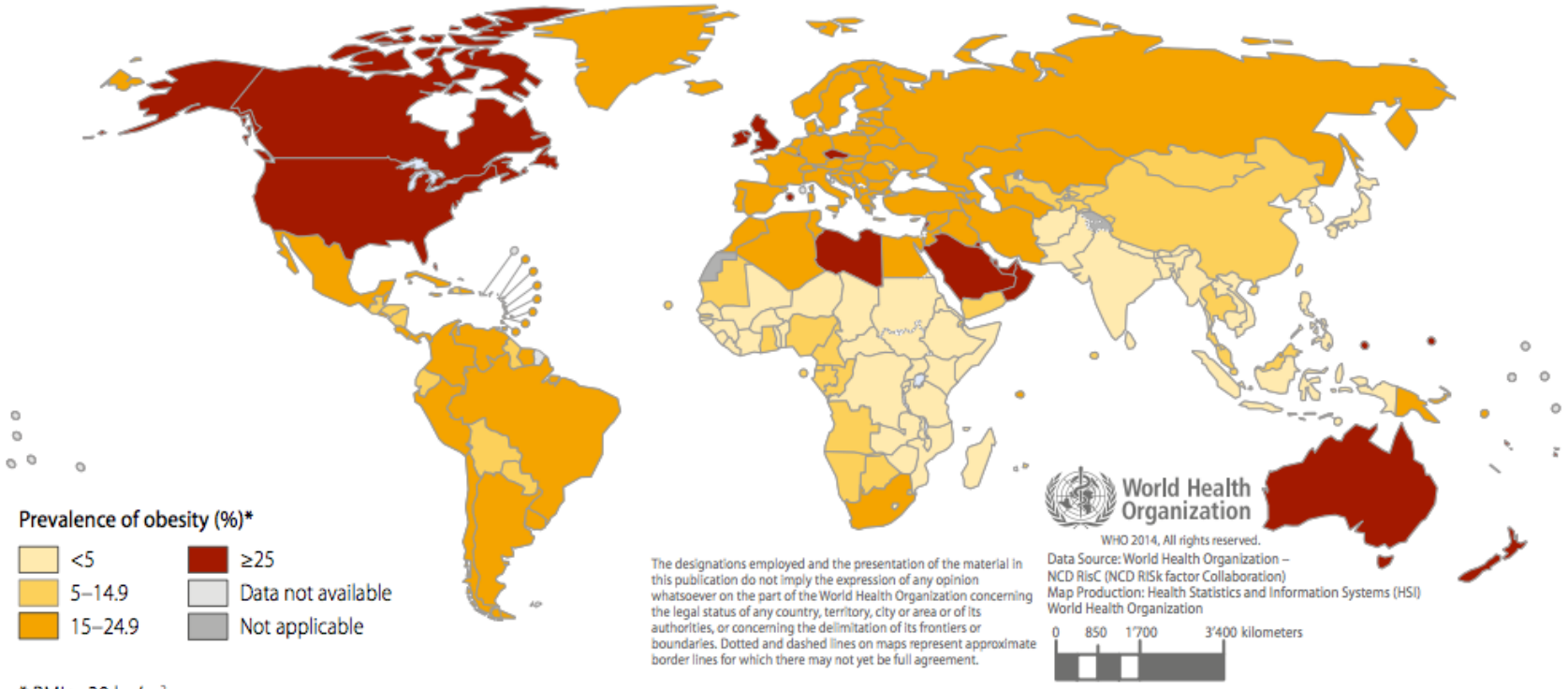
HAROKOPIO UNIVERSITY
Department of Dietetics & Nutritional Science

Μοριακή Γενετική της παχυσαρκίας και αλληλεπιδράσεις με διατροφή και φυσική δραστηριότητα

Γιώργος Δεδούσης
Καθηγητής Βιολογίας του Ανθρώπου

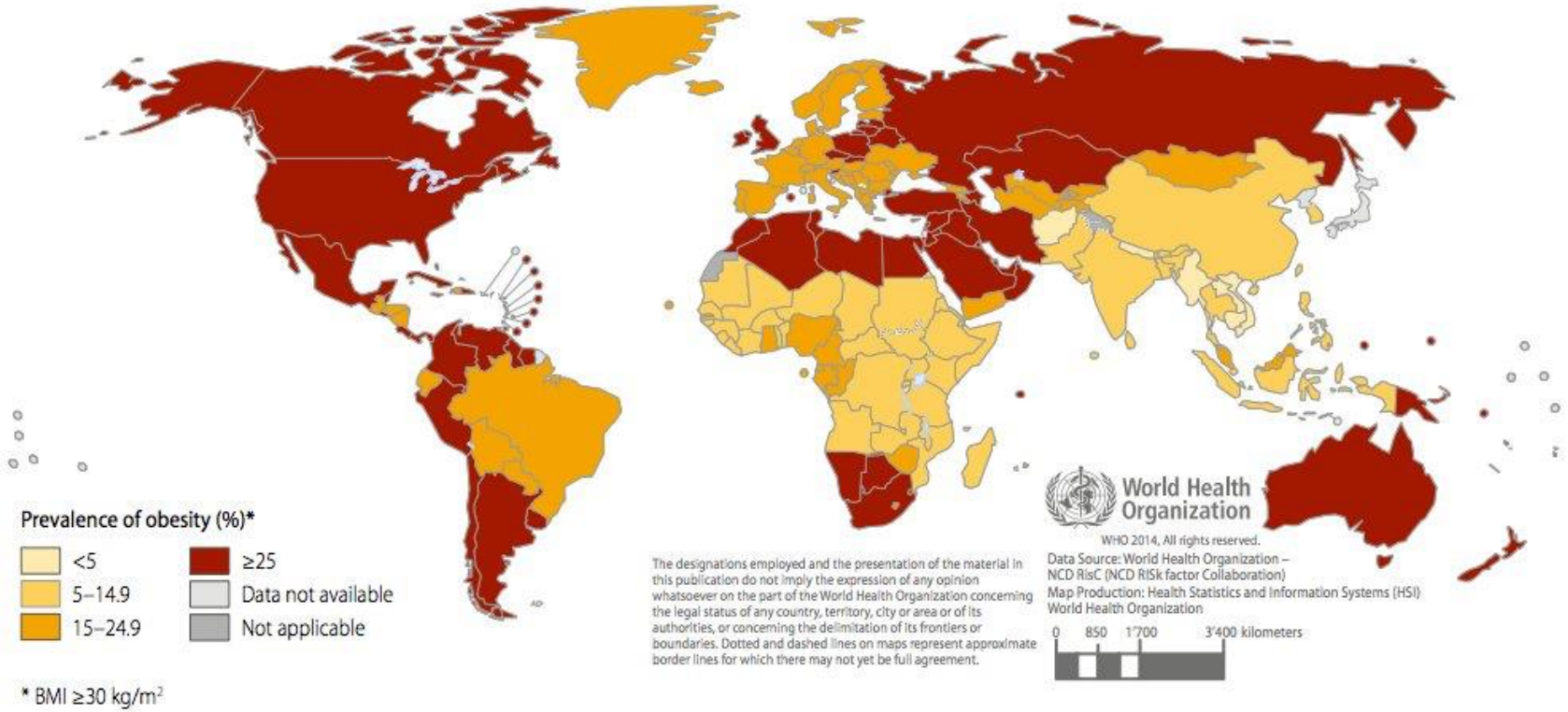
Prevalence of obesity

Fig. 7.1 Age-standardized prevalence of obesity in men aged 18 years and over (BMI ≥30 kg/m^2), 2014

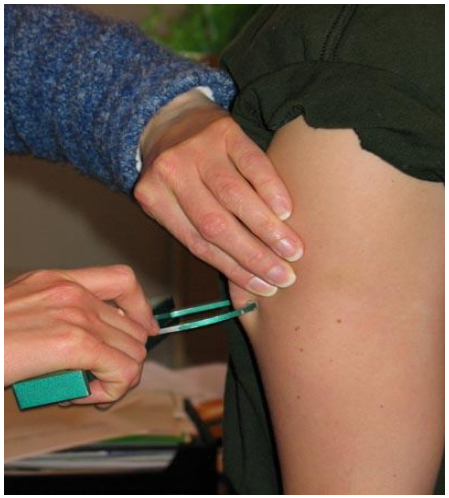


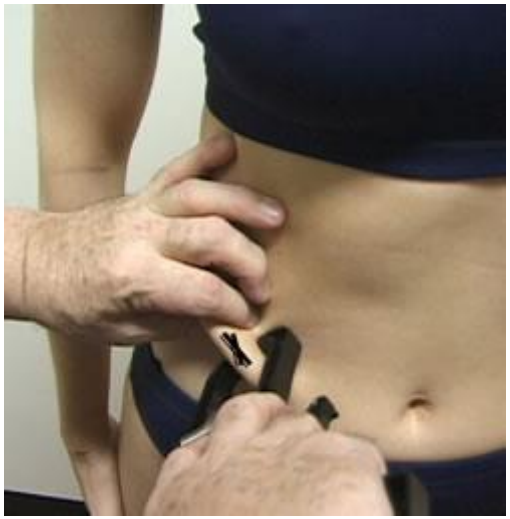
Prevalence of obesity

Fig. 7.2 Age-standardized prevalence of obesity in women aged 18 years and over (BMI ≥30 kg/m²), 2014



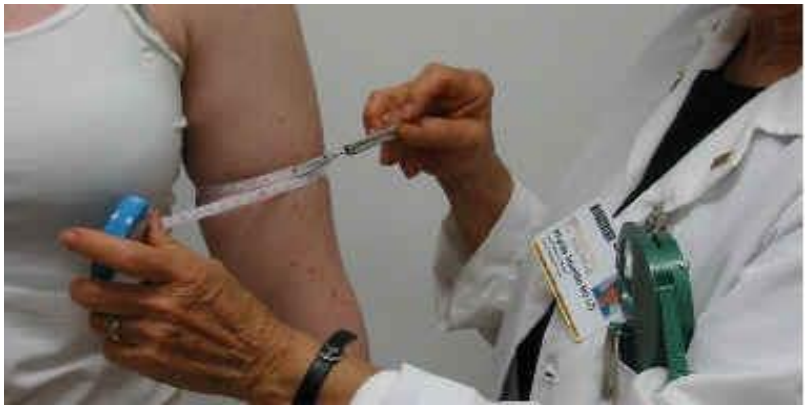
Δερματοπτυχές



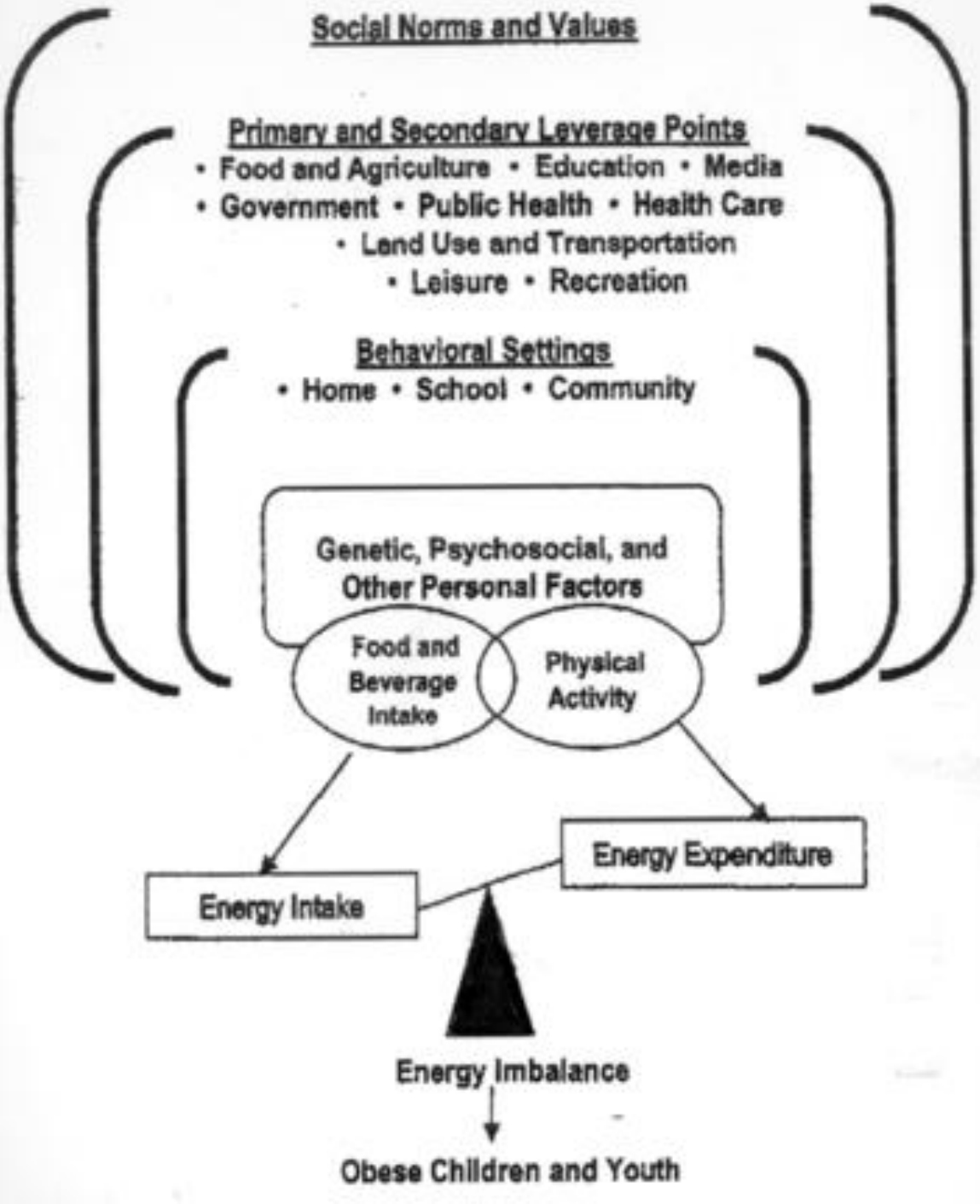


Τα δερματοπτυχόμετρα σε συγκεκριμένα σημεία του σώματος όπως οι δερματοπτυχές τρικεφάλου, δικεφάλου, υπερλαγόνια και ωμοπλατιαία δερματοπτυχή

Περιφέρειες



- Ο υπολογισμός της περιφέρειας μέσης είναι ένας τρόπος πληροφόρησης σχετικά με την **κατανομή του σωματικού λίπους**, συγκεκριμένα του σπλαχνικού λίπους το οποίο έχει συσχετιστεί με αρκετούς κινδύνους για την υγεία και μεταβολικές επιπλοκές.

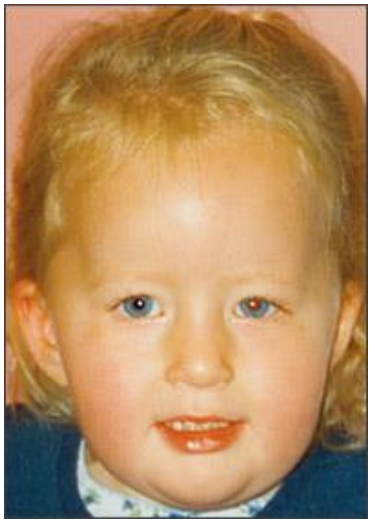


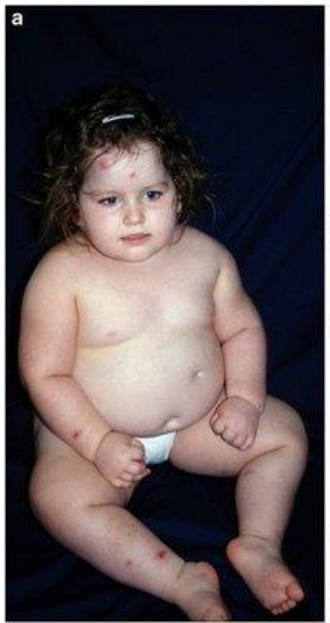
Factors predisposing to an energy imbalance resulting in overweight.

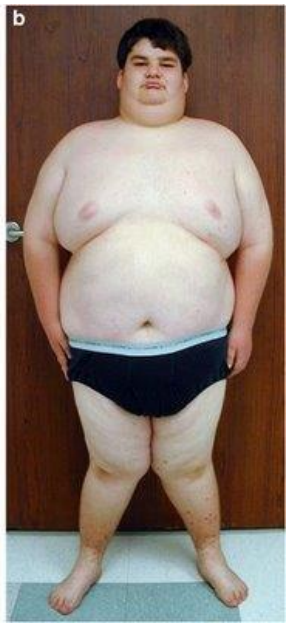
National Academy of Sciences, **Preventing Childhood Obesity: Health in the Balance,** *2005.*

Prader-Willi syndrome (PWS)

- **Ο επιπολασμός είναι από 1:10,000 σε 1:52,000**
- **Ήπια έως μέτρια πνευματική καθυστέρηση**
- **Υποτονία και μειωμένη πρόσληψη τροφής στην νεογνική ηλικία**
- **Μειωμένα αντανακλαστικά θηλασμού, αμυγδαλωτά μάτια, ήπιος στραβισμός, λεπτό πάνω χείλος,**
- **Κοντή σωματοδομή, μικρά άνω και κάτω άκρα, μικρά έξω γεννητικά όργανα**
- **Υπερφαγία από την ηλικία των 2 ετών, παχυσαρκία**

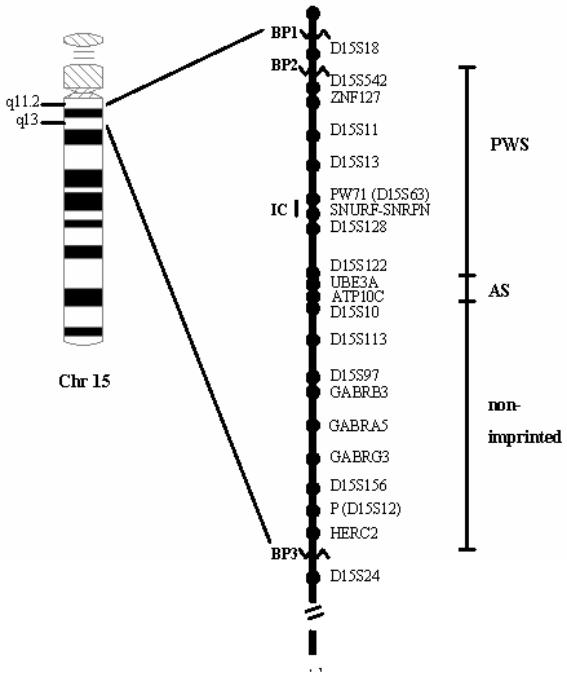


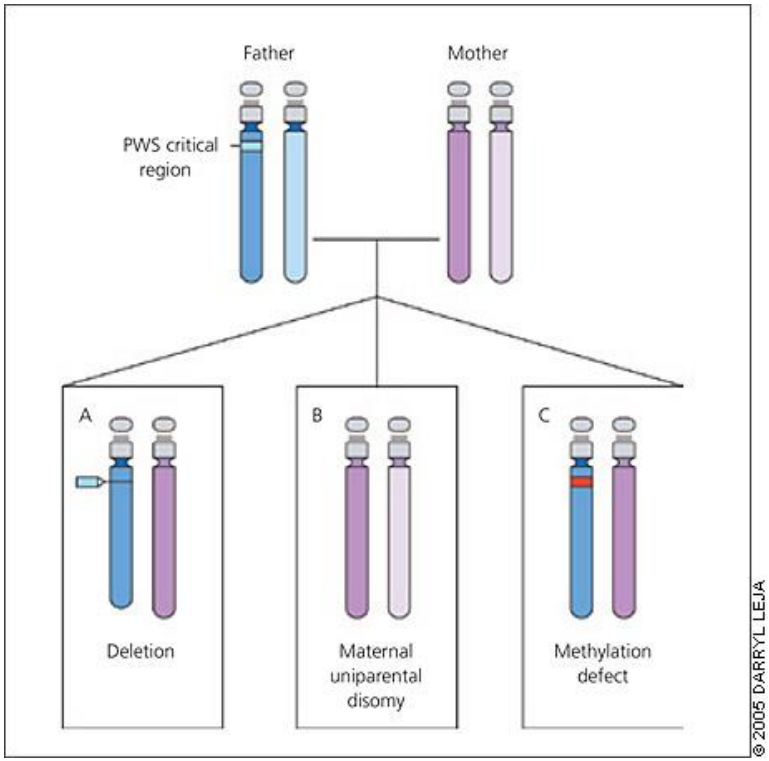




Γενετική αιτιολογία του συνδρόμου

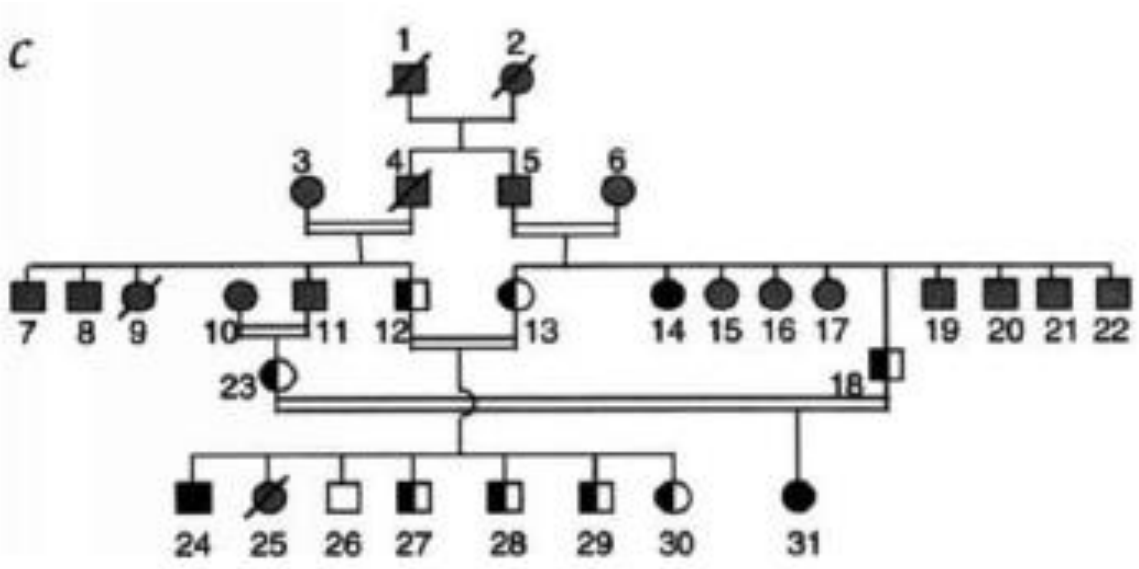
- **Στο 70-75% των PWS απουσία έκφρασης (έλλειψη 15q11-q13) των πατρικών γονιδίων που εδράζουν σε σημαντική περιοχή του χρωμοσώματος 15**
- **Το υπόλοιπο 25% οφείλεται σε μητρικού τύπου μονογονική δισωμία**
- **Λίγες περιπτώσεις σε επιγενετικές τροποποιήσεις της έκφρασης (μεθυλίωση)**





Μονογονιδιακού τύπου παχυσαρκία

A leptin missense mutation associated with hypogonadism and morbid obesity



nature genetics volume 18 march 1998

A Novel Homozygous Missense Mutation of Melanocortin-4 Receptor (*MC4R*) in a Japanese Woman With Severe Obesity

Hiromasa Kobayashi,[1] Yoshihiro Ogawa,[2] Mitsuyo Shintani,[2] Ken Ebihara,[2] Makiko Shimodahira,[1] Toshio Iwakura,[1] Megumu Hino,[3] Takashi Ishihara,[1] Katsuji Ikekubo,[3] Hiroyuki Kurahachi,[1] and Kazuwa Nakao[2]

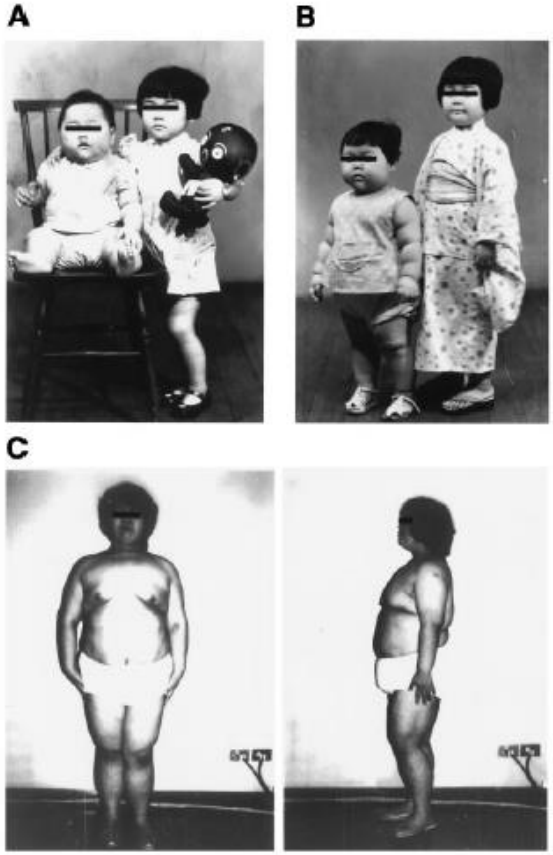


FIG. 2. Photographs of the proband at 2 (*A*) and 3 (*B*) years of age (with her elder sister at 4 and 5 years of age, respectively) and 23 years of age (*C*) (she weighed 115 kg). The photographs are reproduced with the informed consent of the proband and her mother.

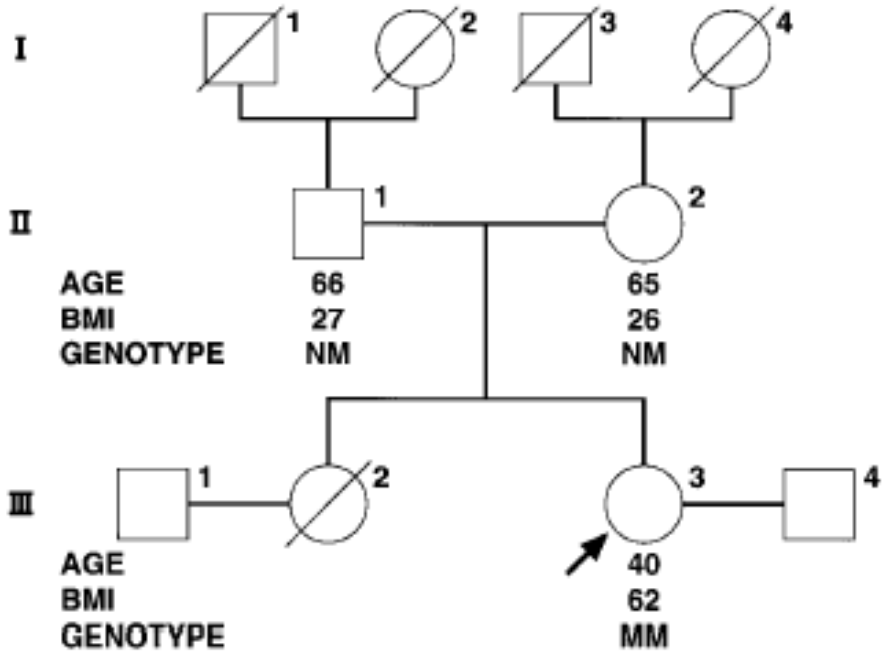


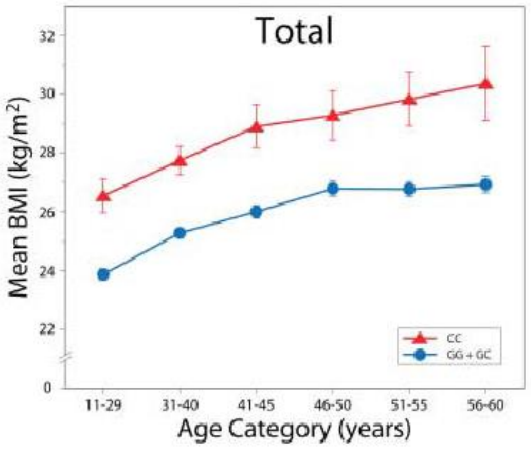
FIG. 1. Pedigree of the family. The arrow indicates the proband. The age, BMI, and *MC4R* genotype of the family members, if available, are shown below each symbol. M, mutant allele (G98R); N, normal allele.

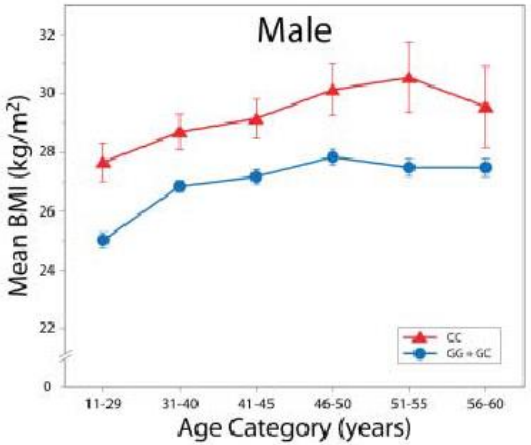
A Common Genetic Variant Is Associated with Adult and Childhood Obesity

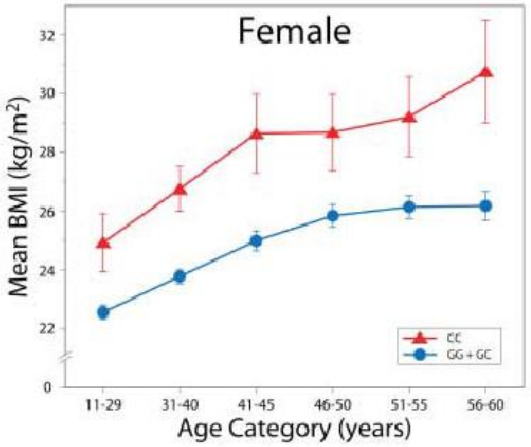
Alan Herbert,[1*] Norman P. Gerry,[1] Matthew B. McQueen,[2] Iris M. Heid,[3,4] Arne Pfeufer,[5,6] Thomas Illig,[3,4] H.-Erich Wichmann,[3,4,7] Thomas Meitinger,[5,6] David Hunter,[2,8,9] Frank B. Hu,[2,8,9] Graham Colditz,[8,9] Anke Hinney,[10] Johannes Hebebrand,[10] Kerstin Koberwitz,[6,10] Xiaofeng Zhu,[11] Richard Cooper,[11] Kristin Ardlie,[12] Helen Lyon,[13,14,15] Joel N. Hirschhorn,[13,14,15] Nan M. Laird,[16] Marc E. Lenburg,[1] Christoph Lange,[9,13] Michael F. Christman[1*]

Table 1. Screening and testing of SNPs for association with BMI. Genome-wide SNPs (86,604) were screened using parental genotypes to find those likely to affect offspring BMI. The top 10 SNPs from the screening step (ranked by power from most likely to least likely) are shown. These SNPs were tested using offspring genotypes for association with BMI using the FBAT. The rs7566605 SNP is highlighted in bold.

Ranking from screen	SNP	Chromosome	Frequency	Informative families	*P* value FBAT
1	rs3897510	20p12.3	0.36	30	0.2934
2	rs722385	2q32.1	0.16	15	0.1520
3	rs3852352	8p12	0.33	34	0.7970
4	**rs7566605**	**2q14.1**	**0.37**	**39**	**0.0026**
5	rs4141822	13q33.3	0.29	27	0.0526
6	rs7149994	14q21.1	0.35	31	0.0695
7	rs1909459	14q21.1	0.39	38	0.2231
8	rs10520154	15q15.1	0.36	38	0.9256
9	rs440383	15q15.1	0.36	38	0.8860
10	rs9296117	6p24.1	0.40	44	0.3652







In all age groups, homozygous for rs7566605 CC had 1 unit of BMI comparing with GC ή GG (P<0.0001), in both sexes

nature genetics

Variation in *FTO* contributes to childhood obesity and severe adult obesity

Christian Dina[1], David Meyre[1], Sophie Gallina[1], Emmanuelle Durand[1], Antje Körner[2], Peter Jacobson[3], Lena M S Carlsson[3], Wieland Kiess[2], Vincent Vatin[1], Cecile Lecoeur[1], Jérome Delplanque[1], Emmanuel Vaillant[1], François Pattou[4], Juan Ruiz[5], Jacques Weill[6], Claire Levy-Marchal[7], Fritz Horber[8], Natascha Potoczna[8], Serge Hercberg[9], Catherine Le Stunff[10], Pierre Bougnères[10], Peter Kovacs[11], Michel Marre[12], Beverley Balkau[13,14], Stéphane Cauchi[1], Jean-Claude Chèvre[1] & Philippe Froguel[1,15]

Science

A Common Variant in the *FTO* Gene Is Associated with Body Mass Index and Predisposes to Childhood and Adult Obesity

Timothy M. Frayling,[1,2*] Nicholas J. Timpson,[3,4*] Michael N. Weedon,[1,2*] Eleftheria Zeggini,[3,5*] Rachel M. Freathy,[1,2] Cecilia M. Lindgren,[3,5] John R. B. Perry,[1,2] Katherine S. Elliott,[3] Hana Lango,[1,2] Nigel W. Rayner,[3,5] Beverley Shields,[2] Lorna W. Harries,[2] Jeffrey C. Barrett,[3] Sian Ellard,[2,6] Christopher J. Groves,[5] Bridget Knight,[2] Ann-Marie Patch,[2,6] Andrew R. Ness,[7] Shah Ebrahim,[8] Debbie A. Lawlor,[9] Susan M. Ring,[9] Yoav Ben-Shlomo,[9] Marjo-Riitta Jarvelin,[10,11] Ulla Sovio,[10,11] Amanda J. Bennett,[5] David Melzer,[1,12] Luigi Ferrucci,[13] Ruth J. F. Loos,[14] Inês Barroso,[15] Nicholas J. Wareham,[14] Fredrik Karpe,[5] Katharine R. Owen,[5] Lon R. Cardon,[3] Mark Walker,[16] Graham A. Hitman,[17] Colin N. A. Palmer,[18] Alex S. F. Doney,[19] Andrew D. Morris,[19] George Davey Smith,[4] The Wellcome Trust Case Control Consortium,† Andrew T. Hattersley,[1,2]‡§ Mark I. McCarthy[3,5]‡

Science

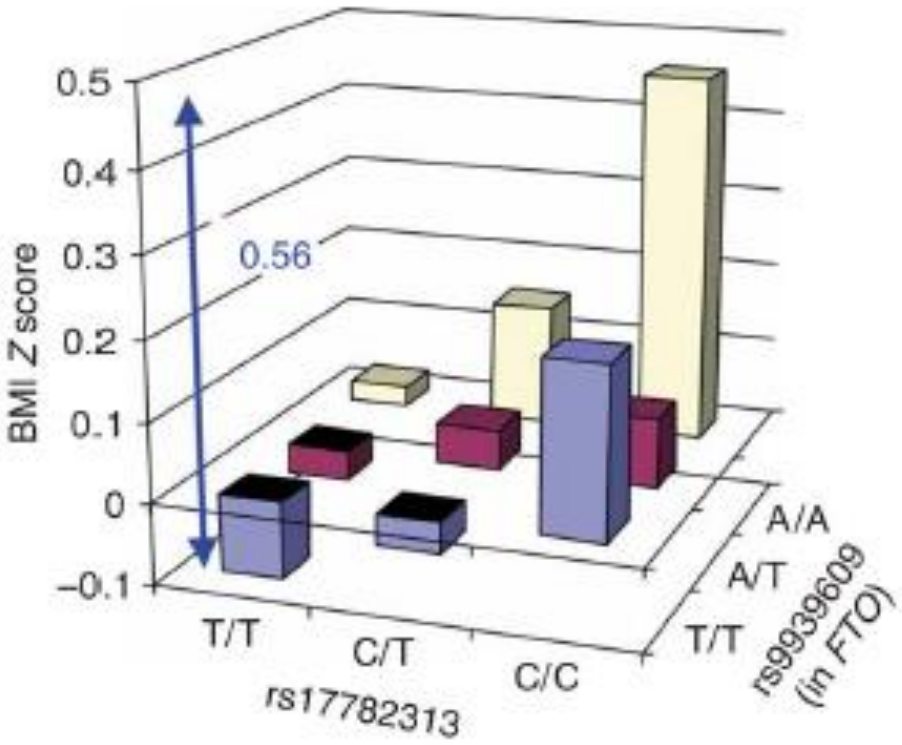
- An additive association of the variant with BMI was replicated in 13 cohorts with 38,759 participants.
- The 16% of adults who are homozygous for the risk allele weighed about **3** kilograms more and had **1.67**-fold increased odds of obesity when compared with those not inheriting a risk allele.
- This association was observed from **age 7** years and reflects a specific increase in fat mass.

Table 2. Association of BMI (corrected for sex) and birth weight (corrected for sex and gestational age) with rs9939609 genotypes in children. *P* values represent the change in log BMI per A allele. BMI presented as geometric means and back-transformed 95% confidence intervals.

Cohort	Age (years)	Males (%)	*N*	Mean trait value (95% CI) by genotype			*P*
				TT	AT	AA	
				Children*			
ALSPAC	7	51	5969	16.00 (15.92, 16.07)	16.11 (16.04, 16.18)	16.31 (16.19, 16.43)	3×10^{-5}
	8	50	4871	16.80 (16.70, 16.90)	17.01 (16.92, 17.09)	17.29 (17.14, 17.45)	1×10^{-7}
	9	50	5459	17.20 (17.08, 17.31)	17.53 (17.43, 17.63)	17.86 (17.69, 18.04)	5×10^{-11}
	10	50	5273	17.66 (17.54, 17.79)	18.05 (17.94, 18.17)	18.37 (18.18, 18.57)	1×10^{-10}
	11	49	5010	18.46 (18.32, 18.61)	18.82 (18.70, 18.94)	19.20 (18.98, 19.42)	7×10^{-9}
NFBC1966 (age 14)	14	47	4203	19.14 (19.02, 19.26)	19.25 (19.14, 19.36)	19.38 (19.19, 19.57)	0.04
				Birth†			
ALSPAC	0	51	7477	3438 (3422, 3455)	3452 (3437, 3466)	3454 (3429, 3480)	0.21
NFBC1966	0	47	4320	3523 (3501, 3546)	3538 (3518, 3558)	3536 (3501, 3571)	0.42

*ALSPAC children are offspring of the participants included in the adult study (Table 1), and data are shown at five available ages. NFBC1966 children are the same participants as those in the adult study (Table 1). †ALSPAC birth data are for the same participants as those in the children study. NFBC1966 birth data are for the same participants as those in the children and adult studies. Non-singleton births and individuals born at gestation <36 weeks were excluded from the birth-weight analysis.

Συνδυαστική δράση των δύο γονιδίων



- Οι ομοζυγώτες και για τα δύο αλληλόμορφα κινδύνου (19%) είχαν 1,17 μονάδες BMI περισσότερες από εκείνους που δεν είχαν κανένα αλληλόμορφο κινδύνου

nature genetics

Meta-analysis identifies 13 new loci associated with waist-hip ratio and reveals sexual dimorphism in the genetic basis of fat distribution

Table 2 Evidence of sex-differences in the WHR association at seven of the 14 associated loci

		Men						Women						Sex difference
		Discovery		Follow up		Combined		Discovery		Follow up		Combined		Combined
SNP	Nearby genes	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*	β	*P*
rs9491696	*RSPO3*	1.68×10^{-4}	0.026	6.97×10^{-9}	0.036	1.05×10^{-11}	0.031	1.62×10^{-12}	0.047	8.84×10^{-22}	0.053	1.93×10^{-32}	0.050	1.94×10^{-3}
rs6905288	*VEGFA*	0.066	0.013	2.09×10^{-4}	0.025	7.38×10^{-5}	0.020	7.72×10^{-13}	0.052	3.14×10^{-15}	0.051	2.27×10^{-26}	0.052	5.20×10^{-6}
rs984222	*TBX15-WARS2*	3.32×10^{-9}	0.041	2.43×10^{-5}	0.029	9.41×10^{-13}	0.035	1.21×10^{-7}	0.036	1.33×10^{-8}	0.033	1.02×10^{-14}	0.034	0.951
rs1055144	*NFE2L3*	6.00×10^{-4}	0.029	5.67×10^{-8}	0.040	2.52×10^{-10}	0.035	2.34×10^{-6}	0.040	7.13×10^{-12}	0.046	1.41×10^{-16}	0.044	0.270
rs10195252	*GRB14*	0.201	0.009	0.114	0.011	0.043	0.010	6.33×10^{-15}	0.053	4.95×10^{-21}	0.054	3.84×10^{-34}	0.054	1.41×10^{-11}
rs4846567	*LYPLAL1*	0.191	0.010	0.982	0.000	0.358	0.005	4.84×10^{-18}	0.064	8.12×10^{-17}	0.055	4.95×10^{-33}	0.059	1.18×10^{-13}
rs1011731	*DNM3-PIGC*	4.88×10^{-7}	0.034	1.95×10^{-3}	0.022	7.81×10^{-9}	0.028	2.13×10^{-5}	0.028	7.03×10^{-7}	0.030	6.90×10^{-11}	0.029	0.855
rs718314	*ITPR2-SSPN*	0.177	0.010	2.02×10^{-3}	0.022	1.41×10^{-3}	0.017	8.29×10^{-10}	0.047	4.21×10^{-9}	0.038	2.41×10^{-17}	0.042	4.67×10^{-4}
rs1294421	*LY86*	4.18×10^{-3}	0.020	7.00×10^{-6}	0.030	1.63×10^{-7}	0.025	3.44×10^{-8}	0.038	7.32×10^{-6}	0.026	2.40×10^{-12}	0.031	0.357
rs1443512	*HOXC13*	0.184	0.011	9.74×10^{-4}	0.024	9.45×10^{-4}	0.018	1.43×10^{-9}	0.048	3.09×10^{-8}	0.035	6.38×10^{-16}	0.040	2.23×10^{-3}
rs6795735	*ADAMTS9*	0.011	0.017	0.614	0.004	0.027	0.011	7.85×10^{-7}	0.033	2.95×10^{-11}	0.042	1.92×10^{-16}	0.038	8.50×10^{-5}
rs4823006	*ZNRF3-KREMEN1*	6.87×10^{-3}	0.019	0.094	0.012	1.94×10^{-3}	0.015	6.86×10^{-8}	0.037	3.81×10^{-5}	0.024	3.24×10^{-11}	0.030	0.032
rs6784615	*NISCH-STAB1*	1.51×10^{-3}	0.045	0.033	0.032	1.68×10^{-4}	0.039	6.23×10^{-5}	0.057	1.72×10^{-3}	0.039	6.01×10^{-7}	0.047	0.574
rs6861681	*CPEB4*	1.88×10^{-3}	0.023	0.045	0.015	3.03×10^{-4}	0.019	2.14×10^{-4}	0.027	1.58×10^{-3}	0.021	1.55×10^{-6}	0.024	0.555

- Οι 14 γενετικοί τόποι εξηγούν το **1,4%** της διακύμανσης του WHR στις γυναίκες και μόλις το **0,46%** στους άνδρες

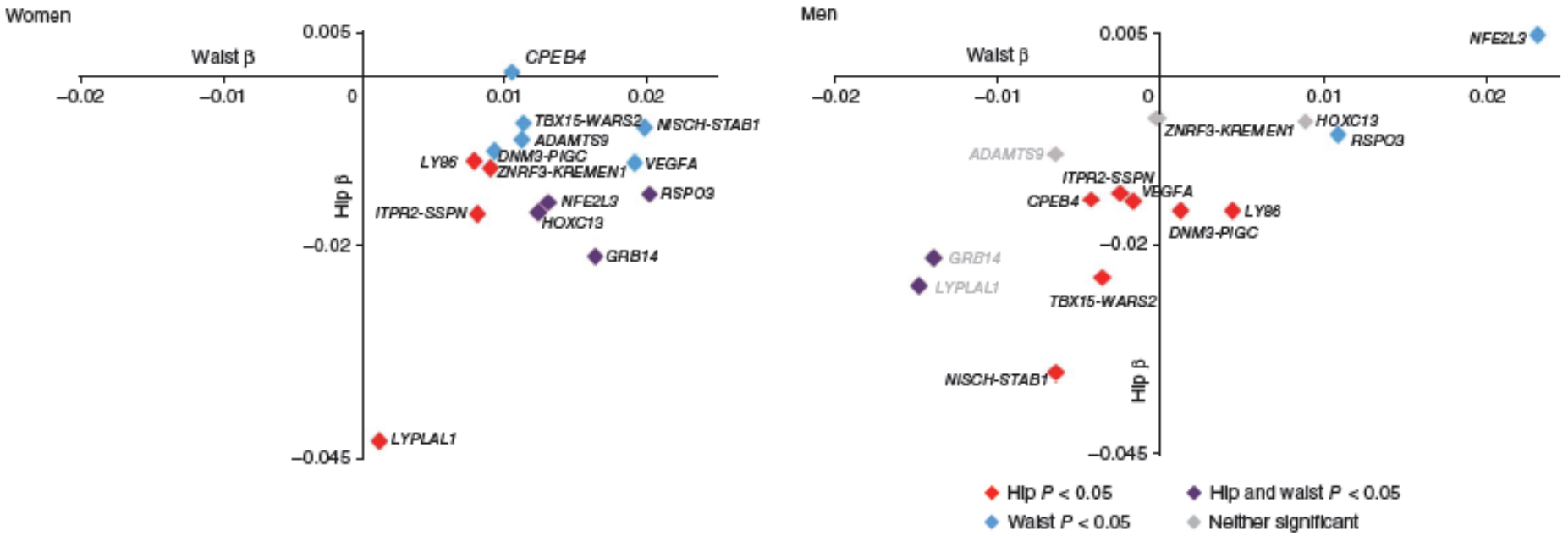


Figure 3 Association of the 14 WHR loci with waist and hip circumference. β coefficients for waist circumference (WC, *x* axis) and hip circumference (HIP, *y* axis) in women and men derived from the joint discovery and follow-up analysis. *P* for WC and HIP are represented by color. In men, gray gene labels refer to those SNPs that were not significant in the male-specific WHR analysis. More details can be found in **Supplementary Table 3**.

nature genetics

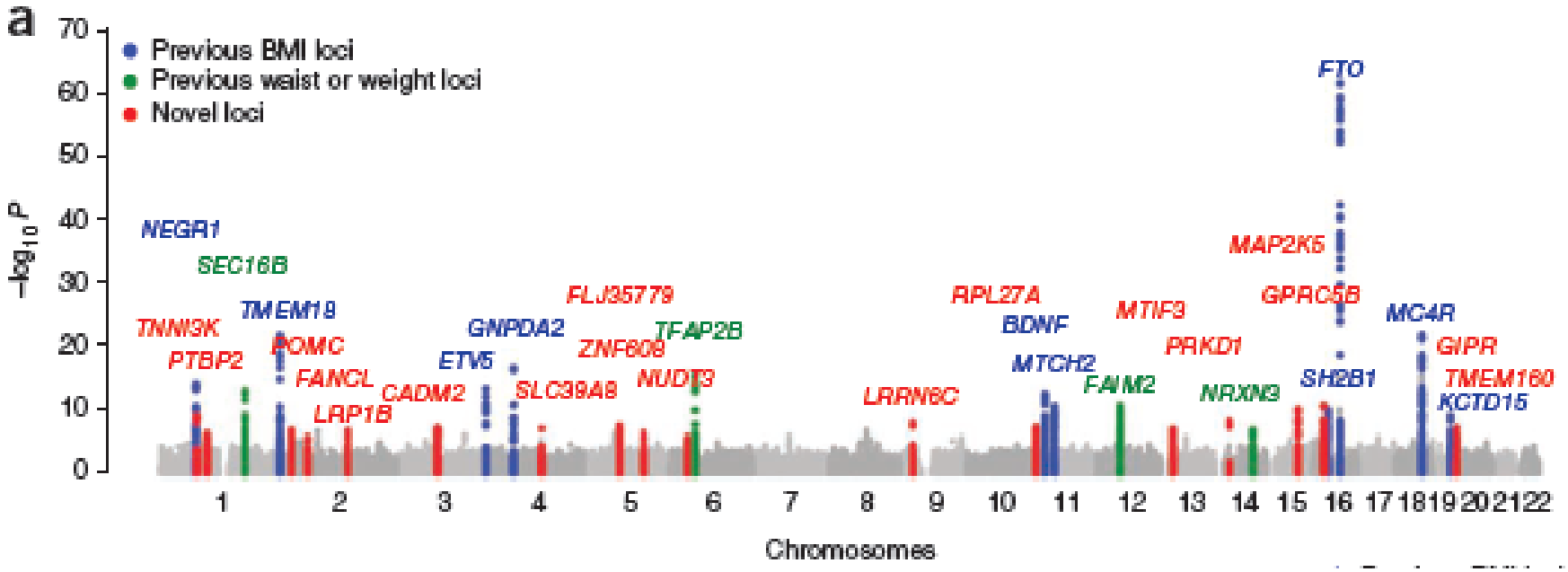
Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index

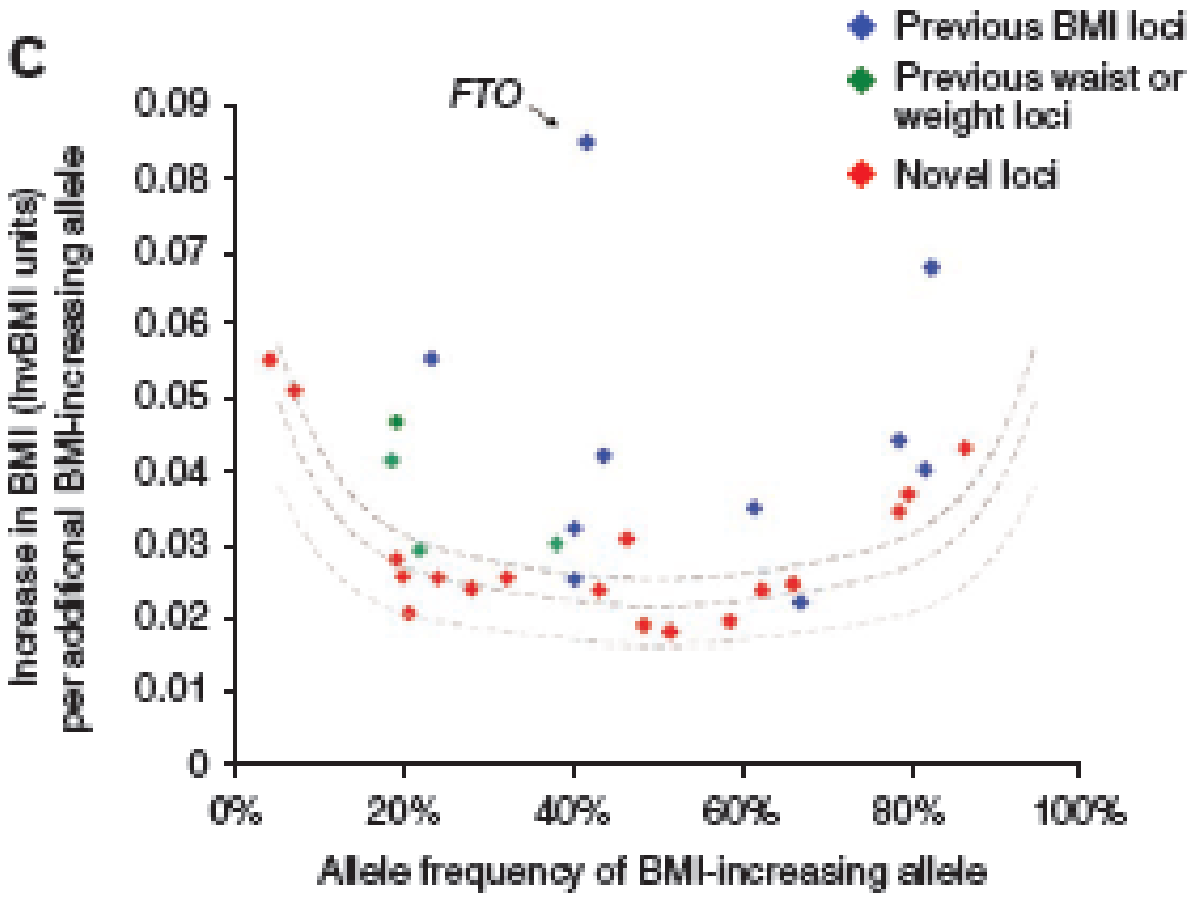
Table 1 Stage 1 and stage 2 results of the 32 SNPs that were associated with BMI at genome-wide significant ($P < 5 \times 10^{-8}$) levels

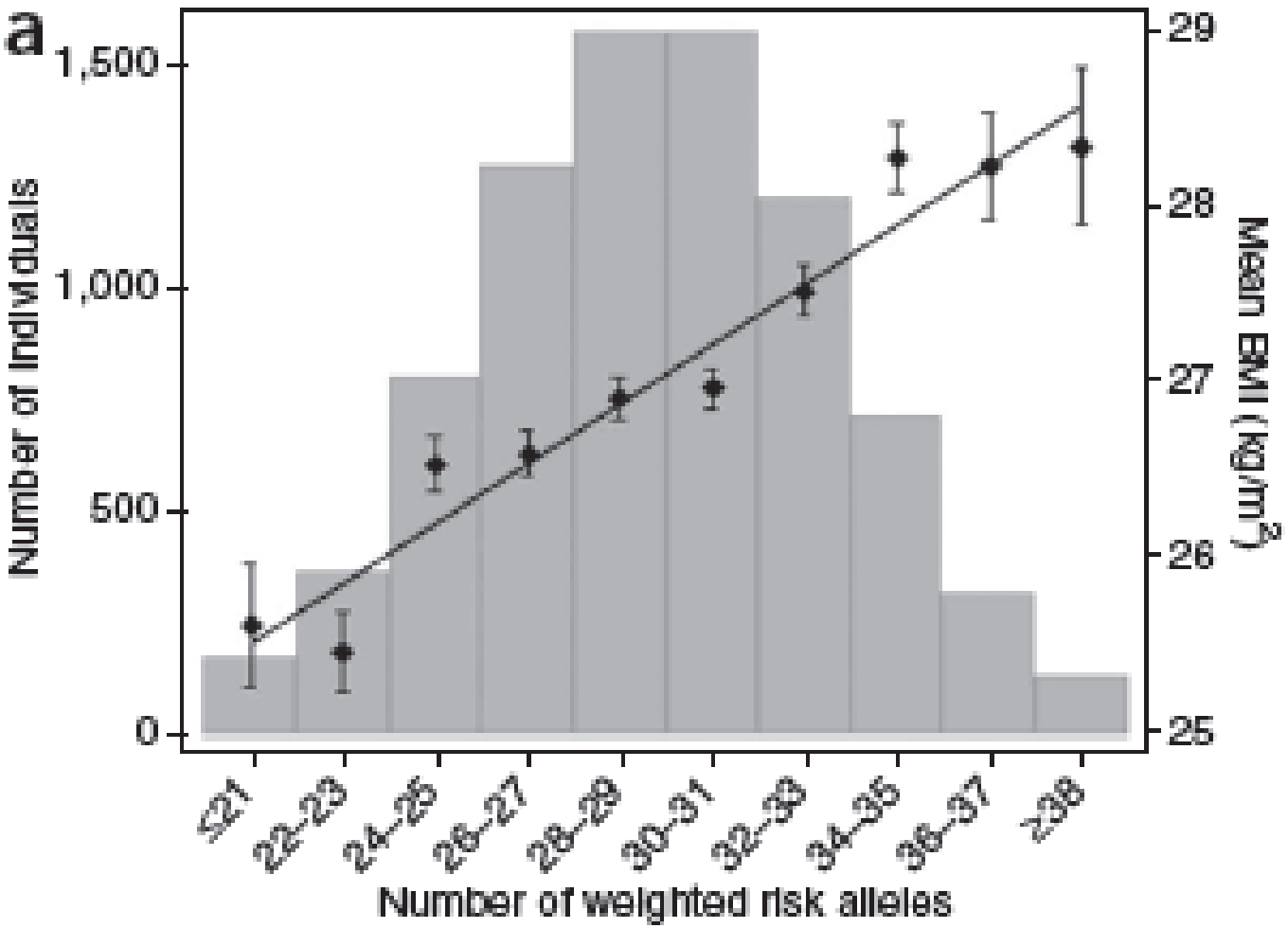
SNP	Nearest gene	Other nearby genes[a]	Chr.	Position[b] (bp)	Alleles[b] Effect	Other	Frequency effect allele	Per allele change in BMI β (s.e.m.)[c]	Explained variance (%)	Stage 1 *P*	Stage 2 *P*	Stage 1 + 2 *n*	Stage 1 + 2 *P*
Previously identified BMI loci													
rs1558902	*FTO*		16	52,361,075	A	T	0.42	0.39 (0.02)	0.34%	2.05×10^{-62}	1.01×10^{-60}	192,344	4.8×10^{-120}
rs2867125	*TMEM18*		2	612,827	C	T	0.83	0.31 (0.03)	0.15%	2.42×10^{-22}	4.42×10^{-30}	197,806	2.77×10^{-49}
rs571312	*MC4R* (B)		18	55,990,749	A	C	0.24	0.23 (0.03)	0.10%	1.82×10^{-22}	3.19×10^{-21}	203,600	6.43×10^{-42}
rs10938397	*GNPDA2*		4	44,877,284	G	A	0.43	0.18 (0.02)	0.08%	4.35×10^{-17}	1.45×10^{-15}	197,008	3.78×10^{-31}
rs10767664	*BDNF* (B,M)		11	27,682,562	A	T	0.78	0.19 (0.03)	0.07%	5.53×10^{-13}	1.17×10^{-14}	204,158	4.69×10^{-26}
rs2815752	*NEGR1* (C,Q)		1	72,585,028	A	G	0.61	0.13 (0.02)	0.04%	1.17×10^{-14}	2.29×10^{-9}	198,380	1.61×10^{-22}
rs7359397	*SH2B1* (Q,B,M)	*APOB48R* (Q,M), *SULT1A2* (Q,M), *AC138894.2* (M), *ATXN2L* (M), *TUFM* (Q)	16	28,793,160	T	C	0.40	0.15 (0.02)	0.05%	1.75×10^{-10}	7.89×10^{-12}	204,309	1.88×10^{-20}
rs9816226	*ETV5*		3	187,317,193	T	A	0.82	0.14 (0.03)	0.03%	7.61×10^{-14}	1.15×10^{-6}	196,221	1.69×10^{-18}
rs3817334	*MTCH2* (Q,M)	*NDUFS3* (Q), *CUGBP1* (Q)	11	47,607,569	T	C	0.41	0.06 (0.02)	0.01%	4.79×10^{-11}	1.10×10^{-3}	191,943	1.59×10^{-12}
rs29941	*KCTD15*		19	39,001,372	G	A	0.67	0.06 (0.02)	0.00%	1.31×10^{-9}	2.40×10^{-2}	192,872	3.01×10^{-9}
Previously identified waist and weight loci													
rs543874	*SEC16B*		1	176,156,103	G	A	0.19	0.22 (0.03)	0.07%	1.66×10^{-13}	2.41×10^{-11}	179,414	3.56×10^{-23}
rs987237	*TFAP2B*		6	50,911,009	G	A	0.18	0.13 (0.03)	0.03%	5.97×10^{-16}	2.40×10^{-6}	195,776	2.90×10^{-20}
rs7138803	*FAIM2*		12	48,533,735	A	G	0.38	0.12 (0.02)	0.04%	3.96×10^{-11}	7.82×10^{-8}	200,064	1.82×10^{-17}
rs10150332	*NRXN3*		14	79,006,717	C	T	0.21	0.13 (0.03)	0.02%	2.03×10^{-7}	2.86×10^{-5}	183,022	2.75×10^{-11}
Newly identified BMI loci													
rs713586	*RBJ*	*ADCY3* (Q, M), *POMC* (Q,B)	2	25,011,512	C	T	0.47	0.14 (0.02)	0.06%	1.80×10^{-7}	1.44×10^{-16}	230,748	6.17×10^{-22}
rs12444979	*GPRC5B* (C,Q)	*IQCK* (Q)	16	19,841,101	C	T	0.87	0.17 (0.03)	0.04%	4.20×10^{-11}	8.13×10^{-12}	239,715	2.91×10^{-21}
rs2241423	*MAP2K5*	*LBXCOR1* (M)	15	65,873,892	G	A	0.78	0.13 (0.02)	0.03%	1.15×10^{-10}	1.59×10^{-9}	227,950	1.19×10^{-18}
rs2287019	*QPCTL*	*GIPR* (B,M)	19	50,894,012	C	T	0.80	0.15 (0.03)	0.04%	3.18×10^{-7}	1.40×10^{-10}	194,564	1.88×10^{-16}
rs1514175	*TNNI3K*		1	74,764,232	A	G	0.43	0.07 (0.02)	0.02%	1.36×10^{-9}	7.04×10^{-6}	227,900	8.16×10^{-14}
rs13107325	*SLC39A8* (Q,M)		4	103,407,732	T	C	0.07	0.19 (0.04)	0.03%	1.37×10^{-7}	1.93×10^{-7}	245,378	1.50×10^{-13}
rs2112347	*FLJ35779* (M)	*HMGCR* (B)	5	75,050,998	T	G	0.63	0.10 (0.02)	0.02%	4.76×10^{-8}	8.29×10^{-7}	231,729	2.17×10^{-13}
rs10968576	*LRRN6C*		9	28,404,339	G	A	0.31	0.11 (0.02)	0.02%	1.88×10^{-8}	3.19×10^{-6}	216,916	2.65×10^{-13}
rs3810291	*TMEM160* (Q)	*ZC3H4* (Q)	19	52,260,843	A	G	0.67	0.09 (0.02)	0.02%	1.04×10^{-7}	1.59×10^{-6}	233,512	1.64×10^{-12}
rs887912	*FANCL*		2	59,156,381	T	C	0.29	0.10 (0.02)	0.03%	2.69×10^{-6}	1.72×10^{-7}	242,807	1.79×10^{-12}
rs13078807	*CADM2*		3	85,966,840	G	A	0.20	0.10 (0.02)	0.02%	9.81×10^{-8}	5.32×10^{-5}	237,404	3.94×10^{-11}
rs11847697	*PRKD1*		14	29,584,863	T	C	0.04	0.17 (0.05)	0.01%	1.11×10^{-8}	2.25×10^{-4}	241,667	5.76×10^{-11}
rs2890652	*LRP1B*		2	142,676,401	C	T	0.18	0.09 (0.03)	0.02%	2.38×10^{-7}	9.47×10^{-5}	209,068	1.35×10^{-10}
rs1555543	*PTBP2*		1	96,717,385	C	A	0.59	0.06 (0.02)	0.01%	7.65×10^{-7}	4.48×10^{-5}	243,013	3.68×10^{-10}
rs4771122	*MTIF3*	*GTF3A* (Q)	13	26,918,180	G	A	0.24	0.09 (0.03)	0.02%	1.20×10^{-7}	8.24×10^{-4}	198,577	9.48×10^{-10}
rs4836133	*ZNF608*		5	124,360,002	A	C	0.48	0.07 (0.02)	0.01%	7.04×10^{-7}	1.88×10^{-4}	241,999	1.97×10^{-9}
rs4929949	*RPL27A*	*TUB* (B)	11	8,561,169	C	T	0.52	0.06 (0.02)	0.01%	7.57×10^{-8}	1.00×10^{-3}	249,791	2.80×10^{-9}
rs206936	*NUDT3*	*HMGA1* (B)	6	34,410,847	G	A	0.21	0.06 (0.02)	0.01%	2.81×10^{-6}	7.39×10^{-4}	249,777	3.02×10^{-8}

Chr., chromosome; Q, association and eQTL data converge to affect gene expression; B, biological candidate; M, BMI-associated variant is in strong LD ($r^2 \geq 0.75$) with a missense variant in the indicated gene; C, CNV.
[a]Genes within ± 500 kb of the lead SNP. [b]Positions according to Build 36 and allele coding based on the positive strand. [c]Effect sizes in kg/m^2 obtained from stage 2 cohorts only.

- Οι επιδράσεις των νέων αλληλομόρφων είναι μικρότερες και η συχνότητα επίσης
- Και οι 32 γενετικοί τόποι εξηγούν μόλις **1,5%** της διακύμανσης του BMI


a
Previous BMI loci
Previous waist or weight loci
Novel loci
$-\log_{10} P$
70
60
50
40
30
20
10
0
NEGR1
SEC16B
TNNI3K
TMEM18
PTBP2
POMC
FANCL
LRP1B
CADM2
ETV5
GNPDA2
SLC39A8
FLJ35779
ZNF608
TFAP2B
NUDT3
LRRN6C
RPL27A
BDNF
MTCH2
FAIM2
MTIF3
PRKD1
NRXN3
FTO
MAP2K5
GPRC5B
SH2B1
MC4R
GIPR
TMEM160
KCTD15
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
Chromosomes


C
Previous BMI loci
Previous waist or weight loci
Novel loci
FTO
Increase in BMI (lnvBMI units) per additional BMI-increasing allele
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
0%
20%
40%
60%
80%
100%
Allele frequency of BMI-increasing allele



- Για κάθε μία μονάδα αύξησης του γενετικού σκορ ισοδυναμεί με αύξηση **0,17 μονάδες BMI**, περίπου **435-551 gr** επιπλέον για ενήλικες ύψους 160-180 cm.

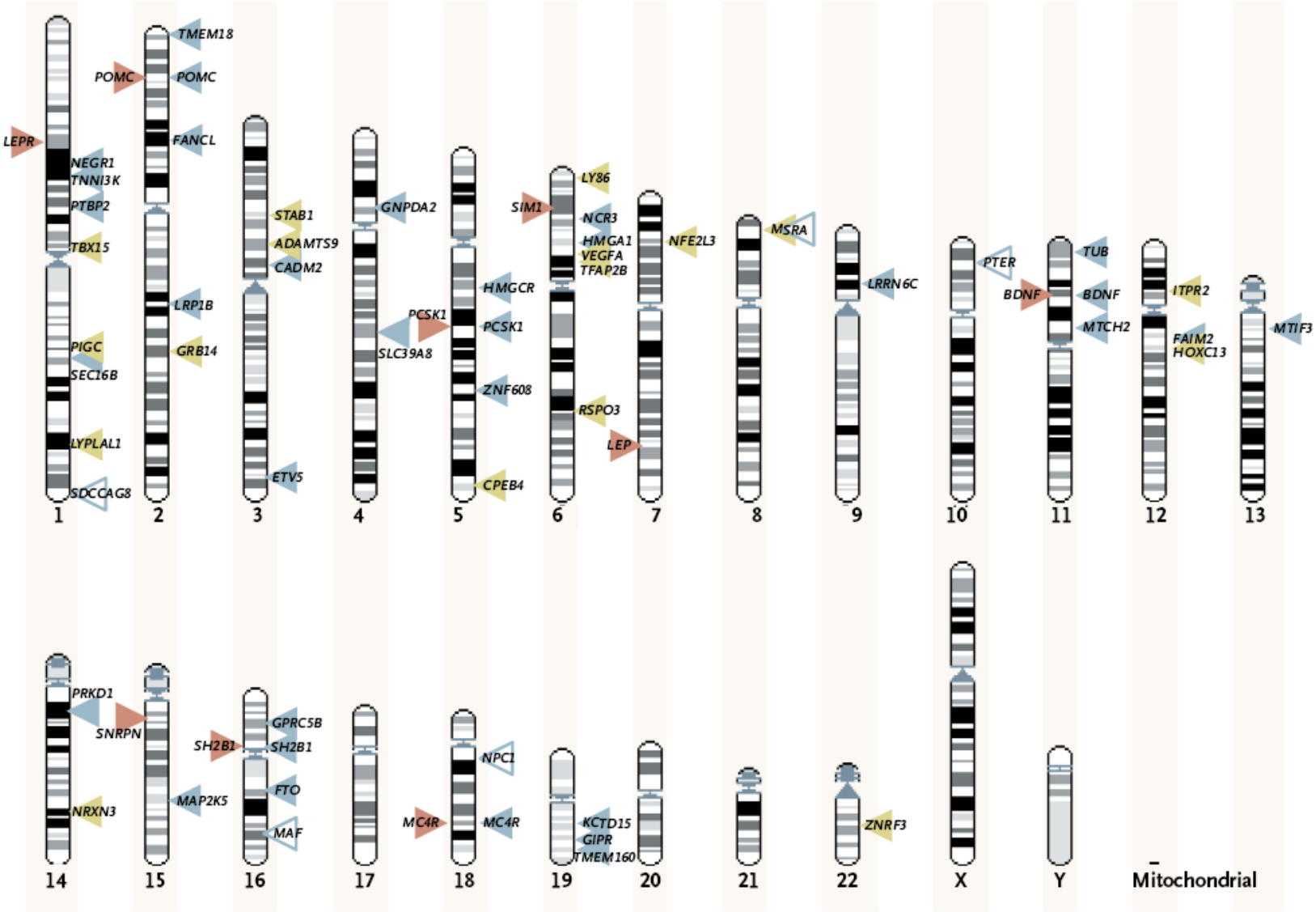


Figure 2. Genomic Locations of Proven Signals of Body-Mass Index (BMI), Obesity, and Related Phenotypes.

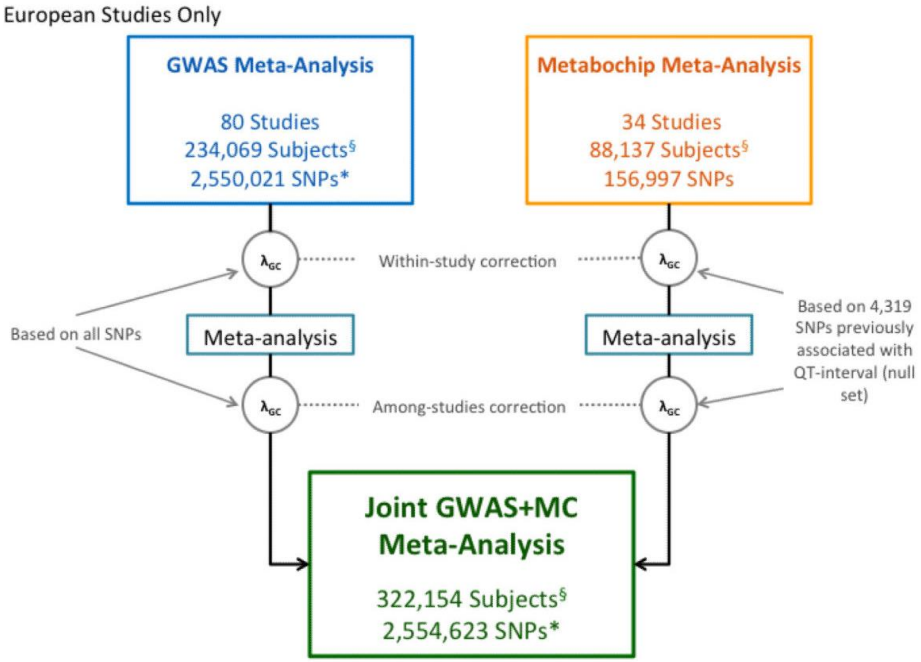
Signals are shown according to their location on each chromosome. Genes causing monogenic and selected syndromic forms of obesity (red triangles) are shown to the left. Common variants that have significant genomewide associations with BMI or multifactorial obesity are shown to the right: loci implicated in BMI or weight variation at the population level (solid blue triangles), additional loci identified in case–control analyses of extreme obesity (open blue triangles), and variants identified primarily because of their association with waist circumference or waist-to-hip ratio (solid green triangles). For the variants shown to the right, the genes named within the triangles are indicative of signal position, but in most instances, formal proof that these are the specific genes responsible for the association is lacking.

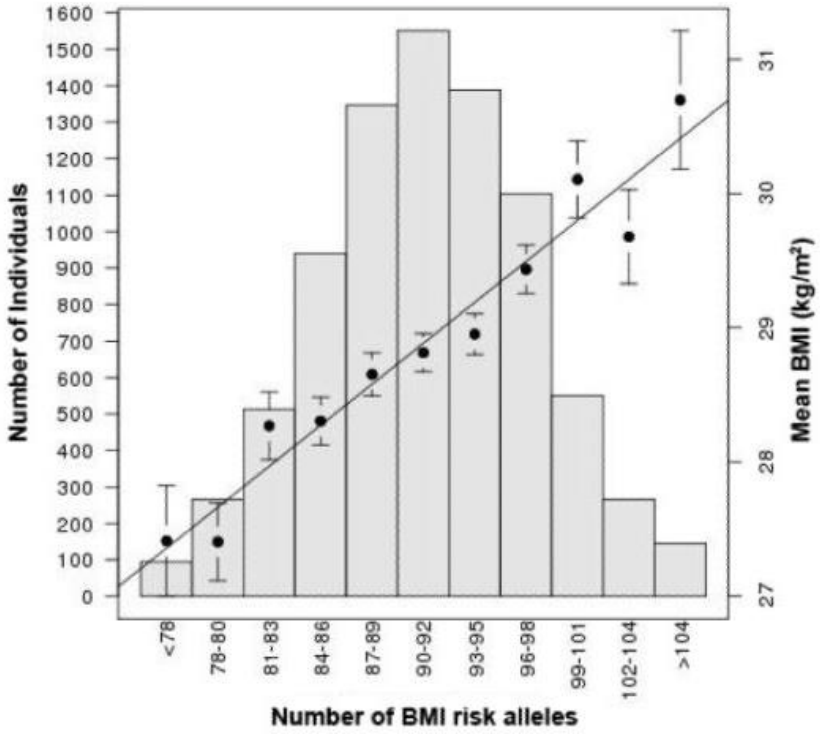
Nature
Author Manuscript HHS Public Access

Genetic studies of body mass index yield new insights for obesity biology

Adam E. Locke, Bratati Kahali, [...], and Elizabeth K. Speliotes

This analysis identified 97 BMI-associated loci, 56 of which are novel. The 97 loci account for ~**2.7% of BMI** variation, and genome-wide estimates suggest that common variation accounts for **>20%** of BMI variation.





Public Health Nutrition: page 1 of 8 doi:10.1017/S1368980013000074

Body composition and eating behaviours in relation to dieting involvement in a sample of urban Greek adolescents from the TEENAGE (TEENs of Attica: Genes & Environment) study

Ioanna Ntalla[1], Margarita Giannakopoulou[2], Panagiota Vlachou[1], Kalliope Giannitsopoulou[1], Vasiliki Gkesou[1], Chrysoula Makridi[1], Maria Marougka[1], Georgia Mikou[1], Kyriaki Ntaoutidou[1], Eirini Prountzou[1], Alexandra Tsekoura[1] and George V Dedoussis[1,*]

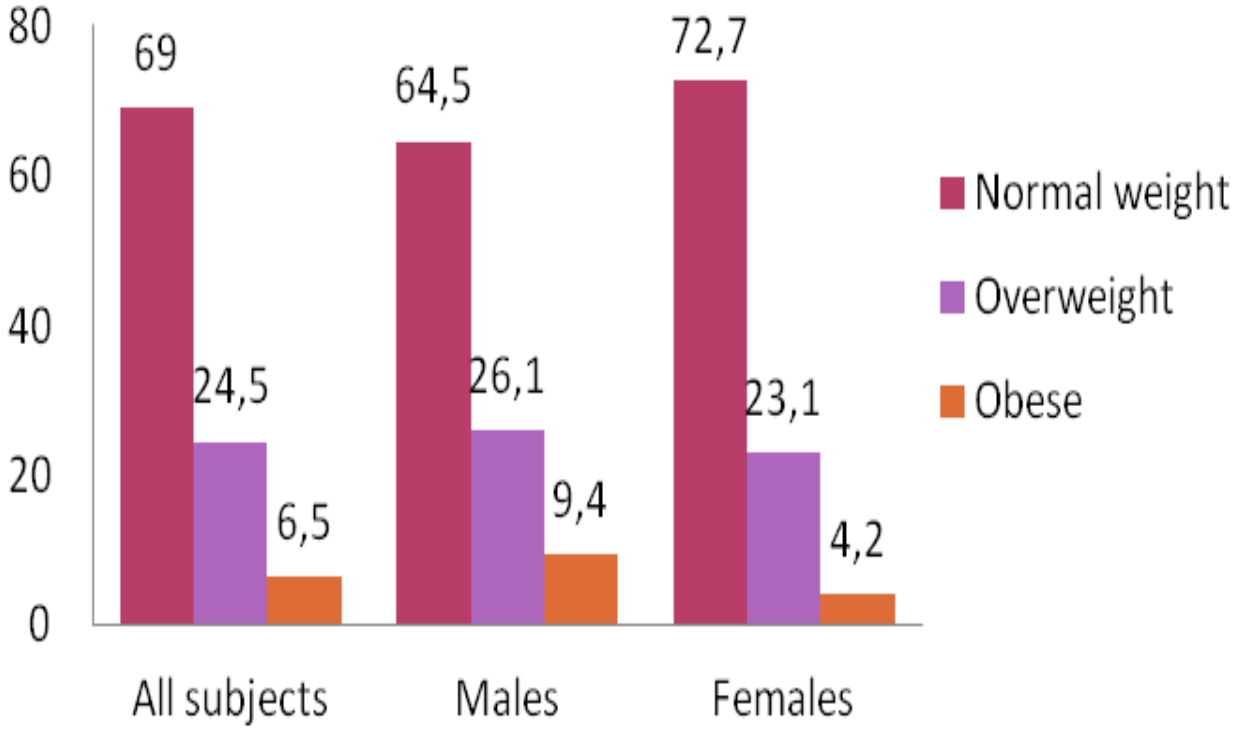


Figure 1 Prevalence (%) of overweight & obesity

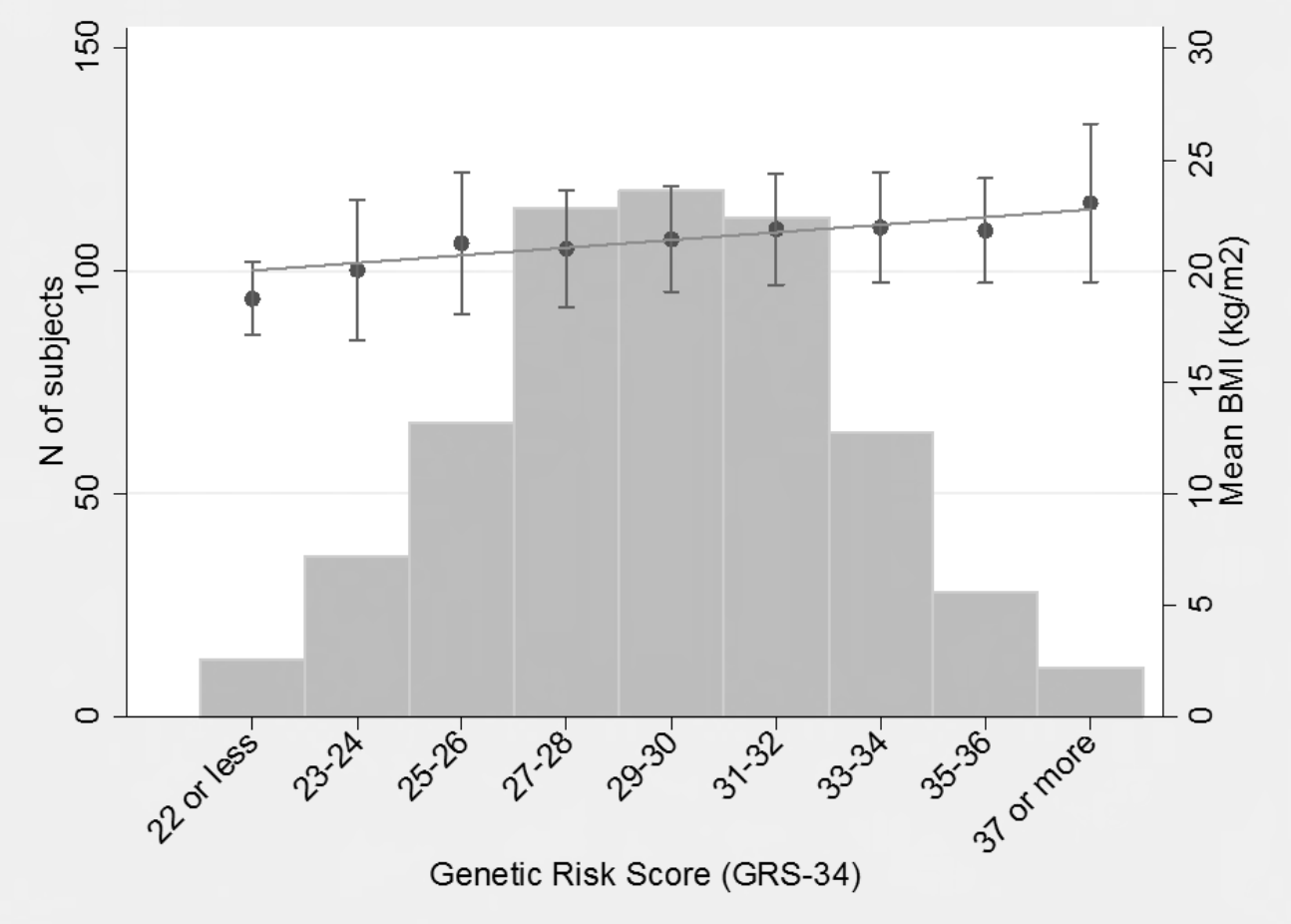
Ntalla et al, 2013

Annals of human genetics

Short Communication

doi: 10.1111/ahg.12012

Replication of Established Common Genetic Variants for Adult BMI and Childhood Obesity in Greek Adolescents: The TEENAGE Study



Ntalla et al, 2013

- Δημιουργήσαμε ένα γενετικό σκορ αθροίζοντας τις αλληλεπιδράσεις των αλληλομόρφων (GRS-34) για κάθε άτομο.
- Επιβεβαιώσαμε τις επιδράσεις των γενετικών τόπων *FTO, TMEM18, FAIM2*, *RBJ, ZNF608* and *QPCTL* στο BMI και στον κίνδυνο για υπέρβαρο ($p<0.05$).
- Ανάλυση στρωματοποιημένη με το φύλο έδειξε για τα TFAP2B and NEGR1 γενετικούς τόπους συσχέτιση με BMI και υπέρβαρο ($p<0.05$) στους άνδρες και στις γυναίκες αντίστοιχα.
- Το σκορ GRS-34 συσχετίστηκε με το BMI (**beta=0.17kg/m^2/allele;** $p<0.001$) και με τον κίνδυνο για υπέρβαρο (OR=1.09/allele; 95%CI: 1.04–1.16; $p=0.001$).

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Sugar-Sweetened Beverages and Genetic Risk of Obesity

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Table 1. Baseline Characteristics of the Participants in the Three Cohorts, According to Intake of Sugar-Sweetened Beverages.*

Characteristic	Servings of Sugar-Sweetened Beverages				P Value†
	<1 per Month	1–4 per Month	2–6 per Week	≥1 per Day	
NHS cohort					
Participants — no.	2843	1776	1496	819	
Age — yr	48.7±6.5	48.0±6.7	46.9±6.9	45.8±6.8	<0.001
BMI‡	24.5±4.6	24.5±4.7	24.9±4.8	25.2±5.7	<0.001
Alcohol consumption — g/day	7.7±11.1	5.8±9.9	5.5±8.9	5.3±9.7	<0.001
Current smoking — no. (%)	722 (25.4)	361 (20.3)	316 (21.1)	248 (30.3)	0.58
Physical activity — MET-hr/wk§	15.5±18.3	13.4±17.8	13.1±16.2	12.6±17.0	<0.001
Time spent watching television — hr/wk	13.4±12.0	13.4±11.5	13.5±11.2	13.6±12.0	0.67
Total energy intake — kcal/day	1460±457	1580±479	1690±475	1840±524	<0.001
Alternative Healthy Eating Index score¶	30.7±9.1	28.6±8.7	28.2±8.4	27.5±8.0	<0.001
Artificially sweetened beverages — servings/day	0.61±0.99	0.32±0.71	0.26±0.55	0.35±0.74	<0.001
Genetic-predisposition score‖	29.3±4.0	29.1±4.0	29.0±4.0	29.1±4.0	0.15
HPFS cohort					
Participants — no.	1627	1058	1338	400	
Age — yr	56.4±8.3	55.4±8.6	53.0±8.6	51.4±8.9	<0.001
BMI‡	25.7±3.4	25.7±3.3	25.9±3.3	26.0±3.3	0.07
Alcohol consumption — g/day	13.0±16.2	11.4±14.7	11.3±14.9	10.7±18.3	0.02
Current smoking — no. (%)	132 (8.1)	97 (9.2)	124 (9.3)	51 (12.8)	0.02
Physical activity — MET-hr/wk§	20.6±28.6	19.2±23.8	18.8±27.0	19.7±27.7	0.62
Time spent watching television — hr/wk	12.0±9.0	11.4±8.5	11.3±8.4	13.0±9.0	0.03
Total energy intake — kcal/day	1853±566	1967±570	2172±600	2458±633	<0.001
Alternative Healthy Eating Index score¶	46.2±11.7	44.9±10.7	43.4±10.1	41.2±10.6	<0.001
Artificially sweetened beverages — servings/day	0.67±1.11	0.40±0.78	0.35±0.67	0.30±0.71	<0.001
Genetic-predisposition score‖	29.3±4.0	29.0±4.0	29.2±4.0	29.0±4.0	0.57
WGHS cohort					
Participants — no.	9759	4780	5531	1670	
Age — yr	54.9±7.0	55.1±7.4	54.3±7.1	52.9±6.2	<0.001
BMI‡	25.8±4.8	25.7±4.7	25.7±4.9	26.1±5.4	0.03
Alcohol consumption — g/day	5.1±9.5	4.0±7.8	3.6±7.1	3.2±7.5	<0.001
Current smoking — no. (%)	985 (10.1)	508 (10.6)	678 (12.3)	326 (19.5)	<0.001
Physical activity — MET-hr/wk§	16.2±19.4	14.4±17.5	13.5±17.3	12.1±17.1	<0.001
Total energy intake — kcal/day	1613±488	1737±505	1847±527	2050±559	<0.001
Artificially sweetened beverages — servings/day	0.97±1.28	0.68±1.02	0.55±0.99	0.41±1.03	<0.001
Genetic-predisposition score‖	29.3±3.8	29.0±3.7	28.9±3.7	28.6±3.8	0.001

Τη δεκαετία **του 80** που έγιναν οι πρώτες μετρήσεις, έδειξαν ότι η κατανάλωση των αναψυκτικών ήταν κατά μέσο όρο, **0.33 αναψυκτικά/ημέρα**. Παρατηρήθηκε συσχέτιση της κατανάλωσης αναψυκτικών με την παχυσαρκία. Επίσης φάνηκε ότι μεγαλύτερη κατανάλωση αναψυκτικών ήταν χαρακτηριστική για νεώτερους σε ηλικία καταναλωτές, οι οποίοι κατανάλωναν λιγότερο αλκοόλ, και φυσική δραστηριότητα και μεγαλύτερη ενεργειακή πρόσληψη

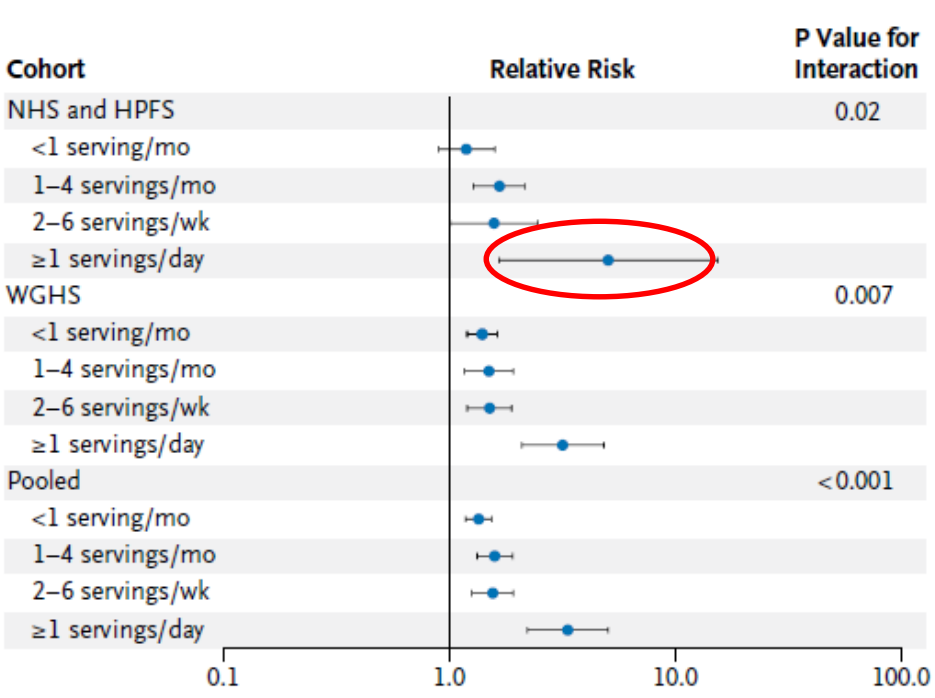


Figure 1. Relative Risk of the Development of Obesity per Increment of 10 Risk Alleles, According to Intake of Sugar-Sweetened Beverages.

For the discovery phase, with data from the Nurses' Health Study (NHS) and Health Professionals Follow-up Study (HPFS) cohorts, the analyses were based on 18 years of follow-up for 6402 initially nonobese women (1980 to 1998, 1107 incident cases of obesity) and 12 years of follow-up for 3889 initially nonobese men (1986 to 1998, 297 incident cases of obesity). Shown are the pooled relative risks of incident obesity, with adjustment for age, source of genotyping data, level of physical activity, status with respect to current smoking, alcohol intake, time spent watching television, Alternative Healthy Eating Index score, and total energy intake. For the replication phase, with data from the Women's Genome Health Study (WGHS) cohort, the analyses were based on a median of 6 years of follow-up for 18,127 initially nonobese women (1992 to 1998, 2280 incident cases of obesity). Shown are the relative risks of incident obesity, with adjustment for age, geographic region, eigenvectors, level of physical activity, status with respect to current smoking, alcohol intake, and total energy intake. Horizontal bars indicate 95% confidence intervals.

Στις τρεις προοπτικές μελέτες, άτομα που παρακολουθήθηκαν για μερικά χρόνια και **δεν ήταν παχύσαρκα** κατά την **πρώτη επίσκεψη**, η αυξημένη κατανάλωση αναψυκτικών συνδέθηκε με ανάπτυξη παχυσαρκίας για κάθε αύξηση 10 αλληλομόρφων κινδύνου. Είναι χαρακτηριστικό ότι άτομα που καταναλώνανε όλα αυτά τα χρόνια τουλάχιστον **1 αναψυκτικό την ημέρα**, είχαν **πενταπλάσιο κίνδυνο** να γίνουν παχύσαρκοι όταν είχαν ταυτόχρονα και αυξημένη γενετική προδιάθεση.

Table 2. Increase in BMI per Increment of 10 Risk Alleles, According to Intake of Sugar-Sweetened and Artificially Sweetened Beverages in the NHS and HPFS Cohorts.*

Analysis	Increase in BMI				P Value for Interaction
	<1 Serving per Month	1–4 Servings per Month	2–6 Servings per Week	≥1 Serving per Day	
Sugar-sweetened beverages					
NHS cohort					
Model 1†	1.17±0.18	1.66±0.16	1.84±0.23	2.12±0.39	0.004
Model 2‡	1.18±0.17	1.56±0.16	1.78±0.22	2.03±0.38	0.008
HPFS cohort					
Model 1†	0.80±0.20	0.42±0.21	1.05±0.19	1.59±0.37	0.06
Model 2‡	0.77±0.19	0.43±0.20	1.08±0.19	1.54±0.37	0.02
Pooled cohorts§					
Model 1†	1.00±0.13	1.20±0.13	1.37±0.15	1.85±0.27	<0.001
Model 2‡	1.00±0.13	1.12±0.12	1.38±0.14	1.78±0.27	<0.001
Artificially sweetened beverages					
NHS cohort					
Model 1†	1.43±0.20	1.37±0.21	1.43±0.20	1.42±0.29	0.88
Model 2‡	1.42±0.18	1.25±0.21	1.39±0.20	1.36±0.27	0.91
HPFS cohort					
Model 1†	0.94±0.18	0.78±0.24	0.40±0.20	1.04±0.31	0.63
Model 2‡	0.95±0.18	0.76±0.23	0.45±0.20	0.92±0.29	0.46
Pooled cohorts§					
Model 1†	1.16±0.13	1.11±0.16	0.92±0.14	1.24±0.21	0.83
Model 2‡	1.19±0.13	1.03±0.16	0.92±0.14	1.16±0.20	0.64

* Plus–minus values are β coefficients ±SE. Data were derived from repeated-measures analysis for women in the NHS (five measures during the period from 1980 to 1998) and for men in the HPFS (three measures during the period from 1986 to 1998). Data on beverage intake were assessed 4 years before the assessment of BMI.

† Data were adjusted for age and source of genotyping data.

‡ Data were further adjusted for level of physical activity, time spent watching television, status with respect to current smoking, alcohol intake, Alternative Healthy Eating Index score, and total energy intake.

§ Results for the two cohorts were pooled by means of inverse-variance–weighted, fixed-effects meta-analyses.

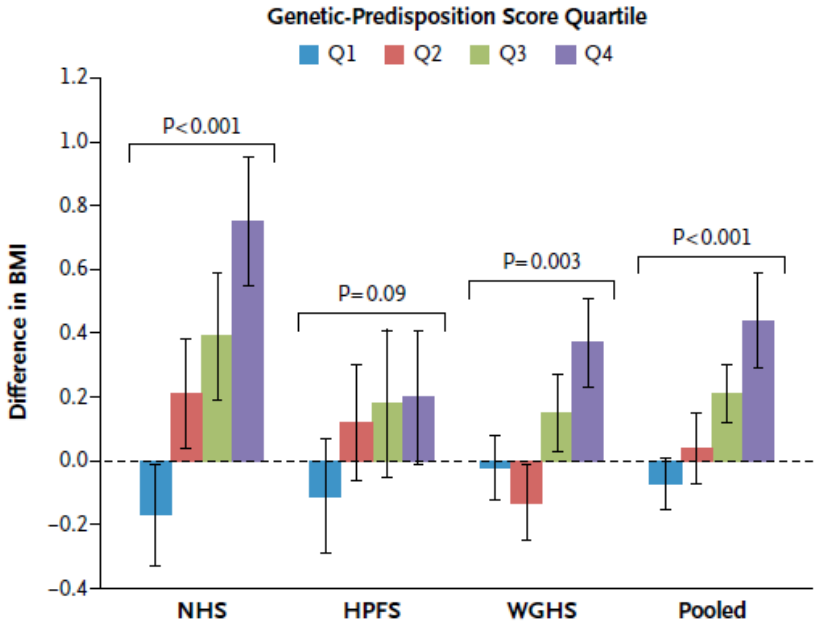
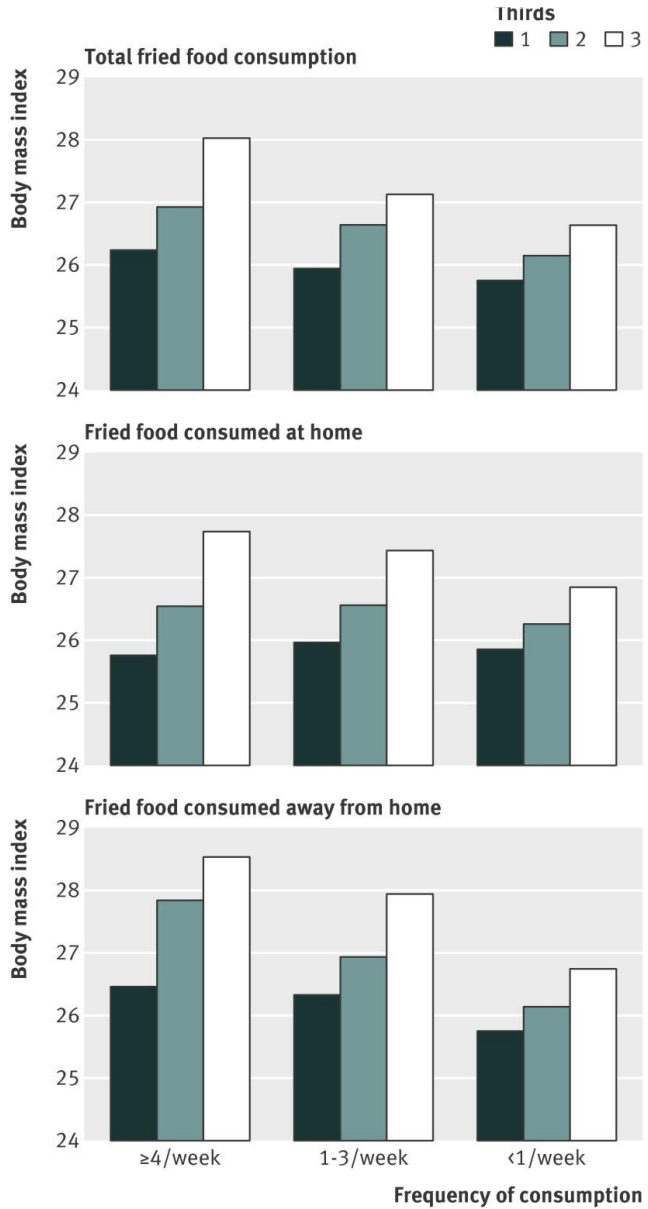


Figure 2. Difference in BMI Associated with One Serving of a Sugar-Sweetened Beverage per Day, According to the Quartile of the Genetic-Predisposition Score.

Data are effect sizes (β coefficients [±SE]) of sugar-sweetened beverage intake (one serving per day) on body-mass index (BMI; the weight in kilograms divided by the square of the height in meters), stratified according to the quartile of the genetic-predisposition score. In the NHS cohort, the median scores across the quartiles were 24.5 (range, 13.1 to 26.3), 27.8 (range, 26.4 to 29.0), 30.3 (range, 29.1 to 31.7), and 33.6 (range, 31.8 to 43.4); in the HPFS cohort, 24.9 (range, 16.0 to 26.5), 27.9 (range, 26.6 to 29.1), 30.4 (range, 29.2 to 31.7), and 33.6 (range, 31.8 to 41.9); and in the WGHS cohort, 24.7 (range, 15.3 to 26.5), 27.8 (range, 26.6 to 29.1), 30.3 (range, 29.2 to 31.6), and 33.4 (range, 31.7 to 43.4). In the NHS and HPFS cohorts, the analyses were based on data from the first 4 years in women (1980 to 1984) and men (1986 to 1990), respectively, with adjustment for age, source of genotyping data, level of physical activity, time spent watching television, status with respect to current smoking, alcohol intake, and Alternative Healthy Eating Index score. In the WGHS cohort, the analyses were based on data from the first 3 years, with adjustment for age, geographic region, eigenvectors, level of physical activity, status with respect to current smoking, and alcohol intake. P values are for interaction. I bars indicate standard errors.

Fried food consumption, genetic risk, and body mass index: gene-diet interaction analysis in three US cohort studies

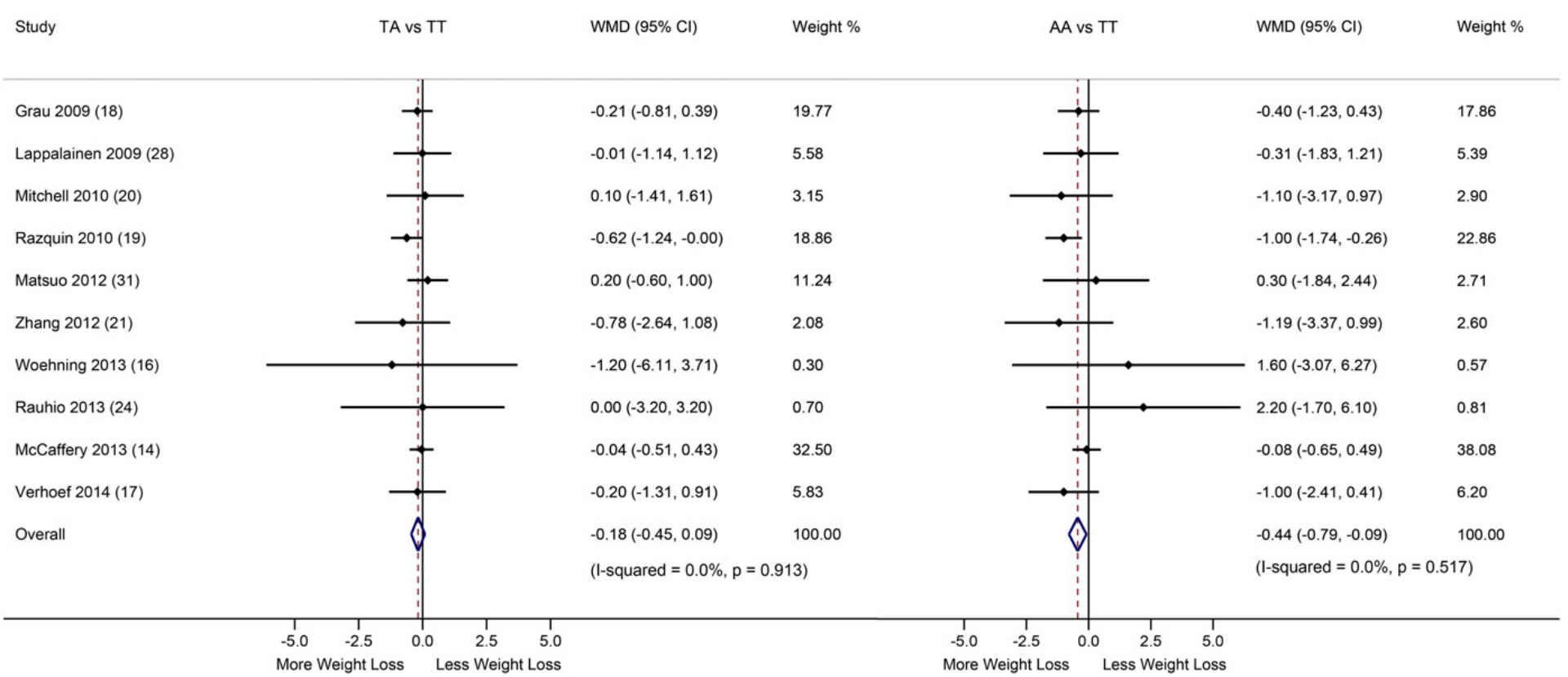


Η σχέση της κατανάλωσης τηγανιτών και παχυσαρκίας διαφέρει με βάση την διαφορετική γενετική προδιάθεση

BMJ 2014;348:g1610 doi: 10.1136/bmj.g1610

FTO genotype and weight loss in diet and lifestyle interventions: a systematic review and meta-analysis[1,2]

*Lingwei Xiang,[3] Hongyu Wu,[4] An Pan,[5] Bhakti Patel,[3] Guangda Xiang,[6] Lu Qi,[4,7] Robert C Kaplan,[3] Frank Hu,[4,7] Judith Wylie-Rosett,[3] and Qibin Qi[3]**



This meta-analysis of 14 studies (comprising 7700 participants) present the results of dominant genetic models indicated **a 0.20-kg** greater weight loss in the TA/AA genotype than in the TT genotype

Am J Clin Nutr doi: 10.3945/ajcn.115.123448

FTO genotype and weight loss: systematic review and meta-analysis of 9563 individual participant data from eight randomised controlled trials

Katherine M Livingstone,[1,2] Carlos Celis-Morales,[1,3] George D Papandonatos,[4] Bahar Erar,[4] Jose C Florez,[5,6] Kathleen A Jablonski,[7] Cristina Razquin,[8,9] Amelia Marti,[9,10] Yoriko Heianza,[11] Tao Huang,[11,12] Frank M Sacks,[13] Mathilde Svendstrup,[14,15] Xuemei Sui,[16] Timothy S Church,[17] Tiina Jääskeläinen,[18,19] Jaana Lindström,[20] Jaakko Tuomilehto,[21,22] Matti Uusitupa,[18] Tuomo Rankinen,[23] Wim H M Saris,[24] Torben Hansen,[14] Oluf Pedersen,[14] Arne Astrup,[25] Thorkild I A Sørensen,[14,26] Lu Qi,[11,13] George A Bray,[17] Miguel A Martinez-Gonzalez,[9,10] J Alfredo Martinez,[9,10,27] Paul W Franks,[13,28] Jeanne M McCaffery,[29] Jose Lara,[1,30] John C Mathers[1]

Table 1 | Characteristics of studies included in qualitative synthesis (n=10 000) and meta-analysis (n=9563)

	No of participants					Intervention				Mean (SD)	
Study	All	Men	Women	SNP	MAF	Type	Length	Region	Ethnicity	Age (years)	BMI
DPP[20]	2835	962	1873	rs9939609	40.9	Drug and lifestyle	1 year	North America	Mixed	51.0 (10.6)	34.0 (6.7)
DREW[14]	278	—	278	rs8050136*	41.0	Exercise	6 months	North America	Mixed	57.3 (6.7)	31.8 (3.8)
Finnish DPS[21]	264	97	167	rs9939609	41.5	Diet and exercise	3 years	Europe	White	54.8 (7.2)	31.1 (4.6)
Food4Me [36]	671	313	358	rs9939609	44.3	Diet and exercise	6 months	Europe	White	43.3 (12.5)	27.8 (4.7)
Look AHEAD[15]	3637	1601	2036	rs9939609	44.5	Diet and exercise	1 year	North America	Mixed	59.1 (6.9)	36.2 (6.0)
POUNDS LOST[16]	600	240	360	rs9939609	45.1	Diet	2 years	North America	White	51.6 (9.1)	32.6 (3.9)
PREDIMED[13]	735	335	400	rs9939609	41.6	Diet	3 years	Europe	White	67.6 (6.0)	29.2 (3.3)
NUGENOB[17]	543	136	407	rs9939609	41.5	Diet	10 weeks	Europe	White	36.8 (7.9)	35.7 (5.0)
Ramos et al[37]	86	-	86	rs9939609	NE	Drug	6 months	South America	White	51 (3.0)	26.6 (2.8)
De Luis et al[38]	305	80	225	rs9939609	44.1	Diet	3 months	Europe	NE	43.5 (15.3)	36.6 (6.6)
MOVE![39]	46	33	13	rs9939609	NE	Diet	8 weeks	North America	Mixed	NE	NE

SNP=single nucleotide polymorphism; MAF=minor allele frequency for all randomised participants who provided genetic consent and whose DNA data passed quality control procedures; BMI=body mass index; NE=not estimable based on data in published manuscript.
*SNP rs8050136 was in high linkage disequilibrium with rs9939609 (HapMap US residents of European ancestry: r^2>0.84).

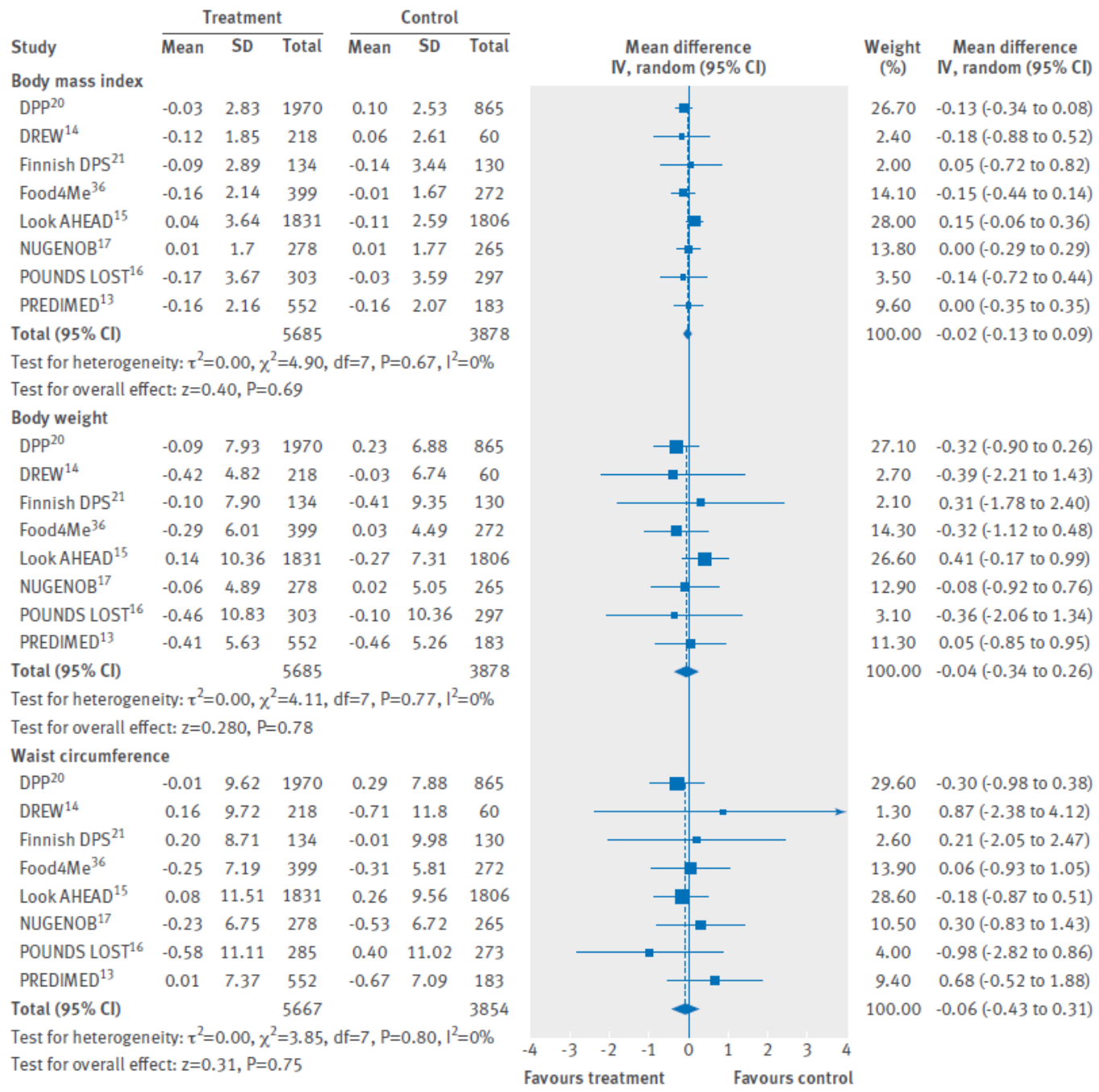


Fig 2 | Forest plot of change in body mass index, body weight, and waist circumference after weight loss intervention for each copy of the FTO minor allele (rs9939609 genotype or a proxy) in treatment versus control arm in random effects

This systematic review and meta-analysis of individual participant data reveals that carriage of the **FTO minor allele**, associated with risk of obesity in the general population as well as baseline adiposity in the present study, **was not associated** with changes in body mass index, body weight, or waist circumference in response to weight loss intervention.

It is shown that weight loss in those carrying the FTO minor allele is similar to the rest of the population after dietary, exercise, or drug based interventions.

Physical activity and FTO genotype by physical activity interactive influences on obesity

Joon Young Kim[1], Jacob T. DeMenna[2], Sobha Puppala[3], Geetha Chittoor[4], Jennifer Schneider[3], Ravindranath Duggirala[5], Lawrence J. Mandarino[2,6], Gabriel Q. Shaibi[1,6,7] and Dawn K. Coletta[2,6*]

Measurements, physical activity questionnaire

Table 1 Descriptive characteristics of participants by groups ("yes" responders vs. "no" responders at regular PA questionaire)[a]

	PA-Yes ($n = 389$)	PA-No ($n = 271$)	Total ($n = 660$)	P-value
Age (years)	31.1 ± 13.6	33.1 ± 13.0	31.7 ± 13.4	0.053
Sex (male/female), *n* (%)	186 (48)/203 (52)	71 (26)/186 (74)	260 (39)/407 (61)	<0.001
BMI (kg/m^2)[b]	27.9 ± 6	30.1 ± 7.3	28.8 ± 6.6	<0.001
Fat mass (kg)[b]	20.4 ± 10.3	25.4 ± 12.1	22.4 ± 11.3	<0.001
Hip circumference (cm)[b]	104.6 ± 12.4	108.5 ± 14.6	106.1 ± 13.5	<0.01
Waist circumference (cm)[b]	93.3 ± 15.2	98.5 ± 16.8	95.3 ± 16.1	<0.001

Data are mean ± SD unless otherwise indicated. A total of 667 participants participated in the study. Of the 667 participants, data for PA questionnaire, body mass index (BMI), fat mass, hip circumference and waist circumference were not available for 7, 3, 8, 7, and 7, respectively

[a]Not accounted for the relatedness of study participants; [b]Adjusted for age and sex effects

Kim *et al. BMC Genetics* (2016) 17:47
DOI 10.1186/s12863-016-0357-6

Table 2 Interaction between PA and FTO SNPs on adiposity-related phenotype

SNP rs no.	Phenotype	Major/major		Major/minor		Minor/minor		P[a]
		PA_Yes	PA_No	PA_Yes	PA_No	PA_Yes	PA_No	
rs3751812 (G/**T**)	BMI	27.8 ± 6.1	28.9 ± 6.4	28.2 ± 5.7	31.2 ± 7.1	30.9 ± 4.8	37.3 ± 8.3	0.08
	Fat mass	20.2 ± 10.9	24.2 ± 11.6	21.1 ± 9.7	27.5 ± 12.8	26.3 ± 8.5	38.4 ± 16.5	0.12
	HC	104.2 ± 12.7	106.5 ± 13.3	105.5 ± 11.5	110.9 ± 13.7	111.2 ± 9.8	122.7 ± 16.1	0.13
	WC	92.7 ± 15.3	96.5 ± 16.3	94.2 ± 14.7	100.4 ± 16.1	102.5 ± 13.3	111.5 ± 19.4	0.46
rs8050136 (C/**A**)	BMI	28.0 ± 6.1	28.9 ± 6.5	27.9 ± 5.7	30.9 ± 7.0	30.7 ± 4.9	34.7 ± 9.0	0.14
	Fat mass	20.5 ± 11.0	24.4 ± 11.8	20.6 ± 9.7	27.1 ± 12.6	25.4 ± 8.6	33.2 ± 17.4	0.10
	HC	104.6 ± 12.5	106.6 ± 13.4	104.8 ± 12.0	110.4 ± 13.7	109.9 ± 10.0	118.3 ± 16.8	0.14
	WC	92.9 ± 15.2	96.8 ± 16.6	93.8 ± 14.9	100.0 ± 15.9	100.7 ± 14.3	105.8 ± 20.8	0.61
rs9939609 (T/**A**)	BMI	27.9 ± 6.2	28.8 ± 6.4	28.0 ± 5.7	30.9 ± 7.0	30.6 ± 4.8	34.7 ± 9.0	0.60
	Fat mass	20.4 ± 11.1	24.3 ± 11.8	20.8 ± 9.6	27.1 ± 11.8	25.3 ± 8.4	33.2 ± 17.4	0.17
	HC	104.4 ± 12.8	106.4 ± 13.2	105.0 ± 11.7	110.3 ± 13.6	109.9 ± 9.7	118.3 ± 16.8	0.21
	WC	92.7 ± 15.5	96.6 ± 16.6	94.1 ± 14.6	100.0 ± 15.8	100.2 ± 14.1	105.8 ± 20.8	0.78

Data are mean ± SD unless otherwise indicated. SNP rs no (Major allele/Minor allele) and bold allele indicates risk allele; BMI, body mass index; HC, hip circumference; WC, waist circumference. rs3751812 (major allele [G]; minor allele [T]); rs8050136 (major allele [C]; minor allele [A]); rs9939609 (major allele [T]; minor allele [A])

[a]P-values from the genetic analyses regarding the significance of the intercation terms

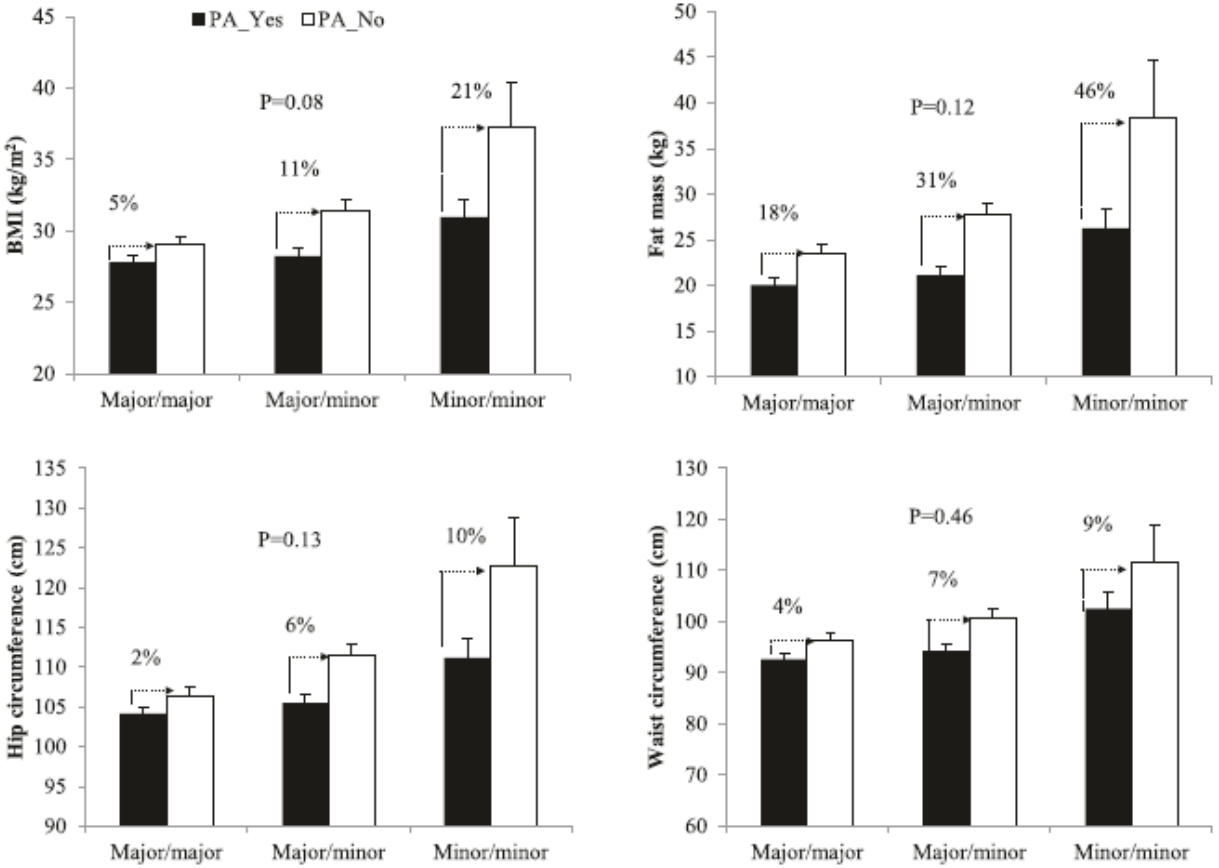


Fig. 1 Interaction between PA and FTO SNP rs3751812 on adiposity-related phenotypes. Major allele (G)/minor allele (T); minor allele T considered risk allele

To our knowledge, the majority of interaction studies have focused on European populations [9, 26] and a lack of data exist in the Latino population, even though it is well established that Latinos are at increased risk for obesity and type 2 diabetes [10]. Therefore, our data are relevant as we exclusively focused on Latino children

Physical Activity Attenuates the Effect of the *FTO* Genotype on Obesity Traits in European Adults: The Food4Me Study

Carlos Celis-Morales[1], Cyril F.M. Marsaux[2], Katherine M. Livingstone[1], Santiago Navas-Carretero[3,4], Rodrigo San-Cristobal[3,4], Clare B. O'donovan[5], Hannah Forster[5], Clara Woolhead[5], Rosalind Fallaize[6], Anna L. Macready[6], Silvia Kolossa[7], Jacqueline Hallmann[7], Lydia Tsirigoti[8], Christina P. Lambrinou[8], George Moschonis[8], Magdalena Godlewska[9], Agnieszka Surwiłło[9], Keith Grimaldi[10], Jildau Bouwman[11], Yannis Manios[8], Iwona Traczyk[9], Christian A. Drevon[12], Laurence D. Parnell[13], Hannelore Daniel[7], Eileen R. Gibney[5], Lorraine Brennan[5], Marianne C. Walsh[4], Mike Gibney[5], Julie A. Lovegrove[6], J. Alfredo Martinez[3,4], Wim H.M. Saris[2], and John C. Mathers[1], on behalf of the Food4Me Study

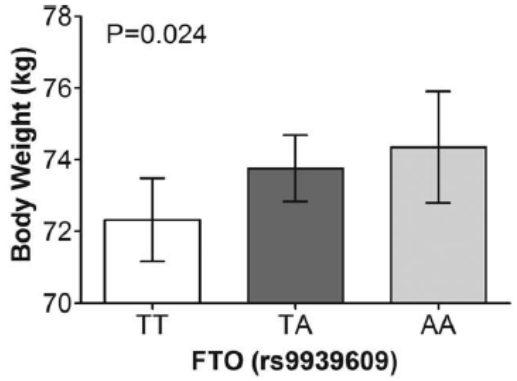
Obesity (2016) **24**, 962-969. doi:10.1002/oby.21422

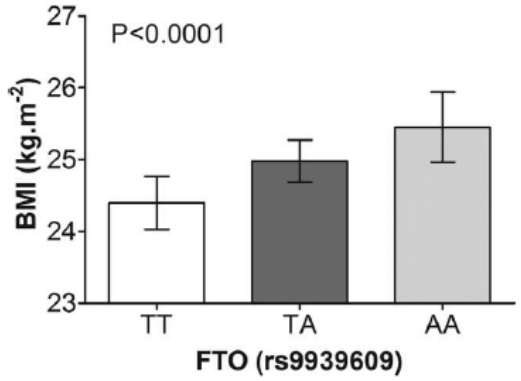
PA measures and analysis

PA levels (PAL) and time spent in sedentary behaviors were measured objectively using triaxial accelerometers (TracmorD, Philips Consumer Lifestyle, The Netherlands) (24). All participants were instructed to wear the accelerometer every day during waking hours, except when taking a shower, for the whole duration of the study. For the analyses reported in this article, data collected over 2 weeks at baseline were used. Participants were instructed to upload their PA data into the study server via the Internet.

TABLE 1 Characteristics of Food4Me study participants

Variable	Overall	Men	Women
N	1,280	537	743
Age (years)	39.9 (13.0)	41.6 (13.4)	38.7 (12.5)
Anthropometric			
Height (m)	1.71 (0.09)	1.79 (0.07)	1.65 (0.06)
Body weight (kg)	74.7 (15.8)	83.4 (13.5)	68.5 (14.3)
BMI (kg m^{-2})	25.5 (4.8)	26.1 (4.1)	24.9 (5.2)
Underweight ($<$18.5 kg m^{-2}; %)	2.6	0.8	3.8
Normal weight ($\geq$18.5 to $<$25.0 kg m^{-2}; %)	51.3	44.7	56.0
Overweight ($\geq$25.0 to $<$30.0 kg m^{-2}; %)	30.3	38.4	24.6
Obesity ($\geq$30.0 kg m^{-2}; %)	15.8	16.1	15.6
WC (cm)	85.7 (13.8)	92.7 (12.1)	80.7 (12.8)
Central obesity (%)[a]	24.3	22.8	25.6
Physical activity (PA)			
PAL	1.73 (0.18)	1.74 (0.2)	1.72 (0.2)
Sedentary time (min day^{-1})	744.8 (76.6)	738.9 (82.3)	749.1 (71.5)
Light PA (min day^{-1})	73.9 (30.4)	74.0 (29.8)	73.9 (30.9)
Moderate PA (min day^{-1})	33.3 (20.4)	37.3 (21.1)	30.3 (19.4)
Vigorous PA (min day^{-1})	11.8 (16.1)	16.7 (18.1)	8.17 (13.1)
Moderate-equivalent PA (min day^{-1})	56.9 (45.0)	70.9 (49.1)	46.7 (38.4)
Moderate-equivalent PA in 10-min bouts (min day^{-1})	29.2 (32.3)	36.5 (35.9)	23.8 (28.1)
Active individuals ($\geq$150 min $week^{-1}$ moderate-equivalent PA in bouts; %)	47.0	56.5	40.0





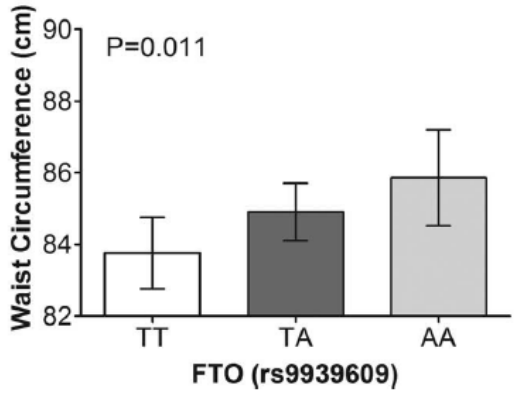


Figure 1 Association between *FTO* rs9939609 genotype and adiposity measures. Least-squares means of genotypes were calculated by using Robust Linear Regression, with adjustment for age, sex, and country.

TABLE 2 Association of *FTO* rs9939609 genotype with obesity-related traits

Variable	Beta or OR (95% CI)	*P*
Anthropometric		
Body weight (kg)	1.09 (0.14 to 2.04)	0.024
BMI (kg m^{-2})	0.54 (0.23 to 0.83)	<0.0001
WC (cm)	1.07 (0.24 to 1.90)	0.011
Overweight or obesity[a]	1.32 (1.12 to 1.54)	0.001
Central obesity[a]	1.13 (0.95 to 1.36)	0.158

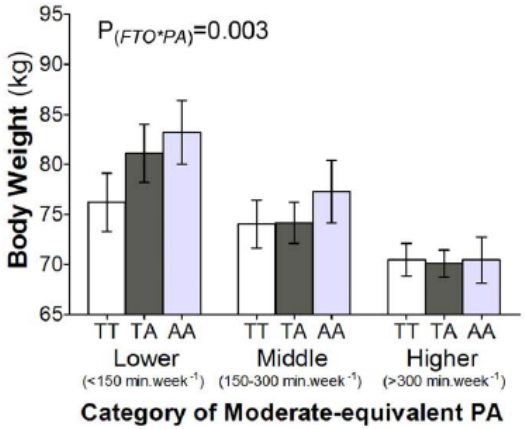
Data presented as beta coefficient or odds ratio (OR) with their corresponding 95% confidence interval (CI).
Models were adjusted for age, sex, and country. Physical activity variables were additionally adjusted for monitor wear time and season. Allele frequencies were TT ($n = 469$), TA ($n = 739$), and AA ($n = 264$).
[a]Overweight or obesity was defined as BMI ≥ 25.0 kg m^{-2}(normal weight was used as reference group). Central obesity was defined as WC >88 cm for women and >102 cm for men (individuals with no central obesity were used as reference group).

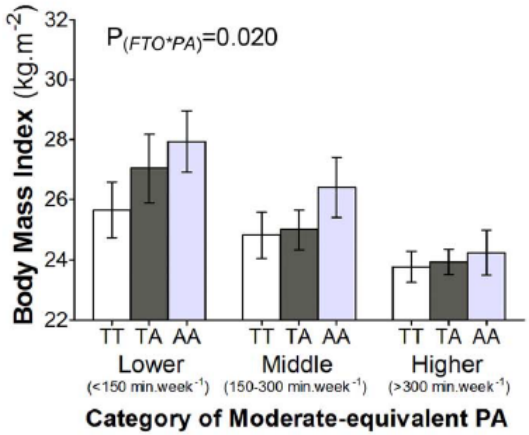
TABLE 3 Association between the *FTO* rs9939609 genotype and obesity measures by category of moderate-equivalent physical activity (PA)

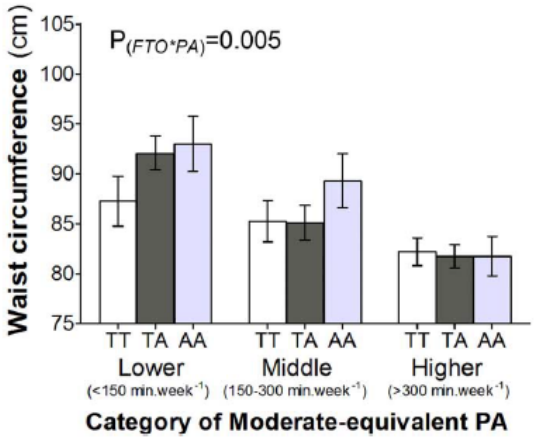
Variables	Low PA ($n = 288$), Beta or OR (95% CI)	*P*	Middle PA ($n = 306$), Beta or OR (95% CI)	*P*	High PA ($n = 686$), Beta or OR (95% CI)	*P*	$P_{(FTO*PA)}$
Body weight (kg)	3.53 (0.93 to 6.11)	0.008	1.42 (−0.84 to 3.67)	0.217	−0.28 (−1.48 to 0.91)	0.644	0.003
BMI (kg m^{-2})	1.06 (0.14 to 1.99)	0.024	0.68 (−0.08 to 0.15)	0.082	0.16 (−0.21 to 0.52)	0.388	0.020
WC (cm)	2.72 (0.43 to 5.01)	0.019	1.81 (−0.22 to 2.84)	0.081	−0.49 (−1.6 2 to 0. 64)	0.393	0.005
BMI ≥ 25.0 (kg m^{-2})[a]	1.65 (1.10 to 2.45)	0.014	1.30 (0.94 to 1.79)	0.112	1.22 (0.93 to 1.56)	0.102	0.173
Central obesity[a]	1.04 (0.71 to 1.51)	0.824	1.22 (0.84 to 1.76)	0.285	1.02 (0.73 to 1.39)	0.923	0.902

Data presented as adjusted beta coefficient or odds ratio (OR) with their corresponding 95% confidence interval (CI).
All models are adjusted for age, sex, country, season and monitor wear time. Beta or OR is the increase in trait per each copy of the risk allele; *P*-value for *FTO* and PA category interaction is the difference in trait per minor allele of rs9939069 comparing individuals with lower (<150 min $week^{-1}$), middle (150-300 min $week^{-1}$) and higher (>300 min $week^{-1}$) levels of moderate-equivalent PA.
[a]Overweight or obesity was defined as BMI ≥ 25.0 kg m^{-2} (normal weight was used as reference group). Central obesity was defined as WC >88 cm for women and >102 cm for men (individuals with no central obesity were used as reference group).

traits. We found that the influence of the *FTO* risk allele on BMI was 36% and 84% lower in individuals achieving between 150 and 300 min $week^{-1}$ or above 300 min $week^{-1}$ of moderate-equivalent PA, respectively, than in inactive individuals (<150 min $week^{-1}$).



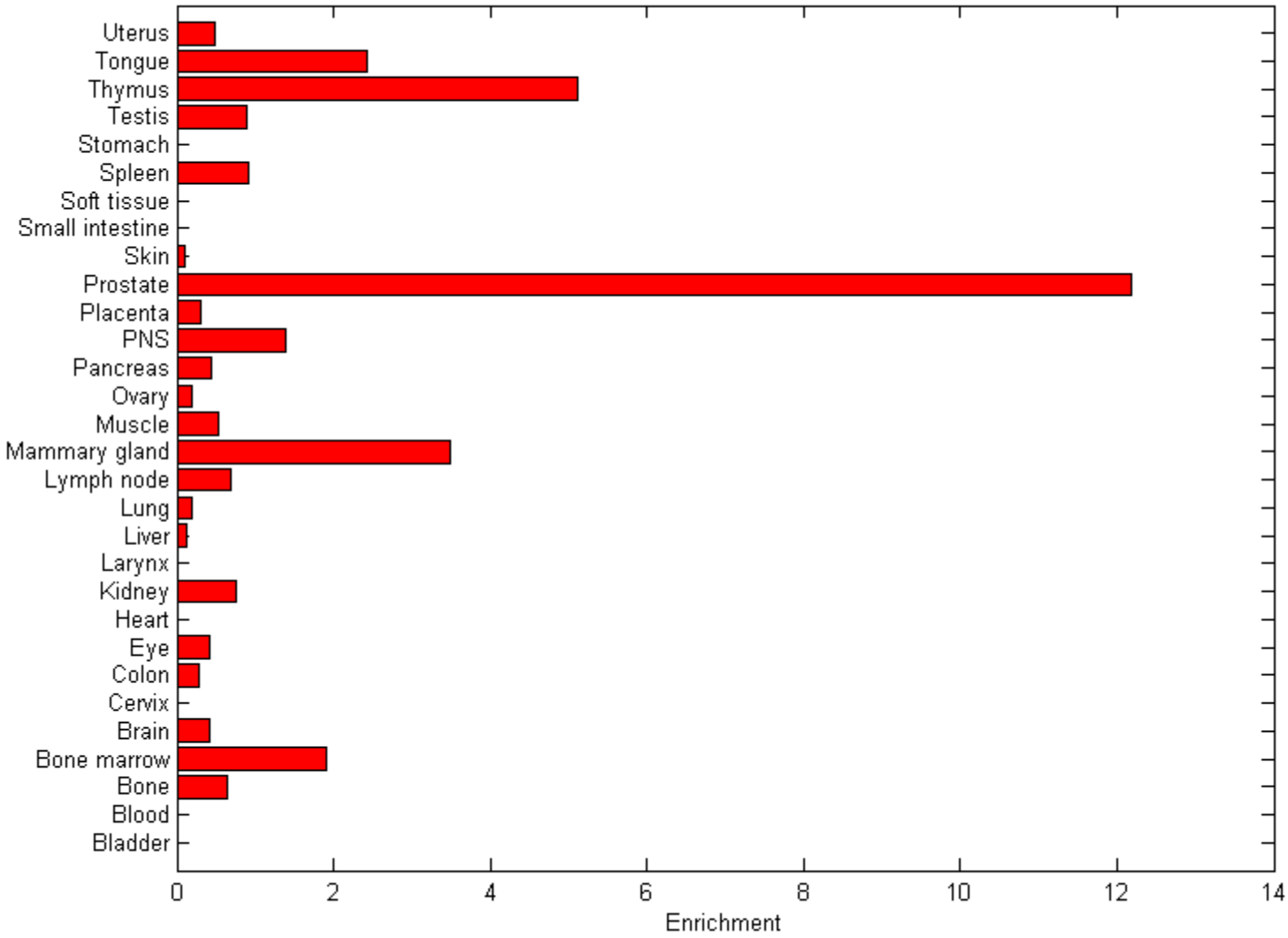




Screen time behaviors may interact with obesity genes, independent of physical activity, to influence adolescent BMI in an ethnically-diverse cohort

M Graff[1,2], **KE North**[1,3], **AS Richardson**[2], **K M Young**[1,2], **KL Mohlke**[3,4], **LA Lange**[3,4], **EM Lange**[3,4], **KM Harris**[2,3,5], and **P Gordon-Larsen**[2,6]

Pediatr Obes. 2013 December ; 8(6): . doi:10.1111/j.2047-6310.2013.00195.x.

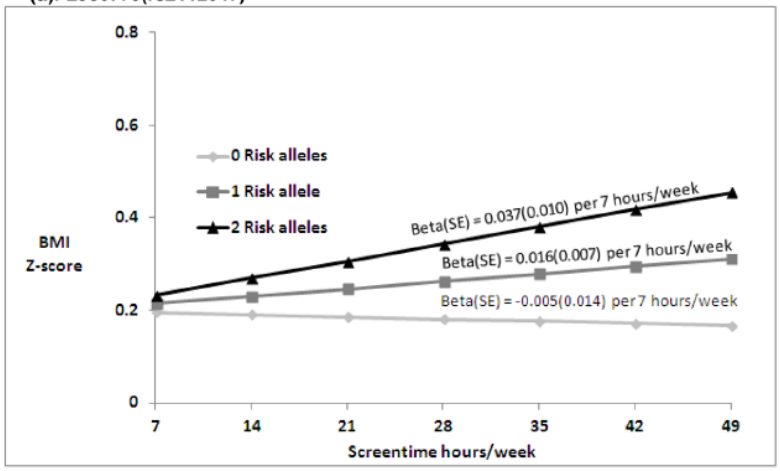


Homo sapiens hypothetical protein FLJ35779 (FLJ35779), mRNA

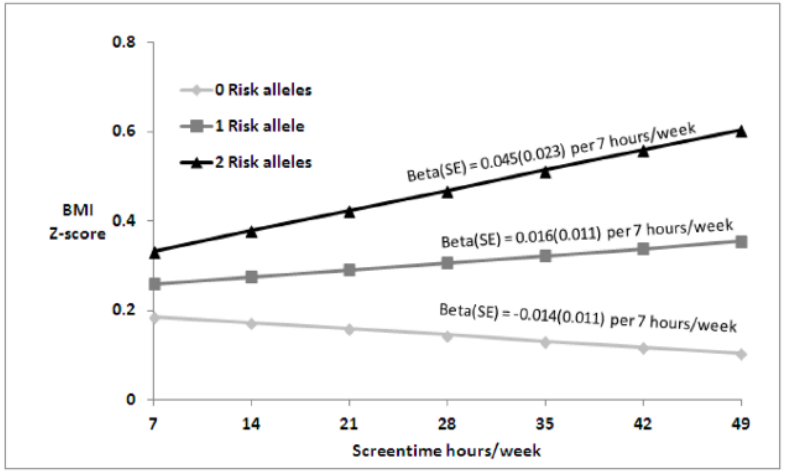
GNPDA2

The protein encoded by this gene is an allosteric enzyme that catalyzes the reversible reaction converting D-glucosamine-6-phosphate into D-fructose-6-phosphate and ammonium. Variations of this gene have been reported to be associated with influencing body mass index and susceptibility to obesity. A pseudogene of this gene is located on chromosome 9. Alternative splicing results in multiple transcript variants that encode different protein isoforms.

(a)*FLJ35779*(rs2112347)



(b)*GNPDA2* (rs10938397)



Although we find suggestive evidence that ST may exacerbate the influence of *FLJ35779 in* EA and *GNPDA2* in AA on BMI Z-score, strong evidence for interaction between the majority of established obesity loci and ST on BMI is lacking. However, our study was powered to detect fairly large interactions, which we did not observe. These estimates are an important resource that should pooled with other samples for meta-analyses. Indeed, our findings are relevant to the larger discussion of obesity susceptibility and modifiable behaviors influencing BMI.

Pediatr Obes. 2013 December ; 8(6): . doi:10.1111/j.2047-6310.2013.00195.x.