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# Do biological measures mediate the relationship between education and health: A comparative study

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#### ABSTRACT

Despite a myriad of studies examining the relationship between socioeconomic status and health outcomes, few have assessed the extent to which biological markers of chronic disease account for social disparities in health. Studies that have examined this issue have generally been based on surveys in wealthy countries that include a small set of clinical markers of cardiovascular disease. The availability of recent data from nationally representative surveys of older adults in Costa Rica and Taiwan that collected a rich set of biomarkers comparable to those in a recent US survey permits us to explore these associations across diverse populations. Similar regression models were estimated on three data sets – the Social Environment and Biomarkers of Aging Study in Taiwan, the Costa Rican Study on Longevity and Healthy Aging, and the Health and Retirement Study in the USA – in order to assess (1) the strength of the associations between educational attainment and a broad range of biomarkers; and (2) the extent to which these biomarkers account for the relationships between education and two measures of health status (self-rated health, functional limitations) in older populations. The estimates suggest non-systematic and weak associations between education and high risk biomarker values in Taiwan and Costa Rica, in contrast to generally negative and significant associations in the US, especially among women. The results also reveal negligible or modest contributions of the biomarkers to educational disparities in the health outcomes. The findings are generally consistent with previous research suggesting stronger associations between socioeconomic status and health in wealthy countries than in middle-income countries and may reflect higher levels of social stratification in the US. With access to an increasing number of longitudinal biosocial surveys, researchers may be better able to distinguish true variations in the relationship between socioeconomic status and health across different settings from methodological differences.

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#### Introduction

Despite a long-standing interest in social inequalities in health and survival, and in the behavioral, psychosocial, and environmental mechanisms that may account for these disparities, social scientists have only recently begun to examine the underlying biological pathways linking social position to mental and physical well-being. Interest in these physiological connections has led to a proliferation of "biosocial surveys" that obtain socio-demographic information through interviews along with biological markers related to chronic disease based on physical assessments and laboratory analyses (Weinstein, Vaupel, & Wachter 2008). These surveys are providing

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E-mail address: ngoldman@princeton.edu (N. Goldman). 0277-9536/\$ - see front matter © 2010 Published by Elsevier Ltd. researchers with measurements of biomarkers related to metabolic and cardiovascular disease, often combined with indicators of immune and neuroendocrine function, for broad population-based samples. The resulting biological markers not only offer researchers more objective assessments of health status and disease than the self-reported information typically collected in household surveys, but they are likely to generate insights into the nature of the physiological dysregulation and, ultimately, the underlying causal pathways linking lower social status to poorer health.

Previous studies examining socioeconomic differentials in biomarkers or the impact of these differentials on social disparities in health have largely been based on data from wealthy Western nations. Moreover, many studies have been limited to a few biological markers derived from small or select samples. The availability of recent data from nationally representative surveys of older adults in

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two middle-income countries in different regions (Costa Rica and Taiwan) that collected a rich set of biological measures comparable to those in a recent US survey permits us to explore these relationships in a diverse set of populations.

These countries provide a fascinating set of comparisons. Despite substantial differences in levels of human development in the recent past, the US. Taiwan and Costa Rica now have almost identical life expectancies at birth (approximately 78 years in Taiwan and the US and 79 in Costa Rica (Population Reference Bureau)). The average educational level is currently the same in Taiwan and the US (schooling life expectancy of 15.6 years in 2005), but several years lower in Costa Rica (11.7 years in 2005) (UNESCO Institute for Statistics, 2009; United Nations Educational, Scientific and Cultural Organization). However, the countries continue to have substantially different levels of economic well-being, health care expenditures and inequities in health care. GDP per capita (PPP) in 2009 is much lower in Costa Rica ( $\approx$ \$11,000) than in either Taiwan ( $\approx$  \$33,000) or the US ( $\approx$  \$47000) (International Monetary Fund, 2010). Moreover, in contrast to the decentralized health care system in the US that leaves a large fraction of the population without health insurance (until age 65) or adequate health services, Taiwan and Costa Rica have national health insurance systems that cover the vast majority of residents. This health care is achieved at a fraction of the cost of health care in the US: health expenditures per capita in the US are about six times as high as in Taiwan and about nine times as high as in Costa Rica (Lu & Hsiao, 2003; Unger, De Paepe, Buitron, & Soors, 2008).

#### **Background**

A huge body of research has examined the relationships between socioeconomic status (SES) — most commonly measured by education, income, and occupational status — and health outcomes. There is a consensus that more educated and wealthier individuals fare better than their lower SES counterparts on most broad measures of health status and that these patterns persist at the older ages, although the differentials are generally smaller than at younger ages (Smith & Goldman, 2007; Zajacova, Goldman, & Rodriguez, 2009). However, the few studies conducted in middle-income countries suggest a more erratic and weaker relationship between measures of SES and health than in rich countries (Rosero-Bixby & Dow, 2009; Smith & Goldman, 2007).

Cardiovascular disease, typically the leading cause-of-death in Western populations, is a presumed source of many of the socioeconomic differentials in health and survival. Many studies have examined the association between SES and clinical markers of cardiovascular and metabolic function (e.g., blood pressure, total and HDL cholesterol, body-mass index, and glucose levels). Relatively few population-based studies have examined other physiological markers related to stress and health, such as neuroendocrine measures (Love, Seeman, Weinstein, & Ryff, 2010), even though exposure and response to stressful experience are presumed to comprise an important pathway linking lower social status to poorer health (Siegrist & Marmot, 2004; Steptoe & Marmot, 2002).

There is a pervasive notion that social inequalities in health are reflected in SES differentials in biomarkers related to chronic disease (see, for example, Banks, Marmot, Oldfield, & Smith, 2006; Kristenson, Eriksen, Sluiter, Starke, & Ursin, 2004), but a more nuanced assessment of findings suggests that the associations between biomarkers and SES are not clear-cut. For example, blood pressure which is one of the most commonly analyzed biomarkers, has an inverse association with SES in numerous studies (Atherton & Power, 2007; Banks, Marmot, Oldfield et al. 2006; Bobak, Hertzman, Skodova, & Marmot, 1999; Martikainen, Ishizaki, Marmot, Nakagawa, & Kagamimori, 2001), no significant association in many others

(Brunner, Marmot, Nanchahal et al. 1997; Kapuku, Treiber, & Davis, 2002; Steptoe, Kunz-Ebrecht, Owen et al. 2003) and a positive association in at least one study (Reddy, Rao, & Reddy, 2002). Moreover, the findings are often not consistent within a given study, showing variations by sex or by type of indicator of SES. Additional evidence from a comparative study in Japan and England suggests that the relationships between SES and cardiovascular risk factors are likely to vary across cultural and socioeconomic settings (Martikainen, Ishizaki, Marmot et al. 2001).

Recent studies in Costa Rica and in Taiwan underscore the nonsystematic associations between SES and biomarkers of chronic disease and suggest that, as with SES disparities in health outcomes, SES differentials in biological risk factors may be weaker in moderate to low income countries than in wealthy nations (Dowd & Goldman, 2006; Rosero-Bixby & Dow, 2009). In this study, we take advantage of the availability of comparable high quality biological and health data from Costa Rica, Taiwan and the US to move beyond single-country analyses in order to assess (1) the strength and direction of the associations between education and a broad range of biomarkers; and (2) the extent to which these biomarkers account for the relationships between education and two measures of health status in older populations. Based on the previous work summarized above, we hypothesize that the associations between education and the biomarkers will be considerably weaker in Taiwan and Costa Rica than in the US, and, consequently, that only in the US are we likely to find that the biomarkers mediate the association between education and our downstream measures of health.

#### Materials and methods

Data

Data for this analysis come from three sources: the Social Environment and Biomarkers of Aging Study (SEBAS) in Taiwan, the Costa Rican Study on Longevity and Healthy Aging (CRELES) and the Health and Retirement Study (HRS) in the US. The three surveys comprise information regarding demographic and socioeconomic characteristics, physical health, health-related behaviors, psychological well-being and health service utilization. In addition, all surveys collected physiological data that provide a comparable set of biological measures. Prior to data collection, institutional review boards at the participating institutions approved all survey procedures and respondents provided written informed consent for participation in the interviews and biomarker collection.

SEBAS is based on a follow-up of the Survey of Health and Living Status of the Near Elderly and Elderly in Taiwan (TLSA), a nationally representative longitudinal survey (including the institutionalized population at baseline) that was administered six times between 1989 and 2007. In 2000, a random subsample of respondents for SEBAS was drawn from surviving respondents in 1999, with an oversampling of persons aged 70 years and older and persons in urban areas. A second wave of the survey was conducted in 2006, but the present analysis relies on data from the first wave. SEBAS, which includes respondents 54 and older at the 2000 interview, consists of a face-to-face in-home interview and a medical exam conducted at a hospital several weeks after the interview.

CRELES is an on-going longitudinal study of a nationally representative sample of adults born in 1945 or earlier (ages 60 and over at the first interview) and residing in Costa Rica, with oversampling of the oldest old. For this analysis we use data for the first wave of interviews, conducted between 2004 and 2006, mostly in 2005. The interview data and biological specimens were collected in the participants' homes, usually in two visits.

HRS started in 1992 as a nationally representative study of the non-institutionalized population aged 51 to 61 and their spouses/

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partners. Since 1998, when HRS was merged with the Study of Assets and Health Dynamics among the Oldest Old (AHEAD), HRS has surveyed a nationally representative sample of Americans over the age of 50 every two years. In the 2006 HRS wave, one-half of the full sample (ages 53 and over) was randomly selected to provide an enhanced face-to-face interview that included anthropometric, physical performance and biomarker measurements (Weir, 2008). The data and specimens were collected at the participants' homes. Table 1 provides a summary of the main characteristics of each survey.

### Variables

In order to preserve comparability across populations, we limit the analysis to biomarkers that were ascertained in at least two of the surveys (SEBAS and CRELES obtained more markers than HRS). Of the ten markers examined here, eight are related to metabolic syndrome and two are nonclinical measures associated with neuroendocrine functioning: urinary cortisol and dehydroepiandrosterone sulfate (DHEAS). We construct dichotomous measures of the biomarkers coded as 1 when the respondent has a high risk value and 0 otherwise to capture values outside established cutoff points of clinical markers as well as the potential for risk at extreme values of nonclinical markers (see Table 2 for cutoff points). Binary measures of biomarkers, which have been used extensively in other analyses (Feldman et al., 2001; Park, Cho, Song, & Sung, 2006), have several advantages over continuous parameterizations. First, a linear specification is unsatisfactory for biomarkers that have risk associated with both low and high values: a non-monotonic specification such as a quadratic function can be readily implemented when biomarkers are explanatory – but not outcome – variables. Second, because most of the markers in this analysis have well-established cutoff points designating clinical risk, an underlying assumption of a threshold effect on health status is at least as plausible as a linear effect throughout the range of the biomarker. Third, research related to the construction of indices of physiological dysregulation has concluded that indices based on counts of biomarkers with high risk values (i.e., a sum of binary variables) perform as well as those based on continuous markers (Seplaki, Goldman, Glei, & Weinstein, 2005). Finally, in contrast to continuous measures, binary variables are robust to outliers.

The metabolic syndrome markers include two indicators of body fatness: waist circumference and BMI. For waist circumference, we code values larger than 88 cm for women and 102 for men as high risk (National Heart, Lung, and Blood Institute, Obesity

Education Initiative). For BMI, calculated as weight divided by height squared (kg/m<sup>2</sup>), we recode the original values to reflect obesity (values larger than or equal to 30) and underweight status (lower than 18.5), following earlier studies that have shown that both excess fat and accelerated loss of lean body-mass are associated with health deterioration (Allison, Faith, Heo, & Kotler, 1997: Seidell & Visscher, 2000). (Some studies recommend the use of lower cutoff points to define obesity in East Asian populations, but this is a controversial issue (World Health Organization 1998)). For systolic and diastolic blood pressure, values > 140 and 90 mmHg respectively (based on two readings for SEBAS and CRELES and three readings for HRS) are defined as high risk (Whitworth, 2003). We also include measures of total serum cholesterol (high risk  $\geq$  240 mg/dL) and triglycerides (high risk  $\geq$  200 mg/dL), based on fasting blood specimens in SEBAS and CRELES and a non-fasting blood specimen in the HRS (Third Report of the National Cholesterol Education Program (NCEP) Expert Panel 2002). Two biomarkers measure glucose metabolism: fasting glucose and glycosylated hemoglobin (HbA1c). High risk cutoff values for these measures are  $\geq$  100 mg/dl and >6.5% respectively (AACE Diabetes Mellitus Clinical Practice Guidelines Task Force 2007).

In the absence of guidelines for normal ranges of nonclinical markers, we use cutoff points for cortisol and DHEAS based on the distributions of these biomarkers in each survey (Seeman, Singer, Rowe, Horwitz, & McEwen, 1997), calculated separately for men and women. Because both low and high cortisol levels may be related to increased risk of dying (Marklund, Peltonen, Nilsson, & Olsson, 2004), this marker equals 1 for respondents who have values in the lowest or highest deciles. DHEAS equals 1 only for individuals in the lowest quartile because low levels of DHEAS have been related to several disorders, including impairments of immune and cognitive function, as well as mortality (Barrett-Connor, Khaw, & Yen, 1986; Mazat, Lafont, Berr et al. 2001). Triglycerides, fasting glucose, cortisol and DHEAS measurements are not available in the HRS, and, thus, are compared only in SEBAS and CRELES.

The health outcomes in this analysis comprise two measures — self-rated health and functional limitations — that have been shown to be associated with a broad range of biomarkers (Goldman, Turra, Glei, Lin, & Weinstein, 2006b; Jylhä, Volpato, & Guralnik, 2006; Koster, Penninx, Bosma et al. 2005). Self-rated health is reported according to the conventional 5-point ordinal scale: excellent, very good, good, fair and poor. The measure of functional limitations is constructed to be comparable across surveys and reflects the number of activities that the respondent reports difficulty performing; this count is derived from four mobility tasks (lifting or

**Table 1**Summary of survey characteristics for SEBAS, CRELES and HRS.

Survey characteristics	SEBAS (2000) Taiwan	CRELES (2004–2006) Costa Rica	HRS (2006) USA
Design	Nationally representative, longitudinal	Nationally representative, longitudinal	Nationally representative, longitudinal
Types of interviews	Face-to-face in-home interview and a medical exam in a hospital	2 face-to-face in-home interviews	Face-to-face in-home interview
Age range	54+	60+	53+
Sample size	1497 interviews	2827 interviews	7819 interviews
Response rates	92% (of located survivors) for interviews	85% (of located survivors) for interviews	93% (of located survivors) for interviews
	Among those interviewed:	Among those interviewed:	Among those eligible:
	68% for medical exam	95% for blood sample	97% for blood sample
		92% for urine sample	93% for height and weight
		91% for anthropometry	96% for blood pressure
Biomarker	•12-h overnight urine	12-h overnight urine	•saliva sample
collection	•fasting blood sample (venipuncture)	•fasting blood sample (venipuncture)	<ul><li>blood sample (finger prick)</li></ul>
	<ul> <li>waist and hip circumference, height,</li> </ul>	<ul> <li>waist and hip circumference, height,</li> </ul>	<ul> <li>waist circumference, height,</li> </ul>
	and weight	and weight	and weight
	•3 blood pressure readings with a mercury sphygmomanometer	•2 blood pressure readings with a digital monitor	•3 blood pressure readings with a digital monitor

**Table 2**Cutoff points and summary measures for high risk values of individual biomarkers in SEBAS. CRELES and HRS.

Sex/Biomarker	Cutoff points for	SEBAS		CRELES		HRS	
	high risk values	Sample Size	Percentage of high risk cases <sup>a</sup>	Sample Size	Percentage of high risk cases <sup>a</sup>	Sample Size	Percentage of high risk cases <sup>a</sup>
Women							
BMI (kg/m <sup>2</sup> )	≥30 or <18.5	433	13.2	1463	36.1	3799	40.7
Waist circumference(cm)	>88	432	27.6	1421	64.6	3897	69.5
Glucose (mg/dl)	≥100	433	42.6	1448	51.2	N/A <sup>b</sup>	
HbA1c (%)	>6.5	432	19.3	1431	14.0	3509	9.5
Systolic blood pressure (mmHg)	>140	433	44.1	1515	54.2	3955	25.9
Diastolic blood pressure (mmHg)	>90	433	22.1	1515	29.3	3955	17.0
Cholesterol (mg/dL)	≥240	433	19.8	1448	36.5	3348	17.8
Triglycerides (mg/dL)	≥200	433	10.6	1447	23.7	N/A <sup>b</sup>	
DHEAS (μg/dl)	<29.9 (SEBAS)	433	24.9			N/A <sup>b</sup>	
	<17.4 (CRELES)			1426	24.8		
Cortisol (µg/g creatinine)	<9.99 or >53.28 (SEBAS)	431	19.9			N/A <sup>b</sup>	
	<8.89 or >48.96 (CRELES)			1209	19.8		
Men	()						
BMI (kg/m <sup>2</sup> )	>30 or <18.5	589	8.5	1235	22.0	2817	39.0
Waist circumference (cm)	>102	589	4.0	1211	21.2	2919	54.5
Glucose (mg/dl)	>100	589	36.6	1211	40.7	N/A <sup>b</sup>	
HbA1c (%)	>6.5	589	9.6	1185	8.8	2506	11.3
Systolic blood pressure (mmHg)	>140	590	37.0	1278	50.4	2931	33.9
Diastolic blood pressure (mmHg)	>90	590	21.4	1278	26.6	2931	19.4
Cholesterol (mg/dL)	>240	589	10.7	1209	21.8	2368	11.5
Triglycerides (mg/dL)	>200	589	10.5	1209	23.5	N/A <sup>b</sup>	
DHEAS (μg/dl)	<53.2 (SEBAS)	588	24.7			N/A <sup>b</sup>	
,	<35.4 (CRELES)			1192	24.9	,	
Cortisol (µg/g creatinine)	<7.56 or >42.86 (SEBAS)	588	19.7			N/A <sup>b</sup>	
	<8.75 or >47.65 (CRELES)			1041	19.7		

<sup>&</sup>lt;sup>a</sup> Weighted estimates.

carrying weight, raising arms above shoulders, walking a specified distance, and climbing stairs), two instrumental activities of daily living (buying personal items and managing money), and three activities of daily living (bathing, eating, and toileting).

We use educational attainment as our measure of SES for several reasons. Educational attainment is not only the most comparable measure across the three settings, but it is also better suited to measure SES at older ages than income and occupation and has less missing data than the other variables. Wealth has been found to be important in some studies of older populations (Avendano & Glymour, 2008; Bond Huie, Krueger, Rogers, & Hummer, 2003), but it is not consistently measured in the studies. In addition, education, which is typically completed early in life, is considerably less likely to be affected by poor health - i.e., reverse causality - than are measures of wealth, income and occupational status (Elo, 2009). Although, we recognize that education is an imperfect measure of social position among older adults, particularly in modernizing societies such as Taiwan that have experienced dramatic increases in educational attainment and social mobility, there is evidence that older adults give more weight to their schooling than to other economic indicators when evaluating their social position (Goldman, Cornman, & Chang, 2006a). In order to preserve comparability, we code education into three categories based on approximate terciles of its (unweighted) distribution in each survey. The cutoff points are similar in Taiwan (men: 0-5, 6, 7+; women: 0, 1-6, 7+) and Costa Rica (men: 0–1, 2–5, 6+; women: 0–2, 3–5, 6+). In the US, where secondary education has been mandatory for a longer period, the cutoff points are 0-1112, and 13 + years of schooling for both sexes. Distributions of educational attainment, as well as self-rated health and functional limitations, are provided in Supplementary Table 1. We include linear and quadratic controls for age in all models.

Analytic strategy

To examine the associations between education and the physiological measures in each of the three countries, we estimate separate logistic regression models for each biomarker, controlling for age. We fit separate models for men and women because of presumed sex differences in the biological mechanisms linking SES and health (Dowd & Goldman, 2006; Rosero-Bixby & Dow, 2009).

To test for the mediating effects of biomarkers in the relation between education and health, we also estimate separate models for each population and sex. Ordered logistic regression models are used for self-rated health and Poisson regression models for the count of functional limitations. We compare two models for each outcome. The first includes only age and education, whereas all biomarkers are included in the second model. The analytic sample sizes vary slightly across models for a given country, due primarily to missing values for biomarkers. We use Stata 10 to estimate the models (StataCorp, 2008).

#### Results

Table 2, which provides weighted estimates of the prevalence of high risk biomarker values, reveals considerable variation across the three countries. The frequencies of extreme BMI values and large waist circumference are higher in the U.S compared to Taiwan and Costa Rica. In contrast, Costa Rica has the largest proportions of persons with high blood pressure and high cholesterol. Estimates that include persons using antihypertensive medication regardless of their blood pressure levels (not shown) reveal that the US and Costa Rica have similarly high rates of hypertension under these revised definitions.

b Not applicable.

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Estimated odds ratios for education from the logistic models of having high risk values of each biomarker are presented in Tables 3 and 4. In Taiwan, only one of the 10 markers is significantly associated with education for both sexes (DHEAS); glucose is significant only for men, whereas three other markers are significant only for women (BMI, diastolic blood pressure and cortisol). Even fewer significant associations are present in Costa Rica — glucose and triglyceride values among men, and systolic blood pressure, glucose, and glycosylated hemoglobin values among women — and the direction of the association with education varies across these markers.

In the US, where we have data on only six of the 10 markers, we find a higher proportion of statistically significant associations: among women, all associations except those for cholesterol are significant, and, for men, three of the biomarkers (diastolic and systolic blood pressure and HbA1c) have a significant odds ratio associated with education. Most of the significant associations in each country pertain to the highest education group, whose members are less likely than those in the lowest level to have high risk values (except for Costa Rican men). Only in the US do we generally find a graded relationship, with the odds ratios becoming progressively smaller for higher levels of education, particularly for women.

Despite only sporadic associations between education and the biomarkers for Costa Rica and Taiwan, education is significantly related to both self-rated health and functional limitations in all samples (Model 1, Tables 5 and 6). The generally larger coefficients (in absolute value) for HRS suggest that the relationship between higher levels of education and better health outcomes is stronger in the US than in Costa Rica or Taiwan, consistent with the literature identifying weaker associations in middle-income countries. As shown by a comparison of estimates from Models 1 and 2, evidence supporting the mediating role of biological markers is modest. In most cases, the coefficients and significance levels for the education variables change little with the inclusion of the biomarkers, suggesting that the biomarkers do not help to explain the SES disparities in these health outcomes. However, for the most educated women in Taiwan and the US, and, to a lesser extent, educated Taiwanese men, the biomarkers appear to mediate part of the association between education and the health measures. Nevertheless, in the presence of controls for biomarkers, all but one of these associations remains statistically significant.

#### Discussion

Overall, these results suggest non-systematic associations between education and high risk biomarker values in Taiwan and Costa Rica, and negligible or modest mediating effects of the biomarkers on educational disparities in two health measures for all three countries. Particularly in light of the fact that the statistical model controls for only six biomarkers in the US in contrast to 10 markers in the other countries, the findings suggest a larger contribution of the biomarkers to educational disparities in the US than in Taiwan and Costa Rica. In models not presented here, we explored the robustness of these findings by specifying educational attainment based on conventional schooling levels. The alternative formulations produced results similar to those described above. We also redefined high blood pressure and high levels of glycosylated hemoglobin to include respondents taking medications for these conditions. The corresponding estimates of prevalence increased under the revised definitions, but there was little effect on the education coefficients. Finally, we evaluated the robustness of our findings to the specification of the biomarkers. After trimming outlying values of the biomarkers, we (1) estimated linear regression models for each biomarker corresponding to the logistic models in Tables 3 and 4 and re-estimated Model 2 in Tables 5 and 6 based on linear, rather than binary, parameterizations of the markers. Overall, about the same number of biomarkers were significantly associated with education in the binary and linear specifications. The one exception was a larger number of significant associations for Costa Rican males based on linear markers, but all of these were in the same direction as those for the binary measures, suggesting that higher levels of education are related to *riskier* values of the markers. The comparison of education coefficients with and without controls for the biomarkers revealed negligible or modest changes under both specifications, but, overall, the reduction in the magnitude of the education coefficients was

**Table 3**Odd ratios from logistic models of having high risk values of each biomarker, by education: men in SEBAS, CRELES and HRS.

	BMI	Waist circumference	Systolic BP	Diastolic BP	Glucose	HbA1c	Cholesterol	Triglycerides	DHEAS	Cortisol
SEBASª										
Education level 1 (reference	ce)									
Education level 2	0.5781 [0.2100]	0.9158 [0.4834]	1.0690 [0.2352]	0.8891 [0.2364]	1.4989 [0.3465]	0.9799 [0.3561]	0.7001 [0.2320]	0.6134 [0.2193]	0.9552 [0.2207]	0.7881 [0.2112]
Education level 3	0.6282 [0.2276]	0.7814 [0.4341]	0.8063 [0.1845]	0.7061 [0.2043]	1.9735** [0.4675]	1.0203 [0.3797]	0.5996 [0.2121]	0.6425 [0.2413]	0.3383** [0.0932]	0.9137 [0.2520]
Number of observations CRELES <sup>a</sup>	589	589	590	590	589	589	589	589	588	588
Education level 1 (reference	ce)									
Education level 2	1.0496 [0.1957]	1.0616 [0.2022]	1.0335 [0.1422]	0.9226 [0.1496]	1.0917 [0.1584]	1.1391 [0.3128]	1.0487 [0.1853]	1.2067 [0.2240]	1.0582 [0.1645]	0.7537 [0.1411]
Education level 3	1.4497 [0.2813]	1.3837 [0.2754]	0.8024 [0.1202]	0.9514 [0.1649]	1.5901** [0.2511]	1.2000 [0.3517]	1.0865 [0.2084]	1.5261* [0.2969]	1.3490 [0.2365]	0.9794 [0.1977]
Number of observations HRS <sup>a</sup>	1235	1211	1278	1278	1211	1185	1209	1209	1192	1041
Education level 1 (reference	ce)									
Education level 2	1.1066 [0.1240]	1.2013 [0.1291]	0.8841 [0.0960]	0.8784 [0.1204]		0.8103 [0.1304]	0.9927 [0.1964]			
Education level 3	0.9058 [0.0946]	0.9527 [0.0940]	0.7699* [0.0780]	0.6998** [0.0900]		0.6055** [0.0943]	0.8211 [0.1506]			
Number of observations	2817	2919	2931	2931		2506	2368			

Standard errors in brackets.

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<sup>\*</sup> significant at 5%; \*\* significant at 1%.

<sup>&</sup>lt;sup>a</sup> All models are unweighted and control for linear and quadratic terms for age. Models for SEBAS control for urban/rural residence.

**Table 4**Odds ratios from logistic models of having high risk values of each biomarker, by education: women in SEBAS, CRELES and HRS.

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	BMI	Waist circumference	Systolic BP	Diastolic BP	Glucose	HbA1c	Cholesterol	Triglycerides	DHEAS	Cortisol
SEBAS <sup>a</sup>										
Education level 1 (referen	ce)									
Education level 2	1.3004	1.2513	0.9471	0.9468	0.9123	0.7109	0.8861	0.8615	0.9274	1.2135
	[0.4005]	[0.3041]	[0.2125]	[0.2545]	[0.2061]	[0.2046]	[0.2442]	[0.3202]	[0.2324]	[0.3215]
Education level 3	0.1117*	0.5521	0.8037	0.3146*	0.6968	0.6400	0.9147	2.1876	0.1287**	0.3221*
	[0.1157]	[0.2182]	[0.2588]	[0.1626]	[0.2304]	[0.2903]	[0.3506]	[0.9356]	[0.0802]	[0.1791]
Number of observations CRELES <sup>a</sup>	433	432	433	433	433	432	433	433	433	431
Education level 1 (referen	ce)									
Education level 2	0.8070	0.8468	1.1107	1.1134	1.3584*	0.9175	1.0514	0.9440	0.8841	1.0533
	[0.1078]	[0.1132]	[0.1412]	[0.1553]	[0.1723]	[0.1722]	[0.1413]	[0.1448]	[0.1276]	[0.1806]
Education level 3	0.8990	0.8353	0.6873**	0.8133	1.2247	0.6566*	1.0405	0.9913	1.3148	1.3389
	[0.1226]	[0.1156]	[0.0887]	[0.1200]	[0.1607]	[0.1324]	[0.1441]	[0.1550]	[0.1930]	[0.2329]
Number of observations HRS <sup>a</sup>	1463	1421	1515	1515	1448	1431	1448	1447	1426	1209
Education level 1 (referen	ce)									
Education level 2	0.7564**	0.7164**	0.7455**	0.7848*		0.5482**	1.0319			
	[0.0676]	[0.0726]	[0.0697]	[0.0849]		[0.0723]	[0.1289]			
Education level 3	0.5719**	0.5356**	0.6248**	0.6579**		0.3705**	0.9863			
	[0.0513]	[0.0527]	[0.0593]	[0.0721]		[0.0526]	[0.1235]			
Number of observations	3799	3897	3955	3955		3509	3348			

Standard errors in brackets.

slightly larger with binary markers for Costa Rica and Taiwan and slightly larger with linear markers for the US.

Although the results for Taiwan and Costa Rica challenge the commonly held assumption that more educated individuals have healthier biological profiles than their less educated peers, the findings are consistent with earlier studies based on SEBAS and CRELES, each of which used a somewhat different set of markers, SES variables, and health outcomes than the present study. The Taiwan study found that biomarkers associated with the cardio-vascular, neuroendocrine, and immune systems explained relatively little of the association between SES and health status, primarily because few biomarker distributions were significantly associated with education and income (Dowd & Goldman, 2006).

Although analyses of the Costa Rican data did not assess the extent to which biomarkers accounted for SES differentials, the results demonstrated that (1) the direction of the SES gradient varied across biomarkers, with lower SES individuals often having *better* indicators than their higher SES counterparts (Rosero-Bixby & Dow, 2009); and (2) fewer cardiovascular risk factors were associated with education in Costa Rica than in the US, based on NHANES (Rehkopf, Dow, & Rosero Bixby, 2010).

The findings for HRS are generally consistent with those in other US studies. For example, analyses based on NHANES indicate that high income and high education levels are negatively associated with high blood pressure and total cholesterol and positively associated with HDL cholesterol, as expected (Kanjilal, Gregg,

**Table 5**Estimated regression coefficients<sup>a</sup> for self-rated health and functional limitations, by education: men in SEBAS, CRELES and HRS.

	SEBAS <sup>b</sup>		CRELES <sup>c</sup>		HRS <sup>d</sup>		
	Self-rated health	Functional limitations	Self-rated health	Functional limitations	Self-rated health	Functional limitations	
Model 1							
Education level 1 (reference	ce)						
Education level 2	-0.1594	-0.5916**	-0.2593	-0.0410	-0.7356**	-0.2767**	
	[0.1999]	[0.1385]	[0.1466]	[0.0577]	[0.1182]	[0.0783]	
Education level 3	-0.6178**	-0.6937**	-1.1289**	-0.4405**	-1.1696**	-0.5813**	
	[0.2099]	[0.1467]	[0.1633]	[0.0794]	[0.1120]	[0.0795]	
Model 2							
Education level 1 (reference	ce)						
Education level 2	-0.1609	-0.5224**	-0.2561	-0.0421	-0.7409**	-0.2956**	
	[0.2018]	[0.1412]	[0.1472]	[0.0578]	[0.1191]	[0.0780]	
Education level 3	-0.5576*	-0.5636**	-1.1252**	-0.4550**	-1.1393**	-0.5761**	
	[0.2164]	[0.1512]	[0.1645]	[0.0798]	[0.1127]	[0.0787]	
Number of observations	580	585	953	848	2203	2200	

Standard errors in brackets.

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<sup>\*</sup> significant at 5%; \*\* significant at 1%.

<sup>&</sup>lt;sup>a</sup> All models are unweighted and control for linear and quadratic terms for age. Models for SEBAS control for urban/rural residence.

significant at 5%; \*\* significant at 1%.

a Ordered logistic regression models are used for self-rated health and Poisson regression models for the count of functional limitations. Models are unweighted.

b Model 1 controls for urban/rural residence and linear and quadratic terms for age. Model 2 controls for urban/rural residence, linear and quadratic terms for age and ten biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose, HbA1c, total cholesterol, triglycerides, DHEAS and cortisol.

<sup>&</sup>lt;sup>c</sup> Model 1 controls for linear and quadratic terms for age. Model 2 controls for linear and quadratic terms for age and ten biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose, HbA1c, total cholesterol, triglycerides, DHEAS and cortisol.

<sup>&</sup>lt;sup>d</sup> Model 1 controls for linear and quadratic terms for age. Model 2 controls for linear and quadratic terms for age and six biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, HbA1c, total cholesterol.

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**Table 6**Estimated regression coefficients<sup>a</sup> for self-rated health and functional limitations, by education: women in SEBAS, CRELES and HRS.

	SEBAS <sup>b</sup>		CRELES <sup>c</sup>		HRS <sup>d</sup>		
	Self-rated health	Functional limitations	Self-rated health	Functional limitations	Self-rated health	Functional limitations	
Model 1							
Education level 1 (referen-	ce)						
Education level 2	-0.4001	-0.4670**	-0.1629	-0.2167**	-1.0879**	-0.3738**	
	[0.2091]	[0.1104]	[0.1344]	[0.0477]	[0.0923]	[0.0373]	
Education level 3	-0.9321**	-0.4582**	-0.9476**	-0.4852**	-1.6026**	-0.5981**	
	[0.2959]	[0.1564]	[0.1390]	[0.0565]	[0.0936]	[0.0391]	
Model 2							
Education level 1 (referen-	ce)						
Education level 2	-0.3964	-0.4488**	-0.1416	-0.1797**	-1.0105**	-0.3123**	
	[0.2104]	[0.1113]	[0.1354]	[0.0484]	[0.0931]	[0.0376]	
Education level 3	-0.7791*	-0.3167	-0.9505**	-0.4874**	-1.4795**	-0.5032**	
	[0.3073]	[0,1627]	[0.1403]	[0.0569]	[0.0946]	[0.0397]	
Number of observations	417	426	1116	942	3037	3033	

Standard errors in brackets.

Cheng et al. 2006; Muennig, Sohler, & Mahato, 2007). However, few of these cardiovascular markers are significantly related to education in an analysis based on the MacArthur Successful Aging Study (Seeman, Crimmins, Huang et al. 2004), perhaps because the MacArthur sample is older (ages 70–79) than the sample in HRS and in most other US studies. The presence of significant inverse associations between SES and markers of obesity among American women but not American men — as found here — has been identified in studies based on NHANES (Chang & Lauderdale, 2005; Zhang & Wang, 2004).

In contrast to a fairly large literature examining links between SES and biomarkers, few studies in the US have looked at the mediating effects of a substantial set of biomarkers (i.e., more than several markers or markers pertaining to more than one physiological system) on SES differentials in health. An analysis based on the MacArthur Study identifies modest effects of cardiovascular and immune parameters, and very small effects of neuroendocrine markers, on the relative risks of dying associated with educational attainment (Seeman, Crimmins, Huang et al. 2004). Findings for other countries vary substantially by time and place. For example, a study in Eastern Finland shows large reductions in the relative hazards of all-cause mortality after adjustment for biologic risk factors (Lynch, Kaplan, Cohen, Tuomilehto, & Salonen, 1996). Yet, another Finnish study demonstrates that, since the 1980s, traditional risk factors have been less able to account for socioeconomic disparities in cardiovascular mortality in Finland as compared with earlier periods, perhaps because of improved access to new medical technologies (Harald et al., 2008). In London, an analysis based on the Whitehall II study finds large effects of metabolic and inflammatory markers on differentials in incident coronary disease by employment grade (Marmot, Shipley, Hemingway, Head, & Brunner, 2008). In contrast, two studies in South Korea fail to find mediating effects of biologic risk factors on either cardiovascular disease or all-cause mortality (Khang & Kim, 2005; Yun-Mi Song, Ferrer, Sung-il Cho, Sung, Ebrahim, & Smith 2006).

Despite a justified appeal for international comparisons of social gradients in health that integrate biological mechanisms (Banks, Marmot, Oldfield et al. 2006; Elo, 2009), such undertakings are generally unable to establish whether divergent findings reflect true variability in the physiological pathways linking SES to health across

countries, regions and time periods; differences across data sets in measurement error or definitions of biomarkers. SES, and health outcomes; differences in analytic strategies; or variations in sample size. In this analysis, measurement error, particularly for the biomarkers – which are collected on a single day – is a serious concern. An additional limitation is the disparity in sample sizes (HRS is the largest and SEBAS the smallest of the surveys) and associated levels of statistical power. In particular, the finding that there are more significant associations between biomarkers and education for the US as compared to Taiwan and Costa Rica could reflect, in part, the larger sample size of the HRS, although sample size considerations would not account for Costa Rica displaying weaker associations than Taiwan. Nevertheless, the similarity in the variables, statistical models, and analytic strategy for the three data sets strengthens our conclusion that the biomarkers are most strongly associated with education in the US and that their mediating effects on health are likely to be larger in the US than in Costa Rica or Taiwan. This finding may partly reflect higher levels of social stratification in the US than in the other countries, including larger inequities in access to health care and a higher concentration of unhealthy behaviors among individuals occupying lower socioeconomic positions. The variability in associations across countries also underscores the dangers of assuming that these relationships are universal.

Recent studies that incorporate "novel coronary risk factors" suggest that immune and inflammatory markers related to cardiovascular risk may play a more important role than traditional cardiovascular risk factors in mediating the associations between SES and health. For example, many studies in the US and the UK identify substantial SES differences in the levels of such markers as interleukin-6, C-reactive protein, fibrinogen, and tumor necrosis factor-α (Albert, Glynn, Buring, & Ridker, 2006; Banks, Marmot, Oldfield et al. 2006; Friedman & Herd, 2010; Gruenewald, Cohen, Matthews, Tracy, & Seeman, 2009; Hemingway, Shipley, Mullen et al. 2003; Koster, Bosma, Penninx et al. 2006; Marmot, Shipley, Hemingway et al. 2008; Pollitt et al., 2008; Ramsay, Morris, Whincup et al. 2009; Tabassum et al., 2008). Once again, however, relatively few of these studies assess the impact of these markers on SES differentials in health, and, among those that do, the results vary across studies (due in part to whether behavioral risk factors are included in the model and the specific measure of SES used).

<sup>\*</sup> significant at 5%; \*\* significant at 1%.

a Ordered logistic regression models are used for self-rated health and Poisson regression models for the count of functional limitations. Models are unweighted.

b Model 1 controls for urban/rural residence and linear and quadratic terms for age. Model 2 controls for urban/rural residence, linear and quadratic terms for age and ten biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose, HbA1c, total cholesterol, triglycerides, DHEAS and cortisol.

<sup>&</sup>lt;sup>c</sup> Model 1 controls for linear and quadratic terms for age. Model 2 controls for linear and quadratic terms for age and ten biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, fasting glucose, HbA1c, total cholesterol, triglycerides, DHEAS and cortisol.

d Model 1 controls for linear and quadratic terms for age. Model 2 controls for linear and quadratic terms for age and six biomarkers: BMI, waist circumference, systolic blood pressure, diastolic blood pressure, HbA1c, total cholesterol.

Still, the strong links between these inflammatory and immune markers and various illnesses, chronic conditions, and healthrelated behaviors, such as smoking and obesity, suggest that their inclusion in biosocial surveys may provide a promising direction for elucidating the pathways linking social disparities to health. In addition, the increasing number of biosocial surveys being fielded in both high and middle-income countries, some of which comprise longitudinal data that permit the identification of incident health conditions and their sequelae, may help researchers to identify true variations in the strength and nature of the relationships between SES and health across different social, economic and cultural settings. At minimum, social scientists need to recognize that the conventional biomarkers of cardiovascular disease used in most studies are only scratching the surface of the complex, multisystem physiological mechanisms through which social disadvantage is likely to get under the skin.

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# Appendix. Supplementary data

Supplementary data related to this article can be found online at doi:10.1016/j.socscimed.2010.11.004.

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