Longitudinal Changes in Aerobic Capacity: Implications for Concepts of Aging

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Background. Whereas aerobic capacity declines with age, major factors responsible for such decline have been poorly defined by past studies.

Methods. Participants were relatively healthy older individuals (339 women, 253 men) in whom demographic information and cardiopulmonary physiological measurements were obtained at baseline and biannually for three additional measurements.

Results. The study identified progressive declines in both forced expiratory volume in 1 second (FEV1) and in maximal exercise heart rate as two variables that accounted primarily for the longitudinal decline of aerobic performance in this cohort of relatively fit older persons who achieved high respiratory exchange ratios (RER; mean = 1.08 for women, 1.12 for men). Whereas women achieved a peak oxygen consumption (VO2peak) only 77% that of men, oxygen uptake became similar to men (to 95%) when measured per kilogram of lean body mass rather than per kilogram of total body mass. During the 6 years of the study (four time points) aerobic capacity declined in both sexes, however, less steeply for women than for men (18% vs 24% per decade, respectively). The rate of decline was independent of baseline variables such as body composition (e.g., lean body mass, lean/fat ratio), smoking status, medications, or concomitant health conditions, even though these variables strongly influenced baseline aerobic performance. Inclusion of FEV1 and maximal exercise heart rate into the statistical models, however, accounted for most of the longitudinal decline of aerobic performance. When adjusted for these two variables, aerobic capacity declined 9.7% and 10.4% per decade in women and men, respectively.

Conclusions. Our findings emphasize the primary importance of declining FEV1 and declining maximal exercise heart rate in accounting for the “aging effect” on aerobic capacity. Thus, when comparing longitudinal studies, all estimates of aerobic decline should be interpreted with respect to the specific variables included in the models, which also need to include FEV1 and maximal exercise heart rate.

MAXIMAL aerobic capacity (maximal oxygen uptake, VO2 max) is reported to decline with age, ~10% per decade in sedentary persons >25 years of age (1,2) and ~15% per decade between the ages of 50 and 75 years (3). Such estimates are based mainly on cross-sectional data. The few studies that used longitudinal data have been based on small numbers of selected individuals [e.g., master/endurance athletes (3–6), physical education students (7), men enrolled in a fitness program (8)] or unselected individuals (9). A recent study by Fleg and colleagues (10) studied 810 participants from ages 20 to mid 80s and observed declines in level of oxygen consumption at peak exercise (VO2peak) and oxygen pulse (VO2 ml/heart beat at maximum exercise) that accelerated with advanced decades.

This study describes the longitudinal changes in cardiopulmonary capacity that occur with aging in a large sample (n = 592) of community-dwelling older participants (median age 70 years at enrollment) not selected on the basis of patterns of physical activity or other lifestyle variables. Specifically, we have investigated how the inclusion of a number of physiological variables into such analyses can change the estimates of age-related decline in fitness. In contrast to most other longitudinal studies that have used only two time points to measure change, we took measurements approximately every 2 years up to four time points. The large numbers of observations allowed us to evaluate the effects of several variables on exercise performance, e.g., pulmonary mechanics, smoking, medications, body composition, and physical activity.

METHODS

Participants

Of 2092 individuals who participated in a population-based longitudinal study of aging in people ≥55 years old who lived in the city of Sonoma, California, 998 relatively healthy persons (419 men and 579 women) were eligible for this substudy of aerobic fitness (11). Individuals were excluded if they had: 1) known cardiac disease (myocardial infarction by history or electrocardiogram, history of angina, coronary artery angioplasty, or bypass grafting); 2) cerebrovascular disease (stroke, transient ischemic attacks, or carotid artery surgery); 3) peripheral vascular disease with intermittent claudication; or 4) musculoskeletal impairment (use of a cane and/or walker; lower extremity arthritis that impaired walking) or inability to perform a treadmill exercise test.

Participants were first interviewed and underwent treadmill exercise between June 1993 and March 1995, which then was repeated approximately biannually: 800 (80%; 473 men, 327
women) a second time (T2, September 1995 through April 1997); 598 (60%; 251 men, 347 women) a third time (T3, August 1997 through October 1999); and 490 (43%; 196 men, 294 women) a fourth time (T4, February 2000 through March 2002). Major reasons for participants not to be retested were death (60), intervening illness (263), refusals (238), and moving from the study area (7). The study was approved by the Committee on Human Research, University of California, San Francisco and the Committee for the Protection of Human Subjects, University of California, Berkeley. Written, informed consent was obtained from all participants prior to testing at each time point. We restricted our analyses to 592 participants (253 men and 339 women) who completed at least 3 of the 4 biannual tests.

### Treadmill Exercise Testing

Participants were exercised on a computer-driven treadmill (CASE 15; Marquette Electronics, Inc., Milwaukee, WI) with the Cornell modification of the Bruce treadmill exercise protocol (12,13). They were exercised to their self-determined maximal capacity or until the physician stopped the test. Participants could stop the test whenever they felt the need to do so. All participants exercised for \( \geq 4 \) minutes.

### Respiratory Gas Measurements and Spirometry

Continuous breath-to-breath respiratory gas measurements were obtained with a Medical Graphics Cardiopulmonary Exercise (CPX) system (Medical Graphics Corp., St. Paul, MN). Direct measurements of oxygen consumption (\( VO_2 \)), carbon dioxide production (\( VCO_2 \)), minute ventilation (\( VE \)), and respiratory rate were obtained. Flow meters and gas analyzers were calibrated daily for accuracy and linearity with precisely analyzed gas mixtures. Gas analyzers were checked by auto-calibration prior to each test. Output from the gas analyses were sampled every 15 seconds and stored for calculation of the Oxygen Uptake Efficiency Slope (OUES). Maximum expiratory maneuvers were performed on a rolling seal Survey Spirometer (Warren E. Collins, Braintree, MA). The mean forced expiratory volume in 1 second (FEV\(_1\)) was based on two or three trials that met all acceptability criteria for spirometry (14).

We have included FEV\(_1\) in our analyses because several long-term follow-up studies (15–18) have demonstrated an association between FEV\(_1\) and various causes of mortality that are independent of cigarette smoking, known coronary heart disease, and a variety of risk factors for heart disease. It has been suggested that FEV\(_1\) is a marker for general aging processes that affect both the heart and lungs (18) and other organ systems as well. Therefore, in these analyses we consider FEV\(_1\) as a surrogate for a number of unmeasured aging processes that could impact aerobic fitness and not as a specific measure of lung function.

### Measures of Cardiopulmonary Fitness

\( VO_2^\text{peak} \) (ml/kg min\(^{-1}\)), the duration of exercise, and the OUES were used to evaluate aerobic fitness. Originally described by Baba and colleagues (19) and verified by us (20), the OUES reflects the relationship between oxygen...
Table 2. Statistical Differences Between Participants Who Did and Did Not Complete at Least Three Biannual Cycles of Treadmill Exercise

<table>
<thead>
<tr>
<th>General</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Body Surface Area (m²)*</td>
<td>.87</td>
<td>.17</td>
</tr>
<tr>
<td>Smoking (% never/ current)</td>
<td>.03/34</td>
<td>&lt;.01/32</td>
</tr>
<tr>
<td>No underlying health condition (%)²</td>
<td>.09</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Diabetes mellitus (%)³</td>
<td>.25</td>
<td>.35³</td>
</tr>
<tr>
<td>Intermittent claudication (%)</td>
<td>.08</td>
<td>.04</td>
</tr>
<tr>
<td>Current asthma, chronic bronchitis, emphysema (%)</td>
<td>.06</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Cancer (except non-melanoma skin) (%)</td>
<td>.02</td>
<td>.02</td>
</tr>
<tr>
<td>Medication for high blood pressure (%) ²</td>
<td>&lt;.01</td>
<td>&lt;.22</td>
</tr>
<tr>
<td>Treadmill Exercise Test²</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peak VO₂ (ml · min⁻¹ · kg⁻¹)²</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peak VE (L · min⁻¹)²</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Peak heart rate (bpm)²</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>RER at peak exercise</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Exercise duration (min)²</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>OUES (ml · min⁻¹ · (L · min⁻¹ · VE))²</td>
<td>&lt;.01</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

Notes: Data shown are for present cohort (≥3 cycles of testing) versus excluded participants (<3 cycles of testing).

*Median.
²Self-report of no asthma, chronic bronchitis/emphysema, cancer, liver or kidney disease, diabetes mellitus, vascular disease, Parkinson’s disease.
³All medical conditions are self-reported.
§β-adrenergic receptor blockers, calcium channel blockers.
Mean.

VO₂peak = level of oxygen consumption at peak exercise; VE = ventilation; RER = respiratory exchange ratio; OUES = Oxygen Uptake Efficiency Slope.

uptake (VO₂ in ml · min⁻¹) and total ventilation (VE in L · min⁻¹), and is described by the following equation:

$$ VO₂ = a \log_{10} VE + b, $$

where a represents the OUES \((\text{VO}_2 \text{ ml} \cdot \text{min}^{-1})/(\text{VE} \cdot \text{L} \cdot \text{min}^{-1})\). OUES can be calculated reliably from a sub-maximal exercise test of at least 4 minutes duration (20). Its use greatly reduces test variability due to motivational and subjective factors—variables that can influence results when exercise duration or VO₂peak are used as test endpoints.

**Lean Body Mass (Bioelectric Impedance) Measurements**

Whole-body resistance and reactance were obtained by bioelectric impedance at each visit (Body Composition Analyzer Model B1A-101; RJL Systems, Clinton Twp, MI; 21). Lean and fat mass were estimated from regression equations derived in a validation substudy of 200 study participants who were free of congestive heart failure and kidney or liver disease, who were not taking diuretics, and who underwent bioelectric impedance measurements and dual x-ray absorptiometry (DEXA) (21).

**Statistical Analysis**

All continuous baseline variables were centered on their median values. Longitudinal effects of interest were estimated with sex-specific repeated measures models (22) that allowed separation of longitudinal effects due to aging from cross-sectional (cohort) effects. Six separate, sex-specific models were tested by repeated measures methods (Appendix A): two cross-sectional models that do not account for time and four longitudinal models to evaluate the effects of time on the estimates of age-related declines.

To account for the effect on the results of various patterns of losses to follow-up, we carried out a series of sensitivity analyses (details of these analyses available from IBT on request). In no instance were the results different from those obtained without adjustment for the censoring.

**RESULTS**

**Participant Characteristics**

The characteristics of our original cohort at baseline (579 women and 419 men) have been reported (13,20). For the present analyses, participants who completed at least three of the four biannual cycles of testing (over a mean period of 6.3 years) were included. Tables 1 and 2 show the baseline clinical and exercise characteristics of these 592 participants compared with those of participants who were not able to complete at least three cycles of testing. Of note, of the 14% (n = 37) of women who were taking blood pressure medication, 33 had no other underlying health condition. If we consider these women to be free of underlying health condition, then 85% of women have no self-reported disease. The comparable figure for men was 97%. Participants

Table 3. Participant General Characteristics at Each of Four Biannual Cycles of Treadmill Testing

<table>
<thead>
<tr>
<th>Round</th>
<th>N</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female/male</td>
<td>Females</td>
</tr>
<tr>
<td>1</td>
<td>339/253</td>
<td>68.1 ± 12.0</td>
</tr>
<tr>
<td>2</td>
<td>336/249</td>
<td>68.1 ± 11.8</td>
</tr>
<tr>
<td>3</td>
<td>326/244</td>
<td>68.0 ± 12.6</td>
</tr>
<tr>
<td>4</td>
<td>211/178</td>
<td>68.1 ± 12.5</td>
</tr>
</tbody>
</table>

Notes: All values expressed as mean ± standard deviation.

BSA = body surface area; BMI = body mass index.
included in the present study generally had better cardiovascular function than those excluded.

Tables 3 and 4 show cross-sectional, physical characteristics and exercise responses at each test cycle. Little within-sex variation in body composition occurred as the study progressed. Women have lower body surface area (BSA), body mass index (BMI), total body mass, lean mass, and lean/fat ratio than do men. Such sex differences in body composition contribute to the apparent sex differences in VO2peak. When normalized for lean body (muscle) mass instead of body weight (kg), the sex difference in VO2peak disappeared, and VO2peak uptake in women, expressed as a percentage of that achieved by men, increased from 77% to 95% (13).

Decline in Aerobic Capacity with Age

Tables 5 and 6 summarize the results for VO2peak and OUES. Models 1 (baseline data only) and 2 (data as repeated measures) are cross-sectional models (time is not modeled explicitly in Model 2). Models 3-6 are longitudinal models in which time is modeled explicitly. In addition to Time (Model 3), Models 4–6 successively add: age (Model 4), baseline FEV1 and change in FEV1, smoking and medications (Model 5), peak heart rate and change peak heart rate from baseline (Model 6).

The cross-section parameter estimate for age (Model 1) largely reflects differences in the varying cohorts that make up the study participants. Model 2 mixes longitudinal and cohort effects together by treating data as repeated measures. The rate of decline of VO2peak with age is similar for men and women but, for OUES, is approximately 2-fold greater in men.

Model 3 estimates unadjusted longitudinal change (Time) in VO2peak and OUES over the average 6.3 years of the follow-up. For both measures, the decline for men is greater than for women, particularly for OUES. In Model 4, the cross-sectional (cohort) effects of age are added into the model (e.g., 0.23 ml O2 min⁻¹·kg⁻¹ needs to be subtracted for each year of a participant’s age over 65 years). There is virtually no change in the estimates of the magnitude of the longitudinal declines (Time), which appear to be larger than the cross-sectional effect (Age) (−0.39 vs −0.23 ml O2 min⁻¹·kg⁻¹ in women, −0.69 vs −0.34 ml O2·kg⁻¹·min⁻¹ in men). Model 5 adds a number of baseline covariates that result in little change in the longitudinal point estimate of decline (−0.39 to −0.36 ml O2·kg⁻¹·min⁻¹ in women; −0.69 to −0.58 ml O2·kg⁻¹·min⁻¹ in men) (−5.8 ml O2·kg⁻¹·min⁻¹ per decade for any given stratum implied in the model). Model 6 includes the change in peak heart rate at the end of the most recent exercise test from the value achieved at the end of the baseline test. With this inclusion, the estimate for longitudinal change (Time) in VO2peak in women is decreased by 39% (−0.36 to −0.22 ml O2·kg⁻¹·min⁻¹) and is similar for men (46%, Table 5, Model 6). Thus, the estimated rate of longitudinal decline in women is −0.22 ml O2·kg⁻¹·min⁻¹·y⁻¹ or 9.7% per decade and in men is −0.31 ml O2·kg⁻¹·min⁻¹·y⁻¹ or 10.4% per decade. Although fewer than 10% of participants were taking beta-adrenergic blocking drugs for hypertension, the above analyses were repeated after censoring these participants. There was little effect on the decline in heart rate (Table 4) and little change in the regression results, most likely due to the small number of participants receiving these medications.

### Table 4. Treadmill Exercise Outcomes

<table>
<thead>
<tr>
<th>Round</th>
<th>F/M</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
<th>Females</th>
<th>Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>339/253</td>
<td>21.9 ± 4.5</td>
<td>28.5 ± 6.0</td>
<td>1642 ± 318</td>
<td>2478 ± 493</td>
<td>11.5 ± 3.8</td>
<td>14.7 ± 4.4</td>
<td>1.08 ± 0.09</td>
<td>1.12 ± 0.08</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>336/249</td>
<td>21.5 ± 4.3</td>
<td>27.8 ± 6.0</td>
<td>1631 ± 299</td>
<td>2468 ± 493</td>
<td>11.5 ± 3.9</td>
<td>14.6 ± 4.3</td>
<td>1.05 ± 0.09</td>
<td>1.09 ± 0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>326/244</td>
<td>20.3 ± 4.3</td>
<td>25.8 ± 5.8</td>
<td>1607 ± 304</td>
<td>2347 ± 478</td>
<td>10.9 ± 3.9</td>
<td>13.7 ± 4.4</td>
<td>1.07 ± 0.11</td>
<td>1.11 ± 0.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>211/178</td>
<td>20.1 ± 3.8</td>
<td>25.1 ± 5.5</td>
<td>1548 ± 284</td>
<td>2225 ± 447</td>
<td>11.1 ± 3.7</td>
<td>13.7 ± 4.3</td>
<td>1.10 ± 0.11</td>
<td>1.14 ± 0.12</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 5. All Participants

<table>
<thead>
<tr>
<th>Round</th>
<th>N</th>
<th>VO2peak (ml·min⁻¹·kg⁻¹)</th>
<th>OUES (ml·min⁻¹·O2/L·min⁻¹·VE)</th>
<th>Exercise Duration (min)</th>
<th>RER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>339/253</td>
<td>21.9 ± 4.5</td>
<td>28.5 ± 6.0</td>
<td>1642 ± 318</td>
<td>2478 ± 493</td>
</tr>
<tr>
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</tr>
<tr>
<td>3</td>
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<td>1607 ± 304</td>
<td>2347 ± 478</td>
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<tr>
<td>4</td>
<td>211/178</td>
<td>20.1 ± 3.8</td>
<td>25.1 ± 5.5</td>
<td>1548 ± 284</td>
<td>2225 ± 447</td>
</tr>
</tbody>
</table>

### Notes:

- All values expressed as mean ± standard deviation.
- VO2 = level of oxygen consumption; OUES = Oxygen Uptake Efficiency Slope; VE = ventilation; RER = respiratory exchange ratio; FEV1 = forced expiratory volume in 1 s.

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Male
decade decline in VO2peak for women and men, respectively, approximately a 40% and 50% decline in the estimated per
in peak heart rate achieved during exercise results in
cross-sectional estimates (Model 1). The inclusion of change
longitudinal estimates of decline per decade are larger than
round. Based on Models 3–5, the conclusion would be that
the study were set to the sex-specific medians for each test
and change in these variables during the course of the study
smaller for OUES (Table 7).

With regard to the cross-sectional parameter point esti-
mates of VO2peak (Age), these also decrease successively
as one progresses from Model 4 to Model 6 (from −0.23
to −0.16 to −0.08 ml O2·kg−1·min−1 in women; from −0.34
to −0.27 to −0.15 ml O2·kg−1·min−1 in men).

Similar results to the above for the variables of Time and
Age are noted when OUES is used as the outcome variable
(Table 6, Model 6), although the percentage changes in the
age and time parameters are not as great as for VO2peak.

Table 7 provides sex-specific estimates of the percentage
deciles in VO2peak and OUES per decade. Each estimate
represents the percentage decline for participants age 65
years at baseline not taking cardiovascular medications and
whose FEV1, peak heart rate, as well as their change during
the study were set to the sex-specific medians for each test
round. Based on Models 3–5, the conclusion would be that
longitudinal estimates of decline per decade are larger than
cross-sectional estimates (Model 1). The inclusion of change
in peak heart rate achieved during exercise results in
approximately a 40% and 50% decline in the estimated per
decade decline in VO2peak for women and men, respectively,
compared to Model 5 where change in heart rate is not
included. The effect of peak heart rate change is much
smaller for OUES (Table 7).

Inclusion of lean body mass, the ratio of lean/fat mass,
and change in these variables during the course of the study
resulted only in small changes in aerobic performance at
baseline (1.8% and 1.3% per kg difference in lean body
mass in women and men, respectively; 1.8% and 0.9% per
0.1 unit difference in the lean/fat ratio in women and men,
respectively). Changes in lean body mass and lean/fat ratio
during the 6.3 years of the study were small and did not
affect the age-related decline in exercise performance.
Inclusion of self-reported physical activity over the 4 years
did not modify the observed age-related decline in exercise
performance. Exclusion of the small number of participants
with underlying health conditions (e.g., diabetes, lung
conditions, cancer) had little effect on the results.

**DISCUSSION**

Few longitudinal studies have been performed to define
age-related decline in aerobic fitness. Dehn and Bruce (23)
suggested that the decline (25% per decade) in individuals
studied serially was approximately double the rate of decline
reported in cross-sectional analyses. In the study by Jackson
and colleagues (8) of persons ages 25–70 years, cross-
section estimates likely are confounded by cohort effects
due to enrollment over an unspecified period of time; their
estimates of longitudinal change are imprecise due to
relatively little change over the study interval (4.1 years).

Although Fleg and colleagues included individuals who

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Table 5. Peak Oxygen Consumption (ml O2/kg/min)

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
<th>Model 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>22.49 (0.28)</td>
<td>21.38 (0.22)</td>
<td>22.05 (0.22)</td>
<td>22.14 (0.21)</td>
<td>22.77 (0.27)</td>
<td>22.72 (0.24)</td>
</tr>
<tr>
<td>Age</td>
<td>−0.08 (0.04)</td>
<td>−0.06 (0.03)</td>
<td>NA</td>
<td>−0.23 (0.03)</td>
<td>−0.16 (0.03)</td>
<td>−0.08 (0.03)</td>
</tr>
<tr>
<td>FEV1</td>
<td>2.40 (0.51)</td>
<td>1.90 (0.39)</td>
<td>NA</td>
<td>NA</td>
<td>2.50 (0.50)</td>
<td>2.05 (0.45)</td>
</tr>
<tr>
<td>FEV1 change from baseline</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1.51 (0.85)</td>
<td>1.16 (0.74)</td>
</tr>
<tr>
<td>Peak heart rate</td>
<td>0.11 (0.01)</td>
<td>0.11 (0.01)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>0.10 (0.01)</td>
</tr>
<tr>
<td>Peak heart rate change from baseline</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>0.10 (0.01)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.68 (0.85)</td>
<td>0.77 (0.72)</td>
<td>NA</td>
<td>NA</td>
<td>−0.58 (0.82)</td>
<td>0.69 (0.74)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>−0.49 (0.47)</td>
<td>−0.49 (0.39)</td>
<td>NA</td>
<td>NA</td>
<td>−0.88 (0.46)</td>
<td>−0.69 (0.41)</td>
</tr>
<tr>
<td>Beta blocker</td>
<td>−0.01 (0.79)</td>
<td>0.00 (0.37)</td>
<td>NA</td>
<td>NA</td>
<td>−0.82 (0.39)</td>
<td>0.21 (0.35)</td>
</tr>
<tr>
<td>Non-beta blocker cardiac drug</td>
<td>−0.06 (0.61)</td>
<td>−0.04 (0.29)</td>
<td>NA</td>
<td>NA</td>
<td>−0.44 (0.31)</td>
<td>−0.50 (0.27)</td>
</tr>
<tr>
<td>Time</td>
<td>NA</td>
<td>NA</td>
<td>−0.39 (0.03)</td>
<td>−0.39 (0.03)</td>
<td>−0.36 (0.04)</td>
<td>−0.22 (0.03)</td>
</tr>
</tbody>
</table>

| **Male**             |         |         |         |         |         |         |
| Intercept            | 29.55 (0.51) | 27.85 (0.39) | 28.66 (0.36) | 28.62 (0.33) | 30.07 (0.49) | 29.75 (0.44) |
| Age                  | −0.11 (0.06) | −0.08 (0.04) | NA       | −0.34 (0.04) | −0.27 (0.06) | −0.15 (0.05) |
| FEV1                 | 1.85 (0.58) | 1.79 (0.42) | NA       | NA       | 1.94 (0.57) | 1.37 (0.51) |
| FEV1 change from baseline | NA       | NA       | NA       | NA       | 4.28 (0.82) | 2.87 (0.70) |
| Peak heart rate      | 0.16 (0.02) | 0.17 (0.01) | NA       | NA       | NA       | 0.15 (0.02) |
| Peak heart rate change from baseline | NA       | NA       | NA       | NA       | −4.29 (1.58) | −2.99 (1.40) |
| Current smoker       | −3.16 (1.60) | −2.48 (1.26) | NA       | NA       | −1.99 (1.70) | −1.70 (0.61) |
| Ex-smoker            | −1.60 (0.71) | −1.06 (0.56) | NA       | NA       | −0.42 (0.63) | 0.64 (0.54) |
| Beta blocker         | 1.20 (1.64) | −0.49 (0.63) | NA       | NA       | NA       | 0.10 (0.35) |
| Non-beta blocker cardiac drug | −0.51 (0.84) | −1.04 (0.38) | NA       | NA       | 0.25 (0.41) | 0.10 (0.35) |
| Time                 | NA       | NA       | −0.69 (0.04) | −0.69 (0.04) | −0.58 (0.05) | −0.31 (0.05) |

**Notes:** All data are estimates (standard error).
*Model based on baseline values.
1Repeated measurements model without Time variable.
2Repeated measurements model with Time variable.
3Values are median centered by rounds, refer to Tables 3 and 4.
4Ex-smoker defined as having ever smoked and either quit less than 20 years prior to their baseline interview or accumulated the equivalent of 10 or
more pack-years.
5Time is in years to 2 decimal places.

FEV1 = forced expiratory volume in 1 s; NA = not applicable.
were much younger than ours, the per decade estimates derived from our mixed Model 5 for VO$_{2\text{peak}}$ (Table 7) are very similar to their results for persons older than 50 years (see Figure 3 of reference 10). In both studies, percentage declines were greater for men than for women. Moreover, our study and the Fleg study show that estimates based on longitudinal analyses are larger than those based on cross-sectional data. Neither the study of Fleg and colleagues nor any of the other studies, however, evaluated the extent to which the estimated rates of decline were sensitive to the variables included in their regression models.

We have demonstrated that estimated rates of decline in VO$_{2\text{peak}}$ and OUES associated with aging are sensitive to two physiological variables. Of note, neither habitual physical exercise nor high aerobic capacity is known to modify the normal deterioration in resting FEV$_1$ or lung function that occurs with age (24). The study by Fleg and colleagues also showed that high intensity physical activity did not affect patterns of decline in VO$_{2\text{peak}}$, although levels at any age were ordered by degree of participation in high level activities (10).

On the basis of our data, we suggest that aging with respect to cardiopulmonary function, and, as with many other age-related processes [e.g., physical functioning and disability (25)], is a relative concept the interpretation of which depends on the types of variables included in models as well as the model that is chosen to characterize the change with age (cross-section vs longitudinal).

Our analysis provides an explanation for the differences between estimates of decline in aerobic capacity based on cross-sectional and longitudinal data. Estimates based on cross-sectional studies mix aging and cohort effects together, whereas those from longitudinal studies can separate the effects. In cross-sectional analyses, the survivor bias will tend to decrease the average estimate of decline compared to what would have been observed longitudinally. Therefore, if one is interested in an estimate of longitudinal
change, then the Time variable in our models is that estimate. If one is interested in the overall effect of aging on aerobic decline, then the sum of the Age (cross-sectional) and Time variables provides that estimate.

Age-related decline in aerobic capacity, when not adjusted for other variables, was less in women than in men (e.g., 18% vs 24% per decade for VO2peak and 12% vs 20% per decade for OUES, Model 3, Table 7). This difference has been found in other studies (2,9,24,26). Adjustment for differences in body composition had little effect on these gender differences in the rates of decline. The decline in peak exercise heart rate with age appears to be the major cardiac determinant of the age-related decline in VO2max. Moreover, the lack of effect of physical activity in unselected older age groups in this process of decline would suggest that activity patterns early in life that maximize aerobic fitness may be particularly important in the preservation of adequate aerobic reserve in the oldest old.

One potential limitation on the interpretation of our results could be the occurrence of selection bias that is suggested by the loss of participants between the 3rd and 4th round of testing. When we dropped the round four data and included participants who completed all of the first three rounds, however, the results were unchanged. In addition, a more formal analysis to reweight the sample for various censoring patterns also gave nearly identical results. Therefore, we believe that the results for the full sample are valid. This view is reinforced by the quantitative and qualitative similarity of our results to those of Fleg and colleagues (10) who also used a population-based sample. Unfortunately, the participants in our study were predominantly white and middle class (as were those in the study of Fleg and colleagues) which does limit the findings of this study to these groups.

Summary
This study demonstrates that estimates of effects of aging on aerobic capacity are sensitive to the inclusion of physiological factors that also decline with age. In the present study, FEV1 and maximal exercise heart rate (together with their changes during the course of the study) accounted for most of the longitudinal decline of aerobic capacity with age. Our findings also corroborate, in a much larger cohort, the findings of others that the rate of decline is greater in men than in women—an observation that remains largely unexplained. In a more general context, quantitative estimates of aging of any physiological process, as measured in clinical and epidemiologic studies, represent the residual variance not explained by factors included in the study and/or any mismeasurement of those factors. The apparently larger estimates of decline observed in some longitudinal analyses likely represent incomplete selection of variables in the models used. Thus, attempts to reconcile differences and/or compare results between studies of the effects of aging on aerobic fitness need to recognize this heretofore neglected concept.

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REFERENCES
APPENDIX A

Statistical Details

Continuous baseline variables were centered on their median values. Longitudinal effects of interest were estimated with sex-specific repeated measures models (5)

\[
VO_{2\text{peak}}/\text{kg} = \beta_0 + \delta_1 x_{1i} + \delta_2 (y_{ij} - \bar{y}_j) + \beta_3 w_{ij} + \epsilon_{ij},
\]

where i indexes participant and j indexes trial number. \(x_{1i}\) is the vector of baseline covariates (age, BSA, median centered mean reproducible FEV, and smoking status). \(y_{ij}\) represents a vector of the variables that captures the change at time \(j\) of FEV, and peak heart rate from their respective baseline values. \(w_{ij}\) is the vector of time-dependent variables (time [years from baseline visit], use of cardiac medications known to affect exercise performance). \(\beta_0\) is the estimated mean \(VO_{2\text{peak}}/\text{kg}\) or OUES adjusted to the median values of baseline age, BSA, and FEV, for nonsmokers who are not on any cardiac medications. \(\delta_1\) represents the cross sectional difference in average \(VO_{2\text{peak}}/\text{kg}\) or OUES for groups that differ by 1 unit in \(x_{1i}\) at baseline, conditional on other covariates. \(\delta_2\) represents the expected longitudinal difference in \(VO_{2\text{peak}}/\text{kg}\) or OUES per unit change in \(y_{ij}\), conditional on other covariates. \(\beta_3\) is the difference in average \(VO_{2\text{peak}}/\text{kg}\) or OUES for groups that differ by 1 unit in \(w_{ij}\) over time, conditional on other covariates. The part of \(\beta_3\) that is the coefficient for time captures changes in \(VO_{2\text{peak}}/\text{kg}\) or OUES due to any other unmeasured variability specific to the settings of different rounds, conditional on all other covariates being held constant. The conditional longitudinal effect of aging on \(VO_{2\text{peak}}/\text{kg}\) or OUES can be estimated through the parameter estimates for Age and Time as follows: \(\delta_1 + \epsilon_1 + \beta_3\). The coefficients for the cardiac medications represent the estimated difference in \(VO_{2\text{peak}}/\text{kg}\) or OUES when switching between being on a drug not thought to influence \(VO_{2\text{peak}}/\text{kg}\) or OUES (or not being on a drug at all) to being on beta blockers or cardiac drugs that influence exercise performance, conditional on all other covariates being held constant.

A baseline visit is defined as the first time that the participant performed treadmill exercise. The OUES regression slope for each participant was calculated by regression of \(VO_2\) on the \(\log_{10}\) (VE) for each time \(j\). The inverse of the variance of the slope estimates (1/Var(OUES)) was used as the weight in the repeated measures model to account for the differences in data available to fit each participant’s OUES (a minimum of eight data points was required). Although longitudinal data were obtained for BSA, only baseline BSA was included in the model, as there was very little variability in the measure over time. A similar, repeated measures model was fit for \(VO_{2\text{peak}}/\text{kg/min}\). BSA was excluded in this latter model, because the measure is already normalized for body weight.

Descriptive and regression analyses were performed using SAS System statistical software (version 8.2; SAS Institute Inc., Cary, NC). Models were fit using the MIXED procedure with the repeated statement.