SUPPLEMENTARY MATERIAL

Supplementary Material

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Supplementary Tables

Table S1 Characteristics of the MPP and MDC cohorts

	MPP (n=9,367)	MDC (n=29,295)
	Mean±SD/%	*Mean±SD/%*
Age, yrs	46.8±6.3	58.0±7.6
Sex, % Male	55.4	39.7
BMI, kg/m^2	24.3±3.4	25.8±4.0
Waist to Hip Ratio	0.92±0.09	0.86±0.15
Body Fat, %	-	26.8±7.0
baseline Systolic Blood Pressure, mmHg	126.5±14.2	141.1±20.0
baseline Diastolic Blood Pressure, mmHg	85.2±8.7	85.6±10.4
follow-up Systolic Blood Pressure, mmHg	144.9±20.0	-
follow-up Diastolic Blood Pressure, mmHg	83.6±10.5	-
Diabetes at baseline, %	3.8	17.4
Smoke, % smokers	32.7	62.1
baseline Hypertensive, %	34.2	61.3
follow-up Hypertensive, %	63.3	-

Legend: BMI, Body Mass index; MPP, Malmö Preventive Project; MDC, Malmö Diet and Cancer

Table S2 Adiposity measurements in the two cohorts.

Adiposity trait	**Measurement**	**MDC**	**MPP**
BMI	weight (kg)/ height^2 (m^2); height and weight measured by trained nurses	Yes	Yes
WHR	waist/hip; i) waist measured between lowest rib margin and iliac crest; ii) hip circumference	Yes	Yes
Body fat	Body fat estimated through Bioelectrical Impedance Analyzer (BIA) according to manufacturer's algorithm (BIA 103, JRL systems, single-frequency analyzer, Detroit, USA)	Yes	No

Legend: BMI, Body Mass Index; WHR, Waist to hip ratio; MPP, Malmö Preventive Project; MDC, Malmö Diet and Cancer.

Table S3. Information about the studies from which weights for GRSs were derived

GRS	Trait	Study	Sample size	Ethnic group
$GRS\text{-}BMI_{565}$	Body m ass index	Pulit et al 2019	n= 694,649 (UKBiobank: n=484,563, GIANT: n=210,086)	European
$GRS\text{-}WHR_{324}$	Waist to hip ratio	Pulit et al 2019	694,649 (UKBiobank, n=484,563+ GIANT, n=210,086)	European
$GRS\text{-}VAT_{208}$	Predicted visceral adiposity trait (VAT)	Karlsson et al 2019	UKBiobank, n=325,153	White and British ancestry
$GRS\text{-}BF_{81}$	Body fat mass; measured with bio-electrical impedance (BIA) and dual energy X-ray absorptiometry (DXA	Rask-Andersen et al 2019	UKBiobank, n= 362,499	White and British ancestry of UKBB

Legend: GRS-VAT208, Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-BF81, Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs.

Table S4 Association of four GRS with blood pressure traits in MPP (a.) and in MDC (b.)

a. MPP	SBP at baseline (n=9,140)				DBP at baseline (n=9,140)			
	Model 1		**Model 2**		**Model 1**		**Model 2**	
	Beta (95%CI)	p-value	Beta (95%CI)		Beta (95%CI)	p-value	Beta (95%CI)	p-value
GRS-BMI_{565}	0.231 (0.131,0.331)	$3.4E^{-6}$	0.233 (0.133,0.333)	$4.2E^{-6}$	0.251 (0.153,0.349)	$4.0E^{-7}$	0.257 (0.157,0.357)	$3.0E^{-7}$
GRS-WHR_{324}	0.426 (0.175,0.677)	0.001	0.288 (0.123,0.453)	0.001	0.529 (0.286,0.772)	$3.24E^{-5}$	0.367 (0.202,0.532)	$1.4E^{-5}$
GRS-BF_{81}	0.247 (-0.07,0.563)	0.125	0.241 (-0.07,0.552)	0.130	0.275 (-0.036,0.586)	0.084	0.269 (-0.017,0.576)	0.087
GRS-VAT_{208}	0.326 (0.173,0.479)	$3.1E^{-5}$	0.336 (0.187,0.485)	$9.7E^{-6}$	0.270 (0.162,0.378)	0.001	0.296 (0.149,0.443)	$8.3E^{-5}$
	SBP at follow-up (n=9,041)				DBP at follow-up (n=9,041)			
GRS-BMI_{565}	0.163 (0.060,0.260)	0.002	0.158 (0.058,0.258)	0.002	0.178 (0.078,0.278)	0.001	0.172 (0.072,0.272)	0.001
GRS-WHR_{324}	0.083 (-0.146,0.312)	0.475	0.048 (-0.050,0.196)	0.053	0.061 (-0.089,0.211)	0.431	0.055 (-0.098,0.208)	0.477
GRS-BF_{81}	-0.166 (-0.497,0.165)	0.327	-0.161 (-0.482,0.160)	0.325	-0.034 (-0.353,0.285)	0.834	-0.033 (-0.343,0.277)	0.834
GRS-VAT_{208}	0.128 (-0.029,0.285)	0.110	0.122 (-0.042,0.286)	0.111	0.200 (0.043,0.357)	0.012	0.190 (0.04,0.339)	0.012
b. **MDC**	SBP at baseline (n=29,247)				DBP at baseline (n=29,247)			
GRS-BMI_{565}	0.166 (0.104,0.222)	$4.0E^{-8}$	0.205 (0.145,0.265)	$8.3E^{-12}$	0.239 (0.18,0.298)	$4.4E^{-16}$	0.248 (0.188,0.308)	$6.8E^{-17}$
GRS-WHR_{324}	0.620 (0.336,0.940)	$2.0E^{-5}$	0.546 (0.311,0.781)	$5.7E^{-6}$	0.767 (0.477,1.057)	$2.5E^{-7}$	0.676 (0.431,0.921)	$6.0E^{-8}$
GRS-BF_{81}	0.129 (0.094,0.164)	0.310	0.142 (-0.038,0.322)	0.305	0.311 (0.274,0.348)	0.02	0.267 (0.089,0.445)	0.003
GRS-VAT_{208}	0.182 (0.096,0.268)	$3.3E^{-5}$	0.226 (0.142,0.310)	$1.6E^{-7}$	0.267(0.183,0.351)	$7.6E^{-10}$	0.284 (0.200,0.368)	$3.1E^{-11}$

Legend:-GRS-$VAT_{208,}$ Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-$BF_{81,}$ Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR_{324} Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI_{565}, Genetic Risk Score for Body Mass Index based on 565 SNPs; BMI, Body Mass Index; BF, Body Fat; WHR, Waist Hip Ratio. Model 1: raw association (without adjustment); Model 2: the exposure trait was used as the residual from linear regression with age, sex, age^2, age*sex.

Table S5 Sensitivity analysis, including in the same model the GRS-BMI_{565} and GRS-WHR_{324}.

MDC		
	Hypertension Prevalence n=29262	
	OR (95%CI)	p-value
GRS_{565}-BMI	1.49 (1.32,1.68)	$1.0E^{-10}$
GRS_{324}-WHR	2.55 (1.51,4.35)	0.001

Legend: GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs.

Table S6 Binary Outcome with first step of regression, computed only on control

	Hypertension Prevalence n=9,137		Hypertension Incidence n=5,971	
	OR (95%CI)	p-value	OR (95%CI)	p-value
GRS-BMI_{565}	1.59 (1.04,2.03)	0.0002	1.42 (1.03,1.96)	0.003
GRS-WHR_{324}	2.49 (1.52,4.08)	0.0003	1.10 (0.54,2.25)	n.s.
GRS-BF_{81}	1.64 (0.66,4.06)	n.s.	0.41 (0.15,1.11)	n.s.
GRS-VAT_{208}	2.47 (1.64,3.72)	1.5e-05	1.42 (0.89,2.23)	0.01

Legend: GRS-VAT208, Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-BF81, Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs; n.s.: not significant; OR, Odd Ratio; CI; Confidence Interval

Table S7 Summarized data analysis

		SBP		DBP	
	Method	**Estimate(95%CI)**	**p-value**	**Estimate(95%CI)**	**p-value**
$GRS\text{-}BMI_{565}$					
	Weighted median	1.90(0.09,3.71)	0.04	2.05(1.15,2.95)	<0.0001
	IVW	2.75(1.66,3.85)	<0.0001	2.00(1.45,2.55)	<0.0001
	MR Egger	1.79(-1.15,4.73)	n.s.	1.32(-0.15,2.81)	n.s.
$GRS\text{-}WHR_{324}$					
	Weighted median	4.67(2.57,7.08)	<0.0001	2.44(1.23,3.65)	<0.0001
	IVW	3.18(1.68,4.67)	<0.0001	1.95(1.19,2.71)	<0.0001
	MR Egger	4.25(1.68,4.67)	0.03	2.51(0.54,4.47)	0.012
$GRS\text{-}BF_{81}$					
	Weighted median	0.19(-0.02,0.40)	n.s.	0.18(-0.04,0.39)	n.s.
	IVW	0.08(-0.10,0.25)	n.s.	0.19(-0.01,0.38)	n.s.
	MR Egger	0.13(-0.11,0.37)	n.s.	0.12(-0.14,0.38)	n.s.
$GRS\text{-}VAT_{208}$					
	Weighted median	0.15(0.05,0.24)	0.003	0.18(0.08,0.28)	<0.0001
	IVW	0.13(0.06,0.20)	<0.0001	0.19(0.12,0.26)	<0.0001
	MR Egger	0.13(-0.10,0.36)	n.s.	0.21(-0.03,0.44)	n.s.

Legend: DBP, Diastolic Blood Pressure; GRS-VAT208, Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-BF81, Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs; IVW, Inverse Weighted Median; SBP, Systolic Blood Pressure.

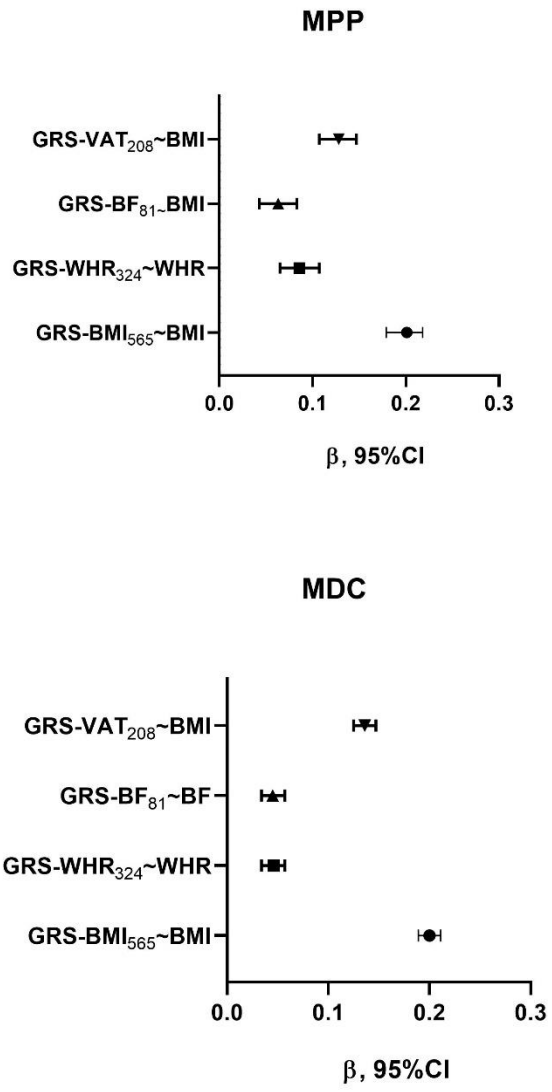
Table S8 Association with hypertension prevalence in MDC, after stratification for age

	Age groups*	OR (95%CI)	p-value
$GRS\text{-}BMI_{565}$	1st tertile age	1.81 (1.49,2.21)	3.14E-9
	2nd tertile age	1.64 (1.34,2.01)	1.45E-6
	3rd tertile age	1.52 (1.19,1.93)	.0006
$GRS\text{-}WHR_{324}$	1st tertile age	2.12 (1.06,4.28)	0.034
	2nd tertile age	3.35 (1.62,6.90)	0.001
	3rd tertile age	6.50 (2.70,15.50)	$2.48E^{-5}$
$GRS\text{-}BF_{81}$	1st tertile age	2.51 (1.34,4.70)	0.004
	2nd tertile age	1.41 (0.73,2.73)	0.304
	3rd tertile age	1.27 (0.59,2.76)	0.541
$GRS\text{-}VAT_{208}$	1st tertile age	1.59 (1.20,2.12)	0.001
	2nd tertile age	1.81 (1.34,2.43)	8.61E-5
	3rd tertile age	1.88 (1.33,2.65)	0.0004

Legend: GRS-VAT208, Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-BF81, Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs; OR Odd Ratio; CI; Confidence Interval. * 1st tertile: from 44.9 to 53.3 years; 2nd tertile: from 53.3 to 62.0 years; 3rd tertile: from 62.0 to 73.6 years.

Supplementary Figures

Figure S1 Association of the four GRSs with the adiposity traits, in the two cohorts



Legend: GRS-VAT208, Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-BF81, Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs; BMI, Body Mass Index; BF, Body Fat; WHR, Waist Hip Ratio. The Forest plot shows the magnitude of the association of 1 SD of the different GRS with the correspondent adiposity trait in the Malmö Preventive Project (MPP) and in the Malmö Diet and Cancer (MDC). I.e. for each SD increase in GRS-VAT208 there is a 0.128 Kg/m2 increase in BMI.

Figure S2 Comparison of different summarized-level data methods in the association of GRS-BMI_{565} with SBP (a.) and DBP (b.)

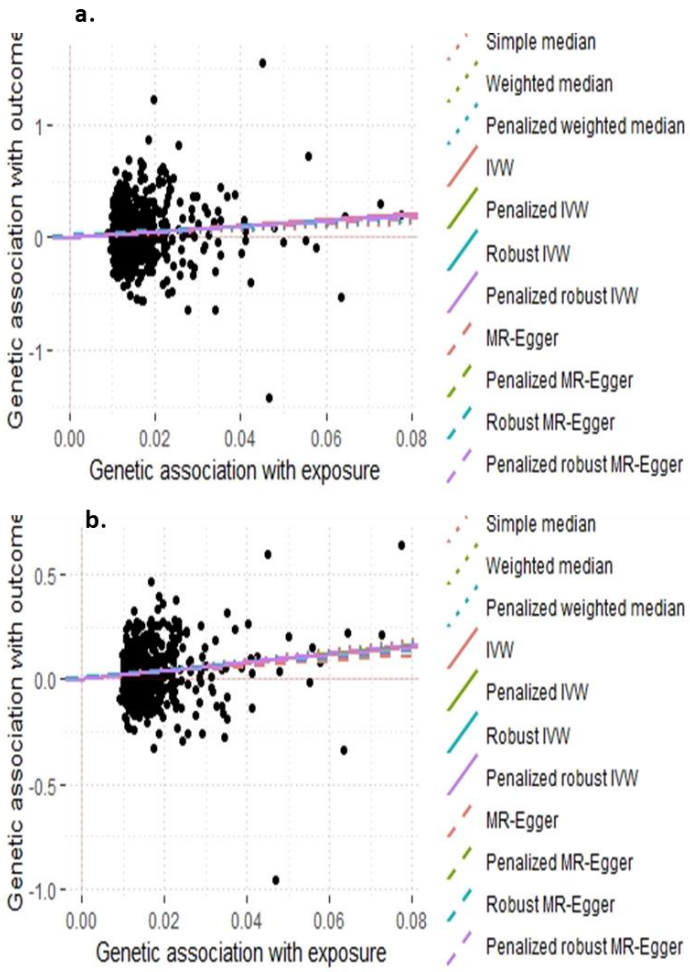


Figure S3 Comparison of different summarized-level data methods in the association of GRS-WHR324 with SBP (a.) a nd DBP (b.)

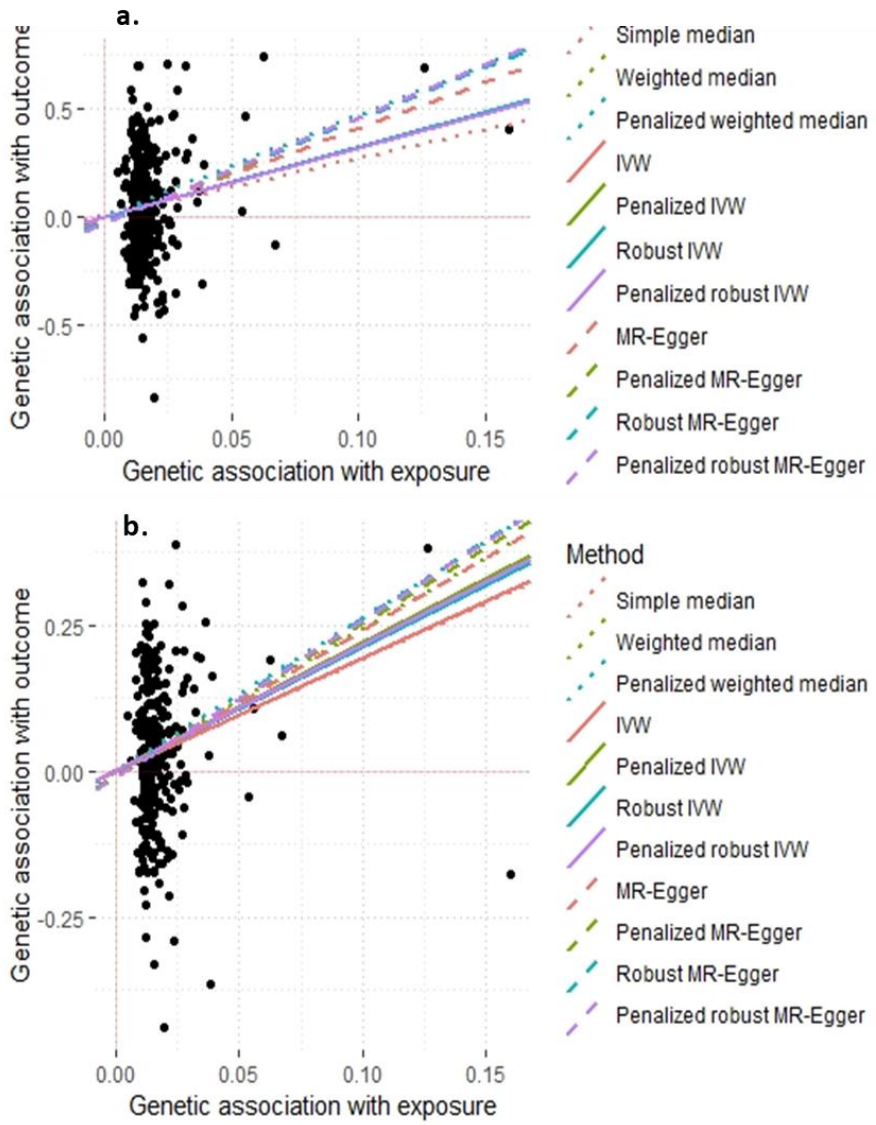


Figure S4 Comparison of different summarized-level data methods in the association of GRS-BF81 with SBP (a.) and DBP (b.)

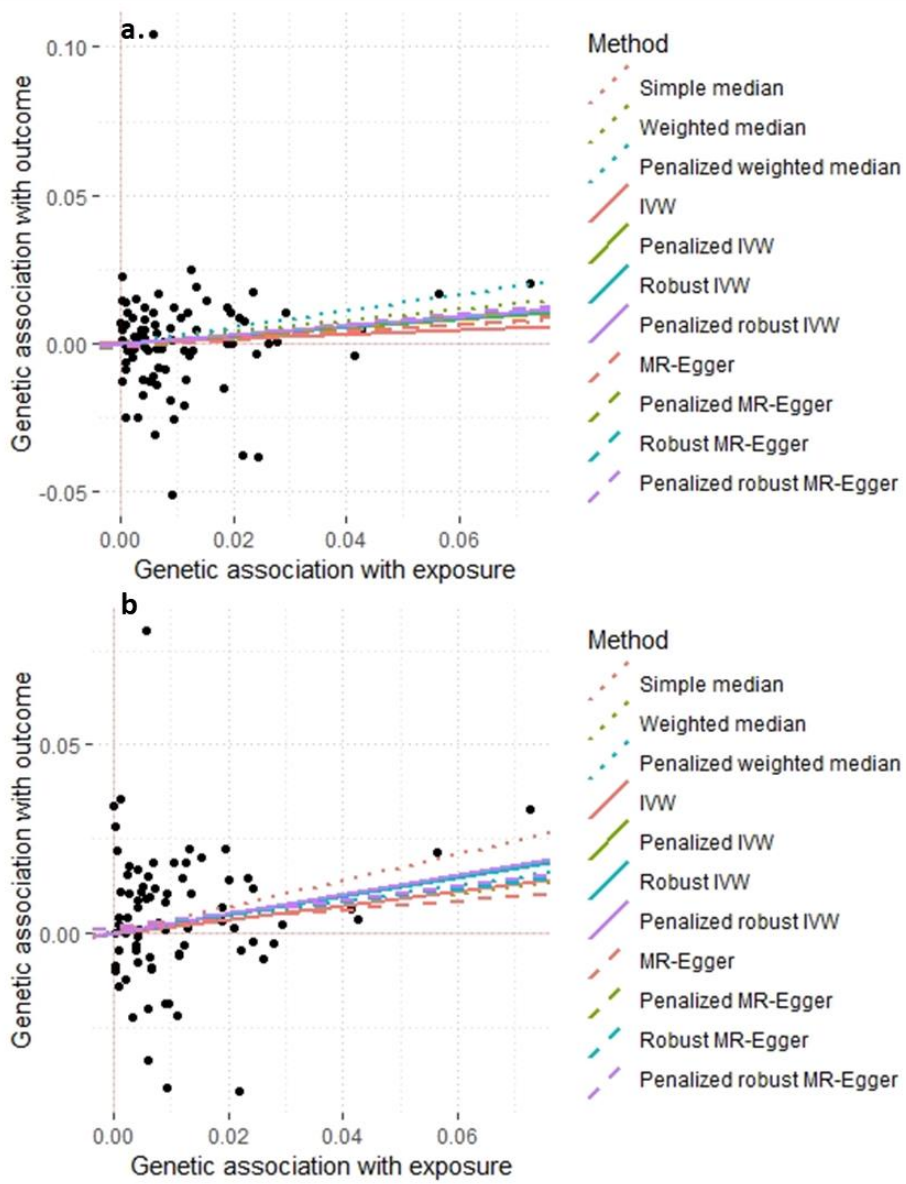


Figure S5 Comparison of different summarized-level data methods in the association of GRS-VAT208 with SBP (a.) and DBP (b.)

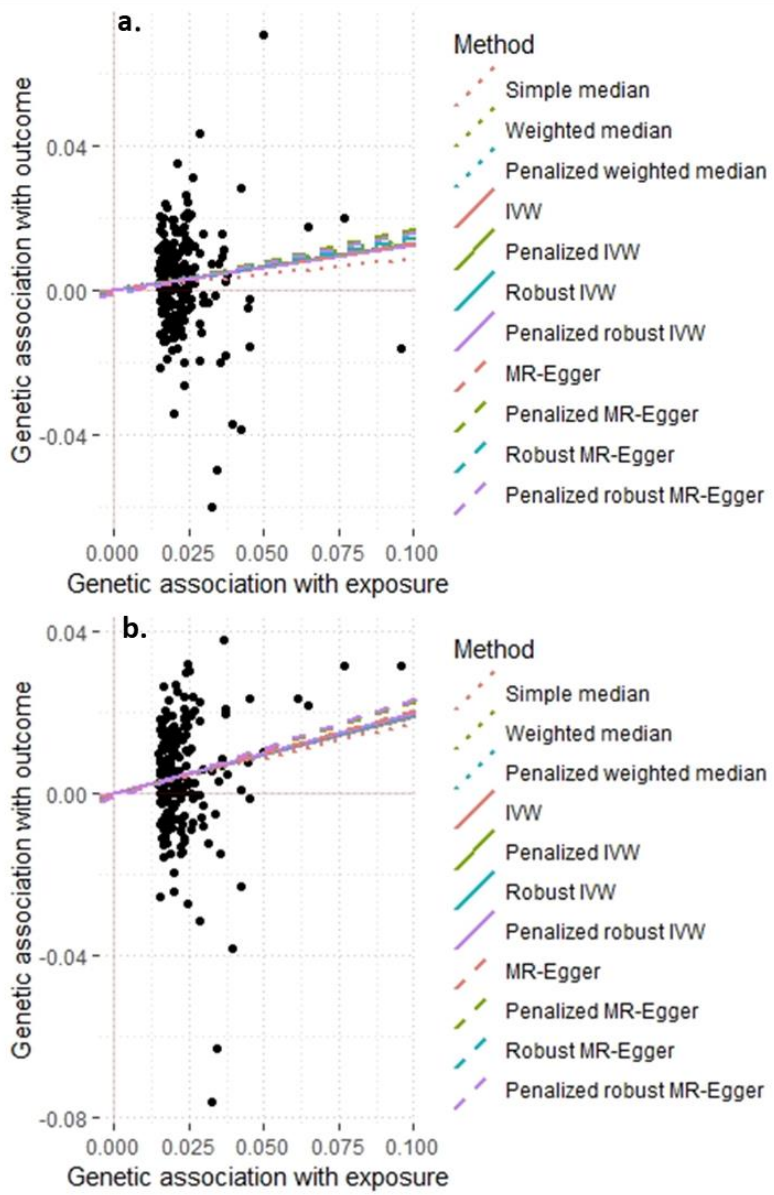
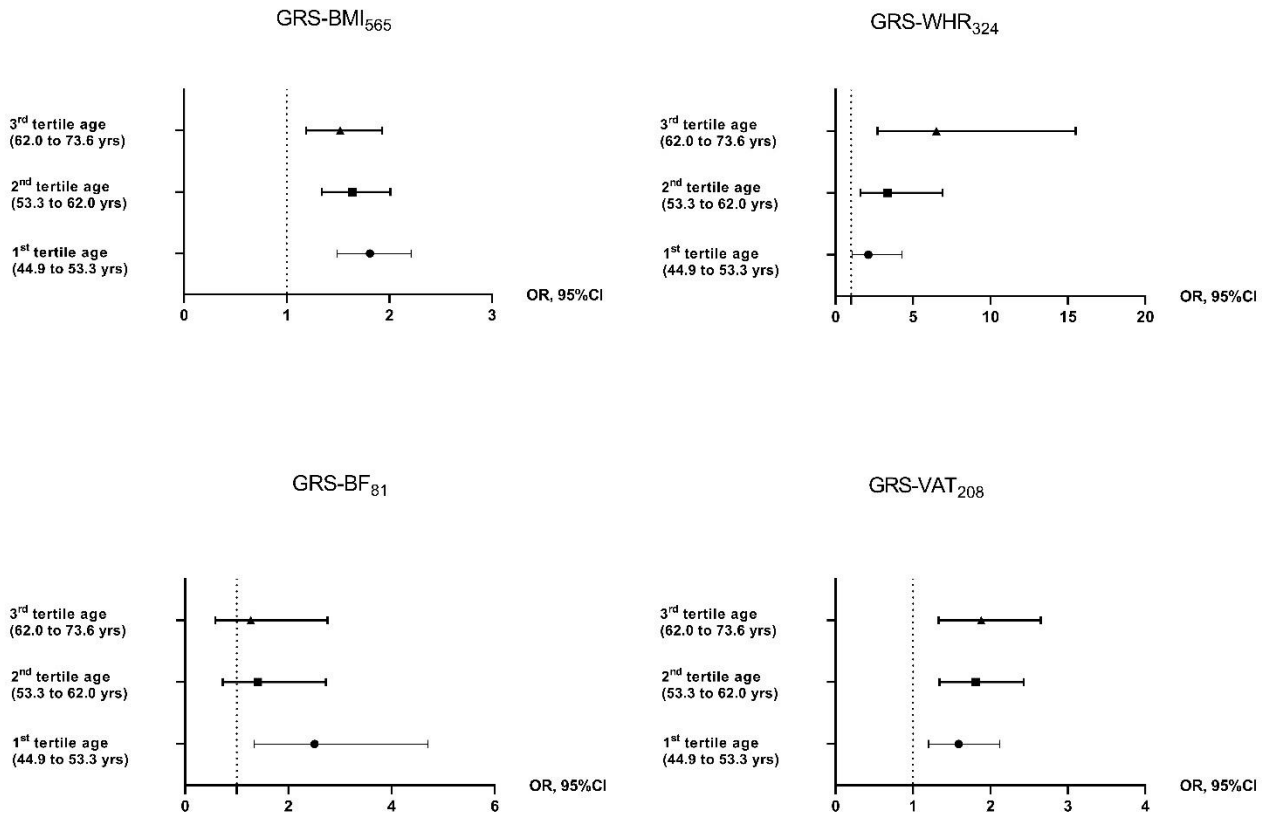


Figure S6 Association of the four GRSs with the prevalence of hypertension in the MDC after stratification for age.



Legend: GRS-VAT208, Genetic risk score for Visceral Adipose Tissue based on 208 SNPs; GRS-BF81, Genetic risk score for Body Fat based on 81 SNPs; GRS-WHR324 Genetic Risk Score for Waist Hip Ratio based on 324 SNPs; GRS-BMI565, Genetic Risk Score for Body Mass Index based on 565 SNPs; BMI, Body Mass Index; BF, Body Fat; WHR, Waist Hip Ratio. The Forest plot shows the magnitude of the association of 1 SD of the different GRS with the correspondent adiposity trait in the Malmö Diet and Cancer (MDC). I.e. for each SD increase in GRS-VAT208 there is a 0.128 Kg/m2 increase in BMI.