Physical activity attenuates the influence of *FTO* variants on obesity; a meta-analysis of 218,166 adults and 19,268 children

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Text S1 - Table 1. Number of individuals, study design, and participant characteristics for studies of adults participating in the meta-analyses

Study		Study design	Primary outcome	Total sample	Participants	Analysis*	Reference
Short name	Full name	Study design	riillary outcome	size	Farticipants	Allalysis	PubMed ID
AGES-Reykjavik	Age/Gene Environment Susceptibility Reykjavik Study	Population-based cohort of adults born between 1907-1935	Disease and disability in old age	3,197	white (1,347 men, 1,850 women)	Locally	17351290
ARIC	Atherosclerosis Risk in Communities	Multi-center cohort of 45-64-year old adults	Atherosclerosis and variation in cardiovascular risk factors	10,890	white (5,128 men, 5,762 women)	Locally	2646917
Birth Cohort 1958	British Birth Cohort 1958	Birth cohort	Health, educational and social development during lifecourse	5,486	white (2,614 men, 2,872 women)	Locally	16155052
BLSA	Baltimore Longitudinal Study of Aging	Population-based cohort of adults	Changes occurring with normal aging	708	white (326 men, 382 women)	Locally	Shock NW, et al. NIH publication no.84-2450 (1984).
BWHHS	British Women's Heart & Health Study	Cohort of 60-79-year-old women	Cardiovascular risk factors and incidence of cardiovascular disease	3,107	white women	Centrally	12540690
CLHNS	Cebu Longitudinal Health and Nutrition Survey	Cohort of women who gave birth in 1983-1984	Maternal health	1,711	Filippino women	Locally	20507864
CoLaus	Cohorte Lausanneoise	Population-based, cross- sectional study of adults	Cardiovascular risk factors	5,342	white (2,530 men, 2,812 women)	Locally	18366642
DESIR	Data from an Epidemiological Study on the Insulin Resistance Syndrome	Cohort of middle-aged adults	Cardiovascular risk factors	4,640	white (2,308 men, 2,332 women) (~0.30% of overall DESIR population estimated to be of non- European ancestry; individuals born outside France excluded for the present study)	Locally	9416436
DPP	The Diabetes Prevention Program	Randomized controlled trial in overweight or obese adults	Incidence of type 2 diabetes	3,364	white (683 men, 1,267 women), African American (179 men, 510 women), Asian (83 men, 66 women), and Hispanic (193 men, 383 women) American-Indian individuals were excluded due to their small number.	Locally	11832527

Study		Study design	Primary outcome	Total sample	Participants	Analysis*	Reference
Short name	Full name	otacy acoign	rimary outcome	size	r artisipants	7 11101 4010	PubMed ID
DPS	The Diabetes Prevention Study	Randomized controlled trial in overweight or obese adults	Incidence of type 2 diabetes	487	white (161 men, 326 women)	Centrally	14633807
ELSA	English Longitudinal Study of Ageing	Cohort of ≥50-year-old adults in the household sector in England	Health, economic position, and quality of life with ageing	5,216	white (2,394 men, 2,822 women)	Locally	
EPIC-NL	The European Prospective Investigation into Cancer and Nutrition - Netherlands Study	Population-based cohort of adults	Incidence of chronic disease	1,729	white (477 men, 1,252 women)	Locally	19483199
EPIC-Norfolk	The European Prospective Investigation into Cancer and Nutrition - Norfolk Study	Population-based cohort of adults	Incidence of chronic disease	20,374	white (10,059 men, 10,315 women)	Centrally	10466767
EPIC-Potsdam	The European Prospective Investigation into Cancer and Nutrition - Potsdam Study	Population-based cohort of adults	Incidence of chronic disease	4,858	white (1,917 men, 2,941 women)	Locally	10592369
ERF	Erasmus Rucphen Family Study	Family-based, cross-sectional study of a genetically isolated Dutch population	Risk of complex disease	1,489	white (655 men, 834 women)	Locally	15054401
FamHS	Family Heart Study	Multi-center cohort of individuals and families	Cardiovascular risk factors, preclinical atherosclerosis, and incidence of coronary heart disease	839	white (403 men, 436 women)	Locally	19557197
FUSION Stage 1	Finland-United States Investigation of NIDDM Genetics Study Stage 1	Case-control	Type 2 diabetes cases vs. controls with normal glucose tolerance	1,955	white (1,054 men, 901 women)	Locally	17463248
FUSION Stage 2	Finland-United States Investigation of NIDDM Genetics Study Stage 2	Case-control	Type 2 diabetes cases vs. controls with normal glucose tolerance	977	white (644 men, 333 women)	Locally	17463248
GLACIER	Gene-Lifestyle Interactions and Complex Traits Involved in Elevated Disease Risk	Population-based cohort of adults	Chronic disease incidence and risk factors	14,828	white (5,806 men, 9,022 women)	Locally	20870969
GOOD	The Gothenburg Osteoporosis and Obesity Determinants Study	Cohort of 18-20-year-old men	Bone and fat mass	938	white men	Centrally	16007330
НАРІ	Heredity and Phenotype Intervention Heart Study	Controlled trial in a healthy, genetically isolated population of adults	Cardiovascular response to lifestyle intervention	768	Amish (408 men, 360 women)	Centrally	18440328

Study		Study design	Primary outcome	Total sample	Participants	Analysis*	Reference
Short name	Full name	. •	•	size	·	·	PubMed ID
HUNT2-DiaB	The HUNT2-Bergen Diabetes Research Collaboration	Case-control	Type 2 diabetes cases vs. non-diabetic controls	2,811	white (1,455 men, 1,356 women)	Locally	17827402
InCHIANTI	InCHIANTI Study	Population-based cohort of adults	Physical functioning in late life	1,132	white (509 men, 623 women)	Locally	11129752
Inter99	Inter99 Population-Based Cohort of Middle-Aged Danes	Randomized controlled trial in a population-based cohort of adults	Incidence of ischemic heart disease	5,922	white (2,891 men, 3,031 women)	Centrally	14663300
METSIM	The Metabolic Syndrome in Men Study	Population-based, cross-sectional study of 45-70-year-old men	Risk of type 2 diabetes and cardiovasular disease	5,144	white men	Locally	19223598
MDC	Malmö Diet and Cancer Cohort	Population-based cohort of adults	Incidence of cancer	26,013	white (10,200 men, 15,813 women)	Locally	8429286 12028859
MONICA/KORA	MONICA/KORA S2, S3 and S4 Surveys	Population-based cohort of adults	Cardiovascular risk factors	11,679	white (5,860 men, 5,819 women)	Locally	16032512 16032514
MPP	Malmö Preventive Project	Population-based cohort of adults	Total death and death from ischemic heart disease	15,925	white (10,330 men, 5,595 women)	Locally	19373445
MRC Ely	The MRC Ely Study	Population-based cohort of adults	Incidence of type 2 diabetes	810	white (336 men, 474 women)	Centrally	17257284
NFBC1966	Northern Finland Birth Cohort 1966	Birth cohort	Pre-term birth, low birth weight, and subsequent morbidity and mortality	4,375	white (2,106 men, 2,269 women)	Locally	4911003
NHS & HPFS	Nurses Health Study and Health Professionals Follow-up Study	Nested case-control	Type 2 diabetes cases vs. healthy controls	5,453	white (2,224 men, 3,229 women)	Locally	18647953
ORGGEN	Obesity Research Group - Genetics	Case-cohort	Obese cases vs. random controls from a population-based cohort	1,629	white men	Locally	2508915 2361809
PPP-Botnia	Prevalence, Prediction, and Prevention of Diabetes in Botnia Study	Population-based cohort of adults	Type 2 diabetes risk factors and prevalence	2,291	white (1,245 men, 1,046 women)	Locally	19373445
QFS	Quebec Family Study	Cohort of healthy parents and offspring	Fitness and risk factors for cardiovascular disease and diabetes	711	white (314 men, 397 women)	Centrally	16355479

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Study		Study design	Primary outcome	Total sample	Participants	Analysis*	Reference
Short name	Full name	,	,	size		, ,	PubMed ID
RISC	Relationship between Insulin Sensitivity and Cardiovascular Disease	Cohort of healthy adults	Insulin resistance and risk of cardiovascular disease	771	white (335 men, 436 women)	Centrally	14968294
Rotterdam	Rotterdam Study	Population-based cohort of adults ≥54 years of age	Diseases frequent in the elderly	3,479	white (1494 men, 1985 women)	Centrally	19728115 1833235
Segovia	The Segovia Study	Population-based, cross-sectional study of adults	Prevalence of anthropometric and physiological parameters related to metabolic syndrome	586	white (271 men, 315 women)	Centrally	Martínez-Larrad MT, et al. Med Clin (Barc). 2005;125:481-6.
Singapore NHS98	1998 Singapore National Health Survey	Population-based, cross-sectional study of adults	Prevalence of diabetes mellitus, hypertension, obesity, smoking, physical inactivity, and hypercholesterolaemia	4,210	Chinese (1,305 men, 1,559 women), Malay (369 men, 394 women), and Indian-Asian (282 men, 301 women)	Centrally	18599522
TUEF & TULIP	Tuebingen Family Study & Tuebingen Lifestyle Intervention Programme	TUEF: Controlled trial in healthy adults; TULIP: Controlled trial in adults with prediabetes phenotypes	TUEF: Incidence of type 2 diabetes and changes in adiposity; TULIP: Incidence of type 2 diabetes and improvement in prediabetes phenotypes	930	white (323 men, 607 women)	Centrally	16205883 17327385
TwinsUK	TwinsUK	Cohort of adult twin pairs	Cardiovascular, metabolic, musculoskeletal, dermatological, and opthalmological diseases	3,964	white (322 men, 3,642 women)	Locally	12537873 19359265
WGHS	Women's Genome Health Study	Cohort of US female health professionals	Incidence of chronic disease	21,674	white women	Locally	18070814
WHI-OS	The Women's Health Initiative - Observational Study	Nested case-control	Incident type 2 diabetes cases vs. healthy controls	3,531	white (n=1,818), African American (n=1,081), Asian (n=239), and Hispanic (n=393) women	Locally	18787525
YFS	The Cardiovascular Risk in Young Finns Study	Population-based cohort of adults	Cardiovascular risk from childhood to adulthood	2,223	white (997 men, 1226 women)	Locally	18263651

^{*}The analyses according to a standardized plan were either performed by each study 'locally' or the dataset was sent to the meta-analysts to be analysed 'centrally'.

Text S1 - Table 2. Number of individuals, study design, and participant characteristics for studies of children and adolescents participating in the meta-analyses

Study		Study design	Primary outcome	Total sample	Participants	Analysis*	Reference
Short name	Full name			size			PubMed ID
ALSPAC	Avon Longitudinal Study of Parents and Children	Cohort of children	Child health and development	3,760	10-13-year old whites (1814 boys 1,946 girls)	Locally	11237119
EYHS	European Youth Heart Study	Cross-sectional, multi-centre study of children and adolescents	Cardiovascular risk factors	1,235	8-17-year old whites (550 boys, 685 girls)	Centrally	15321796
GENDAI	Gene-Diet Attica Investigation on Childhood Obesity	Cross-sectional, multi-centre study of children	Body weight	913	9-13-year old whites (429 boys, 484 girls)	Locally	17378724
HELENA	Healthy Lifestyle in Europe by Nutrition in Adolescence	Cross-sectional, multi-centre study of adolescents	Nutrition and health in European adolescents	755	11-18-year old whites (342 boys, 413 girls)	Locally	20368485
NFBC1966	Northern Finland Birth Cohort 1966	Birth cohort	Pre-term birth, low birth weight, and subsequent morbidity and mortality	4,027	14-year old whites (1,877 boys, 2,150 girls)	Locally	8494831
NFBC1986	Northern Finland Birth Cohort 1986	Birth cohort	Maternal and child health	5,468	16-year old whites (2,692 boys and 2,776 girls)	Locally	4911003
PANIC	The Physical Activity and Nutrition in Children Study	Controlled exercise and diet intervention trial in 6-8-year old children	Influence of lifestyle intervention on overweight and obesity	472	6-8-year old whites (244 boys, 228 girls)	Centrally	21054767
STRIP	The Special Turku Coronary Risk Factor Intervention Project for Children	Controlled trial in healthy children	Influence of dietary counselling on dietary intakes, serum lipid and lipoprotein concentrations, and growth and development of infants and children	382	14-15-year old whites (195 boys and 187 girls)	Locally	18430753 19158205
YFS	The Cardiovascular Risk in Young Finns Study	Population-based cohort of children and adolescents	Cardiovascular risk from childhood to adulthood	2,256	3-18-year old whites (1008 boys and 1,248 girls)	Locally	18263651

^{*}The analyses according to a standardized plan were either performed by each study 'locally' or the dataset was sent to the meta-analysts to be analysed 'centrally'.

Text S1 - Table 3. Methods used for measuring BMI, waist circumference and body fat percentage in studies of adults participating in the meta-analyses

	B	ВМІ		Waist circumference		Body fat percentage			
Study	Measured/ self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Method (instrument)		
AGES-Reykjavik	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (Xitron HYDRA ECF/ICF, Model 4200)		
ARIC	Measured	YES	Measured	YES	NA	NA	NA		
Birth Cohort 1958	Self-reported	YES	Measured	3 years later	NA	NA	NA		
BLSA	Measured	YES	Measured	YES	Measured	On different visit (results excluded from meta-analysis)	Skinfold thickness		
BWHHS	Measured	YES	Measured	YES	NA	NA	NA		
CLHNS	Measured	YES	Measured	YES	NA	NA	NA		
CoLaus	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (Bodystat 1500 Analyzer)		
DESIR	Measured	YES	Measured	YES	Measured	6 years later (results excluded from meta- analysis)	Bioimpedance (Tanita TBF-300P)		
DPP	Measured	YES	Measured	YES	NA	NA	NA		
DPS	Measured	YES	Measured	YES	NA	NA	NA		
ELSA	Measured	YES	Measured	YES	NA	NA	NA		
EPIC-NL	Measured	YES	Measured	YES	NA	NA	NA		
EPIC-Norfolk	Measured	YES	Measured	YES	NA	NA	NA		
EPIC-Potsdam	Measured	YES	Measured	YES	Measured	YES	Skinfold thickness		
ERF	Measured	YES	Measured	YES	Measured	YES	DEXA (DPX Prodigy total body fan-beam densitometer		
FamHS	Measured	YES	Measured	YES	Measured	6-9 years later (results excluded from meta- analysis)	Bioimpedance (RJL bioelectric impedance meter)		
FUSION Stage 1	Measured	YES	Measured	YES	NA	NA	NA		

	B	ВМІ		Waist circumference		Body fat	t percentage
Study	Measured/ self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Method (instrument)
FUSION Stage 2	Measured	YES	Measured	YES	NA	NA	NA
GLACIER	Measured	YES	NA	NA	NA	NA	NA
GOOD	Measured	YES	Measured	YES	Measured	YES	DEXA (Lunar Prodigy, GE Healthcare)
НАРІ	Measured	YES	Measured	YES	Measured	On different visit (individuals with ≥3 years gap between measurements excluded)	DEXA (Hologic QDR-4500W)
HUNT2-DiaB	Measured	YES	Measured	YES	NA	NA	NA
InCHIANTI	Measured	YES	Measured	YES	NA	NA	NA
Inter99	Measured	YES	Measured	YES	NA	NA	NA
MDC	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (BIA 103 single-frequency analyzer)
METSIM	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (Akern Bioimpedance Analyzer model BIA101)
MONICA/KORA	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (KORA Survey 3: Body Composition Analyzer TVI 10; KORA Survey 4 and parts of Survey 3: B.I.A. 2000 Analyzer)
MPP	Measured	YES	NA	NA	NA	NA	NA
MRC Ely	Measured	YES	Measured	YES	Measured	YES	DEXA (GE Lunar Prodigy)
NFBC1966	Measured	YES	Measured	YES	NA	NA	NA
NHS & HPFS	Self-reported	YES	Self-reported	YES	NA	NA	NA
ORGGEN	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (BIA-103 RJL-system-analyzer)
PPP-Botnia	Measured	YES	NA	NA	NA	NA	NA
QFS	Measured	YES	Measured	YES	Measured	YES	Skinfold thickness

	В	ВМІ		Waist circumference		Body fat percentage			
Study	Measured/ self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Method (instrument)		
RISC	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (Tanita TBF-300 Body Composition Analyzer)		
Rotterdam	Measured	YES	Measured	YES	Measured	~5 years later (results excluded from meta- analysis)	DEXA (Lunar Prodigy, GE Healthcare)		
Segovia	Measured	YES	Measured	YES	NA	NA	NA		
Singapore NHS98	Measured	YES	Measured	YES	NA	NA	NA		
TUEF & TULIP	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (RJL Bioelectrical Impedance Analyzer)		
TwinsUK	Measured	On different visit (individuals with ≥3 years gap between measurements excluded)	Measured	On different visit (individuals with ≥3 years gap between measurements excluded)	Measured	On different visit (individuals with ≥3 years gap between measurements excluded)	DEXA (Hologic Discover W' -QDR software ver. 12.6		
WGHS	Self-reported	YES	Self-reported	6 years later (results excluded from meta- analysis)	NA	NA	NA		
WHI-OS	Measured	YES	Measured	YES	NA	NA	NA		
YFS	Measured	YES	Measured	YES	Measured	YES	Skinfold thickness		

^{*} NA, data not available

Text S1 - Table 4. Methods used for measuring BMI, waist circumference and body fat percentage in studies of children and adolescents participating in the meta-analyses

	ВМІ		Waist circ	Waist circumference		Body fat percentage			
Study	Measured/ self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Measured/self- reported?	Measured on the same year with physical activity?	Method (instrument)		
ALSPAC	Measured	YES	Measured	YES	Measured	YES	DEXA (Lunar Prodigy, GE Healthcare)		
EYHS	Measured	YES	Measured	YES	Measured	YES	Skinfold thickness		
GENDAI	Measured	YES	Measured	YES	Measured	YES	Skinfold thickness		
HELENA	Measured	YES	Measured	YES	Measured	YES	Skinfold thickness		
NFBC1966	Self-reported	YES	NA	NA	NA	NA	NA		
NFBC1986	Measured	YES	Measured	YES	NA	NA	NA		
PANIC	Measured	YES	Measured	YES	Measured	YES	Bioimpedance (InBody 720, Biospace)		
STRIP	Measured	YES	Measured	YES	NA	NA	NA		
YFS	Measured	YES	NA	NA	NA	NA	NA		

^{*} NA, data not available

Text S1 - Table 5. Methods used for measuring physical activity and definitions of inactivity for studies of adults participating in the meta-analyses

Study	PA measurement	PA measure used to define physical inactivity	Definition of physical inactivity
AGES-Reykjavik	Interviewer-administered questionnaire	The following question was used: In the past 12 months, how often did you participate in moderate or vigorous physical activities?	Never or rarely participation in moderate or vigorous physical activities
ARIC	Self-administered questionnaire (Baecke Questionnaire of Habitual Physical Activity)	Sport activity PA score	Sex-specific 20% with lowest PA
Birth Cohort 1958	Self-administered questionnaire	The following questions were used: 1) Do you regularly take part in any of these activities; that is, at least once a month, for most of the year? (11 different activities listed) 2) Work class: manual, non-manual, unemployed/other	Response 'No' to question 1 and response 'non-manual' to question 2.
BLSA	Self-administered questionnaire	MET-minutes of leisure-time PA per week	Sex-specific 20% with lowest PA
BWHHS	Self-administered questionnaire	Hours of moderate-to-vigorous PA per typical week	Less than 1 h/wk of moderate-to-vigorous PA
CLHNS	Self-administered questionnaire	A) MET-minutes calculated by summing all individual activities during 24 hours of a typical day; B) MET-minutes calculated after grouping together similar tasks (e.g. personal hygiene) during 24 hours of a typical day	Women with PA in the lowest 20% of population when measured with both A and B. Women with PA in the lowest 40% of A or B but with PA in the lowest 20% of the other
CoLaus	Self-administered questionnaire	The following questions were used: 1) How much time (in minutes) do you walk every day on average to get to work, shops? 2) During working hours does your occupation involve: a) most often sitting, b) often standing, but little or no carrying or lifting of heavy loads, c) most often walking around and carrying light loads, d) important physical load, carrying heavy loads. 3) How many times per week do you take part for at least 20 minutes in leisure physical activities?	3) Less than once a week of participation in 20 minutes
DESIR	Self-administered questionnaire	Number of times person was involved in structured PA per week	0-1 times/week of structured PA
DPP	Self-administered questionnaire (Modified Activity Questionnaire)	MET-min of leisure time PA per week	Sex-specific 20% with lowest PA for each ethnicity separately
DPS	Self-administered questionnaire (Kuopio Ischemic Heart Disease Risk Factor Study 12- Month Leisure-Time Physical Activity Questionnaire)	MET-min of leisure time PA per week	Sex-specific 20% with lowest PA

Study	PA measurement	PA measure used to define physical inactivity	Definition of physical inactivity
ELSA	Self-administered questionnaire	The following questions were used: 1) Do you take part in sports or activities that are vigorous? 2) Do you take part in sports or activities that are moderately energetic?	Hardly ever participation in vigorous sports or activities and less than once a month of moderately energetic sports or activities
EPIC-NL	Self-administered questionnaire (The EPIC Core Questionnaire)	Cambridge Physical Activity Index (four categories: inactive, moderately inactive, moderately active, active)	Inactive category
EPIC-Norfolk	Self-administered questionnaire (The EPIC Core Questionnaire)	Cambridge Physical Activity Index (four categories: inactive, moderately inactive, moderately active, active)	Inactive category
EPIC-Potsdam	Self-administered questionnaire (The EPIC Core Questionnaire)	Cambridge Physical Activity Index (four categories: inactive, moderately inactive, moderately active, active)	Inactive category
ERF	Self-administered questionnaire	The following questions were used: 1) How would you describe the physical intensity of your work (light, fairly heavy, heavy or very heavy)? 2) How often do you practice sports with sweating or getting short of breath? 3) How often do you practice sports with slight sweating or slight increase in heart rate or breathing?	All of the following responses required: 1) Light intensity of work 2) Never or sometimes sports with sweating or getting short of breath 3) Never or sometimes sports with slight sweating or slight increase in heart rate or breathing
FamHS	Self-administered questionnaire	MET-minutes of leisure-time PA per week	Sex-specific 20% with lowest PA
FUSION Stage 1 and 2	Self-administered questionnaire	The following questions were used: 1) How strenuous is your work? 2) How much do you exercise or exert yourself in your spare time?	Both of the following responses required: 1) 'I have not worked because I am retired or not working for other reasons' or 'light deskwork' 2) 'In my spare time I read, watch TV, and work in the household tasks which don't make me move much or physically tax me'
GLACIER	Self-administed questionnaire (Umeå EPIC Questionnaire)	Frequency of structured exercise (coded as exercise never/rarely vs. one or more times weekly)	Exercise never/rarely
GOOD	Self-administered questionnaire	Hours of recreational PA per week	No participation in recreational PA
НАРІ	Accelerometer (Actical ver. 8.2 or 8.3 worn seven full days)	Mean accelerometer counts per minute worn	Sex-specific 20% with lowest PA

Study	PA measurement	PA measure used to define physical inactivity	Definition of physical inactivity
HUNT2-DiaB	Self-administered questionnaire	The following questions were used: 1) Number of times per week with light activity (not sweaty/breathless) 2) Number of times per week with hard physical activity (sweaty/breathless) 3) How will you describe your physical activity at work?	All of the following responses required: 1) Below one time per week of light activity 2) No hard activity per week 3) Mostly sedentary work. If there was no response on question 3, only questions 1 and 2 were used
InCHIANTI	Self-administered questionnaire	The following question was used: What was your physical activity level last year (hardly any physical activity, mostly sitting/some walking, light exercise 2-4 h/wk, moderate 1-2 h/wk or light exercise >4 h/wk, or moderate exercise > 3 h/wk)?	Response 'Hardly any physical activity' or 'Mostly sitting/some walking'
Inter99	Self-administered questionnaire	A combined PA score (three categories: physically passive, light or medium physically active, hard or very hard physically active) calculated based on responses to two questions; one enquiring about the level of physical activity at work and the other of leisure-time PA	Physically passive category
MDC	Self-administered questionnaire	MET-minutes of PA per week	Sex-specific 20% with lowest PA
METSIM	Self-administered questionnaire	The following questions were used: 1) Level of physical activity at work (light/moderate/heavy) 2) Level of leisure-time physical activity ('very low' = almost completely inactive, 'low' = some minor physical activity, 'moderate' = physical activity ≤2 times/wk ≥30 min, 'high' = physical activity ≥3 times/wk ≥30 min)	Both of the following responses required: 1) Light physical activity at work 2) 'Very low' or 'low' leisure-time PA
MONICA/KORA	Self-administered questionnaire	The following questions were used: 1) How often do you carry out sports in the winter? 2) How often do you carry out sports in the summer? 3) How would you classify your work or main employment?	Less than 1 h/wk of sports in the winter and summer and 'no appreciable physical work' in main employment
МРР	Self-administered questionnaire	The following questions were used: 1) Do you walk or cycle to and from work? 2) Do you walk or cycle for recreation during weekdays? 3) Do you walk or cycle for recreation during weekend days? 4) Do you undertake at least 3 h/wk of structured physical exercise? 5) Do you walk to work or do yard work? 6) Do you perform light structured physical exercise each week?	Response 'No' to all questions
MRC Ely	Heart rate sensor (Flex Heart Rate technique)	Physical Activity Level (total daily energy expenditure divided by resting energy expenditure)	Sex-specific 20% with lowest PA
NFBC1966	Self-administered questionnaire	MET-hours of brisk PA per week	Sex-specific 20% with lowest PA

Study	PA measurement	PA measure used to define physical inactivity	Definition of physical inactivity
NHS & HPFS	Self-administered questionnaire	MET-hours of leisure-time PA per week	Sex-specific 20% with lowest PA
ORGGEN	Self-administered questionnaire	Level of PA defined by the following categories: 1) Being almost entirely inactive or engaging in light PA less than 2 hours/week 2) Engaging in light PA 2-4 hours/week 3) Engaging in light PA more than 4 hours/week or in vigorous PA 2-4 hours/week 4) engaging in highly vigorous PA more than 4 hours/week in regular heavy exercise or competitive sports several times per week	Being almost entirely inactive or engaging in light PA less than 2 hours/week
PPP-Botnia	Self-administered questionnaire (Kuopio Ischemic Heart Disease Risk Factor Study 12- Month Leisure-Time Physical Activity Questionnaire)	MET-min of leisure time PA per week	Sex-specific 20% with lowest PA
QFS	Bouchard 3-day physical activity diary	Total daily activity level	Sex-specific 20% with lowest PA
RISC	Accelerometer (Actigraph)	Mean accelerometer counts per minute worn	Sex-specific 20% with lowest PA
Rotterdam	Self-administered questionnaire	MET-minutes of leisure-time PA per week	Sex-specific 20% with lowest PA
Segovia	Self-administered questionnaire	MET-hours of regular leisure-time PA per week	Sex-specific 20% with lowest PA
Singapore NHS98	Interviewer-administered questionnaire	The following questions were used: 1) Level of occupational physical activity (sedentary/light/moderate/heavy) 2) On average, how many times do you participate in sports, exercise or brisk walking in a week (each session should last for at least 20 minutes)?	Sedentary occupation and no participation in ≥20 min of sports, exercise or brisk walking
TUEF & TULIP	Self-administered questionnaire (Baecke Questionnaire of Habitual Physical Activity)	Total habitual PA score	Sex-specific 20% with lowest PA
TwinsUK	Self-administered questionnaire	The following questions were used: 1) During the last 12 months, how would you describe the kind of physical activity at work? (inactive/light/moderate/heavy/not applicable) 2) In the past year, how frequently have you typically engaged in physical exercise that raise your heart rate and last for 20 minutes at a time?	Inactive' or 'light' PA at work and less than once a month of physical exercise that raised heart rate and lasted for 20 minutes at a time

Study	PA measurement	PA measure used to define physical inactivity	Definition of physical inactivity
WGHS	Self-administered questionnaire	MET-hours of leisure-time PA per week	Sex-specific 20% with lowest PA for each ethnicity separately
WHI-OS	Self-administered questionnaire	MET-hours of recreational PA per week	Sex-specific 20% with lowest PA
YFS	Self-administered questionnaire	The following question was used: How often do you engage in rigorous physical activity?	Less than once a week

MET, metabolic equivalent; PA, physical activity

Text S1 - Table 6. Methods used for measuring physical activity and definitions of inactivity for studies of children and adolescents participating in the meta-analyses

Study			
	PA measurement	PA measure used to define physical inactivity	Definition of physical inactivity
ALSPAC	Accelerometer (Actigraph)	Mean accelerometer counts per minute worn	Sex- and age-specific 10% with lowest PA
EYHS	Accelerometer (MTI model WAM 7164 worn 2 weekdays and 2 weekend days)	Mean accelerometer counts per minute worn	Sex- and age-specific 10% with lowest PA
GENDAI	Self-administered PA recall checklist	MET-minutes of PA per day	Sex- and age-specific 10% with lowest PA
HELENA	Accelerometer (Actigraph worn seven full consecutive days)	Mean accelerometer counts per minute worn	Sex- and age-specific 10% with lowest PA
NFBC1966	Self-administered questionnaire	The following question was used: How often do you participate in sports after school hours?	Response 'once in two weeks', 'once a month' or 'usually never'
NFBC1986	Self-administered questionnaire	The following question was used: Outside school hours, how many hours a week do you spend on brisk physical activity?	Less than 1h/wk of brisk PA
PANIC	Self-administered questionnaire (completed by the parents on behalf of their child)	The following measures were used: 1) Distance from home to school commuted by foot or by bicycle. 2) Number of exercise sessions/wk outside school hours.	Commuting to school <3 km/week by foot or <5 km/week by bicycle, and 0-2 exercise sessions/wk outside school hours
STRIP	Self-administered questionnaire	MET-hours of leisure-time PA per week	Sex- and age-specific 10% with lowest PA
YFS	Self-administered questionnaire	The following question was used: How often do you engage in leisure-time physical activity for at least half an hour per session?	Less than once a week of leisure-time PA ≥30 min

MET, metabolic equivalent; PA, physical activity

Text S1 - Table 7. Study-specific descriptive statistics in studies of adults participating in the meta-analyses

	Men								Wo	men		
Study					Waist circumference,						Waist circumference,	
	N	Inactive (%)	Age, yrs mean (sd)	BMI, kg/m² mean (sd)	cm mean (sd)	Fat% mean (sd)	N	Inactive (%)	Age, yrs mean (sd)	BMI, kg/m² mean (sd)	cm mean (sd)	Fat% mean (sd)
AGES-Reykjavik	1,347	59.0	76.7 (5.3)	27.0 (3.8)	102.5 (10.5)	22.0 (5.5)	1,850	66.3	76.7 (5.8)	27.2 (4.9)	99.6 (13.2)	34.0 (5.0)
ARIC	5,128	19.5	54.8 (5.7)	27.4 (4.0)	99.7 (10.4)	-	5,762	16.8	53.9 (5.7)	26.6 (5.5)	93.1 (14.9)	-
Birth Cohort 1958	2,614	10.6	42.0 (0.0)	26.5 (3.9)	98.5 (11.1)	-	2,872	17.4	42.0 (0.0)	24.8 (4.7)	84.8 (12.5)	-
BLSA	326	19.9	50.1 (17.3)	23.9 (3.7)	76.6 (9.3)	-	382	19.9	48.6 (16.8)	25.3 (3.1)	89.4 (9.2)	-
BWHHS	0	-	-	-	-	-	3,107	52.6	68.9 (5.5)	27.5 (5.0)	86.0 (12.2)	-
CLHNS	0	-	-	-	-	-	1,711	21.5	48.4 (6.1)	24.3 (4.4)	81.1 (10.9)	-
CoLaus	2,530	13.0	53.2 (10.9)	26.6 (4.2)	88.7 (13.6)	23.9 (6.0)	2,812	11.2	54.3 (10.7)	25.1 (4.9)	89.8 (13.2)	34.4 (8.2)
DESIR	2,308	49.4	47.2 (10.1)	25.4 (3.3)	89.7 (9.6)	-	2,332	53.9	47.5 (9.9)	24.0 (4.1)	77.1 (10.4)	-
DPP African American	179	19.6	55.1 (10.0)	32.6 (5.9)	106.9 (14.1)	-	510	19.8	49.1 (9.4)	36.2 (7.0)	106.2 (15.3)	-
DPP Asian	83	19.3	51.5 (10.0)	28.5 (3.7)	97.1 (9.4)	-	66	19.7	47.7 (6.5)	31.0 (6.7)	93.5 (14.2)	-
DPP Hispanic	193	19.7	51.8 (10.9)	31.4 (4.9)	104.6 (12.4)	-	383	19.8	47.5 (9.8)	34.0 (5.9)	99.7 (12.5)	-
DPP white	683	19.6	54.0 (10.5)	32.5 (5.8)	110.4 (13.3)	-	1,267	20.0	50.9 (10.3)	35.0 (7.0)	104.3 (14.7)	-
DPS	161	19.9	55.4 (7.6)	29.9 (3.5)	104.2 (9.8)	-	326	19.9	55.1 (7.0)	31.9 (4.8)	99.8 (11.3)	-
ELSA	2,394	54.9	63.3 (9.1)	27.7 (4.1)	101.0 (11.1)	-	2,822	67.2	63.6 (9.4)	27.8 (5.2)	90.4 (12.2)	-
EPIC-NL	477	10.7	44.5 (11.1)	26.1 (3.7)	93.1 (11.5)	-	1,252	8.1	51.4 (11.6)	26.2 (4.1)	83.0 (10.6)	-
EPIC-Norfolk	10,059	30.5	59.1 (9.3)	26.5 (3.3)	95.7 (9.7)	23.5 (6.1)	10,315	30.9	58.5 (9.3)	26.1 (4.2)	82.1 (10.7)	39.6 (9.0)
EPIC-Potsdam	1,917	17.2	51.7 (8.1)	27.0 (3.6)	94.7 (10.0)	24.5 (5.5)	2,941	17.7	48.5 (9.1)	25.8 (4.8)	80.8 (11.8)	35.2 (5.9)
ERF	655	4.1	49.1 (13.7)	27.0 (4.0)	93.2 (11.5)	26.7 (7.1)	834	3.6	47.8 (13.9)	26.3 (4.6)	81.1 (11.4)	38.5 (7.5)
FamHS	403	17.6	53.1 (12.1)	28.1 (4.2)	101.1 (11.0)	-	436	22.9	57.7 (9.1)	27.5 (5.8)	96.0 (15.2)	-
FUSION Stage 1 cases	605	16.7	62.7 (7.1)	29.5 (4.0)	104.3 (10.8)	-	455	29.0	64.1 (7.9)	31.2 (5.3)	99.0 (12.8)	-
FUSION Stage 1 controls	449	12.0	61.3 (7.5)	27.0 (3.3)	96.2 (9.7)	-	446	10.1	61.5 (7.3)	27.2 (4.2)	86.2 (10.9)	-
FUSION Stage 2 cases	366	21.6	56.4 (8.7)	30.9 (5.1)	105.9 (13.6)	-	202	26.7	59.9 (7.2)	32.2 (5.9)	98.2 (13.8)	-
FUSION Stage 2 controls	278	9.0	54.6 (6.4)	27.0 (3.5)	94.1 (9.8)	-	131	13.0	60.5 (3.8)	27.7 (4.2)	83.2 (9.3)	-
GLACIER	5,806	48.0	53.0 (9.7)	26.3 (4.1)	-	-	9,022	48.4	51.7 (8.2)	25.7 (4.1)	-	-
GOOD	938	36.1	18.9 (0.6)	22.4 (3.2)	78.5 (7.2)	17.1 (7.4)	0	-	-	-	-	-
HAPI	408	19.9	42.6 (13.6)	25.6 (3.2)	90.1 (9.9)	19.3 (6.2)	360	20.0	45.6 (14.0)	27.8 (5.4)	84.3 (11.3)	35.4 (6.3)
HUNT2-DiaB cases	461	16.7	61.3 (15.0)	28.0 (3.9)	97.3 (10.9)	-	404	29.0	63.4 (15.7)	30.0 (6.0)	92.7 (13.6)	-
HUNT2-DiaB controls	994	10.1	51.8 (17.4)	26.5 (3.5)	92.2 (9.2)	-	952	15.1	50.7 (18.0)	26.3 (4.5)	81.6 (11.2)	-
InCHIANTI	509	8.6	67.3 (14.9)	27.0 (3.4)	94.5 (9.4)	-	623	19.9	68.4 (15.7)	27.3 (4.7)	88.8 (11.9)	-

MDC 10.000 20 59.1(7.1) 26.3(3.5) 93.8(11) 20.7(5.0) 15.813 20.0 573.7(7.9) 25.5(4.2) 77.9(11.4) 30.8 (MSTSIM 51.44 12.5 56.5(6.7) 26.8(3.7) 97.0(11.5) 23.0(6.0) 0	Inter00	2,891	20.0	46 2 (7 7)	26.8 (4.0)	02.2 (11.0)		2.021	20.0	45 7 (7 0)	2F 8 /F 1\	90.2 (11.0)	
METSIM 5,144 12.5 56.5 (6.7) 26.8 (3.7) 97.0 (10.5) 23.0 (6.0) 0	Inter99	•	30.8	46.3 (7.7)	26.8 (4.0)	93.2 (11.0)	-	3,031	38.9	45.7 (7.8)	25.8 (5.1)	80.3 (11.9)	-
MONICA/KORA 5,860 15.3 49.7 (14.1) 27.3 (3.8) 96.1 (16.6) 28.5 (6.3) 5,819 8.8 49.0 (13.8) 26.6 (5.1) 83.4 (12.3) 36.4 (MPP 10,330 22.0 42.9 (5.9) 24.4 (2.6) 5,595 21.1 50.2 (8.7) 24.0 (4.6) MIKC (19 33.6 19.9) 53.8 (11.1) 26.7 (3.2) 94.9 (9.7) 23.9 (4.6) 474 19.8 53.4 (13.3) 26.2 (4.6) 81.4 (10.9) 37.0 (19.6) 19.6 (19.6) 19.8 (·		, ,		, ,	, ,		20.0	57.3 (7.9)	25.5 (4.2)	77.9 (11.4)	30.8 (5.0)
MPP 10,330 22.0 42,9159 24,4 (2.6) 5,595 21.1 50 2(8.7) 24,0 (4.6) MRC Ely 336 19.9 53.8 (11.1) 26,7 (3.2) 94,9 (9.7) 23,9 (4.6) 474 19.8 53.4 (10.3) 26,2 (4.6) 81.4 (10.9) 37.0 (1.9) 19.0	METSIM	5,144	12.5	56.5 (6.7)	26.8 (3.7)	97.0 (10.5)	23.0 (6.0)	0	-	-	-	-	-
MRC ELY 336 19.9 53.8 (11.1) 26.7 (3.2) 94.9 (9.7) 23.9 (4.6) 474 19.8 53.4 (10.3) 26.2 (4.6) 81.4 (10.9) 37.0 (10.9) 19.6 (10	MONICA/KORA	5,860	15.3	49.7 (14.1)	27.3 (3.8)	96.1 (10.6)	28.5 (6.3)	5,819	8.8	49.0 (13.8)	26.6 (5.1)	83.4 (12.3)	36.4 (6.9)
NFBC1966	MPP	10,330	22.0	42.9 (5.9)	24.4 (2.6)	-	-	5,595	21.1	50.2 (8.7)	24.0 (4.6)	-	=
NHS & HPFS cases 1,040 24.0 55.6 (8.4) 27.8 (4.1) 101.7 (11.1) - 1,384 24.1 54.1 (6.8) 29.8 (6.0) 90.1 (13.7) - 1.8 (15.8) 11.8 (16.8) 11.	MRC Ely	336	19.9	53.8 (11.1)	26.7 (3.2)	94.9 (9.7)	23.9 (4.6)	474	19.8	53.4 (10.3)	26.2 (4.6)	81.4 (10.9)	37.0 (6.4)
NHS & HPFS controls 1,184 16.1 55.7 (8.5) 25.1 (2.8) 94.6 (8.4) - 1,1845 16.9 53.8 (6.8) 25.6 (5.0) 79.1 (1.1.2) - 1.1.2 (1.1.2) 1.1.2 (1.1.2) 34.5 (5.2) 0	NFBC1966	2,106	22.7	31.0 (0.0)	25.2 (3.6)	88.9 (9.9)	-	2,629	20.2	31.0 (0.0)	24.2 (4.8)	79.1 (12.2)	-
ORGGEN cases 751 16.2 43.6 (6.3) 35.7 (5.7) 117.2 (14.2) 34.5 (5.2) 0	NHS & HPFS cases	1,040	24.0	55.6 (8.4)	27.8 (4.1)	101.7 (11.1)	-	1,384	24.1	54.1 (6.8)	29.8 (6.0)	90.1 (13.7)	-
ORGGEN controls 878 9.2 48.1 (8.4) 26.1 (3.6) 93.5 (10.5) 24.5 (5.8) 0 -	NHS & HPFS controls	1,184	16.1	55.7 (8.5)	25.1 (2.8)	94.6 (8.4)	-	1,845	16.9	53.8 (6.8)	25.6 (5.0)	79.1 (11.2)	-
PPP-Bebthia 1,245 19,9 45.4 (14.9) 25.3 (4.4) - - 1,046 20.0 46.4 (16.2) 26.4 (4.0) - - - 1,046 20.0 46.4 (16.2) 26.4 (4.0) - - - - 1,046 20.0 46.4 (16.2) 26.4 (4.0) - - - - - 1,046 20.0 46.4 (16.2) 26.4 (4.0) -<	ORGGEN cases	751	16.2	43.6 (6.3)	35.7 (5.7)	117.2 (14.2)	34.5 (5.2)	0	-	-	-	-	-
OFS 314 19.7 40.4 (15.9) 27.3 (6.4) 93.5 (16.6) 22.8 (9.0) 397 18.9 40.3 (13.8) 27.5 (8.1) 83.8 (18.2) 32.0 (1.1) RISC 335 19.7 44.2 (8.2) 26.0 (3.1) 92.7 (10.0) 21.4 (6.2) 436 20.0 45.7 (8.0) 24.5 (4.2) 80.9 (11.1) 32.0 (1.1) 32.0 (1.1) 32.0 (1.1) 32.0 (1.1) 32.0 (1.1) 32.0 (1.1) 32.0 (1.1) 32.0 (1.1) 44.6 (2.1) 436 20.0 45.7 (8.0) 24.5 (4.2) 80.9 (11.1) 32.0 (1.1) 32.0 (1.1) 40.0 (12.0) 27.4 (3.4) 95.7 (9.0) - 1,985 18.9 73.0 (7.3) 27.3 (4.4) 90.7 (12.3) - 58.0 (11.1) - 40.0 (12.0) 27.4 (3.4) 95.7 (9.0) - 315 19.0 56.4 (11.8) 27.5 (4.6) 85.7 (11.1) - 58.0 (11.1) - - 1,559 26.4 36.9 (12.0) 22.0 (3.6) 73.1 (8.5) - 30.0 (13.0) 39.1 (10.1) - - 30.0 (13.0) 40.8 (12.0) 25.6	ORGGEN controls	878	9.2	48.1 (8.4)	26.1 (3.6)	93.5 (10.5)	24.5 (5.8)	0	-	-	-	-	-
RISC 335 19.7 44.2 (8.2) 26.0 (3.1) 92.7 (10.0) 21.4 (6.2) 436 20.0 45.7 (8.0) 24.5 (4.2) 80.9 (11.1) 32.0 (Rotterdam 1,494 19.0 71.8 (6.3) 26.3 (3.2) 97.5 (9.4) - 1,985 18.9 73.0 (7.3) 27.3 (4.4) 90.7 (12.3) - Segovia 271 16.2 54.7 (12.9) 27.4 (3.4) 95.7 (9.0) - 315 19.0 56.4 (11.8) 27.5 (4.6) 85.7 (11.1) - Singapore NHS98 Chinese 1,305 12.3 38.3 (12.0) 23.5 (3.7) 84.1 (9.9) - 1,555 26.4 36.9 (12.0) 22.0 (3.6) 73.1 (8.5) - Singapore NHS98 Indian Asian 282 14.5 40.6 (12.0) 24.5 (4.1) 88.8 (10.5) - 301 13.3 40.8 (12.9) 25.6 (5.0) 81.7 (11.6) - Singapore NHS98 Malay 369 8.7 39.7 (11.7) 24.9 (4.2) 86.2 (10.7) - 394 17.3 38.1 (11.9) 26.4 (5.5) 79.5 (11.6) - TUEF & TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (TwinsUK 322 25.8 50.5 (14.9) 26.7 (3.9) 93.2 (9.5) 23.3 (5.6) 3,642 29.8 50.0 (13.3) 25.9 (4.9) 79.5 (10.5) 34.2 (WGHS 0 21.6 1,081 21.3 61.2 (6.7) 30.9 (7.1) 91.0 (14.6) - WHI-OS African American 0 23.9 20.1 62.8 (8.1) 24.7 (4.5) 78.2 (11.0) - WHI-OS Afsian 0	PPP-Botnia	1,245	19.9	45.4 (14.9)	25.3 (4.4)	-	-	1,046	20.0	46.4 (16.2)	26.4 (4.0)	-	-
Rotterdam 1,494 19.0 71.8 (6.3) 26.3 (3.2) 97.5 (9.4) - 1,985 18.9 73.0 (7.3) 27.3 (4.4) 90.7 (12.3) - Segovia 271 16.2 54.7 (12.9) 27.4 (3.4) 95.7 (9.0) - 315 19.0 56.4 (11.8) 27.5 (4.6) 85.7 (11.1) - Singapore NHS98 Chinese 1,305 12.3 38.3 (12.0) 23.5 (3.7) 84.1 (9.9) - 1,559 26.4 36.9 (12.0) 22.0 (3.6) 73.1 (8.5) - Singapore NHS98 Indian Asian 282 14.5 40.6 (12.0) 24.5 (4.1) 88.8 (10.5) - 301 13.3 40.8 (12.9) 25.6 (5.0) 81.7 (11.6) - Singapore NHS98 Malay 369 8.7 39.7 (11.7) 24.9 (4.2) 86.2 (10.7) - 394 17.3 38.1 (11.9) 26.4 (5.5) 79.5 (11.6) - TUEF & TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0)	QFS	314	19.7	40.4 (15.9)	27.3 (6.4)	93.5 (16.6)	22.8 (9.0)	397	18.9	40.3 (13.8)	27.5 (8.1)	83.8 (18.2)	32.0 (10.1)
Segovia 271 16.2 54.7 (12.9) 27.4 (3.4) 95.7 (9.0) - 315 19.0 56.4 (11.8) 27.5 (4.6) 85.7 (11.1) - Singapore NHS98 Chinese 1,305 12.3 38.3 (12.0) 23.5 (3.7) 84.1 (9.9) - 1,559 26.4 36.9 (12.0) 22.0 (3.6) 73.1 (8.5) - Singapore NHS98 Indian Asian 282 14.5 40.6 (12.0) 24.5 (4.1) 88.8 (10.5) - 301 13.3 40.8 (12.9) 25.6 (5.0) 81.7 (11.6) - Singapore NHS98 Malay 369 8.7 39.7 (11.7) 24.9 (4.2) 86.2 (10.7) - 394 17.3 38.1 (11.9) 26.4 (5.5) 79.5 (11.6) - TUEF & TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (TwinsUK 322 25.8 50.5 (14.9) 26.7 (3.9) 93.2 (9.5) 23.3 (5.6) 3,642 29.8 50.0 (13.3) <t< td=""><td>RISC</td><td>335</td><td>19.7</td><td>44.2 (8.2)</td><td>26.0 (3.1)</td><td>92.7 (10.0)</td><td>21.4 (6.2)</td><td>436</td><td>20.0</td><td>45.7 (8.0)</td><td>24.5 (4.2)</td><td>80.9 (11.1)</td><td>32.0 (7.6)</td></t<>	RISC	335	19.7	44.2 (8.2)	26.0 (3.1)	92.7 (10.0)	21.4 (6.2)	436	20.0	45.7 (8.0)	24.5 (4.2)	80.9 (11.1)	32.0 (7.6)
Singapore NHS98 Chinese 1,305 12.3 38.3 (12.0) 23.5 (3.7) 84.1 (9.9) - 1,559 26.4 36.9 (12.0) 22.0 (3.6) 73.1 (8.5) - Singapore NHS98 Indian Asian 282 14.5 40.6 (12.0) 24.5 (4.1) 88.8 (10.5) - 301 13.3 40.8 (12.9) 25.6 (5.0) 81.7 (11.6) - Singapore NHS98 Malay 369 8.7 39.7 (11.7) 24.9 (4.2) 86.2 (10.7) - 394 17.3 38.1 (11.9) 26.4 (5.5) 79.5 (11.6) - TUEF & TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (TwinsUK 322 25.8 50.5 (14.9) 26.7 (3.9) 93.2 (9.5) 23.3 (5.6) 3,642 29.8 50.0 (13.3) 25.9 (4.9) 79.5 (10.5) 34.2 (WGHS 0 - - - - - 21,674 20.2 54.2 (7.1) 25.9 (5.0) <td< td=""><td>Rotterdam</td><td>1,494</td><td>19.0</td><td>71.8 (6.3)</td><td>26.3 (3.2)</td><td>97.5 (9.4)</td><td>-</td><td>1,985</td><td>18.9</td><td>73.0 (7.3)</td><td>27.3 (4.4)</td><td>90.7 (12.3)</td><td>-</td></td<>	Rotterdam	1,494	19.0	71.8 (6.3)	26.3 (3.2)	97.5 (9.4)	-	1,985	18.9	73.0 (7.3)	27.3 (4.4)	90.7 (12.3)	-
Singapore NHS98 Indian Asian 282 14.5 40.6 (12.0) 24.5 (4.1) 88.8 (10.5) - 301 13.3 40.8 (12.9) 25.6 (5.0) 81.7 (11.6) - Singapore NHS98 Malay 369 8.7 39.7 (11.7) 24.9 (4.2) 86.2 (10.7) - 394 17.3 38.1 (11.9) 26.4 (5.5) 79.5 (11.6) - TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 39.6 (12.6) 29.5 (5.0) 79.5 (10.5) 34.2 (10.6) 39.6 (12.6) 29.6 (10.6) 39.6 (12.6) 29.6 (10.6)	Segovia	271	16.2	54.7 (12.9)	27.4 (3.4)	95.7 (9.0)	-	315	19.0	56.4 (11.8)	27.5 (4.6)	85.7 (11.1)	-
Singapore NHS98 Malay 369 8.7 39.7 (11.7) 24.9 (4.2) 86.2 (10.7) - 394 17.3 38.1 (11.9) 26.4 (5.5) 79.5 (11.6) - TUEF & TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 32.0 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 33.6 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 33.6 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 33.6 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (12.6) 33.6 (12.6) 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (10.5) 33.6 (12.6) 39.6 (12.6) 29.8 (5.0) 49.2 (10.5) 34.2 (10.5) 34.2 (10.5) 34.2 (10.5) 34.2 (10.5) 34.2 (10.5) 34.2 (10.5) 34.2 (10.5) 34.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) 39.2 (10.5) <	Singapore NHS98 Chinese	1,305	12.3	38.3 (12.0)	23.5 (3.7)	84.1 (9.9)	-	1,559	26.4	36.9 (12.0)	22.0 (3.6)	73.1 (8.5)	-
TUEF & TULIP 323 18.3 40.2 (13.6) 26.8 (5.0) 95.5 (14.0) 21.9 (6.8) 607 18.6 39.6 (12.6) 27.0 (6.0) 88.0 (14.3) 32.9 (14.3)	Singapore NHS98 Indian Asian	282	14.5	40.6 (12.0)	24.5 (4.1)	88.8 (10.5)	-	301	13.3	40.8 (12.9)	25.6 (5.0)	81.7 (11.6)	=
TwinsUK 322 25.8 50.5 (14.9) 26.7 (3.9) 93.2 (9.5) 23.3 (5.6) 3,642 29.8 50.0 (13.3) 25.9 (4.9) 79.5 (10.5) 34.2 (10.5)	Singapore NHS98 Malay	369	8.7	39.7 (11.7)	24.9 (4.2)	86.2 (10.7)	-	394	17.3	38.1 (11.9)	26.4 (5.5)	79.5 (11.6)	=
WGHS 0 - - - - - 21,674 20.2 54.2 (7.1) 25.9 (5.0) - - - WHI-OS African American 0 - - - - 1,081 21.3 61.2 (6.7) 30.9 (7.1) 91.0 (14.6) - WHI-OS Asian 0 - - - - - 239 20.1 62.8 (8.1) 24.7 (4.5) 78.2 (11.0) - WHI-OS Hispanic 0 - - - - 393 22.9 60.2 (6.8) 29.0 (5.8) 87.3 (13.9) - WHI-OS white 0 - - - - 1,818 19.6 63.9 (6.8) 29.5 (6.8) 91.2 (16.1) -	TUEF & TULIP	323	18.3	40.2 (13.6)	26.8 (5.0)	95.5 (14.0)	21.9 (6.8)	607	18.6	39.6 (12.6)	27.0 (6.0)	88.0 (14.3)	32.9 (8.7)
WHI-OS African American 0 - - - - 1,081 21.3 61.2 (6.7) 30.9 (7.1) 91.0 (14.6) - WHI-OS Asian 0 - - - - - 239 20.1 62.8 (8.1) 24.7 (4.5) 78.2 (11.0) - WHI-OS Hispanic 0 - - - - 393 22.9 60.2 (6.8) 29.0 (5.8) 87.3 (13.9) - WHI-OS white 0 - - - - 1,818 19.6 63.9 (6.8) 29.5 (6.8) 91.2 (16.1) -	TwinsUK	322	25.8	50.5 (14.9)	26.7 (3.9)	93.2 (9.5)	23.3 (5.6)	3,642	29.8	50.0 (13.3)	25.9 (4.9)	79.5 (10.5)	34.2 (7.0)
WHI-OS Asian 0 - - - - - 239 20.1 62.8 (8.1) 24.7 (4.5) 78.2 (11.0) - WHI-OS Hispanic 0 - - - - - 393 22.9 60.2 (6.8) 29.0 (5.8) 87.3 (13.9) - WHI-OS white 0 - - - - 1,818 19.6 63.9 (6.8) 29.5 (6.8) 91.2 (16.1) -	WGHS	0	-	-	-	-	-	21,674	20.2	54.2 (7.1)	25.9 (5.0)	-	-
WHI-OS Hispanic 0 393 22.9 60.2 (6.8) 29.0 (5.8) 87.3 (13.9) - WHI-OS white 0 1,818 19.6 63.9 (6.8) 29.5 (6.8) 91.2 (16.1) -	WHI-OS African American	0	-	-	-	-	-	1,081	21.3	61.2 (6.7)	30.9 (7.1)	91.0 (14.6)	-
WHI-OS white 0 1,818 19.6 63.9 (6.8) 29.5 (6.8) 91.2 (16.1) -	WHI-OS Asian	0	-	-	-	-	-	239	20.1	62.8 (8.1)	24.7 (4.5)	78.2 (11.0)	-
	WHI-OS Hispanic	0	-	-	-	-	-	393	22.9	60.2 (6.8)	29.0 (5.8)	87.3 (13.9)	-
YFS 997 29.1 31.7 (5.0) 25.7 (4.1) 89.8 (10.8) 16.1 (6.0) 1,226 22.2 31.5 (5.0) 24.5 (4.6) 79.4 (11.4) 27.0 (WHI-OS white	0	-	-	-	-	-	1,818	19.6	63.9 (6.8)	29.5 (6.8)	91.2 (16.1)	-
	YFS	997	29.1	31.7 (5.0)	25.7 (4.1)	89.8 (10.8)	16.1 (6.0)	1,226	22.2	31.5 (5.0)	24.5 (4.6)	79.4 (11.4)	27.0 (7.6)

Text S1 - Table 8. Study-specific descriptive statistics in children and adolescents participating in the meta-analyses

			oys		Girls							
Study				Waist circumference,								
	N	Inactive (%)	Age, yrs mean (sd)	BMI, kg/m² mean (sd)	cm mean (sd)	Fat% mean (sd)	N	Inactive (%)	Age, yrs mean (sd)	BMI, kg/m² mean (sd)	cm mean (sd)	Fat% mean (sd)
ALSPAC	1,814	9.5	11.7 (0.2)	18.7 (3.1)	68.3 (9.3)	22.8 (9.4)	1,946	9.9	11.7 (0.2)	19.2 (3.4)	67.7 (9.0)	27.9 (8.5)
EYHS	550	9.8	11.5 (2.7)	18.2 (2.8)	63.4 (8.0)	16.3 (4.6)	685	10.1	11.7 (2.8)	18.3 (3.0)	61.5 (7.4)	20.9 (5.2)
GENDAI	429	11.7	11.2 (0.7)	20.3 (3.5)	70.3 (9.7)	25.9 (10.4)	484	10.1	11.1 (0.6)	19.8 (3.4)	67.2 (9.2)	31.3 (11.7)
HELENA	342	9.9	14.5 (1.4)	20.6 (3.3)	72.7 (7.9)	19.3 (10.6)	413	9.9	14.4 (1.3)	21.1 (3.4)	70.6 (8.0)	26.0 (7.2)
NFBC1966	1,877	17.2	14.0 (0.0)	19.1 (2.4)	-	-	2,150	28.9	14.0 (0.0)	19.4 (2.7)	-	-
NFBC1986	2,692	11.9	16.0 (0.0)	21.5 (4.0)	76.0 (9.2)	-	2,776	12.2	16.0 (0.0)	21.0 (3.6)	72.1 (8.1)	-
PANIC	244	7.0	7.6 (0.4)	16.1 (2.0)	57.1 (5.2)	14.6 (6.3)	228	10.1	7.6 (0.4)	16.1 (2.2)	56.0 (5.8)	18.2 (7.0)
STRIP	195	9.7	15.0 (0.0)	20.3 (3.2)	74.6 (8.8)	-	187	10.2	15.0 (0.1)	20.6 (3.1)	70.9 (7.5)	-
YFS	1,008	9.0	10.4 (5.0)	19.1 (3.2)	-	-	1,248	9.5	10.5 (5.0)	19.4 (3.2)	-	-

Text S1 - Table 9. Genotyping methods and quality control for the FTO SNP in all studies participating in the meta-analyses

Cohort	SNP	r² with rs9939609*	Minor allele	Platform	Call rate*	Duplicate concordance	p for HWE
AGES-Reykjavik	rs3751812	1	T	Illumina 370CNV BeadChip	97%	NA	0.57
ALSPAC	rs9939609	1	Α	Genotyped by Kbioscience (http://www.kbioscience.co.uk)	NA	NA	0.49
ARIC	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	95%	97%	0.68
Birth Cohort 1958	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	98%	NA	0.94
BLSA	rs8050136	1	Α	Illumina 550K chip	99%	NA	0.47
BWHHS	rs9939609	-	Α	Genotyped by Kbioscience (http://www.kbioscience.co.uk)	95%	99%	0.91
CLHNS	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	97%	100%	0.27
CoLaus	rs9939609	-	Α	Affymetrix 500K chip	99%	NA	0.75
DESIR	rs1421085	0.93	С	TaqMan® SNP Genotyping Assays (Applied Biosystems)	97%	100%	0.81
DPP	rs9939609	-	Α	iPLEX™ Sequenom MassARRAY®	97%	NA	White: 0.70 African American: 0.99 Asian: 0.20 Hispanic: 0.83
OPS	rs9939609	-	Α	Illumina Golden Gate Assay	99%	NA	0.78
ELSA	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	99%	100%	0.68
PIC-NL	rs9939609	-	Α	Illumina IBC v.3. chip	98%	NA	0.91
PIC-Norfolk	rs1121980	0.84	Т	TaqMan® SNP Genotyping Assays (Applied Biosystems)	98%	99%	0.90
PIC-Potsdam	rs9935401	1	Α	Genotyped by Kbioscience (http://www.kbioscience.co.uk)	99%	99%	0.16
RF	rs3751812	0.99	Α	Illumina 318K, Illumina 370K, and Affymetrix 250K chips	95%	NA	0.03
YHS	rs1121980	0.84	Т	TaqMan® SNP Genotyping Assays (Applied Biosystems)	97%	100%	0.30
amHS	rs3751812	1	Т	Illumina 550K chip	100%	NA	0.01
USION Stage 1	rs8050136	1	Α	Illumina Infinium Human Hap300 BeadChip	100%	100%	0.16
FUSION Stage 2	rs9939609	-	Α	Illumina Infinium Human Hap300 BeadChip	100%	100%	0.16
GENDAI	rs9939609	-	Α	iPLEX™ Sequenom MassARRAY®	98%	99%	0.05
GLACIER	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	>96%	>99 %	0.11
GOOD	rs3751812	1	Т	Illumina HumanHap 610K chip	100%	100%	0.84
НАРІ	rs9939609	-	Α	Affymetrix GenChip Human Mapping 500K chip	99%	NA	0.58
HELENA	rs9939609	-	Α	Illumina Golden Gate Assay	100%	NA	0.56
HUNT2-DiaB	rs9939609	-	Α	iPLEX™ Sequenom MassARRAY®	100%	100%	0.88
nCHIANTI	rs8050136	1	Α	Illumina 500K chip	>98%	NA	0.46
nter99	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	97%	100%	0.73
MDC	rs9939609	-	Α	iPLEX™ Sequenom MassARRAY® or TaqMan® SNP Genotyping	97%	99%	0.99
METSIM	rs9939609	-	Α	Assays (Applied Biosystems) TaqMan® SNP Genotyping Assays (Applied Biosystems)	100%	100%	0.91
MONICA/KORA	rs9935401	1	Α	iPLEX™ Sequenom MassARRAY®	95%	NA	0.50
ИРР	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	>99 %	>99 %	0.35

NFBC1966	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	88%	100%	0.33
NFBC1986	rs1421085	0.93	С	TaqMan® SNP Genotyping Assays (Applied Biosystems)	99%	100%	1.00
NHS	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	>95 %	>99%	0.10
HPFS	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	>95 %	>99%	0.03
ORGGEN	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	96%	100%	0.27
PANIC	rs8050136	1	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	100%	100%	0.95
PPP-Botnia	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	>99 %	>99%	0.37
QFS	rs8050136	1	Α	Illumina Golden Gate Assay	NA	>99%	0.14
RISC	rs9939609	-	Α	Genotyped by Kbioscience (http://www.kbioscience.co.uk)	NA	NA	0.99
Rotterdam	rs8050136	1	Α	Illumina Infinium HumanHap 55 BeadChip v.3.	≥97 %	99%	0.96
Segovia	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	95%	1	0.90
Singapore NHS98	rs9939609	-	Α	iPLEX™ Sequenom MassARRAY®	98%	1	Chinese: 0.65 Malay: 0.59 Asian Indian: 0.23
STRIP	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	97%	1	0.25
TUEF & TULIP	rs8050136	1	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	NA	NA	0.95
TwinsUK	rs8050136	1	Α	Illumina Infinium Assay	100%	NA	0.76
WGHS	rs8050136	1	Α	Illumina Infinium II assay (Human HAP300 panel)	>99 %	NA	0.88
WHI-OS	rs9939609	-	Α	TaqMan® SNP Genotyping Assays (Applied Biosystems)	98%	99%	White: 0.17 African American:0.16 Asian: 0.45 Hispanic: 0.15
YFS	rs9939609	-	А	TaqMan® SNP Genotyping Assays (Applied Biosystems)	100%	100%	0.56

NA, data not available; * r² in the HapMap CEU population