Socioeconomic status and mortality in Moscow: A role for biomarkers?

Megan Todd

DRAFT: Please do not cite

**Abstract** 

Low socioeconomic status has consistently been linked to poor health and elevated mortality risk, though the physiological mechanisms behind this relationship are not well understood. These health disparities are especially large in Russia, where the recent mortality crisis disproportionately affected low-SES individuals.

In this study, I assess whether a number of biomarkers predict subsequent mortality among older adults in Moscow, and whether these factors explain the SES-mortality link. Using data from the survey on Stress, Aging, and Health in Russia, I examine biomarkers related to inflammation, neuroendocrine function, heart rate variability, and cardiovascular risk.

1

### **Background**

Low socioeconomic status (SES) has consistently been linked to poor health outcomes and greater mortality risk. This association has been found in different time periods, in locations around the world, in both genders, in all ages, across the entire range of SES, and for most health conditions (Adams et al. 2004; Phelan et al. 2004; Cutler, Deaton, and Lleras-Muney 2006).

Health disparities by SES are especially troubling in Russia, where disparities are particularly large (Shkolnikov et al. 1998). Between the 1960s and 1990s, mortality rates increased in Russia, representing a dramatic departure from the global trend of decreasing mortality rates (Shkolnikov et al. 2004). This mortality crisis disproportionally affected the least educated groups, which experienced decreases in life expectancy, particularly among men (Shkolnikov et al. 2006; Shkolnikov et al. 2004).

For SES to affect physical health and disease, it must ultimately act on some physiological process (Steptoe and Marmot 2002), but these pathways are not well understood. In this study, I examine socioeconomic disparities in mortality among older adults in Moscow, Russia, determining whether baseline biomarkers can partially explain the SES-mortality link. I examine biomarkers related to inflammation, neuroendocrine function, heart rate variability, and traditional markers of cardiovascular risk.

#### Data and method

The survey on Stress, Aging, and Health in Russia (SAHR) focuses on Moscow residents aged 55 and older. The study consists of a baseline survey fielded 2006-2009, with a follow-up survey wave conducted in 2009-2011, and mortality follow-up planned through 2016 (Shkolnikova et al., 2009). The sample (n=1800) is largely drawn from seven existing epidemiological cohorts in Moscow; prior studies of these cohorts began between the 1970s and 1990s. To ensure more recent immigrants to Moscow are represented in the SAHR sample, a small additional group is drawn from medical registers. The baseline survey collected numerous biomarkers from a venous blood sample.

#### **Variables**

I use educational attainment as a measure of SES, categorized as follows. Lower education includes elementary education and incomplete secondary education (with or without vocational education). Secondary education includes completed secondary education (with or without vocational education), and incomplete higher education. Higher education includes completed higher education and above.

Inflammation is measured as a count of the following measures for which an individual falls into a highrisk category: C-reactive protein, interleukin-6, and fibrinogen. Of these three measures, a clinical highrisk cut-point exists only for C-reactive protein: respondents with C-reactive protein > 3mg/L are considered high risk (Alley et al. 2006). Because there is no such established cut-point for interleukin-6 and fibrinogen, I classify respondents in the top sex-specific quintile of these measures as high risk. This potential range of this inflammation index is 0-3. The neuroendocrine index [0-4] is a count of the four neuroendocrine measures for which a respondent falls into the high-risk category. High risk is categorized as follows: 1) dehydroepiandrosterone sulfate (DHEAS) in lowest sex-specific quintile, 2) cortisol in highest sex-specific quintile, 3) epinephrine in highest or lowest sex-specific decile, 4) norepinephrine in highest sex-specific quintile. The heart rate index [0-4] is a count of the four heart rate markers for which a respondent falls into the high-risk category. High risk is categorized as follows: 1) mean heart rate in the highest sex-specific quintile, 2) ratio of mean daytime heartrate to mean nighttime heartrate in the lowest sex-specific quintile, 3) standard deviation of the normal-to-normal beat-to-beat intervals < 100 ms, 4) square root of mean of sum of squares of differences between normal-to-normal intervals in the highest or lowest sex-specific quintile. The cardiovascular index [0-9] is a count of the nine cardiovascular risk factors for which a respondent falls into the high-risk category. High risk is categorized as follows: 1) systolic blood pressure > 140 mmHG, 2) diastolic blood pressure > 90 mmHG, 3) total cholesterol >= 240 mg/dL, 4) high-density lipoprotein < 40 mg/dL, 5) triglycerides >= 200 mg/dL, 6) glycosylated hemoglobin > 6.5%, 7) homeostasis model assessment-estimated insulin resistance index >= 3.78 for men, >=4.16 for women, 8) BMI < 18.5 or > 30 9) waist circumference > 102 cm for men, >88 for women.

#### **Empirical strategy**

Limiting the sample to respondents with non-missing information on demographic characteristics (age, sex) and biomarkers yields a sample of 1,557.

I use proportional hazard Gompertz models of age-specific mortality through the end of 2011. I use Gompertz models because the Gompertz hazard function has been shown to be a good approximation of mortality among older adults (Horiuchi and Coale, 1982).

### **Preliminary results**

Descriptive statistics of my analytic sample are shown in Table 1 for the full sample, and separately by sex.

Table 2 shows Gompertz hazard models of mortality by December 31, 2011. Model 1 includes only years of education, while subsequent models add potential biological mediators of the education-mortality relationship. The cardiovascular index (Model 3) is not independently associated with mortality; the inflammation index (Model 4) is most strongly predictive of future mortality. The coefficient on education attenuates slightly when each index is sequentially included in the model; when all four indexes are included (Model 2 and 7), the coefficient on education attenuates slightly more, and retains only marginal significance (p = 0.054). Model 7 allows the comparison of all four indexes together. While the association with mortality for each index is slightly weaker in this joint model, the neuroendocrine, inflammation, and heart rate indexes remain significantly associated with subsequent mortality.

### **Conclusion**

My preliminary results suggest that inflammation, neuroendocrine function, and heart rate may mediate the relationship between education and mortality among older adults in Moscow. Inflammation is the most strongly related to mortality. Future work should work to clarify the relationship between education, inflammation, and mortality.

### References

- Adams, P., Hurd, M.D., McFadden, D., Merrill, A., Ribeiro, T., 2004. Healthy, Wealthy, and Wise? Tests for Direct Causal Paths between Health and Socioeconomic Status, in: Wise, D.A. (Ed.), Perspectives on the Economics of Aging. University of Chicago Press.
- Adler, N.E., Boyce, T., Chesney, M.A., Cohen, S., Folkman, S., Kahn, R.L., Syme, S.L., 1994. Socioeconomic status and health. The challenge of the gradient. Am. Psychol. 49, 15–24.
- Aiello, A.E., Kaplan, G.A., 2009. Socioeconomic Position and Inflammatory and Immune Biomarkers of Cardiovascular Disease: Applications to the Panel Study of Income Dynamics. Biodemography Soc. Biol. 55, 178–205.
- Alley, D., Seeman, T., Ki Kim, J., Karlamangla, A., Hu, P., Crimmins, E., 2006. Socioeconomic status and Creactive protein levels in the US population: NHANES IV. Brain. Behav. Immun. 20, 498–504.
- Baum, A., Garofalo, J.P., Yali, A.M., 1999. Socioeconomic Status and Chronic Stress: Does Stress Account for SES Effects on Health? Ann. N. Y. Acad. Sci. 896, 131–144.
- Chen, E., Matthews, K.A., 2001. Cognitive appraisal biases: An approach to understanding the relation between socioeconomic status and cardiovascular reactivity in children. Ann. Behav. Med. 23, 101–111.
- Cohen, S., 2005. Keynote Presentation at the Eight International Congress of Behavioral Medicine: the Pittsburgh common cold studies: psychosocial predictors of susceptibility to respiratory infectious illness. Int. J. Behav. Med. 12, 123–131.
- Cohen, S., Doyle, W.J., Baum, A., 2006. Socioeconomic status is associated with stress hormones. Psychosom. Med. 68, 414–420.
- Cohen, S., Kessler, R.C., Gordon, L.U., 1995. Strategies for measuring stress in studies of psychiatric and physical disorders, in: Cohen, S., Kessler, R.C., Gordon, Lynne Underwood (Eds.), Measuring Stress: A Guide for Health and Social Scientists. Oxford University Press, New York, NY, US, pp. 3–26.
- Crimmins, E., Vasunilashorn, S., Kim, J.K., Alley, D., 2008. Chapter 5 Biomarkers Related To Aging In Human Populations, in: Advances in Clinical Chemistry. Elsevier, pp. 161–216.
- Cutler, D., Deaton, A., Lleras-Muney, A., 2006. The Determinants of Mortality. J. Econ. Perspect. 20, 97–120.
- Danesh, J., Pepys, M.B., 2009. C-Reactive Protein and Coronary Disease Is There a Causal Link? Circulation 120, 2036–2039.
- Danesh, J., Wheeler, J.G., Hirschfield, G.M., Eda, S., Eiriksdottir, G., Rumley, A., Lowe, G.D.O., Pepys, M.B., Gudnason, V., 2004. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. N. Engl. J. Med. 350, 1387–1397.
- Danesh, J., Whincup, P., Walker, M., Lennon, L., Thomson, A., Appleby, P., Gallimore, J.R., Pepys, M.B., 2000. Low grade inflammation and coronary heart disease: prospective study and updated meta-analyses. BMJ 321, 199–204.
- Dowd, J.B., Haan, M.N., Blythe, L., Moore, K., Aiello, A.E., 2007. Socioeconomic Gradients in Immune Response to Latent Infection. Am. J. Epidemiol. 167, 112–120.
- Dowd, J.B., Simanek, A.M., Aiello, A.E., 2009. Socio-economic status, cortisol and allostatic load: a review of the literature. Int. J. Epidemiol. 38, 1297–1309.
- Gallo, L.C., Shivpuri, S., Gonzalez, P., Fortmann, A.L., Monteros, K.E. de los, Roesch, S.C., Talavera, G.A., Matthews, K.A., 2013. Socioeconomic status and stress in Mexican–American women: a multimethod perspective. J. Behav. Med. 36, 379–388.
- Glaser, R., Friedman, S.B., Smyth, J., Ader, R., Bijur, P., Brunell, P., Cohen, N., Krilov, L.R., Lifrak, S.T., Stone, A., Toffler, P., 1999. The differential impact of training stress and final examination stress

- on herpesvirus latency at the United States Military Academy at West Point. Brain. Behav. Immun. 13, 240–251.
- Glei, D.A., Goldman, N., Shkolnikov, V.M., Jdanov, D., Shalnova, S., Shkolnikova, M., Weinstein, M., 2013a. To what extent do biomarkers account for the large social disparities in health in Moscow? Soc. Sci. Med. 77, 164–172.
- Glei, D.A., Goldman, N., Shkolnikov, V.M., Jdanov, D., Shkolnikova, M., Vaupel, J.W., Weinstein, M., 2013b. Perceived stress and biological risk: is the link stronger in Russians than in Taiwanese and Americans? Stress 1–10.
- Godbout, J.P., Glaser, R., 2006. Stress-Induced Immune Dysregulation: Implications for Wound Healing, Infectious Disease and Cancer. J. Neuroimmune Pharmacol. 1, 421–427.
- Grzywacz, J.G., Almeida, D.M., Neupert, S.D., Ettner, S.L., 2004. Socioeconomic Status and Health: A Micro-level Analysis o Exposure and Vulnerability to Daily Stressors. J. Health Soc. Behav. 45, 1–16.
- Hatch, S.L., Dohrenwend, B.P., 2007. Distribution of Traumatic and Other Stressful Life Events by Race/Ethnicity, Gender, SES and Age: A Review of the Research. Am. J. Community Psychol. 40, 313–332.
- Horiuchi, S., Coale, A.J., 1982. A Simple Equation for Estimating the Expectation of Life at Old Ages. Popul. Stud. 36, 317–326.
- Kiecolt-Glaser, J.K., Loving, T.J., Stowell, J.R., Malarkey, W.B., Lemeshow, S., Dickinson, S.L., Glaser, R., 2005. Hostile marital interactions, proinflammatory cytokine production, and wound healing. Arch. Gen. Psychiatry 62, 1377–1384.
- Kiecolt-Glaser, J.K., Marucha, P.T., Mercado, A.M., Malarkey, W.B., Glaser, R., 1995. Slowing of wound healing by psychological stress. The Lancet 346, 1194–1196.
- Kuo, H.-K., Yen, C.-J., Chang, C.-H., Kuo, C.-K., Chen, J.-H., Sorond, F., 2005. Relation of C-reactive protein to stroke, cognitive disorders, and depression in the general population: systematic review and meta-analysis. Lancet Neurol. 4, 371–380.
- Loucks, E.B., Sullivan, L.M., Hayes, L.J., D'Agostino, R.B., Larson, M.G., Vasan, R.S., Benjamin, E.J., Berkman, L.F., 2006. Association of Educational Level with Inflammatory Markers in the Framingham Offspring Study. Am. J. Epidemiol. 163, 622–628.
- Marucha, P.T., Kiecolt-Glaser, J.K., Favagehi, M., 1998. Mucosal wound healing is impaired by examination stress. Psychosom. Med. 60, 362–365.
- McEwen, B.S., 2008. Central effects of stress hormones in health and disease: Understanding the protective and damaging effects of stress and stress mediators. Eur. J. Pharmacol. 583, 174–185.
- McLeod, J.D., Kessler, R.C., 1990. Socioeconomic Status Differences in Vulnerability to Undesirable Life Events. J. Health Soc. Behav. 31, 162–172.
- Mehta, S.K., Stowe, R.P., Feiveson, A.H., Tyring, S.K., Pierson, D.L., 2000. Reactivation and Shedding of Cytomegalovirus in Astronauts during Spaceflight. J. Infect. Dis. 182, 1761–1764.
- Muennig, P., Sohler, N., Mahato, B., 2007. Socioeconomic status as an independent predictor of physiological biomarkers of cardiovascular disease: evidence from NHANES. Prev. Med. 45, 35–40.
- Pearson, T.A., Mensah, G.A., Alexander, R.W., Anderson, J.L., Cannon, R.O., 3rd, Criqui, M., Fadl, Y.Y., Fortmann, S.P., Hong, Y., Myers, G.L., Rifai, N., Smith, S.C., Jr, Taubert, K., Tracy, R.P., Vinicor, F., Centers for Disease Control and Prevention, American Heart Association, 2003. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. Circulation 107, 499–511.
- Phelan, J.C., Link, B.G., Diez-Roux, A., Kawachi, I., Levin, B., 2004. "Fundamental causes" of social inequalities in mortality: a test of the theory. J. Health Soc. Behav. 45, 265–285.

- Pollitt, R.A., Kaufman, J.S., Rose, K.M., Diez-Roux, A.V., Zeng, D., Heiss, G., 2007. Early-life and adult socioeconomic status and inflammatory risk markers in adulthood. Eur. J. Epidemiol. 22, 55–66.
- Ranjit, N., Diez-Roux, A.V., Shea, S., Cushman, M., Ni, H., Seeman, T., 2007. Socioeconomic Position, Race/Ethnicity, and Inflammation in the Multi-Ethnic Study of Atherosclerosis. Circulation 116, 2383–2390.
- Rosvall, M., Engström, G., Janzon, L., Berglund, G., Hedblad, B., 2007. The role of low grade inflammation as measured by C-reactive protein levels in the explanation of socioeconomic differences in carotid atherosclerosis. Eur. J. Public Health 17, 340–347.
- Scuteri, A., Orru, M., Morrell, C., Piras, M.G., Taub, D., Schlessinger, D., Uda, M., Lakatta, E.G., 2011. Independent and additive effects of cytokine patterns and the metabolic syndrome on arterial aging in the SardiNIA Study. Atherosclerosis 215, 459–464.
- Shkolnikova, M., Shalnova, S., Shkolnikov, V.M., Metelskaya, V., Deev, A., Andreev, E., Jdanov, D., Vaupel, J.W., 2009. Biological mechanisms of disease and death in Moscow: rationale and design of the survey on Stress Aging and Health in Russia (SAHR). BMC Public Health 9, 293.
- Steptoe, A., Marmot, M., 2002. The role of psychobiological pathways in socio-economic inequalities in cardiovascular disease risk. Eur. Heart J. 23, 13–25.
- Steptoe, A., Owen, N., Kunz-Ebrecht, S., Mohamed-Ali, V., 2002. Inflammatory cytokines, socioeconomic status, and acute stress responsivity. Brain. Behav. Immun. 16, 774–784.
- Tabassum, F., Kumari, M., Rumley, A., Lowe, G., Power, C., Strachan, D.P., 2008. Effects of socioeconomic position on inflammatory and hemostatic markers: a life-course analysis in the 1958 British birth cohort. Am. J. Epidemiol. 167, 1332–1341.
- Thoits, P.A., 2010. Stress and Health: Major Findings and Policy Implications. J. Health Soc. Behav. 51, S41–S53.
- Wilson, T., Kaplan, G., Kauhanen, J., Cohen, R., Wu, Salonen, R., Salonen, J., 1993. Association between plasma fibrinogen concentration and five socioeconomic indices in the Kuopio Ischemic Heart Disease Risk Factor Study. Am. J. Epidemiol. 137, 292–300.
- Yarnell, J., Yu, S., McCrum, E., Arveiler, D., Hass, B., Dallongeville, J., Montaye, M., Amouyel, P., Ferrières, J., Ruidavets, J.-B., Evans, A., Bingham, A., Ducimetière, P., 2005. Education, socioeconomic and lifestyle factors, and risk of coronary heart disease: the PRIME Study. Int. J. Epidemiol. 34, 268–275.

# **Tables**

Table 1: Descriptive statistics

	Full sample			I	Male		Female			
	Mean/			Mean/			Mean/			
	Prop.	SD	Med.	Prop.	SD	Med.	Prop.	SD	Med.	
Demographic characteristics										
Male (%)	45%			100%			0%			
Age	67.9	7.5	68.0	68.6	8.0	68.0	67.3	7.0	67.0	
Education, completed years	14.0	3.5	15.0	13.9	3.8	15.0	14.1	3.3	15.0	
Education: lower (%)	11.0%			13.9%			8.6%			
Education: secondary (%)	39.6%			39.0%			40.1%			
Education: higher (%)	49.5%			47.2%			51.4%			
Mortality										
Died by 31 December 2011 (%)	8.2%			12.0%			4.9%			
Died of cardiovascular cause by 31 December 2011 (%)	4.9%			7.8%			2.6%			
Biomarkers										
Full index (possible range: 0-20)	4.7	2.6	4.0	4.5	2.6	4.0	4.8	2.6	5.0	
Cardiovascular index (possible range: 0-9)	2.5	1.8	2.0	2.4	1.8	2.0	2.6	1.8	2.0	
Heart rate index (possible range: 0-4)	0.7	0.9	0.0	0.7	1.0	0.0	0.7	0.9	0.0	
Neuroendocrine index (possible range: 0-4)	0.8	0.9	1.0	0.8	0.9	1.0	0.8	8.0	1.0	
Inflammation index (possible range: 0-3)	0.7	8.0	0.0	0.7	0.8	0.0	0.7	0.9	1.0	
N	1,557			706			851			

## Table 2:

	Model 1		Model 2		N	Model 3		1odel 4	Model 5		Model 6		Model 7	
	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Education, years	0.93	(0.89, 0.97)	0.96	(0.91, 1.00)	0.94	(0.89, 0.98)	0.95	(0.91, 0.99)	0.94	(0.90, 0.98)	0.93	(0.89, 0.97)	0.96	(0.91, 1.00)
Biomarkers														
Full index			1.22	(1.15, 1.30)										
Cardiovascular index					1.07	(0.97, 1.19)							1.00	(0.90, 1.11)
Inflammation index							1.68	(1.41, 2.01)					1.63	(1.36, 1.96)
Heart rate index									1.59	(1.38, 1.83)			1.55	(1.35, 1.79)
Neuroendocrine index											1.23	(1.03, 1.47)	1.22	(1.02, 1.46)
Male	2.27	(1.56, 3.29)	2.52	(1.74, 3.65)	2.34	(1.61, 3.39)	2.38	(1.64, 3.45)	2.24	(1.55, 3.25)	2.30	(1.59, 3.33)	2.36	(1.62, 3.44)
N	1,557		1,557		1,557		1,557		1,557		1,557		1,557	
Model Chi squared	29.59		66.60		31.45		61.73		65.12		34.71		97.68	