Supplemental Digital Content 2.

Text. Estimated maximum heart rate after deleting tests that are presumably less than full effort

Methods

Supplemental Paragraph Number 1 Including tests that represent less than full effort may impede assessment of the association of age and observed MHR. We explored several strategies for forming restriction sets that eliminated tests that were less than full effort: 1) If RPE was low, the participant did not perceive working at full effort during the treadmill test; as an example of RPE-based restriction, we studied a restriction set that eliminated any test with RPE <15. 2) Tests of short duration may not represent full effort; we studied a duration-based restriction set that excluded those who did not finish stage 2 of the test, and for another excluding those who did not finish stage 3. 3) We formed restriction sets by excluding tests with low age-specific MHR, using a "trimline". One such "trimline" strategy excludes tests with MHR <85% of predicted MHR using the Tanaka formula 208- 0.7*age, as depicted in Supplemental Digital Content 4. This restriction eliminates tests in 18 year olds with MHR < 166 beats/minute. The cutpoint for exclusion declines to 147 at age 50 by 0.7 beats/minute per year of age. We designate this "trimline" by the cutpoints at age 18 and at age 50, that is trimline (166,147).

Supplemental Paragraph Number 2 Trimline (166,147) makes exclusion proportional to predicted MHR at each age. We explored 600 additional non-proportional "trimlines" in order to see whether a linear age-MHR association emerged in this CARDIA dataset similar to the equations reported by Tanaka and

Gellish (8, 22). This exploration consisted of examining the repeated measures regression of MHR on quadratic age for each trimline (X, Y), with X (the cutpoint at age 18) ranging from 160 to 189 and Y (the cutpoint at age 50) ranging from 120 to 139 (30 x 20 = 600 "trimlines" in total). We recorded size and statistical significance of the coefficient for age^2, with focus on a cutoff line that yielded a small and nonsignificant coefficient for age^2 (indicating a linear age-MHR relationship), then repeated the regression omitting the age^2 term to characterize the linear solution.

Interpretation

Supplemental Paragraph Number 3 We further studied the shape of the eMHR curve under several restriction strategies based on RPE, highest stage of the treadmill test attained, or trimming using a percent of the Tanaka age-predicted MHR (eg, trimline (166,147)) (see Table, Supplemental Digital Content 3, which demonstrates prediction of maximum heart rate (MHR) from age in all available data and in some restriction sets obtained by different trimming methods; see Figure, Supplemental Digital Content 4 which shows distribution of MHR by age after excluding those with values below the 85% TANAKA estimate of MHR (eMHR)). All shapes were quadratic. We explored a wide range of non-proportional "trimlines" and found that many yielded a linear slope similar to what was reported previously (8,22). For example, linearity of the MHR age relationship was maintained for the age 18 cutoff 180-186 combined with any age 50 cutoffs in the range 120-139; the age slope was close to (-0.7) for all these trimlines. Specifically, the trimline (182,130) yielded eMHR=203-0.70*age. However, further adjustment for baseline characteristics that may have been involved

in selection bias, including sex, race, BMI, physical activity, smoking status, lung function and treadmill test duration, restored a quadratic association with quadratic coefficient -0.003. We concluded that we never know what proportion of a true maximal test was performed; even a person achieving a relatively high MHR might have achieved a relatively low proportion of true MHR. Therefore we were not able to distinguish less than full effort from full effort tests, and we deemed restriction strategies for all but a very few low level tests not to be helpful in understanding MHR.

Figure 1: Distribution of Maximum Heart Rate (1 standard deviation error bars and age-specific 5th percentiles) of eligible tests across 20 year follow-up by age at examination (9622 tests in 4844 participants).

Figure 2: Distribution of Maximum Heart Rate of treadmill tests predicted by existing formulae using CARDIA data.

†Constant cohort represents 1479 participants who took treadmill tests at year 0, 7 and 20.

Figure 3: Distribution of Maximum Heart Rate of treadmill tests by age across quartiles of baseline BMI in CARDIA.

List of Supplemental Digital Content

Supplemental Digital Content 1. Table showing number of people excluded from the treadmill tests according to different criteria in CARDIA study. doc.

Supplemental Digital Content 2. Text explaining several strategies for forming restriction sets that eliminated tests that might be less than full effort. doc.

Supplemental Digital Content 3. Table demonstrating prediction of maximum heart rate (MHR) from age in all available data and in some restriction sets obtained by different trimming methods. doc.

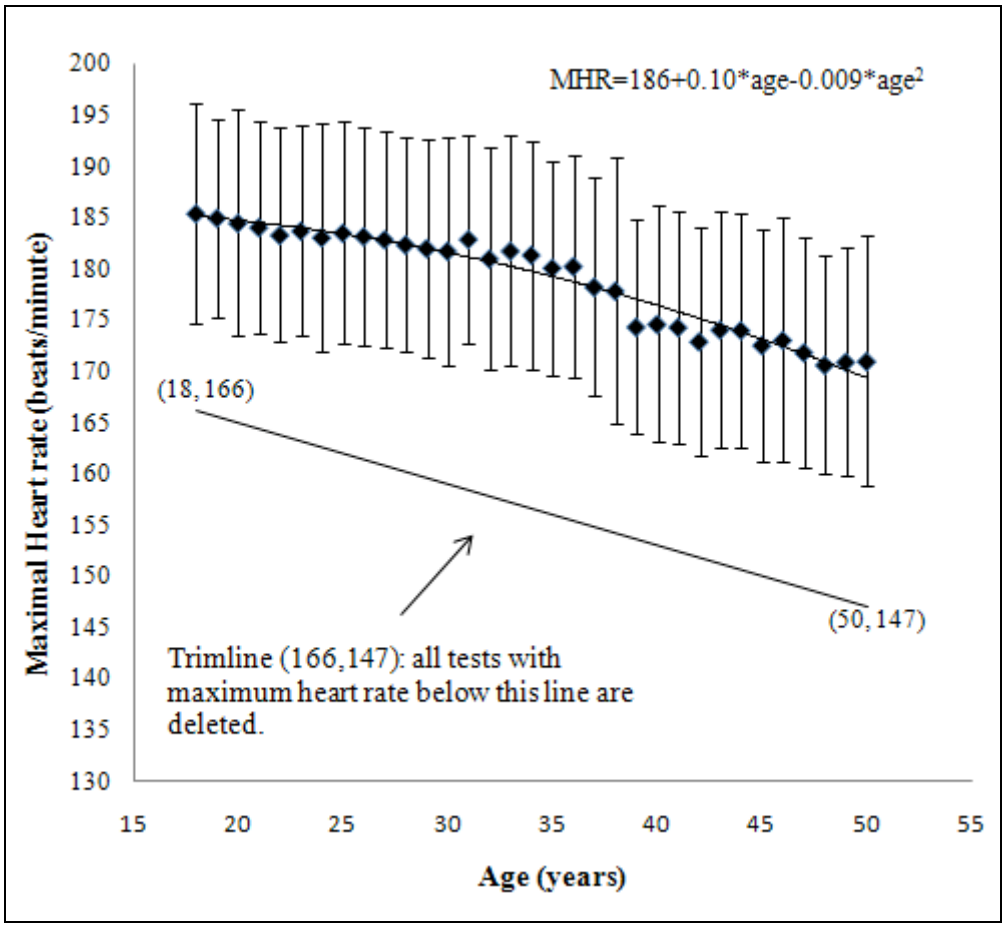
Supplemental Digital Content 4. Figure showing distribution of MHR by age after excluding those with values below the 85% TANAKA estimate of MHR (eMHR). tif.

Supplemental Digital Content 5. Table showing the equations for year 0, year 0 and 7, and then for year 0, 7, and 20 with multiple baseline variables. doc.

Type of file: figure
Label: 1
Filename: D.R.JACOBS_SDC 4 Figure.pdf

Supplemental Digital Content 4.

Figure. Distribution of Maximum Heart Rate (1 standard deviation error bars) of treadmill tests by age at examination after excluding those with values below the 85% eMHR as predicted by Tanaka formula, 208-0.7*age (trimline (166,147)).



Type of file: table
Label: 1
Filename: D.R.JACOBS_SDC 1 Table.pdf

Supplemental Digital Content 1.

Table. Number of people excluded from the treadmill tests according to different criteria in the CARDIA study.

	Year 0	Year 7	Year 20
Permanent Exclusion Criteria			
History of exercise-induced asthma	15	17	11
History of heart, blood vessel or lung conditions *	11	28	61
Elevated resting blood pressure †	14	36	17
Abnormal ECG ‡	14	8	8
Abnormal chest exam ¶	17	13	3
Subject refusal	3	16	3
Other diseases Δ	57	134	27
Pregnancy	0	0	6
Discretion of exam personnel	68	150	57
Exclusion where rescheduling is possible but never happen			
Equipment malfunction	10	0	1
Fever/cold on exam day	5	7	11
Injury on exam day	15	49	17
	229	458	222

*History of any of the following heart, blood vessel or lung conditions: heart attack, angina, infarction, valvular heart disease, heart failure, stroke cardiomyopathy, aneurysm, myocarditis or pericarditis, pulmonary embolus or infarction.

† Systolic blood pressure ≥160mmHg or diastolic blood pressure≥100mmHg at year 0 or year 7; Systolic blood pressure ≥200 mmHg or diastolic blood pressure≥110 mmHg at year 20.

‡Resting ECG showing evidence of possible significant ischemia, high-degree atrioventricular block, tachyarrhythmia or bradyarrhythmia other than sinus tachycardia or sinus bradycardia.

¶Any of the following findings on chest and cardiac examination: rales, wheeze, systolic murmur which study physician feels is likely to represent aortic stenosis, S3 gallop.

ΔAny of the following medical conditions: disorder of the muscles, joints or nervous system that is made worse by exercise, uncontrolled metabolic disease, chronic infectious disease, or uncontrolled HIV.

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Filename: D.R.JACOBS_SDC 3 Table.pdf

Supplemental Digital Content 3.

Table. Prediction of MHR from age in all available data and in some restriction sets obtained by different trimming methods.

	Number of tests	MHR best fitting formula
A. All available tests		
Completed any test * (ages 18 – 50)	9622	$179+0.29*age-0.011*age^2$ ($p<0.0001$)
Completed yr0+yr7 tests (ages 18 – 37)	4432	$190-0.37*age$ ($p<0.0001$)
Completed yr7+yr20 tests (ages 25 – 50)	3148	$199-0.63*age$ ($p<0.0001$)
B. Restricted sets of tests		
Maximum RPE ≥15 †	8622	$178+0.39*age-0.012*age^2$
Highest stage achieved >2 †	9130	$178+0.36*age-0.012*age^2$
Highest stage achieved >3 †	7779	$175+0.63*age-0.015*age^2$
MHR >75% * (208-0.7*age) †	9380	$182+0.19*age-0.010*age^2$
MHR >85% * (208-0.7*age) †	8588	$186+0.10*age-0.009*age^2$
Above trimline (182,130)	7549	$203-0.70*age$
Above trimline (182,130) adjusted for baseline differences¶	7549	$198 – 0.47*age – 0.003* age^2$

*The quadratic form was significant for all eligible tests.

†The quadratic form is significant at $\alpha=0.05$.

¶Further adjustment for baseline characteristics that may have been involved in selection bias, including sex, race, BMI, physical activity, smoking status, lung function and treadmill test duration, restored a quadratic association; the intercept includes those covariates evaluated at their means.

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Filename: D.R.JACOBS_SDC 5 Table.pdf

Supplemental Digital Content 5

Table. The predicting equation of Maximum Heart Rate at year 0, year 0 and 7, and year 0, 7, and 20 from multiple baseline variables.

	Year 0*			Year 0 and 7*			Year 0, 7 and 20*		
	Estimate	SE	P	Estimate	SE	P	Estimate	SE	P
Intercept	179.06	6.90	<.0001	192.98	6.19	<.0001	189.38	6.12	<.0001
Age (years)	-0.16	0.07	0.02	-0.27	0.03	<.0001	0.36	0.11	0.0009
Age*Age (years square)							-0.01	0.00	<.0001
Gender (women)	-2.97	0.74	<.0001	-3.86	0.67	<.0001	-3.61	0.64	<.0001
Race (black)	-3.05	0.58	<.0001	-3.67	0.52	<.0001	-3.61	0.49	<.0001
BMI (kg/m^2)	-0.31	0.05	<.0001	-0.35	0.04	<.0001	-0.41	0.04	<.0001
Height(m)	-0.11	0.04	0.01	-0.12	0.04	0.0012	-0.11	0.04	0.0034
Pre-exercise heart rate (beats/min)	0.23	0.02	<.0001	0.19	0.02	<.0001	0.16	0.01	<.0001
Systolic Blood Pressure (mmHg)	0.06	0.02	0.01	0.03	0.02	0.129	0.02	0.02	0.3888
FVC (l)¶	2.46	0.45	<.0001	2.30	0.41	<.0001	1.99	0.39	<.0001
Physical activity score (exercise units)	0.0039	0.0008	<.0001	0.00	0.00	<.0001	0.00	0.00	<.0001
TV watching (hours/week)†	-0.11	0.02	<.0001	-0.12	0.02	<.0001	-0.12	0.02	<.0001
Smoking status (versus never)									
current	-7.99	0.53	<.0001	-7.75	0.48	<.0001	-7.59	0.46	<.0001
former	-2.00	0.68	0.003	-1.99	0.62	0.0013	-1.98	0.58	0.0007

*At year 0, 3591 treadmill tests were included in the analysis; At year 0 and 7, 5644 tests from 3697 participants (each took 1 or 2 tests during the 7 year follow-up) were included; at year 0, 7 and 20, 7938 tests of 3776 participants (each took 1, 2, or 3 during 20 year follow-up).

¶Since year 7 lung function data were not collected, year 10 lung function data were used in the analysis when baseline was year 7.

†Year 5 data were used in the analysis when baseline was year 0; year 10 data were used when baseline was year 7.