

ΔΙΑΤΡΟΦΗ, ΤΡΟΠΟΣ ΖΩΗΣ ΚΑΙ ΓΕΝΕΤΙΚΗ ΠΡΟΔΙΑΘΕΣΗ: ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ



ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
«ΕΦΑΡΜΟΣΜΕΝΗ ΔΙΑΙΤΟΛΟΓΙΑ – ΔΙΑΤΡΟΦΗ»

Δρ Νάνα Καλαφάτη
Διαιτολόγος – Διατροφολόγος, PhD
Μεταδιδακτορική ερευνήτρια
nkalafati@gmail.com

Αθήνα, Μάιος 2021



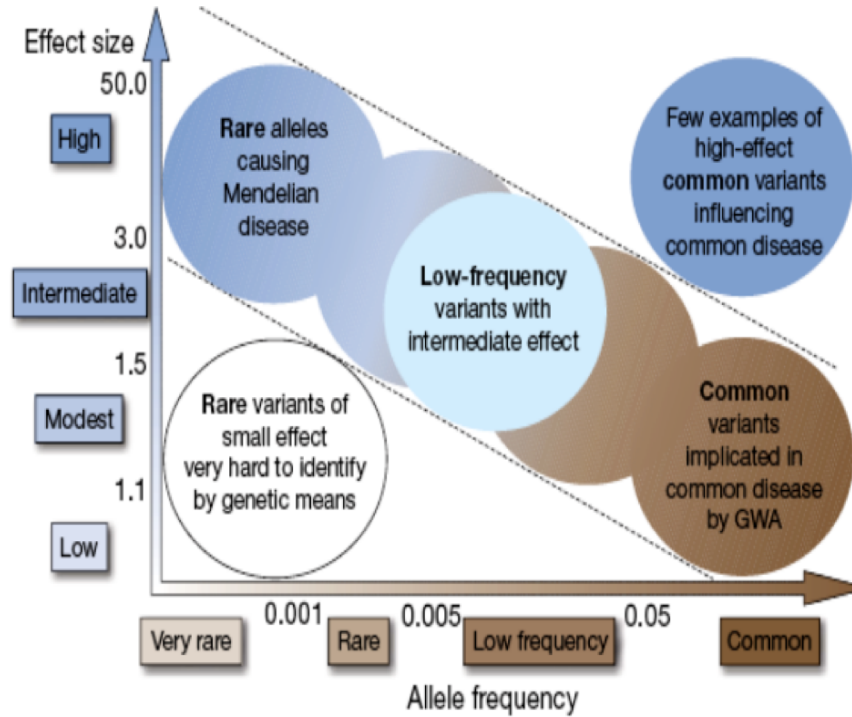
ΧΑΡΟΚΟΠΕΙΟ ΠΑΝΕΠΙΣΤΗΜΙΟ
HAROKOPIO UNIVERSITY

Ελληνικός όρος	Διεθνής όρος	Σημασία
Γονίδιο	Gene	Συγκεκριμένη περιοχή του DNA, η οποία κωδικοποιεί μία πρωτεΐνη.
Γενετικός Τόπος	Locus	Περιοχή του χρωμοσώματος.
Αλληλόμορφο	Allele	Εναλλακτικές μορφές ενός γονιδίου σε ένα δεδομένο γενετικό τόπο.
Πολυμορφισμός	Polymorphism	Διαφορετική αλληλουχία βάσης/βάσεων στο ίδιο γονίδιο, με υψηλή συχνότητα στον πληθυσμό. Δεν οδηγεί σε εμφάνιση ασθένειας - rsID
Μετάλλαξη	Mutation	Αλλαγή βάσης/βάσεων ενός γονιδίου, η οποία οδηγεί σε έκφραση μη φυσιολογικής πρωτεΐνης και ασθένειας. Σπάνια στον πληθυσμό.
Φαινότυπος	Phenotype	Παρατηρούμενη έκφραση ενός ή πολλών γονιδίων.
Γονότυπος	Genotype	Γενετική σύσταση ενός ατόμου.

Βασικοί όροι

Στατιστικός όρος	Σημασία
Odds ratio (OR)	OR = 1: Δεν υπάρχει διαφορά ως προς την πιθανότητα εμφάνισης της νόσου μεταξύ των 2 ομάδων OR < 1: Η νόσος είναι λιγότερο πιθανό να εκδηλωθεί στα άτομα που εκτέθηκαν σε σύγκριση με αυτά που δεν εκτέθηκαν (ΠΡΟΣΤΑΤΕΥΤΙΚΗ ΕΠΙΔΡΑΣΗ) OR > 1: Η νόσος είναι πιθανότερο να εκδηλωθεί στα άτομα που εκτέθηκαν σε σύγκριση με αυτά που δεν εκτέθηκαν (ΕΠΙΒΑΡΥΝΤΙΚΗ ΕΠΙΔΡΑΣΗ)
Relative Risk (RR)	RR>1: ο κίνδυνος εμφάνισης της νόσου αυξάνεται μετά την έκθεση στον παράγοντα μελέτης
Beta coefficient	Σχέση μεταξύ Y και X – βαρύτητα
p-value	p-value ≤ 0.05: Η απόρριψη της H0 είναι ισχυρή
Meta-analysis	Στατιστική ανάλυση αποτελεσμάτων μελετών με κοινή υπόθεση, με σκοπό να βγει ένα κοινό συμπέρασμα
Candidate-gene analysis	Έλεγχος συγκεκριμένων γονιδίων (a priori)
GWAS	Τυχαία αναζήτηση συσχέτισης – Σάρωση γονιδιώματος (a posteriori)

Βασικοί όροι



Βασικοί όροι

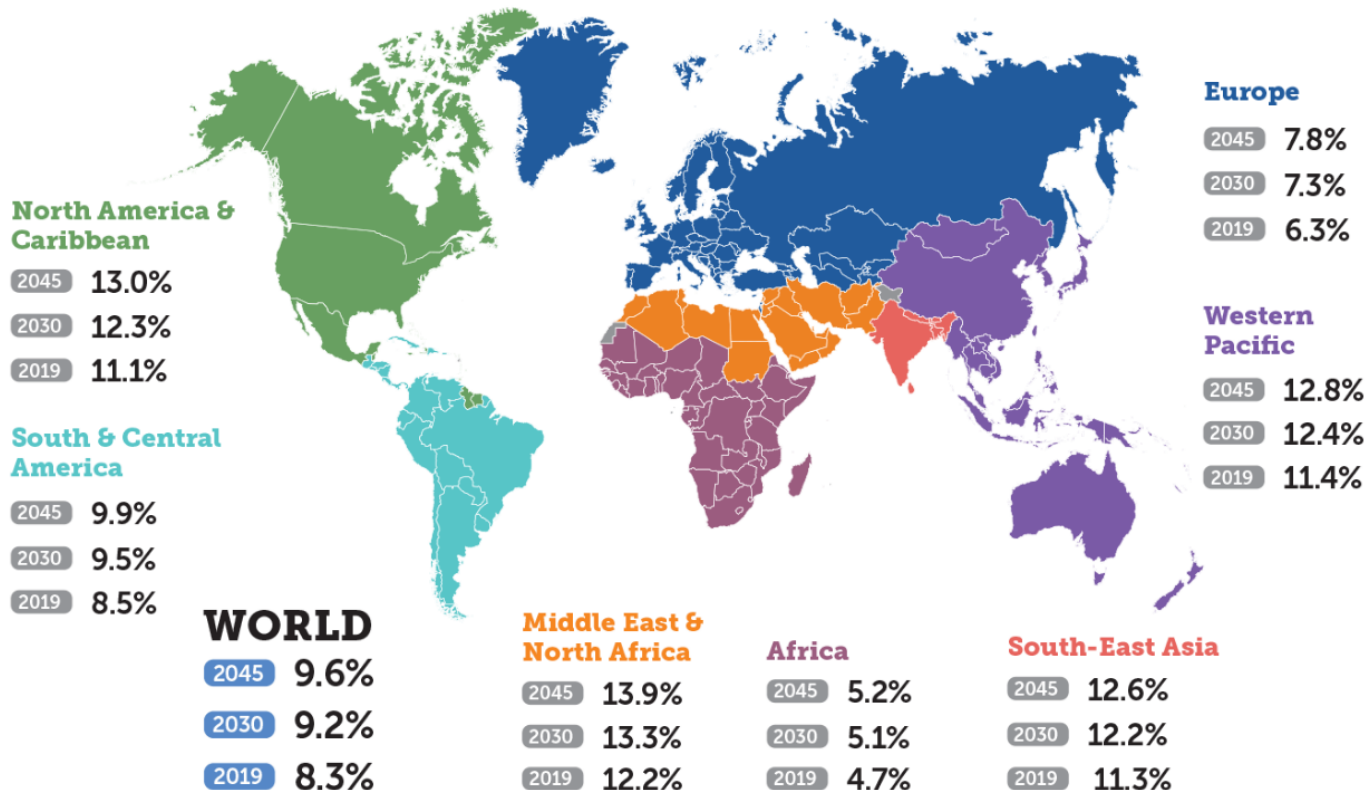
Επιπολασμός

Α ν α μ έ ν ε τ α ι
π ε ρ α ι τ έ ρ ω α ύ ξ η σ η
τ ο υ π α γ κ ό σ μ ι ο υ
ε π ι π ο λ α σ μ ο ύ τ η ς
ν ό σ ο υ .



Η α ν ά γ κ η
ε ξ α τ ο μ ι κ ε υ μ έ ν η ς
θ ε ρ α π ε ί α ς ε ί ν α ι
π λ έ ο ν ε π ι τ α κ τ ι κ ή .

Map Prevalence of diabetes in adults (20–79 years) in IDF Regions, by age-adjusted comparative diabetes prevalence



Factors that affect insulin secretion and action

- Body weight
- Level of physical activity
- Smoking
- Heavy alcohol consumption
- Genetic predisposition
- Gene-environment interaction
- Epigenetics
- Gestational diabetes mellitus

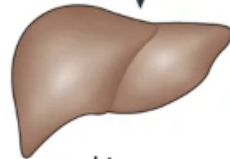
Positive risk profile

Normoglycaemia

Negative risk profile

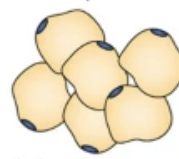
β -cell dysfunction and insulin resistance

Insulin-mediated glucose production $\uparrow$



Liver

Insulin-mediated glucose uptake $\downarrow$



Adipose tissue

Insulin-mediated glucose uptake $\downarrow$



Skeletal muscle

Hyperglycaemia

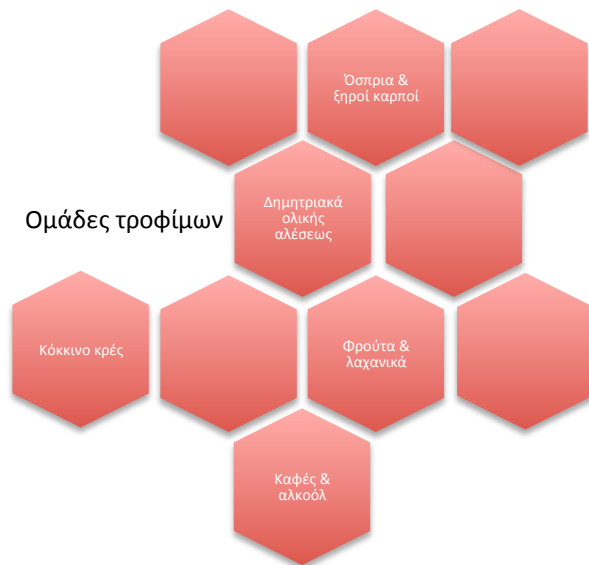
****Σημαντικός ο ρόλος των γονιδίων**

Βασικοί παράγοντες κινδύνου

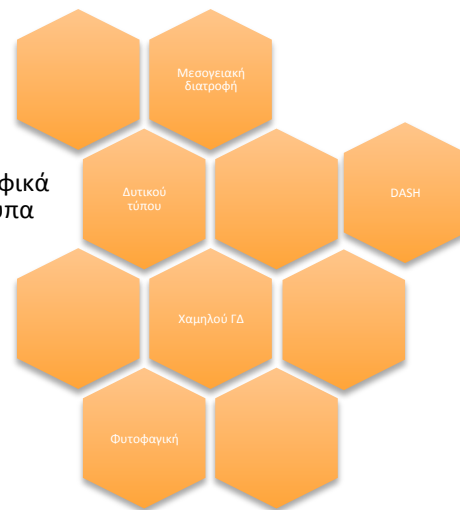
- ✧ Μεγαλύτερη ηλικία
 - ✧ Μη λευκή καταγωγή
 - ✧ Οικογενειακό ιστορικό σακχαρώδους διαβήτη τύπου 2
 - ✧ Χαμηλή κοινωνικοοικονομική κατάσταση
 - ✧ Γενετικοί παράγοντες
 - ✧ Συστατικά του μεταβολικού συνδρόμου
 - ✧ Υπέρβαρο ή παχύσαρκο ($\Delta\text{ΜΣ} \geq 25 \text{ kg / m}^2$)
 - ✧ Κεντρικού τύπου παχυσαρκία (ανεξάρτητη από τον $\Delta\text{ΜΣ}$)
 - ✧ Ανθυγιεινές διατροφικές συνήθειες
 - ✧ Κάπνισμα
 - ✧ Καθιστική ζωή
 - ✧ Ιστορικό σακχαρώδους διαβήτη κύησης ή παράδοση νεογνών $> 4 \text{ kg}$ σε βάρος
 - ✧ Μερικά φάρμακα, όπως στατίνες, θειαζίδες και βήτα-αποκλειστές
 - ✧ Ψυχοκοινωνικό στρες και κατάθλιψη
- ΓχΠ αλληλεπιδράσεις
-
- The diagram illustrates the synergistic interactions between various risk factors for Gestational Diabetes Mellitus (GDM). Green arrows point from the 'Genetic factors' and 'Unhealthy dietary habits' categories to the 'GDM interactions' label, indicating their combined impact. Additionally, green arrows point from 'Smoking', 'Sedentary lifestyle', and 'History of gestational diabetes or birth weight' towards the 'GDM interactions' label, suggesting these factors also contribute to the overall risk through their interactions with other factors.

Παράγοντες διατροφής

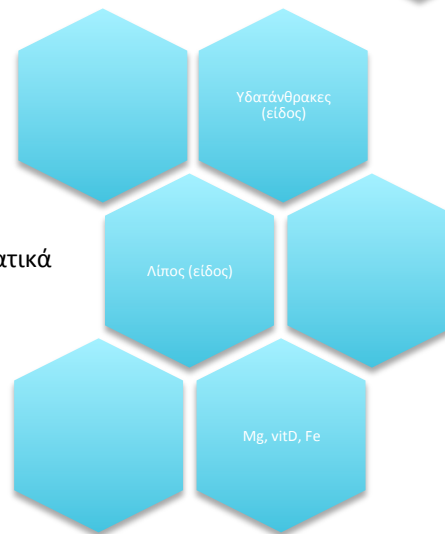
Ομάδες τροφίμων



Διατροφικά πρότυπα



Θρεπτικά συστατικά



ΕΝΕΡΓΕΙΑΚΟ ΙΣΟΖΥΓΙΟ

Αποτελέσματα μεγάλων
διατροφικών μελετών
παρατήρησης και
παρέμβασης.

Nutritional factor assessed	Relative risk (95% CI)
Nutrients	
Haeme (iron)	1.31 (1.21–1.43) extreme groups*
Glycaemic index	1.19 (1.14–1.24) extreme groups*
Glycaemic load	1.13 (1.08–1.17) extreme groups*
Docosahexaenoic acid (DHA) or eicosapentaenoic acid (EPA)	1.04 (0.97–1.10) per 250 mg per day
Vegetable fibre	1.04 (0.94–1.15) extreme groups*
Fruit fibre	0.96 (0.88–1.04) extreme groups*
α -Linolenic acid	0.93 (0.83–1.04) per 0.5 g per day
Magnesium	0.78 (0.73–0.84) extreme groups*
Cereal fibre	0.67 (0.62–0.72) extreme groups*
Vitamin D	0.62 (0.54–0.70) extreme groups*
Food groups	
Processed red meat	1.51 (1.25–1.83) per 50 g per day
Unprocessed red meat	1.19 (1.04–1.37) per 100 g per day
Fish or seafood	1.12 (0.94–1.34) per 100 g per day
White rice	1.11 (1.08–1.14) per 1 serving per day
Green leafy vegetables	0.86 (0.77–0.97) extreme groups*
Green leafy vegetables	0.84 (0.74–0.94) extreme groups*
Dairy products	0.86 (0.79–0.92) extreme groups*
Whole grains	0.68 (0.58–0.81) per 3 servings per day
Sugar-sweetened beverages	1.26 (1.12–1.41) extreme groups*
Sugar-sweetened beverages	1.18 (1.06–1.32) per 336 g per day
Decaffeinated coffee	0.80 (0.70–0.91) extreme groups*
Total coffee	0.70 (0.65–0.75) extreme groups*
Dietary patterns	
Mediterranean diet	0.60 (0.43–0.85) Mediterranean diet supplemented with extra-virgin olive oil compared with control group (advice on a low-fat diet), 0.82 (0.61–1.10) Mediterranean diet supplemented with nuts compared with control group
Alternate healthy eating index (AHEI) 2010	0.77 (0.67–0.88) the highest compared with the lowest quintiles
Dietary approaches to stop hypertension (DASH)	0.75 (0.65–0.85) the highest compared with the lowest quintiles

Φυσική δραστηριότητα

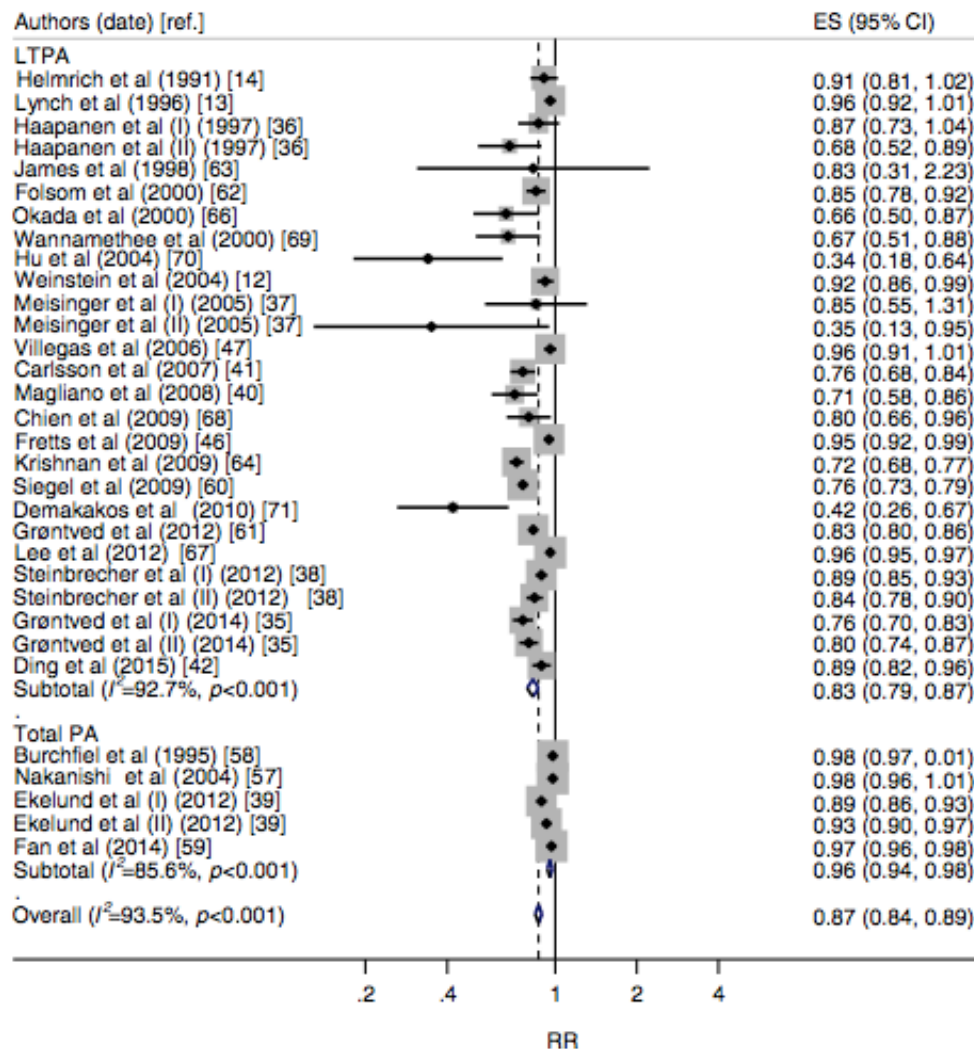
Άσκηση

- Υψηλή vs χαμηλή ΦΔ συσχετίζεται με μείωση του σχετικού κινδύνου εμφάνισης ΣΔ κατά περίπου 30%
- Βελτίωση ινσουλινοευαισθησίας και γλυκαιμικού ελέγχου σε μη-διαβητικά άτομα.
- Συμπεριλαμβάνονται όλοι οι τύποι άσκησης (εντός & εκτός εργασίας).
- Δεν αφορά μόνο στην κατανάλωση θερμίδων.

Δραστηριότητες καθιστικές

- Αυξημένη διάρκεια καθιστικών δραστηριοτήτων → 2πλάσιος κίνδυνος εμφάνισης ΣΔ
- 1 ώρα επιπλέον μπροστά στην τηλεόραση → 3,4% μεγαλύτερο κίνδυνο εμφάνισης ΣΔ μέσα σε 3,2 έτη

→ Σύσταση για αντικατάσταση καθιστικών δραστηριοτήτων με δραστηριότητες που περιλαμβάνουν κίνηση και άσκηση.

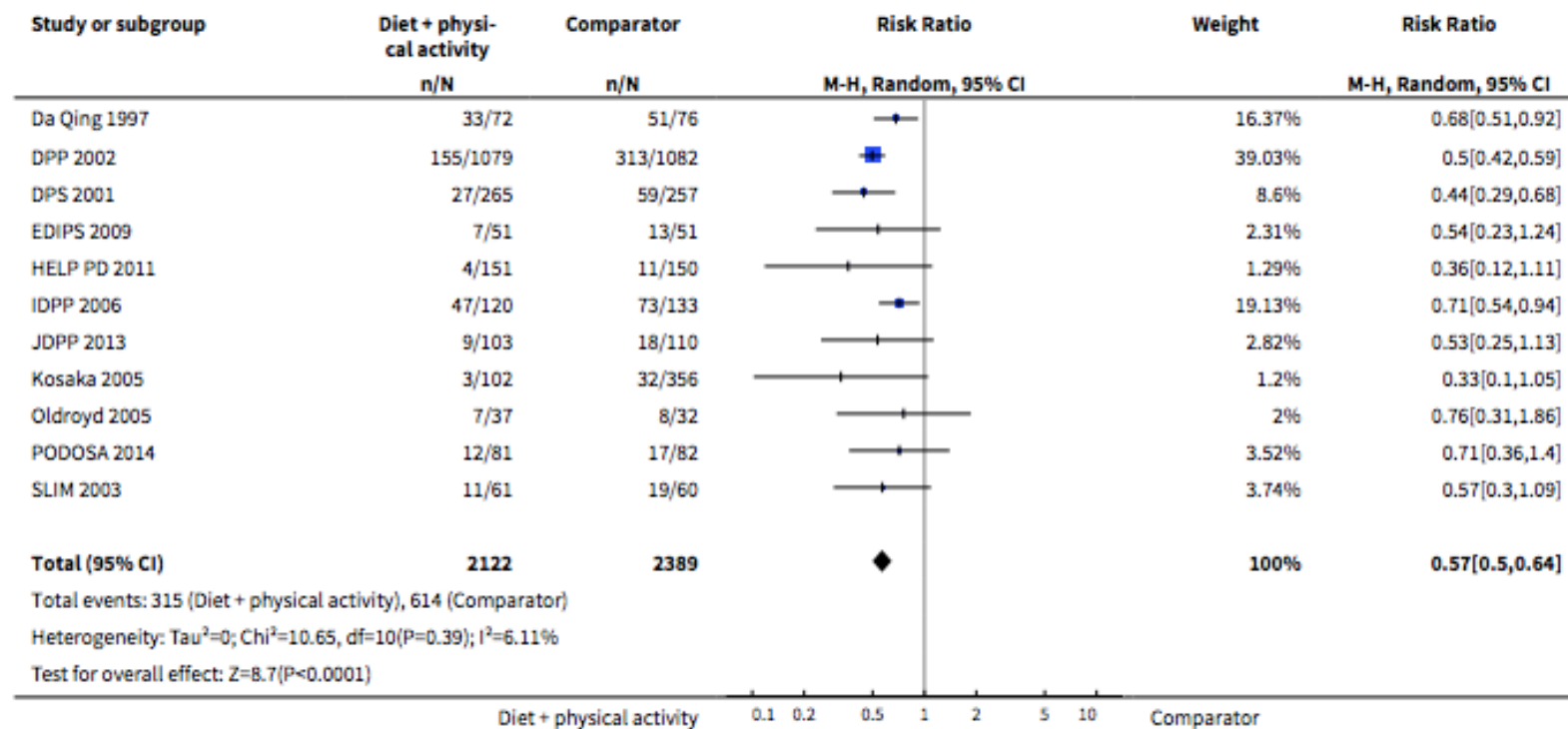


- Σχετικοί κίνδυνοι για ΣΔ ανά 10 MET h/wk
- LTPA: Leisure-time PA

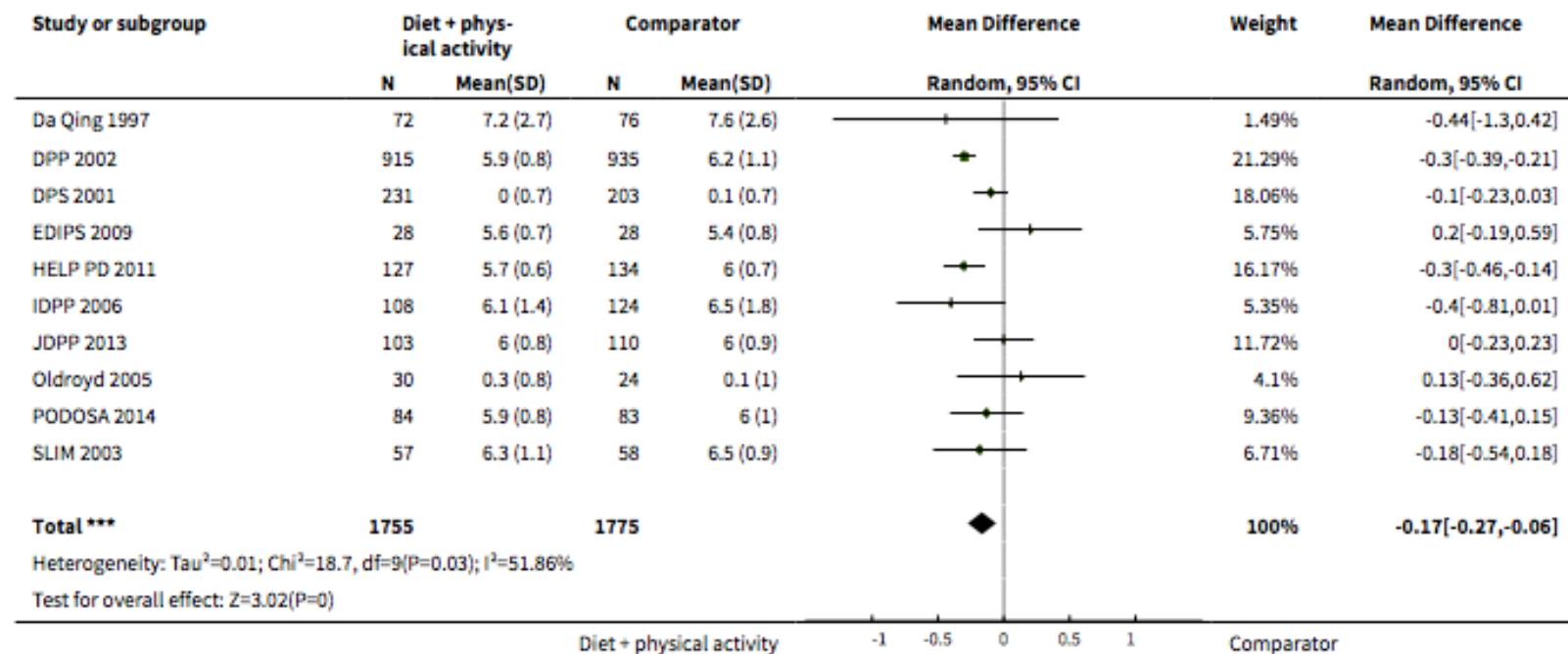
- Δοσο-εξαρτώμενη συσχέτιση
- a-d: διαφορετικά σενάρια όσον αφορά τα MET h/wk αναφοράς και τη διάρκεια της κάθε συνεδρίας

LTPA MET h/week	a		b		c		d	
	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
2.25	0.93	(0.92, 0.95)	0.92	(0.90, 0.94)	0.92	(0.90, 0.94)	0.88	(0.85, 0.92)
4.50	0.87	(0.84, 0.90)	0.85	(0.82, 0.89)	0.85	(0.82, 0.89)	0.82	(0.77, 0.87)
10.00	0.76	(0.71, 0.81)	0.73	(0.67, 0.80)	0.73	(0.67, 0.79)	0.68	(0.60, 0.76)
11.25	0.74	(0.69, 0.80)	0.72	(0.65, 0.79)	0.71	(0.65, 0.77)	0.67	(0.58, 0.75)
22.50	0.64	(0.56, 0.73)	0.61	(0.52, 0.71)	0.61	(0.52, 0.70)	0.55	(0.45, 0.67)
30.00	0.60	(0.51, 0.70)	0.58	(0.48, 0.69)	0.57	(0.47, 0.68)	0.52	(0.41, 0.65)
60.00	0.47	(0.34, 0.65)	0.45	(0.31, 0.68)	0.44	(0.31, 0.63)	0.39	(0.26, 0.60)

Analysis 2.8. Comparison 2 Diet plus physical activity versus comparator, Outcome 8 Incidence of type 2 diabetes.



Analysis 2.18. Comparison 2 Diet plus physical activity versus comparator, Outcome 18 Fasting plasma glucose.



Καπνιστικές συνήθειες

- Υψηλότερος κίνδυνος εμφάνισης ΣΔ σε ενεργητικούς & παθητικούς καπνιστές σε σύγκριση με μη-καπνιστές
- Μετα-ανάλυση προοπτικών μελετών: RR=1,6 βαρείς | RR=1,3 ελαφρείς καπνιστές | RR=1,2 πρώην καπνιστές

Tobacco Use, Insulin Resistance, and Risk of Type 2 Diabetes: Results from the Multi-Ethnic Study of Atherosclerosis

Rachel J. Keith^{1,2,3,*}, Mahmoud Al Rifai^{3,4}, Christopher Carruba⁵, Natasha De Jarnett^{1,3}, John W. McEvoy⁴, Aruni Bhatnagar^{1,2,3}, Michael J. Blaha^{3,4}, Andrew P. Defilippis^{1,2,3,4}

- 5931 άτομα διαφόρων εθνικοτήτων
- Σχέση καπνού – παρουσίας προδιαβήτη
- Σχέση καπνού – Επίπτωση ΣΔ

Table 6. Odds Ratios (95%) for the association of tobacco exposure and baseline prediabetes.

	Unadjusted	Model 1	Model 2
Cigarette			
Never	1 (reference)	1 (reference)	1 (reference)
Former	1.05 (0.90,1.22)	0.90 (0.75,1.07)	0.88 (0.72,1.08)
Current	0.91 (0.73,1.14)	0.86 (0.67,1.11)	1.02 (0.76,1.36)
Cigar			
Never	1 (reference)	1 (reference)	1 (reference)
Former	1.54 (1.11,2.14)	1.51 (1.02,2.21)	1.30 (0.86,1.98)
Current	1.88 (0.88,4.00)	2.16 (0.93,5.01)	1.91 (0.76,4.77)
Pipe			
Never	1 (reference)	1 (reference)	1 (reference)
Former	1.10 (0.83,1.46)	1.05 (0.76,1.46)	0.91 (0.63,1.32)
Current	1.85 (0.73,4.67)	2.05 (0.71,5.91)	2.04 (0.62,6.70)
Smokeless			
Never	1 (reference)	1 (reference)	1 (reference)
Former	1.47 (0.77,2.79)	1.28 (0.59,2.77)	0.92 (0.35,2.45)
Current	1.84 (0.50,6.80)	1.41 (0.31,6.47)	0.50 (0.04,5.66)

Tobacco Use, Insulin Resistance, and Risk of Type 2 Diabetes: Results from the Multi-Ethnic Study of Atherosclerosis

Rachel J. Keith^{1,2,3*}, Mahmoud Al Rifai^{3,4}, Christopher Carruba⁵, Natasha De Jarnett^{1,3}, John W. McEvoy⁴, Aruni Bhatnagar^{1,2,3}, Michael J. Blaha^{3,4}, Andrew P. Defilippis^{1,2,3,4}

- Δεν παρατηρήθηκε κάποια στατιστικά σημαντική ανεξάρτητη σχέση.

Table 7. Hazard ratios (95% CI) for the association of tobacco exposure and incident diabetes.

	N events	Unadjusted	Model 1	Model 2
Cigarette				
Never	154	1 (reference)	1 (reference)	1 (reference)
Former	160	1.35 (1.08,1.68)	1.20 (0.95,1.51)	1.02 (0.77,1.37)
Current	45	1.07 (0.77,1.49)	1.04 (0.74,1.46)	0.86 (0.55,1.34)
Cigar				
Never	331	1 (reference)	1 (reference)	1 (reference)
Former	24	1.74 (1.13,2.69)	1.51 (0.96,2.39)	1.58 (0.85,2.94)
Current	4	0.92 (0.23,3.68)	0.89 (0.22,3.61)	1.90 (0.39,9.11)
Pipe				
Never	321	1 (reference)	1 (reference)	1 (reference)
Former	36	1.46 (1.02,2.10)	1.43 (0.97,2.12)	1.36 (0.83,2.25)
Current	2	0.69 (0.10,4.91)	0.63 (0.09,4.49)	1.10 (0.14,8.88)
Smokeless tobacco				
Never	343	1 (reference)	1 (reference)	1 (reference)
Former	12	3.38 (1.85,6.16)	3.18 (1.72,5.86)	2.19 (0.83,5.76)
Current	4	3.09 (0.77,12.41)	2.75 (0.68,11.10)	–

Tobacco Use, Insulin Resistance, and Risk of Type 2 Diabetes: Results from the Multi-Ethnic Study of Atherosclerosis

Rachel J. Keith^{1,2,3,*}, Mahmoud Al Rifai^{3,4}, Christopher Carruba⁵, Natasha De Jarnett^{1,3}, John W. McEvoy⁴, Aruni Bhatnagar^{1,2,3}, Michael J. Blaha^{3,4}, Andrew P. Defilippis^{1,2,3,4}

Table 4. Beta coefficients (95% CI) for the cross-sectional association of dose and intensity of tobacco exposure and levels of insulin resistance biomarkers.

	Dose of tobacco exposure			Intensity of tobacco exposure		
	Unadjusted	Model 1	Model 2	Unadjusted	Model 1	Model 2
Cigarette						
Glucose, mg/dL	3.49 (1.01,5.97)	2.60 (0.10,5.11)	1.93 (-0.43,4.29)	3.52 (-0.26,7.31)	3.75 (-0.11,7.61)	2.52 (-1.10,6.14)
Insulin, mU/L	0.03 (-0.03,0.10)	0.08 (0.01,0.14)	0.02 (-0.03,0.07)	0.05 (-0.0,0.15)	0.12 (0.02,0.22)	0.005 (-0.079,0.084)
HOMA-IR, %	0.07 (-0.04,0.14)	0.10 (0.03,0.17)	0.04 (-0.02,0.10)	0.09 (-0.02,0.20)	0.16 (0.05,0.27)	0.02 (-0.07,0.12)
Cigar						
Glucose, mg/dL	2.78 (0.06,5.50)	1.25 (-1.44,3.95)	1.08 (-1.43,3.60)	99.96 (30.32,169.59)	56.04 (-13.62,125.70)	34.67 (-30.84,100.17)
Insulin, mU/L	0.04 (-0.03,0.11)	0.06 (-0.01,0.13)	-0.10 (-0.03,0.08)	2.43 (0.68,4.17)	3.21 (1.44,4.96)	1.31 (-0.15,2.80)
HOMA-IR, %	0.07 (0.01,0.15)	0.076 (-0.002,0.153)	0.04 (-0.03,0.10)	3.48 (1.48,5.48)	3.82 (1.81,5.83)	1.69 (0.02,3.36)
Pipe						
Glucose, mg/dL	0.06 (-1.40,2.58)	-0.44 (-2.43,1.55)	-0.41 (-2.36,1.54)	3.43 (-14.77,8.33)	1.08 (-48.93,51.10)	-11.02 (-58.64,36.59)
Insulin, mU/L	0.03 (0.02,0.08)	0.06 (0.01,0.11)	0.04 (-0.01,0.08)	1.59 (0.36,2.82)	2.60 (1.33,3.86)	1.060 (0.006,2.212)
HOMA-IR, %	0.04 (-0.02,0.10)	0.059 (0.002,0.117)	0.03 (-0.02,0.08)	1.98 (0.57,3.38)	2.66 (1.22,4.10)	0.96 (-0.25,2.18)
Smokeless tobacco						
Glucose, mg/dL	1.15 (-3.69,5.99)	1.22 (-3.54,5.97)	1.13 (-3.63,5.89)	9.81 (-66.55,86.16)	17.33 (-57.59,92.25)	14.97 (-57.44,87.39)
Insulin, mU/L	-0.01 (-0.13,0.11)	0.002 (-0.118,0.122)	-0.05 (-0.15,0.06)	-0.33 (-2.24,1.58)	-0.19 (-2.07,1.70)	-0.26 (-1.88,1.36)
HOMA-IR, %	0.01 (-0.13,0.15)	0.02 (-0.12,0.16)	-0.03 (-0.15,0.09)	-0.15 (-2.34,2.04)	0.08 (-2.08,2.22)	-0.02 (-1.86,1.82)

Συνήθειες ύπνου

Διάρκεια Ύπνου

- 7-8 ώρες ύπνου ημερησίως → χαμηλότερος κίνδυνος ΣΔ
 - Αύξηση κινδύνου κατά 9% για κάθε μείωση διάρκειας ύπνου κατά 1 ώρα
 - Μεγαλύτερη διάρκεια ύπνου ή ύπνος κατά τη διάρκεια της ημέρας → αύξηση κινδύνου (;)

Διαταραχές Ύπνου

- Σκορ ποιότητας ύπνου (PSQI): συσχέτιση με επίπεδα HbA1c και γλυκόζης νηστείας.
- Συμπτώματα αυπνίας → μεγαλύτερη επίπτωση ΣΔ
- Κοινωνικό jetlag
- Χρονότυπος

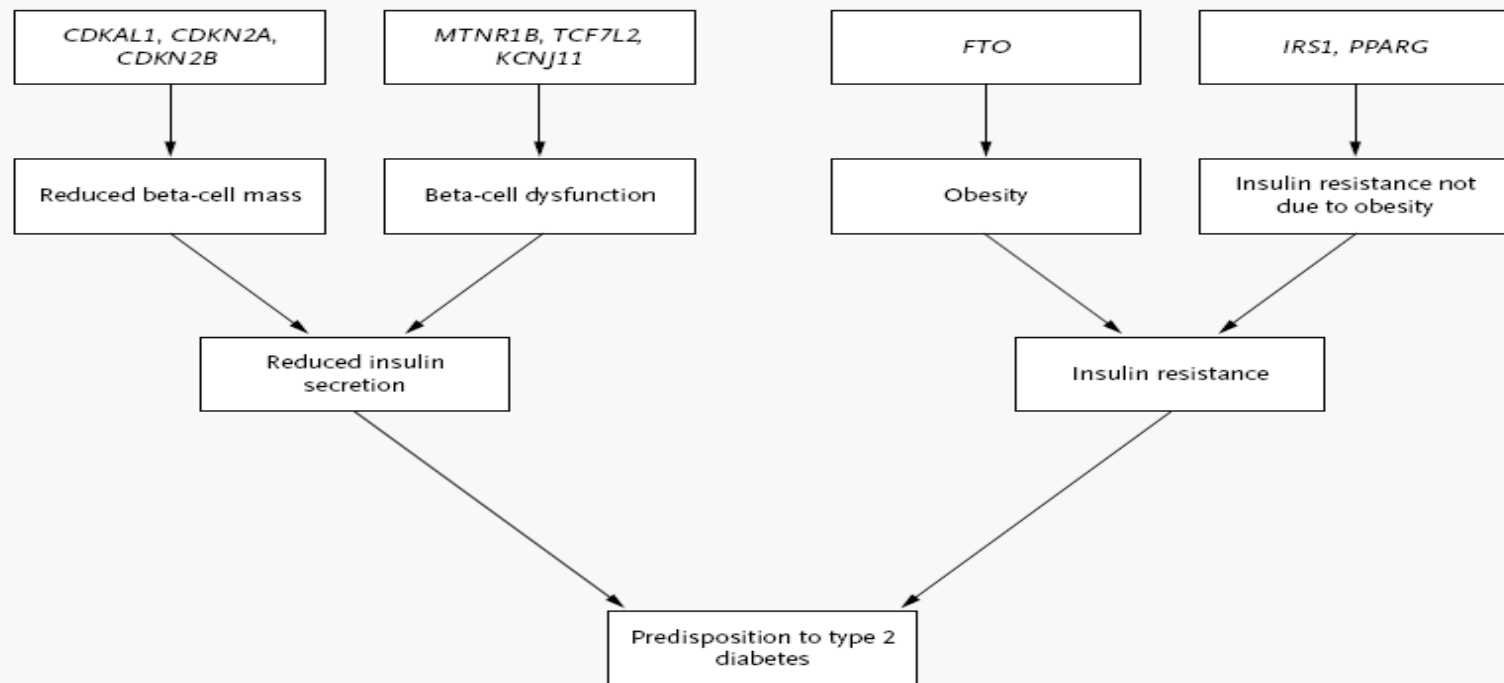


Figure 3. Pathways to Type 2 Diabetes Implicated by Identified Common Variant Associations.

Type 2 diabetes results when pancreatic beta cells are unable to secrete sufficient insulin to maintain normoglycemia, typically in the context of increasing peripheral insulin resistance. The beta-cell abnormalities fundamental to type 2 diabetes are thought to include both reduced beta-cell mass and disruptions of beta-cell function. Insulin resistance can be the consequence of obesity or of obesity-independent abnormalities in the responses of muscle, fat, or liver to insulin. Examples of susceptibility variants that, given current evidence, are likely to influence predisposition to type 2 diabetes by means of each of these mechanisms are shown.

Variant of transcription factor 7-like 2 (TCF7L2) gene confers risk of type 2 diabetes

Struan F A Grant¹, Gudmar Thorleifsson, Inga Reynisdottir, Rafn Benediktsson, Andrei Manolescu, Jesus Sainz, Agnar Helgason, Hreinn Stefansson, Valur Emilsson, Anna Helgadóttir, Unnur Styrkarsdóttir, Kristinn P Magnusson, G Bragi Walters, Ebba Palsdóttir, Thorbjorg Jonsdóttir, Thorunn Gudmundsdóttir, Arnaldur Gylfason, Jona Saemundsdóttir, Robert L Wilensky, Muredach P Reilly, Daniel J Rader, Yu Bagger, Claus Christiansen, Vilmundur Gudnason, Gunnar Sigurdsson, Unnur Thorsteinsdóttir, Jeffrey R Gulcher, Augustine Kong, Karl Stefansson

	Allele	Affected frequency ^a	Control frequency ^a	RR ^b	Two sided P ^c
All alleles of DG10S478^d					
Iceland (1,185/931)	0	0.636	0.724	0.67	2.1 × 10 ⁻⁹
	4	0.005	0.002	2.36	0.12
	8	0.093	0.078	1.21	0.090
	12	0.242	0.178	1.48	4.6 × 10 ⁻⁷
	16	0.022	0.015	1.53	0.076
Denmark (228/539)	0	0.669	0.740	0.71	0.0048
	4	0.002	0.004	0.59	0.62
	8	0.070	0.048	1.49	0.091
	12	0.239	0.190	1.34	0.032
	16	0.020	0.018	1.12	0.78
USA (361/530)	-4	0.001	0.000	-	-
	0	0.615	0.747	0.54	3.3 × 10 ⁻⁹
	4	0.003	0.004	0.73	0.72
	8	0.085	0.049	1.79	0.0029
	12	0.256	0.180	1.57	1.2 × 10 ⁻⁴
	16	0.040	0.020	2.07	0.012

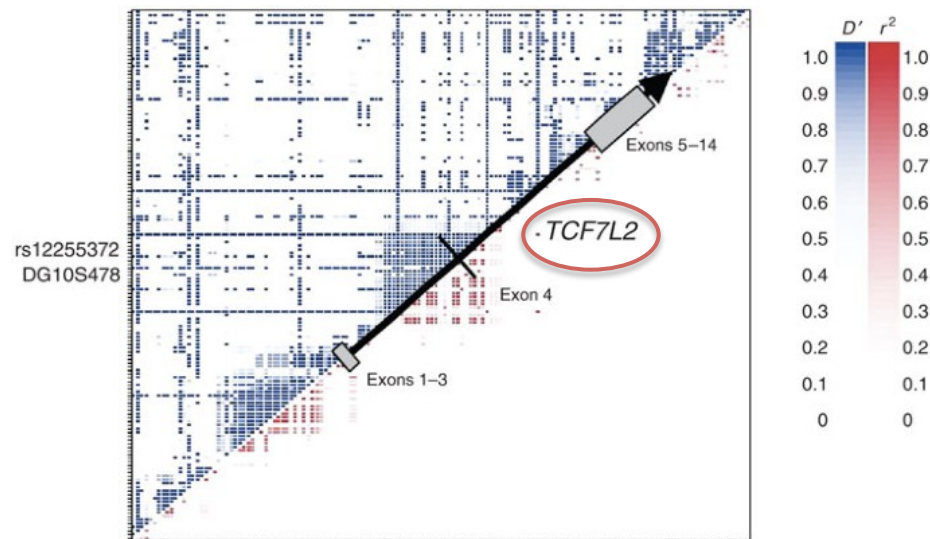
Allele X of DG10S478^e					
Iceland (1,185/931)	X	0.364	0.276	1.50 [1.31, 1.71]	2.1 × 10 ⁻⁹
Denmark (228/539)	X	0.331	0.260	1.41 [1.11, 1.79]	0.0048
USA (361/530)	X	0.385	0.253	1.85 [1.51, 2.27]	3.3 × 10 ⁻⁹
Combined	X	-	-	1.56 [1.41, 1.73]	4.7 × 10 ⁻¹⁸

^aShown is the allele frequency in affected individuals and controls and the corresponding association of DG10S478 to type 2 diabetes, together with the number (n) of subjects (individuals with type 2 diabetes/controls), the haplotype relative risk (RR) and P values.

^bAllelic frequencies, rather than carrier frequencies, are presented in the table. ^cRR calculated assuming a multiplicative model; 95% confidence interval indicated by brackets. ^dTwo-sided P values calculated for each allele using a likelihood ratio test statistic with adjustment for the relatedness of Icelandic individuals with type 2 diabetes. (**Supplementary Methods**).

^eFrequency and association for all the alleles of DG10S478 in the Icelandic, Danish and US cohorts are shown separately.

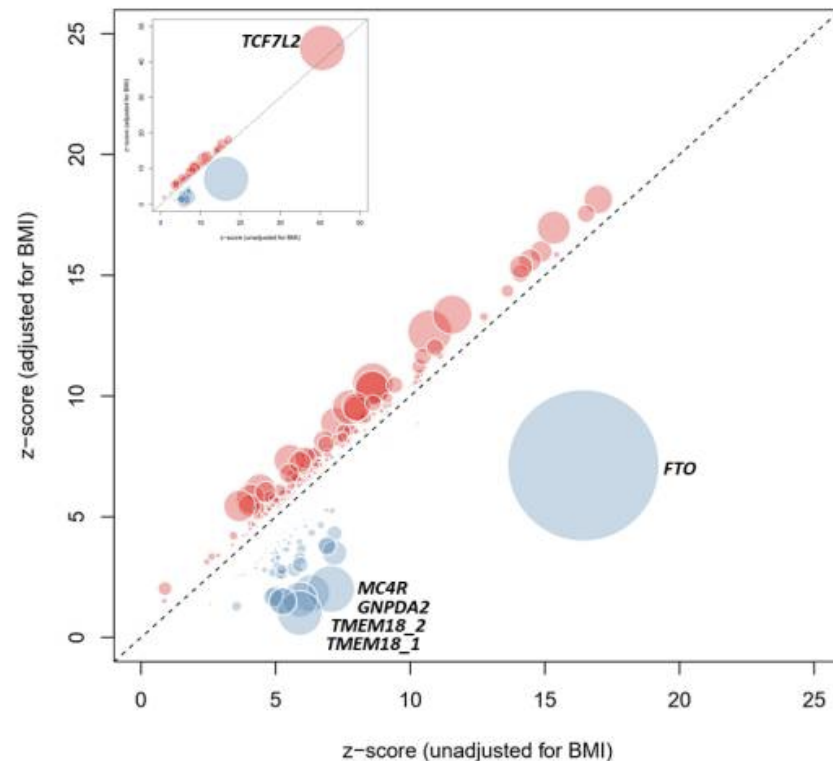
^fFrequency and association for the composite at-risk allele X (nonzero alleles) of DG10S478 in all three cohorts and in the cohorts combined using a Mantel-Haenszel model¹¹.



Cohort	Genotype relative risk (GRR) ^a			
	00	0X [95% c.i.]	XX [95% c.i.]	PAR
Iceland	1	1.41 [1.17,1.70]	2.27 [1.70, 3.04]	0.21
Denmark	1	1.37 [0.98,1.90]	1.92 [1.13, 3.26]	0.17
USA	1	1.64 [1.23, 2.19]	3.29 [2.13, 5.07]	0.28
Combined	1	1.45 [1.26, 1.67]	2.41 [1.94, 3.00]	0.21

^aRisk for heterozygous carriers (0X) and homozygous carriers (XX) compared with risk for non-carriers (00). c.i., confidence interval. PAR, population attributable risk.

Fine-mapping of an expanded set of type 2 diabetes loci to single-variant resolution using high-density imputation and islet-specific epigenome maps



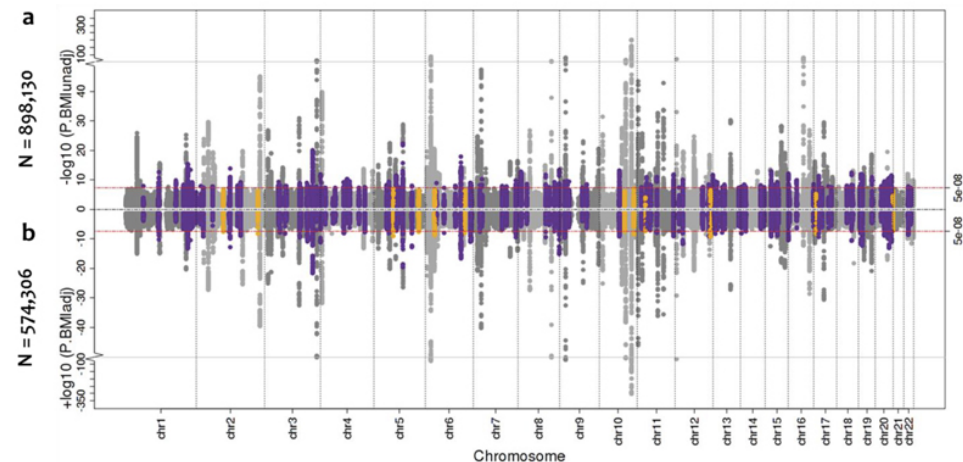
-32 European-descent GWAS – imputed
74124 T2D ασθενείς, 824006 μάρτυρες

-135 novel loci (μωβ)

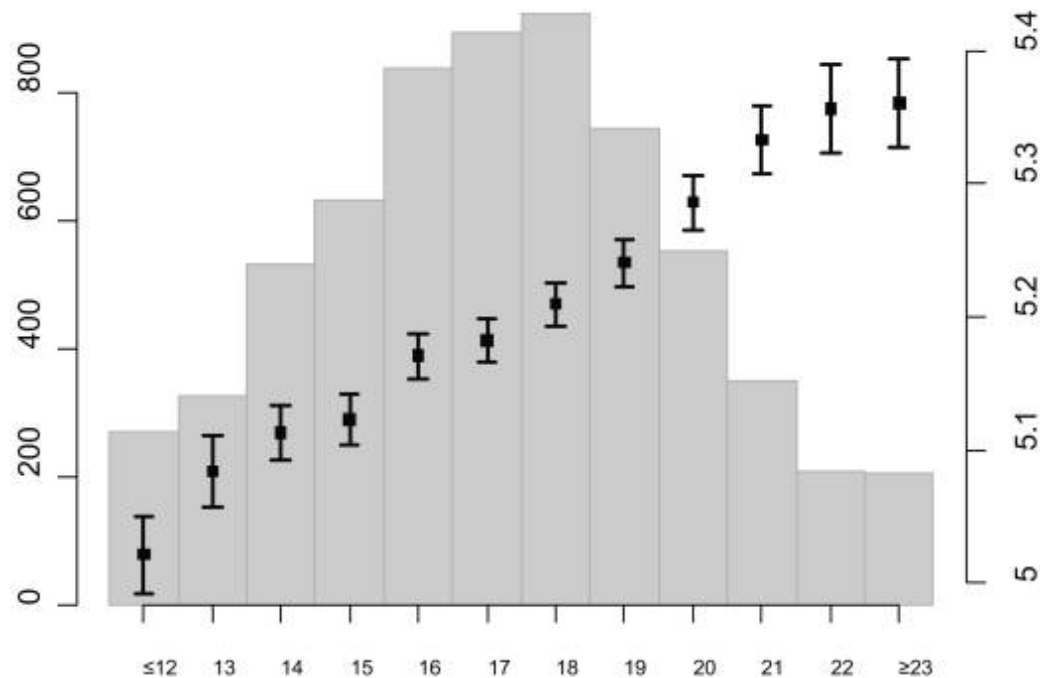
-Το μέγεθος της επίδρασης κάθε γονιδίου
ορίζεται από το μέγεθος του κύκλου.

-Με μπλε χρώμα τα bmi-unadjusted

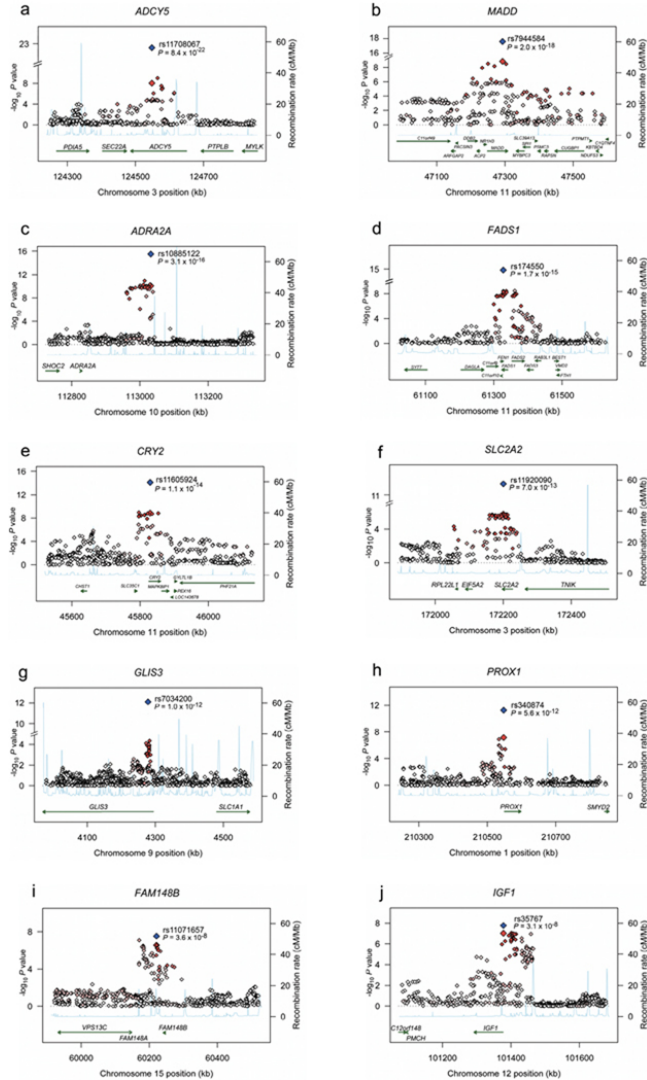
-Με κόκκινο χρώμα τα bmi-adjusted



New genetic loci implicated in fasting glucose homeostasis and their impact on type 2 diabetes risk



Νέοι γενετικοί τόποι & γενετικό σκορ που αυξάνει την πιθανότητα εμφάνισης ΣΔ2.



A Polygenic Lipodystrophy Genetic Risk Score Characterizes Risk Independent of BMI in the Diabetes Prevention Program

Shylaja Srinivasan,¹ Kathleen A. Jablonski,² William C. Knowler,³ Samuel Dagogo-Jack,⁴ Steven E. Kahn,⁵ Edward J. Boyko,⁶ George A. Bray,⁷ Edward S. Horton,⁸ Marie-France Hivert,^{9,10,11} Ronald Goldberg,¹² Ling Chen,^{13,14} Josep Mercader,^{13,14} Maegan Harden,¹⁴ and Jose C. Florez,^{9,10,13,14} for the Diabetes Prevention Program Research Group

Δημιουργία GRS από 11 SNPs που σχετίζονται με χαμηλή ινσουλινοευαισθησία και λιποδυστροφία – ανεξάρτητα από ΔΜΣ

Table 1. Effect Sizes for Fasting Insulin Along With Frequencies of Genetic Variants in Published Reports from MAGIC and in the DPP Participants

Gene	SNP	β Estimates for ln FI (μ U/mL) in MAGIC	Risk Allele Frequency in MAGIC (%)	Frequency of High-Risk Alleles in DPP (%)					
				Overall N = 2713	Caucasian N = 1503	Black N = 554	Hispanic N = 458	Asian/ Pacific Islanders N = 120	American Indian N = 78
<i>IRS1</i>	rs2943634	0.027	66	67	68	45	77	92	92
<i>COBL11/GRB14</i>	rs1607080	0.027	88	87	85	90	98	98	97
<i>ARL15</i>	rs4865796	0.011	67	74	70	75	82	81	94
<i>FAM13A</i>	rs3822072	0.013	48	49	49	53	42	54	40
<i>LYPLAL1</i>	rs2785980	0.015	67	70	67	84	53	71	44
<i>PEPD</i>	rs731839	0.014	34	34	34	39	40	58	47
<i>PDGFC</i>	rs4691380	0.017	67	59	66	29	61	64	71
<i>RSPOR2</i>	rs2745353	0.011	39	35	50	63	56	60	66
<i>PPARG</i>	rs18001282	0.022	87	91	90	98	91	90	81
<i>TET2</i>	rs9884482	0.012	39	35	38	11	45	58	40
<i>ANKRD55</i>	rs459193	0.013	73	70	75	58	73	53	74

Abbreviation: FI, fasting insulin.

Table 4. Association of the GRS with Change in Traits at 1 Year

Year 1-Baseline	Sample Size (n)	β Estimate per Allele	SE	P
Weight, kg ^a	2568	0.1234	0.0529	0.020
BMI, kg/m ^{2a}	2568	0.0461	0.0190	0.015
Waist circumference, cm ^a	2568	0.0754	0.0593	0.204
FI, μ U/mL, ln	2568	0.0130	0.0043	0.002
Fasting glucose, mg/dL, ln ^a	2568	0.0003	0.0009	0.722
ISI, ln ^b	2506	-0.0136	0.0047	0.004
Systolic blood pressure, mm Hg	2568	0.0874	0.1134	0.441
Diastolic blood pressure, mm Hg	2568	0.0277	0.0740	0.708
HDL-cholesterol, mg/dL	2559	0.0043	0.0591	0.942
LDL-cholesterol, mg/dL	2559	0.0067	0.2033	0.974
Triglycerides, mg/dL, ln +	2559	0.0047	0.0033	0.154
ALT, U/L, ln +	1857	0.0801	0.1211	0.509
Visceral adipose tissue, cm ² , L4-5	618	-0.0006	0.0017	0.721
Subcutaneous adipose tissue, cm ² , L4-5	618	0.4760	1.0300	0.644

All measures adjusted for baseline value, age at randomization, sex and self-reported race/ethnicity, waist circumference and treatment group except where indicated.

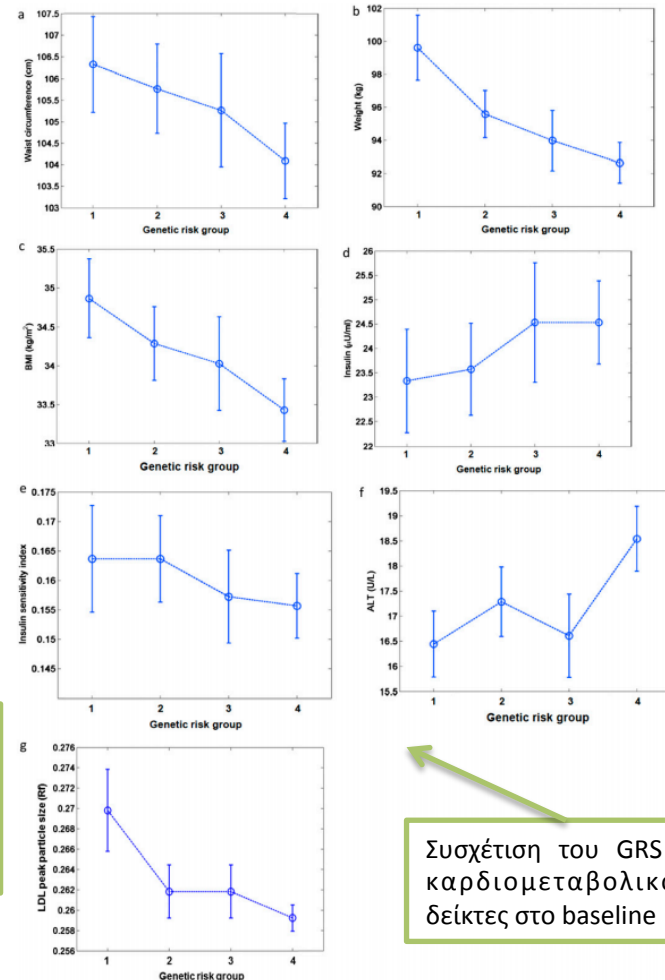
Abbreviation: FI, fasting insulin.

^aAdjusted for age at randomization, sex, and race/ethnicity

^bln (Year 1 measurement) - ln (Baseline measurement)

Συσχέτιση του GRS με αλλαγή σε καρδιομεταβολικούς δείκτες μετά από 1 έτος παρέμβασης

Συσχέτιση του GRS με καρδιομεταβολικούς δείκτες στο baseline



T2D susceptibility loci achieving genome-wide significance (combined meta-analysis $P < 5 \times 10^{-8}$) for the first time in European descent populations

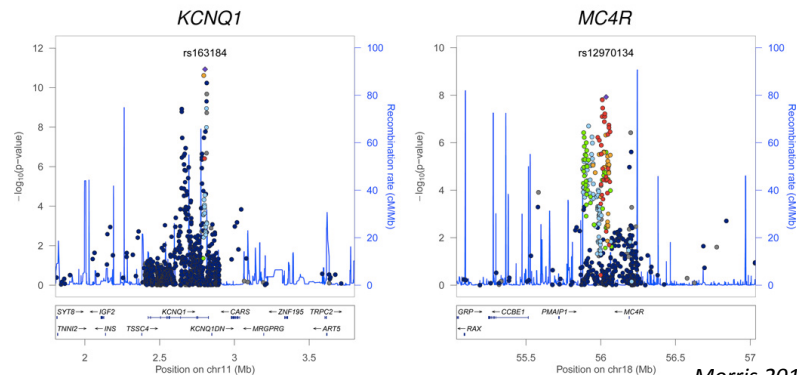
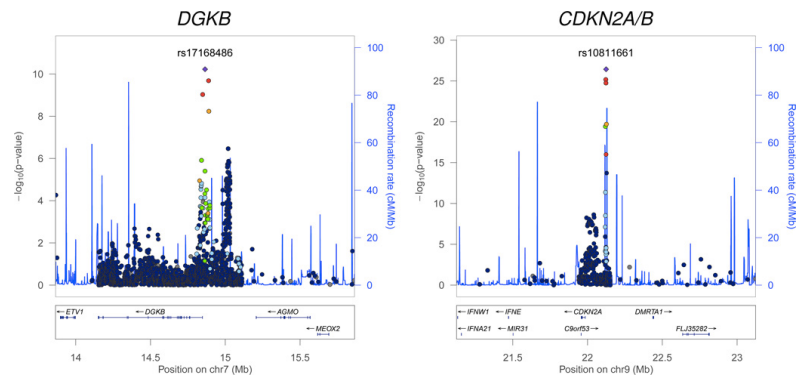
SNP	Chr	Position (Build 36)	Alleles ^a		Risk allele frequency ^b	Nearby gene	Stage 1 meta-analysis: up to 12,171 cases and 56,862 controls		Stage 2 meta-analysis: up to 22,669 cases and 58,119 controls		Combined meta-analysis: up to 34,840 cases and 114,981 controls	
			Risk	Other			OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
New loci not previously reported in any population												
rs12571751	10	80,612,637	A	G	0.52	ZMIZ1	1.09 (1.06–1.13)	7.0×10 ^{−7}	1.07 (1.04–1.10)	1.5×10 ^{−6}	1.08 (1.05–1.10)	1.0×10 ^{−10}
rs516946	8	41,638,405	C	T	0.76	ANK1	1.10 (1.06–1.15)	2.1×10 ^{−6}	1.08 (1.05–1.12)	1.1×10 ^{−6}	1.09 (1.06–1.12)	2.5×10 ^{−10}
rs10842994	12	27,856,417	C	T	0.80	KLHDC5	1.09 (1.04–1.13)	3.0×10 ^{−4}	1.10 (1.07–1.14)	2.8×10 ^{−8}	1.10 (1.06–1.13)	6.1×10 ^{−10}
rs2796441	9	83,498,768	G	A	0.57	TLE1	1.07 (1.03–1.12)	4.8×10 ^{−4}	1.07 (1.04–1.10)	3.3×10 ^{−7}	1.07 (1.05–1.10)	5.4×10 ^{−9}
rs459193	5	55,842,508	G	A	0.70	ANKRD55	1.05 (1.01–1.10)	2.7×10 ^{−2}	1.10 (1.06–1.13)	2.0×10 ^{−9}	1.08 (1.05–1.11)	6.0×10 ^{−9}
rs10401969	19	19,268,718	C	T	0.08	CILP2	1.13 (1.05–1.21)	9.2×10 ^{−4}	1.14 (1.08–1.20)	2.0×10 ^{−7}	1.13 (1.09–1.18)	7.0×10 ^{−9}
rs12970134	18	56,035,730	A	G	0.27	MC4R	1.08 (1.03–1.12)	2.3×10 ^{−4}	1.08 (1.05–1.11)	2.0×10 ^{−6}	1.08 (1.05–1.11)	1.2×10 ^{−8}
rs7202877	16	73,804,746	T	G	0.89	BCAR1	1.15 (1.07–1.23)	5.0×10 ^{−5}	1.10 (1.05–1.15)	1.9×10 ^{−5}	1.12 (1.07–1.16)	3.5×10 ^{−8}
Loci not previously reported in European descent populations												
rs7177055	15	75,619,817	A	G	0.68	HMG20A	1.08 (1.04–1.12)	1.2×10 ^{−4}	1.08 (1.05–1.11)	8.8×10 ^{−7}	1.08 (1.05–1.10)	4.6×10 ^{−9}
rs13389219	2	165,237,122	C	T	0.60	GRB14	1.05 (1.01–1.09)	1.3×10 ^{−2}	1.09 (1.06–1.12)	9.5×10 ^{−9}	1.07 (1.05–1.10)	1.0×10 ^{−8}

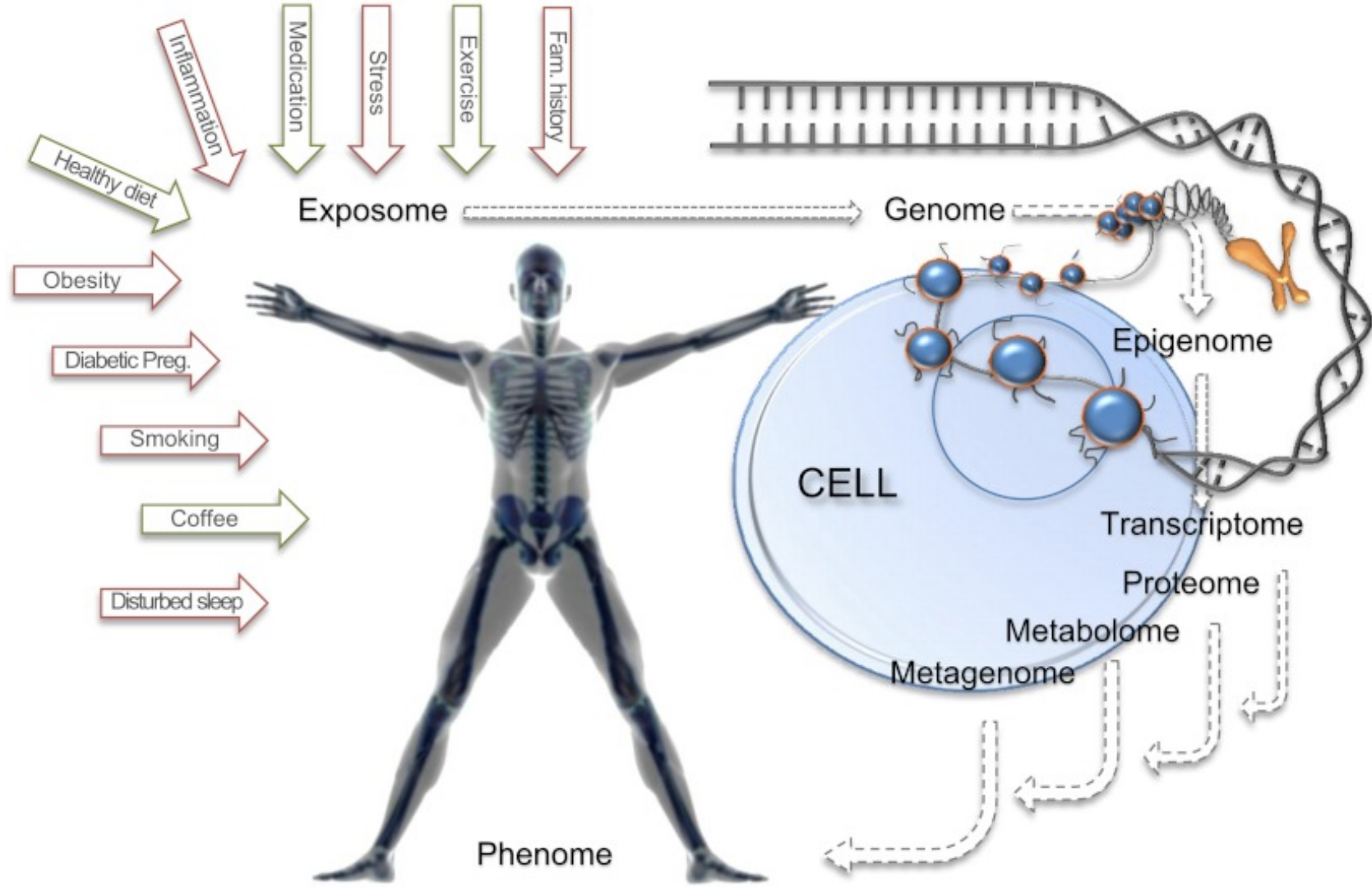
T2D susceptibility loci with sex-differentiated evidence of association

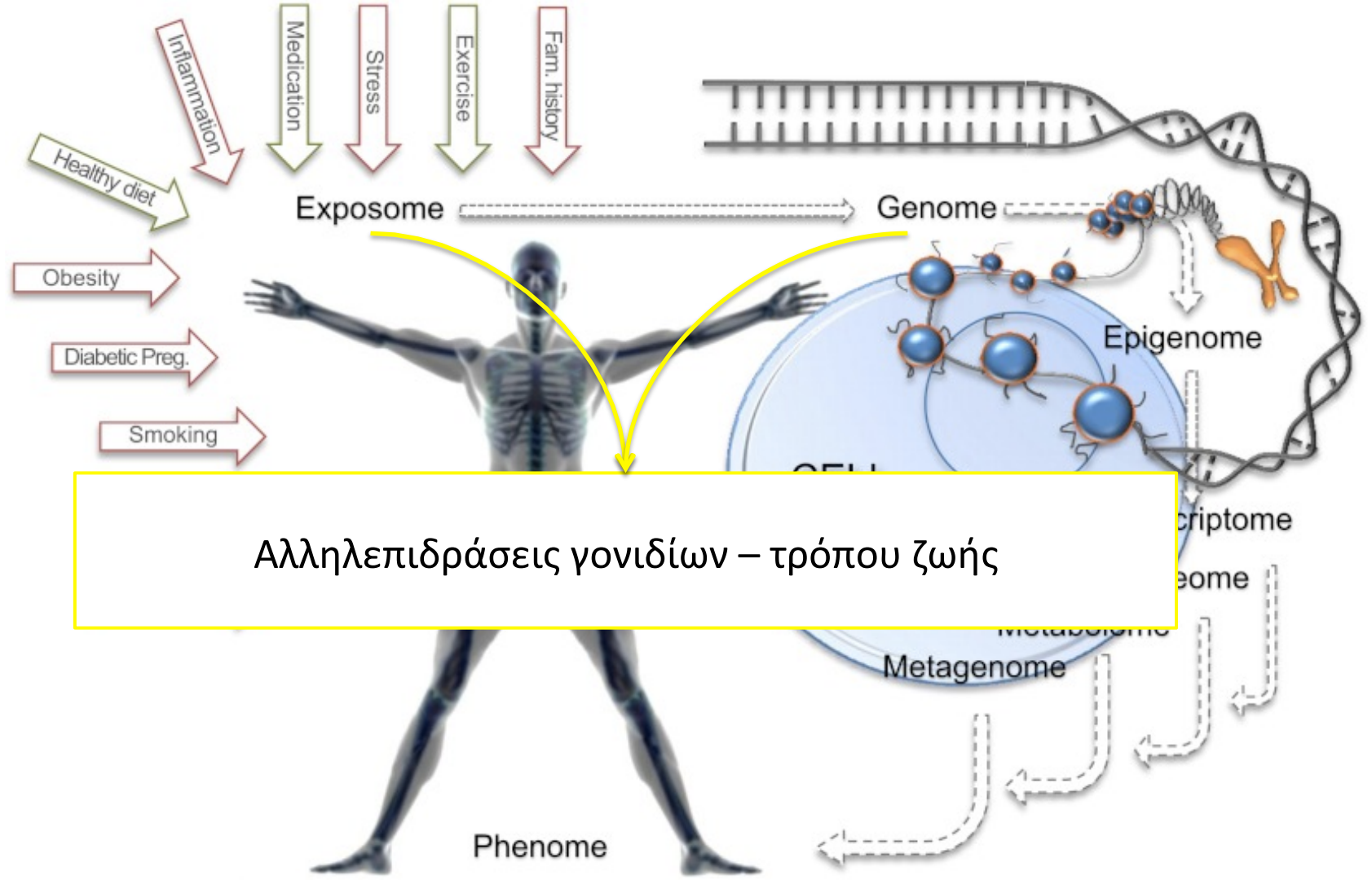
SNP	Chr	Position (Build 36)	Alleles ^a		Risk allele frequency ^b	Nearby gene	Male meta-analysis: up to 20,219 cases and 54,604 controls		Female meta-analysis: up to 14,621 cases and 60,377 controls		Sex-differentiated meta- analysis: up to 34,840 cases and 114,981 controls	
			Risk	Other			OR (95% CI)	P-value	OR (95% CI)	P-value	Association P-value	Heterogeneity P-value
New loci identified through sex-differentiated meta-analysis achieving genome-wide significance ($P < 5 \times 10^{-8}$)												
rs11063069	12	4,244,634	G	A	0.21	CCND2	1.12 (1.08–1.16)	1.1×10^{-9}	1.04 (1.00–1.09)	3.6×10^{-2}	9.8×10^{-10}	1.3×10^{-2}
rs8108269	19	50,850,353	G	T	0.31	GIPR	1.05 (1.02–1.08)	3.7×10^{-3}	1.10 (1.06–1.14)	2.2×10^{-7}	2.1×10^{-8}	5.7×10^{-2}
Other loci with nominally significant evidence ($P < 0.05$) of heterogeneity in allelic odds ratios between sexes												
rs163184	11	2,803,645	G	T	0.50	KCNQ1	1.12 (1.09–1.16)	8.5×10^{-15}	1.05 (1.01–1.08)	7.8×10^{-3}	2.4×10^{-15}	1.3×10^{-3}
rs17168486	7	14,864,807	T	C	0.19	DGKB	1.15 (1.11–1.19)	6.5×10^{-13}	1.06 (1.02–1.11)	5.2×10^{-3}	1.2×10^{-13}	6.8×10^{-3}
rs3923113	2	165,210,095	A	C	0.63	GRB14	1.05 (1.01–1.08)	4.9×10^{-3}	1.11 (1.08–1.15)	1.8×10^{-9}	2.6×10^{-10}	8.0×10^{-3}
rs243088	2	60,422,249	T	A	0.45	BCL11A	1.10 (1.06–1.13)	6.5×10^{-10}	1.04 (1.00–1.07)	2.8×10^{-2}	4.7×10^{-10}	1.2×10^{-2}

-Νέοι γενετικοί τόποι που σχετίζονται με ΣΔ2 σε Ευρωπαϊκό πληθυσμό

- Η επίδραση του φύλου
- >1 ανεξάρτητα σήματα







**Μελετες αλληλεπιδράσεων γονιδίων -
διατροφής**

-Συγκεντρωτικός πίνακας μελετών αλληλεπιδράσεων ΓΧΔ ως προς τον κίνδυνο εμφάνισης ΣΔ2

- Με **κόκκινο** χρώμα: απουσία αλληλεπίδρασης
- Με **πράσινο** χρώμα: παρουσία αλληλεπίδρασης
- Με **πορτοκαλί** χρώμα: διφορούμενα αποτελέσματα
- Ο αριθμός στο κάθε κουτάκι αντιστοιχεί στο πλήθος των μελετών
- *: nominal συσχετίσεις

Nearest gene	Variant	Reference	Protein	Total FA	Saturated FA	Polysaturated FA	Monounsaturated FA	Carbohydrate	Sucrose	Glycemic load	Glycemic index	Fiber	Cereal fiber	Whole grain	Coffee	Olive oil	Whey containing dairy	Milk intake	Red meat	Processed meat	Alcohol	Mediterranean diet	Wester dietary pattern	Prudent dietary pattern	Diet risk score	Change in diet	Dietary Magnesium	Dietary iron	Heme iron	Zinc	Retinol	Plasma Vitamin A
TCF7L2	rs7903146	(14, 19-22, 24)	1	1				1				2	2	2	1	1	1															
	rs4506565	(20)											1	1																		
	rs12255372	(14, 22-24)						1		2	1*	1	2	1		1*	1	1														
PPARG	rs1801282	(22, 25, 29, 32)	2*	1	1	1	1					1				1																
	rs3856806	(25)	1*																													
NOTCH2	rs10923931	(22)										1																				
ZBED3	rs4457053	(22)										1																				
GIPR	rs10423928	(14, 24, 27)	1	2				2	1			1	1		1	1*	1															
IRS1	rs2943641	(26)	1	1				1				1																				
FFAR4	p.R270H	(28)	1																													
CAV2	rs2270188	(14, 29)		2	2	1	1																									
LCT	rs4988235	(31)																	1													
IGF2BP2	rs4402960	(32)														1																
CDKAL1	rs7754840	(32)														1																
	rs9465871	(69)																											1			
KCNJ11	rs5215	(32)																														
ADH1C	*1/*2	(34)														1*					1											
HFE	rs1799945	(38, 40)																													2	
	rs1800562	(38, 40)																													2	
SLC40A1	rs744653	(40)																												1		
TMPRSS6	rs855791	(38, 40)																													2	
SLC30A8	8_118252314	(69)																					1*								1	
	8_118252435	(69)																													1	
	rs16889462	(69)																													1	
	58 SNPs	(43, 69)																													1	
CLOCK	rs4580704	(53)																				1*										
HHEX	rs1111875	(22)										1																				
HNF1A	rs7957197	(22)										1																				
TLE4	rs13292136	(22)										1																				
KCNQ1	rs163171	(24)											1	1	1	1																
	rs163184	(24)											1	1	1	1																
	rs2237892	(24)											1	1	1	1																
	rs163177	(42)																												1		
WFS1	rs10010131	(24)										1		1	1	1																
GCKR	rs780094	(32)											1																			
JAZF1	rs864745	(32)														1																
CDKN2A/B	rs10811661	(32)														1																
SPRY2	rs1359790	(32)														1																
FTO	rs8050136	(32)														1																
HECTD4	2 SNPs	(36)																			1											
TRPM6	20 SNPs	(37)																														
TRPM7	5 SNPs	(37)																														
TPMRSS6	rs855791	(39, 40)																														
TF	3 SNPs	(39)																														
PCK7	rs236918	(40)																														
JMJD1C	rs10761745	(42)																														
RBP4	rs3758539	(44)																														
ADRA2B	12Glu9	(55)																														
ferritin-GRS		(40)																														
IR-GRS		(30)											1	1	1	1	1														1	
T2D-GRS		(30, 33, 35, 45, 46)											1	2	2	2	1	1														

Interactions of Dietary Whole-Grain Intake With Fasting Glucose- and Insulin-Related Genetic Loci in Individuals of European Descent

A meta-analysis of 14 cohort studies

Table 2—Meta-analyzed association between daily whole-grain intake and fasting glucose and fasting insulin in 14 cohorts

	n	Regression coefficient (β [95% CI] representing expected change in fasting glucose [mmol/L] per one-daily-serving-greater whole-grain intake)	P	n	Regression coefficient (β [95% CI] representing expected change in fasting insulin [ln]pmol/L per one-daily-serving-greater whole-grain intake)	P
Model 1: age, sex, energy intake, field center, or population structure*	48,723	-0.019 (-0.022 to -0.015)	<0.0001	34,201	-0.021 (-0.025 to -0.017)	<0.0001
Model 2: model 1 + education level, physical activity, alcohol intake, and smoking status†	48,207	-0.013 (-0.017 to -0.010)	<0.0001	34,108	-0.022 (-0.026 to -0.017)	<0.0001
Model 3: model 2 + red or processed meat, fish, vegetables, fruit, coffee, nuts, and seeds‡	46,985	-0.012 (-0.016 to -0.008)	<0.0001	33,993	-0.016 (-0.021 to -0.011)	<0.0001
Model 4: model 3 + BMI§	46,928	-0.009 (-0.013 to -0.005)	<0.0001	33,937	-0.011 (-0.015 to -0.007)	0.0003

*Energy intake was not estimated in the Age, Gene/Environment Susceptibility-Reykjavik Study cohort. Field center was included as a covariate in the Health, Aging, and Body Composition Study; the Cardiovascular Model Study; the Atherosclerosis Risk in Communities Study; the Family Heart Study; and the Invecchiare in Chianti (Aging in the Chianti Area) Study. Principal components were used to adjust for population structure in the Framingham Heart Study and the Family Heart Study. †Education level and physical activity were defined uniquely by cohort. Smoking status was characterized as current, former, or never in 12 cohorts and as current or not current in 3 cohorts (Framingham Heart Study; Age, Gene/Environment Susceptibility-Reykjavik Study; Uppsala Longitudinal Study of Adult Men). ‡Education level, smoking status, and alcohol intake were not adjusted in the Gene-Diet Attica Investigation on Childhood Obesity cohort (fifth and sixth graders). §Most cohorts included each of dietary covariates listed in the table as servings per day or grams per day; exceptions are noted in the online supplement. §BMI was modeled as a continuous variable in all cohorts (kg/m^2).

Table 3—Meta-analyzed interactions between daily whole-grain intake and genotype for select SNPs for fasting glucose and fasting insulin in 14 cohorts*

SNP	Nearest gene	Glucose- or insulin-raising allele/other allele	Number of cohorts	n	Regression coefficient for interaction between daily servings of whole grains $\times$ SNP for fasting glucose (mmol/l)			I^2 (95% uncertainty interval) (%)
					β	SE	P	
Glucose-related SNP								
rs340874	PROX1	C/T	13	43,527	-0.0011	0.0030	0.71	0 (0-57)
rs780094	GCKR	C/T	14	48,303	0.0040	0.0027	0.13	0 (0-55)
rs560887	G6PC2	C/T	13	43,488	-0.0001	0.0032	0.98	0 (0-57)
rs11708067	ADCY5	A/G	13	43,555	0.0039	0.0036	0.28	24 (0-61)
rs11920090	SLC2A2	T/A	13	43,451	0.0006	0.0043	0.89	0 (0-57)
rs2191349	DGKB/TMEM195	T/G	13	43,561	-0.0044	0.0029	0.13	0 (0-57)
rs4607517	GCK	A/G	14	48,323	0.0002	0.0035	0.95	0 (0-55)
rs11558471	SLC30A8	A/G	10	40,776	-0.0007	0.0034	0.84	0 (0-62)
rs7034200	GLIS3	A/C	13	43,362	0.0015	0.0029	0.60	0 (0-57)
rs10885122	ADRA2A	G/T	13	43,391	0.0082	0.0044	0.06	0 (0-57)
rs4506565	TCF7L2	T/A	12	45,911	0.0004	0.0030	0.88	51 (6-75)
rs11605924	CRY2	A/C	13	43,567	-0.0016	0.0029	0.58	0 (0-57)
rs7944584	MADD	A/T	13	43,361	0.0049	0.0033	0.14	0 (0-57)
rs174550	FADS1	T/C	14	48,162	-0.0027	0.0028	0.34	32 (0-64)
rs10830963	MTNR1B	G/C	13	43,433	0.0028	0.0035	0.42	32 (0-65)
rs11071657	C2CD4B	A/G	13	42,500	0.0035	0.0031	0.26	0 (0-57)
					Regression coefficient for interaction between daily servings of whole grains $\times$ SNP for fasting insulin [(ln)pmol/l]			
Insulin-related SNP								
rs780094	GCKR	C/T	14	33,784	0.0091	0.003	0.006	1 (0-36)
rs33767	IGF1	G/A	13	29,078	0.0022	0.003	0.09	0 (0-57)

*Regression coefficient for interaction between daily servings of whole grains $\times$ SNP for fasting glucose (mmol/l) and fasting insulin [(ln)pmol/l], adjusted for age, sex, energy intake (not in the Age, Gene/Environment Susceptibility-Reykjavik Study), and field center (Health, Aging, and Body Composition Study; the Cardiovascular Health Study; the Atherosclerosis Risk in Communities Study; and the Invecchiare in Chianti [Aging in the Chianti Area] Study) and population structure by principal components in the Framingham Heart Study and the Family Heart Study.

Several type 2 diabetes-associated variants in genes annotated to WNT signaling interact with dietary fiber in relation to incidence of type 2 diabetes

George Hindy,  Inês G. Mollet, Gull Rukh, Ulrika Ericson, and Marju Orho-Melander

-Μελέτη 8 γονιδίων ως προς primary & secondary outcomes.
- Παρατηρήθηκαν στατιστικά σημαντικές αλληλεπιδράσεις μεταξύ πολυμορφισμών των 3 γονιδίων και της πρόσληψης διαιτητικών ινών.

HR of incident type 2 diabetes by genotype and quintiles of fiber intake

	Genotype					
	XX	XR ^a	RR	HR per R allele	<i>P</i> trend ^b	<i>P</i> interaction ^c
<i>TCF7L2</i> rs7903146						
Q1	1.16 (0.98–1.39)	1.58 (1.32–1.89)	1.56 (1.14–2.15)	1.24 (1.09–1.40)	0.001	0.034
Q2	1.13 (0.95–1.35)	1.52 (1.27–1.82)	1.92 (1.43–2.60)	1.26 (1.11–1.42)	0.0002	
Q3	1.15 (0.97–1.37)	1.62 (1.36–1.93)	2.10 (1.60–2.77)	1.37 (1.22–1.55)	1 × 10 ^{−7}	
Q4	1.02 (0.85–1.22)	1.35 (1.12–1.62)	1.93 (1.48–2.58)	1.31 (1.15–1.49)	5 × 10 ^{−5}	
Q5	1 (ref)	1.70 (1.42–2.03)	2.00 (1.49–2.70)	1.47 (1.30–1.66)	2 × 10 ^{−9}	
HR per Q	0.97 (0.93–1.01)	0.99 (0.95–1.03)	1.05 (0.95–1.15)			
<i>P</i> trend ^c	0.19	0.64	0.37			
<i>TCF7L2</i> rs12255372						
Q1	1.22 (1.03–1.45)	1.44 (1.20–1.73)	1.27 (0.90–1.78)	1.08 (0.95–1.22)	0.26	0.005
Q2	1.16 (0.98–1.38)	1.32 (1.10–1.58)	1.74 (1.31–2.32)	1.16 (1.02–1.31)	0.02	
Q3	1.07 (0.90–1.28)	1.53 (1.29–1.82)	1.89 (1.44–2.47)	1.36 (1.21–1.53)	3 × 10 ^{−7}	
Q4	1.02 (0.86–1.22)	1.27 (1.05–1.52)	1.68 (1.25–2.26)	1.23 (1.08–1.40)	0.002	
Q5	1 (ref)	1.41 (1.18–1.68)	1.99 (1.48–2.67)	1.40 (1.23–1.59)	4 × 10 ^{−7}	
HR per Q	0.96 (0.92–1.00)	0.98 (0.94–1.02)	1.05 (0.96–1.16)			
<i>P</i> trend ^d	0.060	0.37	0.28			

NOTCH2 rs10923931

Q1	1.00 (0.87–1.14)	1.14 (0.92–1.42)	1.66 (0.86–3.23)	1.12 (0.93–1.34)	0.24	0.017
Q2	1.00 (0.88–1.14)	1.04 (0.85–1.28)	0.76 (0.28–2.04)	1.06 (0.88–1.28)	0.51	
Q3	1.03 (0.91–1.18)	1.10 (0.90–1.35)	1.05 (0.47–2.34)	1.08 (0.90–1.30)	0.41	
Q4	0.97 (0.85–1.11)	0.70 (0.55–0.90)	0.75 (0.28–2.00)	0.75 (0.60–0.95)	0.015	
Q5	1 (ref)	1.00 (0.80–1.25)	0.25 (0.04–1.80)	0.93 (0.75–1.15)	0.50	
HR per Q	1.00 (0.97–1.03)	0.93 (0.87–0.996)	0.63 (0.44–0.90)			
P trend	0.89	0.038	0.010			

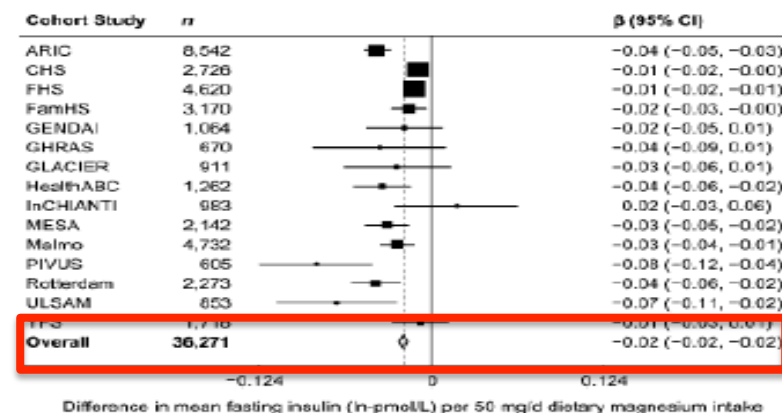
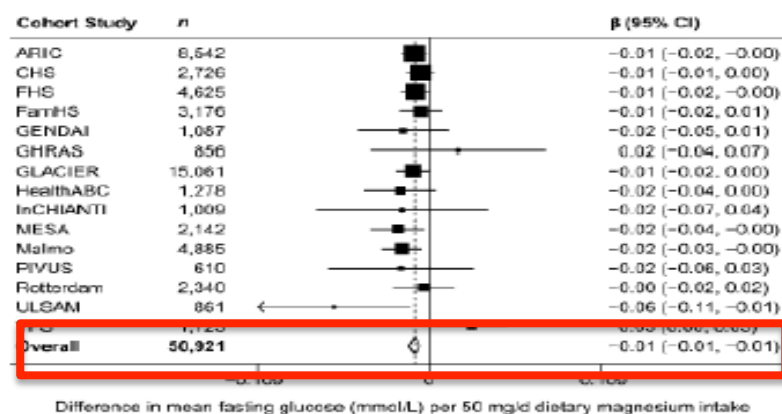
ZBED3 rs4457053

Q1	0.96 (0.81–1.13)	1.03 (0.86–1.23)	1.51 (1.14–2.01)	1.16 (1.02–1.31)	0.06	0.002
Q2	0.96 (0.81–1.12)	1.00 (0.84–1.20)	1.04 (0.74–1.46)	1.03 (0.90–1.17)	0.36	
Q3	1.04 (0.89–1.21)	1.04 (0.88–1.24)	0.85 (0.59–1.22)	0.99 (0.87–1.12)	0.97	
Q4	0.93 (0.79–1.09)	0.93 (0.78–1.12)	0.67 (0.46–0.99)	0.95 (0.83–1.10)	0.55	
Q5	1 (ref)	0.98 (0.82–1.17)	0.72 (0.50–1.04)	0.94 (0.81–1.07)	0.25	
HR per Q	1.01 (0.97–1.05)	0.98 (0.94–1.03)	0.85 (0.76–0.95)			
P trend	0.69	0.40	0.003			

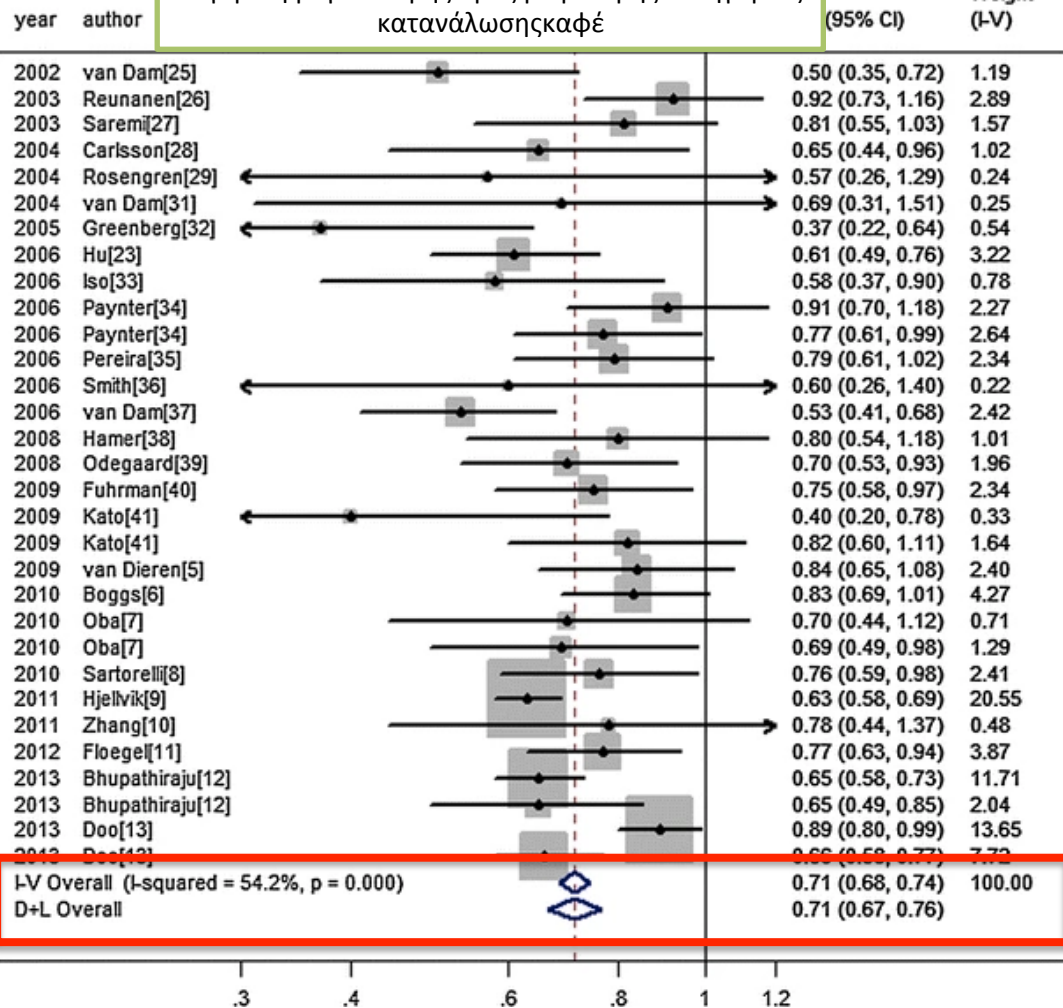
Higher Magnesium Intake Is Associated with Lower Fasting Glucose and Insulin, with No Evidence of Interaction with Select Genetic Loci, in a Meta-Analysis of 15 CHARGE Consortium Studies¹⁻⁴

Adela Hruby,⁵ Julius S. Ngwa,⁶ Frida Renström,⁷⁻⁸ Mary K. Wojczynski,¹⁰ Andrea Ganna,¹¹ Göran Hallmans,¹² Denise K. Houston,¹³ Paul F. Jacques,⁵ Stavroula Kanoni,^{14, 15} Terho Lehtimäki,¹⁶ Rozenn N. Lemaitre,¹⁷ Ani Manichaikul,¹⁸ Kari E. North,¹⁹ Ioanna Ntalla,²⁰ Emily Sonestedt,⁸ Toshiko Tanaka,²⁰ Frank J. A. van Rooij,^{21, 22} Stefania Bandinelli,²³ Luc Djoussé,²⁴ Efi Grigoriou,¹⁵ Ingegerd Johansson,²⁵ Kurt K. Lohman,²⁶ James S. Pankow,²⁷ Olli T. Raitakari,²⁸ Ulf Riserus,²⁹ Mary Yannakoulia,¹⁵ M. Carola Zillikens,^{21, 22, 30} Neelam Hassanali,³¹ Yongmei Liu,³² Dariush Mozaffarian,³³ Constantina Papoutsakis,¹⁵ Ann-Christine Syvänen,³⁴ André G. Uitterlinden,^{21, 22, 30} Jorma Viikari,³⁵ Christopher J. Groves,³¹ Albert Hofman,^{21, 22} Lars Lind,³⁶ Mark L. McCarthy,^{31, 37} Vera Mikkilä,³⁸ Kenneth Mukamal,³⁹ Oscar H. Franco,^{21, 22} Ingrid B. Borecki,¹⁰ L. Adrienne Cupples,^{6, 40} George V. Dedoussis,¹⁵ Luigi Ferrucci,²⁰ Frank B. Hu,⁷ Erik Ingelsson,⁴¹ Mika Kahönen,⁴¹ W. H. Linda Kao,⁴² Stephen B. Kritchevsky,¹³ Marju Orho-Melander,⁸ Inga Prokopenko,^{31, 43} Jerome I. Rotter,⁴⁴ David S. Siscovick,^{37, 45} Jacqueline C. M. Witteman,^{21, 22} Paul W. Franks,⁷⁻⁹ James B. Meigs,⁴⁶ Nicola M. McKeown,^{5*} and Jennifer A. Nettleton⁴⁷

- Οι ελληνικοί πληθυσμοί παρουσίασαν χαμηλά επίπεδα πρόσληψης Mg.
- Nominal αλληλεπίδραση για επίπεδα γλυκόζης νηστείας: rs11558471 στο SLC30A8 και rs3740393 κοντά στο CNNM2



Σύγκριση μεγαλύτερης προς μικρότερης κατηγορίας κατανάλωσης καφέ



Μετανάλυση 26 προοπτικών μελετών ανέδειξαν σχέση **δόσης-απόκρισης** μεταξύ της πρόσληψης καφέ και του κινδύνου εμφάνισης ΣΔ2.

Κάθε αύξηση της πρόσληψης καφέ και decaf καφέ κατά 2 φλ.ημέρα συσχετίστηκε με μείωση του κινδύνου κατά **12% και 11%, αντίστοιχα.**

Eur J Nutr (2014) 53:25–38
DOI 10.1007/s00394-013-0603-x

REVIEW

Coffee and caffeine intake and incidence of type 2 diabetes mellitus: a meta-analysis of prospective studies

Xiubo Jiang · Dongfeng Zhang · Wenjie Jiang

Investigation of gene–diet interactions in the incretin system and risk of type 2 diabetes: the EPIC-InterAct study

The InterAct Consortium

Multivariable-adjusted HR (95% CI) for risk of type 2 diabetes per one serving per day increment of each dietary factor, stratified by incretin-related SNPs, in the EPIC-InterAct study (*n* = 18,638)

SNP	HR (95% CI)			<i>P</i> Interaction
TCF7L2 rs12255372 (<i>n</i> cases / <i>n</i> total)	GG (3,216/8,171)	GT (3,520/7,661)	TT ^a (906/1,807)	
Whey-containing dairy (150 g/day)	1.04 (1.00, 1.08)	0.98 (0.94, 1.02)	1.06 (0.97, 1.15)	0.67
Cereal fibre (10 g/day)	0.94 (0.81, 1.09)	1.06 (0.92, 1.23)	1.35 (0.97, 1.88)	0.08
Coffee (125 g/day)	0.99 (0.97, 1.02)	0.96 (0.93, 0.98)	0.93 (0.88, 0.98)	0.048
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	0.97 (0.91, 1.04) (2,546/6,459)	0.98 (0.92, 1.04) (2,919/6,475)	0.97 (0.88, 1.08) (781/1,585)	0.67
TCF7L2 rs7903146 (<i>n</i> cases / <i>n</i> total)	CC (3,197/8,196)	CT (3,622/7,896)	TT ^a (977/1,879)	
Whey-containing dairy (150 g/day)	1.04 (1.00, 1.08)	0.99 (0.95, 1.03)	1.02 (0.94, 1.11)	0.89
Cereal fibre (10 g/day)	0.94 (0.81, 1.09)	1.06 (0.92, 1.24)	1.13 (0.83, 1.54)	0.30
Coffee (125 g/day)	0.99 (0.97, 1.01)	0.95 (0.93, 0.98)	0.95 (0.90, 1.00)	0.08
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	0.98 (0.92, 1.04) (2,539/6,500)	1.00 (0.94, 1.06) (3,002/6,659)	0.90 (0.81, 0.98) (835/1,630)	0.90

GIPR rs10423928 (<i>n</i> cases / <i>n</i> total)	TT (4,925/11,548)	AT (2,684/6,014)	AA ^a (345/784)	
Whey-containing dairy (150 g/day)	1.04 (1.00, 1.07)	0.99 (0.95, 1.04)	1.04 (0.90, 1.22)	0.51
Cereal fibre (10 g/day)	0.98 (0.87, 1.12)	1.18 (1.00, 1.40)	0.66 (0.43, 1.01)	0.55
Coffee (125 g/day)	0.97 (0.95, 0.99)	0.97 (0.94, 0.99)	0.93 (0.85, 1.02)	0.92
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	0.93 (0.88, 0.98) (3,989/9,439)	1.04 (0.97, 1.11) (2,226/5,003)	1.38 (1.02, 1.85) (283/657)	0.050
WFS1 rs10010131 (<i>n</i> cases / <i>n</i> total)	GG ^a (2,857/6,392)	AG (3,424/8,095)	AA (1,185/2,773)	
Whey-containing dairy (150 g/day)	1.00 (0.96, 1.04)	1.04 (1.00, 1.08)	0.99 (0.92, 1.07)	0.95
Cereal fibre (10 g/day)	1.02 (0.86, 1.20)	0.99 (0.85, 1.14)	0.81 (0.63, 1.04)	0.72
Coffee (125 g/day)	0.97 (0.95, 1.00)	0.98 (0.96, 1.00)	0.94 (0.91, 0.98)	0.49
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	0.98 (0.92, 1.04) (2,378/5,346)	0.97 (0.91, 1.03) (2,783/6,616)	0.92 (0.84, 1.01) (935/2,215)	0.27
KCNQ1 rs163171 (<i>n</i> cases / <i>n</i> total)	CC (4,647/10,652)	CT (2,605/6,110)	TT ^a (391/883)	
Whey-containing dairy (150 g/day)	1.03 (0.99, 1.06)	1.01 (0.96, 1.05)	1.09 (0.94, 1.25)	0.77
Cereal fibre (10 g/day)	1.04 (0.92, 1.19)	0.93 (0.79, 1.11)	0.64 (0.36, 1.16)	0.18
Coffee (125 g/day)	0.98 (0.96, 1.00)	0.95 (0.92, 0.98)	1.03 (0.95, 1.11)	0.75
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	0.99 (0.94, 1.04) (3,862/8,841)	0.95 (0.89, 1.02) (2,083/4,985)	0.97 (0.78, 1.22) (302/699)	0.56
KCNQ1 rs163184 (<i>n</i> cases / <i>n</i> total)	TT (2,007/4,850)	GT (3,971/9,135)	GG ^a (1,977/4,367)	
Whey-containing dairy (150 g/day)	1.01 (0.96, 1.07)	1.00 (0.97, 1.04)	1.02 (0.97, 1.07)	0.59
Cereal fibre (10 g/day)	0.97 (0.80, 1.17)	0.89 (0.77, 1.03)	1.17 (0.98, 1.40)	0.69
Coffee (125 g/day)	0.97 (0.94, 1.00)	0.97 (0.95, 0.99)	0.97 (0.93, 1.00)	0.22
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	1.00 (0.93, 1.08) (1,668/4,025)	0.96 (0.91, 1.01) (3,240/7,551)	0.94 (0.87, 1.01) (1,591/3,529)	0.97
KCNQ1 rs2237892 (<i>n</i> cases / <i>n</i> total)	CC ^a (6,148/13,869)	CT (701/1,647)	TT (20/61)	
Whey-containing dairy (150 g/day)	1.01 (0.98, 1.04)	1.09 (1.00, 1.19)	— ^c	0.56
Cereal fibre (10 g/day)	0.99 (0.88, 1.11)	0.97 (0.69, 1.37)	— ^c	0.81
Coffee (125 g/day)	0.98 (0.96, 0.99)	0.97 (0.92, 1.02)	— ^c	0.27
Olive oil (10 g/day) (<i>n</i> cases / <i>n</i> total) ^b	0.95 (0.91, 0.99) (5,100/11,579)	1.17 (0.98, 1.39) (529/1,250)	— ^c (13/38)	0.07

-Παρατηρήθηκε στατιστικά σημαντική αλληλεπίδραση του GRS με την πρόσληψη 125γρ καφέ ημερησίως.

Multivariable-adjusted HR (95% CI) stratified by genetic risk score and *p* value for the interaction of each dietary factor with incident type 2 diabetes in the EPIC-InterAct study (*n* = 18,638)

	Genetic risk score ^a					<i>p</i>
	0-3	4	5	6	7-10	Interaction
<i>n</i> cases/ <i>n</i> total	642/1710	1188/2890	1684/3780	1509/3331	1147/2326	
Whey-containing dairy (150 g/day)	0.96 (0.86, 1.06)	1.09 (1.03, 1.16)	0.98 (0.93, 1.03)	1.00 (0.95, 1.06)	1.03 (0.96, 1.10)	0.90
Cereal fibre (10 g/day)	0.96 (0.70, 1.30)	0.84 (0.65, 1.09)	0.85 (0.68, 1.05)	0.96 (0.77, 1.21)	1.07 (0.84, 1.36)	0.79
Coffee (125 g/day)	0.99 (0.94, 1.04)	0.97 (0.93, 1.02)	0.97 (0.94, 1.00)	0.96 (0.92, 0.99)	0.95 (0.90, 0.99)	0.005
<i>n</i> cases/ <i>n</i> total	489/1304	945/2338	1383/3131	1249/2776	972/1984	
Olive oil ^b (10 g/day)	0.88 (0.75, 1.03)	0.98 (0.88, 1.08)	0.97 (0.88, 1.06)	0.96 (0.88, 1.05)	0.98 (0.89, 1.08)	0.27

Gene-diet quality interactions on haemoglobin A1c and type 2 diabetes risk: The Airwave Health Monitoring Study

Rebeca Eriksen¹ | Rachel Gibson^{1,2} | Maria Aresu³ | Andy Heard³ | Queenie Chan³ | Evangelos Evangelou³ | He Gao³ | Paul Elliott³ | Gary Frost¹

- 14089 Βρετανοί (3733 με διατροφικά δεδομένα)
- Δημιουργία GRS από 87 κοινούς SNPs
- Επίδραση στα επίπεδα %HbA1c και στον κίνδυνο εμφάνισης ΣΔ2

TABLE 1 Genetic score association with HbA1c% in the Airwave Health Monitoring Study (n = 14 085)

	Model 1 ^a			Model 2 ^b			Model 3 ^c		
	β	95% CI	P-value	β	95% CI	P-value	β	95% CI	P-value
HbA1c (%)	0.03	0.03, 0.05	<0.0001	0.03	0.03, 0.05	<0.0001	0.03	0.02, 0.04	<0.0001

Abbreviations: CI, confident interval; β , beta-coefficient.

^aAdjusted for body mass index, age and sex.

^bAdjusted for waist circumference, age and sex.

^cAdjusted for age, sex, body mass index, smoking, physical activity, diabetes diagnosis and glucose lowering medication.

	Cases/Subcohort	OR ^a	95% CI	P-value
Prediabetes ^b	5253/8820	1.09	1.05, 1.13	<0.0001
Type 2 diabetes ^c	516/13 569	1.14	1.04, 1.24	0.006

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

^aAdjusted for age, sex, BMI, smoking, physical activity.

^bHbA1c > 5.7 ≤ 6.5% and not on glucose lowering medication or previously diagnosed with diabetes.

^cHbA1c ≥6.5% and/or diagnosed with diabetes and/or glucose-lowering medication.

TABLE 2 Risk of prediabetes and type 2 diabetes by per one point (standardized) increase in genetic score, the Airwave Health Monitoring Study (n = 14 085)

Gene-diet quality interactions on haemoglobin A1c and type 2 diabetes risk: The Airwave Health Monitoring Study

Rebeca Eriksen¹ | Rachel Gibson^{1,2} | Maria Aresu³ | Andy Heard³ | Queenie Chan³ | Evangelos Evangelou³ | He Gao³ | Paul Elliott³ | Gary Frost¹

Interacting variables	n	HbA1c (%)		P _{interaction}
		β ^a	95% CI	
Alcohol categories				
No alcohol intake	767	Ref		0.6
Within UK allowance ^b	1670	-0.19	-1.57, 1.18	
Above UK allowance ^c	1296	0.34	-1.08, 1.76	
BMI categories				
BMI (18.50-24.99 kg/m ²)	1273	Ref		0.03
BMI (25-29.99 kg/m ²)	1741	0.11	-0.01, 1.22	
BMI (>30 kg/m ²)	711	1.88	0.41, 3.34	

Abbreviations: Beta, beta-coefficient interaction effect; BMI, body mass index; CI, confident interval; HbA1c, glycated haemoglobin.

^aBeta-coefficient for the estimated difference in HbA1c% per unit increase in genetic risk score interacting with alcohol or BMI category adjusted for age, gender, smoking, physical activity, (BMI), (alcohol). Note: alcohol included in BMI model and BMI in alcohol model.

^b>0 unit and <2 units of alcohol/d.

^c>2 units of alcohol/d.

Gene-diet quality interactions on haemoglobin A1c and type 2 diabetes risk: The Airwave Health Monitoring Study

Rebeca Eriksen¹ | Rachel Gibson^{1,2} | Maria Aresu³ | Andy Heard³ | Queenie Chan³ | Evangelos Evangelou³ | He Gao³ | Paul Elliott³ | Gary Frost¹

TABLE 3 The effect of genetic-diet interactions on HbA1c across genetic risk tertiles, the Airwave Health Monitoring Study (n = 3733)

		GRS tertile 1		GRS tertile 2		GRS tertile 3	
		Lowest risk				Highest risk	
		n = 1085		n = 1485		n = 1161	
Dietary components			β^a	95% CI		β^a	$P_{\text{interaction}}$
DRV score ^b	Ref		-0.01	-0.02, 0.003		-0.01	0.15
Carbohydrates (per 10 g)	Ref		-0.001	-0.01, 0.005		-0.04	0.41
Fibre (per 10 g)	Ref		-0.02	-0.1, 0.1		-0.04	0.71
Fruit, vegetable (per 100 g)	Ref		-0.02	-0.04, -0.01		-0.01	0.12
Wholegrains (per 100 g)	Ref		-0.1	-0.1, 0.01		-0.07	0.04
Total fat (per 10 g)	Ref		0.005	-0.01, 0.02		0.01	0.64
Saturated fat (per 10 g)	Ref		0.01	-0.03, 0.05		0.006	0.86
Added sugars (per 10 g)	Ref		-0.002	-0.01, 0.009		-0.006	0.55

Abbreviations: CI, confident interval; DRV, dietary reference value score; GRS, genetic risk score; $P_{\text{interaction}}$; P -value type III error; β , beta-coefficient.

^aEstimated effect on HbA1c% per increase in nutrient variable interaction with GRS tertiles adjusted for age, gender, smoking, alcohol, energy intake, physical activity, BMI, diabetes diagnosis and treatment.

^bCoefficients represent per 1 point increase in DRV score.

ORIGINAL INVESTIGATION

Open Access



CLOCK gene variation is associated with incidence of type-2 diabetes and cardiovascular diseases in type-2 diabetic subjects: dietary modulation in the PREDIMED randomized trial

Dolores Corella^{1,2*}, Eva. M. Asensio^{1,2}, Oscar Coltell^{2,3}, José V. Sorlí^{1,2}, Ramón Estruch^{2,4,5}, Miguel Ángel Martínez-González^{2,5,6,15}, Jordi Salas-Salvadó^{2,5,7}, Olga Castañer^{2,8}, Fernando Arós^{2,5,9}, José Lapetra^{2,5,10}, Lluís Serra-Majem^{2,5,11}, Enrique Gómez-Gracia^{5,12}, Carolina Ortega-Azorín^{1,2}, Miquel Fiol^{1,3}, Javier Díez Espino^{2,5,14,15}, Andrés Díaz-López^{2,7}, Montserrat Fitó^{2,8}, Emilio Ros^{2,16} and José M. Ordovás^{1,7,18,19}

- 7098 συμμετέχοντες, 4,8 έτη follow-up
- Παρέμβαση για MedDiet
- CLOCK gene: κικκάδειος ρυθμός

Table 1 Demographic, clinical, lifestyle and genetic characteristics of the study participants at baseline according to the CLOCK-rs4580704 genotype

Age (years)	CC (n = 2667)		CG (n = 3415)		GG (n = 1016)		P ¹
	66.9	(6.2)	67.0	(6.2)	67.0	(6.3)	
Weight (Kg)	76.9	(12.0)	77.1	(12.1)	75.4	(11.5)	<0.001
BMI (Kg/m ²)	30.0	(3.8)	30.0	(3.9)	29.7	(3.8)	0.030
Waist circumference (cm)	100.5	(10.3)	100.6	(10.9)	99.3	(10.3)	0.002
Female sex n, %	1551	(58.2)	1932	(56.6)	587	(57.8)	0.444
Current smokers n, %	365	(13.7)	494	(14.5)	143	(14.1)	0.399
T2D prevalence n, %	1314	(49.3)	1616	(47.3)	497	(48.9)	0.291
CLOCK-rs4580704 n, %							0.570
MedDiet with EVOO	901	(33.8)	1208	(35.4)	339	(33.4)	
MedDiet with nuts	927	(34.8)	1078	(31.6)	328	(32.3)	
Control	839	(31.5)	1129	(33.1)	349	(34.4)	
SBP (mm Hg)	149.1	(20.8)	149.6	(20.7)	149.5	(21.0)	0.676
DBP (mm Hg)	83.5	(11.1)	83.5	(10.9)	83.0	(11.0)	0.389
Heart rate (bpm)	71.5	(11.1)	71.4	(11.3)	70.7	(10.8)	0.117
Total cholesterol (mg/dL)	209.9	(37.8)	211.2	(39.0)	210.0	(36.2)	0.417
LDL-C (mg/dL)	129.2	(33.7)	130.0	(34.0)	129.6	(32.7)	0.635
HDL-C (mg/dL)	53.8	(13.7)	53.6	(13.9)	54.5	(14.3)	0.224
Triglycerides (mg/dL)	137.5	(75.5)	137.6	(75.1)	132.6	(68.6)	0.109
Fasting glucose (mg/dL)	122.9	(41.8)	121.8	(41.8)	120.4	(39.1)	0.268
Energy intake (kcal/d)	2275	(603)	2281	(605)	2272	(605)	0.887
Total fat (g/d)	98.8	(30.3)	99.1	(30.6)	97.8	(29.9)	0.510
Saturated fat (g/d)	25.2	(9.2)	25.5	(9.3)	25.0	(8.9)	0.313
MUFA (g/d)	48.9	(16.0)	49.0	(16.0)	48.6	(16.0)	0.832
PUFA (g/d)	15.8	(6.9)	15.9	(7.2)	15.6	(6.6)	0.380
Proteins (g/d)	92.3	(22.8)	92.6	(23.2)	93.2	(23.5)	0.558
Carbohydrates (g/d)	230.6	(80.6)	230.5	(81.1)	230.0	(81.2)	0.987
Adherence to the MedDiet (points) ^a	8.6	(2.0)	8.7	(2.0)	8.7	(2.0)	0.037
Alcohol consumption (g/d)	8.3	(14.4)	8.6	(14.1)	8.4	(14.6)	0.718
Physical activity (METs-min/day)	232	(238)	227	(237)	243	(253)	0.218

Total indicates the maximum number of participants included with genotype data and demographic, anthropometric, adherence to MedDiet, physical activity and clinical variables. For dietary intake obtained by food-frequency questionnaires n = 7040 subjects were analyzed after exclusion of n = 58 subjects with invalid data. Biochemical data were available for fasting glucose (n = 6716 participants) total cholesterol (n = 6834 participants), HDL cholesterol (n = 6753 participants), LDL cholesterol (n = 6698 participants), and triglycerides (n = 6795 participants)

MUFA Monounsaturated fatty acids, MedDiet Mediterranean diet, EVOO extra virgin olive oil

^a Based on a 14-point screener of adherence

ORIGINAL INVESTIGATION

Open Access



CLOCK gene variation is associated with incidence of type-2 diabetes and cardiovascular diseases in type-2 diabetic subjects: dietary modulation in the PREDIMED randomized trial

Dolores Corella^{1,2*}, Eva. M. Asensio^{1,2}, Oscar Coltell^{2,3}, José V. Sorlí^{1,2}, Ramón Estruch^{2,4,5}, Miguel Ángel Martínez-González^{2,5,6,15}, Jordi Salas-Salvadó^{2,5,7}, Olga Castañer^{2,8}, Fernando Arós^{2,5,9}, José Lapetra^{2,5,10}, Lluís Serra-Majem^{2,5,11}, Enrique Gómez-Gracia^{5,12}, Carolina Ortega-Azorín^{1,2}, Miquel Fiol^{1,3}, Javier Díez Espino^{2,5,14,15}, Andrés Díaz-López^{2,7}, Montserrat Fitó^{2,8}, Emilio Ros^{2,16} and José M. Ordovás^{17,18,19}

Table 2 Incidence rate and hazard ratios (HR) for type-2 diabetes (T2D) depending on the CLOCK-rs4580704 in non-T2D subjects

CLOCK genotypes	Non-T2D subjects at baseline (n = 3671)								
	Cases	Person-y	Incidence rate ^a	Model 1			Model 2		
				HR	95 % CI	P value	HR	95 % CI	P value
Dominant model									
CC	130	6088.5	21.4	1.00	(Reference)		1.00	(Reference)	
CG + GG	156	10727.7	14.5	0.68	(0.54–0.86)	0.001	0.69	(0.54–0.87)	0.002

Model 1: adjusted for sex, age, center and dietary intervention group

Model 2: adjusted for variables in model 1 plus BMI, drinking, physical activity, medication (hypertension, dyslipemia and glucose), adherence to the Mediterranean Diet and total energy intake at baseline

^a Crude incidence rates were expressed per 1000 person-years of follow-up

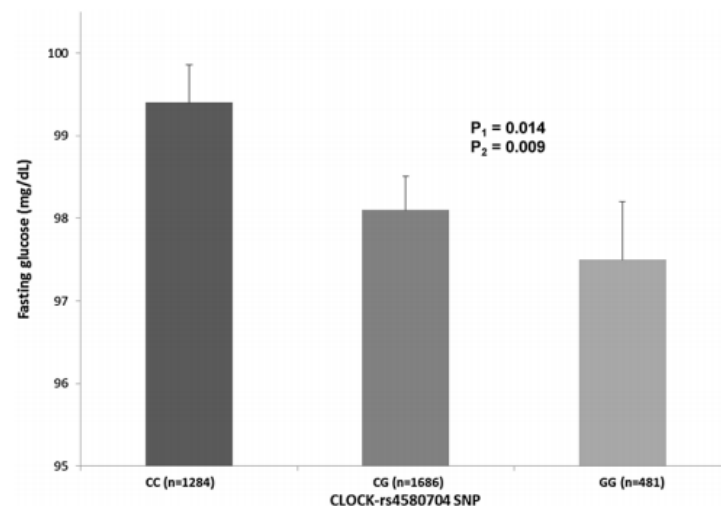


Fig. 1 Association between the CLOCK-rs4580704 SNP and fast-ing glucose in non-T2D subjects at baseline. Means values and SE of means (error bars) are represented depending on the CLOCK genotypes. The P-values for the polymorphism were obtained in the dominant model for G-carriers vs CC subjects. P_1 Unadjusted model. P_2 Model adjusted for sex, age, field center and BMI

ORIGINAL INVESTIGATION

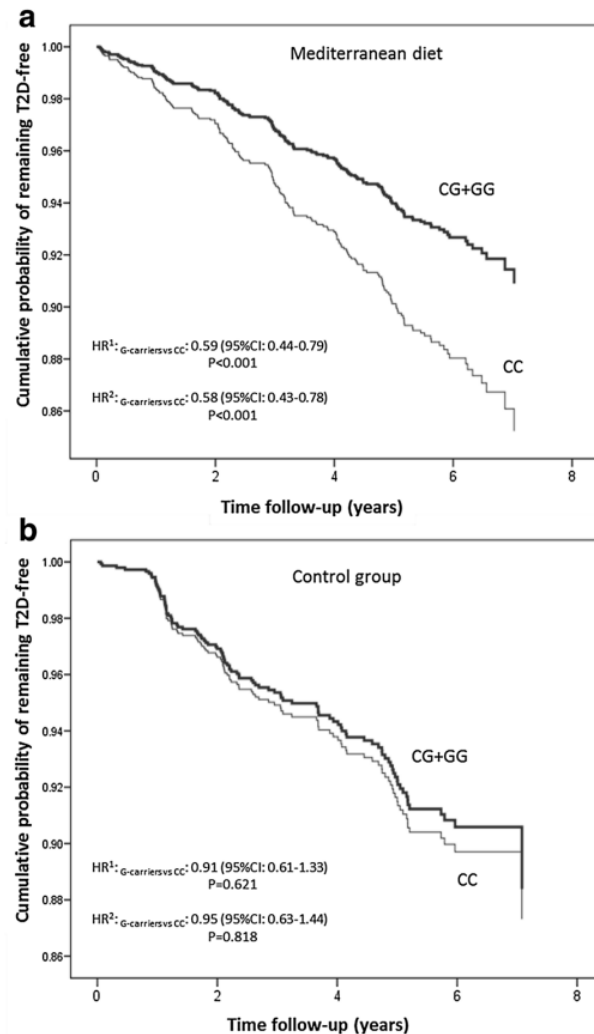
Open Access



CLOCK gene variation is associated with incidence of type-2 diabetes and cardiovascular diseases in type-2 diabetic subjects: dietary modulation in the PREDIMED randomized trial

Dolores Corella^{1,2*}, Eva. M. Asensio^{1,2}, Oscar Coltell^{2,3}, José V. Sorlí^{1,2}, Ramón Estruch^{2,4,5}, Miguel Ángel Martínez-González^{2,5,6,15}, Jordi Salas-Salvadó^{2,5,7}, Olga Castañer^{2,8}, Fernando Arós^{2,5,9}, José Lapetra^{2,5,10}, Lluís Serra-Majem^{2,5,11}, Enrique Gómez-Gracia^{5,12}, Carolina Ortega-Azorín^{1,2}, Miquel Fiol^{1,3}, Javier Díez Espino^{2,5,6,14,15}, Andrés Díaz-López^{2,7}, Montserrat Fitó^{2,8}, Emilio Ros^{2,16} and José M. Ordovás^{1,7,18,19}

- Στατιστικά σημαντική επίδραση της προσκόλλησης στη Μεσογειακή διατροφή στη σχέση του γονιδίου με την πιθανότητα εμφάνισης ΣΔ2



Genetic predisposition, Western dietary pattern, and the risk of type 2 diabetes in men¹⁻³

Lu Qi, Marilyn C Cornelis, Cuilin Zhang, Rob M van Dam, and Frank B Hu

Am J Clin Nutr 2009;89:1453-8. Printed in USA. © 2009 American Society for Nutrition

TABLE 3

Interactions between dietary patterns and the genetic risk score in relation to diabetes risk¹

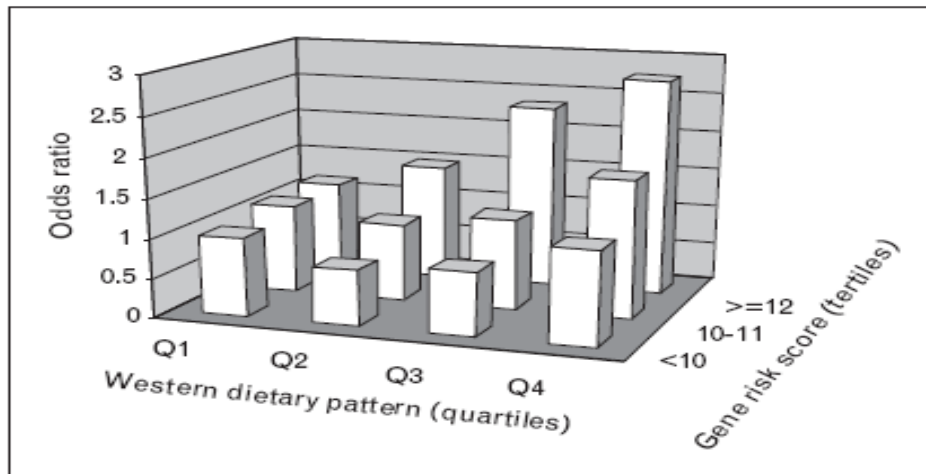
Genetic risk score ²	Dietary patterns ³				P for trend	P for interaction
	Q1 (lowest)	Q2	Q3	Q4 (highest)		
Western dietary pattern						
<10 (n = 503)	1	0.79 (0.46, 1.38)	0.81 (0.48, 1.37)	1.07 (0.65, 1.76)	0.69	0.02
10–11 (n = 904)	1	0.98 (0.67, 1.44)	1.02 (0.69, 1.49)	1.40 (0.97, 2.01)	0.06	—
≥12 (n = 1126)	1	1.23 (0.88, 1.73)	1.49 (1.06, 2.09)	2.06 (1.48, 2.88)	0.01	—
Prudent dietary pattern						
<10 (n = 503)	1	0.85 (0.50, 1.44)	1.07 (0.65, 1.76)	1.29 (0.79, 2.11)	0.24	NS
10–11 (n = 904)	1	0.75 (0.52, 1.07)	0.81 (0.56, 1.18)	0.77 (0.53, 1.11)	0.21	—
≥12 (n = 1126)	1	0.81 (0.58, 1.14)	0.71 (0.51, 0.99)	0.81 (0.59, 1.13)	0.16	—

¹ The analyses were adjusted for age, BMI, smoking, alcohol consumption, physical activity, family history of diabetes, and total energy intakes. Q, quartile.

² Defined by counting the number of risk alleles of 10 single nucleotide polymorphisms from a genome-wide association study, including *HHEX* (rs11111875), *CDKALI* (rs7756992), *IGF2BP2* (rs4402960), *SLC30A8* (rs13266634), *WFS1* (rs10010131), *CDKN2A/B* (rs564398, rs10811661), *TCF7L2* (rs12255372), *PPARG* (rs1801282), and *KCNJ11* (rs5219).

³ Values are odds ratios (95% CIs) calculated by using an unconditional logistic regression model.

- 1196 Ασθενών- 1337 μαρτύρων
- A posteriori dietary patterns
 - GRS από 10 SNPs



**Μελέτες αλληλεπιδράσεων γονιδίων –
φυσικής δραστηριότητας**

Previously Associated Type 2 Diabetes Variants May Interact With Physical Activity to Modify the Risk of Impaired Glucose Regulation and Type 2 Diabetes

A Study of 16,003 Swedish Adults

Ema C. Brito,¹ Valeriya Lyssenko,² Frida Renström,¹ Göran Berglund,³ Peter M. Nilsson,³ Leif Groop,² and Paul W. Franks^{1,2}

- 17 SNPs
- 16003 Μη-διαβητικοί, Σουηδικής καταγωγής

Participant characteristics stratified by level of physical activity
(*n* = 16,003)

Variable	Physically inactive	Physically active	<i>P</i>
<i>n</i>	3,455	12,548	—
Sex (M/F)	2,287/1,168	8,115/4,433	0.097
Baseline age (years)	44.7 ± 7.3	45.7 ± 6.8	<0.0001
Baseline BMI (kg/m ²)	24.6 ± 3.7	24.2 ± 3.1	<0.0001
Baseline fasting glucose (mmol/l)	4.87 ± 0.48	4.81 ± 0.49	<0.0001
Baseline 2-h glucose (mmol/l)*	5.67 ± 1.54	5.64 ± 1.44	0.480
Baseline glucose regulation (NGR/IGR)	2,585/870	9,601/2,947	0.038
Developed diabetes (no/yes)	2,958/497	10,982/1,566	0.003

Previously Associated Type 2 Diabetes Variants May Interact With Physical Activity to Modify the Risk of Impaired Glucose Regulation and Type 2 Diabetes

A Study of 16,003 Swedish Adults

Ema C. Brito,¹ Valeriya Lyssenko,² Frida Renström,¹ Göran Berglund,³ Peter M. Nilsson,³ Leif Groop,² and Paul W. Franks^{1,2}

TABLE 2
Tests of association and gene × physical activity interaction for 17 polymorphisms on IGR risk (vs. NGR) and 2-h glucose levels (mmol/l)

Nearest gene (variant)	Main effects (OR or β-coefficient) and P values (for main effects and interactions)							
	Overall		<i>P</i> _{interaction}		Physically inactive		Physically active	
	IGR risk (OR, <i>P</i> value)	2-h glucose (β-coefficient, <i>P</i> value)	IGR risk	2-h glucose	IGR risk (OR, <i>P</i> value)	2-h glucose (β-coefficient, <i>P</i> value)	IGR risk (OR, <i>P</i> value)	2-h glucose (β-coefficient, <i>P</i> value)
<i>CDKN2A/B</i> (rs10811661)*	1.08, 0.084	0.02, 0.432	0.015	0.013	0.91, 0.197	−0.12, 0.064	1.12, 0.0075	0.06, 0.070
<i>HNF1B</i> (rs4430796)	1.02, 0.361†	0.02, 0.651†	0.026	0.0009	0.92, 0.126	−0.13, 0.005	1.06, 0.066	0.04, 0.056
<i>PPARG</i> (rs1801282)	1.01, 0.744	0.01, 0.790	0.041	0.776	0.88, 0.097	−0.01, 0.877	1.05, 0.221	0.01, 0.717
<i>SLC30A8</i> (rs13266634)	1.04, 0.169	0.02, 0.669	0.134	0.960	0.96, 0.540	0.01, 0.798	1.06, 0.055	0.05, 0.047
<i>WFS1</i> (rs10010131)	1.03, 0.231	−0.01, 0.651	0.140	0.082	0.96, 0.456	−0.08, 0.087	1.05, 0.082	0.01, 0.748
<i>TCF7L2</i> (rs7903146)	1.10, 0.001	0.06, 0.012	0.141	0.600	1.01, 0.858	0.03, 0.538	1.13, 0.0005	0.06, 0.012
<i>ADAMTS9</i> (rs4607103)	1.03, 0.351	−0.02, 0.420	0.155	0.784	0.94, 0.420	−0.01, 0.886	1.05, 0.138	−0.02, 0.405
<i>CDKAL1</i> (rs7754840)	1.06, 0.024	0.04, 0.049	0.222	0.715	1.14, 0.033	0.02, 0.659	1.04, 0.165	0.05, 0.051
<i>CAMK1D</i> (rs12779790)	1.03, 0.306	0.01, 0.633	0.238	0.753	0.96, 0.565	−0.00, 0.978	1.05, 0.143	0.02, 0.565
<i>NOTCH2</i> (rs10923931)	1.11, 0.013	0.04, 0.190	0.313	0.281	1.20, 0.042	0.12, 0.129	1.09, 0.092	0.03, 0.471
<i>KCNJ11</i> (rs5219)	1.04, 0.144	0.04, 0.047	0.391	0.974	1.09, 0.148	0.04, 0.391	1.03, 0.388	0.04, 0.072
<i>THADA</i> (rs7578597)*	1.04, 0.357	−0.03, 0.511	0.472	0.484	0.98, 0.858	0.02, 0.774	1.06, 0.249	−0.03, 0.358
<i>IGFBP2</i> (rs4402960)	1.10, 0.002	0.02, 0.012	0.627	0.871	1.12, 0.057	0.06, 0.289	1.09, 0.014	0.06, 0.025
<i>JAZF1</i> (rs864745)*	1.04, 0.154	0.05, 0.008	0.830	0.435	1.05, 0.384	0.08, 0.078	1.04, 0.253	0.04, 0.034
<i>HHEX</i> (rs1111875)	1.08, 0.005	0.05, 0.024	0.862	0.802	1.08, 0.220	0.03, 0.485	1.09, 0.010	0.05, 0.031
<i>MTNR1B</i> (rs10830963)	1.18, <0.0001	0.06, 0.009	0.912	0.300	1.20, 0.004	0.10, 0.067	1.18, <0.0001	0.05, 0.048
<i>TSPAN8</i> (rs7961581)	1.04, 0.141	0.02, 0.053	0.989	0.857	1.04, 0.502	0.06, 0.286	1.04, 0.210	0.04, 0.091

P values are unadjusted for multiple statistical comparisons. Effect estimates are expressed as ORs (IGR vs. NGR) or β-coefficient (mmol/l of 2-h glucose) per copy of the risk allele at each locus. Data are adjusted for age, sex, and BMI and are ranked by *P* value for the test of gene × physical activity interaction on IGR risk. *The major allele is shown as the risk allele. In all other cases the minor allele is the risk allele. †This result has previously been reported (14). Fasting glucose and type 2 diabetes data also have previously been reported in this cohort for *MTNR1B* (15). Associations with type 2 diabetes have been reported for all other SNPs (10).

Previously Associated Type 2 Diabetes Variants May Interact With Physical Activity to Modify the Risk of Impaired Glucose Regulation and Type 2 Diabetes

A Study of 16,003 Swedish Adults

Ema C. Brito,¹ Valeriya Lyssenko,² Frida Renström,¹ Göran Berglund,³ Peter M. Nilsson,³ Leif Groop,² and Paul W. Franks^{1,2}

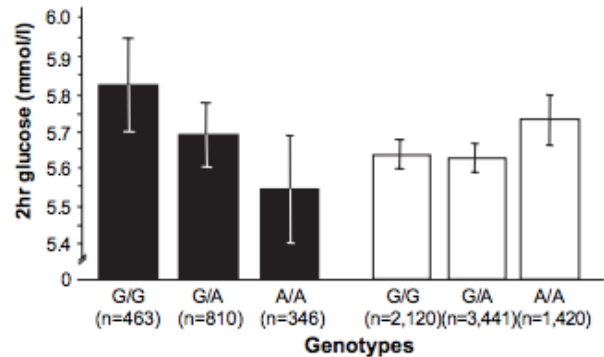
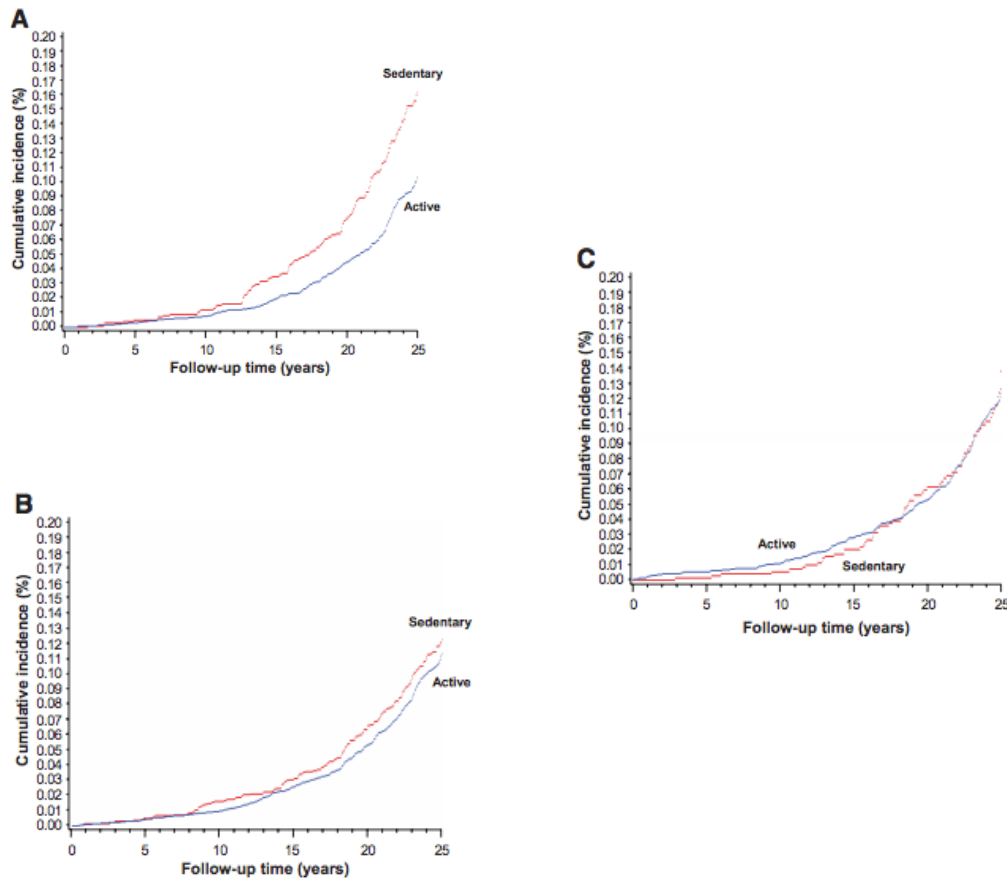


FIG. 1. Interaction between the *HNF1B* rs4430796 variant and physical activity on 2-h glucose levels in 8,600 Swedish middle-aged men and women. ■, physically inactive; □, physically active. Data are means adjusted for age and sex. Error bars are 95% CIs. $P_{\text{interaction}} = 0.0009$.



Genetic variants near the *IRS1* gene, physical activity and type 2 diabetes in US men and women

M. A. He,

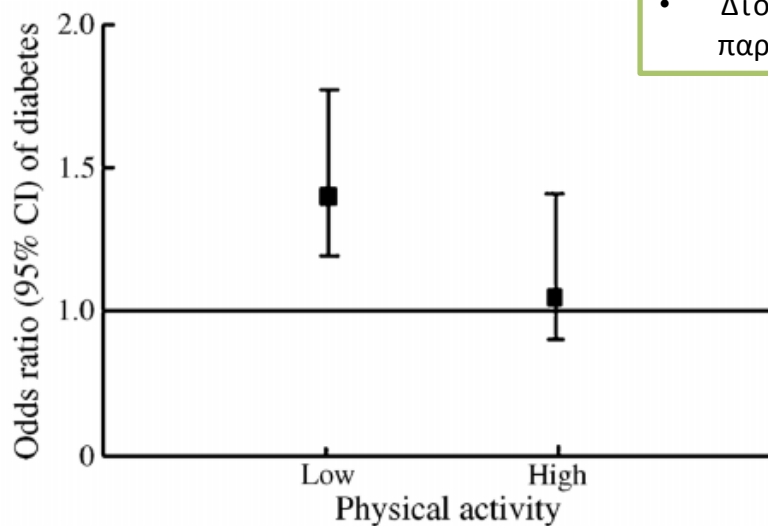
Table 1 Associations between SNPs rs1522813 and rs2943641 and type 2 diabetes in NHS and HPFS

SNP	Genotype	NHS (women)						HPFS (men)						Meta-analysis	
		Cases (n=1,467)	Controls (n=1,754)	Crude OR (95% CI)	p value	Adjusted OR (95% CI) ^a	p value	Cases (n=1,124)	Controls (n=1,298)	Crude OR (95% CI)	p value	Adjusted OR (95% CI) ^a	p value	OR (95% CI)	p value
rs1522813	GG	784 (53.4)	1,003 (57.2)	1.00	–	1.00	–	550 (48.9)	691 (53.2)	1.00	–	1.00	–	–	–
	GA	581 (39.6)	630 (35.9)	1.18 (1.02–1.37)	0.03	1.25 (1.03–1.51)	0.02	470 (41.8)	510 (39.3)	1.16 (0.98–1.37)	0.09	1.21 (1.00–1.46)	0.06	1.23 (1.07–1.41)	0.003
	AA	102 (7.0)	121 (6.9)	1.08 (0.82–1.43)	0.60	1.21 (0.84–1.74)	0.30	104 (9.3)	97 (7.5)	1.35 (1.00–1.83)	0.05	1.38 (0.98–1.94)	0.07	1.30 (1.01–1.66)	0.042
Additive model		–	–	1.10 (0.99–1.23)	0.09	1.17 (1.01–1.35)	0.03	–	–	1.16 (1.02–1.31)	0.02	1.19 (1.03–1.37)	0.019	1.18 (1.06–1.30)	0.002
rs2943641	CC	641 (43.7)	722 (41.2)	1.00	–	1.00	–	510 (45.4)	539 (41.5)	1.00	–	1.00	–	–	–
	CT	636 (43.4)	798 (45.5)	0.90 (0.77–1.04)	0.16	0.91 (0.75–1.11)	0.36	489 (43.5)	570 (43.9)	0.91 (0.76–1.08)	0.26	0.92 (0.76–1.12)	0.41	0.92 (0.80–1.05)	0.218
	TT	190 (13.0)	234 (13.3)	0.91 (0.74–1.14)	0.42	0.83 (0.62–1.11)	0.21	125 (11.1)	189 (14.6)	0.70 (0.54–0.90)	0.006	0.67 (0.50–0.90)	0.008	0.75 (0.61–0.92)	0.006
Additive model		–	–	0.94 (0.85–1.04)	0.23	0.91 (0.80–1.04)	0.18	–	–	0.86 (0.76–0.96)	0.009	0.85 (0.74–0.97)	0.016	0.88 (0.80–0.97)	0.008

^a Adjusted for age, BMI (five categories), family history of diabetes (yes, no), smoking (never, past or current), alcohol (five categories), menopausal status (pre- or post-menopausal [never, past or current hormone use]; women only), quintiles of physical activity (MET h/week for men in HPFS, h/week for women in NHS) and quintiles of energy-adjusted polyunsaturated fatty acid:saturated fatty acid ratio, and intakes of *trans* fat and cereal fibre

Genetic variants near the *IRS1* gene, physical activity and type 2 diabetes in US men and women

M. A. He,



- *IRS1*: insulin receptor substrate
- Rs1522813 x PA σε γυναίκες
- PA χωρισμένο με βάση τον διάμεσο
- Επικρατές μοντέλο κληρονομής
- Διόρθωση για πολλούς συγχυτικούς παράγοντες.

Interaction of single nucleotide polymorphisms in *ADRB2*, *ADRB3*, *TNF*, *IL6*, *IGF1R*, *LIPC*, *LEPR*, and *GHRL* with physical activity on the risk of type 2 diabetes mellitus and changes in characteristics of the metabolic syndrome: The Finnish Diabetes Prevention Study

Tuomas O. Kilpeläinen^{a,*}, Timo A. Lakka^{a,b}, David E. Laaksonen^{a,c}, Ursula Mager^d, Titta Salopuro^d, Agata Kubaszek^e, Boryana Todorova^e, Olli Laukkanen^e, Jaana Lindström^e, Johan G. Eriksson^{e,f}, Helena Hämäläinen^g, Sirkka Aunola^h, Pirjo Ilanne-Parikka^{i,j}, Sirkka Keinänen-Kiukaanniemi^{k,l}, Jaako Tuomilehto^{e,f,m}, Markku Laakso^e, Matti Uusitupa^d for the Finnish Diabetes Prevention Study Group

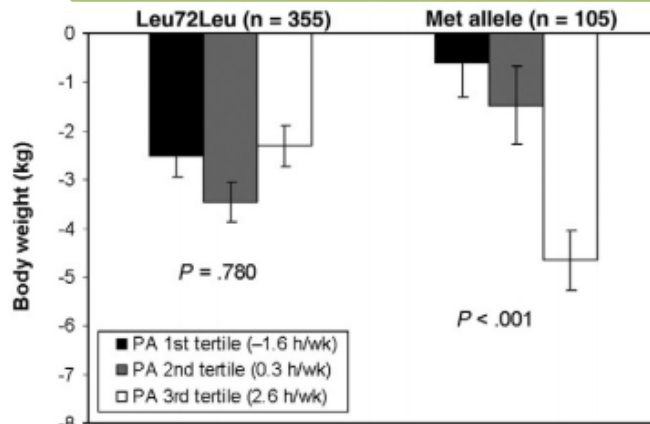
- Finnish DPS
- Παχύσαρκοι με IGT
- Παρακολούθηση για 4,1 έτη

Table 2

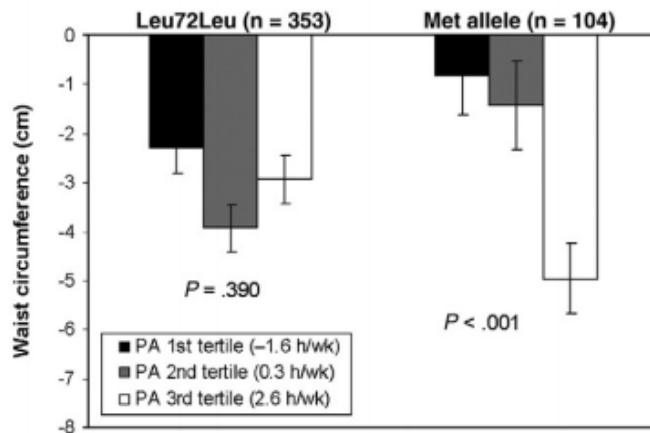
Baseline characteristics of participants in the Finnish DPS

Characteristic	Level at baseline
n	487
Sex (male/female)	162/325
Age (y)	55.4 ± 7.0
Weight (kg)	86.3 ± 14.3
BMI (kg/m ²)	31.3 ± 4.5
Waist circumference (cm)	101.2 ± 11.0
Fasting plasma glucose (mmol/L)	6.1 ± 0.7
2-h plasma glucose (mmol/L)	8.9 ± 1.5
Fasting serum insulin (mU/L)	14.7 ± 7.3
2-h serum insulin (mU/L)	95.4 ± 65.5
Energy intake (kcal)	1767 ± 527
Total fat intake, energy adjusted (g)	72.2 ± 12.7
Saturated fat intake, energy adjusted (g)	32.8 ± 8.2
Fiber intake, energy adjusted (g)	19.9 ± 6.6
Total PA (h/wk) ^a	5.7 (3.1-9.3)
Moderate-to-vigorous PA (h/wk)	1.7 (0.5-4.0)
Low-intensity PA (h/wk)	3.0 (1.2-5.9)

GHRL - change in moderate-to-vigorous PA



P for interaction* = 0.001

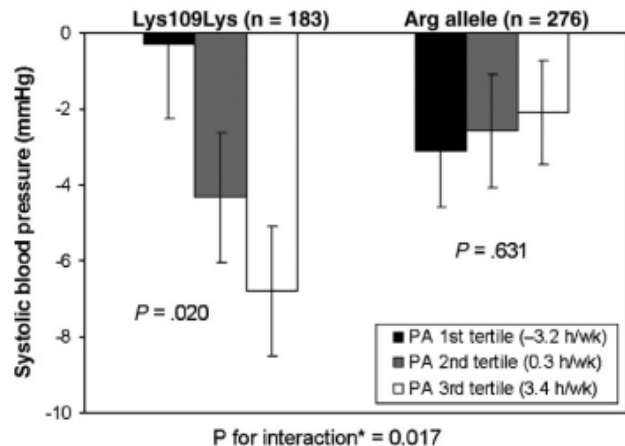


P for interaction* = 0.006

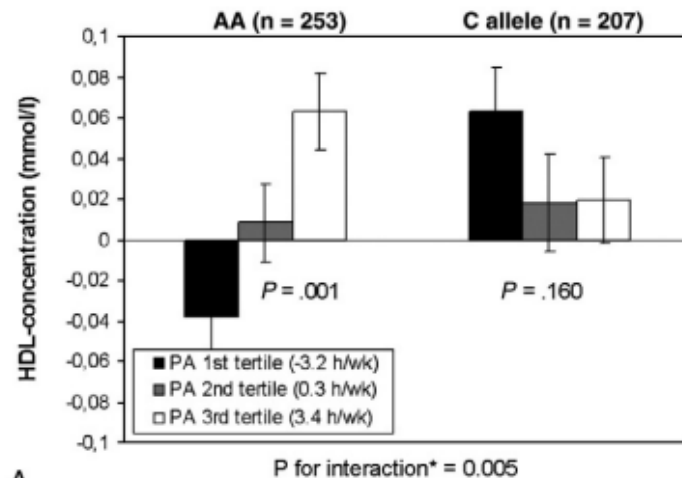
- 3 ομάδες ΦΔ
- Αποτελέσματα 1 ου έτους παρέμβασης
- Δεν παρατηρήθηκε στατιστική αλληλεπίδραση ως προς τον ΣΔ

Interaction of single nucleotide polymorphisms in *ADRB2*, *ADRB3*, *TNF*, *IL6*, *IGF1R*, *LIPC*, *LEPR*, and *GHRL* with physical activity on the risk of type 2 diabetes mellitus and changes in characteristics of the metabolic syndrome: The Finnish Diabetes Prevention Study

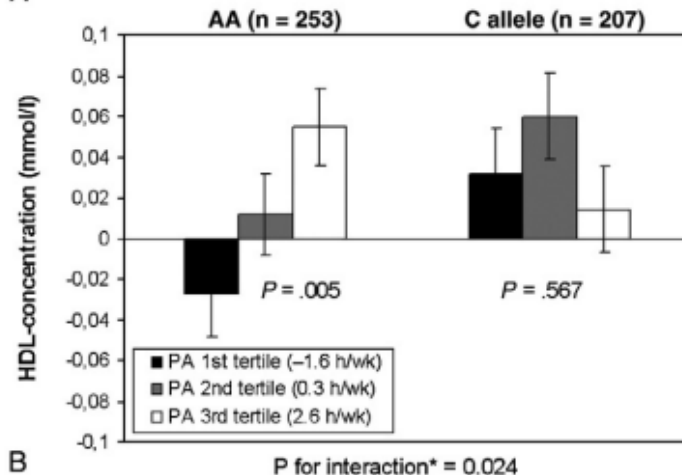
Tuomas O. Kilpeläinen^{a,*}, Timo A. Lakka^{a,b}, David E. Laaksonen^{a,c}, Ursula Mäger^d, Titta Salopuro^d, Agata Kubaszek^e, Boryana Todorova^e, Olli Laukkanen^e, Jaana Lindström^e, Johan G. Eriksson^{e,f}, Helena Hämäläinen^g, Sirkka Aunola^h, Pirjo Ilanne-Parikka^{i,j}, Sirkka Keinänen-Kiukkaanniemi^{k,l}, Jaako Tuomilehto^{e,f,m}, Markku Laakso^e, Matti Uusitupa^d
for the Finnish Diabetes Prevention Study Group



LEPR – change in total PA



A



B

GHRL
A. Change in total PA
B. Change in moderate to vigorous PA

- Finnish DPS
- Υπερβαροι με IGT
- Παρακολούθηση για 4,1 έτη

Physical activity modifies the effect of SNPs in the *SLC2A2* (GLUT2) and *ABCC8* (SUR1) genes on the risk of developing type 2 diabetes

T. O. Kilpeläinen,¹ T. A. Lakka,^{1,2} D. E. Laaksonen,^{1,3} O. Laukkanen,⁴ J. Lindström,⁴ J. G. Eriksson,^{4,5} T. T. Valle,⁴ H. Hämäläinen,⁶ S. Aunola,⁷ P. Ilanne-Parikka,^{8,9} S. Keinänen-Kiukkaanniemi,^{10,11} J. Tuomilehto,^{4,5,12} M. Uusitupa,¹³ M. Laakso,³ for the Finnish Diabetes Prevention Study Group

Table 3. Association of SNPs in *SLC2A2* with the risk of developing type 2 diabetes according to thirds of the change in moderate-to-vigorous physical activity

	Change in Moderate-to-Vigorous Physical Activity,* h/wk			P for Difference	P for Interaction†
	–1.5 (–13.5 to –0.1)	0.5 (–0.1 to 1.3)	2.6 (1.3 to 14.4)		
Relative risk of conversion to type 2 diabetes (95% CI)					
SLC2A2 rs5393 (A/C)					
AA (n = 374)	2.67 (1.25–5.70)	2.23 (1.13–4.37)	1	0.010	0.027
C allele (n = 105)	0.26 (0.05–1.27)	0.43 (0.12–1.53)	1	0.082	
Conversions (%), AA vs. C allele	36 (30) vs. 7 (19)	35 (29) vs. 8 (22)	12 (9) vs. 6 (19)		
Relative risk of conversion to type 2 diabetes (95% CI)					
SLC2A2 rs5394 (C/T)					
CC (n = 387)	2.67 (1.25–5.72)	2.25 (1.14–4.41)	1	0.010	0.022
T allele (n = 92)	0.21 (0.04–1.19)	0.37 (0.10–1.42)	1	0.064	
Conversions (%), CC vs. T allele	37 (29) vs. 6 (20)	36 (28) vs. 7 (21)	12 (9) vs. 6 (21)		
Relative risk of conversion to type 2 diabetes (95% CI)					
SLC2A2 rs5400 (C/T) (T110I)					
CC (n = 356)	2.42 (1.11–5.29)	2.37 (1.17–4.78)	1	0.023	0.057
T allele (n = 123)	0.67 (0.18–2.58)	0.51 (0.17–1.53)	1	0.473	
Conversions (%), CC vs. T allele	33 (29) vs. 10 (23)	34 (29) vs. 9 (21)	11 (9) vs. 7 (19)		
Relative risk of conversion to type 2 diabetes (95% CI)					
SLC2A2 rs5404 (G/A) (T198T)					
GG (n = 387)	2.62 (1.23–5.60)	2.27 (1.15–4.45)	1	0.011	0.022
A allele (n = 92)	0.22 (0.04–1.23)	0.37 (0.10–1.40)	1	0.068	
Conversions (%), GG vs. A allele	37 (29) vs. 6 (21)	36 (29) vs. 7 (21)	12 (9) vs. 6 (21)		

Table 6. Association of SNPs in *ABCC8* and *KCNJ11* with changes in 2-h glucose concentration according to thirds of the change in moderate-to-vigorous physical activity

	Change in Moderate-to-Vigorous Physical Activity,* h/wk			P for Trend	P for Interaction†
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)		
Change in plasma 2-h glucose, mean ± SE, mmol/l					
ABCC8 rs3758947 (G-2886A)					
GG (n = 270)	0.15 ± 0.23	−0.50 ± 0.18	−0.58 ± 0.18	0.020	0.015
A allele (n = 207)	−0.64 ± 0.20	−0.36 ± 0.20	−0.28 ± 0.19	0.224	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
ABCC8 rs3758953 (A-1273G)					
AA (n = 123)	0.20 ± 0.38	−0.53 ± 0.28	−0.98 ± 0.26	0.021	0.001
G allele (n = 354)	−0.42 ± 0.16	−0.34 ± 0.15	−0.21 ± 0.15	0.369	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
ABCC8 rs1799859 (A/G) (R1273R)					
A allele (n = 146)	0.83 ± 0.33	−0.18 ± 0.23	−0.49 ± 0.26	0.004	0.002
GG (n = 331)	−0.74 ± 0.17	−0.46 ± 0.16	−0.41 ± 0.15	0.158	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
KCNJ11 rs5219 (T/C) (E23K)					
TT (n = 126)	−0.15 ± 0.35	−0.10 ± 0.25	−0.33 ± 0.26	0.702	0.435
C allele (n = 351)	−0.28 ± 0.18	−0.61 ± 0.16	−0.45 ± 0.15	0.502	

Table 4. Association of SNPs in *ABCC8* and *KCNJ11* with the risk of developing type 2 diabetes according to thirds of the change in moderate-to-vigorous physical activity

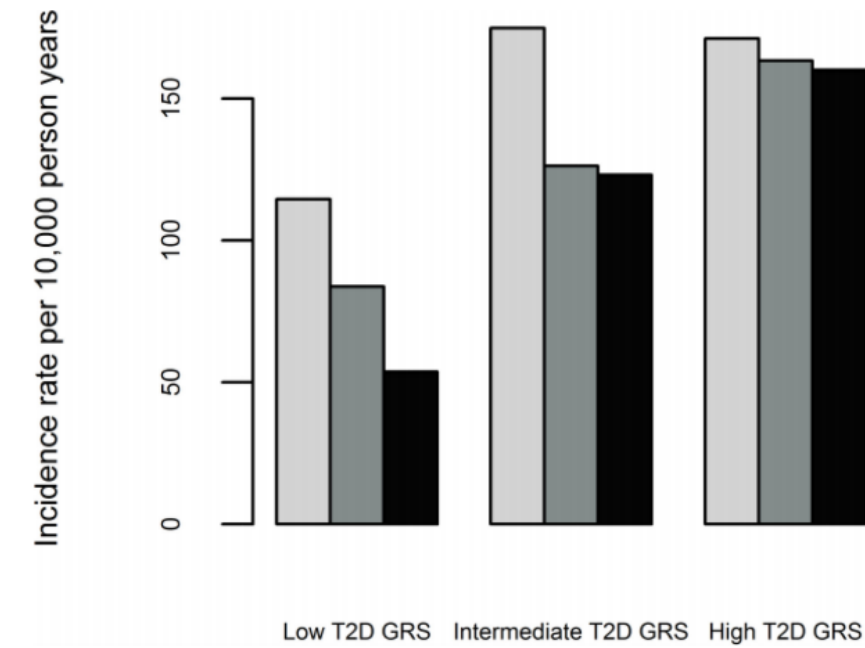
	Change in Moderate-to-Vigorous Physical Activity,* h/wk			P for Difference	P for Interaction†
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)		
Relative risk of conversion to type 2 diabetes (95% CI)					
ABCC8 rs3758947 (G/A)					
GG (n = 272)	3.65 (1.60–8.33)	1.42 (0.71–2.84)	1	0.003	0.007
A allele (n = 207)	1.04 (0.31–3.46)	2.25 (0.76–6.68)	1	0.972	
Conversions (%), GG vs. A allele	32 (38) vs. 11 (15)	25 (27) vs. 18 (27)	13 (14) vs. 5 (8)		
Relative risk of conversion to type 2 diabetes (95% CI)					
ABCC8 rs3758953 (A/G)					
AA (n = 123)	5.16 (1.51–17.6)	1.80 (0.67–4.85)	1	0.012	0.128
G allele (n = 356)	1.32 (0.59–2.99)	1.72 (0.83–3.57)	1	0.548	
Conversions (%), AA vs. G allele	18 (47) vs. 25 (21)	13 (30) vs. 30 (26)	7 (17) vs. 11 (9)		
Relative risk of conversion to type 2 diabetes (95% CI)					
ABCC8 rs1799859 (A/G) (R1273R)					
GG (n = 332)	5.60 (1.72–18.2)	2.40 (0.84–6.91)	1	<0.001	0.111
A allele (n = 147)	0.85 (0.39–1.87)	1.61 (0.80–3.25)	1	0.814	
Conversions (%), GG vs. A allele	20 (48) vs. 23 (20)	18 (32) vs. 25 (24)	5 (10) vs. 13 (12)		
Relative risk of conversion to type 2 diabetes (95% CI)					
KCNJ11 rs5219 (T/C) (E23K)					
TT (n = 127)	9.81 (1.53–63.1)	5.99 (1.46–24.7)	1	0.006	0.203
C allele (n = 352)	1.28 (0.64–2.57)	1.26 (0.65–2.46)	1	0.498	
Conversions (%), TT vs. C allele	11 (30) vs. 32 (26)	14 (30) vs. 29 (26)	3 (7) vs. 15 (13)		

Table 5. Association of SNPs in *SLC2A2* with changes in plasma 2-h glucose concentration according to thirds of the change in moderate-to-vigorous physical activity

	Change in Moderate-to-Vigorous Physical Activity,* h/wk			P for Trend	P for Interaction†
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)		
Change in plasma 2-h glucose, mean ± SE, mmol/l					
SLC2A2 rs5393 (A/C)					
AA (n = 373)	−0.17±0.17	−0.22±0.15	−0.46±0.15	0.222	0.013
C allele (n = 104)	−0.80±0.29	−1.24±0.23	−0.01±0.27	0.077	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
SLC2A2 rs5394 (C/T)					
CC (n = 385)	−0.18±0.17	−0.24±0.15	−0.46±0.15	0.233	0.023
T allele (n = 92)	−0.87±0.31	−1.19±0.24	−0.03±0.28	0.070	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
SLC2A2 rs5400 (C/T) (T110I)					
CC (n = 355)	−0.26±0.17	−0.18±0.16	−0.46±0.15	0.414	0.016
T allele (n = 122)	−0.42±0.27	−1.22±0.21	−0.05±0.25	0.375	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
SLC2A2 rs5404 (G/A) (T198T)					
GG (n = 385)	−0.18±0.17	−0.23±0.15	−0.46±0.14	0.231	0.016
A allele (n = 92)	−0.93±0.31	−1.17±0.24	0.01±0.28	0.048	
Change in plasma 2-h glucose, mean ± SE, mmol/l					
SLC2A2 CTTA haplotype†					
Noncarriers (n = 386)	−0.15±0.17	−0.26±0.15	−0.45±0.15	0.207	0.022
CTTA carriers (n = 91)	−0.95±0.31	−1.14±0.25	0.01±0.28	0.043	

Association of physical activity with lower type 2 diabetes incidence is weaker among individuals at high genetic risk

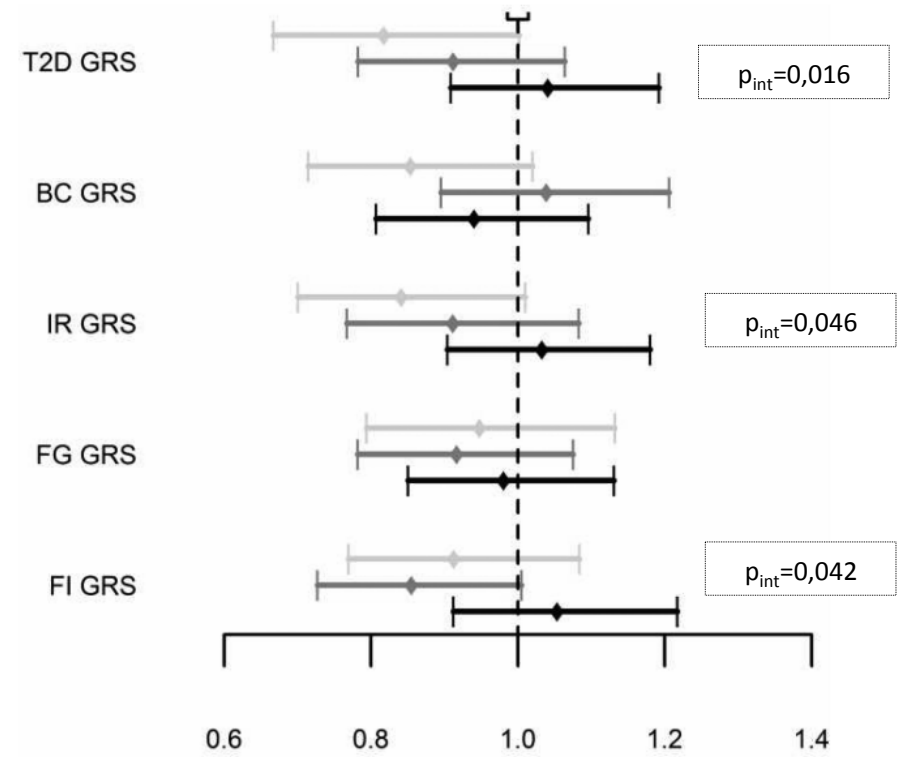
Yann C. Klimentidis^{1,*}, Zhao Chen¹, Amit Arora¹, and Chiu-Hsieh Hsu¹



- Άσπρο: χαμηλή ΦΔ
- Γκρι: μέτρια ΦΔ
- Μαύρο: υψηλή ΦΔ

- 8.101 άτομα από την ARIC
- Προοπτική μελέτη – 12 έτη
- 65 ΣΔ-SNPs, 36 Γλυ-SNPs, 16 Ινσ-SNPs

Καμία αλληλεπίδραση με τα SNPs ξεχωριστά δεν έφτασε το επίπεδο στατιστικής σημαντικότητας.



- Σχετικός κίνδυνος εμφάνισης ΣΔ για κάθε 1 μονάδα αύξησης ΦΔ.
- Διαχωρισμός ανά κατηγορία GRS (άσπρο: χαμηλό GRS)

**Μελέτες αλληλεπιδράσεων γονιδίων -
ύπνου**

Associations between chronotype, *MTNR1B* genotype and risk of type 2 diabetes in UK Biobank

■ X. Tan¹ , D.-M. Ciuculete¹, H.B. Schiöth^{1,2} & C. Benedict¹ 

- 337083 άτομα από την UKBB – Λευκοί Βρετανοί
- *MTNR1B*: μελατονίνη
- Rs10830963: παρατεταμένη απέκκριση μελατονίνης & μειωμένη απέκκριση ινσουλίνης → υπεργλυκαιμία

Table 3. Odds ratios and 95% CIs for type 2 diabetes, separated by rs10830963 genotype and chronotype

Exposure	Model 1			Model 2			Model 3			Model 4		
	OR (95% CI)	P*	R ²	OR (95% CI)	P*	R ²	OR (95% CI)	P*	R ²	OR (95% CI)	P*	R ²
rs10830963 genotype												
CC	1		0.056	1		0.059	1		0.063	1		0.184
CG	1.10 (1.07, 1.14)	4.0051E-8		1.10 (1.07, 1.14)	3.8816E-8		1.10 (1.08, 1.12)	4.1039E-8		1.10 (1.07, 1.15)	1.1282E-7	
GG	1.19 (1.12, 1.27)	3.3262E-8		1.19 (1.12, 1.27)	2.5537E-8		1.19 (1.16, 1.23)	2.7255E-8		1.21 (1.14, 1.29)	5.6032E-9	
Chronotype												
Definitely morning	1		0.058	1		0.059	1		.065	1		0.184
More morning than evening	0.84 (0.80, 0.89)	2.3055E-10		0.84 (0.80, 0.89)	2.8277E-10		0.84 (0.80, 0.88)	9.9992E-11		0.96 (0.91, 1.01)	0.088	
More evening than morning	1.01 (0.96, 1.05)	0.791		1.01 (0.96, 1.05)	0.769		1.00 (0.95, 1.04)	0.833		1.06 (1.01, 1.12)	0.012	
Definitely evening	1.38 (1.29, 1.46)	0.0E0		1.37 (1.29, 1.46)	0.0E0		1.34 (1.26, 1.43)	0.0E0		1.25 (1.17, 1.33)	7.0805E-11	

Model 1: adjusted for age and sex.

Model 2: adjusted for confounders in Model 1 + self-reported chronotype (or rs10830963 genotype when investigating the association between self-reported chronotype and T2D).

Model 3: adjusted for confounders in Model 1 + self-reported sleep duration + insomnia.

Model 4: adjusted for confounders in Model 2 + self-reported sleep duration + insomnia + BMI + systolic blood pressure + smoking + alcohol intake frequency + test centre + principal components of ancestry + Townsend index.

Associations between chronotype, *MTNR1B* genotype and risk of type 2 diabetes in UK Biobank

■ X. Tan¹ , D.-M. Ciuculete¹, H.B. Schiöth^{1,2} & C. Benedict¹ 

- Δεν παρατηρήθηκε κάποια σημαντική αλληλεπίδραση
- Ξεχωριστές επιδράσεις γονοτύπου-χρονотύπου

Table 4. (a) Odds ratios and 95% CIs for the association between *MTNR1B* rs10830963 genotype and type 2 diabetes, separated by chronotype. (b) Odds ratios and 95% CIs for the association between chronotype and type 2 diabetes, separated by the *MTNR1B* rs10830963 genotype

	Chronotype			
	Definitely morning	More morning than evening	More evening than morning	Definitely evening
rs10830963 genotype	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
(a)				
CC (reference group)	1	1	1	1
CG	1.17 (1.08, 1.25)	1.11 (1.04, 1.18)	1.05 (0.98, 1.12)	1.11 (0.97, 1.27)
GG	1.25 (1.10, 1.42)	1.24 (1.10, 1.39)	1.20 (1.06, 1.35)	1.10 (0.87, 1.39)

Chronotype	rs10830963 genotype		
	CC	CG	GG
	OR (95% CI)	OR (95% CI)	OR (95% CI)
(b)			
Definitely morning (reference group)	1	1	1
More morning than evening	0.98 (0.92, 1.05)	0.93 (0.86, 1.00)	0.99 (0.84, 1.17)
More evening than morning	1.11 (1.03, 1.19)	1.01 (0.93, 1.08)	1.10 (0.93, 1.29)
Definitely evening	1.27 (1.16, 1.40)	1.23 (1.10, 1.38)	1.16 (0.90, 1.49)

Logistic regression analysis adjusted for age, sex, self-reported sleep duration, insomnia, BMI, systolic blood pressure, smoking, alcohol intake frequency, test centre, principal components of ancestry and Townsend index.

Assessment of *MTNR1B* Type 2 Diabetes Genetic Risk Modification by Shift Work and Morningness-Eveningness Preference in the UK Biobank

Hassan S. Dashti,^{1,2,3} Céline Vetter,^{2,4} Jacqueline M. Lane,^{1,2,3} Matt C. Smith,⁵ Andrew R. Wood,⁵ Michael N. Weedon,⁵ Martin K. Rutter,^{6,7} Marta Garaulet,^{8,9} Frank A.J.L. Scheer,^{10,11} and Richa Saxena^{1,2,3}

- Ο χρονότυπος και οι βάρδιες εργασίας συσχετίστηκαν με την παρουσία ΣΔ.

Table 3—Adjusted ORs of type 2 diabetes and adjusted β s of HbA_{1c} with each additional copy of the *MTNR1B* G risk allele across categories of current work schedule

	Type 2 diabetes case/control subjects, <i>n/n</i>	Type 2 diabetes		HbA _{1c} (mmol/mol)		
		OR (95% CI)	<i>P</i> _{int}	<i>N</i>	β (95% CI)	<i>P</i> _{int}
Overall (<i>n</i> = 189,488)	5,042/184,446	1.10 (1.05–1.15)	0.15	175,156	0.26 (0.23–0.28)	0.25
Day workers	4,047/154,792	1.09 (1.03–1.14)		146,993	0.25 (0.22–0.28)	
Shift work without nights	475/14,863	1.24 (1.07–1.43)		14,110	0.32 (0.22–0.41)	
Sometimes night shift work	284/8,434	0.99 (0.82–1.20)		8,005	0.36 (0.24–0.48)	
Usual night shift work	80/2,171	0.85 (0.58–1.25)		2,069	0.20 (–0.04 to 0.45)	
Always night shift work	156/4,186	1.28 (0.99–1.65)		3,979	0.19 (0.02–0.37)	

Association results are adjusted ORs (95% CI) of type 2 diabetes per each additional copy of the *MTNR1B* G risk allele or adjusted β s (95% CI) describing differences in HbA_{1c} in mmol/mol per each additional copy of the *MTNR1B* G risk allele across categories of current work schedule. Association analyses are adjusted for age, sex, BMI, genotyping array, and 10 principal components of ancestry. *P*_{int} is log likelihood ratio test comparing models with and without cross-product interaction terms (*MTNR1B* and current work schedule) including main effect terms in logistic or linear regression models adjusted for the aforementioned covariates.

Assessment of *MTNR1B* Type 2 Diabetes Genetic Risk Modification by Shift Work and Morningness-Eveningness Preference in the UK Biobank

Hassan S. Dashti,^{1,2,3} Céline Vetter,^{2,4} Jacqueline M. Lane,^{1,2,3} Matt C. Smith,⁵ Andrew R. Wood,⁵ Michael N. Weedon,⁵ Martin K. Rutter,^{6,7} Marta Garaulet,^{8,9} Frank A.J.L. Scheer,^{10,11} and Richa Saxena^{1,2,3}

- Κατανάλωση πρωινού;
- Έκθεση στο φως;

Table 4—Adjusted ORs of type 2 diabetes and adjusted β s of HbA_{1c} with each additional copy of the *MTNR1B* G risk allele across categories of morningness-eveningness preference

	Type 2 diabetes			HbA _{1c} (mmol/mol)		
	Type 2 diabetes case/control subjects, <i>n/n</i>	OR (95% CI)	<i>P_{int}</i>	<i>N</i>	β (95% CI)	<i>P_{int}</i>
Overall (<i>n</i> = 169,926)	4,519/165,407	1.10 (1.04–1.15)	0.044	157,256	0.26 (0.23–0.29)	0.87
Definite morning	1,272/42,097	1.17 (1.07–1.28)		39,976	0.30 (0.25–0.36)	
More morning than evening	1,482/60,064	1.09 (1.00–1.18)		57,127	0.23 (0.19–0.28)	
More evening than morning	1,268/48,593	1.06 (0.97–1.16)		46,267	0.23 (0.18–0.28)	
Definite evening	497/14,653	1.02 (0.88–1.18)		13,886	0.36 (0.27–0.45)	

Association results are adjusted ORs (95% CI) of type 2 diabetes per each additional copy of the *MTNR1B* G risk allele or adjusted β s (95% CI) describing differences in HbA_{1c} in mmol/mol per each additional copy of the *MTNR1B* G risk allele across categories of morningness-eveningness preference. Association analyses are adjusted for age, sex, BMI, genotyping array, and 10 principal components of ancestry. *P_{int}* is log likelihood ratio test comparing models with and without cross-product interaction terms (*MTNR1B* and morningness-eveningness preference) including main effect terms in logistic or linear regression models adjusted for the aforementioned covariates.

**Μελέτες αλληλεπιδράσεων γονιδίων –
τρόπου ζωής**

Gene-Lifestyle Interaction and Type 2 Diabetes: The EPIC InterAct Case-Cohort Study

Claudia Langenberg^{1,2}, Stephen J. Sharp^{1,3}, Paul W. Franks^{2,3,5}, Robert A. Scott¹, Panos Deloukas⁴, Nita G. Forouhi¹, Philippe Froguel¹, Leif C. Groop^{6,7}, Torben Hansen^{8,9}, Luigi Palla¹, Oluf Pedersen^{8,10,11}, Matthias B. Schulze¹², Maria-Jose Tormo^{13,14,15}, Eleanor Wheeler¹², Claudia Agnoli¹⁶, Larraitz Arriola^{16,17,18}, Aurelio Barricarte^{14,19}, Heiner Boeing¹², Geraldine M. Clarke²⁰, Françoise Clavel-Chapelon^{21,22}, Eric J. Duell²³, Guy Fagherazzi^{21,22}, Rudolf Kaaks²⁴, Nicola D. Kerrison¹, Timothy J. Key²⁵, Kay Tee Khaw²⁶, Janine Kröger¹², Martin Lajous^{21,27,28}, Andrew P. Morris²⁰, Carmen Navarro^{13,14,29}, Peter M. Nilsson³, Kim Overvad^{30,31}, Domenico Palli³², Salvatore Panico³³, J. Ramón Quirós³⁴, Olov Rolandsson³, Carlotta Sacerdote^{35,36,37}, Maria-José Sánchez^{14,38}, Nadia Slimani³⁹, Annemieke M. W. Spijkerman⁴⁰, Rosario Tumino^{41,42}, Daphne L. van der A⁴⁰, Yvonne T. van der Schouw⁴³, Inês Barroso^{4,44}, Mark I. McCarthy^{20,45,46}, Elio Riboli⁴⁷, Nicholas J. Wareham¹⁴

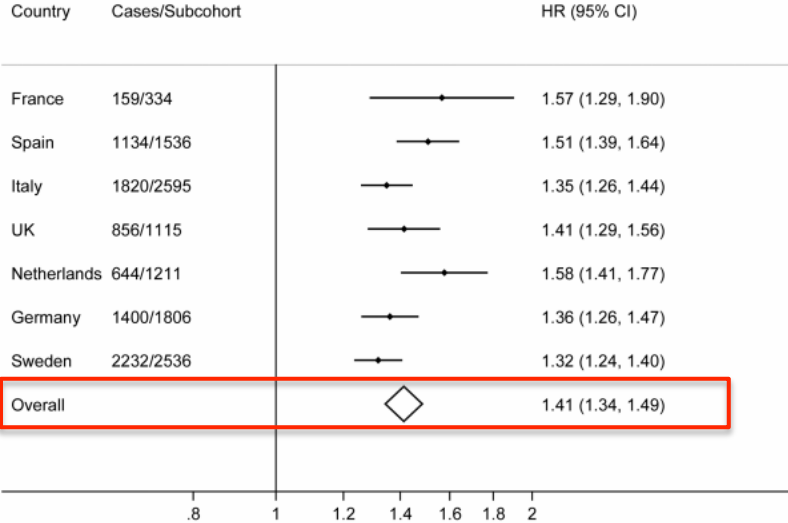


Figure 1. Hazard ratios for type 2 diabetes per standard deviation (4.4 alleles) increase in the imputed, unweighted genetic risk score by country and overall: the InterAct study.

- Προοπτική μελέτη – 4 έτη μ.ο.
- GRS – 49 γενετικοί τόποι

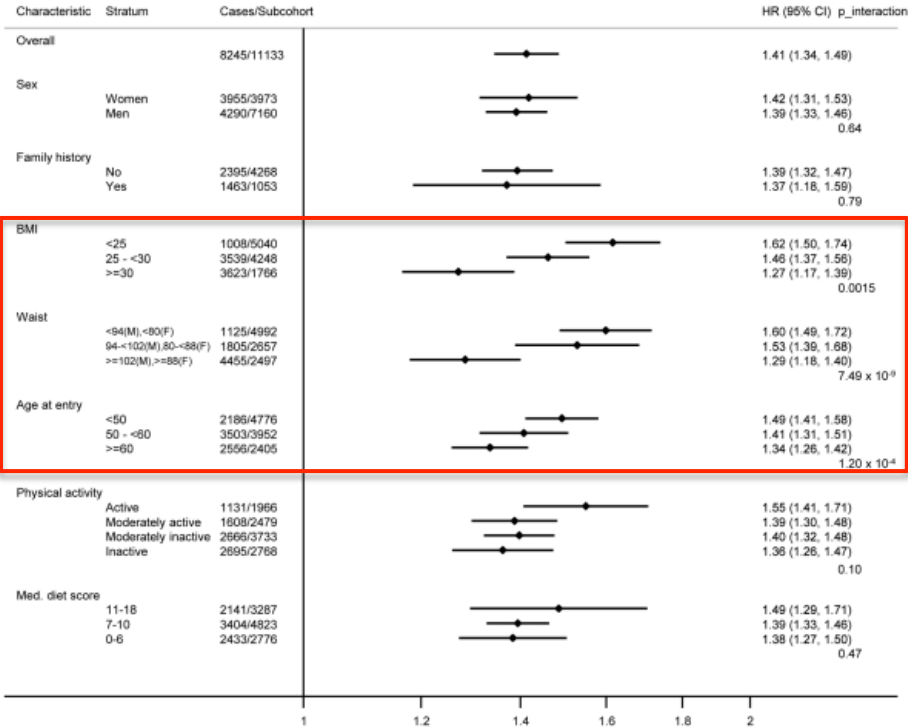


Figure 2. Hazard ratios for type 2 diabetes per standard deviation (4.4 alleles) increase in the imputed, unweighted genetic risk score within strata defined by sex, diabetes family history, body mass index, waist circumference, age, physical activity, and Mediterranean diet score: the InterAct study. Prentice-weighted Cox regression models are adjusted for age, sex, and centre. F, female; M, male; Med., Mediterranean.

Associations of Combined Genetic and Lifestyle Risks With Incident Cardiovascular Disease and Diabetes in the UK Biobank Study

E Type 2 diabetes

