The Impact of Late-Career Job Loss and Genotype on BMI

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Are changes in weight after a job loss moderated by genotype?

- Corrosive effects of job loss documented extensively in the social science literature
- Scarring effects for older workers are particularly severe
  - Associated with longer periods of unemployment, lower levels of income, gaps in health insurance, elevated stress levels, higher rates of depression and anxiety, and increased smoking and drinking
    - Kalil & DeLeire 2013; Stevens & Moulton 2013; Deb et al. 2011; Munnell & Sass 2009; Tu & Liebhaber 2009; Falba et al. 2005; Gallo et al. 2001
- All these factors could disrupt appetite, energy balance, and metabolic function—endophenotypes that are associated with obesity and regulated by genetic variants

The genetics of obesity

- Obesity is a global epidemic that is highly heritable
  - Heritability accounts for ~30%-70% of obesity risk (e.g. Maes et al. 1997; Stunkard et al. 1986)
- GWAS: 32 genome-wide significant loci explain ~ 1.45% of the individual variation in BMI (Speliotes et al. 2010)
- Lifestyle and social context fuel onset and persistence
  - Evidence of FTO by environment interactions of exercise on the attenuation of BMI (Kilpeläinen et al. 2011), possibly mediated by DNA methylation (Bell et al. 2010; Almén et al. 2012)
  - G x E effects on BMI related to lifetime SES, social norms, and institutional policies (Liu & Guo 2015; Boardman et al. 2012)

The endogeneity problem in applied G x E research

- A significant shortcoming of many G x E studies is they rely on endogenous measures of the environment, which may be correlated with unobserved genetic or environmental influences
- Outcomes of interest in the social sciences are highly polygenic—risk of allelic association spread across the genome
  - Candidate gene studies may suffer from omitted variable bias
  - Studies rarely account for population stratification
- Need both "G" and "E" to be independent of each other to properly identify G x E effects
  - Schmitz & Conley 2015; Fletcher & Conley 2013; Conley 2009

Exogenous "E": Job loss due to a business closure

- Exogenous source of stress to employee health—driven by external influences/events, whereas layoffs or firings may be linked to worker health or other unobserved characteristics
  - Deb et al. 2011; Salm 2009; Strully 2009; Sullivan & von Wachter 2009
- Using business closures, studies have been unable to identify changes in BMI at the mean (e.g. Marcus 2014; Salm 2009)
- However increases of approx. 1 kg/m^2 have been identified for workers who were overweight pre-job loss (Deb et al. 2011)
  - Effects of job loss especially problematic for high-risk individuals

Dataset combines socio-demographic and genotype data from the HRS

- For each respondent, we use information from two waves in the HRS (1992-2012)
  - Baseline sample: individuals 63 years old or younger who were working for pay and not self-employed
  - Two years later, treatment group comprised of individuals who report they are no longer working for their previous wave employer due to a business closure
  - In total, we identify 311 genotyped respondents of European ancestry who lost their job due to a business closure

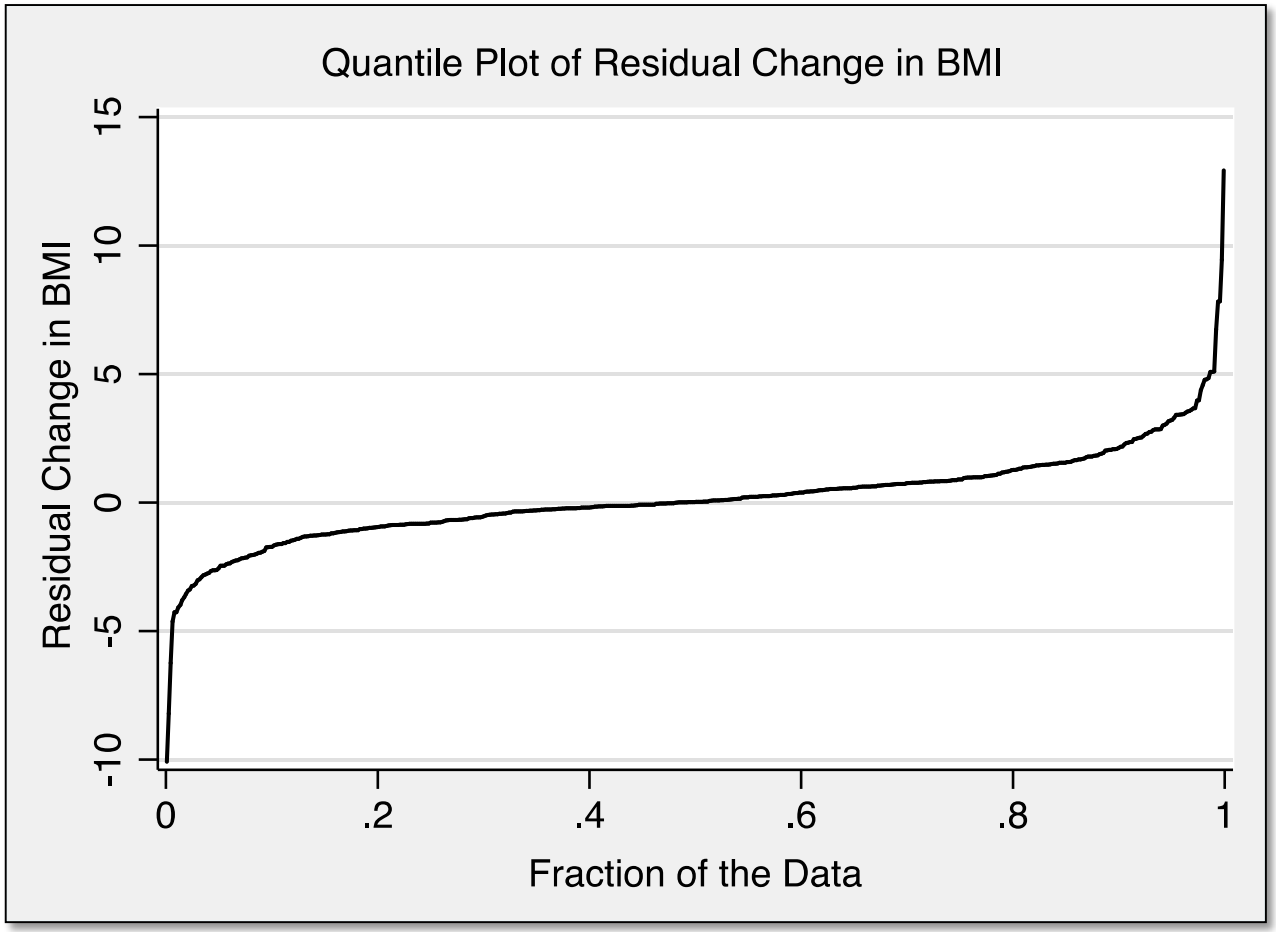
"G": Polygenic score for BMI

- Construct a linear genetic risk score (GRS) for BMI based on a GWAS meta-analysis conducted across 46 studies by the GIANT consortium (Speliotes et al. 2010)
- GRS is a weighted average across the number of SNPs (*n*) of the number of reference alleles *x* (0,1 or 2) at that SNP multiplied by the score for that SNP (β):

$$GRS_i = \sum_{j=1}^{n} (\beta_j x_{ij})$$

- We do not use imputed data or impose a p-value threshold
- In total, 838,490 SNPs were used to construct the BMI GRS for each HRS respondent

Not all individuals respond to a job loss by gaining weight



GRS measures genetic susceptibility to obesity

→Genotypic effects may play a larger role above the median

Use a quantile DID matching strategy to estimate G x E effect

Two-step approach:

- Marcus 2014; Athey & Imbends 2006; Heckman et al. 1997

1. Use one-to-one nearest-neighbor propensity score matching to find control cases that are similar to treatment cases

   → Eliminate any (observable) association between covariates and the treatment assignment

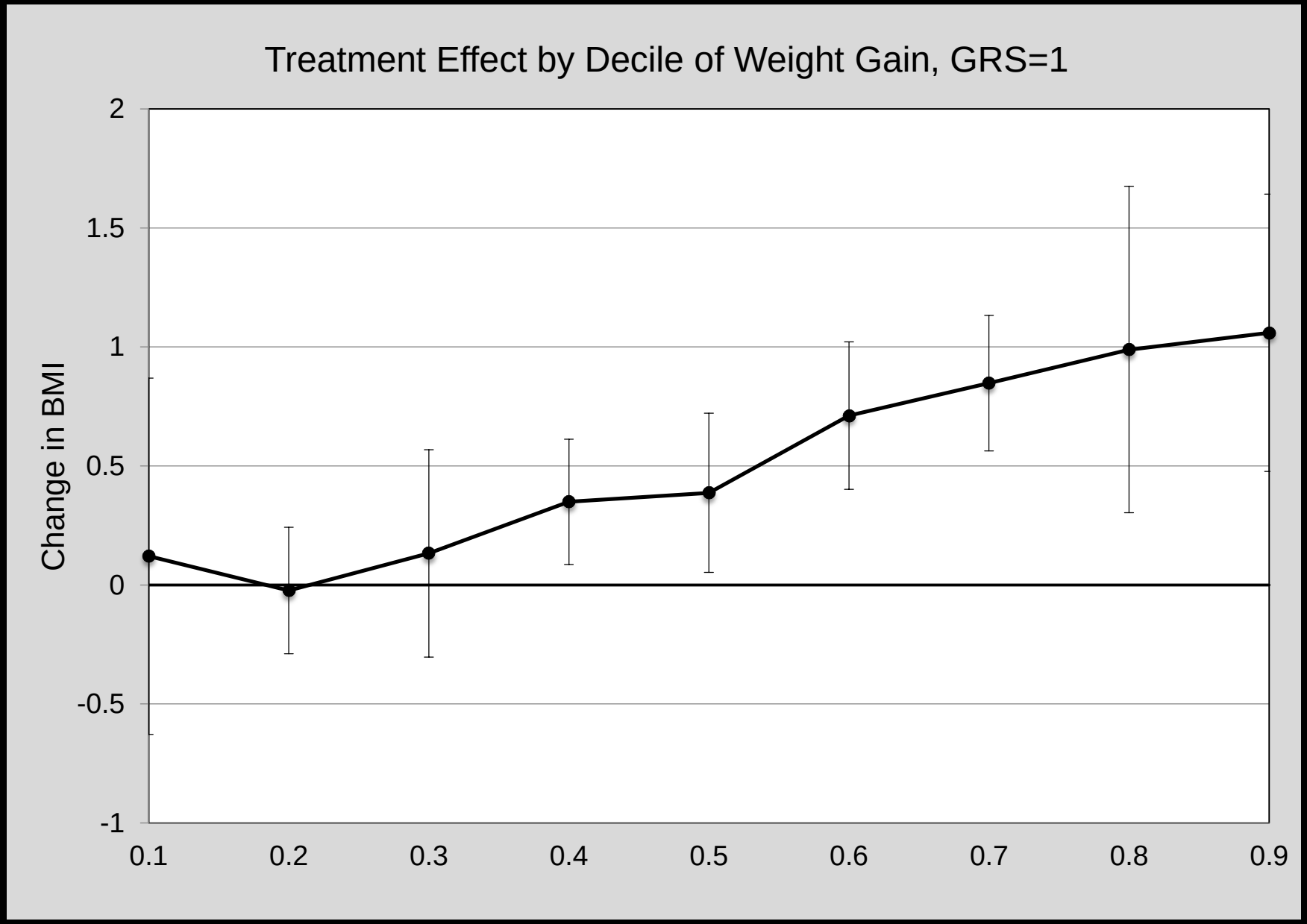
1. Use treatment and control groups determined from matching to estimate treatment effect by genotype at all portions of the distribution of changes in BMI:

$$Q_t\left(BMI_{it} \mid BC_{it-1}, BMI_{it-1}, G_i, X_{it-1}\right) = \alpha_t BC_{it-1} + \gamma_t BMI_{it-1} + \rho_t G_i + \delta_t \left(BC_{it-1} \times G_i\right) + X_{it-1}\beta_t$$

G x E effect significant at 75th percentile of weight gain

	OLS (No GRS)	OLS	Q25	Q50	Q75
Business closure	0.201	0.470***	0.0834	0.267**	0.603***
	(0.134)	(0.140)	(0.135)	(0.111)	(0.142)
Business closure*GRS		0.0579	-0.114	0.120	0.320**
		(0.156)	(0.137)	(0.110)	(0.144)
GRS		-0.0469	0.0358	-0.0740	-0.191**
		(0.0970)	(0.104)	(0.0678)	(0.0846)
BMI *(t-1)*	0.935***	0.928***	0.910***	0.952***	0.975***
	(0.0289)	(0.0269)	(0.0195)	(0.012)	(0.0186)
N	622	622	622	622	622
R2 or Pseudo-R2	0.876	0.880	0.655	0.692	0.704
Treatment Effect (GRS=1)		0.528**	-0.0301	0.387**	0.924***
		(0.219)	(0.175)	(0.170)	(0.237)

Notes: Regressions include controls for baseline age, gender, marital status, (log) income, wealth, education, part-time status, industry, smoking, exercise behavior and the first four principal components. Robust standard errors are in parenthesis.


Treatment Effect by Decile of Weight Gain, GRS=1
Change in BMI
2
1.5
1
0.5
0
-0.5
-1
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9

Endogenous job losers gained less weight

	OLS (No GRS)	OLS	Q25	Q50	Q75
Job loss	0.279***	0.257***	0.169	0.279***	0.272
	(0.0517)	(0.0518)	(0.194)	(0.0423)	(0.401)
Job loss*GRS		-0.216***	-0.193***	-0.197*	-0.232**
		(0.0521)	(0.0743)	(0.105)	(0.111)
GRS		0.280***	0.249	0.282*	0.292**
		(0.0294)	(0.175)	(0.155)	(0.122)
BMI *(t-1)*		0.932***	0.888***	0.963***	1.004***
		(0.00956)	(0.0312)	(0.0120)	(0.0534)
N	5340	5340	5340	5340	5340
R2 or Pseudo-R2	0.874	0.876	0.674	0.692	0.706
Treatment Effect (GRS=1)		0.0411	-0.0239	0.0814	0.0397
		(0.0761)	(0.203)	(0.135)	(0.486)

Notes: Regressions include controls for baseline age, gender, marital status, (log) income, wealth, education, part-time status, industry, smoking, exercise behavior and the first four principal components. Robust standard errors are in parenthesis.

Discussion

- We find evidence that the effects of job loss from a business closure on BMI are moderated by genotype
- Genotypic effects are significant at higher percentiles of weight gain only
  - Older workers at high genetic risk for weight gain (GRS=1) who lost their job gained approximately 0.39-0.92 kg/m^2 more than comparable workers who did not lose their job
  - Equivalent to a 4-7 lb. weight gain for a man who is 5'10" tall and weighs 180 lbs. at baseline
  - Stress related to job loss may amplify polygenic risk for weight gain

Summary & Implications

- Preliminary results show importance of using plausibly exogenous sources of environmental variation to identify G x E effects
  - G x E results from endogenous job loss indicate that workers who lost their job for personal or health reasons gained less weight on average than workers who did not lose their job
  - No detectable effect on high-risk genotypes (GRS=1)

Future Work

- Overall, further robustness checks and alternative specifications are needed to confirm our results
  - Placebo GREML of job loss (endogenous and exogenous)
  - Placebo Bivariate GREML of job loss and BMI (and Δ BMI)
  - Rosenbaum bounds analysis of γ for unobservable joint correlation between exogenous job loss and Δ BMI
- Further analysis on differential impacts by education and health behaviors
- Cross-country G x E analysis → determine if different welfare regimes further mediate polygenic risk and the accumulation of health advantage

THANKS!

- Questions?