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Reproducibility of Resting Blood Pressure and Heart Rate Measurements: The HERITAGE Family Study

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PURPOSE: This study determined the reproducibility of resting systolic and diastolic blood pressure, mean arterial pressure, and heart rate (the average of three measures/day).
METHODS: The data were obtained on two separate days prior to an exercise training intervention in a sample of 822 subjects participating in the HERITAGE Family Study. The same protocol was conducted across three days in an intracenter quality control substudy, which included an additional 60 subjects.
RESULTS: Reproducibility estimates included technical error, coefficient of variation within subjects, and intraclass correlation with results expressed by sex, race, age, cuff size, BMI, and %fat. Since the data were collected across four Clinical Centers, the reproducibility estimates were also computed separately for each Center. The systolic, diastolic, and mean arterial blood pressures were highly reproducible with technical errors less than 5.1 mmHg, coefficients of variation of less than 7.0% and intraclass correlations > 0.75. The heart rates were slightly less reproducible. These results were fairly consistent across subject populations and across all four Clinical Centers.
CONCLUSION: It is concluded that within subject day-to-day variations are small compared to between subject variance for resting systolic, diastolic, and mean arterial blood pressure and heart rate at each of the Clinical Centers for all of the HERITAGE Family Study data. This makes it appropriate to pool the data and analyze it for changes subsequent to endurance exercise training and to determine the possible genetic basis for these changes.
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KEY WORDS: Blood Pressure Determination, Reproducibility of Results, Blood Pressure Variability, Quality Control

INTRODUCTION

The ability to accurately track change in cardiovascular risk factors consequent to any intervention is dependent in part on the reproducibility of the measurements. When measurements are less reliable or when the phenotypes are characterized by wide day-to-day variation, it is difficult to accurately identify statistically significant change. In addition, for the HERITAGE Family Study, which uses an exercise intervention, it is imperative to have high reproducibility to be able to establish the possible genetic basis for the heterogeneity in response. Even under standardized conditions of measurement, the within-subject standard deviation for resting blood pressure has been shown to be about half of the real between-subject standard deviation (1), making accurate determination of statistically significant change in resting blood pressure difficult.

The reproducibility of measurements may reflect trial-to-trial reliability as well as day-to-day variability. Blood pressure variability has been shown to vary considerably based on a number of factors including: number of measurements (2, 3), number of days on which measurements are taken (2, 3), level of blood pressure (2, 4), and age (4). Far fewer studies (5, 6) exist that investigate the reproducibility of resting heart rate, but heart rate has been shown to decrease daily over a 5-day period (7).

The HERITAGE Family Study is a large multicenter clinical trial investigating possible genetic bases for the variability in the response of physiological measures, and risk factors for cardiovascular disease and non-insulin-dependent diabetes mellitus, to endurance exercise training. The purpose of this study was to establish the reproducibility of

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Selected Abbreviations and Acronyms

SBP = Systolic blood pressure
DBP = Diastolic blood pressure
MAP = Mean arterial pressure
ICQC = Intracenter quality control substudy
BMI = Body mass index
TE = Technical error
CV = Coefficient of variation
ICC = Intraclass correlations

resting blood pressure and heart rate values before a 20-week endurance training program in HERITAGE Family Study subjects, and in a separate group of quality control subjects, across four participating Clinical Centers. Details of the HERITAGE Family Study have been published previously (8).

METHODS

Subjects

The HERITAGE Family Study subject population consists of Black and White families, including the natural father and mother and their offspring 16 years of age and older. Subjects were recruited over a period of about four years by each of the four Clinical Centers located at Arizona State University (relocated to Indiana University), Laval University, the University of Minnesota, and The University of Texas at Austin. Subjects for this study were the 822 subjects who completed a minimum of pre-training blood pressure and heart rate measurements on two separate days. Of these subjects, 108 were Black men, 199 were Black women, 255 were White men, and 260 were White women. Physical characteristics are presented in Table 1. All subjects were healthy, were not on any anti-hypertension medication at the time of the study or for 3 months prior to the start of the study, and had a screening blood pressure below 160/90 mm Hg. All subjects met additional inclusionary criteria, and passed a physician-administered physical examination, including a resting and exercise 12-lead electrocardiogram (8). The study protocol had been previously approved by each Clinical Center's Institutional Review Board, and informed consent was obtained from each subject.

During the second and third years of data collection, an intracenter quality control substudy (ICQC) was conducted to determine the reproducibility of measurements within each center. During this time, each Clinical Center recruited additional subjects every 6 months over three consecutive 6-month periods. Subjects in the ICQC were required to meet all the criteria for admission to the HERITAGE Family Study with the exception of family membership and degree of sedentariness. The physical characteristics for these 60 subjects are also presented in Table 1. The ICQC subjects were younger and had lower body mass and BMI than the main HERITAGE subjects.

Experimental Design

Each subject in the HERITAGE Family Study completed an extensive battery of tests prior to starting the 20-week endurance training program. A series of 4 to 8 blood pressure and heart rate measurements were conducted on two separate days. The mean systolic pressure (SBP), diastolic pressure (DBP), mean arterial pressure (MAP), and heart rate from each day were used in the analysis.

Blood Pressure and Heart Rate Methodolgy

Blood pressure and heart rate measures were taken using the Colin STBP-780 automated blood pressure unit. This system employs two electrocondenser microphones embedded in the cuff. The sound signal is synchronized to the electrocardiograph R wave, and a detection algorithm is used to determine both SBP and DBP. Earphones worn by the technician allowed for a manual confirmation of the

TABLE 1. Physical characteristics of the subjects in the HERITAGE Family Study and in the ICQC Substudy*

Subjects	n	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m²)
HERITAGE					
Black men	108	33.0 ± 12.3	176.6 ± 6.8	84.9 ± 16.9	27.4 ± 5.6
Black women	199	32.9 ± 11.3	162.3 ± 6.7	74.7 ± 18.0	28.3 ± 6.6
White men	255	35.9 ± 15.0	177.7 ± 6.5	84.4 ± 16.3	26.7 ± 4.9
White women	260	34.8 ± 14.0	163.8 ± 6.5	67.1 ± 13.6	25.0 ± 4.8
Total	822	34.4 ± 13.5	169.3 ± 9.6	76.6 ± 17.9	26.7 ± 5.6
ICQC					
Men	25	28.5 ± 9.5	176.0 ± 6.1	76.4 ± 11.4	24.7 ± 3.3
Women	35	27.4 ± 8.4	165.6 ± 6.9	64.3 ± 11.5	23.4 ± 3.6
Total	60	28.1 ± 9.0	171.7 ± 8.2	71.4 ± 12.9	24.1 ± 3.5

* Data are expressed as mean ± SD.
ICQC, Intracenter Quality Control Substudy with 15 subjects provided by each of the four clinical centers.

algorithm-determined blood pressure values. In addition, the printer function enabled the technician to visually confirm the accuracy of the reading with its graphic Korotkoff sounds (K-sounds).

Subjects reported to the laboratory before 11:00 A.M. having refrained from tobacco, caffeine and any blood pressure or heart rate altering medication for 2 hours prior to testing. Proper cuff size (child, regular adult, or large adult) was determined using the guidelines from the 1988 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (9) and the size was recorded in the subject's file. The blood pressure cuff was placed snugly around the right upper arm so that the microphones were over the brachial artery and the lower margin of the cuff was 2–3 cm above the antecubital space. Electrodes were placed over the manubrium, and on the midclavicular line over the lower left and right ribs. The subject was then seated in a reclining chair in a semi-recumbent position (legs supported parallel to the floor and the back support reclined at 45° angle from the floor), with the arms relaxed and supported. The laboratory was quiet, with little or no light and a room temperature between 23°C and 26°C. A sheet or blanket was available if the subject requested it. The blood pressure equipment and technician were to the side or behind the subject so that the subject could not see the blood pressure monitor or the technician.

Following a rest period of at least 5 minutes, four blood pressure and heart rate readings were taken at 2-minute intervals (2 minutes from the start of one to the start of the next blood pressure measurement). The first reading was always deleted. If the next three measurements were considered "reliable", no more measurements were taken. If one or more of these measurements were considered "unreliable", additional measurements were taken until there were three reliable measurements or until eight measurements had been taken. Even though several blood pressures were taken on a subject each day, there was only one blood pressure measure reported each day. This reported blood pressure was the mean of the three reliable measurements or the mean of all available reliable readings. Subjects reported to the laboratory on a second day and the same procedures were repeated. Most subjects reported within ± 2 hours of time for the first day.

Unreliable measurements were those considered to be invalid because of subject movement, machine malfunction, technician error or where by checking the graph of K-sounds it was obvious that the Colin STBP-780 had chosen the wrong systolic or diastolic blood pressure. For each blood pressure measurement two separate readings were manually recorded; the automated value determined by the Colin STBP-780 and the manual reading value determined by the technician listening through headphones. The technician first recorded the manual reading without looking at the automated reading and then recorded the automated reading from the print out from the Colin STBP-780. When there was a significant discrepancy between the automated and manual reading the technician examined the graph of the K-sounds to determine if the Colin STBP-780 reading was valid.

Heart rate was measured by the STBP-780 as a moving average of six beats. The heart rate measured during each blood pressure measurement was printed out by the STBP-780 and recorded. Heart rate values reported were those on the STBP printout corresponding to the blood pressure measurement used.

SBP was defined as the first sound (appearance of K-sounds) and DBP was defined as the fifth sound (disappearance of K-sounds). The Colin STBP-780 was calibrated using a mercury manometer at the beginning of most testing days. Colin STBP-780 values were recorded at mercury manometer pressures of 200, 150, 100, 50 and 0 mmHg. The Colin STBP-780 was considered calibrated if its values were within ± 2 mmHg of the mercury manometer values. If the Colin STBP-780 failed calibration, the Colin STBP-780 was recalibrated.

Quality Assurance, Quality Control, and Statistical Methodology

Important quality assurance and quality control procedures were instituted across all four Clinical Centers, as detailed by Gagnon et al. (10), including, a) central training for staff members, b) development and use of a detailed Manual of Procedures, and c) testing on two separate occasions during each of the first 2 yr of 4 subjects who went to each of the Clinical Centers over a 3- to 4-week period.

All statistical analyses were performed from one blood pressure and heart rate measurement, which was the mean of the reliable measures taken on that day. Technical errors (TE), coefficients of variation within subjects (CV), and intraclass correlations (ICC) were computed to evaluate the reproducibility of SBP, DBP, and heart rate measurements using the model of Shrout and Fleiss (11). With this model, the i^{th} measurement on the j^{th} subject, x_{ij}, is given by:

$$x_{ij} = \mu + b_j + w_{ij}$$

where μ is the population mean, b_j is the difference from μ of the mean of the measurements on the j^{th} subject, and w_{ij} is the difference from $\mu + b_j$ of the i^{th} measurement on the j^{th} subject (w_{ij} is a residual that encompasses the effects of the rater, the rater x subject ineraction, and the error). Both b_j and w_{ij} are assumed to be normally distributed and independent with standard deviations of σ_T and σ_w. σ_w is the within-subjects standard deviation, also called TE. The CV was computed as :

$$CV = (100 \times \sigma_w)/\mu$$

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To compute the ICC, PROC GLM in SAS was used to run an ANOVA, providing between-subjects mean square (BMS) and within-subjects mean square (WMS) values. These were used to estimate the intraclass correlation (ICC) according to Shrout and Fleiss (11):

$$ICC = (BMS - WMS)/[BMS + (k - 1) \times WMS],$$

where k is the number of replicate measurements on a subject. TE, the within-subject standard deviation, is computed as the square root of the WMS from the ANOVA. TE, CV, and ICC were calculated for SBP, DBP, MAP and heart rate for the overall sample; by sex; by race; by category of age, cuff size, BMI, and %fat; by Clinical Center; and for the entire ICQC sample.

A 5-factor (sex, race, age, cuff size, and time) repeated measures ANOVA was used to determine if there were any significant within-subject (Day-1 vs. Day-2) or between subject differences for the entire HERITAGE sample. A one factor repeated measures ANOVA was used to determine if there were any significant day within-subjects or between subject differences among the three days in the ICQC study.

Age categories were: 17–25; 26–35; 36–45; 46–55; > 55. The cuff-size categories were: small, regular, and large. The two categories for BMI and %fat were: above the median and below the median.

RESULTS

The SBP, DBP, MAP, and heart rate values for the total sample and for the total sample split by race and sex for Day 1 and Day 2 are presented in Table 2. Fleiss (12) considers ICC values > 0.75 to represent excellent reliability, between 0.40 and 0.75 to represent fair to good reliability, and values less than 0.40 to represent poor reliability. All of the ICC values from the current study, except for heart rate, exceeded 0.75 and would therefore be considered excellent. According to Scott et al. (13), for most biological data, a CV of < 10% is considered good. According to this criterion, the CVs in the current study (4.1–4.3% for SBP, 6.1–6.7% for DBP, 4.6–5.0% for MAP, and 7.4–8.0% for heart rate) for the HERITAGE Family Study data, would be very good. The TE, CV, and ICC were similar for men, women, Blacks and Whites. The TE, CV, and ICC values by category for age, BMI and %fat are not presented since they were nearly identical to those presented in Table 2. Using TE, CV, and ICC as the criteria, the SBP was the most reproducible and heart rate was the least reproducible.

Table 3 gives the TE, CV and ICC for SBP, DBP, MAP, and heart rate for each of the four Clinical Centers in the HERITAGE Family Study. All of the CV values were under 10% and all of the ICC values were 0.75 and above except for DBP for Center C and heart rate for Centers A, B, and C.

A 5-factor (sex, race, age, cuff size, and time) repeated measures ANOVA was used to test for within-subject differences (Day-1 and Day-2) or between subject differences for SBP, DBP, MAP and heart rate. Although interactions were not the focus of the study, they were examined to ensure that main effect interpretation was unambiguous. The time effect was examined first. Interactions (between this factor and others) were not significant (SBP, 0/15 interactions significant; DBP, 0/15 significant; MAP, 0/15 significant; heart rate 0/15 significant). The time main effect also was not significant (SBP, $F = 2.2$, $p = 0.138$; DBP, $F = 0.66$, $p = 0.417$; MAP, $F = 1.52$, $p = 0.217$; HR, $F = 1.03$, $p = 0.311$).

Because it was not a focus of the study, only the main effects of between-subject differences were analyzed. For the between-subject terms, means averaged over Day 1 and 2 were examined. Men had significantly higher SBP ($F = 3.9$, $p = 0.049$), DBP ($F = 5.82$, $p = 0.016$) and MAP ($F = 6.00$, $p = 0.015$) than women. Blacks had significantly higher SBP ($F = 11.42$, $p = 0.001$), DBP ($F = 6.74$, $p = 0.010$) and MAP ($F = 10.18$, $p = 0.001$) than whites. Older age categories had higher SBP ($F = 3.33$, $p = 0.010$), DBP ($F = 9.01$, $p = 0.000$), and MAP ($F = 7.08$, $p = 0.001$) than younger age categories. There was a significant cuff size main effect for SBP ($F = 3.82$, $p = 0.022$) and MAP ($F = 3.62$, $p = 0.027$), but not for DBP ($F = 2.65$, $p = 0.071$). A Bonferonni/Dunn post-hoc test determined that: (1) for SBP those with large cuffs had higher values (123.0 ± 13.4) than those with small (118.5 ± 12.1) or regular cuffs (118.3 ± 12.0); and (2) for MAP those with large cuffs had higher values (88.3 ± 9.7) than those with regular cuffs (84.7 ± 9.0), but there was no significant difference between those with small cuffs (85.1 ± 9.2) and those with regular or large cuffs. There were no significant main effects for heart rate ($F = 0.00$–2.09, $p > 0.05$).

The resting SBP, DBP, MAP and heart rate values for the ICQC subjects are presented in Table 4. As with data from the entire HERITAGE Family Study, the SBP measures were the most reproducible and heart rate was the least reproducible. All CV values were under 10%. The ICC values were above 0.75 for SBP and MAP and below 0.75 for DBP and heart rate. A one-way repeated measures ANOVA determined that there were no significant differences among the three days for SBP ($F = 0.66$, $p = 0.521$), DBP ($F = 0.30$, $p = 0.744$), MAP ($F = 0.44$, $p = 0.649$) or heart rate ($F = 0.19$, $p = 0.828$).

DISCUSSION

The reproducibility of resting blood pressure for HERITAGE subjects (Table 2), for the HERITAGE study by Clinical Center (Table 3) and for the ICQC subjects (Table 4) compare favorably with that found in other studies. The ICCs in the current study ranged from 0.76 to 0.87 for SBP

TABLE 2. Reproducibility of resting systolic, diastolic and mean arterial blood pressures and heart rate across two days

	n	Day 1 (Mean ± SD)	Day 2 (Mean ± SD)	TE (mmHg or beats/min)	CV (%)	ICC
Systolic						
Men	363	121.3 ± 11.5	122.1 ± 10.8	5.1	4.2	0.80
Women	459	117.3 ± 12.9	116.5 ± 12.6	5.0	4.2	0.85
Black	307	123.4 ± 12.8	123.1 ± 12.3	5.0	4.2	0.84
White	515	116.4 ± 11.5	116.5 ± 11.4	5.0	4.3	0.81
Total	822	119.1 ± 12.4	119.0 ± 12.2	5.0	4.2	0.84
Diastolic						
Men	363	69.7 ± 9.5	69.2 ± 9.3	4.6	6.7	0.76
Women	459	68.0 ± 9.6	67.3 ± 9.5	4.2	6.2	0.81
Black	307	72.7 ± 9.4	72.3 ± 8.7	4.4	6.1	0.76
White	515	66.4 ± 8.9	65.6 ± 8.9	4.4	6.7	0.76
Total	822	68.7 ± 9.6	68.1 ± 9.4	4.4	6.4	0.79
MAP						
Men	363	86.9 ± 9.2	86.8 ± 8.7	4.0	5.0	0.81
Women	459	84.4 ± 10.0	83.7 ± 9.9	3.9	4.6	0.85
Black	307	89.6 ± 9.6	89.3 ± 9.1	3.9	4.4	0.83
White	515	83.1 ± 9.0	82.6 ± 8.8	3.9	4.7	0.81
Total	822	85.5 ± 9.7	85.1 ± 9.5	3.9	4.6	0.84
Heart rate						
Men	363	62.1 ± 9.0	62.4 ± 9.2	4.6	7.4	0.74
Women	459	67.7 ± 9.1	68.4 ± 9.7	5.4	7.9	0.68
Black	307	66.6 ± 9.7	67.7 ± 9.8	5.4	8.0	0.70
White	515	64.4 ± 9.3	64.6 ± 9.8	4.8	7.5	0.74
Total	822	65.2 ± 9.5	65.7 ± 9.9	5.0	7.7	0.73

TE, technical error; CV, coefficient of variation; ICC, intraclass correlation; MAP, mean arterial pressure.

TABLE 3. Reproducibility of resting systolic, diastolic, and mean arterial blood pressure and heart rate across Clinical Centers for the HERITAGE Family Study Subjects

Clinical Center	N	TE (mmHg or beats/min)	CV (%)	ICC
Systolic				
Center A	195	4.5	3.6	0.86
Center B	211	6.5	5.6	0.77
Center C	212	4.6	4.0	0.81
Center D	204	4.1	3.4	0.87
Diastolic				
Center A	195	4.4	6.1	0.80
Center B	211	4.6	7.0	0.75
Center C	212	4.4	6.9	0.69
Center D	204	4.2	5.9	0.78
MAP				
Center A	195	3.8	4.2	0.85
Center B	211	4.4	5.3	0.79
Center C	212	4.0	4.9	0.75
Center D	204	3.5	4.0	0.85
Heart Rate				
Center A	195	5.7	8.6	0.66
Center B	211	5.0	7.6	0.72
Center C	212	5.2	7.8	0.72
Center D	204	4.2	6.6	0.80

TE, technical error; CV, coefficient of variation; ICC, intraclass correlation; MAP, mean arterial pressure.

and from 0.69 to 0.81 for DBP. The ICC values of 0.84 and 0.79 for SBP and DBP for the total HERITAGE population, compare favorably with those from previous studies (see Table 5). Llabre et al. (2) took six resting seated blood pressures on each of 5 days on 128 normotensive Black and White males and females. They determined the ICC for a matrix of 1 to 5 days and 1 or 2 measurements. The ICCs for 2 replications and 2 days (the combination most similar to the HERITAGE sample) were 0.84 and 0.74 for SBP and DBP, respectively. Llabre et al. (3) also studied 40 mild hypertensives and 79 normotensive Black and White males and females with the same study design. They determined the ICCs for a matrix of 1 to 3 days and 1 to 6 measurements. For 2-days and 3-measurements, their ICCs for SBP and DBP were 0.91 and 0.89, respectively, for the entire sample. Values for the normotensives were slightly better than those of the hypertensives. Wattigney et al. (14) determined ICCs in the Bogalusa Heart Study, measuring blood pressures on 417 children, 6–18 years of age, on two separate days using both a mercury sphygmomanometer and a Dinamap automatic blood pressure monitor. They had ICCs of 0.90 and 0.82 for SBP measured with the sphygmomanometer and Dinamap, respectively, and ICCs of 0.76 and 0.68 for DBP measured with the sphygmomanometer and Dinamap, respectively.

The TE and (CV) in the current study ranged from 4.1–6.5 mmHg (3.4–5.6 %) and from 4.2–4.6 mmHg (5.9–

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TABLE 4. Reproducibility of resting systolic, diastolic, and mean arterial blood pressures and heart rate across three days for the ICQC substudy (n = 60)

	Day 1 (Mean ± SD)	Day 2 (Mean ± SD)	Day 3 (Mean ± SD)	TE (mmHg or beats/min)	CV (%)	ICC
Systolic	118.7 ± 10.3	119.1 ± 9.6	117.9 ± 10.1	4.9	4.1	0.76
Diastolic	64.8 ± 7.8	65.0 ± 8.8	64.2 ± 8.3	4.6	7.2	0.69
MAP	82.9 ± 7.7	81.7 ± 13.4	82.3 ± 8.4	4.0	4.8	0.75
Heart rate	60.5 ± 9.7	61.2 ± 11.0	60.6 ± 10.7	6.0	9.8	0.67

TE, technical error; CV, coefficient of variation; ICC, intraclass correlation; MAP, mean arterial pressure.

7.2%) for SBP and DBP, respectively. The TE and (CV) values of 5.0 mmHg (4.2%) and 4.4 mmHg (6.4%) for SBP and DBP for the total HERITAGE population, compare favorably with those from previous studies (see Table 5.) Scott et al. (13) measured resting SBP and DBP on days 1, 2, and 30 in 10 healthy subjects, 21–35 yrs of age, and reported TE and (CVs) of 5.7 mmHg (5.3%) and 4.2 mmHg (5.8%) for SBP and DBP, respectively. (The number of blood pressure measurements was not explicitly given, but was assumed to be one per visit.) Sime et al. (17) conducted one blood pressure measurement on 46 men, 40–57 years of age, seated on a cycle ergometer immediately prior to an exercise test on two occasions, one week apart. The TE (CV) was 10.6 mmHg (8.4%) and 7.8 mmHg (9.6%) for SBP and DBP, respectively. In the Hypertension Detection and Follow-up Program (16), approximately 159,000 men and women, 30–69 years of age, were screened for hypertension in their home by trained professionals and then 72 hours later at a clinic. During the in-home visit three blood pressure measurements were taken. Using DBP measurement 2 and 3, the CV was calculated by 10-year age categories for Black and White males and females for those with no history of high blood pressure, those with a history of high blood pressure but not on anti-hypertension medication, and those currently on hypertensive medication. The TEs (CVs) ranged from a low of 10.6 mmHg (11.4%) to a high of 15.2 mmHg (16.6%). Other studies only report TE or CV data. Glasgow et al. (18) had 254 subjects with borderline or established hypertension, 186 of whom were taking hypertension medication, monitor their own blood pressure by taking three consecutive readings and averaging them into one reading. They did this three times a day (morning, midday, and evening) for 28 successive days. The TEs comparing one day one week vs the same day of the week the next week ranged from 2.5–4.5 mmHg and 1.5–3.4 mmHg, for SBP and DBP, respectively. Wattigney et al. (14) reported CVs of 3.6 and 4.6% for SBP measured using a sphygmomanometer and Dinamap, respectively, and 17.1 and 7.4% for DBP measured using a sphygmomanometer and Dinamap, respectively, in the Bogalusa Heart Study. Canner et al. (15) determined CVs for the Hypertension Prevention Trial, where two blood pressure measurements were made at least 30 seconds apart at three baseline visits and at six follow-up visits on 841 participants. The CVs were 3.8 and 4.5% for SBP and DBP, respectively.

The reproducibility of resting heart rate for HERITAGE subjects (Table 2), for the HERITAGE study by Clinical Center (Table 3) and for the ICQC subjects (Table 4), was slightly less than reported in the limited number of studies found for comparison. The TE and (CV) for the total HERITAGE population was 5.0 beats/min (7.7%). Scott et al. (13) measured resting heart rate on days 1, 2, and 30 in 10

TABLE 5. Reproducibility of resting systolic and diastolic blood pressure from previously published studies and the HERITAGE Family Study

Study	N	TE (mmHg) (SBP/DBP)	CV (%) (SBP/DBP)	ICC (SBP/DBP)
Canner et al. (15)	841		3.8/4.5	
Glasgow et al. (18)	254	2.5–4.5/1.5–3.4		
HERITAGE Family Study	822	5.0/4.4	4.2/6.4	0.84/0.79
Hypertension Detection (16)	159,000	?/10.6–15.2*	?/11.4–16.6	
Llabre et al. (2)	128			0.84/0.74
Llabre et al. (3)	119			0.91/0.89
Scott et al. (13)	10	5.7/4.2*	5.3/5.8	
Sime et al. (17)	17	10.6/7.8	8.4/9.6*	
Wattingly et al. (14) (sphygmomanometer)	417		3.6/17.1	0.90/0.76
Wattingly et al. (14) (Dinamap)	417		4.6/7.4	0.82/0.68

* These values were derived from the data given in the original manuscript. TE, technical error; CV, coefficient of variation; ICC, intraclass correlation.

healthy subjects, 21–35 yrs of age, and reported a TE of 4.8 beats/min and a CV of 7.1%. (The number of heart rate measurements was not explicitly given, but was assumed to be one per visit.) Laird and Campbell (6) had six men and six women, ages 21–90 years, measure their own heart rate at roughly the same time of day after sitting for 5 min on three separate days. Heart rate was palpated at the radial artery and measured as the number of beats counted in one minute. The CV was 5.7%. Bacon et al. (5) measured resting heart rate after 10 minutes of seated rest using an electrocardiogram on four men and four women, ages 34–58 years, on four occasions before administering eye drops at the same time of day separated by at least 7 days. The CV was 7.1%.

In pooling the data for analysis in a study involving different clinical centers, it is important to ensure that a standardized protocol is strictly enforced and that the reproducibility of the measures is high in each of the centers (10). As shown in Table 3, the reproducibility values among the 4 Clinical Centers in the HERITAGE Family Study were quite high.

Because it is possible for initial blood pressure and heart rate values to be higher than the true blood pressure and heart rate due to test anxiety, the protocol of the HERITAGE Family Study involved taking up to eight blood pressure and heart rate measurements on two separate occasions before training. The fact that there were no significant differences between Day-1 and Day-2 for SBP, DBP, MAP, and heart rate indicates that true resting values were achieved.

In conclusion, in the HERITAGE Family Study the reproducibility of the SBP, DBP, and MAP was excellent and the reproducibility of heart rate was good. This makes it appropriate for the data from the four Clinical Centers to be pooled and to analyze this data set for changes subsequent to endurance exercise training and to determine the possible genetic basis for these changes.

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