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eTable 4. Levels of Activity and Life Satisfaction Across US Geographic Regions

This supplementary material has been provided by the authors to give readers additional information about their work.
eFigure 1

Legend:
e1: Screenshots from MyHeart Counts App with Consent Form.
eFigure2

Legend:
e2: Data returned to the user by the MyHeart Counts application. Returned metrics include heart age (left), 6 minute walk statistics (center), and insights (right).
Legend:

e3A: Physical Activity Readiness Questionnaire (PAR-Q).
e3B: Activity and Sleep Survey: on-the-job activity, leisure-time activity.
EFigure 4

Legend:

e4A: Activity and Sleep Survey: Moderate or Vigorous Physical Activity\(^2\), sleep\(^7\)
e4B: Well-Being\(^9\) and Risk Perception\(^10\)
**Diet Survey**

How many cups of fruit do you eat in an average day? __ cups

How many cups of vegetables do you eat in an average day? __ cups

How many servings of fish do you eat in an average week? __ servings

How many servings of whole grains do you eat in an average day? __ servings

How many beverages with added sugar do you drink every week? __ (Y/N)

Select the statements that apply to you.

- I avoid eating prepackaged and processed foods.
- I avoid eating out, but when I do, I seek out low-sodium options.
- I avoid salt when I’m cooking at home.


**Cardiovascular Health Survey**

Do you have any of the following risk factors (if yes, indicate all that apply)? Y/N

- Abnormal Cholesterol (low HDL or high total cholesterol, LDL, or triglycerides)
- High Blood Pressure/Hypertension
- Diabetes
- Pre-Diabetes, Insulin Resistance, or Metabolic Syndrome
- Cigarette Smoking – Current or Former

Do you have a family history of heart disease (if yes, indicate all that apply)? Y/N

- Father or brother with heart attack or coronary artery disease before age 55
- Mother or sister with heart attack or coronary artery disease before age 55

Do you take medications to treat the following risk factors (indicate all that apply)?

- To treat and lower cholesterol
- To treat hypertension and lower blood pressure
- To treat diabetes or diabetes and lower blood sugar

Have you been diagnosed with heart disease (if yes, indicate all that apply)? Y/N

- Heart Attack/Myocardial Infarction
- Heart Bypass Surgery
- Coronary Blockage/Stenosis
- Coronary Stent/Surgery
- Angina (heart/chest pain)
- High Coronary Calcium Score
- Heart Failure or CHF
- Arrhythmia (Atrial fibrillation or Atrial)
- Congenital Heart Disease

Have you been diagnosed with vascular disease (if yes, indicate all that apply)? Y/N

- Stroke
- Transient Ischemic Attack (TIA)
- Carotid Artery Blockage/Stenosis
- Carotid Artery Surgery or Stent
- Peripheral Vascular Disease (Blockage/Stenosis, Surgery, or Stent)
- Abdominal Aortic Aneurysm

1Adapted from ISCHEMIA trial. http://www.ischemia2011.org/CT04471572

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**Legend:**

**e5A:** Diet Survey

**e5B:** Cardiovascular Health Survey

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**Legend**

e6: K-means clustering of subjects' activity patterns based on 10 features: proportion of time spent in the “stationary”, “automotive” (driving), “walking”, “cycling”, and “running” states during the weekdays as well as during the weekends.
eFigure 7

Legend:

e7A: Clusters of physical data based on the number of times subjects changed state from active to inactive and vice versa over the course of 2 weekdays and 2 weekend days.

eB: Association of physical activity clusters with probability of health conditions. Y-axis indicates the Chi-squared difference in observed minus expected standardized residuals for each cluster. Significant associations were identified for chest pain (p<0.001, N=17500, $\chi^2=43.38$, $V=0.025$), diabetes (p<0.001, N=17500, $\chi^2=25.96$, $V=0.0172$), heart condition (p<0.001, N=17500, $\chi^2=41.57$, $V=0.0217$), heart disease (p<0.001, N=17500, $\chi^2=97.765$, $V=0.0343$), hypertension (p=2.0e-2, N=17500, $\chi^2=13.857$, $V=0.0126$), joint problems (p=3.04e-4, N=17500, $\chi^2=23.197$, $V=0.0162$), and vascular disease (p=9.0e-2, N=17500, $\chi^2=40.636$, $V=0.0216$).

eC: Distribution of job activity levels by physical activity cluster.

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eFigure 8

Legend
e8: Assessment of subjects’ cardiovascular risk. A. Subject’s calculated 10-year cardiovascular risk is compared to how they rank themselves compared to others of the same sex and age. A rank of 1 indicates that a subject considers him/herself at lower risk for cardiovascular disease as compared to others; a rank of 5 indicates that a subject considers him/herself at a much higher risk. B. Linear regression of subjects’ predicted heart age onto true age.

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eFigure 9

Legend:

e9: Bland Altman analysis of app-reported six minute walk distance vs. measured six minute walk distance.
**eMethods. Supplementary Methods**

Screen shots from the application demonstrating the consent process and the return of data dashboard are shown in [eFigures 1-2](#).

**Data Access**

Data are stored on the phone and uploaded directly to a secure server (Sage Bionetworks, Seattle, WA) where they are de-identified. No data are sent to Apple Inc. Security measures exceed those specified by the Health Insurance Portability and Accountability Act (HIPAA). Incremental updates are downloaded to Stanford University servers using the Synapse R API. Personal and cohort average 6-minute walk scores were returned to participants within the application.

The application sends a combination of structured json and tabular HealthKit files to an intermediate bridge server controlled by Sage Bionetworks. Synchronization happens over the internet at scheduled intervals through the day or when the local cache size reaches a minimum threshold. The purpose of the bridge server is two-fold. First, Apple account emails are mapped to internal anonymized identifiers designated as HealthCodes. Second, the structured json files are formatted as tabular data using a priori defined and versioned schema for display through Synapse. During the mapping process, metadata including timestamps and application versions are extracted and associated with the results. Each record in the Synapse table corresponds to a discrete synchronization event. For HealthKit related data such as Activity State, Geographical Displacement and Heart Rate there will be links to data blobs that contain high resolution time-series data collected over a specific time interval. At the time of writing, there are 22 tables being updated of which 7 include links to external HealthKit blob data. All data is programmatically queried and downloaded through the R API v1.11.1.

**Motion Tracking Calculations**

We used the motion data from participants’ iPhones to calculate the number of seconds each individual spent in each of these states: walking, running, cycling, automotive, and stationary. Individuals with short durations (less than 2 consecutive days of data) or few entries of motion tracking data (less than 2000 data points) were excluded. To maximize the inclusion of participants who did not contribute a full 7 days of motion tracking, feature extraction was performed on data from two weekday and two weekend day samples. We calculated the total proportion of time an individual spent active (running, walking, cycling) and the proportion of time an individual spent inactive (stationary and automotive). The physical activity data was sampled and filtered to select two consecutive weekdays as well as two consecutive weekend days of activity for each subject. “Unknown” states were resolved by forward-carrying the immediately preceding known activity state. Data was analyzed at a two-minute granularity. For each consecutive two-minute window of data, the mode of the reported activity states was computed. The physical activity data was sampled and filtered to select two consecutive weekdays as well as two consecutive weekend days of activity for each subject. “Unknown” states were resolved by forward-carrying the immediately preceding known activity state. Data was analyzed at a two-minute granularity. For each consecutive two-minute window of data, the mode of the reported activity states was computed. The state for the window was assigned in accordance with the majority vote. Any gap in data greater than 15 minutes was assigned to the stationary state.

K-means clustering was then performed using K=10 (as determined by minimizing the Bayesian information content) ([Supplementary Figure e8](#)). 10 features were selected for clustering: fraction of time spent in the stationary, automotive, walking, running, and cycling states during the weekend as well as the fractions of time spent in each of these five states during the weekday. Four meta-clusters were generated by hierarchical clustering on the centroid coordinates of the 10 K-means clusters. The closest pair of centroids in N-dimensional space were successively merged to reduce the 10 clusters to four. The four meta-clusters consisted of inactive individuals, individuals who spent a significant portion of the day driving, active walkers/cyclists, and individuals who were inactive during the weekdays but active on weekends. In subsequent iterations of the app, the goal is to use the meta-clusters to track subject behavior over time and provide feedback indicating when a subject’s activity levels lead them to shift from a cluster with significant correlations for poor health outcomes to a cluster with more favorable health metrics.

**Unsupervised Machine Learning Analysis**

Participants with low amounts of motion tracking data were removed from the motion tracking and 6-minute walk analysis.

Physical activity clusters were correlated with health outcomes collected from survey questionnaires via several statistical analysis techniques. A Chi-squared test was performed to check for associations between activity cluster membership and the presence/absence of multiple health conditions (heart disease, vascular disease, diabetes, joint problems, chest pain, hypertension). Tukey’s HSD test in conjunction with ANOVA.
was applied to compare cluster means for quality of life metrics such as happiness, depression, worry, and overall life satisfaction, as well as continuous (rather than categorical) health outcomes such as blood pressure and HDL/LDL levels.

Heart Age and 10 Year Risk Assessment
A participant’s ten-year risk and lifetime risk of stroke and myocardial infarction were calculated utilizing formulas published by the American Heart Association. Ten-year risk was calculated for participants in the 40-80 age range, while lifetime risk was calculated for subjects in the 20-60 age range. The calculations incorporate age, race, sex, HDL levels, total cholesterol levels, treated/unreated systolic blood pressure, smoking status, and diabetes status, as well as population estimates of baseline survival.

These metrics were acquired through a cardiovascular health questionnaire. To provide the participants a risk estimate that was more meaningful, we calculated their “heart age” by identifying the age of an individual with the same 10-year risk as the subject, but with optimal predictor values.

Predicted heart age and risk calculations were compared to subjects’ self-reported perceptions of risk, as obtained through the risk perception questionnaire. Linear regression was performed to identify the relationship between a subject’s calculated heart age and true biological age.

Validation studies
Validation studies were carried out for the 6 minute walk measurements. We measured an individual’s walking distance using a measuring wheel (Komelon MK45M Merteman) and the MyHeart Counts App and compared the two values. Individuals walked outside, in a straight line with no stopping. Individuals were instructed to walk at a normal, very brisk or very slow pace.

Survey instruments
Survey instruments used in the study are shown in eFigures 3-5.

The Physical Activity Readiness Questionnaire (PAR-Q+ c.2012, eFigure 3A) originates from and is used with the permission of The Canadian Society for Exercise Physiology. The PAR-Q+ is a self-guided screening instrument completed by the participant before they become more physically active. Participants are required to read each question in its entirety and respond to each question carefully. If the answer to all questions is NO the participant is informed that they cleared for physical activity. If one or more answers is a YES users are prompted to consult with a physician prior to starting and/or increasing activity.

The Activity and Sleep survey (eFigures 3B, 4A) is a fusion of existing validated activity and sleep surveys assessing on-the-job activity, leisure-time activity and sleep. More specifically questions 1 and 2 ("On-the-Job Activity" and “Leisure-Time Activity") are from the Stanford Brief Activity Survey (SBAS) and the updated Stanford Leisure-Time Categorical Item. This is a self administered clinically validated survey that is intended to provide a swift appraisal (less than 5 minutes) of the quantity as well as intensity of physical activity that the user does over the course of a day. The SBAS is composed of two questions, each question has five possible responses. The participant is asked to choose a response that most closely depicts their work-place activity as well as their leisure time activity. Each of the five response statements are phrased as comprehensive statements to include the type of activity, its duration, frequency and its intensity. The activity survey also includes two additional questions from the AHA’s MyLifeCheck on minutes per week of moderate and vigorous activity, adapted from the short-form IPAQ questionnaire. Questions related to sleep are derived from the 2011-12 National Health and Nutrition Examination Survey (NHANES). The user is asked to estimate the actual sleep hours per weekday and if they have any sleep disorder. The latter was modified by Dr. Mignot (Director, Stanford Sleep Medicine Center) to include a list of seven specific sleep disorders.

The Well-Being survey questions (eFigure 4B) approach Well-Being and Risk Perception. Questions stem from the Organisation for Economic Co-operation and Development guidelines on measuring subjective well being. The questions are designed to have a minimal demand on participants time while measuring the topics for which there is the strongest validity and relevance to well being. The first question asks the user to evaluate their overall life satisfaction with 0 being completely dissatisfied and 10 meaning completely satisfied, question two encompases the eudaimonic concept of whether the things a user is doing in their life are worthwhile with 0 signifying “not at all worthwhile” and 10 signifying “completely satisfied”. The last 3 questions are designed to capture the affective state of the individual in regards to the previous day period, with 0 meaning the feeling of happiness was not experienced at all and a rating of 10 meaning the feeling of happiness was experienced all day.

The Risk Perception Survey was adapted from Knowles et al (2012) and consists of four questions whose aim is to assess the participants perceived risk of ten year and overall lifetime mortality due to heart attack, © 2016 American Medical Association. All rights reserved.
stroke or death due to cardiovascular disease. Participants are asked to rate their own risk of having a heart attack, stroke or death relative to others their age and gender over the subsequent decade as well as over their entire lifetime. Response options are: much lower than average, about average, higher than average, and much higher than average. The responses are assigned a numerical value (-3, -2, -1, 0, 1, 2, 3 respectively). Perceived risk is stratified based on the mean of values indicated above thus a mean less than zero indicates an optimistic bias and means that the individual perceives themselves as lower risk than their peers.

The Diet Survey (eFigure 5A) was based on the American Heart Association’s MyLifeCheck questions, with permission, adapted from Policy Statement on The Role of Worksite Health Screening (2014). The questions regarding diet were used in order to determine if a healthy dietary pattern is followed. The document identifies a healthy dietary pattern as one that is consistent with a Dietary Approaches to Stop Hypertension (DASH)-type eating pattern, to consume ≥4.5 cups/d of fruits and vegetables, ≥2 servings/wk of fish, and ≥3 servings/d of whole grains and no more than 36 oz/wk of sugar-sweetened beverages and 1500 mg/d of sodium.

The Cardiovascular Health Survey (eFigure 5B) is based on the AHA’s MyLifeCheck questions, supplemented with baseline questions from the International Study on Comparative Health Effectiveness With Medical and Invasive Approaches (ISCHEMIA Trial, NCT01471522) designed by the ISCHEMIA Trial investigators.
Physical activity

Though the study protocol indicated that subjects should generate 7 days of activity data, participant compliance with this guideline varied widely. 22,790 subjects uploaded 2 consecutive days of data, 13,990 uploaded 3 consecutive days, and 8,877 uploaded 4 consecutive days. Most subjects did not complete a single full week of data collection, leading us to select 2 consecutive weekday days and 2 consecutive weekend days as the minimum participation level to include a subject in the physical activity analysis. Most subjects recorded activity data for 15-20 hours per day, with gaps in data typically appearing during the night time hours. Estimates of minutes spent in moderate or vigorous activity were stable through different age groups (IQR= 43 - 172 minutes of physical activity per day). Confidence estimates are provided by the low power sensor algorithm.

The assignment of individuals to activity clusters correlates with reported on-the-job activity levels. Individuals in cluster 1 spend the lowest fraction of time sitting/standing and the highest fraction of time walking and performing tasks that required moderate exertion. Conversely, individuals in clusters 5 and 6 spent the highest fraction of time sitting/standing. Individuals in cluster 3, the “weekend warriors”, spent a similarly high fraction in the sitting/standing state.

A more finely-grained clustering analysis grouped individuals by fraction of time spent in each of five activity states during two consecutive weekdays and weekend days. A K-means clustering on these features yielded 10 clusters grouped into three meta-clusters. A pairwise ANOVA of cluster membership versus answers to the well-being survey indicated significant correlations between activity level and reported happiness, worry, depression, and overall life satisfaction (eFigure 6c). A Tukey HSD analysis of difference in means between the most active cluster (“walkers”) and the inactive cluster revealed that the active subjects reported feeling 7.3% less worried (p<0.001), 5.4% less depressed (p<0.001), 5.5% happier (p<0.001), 5.2% more satisfied with life (p<0.001), and 4.1% more worthwhile (p<0.001) than their inactive counterparts. Similarly, cluster membership was found to correlate with disease (eFigure 2b); the active participants were found to have on average 5% reduced risk for chest pain, dizziness, heart condition, heart disease, and joint problems.

Validation study

Although extensive testing of activity and distance measurements from the internal motion co-processor chip functionalities was carried out by Apple Inc, we carried out an independent validation study comparing self-administered 6 minute walk distance to clinically administered tests at Stanford Hospital. eFigure 7 shows a result of the Bland-Altman analysis of app-reported vs. measured distance. The mean absolute percentage error of the six minute walk was 8.7% (52.3 (SD: 37.4) yards).

Models of life satisfaction and self-reported disease

We tested the association of life satisfaction and self-reported disease status in our population with dietary, lifestyle, and other factors. Significant univariate predictors of life satisfaction in a linear model adjusting for covariates of age and sex were: family history of heart disease (β=-.31 95% CI(-0.52, -0.08), p=0.0057), proportion of time recorded as active (β= 3.03 95% CI(0.97, 5.09), p=0.0041), self-reported minutes of moderate (β= 0.0018, 95% CI(0.0011, 0.0025), p=0.0001) and vigorous activity (β= 0.0032, 95% CI(0.0022, 0.0042), p<0.001), diet including daily servings of fruit (β= 0.18, 95% CI(0.10, 0.25), p=0.001) and vegetables (β= 0.13, 95% CI(0.06, 0.19), p<0.001), weekly servings of fish (β= 0.12, 95% CI(0.05, 0.19), p=0.0011), and weekly sugary drink intake (β= -0.03, 95% CI(-0.01, -0.05), p<0.001). Since many of these univariate predictors are correlated, we derived a multivariate linear model using stepwise selection on all significant univariate predictors, once again including age and sex as covariates. We found that fruit intake, sugary drink intake, recorded activity, and self-reported vigorous activity remained as significant predictors.

Significant univariate predictors of disease in a logistic regression of disease status that included age and sex as covariates were: family history of cardiovascular disease (OR: 1.88 95% CI (1.32, 2.67), p<0.001), consumption of whole grains (OR: 1.07 95% CI (1.00, 1.13), p=0.044), life satisfaction (OR: 0.89, 95% CI (0.82, 0.98), p=0.015), and having an active job (OR: 0.54, 95% CI (0.30, 0.97), p=0.041). We used stepwise selection on the significant predictors to derive a multivariate logistic regression model, with age and sex as covariates, that showed family history, whole grain consumption, and job activity as significant predictors.
Table 1:

Subject demographic information.

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Number of participants</th>
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<tbody>
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<td>Male</td>
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<tr>
<td>Female</td>
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<td>No response</td>
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<tr>
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<tr>
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<td>I prefer not to indicate</td>
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**Table 2**

X^2 statistical associations between K-means activity clusters and self-reported health conditions.

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<th>Heart Disease</th>
<th>Joint Pain</th>
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<td>X^2</td>
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<td>22.682</td>
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<tr>
<td>Cramer V</td>
<td>0.0149</td>
<td>0.0122</td>
<td>0.0121</td>
<td>0.0149</td>
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<tr>
<td>ϕ for weekend warrior cluster</td>
<td>0.0420</td>
<td>0.0380</td>
<td>0.0465</td>
<td>0.0429</td>
</tr>
</tbody>
</table>
Table 3

Significant predictors of life satisfaction and disease status, as determined by a multivariate linear model (life satisfaction) and multivariate logistic regression model (for disease status) using stepwise selection on all significant univariate predictors, including age and sex as covariates. Fruit intake, sugary drink intake, recorded activity, and minutes of self-reported vigorous activity remained as significant predictors of life satisfaction.

<table>
<thead>
<tr>
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<th>Significant predictors of life satisfaction</th>
<th>Significant predictors of disease</th>
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</thead>
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<tr>
<td>Fruit intake</td>
<td>Sugary drink intake</td>
<td>Recorded activity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Minutes of self-reported vigorous activity</td>
</tr>
<tr>
<td>P-value</td>
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<td>0.04</td>
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<tr>
<td>95% CI</td>
<td>0.01, 0.27</td>
<td>-0.063 , -0.002</td>
</tr>
<tr>
<td>β</td>
<td>0.14</td>
<td>-0.032</td>
</tr>
<tr>
<td>OR</td>
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</table>

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Levels of activity and life satisfaction across U.S. geographic regions.

<table>
<thead>
<tr>
<th>Region</th>
<th>Activity levels (% of day spent active)</th>
<th>Life satisfaction (score on a scale of 1 - 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>West</td>
<td>15.6% 95% CI (15.2%, 16.0%)</td>
<td>7.18 95% CI (7.09, 7.27)</td>
</tr>
<tr>
<td>Midwest</td>
<td>15.1% 95% CI (14.8%, 15.4%)</td>
<td>7.15 95% CI (7.08, 7.22)</td>
</tr>
<tr>
<td>South</td>
<td>14.9% 95% CI (14.5%, 15.3%)</td>
<td>7.13 95% CI (7.04, 7.21)</td>
</tr>
<tr>
<td>Northeast</td>
<td>14.8% 95% CI (14.3%, 15.2%)</td>
<td>6.96 95% CI (6.86, 7.06)</td>
</tr>
</tbody>
</table>
References


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