Genetic and Economic Interaction in the Formation of Health: The Case of Obesity

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Genes, Biology, and Choices

What:

- How genetic differences influence health investments and life-cycle evolution of health
    - via changes in **production function**
    - via changes in **preferences**

How:

- Integrate genes into a standard economic model of health
    - Genes = measures of heterogeneity in parameters

Why:

- Inequality at birth and impact over the life
- Differential response to prices, taxes, policies

Simple Model

$$\max_{E,F} U(B, F, \ell, c; g)$$

$$s.t$$

$$\Omega = \ell + E \quad (1)$$

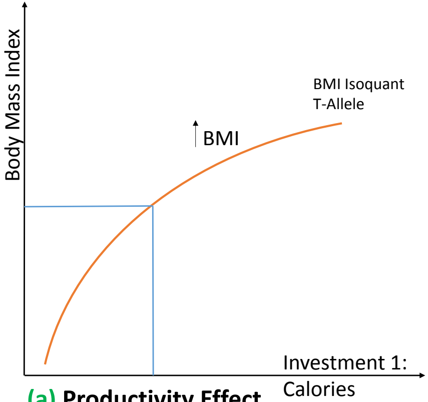
$$Y = p_F F + c \quad (2)$$

$$B = I(F, E; g) + (1 - \delta)B' + \varepsilon \quad (3)$$

- Utility from BMI B, consumption c, food consumption F, and leisure ℓ
- Income Y is devoted to buying food F and non-food consumption c
- time Ω devoted to exercise E vs leisure ℓ
- Genotype g influences:
  - **Cost** of investment [disutility: U(.;g)]
  - **Productivity** of investment [$I(.; g)$]

The Model: Genetic-Economic Interaction

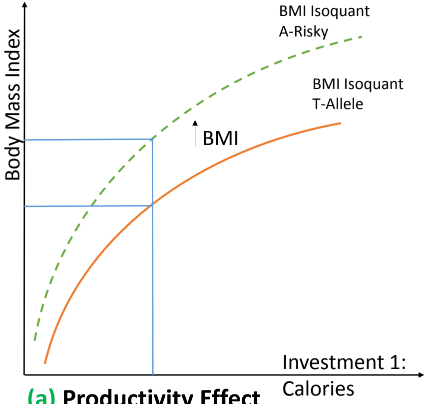
(a) Shift the **production** function



(a) Productivity Effect

The Model: Genetic-Economic Interaction

(a) Shift the **production** function

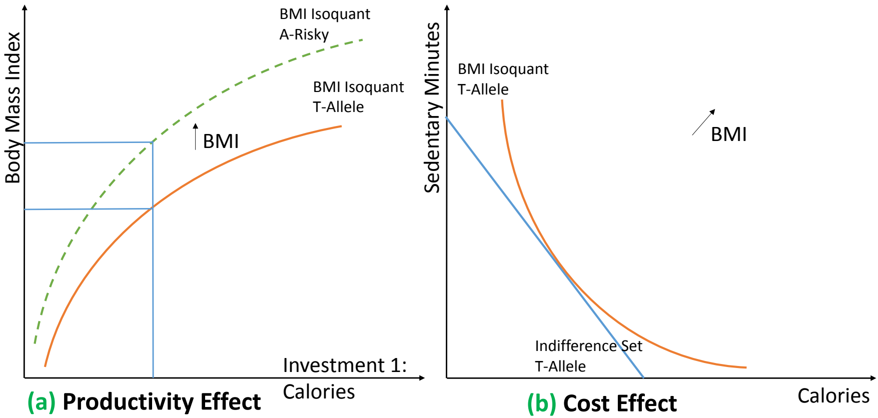


(a) Productivity Effect

The Model: Genetic-Economic Interaction

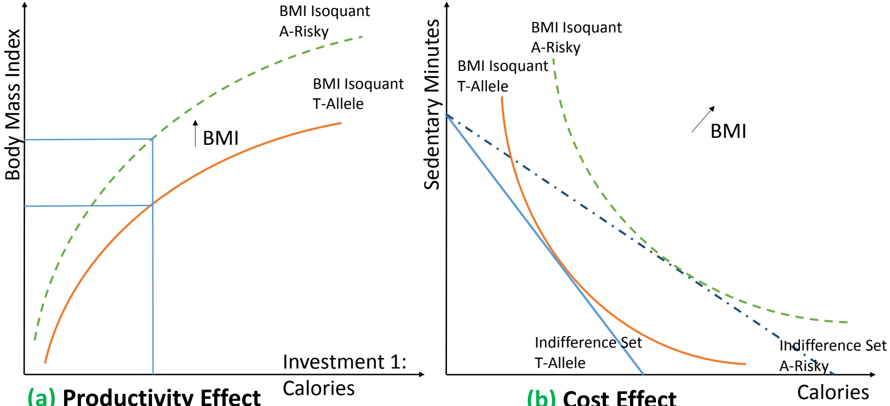
(a) Shift the **production** function

(b) Change the **utility cost** of investment



The Model: Genetic-Economic Interaction

(a) Shift the **production** function
(b) Change the **utility cost** of investment



(a) Productivity Effect **(b) Cost Effect**

The gene variant rs9939609

Gene: FTO intron, long-range connection with IRX [Smemo et al., 2014]
Risky A-allele connected to obesity by GWAS

- *How?:* Regulates appetite
  - Appetite-stimulant hormone (ghrelin)
  - Neural responsiveness to food images
  - Expressed in the hunger-related sites of the brain

$\Rightarrow$ could increase the **utility cost** of dieting

[Karra et al., 2013, Speakman et al., 2008, Fawcett and Barroso, 2010, Wardle et al., 2008, Cecil et al., 2008, Olszewski et al., 2009, Fredriksson et al., 2008, Timpson et al., 2008, Smemo et al., 2014] pics

- More exercise associated with lower genetic differences in BMI
- Weight-loss in dieting programs associated with FTO

$\Rightarrow$ could change the **productivity** of investments

[Andreasen et al., 2008, Franks et al., 2008, Kilpeläinen et al., 2011, Huang et al., 2014, Zhang et al., 2012]

ALSPAC Data

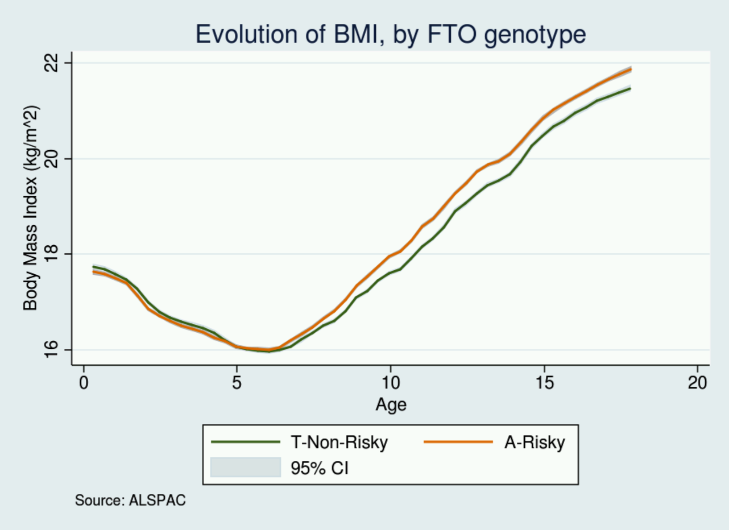
Avon Longitudinal Study of Parents and Children (ALSPAC)

- Cohort of children born in 1991-1992 near Bristol (UK)
- Data from clinic visits
- Enrolled ≈ 14,000 pregnant mothers, ≈ 8,000 children with genetic data

- **Obesity**: Body Mass Index (BMI), ages 1 to 18
- **Investments**: ages 11 and 13
  - Child Physical Activity: uni-axial accelerometer
    MTI Actigraph; see [Mattocks et al., 2008]
  - Child Diet: 3-day dietary diary
    Nutrients with reporting adjustment, see [Noel et al., 2010]
- Genetic data collected at age 7

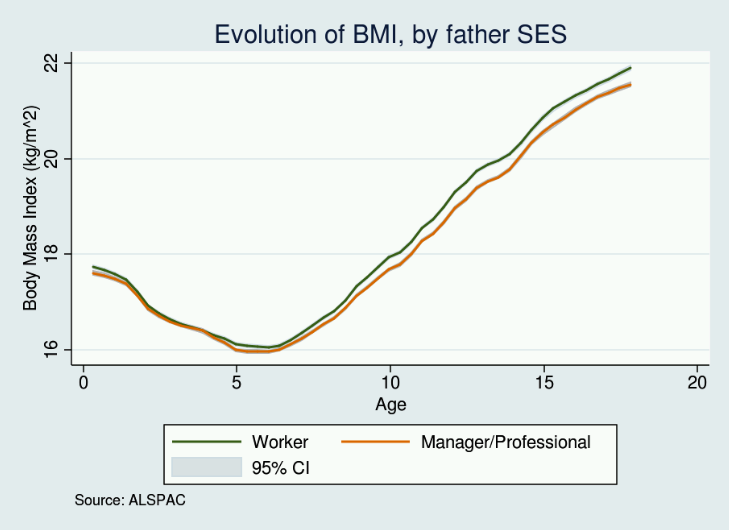
The Children of the 90s

Evolution of Body Mass Index



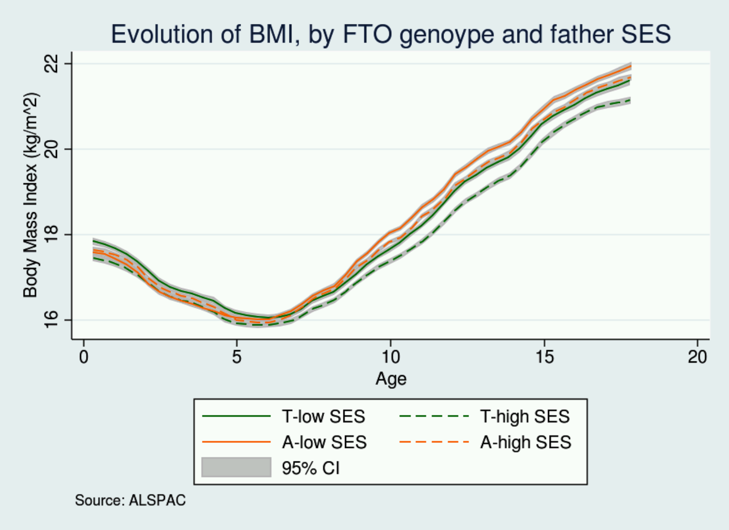
▸ Mom SES ▸ Dad Edu ▸ Mom Edu ▸ Income

Evolution of Body Mass Index



Mom SES Dad Edu Mom Edu Income

Evolution of Body Mass Index



Mom SES Dad Edu Mom Edu Income

Gene×Calories Interaction

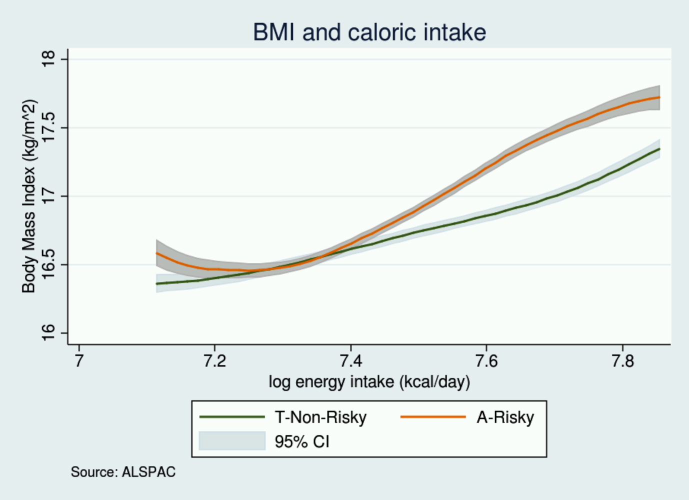


Figure: Nonparametric local-mean smoothing using Epanechnikov kernel and Silverman's Rule-of-Thumb bandwidth. Combining information from successive clinical visits, age 11 and 13; excluding outliers in the top and bottom 5% of the distributions of BMI and log(energy intake).

Gene×Exercise Interaction

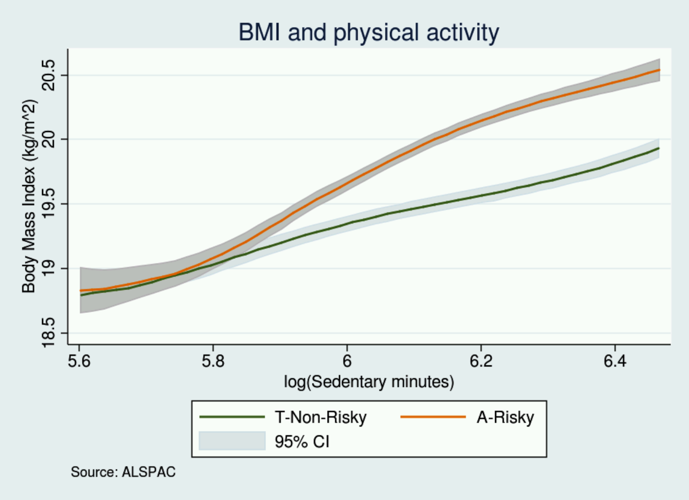


Figure: Nonparametric local-mean smoothing using Epanechnikov kernel and Silverman's Rule-of-Thumb bandwidth. Combining information from successive clinical visits, age 11 and 13; excluding outliers in the top and bottom 5% of the distributions of BMI and log(sedentary minutes).

Genetic Productivity Effect

Log-linearize a Cobb Douglas production function for obesity

$$\begin{aligned} log(B_{i,t}) =& \mu + \mu_g g + \alpha_e log(E_{i,t}) + \alpha_f log(F_{i,t}) + \\ & + \alpha_{g\times e} log(E_{i,t}) \cdot g + \alpha_{g\times f} log(F_{i,t}) \cdot g + \\ & + \delta log(B_{i,t-1}) \\ & + \gamma_b log(B_i^{mom}) + h(X_{i,t}) + \kappa_t + \varepsilon_{i,t} \end{aligned}$$

- Level effect: $\mu_g = \frac{\partial f}{\partial g}$
- Productivity effect: $\alpha_{GxK} = \frac{\partial f}{\partial investment}\Big|_{g=A} - \frac{\partial f}{investment}\Big|_{g=T}$
- X_i covariates: mom and dad education and SES; mother age at pregnancy; parity; birth weight; age of child at clinic date; dummy for single mother; time dummy; seasonal dummies; month effects; low kilo-calories reporting; late respondent;

Reduced Form

Table: Gene and Investment Interaction - FTO

		log(Body Mass Index$_t$)				
		(1)	(2)	(3)	(4)	(5)
Risky FTO Gene	β_g	0.019 [0.005]***	0.006 [0.002]***	0.010 [0.002]***	0.010 [0.003]***	0.010 [0.003]***
log(Food Intake)	α_f			0.067 [0.009]***	0.059 [0.010]***	0.069 [0.009]***
G X Food Intake	$\alpha_{g\times f}$			0.025 [0.011]**	0.027 [0.011]**	0.026 [0.011]**
log(Sedentary min.)	α_e			0.027 [0.009]***	0.028 [0.011]***	0.024 [0.009]***
G X Sedentary min.	$\alpha_{g\times e}$			0.011 [0.011]	0.010 [0.011]	0.012 [0.011]
log$(BMI)_{t-1}$	$(1-\delta)$		0.969 [0.007]***	0.939 [0.008]***	0.947 [0.013]***	0.967 [0.008]***
log$(BMI)_{mom}$	γ_b		0.090 [0.007]***	0.090 [0.007]***	0.097 [0.012]***	
Covariates			X	X	X	
Mom Gene					X	
R^2		0.32%	78%	78%	78%	78%
Observations		7052	7052	7052	7052	7052
n		3526	3526	3526	3526	3526

Dependent variable: log BMI (kg/m^2); Risky FTO gene $g = 1$ if rs9939609 gene variant contains one or more A-Alleles; $g = 0$ otherwise; Covariates: gender; parity; age of child at clinic date; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets.

Sizable effect: $\approx 1/4$ kg

Utility Cost

- Second genetic effect: change in the demand for investments
- A-Allele
  - Higher food intake
  - No differences in activity

Table: Utility Cost Effect

	Calories		Sedentary Activity	
	Male	Female	Male	Female
	(1)	(2)	(3)	(4)
Risky FTO	0.020	0.018	0.006	0.005
Gene	[0.009]**	[0.008]**	[0.007]	[0.006]
Covariates	X	X	X	X
Observations	3,347	3,711	3,347	3,711

Dependent variables: log of daily kilocalories intake (columns (1) and (2)), and log of daily sedentary minutes (columns (3) and (4)). Covariates: $\log(BMI)_{t-1}$; log mom BMI during pregnancy; parity; age of child at clinic date; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; month dummies; late respondent; birth weight. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets.

- Sizable effect: $\approx$ 1.5 kg/year

Robustness

- Check the robustness of the results:

→ Polygenic Score

→ Dropping underweight children (≈ 4%) ▸ Gender+NoUnder

→ Different measures of fat-mass ▸ Fat Mass

→ Different measures of investments ▸ Food

→ Different quantiles ▸ Quantiles

→ Different dataset: FHS ▸ FHS

Polygenic Approach

- Construct a PGS by adding up the number of obesity-related alleles of 24 different genes, following [Belsky et al., 2013] MC4R TMEM18 FTO TFAP2B BCDIN3D ETV5 BDNF GNPDA2 PPARG THADA IGF2BP2 TCF7L2 NPC1 MTCH2 PCSK1 KCTD15 SH2B1 NRXN3 HHEX LYPLAL1 GCK NEGR1 PTER GCKR ▸ dist
- Unweighted
- Split the sample into higher and lower than median PGS

Polygenic Approach

Table: Gene and Investment Interaction - Genetic Score

		(1)	(2)	(3)	(4)
Risky Genetic Score	β_g	0.034 [0.005]***	0.009 [0.002]***	0.012 [0.002]***	0.012 [0.002]***
log(Energy Intake)	α_f			0.065 [0.008]***	0.066 [0.008]***
G X Energy Intake	$\alpha_{g\times f}$			0.025 [0.011]**	0.026 [0.011]**
log(Sedentary min.)	α_e			0.019 [0.008]**	0.014 [0.008]*
G X Sedentary min.	$\alpha_{g\times e}$			0.000 [0.011]	-0.003 [0.011]
$\log(BMI)_{t-1}$	$(1-\delta)$		0.967 [0.007]***	0.938 [0.008]***	0.965 [0.008]***
$\log(BMI)_{mom}$	γ_b		0.089 [0.007]***	0.090 [0.007]***	
Covariates			X	X	
R^2		1.05%	78%	78%	78%
Observations		7052	7052	7052	7052

* significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets. Dependent variable: log BMI (kg/m^2); Risky genetic score $g = 1$ if genetic score > 25; $g = 0$ otherwise; Covariates: gender; parity; age of child at clinic date; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

Utility Cost Effect

- Effect of the genetic score on the investments:
  - Varies by gender
  - Differences also in activity levels

Table: Genetic Effect on Investments - Genetic Score

	Caloric Consumption		**Sedentary Minutes**	
	Male	Female	Male	Female
	(1)	(2)	(3)	(4)
Risky Genetic	0.011	0.014	0.001	0.022
Score	[0.009]	[0.008]*	[0.007]	[0.006]***
Covariates	X	X	X	X
Observations	3,347	3,371	3,347	3,371

* significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets. Dependent variables: logarithm of daily kilocalories intake (columns (1) and (2)), and logarithm of daily sedentary minutes (columns (3) and (4)). Covariates: log(sedentary min.) in columns (1) and (2), and log(kilocalories) in columns (3) and (4); $\log(BMI)_{t-1}$; log mom BMI during pregnancy; parity; age of child at clinic date; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; month dummies; late respondent; birth weight.

→ Must understand better the biological function of the various genes

Life-cycle Model

$$V_t(B_t, Y_t, \varepsilon_t; g) = \max_{E_t, F_t} u(B_t, F_t, \ell_t, c_t; g) + \beta E V_{t+1}(B_{t+1}, Y_{t+1}, \varepsilon_{t+1}; g)$$

$$s.t$$

$$\Omega = \ell_t + E_t \tag{4}$$

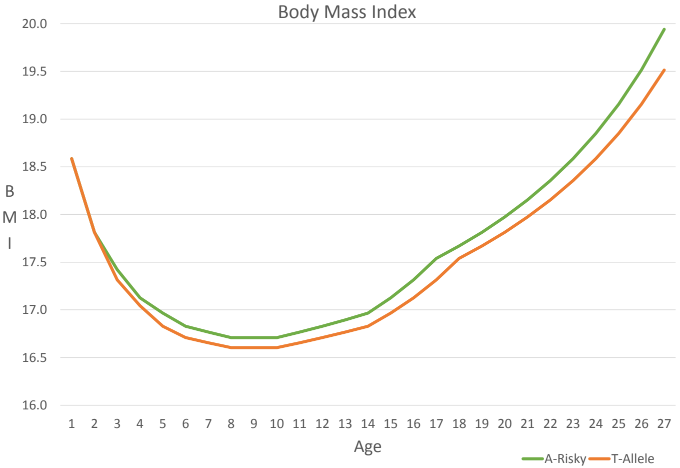
$$Y_t = p_{F_t} F_t + c_t \tag{5}$$

$$B_{t+1} = I(F_t, E_t; g) + (1 - \delta_t) B_t + \varepsilon_t \tag{6}$$

- Take into account expected future value of current choices $\beta E V_{t+1}$
- Genotype g influences:
  - **Cost** of investment [disutility: U(.;g)]
  - **Productivity** of investment [$I(.; g)$]

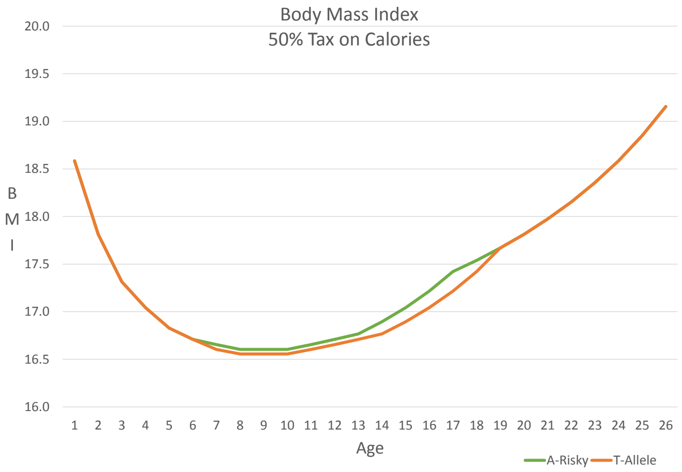
Calibration

Use parameters estimated in reduced form to calibrate:

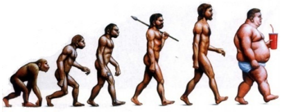


Policy A: Food Tax

Higher food prices

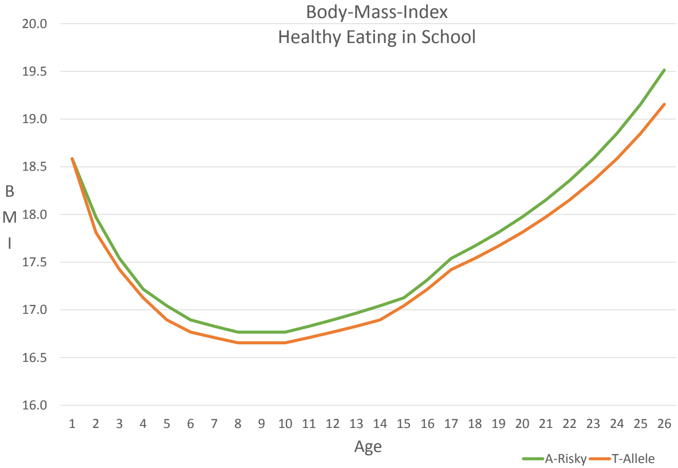


Thank You



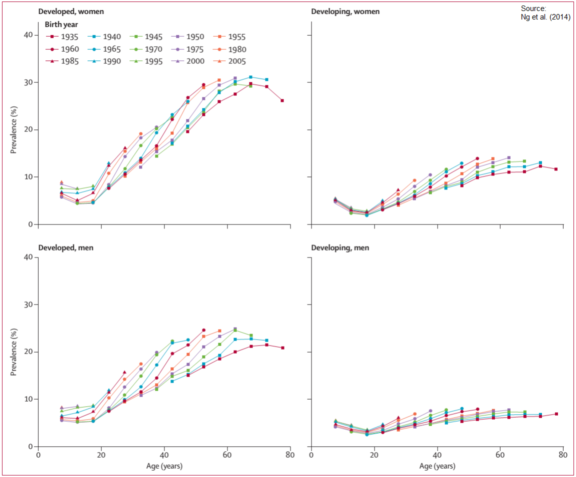
Policy B: School Eating

Reduce caloric consumption by 25% in the first 10 years of life



Appendix

Body-Mass-Index and obesity: major health problem



Cost Consequences

- Health: (US) $14.3 billion for children, $147 billion for adults, 400k deaths;
- Economic: lower skills acquisition, wages, labor force, and productivity.
  ↪ see [Cawley, 2010, Kline and Tobias, 2008, Ng et al., 2014]

Summary Statistics

Table: Summary Statistics, Age 11 and 13 by genotype and father SES

	Genotype		Father SES		Total
	T-Allele	A-Risky	High	Low	
Body Mass Index	19.10	19.47	19.17	19.39	19.33
	(11.24)	(11.07)	(10.09)	(11.68)	(11.17)
	[0.07]***	[0.05]***	[0.06]**	[0.06]**	
Overweight (%)	22.17	28.48	23.39	27.47	26.19
	(17.26)	(20.37)	(17.92)	(19.93)	(19.33)
	[0.82]***	[0.67]***	[0.75]***	[0.82]***	
Kilocalories/day	1.89	1.92	1.91	1.90	1.91
	(0.21)	(0.19)	(0.19)	(0.20)	(0.20)
	[0.01]**	[0.01]**	[0.01]	[0.01]	
Sedentary Hours/day	7.51	7.55	7.67	7.43	7.54
	(1.54)	(1.59)	(1.46)	(1.65)	(1.58)
	[0.02]	[0.02]	[0.02]**	[0.02]**	
n obs.	2562	4490	3722	3330	7052

Mean of Body Mass Index (BMI kg/m^2), percentage overweight (BMI greater than 85% pct), sedentary hours, and Kilocalories (x1000), by FTO variant and father SES. Sample variance in parenthesis; mean standard-error in brackets.

49% of the sample is male. 63% of the sample carries one or two A-Alleles in the rs9939609 SNP of the FTO gene (15% are heterozygous AA, Minor Allele Frequency of 0.39 representative of UK population). High SES: manager or professional (47%); low: worker (skilled or unskilled), based on OPCS occupation codes.

Identification and limitations

Identification:

- Mendelian Randomization: Mendel's first law of segregation
- Genotype random conditional on parental g
- Dad genotype unobserved $\rightarrow$ bound using [Altonji et al., 2008]

Limitations:

- Measurement error and misreporting $\rightarrow$ attenuation
- Potential endogeneity of investments

Parametrization of the Model

Utility

$$u\left(B,F,\ell,c;g\right)=\zeta_B\log B+\zeta_F(g)\log F+\zeta_\ell\log\ell+\zeta_c\log c$$

Production function

$$\log B_{t+1}=\log\phi(g)+a(g)\log F_t+b(g)\log E_t+(1-\delta_1-t/T\delta_2)\log B_t+\varepsilon_t$$

- 10 Parameters $\left(\zeta_B,\zeta_F(g),\zeta_\ell,\zeta_c,\phi(g),a(g),b(g),\delta_1,\delta_2,\sigma^2_\varepsilon\right)$
- 4 vary by genotype

back

Calibrated Parameters

Parameters taken from the literature:

- $\beta = 0.97$ (As in Hubbard, Skinner, and Zeldes (1995); and Engen, Gale, and Uccello (1999))
- $\zeta_c = 0.36$ (As in Scholz and Seshadri (2013))

Calibrated:

- $\zeta_B = 0.4$
- $\zeta_\ell = 0.4$
- $\zeta_{F(0)} = 0.1$
- $\zeta_{F(1)} = 0.2$
- $a(0) = 0.06$
- $a(1) = 0.09$
- $b(0) = 0.3$
- $b(1) = 0.3$
- $\phi(0) = 1.0$
- $\phi(1) = 1.1$
- $\delta_1 = 0.02$
- $\delta_2 = 0.04$

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Alternative Parametrization of the Model

Utility

$$u\left(B, F, \ell; g\right) = \frac{\left\{\lambda\left[F^{\eta(g)}\ell^{1-\eta(g)}\right]^{\rho} + (1-\lambda)B^{\rho}\right\}^{\frac{1-\sigma}{\rho}}}{1-\sigma} + \alpha c_t$$

- 11 Parameters: $\lambda, \eta(g), \rho, \sigma, \alpha, \phi(g), a(g), b(g), \delta_1, \delta_2, \sigma_\varepsilon^2$
- 4 vary by genotype

back

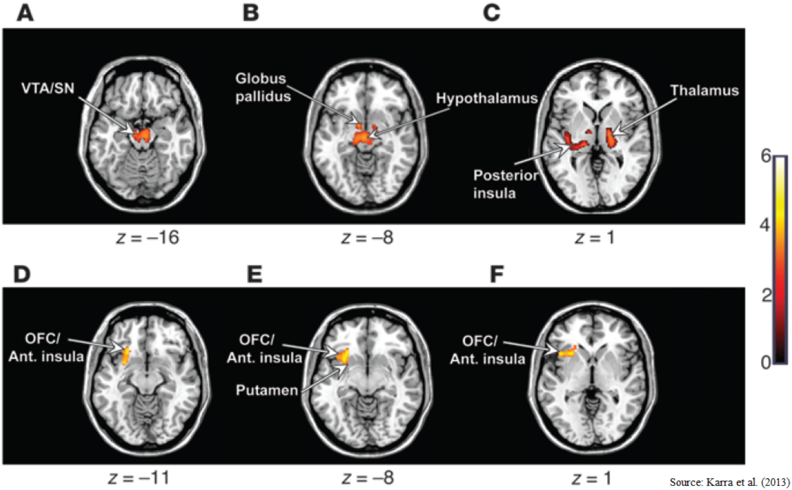
Moments to Match

Match the following moments from the ALSPAC data:

- F_t, E_t at ages 11 and 13
- Average, median, and BMI cutoff at different ages
- $Cov(B_t, F_{t-1})$
- $Cov(B_t, E_{t-1})$
- $Cov(B_t, B_{t-1})$
- $Cov(F_t, E_t)$

back

Brain Imaging, Appetite, and FTO

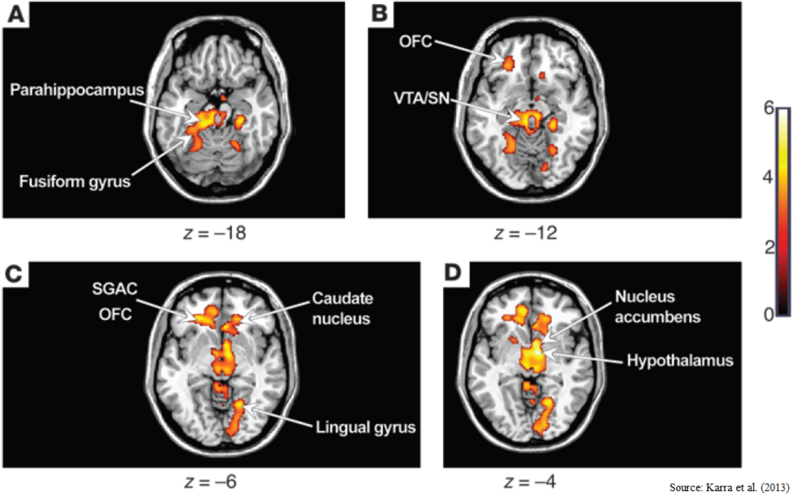


Source: Karra et al. (2013)

Figure: Brain regions where the TT and AA genotypes exhibited different BOLD responses in fMRI when viewing food/non-food images while fasting (A-F); or comparing interaction between fed/fasting and high-incentive/low-incentive-value food (D-F)

Back

Brain Imaging, Appetite, and FTO



Source: Karra et al. (2013)

Figure: Brain regions where the circulating acyl-ghrelin differentially affected brain fMRI responses in TT and AA genotypes

Back

Endogeneity of Inputs

- So far, assumed $I_e, I_d \perp\!\!\!\perp \varepsilon_H$
- Now, consider system of equations:

$$\begin{cases} B_t & = f(I_d, I_e, B_{t-1}, X; g) + \varepsilon_H \\ I_d & = I_d\left(I_e, B_{t-1}, X, Z; g\right) + \varepsilon_d \\ I_e & = I_e\left(I_d, B_{t-1}, X, Z; g\right) + \varepsilon_e \end{cases}$$

- Exclusion restriction: $Z \perp\!\!\!\perp \varepsilon_k$
  - Lagged investments $I_{k,t-1}$
  - Income Y, family composition, distance to school
  - Mother and Father behaviors

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Instrumented Regression

Table: Health Production Function - Instrumented Regression

		(1) OLS	(2) Lagged Invest	(3) Income	(4) Parental Behavior
Risky FTO Gene	β_g	0.010	0.006	0.025	0.037
		[0.002]***	[0.002]**	[0.020]	[0.026]
log(Food Intake)	α_f	0.067	0.073	0.365	0.660
		[0.009]***	[0.039]*	[0.346]	[0.639]
G X Food Intake	$\alpha_{g \times f}$	0.025	0.029	0.354	0.724
		[0.011]**	[0.026]	[0.366]	[0.580]
log(Sedentary min.)	α_e	0.027	-0.001	-0.203	-0.250
		[0.009]***	[0.030]	[0.248]	[0.481]
G X Sedentary min.	$\alpha_{g \times e}$	0.012	0.102	-0.195	-0.086
		[0.011]	[0.026]***	[0.364]	[0.634]
$\log(BMI)_{t-1}$	$(1 - \delta)$	0.939	0.952	0.927	0.929
		[0.008]***	[0.009]***	[0.020]***	[0.034]***
$\log(BMI)_{mom}$	γ_b	0.090	0.024	0.005	0.091
		[0.007]***	[0.022]	[0.015]	[0.008]***
Covariates		X	X	V	X
Observations		7052	6264	7052	7052

Dependent variable: log BMI (kg/m^2). 3-stage-least-square estimation. Column (1) reports the baseline results from OLS regression in table (1). Column (2) uses lagged values of food intake, protein intake, and sugar intake as instruments for caloric intake; lagged sedentary minutes, moderate to vigorous activity, and counts per minutes as instruments for investment in exercise. Column (3) uses income and financial difficulties, mother and father SES, mother and father education, distance to school, and number of siblings as instruments for both investments. Column (4) uses mother and father Food intake when child was 4-years old, and mother self-reported level of physical activity as instruments for investments. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level and correlated across equations in brackets. Risky FTO gene $g = 1$ if rs9939609 gene variant contains one or more A-alleles; $g = 0$ otherwise; Covariates X: gender; parity; age of child at clinic date; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight. Covariates V: gender; age of child at clinic date; mother age at pregnancy; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight. back

Utility Cost Effect

Table: Investment Equation - Food Intake

(2)		(3)		(4)	
Risky FTO	0.017	Risky FTO	0.109	Risky FTO	0.112
Gene	[0.006]***	Gene	[0.077]	Gene	[0.076]
log(Sed	-0.222	log(Sed	-19.590	log(Sed	-19.459
Min)	[0.052]***	Min)	[0.128]***	Min)	[0.184]***
Lagged	0.198	Income	0.009	Mom Food Int.	0.063
Food Int.	[0.021]***		[0.073]	(age 4)	[0.143]
Lagged	0.074	Mom SES	-0.012	Dad Food Int.	0.018
Protein Int.	[0.014]***		[0.045]	(age 4)	[0.183]
Lagged	0.042	Dad SES	-0.106	Mom Physical	-0.227
Sugar Int.	[0.009]***		[0.036]***	Activity	[0.099]**
		Mom Edu	0.259		
			[0.041]***		
		Dad Edu	0.071		
			[0.036]**		
		Distance	0.176		
			[0.041]***		
		Num Sibling	-0.153		
			[0.048]***		
Covariates	X		V		X
Observations	6264		7052		7052
Instrument: Lag Investment		Income and distance to school		Parental Behavior	

Dependent variable: log(Food Intake). 3-stage-least-square estimation. Column (2) uses lagged values of food intake, protein intake, and sugar intake as instruments for caloric intake; lagged sedentary minutes, moderate to vigorous activity, and counts per minutes as instruments for investment in exercise. Column (3) uses income and financial difficulties, mother and father SES, mother and father education, distance to school, and number of siblings as instruments for both investments. Column (4) uses mother and father Food intake when child was 4-years old, and mother self-reported level of physical activity as instruments for investments. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level and correlated across equations in brackets. Risky FTO gene $g = 1$ if rs9939609 gene variant contains one or more A-alleles; $g = 0$ otherwise; Covariates X: gender; parity; age of child at clinic date; log mom BMI during pregnancy; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight. Covariates V: gender; age of child at clinic date; mother age at pregnancy; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

Utility Cost Effect - 2

Table: Investment Equation - Sedentary Minutes

(2)		(3)		(4)	
Risky FTO	0.008	Risky FTO	0.006	Risky FTO	0.006
Gene	[0.004]*	Gene	[0.004]	Gene	[0.004]
log(Food	-0.187	log(Food	-0.051	log(Food	-0.051
Intake)	[0.010]***	Intake)	[0.000]***	Intake)	[0.000]***
Lagged	0.191	Income	0.000	Mom Food Int.	0.003
Sedentary Min	[0.020]***		[0.004]	(age 4)	[0.007]
Lagged	0.021	Mom SES	-0.001	Dad Food Int.	0.001
Vig. Activity	[0.006]***		[0.002]	(age 4)	[0.009]
Lagged	-0.140	Dad SES	-0.005	Mom Physical	-0.012
Counts per min	[0.019]***		[0.002]***	Activity	[0.005]**
		Mom Edu	0.013		
			[0.002]***		
		Dad Edu	0.004		
			[0.002]**		
		Distance	0.009		
			[0.002]***		
		Num Sibling	-0.008		
			[0.002]***		
Covariates	X		V		X
Observations	6264		7052		7052
Instrument: Lag Investment		Income and distance to school		Parental Behavior	

Dependent variable: log(Sedentary min.). 3-stage-least-square estimation. Column (2) uses lagged values of food intake, protein intake, and sugar intake as instruments for caloric intake; lagged sedentary minutes, moderate to vigorous activity, and counts per minutes as instruments for investment in exercise. Column (3) uses income and financial difficulties, mother and father SES, mother and father education, distance to school, and number of siblings as instruments for both investments. Column (4) uses mother and father Food intake when child was 4-years old, and mother self-reported level of physical activity as instruments for investments. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level and correlated across equations in brackets. Risky FTO gene $g = 1$ if rs9939609 gene variant contains one or more A-alleles; $g = 0$ otherwise; Covariates X: gender; parity; age of child at clinic date; log mom BMI during pregnancy; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight. Covariates V: gender; age of child at clinic date; mother age at pregnancy; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

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Summary Statistics, Investments

Table: Summary Statistics, Food Intake and Exercise

	FTO genotype		
	T-Allele	A-Risky	Total
Kilocalories	1.89**	1.92**	1.91
(x1000)	[0.01]	[0.01]	[0.01]
Fat Intake	75.82**	77.10**	76.64
(grams/day)	[0.45]	[0.33]	[0.27]
Dietary Cholesterol Intake	188.66**	193.39**	191.67
(grams/day)	[1.88]	[1.44]	[1.15]
Carbohydrate Intake	252.83*	255.58*	254.58
(grams/day)	[1.30]	[0.94]	[0.76]
Total Sugar Intake	114.74	115.87	115.46
(grams/day)	[0.91]	[0.64]	[0.53]
Physical Activity	7.51	7.55	7.54
(Sedentary Hours)	[0.02]	[0.02]	[0.01]
Physical Activity	23.92	23.68	23.77
(Moderate To Vigorous)	[0.32]	[0.25]	[0.20]
Physical Activity	581.96	576.78	578.66
(counts per minute)	[3.73]	[2.84]	[2.26]
Very Active	3.69	3.71	3.7
(self-report)	[0.02]	[0.01]	[0.01]

Average measures of investment in diet, and investment in exercise. Pooled across gender and ages, separated by FTO-genotype. Standard errors of means in brackets. Mean difference * significant at 10%; ** significant at 5%; *** significant at 1%. 3-day dietary records coded using the Diet In Data Out software. Actigraph data: counts per min., min. of sedentary activity, and moderate to vigorous activity. Self-reported activity ranged from 1 (never) to 5 (daily). Back

Summary Statistics, by age

Table: Summary Statistics by age, gender, and genotype

	Body Mass Index				Sedentary Hours			
	Female		Male		Female		Male	
Age	T-Allele	A-Allele	T-Allele	A-Allele	T-Allele	A-Allele	T-Allele	A-Allele
8	16.25	16.42	16.06	16.13	.	.	.	.
	(4.71)	(4.57)	(3.37)	(3.59)	.	.	.	.
	[0.07]	[0.05]	[0.06]	[0.04]	.	.	.	.
11	18.50	18.99	18.17	18.62	7.18	7.25	6.89	6.98
	(10.39)	(10.80)	(8.56)	(10.29)	(1.19)	(1.21)	(1.27)	(1.45)
	[0.10]	[0.08]	[0.09]	[0.07]	[0.04]	[0.03]	[0.04]	[0.03]
13	20.41	20.87	19.74	20.08	8.26	8.24	7.73	7.77
	(11.84)	(12.56)	(10.29)	(11.68)	(1.32)	(1.31)	(1.50)	(1.54)
	[0.12]	[0.09]	[0.11]	[0.09]	[0.05]	[0.03]	[0.05]	[0.04]

Mean of Body Mass Index (BMI kg/m^2), sedentary hours, and Kilocalories (in thousands), by age, gender, and FTO genotype. Sample variance in parenthesis; mean standard-error in brackets.

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Summary Statistics, by age

Table: Summary Statistics by age, gender, and genotype

	Kilocalories				Whole Sample		
	Female		Male				
Age	T-Allele	A-Allele	T-Allele	A-Allele	BMI	Sed	Kcal
8	1.64	1.64	1.75	1.79	16.23	.	1.71
	(0.08)	(0.08)	(0.09)	(0.11)	(4.08)	.	(0.10)
	[0.01]	[0.01]	[0.01]	[0.01]	[0.03]	.	[0.00]
11	1.75	1.78	1.92	1.97	18.64	7.10	1.86
	(0.13)	(0.12)	(0.15)	(0.16)	(10.23)	(1.31)	(0.15)
	[0.01]	[0.01]	[0.01]	[0.01]	[0.04]	[0.02]	[0.01]
13	1.77	1.76	2.12	2.15	20.34	8.02	1.95
	(0.21)	(0.18)	(0.30)	(0.27)	(11.92)	(1.47)	(0.27)
	[0.02]	[0.01]	[0.02]	[0.01]	[0.05]	[0.02]	[0.01]

Mean of Body Mass Index (BMI kg/m^2), sedentary hours, and Kilocalories (in thousands), by age, gender, and FTO genotype. Sample Variance in parenthesis; mean standard-error in brackets.

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Summary Statistics, by gender

Table: Summary Statistics, by gender

	Female		Male		Total
	T-Allele	A-Risky	T-Allele	A-Risky	
Body Mass Index	19.34	19.77	18.83	19.14	19.33
	(11.80)	(11.73)	(10.49)	(10.16)	(11.17)
	[0.09]***	[0.07]***	[0.09]***	[0.07]***	
Kilocalories/day	1.77	1.79	2.02	2.06	1.91
	(0.16)	(0.14)	(0.23)	(0.21)	(0.20)
	[0.01]	[0.01]	[0.01]***	[0.01]***	
Sedentary Hours/day	7.70	7.72	7.29	7.36	7.54
	(1.51)	(1.52)	(1.50)	(1.62)	(1.58)
	[0.03]	[0.03]	[0.04]	[0.03]	

Mean of Body Mass Index (BMI kg/m^2), sedentary hours, and Kilocalories (x1000), by gender and FTO variant. Sample variance in parenthesis; mean standard-error in brackets.

49% of the sample is male. 63% of the sample carries one or two A-Alleles in the rs9939609 SNP of the FTO gene (15% are heterozygous AA, Minor Allele Frequency of 0.39, representative of UK population)

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Summary Statistics, Anthropometrics

Table: Summary Statistics, Anthropometrics

	FTO genotype		
	T-Allele	A-Risky	Total
Height	154.51	154.81	154.7
(cm)	[0.21]	[0.16]	[0.13]
Weight	46.22***	47.26***	46.88
(kg)	[0.24]	[0.18]	[0.14]
BMI	19.10***	19.47***	19.33
kg/cm^2	[0.07]	[0.05]	[0.04]
BMI z-score	0.20***	0.35***	0.3
	[0.02]	[0.02]	[0.01]
Fat Percentage	24.31***	25.42***	25.02
	[0.19]	[0.15]	[0.12]
Overweight (%)	22.17***	28.49***	26.19
	[0.82]	[0.67]	[0.52]
Underweight (%)	4.18	3.56	3.79
	[0.40]	[0.28]	[0.23]
Arm Circ.	23.90***	24.34***	24.18
(cm)	[0.07]	[0.05]	[0.04]
Waist Circ.	68.45***	69.39***	69.05
(cm)	[0.19]	[0.14]	[0.11]
Waist/Hip ratio	0.82	0.82	0.82
	[0.00]	[0.00]	[0.00]

Body mass index normal z-scores calculated using 1990 British Growth Reference. Fat percentage: ratio of fat mass to total mass. Overweight and Underweight calculated using the BMI z-scores with a cutoff of 5% and 85%. Standard errors of means in brackets. Mean difference * significant at 10%; ** significant at 5%; *** significant at 1%.

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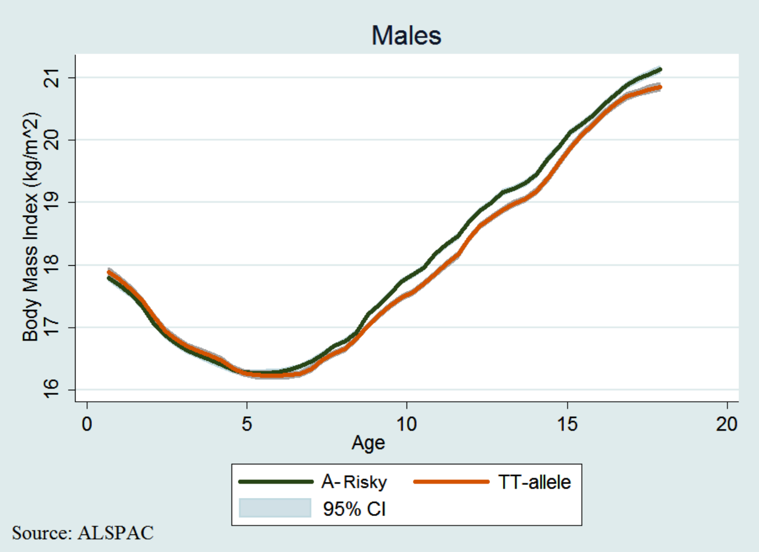
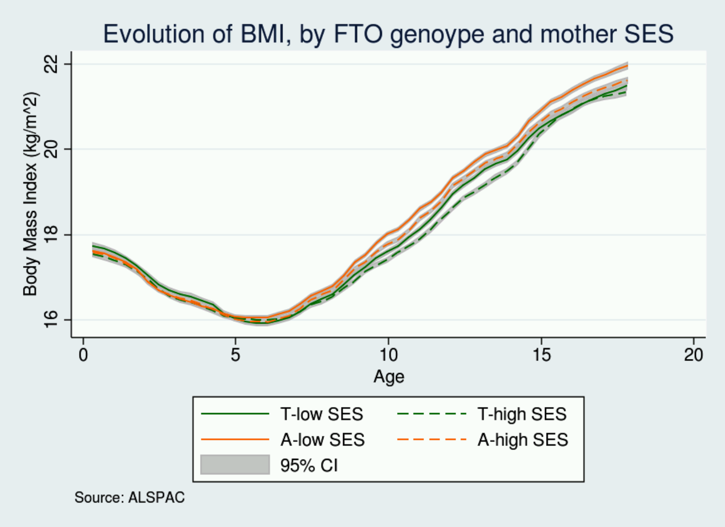
Evolution of Body Mass Index



Back Density

Evolution of Body Mass Index



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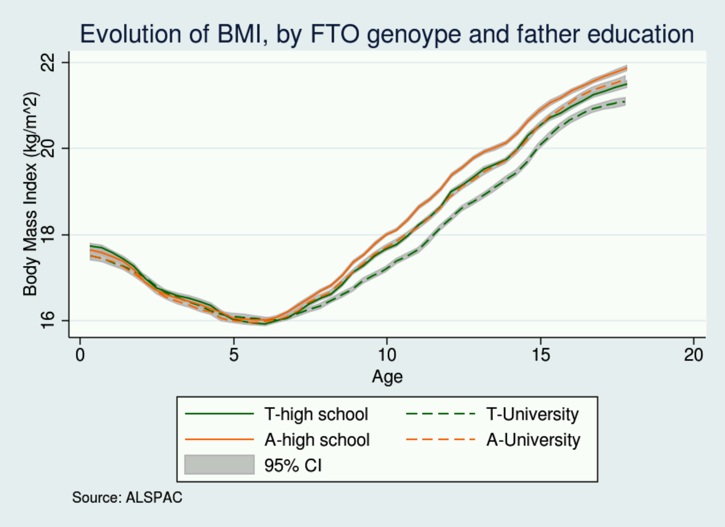
Evolution of Body Mass Index



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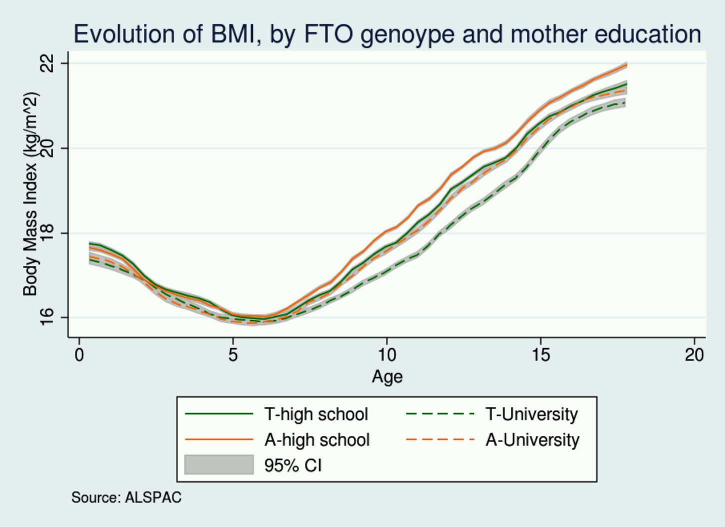
Evolution of Body Mass Index



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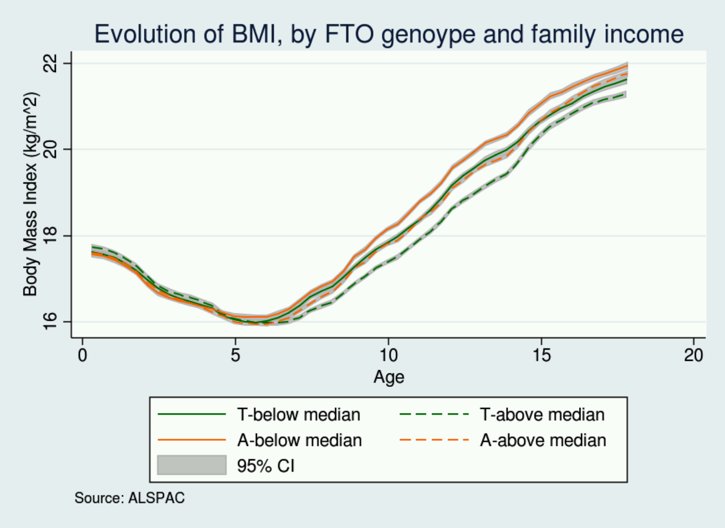
Evolution of Body Mass Index



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Summary Statistics, Environment and Covariates

Table: Family Characteristics, by Child FTO genotype

	FTO genotype		
	T-Allele	A-Risky	Total
Mother Edu	3.36	3.33	3.34
	[0.03]	[0.02]	[0.02]
Father Edu	3.32	3.34	3.33
	[0.04]	[0.03]	[0.02]
Mother SES	2.75	2.78	2.77
	[0.02]	[0.02]	[0.02]
Father SES	2.88	2.84	2.86
	[0.03]	[0.02]	[0.02]
Mother BMI	22.74**	23.00**	22.90
	[0.10]	[0.08]	[0.06]
Mother age	29.33	29.35	29.34
at birth	[0.12]	[0.09]	[0.07]
Teen mother (%)	1.51	2.10	1.88
	[0.33]	[0.29]	[0.22]
Single Mother (%)	15.85	15.28	15.49
	[0.98]	[0.73]	[0.58]
Parity	0.69	0.73	0.72
	[0.02]	[0.02]	[0.01]
Birth Weight (kg)	3.42	3.43	3.42
	[0.01]	[0.01]	[0.01]

Average value of the covariates for the sample used in the main analysis. Pooled across genders and separated by FTO-genotype. Standard errors of means in brackets. Mean difference * significant at 10%; ** significant at 5%; *** significant at 1%.
Education ranges from lowest (1 = CSE or less) to highest (5 = degree). Socio-Economic-Status ranges from from highest (1 = professional) to lowest (6 = unskilled). Teen mother is a dummy for mothers who were pregnant before age 19. Single mother is a dummy for a household without a male figure.

Gene×Calories Interaction

Figure: Nonparametric local-mean smoothing using Epanechnikov kernel and Silverman's Rule-of-Thumb bandwidth. Combining information from successive clinical visits, age 11 and 13; excluding outliers in the top and bottom 5% of the distributions of BMI and log(energy intake). ▸ Density ▸ Back

Gene×Calories Interaction

Figure: Nonparametric local-mean smoothing using Epanechnikov kernel and Silverman's Rule-of-Thumb bandwidth. Combining information from successive clinical visits, age 11 and 13; excluding outliers in the top and bottom 5% of the distributions of BMI and log(energy intake). ▸ Density ▸ Back

Gene×Exercise Interaction

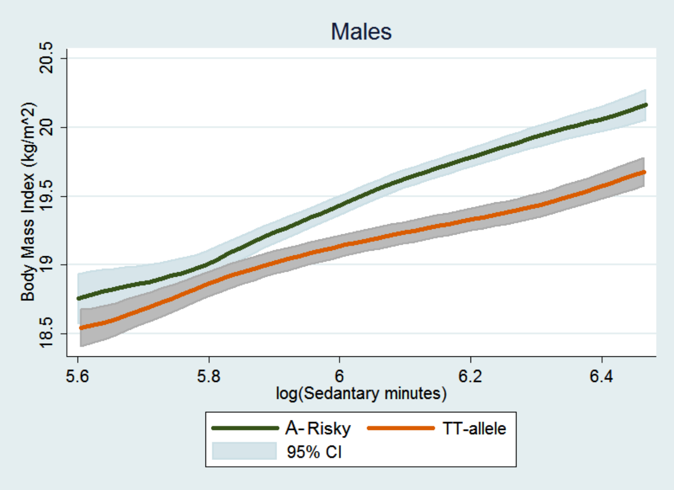

Figure: Nonparametric local-mean smoothing using Epanechnikov kernel and Silverman's Rule-of-Thumb bandwidth. Combining information from successive clinical visits, age 11 and 13; excluding outliers in the top and bottom 5% of the distributions of BMI and log(sedentary minutes).

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Gene×Exercise Interaction

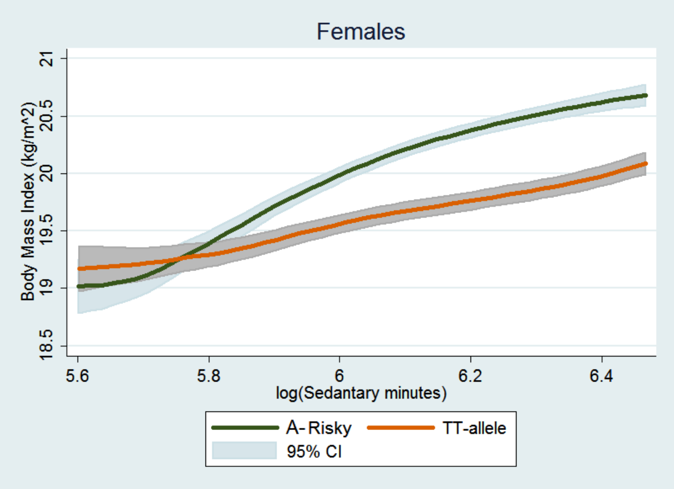

Figure: Nonparametric local-mean smoothing using Epanechnikov kernel and Silverman's Rule-of-Thumb bandwidth. Combining information from successive clinical visits, age 11 and 13; excluding outliers in the top and bottom 5% of the distributions of BMI and log(sedentary minutes).

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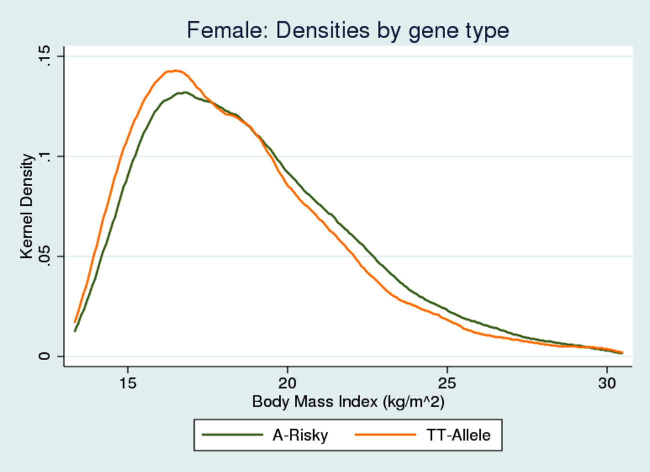
Distribution of BMI, Females



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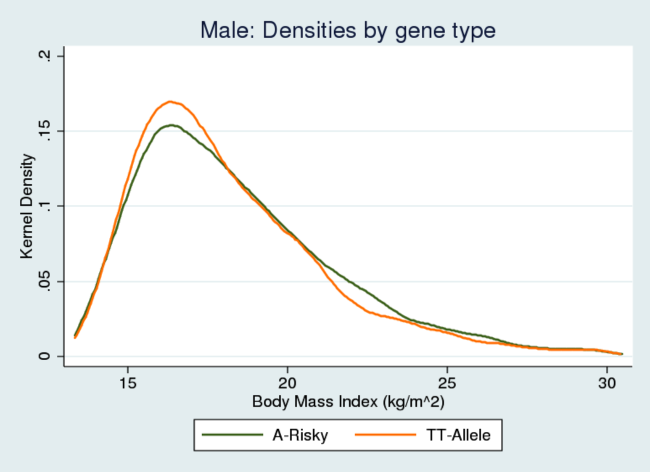
Distribution of BMI, Males



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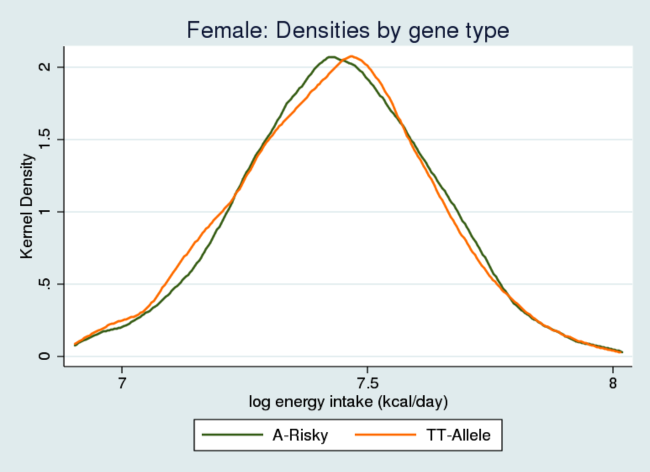
Distribution of Caloric Intake, Females



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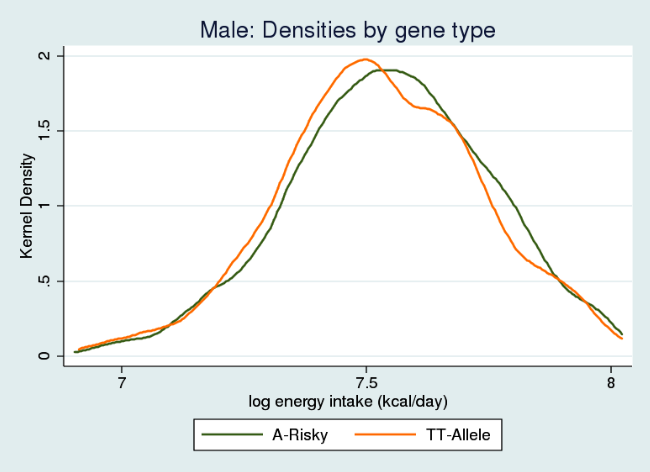
Distribution of Caloric Intake, Males



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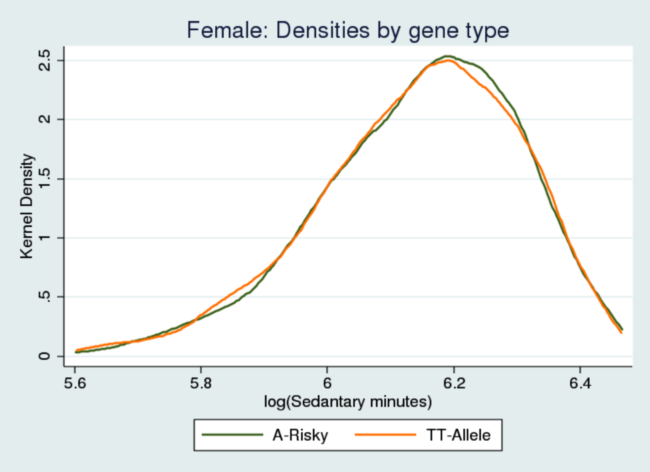
Distribution of Exercise, Females



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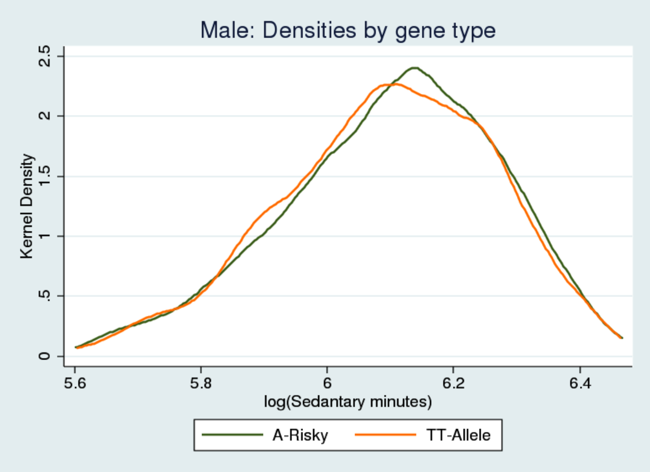
Distribution of Exercise, Males



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Heterogeneity by group

Table: By Gender and Without Underweight

		(1) Baseline	(2) Males	(3) Females	(4) No Underweight
Risky FTO Gene	β_g	0.010	0.006	0.010	0.011
		[0.002]***	[0.004]	[0.003]***	[0.003]***
log(Food Int.)	α_f	0.067	0.067	0.082	0.069
		[0.009]***	[0.013]***	[0.014]***	[0.009]***
G X Food Int.	$\alpha_{g\times f}$	0.025	0.004	0.044	0.030
		[0.011]**	[0.016]	[0.018]**	[0.011]***
log(Sedentary m.)	α_e	0.027	0.042	0.007	0.028
		[0.009]***	[0.013]***	[0.013]	[0.009]***
G X Sedentary m.	$\alpha_{g\times e}$	0.012	0.026	-0.007	0.009
		[0.011]	[0.016]*	[0.016]	[0.011]
B_{t-1}	$(1-\delta)$	0.939	0.947	0.928	0.911
		[0.008]***	[0.012]***	[0.011]***	[0.008]***
Controls		X	X	X	X
R^2		78%	79%	79%	77%
Observations		7,052	3,346	3,706	6,785

Column (1) reports the baseline estimates (same as table 1). Column (2) and (3) run the model separately for males and females. Column (4) runs the model dropping the children who are below the 5^{th} percentile of the z-BMI standard distribution for the UK (they represent 4% of the sample).

* significant at 10%; ** significant at 5%; *** significant at 1%. Standard errors in brackets. Risky FTO gene $g = 1$ if rs9939609 gene variant contains one or more A-Alleles; $g = 0$ otherwise. Covariates: gender; parity; age of child at clinic date; log mom BMI during pregnancy; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

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Measurement of Adiposity

Table: Different Measures of Adiposity

		(1) Prob Overweight	(2) BMI and Height	(3) Weight	(4) zBMI	(5) Fat %
Risky FTO Gene	β_g	0.228	0.010	0.012	0.081	-0.011
		[0.065]***	[0.002]***	[0.003]***	[0.019]***	[0.019]
log(Food Int.)	α_f	0.500	0.060	0.072	0.490	0.036
		[0.224]**	[0.009]***	[0.011]***	[0.070]***	[0.078]
G X Food Int.	$\alpha_{g\times f}$	0.091	0.025	0.030	0.199	0.029
		[0.274]	[0.011]**	[0.013]**	[0.083]**	[0.093]
log(Sedentary m.)	α_e	0.554	0.026	0.031	0.189	0.141
		[0.218]**	[0.009]***	[0.011]***	[0.067]***	[0.068]**
G X Sedentary m.	$\alpha_{g\times e}$	0.082	0.012	0.009	0.076	0.021
		[0.252]	[0.011]	[0.013]	[0.080]	[0.081]
B_{t-1}	$(1-\delta)$	2.101	0.934	0.761	0.869	0.306
		[0.052]***	[0.008]***	[0.008]***	[0.008]***	[0.022]***
log(Height)			0.106	0.92		
			[0.021]***	[0.031]***		
Controls		X	X	X	X	X
R^2			78%	88%	77%	55%
Observations		7,052	7,050	7,048	7,052	5,305

Column (1) runs a probit model on the probability of being obese. Column (2) uses B_t =log(weight) as dependent variable, controlling for log(height). Column (3) uses z-BMI as dependent variable. Column (4) uses the estimated percentage of body fat as dependent variable. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard errors in brackets. Risky FTO gene $g=1$ if rs9939609 gene variant contains one or more A-Alleles; $g=0$ otherwise. Covariates: gender; parity; age of child at clinic date; log mom BMI during pregnancy; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

Measurement of Food Intake

Table: Different Measures of Food Intake - FTO gene

		(1) Calories	(2) Proteins	(3) Fat	(4) Carbs	(5) Dietary Cholesterol	(6) Sugar	(7) Starch
Risky FTO Gene	β_g	0.010	0.010	0.009	0.008	0.008	0.007	0.008
		[0.002]***	[0.002]***	[0.002]***	[0.002]***	[0.002]***	[0.002]***	[0.002]***
log(Food)	α_f	0.067	0.046	0.037	0.047	0.010	0.011	0.046
		[0.009]***	[0.007]***	[0.007]***	[0.008]***	[0.004]***	[0.005]**	[0.007]***
G X Food	$\alpha_{g \times f}$	0.025	0.027	0.015	0.013	0.009	0.002	0.011
		[0.011]**	[0.009]***	[0.008]*	[0.010]	[0.005]*	[0.006]	[0.009]
log(Sedentary min.)	α_e	0.027	0.025	0.027	0.026	0.024	0.024	0.027
		[0.009]***	[0.009]***	[0.009]***	[0.009]***	[0.009]**	[0.009]**	[0.009]***
G X Sedentary min.	$\alpha_{g \times e}$	0.012	0.010	0.013	0.011	0.010	0.010	0.011
		[0.011]	[0.011]	[0.011]	[0.011]	[0.011]	[0.011]	[0.011]
$\log(BMI)_{t-1}$	$(1-\delta)$	0.939	0.939	0.944	0.942	0.945	0.946	0.943
		[0.008]***	[0.008]***	[0.008]***	[0.008]***	[0.008]***	[0.008]***	[0.008]***
Covariates		X	X	X	X	X	X	X
R^2		78%	78%	78%	78%	78%	78%	78%
Observations		7052	7052	7052	7052	7051	7052	7052

Column (1) reports the baseline estimates (same as table 1). The different measures of dietary intake used are: Food intake (kilocalories/day - column 1); protein intake (grams/day - column 2); fat intake (grams/day - column 3); carbohydrate intake (grams/day - column 4); dietary cholesterol intake (mg/day - column 5); total sugar intake (grams/day - column 6); starch intake (grams/day - column 7); non-starch polysaccharide (fibre) intake (grams/day - column 8); factor score of all the dietary measures (column 9); * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets. Dependent variable: log BMI (kg/m^2); Covariates: gender; parity; age of child at clinic date; log mom BMI during pregnancy; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

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Measurement of Exercise

Table: Different Measures of Physical Activity - FTO gene

		(1) Sedentary min	(2) MVPA	(3) Counts per min	(4) Factor Score
Risky FTO Gene	β_g	0.010	0.009	0.009	0.009
		[0.002]***	[0.002]***	[0.003]***	[0.002]***
log(Food Intake)	α_f	0.067	0.068	0.069	0.069
		[0.009]***	[0.009]***	[0.009]***	[0.009]***
G X Food Intake	$\alpha_{g \times f}$	0.025	0.021	0.024	0.023
		[0.011]**	[0.011]*	[0.011]**	[0.011]**
log(Exercise)	α_e	0.027	-0.011	-0.028	-0.008
		[0.009]***	[0.002]***	[0.005]***	[0.002]***
G X Exercise	$\alpha_{g \times e}$	0.012	-0.001	-0.009	-0.002
		[0.011]	[0.002]	[0.006]	[0.002]
$\log(BMI)_{t-1}$	$(1-\delta)$	0.939	0.934	0.936	0.936
		[0.008]***	[0.008]***	[0.008]***	[0.008]***
Covariates		X	X	X	X
R^2		78%	79%	79%	79%
Observations		7052	7043	7052	7043

Column (1) reports the baseline estimates (same as table 1). The different measures of exercise used are: sedentary minutes (column 1); moderate to vigorous physical activity (MVPA - column 2); counts per minute (column 3) factor score of all the exercise measures (column 4);

* significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets. Dependent variable: log BMI (kg/m^2); Covariates: gender; parity; age of child at clinic date; log mom BMI during pregnancy; mom and dad education and SES; mother age at pregnancy; dummy for single mother; reliable dietary report; time dummy; seasonal dummies; late respondent; birth weight.

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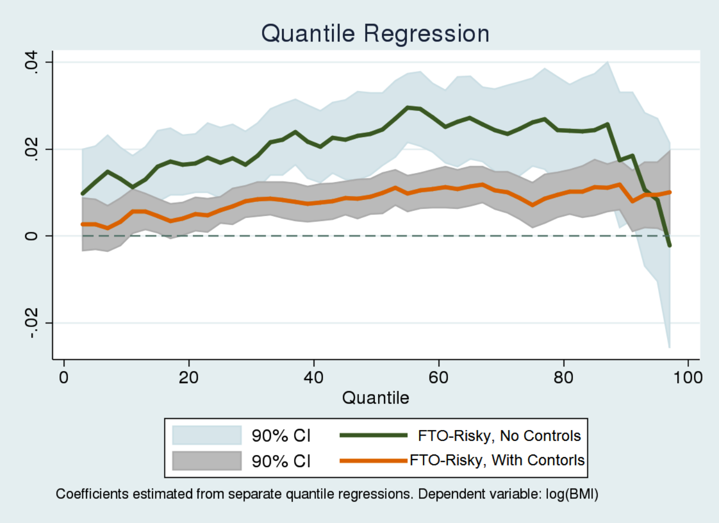
Quantile Regression



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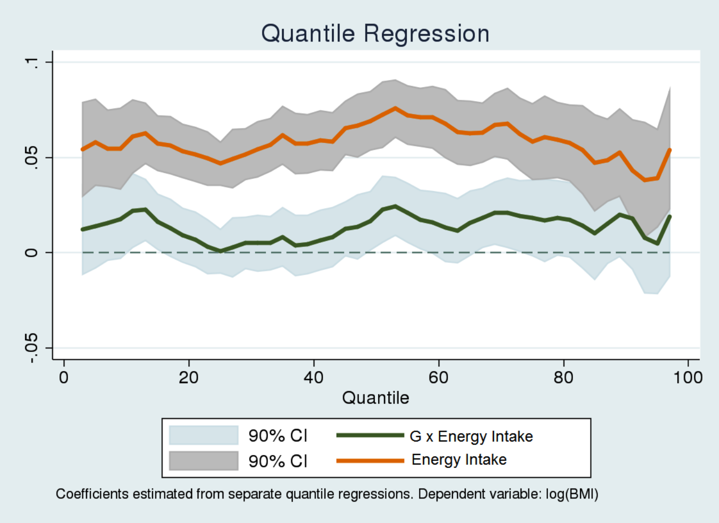
Quantile Regression



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Replication of the Results

Framingham Heart Study (FHS), Offspring Cohort

- Information on 5,124 individuals, children of the original cohort population (1948)
- Born over a 60-year period (1905-1965)
- 8 clinical exams from 1971 to 2008
- Genetic info: 1987-1991, 98% consent
- 4 waves with BMI, caloric intake, and physical activity

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FHS: Log-Linear Regression

Table: FHS: Gene and Investment Interaction - FTO

		log(Body Mass Index$_t$)			
		(1)	(2)	(3)	(4)
			born after 1940		born after 1940
Risky FTO variant	β_g	0.024***	0.043***	0.002	0.005**
		[0.007]	[0.010]	[0.001]	[0.002]
log(Energy Intake)	α_f			0.013***	0.022***
				[0.004]	[0.005]
G X Energy Intake	$\alpha_{g \times f}$			0.010**	0.016**
				[0.005]	[0.006]
log(Physical Activity)	α_e			-0.005**	-0.009***
				[0.002]	[0.003]
G X Physical Activity	$\alpha_{g \times e}$			0.003	0.001
				[0.003]	[0.004]
$\log(BMI)_{t-1}$	$(1-\delta)$			0.937***	0.927***
				[0.006]	[0.009]
Covariates				x	x
R^2		0.4%	1.2%	85.3%	84.7%
Observations		8258	4918	8258	4642
n		2753	1639	2753	1547

Dependent variable: log BMI (kg/m^2); Risky FTO gene $g = 1$ if rs9939609 gene variant contains one or more A-Alleles; $g = 0$ otherwise; Covariates: gender; 3-degree polynomial in age; dummies education and income; dummies for marital status; reliable dietary report; time dummies; birth cohort dummies; 20 first principal components of genome. * significant at 10%; ** significant at 5%; *** significant at 1%. Standard error clustered at the individual level in brackets.

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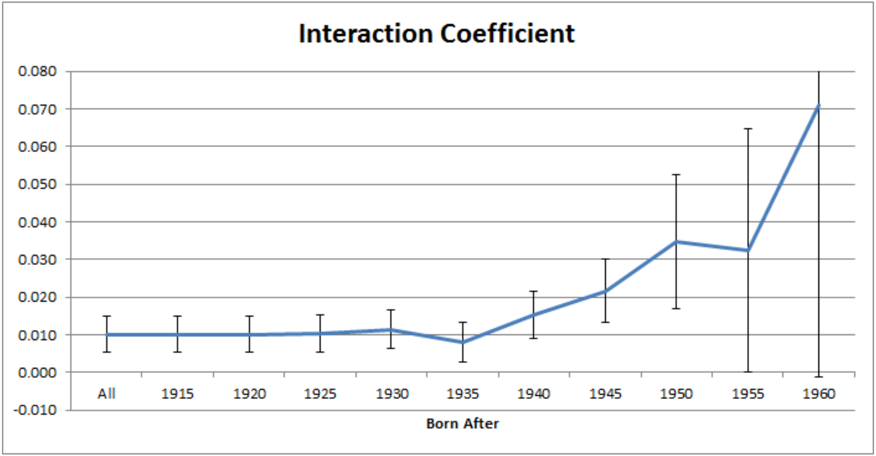
Birth Year Effects



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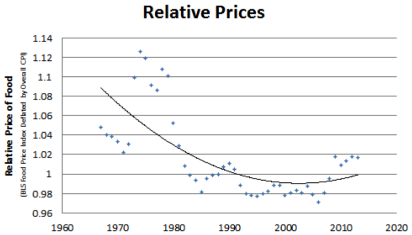
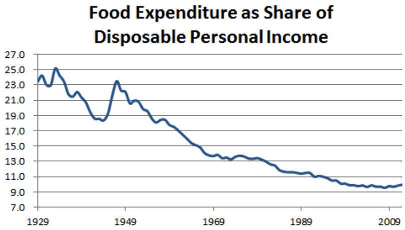
Prices, Income, Food Availability





Source: Economic Research Service, USDA; U.S. Census Bureau; and the Bureau of Labor Statistics.

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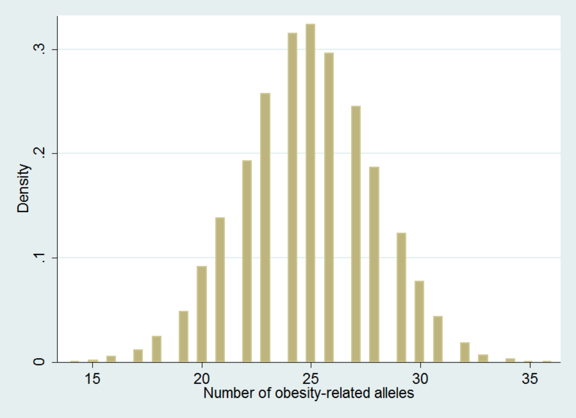
According to Mendel's laws of independent assortment, we expect a bell-shaped distribution



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Decomposition of the Genetic Effect

- Decompose the overall effect in difference in *parameters* and difference in *inputs* (Oaxaca 1973):

$$\overline{BMI}_g = \overline{W}_g \alpha_g$$

$$\Rightarrow \underbrace{\overline{BMI}_A - \overline{BMI}_T}_{\Delta\ BMI} = \underbrace{\overline{W}_T(\alpha_A - \alpha_T)}_{\Delta\ parameters} + \underbrace{(\overline{W}_A - \overline{W}_T)\alpha_A}_{\Delta\ inputs}$$

- Difference in Parameters: 35.4% [26%,39%] → productivity
- Difference in Inputs: 64.6% [47%,72%] → prefernecees