Allostatic Load as a Predictor of Morbidity and Mortality – Empirical Evidence

"A focus on individual biological parameters does not address the possibility that physiological risks cumulate across systems and across time, resulting in differential health risks within populations. The concept of allostatic load (AL), introduced by McEwen and Stellar (1993), reflects this more cumulative view of physiological risk. The basic proposition is that wear and tear across multiple physiological systems is a significant contributor to overall health risk. . . . Wear and tear across multiple physiological systems is consistent with evidence that many people, particularly at later ages, suffer from multiple, co-occurring chronic conditions (i.e., multiple pathophysiologies). Forty-five percent of women and 35% of men age 60 to 69 report two or more chronic conditions; these figures rise to 61% of women and 47% of men age 70 to 79 and 70% of women and 53% of men age 80 to 89 (Jaur et al. 1999). … Previous analyses from the MacArthur Studies of Successful Aging (25) have shown that although the overall summary measure of AL significantly predicts risk for major health outcomes, including mortality, none of the individual components is a significant independent "risk factor."" [Source: Seeman et al. 2002]

- McEwen BS, Stellar E. Stress and the individual: mechanisms leading to disease. *Arch Intern Med* 1993;153:2093–101.

- Jaur L, Stoddard S. Chartbook on women and disability in the U.S. Washington DC: US National Institute on Disability and Rehabilitation Research; 1999.

- Seeman TE, Singer BH, Ryff CD, Love GD, Levy-Storms L. Social relationships, gender, and allostatic load across two age cohorts. *Psychosomatic Medicine* 2002;64:395-406.

"Higher levels of allostatic load were observed in individuals with higher levels of ischaemic heart disease and periodontal disease. Markers of allostatic load had a similar effect in both ischaemic heart disease and periodontitis and explained part of the education and income gradients in the aforementioned chronic diseases." [Source: Sabbah et al 2008]

- Sabbah W. Watt RG, Sheiham A, Tsakos G. Effects of allostatic load on the social gradient in ischaemic heart disease and periodontal disease: evidence from the Third National Health and Nutrition Examination Survey. *J Epidemiol Community Health* 2008;62:415-420.

In a national sample (NHANES III), across ages 20–90, allostatic load is associated with poorer physical functioning and this relationship remains statistically significant after controlling for age and gender. Similarly, allostatic load is associated with a 1.2 times greater odds of having cardiovascular disease after controlling for age and gender. [Source: Crimmins et al. 2006]

- Crimmins EM, Johnston ML, Hayward M, Seeman T. Chapter 7. Age Differences in Allostatic Load: An Index of Frailty. In Zeng Yi et al. (eds.), *Longer Life and Healthy Aging*, Netherlands: Springer 2006.

A longitudinal, community-based study of relatively high-functioning men and women aged 70-79 years found after 24 to 32 months that higher allostatic load scores were associated with poorer cognitive and physical functioning and predicted larger decrements in cognitive and physical functioning, as well as being associated with an increased risk for the incidence of cardiovascular disease, independent of sociodemographic and health status risk factors. None of the individual CVD risk factors (components of allostatic load) exhibited a significant association with incident CVD. The comprehensive measure of allostatic load was more strongly predictive of incident CVD and declines

in cognitive and physical functioning than either individual risk factors or alternative reduced forms of allostatic load. [Source: Seeman et al. 1997]

- Seeman TE, Singer BH, Rowe JW, Horwitz RI, McEwen BS. Price of adaptation – allostatic load and its health consequences. *Archives of Internal Medicine* 1997;157:2259-2268.

A longitudinal, community-based study of relatively high-functioning men and women aged 70-79 years found that higher baseline allostatic load scores were associated with significantly increased risk for 7-year mortality as well as declines in cognitive and physical functioning and were marginally associated with incident cardiovascular disease events, independent of standard socio-demographic characteristics and baseline health status. Allostatic load was a better predictor of mortality and decline in physical functioning than either the syndrome X or primary mediator components alone. [Source: Seeman et al. 2001]

- Seeman TE, McEwen BS, Rowe JW, Singer BH. Allostatic load as a marker of cumulative biological risk: MacArthur Studies of Successful Aging. *Proc Natl Acad Sci* 2001;98(8):4770-4775.

A longitudinal, community-based study of relatively high-functioning men and women aged 70-79 years found that a summary measure of physiologic dysregulation (allostatic load) reflecting activity across multiple physiological systems had strong associations with both short-term (21/2 year) and long-term (71/2 year) physical and cognitive functional declines using canonical correlation analyses. This association was independent of cardiovascular disease, and had significant contributions from both traditional cardiovascular risk factors as well as other parameters reflecting HPA axis and sympathetic dysregulation. [Source: Karlamangla et al. 2002)

- Karlamangla AS, Singer BH, McEwen BS, Rowe JW, Seeman TE. Allostatic load as a predictor of functional decline: MacArthur studies of successful aging. *Journal of Clinical Epidemiology* 2002;55:696-710.

A longitudinal, community-based study of relatively high-functioning men and women aged 70-79 years found that higher allostatic load scores were associated with a gradient of increasing 7.5-year mortality. Analyses revealed that allostatic load explained 35.4% of the difference in mortality risk between those with higher versus lower SES (as measured by less than high school education versus high school o rgreater educational attainment). Importantly, allostatic load provided independent explanatory power, over and above a measure of doctor-diagnosed disease, though the latter also contributed to education-related variation in mortality risks. The summary measure of biological risk also accounted for more variance than individual biological parameters, suggesting the potential value of a multi-systems view of biological pathways through which SES ultimately affects morbidity and mortality. [Source: Seeman et al. 2004]

- Seeman TE, Crimmins E, Huang M, Singer B, Bucur A, Gruenewald T, Berkman LF, Reuben DB. Cumulative biological risk and socio-economic differences in mortality: MacArthur Studies of Successful Aging. *Social Science & Medicine* 2004;58:1985-1997.

A longitudinal, community-based study of relatively high-functioning men and women aged 70-79 years found that individuals whose allostatic load score increased had significantly higher risk of all-cause mortality between 1991 and 1995 as compared with participants whose allostatic load score decreased between 1988 and 1991 (15% versus 5%). Adjusted for age and baseline allostatic load, each unit increment in the allostatic load change score was associated with mortality odds ratio of 3.3 (95% confidence interval, 1.1–9.8). [Source: Karlamangla et al. 2006]

- Karlamangla AS, Singer BH, Seeman TE. Reduction in allostatic load in older adults is associated with all-cause mortality risk: MacArthur Studies of Successful Aging. *Psychosomatic Medicine* 2006;68:500-507.

A longitudinal, community-based study of relatively high-functioning men and women aged 70-79 years found that an allostatic load measure based on recursive partitioning techniques was associated with a high-risk of mortality over the 12-year period. [Source: Gruenewald et al. 2006]

- Gruenewald TL, Seeman TE, Ryff CD, Karlamangla AS, Singer BH. Combinations of biomarkers predictive of later life mortality. *Proc Natl Acad Sci* 2006;103(38):14158-14163.

A study of a national sample of Taiwanese persons aged 54 years or older found that allostatic load was significantly associated with 3-year mortality. Inclusion of neuroendocrine and immune biomarkers into the allostatic load measure had better explanatory and discriminatory power than the one with just clinical measures, suggesting that the nonclinical measures provide additional warning signs of deteriorating health above and beyond what can be learned from standard clinical measures. [Source: Goldman et al. 2006]

- Goldman N, Turra CM, Glei DA, Seplaki CL, Lin Y, Weinstein M. Predicting mortality from clinical and nonclinical biomarkers. *Journal of Gerontology* 2006;61A(10), 1070–1074.