# Sex and SES paradox in health status
# and mortality among elderly populations

**(DRAFT)**

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***Abstract***

*Adult males have higher mortality than females, while, paradoxically, health status indicators often show the contrary: males are better off than females. Mortality indicators are hard, indisputable data. Health indicators, however, are often based on "soft" data, dependent on definitions, interpretations, and subjective self-reports. Based on panel data for elderly Mexicans (MHAS study) and biomarkers for elderly Costa Ricans (CRELES), we conclude that self-reported health indicators may be misleading. The sex gap showing elderly women with poorer health than men is to some extent a spurious result of differential age structure, survival selection, and sex-bias in self-reports. The paper also explores whether the large socioeconomic gap in self-reported health suffers similar problems like the sex gap. Elderly Costa Ricans do not show the inverse gradient in health by socioeconomic status (SES) for important biomarkers. This finding contradicts the results obtained when using self reported indicators.*

## Introduction

In this paper we investigate a well-known paradox existing in data for adult and elderly populations: while everywhere there is over-mortality for males, health status indicators are usually much better for males than for females. Mortality indicators are "hard", clear-cut data. They are indisputable. Health status indicators, in contrast, are often based on "soft" data, dependent on definitions, interpretations and subjective self-reports. Is this paradox real or just a result of biases in data on health status? If it were real, then the paradox would mean that elderly women live longer but a life of lower quality, an inequity that should be corrected as feminist and gender-approach literature proclaim. But if the paradox is originated in bad survey data, people would be making wrong inferences and bad decisions. Furthermore, if sex differentials in health status are biased, socioeconomic and other differentials may also be so. As a matter of fact, Costa Rican mortality data for old ages do not show the expected socioeconomic gradient (more educated or richer individuals do not show lower mortality), whereas some self-reported, survey data show substantially better health indicators for the affluent or more educated (Rosero-Bixby, 2005; Rosero-Bixby, Dow, & Lacle, 2005). In this paper we also explore whether socioeconomic differentials in health are afflicted by similar problems as the sex-gap.

Comparative studies for four Asian countries (Zimmer, Natividad, Ofstead, & Lin, 2002), and seven Latin American cities (Wong, Pelaez, & Palloni, 2005; Menendez et al., 2005) show clear advantage of elderly males over females in self-assessed health status, as well as in performing activities of daily living (ADL), and chronic conditions with the exception of some life-threatening conditions that are more prevalent among men. However, a study of elderly Taiwanese show that the health sex-gap disappears or becomes less consistent when measured by objectively biomarkers (Goldman et al., 2004). It is important to mention that all these evidences come from cross-sectional data.

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One possible explanation for the sex paradox is that females have higher prevalence of debilitating conditions, while males have higher prevalence of life-threatening conditions (Zimmer et al. 2002; Case & Paxson, 2005; Arber & Cooper, 1999). The paradox may also be originated in confounding effects of third variables, selection effects, or just sex-biased responses.

The most common confounding effect comes from the age structure, which is older for elderly females than that for males. This confounding element can --and should-- be easily controlled for. Second, the selection bias may come from the fact that in surveys we are dealing with just survivors and the rare male survivor could be healthier than the average female survivor. Third, females may simply be more aware of diseases and health problems than males, either because the former have the social responsibility for health in their families, so, they pay more attention or are in closer contact with health providers, or males may try to hide disease or poor health on the premises that those are signs of weakness, which men should not exhibit.

Differentials in both health and mortality by socioeconomic status (SES) at older ages are less clear and rarely studied because of the lack of proper information. In general terms, SES differentials tend to be smaller at older ages than at earlier ages (Crimmins, 2005). Surveys in Asia and Latin America show substantially poorer self-assessed health among the low-educated (Zimmer et al., 2002; Palloni & McEniry, 2004). These studies show that in Asia the SES differentials are less clear for ADL indicators and it reverses for life-threatening measures, while in Latin America the SES gradient persists for ADLs and chronic conditions like diabetes, although with less strength than that observed in self-assessed health indicators.

In both, Asia and Latin America, socioeconomic differentials are substantially lower than those observed in the USA (Zimmer et al., 2002; Palloni & McEniry, 2004). However, SES differentials for adult and old age mortality are less known in developing countries. Recent studies have found that mortality by cardiovascular diseases and diabetes tends to be higher in the more developed areas of Costa Rica (Rosero-Bixby, 1996). Similarly, a 17-year follow-up study in Costa Ricans shows no significant differences in survival by SES among elderly (Rosero-Bixby, et al., 2005)

Some authors attribute to selection effects the weakening of sex differentials by age, that is, mortality eliminates the frailest individuals at early ages in groups with lower SES (Crimmings, 2005). Other authors attribute to differential in access to health care the fact that life-threatening conditions are less prevalent in lower SES groups (Zimmer, 2002).

New surveys on health status among elderly in developing countries have gone beyond cross-sectional designs and self-reported health data. These surveys are based on longitudinal designs and include biomarkers as more objective health indicators (Rieker & Bird, 2005). These new data allow more valid assessments on sex and SES differentials in health. This paper uses data from two of these new generations of studies: a Mexican longitudinal survey (MHAS project) and a Costa Rican longitudinal survey, which includes various biomarkers (CRELES project), with the purpose of refining measurements on health status and validating traditional indicators.

By using transitions from longitudinal studies, instead of just prevalences, one can assess the volatility of data and also remove biases that stay fixed over time. If a health indicator has two components: (1) a true health status $H(t)$ varying over time, and (2) a bias or error $E$ fixed over time; then, the growth rate $rh$ of the health status calculated from observations at times $t_0$ and $t_1$, will be free of the bias $E$, and it will measure only health status and its change as follows:

$$rh = \frac{H(t_0)E}{H(t_1)E} - 1 = \frac{H(t_0)}{H(t_1)} - 1$$

Similarly, when using biomarkers, one can check if sex and SES differentials persist. Biomarkers permit also to validate self-reported data on specific conditions such as diabetes or high blood pressure, as well as to identify cultural biases in reporting individuals' own health status that vary systematically by sex or socioeconomic status.

**Data and methods**

**The data**

Data for this study come primarily from the Mexican Health and Aging Study (MHAS), which is a prospective panel in a nationally representative sample of about 8,000 individuals born before 1951 and interviewed during 2001 and 2003. This paper uses data on self-assessed health ("Would you say your health is excellent, very good, good, fair or poor?"), mortality, age, sex and education from data files available at the study's web page (MHAS, 2005).

The second data set used in this study comes from the Costa Rican Study on Longevity and Healthy Aging (CRELES). This is a on-going longitudinal study of a nationally representative sample of 3,000 adults aged 60 and over, with over-sampling of the older old. For this analysis, a sub-sample of 1,800 individuals was available. We use data on physical assessments (anthropometric measures), and laboratory tests on blood specimens, and 12-hour (overnight) urine collections, which together yielded information on the biomarkers considered in this paper. Because of over-sampling of older individuals, results of this survey must be weighted in order to reflect the age structure of the population aged 60 and over.

**Measures**

Two unconditional transition probabilities (called "rates" for simplicity) are considered to measure the self-assessed health category "fair and poor health", which were computed for individuals with information for the two waves in the Mexican study:

1. *Deterioration rate* = proportion of individuals with "poor or fair" health in wave 2 and with "good to excellent" health in wave 1.

2. *Improvement rate* = proportion of individuals with "good to excellent" health in wave 2 and with "poor or fair" health in wave 1

To assess mortality selection effects between waves, individuals who died before o during the second wave were included in the category "poor or fair health" in the second wave, keeping their reported status in wave 1.

Table 1 summarizes16 biomarkers and physical assessments used in this paper, collected by the on-going CRELES Project. For each biomarker we define a cut-off value to establish individuals at risk of health damage. The table shows the cut-off points and the percentage of individuals at risk. There are two anthropometric indicators: body mass index that allows us to identify individuals with obesity problems, and waist-to-hip ratio, which is an index of metabolism and adipose tissue deposition. Systolic and diastolic blood pressures were measured twice during the interview. We consider that individuals suffer high blood pressure—a cardiovascular condition, when both measurements resulted in readings above the cut-off points. Total and HDL cholesterol, as well as the ratio among them, along with triglycerides are well-established biomarkers of cardiovascular disease. High levels of glucose in the blood are measured with two biomarkers: glycated hemoglobin and fasting glucose. The former is an indicator of a chronic condition while the latest indicates an acute condition. Serum creatinine and creatinine clearance in urine are indicators of renal functioning often associated to high blood pressure. Twelve hours urinary excretion of epinephrine and nor-epinephrine indicate the level of activity in the hypothalamic-pituitary-adrenal axis. Prolonged levels of activity increase these hormones, which are associated with atherosclerosis and cardiovascular disease. Low grip strength is an indicator of physical limitations and low peak flow is an indicator of lung conditions.

In addition to self-reported health and biomarkers, we use CRELES self reports about functioning in 14 daily and instrumental life activities, such as walking, lifting objects, bathing, and eating, as well as self reports of medical diagnoses of several conditions, such as diabetes, high blood pressure, osteoporosis or infarction.

Our indicator of SES was the variable "education" recoded in two categories: (1) less than 6 years, i.e. individuals who did not completed elementary school; and (2) six or more years or individuals with completed elementary school or higher education.

To compute age-adjusted indicators, we assumed a rectangular age-structure; i.e., with equal population in each 5-year age group. It is worth noting that these age-adjusted indicators give more weight to older ages than the one they have in real populations.

**Results**

The longitudinal data from MHAS recorded whether the individual died in the about two years between waves. Four percent of individuals in the sample died, according to figures in Table 2. Mortality was 20% higher for males and this percentage does not change after adjustment for age. Mortality among individuals who did not complete elementary school was 77% higher than mortality among the better educated. This over-mortality, however, disappears after controlling for age, as can be seen in Table 2, given that low educated individuals tend to also be older. The Mexican data thus confirm that SES differentials in mortality at old ages do not exist or are not as clear as at younger ages.

Table 3 provides evidence of the sex and SES paradoxes.  Using data from the two-wave Mexican survey we can observe the well-known pattern of poorer self reported health for women: 18% of women reported "poor" health compared to 13% reported by males, which contrast with the 20% lower mortality of females. During the second wave, carried out 2 years later, the sex differential is 20% for females against 15% for males. Thus, the likelihood of reporting poor health is more than 30% higher for women.  This sharply contrasts with 20% higher mortality of males.

After controlling for age, as expected, the sex gap (measured by the sex ratio in poor health) narrows to 23% in the first wave, when compared to 37% with no age-adjustment, and to 9% in the second wave. A second adjustment takes care of mortality selection bias --those who died between the two waves are included in the group of "poor health" in the second wave. This adjustment corrects the death selection bias occurred in the two years between waves. The adjustment, which is relevant only for the second wave estimate, makes the sex gap to disappear. In fact, the percentages of poor-health for males and females are 27.0 % and 27.6%, respectively. It seems that the entire sex gap in self reported health is result of the female older age structure and the selection bias due to higher male mortality.

In the lowest panel of Table 3, we see the growth rate for the poor-health individuals. Females exhibit lower rates: poor-health males increase by 24%, while females did by about 10% (age-adjusted indicators). Thus, health deterioration seems to occur faster in males than females for this longitudinal study.

Table 3 also shows a huge gap in self-reported poor health by education.  Twenty percent of low educated individuals report poor health compared to only 9% among the better educated.  The gap as measured by the ratio in these two percentages is 2.14, i.e., low educated individuals are 114% more likely to die than the better educated ones. This huge gap however shrinks to about 70% when data is adjusted for age, and it shrinks again to 40% in the second wave, when data is adjusted for death-selection effect. The gap reverses when the rate of health deterioration over time is calculated.

The transition rates shown in Table 4 confirm the results presented above. First, females seem to be more volatile on this regard, that is, more women enter and leave the poor health state than men, but the net health deterioration rate is about the same for both sexes: 1.7 per cent over two years. However, after adjusting for the age structure, the net health deterioration rate among women is about half that for men, 1.6 and 3.1, respectively -- a result completely different than the observed in non-adjusted cross-sectional data, where more women self-report poor health.

Regarding SES differentials in the transition rates to poor health, respondents with lower education show more volatility in both deterioration and improvement rates. The net-deterioration rate is 54% higher for the low educated, but this gap disappears after adjusting for age and death-selection effects.

The panel from MHAS thus shows that cross-sections of self-reported health status can be severely misleading regarding to the sex and SES gaps, especially if results are not adjusted by age.

The story is somewhat different with the Costa Rican data on biomarkers. It is important to mention that all Costa Rican figures have been adjusted using a rectangular age structure. In Figure 1, panel A, it can be seen that the likelihood of reporting poor or fair health is higher among females: 53% compared to 49% of males. Women are also more likely to report problems when performing activities of daily living (ADLs) and instrumental ADLs (IADL): 38% of women cannot perform four or more ADL/IADL (out of 14), compared to 32% of men. Given the sample size of this study, differences of less than five percentage points are statistically non significant. These two sex gaps in self reported health status are thus borderline significant. Regarding specific health conditions (diagnosed by a physician), women report significantly higher prevalence of high blood pressure, high cholesterol, arthritis, diabetes, and osteoporosis. There is no significant sex gap in respiratory and heart disease, stroke, and infarction.

Interestingly, many of the biomarkers confirm that women may have higher morbidity or risk of health conditions (panel B in Figure 1). That is the case for high systolic blood pressure, triglycerides, total cholesterol, epi- and nor-epinephrine, as well as body mass index, and tests on physical performance and grip strength. There are, however, three biomarkers in which men have significantly higher health risks: serum creatinine, HDL cholesterol, and waist/hip ratio. There is not enough statistical power in this data as to identify significant sex gaps in diastolic blood pressure, urine creatinine, fasting glucose and glycated hemoglobin.

Therefore, Costa Rican data reproduce to some extent the pattern of women self-reporting lower health status than men. However, results from biomarkers in this dataset are not conclusive regarding the sex paradox: in some biomarkers women are not doing well, but in other biomarkers men are the ones in disadvantage. These results are adjusted for age. It is possible, however, that part of this phenomenon come from the selection of the fittest effect, which we were able to control in part in the Mexican, panel data.

Now, we can take a closer look at two conditions --diabetes and high blood pressure (HBP) -- and compare self-reports (medical diagnoses) and biomarkers. Actually, biomarkers allow us to assess only the negative predictive value of self-reports, i.e., those that report themselves free of the condition but biomarkers show this is not the case. False-positive reports, instead, cannot be detected since an apparent discrepancy with biomarkers can be explained by the fact respondents are taking medicine and keeping the condition under control. In Table 4 we identify those individuals that are free of the condition mentioned (according to both self report and biomarker), those who have the condition (self report) but keep it under control (negative biomarker), those not controlling the condition and knowing they have it, and those with a "hidden" condition since biomarkers show they are sick but they did not know that.

For diabetes, we have two biomarkers: fasting glucose ($\geq$126 mg/dL) and glycosylated hemoglobine (HbA1c $\geq$ 6.5%). The second measures glucose metabolism in the last 3 months; thus, it may have a superior predictive value. Fasting glucose may vary because of temporary conditions or because subjects did not fast (even though they reported fasting). For HBP our "biomarker" is the average of two readings during the 1.5-hour long interview (diastolic BP > 90 OR systolic BP > 140).

Women are more likely of having both diabetes and HBP, but men are more likely to be uncertain about having these health conditions. For example, 36% (age adjusted) of males in the sample did not report having HBP but our two readings suggested they have it, compared to 26% of women. These results confirm that women may be more aware than men of their health condition. In other words, men are more likely to underreport morbidity.

Biomarkers also allow us to check early findings that show that among Costa Rican elderly there is no a clear socioeconomic gradient in mortality. Figure 2 shows that in Costa Rica, as everywhere, less educated individuals are substantially more likely to self report poor-fair health, as well as to report they need more help performing ADLs and IADLs (note these figures are age-adjusted). Biomarkers, in turn, provide a much more complex picture. For a few biomarkers, the low educated are at higher risk: systolic BP, urine creatinine, and epi- nor-epinephrine. In contrast, the low educated are better off in triglycerides, fasting glucose and obesity. For all the other biomarkers educational differences are to small to be detected as significant in this sample. The hard data on biomarkers thus suggest that among elderly Costa Ricans, those in low SES do not necessarily have higher morbidity.

**Conclusion**

Self-reported health indicators widely used to illustrate cross-sectional differences in health status among adult populations may be misleading. Many times, they are severely misleading. The sex and SES health paradoxes to some extent come from deficiencies in cross-sectional, soft data.

A rather basic deficiency in some studies of sex and SES health gaps is the failure to control for age structures. Women and lower-SES individuals tend to be older and, thus, to present more health problems. The sex and SES gaps appearing in self-reported health data narrow substantially after adjusting age effects.

Death selection bias is a second spurious component of those gaps, especially when studying sex differences in health. The Mexican panel data allowed us to include the death in the "poor-health" group, which resulted in a reduction of the sex and SES health gaps.

Moreover, panel data as those from the Mexican study; allow us to compute transition rates, which automatically control confounding effects that are fixed over time, such as a cultural, gender specific bias in reporting health status. The net progression rate into the poor-health status did not show that women and low-SES adults have more health problems.

Mortality in the Mexican panel confirmed the better prospects of survival of females and showed no education differentials in age-adjusted death rates. Early studies for Costa Rican adults and elders also have failed to show a SES gradient in mortality. The SES paradox is thus real since low-SES individuals are substantially more likely to report poor health status.

Hard data on biomarkers from Costa Rican elderly show no clear indication that women or low-SES individuals are doing bad. In some biomarkers these groups are worse-off, whereas in other biomarkers they are better-off, and in many there are no significant differences. Biomarkers also

gave us evidence of sex biases in the accuracy of reporting health conditions. Men were more likely to fail to report they have diabetes or high blood pressure.

The results in this paper strongly support the need that social researchers to pay more attention to panel survey designs and biomarker collection efforts.

Table 1. Cut-off points to define at risk biomarkers in the CRELES study, 2006

| Biomarker | Cut-point at risk | (N) | Percent at risk | |
| --- | --- | --- | --- | --- |
| | | | Observed | Weighted |
| Body Mass Index | >30 | -1,628 | 16 | 19 |
| High Waist / Hip Ratio | ≥1.0 | -1,668 | 24 | 24 |
| High Diastolic Pressure (mmHg) | ≥90 | -1,808 | 20 | 22 |
| High Systolic Pressure (mmHg) | ≥140 | -1,808 | 48 | 45 |
| High triglycerides (mg/dl) | ≥150 | -1,536 | 40 | 43 |
| High total Cholesterol | >250 | -1,536 | 21 | 24 |
| Low HDL Cholesterol (mg/dl) | ≤40 | -1,533 | 29 | 31 |
| High total/HDL cholesterol ratio | ≥5.92 | -1,533 | 18 | 20 |
| High Glycated Hemoglobin (%) | ≥6.5 | -1,494 | 9 | 11 |
| High fasting Glucose | ≥126 | -1,537 | 16 | 18 |
| High serum Creatinine | ≤0.5 ≥1.2 | -1,537 | 39 | 35 |
| Low Creatinine clearance (mg/dl) | ≤44.64 | -1,409 | 17 | 11 |
| High Urinary excretion of epinephrine (ug/g creatinine) | ≥4.99 | -1,314 | 47 | 46 |
| High Urinary excretion of nor-epinephrine (ug/g creatinine) | ≥48 | -1,357 | 22 | 20 |
| Low grip Strength | ≤33 | -1,639 | 25 | 16 |
| Low best Peak Flow (L/min) | ≤300 | -1,736 | 74 | 67 |

Table 2.  Percentage of deaths between waves, MHAS

| Variable | (N) | Observed | Adjusted |
|---|---|---|---|
| Total | (7,717) | 4.1% | 7.3% |
| Sex | | | |
| Male | (3,393) | 4.5% | 8.1% |
| Female | (4,324) | 3.7% | 6.7% |
| Male/female | | 1.20 | 1.20 |
| | | | |
| Education | | | |
| <6yrs | (4,651) | 4.9% | 8.0% |
| 6+ yrs | (3,061) | 2.8% | 8.4% |
| <6yrs/6+y | | 1.77 | 0.95 |

Table 3. Percentage of persons self reporting poor health conditions.
MHAS waves 1 and 2 and growth rate (percentages)

| Wave & indicator | Sex | | | Education | | |
|---|---|---|---|---|---|---|
| | Male | Female | Fem/Mal | <6yrs | 6+ yrs | Low/High |
| (N) | (3,241) | (4,163) | | (4,423) | (2,976) | |
| (N with deaths) | (3,393) | (4,324) | | (4,651) | (3,061) | |
| | | | | | | |
| *Wave 1* | | | | | | |
| Observed | 13.3% | 18.2% | 1.37 | 20.5% | 9.5% | 2.14 |
| Age adjusted | 16.6% | 20.4% | 1.23 | 22.0% | 12.7% | 1.73 |
| | | | | | | |
| *Wave 2* | | | | | | |
| Observed | 15.3% | 20.2% | 1.32 | 22.8% | 11.1% | 2.07 |
| Age adjusted | 20.6% | 22.4% | 1.09 | 25.0% | 15.0% | 1.67 |
| Death & age adjusted | 27.0% | 27.6% | 1.02 | 31.0% | 22.1% | 1.40 |
| | | | | | | |
| *Growth rate* | | | | | | |
| Observed | 15.6% | 11.1% | 0.71 | 11.6% | 15.8% | 0.73 |
| Age adjusted | 23.8% | 9.5% | 0.40 | 13.8% | 17.8% | 0.78 |

Table 4. Transition rates for self reported poor health status.
MHAS waves 1 and 2 and growth rate (rates per 100)

| Rate type | Sex | | | Education | | |
|---|---|---|---|---|---|---|
| | Male | Female | Fem/male | <6yrs | 6+ yrs | Low/high |
| (N) | (3,393) | (4,324) | | (4,651) | (3,061) | |
| | | | | | | |
| *Deterioration rate* | | | | | | |
| Observed | 8.07 | 9.88 | 1.22 | 12.71 | 6.89 | 1.84 |
| Age adjusted | 10.84 | 9.97 | 0.92 | 13.50 | 8.02 | 1.68 |
| Death & age adjusted | 15.17 | 13.65 | 0.90 | 18.16 | 14.36 | 1.26 |
| | | | | | | |
| *Improvement rate* | | | | | | |
| Observed | 6.40 | 8.15 | 1.27 | 10.45 | 5.42 | 1.93 |
| Age adjusted | 7.72 | 8.37 | 1.08 | 10.70 | 5.94 | 1.80 |
| Death & age adjusted | 7.72 | 8.37 | 1.08 | 10.70 | 5.94 | 1.80 |
| | | | | | | |
| *Net\* deterioration rate* | | | | | | |
| Observed | 1.67 | 1.73 | 1.04 | 2.26 | 1.47 | 1.54 |
| Age adjusted | 3.12 | 1.60 | 0.51 | 2.80 | 2.08 | 1.35 |
| Death & age adjusted | 7.45 | 5.28 | 0.71 | 7.46 | 8.42 | 0.89 |

* Deterioration minus improvement in health status

Table 5. Age adjusted percent distributions of diabetic and high blood pressure conditions, self reported and biomarkers. CRELES

| Groups | **Total** | Male | Female | **Total** | Male | Female |
|---|---|---|---|---|---|---|
| *Diabetic* | *Fasting glucose >=126* | | | *Glyc. hemoglobine >= 6.5* | | |
| (N) | **(1486)** | (694) | (792) | **(1495)** | (692) | (803) |
| No diabetic* | **75.7** | 79.7 | 72.3 | **80.7** | 84.7 | 77.2 |
| Controlled | **8.0** | 6.5 | 9.3 | **10.3** | 8.8 | 11.6 |
| Uncontrolled | **10.2** | 7.9 | 12.2 | **7.8** | 5.5 | 9.8 |
| Hidden | **6.1** | 5.9 | 6.3 | **1.3** | 1.1 | 1.4 |
| Total | **100.0** | 100.0 | 100.0 | **100.0** | 100.0 | 100.0 |
| | | | | | | |
| *High blood pressure* | | | | | | |
| *Diastolic > 90 OR Systolic >140* | | | | | | |
| (N) | **(1808)** | (839) | (969) | | | |
| No HBP* | **31.1** | 36.4 | 26.4 | | | |
| Controlled | **19.4** | 17.9 | 20.7 | | | |
| Uncontrolled | **27.3** | 21.2 | 32.5 | | | |
| Hidden | **22.3** | 24.5 | 20.4 | | | |
| Total | **100.0** | 100.0 | 100.0 | | | |

* No reported MD diagnose nor biomarker

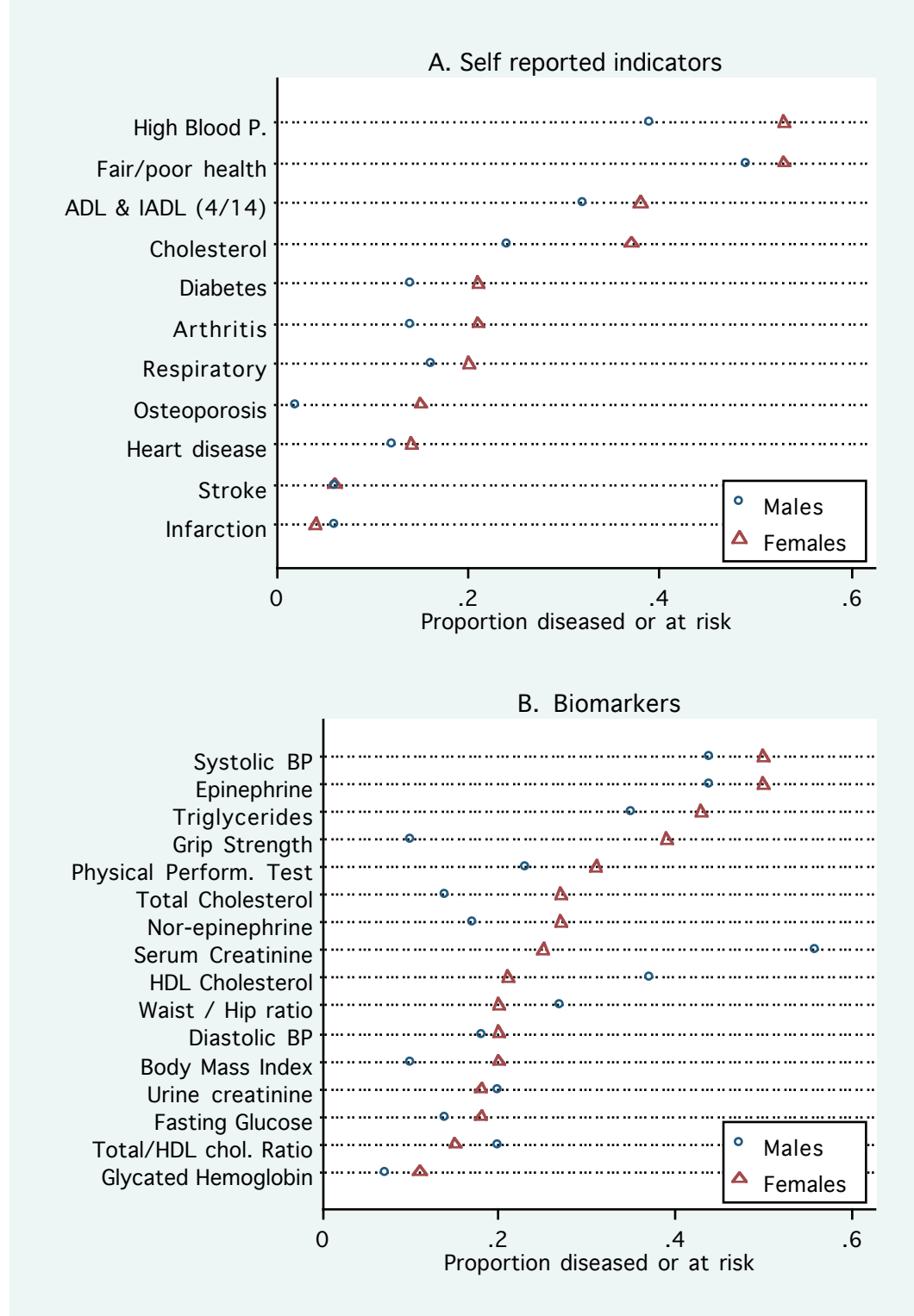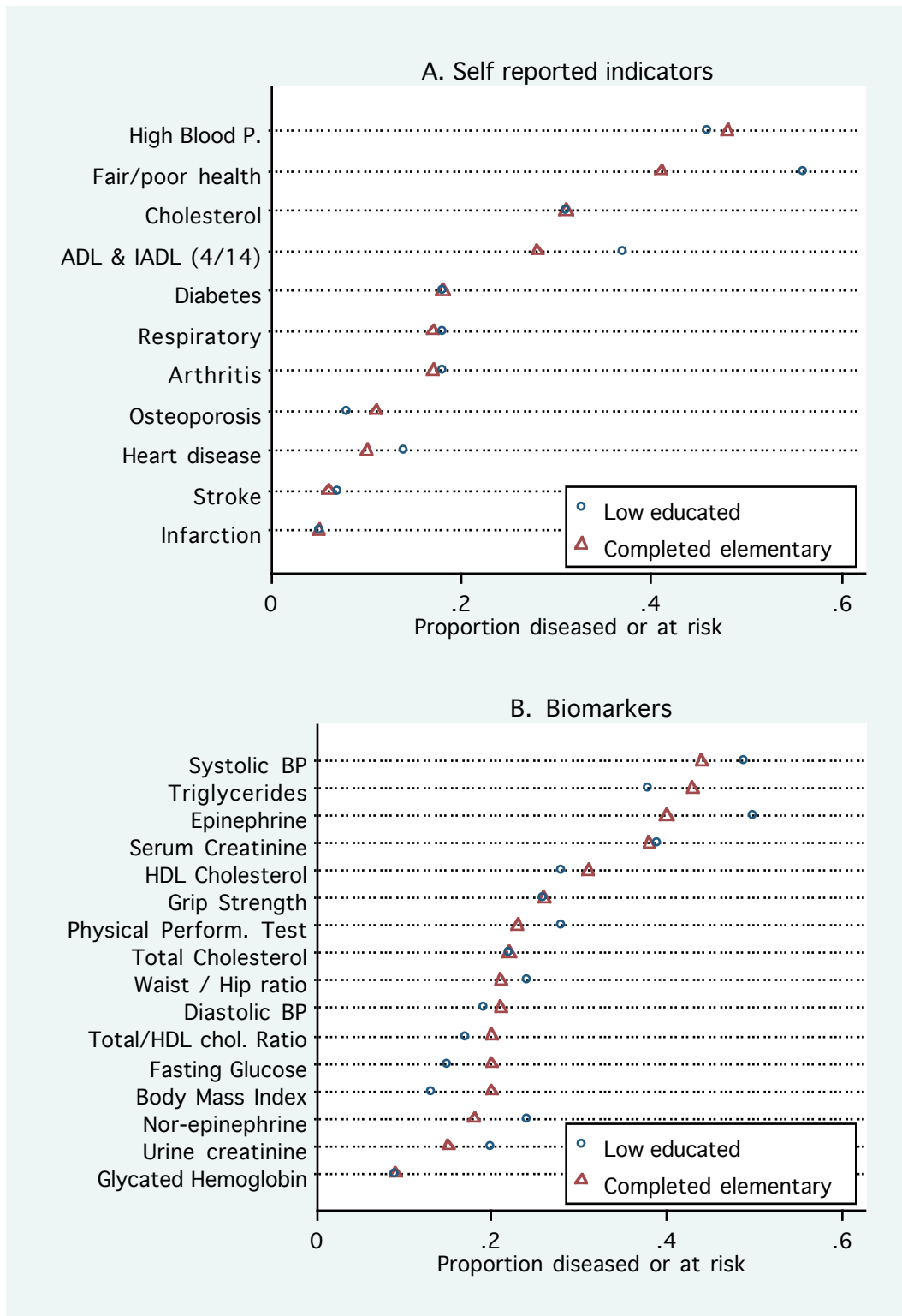Figure 1. Percent diseased or at risk by sex, self-reported and biomarker indicators. CRELES



A. Self reported indicators

B. Biomarkers

Figure 2. Percent diseased or at risk by education, self-reported and biomarker indicators.
CRELES



A. Self reported indicators

B. Biomarkers

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