# Resting Heart Rate and Associations with Clinical Measures from the Project Baseline Health Study: An Observational Study

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Submitted to: Journal of Medical Internet Research
on: May 13, 2024

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## *Abstract*

**Background:** Though widely used, resting heart rate (RHR) as measured by a wearable device has not been previously evaluated in a large cohort against a variety of important baseline characteristics.

**Objective:** This study aimed to assess the validity of the RHR measured by a wearable device compared against the gold standard of ECG, and assess the relationships between device-measured RHR and a broad range of clinical characteristics.

**Methods:** The Project Baseline Health Study (PHBS) captured detailed demographic, occupational, social, lifestyle, and clinical data to generate a deeply phenotyped cohort. We selected an analysis cohort within it, which included participants who had RHR determined by both electrocardiogram (ECG) and by the Verily Study Watch (VSW). We examined the correlation between these simultaneous RHR measures, and assessed the relationship between VSW RHR and a range of baseline characteristics including demographic, clinical, laboratory, and functional assessments.

**Results:** From the overall PBHS cohort (N=2502), 875 (35%) participants entered the analysis cohort, 519 (59%) female and 356 (41%) male participants. The mean and standard deviation of VSW RHR was 66.6 ± 11.2 beats per minute (bpm) for female participants, and 64.4 ± 12.3 bpm for male participants. There was excellent reliability between the two measures of RHR (ECG and VSW) with an intraclass correlation coefficient of 0.946. By univariate analyses, female and male participants had similar baseline characteristics that trended with higher VSW RHR: lack of healthcare insurance (both $p < 0.05$), higher BMI (both $p<0.0001$), higher C-reactive protein (both $p<0.0001$), presence of type 2 diabetes mellitus (both $p<0.0001$), and higher World Health Organization Disability Assessment Schedule (WHODAS) 2.0 score (both $p<0.0001$) were associated with higher RHR. By regression analyses, within each domain of baseline characteristics, different characteristics were most associated with VSW RHR in female compared to male participants: demographics and socioeconomic status (unemployment vs. lack of health insurance), medical conditions (chronic obstructive pulmonary disease with emphysema vs. type 2 diabetes mellitus), laboratory assessments (C-reactive protein vs. blood glucose), and patient reported outcomes (eWHO Disability Assessment Schedule 2.0 score vs. Behavior Risk Factor Surveillance System score). Diastolic blood pressure was the most associated characteristic with higher VSW RHR for both sexes within the vitals and physical function domain.

**Conclusions:** RHR determined by the VSW had excellent correlation with RHR determined by ECG. Participants with higher VSW RHR had similar trends in socioeconomic status, medical conditions, vitals, laboratory assessments, physical function, and patient reported outcomes irrespective of sex. However, within each domain of baseline characteristics, different characteristics were most associated with VSW RHR in female versus male participants. Clinical Trial: clinicaltrials.gov identifier NCT03154346

(JMIR Preprints 13/05/2024:60493)
DOI: https://doi.org/10.2196/preprints.60493

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## Title Page

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Word count: Abstract, 422; main text, 3232

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**Keywords:** resting heart rate; wearable devices; remote monitoring; physiology; PBHS; Project Baseline Health Study; Verily Study Watch

## INTRODUCTION

Resting heart rate (RHR) has been extensively studied in healthy individuals and those with specific disease states such as cardiovascular disease (CVD) [1,2]. Increasing RHR is linked to the development of CVD risk factors such as diabetes mellitus and hypertension and is implicated as an important prognostic factor in those with CVD and cancer [3,4]. Because of these links with important clinical outcomes such as the development of disease and mortality, RHR and RHR trends are of high interest to clinicians and patients alike and have become highly accessible, particularly with the recent ubiquity of wearable devices capable of recording heart rate (HR) and even detecting concerning arrhythmias such as atrial fibrillation [5].

Traditionally, RHR is determined through clinical measurements during physical exams as well as electrocardiography (ECG), and ambulatory devices. In the recent decade, wearable devices have become increasingly popular; many have the capability to track fitness levels with a variety of metrics including steps, HR, and sleep. Commercially available devices have been shown to be accurate in measuring HR and steps and studies suggest that wearable devices may improve physical activity [6-8].

The Project Baseline Health Study (PBHS) was a prospective, multicenter, longitudinal cohort study launched in 2017 to establish a comprehensive reference health state using a wide range of modalities, evaluate different technologies in measuring disease trajectory and participant diversity, and share this information with both scientists and participants. The PBHS enrolled 2502 participants to include a broad range of healthy individuals, with varying disease risk (specifically CVD, breast/ovarian cancer, and lung cancer), as well as those with known disease diagnoses. The PBHS provides an opportunity to describe and assess RHR using a wearable device (Verily Study Watch [VSW]) in a contemporary population and to do so in a comprehensive and more continuous manner than previously done [9]. Prior studies have limited comparisons to clinical measurements or have

small sample sizes focused on specific disease states [10-12]. The design of the PBHS allows for an extensive analysis of RHR as they relate to multimodal clinical data collected from remote and in-person visits in a deeply phenotyped cohort. In this study, we (1) identify an analysis cohort within the PBHS and compare baseline characteristics with the overall study cohort at large, (2) validate the VSW's determination of RHR (VSW RHR) by comparing against the gold standard of RHR by ECG, and (3) assess the relationships between VSW RHR and a broad range of baseline clinical characteristics.

## METHODS

### Overview

The design of the PBHS has been previously described [9]. Informed consent was obtained from all participants enrolled in PBHS and the study was approved by a central institutional review board (IRB; Western IRB) and the IRB at each of the participating institutions (Stanford University, Duke University, and the California Health and Longevity Institute). The PBHS was registered in clinicaltrials.gov (identifier NCT03154346).

### Participants

PBHS participants were selected from an online registry; ultimately, 2502 participants were included. The inclusion criteria for the registry were: age ≥18 years, residency in the U.S, ability to speak and read English, willingness to provide health information, and ability to interact with certain study activities using a personal smartphone/device. In this study cohort, 60% of the enrolled population in each age strata had ~60% higher risk relative to the participants of the same age and sex for atherosclerotic cardiovascular disease, lung cancer, and/or breast/ovarian cancer.

### Measurements and Definitions

#### *Study Assessments*

PBHS participants underwent a deep phenotyping process, with extensive multimodal assessments during enrollment to measure their health characteristics including demographics, vitals, laboratory, functional testing, imaging, surveys, and wearable sensor data from the VSW, an investigational medical device used in medical research and clinical care. For this study, baseline characteristics, as listed in **Multimedia Appendix Tables 1-3**, were selected for each participant and were chosen due to their ubiquity in clinical practice and physiological relevance to RHR.

### *Resting Heart Rate*

Baseline RHR measurements were determined with two different techniques: in-clinic ECG RHR and VSW RHR. During the enrollment study site visit, 12-lead ECG was recorded and HR from the computerized interpretation of the ECG was computed as the ECG RHR. An ECG was considered “Excellent” or “Good” when all 12 leads were analyzable and either no noise/artifact or minimal noise/artifact (respectively) were noted; only ECG readings that met these criteria were considered.

VSW RHR was determined using a proprietary study wrist-wearable device which was an integral part of the continuous assessments of PBHS. Participants were encouraged to wear it consistently during the entire study duration. The VSW captures biological signals via several sensors including photoplethysmography (PPG) at 30 hertz and accelerometry at 30Hz. It also provides several derived metrics using proprietary algorithms that process these signals. In this study, we use the following derived metrics:

- PPG Interbeat Intervals (IBI), which measure the time interval between PPG-derived heart beats, in milliseconds. The IBIs are calculated at each heart beat, and each IBI value is also accompanied by a binary quality metric (“good” vs “bad” quality). To determine the quality of IBIs, in this study, we use the “jump distance” metric which is defined as the following for each sample i:

$$J_i = \sqrt{(I_i - I_{i-1})^2 - (I_{i+1} - I_i)^2}$$

  where $I_i$ is the IBI value in milliseconds at sample $i$. When the jump distance is smaller than 100ms, we label that IBI as having “good” quality and otherwise as having “bad” quality. The reason is that very high jump distance values indicate the presence of artifacts or the failure of the PPG peak detection algorithm. The threshold value of 100ms was chosen as the optimal value in a trade-off between heart rate error and coverage on an internally-collected

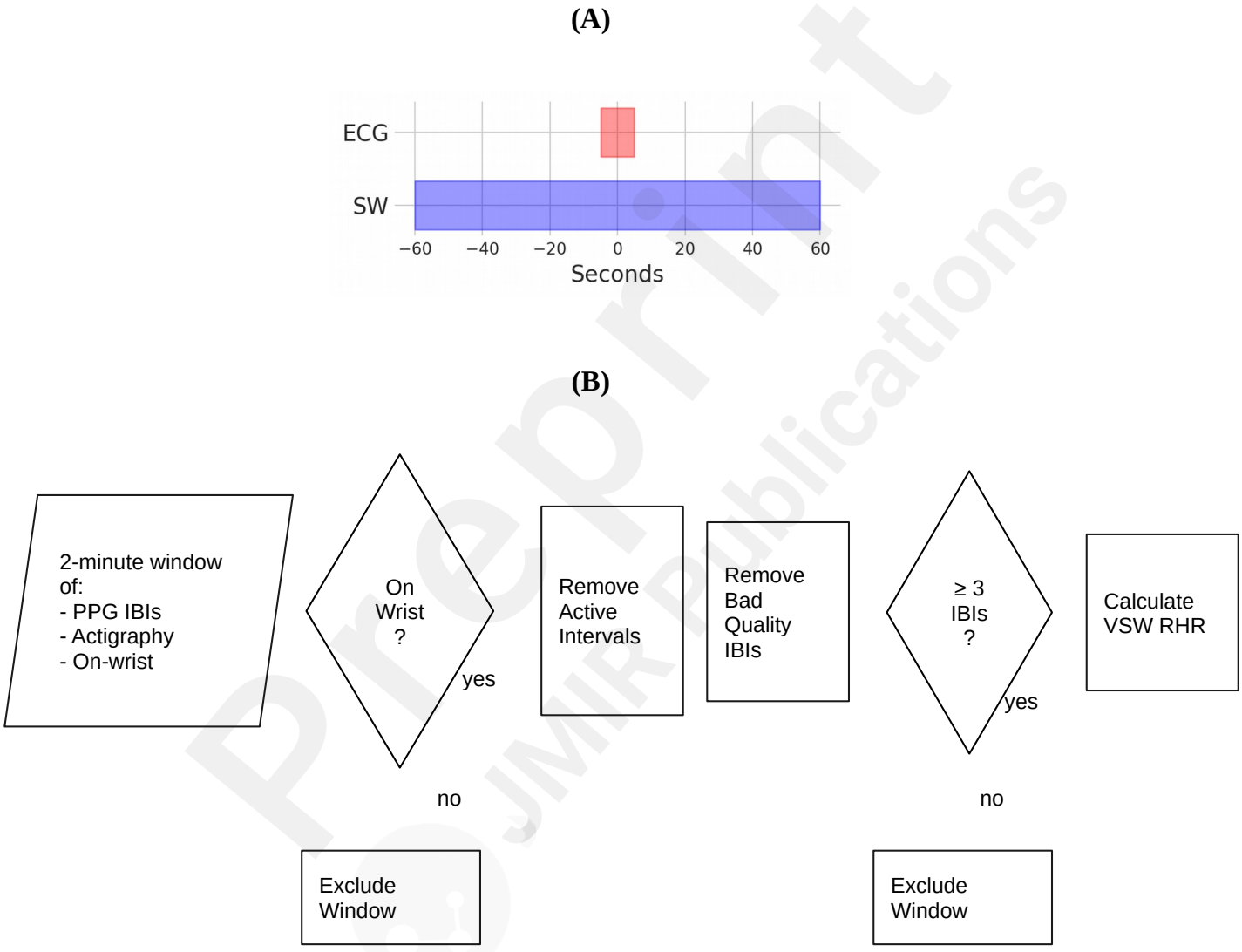
dataset.

- Actigraphy counts, which estimate the level of physical activity and are calculated every 30 seconds.
- On-wrist states, which indicate whether the VSW was worn or not, are computed every 1 minute, and every time the on-wrist state changes.

Since the goal of this analysis was to compare the RHR estimated by VSW to ECG RHR, we used the VSW sensor data captured during the ECG RHR measurement in order to evaluate the performance of the VSW RHR. Thus, we gathered VSW data using a 2-minute measurement window centered at the middle of the ECG acquisition period, as shown in **Figure 1A**.

## Figure 1: VSW RHR Determination

(A) The positioning of the 2-minute VSW data acquisition window relative to the 10-second ECG acquisition window in time. (B) Flowchart showing the processing steps to calculate the VSW RHR for each participant.




Abbreviations: ECG, electrocardiogram; VSW, Verily Study Watch; PPG, photoplethysmography; IBI, interbeat interval; VSW RHR, Verily Study Watch resting heart rate

The processing steps to calculate the VSW RHR for each participant is shown in **Figure 1B**. First, we gathered PPG IBIs, actigraphy counts, and on-wrist states in the 2-minute window mentioned above. Then, we excluded 2-minute windows containing any off-wrist states and we removed the IBIs associated with active intervals from the window (defined as any 30-second interval with a non-zero actigraphy count value, which we define as “Active”). Those intervals for which there was a zero actigraphy count were defined as “Still”. Finally, we removed the “bad” quality IBIs from the 2-minute window. If the remaining number of IBIs was less than 3, we excluded the participant; otherwise, we calculated the VSW RHR from the remaining IBIs as the following:

$$\text{VSW RHR} = \frac{60,000}{\frac{1}{N}\sum_{i=1}^{N} I_i}$$

where $I_i$ is the $i$th IBI value (milliseconds) in the 2-minute window, and N is the number of IBI values in the window.

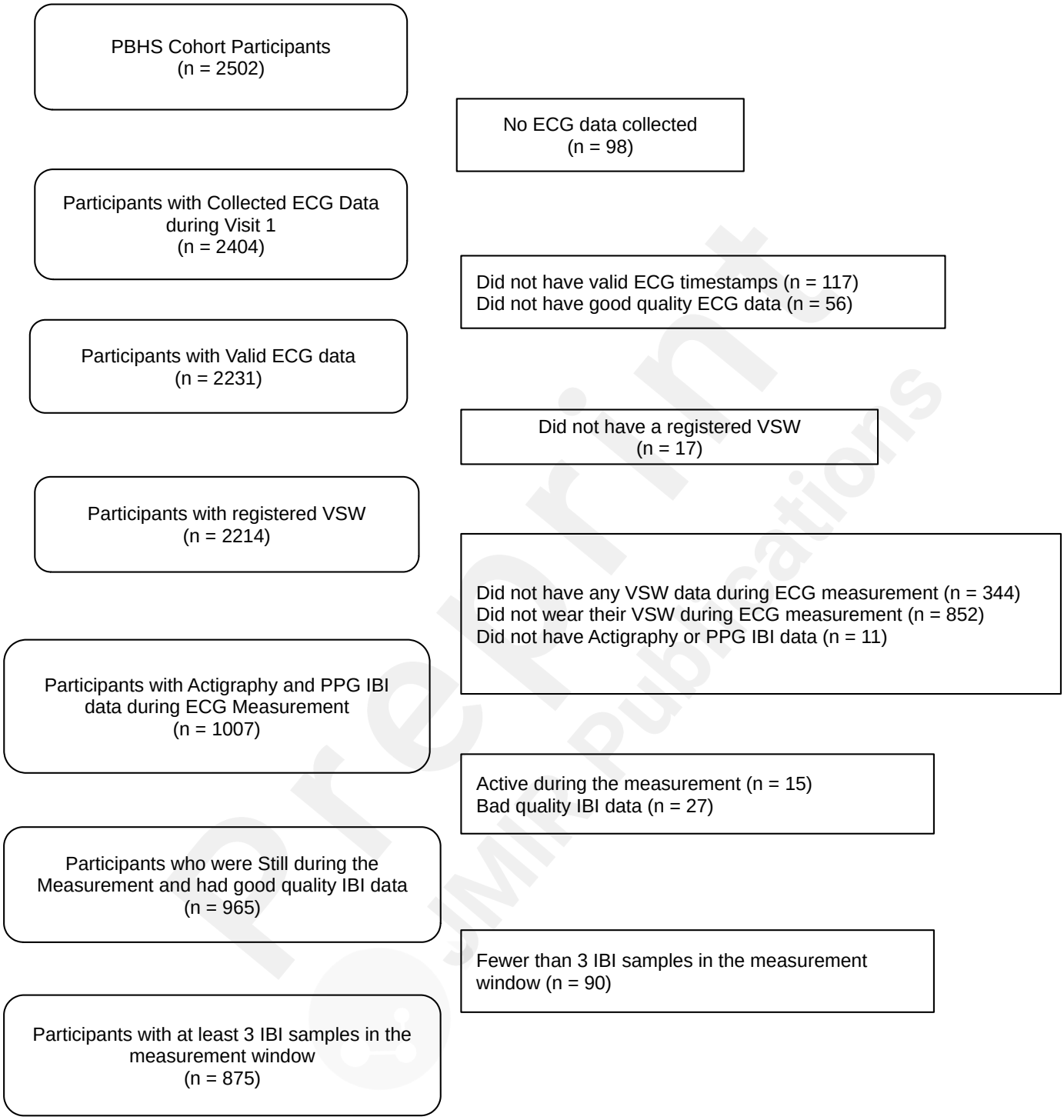
### *Mean daily steps in first 30 days*

Mean daily steps in the first 30 days of the study were calculated for each participant using previously validated step counts captured by the VSW RHR (13)(14). Specifically, daily step count values were averaged across the 30 days following enrollment, only considering days during which the participant wore the VSW for at least ten hours.

## Analysis Cohort

For this analysis, the cohort included only participants who fulfilled the following criteria: (1) recorded ECG RHR during the initial onsite visit and (2) concurrent RHR as recorded by the VSW. Additional exclusion criteria were applied during the VSW RHR calculation procedure, as described in the previous section. Inclusion and exclusion criteria are further described in **Figure 2**.

## Figure 2: Analysis Cohort Flowchart




Abbreviations: PBHS, Project Baseline Health Study; ECG, electrocardiogram; PPG, photoplethysmography; IBI, interbeat interval; VSW, Verily Study Watch

## Statistical Analysis

Descriptive statistics were calculated for selected demographic and other baseline characteristics. Categorical variables were reported as the number of participants with corresponding percentages, and continuous variables were reported as mean and standard deviation (SD).

In addition to descriptive statistics, tests for trend were used to evaluate the relationship between each characteristic and ordinal categories of VSW RHR, separately for males and females. Three VSW RHR categories were created using sex-specific percentile cutpoints: 0-25th, 25th-75th, and 75th-100th. The Cochran-Armitage Trend Test was used to evaluate binary variables, and Spearman Rank Correlation was used to evaluate categorical variables.

Associations with VSW RHR among candidate baseline characteristics were identified using multivariable linear regression models. Prior to modeling, missing data were imputed using five rounds of multiple imputation using chained equations (MICE) methods with predictive mean matching (PMM). Box-Cox transformations were used to approximate a normal distribution for continuous variables (laboratory values, vitals, and physical function measures). In addition to observed age, age-squared was added to the list of baseline variables to account for the inverted U-shaped relationship between age and VSW RHR.

Baseline characteristics were grouped into domains: (1) demographics and socioeconomic status (SES), (2) medical conditions, (3) vitals and physical function, (4) laboratory assessments, and (5) patient reported outcomes (PROs); separate models were built for each domain and separately for male and female. Elastic net (ENET) regularization methods were used to fit regression models. In order to address the multiply-imputed data, a stacked objective function (sENET) method was employed, with 5-fold cross-validation to penalize and select regression coefficients [15,16]. Due to limitations in computational power, ENET alpha values were restricted to 0.5 or 1, where alpha = 1 equates to a least absolute shrinkage and selection operator (LASSO) regression.

## RESULTS

### *Analysis cohort compared with overall PBHS cohort*

Using the criteria as described in **Figure 2**, the analysis cohort consisted of 875 participants: 519 (59%) female and 356 (41%) male. Selected baseline characteristics of the analysis cohort and the PBHS cohort are shown in **Table 1**.

**Table 1. Selected baseline characteristics of the analysis cohort and the PBHS**

| | | | PBHS Cohort (N = 2502) | Analysis Cohort (n = 875) |
|---|---|---|---|---|
| **Demographics** | Mean age at enrollment, years (SD) | | 50 (17.2) | 50.9 (16.5) |
| | Female, n (%) | | 1375 (55.0) | 519 (59.3) |
| | Race, n (%) | White | 1582 (63.2) | 575 (65.7) |
| | | Black | 400 (16.0) | 138 (15.8) |
| | | Asian | 260 (10.4) | 80 (9.1) |
| | | Other | 259 (10.4) | 82 (9.4) |
| | Hispanic, n (%) | | 290 (11.6) | 98 (11.2) |
| **Socioeconomic status, n (%)** | Married | | 1116 (44.6) | 433 (49.5) |
| | Employed | | 1523 (60.9) | 528 (60.3) |
| | Current or former smoker | | 881 (35.2) | 331 (37.8) |
| **Medical conditions, n (%)** | Asthma | | 371 (14.8) | 124 (14.2) |
| | Diabetes, type 2 | | 276 (11.0) | 112 (12.8) |
| | Generalized anxiety disorder | | 327 (13.1) | 121 (13.8) |
| | GERD | | 424 (16.9) | 176 (20.1) |
| | Hypertension | | 675 (27.0) | 262 (29.9) |
| | Hypercholesterolemia | | 314 (12.5) | 118 (13.5) |
| | Major depressive disorder | | 354 (14.1) | 142 (16.2) |
| | Migraines | | 306 (12.2) | 116 (13.3) |
| | Osteoarthritis | | 477 (19.1) | 179 (20.5) |
| | Sleep apnea | | 245 (9.8) | 88 (10.1) |
| **Vitals** | Mean systolic BP (SD) | | 123.4 (16) | 125 (15.5) |
| | Mean diastolic BP (SD) | | 75.9 (9.9) | 77.4 (9.9) |
| | Mean BMI (SD) | | 28.4 (6.9) | 29.4 (7.1) |
| | Mean 6-minute walk distance, m (SD) | | 474.5 (82.7) | 475.4 (88.2) |

| | | | |
|---|---|---|---|
| **Physical performance** | Mean Left ventricular ejection fraction (SD) | 58.7 (4.2) | 58.6 (4.5) |
| **Labs** | Mean hemoglobin A1C (SD) | 5.7 (1.0) | 5.8 (1.1) |
| | Mean hemoglobin, g/dL (SD) | 14.2 (1.3) | 14.1 (1.3) |
| | Mean white blood cell count, thousand/mcl (SD) | 6.4 (1.9) | 6.6 (1.9) |
| | Mean MDRD (eGFR) (SD) | 88.3 (20.4) | 87.5 (21.1) |
| | Mean C-reactive protein, mg/L (SD) | 2.9 (5.9) | 3.4 (7.2) |
| **Patient-reported outcomes** | Mean PHQ-9 score (SD) | 3.7 (4.2) | 3.9 (4.3) |
| | Mean GAD-7 score (SD) | 3.2 (4.1) | 3.3 (4.2) |

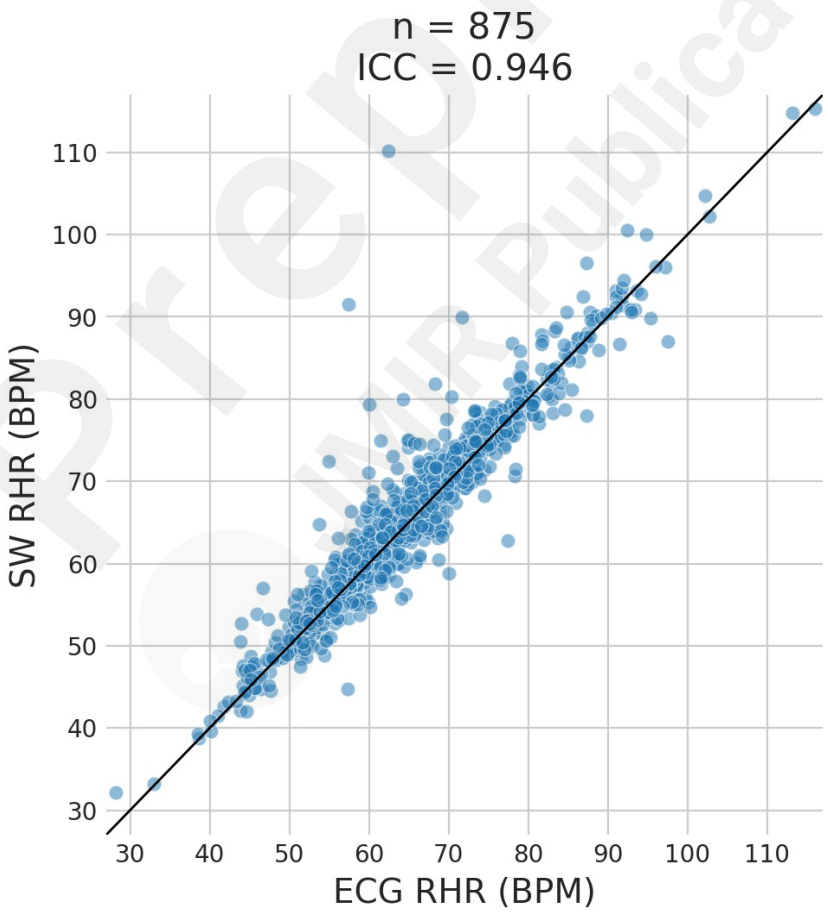
BMI = body mass index; BP = blood pressure; eGFR = estimated glomerular filtration rate; GAD-7 = general anxiety disorder -7; GERD = gastro-esophageal reflux disease; MDRD = modification of diet in renal disease ; PBHS = Project Baseline Health Study; PHQ-9 = patient health questionnaire -9; SD = standard deviation

### Study watch validity

The comparison of the RHR by ECG with VSW is shown in **Figure 3**. There was excellent reliability between the two measures with an intraclass correlation coefficient of 0.946. An agreement plot between RHR by ECG and VSW of all participants also showed high consistency between the two measures (**Multimedia Appendix Figure 1**).

**Figure 3. Correlation between baseline ECG-based and Study Watch measured RHR.** Each dot corresponds to one participant. There is excellent reliability between ECG RHR and VSW RHR (intraclass correlation coefficient of 0.946).

BPM = beats per minute; ECG=electrocardiogram; ICC=Intraclass correlation coefficient; RHR=resting heart rate; SW=study watch

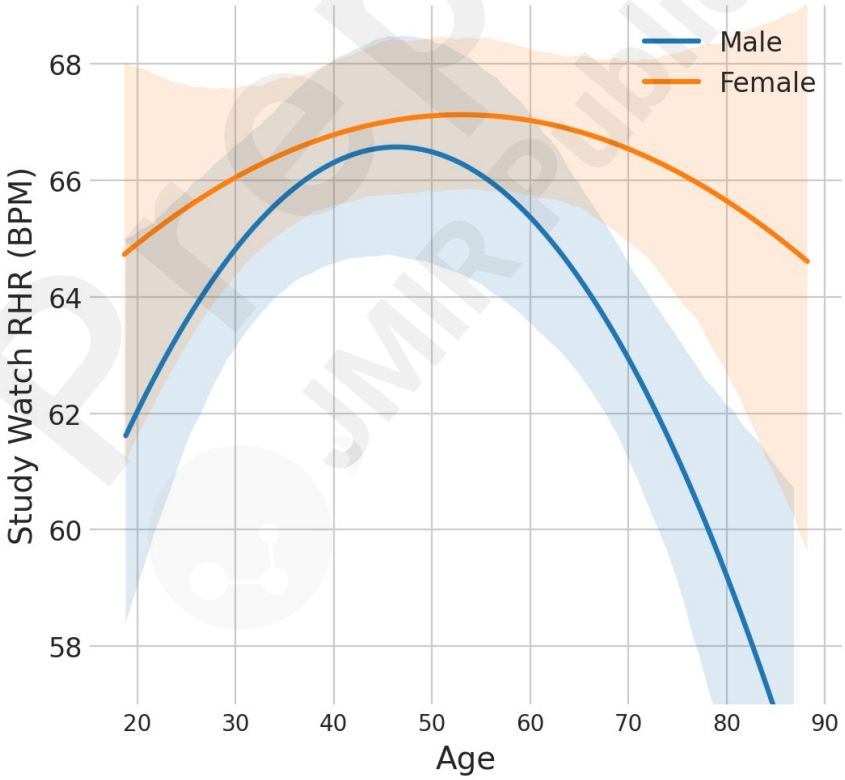


*Analysis cohort baseline characteristics by sex and resting heart rate (age-adjusted)*

The VSW RHR as a function of age and sex is shown in **Figure 4**, with both curves demonstrating the expected upside-down U-shaped relationship (10). The mean and standard deviation of VSW RHR was 66.6 ± 11.2 beats per minute (bpm) for female participants, and 64.4 ± 12.3 bpm for male participants. For ECG RHR, the mean and standard deviation were 65.8 ± 10.9 bpm for females, and 63.7 ± 12.0 bpm for males.

**Figure 4. Baseline SW RHR by age and sex.** A U-shaped curve was observed for both female and male participants when VSW RHR was plotted against age. The lines show fitted quadratic models to female and male data, separately. The shaded areas show the 95% confidence intervals of the models.

BPM = beats per minute; RHR=resting heart rate




The study cohort was then separated by sex and stratified by VSW RHR to assess for trends of selected baseline characteristics: demographics and SES (**Tables 2a-b**); vitals, physical function, and

laboratory assessments (**Tables 3a-b**); and medical conditions and participant reported outcomes (PROs) (**Tables 4a-b**). Full variable comparison lists are included in **the Multimedia Appendix Tables 1-3**.

**Table 2. Analysis cohort: Selected demographics and socioeconomic status at baseline.**

**a. female participants**

| | | VSW RHR percentile* | | | |
|---|---|---|---|---|---|
| | | **0-25th (n = 130)** | **25-75th (n = 259)** | **75-100th (n = 130)** | **p-value** |
| Mean age, years (SD) | | 48.7 (16.3) | 51.1 (16.1) | 49.3 (15.8) | 0.7635 |
| Race, n (%) | White | 93 (71.5) | 164 (63.3) | 83 (63.8) | 0.1924 |
| | Black | 18 (13.8) | 44 (17.0) | 26 (20.0) | 0.1865 |
| | Asian | 10 (7.7) | 27 (10.4) | 6 (4.6) | 0.3686 |
| | Other (NHPI, AIAN, Other) | 9 (6.9) | 24 (9.3) | 15 (11.5) | 0.1994 |
| Hispanic ethnicity, n (%) | | 14 (10.8) | 40 (15.4) | 17 (13.1) | 0.5886 |
| Education, n (%) | High school or less | 11 (9.7) | 21 (9.5) | 24 (20.9) | 0.0107 |
| | Any college | 65 (57.5) | 143 (64.7) | 66 (57.4) | 0.9761 |
| | Graduate degree or higher | 37 (32.7) | 57 (25.8) | 25 (21.7) | 0.0604 |
| Income, n (%) | < $100,000 | 58 (51.3) | 123 (55.7) | 82 (71.3) | 0.0022 |
| | > $100,000 | 46 (40.7) | 82 (37.1) | 25 (21.7) | 0.0025 |
| Marital status, n (%) | Married | 63 (55.8) | 131 (59.3) | 50 (43.5) | 0.0614 |
| | Divorced or separated | 21 (18.6) | 36 (16.3) | 22 (19.1) | 0.9103 |
| | Single | 24 (21.2) | 43 (19.5) | 33 (28.7) | 0.1738 |
| | Widowed | 3 (2.7) | 7 (3.2) | 10 (8.7) | 0.0267 |
| Employment status, n (%) | Employed or homemaker | 92 (74.2) | 164 (68.3) | 69 (57.5) | 0.0057 |
| | Unemployed | 6 (4.8) | 17 (7.1) | 24 (20.0) | <0.0001 |

| | | | | | |
|---|---|---|---|---|---|
| | Retired | 19 (15.3) | 52 (21.7) | 23 (19.2) | 0.4399 |
| | Student | 5 (4.0) | 4 (1.7) | 2 (1.7) | 0.2119 |
| Insured (health insurance, yes), n (%) | | 109 (96.5) | 202 (91.4) | 101 (89.4) | 0.0479 |
| Smoking status, n (%) | Current smoker | 12 (9.2) | 41 (15.8) | 31 (23.8) | 0.0014 |
| | Former smoker | 27 (20.8) | 54 (20.8) | 24 (18.5) | 0.6436 |
| | Never smoker | 91 (70.0) | 164 (63.3) | 75 (57.7) | 0.0394 |

* Percentile cutpoints for females: 25th = 59.38 bpm; 75th = 73.66 bpm. Shading for significant observations. AIAN=American Indians and Alaska Natives ; NHPI=Native Hawaiian, and Pacific Islander ; RHR=resting heart rate; SD=standard deviation; VSW=Verily study watch

## b. male participants

| | | VSW RHR percentile* | | | |
|---|---|---|---|---|---|
| | | **0-25th (n = 89)** | **25-75th (n = 178)** | **75-100th (n = 89)** | **p-value** |
| Mean age, years (SD) | | 55.5 (16.6) | 50.7 (18.5) | 51.6 (14.3) | 0.1055 |
| Race, n (%) | White | 71 (79.8) | 107 (60.1) | 57 (64.0) | 0.027 |
| | Black | 11 (12.4) | 24 (13.5) | 15 (16.9) | 0.3889 |
| | Asian | 4 (4.5) | 24 (13.5) | 9 (10.1) | 0.2201 |
| | Other (NHPI, AIAN, Other) | 3 (3.4) | 23 (12.9) | 8 (9.0) | 0.2029 |
| Hispanic ethnicity, n (%) | | 6 (6.7) | 12 (6.7) | 9 (10.1) | 0.3964 |
| Education, n (%) | High school or less | 7 (9.7) | 16 (10.7) | 12 (15.4) | 0.2757 |
| | Any college | 34 (47.2) | 74 (49.7) | 48 (61.5) | 0.076 |
| | Graduate degree or higher | 31 (43.1) | 59 (39.6) | 18 (23.1) | 0.01 |
| Income, n (%) | < $100,000 | 34 (47.2) | 80 (53.7) | 41 (52.6) | 0.5256 |
| | > $100,000 | 35 (48.6) | 64 (43.0) | 28 (35.9) | 0.1152 |
| Marital status, n (%) | Married | 57 (79.2) | 86 (57.7) | 46 (59.0) | 0.0124 |
| | Divorced or separated | 5 (6.9) | 11 (7.4) | 7 (9.0) | 0.6378 |

| | | | | | |
|---|---|---|---|---|---|
| | Single | 9 (12.5) | 49 (32.9) | 22 (28.2) | 0.0358 |
| | Widowed | 0 (0.0) | 1 (0.7) | 2 (2.6) | 0.2768 |
| Employment status, n (%) | Employed or homemaker | 43 (53.8) | 103 (65.6) | 57 (67.1) | 0.0806 |
| | Unemployed | 9 (11.2) | 9 (5.7) | 11 (12.9) | 0.6738 |
| | Retired | 28 (35.0) | 40 (25.5) | 16 (18.8) | 0.0185 |
| | Student | 0 (0.0) | 4 (2.5) | 1 (1.2) | 0.7997 |
| Insured (health insurance, yes), n (%) | | 69 (95.8) | 137 (91.9) | 67 (85.9) | 0.0304 |
| Smoking status, n (%) | Current smoker | 16 (18.0) | 22 (12.4) | 17 (19.1) | 0.8359 |
| | Former smoker | 21 (23.6) | 41 (23.0) | 25 (28.1) | 0.486 |
| | Never smoker | 52 (58.4) | 115 (64.6) | 47 (52.8) | 0.4447 |

* Percentile cutpoints for males: 25th = 55.50 bpm; 75th = 72.25 bpm. Shading for significant observations. AIAN=American Indians and Alaska Natives; NHPI=Native Hawaiian, and Pacific Islander ; RHR=resting heart rate; SD=standard deviation; VSW=Verily study watch

## Table 3. Analysis cohort: Selected vitals, physical function, and labs at baseline.

## a. female participants

| | | VSW RHR percentile* | | | |
|---|---|---|---|---|---|
| | | **0-25th (n = 130)** | **25-75th (n = 259)** | **75-100th (n = 130)** | **p-value** |
| Vitals | Mean systolic blood pressure (SD) | 119.5 (15.2) | 122.6 (15.5) | 126.5 (15.6) | 0.0002 |
| | Mean diastolic blood pressure (SD) | 73.2 (8.3) | 76.0 (9.2) | 81.1 (10.0) | <0.0001 |
| | Mean waist circumference, cm (SD) | 85.3 (14.4) | 89.8 (15.9) | 98.5 (18.0) | <0.0001 |
| | Mean BMI (SD) | 27.1 (6.4) | 28.5 (6.7) | 32.9 (8.4) | <0.0001 |
| Phys. function | Mean 6-minute walk (SD) | 498.1 (82.7) | 469.3 (81.9) | 433.8 (93.0) | <0.0001 |
| | Mean 10-meter walk speed (SD) | 2.0 (0.6) | 1.9 (0.4) | 1.8 (0.5) | 0.0086 |
| | Mean handgrip (SD) | 28.9 (6.9) | 28.1 (6.9) | 27.4 (7.0) | 0.2264 |

| | | | | | |
|---|---|---|---|---|---|
| | Mean leg balance time (SD) | 44.3 (20.6) | 39.8 (22.1) | 37.8 (23.1) | 0.0159 |
| | Mean sit-rise score (SD) | 7.5 (2.3) | 6.9 (2.5) | 7.0 (2.4) | 0.1137 |
| | Mean 30-second chair stand (SD) | 14.8 (4.7) | 13.9 (5.0) | 12.9 (4.3) | 0.0016 |
| | Mean ejection fraction at rest (SD) | 59.0 (3.6) | 59.4 (4.3) | 58.5 (5.4) | 0.3258 |
| | Mean coronary calcium score (SD) | 66.6 (214.3) | 60.9 (250.0) | 76.6 (249.1) | 0.0289 |
| | Ankle brachial index abnormal, n (%) | 4 (3.1) | 10 (3.9) | 3 (2.5) | 0.7888 |
| | Mean FEV1/FVC (SD) | 0.8 (0.1) | 0.8 (0.1) | 0.8 (0.1) | 0.2469 |
| | Mean daily steps in first 30 days (SD) | 8360 (2990) | 8040 (3187) | 6865 (3243) | 0.0001 |
| Labs | Mean hemoglobin, g/dL (SD) | 13.5 (1.0) | 13.5 (1.2) | 13.7 (1.2) | 0.099 |
| | Mean serum creatinine, mg/dL (SD) | 0.8 (0.1) | 0.8 (0.2) | 0.8 (0.2) | 0.1922 |
| | Mean HDL, mg/dL (SD) | 66.4 (18.4) | 64.3 (20.5) | 57.2 (14.4) | <0.0001 |
| | Mean LDL, mg/dL (SD) | 96.0 (29.1) | 105.5 (33.9) | 105.8 (30.4) | 0.0175 |
| | Mean HbA1c, % (SD) | 5.4 (0.7) | 5.6 (0.8) | 6.0 (1.5) | <0.0001 |
| | Mean C-reactive protein, mg/L (SD) | 2.3 (4.1) | 3.3 (5.1) | 5.6 (8.2) | <0.0001 |
| | Mean blood glucose, mg/dL (SD) | 88.7 (19.0) | 94.1 (27.2) | 108.9 (54.6) | <0.0001 |
| | Mean hematocrit, % (SD) | 41.2 (2.9) | 41.2 (3.4) | 42.0 (3.5) | 0.0465 |
| | Mean platelets, per uL (SD) | 249,836 (56,779) | 259,269 (61,124) | 278,790 (61,889) | 0.0002 |
| | Mean WBC count, thousand/uL (SD) | 6.2 (1.6) | 6.5 (1.8) | 7.5 (2.2) | <0.0001 |
| | Mean sodium, mEq/L (SD) | 139.0 (1.8) | 138.8 (2.1) | 138.6 (2.2) | 0.1538 |
| | Mean GFR MDRD, ml/min (SD) | 86.2 (19.2) | 87.5 (20.1) | 91.0 (24.9) | 0.1876 |
| | Mean TSH, mIU/L (SD) | 1.5 (0.8) | 1.6 (1.2) | 1.6 (0.9) | 0.3462 |

* Percentile cutpoints for females: 25th = 59.38 bpm; 75th = 73.66 bpm. Shading for significant observations. BMI=body mass index; FEV1/FVC=forced expiratory volume in 1 s /forced vital capacity; HbA1c=glycated hemoglobin A1c; HDL=high-density lipoprotein; LDL=low-density lipoprotein; GFR MDRD=glomerular filtration rate, modification of diet in renal disease; RHR=resting heart rate; SD=standard deviation; TSH=thyroid-stimulating hormone; VSW=Verily study watch; WBC=white blood cell.

## b. male participants

| | | VSW RHR percentile* | | | |
|---|---|---|---|---|---|
| | | 0-25th (n = 89) | 25-75th (n = 178) | 75-100th (n = 89) | p-value |
| Vitals | Mean systolic blood pressure (SD) | 127.7 (16.2) | 128.1 (14.1) | 129.3 (14.3) | 0.3677 |
| | Mean diastolic blood pressure (SD) | 76.1 (10.4) | 78.3 (9.7) | 81.2 (10.1) | 0.0015 |
| | Mean waist circumference, cm (SD) | 95.5 (12.3) | 98.7 (15.7) | 108.4 (18.5) | <0.0001 |
| | Mean BMI (SD) | 27.6 (4.5) | 29.3 (5.7) | 32.5 (8.5) | <0.0001 |
| Phys. Function | Mean 6-minute walk (SD) | 501.5 (83.1) | 490.2 (89.8) | 465.2 (84.6) | 0.0017 |
| | Mean 10-meter walk speed (SD) | 2.1 (0.6) | 2.1 (0.6) | 1.9 (0.5) | 0.0211 |
| | Mean handgrip (SD) | 46.0 (9.4) | 44.5 (10.6) | 42.4 (10.3) | 0.0879 |
| | Mean leg balance time (SD) | 38.4 (22.8) | 37.7 (23.1) | 30.6 (22.6) | 0.0117 |
| | Mean sit-rise score (SD) | 7.5 (2.1) | 7.0 (2.3) | 6.7 (2.3) | 0.0152 |
| | Mean 30-second chair stand (SD) | 15.4 (5.3) | 14.9 (5.5) | 13.4 (4.4) | 0.0015 |
| | Mean ejection fraction at rest (SD) | 58.2 (3.7) | 57.7 (4.7) | 58.7 (4.4) | 0.7558 |
| | Mean coronary calcium score (SD) | 361.8 (1012.1) | 254.6 (653.9) | 209.5 (632.9) | 0.9963 |
| | Ankle brachial index abnormal, n (%) | 3 (3.5%) | 7 (3.9%) | 2 (2.3%) | 0.6548 |
| | Mean FEV1/FVC (SD) | 0.7 (0.1) | 0.8 (0.1) | 0.8 (0.1) | 0.0034 |
| | Mean daily steps in first 30 days (SD) | 8970 (3994) | 8565 (3537) | 7869 (4120) | 0.0746 |
| Labs | Mean hemoglobin, g/dL (SD) | 14.8 (0.9) | 14.9 (1.0) | 15.1 (1.1) | 0.0247 |
| | Mean serum creatinine, mg/dL (SD) | 1.0 (0.2) | 1.0 (0.3) | 1.1 (0.5) | 0.9464 |
| | Mean HDL, mg/dL (SD) | 54.3 (17.4) | 48.3 (15.4) | 43.9 (12.8) | <0.0001 |
| | Mean LDL, mg/dL (SD) | 93.3 (36.3) | 95.0 (33.1) | 101.6 (38.5) | 0.2222 |
| | Mean HbA1c, % (SD) | 5.5 (0.5) | 5.7 (1.0) | 6.5 (1.9) | 0.0034 |
| | Mean C-reactive protein, mg/L (SD) | 3.0 (14.4) | 2.5 (4.5) | 4.6 (7.3) | <0.0001 |
| | Mean blood glucose, mg/dL (SD) | 92.2 (12.4) | 102.0 (35.9) | 130.1 (72.8) | <0.0001 |

| | | | | |
|---|---|---|---|---|
| Mean hematocrit, % (SD) | 44.7 (2.9) | 45.2 (3.1) | 45.8 (3.2) | 0.0126 |
| Mean platelets, per uL (SD) | 212,529 (48,991) | 228,567 (53,411) | 248,264 (68,746) | 0.0001 |
| Mean WBC count, thousand/uL (SD) | 6.2 (1.9) | 6.2 (1.5) | 6.9 (1.9) | 0.0095 |
| Mean sodium, mEq/L (SD) | 139.4 (1.7) | 138.9 (2.1) | 138.6 (2.4) | 0.0218 |
| Mean GFR MDRD, ml/min (SD) | 84.3 (16.5) | 88.2 (20.7) | 86.6 (25.2) | 0.3824 |
| Mean TSH, mIU/L (SD) | 1.8 (1.0) | 1.9 (1.1) | 1.7 (0.9) | 0.7056 |

* Percentile cutpoints for males: 25th = 55.50 bpm; 75th = 72.25 bpm. Shading for significant observations. BMI=body mass index; FEV1/FVC=forced expiratory volume in 1 s /forced vital capacity; HbA1c=glycated hemoglobin A1c; HDL=high-density lipoprotein; LDL=low-density lipoprotein; GFR MDRD=glomerular filtration rate, modification of diet in renal disease; RHR=resting heart rate; SD=standard deviation; TSH=thyroid-stimulating hormone; VSW=Verily study watch; WBC=white blood cell.

## Table 4. Analysis cohort: Selected medical conditions and participant-reported outcomes (PROs) at baseline

### a. female participants

| | | VSW RHR percentile* | | | |
|---|---|---|---|---|---|
| | | **0-25th (n = 130)** | **25-75th (n = 259)** | **75-100th (n = 130)** | **p-value** |
| Medical history, n (%) | Asthma | 16 (12.3%) | 35 (13.5%) | 23 (17.7%) | 0.2148 |
| | Cataracts | 12 (9.2%) | 38 (14.7%) | 22 (16.9%) | 0.0731 |
| | Colon polyps | 7 (5.4%) | 26 (10.0%) | 10 (7.7%) | 0.5001 |
| | Major depressive disorder | 15 (11.5%) | 43 (16.6%) | 29 (22.3%) | 0.0202 |
| | Diabetes type 2 | 6 (4.6%) | 27 (10.4%) | 26 (20.0%) | <0.0001 |
| | GERD | 20 (15.4%) | 42 (16.2%) | 36 (27.7%) | 0.0113 |
| | Hypertension | 27 (20.8%) | 70 (27.0%) | 40 (30.8%) | 0.0677 |
| | Hypercholesterolemia | 14 (10.8%) | 40 (15.4%) | 13 (10.0%) | 0.8534 |
| | Osteoarthritis | 25 (19.2%) | 49 (18.9%) | 32 (24.6%) | 0.282 |

| | | | | | |
|---|---|---|---|---|---|
| | Sleep apnea | 6 (4.6%) | 16 (6.2%) | 11 (8.5%) | 0.2042 |
| PROs, mean (SD) scores | Sheehan Disability Scale | 2.9 (4.5) | 2.7 (4.8) | 5.0 (7.6) | 0.0971 |
| | PHQ-9 | 3.4 (3.6) | 3.6 (4.0) | 5.4 (4.8) | 0.0002 |
| | GAD-7 | 3.2 (3.9) | 3.4 (4.1) | 4.1 (4.9) | 0.2798 |
| | WHODAS 2.0 | 2.2 (3.3) | 3.0 (4.4) | 5.0 (6.7) | <0.0001 |
| | BRFSS ACE | 2.2 (2.2) | 2.4 (2.3) | 2.7 (2.6) | 0.2394 |
| | PROMIS pain intensity | 6.0 (2.3) | 6.1 (2.3) | 7.0 (2.8) | 0.0152 |
| | PROMIS pain interference | 10.2 (5.1) | 10.5 (5.2) | 12.2 (6.3) | 0.0295 |
| | PANAS positive affect | 34.7 (6.4) | 34.8 (7.0) | 33.0 (7.3) | 0.0792 |
| | PANAS negative affect | 15.6 (6.7) | 15.5 (6.5) | 15.0 (6.1) | 0.4481 |
| | Subjective Happiness | 21.6 (4.8) | 21.7 (4.8) | 20.9 (4.3) | 0.1264 |
| | Satisfaction with Life | 26.1 (6.6) | 25.9 (6.3) | 24.2 (7.4) | 0.0437 |
| | Perceived Social Support | 70.1 (11.8) | 66.8 (15.2) | 66.9 (13.9) | 0.0811 |
| | AUDIT-C | 2.0 (1.5) | 2.0 (1.9) | 1.9 (1.8) | 0.3505 |

* Percentile cutpoints for females: 25th = 59.38 bpm; 75th = 73.66 bpm. Shading for significant observations. AUDIT-C=Alcohol Use Disorders Identification Test-Concise; BRFSS ACE=Behavioral Risk Factor Surveillance System Adverse Childhood Experience ; GAD-7 = general anxiety disorder -7; GERD = gastro-esophageal reflux disease; PHQ-9 = patient health questionnaire -9; PANAS=Positive and Negative Affect Schedule ; PROMIS=Patient-Reported Outcomes Measurement Information System; RHR=resting heart rate; SD = standard deviation; VSW= Verily study watch; WHODAS=World Health Organization Disability Assessment Schedule

## b. male participants

| | | VSW RHR percentile* | | | |
|---|---|---|---|---|---|
| | | **0-25th e (n = 89)** | **25-75th (n = 178)** | **75-100th (n = 89)** | **p-value** |
| Medical history, n (%) | Asthma | 12 (13.5) | 22 (12.4) | 16 (18.0) | 0.3889 |
| | Cataracts | 14 (15.7) | 28 (15.7) | 5 (5.6) | 0.0466 |
| | Colon polyps | 14 (15.7) | 23 (12.9) | 6 (6.7) | 0.0661 |
| | Major depressive disorder | 8 (9.0) | 28 (15.7) | 19 (21.3) | 0.0227 |
| | Diabetes type 2 | 3 (3.4) | 23 (12.9) | 27 (30.3) | <0.0001 |
| | GERD | 21 (23.6) | 37 (20.8) | 20 (22.5) | 0.8564 |

| | | | | | |
|---|---|---|---|---|---|
| | Hypertension | 29 (32.6) | 61 (34.3) | 35 (39.3) | 0.3468 |
| | Hypercholesterolemia | 15 (16.9) | 27 (15.2) | 9 (10.1) | 0.1999 |
| | Osteoarthritis | 21 (23.6) | 33 (18.5) | 19 (21.3) | 0.7108 |
| | Sleep apnea | 9 (10.1) | 29 (16.3) | 17 (19.1) | 0.0976 |
| PROs, mean scores (SD) | Sheehan Disability Scale | 3.3 (6.6) | 3.1 (5.6) | 4.2 (5.7) | 0.0587 |
| | PHQ-9 | 3.2 (4.1) | 3.8 (4.4) | 4.6 (4.4) | 0.0149 |
| | GAD-7 | 2.1 (3.2) | 2.9 (4.0) | 3.9 (4.8) | 0.0207 |
| | WHODAS 2.0 | 2.2 (4.5) | 3.2 (5.2) | 4.4 (5.4) | <0.0001 |
| | BRFSS ACE | 1.6 (1.9) | 1.9 (2.2) | 2.7 (2.6) | 0.0115 |
| | PROMIS pain intensity | 6.1 (2.7) | 6.4 (2.3) | 6.5 (2.5) | 0.1839 |
| | PROMIS pain interference | 10.0 (5.7) | 10.6 (4.7) | 12.4 (6.1) | 0.0025 |
| | PANAS positive affect score | 35.5 (7.7) | 33.7 (7.6) | 32.1 (8.1) | 0.0095 |
| | PANAS negative affect | 14.9 (5.7) | 15.2 (5.9) | 15.1 (5.8) | 0.9349 |
| | Subjective Happiness | 22.0 (4.3) | 20.7 (4.8) | 18.9 (4.6) | <0.0001 |
| | Satisfaction with Life | 26.1 (6.6) | 24.7 (6.7) | 22.5 (6.2) | 0.0001 |
| | Perceived Social Support | 65.8 (13.8) | 61.6 (16.7) | 59.3 (14.5) | 0.0025 |
| | AUDIT-C | 2.3 (1.7) | 2.1 (1.8) | 1.8 (1.8) | 0.0222 |

* Percentile cutpoints for males: 25th = 55.50 bpm; 75th = 72.25 bpm. Shading for significant observations. AUDIT-C=Alcohol Use Disorders Identification Test-Concise; BRFSS ACE=Behavioral Risk Factor Surveillance System Adverse Childhood Experience ; GAD-7 = general anxiety disorder -7; GERD = gastro-esophageal reflux disease; PHQ-9 = patient health questionnaire -9; PANAS=Positive and Negative Affect Schedule ; PROMIS=Patient-Reported Outcomes Measurement Information System; RHR=resting heart rate; SD = standard deviation; VSW= Verily study watch; WHODAS=World Health Organization Disability Assessment Schedule

There were similar trends seen in female and male participants. For instance, from a SES standpoint, those with higher baseline VSW RHR were more likely to have lower household income, less likely to be married, less likely to have healthcare insurance, and more likely to be smokers.

Medical conditions such as major depressive disorder, type 2 diabetes mellitus, hypertension, and sleep apnea were also more common in those with higher VSW RHR.

Participants with higher VSW RHR tended to have higher systolic and diastolic blood pressures, body mass index (BMI), and waist circumference.

In terms of laboratory assessments, those with higher VSW RHR tended to have hemoglobin A1c %, C-reactive protein levels, and white blood cell counts.

Participants with higher VSW RHR had shorter 6-minute walk distances and fewer mean daily steps as recorded by the VSW.

From a PRO standpoint, participants with higher VSW RHR had higher PHQ-9 scores and WHODAS 2.0 scores.

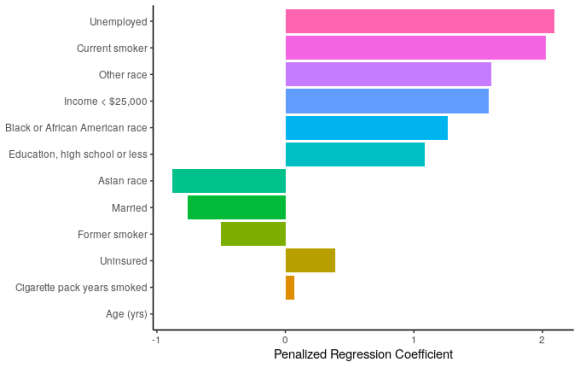
*Associations with VSW RHRs by domain*

The results of the sex-stratified sENET regression models are presented in **Figure 5**. Penalized regression coefficients reflect the relative strength and direction of each association based on standardized predictors. Within each domain of baseline characteristics (demographics and SES, medical conditions, vitals and physical function, laboratory assessments, and PROs), analyses showed that different characteristics were associated with VSW RHR in females compared with male participants. For instance, in the demographics and SES domain, unemployment had the highest association with VSW RHR in females, whereas lack of health insurance had the highest association in male participants. This was the case in the medical conditions, laboratory assessments, and PRO domains as well. For the vitals and physical function domain, the diastolic blood pressure was the most associated characteristic with VSW RHR for both sexes.

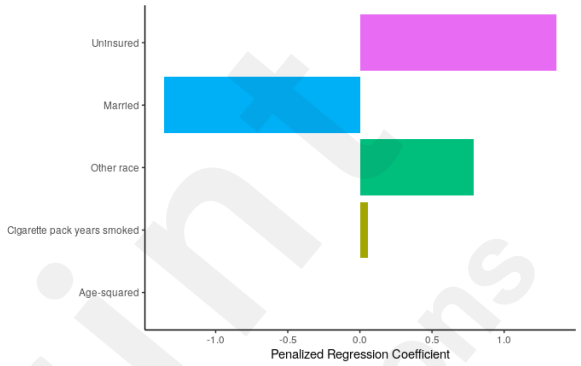
## Figure 5. LASSO regressions

### (A) Demographics and socioeconomic status

#### Female

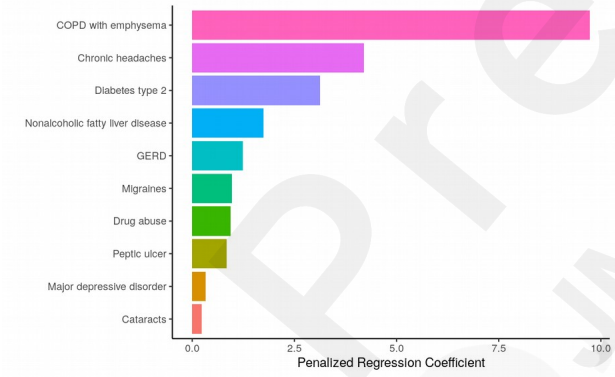



#### Male

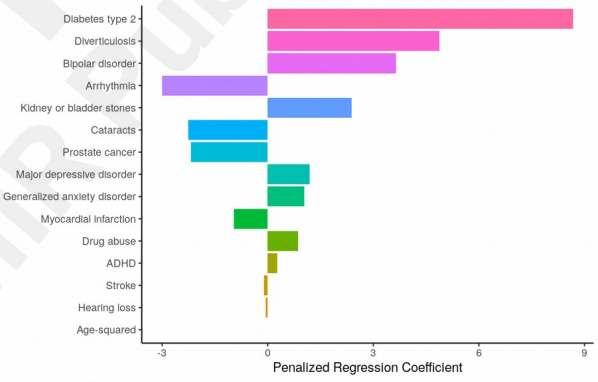



### (B) Medical conditions

#### Female

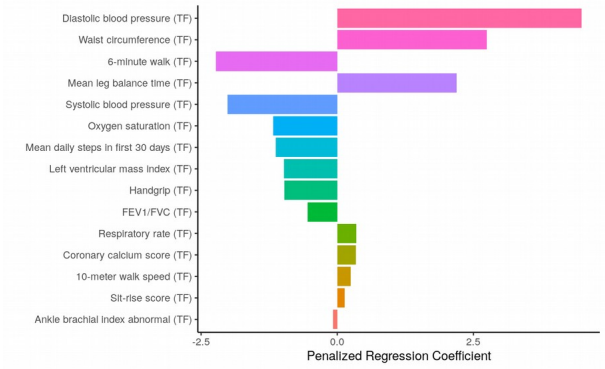



#### Male

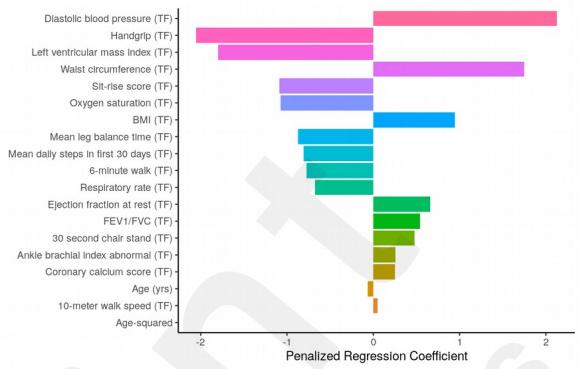


## (C) Vitals and physical function

### Female

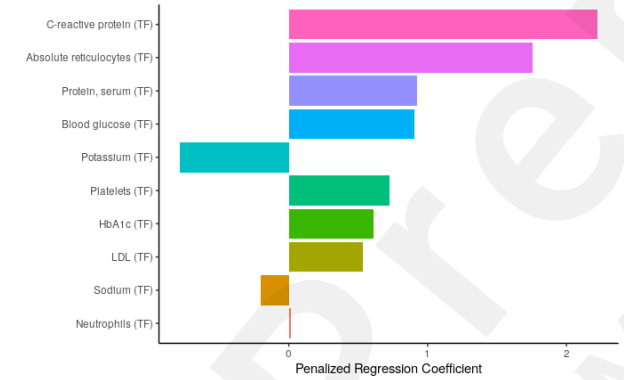



### Male

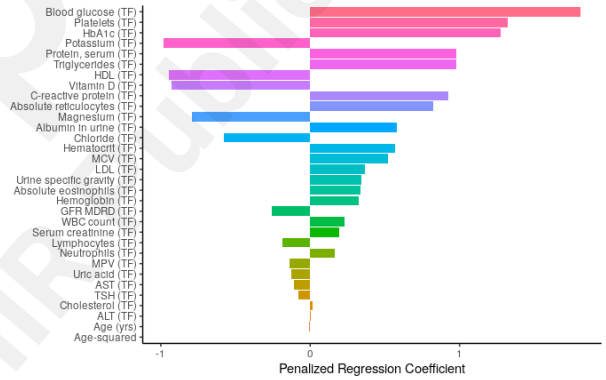



## (D) Laboratory assessments

### Female

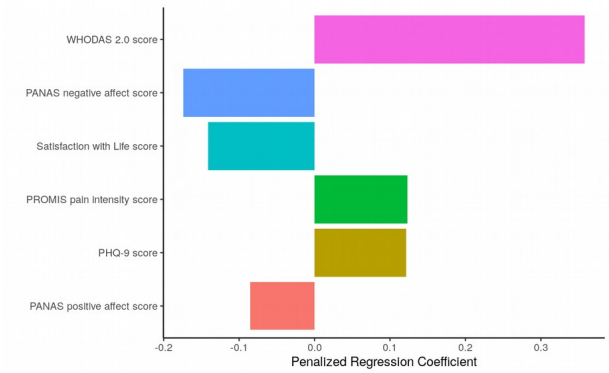



### Male

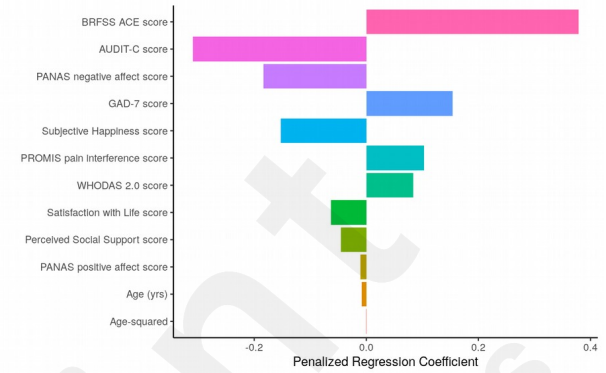


## (E) Patient reported outcomes

### Female




### Male



## DISCUSSION

These analyses from a large deeply phenotyped population show (1) strong agreement between ECG determined RHR and a proprietary VSW determined RHR, (2) significant trends of VSW RHR with clinically important baseline characteristics, and (3) clinical baseline characteristics highly associated with VSW RHR. These findings demonstrate that, in a relatively heterogeneous cohort of participants, RHR can be measured easily and accurately using a wearable device and may have utility in light of strong associations with clinically relevant baseline characteristics.

In the last decade, use of consumer wearables with ability to detect HR and arrhythmias such as atrial fibrillation has become increasingly available [5]. Despite their high accuracy in measuring HR at rest and the ubiquity of these devices in modern life, an in-clinic ECG is still the gold standard method to determine RHR [17]. In clinical research, there are a variety of methodologies used depending on the availability of data and clinical feasibility [10,11,18,19]. In this study, we investigated the viability of the VSW in determining RHR by comparing it with RHR determined by ECG. Using PPG data combined with actigraphy data, we isolated periods of time when the participant wearing the VSW was not in motion during the time of ECG recording, thus allowing us to estimate RHR values from VSW data. With this method, we demonstrated that there is excellent agreement between RHR determined by ECG and VSW, suggesting that the VSW is capable of determining a reliable RHR. In a world where telehealth is increasingly utilized, reliable wearable device-based data such as this may be useful to clinicians, providing them with clinical information that would otherwise be more cumbersome to obtain [20].

While most studies in the past have focused on analyzing the relationship of RHR with objective, lab-based measurements, we also extensively evaluated the relationship of RHR with participants'

wellbeing and quality of life including psychosocial and socioeconomic aspects. In the univariate analyses, we demonstrated that participants who had higher education, married, had health care insurance, and lower PHQ-9 scores were more likely to have a lower VSW RHR. Furthermore, we found similar and significant associations in our regression models when stratified by sex: lack of healthcare insurance, psychiatric conditions (major depressive disorder, generalized anxiety disorder), and higher WHO-DAS 2.0 scores were significantly associated with higher HR. These findings are consistent with prior studies suggesting that more difficult SES and psychosocial circumstances were associated with higher chronic stress and higher HR [21-27]. However, in our analyses, we also found that there were differences by sex in which baseline characteristics were most associated with RHR. For instance, within the demographics and SES domain, unemployment was most significantly associated with higher RHR for female participants but lack of healthcare insurance was the most significantly associated with higher RHR for male participants. Similarly, within the PRO domain, higher WHODAS 2.0 score was most associated with higher RHR for female participants but the Behavioral Risk Factor Surveillance System Adverse Childhood Experience score was most associated with higher RHR for male participants. This may be the result of a multitude of factors including physiological differences between the two sexes, societal influences, and diverse cultural and personal experiences that could impact HR [28-31]. In the laboratory setting, it has been demonstrated that there are sex differences in HR responses to physical and mental stressors [32-34]. A recent study using a contemporary wearable device investigated the effects of occupational stressors in the real world and found that female participants, compared to male participants, had a higher maximum HR and greater changes in HR when confronted with a moderate stressor during a work shift in a retail store [35]. Future studies will be needed to elucidate the relationships and mechanisms underlying how different clinical characteristics affect RHR in females and males.

We observed significant trends of VSW RHR with objective clinical measurements in both our

univariate and regression analyses. Higher VSW RHR was associated with higher blood pressures, BMI, and waist circumference, all previously established in the literature [36,37]. Laboratory findings of higher C-reactive protein and platelet counts in those participants with higher SW RHR was also consistent with the literature [38]. Analyses of physical function showed significant trends with VSW RHR. Lower VSW RHR was significantly correlated with a higher 6-minute walk distance, an important clinical surrogate for fitness [39]. It has been demonstrated previously that HR profiles determined by wrist-worn devices can predict 6-minute walk distances in patients with mitral or aortic valve disease [11]. Another more commonplace measure of physical activity and fitness is step count, a measure that has been associated with mortality [40]. We observed that participants with lower VSW RHR had significantly higher step count, consistent with prior studies demonstrating a negative relationship with VSW RHR and physical fitness [27,41,42]. Though causality cannot be determined from these analyses, the relationship of VSW RHR and step count is of high interest to clinicians and patients alike given step count and other surrogates of physical fitness are integral elements of wearable devices that are often promoted as a method of remote monitoring. Interestingly, the relationship demonstrated in our study was of VSW RHR and *future* step count, suggesting that even a single RHR measurement could be indicative of a person's future physical activity and therefore may identify a population with higher RHR for targeted interventions aimed to improve physical fitness. Future studies will need to longitudinally track both RHR and physical activity levels to determine if their long-term trends are indeed correlated.

There are several limitations to our analysis. Our cohort may have a slight healthy user bias given it was derived from the PBHS registry. The analysis cohort was also more limited in size than expected primarily due to lack of procedural consistency (wearing the VSW at the time of ECG recording) during the participant enrollment visit. In this study, hard clinical outcomes such as mortality and hospitalizations were not assessed but would be highly valuable for future studies, particularly those that evaluate not only associations of RHR with clinical outcomes but also of "free-living" HR with

clinical outcomes. Other studies have examined the validity of using wearable devices to measure HR under free-living conditions which is currently under investigation in the PBHS [43,44].

In conclusion, VSW RHR correlates strongly with RHR obtained using resting ECG. VSW RHR has significant trends with important clinical characteristics that closely mirror those already established in the literature. Further investigations will be needed to inform clinicians and patients alike on how to use wearable technologies that perform noninvasive measurements–not only of RHR–in conjunction with other clinical measurements to potentially detect disease or enhance their shared decision-making process for behavioral change.

## DISCLOSURES/ACKNOWLEDGEMENTS

**Study funding statement:** The Project Baseline Health Study and this analysis were funded by Verily Life Sciences, South San Francisco, California.

**Role of the sponsor statement:** Verily Life Sciences is the funding source for the PBHS and is responsible for data collection. Authors were fully responsible for the data analysis and interpretation presented herein and the writing of this article. The following individuals SAS, SS, MKC had access to the raw data. Authors had access to the full dataset for the study, reviewed and approved the final manuscript for submission.

**Prior disclosure of these data:** NA

**Data [/code/materials] sharing statement:** The deidentified PBHS data corresponding to this study are available upon request for the purpose of examining its reproducibility. Interested investigators should direct requests to jsaiz@verily.com. Requests are subject to approval by PBHS governance.

**Authors' disclosures:**

SAS, SS, MKC, EPS report employment and equity ownership in Verily Life Sciences.

KWM reports research grants from Verily, American Heart Association, Apple Inc., Bayer, the California Institute of Regenerative Medicine, Eidos, Gilead, Idorsia, Johnson & Johnson, Luitpold, Pac-12, Precordior, Sanifit; consulting fees from Amgen, Applied Therapeutics, BMS, BridgeBio, Elsevier, Lexicon, Moderna, Sanofi; equity ownership in Precordior, Regencor.

The rest of the authors report no relevant disclosures.

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Study concept and design: KYF, SAS, SS, KWM

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Data analysis and interpretation: KYF, SAS, SS, MKC

Draft writing and review: All

Draft approval for submission: All

**Acknowledgements**:

Authors wish to thank the Project Baseline Health Study investigators, study sites and participants.

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## ABBREVIATIONS

AIAN=American Indians and Alaska Natives
AUDIT-C=Alcohol Use Disorders Identification Test-Concise
BMI = body mass index
BP = blood pressure
BRFSS ACE=Behavioral Risk Factor Surveillance System Adverse Childhood Experience
ECG=electrocardiogram
eGFR = estimated glomerular filtration rate
FEV1/FVC=forced expiratory volume in 1 s /forced vital capacity
GAD-7 = general anxiety disorder -7
GERD = gastro-esophageal reflux disease
HbA1c=glycated hemoglobin A1c
HDL=high-density lipoprotein
IBI=interbeat interval
LDL=low-density lipoprotein
MDRD = modification of diet in renal disease
NHPI=Native Hawaiian, and Pacific Islander
PANAS=Positive and Negative Affect Schedule
PBHS = Project Baseline Health Study
PHQ-9 = patient health questionnaire -9
PPG=photoplethysmography
PROMIS=Patient-Reported Outcomes Measurement Information System
RHR=resting heart rate
SD = standard deviation
TSH=thyroid-stimulating hormone
VSW=Verily Study Watch
VSW RHR=Verily Study Watch resting heart rate
WBC=white blood cell
WHODAS=World Health Organization Disability Assessment Schedule

# Supplementary Files

# Multimedia Appendixes

Untitled.
URL: http://asset.jmir.pub/assets/a930c1029c229c8c1287fb17048e24da.docx