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**Association of education and receiving social transfers with allostatic load in the Swiss population-based CoLaus study**

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**Running Title:** Socioeconomic status and allostatic load

## **Abstract**

**Background.** Allostatic load reflects cumulative exposure to stressors throughout lifetime and has been associated with several adverse health outcomes. It is hypothesized that people with low socioeconomic status (SES) are exposed to higher chronic stress and have therefore greater levels of allostatic load.

**Objective.** To assess the association of receiving social transfers and low education with allostatic load.

**Methods.** We included 3'589 participants (1'812 women) aged over 35 years and under retirement age from the population-based CoLaus study (Lausanne, Switzerland, 2003-2006). We computed an allostatic load index aggregating cardiovascular, metabolic, dyslipidemic and inflammatory markers. A novel index additionally including markers of oxidative stress was also examined.

**Results.** Men with low vs high SES were more likely to have higher levels of allostatic load (Odds ratio (OR)=1.93/2.34 for social transfers/education, 95%CI from 1.45 to 4.17). The same patterns were observed among women. Associations persisted after controlling for health behaviors and marital status.

**Conclusions.** Low education and receiving social transfers independently and cumulatively predict high allostatic load and dysregulation of several homeostatic systems in a Swiss population-based study. Participants with low SES are at higher risk of oxidative stress, which may justify its inclusion as a separate component of allostatic load.

**Keywords.** Allostatic load; Socioeconomic status; Chronic stress; Oxidative stress; population-based; education

## INTRODUCTION

An association between socioeconomic status (SES) and health, with lower SES being associated with poorer health in a dose-response manner, has been extensively documented and is consistently found across health outcomes, places and time (Adler et al., 1994; Marmot and Wilkinson, 2006). SES differences in health can be found even in prosperous countries such as Switzerland, which ranked 11<sup>th</sup> in the 2011 Human Development Index (UNDP, 2011) and has one of the highest gross domestic product per capita in the world (World Bank, 2012). The socioeconomic gradient in health seems to be even steeper in Switzerland than in other European countries, at least in men (Bopp and Minder, 2003).

Among the factors that have been proposed to explain social inequalities in health are a higher exposure of low SES individuals to environmental factors such as air pollution (Evans and Kantrowitz, 2002; Forastiere et al., 2007), psychosocial factors such as stress (Kristenson et al., 2004; McCartney et al., 2012; Pearlin et al., 2005) or health-risk behaviors such as smoking (Stringhini et al., 2010). Recently, research has started addressing the issue of how SES is biologically embedded to generate differences in health (Hertzman, 1999; Hertzman and Boyce, 2010; Seeman et al., 2010). In this context, the pathway of chronic stress has received a lot of attention.

The concept of allostatic load (AL) has been introduced in the early 1990s by McEwen and Stellar to represent the physiological consequences of exposure to chronic stress (McEwen, 1998, 2004; McEwen and Stellar, 1993). AL is generally operationalized through an index, which is an indicator of the cumulative physiological toll on multiple biological systems over the years (Seeman et al., 2010). Several studies have shown AL to capture the physiological dysregulation that occurs in response to chronic stress (Gallo et al., 2011; Juster et al., 2011). AL has also been associated with cardiovascular morbidity and mortality (Crimmins et al., 2003; Seeman et al., 2004; Seeman et al., 2001), as well as with poorer cognitive and physical functioning (Juster et al., 2010; Seeman et al., 1997).

Studies that have investigated the relationship between SES and AL have generally observed strong SES gradients in cumulative physiological dysregulation (Gruenewald et al., 2012; Seeman et al., 2010). Moreover, in one study SES associated differences in AL were shown to explain up to one third of SES differences in mortality (Seeman et al., 2004).

Studies have examined a variety of indicators of SES in relation to AL (Dowd et al., 2009), including education(Hu et al., 2007; Seeman et al., 2004), income (Hu et al., 2007) and socio-economic disadvantage (Gruenewald et al., 2012). However, which component of low SES (i.e. financial adversity, lack of coping resources, or deleterious lifestyle) represent a challenge for physiological dysregulation is still not clear. Moreover, most studies in this area have been conducted in North American populations (United States) and it remains to be known if SES differences in AL exist even in prosperous countries where health insurance is mandatory and access to health-care is relatively universal.

Although there is still an ongoing debate on which is the best way to capture the multiple and interrelated components of AL (Seeman et al., 2010), studies have generally operationalized AL by creating an index aggregating cardiovascular, metabolic, dyslipidemic, neuroendocrine and inflammatory markers.

To our knowledge, no component specifically targeting oxidative stress has been used so far when generating AL, although mammalian organisms under chronic stress display increased oxidative stress at the cellular level(Devaki et al., 2013). Oxidative stress results from an imbalance between pro- and anti-oxidant molecules, which leads to cell damage. Reactive derivatives of oxygen or nitrogen are the hallmark of oxidative stress, but their instability precludes their use as biomarkers. Serum gamma-glutamyltransferase (GGT) is considered as a suitable marker for oxidative stress in epidemiological settings (Lee et al., 2004). Both homocysteine (Liu et al., 2013) and uric acid (So and Thorens, 2010; Strazzullo and Puig, 2007) are considered as markers of oxidative stress and their circulating levels can be easily assessed in large scale population-based studies.

As most studies assessing the association between SES and AL have been conducted in North American populations, the first objective of the present study is to assess whether SES is associated with allostatic load also in a Swiss population-based study (Colaus). In this context, we use two indicators of SES, education, which has been consistently found to be associated with AL in previous studies, and receiving social transfers, which we consider here as a proxy indicator of financial difficulties. The second objective of this study is to compare two indexes of allostatic load, a “classic” index aggregating cardiovascular, metabolic, dyslipidemic and inflammatory markers, and a novel index additionally including markers of oxidative stress, in relation to SES.

## DATA AND METHODS

### Study population

The CoLaus Study was implemented in Lausanne, a French-speaking Swiss town counting approximately 120,000 inhabitants, after approval of the Institutional Ethics Committee of the University of Lausanne. Participants' recruitment took place between June 2003 and May 2006 at the University Hospital of Lausanne (CHUV). A random sample of 19,830 subjects (35% of registered Swiss citizens) was drawn, out of which 8,121 subjects (41% of the random sample) agreed to participate. Individuals who had moved out of Lausanne, who had died in 2003 or who didn't meet the age criteria were considered as non-eligible. Out of the 8,121 subjects, only 6,738 completed the interview, from which 549 subjects were withdrawn because they were non-Caucasian and one person self-withdrew, reducing the final sample size to 6,188. Further details on sampling, recruitment and inclusion criteria are provided in Firmann et al (Firmann et al., 2008).

Data were collected by trained research nurses, supervised by a medical doctor and a senior research nurse. Venous blood samples were drawn after an overnight fast, and assays were performed by on fresh plasma samples within 2 hour of blood collection in a Modular P apparatus (Roche Diagnostics, Switzerland). Information on demographic data, socioeconomic and marital status, lifestyle factors, personal and family history of disease, cardiovascular risk factors and treatment was collected through questionnaire.

### Measures

#### *Socioeconomic status (SES)*

Two indicators of SES were used: receiving social transfers (ST) and educational level. *Social transfer status* was assessed with the question: "Do you receive social help (for instance for the health insurance, retirement benefits or the invalidity insurance)?" Answer: "Yes/No". In Switzerland, social transfers are provided as financial support by the government to people with disabilities, whose income is insufficient to support themselves or their family, or who are retired (Statistique suisse, 2012). Because all individuals residing in Switzerland receive financial compensation when they retire, the response to this variable is not informative beyond the retirement age. Therefore, men older than 65 years and women older than 63 or 64 years were excluded from the analyses (N=1110). More precisely, because women age at retirement changed over the recruitment period, if the examination took place before January

1<sup>st</sup> 2005, we dropped women older than 63, otherwise we dropped only those older than 64 ( Jacques Méry, OFAS. Statistique de l'AVS 2009, p. 26).

*Educational level* was categorized as (1) primary education (20.1%) , (2) vocational secondary education (24.3 %), (3) secondary education (36.6 %) and (4) university (19%) as described in FirmaNN et al (FirmaNN et al., 2008).

In order to examine the cumulative impact of low education and receiving social transfers on physiological dysregulation, we built a SES score combining both indicators. Only for constructing a SES score, education was further dichotomized as *high* (secondary education or university) or *low* (primary education or vocational secondary education). The *SES score* was then calculated as follows: (1) high education and no ST, (2) high education and ST, (3) low education and no ST and (4) low education and ST.

#### ***Other covariates***

Marital status, that can be considered an indicator of social support (Stringhini et al., 2012), was categorized as single, married or living in couple, divorced, or widowed. Smoking was classified as current or non-current smoking. Alcohol consumption was categorized into regular alcohol intake (at least 1/unit of alcohol per day, corresponding to 10 grams of alcohol) versus non-regular alcohol intake. Physical activity was dichotomized into never versus at least once per week with respect to leisure physical activity sessions (jogging, swimming, cycling, etc.) of at least 20 minutes.

#### ***Clinical and biological data***

Body weight (kg), height (cm), and waist and hip circumferences (cm) were measured according to standard procedures (FirmaNN et al., 2008) (Lean et al., 1995). Body mass index (BMI) was defined as weight in kg divided by height in meters squared. Blood pressure (mmHg) and heart rate were measured thrice on the left arm, with an appropriately sized cuff, after at least 10 minute rest in the seated position using an Omron® HEM-907 automated oscillometric sphygmomanometer (Matsusaka, Japan). The average of the last two measurements was used for analyses (FirmaNN et al., 2008).

### **Allostatic Load**

Constituting risk factors of AL are often analyzed in groups corresponding to five homeostatic systems or processes: cardiovascular system, metabolism, hypothalamic-pituitary-adrenal (HPA) axis, autonomic nervous system (ANS) and inflammation (Seeman et al., 2010). Two indices of AL were generated. The first “classic” index (AL1), described in **eTable 1**, was based on cardiovascular, metabolic, dyslipidemic and inflammatory markers. Compared to the markers usually included in the assessment of AL, we had to omit the neuroendocrine stress factors as they were not available in the CoLaus dataset. However, we distinguished a “lipids” dimension, usually integrated in “metabolism” (Seeman et al., 2010). The second “extended” index (AL2) additionally included markers of oxidative stress (**eTable 1**). We dichotomized the markers into high-risk versus low-risk (1-0) according to gender-specific quartiles. The high-risk quartile was the top quartile of all markers, with the exception of adiponectin and high-density lipoprotein cholesterol (HDL) (lowest quartile, **eTable 1**). The AL scores were then computed by summing the dichotomized values. In logistic regressions, AL1, AL2 and the five homeostatic dimensions were dichotomized using as a cut-off the value closest to the median (**eTable 2**). This latter analysis was chosen to provide a robust association metric that allow comparing the associations of high AL values with SES with those of high values for each dimension.

In total, we assessed nine new risk markers which were not included in previous studies: high leptin and low adiponectin (metabolism), high triglycerides and high apolipoprotein B (lipids), high interleukin 1-B and high tumor necrosis factor alpha (TNF- $\alpha$ ) (inflammation) and, finally, high uric acid, high homocysteine and high gamma-glutamyl transferase (gGT) were the markers constituting the new dimension of oxidative stress. Validity assessment analyses of the five dimensions of AL showed that although all dimensions were significantly interdependent, their non-parametric Spearman correlations were reasonably low (range 0.047 to 0.350). We thus considered the five dimensions as reasonably subdivided.

### **Statistical analyses**

All analyses were conducted in Stata 12.1 (Stata Corp, College Station, Texas, USA) and were stratified by gender. In preliminary analysis, mean values of the two AL scores and of the five system components were calculated for each gender and socioeconomic category. Chi-squared test was used to examine differences in the distribution of socio-demographic

and behavioral factors across categories of education and receiving social transfers. The association of education and receiving social transfers with physiological dysregulation scores was further explored with age-adjusted logistic regression for dichotomized scores (Model 1). After testing that the association between education and AL did not depart from a linear trend (all  $p$  for departure from a linear trend  $>0.05$ ), the four-level education variable was entered as a continuous variable in multivariable analyses. The odds ratio associated with a unit change in education was cubed to yield the odds ratio for the lowest versus the highest educational category. To assess the extent to which the two measures of SES were independently related to AL and the five systems components, we introduced in the regression models the alternative SES indicator and calculated a percent attenuation of the OR with the formula:  $\% \text{ attenuation} = 100 * (\text{OR Model 1}_{\text{age-adjusted}} - \text{OR Model 2}_{\text{Model 1+ST or education}}) / (\text{OR Model 1}_{\text{age-adjusted}} - 1)$ .

We additionally assessed the extent to which health behaviors and marital status contributed to the association between SES indicators and AL by including them as covariates and then calculating the % attenuation as described above.

To investigate further the association between AL and SES without losing precision to dichotomization, quantile regressions were performed on the original AL scores using multivariable age-adjusted quantile regression for quasi-continuous dependent variables (AL1 and AL2 scores).

## RESULTS

Of the 6184 participants of the CoLaus study, 1110 were excluded because in age of receiving retirement benefits, as described previously. Of the remaining 5074, we excluded 1485 participants for one or more of the following reasons: missing information on SES ( $N=25$ ), missing data for at least one marker used to compute the AL ( $N=1384$ , of which 454 for Interleukin-6, 495 for insulin and 326 for leptin), or missing data on other covariates ( $N=75$ ), categories not mutually excluded. In total, 3589 individuals were included in the present study. Excluded participants were more frequently females (44% vs. 39%,  $p<0.001$ ), were older (mean age 56 vs. 50 years,  $p<0.001$ ) and tended to have a more disadvantaged socioeconomic profile ( $p<0.001$ ).

## **Sample characteristics**

The main characteristics of the sample according to gender and SES are summarized in **Table 1**.

Men and women receiving ST had a lower educational attainment ( $p<0.001$ ). In general, participants with low SES (either measured as low education or receiving social transfers) were more likely to follow unhealthy behaviors, although no significant difference was apparent for alcohol consumption. **Figure 1** illustrates mean scores of AL1 and AL2 and of the five system components in men and in women, by ST status and educational category. AL1 and AL2 were significantly higher in individuals receiving ST and a dose-response relationship between allostatic load and education was observed ( $p<0.001$ ).

## **Social transfers and allostatic load**

Results from logistic regressions for the association of AL1, AL2 and the five composing systems with ST are presented in **Table 2**. Men receiving ST were more likely to have inflammatory ( $OR=1.30, 95\%CI: 0.99;1.71$ ), cardiovascular ( $OR=1.31, 95\%CI:1.00;1.71$ ) and metabolic ( $OR=1.67, 95\%CI:1.28;2.20$ ) dysregulation, higher oxidative stress ( $OR=1.28, 95\%CI:0.97;1.78$ ) as well as higher AL1 ( $OR=1.93, 95\%CI:1.45;2.55$ ) and AL2 ( $OR=1.83, 95\%CI:1.38;2.41$ ), although some of these associations were not significant at  $p=0.05$ . Adjustment for education explained about 30% of the associations between ST and AL1/AL2, but there remained a ~60% increased risk of AL for men receiving vs. non receiving ST ( $OR=1.59, 95\%CI: 1.19;2.11$  for AL2).

The association was also partially attenuated after adjustment for health behaviors and marital status. In women, receiving ST was associated with greater physiological dysregulation for all scores except for the cardiovascular component. The association between ST and AL was largely attenuated after adjustment for education (% attenuation: 47% for AL1 and 41% for AL2), but the association between AL2 and ST remained statistically significant. Health behaviors and marital status did not contribute much to the association between ST and AL in women (4% and 12%).

## **Education and allostatic load**

Results for education are shown in **Table 3**. Education was strongly associated with dysregulation of the five homeostatic systems examined (with the exception of cardiovascular and oxidative stress component in women), the metabolic component in particular (OR=2.09/3.09 for men/women). Participants with a low education were about 3 times more likely to have high levels of AL1 and AL2 than those with a high education (OR=3.24/3.04 for men/women for AL2). These associations were only slightly attenuated when controlling for ST. Control for health behaviors and marital status contributed to explain about 30% of the association between education and AL in men and about 20% in women. A strong dose-response association was observed between the SES score and high AL1/AL2 (**Figure 2**).

In analyses using quantile regressions performed on the original AL scores, receiving ST and having a low educational attainment remained strongly associated with AL1 and AL2 in the fully adjusted models, for both genders (**Table 4**).

### Sensitivity Analyses

In additional sensitivity analyses, we assessed whether there were interactive effects between education and social transfer on AL, but found no evidence for such effects (all p-values for interaction between education and receiving social transfers in relation to AL >0.05).

## DISCUSSION

In this study, we found strong and robust associations between SES and AL in adult men and women from a population-based study in Switzerland. The two indicators of SES used in this study, receiving social transfers and having a low education, independently and cumulatively predicted high AL and dysregulation of several homeostatic systems. Additionally, this study hints to the potentials of including markers of oxidative stress in computing allostatic load indexes.

The finding of an association between SES and AL is in line with previous research showing strong socioeconomic differences in physiological dysregulation (Dowd and Goldman, 2006; Gersten, 2008; Hu et al., 2007; Kubzansky et al., 1999; Seeman et al., 2008; Seeman et al., 2004). Multivariable analyses showed that this association was independent of age, health

behaviors and marital status. Moreover, the two measures of SES independently predicted AL, suggesting that they capture different dimensions of SES, in line with previous studies (Geyer et al., 2006; Stringhini et al., 2011).

Previous studies had reported association between a variety of indicators of SES(Dowd et al., 2009), including education(Hu et al., 2007; Seeman et al., 2004), income (Hu et al., 2007) and socio-economic disadvantage(Gruenewald et al., 2012) with AL. This study points to an important link between receiving ST and health, and hints to the potentials of such a marker in predicting financial distress in studies conducted in high income countries, given the difficulty of collecting measures of income and wealth in epidemiological studies (Krieger et al., 1997). In particular, we might speculate that receiving ST captures aspects related to a stressful life (such as financial adversity) that might not be accounted for by education. On the other hand, the association of education with AL was only slightly attenuated by controlling for ST, implying residual confounding or that other aspects than economic resources might be implicated. For example, the strong association of education with AL might be related to the fact that 1) education, at least in Europe, strongly correlates with occupational position (Miech and Hauser, 2001), and people with low education might occupy jobs that are more stressful in their everyday life; 2) education is related to several aspects that might buffer the effect of chronic stress on health, such as social support, social relationships or better ability to cope with stressful situations (Seeman, 1996; Stringhini et al., 2012).

In our study, we used two measures of AL, one including markers typically assessed to compute the AL scores (with the exception of neuroendocrine markers), and a new score including six additional markers of metabolic dysregulation, inflammation and dyslipidemia, as well as a whole new component reflecting oxidative stress. We believe that the additional inclusion of these risk markers would be particularly helpful in future studies. For example, high gamma-glutamyl transferase (gGT) is a recognized risk factor for cardiovascular disease, the metabolic syndrome, and all-cause mortality, and is perceived as an important marker of oxidative stress (Mason et al., 2010). Although high gGT is strongly linked to metabolism, atherosclerosis and hepatic inflammation (Mason et al., 2010), we placed it into the component of “oxidative stress”, in which we also included high serum uric acid and high homocysteine levels. Mechanisms by which low SES could lead to oxidative stress are via chronic stress-induced inflammation and/or anti-oxidant dysbalance (Devaki et al., 2013). To our knowledge, this is the first study to show an association between SES and oxidative stress

in a population-based sample. Further research should assess whether it also strongly predicts adverse health outcomes.

Several pathways have been proposed to explain the higher burden of AL among the lower socioeconomic groups, and include psychological characteristics, coping strategies, social relationships and support, and health behaviors (Hawley et al., 2011). In our study, health behaviors and marital status (a measure of social support) partly attenuated the association between SES and AL, but a large part remained unexplained. Other measures of social support, such as social networks or perceived support were not available in our study.

The association of SES with AL (and their components) seemed to differ in men and women. For example, receiving ST was associated with high oxidative stress in women but not in men while having a low education predicted higher oxidative stress in men but not in women. These results are consistent with previous findings showing important gender differences in the physiologic response to stress. For example, men show greater cortisol responses to stress than women (Chrousos, 2010; Heraclides et al., 2012; Kirschbaum et al., 1992; Lipinska-Grobelny, 2011; Maestripieri et al., 2010; McEwen, 2010; Vassalle et al., 2011).

### **Strengths and limitations**

The major strengths of this study are in the richness of available cardiometabolic phenotypes and its population-based nature. Moreover, the use of two indicators of SES allowed us to show how different dimensions of SES might relate to different aspects of Al. Finally, this is the first study to assess associations between SES and markers of oxidative stress.

This study also has some limitations. First, the new AL score needs to be validated in further studies. Also, the overall prevalence of receiving ST was high (16%). This might be partly due to the ambiguity of the question on receiving “social help”, which mentioned as examples of social help “[help] for the health insurance, retirement allocations or allocations for the invalids”. In future work, it would be useful to have more precise information on the different types of financial compensation received, along with information on the amount of time over which they have been received.

Further, reverse causation could also partly explain the association between ST and AL. This direction of causality should be further explored, for instance using genetic instrumental variables which could predict chronic stress. Finally, given the large number of associations explored, several covariates (i.e.: smoking, alcohol consumption and physical activity) were assessed as dichotomous variables and this might have lead to loss of precision. However, we repeated the analysis using finer categorizations for these variables and results did not vary.

## CONCLUSIONS

In Switzerland, a high income European country with mandatory health insurance, men and women reporting to receive social transfers or with a low educational attainment had higher measured cumulative homeostatic dysregulation, independently of age, marital status, and health behaviors. These results are in line with previous results on North American populations. Moreover, we showed that the two measures of SES examined independently predicted higher levels of allostatic load, suggesting that multiple dimensions of SES contribute to engender a higher burden of allostatic load. This study is also one of the first to show that participants with low SES are at higher risk of oxidative stress, which may justify its inclusion as a separate component of allostatic load.

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**CONFLICT OF INTEREST STATEMENT:** The Authors declare that there is no conflict of interest.

**Table 1. Characteristics of men (N=1777) and women (N=1812) included in the study by socioeconomic indicators, Colaus Study (Lausanne, Switzerland, 2003-2006)**

	MEN								WOMEN							
	Social transfers			Educational attainment				Social transfers			Educational attainment					
	Yes (N=256)	No (N=1521)	% ST	P <sup>a</sup>	Low (N=941)	High (N=836)	% Low	P <sup>a</sup>	Yes (N=317)	No (N=1495)	% ST	P <sup>a</sup>	Low (N=1054)	High (N=758)	% Low	P <sup>a</sup>
<b>Age, Mean (SD, years)</b>	52.0 (± 8.7)	50.0 (± 8.5)	NA		50.7 (± 8.6)	49.7 (± 8.5)	NA		49.4 (± 8.0)	51.1 (± 8.8)	NA		50.5 (± 8.1)	48.5 (± 8.3)	NA	
<b>Social transfers</b>					NA			<0.001					NA			<0.001
Yes	NA	NA	NA		191	65	74.6%		NA	NA	NA		817	678	54.7%	
No	NA	NA	NA		750	771	49.3%		NA	NA	NA		237	80	74.8%	
<b>Educational Attainment</b>				<0.001				NA				<0.001				NA
Primary	74	214	25.7%		NA	NA	NA		276	117	29.8%		NA	NA	NA	
Apprenticeship	117	536	17.9%		NA	NA	NA		541	120	18.2%		NA	NA	NA	
High school/college	36	377	8.7%		NA	NA	NA		401	59	12.8%		NA	NA	NA	
University	29	394	6.9%		NA	NA	NA		277	21	7.0%		NA	NA	NA	
<b>Marital Status</b>				0.142				0.018				<0.001				<0.001
Single	39	235	14.2%		121	153	44.2%		276	54	16.4%		162	168	49.1%	
Married	158	1017	13.4%		640	535	54.5%		855	115	11.9%		589	381	60.7%	
Divorced	54	254	17.5%		169	139	54.9%		325	115	26.1%		252	188	57.3%	
Widow	5	15	25.0%		11	9	55.0%		39	33	45.8%		51	21	70.8%	
<b>Smoking</b>				0.001				<0.001				0.010				0.242
No	158	1100	12.6%		631	627	50.2%		1114	213	16.1%		761	566	57.4%	
Yes	98	421	18.9%		310	209	59.7%		381	104	21.4%		293	192	60.4%	
<b>Alcohol consumption</b>				0.433				<0.001				0.933				0.822
No	167	1030	14.0%		583	614	48.7%		1318	280	17.5%		928	670	58.1%	
Yes	89	491	15.3%		538	222	61.7%		177	37	17.3%		126	88	58.9%	
<b>Physical activity</b>				<0.001				<0.001				<0.001				<0.001
Never	134	524	20.4%		456	202	69.3%		490	138	22.0%		444	184	70.7%	
Once a week	122	997	10.9%		485	634	43.3%		1005	179	15.1%		610	574	51.5%	

SD: Standard Deviation; ST: Social transfers.

<sup>a</sup>P value for difference of ST or education from Chi-squared test.

**Table 2. Association of receiving social transfers with dichotomized allostatic loads and five system components, Colaus Study (Lausanne, Switzerland, 2003-2006)**

	Model 1: age-adjusted		Model 1 + education			Model 1+ health behaviors <sup>a</sup> & marital status		
	OR <sup>b</sup>	95% CI	OR <sup>b</sup>	95% CI	%Δ <sup>c</sup>	OR <sup>b</sup>	95% CI	%Δ <sup>c</sup>
<b>Men</b>								
Inflammation	1.30	(0.99; 1.71)	1.22	(0.92; 1.62)	NA	1.22	(0.92; 1.62)	NA
Cardiovascular	1.31	(1.00; 1.71)	1.19	(0.91; 1.57)	-39%	1.21	(0.92; 1.59)	-32%
Lipidemia	1.09	(0.82; 1.44)	0.97	(0.73; 1.29)	NA	0.99	(0.75; 1.32)	NA
Metabolic	1.67	(1.28; 2.20)	1.43	(1.09; 1.89)	-36%	1.49	(1.13; 1.97)	-27%
Oxidative stress	1.28	(0.97; 1.68)	1.17	(0.88; 1.54)	NA	1.18	(0.89; 1.56)	NA
Allostatic Load 1	1.93	(1.45; 2.55)	1.62	(1.21; 2.15)	-33%	1.67	(1.25; 2.23)	-28%
Allostatic Load 2	1.83	(1.38; 2.41)	1.52	(1.14; 2.02)	-37%	1.59	(1.19; 2.11)	-29%
<b>Women</b>								
Inflammation	1.33	(1.03; 1.71)	1.20	(0.93; 1.56)	-39%	1.36	(1.04; 1.76)	9%
Cardiovascular	0.97	(0.76; 1.25)	0.94	(0.73; 1.20)	NA	1.00	(0.77; 1.29)	NA
Lipidemia	1.62	(1.23; 2.12)	1.47	(1.12; 1.94)	-24%	1.48	(1.12; 1.96)	-23%
Metabolic	1.64	(1.28; 2.10)	1.40	(1.09; 1.81)	-38%	1.63	(1.26; 2.11)	-2%
Oxidative stress	1.61	(1.25; 2.08)	1.57	(1.21; 2.04)	-7%	1.49	(1.14; 1.93)	-20%
Allostatic Load 1	1.45	(1.13; 1.87)	1.24	(0.95; 1.60)	-47%	1.43	(1.10; 1.85)	-4%
Allostatic Load 2	1.59	(1.23; 2.05)	1.35	(1.04; 1.75)	-41%	1.52	(1.17; 1.99)	-12%

**CI:** 95% Confidence Interval; **NA:** not applicable (percent attenuations were calculated only if there was a significant association); **OR:** Odds ratio; **Δ:** Attenuation.

<sup>a</sup> Smoking, alcohol consumption, physical activity.

<sup>b</sup> Odds ratio for receiving versus non-receiving social transfers.

<sup>c</sup> Percent attenuation of the OR in Model 1 after inclusion of the variable in question.

**Table 3. Association of education<sup>a</sup>with dichotomized allostatic loads and five system components , Colaus Study (Lausanne, Switzerland, 2003-2006)**

	Model 1: age-adjusted		Model 1 + ST		Model 1+ health behaviors <sup>b</sup> & marital status			
	OR <sup>c</sup>	95% CI	OR <sup>c</sup>	95% CI	%Δ <sup>d</sup>	OR <sup>c</sup>	95% CI	%Δ <sup>d</sup>
<b>Men</b>								
Inflammation	1.46	(1.11; 1.93)	1.41	(1.06; 1.86)	-11%	1.45	(1.08; 1.94)	-2%
Cardiovascular	1.76	(1.33; 2.33)	1.71	(1.28; 2.27)	-7%	1.51	(1.12; 2.03)	-33%
Lipidemia	1.87	(1.41; 2.49)	1.88	(1.41; 2.52)	1%	1.63	(1.20; 2.20)	-28%
Metabolic	2.68	(2.00; 3.59)	2.50	(1.86; 3.37)	-11%	2.19	(1.61; 2.99)	-29%
Oxidative stress	1.71	(1.29; 2.26)	1.66	(1.25; 2.21)	-7%	1.44	(1.07; 1.94)	-38%
Allostatic Load 1	3.12	(2.34; 4.17)	2.87	(2.14; 3.85)	-12%	2.51	(1.84; 3.41)	-29%
Allostatic Load 2	3.24	(2.43; 4.33)	3.02	(2.24; 4.04)	-10%	2.53	(1.87; 3.43)	-32%
<b>Women</b>								
Inflammation	1.92	(1.44; 2.56)	1.85	(1.38; 2.47)	-8%	1.78	(1.32; 2.40)	-15%
Cardiovascular	1.26	(0.95; 1.68)	1.28	(0.96; 1.71)	NA	1.19	(0.89; 1.61)	NA
Lipidemia	1.87	(1.39; 2.51)	1.73	(1.28; 2.33)	-16%	1.73	(1.27; 2.35)	-16%
Metabolic	3.09	(2.29; 4.19)	2.89	(2.12; 3.92)	-10%	2.63	(1.92; 3.60)	-22%
Oxidative stress	1.26	(0.94; 1.68)	1.14	(0.85; 1.53)	NA	1.15	(0.85; 1.55)	NA
Allostatic Load 1	2.88	(2.14; 3.88)	2.76	(2.04; 3.73)	-6%	2.50	(1.83; 3.40)	-20%
Allostatic Load 2	3.04	(2.26; 4.10)	2.86	(2.12; 3.87)	-9%	2.65	(1.94; 3.61)	-19%

CI: 95% Confidence Interval; NA: not applicable (percent attenuations were calculated only if there was a significant association); OR: Odds ratio; ST: Social transfers; Δ: Attenuation.

<sup>a</sup> Education (4-level categorical variable) is entered as a continuous variable.

<sup>b</sup> Smoking, alcohol consumption, physical activity.

<sup>c</sup> Odds ratio for lowest versus highest educational category.

<sup>d</sup> Percent attenuation of the OR in Model 1 after inclusion of the variable in question.

**Table 4 Association of receiving social transfers and education<sup>b</sup> with continuous allostatic load scores, Colaus Study (Lausanne, Switzerland, 2003-2006)**

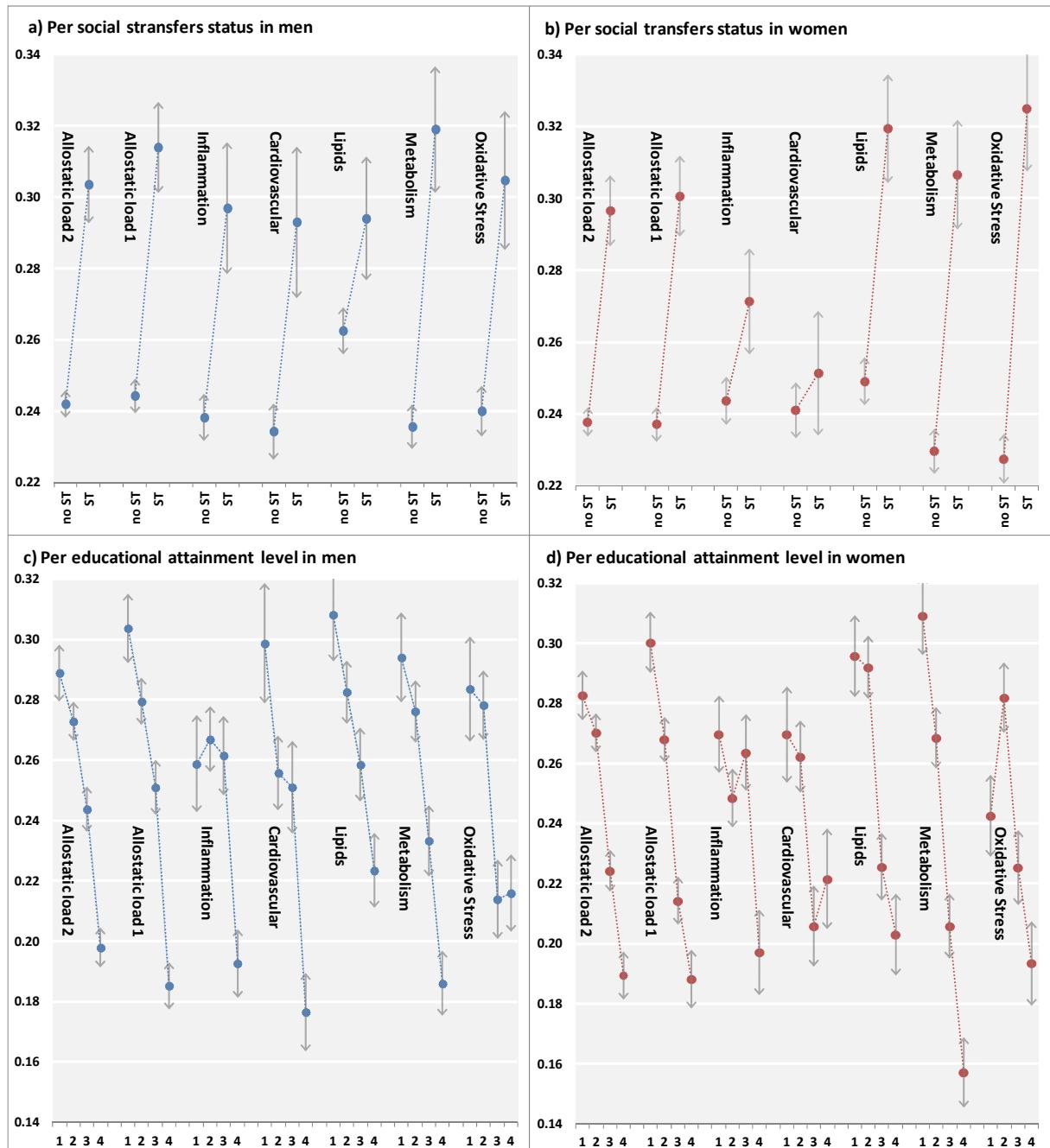
	Social transfers									
	Model 1: age-adjusted			Model 1 + education			Model 1+ health behaviors <sup>a</sup> & marital status			P
	$\beta$	SE	P	$\beta$	SE	P	$\beta$	SE	P	
<b>Men</b>										
Allostatic Load 1 [0;11]	0.90	0.16	<0.001	0.73	0.18	<0.001	0.42	0.19	0.022	
Allostatic Load 2 [0; 20]	1.43	0.30	<0.001	1.03	0.28	<0.001	0.88	0.34	0.010	
<b>Women</b>										
Allostatic Load 1 [0;11]	0.61	0.16	<0.001	0.38	0.16	0.017	0.66	0.13	<0.001	
Allostatic Load 2 [0; 20]	0.90	0.24	<0.001	0.60	0.23	0.010	0.70	0.23	0.003	
Educational attainment										
Model 1: age-adjusted			Model 1 + ST			Model 1+ health behaviors <sup>a</sup> & marital status				
$\beta$	SE	P	$\beta$	SE	P	$\beta$	SE	P		
<b>Men</b>										
Allostatic Load 1 [0;11]	1.37	0.18	<0.001	1.23	0.19	<0.001	0.92	0.19	<0.001	
Allostatic Load 2 [0; 20]	1.97	0.29	<0.001	1.83	0.26	<0.001	1.28	0.31	<0.001	
<b>Women</b>										
Allostatic Load 1 [0;11]	1.17	0.17	<0.001	1.10	0.18	<0.001	0.93	0.18	<0.001	
Allostatic Load 2 [0; 20]	1.73	0.26	<0.001	1.67	0.27	<0.001	1.36	0.26	<0.001	

B: Beta coefficient; P: p-value; SE: Standard Error; ST: Social transfers.

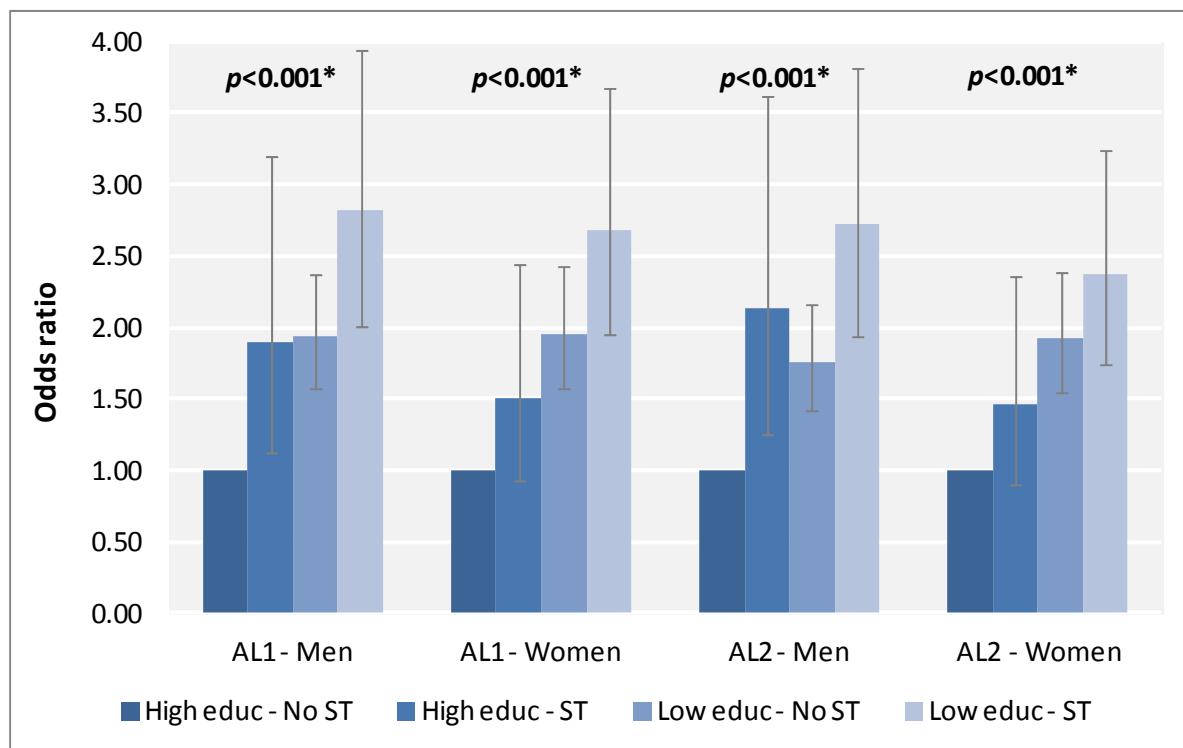
<sup>a</sup> Smoking, alcohol consumption, physical activity.

<sup>b</sup> Education (4-level categorical variable) is entered as a continuous variable. Results are thus for the lower versus the highest educational category (also see methods section).

**Figure 1. Mean score of allostatic loads and their components by gender and socioeconomic indicator, Colaus Study (Lausanne, Switzerland, 2003-2006)**



**Figure 2. Association of a composite socioeconomic score with allostatic load (AL1 and AL2) , Colaus Study (Lausanne, Switzerland, 2003-2006)**



AL: Allostatic Load; educ: education; ST: Social transfers.

"Low education" includes primary and vocational secondary education and "high education" includes secondary and university education.

\* P-value for linear trend across SES score categories

**eTable 1. Components of classic (AL1) and extended (AL2) allostatic loads, Colaus Study (Lausanne, Switzerland, 2003-2006)**

Homeostatic System**	Component (Risk Factor)	Risk quartile	AL1	AL2
<b>Cardiovascular system</b>				
	Systolic blood pressure (mm Hg)	top	X	X
	Diastolic blood pressure (mm Hg)	top	X	X
	Heart rate (BPM)	top	X	X
<b>Metabolism</b>				
	Insulin (microlU/mL)	top	X	X
	Glucose (mmol/l)	top	X	X
	Body mass index (kg/m <sup>2</sup> )	top	X	X
	Waist-to-hip ratio (cm)	top	X	X
	Leptin* (ng/mL)	top		X
	Adiponectin* (ng/mL)	bottom		X
<b>Lipids</b>				
	HDL cholesterol (mmol/l)	bottom	X	X
	Total cholesterol (mmol/l)	top	X	X
	Tryglycerides* (mmol/l)	top		X
	Apolipoprotein B* (mg/dL)	top		X
<b>Inflammation</b>				
	C-reactive protein (mg/l)	top	X	X
	Interleukin-6 (pg/ml)	top	X	X
	Interleukin-1B* (pg/ml)	top		X
	Tumor-necrosis factor alpha* (pg/ml)	top		X
<b>Oxidative Stress (in serum)</b>				
	Uric acid* (μmol/l)	top		X
	Homocysteine* (μmol/l)	top		X
	Gamma-glutamyl transferase* (mmol/l)	top		X

\*Nine extra components included in AL2. \*\*Parameters for the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system (ANS) could not be included in AL1 or AL2, since data was not available.

**eTable 2. Dichotomisation of scores by proximity to the median, Colaus Study (Lausanne, Switzerland, 2003-2006)**

Score	Number of observations and cumulative frequencies							Dichotomisation	
	0	1	2	3	4	5	6	Group 1	Group 2
Inflammation [0; 4]	<b>1486</b> 41.47%	1102 72.23%	607 89.17%	322 98.16%	66 100%	-	-	0	1-4
Cardiovascular [0; 3]	<b>1929</b> 53.84%	905 79.10%	533 93.97%	216 100%	-	-	-	0	1-3
Lipids [0;4]	<b>1310</b> 36.56%	1218 70.56%	689 89.79%	275 97.46%	91 100%	-	-	0	1-4
Metabolic [0;6]	1181 32.96%	<b>1017</b> <b>61.35%</b>	561 77%	385 87.75%	253 94.81%	149 98.97%	37 100%	0-1	2-6
Oxidative stress [0;3]	<b>1724</b> 48.12%	1205 12.45%	513 96.06%	141 100%	-	-	-	0	1-3
AL1 [0;11]	0 12.56%	1 33.38%	2 <b>52.53%</b>	3 67.51%	4 79.82%	5 87.64%	≥6 ....	0-2	3-11
AL2 [0;20]	118 3.29%	328 25.29%	460 38.01%	456 <b>51.13%</b>	470 61.71%	379 ...	...	0-4	5-20

Descriptions of classic (AL1) and extended (AL2) and allostatic loads only go up to 5, for readability. Scores closest to median (upper limit of "group 1") are marked in bold.

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