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Index of Cardiometabolic Health: A New Method of Measuring Allostatic Load Using Electronic Health Records

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Abstract

Objective—We developed a measure of allostatic load from electronic medical records (EMRs), which we named "Index of Cardiometabolic Health" (ICMH).

Methods—Data were collected from participants' EMRs and a written survey in 2005. We computed allostatic load scores using the ICMH score and 2 previously described approaches.

Results—We included 1,865 employed adults who were 25–59 years old. Although the magnitude of the association was small, all methods of were predictive of SF-12 Physical component subscales (all $p<0.001$).

Conclusion—We found that the ICMH had similar relationships with health-related quality of life as previously reported in the literature.

Introduction

Allostatic load has been conceived as an early warning system that is comprised of biomarkers that could indicate early cumulative physiologic dysregulation across many cardiometabolic physiologic systems (Seeman et al., 2001), which may lead to the development of these chronic health conditions. Unlike the Framingham Risk Score (FRS), allostatic load is meant to be indicative of underlying wear and tear and not predictive on an individual basis of future cardiac events (D'Agostino et al., 2008). However, allostatic load is predictive of worse health outcomes including mortality (Wu et al., 2010, Seeman et al., 2004b, Seeman et al., 2001, Borrell et al., 2010), future cardiac events (Seeman et al., 1997, Mottillo et al., 2010), functional decline (Seeman et al., 2001, Karlamangla et al., 2002), and frailty (Gruenewald et al., 2009, Szanton et al., 2009). Likewise, greater allostatic load is also associated with worse patient reported health outcomes such as poorer self-rated health

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Disclosure of Interest

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and poorer performance on activities of daily living (Seplaki et al., 2004, Seplaki et al., 2006). However, the effect sizes of these relationships are small with studies finding that an increase in one point in allostatic load (on a 11 point scale) was associated with a 0.04 to 0.06 increase in units of self-rated health (measured with Excellent being 5 points and poor being 1 point) (Todorova et al., 2013, Read and Grundy, 2014). The association between allostatic load and both self-rated and functional status has also been found to be modest with allostatic load only explaining small 0.2–5% in the variance of these outcomes over and age and sex (Seplaki et al., 2006). Despite the small magnitude of the associations between allostatic load and self-rated health / functional status, these associations have consistently been reported in the literature.

Allostatic load may also represent an important mechanism of action for the effects of stress on health. Several studies have found that individuals with higher cumulative stress levels, such as African Americans and individuals with lower socioeconomic status, have higher allostatic load (Gruenewald et al., 2012, Deuster et al., 2011, Geronimus et al., 2006, Chyu and Upchurch, 2011, Bird et al., 2010, Gustafsson et al., 2011). Chronic stress is also associated with both increased likelihood of having higher allostatic load (Gustafsson et al., 2012).

Although allostatic load and metabolic syndrome have been found to be predictive of other health outcomes, the current process of ascertaining allostatic load in population health research studies includes many biomarkers that are difficult to obtain on a population level such as epinephrine, norepinephrine, cortisol, dehydroepiandrosterone sulfate, insulin-like growth factor-1 and interleukin-6 (Seplaki et al., 2006). This is why prospective studies, with extensive biomarker collection on small samples, have historically been the basis for allostatic load measurement. The complexity involved in measuring allostatic load and the difficulty associated with obtaining extensive biomarkers has constrained research using allostatic load to select populations including cohorts of seniors (for example, the MacArthur Study of Successful Aging), the National Health and Nutrition Examination Survey and specific clinical populations (Beckie, 2012).

With implementation of electronic medical records (EMRs), collection of component items of allostatic load has become increasingly common in large patient populations. However, uncertainty remains about whether the concept of allostasis can be operationalized using the unplanned but extensive collection of biomarkers that occurs routine medical care delivery. In this study, we outline and evaluate a method for evaluating physiologic dysregulation using a z-score based methodology, the Index of Cardiometabolic Health (ICMH). The ICMH follows the conceptual model of allostasis and its operationalization using z-scores that has been put forth in previous other studies (Seplaki et al., 2005). We examine ICMH based on biomarkers collected in routine practice among three condition cohorts (patients with diabetes, multiple cardiovascular risks, and healthy individuals). We aim introduce a new measure of allostatic load that is easily obtained from data routinely collected from healthcare. Thus, the primary objective was to describe the approach to calculating and creating the ICMH. The secondary objective is to compare the performance of the ICMH to other allostatic load measures. Unlike the ICMH, these other allostatic load measures (further description included in Table 1) are based on cut points and include some hard to

measure biomarkers, measures that are very rarely collected in routine primary care. The ICMH also includes 8 of the biomarker measures commonly used in other allostatic load measures. The third objective is to demonstrate the construct validity of the ICMH by determining its' association with health-related quality of life. Specifically, we will determine the construct validity of ICMH and other measures of allostatic load using EMR data by determining whether they are associated with worse health-related quality of life. Several articles have found that worse allostatic load is associated with worse aspects of health-related quality of life such as self-rated health (Seplaki et al., 2004, Seplaki et al., 2006) .

Methods

Study Setting

Kaiser Permanente Georgia (KPGA) is a federally-qualified HMO (health maintenance organization) that at the time of this study provided comprehensive medical services to approximately 275,000 residents in the Atlanta metropolitan area. The study protocol (including survey and survey administration) was reviewed, approved and monitored by the KPGA Institutional Review Board.

Study Sample

Participants were given the survey in written form, with an option to complete the survey on a website, during the period from October to December 2005. The survey was administered by a professional survey service, which handled data collection. A $2 incentive was given in the initial mailing. If participants did not respond after 5–6 weeks, reminder postcards, an additional full survey packet, and a friendly phone call reminder to non-respondents followed in this order.

Inclusion in the KPGA sample required: 1) enrollment with KPGA since January 2004; 2) subscriber within the enrolled family; 3) employment by one of the 100 largest private or public employer groups offering KPGA as an insurance option, and 4) participant age between 25 and 59 years, inclusive, as of August 31, 2005. A stratified randomized design was used to collect relatively well-balanced samples of respondents by condition cohort and by primary care practice. Three condition cohorts were identified for sampling: adults with diabetes, adults with elevated lipids and at least one other cardiovascular disease risk factor (e.g. hypertension or current tobacco smoking) but no history of advanced coronary artery disease (herein after "adults with cardiovascular risks"), and "low risk" adults (i.e. adults without any identifiable major physical or mental morbidities). Identification of these cohorts was accomplished by application of computer algorithms that ascertained evidence of disease from diagnoses on outpatient and inpatient care (e.g. ICD-9 or International Classification of Disease version 9 codes for diabetes), pharmacy dispensing's (e.g. insulin and oral hypoglycemic), and laboratory results (e.g. HbA1c>7.0%). These sampling criteria identified 5,309 potential participants. Of these, 2,224 (43%) completed the 2005 survey. Only individuals who self-categorized themselves as African American or white were included in this analysis (2,029 of 2,224).

Outcome Ascertainment

Participants reported physical and emotional functioning. These were measured in the survey using the Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) scales of the SF-12 (Ware et al., 1996). The scales have been standardized to have a mean of 50 and a standard deviation of 10 and are bounded by 0 and 100, with low scores representing poor physical or emotional functioning and high scores representing excellent physical or emotional functioning. PCS-12 and MCS-12 from the SF-12 have been shown to have good validity and high test-retest reliability (Ware et al., 1996). Estimates of test-retest reliability for PCS-12 and MCS-12 are 0.89 and 0.76 respectively.

Ascertainment of ICMH

Component measures for computing allostatic load were extracted from KPGA's EMR data system. There were two primary data sources within the system: primary care visits and laboratory results. Primary care visits were defined as a face-to-face visit with a physician, physician's assistant or a nurse practitioner in adult medicine or obstetrics/gynecology during routine office hours (i.e. after hours visits for urgent care were excluded). Height and weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) assessed on primary care visits. Height and weight were used to compute body mass index (BMI) calculated by weight in kilograms divided by a square of the height in meters, SBP and DBP were used individually and also to compute mean arterial pressure (MAP) by using the formula: the sum of one third of the systolic blood pressure and two thirds of the diastolic blood pressure.

Laboratory results (e.g. hemoglobin A1c, total cholesterol, low density lipoprotein, high density lipoprotein, serum creatinine, serum albumin, C-reactive protein) associated with outpatient (but not inpatient) services were obtained. Estimated glomerular filtration rate (eGFR) was calculated from serum creatinine, gender, and age at time of the test, using the Cockroft-Gault formula. Most laboratory tests are ordered by primary care physicians; but because there was no screen by ordering physician specialty, the laboratory test results also included tests ordered by medical subspecialists.

For each respondent, component measures were summarized into a measure for 2005. If a respondent had more than one result for a component measure in 2005 (e.g. 2 HbA1c results), then the median of the results for that respondent was retained for the component measure. Since most respondents had none, one, or two results on a component measure in 2005, the mean and median were equivalent for most respondents.

We computed allostatic load scores based on three approaches previously described in the literature, including the approach by Geronimus et. al.(Geronimus et al., 2006), Crimmins et. al. (Crimmins et al., 2003), as well as the ICMH, which is a z-score based approach. For the 3 previously published allostatic load approaches, a higher score was associated with worse physiologic status. For the ICMH measure – in which we wanted to emphasize good physiologic health – a higher score was associated with better physiologic status. Due to the nature of the EMR data, not all participants had values for all component measures. The Seeman et. al. method includes 10 components and participants were given one point for

each measure that exceeded an adverse (high or low) threshold, with cut points established using NHANES data (Beckie, 2012). The Crimmins allostatic load measurement method refers to a method of computing allostatic load based on 12 bio-markers and both clinical and NHANES cut points first described by Crimmins et. al. (Crimmins et al., 2003). The Crimmins measures includes all the components of the Seeman et. al. method, but also includes fasting blood glucose and high density lipoprotein (Crimmins et al., 2003). Moreover, the Crimmins-based method uses cut points based on both NHANES and clinical criteria for some component measures such as blood pressure (Table 1). The index of cardiometabolic health (ICMH), a z-score based approach, standardizes each component measure based on the sample mean on a scale of 0–100, and with a mean of 50 and a standard deviation of 12.5. The mean of the component measures is the overall ICMH score. Thus, higher values on ICMH represent lower allostatic load, or better physiologic health. The ICMH includes 8 biomarkers that are commonly used in the Crimmins et. al. and the Seeman's et.al. approach.

Covariates

Respondent-level covariates included: condition cohort, age group, gender, race/ethnicity, and educational attainment. Condition cohort (diabetes, cardiovascular risks, low risk), age in years, and gender were assessed from KPGA computerized data. Race/ethnicity (African American, white, other/unknown) and educational attainment (less than a high-school education, high school education, some college, and college graduate, post-graduate) were also assessed using survey data.

Statistical Analysis

We conducted descriptive statistics analysis in order to determine and compare the characteristics of the three cohorts (diabetes, cardiovascular risks, and low risk). We also conducted descriptive statistics to examine all three allostatic load measures and their components. For each method of calculating allostatic load, we examined the mean number of component measures per person. Bivariate relationships between demographic characteristics and allostatic load scores of all three measures were conducted using one-way ANOVA tests. We then used ordinary least squares linear regression to determine the multivariate relationships between baseline demographic characteristics and all three measures of allostatic load.

We determined both the bivariate and multivariate relationship between both PCS-12 and MCS-12 and all 3 measures of allostatic load, using one-way ANOVA tests and linear regression. We regressed all three measures of allostatic load and both PCS-12 and MCS-12 respectively as outcomes. Thus, we generated 6 separate linear regressions adjusting for all covariates. We then conducted analyses stratified based on sex and then race in order to determine whether the relationship between all measures of allostatic load and PCS-12 and MCS-12 differed by sex or race. Due to the inherent differences in the allostatic load and ICMH measurement specifications, we reported only standardized beta coefficients. To create standardized beta coefficients, we divided each allostatic load score or ICMH by the standard deviation of the allostatic load score, respectively, that was calculated from the study sample. We used the same standard deviation regardless of whether the analysis was

stratified or not. Thus, each beta-coefficient was only x-standardized and not fully standardized, so that each co-efficient corresponds to the average effect of a one standard deviation unit change in allostatic load on MCS-12 or PCS-12 after adjusting for baseline demographic characteristics. For each regression model, we calculated the semi-partial correlation (or the incremental increase in R-squared), after adding each method of allostatic measurement to a linear regression model adjusted for age, sex, race and education. We examined relevant interactions including those for all of the covariates mentioned previously with each measurement of allostatic load. All statistical tests were performed using Stata 11 (StataCorp., 2009).

Results

Excluding individuals with missing information for race, education, PCS-12, MCS-12, and any allostatic load or ICMH component measure, there were a total of 1,865 of the original sample of 2,029 individuals (91.9%) White or African American participants with complete data for analysis: 546 with diabetes, 666 with cardiovascular risks, and 653 “low risk adults”. Our sample was predominantly female (60.7%) with approximately half of the participants being white (51.3%) and middle aged (average age 48.4 (SD 6.8)). Most participants were well educated, with 82.6% of participants having had at least some college. Table 2 shows participant characteristics and their relationship to the condition cohort. Individuals in the “low risk” category tended to be more likely to be in the highest quartile of PCS-12, while those in the other condition cohorts had lower scores ($p<0.01$). However, MCS-12 did not show any apparent relationship with condition cohort.

Table 3 demonstrates that regardless of the method of allostatic load measurement, individuals who were older tended to have more allostatic load (Crimmins $p<0.01$, Seeman $p<0.01$, ICMH $p<0.01$). Regardless, of the method of measuring allostatic load, there were significant differences in allostatic load score between African Americans and whites (Crimmins $p=0.02$, Seeman $p<0.01$, ICMH $p<0.01$), but there were no differences found between males and females (Crimmins $p=0.48$, Seeman $p=0.38$, ICMH $p=0.64$). Participants with lower scores of physical component score of the SF-12 (PCS-12) tended to have significantly higher allostatic load, regardless of the method of measurement of allostatic load (Crimmins $p<0.01$, Seeman $p<0.01$, ICMH $p<0.01$). However, there were no differences in allostatic load between participants with different mental component scores of the SF-12 (MCS-12) (Crimmins $p=0.13$, Seeman $p=0.10$, ICMH $p=0.64$).

Table 4 demonstrates the mean number of components included in each separate measure of allostatic load. The mean number of component measures included in each of the different methods of computing allostatic load scores varied from an average of 4.43 (SD 1.68) for the Seeman measure to an average of 5.48 (SD 2.96) for ICMH. Everyone in the sample had a measure for body mass index and the majority of participants had values for cholesterol (74.0%), high density lipoproteins (73.1%) and low density lipoproteins (72.9%). Approximately half of participants had information regarding triglycerides (56.9%) and mean arterial pressure (54.1%). Biomarkers that were less likely to have values included albumin (24.2%), hemoglobin A1c (25.7%), Urine albumin/creatinine ratio (16.3%), and estimated glomerular filtration ratio (36.3%). There were no significant differences in the

number of component measures per participant by gender for all of the methods of determining allostatic load (Crimmins p=0.57, Seeman p=0.42, ICMH p=0.84). However, African Americans tended to have a higher number of mean component measures per participant when compared to whites for all of the methods of determining allostatic load (Crimmins p<0.01, Seeman p<0.01, ICMH p<0.01). Older individuals also tended to have a higher mean number of component measures per participant when compared to younger individuals (Crimmins p<0.01, Seeman p<0.01, ICMH p<0.01).

Table 5 presents socio-demographic factors associated with both allostatic load and ICMH at baseline. African Americans and older individuals had significantly worse allostatic load and cardiometabolic health, as measured by the ICMH (Table 5). Gender and education did not have statistically significant relationships with either allostatic load or the ICMH.

Standardized beta coefficients from multiple linear regressions, regressing each different method of allostatic load onto the outcome of PCS-12 and MCS-12 are shown in Table 6. For example, the standardized beta coefficients for the regression of Crimmins onto PCS-12 shows that for each standard deviation increase in the Crimmins score, the PCS-12 score decreases on average 1.51 (95% CI −1.89, −1.13) points after adjusting for age, sex, race and education. All of the methods of allostatic load measurement showed that increased allostatic load was associated with statistically significant lower PCS-12 scores. ICMH was scored in terms of physiologic health (or less allostatic load) and thus had an opposite direction. This remained true regardless of whether the data were stratified by sex or race. However, there was no consistent pattern between methods of allostatic load measurement and MCS-12 scores either overall or stratified by sex or race.

For all of the methods of allostatic load measurement, there was a statistically significant R-squared for the outcome of PCS-12. The semi-partial correlations (or incremental increase in R-squared) represents the percentage of the additional variance of PCS-12 or MCS-12 that is explained by each method of allostatic load measurement, after adjustment for age, sex, race and education. However, the amount of additional variation explained by these methods of allostatic load measurement was relatively small, whereby all of the methods explained less than 4% of the additional variance of R-squared after adjustment for other covariates. This remained true for all strata. For MCS-12 however, there was no clear pattern of different methods of allostatic load measurement having statistically significant adjusted R-squares.

Discussion

The primary objective of this study was to present a new measure of cardiometabolic health, the ICMH, and to examine the validity of the ICMH. We were able to determine the validity of the ICMH in several ways. First, we found that individuals in previous studies who had greater allostatic load using other conceptualizations of allostatic load also had worse ICMH. Second, we were able to reproduce the typical associations between socio-demographic data and allostatic load. Older individuals, African Americans and those with lower educational attainment had higher allostatic load across all measures. Third, we found that the ICMH and 2 established measures for assessing allostatic load using routinely collected vital status and laboratory measures were predictive of physical functioning in the

same way that prospective collection of vital status and laboratory measures stratifies nationally representative samples of adults. Although the magnitude of the association was small, all methods of allostatic load measurement were predictive of the physical component score of the SF-12. In contrast, none of the measures of the methods of calculating allostatic load were associated with the mental components of the SF-12.

Our findings using the ICMH parallel the findings of other studies who have found that African Americans and those who are older or have lower socio-economic status have worse allostatic load (Seeman et al., 2004a, HU et al., 2007). This provides evidence that the ICMH is an effective tool to measure allostatic load using electronic health records amongst the general working age population. However, our study, in contrast to other studies in the literature did not find any gender differences in allostatic load score (Yang and Kozloski, 2011). This may in part be due to a limitation in EMRs as a source for our measure of allostatic load as women tended to have higher inflammatory biomarkers when compared to their male counterparts (Beckie, 2012). Because our inflammatory markers such as CRP are less likely to be routinely ordered in primary care it is likely that the index of physiologic health may underestimate allostatic load for women.

Several studies have found that worse allostatic load using prospectively collected data on samples of large populations is associated with worse self-rated health and worse performance on activities of daily living (Seplaki et al., 2004, Seplaki et al., 2006). Like, previous studies, our study found that allostatic load measured using biomarkers collected during routine practice was associated with worse physical functioning. This remained true, regardless of what gender, racial, or clinical condition (diabetes, cardiovascular risks, low risk) subgroups we examined. Our study used electronic medical records that collect data from patient visits as compared with prospective data collection; and, we found concordant associations of physiologic dysregulation with self-reported physical health that were similar to the concordance found in studies of allostatic load using prospectively collected biomarker samples. However, although we found a statistically significant association between all measures of allostatic load (including the ICMH) and PCS-12, the magnitude of the association was small where a two standard deviation change in ICMH score was associated with a 3 points change in PCS-12 which may be equivalent to a minimally important difference in PCS (Revicki et al., 2006). The magnitude of relationship between all measures of allostatic load or ICMH explored in this study and worse SF-12 scores may be explained by the short time frame of this study. This is largely expected as allostatic load and the ICMH is meant to measure physiologic dysregulation and while stress and mental health issues may result in higher allostatic load or a poorer ICMH score, it is unlikely that higher allostatic load or a poorer ICMH score would be the cause in a 1–2 year time frame.

One of the more unexpected findings of our study was that allostatic load or ICMH, regardless of the scoring algorithm used, only accounted for a very small portion of the variance in physical functioning scores. This may in partbe due to the fact that the wear and tear associated with allostatic load takes time to develop and result in measurable health impairments. This would be especially true amongst our healthy working study population. This is especially supported by the strong association of worse allostatic load and ICMH with higher age, thereby implying that over the life course the wear and tear of allostatic

load as measured by ICMH had time to accumulate. Moreover, although our estimates of the percentage of variance explained by allostatic load were low, they are not unreasonable given the current literature (Seeman et al., 1997, Beckie, 2012).

Due to the plethora of different techniques used to measure allostatic load, several studies have examined whether the method of allostatic load measurement changes any findings. In particular, Seplaki et. al. found that allostatic load measures based on a set of cut-points, such as the methods by Crimmins et. al. (Crimmins et al., 2003) and Seeman et. al. (Beckie, 2012), did not perform as well as those based on z-scores such as the ICMH (Seplaki et al., 2005). Our study found that the association between both more traditional cut point based methods and the z-score based ICMH with PCS-12 did not differ substantially between types of allostatic load measurement. This is in line with the conclusions of a recent systematic review by Beckie et. al which concluded that the association between allostatic load and health impairment did not vary according which individual biomarkers were included or whether the measure of allostatic load was based on a z-score based measure or cut points (Beckie, 2012).

Other indices of short- and long-term predictive effects of cardiometabolic risk have been proposed, most notably the Framingham Risk Score (FRS) (Wilson et al., 1998). The ICMH differs from the FRS in several ways. ICMH is not intended to predict any specific endpoint at the individual level, but rather represents a general measure of cardiometabolic risk to be used on the population level. FRS is calibrated specifically to predict the risk of coronary heart disease (CHD) – one of many endpoints that can occur as a consequence of a range of pre-existing cardiometabolic risks. Additionally, the ICMH can include the following measures which are not included in the Framingham risk score such as GFR, serum and urinary albumin levels etc. Moreover, ICMH is not based on age or gender or disease; and, in fact can explain some variation in health independent of age or gender or disease. FRS substantially relies on age and gender for prediction of cardiometabolic risk. In fact, among men the strongest association of CHD with the FRS risk factors is with age; and, among women, age is as strong as SBP or DBP in predicting CHD (Table 1) (D'Agostino et al., 2008). ICMH does not rely on specific indicators of presence of a specific cardiometabolic disease – as does FRS (e.g. diabetes) – but rather relies on biomarkers indicative of gradients in physiologic status indicative of a disease or level of control of an existing disease (e.g. HbA1c levels). These biomarkers indicate level of glycemic control which is the most important factor explaining risk of subsequent micro- and macro-vascular disease (Stratton et al., 2000, 1993).

Our study is not the first to investigate the ability of using EMR data to measure indices of health. A previous study by Hivert et. al. found that metabolic syndrome could be measured using EMRs (Hivert et al., 2012). The creation of the ICMH builds on this previous work and is the first measure of allostatic load based on data contained in electronic health records. However, metabolic syndrome as defined by the International Diabetes Federation includes measures of central obesity, lipid abnormalities, high blood pressure, high glucose or fasting glucose (Alberti et al., 2006). Unlike the current definition of metabolic syndrome, the ICMH also includes measures of renal function such as eGFR and is a z-score based method and not based on cut points.

Our development and evaluation of the ICMH has several important implications for extension of the concept of allostatic load to measurement of physiologic dysregulation in routine research practice. One of the major limitations of previous work on allostatic load is that it requires many biomarkers that may require multiple measurements at pre-specified times of day (e.g., morning salivary cortisol) (Beckie, 2012). In addition, other typical components of allostatic load measures, such as neuroendocrine markers (like cortisol and epinephrine etc.) and inflammatory markers (like interleukin-6 and tumor necrosis factor), are rarely assayed in routine clinical care. This is largely because physicians are much more likely to order tests for biomarkers that are related to cardiac and metabolic health (e.g., low density lipoprotein or hemoglobin A1c) which the ICMH emphasizes. The majority of current studies on allostatic load have been confined to specialized samples that either include only older individuals (for example MacArthur cohort of aging, Taiwanese and Swedish Aging studies), NHANES and measurement of allostatic load in specific clinical populations (Beckie, 2012). However, the ICMH broadens the ability to conduct allostatic load research by using data from EMRs and not including any neuroendocrine or inflammatory measures side from c-reactive protein. Therefore, the ICMH can be used in more settings and using fewer resources.

Some might argue that the emphasis of the ICMH on cardiac and metabolic component measures is a limitation of the concept of allostatic load. This may be especially important for women given that the inflammatory bio-markers may be more important markers of allostatic load amongst women (Beckie, 2012). Although the lack of inflammatory bio-markers may be a problem, we found that on average 4–5 biomarkers in patients' EMRs were applicable to measurement of allostatic load. One additional limitation may be measurement bias due to the fact that individuals without any symptoms may be less likely to obtain regular healthcare and get the required clinical evaluation that would reveal underlying allostatic load buildup. In order to attempt to counteract this measurement bias we sampled 3 cohorts based on prior history of medical condition (diabetes, cardiovascular risks, low risk). However, this means that our sample is not strictly a random sample.

Conclusion

In conclusion, we propose that the ICMH represents a new way to use EMR data in order to measure and track allostatic load in the general population. Being able to track ICMH over time through EMR data allows us to extend the breadth of allostatic load research by allowing investigators to research allostatic load using more available electronic health record data as opposed to expensive and difficult to obtain physiologic bio-markers. As we enter an era where the adoption and usability of electronic health record data increases we will be able to use this data to measure previously hard to measure concepts such as allostatic load on a wider variety of populations. Moreover as the research using electronic health record data on allostatic load increases, public health officials could track the allostatic load of large portions of the population once as electronic health record data continue to become more common and standardized across multiple health care systems.

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List of Abbreviations

BMI	Body Mass Index
BP	Blood Pressure
DBP	Diastolic Blood Pressure
eGFR	Estimated Glomerular Filtration Rate
EMR	Electronic Medical Record
FRS	Framingham Risk Score
HbA1c	Hemoglobin A1c
HDL	High Density Lipoproteins
HMO	Health Maintenance Organization
ICD-9	International Classification of Diseases version 9
ICMH	Index of Cardiometabolic Health
KPGA	Kaiser Permanente Georgia
LDL	Low Density Lipoprotein
MAP	Mean Arterial Pressure
MCS-12	Mental Components Subscale of the SF-12
NHANES	National Health and Nutrition Examination Survey
PCS-12	Physical Components Subscale of the SF-12
SBP	Systolic Blood Pressure
SF-12	Short Form 12-item survey of Health-related Quality of Life

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Table 1

Description of Methods for calculating allostatic load

	Seeman et al.	Crimmins et al.	ICMH
N of Component Measures	**10**	**12**	**10**
Itemized Component Measures	Creatinine Clearance	Creatinine Clearance	eGFR
	Albumin (Serum)	Albumin (Serum)	Albumin (Serum)
	BMI	BMI	BMI
	SBP	SBP	MAP
	DBP	DBP	--
	HbA1c	HbA1c	HbA1c
	--	Fasting blood glucose	--
	Total Cholesterol	Total Cholesterol	Total cholesterol
	--	HDL	HDL
	--	--	LDL
	Triglycerides	Triglycerides	Triglycerides
	C-reactive protein	C-reactive protein	--
	Homocysteine	Homocysteine	--
	---	---	Urine albumin/creatinine ratio
Scoring Rules	1 point for each measure exceeding an adverse (high or low) threshold established using NHANES distributions	1 point for each measure (*) exceeding and adverse (high or low) threshold established using either clinical criteria (e.g. BP) or NHANES distributions	Each measure standardized to a mean of 0 and std. deviation of 1 in each year (**). Standard deviations beyond ± 4 recoded to ± 4. Standardized [0, 1] values recoded to [50, 12.5] Z-score Method 1: standardizes to the total sample average.

Table 2

Overall Sample Characteristics and by Condition Cohort (Diabetes, High Lipids, Low Risk) amongst 1865 Kaiser Permanente Enrollees, 2005

	All (n=1865)		Diabetes (n=546)		Cardiovascular (n=666)		Low Risk (n=653)		p-value
Age, N (%)									
Under 40	227	12.2	65	11.9	59	8.9	103	15.8	P<0.01
40–49	742	39.8	167	30.6	220	33.0	355	54.4	
50+	896	48.0	314	57.5	387	58.1	195	29.9	
Race, N (%)									
African American	909	48.7	294	53.8	299	44.9	316	48.4	P<0.01
White	956	51.3	252	46.2	367	55.1	337	51.6	
Gender, N (%)									
Female	1126	60.4	223	40.8	299	44.9	217	33.2	P<0.01
Male	739	39.6	323	59.2	367	55.1	436	66.8	
Education, N (%)									
At least HS Grad or GED	326	17.5	125	22.9	105	15.8	96	14.7	P<0.01
Some College	641	34.4	197	36.1	217	32.6	227	34.8	
At least College Degree	898	48.2	224	41.0	344	51.7	330	50.5	
Mean SF-12 PCS (SD)	50.5	(7.4)	48.1	(8.1)	50.6	(7.5)	52.6	(5.9)	P<0.01
Mean SF-12 MCS (SD)	54.5	(8.6)	51.3	(8.8)	51.7	(9.0)	52.5	(8.0)	P=0.01

Table 3

Average Allostatic Load Scores by Participants' Characteristics Amongst 1865 Kaiser Permanente Enrollees, 2005

	Crimmins*				Seeman†				ICMH‡			
Characteristic	**Mean**	**(SD)**	**One way ANOVA**	**Trend Test**	**Mean**	**(SD)**	**One way ANOVA**	**Trend Test**	**Mean**	**(SD)**	**One way ANOVA**	**Trend Test**
All participants	1.46	(1.42)			1.91	(1.56)			49.95	(10.71)		
Cohort												
Diabetes	2.61	(1.39)	F 404.26	NA§	2.96	(1.49)	F 295.65	NA§	48.54	(8.78)	F 76.75	NA§
Cardiovascular Risk	1.28	(1.24)	P<0. 01		1.90	(1.44)	P<0.01		47.22	(9.75)	P<0.01	
Low Risk	0.68	(0.92)			1.05	(1.14)			53.91	(11.98)		
Age												
25–39	1.27	(1.31)	F 13.58		1.61	(1.44)	F15.06		50.7	(12.8)	F 4.76	
40–44	1.11	(1.26)	P<0.01	P<0.01	1.53	(1.50)	P<0.0001	P<0.01	51.71	(11.79)	P<0.01	P<0.01
45–49	1.43	(1.48)			1.93	(1.59)			49.58	(10.91)		
50–54	1.60	(1.46)			2.09	(1.57)			49.72	(9.72)		
55–59	1.71	(1.44)			2.16	(1.53)			48.78	(9.17)		
Race												
African American	1.54	(1.35)	F 5.18	NA§	2.08	(1.52)	F 20.06	NA§	51.45	(10.72)	F 39.00	NA§
White	1.39	(1.49)	P=0.02		1.76	(1.58)	P<0. 01		48.38	(10.48)	P<0.01	
Gender												
Female	1.44	(1.41)	F 0.49	NA§	1.94	(1.57)	F 0.78	NA§	49.86	(11.57)	F 0.22	NA§
Male	1.49	(1.44)	P=0.48		1.87	(1.55)	P=0.38		50.10	(9.25)	P=0.64	
Education												
Some college or less	1.56	(1.45)	F 9.64		2.02	(1.56)	F 9.98		48.93	(10.54)	F 18.41	
At least a college degree	1.35	(1.39)	P<0.01	P<0.01	1.79	(1.55)	P<0.01	P<0.01	51.05	(10.71)	P<0.01	P<0.01
PCS-12 Quartile												
Highest	0.82	(1.12)	F 60.48		1.26	(1.34)	F 52.19		54.09	(11.29)	F 37.86	
Upper Middle	1.39	(1.33)	P<0.01	P<0.01	1.83	(1.49)	P<0.01	P<0.01	50.06	(9.69)	P<0.01	P<0.01
Lower Middle	1.61	(1.47)			2.05	(1.58)			48.94	(10.96)		
Lowest	2.03	(1.50)			2.50	(1.58)			46.81	(9.78)		
MCS-12 Quartile												

Characteristic	Crimmins*				Seeman†				ICMH‡			
	Mean	(SD)	One way ANOVA	Trend Test	Mean	(SD)	One way ANOVA	Trend Test	Mean	(SD)	One way ANOVA	Trend Test
Highest	1.39	(1.40)	F 1.93		1.83	(1.54)	F 2.08		50.31	(9.79)	F 0.56	
Upper Middle	1.37	(1.44)	P=0.12	P=0.02	1.83	(1.55)	P=0.10	P=0.02	50.08	(11.05)	P=0.64	P=0.15
Lower Middle	1.50	(1.41)			1.94	(1.55)			49.97	(11.10)		
Lowest	1.56	(1.45)			2.04	(1.58)			49.47	(10.99)		

*The Crimmins allostatic load measurement method refers to a method of computing allostatic load based on 12 bio-markers and both clinical and NHANES cut points first described by Crimmins et. al. (Crimmins et al., 2003) Higher scores on the Crimmins et. al. measure represent higher allostatic load. Refer to Table 1 for further information on specific bio-markers included in the Crimmins method of computing an allostatic load score.

†The Seeman method of calculating allostatic load, first published by Geronimus et. al., (Geronimus et al., 2006) uses 10 biomarkers and clinical cut points. Like the Crimmins measure, higher scores are associated with higher levels of allostatic load. Refer to Table 1 for further information on specific bio-markers included in the Seeman method of computing an allostatic load score.

‡The ICMH or "Index of Cardiometabolic Health" is a z-score based approach, whereby higher scores are associated with lower allostatic load. The ICMH is calculated by standardizing each biomarker to have a mean of 50 (range 0–100) and standard deviation of 12.5. The average of all the biomarkers is taken to get the ICMH score. Refer to Table 1 for further information on specific bio-markers included in the ICMH method of computing an allostatic load score.

§NA stands for not applicable.

Table 4

Mean Number of Measures per Participant in Allostatic Load Measures Amongst 1865 Kaiser Permanente Enrollees, 2005

			Gender					Race				
	Overall (n=1865)		Male (n=739)		Female (n=1126)			African American (n=909)		White (n=956)		
	Mean	(SD)	Mean	(SD)	Mean	(SD)	p-value	Mean	(SD)	Mean	(SD)	p-value
Crimmins*	5.04	(2.11)	5.01	(2.31)	5.07	(1.98)	0.5743	5.19	(2.01)	4.90	(2.20)	0.0026
Seeman†	4.43	(1.68)	4.40	(1.88)	4.46	(1.55)	0.4157	4.54	(1.60)	4.33	(1.75)	0.0063
ICMH‡	5.48	(2.96)	5.50	(3.09)	5.47	(2.88)	0.8337	5.72	(2.87)	5.24	(3.03)	0.0005

*The Crimmins allostatic load measurement method refers to a method of computing allostatic load based on 12 bio-markers and both clinical and NHANES cut points first described by Crimmins et. al. (Crimmins et al., 2003) Higher scores on the Crimmins et. al measure represent higher allostatic load. Refer to Table 1 for further information on specific bio-markers included in the Crimmins method of computing an allostatic load score.

†The Seeman method of calculating allostatic load, first published by Geronimus et. al., (Geronimus et al., 2006) uses 10 biomarkers and clinical cut points. Like the Crimmins measure, higher scores are associated with higher levels of allostatic load. Refer to Table 1 for further information on specific bio-markers included in the Seeman method of computing an allostatic load score.

‡The ICMH or "Index of Cardiometabolic Health" is a z-score based approach whereby higher scores are associated with lower allostatic load. The ICMH is calculated by standardizing each biomarker to have a mean of 50 (range 0–100) and standard deviation of 12.5. The average of all the biomarkers is taken to get the ICMH score. Refer to Table 1 for further information on specific bio-markers included in the ICMH method of computing an allostatic load score.

Table 5

Predictors of Standardized Allostatic* Load Amongst 1865 Kaiser Permanente Enrollees, 2005

	Seeman†		Crimmins‡		ICMH§	
Predictors	**Beta**	**(95% CI)**	**Beta**	**(95% CI)**	**Beta**	**(95% CI)**
Age (per year)	0.23	(0.16, 0.30)	0.21	(0.14, 0.27)	−0.15	(−0.22, −0.08)
Female	0.03	(−0.06, 0.12)	−0.034	(−0.13, 0.06)	0.004	(−0.087, 0.096)
African American	0.24	(0.15, 0.33)	0.14	(0.04, 0.22)	−0.296	(−0.388, −0.204)
Education						
HS grad or less	Referent		Referent		Referent	
Some college	−0.024	(−0.16, 0.11)	−0.02	(−0.15, 0.11)	−0.021	(−0.15, 0.11)
College degree+	−0.12	(−0.25, 0.0004)	−0.14	(−0.26, −0.01)	0.14	(0.014, 0.264)

*All measures of allostatic load were x-standardized so that each beta coefficient represents the effect of an increase in one unit of the predictor on standard deviations allostatic load. Therefore, the beta coefficient of 0.23 for age for the Seeman method, would be interpreted as follows: a one year increase in age results on average in a 0.23 standard deviation increase in Seeman et. al. allostatic load score after adjustment for gender, race, and education.

†The Crimmins allostatic load measurement method refers to a method of computing allostatic load based on 12 bio-markers and both clinical and NHANES cut points first described by Crimmins et. al. (Crimmins et al., 2003) Higher scores on the Crimmins et. al. measure represent higher allostatic load. Refer to Table 1 for further information on specific bio-markers included in the Crimmins method of computing an allostatic load score.

‡The Seeman method of calculating allostatic load, first published by Geronimus et. al., (Geronimus et al., 2006) uses 10 biomarkers and clinical cut points. Like the Crimmins measure, higher scores are associated with higher levels of allostatic load. Refer to Table 1 for further information on specific bio-markers included in the Seeman method of computing an allostatic load score.

§The ICMH or "Index of Cardiometabolic Health" is a z-score based approach whereby higher scores are associated with lower allostatic load. The ICMH is calculated by standardizing each biomarker to have a mean of 50 (range 0–100) and standard deviation of 12.5. The average of all the biomarkers is taken to get the ICMH score. Refer to Table 1 for further information on specific bio-markers included in the ICMH method of computing an allostatic load score.

Table 6

Association between Measure of Allostatic Load and Physical and Mental Component Subscales of the SF-12*

Measure of Allostatic Load	Physical Component Subscale of SF-12		Mental Component Subscale of SF-12	
	Beta	(95% CI)	Beta	(95% CI)
Crimmins	−1.51	(−1.89, −1.13)	−0.46	(−0.92, 0.01)
Seeman	−1.34	(−1.71, −0.97)	−0.52	(−0.97, −0.07)
ICMH	1.14	(0.80, 1.48)	0.29	(−0.11, 0.70)

* Linear regressions were adjusted for age, sex, race and education. Each method of allostatic load was x-standardized so that it corresponds to the average effect of a one standard deviation unit change in allostatic load on MCS-12 or PCS-12.