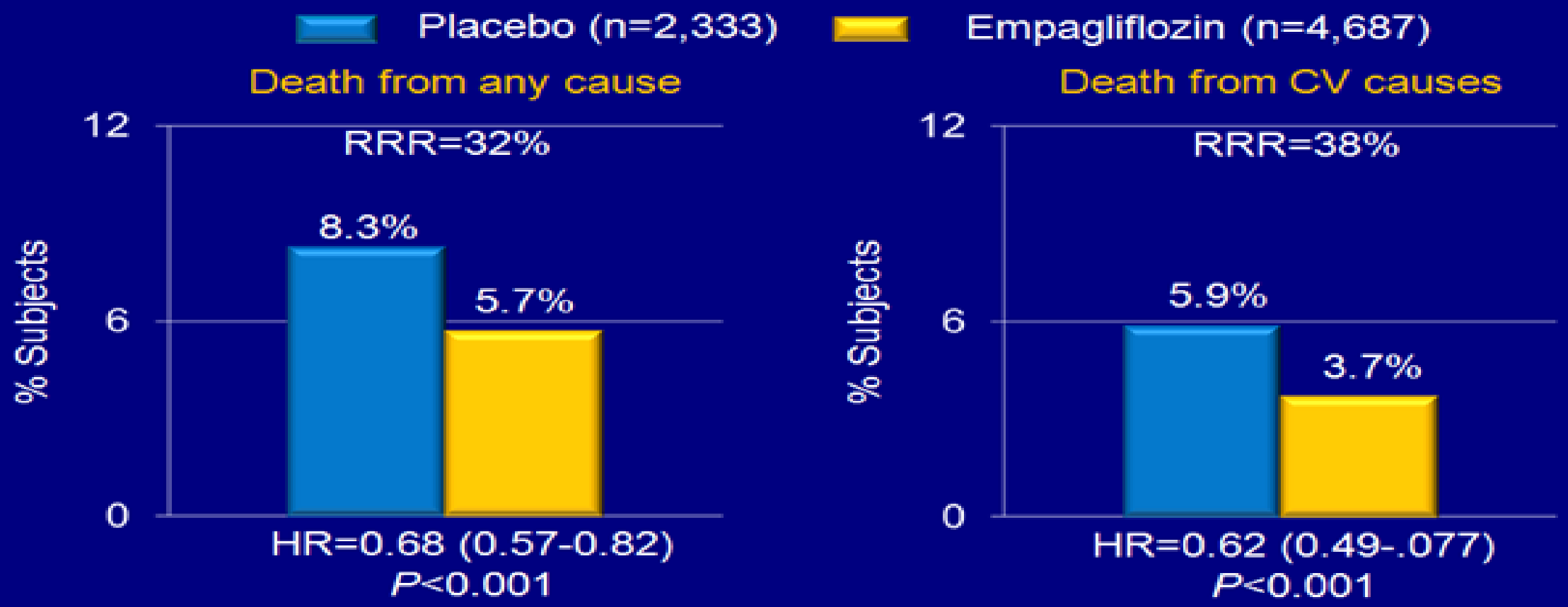
CV=cardiovascular; MI=myocardial infarction; RRR=relative risk reduction; UA=unstable angina

Zinman B, et al; for the EMPA-REG OUTCOME Investigators. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1504720.

Lower All-Cause & CV Mortality With Empagliflozin Vs Placebo in High-Risk Patients

EASD 2015

EMPA-REG OUTCOME



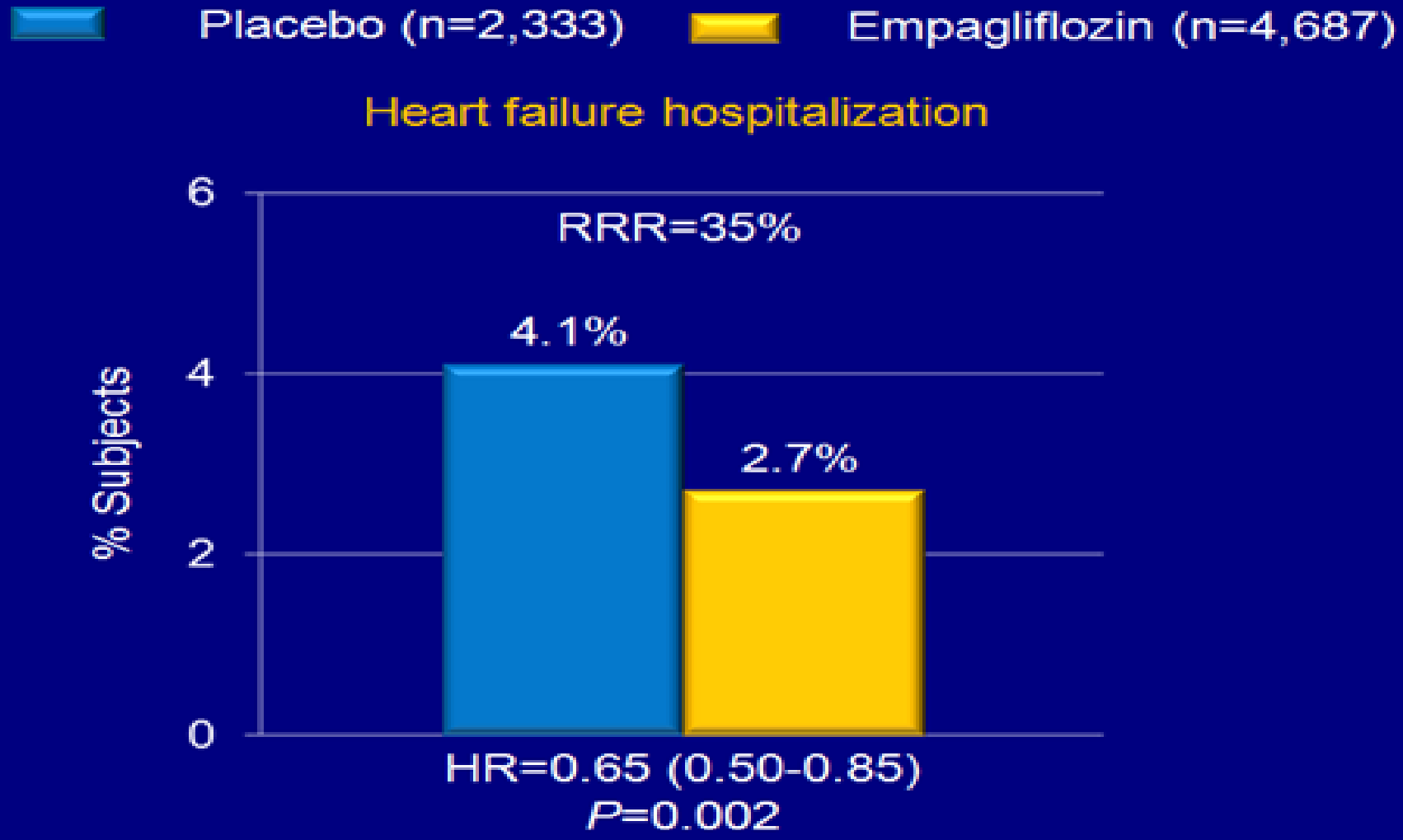
CV=cardiovascular; MI=myocardial infarction; RRR=relative risk reduction

Zinman B, et al; for the EMPA-REG OUTCOME Investigators. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1504720.

Lower Heart Failure Hospitalization With Empagliflozin Vs Placebo in High-Risk Patients

EASD 2015

EMPA-REG OUTCOME



RRR=relative risk reduction

Zinman B, et al; for the EMPA-REG OUTCOME Investigators. *N Engl J Med*. 2015. DOI: 10.1056/NEJMoa1504720.

Συμπεράσματα

- Είναι λογικό και ηθικό να ξαναχρησιμοποιηθούν οι σουλφονυλουρίες ;
- Θα πρέπει **<u>οπωσδήποτε</u>** να χρησιμοποιούμε τους αναστολείς SGLT2 μετά τα θεαματικά αποτελέσματα της EMPA-REG ;