ΔΙΑΤΡΟΦΗ, ΤΡΟΠΟΣ ΖΩΗΣ ΚΑΙ ΓΕΝΕΤΙΚΗ ΠΡΟΔΙΑΘΕΣΗ: ΣΑΚΧΑΡΩΔΗΣ ΔΙΑΒΗΤΗΣ

ΠΡΟΓΡΑΜΜΑ ΜΕΤΑΠΤΥΧΙΑΚΩΝ ΣΠΟΥΔΩΝ
«ΕΦΑΡΜΟΣΜΕΝΗ ΔΙΑΙΤΟΛΟΓΙΑ – ΔΙΑΤΡΟΦΗ»

Δρ Νάνα Καλαφάτη

Διαιτολόγος – Διατροφολόγος

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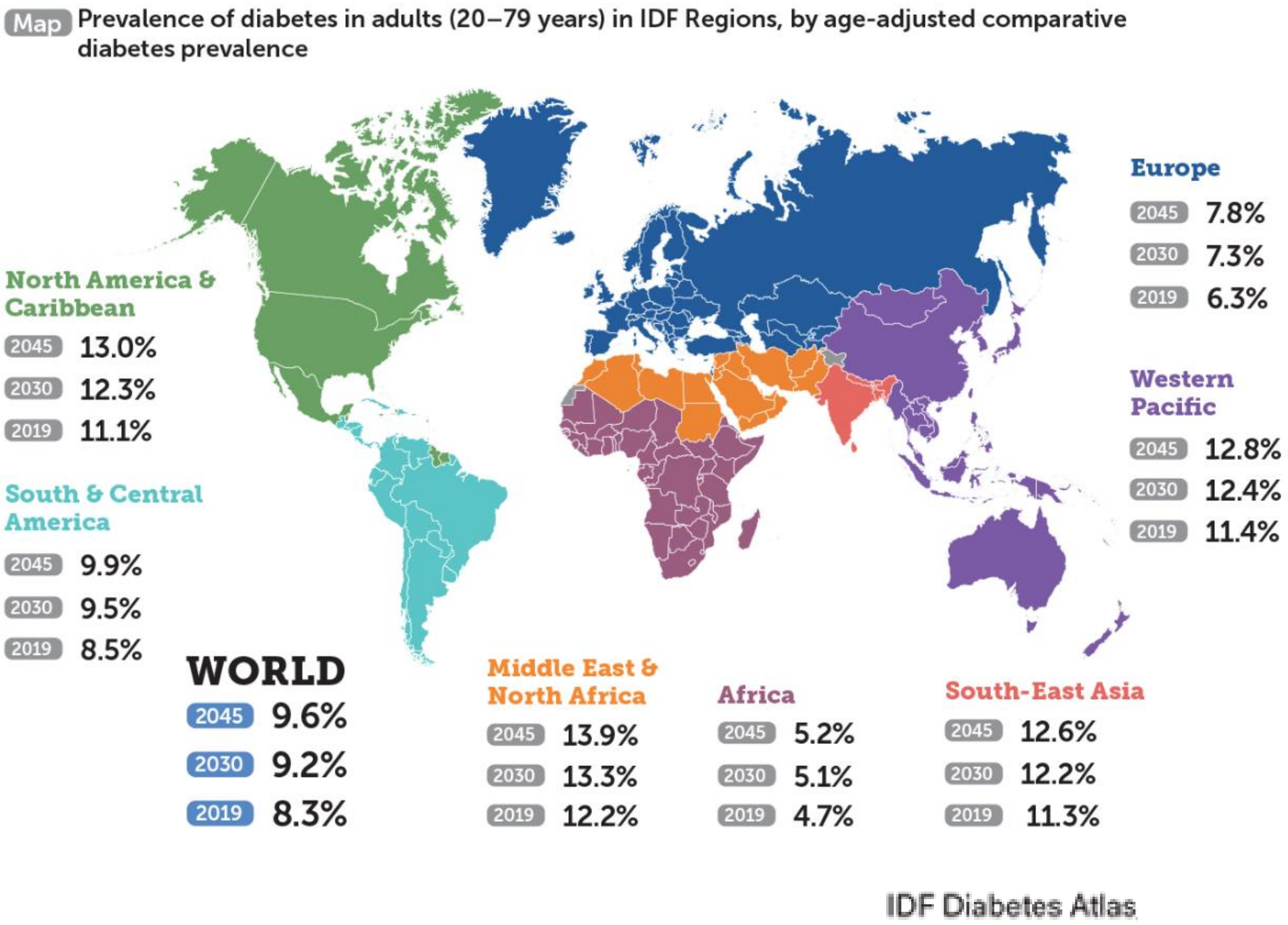
HAROKOPIO UNIVERSITY

Επιπολασμός

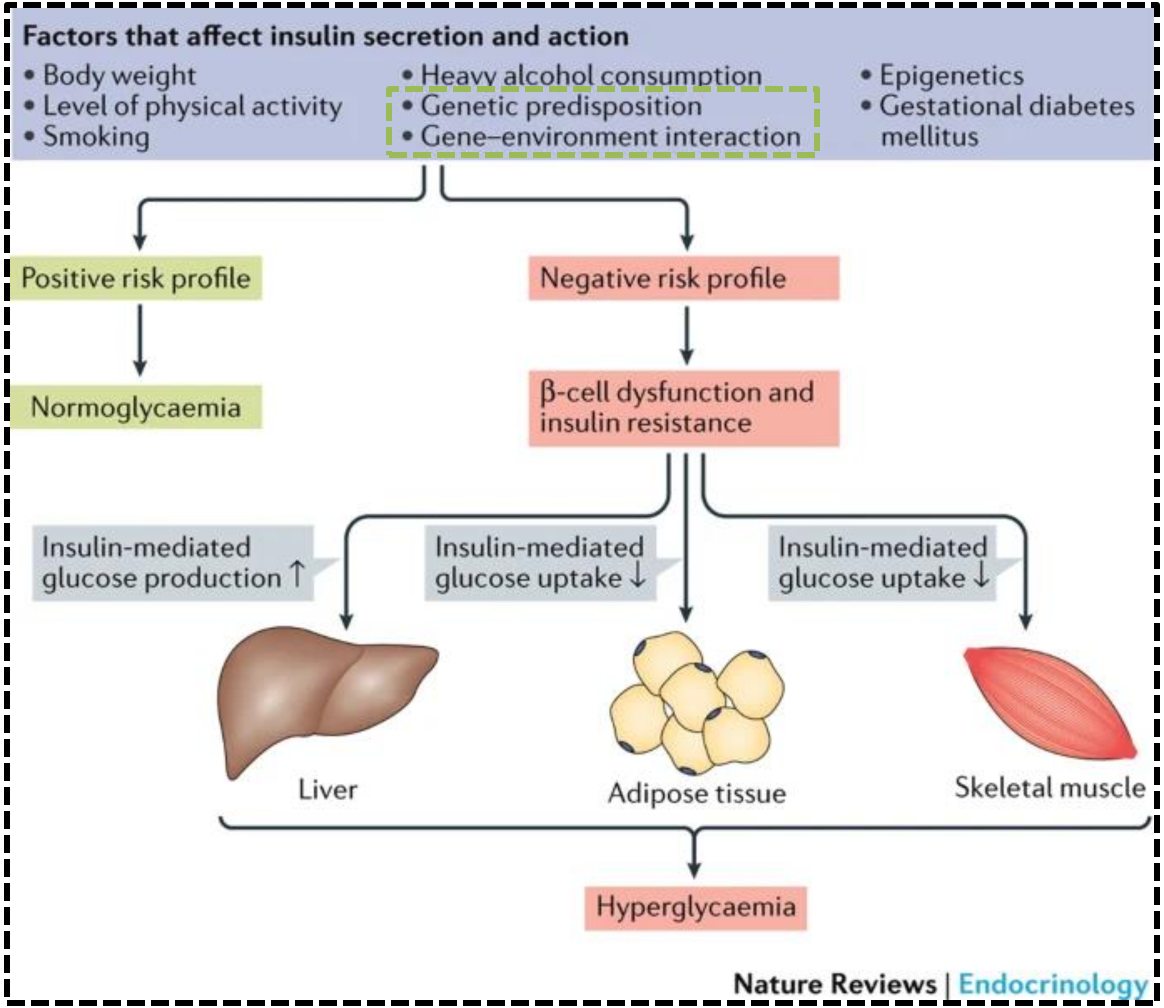
Αναμένεται περαιτέρω αύξηση του παγκόσμιου επιπολασμού της νόσου.

↓

Η ανάγκη εξατομικευμένης θεραπείας είναι πλέον επιτακτική.



Παθοφυσιολογία



**Σημαντικός ο ρόλος των γονιδίων

Zheng 2018

Παράγοντες διατροφής

Διατροφικά πρότυπα

- Μεσογειακή διατροφή
- Δυτικού τύπου
- DASH
- Χαμηλού ΓΔ
- Φυτοφαγική

Ομάδες τροφίμων

- Όσπρια & ξηροί καρποί
- Δημητριακά ολικής αλέσεως
- Κόκκινο κρές
- Φρούτα & λαχανικά
- Καφές & αλκοόλ

Θρεπτικά συστατικά

- Υδατάνθρακες (είδος)
- Λίπος (είδος)
- Mg, vitD, Fe

ΕΝΕΡΓΕΙΑΚΟ ΙΣΟΖΥΓΙΟ

Ley 2014

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

Zheng 2018

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.

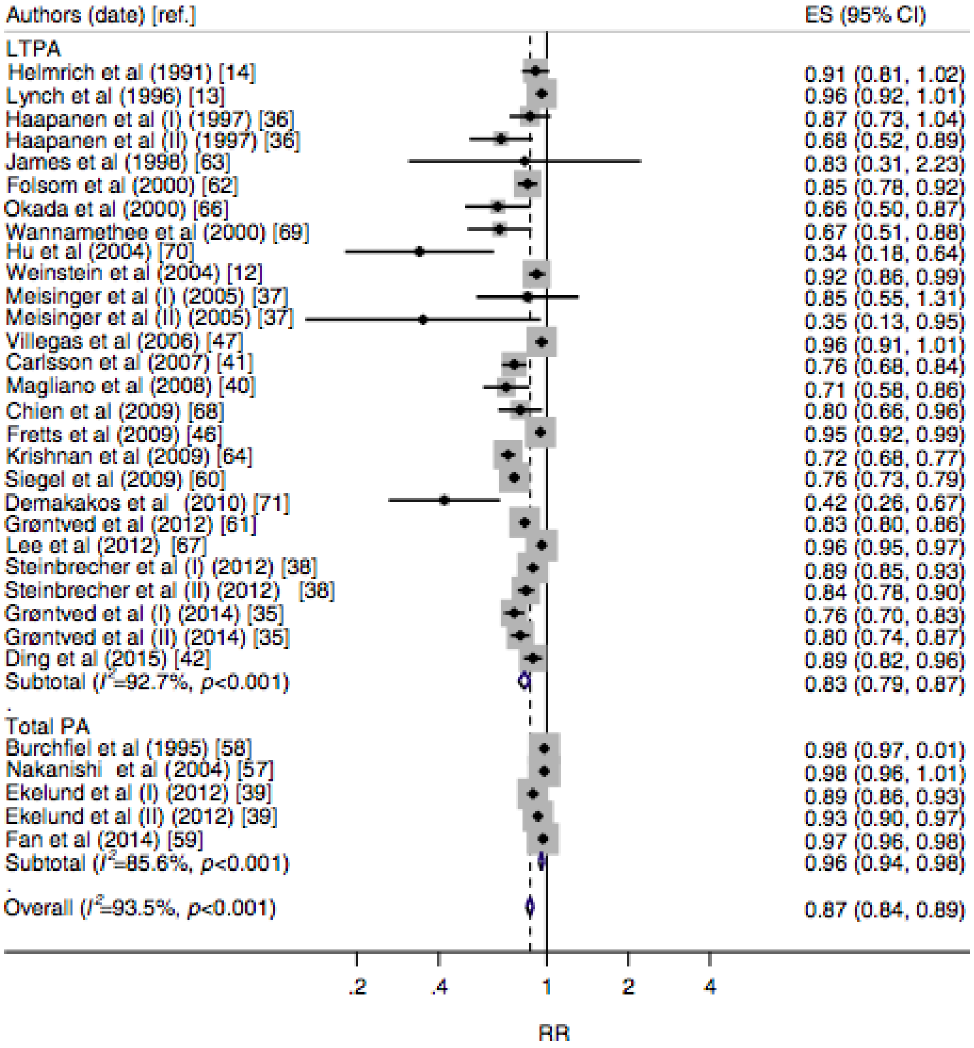
Δραστηριότητες καθιστικές

- 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.

Kolb & Martin, 2017

Φυσική δραστηριότητα



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

Smith A et al, 2016

Φυσική δραστηριότητα

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

	a		b		c		d	
LTPA MET h/week	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)

Smith A et al, 2016

Φυσική δραστηριότητα & Δίαιτα

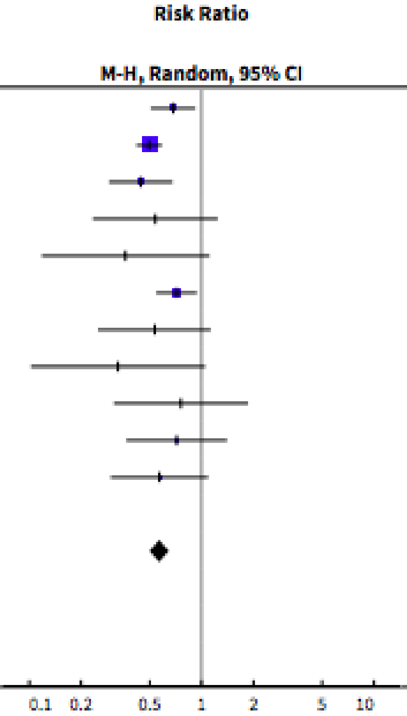
Analysis 2.8. Comparison 2 Diet plus physical activity versus comparator, Outcome 8 Incidence of type 2 diabetes.

Study or subgroup	Diet + physical activity n/N	Comparator n/N	Weight	Risk Ratio M-H, Random, 95% CI
Da Qing 1997	33/72	51/76	16.37%	0.68[0.51,0.92]
DPP 2002	155/1079	313/1082	39.03%	0.5[0.42,0.59]
DPS 2001	27/265	59/257	8.6%	0.44[0.29,0.68]
EDIPS 2009	7/51	13/51	2.31%	0.54[0.23,1.24]
HELP PD 2011	4/151	11/150	1.29%	0.36[0.12,1.11]
IDPP 2006	47/120	73/133	19.13%	0.71[0.54,0.94]
JDPP 2013	9/103	18/110	2.82%	0.53[0.25,1.13]
Kosaka 2005	3/102	32/356	1.2%	0.33[0.1,1.05]
Oldroyd 2005	7/37	8/32	2%	0.76[0.31,1.86]
PODOSA 2014	12/81	17/82	3.52%	0.71[0.36,1.4]
SLIM 2003	11/61	19/60	3.74%	0.57[0.3,1.09]
Total (95% CI)	**2122**	**2389**	**100%**	**0.57[0.5,0.64]**

Total events: 315 (Diet + physical activity), 614 (Comparator)

Heterogeneity: $Tau^2=0$; $Chi^2=10.65$, df=10(P=0.39); $I^2=6.11\%$

Test for overall effect: Z=8.7(P<0.0001)



Diet + physical activity | Comparator

Hemmingsen B et al, Cochrane Database of Systematic Reviews, 2017

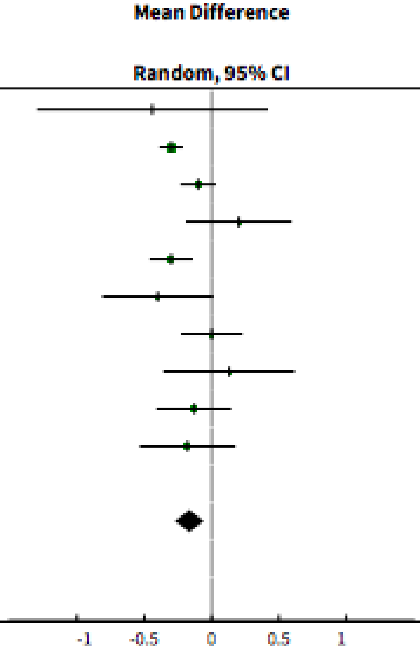
Φυσική δραστηριότητα & Δίαιτα

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

Study or subgroup	Diet + physical activity N	Diet + physical activity Mean(SD)	Comparator N	Comparator Mean(SD)	Weight	Mean Difference Random, 95% CI
Da Qing 1997	72	7.2 (2.7)	76	7.6 (2.6)	1.49%	-0.44[-1.3,0.42]
DPP 2002	915	5.9 (0.8)	935	6.2 (1.1)	21.29%	-0.3[-0.39,-0.21]
DPS 2001	231	0 (0.7)	203	0.1 (0.7)	18.06%	-0.1[-0.23,0.03]
EDIPS 2009	28	5.6 (0.7)	28	5.4 (0.8)	5.75%	0.2[-0.19,0.59]
HELP PD 2011	127	5.7 (0.6)	134	6 (0.7)	16.17%	-0.3[-0.46,-0.14]
IDPP 2006	108	6.1 (1.4)	124	6.5 (1.8)	5.35%	-0.4[-0.81,0.01]
JDPP 2013	103	6 (0.8)	110	6 (0.9)	11.72%	0[-0.23,0.23]
Oldroyd 2005	30	0.3 (0.8)	24	0.1 (1)	4.1%	0.13[-0.36,0.62]
PODOSA 2014	84	5.9 (0.8)	83	6 (1)	9.36%	-0.13[-0.41,0.15]
SLIM 2003	57	6.3 (1.1)	58	6.5 (0.9)	6.71%	-0.18[-0.54,0.18]
Total ***	**1755**		**1775**		**100%**	**-0.17[-0.27,-0.06]**

Heterogeneity: $Tau^2=0.01$; $Chi^2=18.7$, df=9(P=0.03); $I^2=51.86\%$

Test for overall effect: Z=3.02(P=0)



Hemmingsen B et al, Cochrane Database of Systematic Reviews, 2017

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

Kolb & Martin, 2017

RESEARCH ARTICLE

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 Carruba[5], Natasha De Jarnett[1,3], John W. McEvoy[4], 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)

Keith RJ etal, 2016

RESEARCH ARTICLE

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Rachel J. Keith[1,2,3]*, Mahmoud Al Rifai[3,4], Christopher Carruba[5], Natasha De Jarnett[1,3], John W. McEvoy[4], 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)	–

Keith RJ et al, 2016

RESEARCH ARTICLE

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

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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)

Keith RJ et al, 2016

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

Kolb & Martin, 2017, Reutrakul S et al 2013

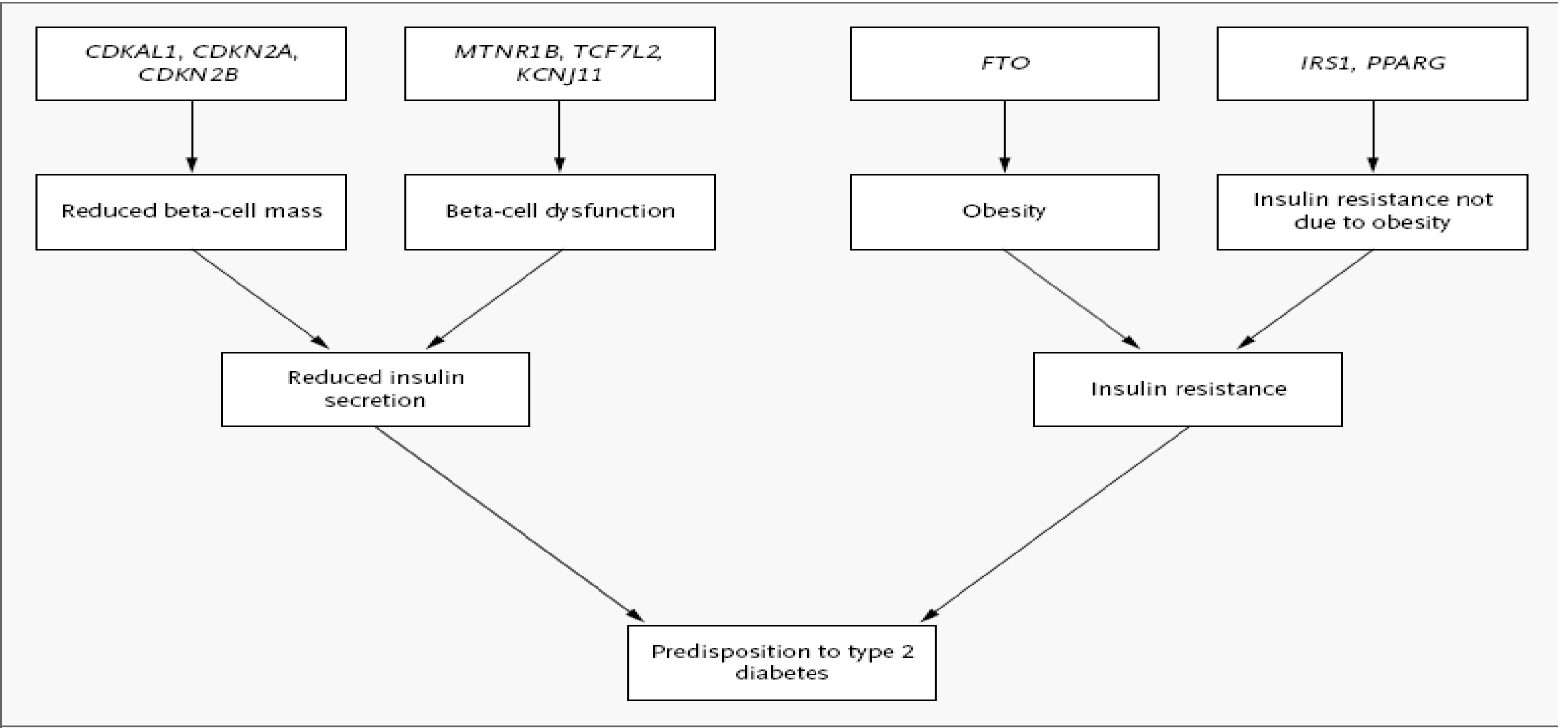


Figure 3. Pathways to Type 2 Diabetes Implicated by Identified Common Variant Associations.
Type 2 diabetes results when pancreatic beta cells are unable to secrete sufficient insulin to maintain normoglycemia, typically in the context of increasing peripheral insulin resistance. The beta-cell abnormalities 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.

Γενετικοί Παράγοντες

McCarthy 2010

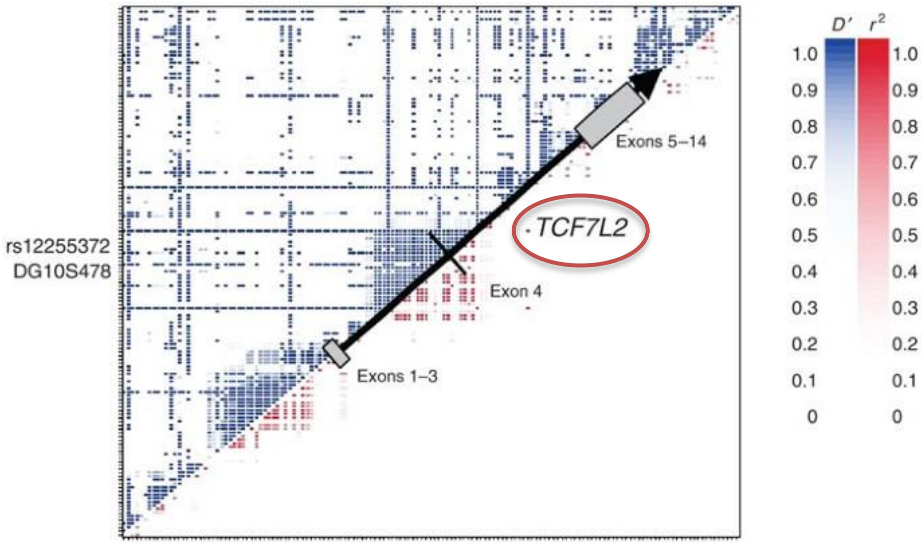
> Nat Genet. 2006 Mar;38(3):320–3. doi: 10.1038/ng1732. Epub 2006 Jan 15.

Variant of transcription factor 7-like 2 (TCF7L2) gen[e] confers risk of type 2 diabetes

Struan F A Grant [1], Gudmar Thorleifsson, Inga Reynisdottir, Rafn Benediktsson, Andrei Manolescu, Jesus Sainz, Agnar Helgason, Hreinn Stefansson, Valur Emilsson, Anna Helgadottir, Unnur Styrkarsdottir, Kristinn P Magnusson, G Bragi Walters, Ebba Palsdottir, Thorbjorg Jonsdottir, Thorunn Gudmundsdottir, Arnaldur Gylfason, Jona Saemundsdottir, Robert L Wilensky, Muredach P Reilly, Daniel J Rader, Yu Bagger, Claus Christiansen, Vilmundur Gudnason, Gunnar Sigurdsson, Unnur Thorsteinsdottir, Jeffrey R Gulcher, Augustine Kong, Kari 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
	20	0.001	0.003	0.39	0.17
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}

Shown 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.
[a]Allelic frequencies, rather than carrier frequencies, are presented in the table. [b]RR calculated assuming a multiplicative model; 95% confidence interval indicated for RR of composite allele X. [c]Two-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**).
[d]Frequency and association for all the alleles of DG10S478 in the Icelandic, Danish and US cohorts are shown separately.
[e]Frequency 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 model[11].



	Genotype relative risk (GRR)[a]			
Cohort	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

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

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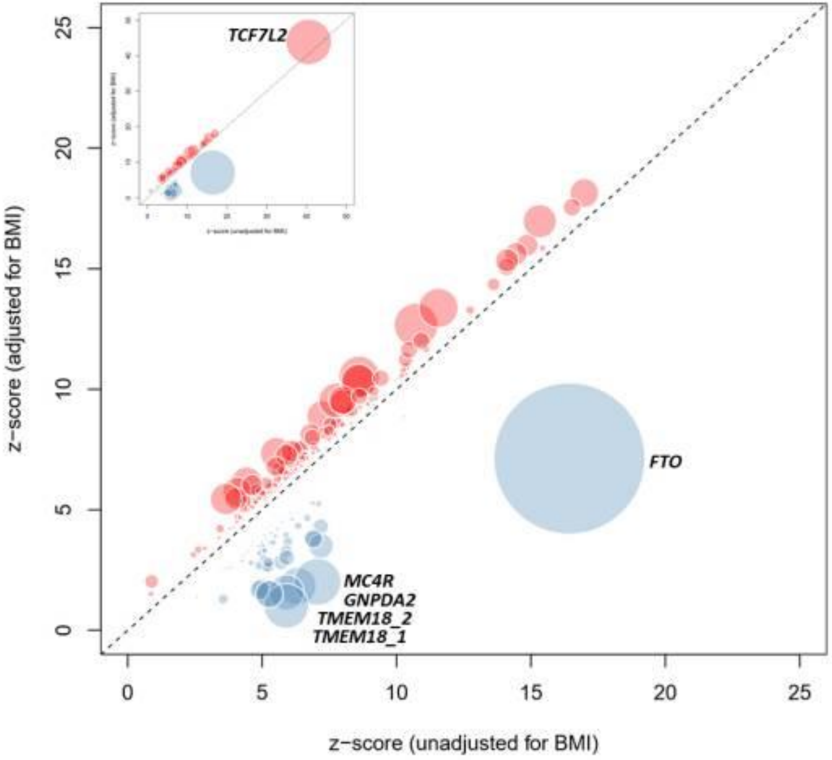
PMCID: PMC6287706
EMSID: EMS80721
PMID: 30297969

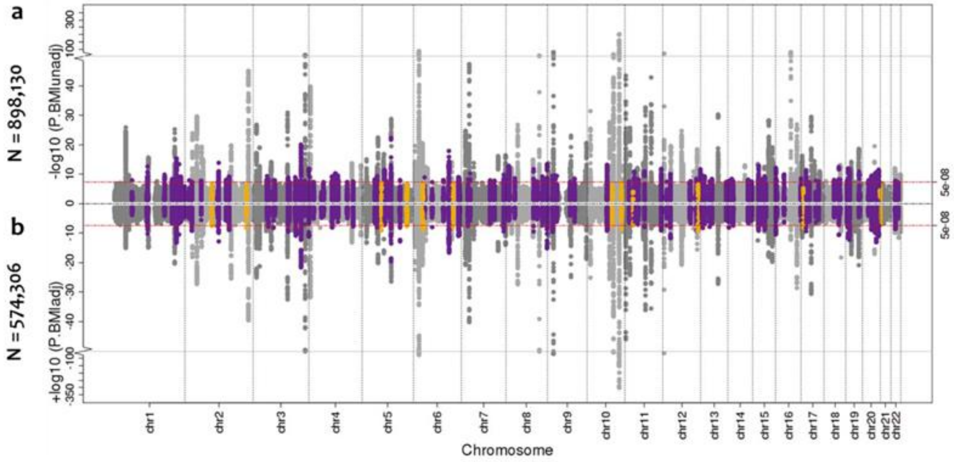
Fine-mapping of an expanded set of type 2 diabetes loci to single-variant resolution using high-density imputation and islet-specific epigenome maps

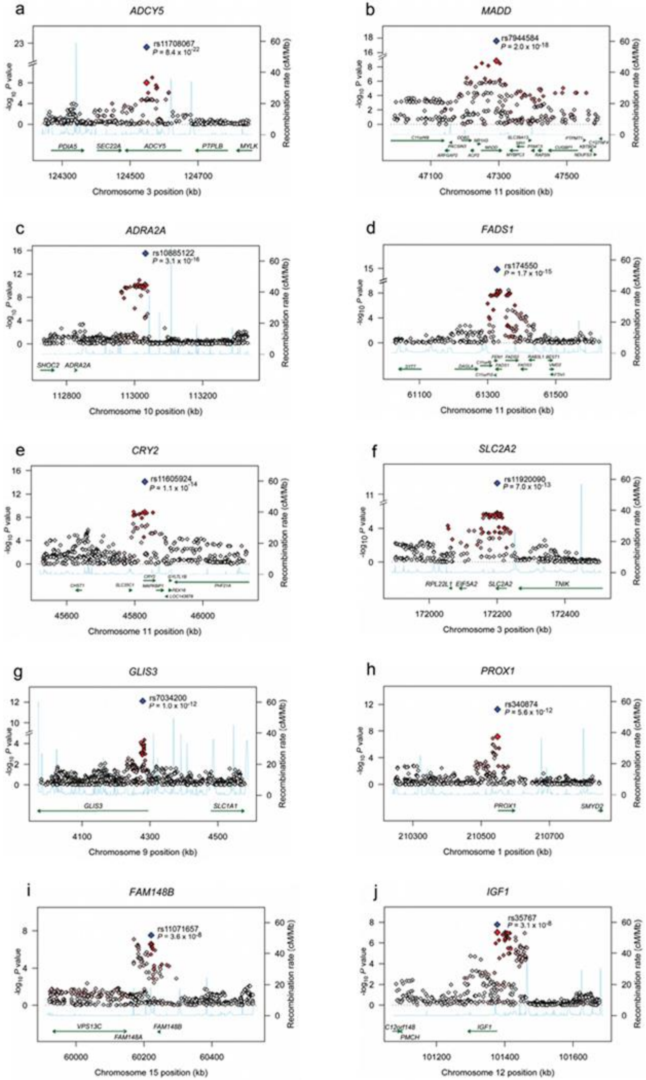
-32 European-descent GWAS – imputed
74124 T2D ασθενείς, 824006 μάρτυρες

-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

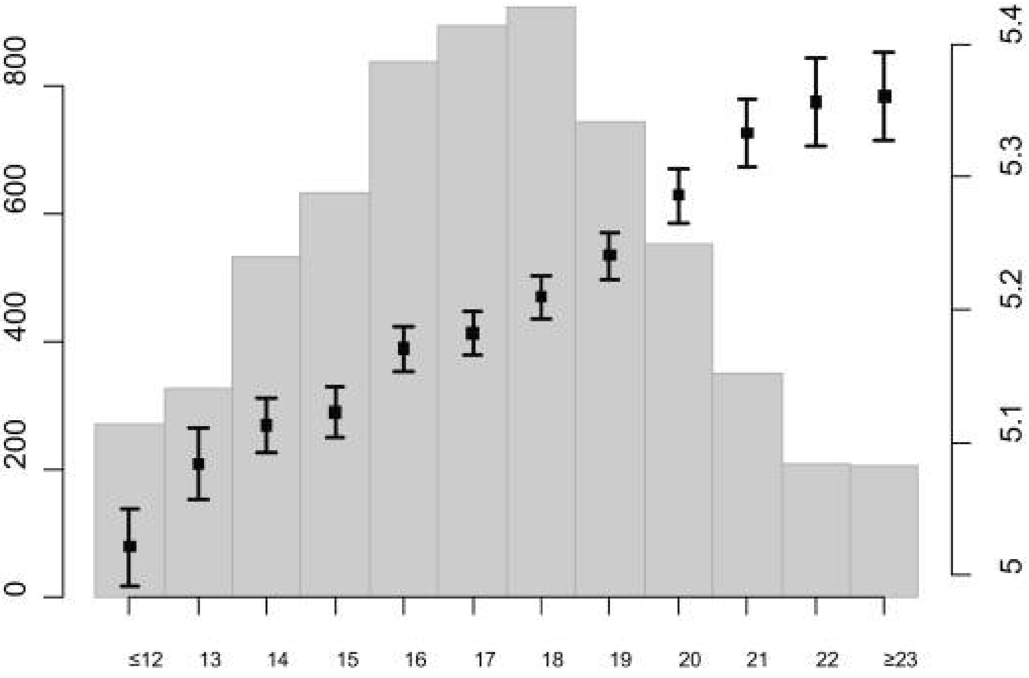






Nat Genet. 2010 February ; 42(2): 105–116. doi:10.1038/ng.520.

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.

nature genetics

LETTERS

https://doi.org/10.1038/s41588-018-0183-z

Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations

Amit V. Khera[1,2,3,4,5], Mark Chaffin[4,5], Krishna G. Aragam[1,2,3,4], Mary E. Haas[4], Carolina Roselli[4], Seung Hoan Choi[4], Pradeep Natarajan[2,3,4], Eric S. Lander[4], Steven A. Lubitz[2,3,4], Patrick T. Ellinor[2,3,4] and Sekar Kathiresan[1,2,3,4*]

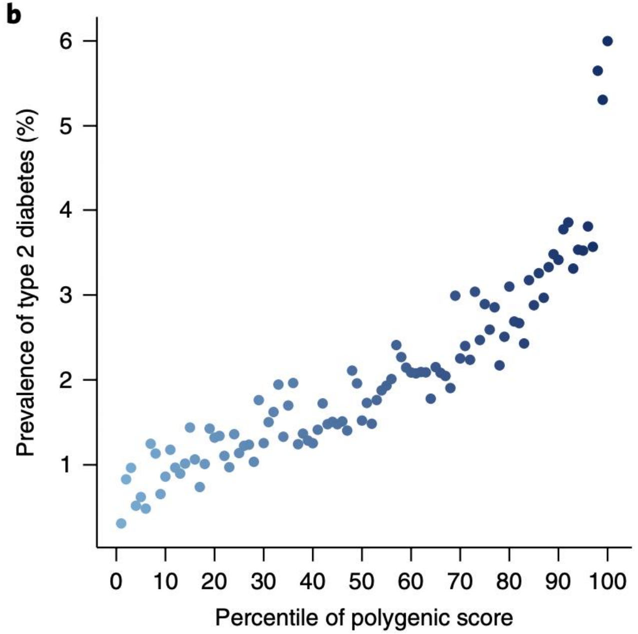


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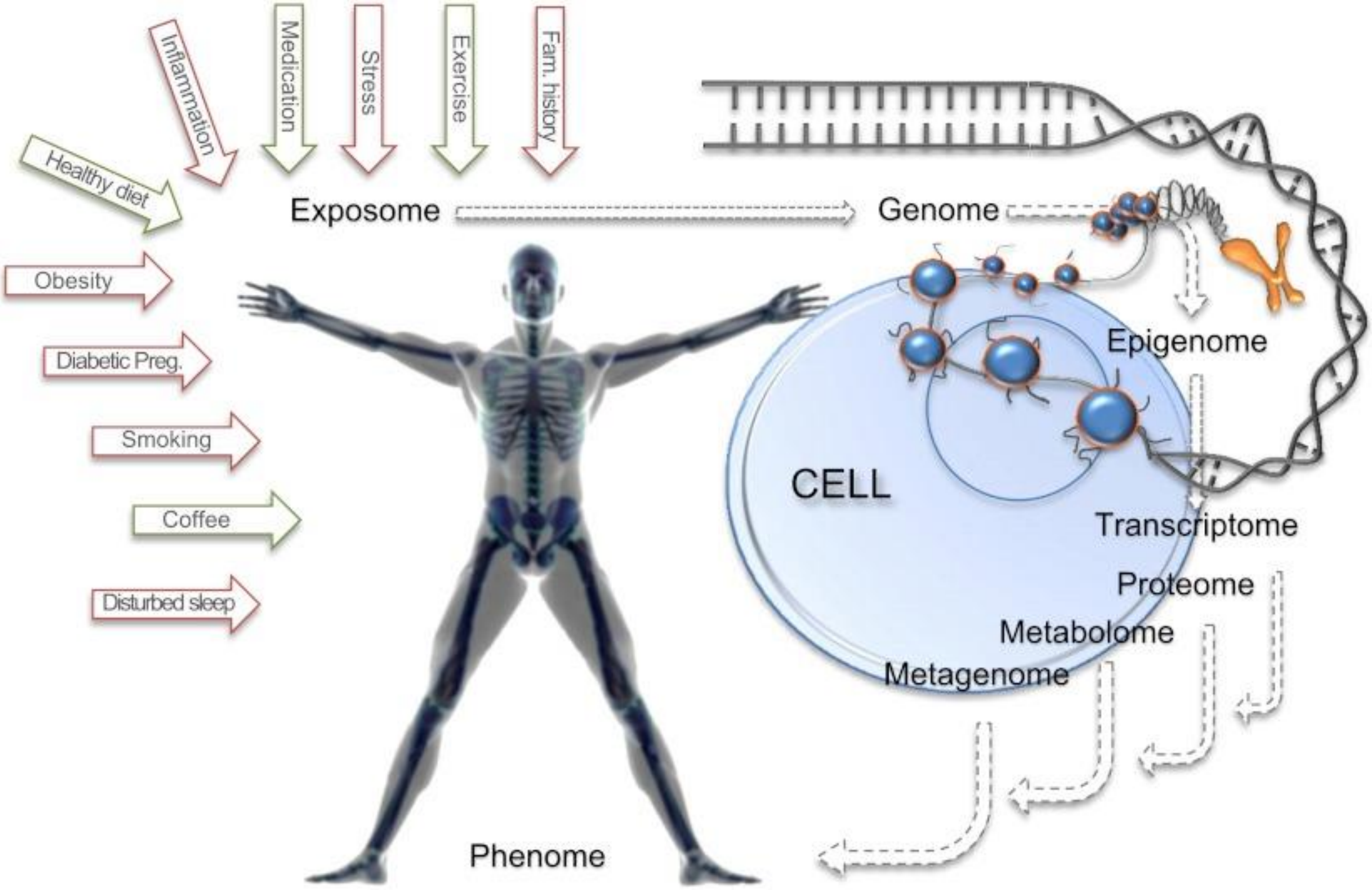
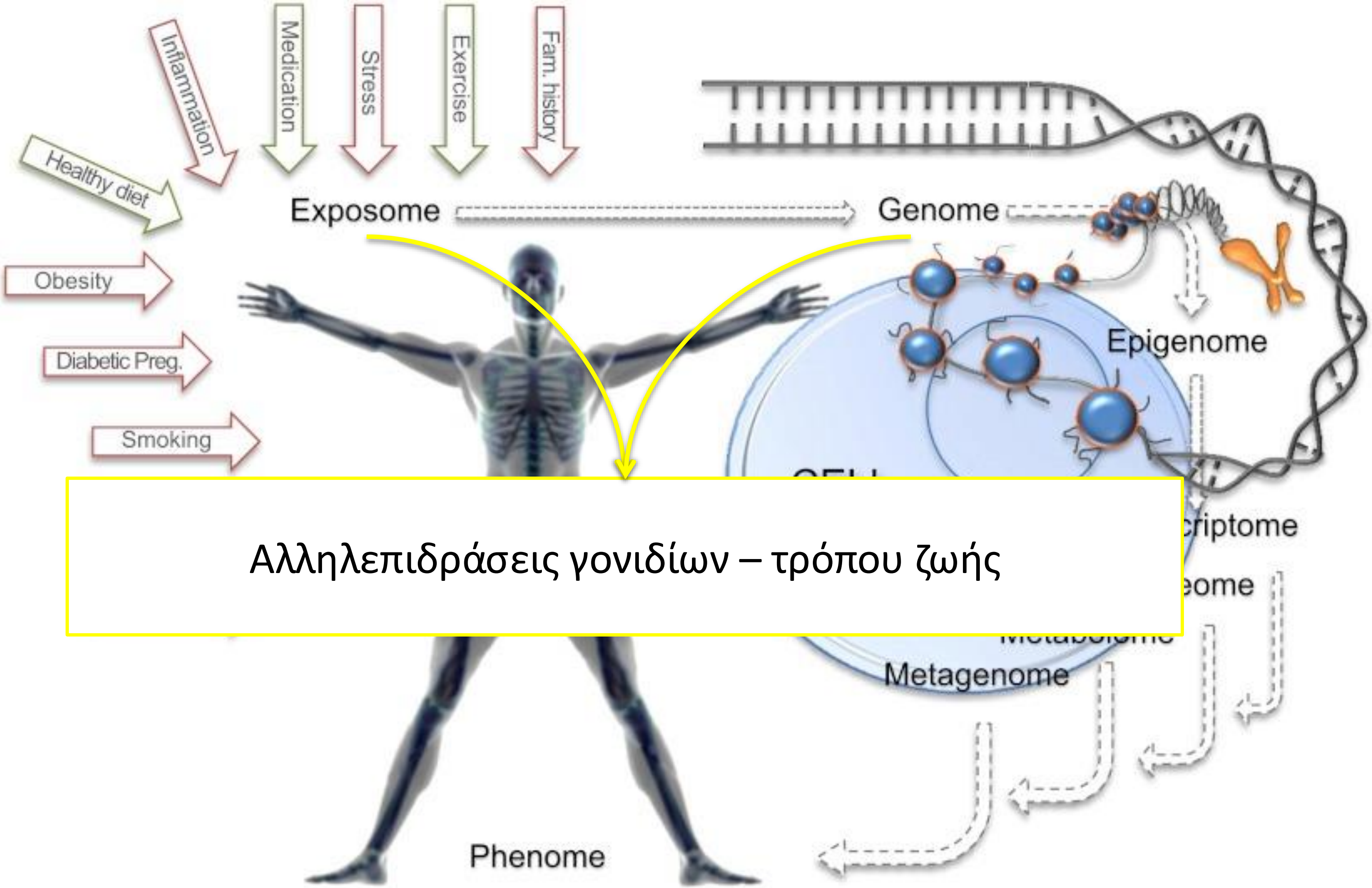
Table 3 | Prevalence and clinical impact of a high GPS

High GPS definition	Reference group	Odds ratio	95% CI	*P* value
CAD				
Top 20% of distribution	Remaining 80%	2.55	2.43–2.67	$<1\times10^{-300}$
Top 10% of distribution	Remaining 90%	2.89	2.74–3.05	$<1\times10^{-300}$
Top 5% of distribution	Remaining 95%	3.34	3.12–3.58	6.5×10^{-264}
Top 1% of distribution	Remaining 99%	4.83	4.25–5.46	1.0×10^{-132}
Top 0.5% of distribution	Remaining 99.5%	5.17	4.34–6.12	7.9×10^{-78}
Atrial fibrillation				
Top 20% of distribution	Remaining 80%	2.43	2.29–2.59	2.1×10^{-177}
Top 10% of distribution	Remaining 90%	2.74	2.55–2.94	7.0×10^{-169}
Top 5% of distribution	Remaining 95%	3.22	2.95–3.51	1.1×10^{-152}
Top 1% of distribution	Remaining 99%	4.63	3.96–5.39	2.9×10^{-84}
Top 0.5% of distribution	Remaining 99.5%	5.23	[illegible]	3.5×10^{-56}
Type 2 diabetes				
Top 20% of distribution	Remaining 80%	2.33	2.20–2.46	3.1×10^{-201}
Top 10% of distribution	Remaining 90%	2.49	2.34–2.66	1.2×10^{-167}
Top 5% of distribution	Remaining 95%	2.75	2.53–2.98	1.7×10^{-130}
Top 1% of distribution	Remaining 99%	3.30	2.81–3.85	1.4×10^{-49}
Top 0.5% of distribution	Remaining 99.5%	3.48	2.79–4.29	4.3×10^{-30}



Inflammation
Medication
Stress
Exercise
Fam. history
Healthy diet
Exposome
Genome
Obesity
Diabetic Preg.
Smoking
Coffee
Disturbed sleep
Epigenome
CELL
Transcriptome
Proteome
Metabolome
Metagenome
Phenome

Αλληλεπιδράσεις γονιδίων – τρόπου ζωής



ΜΕΛΕΤΕΣ ΑΛΛΗΛΕΠΙΔΡΆΣΕΩΝ ΓΟΝΙΔΊΩΝ - ΔΙΑΤΡΟΦΉΣ

-Συγκεντρωτικός πίνακας μελετών αλληλεπιδράσεων ΓxΔ 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	Polyunsaturated 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 (red)	1 (red)				1 (red)				2 (orange)	2 (orange)	2 (green)	1 (red)	1 (red)	1 (red)															
	rs4506565	(20)											1 (green)	1 (green)																		
	rs12255372	(14, 22-24)						1 (red)		2 (orange)	1* (green)	1 (green)	2 (red)		1* (green)	1 (red)	1 (red)															
PPARG	rs1801282	(22, 25, 29, 32)		2* (orange)	1 (red)	1 (red)	1 (red)					1 (red)			1 (red)																	
	rs3856806	(25)		1* (green)																												
NOTCH2	rs10923931	(22)										1 (green)																				
ZBED3	rs4457053	(22)										1 (green)																				
GIPR	rs10423928	(14, 24, 27)	1 (red)	2 (orange)				2 (orange)	1 (red)			1 (red)	1 (red)		1 (red)	1* (green)	1 (red)															
IRS1	rs2943641	(26)	1 (red)	1 (green)				1 (green)				1 (red)																				
FFAR4	p.R270H	(28)		1 (green)																												
CAV2	rs2270188	(14, 29)		2 (orange)	2 (orange)	1 (red)	1 (red)																									
LCT	rs4988235	(31)																1 (green)														
IGF2BP2	rs4402960	(32)													1 (green)																	
CDKAL1	rs7754840	(32)													1 (green)																	
	rs9465871	(69)																										1 (red)				
KCNJ11	rs5215	(32)													1* (green)																	
ADH1C	*1/*2	(34)																			1 (green)											
HFE	rs1799945	(38, 40)																											2 (orange)			
	rs1800562	(38, 40)																											2 (orange)			
SLC40A1	rs744653	(40)																											1 (green)			
TMPRSS6	rs855791	(38, 40)																											2 (orange)			
SLC30A8	8_118252314	(69)																												1 (green)		
	8_118252435	(69)																												1 (green)		
	rs16889462	(69)																												1 (green)		
	58 SNPs	(43, 69)																												1 (red)		
CLOCK	rs4580704	(53)																				1* (green)										
HHEX	rs1111875	(22)										1 (red)																				
HNF1A	rs7957197	(22)										1 (red)																				
TLE4	rs13292136	(22)										1 (red)																				
KCNQ1	rs163171	(24)											1 (red)		1 (red)	1 (red)	1 (red)															
	rs163184	(24)											1 (red)		1 (red)	1 (red)	1 (red)															
	rs2237892	(24)											1 (red)		1 (red)	1 (red)	1 (red)															
	rs163177	(42)																										1 (red)				
WFS1	rs10010131	(24)											1 (red)		1 (red)	1 (red)	1 (red)															
GCKR	rs780094	(32)													1 (red)																	
JAZF1	rs864745	(32)													1 (red)																	
CDKN2A/B	rs10811661	(32)													1 (red)																	
SPRY2	rs1359790	(32)													1 (red)																	
FTO	rs8050136	(32)													1 (red)																	
HECTD4	2 SNPs	(36)																			1 (red)											
TRPM6	20 SNPs	(37)																									1 (red)					
TRPM7	5 SNPs	(37)																									1 (red)					
TPMRSS6	rs855791	(39, 40)																										1 (red)				
TF	3 SNPs	(39)																										1 (red)				
PCK7	rs236918	(40)																											1 (red)			
JMJD1C	rs10761745	(42)																										1 (red)				
RBP4	rs3758539	(44)																													1 (red)	1 (red)
ADRA2B	12Glu9	(55)																								1 (red)						
ferritin-GRS		(40)																											1 (green)			
IR-GRS		(30)	1 (red)	1 (red)	1 (red)	1 (red)	1 (red)	1 (red)					1 (red)																			
T2D-GRS		(30, 33, 35, 45, 46)	1 (red)	2 (red)	2 (red)	2 (red)	1 (red)	1 (red)					1 (red)						1 (green)	1 (green)	1 (red)	1 (red)	1 (green)	1 (red)	1 (red)				1 (green)			

Dietrich *2019*

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 Health 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 × 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 × 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)
rs35767	*IGF1*	G/A	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	0 (0–57)

*Regression coefficient for interaction between daily servings of whole grains × 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.

Genes Nutr. 2016; 11: 6.
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PMCID: PMC4968454
PMID: 27551309

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

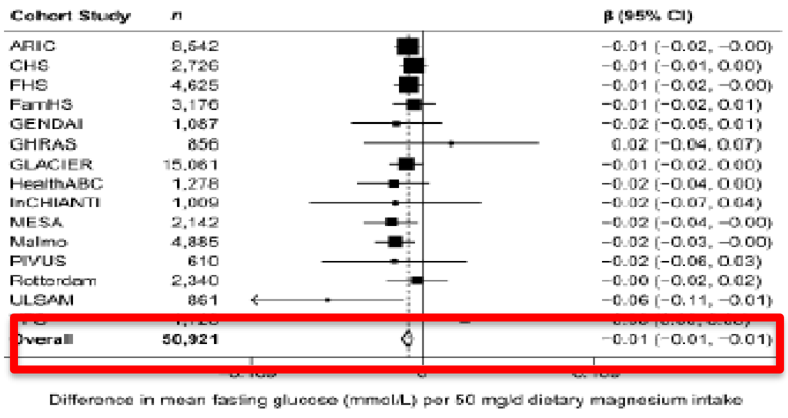
-Μελέτη 8 γονιδίων ως προς primary & secondary outcomes.
-Παρατηρήθηκαν στατιστικά σημαντικές αλληλεπιδράσεις μεταξύ πολυμορφισμών των 3 γονιδίων και της πρόσληψης διαιτητικών ινών.

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

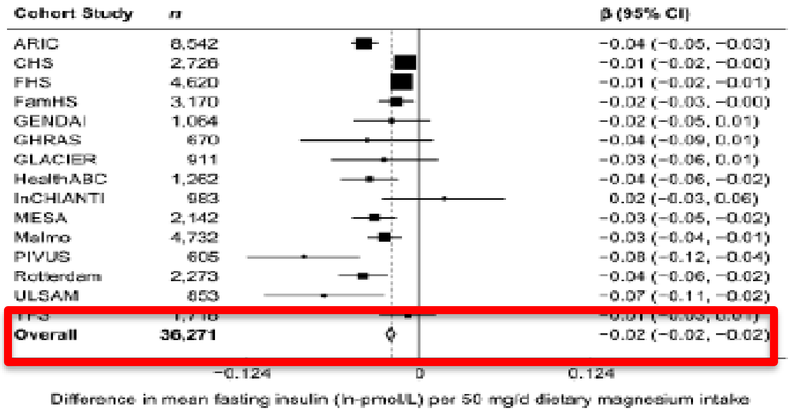
		Genotype					
		XX	XR[a]	RR	HR per R allele	P trend[b]	P interaction[c]
TCF7L2 rs7903146							
	Q1	1.16 (0.98–1.39)	1.58 (1.32–1.89)	1.56 (1.14–2.15)	1.24 (1.09–1.40)	0.001	0.034
	Q2	1.13 (0.95–1.35)	1.52 (1.27–1.82)	1.92 (1.43–2.60)	1.26 (1.11–1.42)	0.0002	
	Q3	1.15 (0.97–1.37)	1.62 (1.36–1.93)	2.10 (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)			
	P trend[c]	0.19	0.64	0.37			
TCF7L2 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)			
	P trend	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			

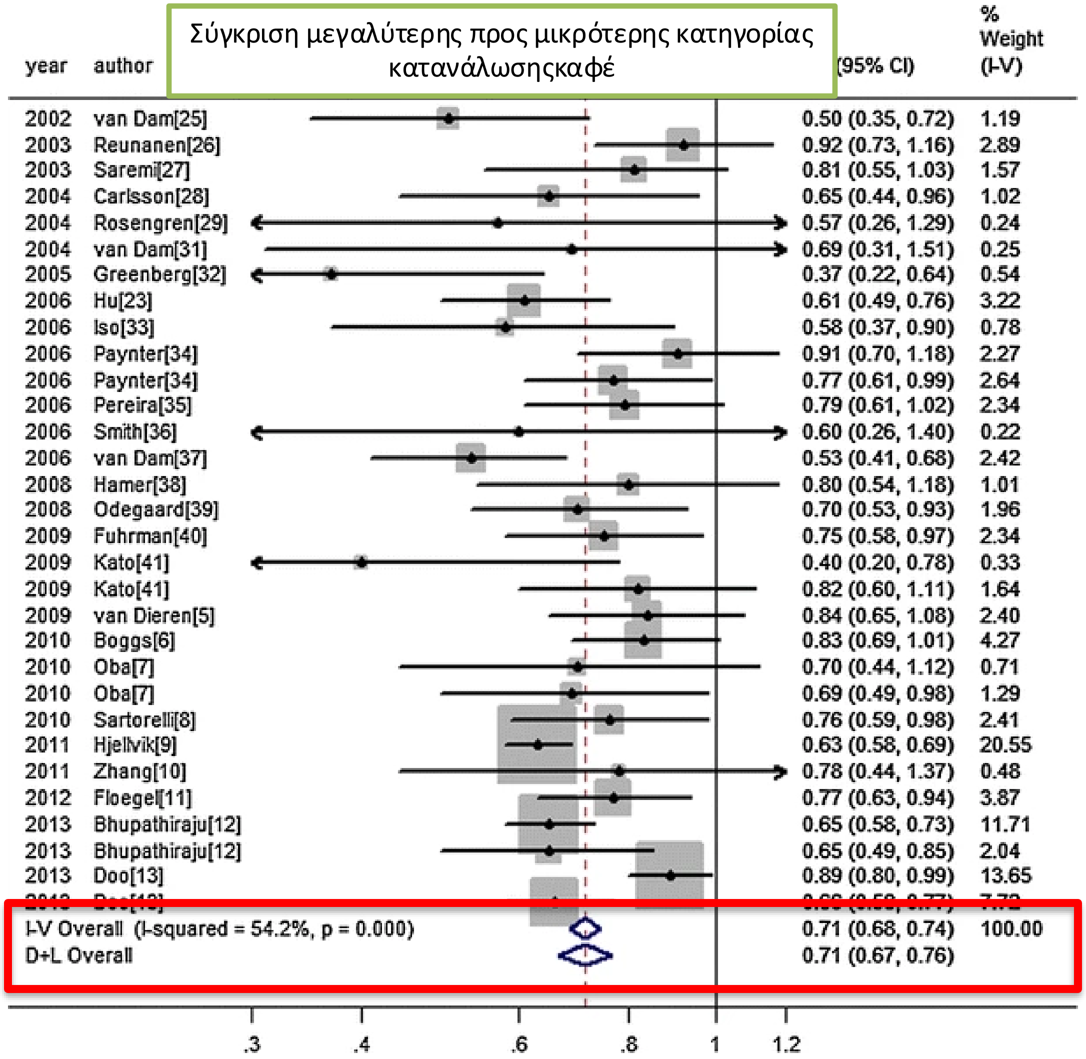
Higher Magnesium Intake Is Associated with Lower Fasting Glucose and Insulin, with No Evidence of Interaction with Select Genetic Loci, in a Meta-Analysis of 15 CHARGE Consortium Studies[1–4]

Adela Hruby,[5] Julius S. Ngwa,[6] Frida Renström,[7–9] 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 I. McCarthy,[31,37] Vera Mikkila,[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,[11] Mika Kähönen,[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,[17, 45] Jacqueline C. M. Witteman,[21, 22] Paul W. Franks,[7–9] James B. Meigs,[46] Nicola M. McKeown,[5*] and Jennifer A. Nettleton[47]



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





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

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Published online 2016 Sep 13. doi: 10.1007/s00125-016-4090-5

PMCID: PMC6518069
PMID: 27623947

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)			p Interaction
TCF7L2 rs12255372 (n cases/n 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) (n cases/n 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 (n cases/n 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) (n cases/n 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 (n cases/n 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) (n cases/n 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 (n cases/n 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) (n cases/n 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 (n cases/n 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) (n cases/n 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 (n cases/n 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) (n cases/n 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 (n cases/n 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) (n cases/n 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]					***p***
	0–3	**4**	**5**	**6**	**7–10**	**Interaction**
n cases/*n* 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
n cases/*n* 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

ORIGINAL ARTICLE

Endocrinology, Diabetes & Metabolism Open Access WILEY

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

Rebeca Eriksen[1] | Rachel Gibson[1,2] | Maria Aresu[3] | Andy Heard[3] | Queenie Chan[3] | Evangelos Evangelou[3] | He Gao[3] | Paul Elliott[3] | Gary Frost[1]

- 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.
[a]Adjusted for body mass index, age and sex.
[b]Adjusted for waist circumference, age and sex.
[c]Adjusted for age, sex, body mass index, smoking, physical activity, diabetes diagnosis and 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)

	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.
[a]Adjusted for age, sex, BMI, smoking, physical activity.
[b]HbA1c > 5.7 ≤ 6.5% and not on glucose lowering medication or previously diagnosed with diabetes.
[c]HbA1c ≥6.5% and/or diagnosed with diabetes and/or glucose-lowering medication.

ORIGINAL ARTICLE

Endocrinology, Diabetes & Metabolism Open Access WILEY

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

Rebeca Eriksen[1] | Rachel Gibson[1,2] | Maria Aresu[3] | Andy Heard[3] | Queenie Chan[3] | Evangelos Evangelou[3] | He Gao[3] | Paul Elliott[3] | Gary Frost[1]

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/m²)	1273	Ref		0.03
BMI (25-29.99 kg/m²)	1741	0.11	−0.01, 1.22	
BMI (>30 kg/m²)	711	1.88	0.41, 3.34	

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

[a]Beta-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.

ORIGINAL ARTICLE

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

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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	95% CI	$P_{interaction}$
DRV score[b]	Ref	−0.01	−0.02, 0.003	−0.01	−0.03, 0.01	0.15
Carbohydrates (per 10 g)	Ref	−0.001	−0.01, 0.005	−0.04	−0.01, 0.002	0.41
Fibre (per 10 g)	Ref	−0.02	−0.1, 0.1	−0.04	−0.1, −0.004	0.71
Fruit, vegetable (per 100 g)	Ref	−0.02	−0.04, −0.01	−0.01	−0.03, 0.01	0.12
Wholegrains (per 100 g)	Ref	−0.1	−0.1, 0.01	−0.07	−0.1, 0.01	0.04
Total fat (per 10 g)	Ref	0.005	−0.01, 0.02	0.01	−0.01, 0.03	0.64
Saturated fat (per 10 g)	Ref	0.01	−0.03, 0.05	0.006	−0.03, 0.05	0.86
Added sugars (per 10 g)	Ref	−0.002	−0.01, 0.009	−0.006	−0.02, 0.01	0.55

Abbreviations: CI, confident interval; DRV, dietary reference value score; GRS, genetic risk score; *P* interaction; *P*-value type III error; β, beta-coefficient.

[a]Estimated 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.

[b]Coefficients represent per 1 point increase in DRV score.

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Cardiovascular Diabetology

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[13], 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[17,18,19]

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

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

	CC (n = 2667)		CG (n = 3415)		GG (n = 1016)		P[1]
Age (years)	**66.9**	**(6.2)**	**67.0**	**(6.2)**	**67.0**	**(6.3)**	**0.961**
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)	239.6	(80.6)	239.5	(81.1)	239.9	(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

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Cardiovascular Diabetology

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[13], 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[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, smoking, 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

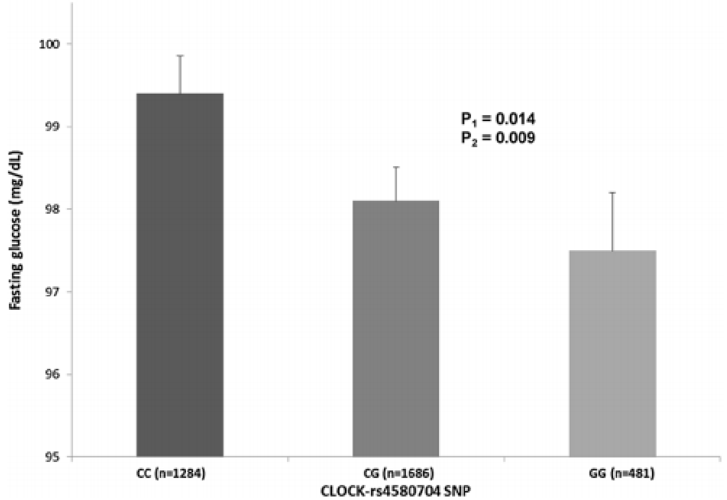

Fig. 1 Association between the CLOCK-rs4580704 SNP and fasting glucose in non-T2D subjects at baseline. Means values and SE of means (*error bars*) are represented depending on the CLOCK genotypes. The P-values for the polymorphism were obtained in the dominant model for G-carriers vs CC subjects. P_1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

Corella et al. Cardiovasc Diabetol (2016) 15:4
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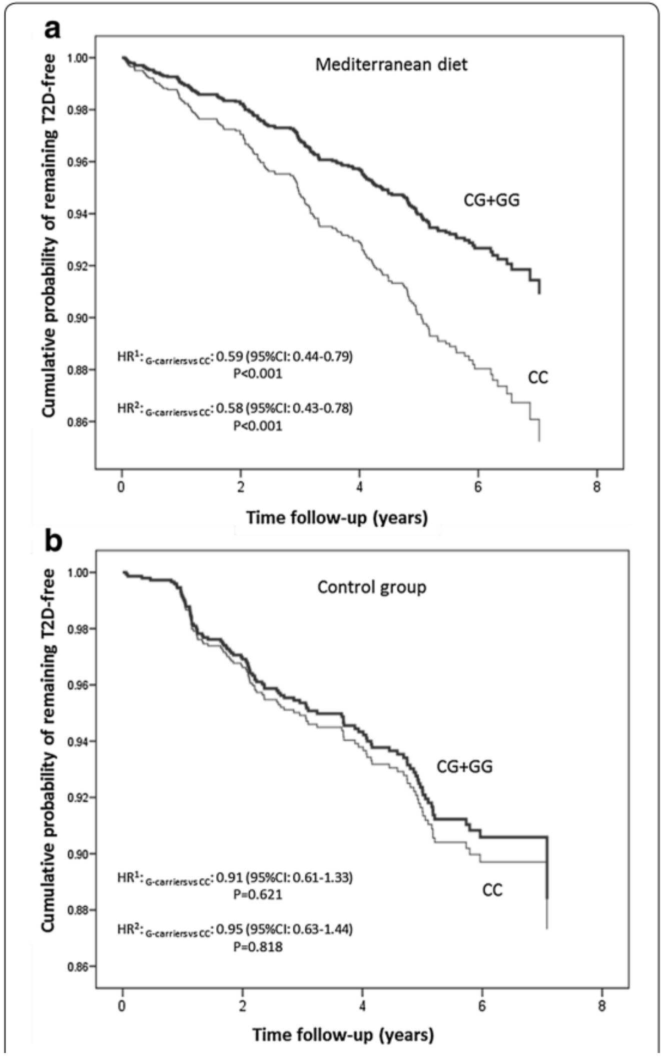


- Στατιστικά σημαντική επίδραση της προσκόλλησης στη Μεσογειακή διατροφή στη σχέση του γονιδίου με την πιθανότητα εμφάνισης ΣΔ2

Genetic predisposition, Western dietary pattern, and the risk of type 2 diabetes in men[1–3]

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 risk[1]

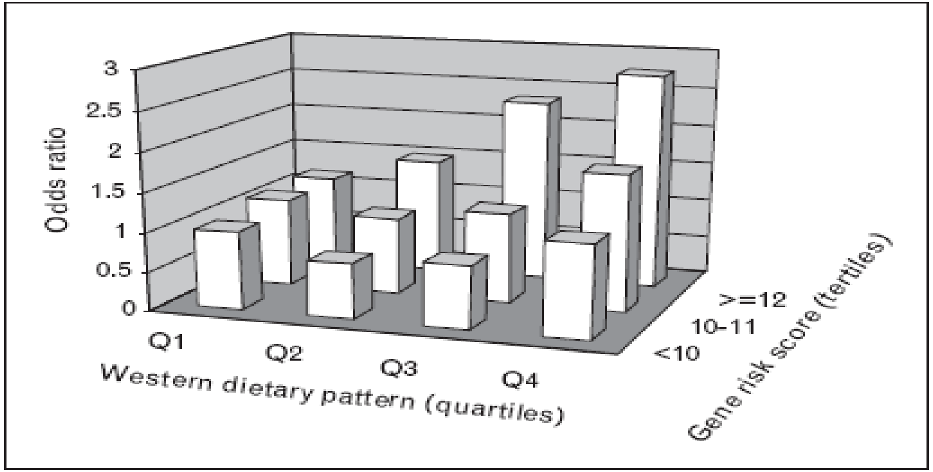
Genetic risk score[2]	Dietary patterns[3] Q1 (lowest)	Q2	Q3	Q4 (highest)	*P* for trend	*P* for interaction
Western dietary pattern						
<10 (*n* = 503)	1	0.79 (0.46, 1.38)	0.81 (0.48, 1.37)	1.07 (0.65, 1.76)	0.69	0.02
10–11 (*n* = 904)	1	0.98 (0.67, 1.44)	1.02 (0.69, 1.49)	1.40 (0.97, 2.01)	0.06	—
≥12 (*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 genomewide association study, including *HHEX* (rs1111875), *CDKAL1* (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-διαβητικοι, Σουηδικής καταγωγής

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

Variable	Physically inactive	Physically active	P
n	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/m²)	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

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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)

	Main effects (OR or β-coefficient) and *P* values (for main effects and interactions)							
	Overall		$P_{interaction}$		Physically inactive		Physically active	
Nearest gene (variant)	IGR risk (OR, *P* value)	2-h glucose (β-coefficient, *P* value)	IGR risk	2-h glucose	IGR risk (OR, *P* value)	2-h glucose (β-coefficient, *P* value)	IGR risk (OR, *P* value)	2-h glucose (β-coefficient, *P* value)
CDKN2A/B (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
HNF1B (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
PPARG (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
SLC30A8 (rs13266634)	1.04, 0.169	0.02, 0.055	0.134	0.560	0.96, 0.540	0.01, 0.798	1.06, 0.055	0.05, 0.047
WFS1 (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
TCF7L2 (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
ADAMTS9 (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
CDKAL1 (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
CAMK1D (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
NOTCH2 (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
KCNJ11 (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
THADA (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
IGFBP2 (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
JAZF1 (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
HHEX (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
MTNR1B (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
TSPAN8 (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]

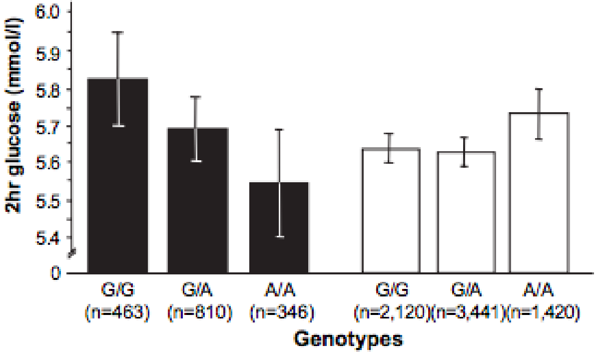
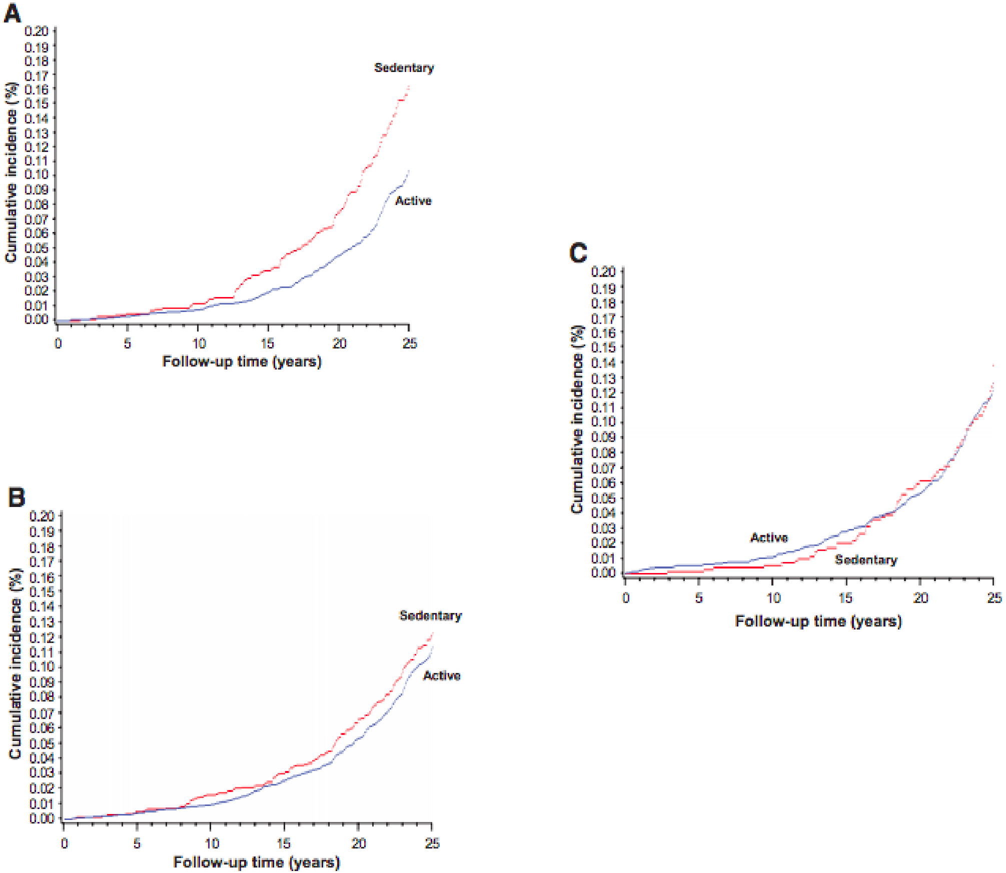


FIG. 1. Interaction between the *HNF1B* rs4430796 variant and physical activity on 2-h glucose levels in 8,600 Swedish middle-aged men and women. ■, physically inactive; □, physically active. Data are means adjusted for age and sex. Error bars are 95% CIs. $P_{interaction} = 0.0009$.



Diabetologia. 2011 June ; 54(6): 1579–1582. doi:10.1007/s00125-011-2123-7.

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 (1.00–1.82)	0.05	1.38 (0.98–1.94)	0.07	1.29 (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

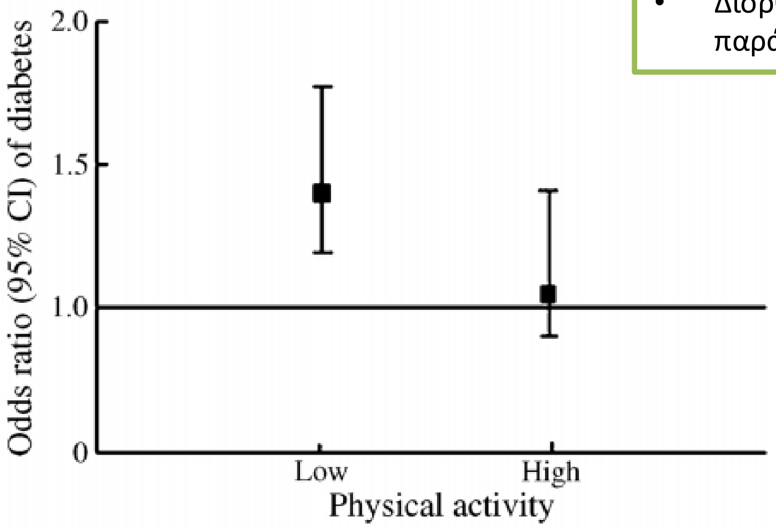
[a] Adjusted for age, BMI (five categories), family history of diabetes (yes, no), smoking (never, past or current), alcohol (five categories), menopausal status (pre- or post-menopausal [never, past or current hormone use]; women only), quintiles of physical activity (MET h/week for men in HPFS, h/week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

Diabetologia. 2011 June ; 54(6): 1579–1582. doi:10.1007/s00125-011-2123-7.

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 κληρονόμησης
- 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

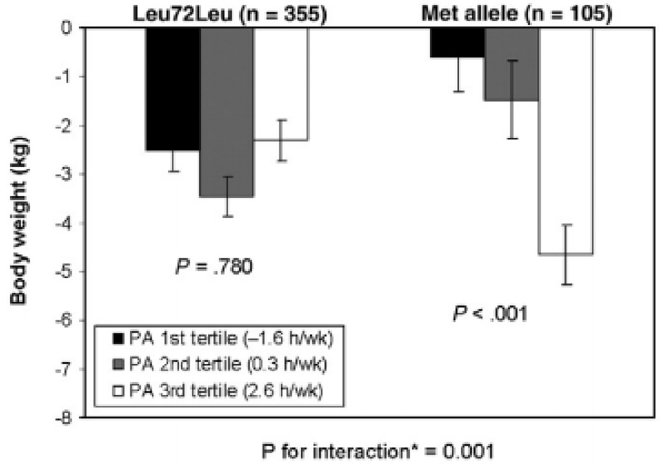
Tuomas O. Kilpeläinen[a,*], Timo A. Lakka[a,b], David E. Laaksonen[a,c], Ursula Mager[d], Titta Salopuro[d], Agata Kubaszek[c], Boryana Todorova[c], Olli Laukkanen[c], Jaana Lindström[e], Johan G. Eriksson[e,f], Helena Hämäläinen[g], Sirkka Aunola[h], Pirjo Ilanne-Parikka[i,j], Sirkka Keinänen-Kiukaanniemi[k,l],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

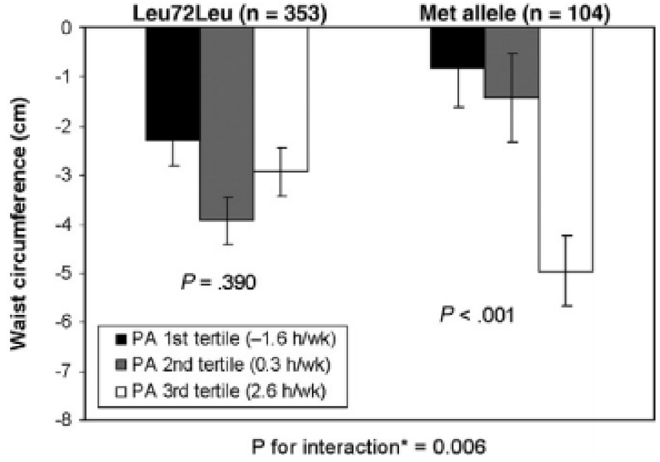
- Finnish DPS
- Παχύσαρκοι με IGT
- Παρακολούθηση για 4,1 έτη

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





- 3 ομάδες ΦΔ
- Αποτελέσματα 1ου έτους παρέμβασης
- Δεν παρατηρήθηκε στατιστικά σημαντική 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

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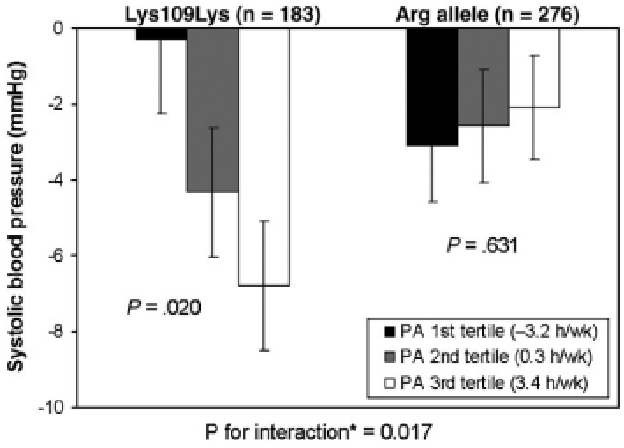
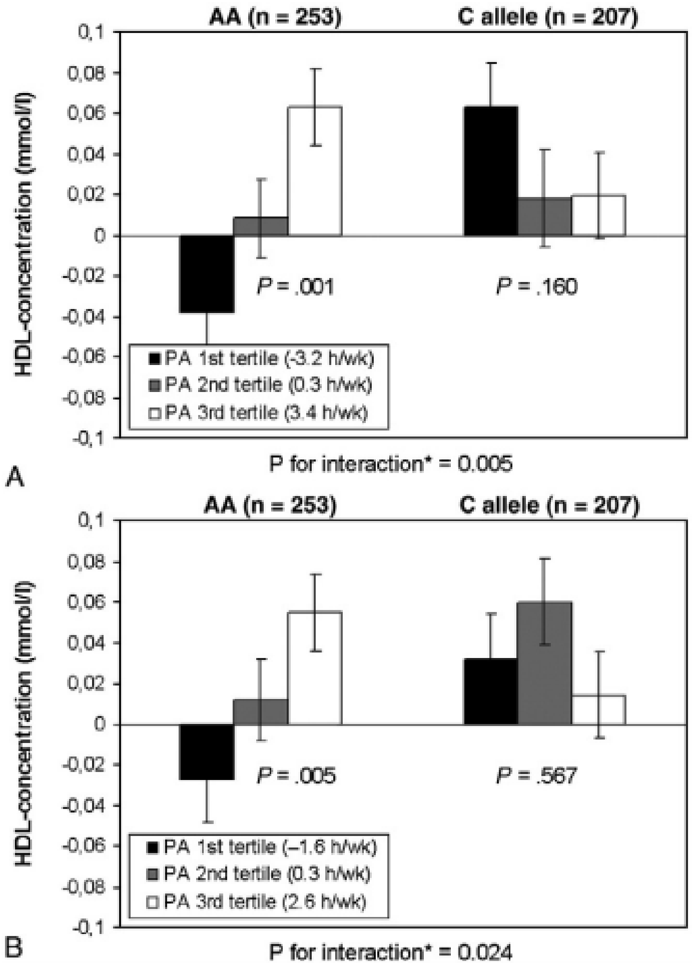


LEPR – change in total PA



GHRL

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

Physiol Genomics 31: 264–272, 2007.
First published July 17, 2007; doi:10.1152/physiolgenomics.00036.2007.

- Finnish DPS
- Υπέρβαροι 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,[3] 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-Kiukaanniemi,[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				
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)	*P* for Difference	*P* for Interaction†
	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	
C allele (*n* = 105)	0.26 (0.05–1.27)	0.43 (0.12–1.53)	1	0.082	0.027
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	
T allele (*n* = 92)	0.21 (0.04–1.19)	0.37 (0.10–1.42)	1	0.064	0.022
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	
T allele (*n* = 123)	0.67 (0.18–2.58)	0.51 (0.17–1.53)	1	0.473	0.057
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	
A allele (*n* = 92)	0.22 (0.04–1.23)	0.37 (0.10–1.40)	1	0.068	0.022
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				
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)	*P* for Trend	*P* for Interaction†
	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	
A allele (*n* = 207)	−0.64±0.20	−0.36±0.20	−0.28±0.19	0.224	0.015
	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	
G allele (*n* = 354)	−0.42±0.16	−0.34±0.15	−0.21±0.15	0.369	0.001
	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	
GG (*n* = 331)	−0.74±0.17	−0.46±0.16	−0.41±0.15	0.158	0.002
	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	
C allele (*n* = 351)	−0.28±0.18	−0.61±0.16	−0.45±0.15	0.502	0.435

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				
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)	*P* for Difference	*P* for Interaction†
	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	
A allele (*n* = 207)	1.04 (0.31–3.46)	2.25 (0.76–6.68)	1	0.972	0.007
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	
G allele (*n* = 356)	1.32 (0.59–2.99)	1.72 (0.83–3.57)	1	0.548	0.128
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	
A allele (*n* = 147)	0.85 (0.39–1.87)	1.61 (0.80–3.25)	1	0.814	0.111
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	
C allele (*n* = 352)	1.28 (0.64–2.57)	1.26 (0.65–2.46)	1	0.498	0.203
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				
	−1.5 (−13.5 to −0.1)	0.5 (−0.1 to 1.3)	2.6 (1.3 to 14.4)	*P* for Trend	*P* for Interaction†
	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	
C allele (*n* = 104)	−0.80±0.29	−1.24±0.23	−0.01±0.27	0.077	0.013
	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	
T allele (*n* = 92)	−0.87±0.31	−1.19±0.24	−0.03±0.28	0.070	0.023
	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	
T allele (*n* = 122)	−0.42±0.27	−1.22±0.21	−0.05±0.25	0.375	0.016
	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	
A allele (*n* = 92)	−0.93±0.31	−1.17±0.24	0.01±0.28	0.048	0.016
	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	
CTTA carriers (*n* = 91)	−0.95±0.31	−1.14±0.25	0.01±0.28	0.043	0.022

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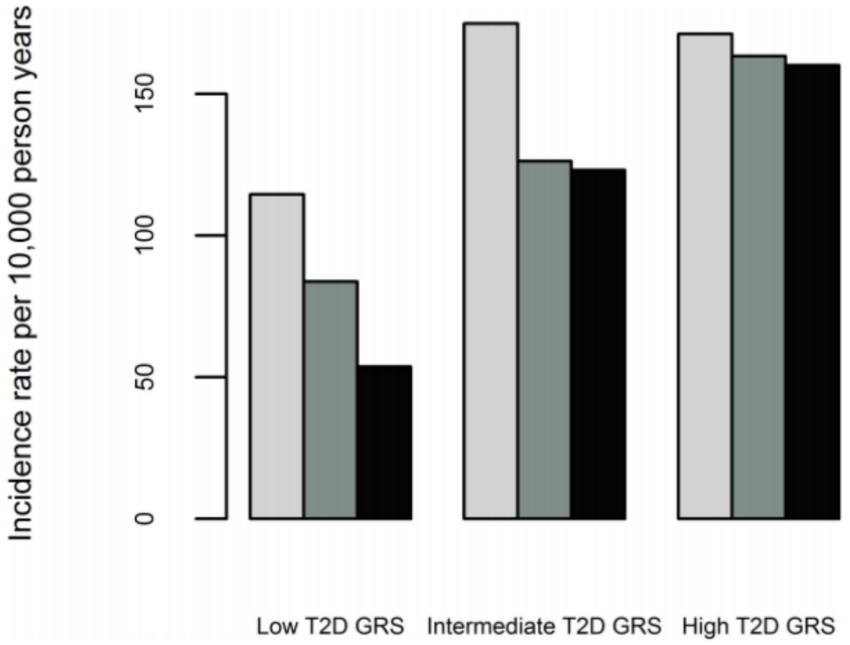
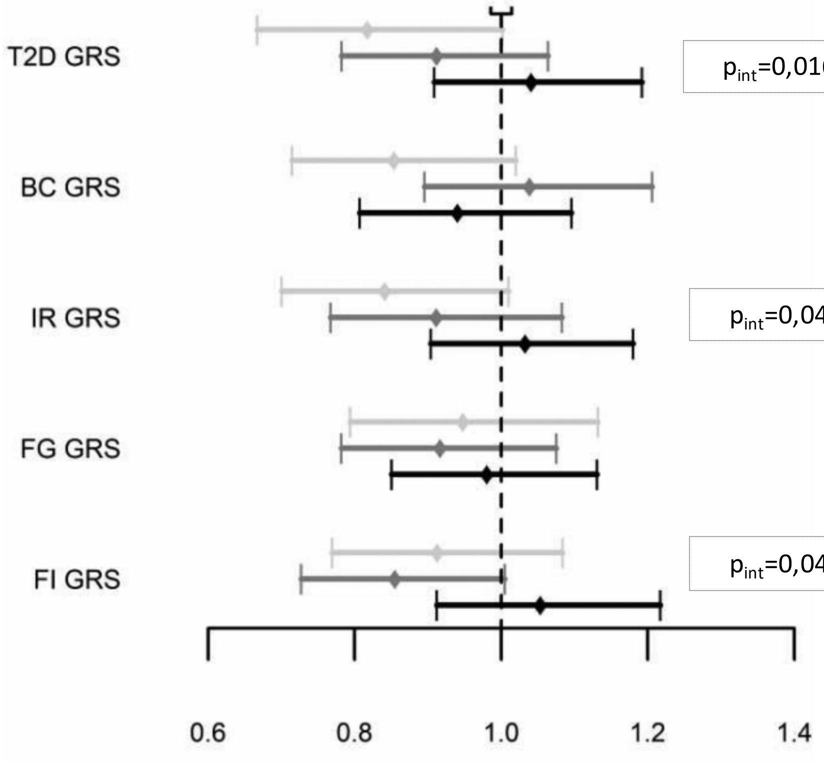
Association of physical activity with lower type 2 diabetes incidence is weaker among individuals at high genetic risk

Yann C. Klimentidis[1,*], Zhao Chen[1], Amit Arora[1], and Chiu-Hsieh Hsu[1]

- 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.





p_{int}=0,016

p_{int}=0,046

p_{int}=0,042

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

- 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. Tan[1], D.-M. Ciuculete[1], H.B. Schiöth[1,2] & C. Benedict[1]

- 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*

	Model 1			Model 2			Model 3			Model 4		
Exposure	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. Tan[1], D.-M. Ciuculete[1], H.B. Schiöth[1,2] & C. Benedict[1]

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

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			
rs10830963 genotype	Definitely morning OR (95% CI)	More morning than evening OR (95% CI)	More evening than morning OR (95% CI)	Definitely evening 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)

	rs10830963 genotype		
Chronotype	CC OR (95% CI)	CG OR (95% CI)	GG 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 βs of HbA_{1c} with each additional copy of the *MTNR1B* G risk allele across categories of current work schedule

	Type 2 diabetes			HbA_{1c} (mmol/mol)		
	Type 2 diabetes case/control subjects, *n/n*	OR (95% CI)	P_{int}	*N*	β (95% CI)	P_{int}
Overall (*n* = 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 βs (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 βs 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, *n*/*n*	OR (95% CI)	P_{int}	*N*	β (95% CI)	P_{int}
Overall (*n* = 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 βs (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 ΓΟΝΙΔΊΙΩΝ – ΤΡΌΠΟΥ ΖΏΗΣ

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

Claudia Langenberg[1¶]*, Stephen J. Sharp[1¶], Paul W. Franks[2,3¶], Robert A. Scott[1], Panos Deloukas[4], Nita G. Forouhi[1], Philippe Froguel[5], Leif C. Groop[6,7], Torben Hansen[8,9], Luigi Palla[1], Oluf Pedersen[8,10,11], Matthias B. Schulze[12], Maria-Jose Tormo[13,14,15], Eleanor Wheeler[4], Claudia Agnoli[16], Larraitz Arriola[14,17,18], Aurelio Barricarte[14,19], Heiner Boeing[12], Geraldine M. Clarke[20], Françoise Clavel-Chapelon[21,22], Eric J. Duell[23], Guy Fagherazzi[21,22], Rudolf Kaaks[24], Nicola D. Kerrison[1], Timothy J. Key[25], Kay Tee Khaw[26], Janine Kröger[12], Martin Lajous[21,27,28], Andrew P. Morris[20], Carmen Navarro[13,14,29], Peter M. Nilsson[2], Kim Overvad[30,31], Domenico Palli[32], Salvatore Panico[33], J. Ramón Quirós[34], Olov Rolandsson[3], Carlotta Sacerdote[35,36,37], María-José Sánchez[14,38], Nadia Slimani[39], Annemieke M. W. Spijkerman[40], Rosario Tumino[41,42], Daphne L. van der A[40], Yvonne T. van der Schouw[43], Inês Barroso[4,44], Mark I. McCarthy[20,45,46], Elio Riboli[47], Nicholas J. Wareham[1]*

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

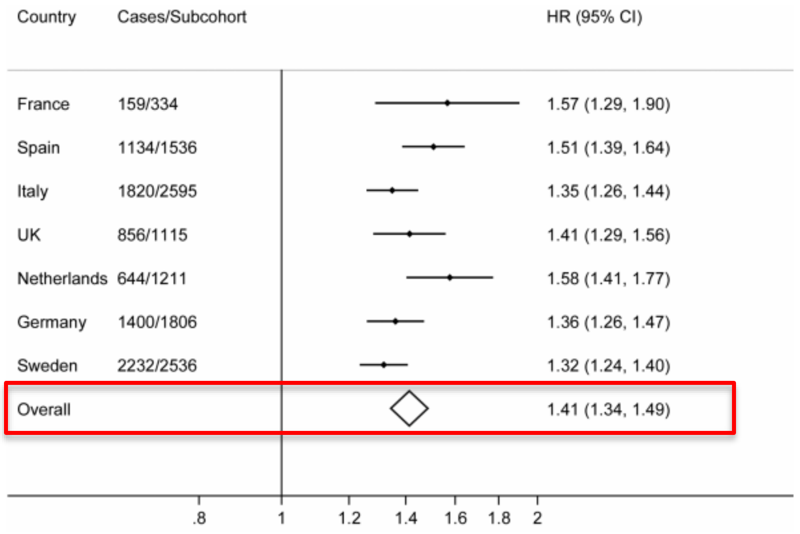


Figure 1. Hazard ratios for type 2 diabetes per standard deviation (4.4 alleles) increase in the imputed, unweighted genetic risk score by country and overall: the InterAct study.

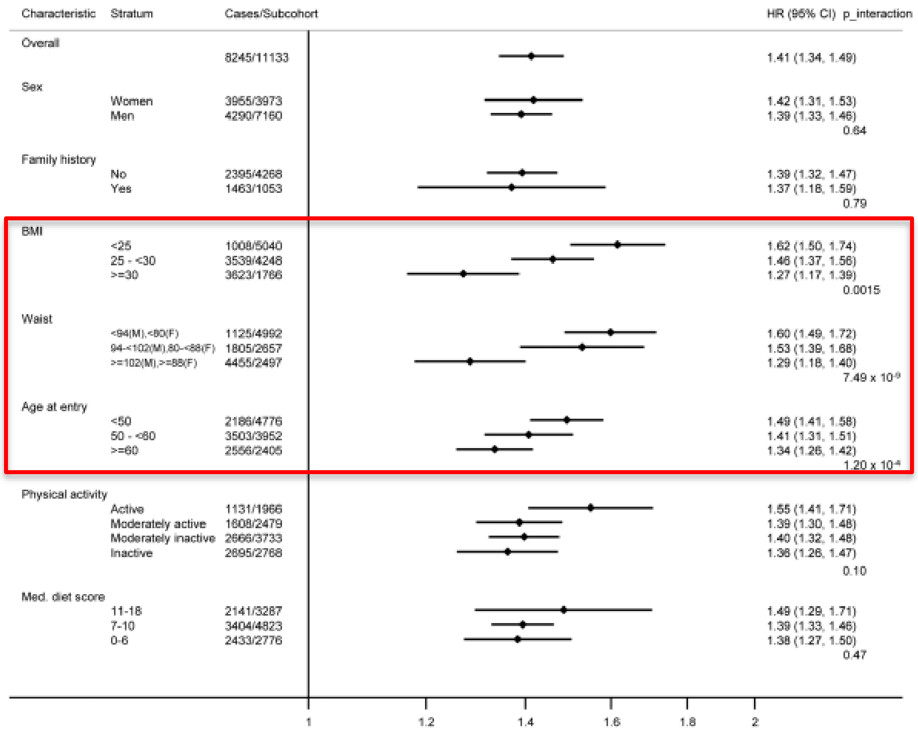


Figure 2. Hazard ratios for type 2 diabetes per standard deviation (4.4 alleles) increase in the imputed, unweighted genetic risk score within strata defined by sex, diabetes family history, body mass index, waist circumference, age, physical activity, and Mediterranean diet score: the InterAct study. 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

Group	HR (95% CI)	AR, %
Low genetic risk		
Ideal lifestyle	1 [Reference]	0.27
Intermediate lifestyle	3.09 (2.22-4.30)	1.00
Poor lifestyle	10.82 (7.54-15.54)	3.87
Intermediate genetic risk		
Ideal lifestyle	1.33 (0.93-1.90)	0.35
Intermediate lifestyle	4.40 (3.19-6.07)	1.41
Poor lifestyle	12.33 (8.84-17.22)	4.50
High genetic risk		
Ideal lifestyle	1.94 (1.30-2.90)	0.52
Intermediate lifestyle	6.27 (4.53-8.68)	1.99
Poor lifestyle	15.46 (10.82-22.08)	5.54