How Long Can and Should We Live

Luigi Ferrucci, MD, PhD
IRP/NIA/NIH
Can we age gracefully?

1. Eat and drink well in good company
2. Exercise (aerobic, resistance and core)
3. Fight afternoon fatigue
4. Change the way you think about aging
5. Sleep well
6. Avoid chronic inflammation (belly fat and oral health)
7. Stay connected
8. Don’t smoke
9. Get busy, have fun, learn something new
10. See regularly your doctor
11. Check your hearing and vision
What and How Much We Eat and Drink
The retardation of aging in mice by dietary restriction: longevity, cancer, immunity and lifetime energy intake.
Caloric restriction reduces age-related and all-cause mortality in rhesus monkeys

Ricki J. Colman et al.

**Figure a:** Age-related mortality

**Figure b:** All-cause mortality

![Graphs showing age-related and all-cause mortality](image-url)
Impact of caloric restriction on health and survival in rhesus monkeys from the NIA study
Julie A. Mattison et al.
Intentional Weight Loss and All-Cause Mortality: A Meta-Analysis of Randomized Clinical Trials


<table>
<thead>
<tr>
<th>Study</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stamler (1987)</td>
<td>1.42 (0.24, 8.32)</td>
</tr>
<tr>
<td>Davis (1993)</td>
<td>2.03 (0.38, 11.02)</td>
</tr>
<tr>
<td>TOHP I (1992)</td>
<td>1.91 (0.12, 30.47)</td>
</tr>
<tr>
<td>TOHP II (1997)</td>
<td>1.40 (0.44, 4.39)</td>
</tr>
<tr>
<td>Knowler (2002)</td>
<td>0.60 (0.14, 2.51)</td>
</tr>
<tr>
<td>Shea (2010)</td>
<td>0.50 (0.28, 0.89)</td>
</tr>
<tr>
<td>Shea (2011)</td>
<td>0.93 (0.65, 1.33)</td>
</tr>
<tr>
<td>Gabriel (2011)</td>
<td>0.50 (0.05, 5.52)</td>
</tr>
<tr>
<td>Rejeski (2011)</td>
<td>0.97 (0.09, 10.56)</td>
</tr>
<tr>
<td>van Wier (2011)</td>
<td>0.99 (0.09, 10.93)</td>
</tr>
<tr>
<td>Wing (2013)</td>
<td>0.86 (0.71, 1.05)</td>
</tr>
<tr>
<td>Daumit (2013)</td>
<td>0.68 (0.12, 4.01)</td>
</tr>
<tr>
<td>Overall</td>
<td>0.85 (0.73, 1.00)</td>
</tr>
</tbody>
</table>
The Science of Fat
After ‘The Biggest Loser,’ Their Bodies Fought to Regain Weight

Contestants lost hundreds of pounds during Season 8, but gained them back. A study of their struggles helps explain why so many people fail to keep off the weight they lose.

By GINA KOLATA MAY 2, 2016
GAINING LOST WEIGHT

Of the 14 contestants studied, all regained weight in the six years after the competition. Four contestants are heavier now than before the competition.

Erinn Egbert is the only contestant who weighs less today than six years ago.

Rudy Pauls regained 80 percent of his lost weight, then had surgery to reduce the size of his stomach.

Danny Cahill lost 239 pounds and won the competition, but has regained over 100 pounds.

A SLOWING METABOLISM

Nearly all the contestants have slower metabolisms today than they did six years ago, and burn fewer calories than expected when at rest.

Danny Cahill now burns 800 fewer calories a day than expected.

“THE BIGGEST LOSER”
Season 8 (2009)
A 2-Year Randomized Controlled Trial of Human Caloric Restriction: Feasibility and Effects on Predictors of Health Span and Longevity

A 2-Year Randomized Controlled Trial of Human Caloric Restriction: Feasibility and Effects on Predictors of Health Span and Longevity

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet
Ramón Estruch, et al.

- Olive oil ≥4 tbsp/day
- Tree nuts and peanuts† ≥3 servings/wk
- Fresh fruits ≥3 servings/day
- Vegetables ≥2 servings/day
- Fish (especially fatty fish), seafood ≥3 servings/wk
- Legumes ≥3 servings/wk
- Sofrito ≥2 servings/wk
- White meat Instead of red meat
- Wine with meals ≥7 glasses/wk

N Engl J Med 2013; 14:368
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet
Ramón Estruch, et al.

A Primary End Point (acute myocardial infarction, stroke, or death from cardiovascular causes)

Med diet, EVOO: hazard ratio, 0.70 (95% CI, 0.53–0.91); P=0.009
Med diet, nuts: hazard ratio, 0.70 (95% CI, 0.53–0.94); P=0.02

No. at Risk
Control diet 2450 2268 2020 1583 1268 946
Med diet, EVOO 2543 2486 2320 1987 1687 1310
Med diet, nuts 2454 2343 2093 1657 1389 1031

N Engl J Med 2013; 14:368
Low-Fat Dietary Pattern and Risk of Cardiovascular Disease
The Women's Health Initiative Randomized Controlled Dietary Modification Trial
Barbara V. Howard et al. JAMA. 2006;295(6):655-666

This long-term dietary intervention in postmenopausal women, intended to reduce fat intake and increase intake of vegetables, fruits, and grains . . . did not reduce risk of CHD or stroke . . . possibly this was because of low compliance.
Minnesota Coronary Experiment (1968 to 1973), study of diets of more than 9,000 people at state mental hospitals and a nursing home. Half of those subjects were fed meals rich in saturated fats from milk, cheese and beef. The remaining group ate a diet in which much of the saturated fat was removed and replaced with corn oil, an unsaturated fat that is common in many processed foods today. A diet low in saturated fat and enriched with corn oil reduced cholesterol (14% versus 1% in controls) but not mortality. In fact, the greater the drop in cholesterol, the higher the risk of death during the trial.
The Fast Food Study

Change Over Time in IL-6 According to Meal Type

![Graph showing change in IL-6 over time for Fast-Food Like Meal and Healthy Meal](image)

- Fast-Food Like Meal
- Healthy Meal

Log(IL-6, pg/mL) vs. Time (min)

- * p<.05
- # p<.01

Fat
What about Exercise
World record times for running 5,000 meters according to age and sex.
CORONARY HEART-DISEASE AND PHYSICAL ACTIVITY OF WORK

J. N. Morris
M.A. Glasg., M.R.C.P., D.P.H.

J. A. Heady
M.A. Oxf.

OF THE SOCIAL MEDICINE RESEARCH UNIT, MEDICAL RESEARCH COUNCIL

P. A. B. Raffle
M.D. Lond., D.P.H., D.I.H.

OF THE MEDICAL DEPARTMENT, LONDON TRANSPORT EXECUTIVE

C. G. Roberts
B.A., M.D. Camb.

J. W. Parks
M.B.E., M.D. Camb., D.C.H.

OF THE TREASURY MEDICAL SERVICE

This report is one of a series on the epidemiology of coronary disease. Study of coronary heart-disease suggests that there has been a true increase of it, and that this is not due simply to an increase of coronary atheroma. The atheroma, it seems, is the basic condition of the heart-disease; but other conditions are necessary, and the complex of atheroma, thrombosis, and the capacity of the heart to deal with these in relation to the demands made upon it, all need to be studied.

Surveys have been made from the Social Medicine Research Unit to gain some knowledge of coronary heart-disease as a problem in public health, and in the hope of uncovering social factors which may be favourable or unfavourable to its occurrence. Observations on a group of medical practitioners indicated that such epidemiological study can be carried out with relatively small numbers, and that it may be rewarding. The present report extends this study to other workers and describes the findings among them. Readers are referred to the previous papers where the possibilities and limitations of this type of investigation are considered, and points of theory and method are discussed in some detail.

I. CORONARY HEART-DISEASE IN DIFFERENT OCCUPATIONAL GROUPS

Absences of any duration are so examined. All diagnoses are coded by the international three-figure code. Details of all deaths and of all retirements due to ill health are also recorded and the medical causes are similarly coded. Copies of the death certificates were available, as were the diagnoses of the London Transport medical officers for ill-health retirements. Routine checks are imposed in the Central Record of Staff Statistics to ensure accuracy of data.

By special arrangement for the present inquiry, all absences, ill-health retirements, and deaths, the diagnoses of which were assigned to any code number from 420 to 434 (inclusive) were reported to the medical department for detailed scrutiny; and cases of coronary heart-disease, presumptively atherosclerotic, and doubtful cases for consideration, were then "notified" to the unit. (It is, of course, to be appreciated that all clinical presentations of the disease, whether occurring on or off duty, were included.)

From the Central Record of Staff Statistics population counts in appropriate age-groups for each occupational group were available at the beginning and end of each year the investigation covered.

RESULTS

Incidence and Early Mortality

Men may retire from work because of coronary heart-disease; so information from industrial sources on

TABLE I—FIRST CLINICAL EPISODES (INCIDENCE) OF CORONARY HEART-DISEASE IN WEEKLY PAID STAFF (MEN AGED 35–64 INCLUSIVE) OF LONDON TRANSPORT EXECUTIVE, 1949–50

<table>
<thead>
<tr>
<th>Ages (years)</th>
<th>(1) Angina pectoris</th>
<th>&quot;Coronary thrombosis&quot;</th>
<th>Total incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of cases</td>
<td>Rate per 1000 p.a.</td>
<td>No. of cases</td>
</tr>
<tr>
<td>35–39</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>
### Dose of Jogging and Long-Term Mortality. The Copenhagen City Heart Study

Peter Schnohr et al. JACC 2015; 5:411-419

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**Central Illustration: Dose of Jogging and Long-Term Mortality**

<table>
<thead>
<tr>
<th>DOSE OF JOGGING</th>
<th>NO. OF PARTICIPANTS</th>
<th>ALL-CAUSE MORTALITY</th>
<th>FOREST PLOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjusted for age and sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary nonjogger (reference)</td>
<td>413</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>Light jogger</td>
<td>576</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Moderate jogger</td>
<td>262</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Strenuous jogger</td>
<td>40</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Adjusted for age, sex, smoking, alcohol intake, education, and diabetes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sedentary nonjogger (reference)</td>
<td>394</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>Light jogger</td>
<td>570</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Moderate jogger</td>
<td>252</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Strenuous jogger</td>
<td>36</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>


Forest plot indicating all-cause mortality in light, moderate, and strenuous joggers compared with sedentary nonjoggers.
Leisure Time Physical Activity and Mortality
A Detailed Pooled Analysis of the Dose-Response Relationship
Hannah Arem, et al.

Figure. Hazard Ratios (HRs) and 95% CIs for Leisure Time Moderate- to Vigorous-Intensity Physical Activity and Mortality
Smoking, physical activity, and active life expectancy.
Effect of Structured Physical Activity on Prevention of Major Mobility Disability in Older Adults. The LIFE Study Randomized Clinical Trial

**Figure 3. Effect of a Moderate Physical Activity Intervention on the Onset of Major Mobility Disability and Persistent Mobility Disability**

- **Major mobility disability**
  - HR, 0.82 (95% CI, 0.69-0.98); P = .03
  - Physical activity
  - Health education

- **Persistent mobility disability**
  - HR, 0.72 (95% CI, 0.57-0.91); P = .006
  - Physical activity
  - Health education

<table>
<thead>
<tr>
<th>No. at risk</th>
<th>Follow-up Time, y</th>
<th>Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity</td>
<td>818</td>
<td>0</td>
</tr>
<tr>
<td>Health education</td>
<td>817</td>
<td>0</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio. The graph for major mobility disability was truncated at 3.5 years and the health education group had 4 additional failures between 3.5 and 3.6 years of follow-up. Number of events represents cumulative events and adjusted HRs and P values are from proportional hazards regression models defined in the Methods section.
Assessing the “Physical Cliff”: Detailed Quantification of Age-Related Differences in Daily Patterns of Physical Activity

Jennifer A. Schrack,1,2 Vadim Zipunnikov,3 Jeff Goldsmith,4 Jiawei Bai,3 Eleanor M. Simonsick,2 Ciprian Crainiceanu,3 and Luigi Ferrucci2

<60
60 – 67
68 – 74
≥ 75

N = 611, BLSA subjects
Assessing the “Physical Cliff”: Detailed Quantification of Age-Related Differences in Daily Patterns of Physical Activity

Jennifer A. Schrack,1,2 Vadim Zipunnikov,3 Jeff Goldsmith,4 Jiawei Bai,3 Eleanor M. Simonsick,2 Ciprian Crainiceanu,3 and Luigi Ferrucci2

N = 611, BLSA subjects

Schrack et al, JGMS 2014
Attitude about Aging
Age Stereotypes Held Earlier in Life Predict Cardiovascular Events in Later Life
Becca R. Levy, Alan B. Zonderman, Martin D. Slade, and Luigi Ferrucci

Association of Positive Age Stereotypes with Lower Repeated Measures of Cortisol over Time for Older Participants

Becca R. Levy et al. A Buffer against Chronic Stress: Positive Aging Self-stereotypes Predict Reduced Cortisol over Time. Submitted
A Buffer against Chronic Stress:
Positive Aging Self-stereotypes Predict Reduced Cortisol over Time

Becca R. Levy, Scott Moffat, Susan M. Resnick, Martin D. Slade, and Luigi Ferrucci

Association of Age Stereotypes with AD Neuropathology at Autopsy

Association of Age Stereotypes with Hippocampal-Volume Decline over Time

Composite of Neurofibrillary-tangle and Amyloid-plaque Groups

Negative-age-stereotype Score

Yearly Measurements of Hippocampal Volume

p-value for linear trend = .016
p-value for difference in slopes = .025
Lower Neuroticism and Higher Conscientiousness in ASYMAD vs AD

Conversely, high N and low C predict AD (Alz & Dementia 2013)
Self-Reported Sleep and β-Amyloid Deposition in Community-Dwelling Older Adults
Avoid Inflammation
Interleukin-6 Serum Levels Predict Incident Disability
A Case Cohort Study Nested in the EPESE

Probability of Mobility Disability

2.5 pg/ml

Adjusted probability

95% CI

Ln (IL-6)
IL-6 is a Cross-Sectional and Longitudinal Predictor of Comorbidity

Chronic intestinal inflammation alters hippocampal neurogenesis

DSS=Dextran Sodium Sulphate; DCX=cytoplasmic marker doublecortin; Ki-67= nuclear, green
Avoid Belly Fat: Abdominal obesity is associated with higher level of inflammatory markers and dietary intervention that reduce abdominal obesity also reduce inflammation
Periodontal disease associates with higher brain amyloid load in normal elderly

N. V. Shock, Gomez, Courmand, ?, and Ogden
meetings of the Am. Physiological Society
Atlantic City, March 15 to 20, 1948
So far they can give you only few pointers. A few of the “don’ts” Dr. Shock said, are these:

• “Don’t over-exert – Exercise after the age of forty won’t keep you young and may, if overdone, hasten old age.

• “If you are already ‘middle-aged’ don’t play or work to the point of being ‘short of breath’.”

• “Don’t indulge in ‘diet fads’ in the hope of staying young. If you want to give up eating eggs or drinking milk, it’s probably all right – provide you substitute other items which are equally nutritious”.

• “Don’t try to substitute vitamin pills for the vitamins in ‘normal all around diet.”

• “There is no indication that alcoholic beverages, or smoking – in moderation – have any affect on longevity”

The Baltimore New Post – October 1950
Thank you for your attention!