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TO WHAT EXTENT DO BIOMARKERS ACCOUNT FOR THE LARGE SOCIAL DISPARITIES IN HEALTH IN MOSCOW?

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Abstract

The Russian population continues to face political and economic challenges, has experienced poor general health and high mortality for decades, and has exhibited widening health disparities. The physiological factors underlying links between health and socioeconomic position in the Russian population are therefore an important topic to investigate. We used data from a population-based survey of Moscow residents aged 55 and older (n=1495), fielded between December 2006 and June 2009, to address two questions. First, are social disparities evident across different clusters of biomarkers? Second, does biological risk mediate the link between socioeconomic status and health?

Health outcomes included subscales for general health, physical function, and bodily pain. Socioeconomic status was represented by education and an index of material resources. Biological risk was measured by 20 biomarkers including cardiovascular, inflammatory, and neuroendocrine markers as well as heart rate parameters from 24-hour ECG monitoring.

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For both sexes, the age-adjusted educational disparity in standard cardiovascular risk factors was substantial (men: standardized β= −0.16, 95% CI = −0.23 to −0.09; women: β= −0.25, CI = −0.32 to −0.18). Education differences in inflammation were also evident in both men (β= −0.17, CI = −0.25 to −0.09) and women (β= −0.09, CI = −0.17 to −0.01). Heart rate parameters differed by education only in men (β= −0.10, CI = −0.18 to −0.02). The associations between material resources and biological risk scores were generally weaker than those for education. Social disparities in neuroendocrine markers were negligible for men and women.

In terms of mediating effects, biological risk accounted for more of the education gap in general health and physical function (19–36%) than in bodily pain (12–18%). Inclusion of inflammatory markers and heart rate parameters—which were important predictors of health outcomes—may explain how we accounted for more of the social disparities than previous studies.

Keywords

Russia; biological markers; socioeconomic status; education; health

INTRODUCTION

Social disparities in Russian mortality appear to be wider than those observed in the West, they are greater for men than for women, and they are continuing to increase (Shkolnikov et al., 1998). The least advantaged segments of the population bore the brunt of the mortality crisis, whereas highly educated Russians enjoyed modest improvements in life expectancy in the late 20th century (Shkolnikov et al., 2006). For health outcomes other than mortality, there is much less research regarding social disparities. On one hand, some evidence indicates a sizeable socioeconomic gradient in self-assessed health status (Bobak et al., 2000; Dubikaytis et al., 2010; Nicholson et al., 2005; Perlman & Bobak, 2008). On the other hand, the results of one study suggest that material deprivation, but not education, is associated with poor physical function in Russia (Bobak et al., 1998).

Researchers have argued that, at least in part, the social gradient in health reflects differences in the burden of physiological stress (Kristenson et al., 2004; Steptoe & Marmot, 2002). The allostatic load framework proposes that repeated or prolonged exposure to environmental challenge scan result in multi -system physiological dysregulation, which may ultimately lead to health decline (McEwen & Stellar, 1993). Such dysregulation is typically operationalized by examining elevated (or reduced) operating levels of biological parameters (“biomarkers”) related to cardiovascular, inflammatory, and neuroendocrine function. These measures have been shown to predict diverse health outcomes including self-assessed health status, physical function, and mortality (see review by Juster et al., 2010). Many factors (e.g., health behaviors, access to health care, exposure to infection, and genes), which may be unrelated to stress exposure, could play a role in generating social disparities in health (see reviews by Crimmins & Seeman, 2004; Steptoe & Marmot, 2002). Nonetheless, any individual characteristic or social factor that might explain social disparities in health (except for mortality from external causes) would likely operate via physiological pathways. The question is whether we can identify the biomarkers that account for the association between socioeconomic status and health.

Most prior studies that have investigated social disparities in biomarkers are based on Western samples and focus on a small number of standard cardiovascular risk factors related to hypertension, dyslipidemia, obesity, and hyperglycemia(e.g., Kanjilal et al., 2006; Winkleby et al., 1992). More recently, studies have examined the association between socioeconomic status and inflammatory markers (e.g., C-reactive protein, interleukin-6). Some research has also explored the social gradient in a multi-system measure of biological

risk. Most of these studies find the expected association between higher status and lower biological risk (Gustafsson et al., 2011; Hu et al., 2007; Kubzansky et al., 1999; Seeman et al., 2008; Singer & Ryff, 1999; Weinstein et al., 2003), although one study finds a significant relationship only for females (Dowd & Goldman, 2006)and another reports a non -significant relationship (Seeman et al., 2004).

Although several studies have investigated whether biological parameters mediate the association between socioeconomic status and mortality (Beauchamp et al., 2010; Harald et al., 2008; Khang & Kim, 2005; Lynch et al., 1996; Ramsay et al., 2009; Seeman et al., 2004; Song et al., 2006), including three studies in Russia (Dennis et al., 1993; Malyutina et al., 2004; Shkolnikov et al., 2000), few have evaluated the extent to which biomarkers account for social disparities in general measures of physical health. Three studies that explored this issue with respect to overall self-rated health found that biomarkers explained only a small share of the socioeconomic gap in Taiwan (≤11%) (Dowd & Goldman, 2006; Goldman et al., 2011; Hu et al., 2007) and the U.S. (2–4%) (Goldman et al., 2011)and none of the gap in Costa Rica (Goldman et al., 2011). These same studies and one other in the U.S. (Koster et al., 2005) examined social disparities in physical function; again, the results suggested that biomarkers account for, at most, a small fraction of the gap.

This paper uses data from a population -based survey of older Moscow residents to address two research questions. First, are social disparities evident across different clusters of biomarkers? Our measure of biological risk incorporates not only standard cardiovascular risk factors (hereafter referred to as “standard markers”), but also markers of inflammation and neuroendocrine activity as well as information about heart function based on a 24h ambulatory ECG—data that are rarely collected in a population-based survey. These data could be especially important in light of the huge role that cardiovascular disease plays in excess Russian mortality.

Second, does this measure of biological risk mediate the link between socioeconomic status and health? In light of the burden of chronic stressors experienced by Russians throughout the 20th century and especially during recent decades—particularly by persons of lower social status—we anticipate that these biological parameters will account for a substantial share of the social gradient in health outcomes. At the same time, we recognize that previous studies in other countries have found very modest effects (Dowd & Goldman, 2006; Goldman et al., 2011; Hu et al., 2007; Koster et al., 2005), underscoring the importance of evaluating these relationships in the Russian context.

METHODS

Data

The data come from the Survey on Stress, Aging, and Health in Russia (SAHR), a population-based sample of Muscovites aged 55 and older that has been described in detail elsewhere(Shkolnikova et al., 2009). The survey was fielded between December 1, 2006 and June 30, 2009. The fieldwork and data processing were conducted jointly by the National Research Center for Preventive Medicine (NRCPM) in Moscow, the Max Planck Institute for Demographic Research in Rostock (Germany) and Duke University in Durham (USA). The study protocols were approved by the Ethics Committee of the NRCPM and the Institutional Review Board at Duke University. Before being interviewed and medically tested, all participants in the SAHR received information about the survey program and provided informed consent. The study was also approved by the Local Committee for Medical Ethics of the NRCPM.

Most of the study participants were selected randomly from seven epidemiological cohorts formed in Moscow between the mid-1970s and the 1990s. Because most of the individuals in the epidemiological cohorts were residents of Moscow before the mid-1980s, an additional small part of the SAHR sample was designed to represent those who moved to Moscow after 1985. These newer residents of Moscow were identified from the Moscow Outpatient Clinics' registry. More information about sample selection is provided in Supplementary Material [INSERT LINK TO ONLINE FILES]. The final SAHR sample includes 1800 respondents (961 women and 839 men) who agreed to participate and who completed an interview and medical testing (response rate = 64%). The sample was aged 68.3 years on average with 1763 individuals originating from the epidemiological cohorts and 37 individuals originating from the Moscow Outpatient Clinics' registry.

In most cases, the interview and medical tests were administered during a hospital visit, but participants who were unable or unwilling to come to the hospital (8%) were interviewed and examined in their home using the hospital protocol. The clinical data include: anthropometry; measurements of blood pressure, resting heart rate, and grip strength; a fasting blood specimen; a 12-lead standard ECG in a supine position; and a 12-hour overnight urine specimen(8 pm to 8 am; cortisol and creatinine were measured the night prior to the first appointment; epinephrine and norepinephrine were measured in a second specimen that was collected the night following the first visit). In addition, respondents self-monitored morning and evening home blood pressure over three days using an Omron HEM-712 semi-automatic arm monitor (92% participation) and completed continuous 24-hour ECG monitoring(96% participation) using the Schiller Holter system with 3-channel MICROVIT MT-101 digital devices.

Measures

Health outcomes—Health outcomes comprised three subscales from the 36-item Short Form Health Survey (SF-36) (RAND, 2011). The general health subscale was based on five questions related to overall health status(α=0.67), including a question commonly referred to as "self-rated health". The physical function subscale was based on 10 questions about the respondent's ability to perform various physical tasks (α=0.91). The bodily pain subscale was constructed from two questions about the level of pain and how much pain interfered with normal activities over the past four weeks (α=0.84). All three SF-36 subscales were scored so that higher values indicate better health.

Socioeconomic status—We included two measures of socioeconomic status: education (measured by completed years of schooling)and an index of material resources. The material resources index was based on eight items: 1) personal income; 2) ownership of a summer/winter country house (warm/cold *dacha*);3) car ownership; 4) garage ownership; 5) number of rooms in dwelling not including kitchen, corridors, toilet/bathrooms or basement; 6) area of the living space; 7) proportion of household income normally spent on food (five categories from "almost all" to "10% or less"); and 8) household's ability to finance basic necessities and expensive durable goods (five categories from "unable to purchase basic necessities" to "able to purchase even very expensive things"). We standardized each item and calculated the mean across valid items (α=0.73); the index was coded as missing if more than half of items were missing.

Biological Risk—This measure was based on 20 biomarkers that have been linked with all-cause mortality (see Supplemental Material for details and information about laboratory assays, [INSERT LINK TO ONLINE FILES]). We also created four system-level subscores representing different clusters of biomarkers.

The first cluster comprised nine standard markers: 1) systolic blood pressure (SBP); 2) diastolic blood pressure (DBP); 3) total cholesterol(TC); 4) high-density lipoprotein (HDL); 5) triglycerides(TG); 6) glycoslyated hemoglobin (HbA_{1c}); 7) insulin resistance; 8) body mass index (BMI); and 9) waist circumference. Because 8% of the sample did not complete home blood pressure monitoring, blood pressure was based on the average of two measurements taken by a clinician.

The heart rate subscore included four markers from the 24-hour ECG monitoring: 1) 24-hour mean heart rate; 2) day/night heart rate averages; 3) SD of the normal-to-normal (NN) beat to beat intervals (SDNN); and 4) square root of the mean of the sum of the squares of differences between successive NN intervals (RMSSD). SDNN represents a time-domain measure of overall heart rate variability (HRV), while RMSSD provides a time-domain estimate of short-term components of HRV. Respondents with a pacemaker (n=10) were coded as missing for all four markers. Those with fewer than 18 hours of recording (n=9) or more than 20% artifacts (n=3) were coded as missing for SDNN and RMSSD. The HRV parameters were calculated using only the normal intervals from the ECG recording.

The inflammation subscore comprised three markers: 1) interleukin-6 (IL-6); 2) high-sensitivity C-reactive protein (hsCRP); and 3) fibrinogen. Finally, the cluster of neuroendocrine markers included dehydroepiandrosterone sulfate (DHEAS) and three measures based on the 12h urine collection: cortisol, epinephrine, and norepinephrine.

When possible, we coded high risk values based on established cutoffs (SDNN, SBP, DBP, TC, HDL, TG, HbA_{1c}, BMI, waist circumference, and hsCRP; see Supplemental Table S-3, [INSERT LINK TO ONLINE FILES]). For the remaining biomarkers—where there are no generally accepted clinical cutoffs—we defined high risk levels based on the sex-specific distribution. Based on prior evidence regarding the association between each biomarker and mortality, high risk was defined by the top quintile (i.e., heart rate, insulin resistance, IL-6, fibrinogen, cortisol, and norepinephrine), bottom quintile (i.e., day/night heart rate, RMSSD, and DHEAS), or for epinephrine, top and bottom deciles were coded as high risk because both extremes have been linked with increased mortality. We created the four subscores by counting the number of markers in each group that fell at high risk levels. The overall score was constructed by summing the subscores.

Health Behaviors—Smoking status was coded as never, former, or current smoker. Current and former smokers were asked the average number of cigarettes smoked daily. Reported frequency of alcohol consumption over the past 12 months was coded as never, once or twice a week, or more than twice a week. The CAGE score for alcohol dependence was based on four questions and ranges from 0 to 4 (Ewing, 1984).

Analytical Strategy

We excluded 224 respondents who were missing data for at least one of the 20 biomarkers and another 81 persons who were missing data for another variable in the analysis. Thus, the analysis sample comprised 1495 respondents. Compared with those who had complete data for all analysis variables, respondents with missing data (n=305) were significantly older, had fewer material resources, and were more likely to be male. We used multiple imputation to assess how the results may have been affected by missing data (see Supplementary Material, [INSERT LINK TO ONLINE FILES]).

Descriptive statistics for analysis variables were weighted using post-stratification weights that adjust for differences in age and education (within each sex) between the sample and the population of Moscow (based on the 2002 census). Linear regression models that predicted biological risk and health outcomes were based on unweighted data. Standard errors were

calculated using the robust estimator (StataCorp, 2007). In order to compare the magnitude of coefficients across different measures, we present standardized coefficients.

In mediation analysis, estimates of direct and indirect effects would be biased if there was unmeasured confounding or if there was an interaction between the exposure (in this case, socioeconomic status) and mediator (biomarkers) on the outcome (health) (Kaufman et al., 2004; Robins & Greenland, 1992). For our study, age and sex were important potential confounders of the exposure-mediator and exposure-outcome relationships. Thus, we estimated models separately by sex and controlled for age (linear and quadratic terms). Because health behaviors may also confound the mediator -outcome relationship, we adjusted for smoking and alcohol consumption. We found no evidence of any interaction between socioeconomic status and biological risk. In the absence of an exposure-mediator interaction, the direct effect represents the net effect of exposure on the outcome after controlling for the mediator and the indirect effect is the effect of exposure operating through the mediator (Valeri & VanderWeele, Forthcoming). We used the software developed by Valeri & VanderWeele (Forthcoming) for the mediation analysis and Stata 10 (StataCorp, 2007) for all other analyses.

Although models were fit separately by sex, we also formally tested for sex differences in the associations between socioeconomic status, biological risk, and health. We pooled both sexes and refit the models including the main effect for sex and interactions between sex and all covariates. Thus, the regression results were exactly the same as fitting models separately by sex, but enabled us to determine whether sex interactions were significant.

RESULTS

On average (based on weighted analyses), men were younger, better educated, and had more material resources than women (Table 1). They also scored better than women in terms of self-reported general health, physical function and bodily pain.

Are Social Disparities Evident Across Different Clusters of Biomarkers?

Education was associated with overall biological risk in both sexes (Table 2). Among women, the educational disparity arose primarily from standard markers, although there was also a weak association with inflammation. Men exhibited a sizeable educational disparity in these two groups of markers and a smaller disparity in heart rate parameters. There was no significant relationship between schooling and neuroendocrine markers in either sex.

The association between material resources and biological risk scores followed a similar pattern, although the coefficients were generally smaller than those for education. One exception was the relatively large association with the heart rate subscore among men. The addition of controls for health behaviors generally had little effect on the coefficients for schooling or material resources.

Sex differences in the relationship between socioeconomic status and biological risk were significant in only one case (out of 10 sex interactions tested). Material resources appeared to be more strongly associated with the heart rate subscore for men than for women.

The relationships between socioeconomic status and individual biomarkers are shown in Supplemental Table S-4 [INSERT LINK TO ONLINE FILE]. In sum, both sexes exhibited educational differentials in most of the standard markers, although women showed larger disparities in diastolic blood pressure and waist circumference than men. In contrast, educational differentials in fibrinogen and material resource disparities in SDNN were greater for men.

Absolute and relative social inequalities in biological risk are shown in Supplemental Table S-5 [INSERT LINK TO ONLINE FILE]. For example, men with low education (10 years) are predicted to score 0.8 points higher on overall biological risk (potential range 0–20) than men with high education (16 years). The relative ratio is 1. 20: at the mean age, men with low education are expected to score 20% higher on biological risk than their counterparts with high education.

Is the Measure of Biological Risk Associated with Health Outcomes?

If biomarkers act as mediators between socioeconomic status and health outcomes, then they must be associated not only with social status, but also with health outcomes. The results in Table 3 show that higher biological risk scores were indeed associated with worse health outcomes. The association was strongest for physical function: a one SD increase in overall biological risk was associated with a one-fifth SD decrease in physical function (Model 1). The addition of controls for health behaviors had little effect on the coefficients.

Model 2 shows the effects by subscore. Heart rate, inflammatory, and standard markers were significantly but weakly associated with most health outcomes in both sexes. There was little evidence that neuroendocrine activity was associated with these health outcomes: the coefficient was significant and in the expected direction in only one model.

Sex differences in the relationship between biological risk scores and health outcomes were significant in only one of 15 tests. The relationship between inflammation and physical function was stronger for men.

Does the Measure of Biological Risk Mediate Social Disparities in Health?

Table 4 shows the association between socioeconomic status and health outcomes, before introducing biomarkers as potential mediators. Among men, but not women, disparities in general health and bodily pain were greater when measured by material resources than by education. Whereas the association between education and health did not differ significantly by sex, men exhibited larger health disparities by material resources than women ($p<0.05$ for all three sex interactions in age-adjusted models).

Absolute and relative social inequalities for health outcomes are shown in Supplemental Table S-6 [INSERT LINK TO ONLINE FILE]. We compare the predicted scores on health outcomes at high (80^{th} percentile) and low (20^{th} percentile) levels for both measures of socioeconomic status. For example, men with high education score 3.8 points (8% in relative terms) higher on general health than those with low education, but the difference by material resources is even greater (5.9 points; 14% in relative terms).

Our key interest is to determine the extent to which biomarkers account for social disparities in health. The decomposition of educational disparities into a direct and indirect effect is presented in Table 5. The corresponding estimates for material resources are shown in Table 6. The results suggested that these biomarkers were important mediators linking social status and health. The indirect effects for education mediated by overall biological risk were generally significant. Indeed, overall biological risk accounted for a sizeable fraction(19–36%) of the educational gap in general health and physical function, but played a lesser role for pain (12% for men, 18% for women; Table 5). The indirect effects for material resources (Table 6) were smaller than for education and significant only for general health and physical function in men.

We also evaluated the contribution of each biological risk subscore. The standard markers accounted for most of the mediating effect among women, but a lesser part for men. Among men, inflammation was also a significant mediator of educational disparities, whereas the

heart rate score was a significant mediator for material resources. There was no evidence that neuroendocrine markers accounted for any of the social disparities in health.

Robustness of the Results to Alternative Specifications

We explored the robustness of the results to a Z-score measure of biological risk that retained continuous values for each of the 20 biomarkers. The indirect effects via the Z-score were generally smaller than those using the count-based formulation as the mediator (see Supplementary Material) [insert link to online files here].

We also used multiple imputation to re-estimate the results based on all 1,800 respondents in the sample (see Supplementary Material for details) [insert link to online files here]. In general, the results were similar to those presented here.

DISCUSSION

To the best of our knowledge, this is the first study exploring relationships between social disparities in health and biomarkers in Russia. This analysis, made possible by the rich health interview and biomarker data collected in SAHR, identified the major links among two measures of socioeconomic position, biomarkers related to several physiological systems, and broad indicators of health among Muscovites.

The magnitude of social inequalities in biological risk varied across systems. We found substantial educational differences in biomarkers related to cardiovascular function, including standard markers in both sexes as well as heart rate parameters in men. There were also notable educational disparities in inflammation. Low-grade inflammation is regarded as a marker of vascular changes associated with heart and cerebrovascular diseases, diabetes, and all-cause mortality (Ford et al., 2005; Hansson, 2005; Pradhan et al., 2001). When measured by material resources, differences in biological risk scores followed a similar pattern, although disparities in standard and inflammatory markers were smaller than those for education.

In general, men appear to exhibit social differentials across a broader range of markers than women. Apparent sex differences should be viewed in the context of the large contrasts between recent male and female patterns of mortality and ill-health in Russia. During the 1990s and 2000s, the sex gap in life expectancy was exceptionally high, varying between 11 and 14 years. Compared with Russian women, men experienced twice the rate of all-cause and cardiovascular mortality (Shkolnikov et al., 2004), five times the smoking prevalence, and 15 times the prevalence of heavy drinking (Perlman et al., 2007; Perlman, 2010). At the same time, poor self-reported health, limited physical function, obesity, and metabolic syndrome were substantially more prevalent among Russian women than men (Andreev et al., 2003; Metelskaya et al., 2011; Sidorenkov et al., 2010). These observations are consistent with our own findings and imply an unusually pronounced male-female health-mortality paradox. A similar paradox has been found in other countries (i.e., men are more likely to die, whereas women are more likely to report ill health), and probably arises, at least in part, from a higher prevalence of life-threatening conditions among men (Case & Paxson, 2005). In the case of Russia, the sex reversal is undoubtedly exacerbated by large differences between men and women in unhealthy behaviors, primarily binge drinking and smoking.

Although women in this study reported worse health than men, the disparities in health outcomes by material resources were larger for men. These disparities may contribute to greater socioeconomic differences in mortality among men than among women. Other studies in Russia have found that men exhibit larger social disparities in general health

(Palosuo et al., 1998; Perlman & Bobak, 2008), but no study has examined how social disparities in physical function vary by sex in Russia. Our results also suggest that the association between material resources and heart rate parameters may be stronger for men than for women in Russia. To our knowledge, there are no previous studies of social disparities in ECG heart rate parameters, much less an investigation of differences by sex.

Neuroendocrine markers differed little by socioeconomic status in either sex. This result is surprising given our expectation that social disparities in health reflect a differential burden of stress. Studies in Taiwan (Dowd & Goldman, 2006; Gersten, 2008) have demonstrated a similar lack of association between socioeconomic status and neuroendocrine activity. One possible explanation is that our measures do not capture the neuroendocrine variation that represents physiological stress. Overnight values for cortisol and catecholamines represent resting levels, but perhaps the differences that matter pertain to variation throughout the day or the response to stressful conditions. Yet, even studies that measured diurnal patterns of salivary cortisol yielded inconsistent relationships with socioeconomic status (Dowd & Goldman, 2006).

We found that biological risk accounted for a substantial portion of social disparities in health, more so than in similar studies conducted elsewhere. This finding was likely to owe, at least in part, to the inclusion of inflammatory markers and heart rate parameters—two sets of markers that appeared to be important predictors of health outcomes.

There were several limitations to this study. First, with cross-sectional data we could not establish the direction of the relationships. For example, among men, the social gradient in health was stronger when measured by material resources than by education, a result that may be partly the consequence of reverse causality (i.e., the effects of illness on income and wealth). Second, people who died before age 55 could not be sampled. Higher mortality among poorly educated Muscovites would attenuate the observed gap in health outcomes among survivors. The effect of mortality selection was likely to be especially acute for men given the exceptionally high death rates among middle-aged Russian men. Based on 2009 mortality rates in Russia, 29% of men and 11% of women were expected to die before age 55; the percentage by age 70 surged to 60% of men and 28% of women (Human Mortality Database (HMD), 2011 accessed 22 Nov 2011). Third, the biomarker measurements captured only a snapshot of intricate processes that are inherently dynamic in nature and subject to measurement error. Fourth, the self-reported measures of health outcomes may have been affected by reporting bias and other unobserved factors that influence perceptions. Correlation between the unobserved factors and socioeconomic status may have biased the estimates of social disparity. Finally, health behaviors may be part of the causal pathway through which socioeconomic status affects biomarkers. The inclusion of controls for health behaviors attenuated the association between socioeconomic status and health (Table 4), probably because smoking and alcohol consumption are important mechanisms through which social status affects biomarkers and ultimately, health. If health behaviors act as both simultaneous mediators (of the link between socioeconomic status and biomarkers) and as confounders (of the relationship between biomarkers and health), then the controlled direct effect of socioeconomic status could be identified using marginal structural models (VanderWeele, 2009).

Russian mortality has varied considerably by both sex and social status in recent years. This study demonstrated that socioeconomic differentials in self-reported measures of general health, physical function, and bodily pain have also been sizeable. In addition, the physiological pathways through which social position affects health may differ by sex. If inflammation and heart rate parameters played a more important role for men than women, as our results suggested, then it is worth investigating whether these markers might also

account for why men, particularly those with low social status, suffer such high mortality relative to women and their more socially advantaged brethren. Future availability of mortality data for this cohort will enable us to investigate this question.

A useful starting point for understanding the disparities in physiological pathways would be an examination of the behavioral and psychosocial factors that influence biological processes. For example, smoking, alcohol consumption, diet, exercise, obesity, psychological stress, and social isolation may affect numerous physiological systems, including inflammatory and cardiovascular mechanisms. We have some evidence that the pattern of social differentials in health-related behaviors differs by sex in Russia. For example, Perlman et al.(2007) demonstrated that educational disparities in smoking prevalence have been larger and were evident much earlier among men than women in Russia. Similarly, the educational gap in frequent, heavy drinking has been much wider in men than women (Perlman, 2010). Given that smoking and binge drinking are associated with a broad range of diseases, variation in such health-related behaviors may provide further insights into the biological linkages among socioeconomic status, sex, health, and survival.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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RESEARCH HIGHLIGHTS

- Older Muscovites of both sexes exhibited substantial educational disparities in standard cardiovascular risk factors.
- Both sexes had an educational gradient with inflammatory markers; men had an educational gradient with heart rate parameters.
- Overall, biomarkers accounted for 19–36% of the education gap in general health and physical function.
- This share is larger than that found in prior studies, perhaps owing to the inclusion of inflammatory and heart parameters.
- These two sets of markers appeared to be important predictors of health outcomes.

Table 1

Descriptive statistics for analysis variables, by sex, weighted analyses[a]

Variable (observed range)	Total (n=1495)	Men (n=671)	Women (n=824)
Age (55–91), mean (SD), y	68.1 (8.4)	67.1 (8.2)	69.0 (8.6)
Male, %	45.4	--	--
Socioeconomic status			
Years of schooling (2–27), mean (SD)	13.0 (3.8)	13.5 (3.9)	12.5 (3.7)
Index of material resources (−1.3 to 4.6), mean (SD)	0.0 (0.6)	0.1 (0.6)	−0.2 (0.5)
Health behaviors			
Smoking status			
Never, %	60.4	33.7	82.6
Former, %	23.2	39.2	9.9
Current, %	16.4	27.1	7.5
Number of cigarettes smoked daily (0–60), mean (SD)	5.9 (9.3)	11.2 (10.8)	1.5 (4.2)
Frequency of alcohol consumption			
Never, %	18.9	14.2	22.9
Once or twice a week, %	64.8	55.0	73.0
More than twice a week, %	16.2	30.8	4.1
CAGE score for alcohol dependence (0–4), mean (SD)	0.3 (0.9)	0.6 (1.2)	0.1 (0.5)
Biological risk			
Overall (0–14), mean (SD)	4.8 (2.6)	4.6 (2.6)	5.0 (2.6)
Standard cardiovascular markers (0–8), mean (SD)	2.6 (1.8)	2.4 (1.9)	2.8 (1.8)
Heart rate (24h ECG) parameters (0–4), mean (SD)	0.7 (0.9)	0.7 (0.9)	0.7 (0.9)
Inflammation (0–3), mean (SD)	0.7 (0.8)	0.7 (0.8)	0.7 (0.9)
Neuroendocrine (0–4), mean (SD)	0.8 (0.9)	0.8 (0.9)	0.8 (0.9)
Health outcomes			
SF-36 general health subscale (0–95), mean (SD)	44.1 (16.4)	46.7 (15.1)	41.9 (17.0)
SF-36 physical function subscale (0–100), mean (SD)	74.3 (23.4)	80.4 (20.7)	69.3 (24.2)
SF-36 bodily pain subscale[b] (0–100), mean (SD)	69.4 (26.1)	75.9 (24.7)	64.1 (26.0)

[a]The data are weighted using post-stratification weights (see “Analytical Strategy” for details).

[b]Coded so that higher values indicate better health (i.e., less bodily pain).

Table 2

Standardized coefficients from models that regress biological risk scores on socioeconomic status, by sex

	Overall Biological Risk		Standard markers		Heart rate		Inflammation		Neuroendocrine	
	β	95% CI	β	95% CI	β	95% CI	β	95% CI	β	95% CI
Men										
Education										
a) Age-adjusted[a]	−0.20	(−0.28, −0.13)	−0.16	(−0.23, −0.09)	−0.10	(−0.18, −0.02)	−0.17	(−0.25, −0.09)	0.00	(−0.08, 0.08)
b) Fully-adjusted[b]	−0.19	(−0.27, −0.11)	−0.16	(−0.23, −0.08)	−0.09	(−0.17, −0.01)	−0.13	(−0.21, −0.06)	0.01	(−0.07, 0.09)
Material resources										
a) Age-adjusted[a]	−0.15	(−0.23, −0.07)	−0.09	(−0.16, −0.02)	−0.15	(−0.23, −0.08)	−0.05	(−0.14, 0.04)	−0.03	(−0.11, 0.05)
b) Fully-adjusted[b]	−0.15	(−0.24, −0.07)	−0.11	(−0.18, −0.03)	−0.17	(−0.25, −0.09)	−0.04	(−0.12, 0.05)	−0.01	(−0.10, 0.07)
Women										
Education										
a) Age-adjusted[a]	−0.21	(−0.29, −0.13)	−0.25	(−0.32, −0.18)	−0.02	(−0.11, 0.06)	−0.09	(−0.17, −0.01)	−0.01	(−0.09, 0.07)
b) Fully-adjusted[b]	−0.20	(−0.28, −0.13)	−0.25	(−0.32, −0.17)	−0.02	(−0.10, 0.07)	−0.09	(−0.17, −0.01)	−0.00	(−0.09, 0.08)
Material resources										
a) Age-adjusted[a]	−0.07	(−0.14, 0.00)	−0.08	(−0.15, −0.01)	−0.04	(−0.11, 0.03)	−0.03	(−0.09, 0.04)	0.03	(−0.04, 0.09)
b) Fully-adjusted[b]	−0.05	(−0.12, 0.02)	−0.07	(−0.15, 0.00)	−0.02	(−0.09, 0.05)	−0.02	(−0.09, 0.05)	0.03	(−0.03, 0.10)

[a]Model adjusts for age and age-squared.

[b]Model includes additional controls for health behaviors (see Table 1).

Table 3

Standardized coefficients from models that regress health outcomes on biological risk scores[a], by sex

	General Health		Physical Function		Bodily Pain	
	β	95% CI	β	95% CI	β	95% CI
Men						
Age-adjusted[b]						
1a) Overall biological risk	−0.17	(−0.24, −0.09)	−0.21	(−0.28, −0.15)	−0.09	(−0.17, −0.01)
2a) Biological risk subscores						
Standard markers	−0.08	(−0.16, −0.01)	−0.07	(−0.14, −0.01)	−0.06	(−0.14, 0.02)
Heart rate (24h ECG)	−0.12	(−0.20, −0.05)	−0.11	(−0.19, −0.03)	−0.08	(−0.16, −0.00)
Inflammation	−0.11	(−0.19, −0.04)	−0.19	(−0.26, −0.12)	−0.06	(−0.14, 0.02)
Neuroendocrine	0.01	(−0.07, 0.08)	−0.04	(−0.12, 0.04)	0.06	(−0.01, 0.13)
Fully-adjusted[c]						
1a) Overall biological risk	−0.16	(−0.23, −0.08)	−0.21	(−0.28, −0.14)	−0.08	(−0.17, −0.00)
2a) Biological risk subscores						
Standard markers	−0.08	(−0.16, −0.00)	−0.08	(−0.15, −0.02)	−0.07	(−0.15, 0.02)
Heart rate (24h ECG)	−0.12	(−0.20, −0.05)	−0.10	(−0.17, −0.02)	−0.09	(−0.17, −0.01)
Inflammation	−0.10	(−0.18, −0.02)	−0.18	(−0.25, −0.10)	−0.05	(−0.13, 0.03)
Neuroendocrine	0.02	(−0.06, 0.10)	−0.04	(−0.12, 0.04)	0.08	(0.01, 0.14)
Women						
Age-adjusted[b]						
1a) Overall biological risk	−0.18	(−0.24, −0.12)	−0.21	(−0.27, −0.16)	−0.14	(−0.21, −0.07)
2a) Biological risk subscores						
Standard markers	−0.09	(−0.15, −0.02)	−0.15	(−0.21, −0.09)	−0.09	(−0.16, −0.03)
Heart rate (24h ECG)	−0.06	(−0.12, −0.00)	−0.07	(−0.13, −0.01)	−0.04	(−0.11, 0.04)
Inflammation	−0.10	(−0.17, −0.03)	−0.08	(−0.15, −0.02)	−0.07	(−0.15, −0.00)
Neuroendocrine	−0.07	(−0.13, −0.00)	−0.03	(−0.10, 0.03)	−0.02	(−0.09, 0.05)
Fully-adjusted[c]						
1a) Overall biological risk	−0.17	(−0.23, −0.10)	−0.22	(−0.28, −0.16)	−0.12	(−0.19, −0.06)
2a) Biological risk subscores						
Standard markers	−0.08	(−0.15, −0.02)	−0.15	(−0.21, −0.09)	−0.09	(−0.15, −0.02)

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	General Health		Physical Function		Bodily Pain	
	β	95% CI	β	95% CI	β	95% CI
Heart rate (24h ECG)	−0.05	(−0.11, 0.01)	−0.07	(−0.13, −0.02)	−0.03	(−0.10, 0.04)
Inflammation	−0.10	(−0.17, −0.03)	−0.09	(−0.15, −0.02)	−0.07	(−0.14, 0.00)
Neuroendocrine	−0.06	(−0.13, 0.01)	−0.04	(−0.10, 0.03)	−0.01	(−0.08, 0.06)

[a] Model 1 includes overall biological risk as the predictor and Model 2 substitutes the four biological subscores as the predictors.

[b] Model adjusts for age and age-squared.

[c] Model includes additional controls for health behaviors (see Table 1).

Table 4

Standardized coefficients from models that regress health outcomes on socioeconomic status, by sex

	General Health		Physical Function		Bodily Pain	
	β	95% CI	β	95% CI	β	95% CI
Men						
Years of schooling						
a) Age-adjusted[a]	0.16	(0.08, 0.24)	0.18	(0.10, 0.26)	0.13	(0.06, 0.21)
b) Fully-adjusted[b]	0.13	(0.05, 0.21)	0.16	(0.08, 0.24)	0.10	(0.03, 0.18)
Material resources						
a) Age-adjusted[a]	0.22	(0.15, 0.29)	0.18	(0.11, 0.25)	0.27	(0.20, 0.34)
b) Fully-adjusted[b]	0.21	(0.13, 0.28)	0.17	(0.10, 0.25)	0.23	(0.16, 0.31)
Women						
Years of schooling						
a) Age-adjusted[a]	0.14	(0.05, 0.22)	0.12	(0.04, 0.19)	0.13	(0.05, 0.21)
b) Fully-adjusted[b]	0.13	(0.04, 0.21)	0.12	(0.04, 0.19)	0.12	(0.04, 0.20)
Material resources						
a) Age-adjusted[a]	0.06	(−0.01, 0.12)	0.08	(0.02, 0.14)	0.13	(0.06, 0.20)
b) Fully-adjusted[b]	0.05	(−0.02, 0.11)	0.08	(0.02, 0.14)	0.12	(0.05, 0.19)

[a]Model adjusts for age and age-squared.

[b]Model includes additional controls for health behaviors (see Table 1).

Table 5

Direct and indirect effects (95% CI) of education on health outcomes[a], by sex

	Men			Women		
	General Health	**Phys. Function**	**Bodily Pain**	**General Health**	**Phys. Function**	**Bodily Pain**
Mediator = **Overall biological risk**						
Direct effect	0.108 (0.031, 0.184)	0.123 (0.051, 0.195)	0.090 (0.013, 0.167)	0.095 (0.019, 0.172)	0.074 (0.005, 0.143)	0.102 (0.021, 0.183)
Indirect effect	0.026 (0.008, 0.043)	0.035 (0.015, 0.054)	0.013 (−0.002, 0.028)	0.031 (0.013, 0.049)	0.042 (0.022, 0.062)	0.022 (0.006, 0.039)
Total effect	0.133 (0.057, 0.210)	0.158 (0.086, 0.231)	0.102 (0.027, 0.178)	0.126 (0.051, 0.202)	0.116 (0.046, 0.186)	0.124 (0.044, k 0.204)
Indirect as a % of Total	19	22	12	25	36	18
Mediator = **Standard markers**						
Direct effect	0.119 (0.042, 0.196)	0.142 (0.069, 0.215)	0.092 (0.015, 0.168)	0.104 (0.026, 0.181)	0.075 (0.005, 0.145)	0.103 (0.021, 0.184)
Indirect effect	0.014 (0.000, 0.028)	0.016 (0.002, 0.030)	0.011 (−0.002, 0.024)	0.023 (0.005, 0.041)	0.041 (0.022, 0.061)	0.021 (0.003, 0.039)
Indirect as a % of Total	11	10	11	18	36	17
Mediator = **Heart rate (24h ECG)**						
Direct effect	0.122 (0.046, 0.198)	0.149 (0.077, 0.221)	0.094 (0.019, 0.170)	0.125 (0.050, 0.201)	0.114 (0.045, 0.184)	0.123 (0.043, 0.203)
Indirect effect	0.011 (0.000, 0.023)	0.009 (−0.001, 0.019)	0.008 (−0.002, 0.017)	0.001 (−0.005, 0.007)	0.002 (−0.006, 0.009)	0.001 (−0.003, 0.004)
Indirect as a % of Total	9	6	8	1	1	1
Mediator = **Inflammation**						
Direct effect	0.119 (0.043, 0.196)	0.133 (0.062, 0.205)	0.096 (0.020, 0.173)	0.116 (0.040, 0.191)	0.105 (0.036, 0.174)	0.116 (0.036, 0.197)
Indirect effect	0.014 (0.001, 0.027)	0.025 (0.008, 0.042)	0.006 (−0.005, 0.017)	0.011 (−0.001, 0.022)	0.011 (0.000, 0.022)	0.007 (−0.002, 0.016)
Indirect as a % of Total	10	16	6	9	9	6
Mediator = **Neuroendocrine**						
Direct effect	0.133 (0.057, 0.209)	0.159 (0.087, 0.231)	0.102 (0.026, 0.177)	0.126 (0.050, 0.202)	0.116 (0.046, 0.185)	0.124 (0.044, 0.204)
Indirect effect	0.000 (−0.001, 0.001)	−0.001 (−0.005, 0.004)	0.001 (−0.005, 0.007)	0.000 (−0.005, 0.005)	0.000 (−0.003, 0.003)	0.000 (−0.001, 0.001)
Indirect as a % of Total	0	0	1	0	0	0

[a]All models control for age, age-squared, and health behaviors (see Table 1).

Table 6

Direct and indirect effects of material resources on health outcomes[a], by sex

	Men			Women		
	General Health	**Phys. Function**	**Bodily Pain**	**General Health**	**Phys. Function**	**Bodily Pain**
Mediator = **Overall biological risk**						
Direct effect	0.185 (0.107, 0.263)	0.145 (0.071, 0.219)	0.225 (0.148, 0.302)	0.038 (−0.027, 0.103)	0.071 (0.012, 0.129)	0.110 (0.041, 0.179)
Indirect effect	0.020 (0.005, 0.036)	0.029 (0.011, 0.048)	0.008 (−0.004, 0.020)	0.008 (−0.004, 0.020)	0.011 (−0.004, 0.026)	0.006 (−0.003, 0.015)
Total effect	0.205 (0.127, 0.283)	0.174 (0.100, 0.249)	0.233 (0.157, 0.310)	0.046 (−0.020, 0.112)	0.082 (0.021, 0.142)	0.116 (0.046, 0.185)
Indirect as a % of Total	10	17	4	18	13	5
Mediator = **Standard markers**						
Direct effect	0.196 (0.118, 0.274)	0.163 (0.088, 0.237)	0.227 (0.150, 0.304)	0.038 (−0.027, 0.104)	0.069 (0.010, 0.128)	0.109 (0.040, 0.178)
Indirect effect	0.009 (−0.001, 0.020)	0.012 (0.000, 0.023)	0.006 (−0.003, 0.016)	0.008 (−0.001, 0.017)	0.013 (0.000, 0.026)	0.007 (−0.001, 0.015)
Indirect as a % of Total	5	7	3	17	15	6
Mediator = **Heart rate (24h ECG)**						
Direct effect	0.187 (0.109, 0.266)	0.159 (0.084, 0.234)	0.223 (0.146, 0.301)	0.045 (−0.021, 0.111)	0.080 (0.020, 0.140)	0.115 (0.046, 0.184)
Indirect effect	0.018 (0.003, 0.033)	0.015 (0.001, 0.029)	0.010 (−0.003, 0.024)	0.001 (−0.004, 0.007)	0.002 (−0.005, 0.009)	0.001 (−0.002, 0.004)
Indirect as a % of Total	9	9	4	3	2	1
Mediator = **Inflammation**						
Direct effect	0.201 (0.124, 0.279)	0.167 (0.094, 0.240)	0.231 (0.155, 0.308)	0.044 (−0.021, 0.109)	0.079 (0.020, 0.139)	0.114 (0.045, 0.183)
Indirect effect	0.004 (−0.005, 0.014)	0.007 (−0.008, 0.023)	0.002 (−0.003, 0.007)	0.002 (−0.007, 0.011)	0.002 (−0.007, 0.011)	0.002 (−0.005, 0.008)
Indirect as a % of Total	2	4	1	5	3	1
Mediator = **Neuroendocrine**						
Direct effect	0.205 (0.128, 0.283)	0.174 (0.099, 0.248)	0.234 (0.158, 0.311)	0.048 (−0.017, 0.114)	0.083 (0.023, 0.143)	0.116 (0.047, 0.186)
Indirect effect	0.000 (−0.002, 0.001)	0.001 (−0.004, 0.005)	−0.001 (−0.007, 0.005)	−0.002 (−0.007, 0.003)	−0.001 (−0.005, 0.002)	−0.001 (−0.003, 0.002)
Indirect as a % of Total	0	0	0	−5	−2	−1

[a]All models control for age, age-squared, and health behaviors (see Table 1).