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Fondazione Policlinico Universitario A. Gemelli
Università Cattolica del Sacro Cuore

Active and healthy aging: physical activity

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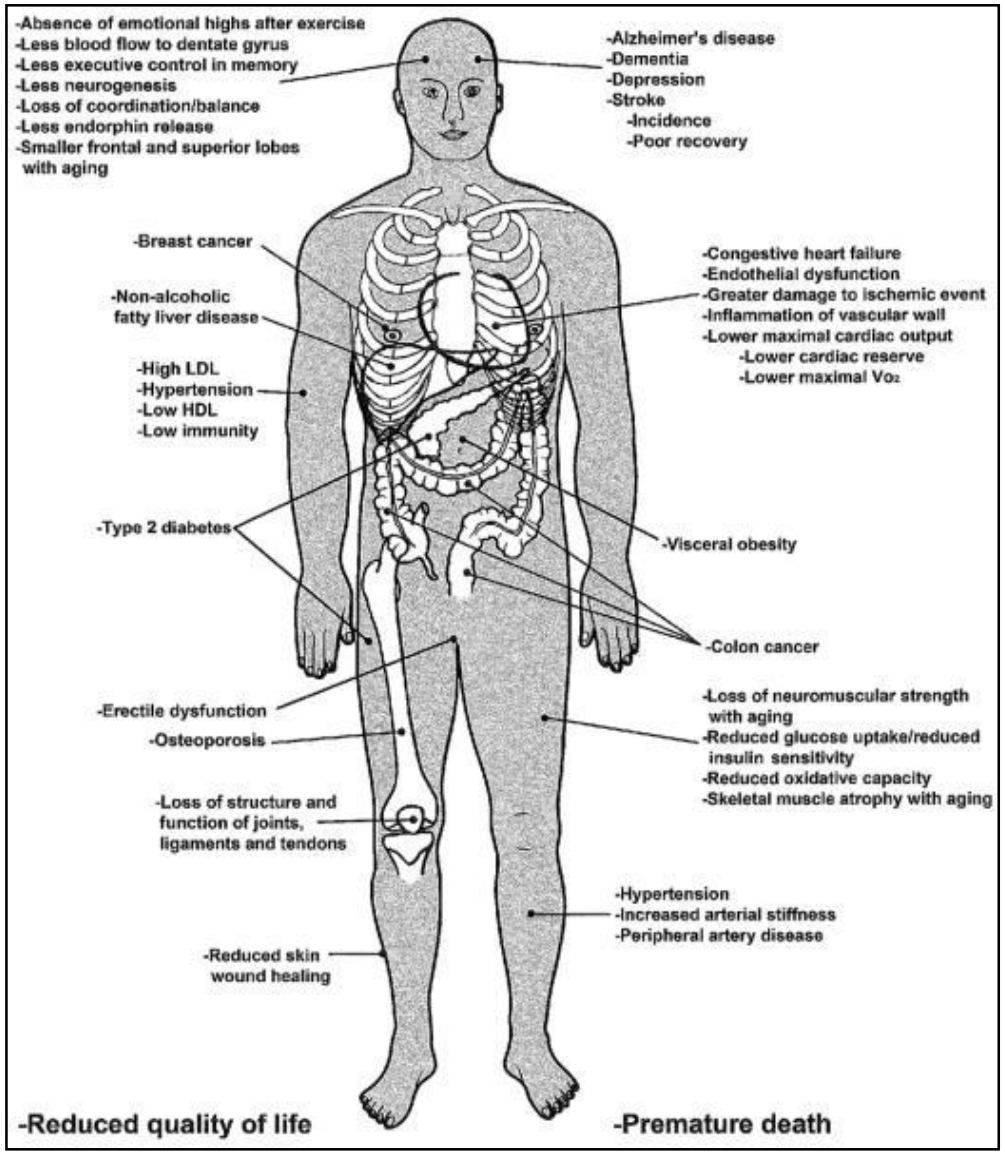
Rome - Italy

Napoli, 26 Novembre 2015

Compr Physiol. 2012 April ; 2(2): 1143–1211. doi:10.1002/cphy.c110025.

Lack of exercise is a major cause of chronic diseases

Frank W. Booth, Ph.D.[1], **Christian K. Roberts, Ph.D.**[2], and **Matthew J. Laye, Ph.D.**[3]



- Physical inactivity is the fourth leading risk factor for global mortality (6% of deaths globally) (WHO, 2009).
- Annual cost in lives lost due to inactivity ranges from 200,000 to 300,000 in the US (Mokdad et al., JAMA. 2000).
- In the US, annual medical costs due to inactivity and its consequences are estimated at $76 billion (Pratt et al., Phys Sportsmed. 2000).

J Physiol 0.0 (2015) pp 1–24

TOPICAL REVIEW

Physiological geroscience: targeting function to increase healthspan and achieve optimal longevity

Douglas R. Seals, Jamie N. Justice and Thomas J. LaRocca

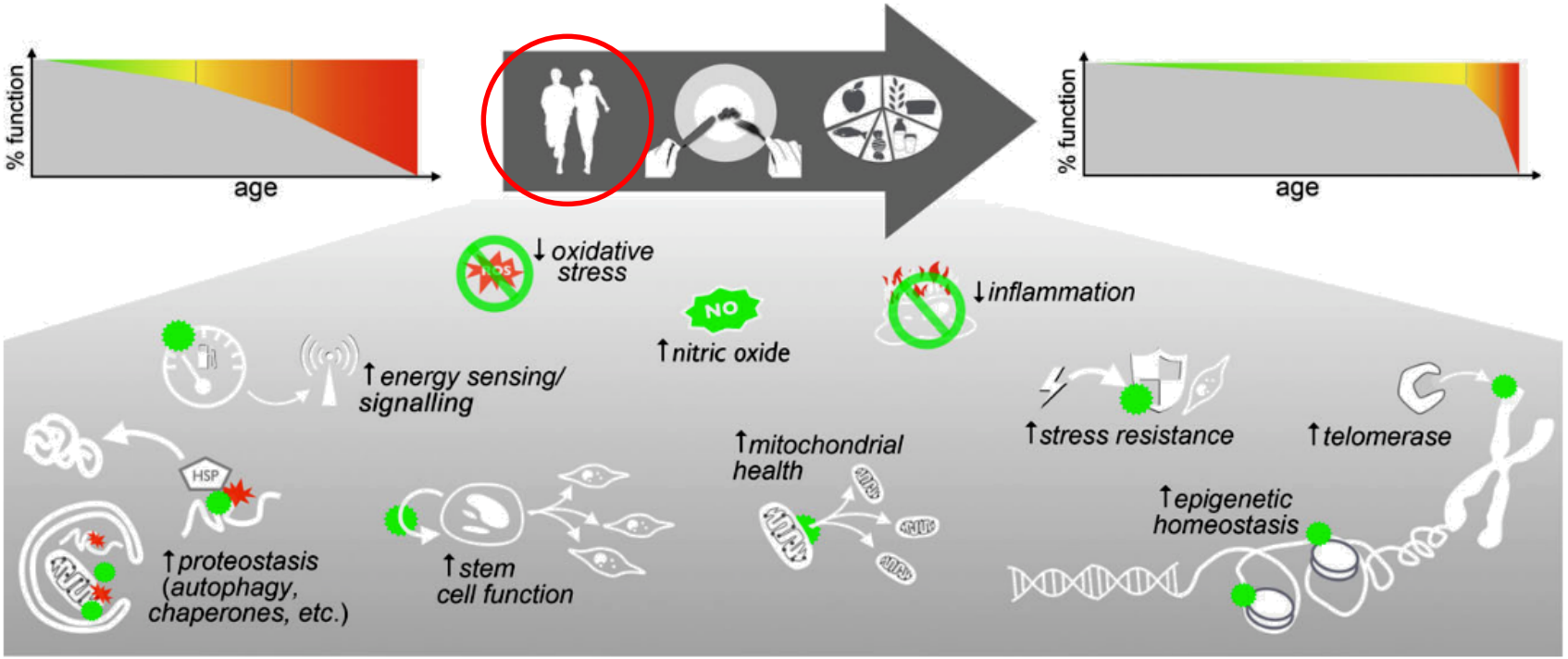


Figure 6. Lifestyle–behavioural strategies that increase function and potential underlying mechanisms
Regular physical activity, restricted energy intake and healthy diet composition enhance physiological function and healthspan, promoting optimal longevity. The molecular/biological mechanisms underlying these benefits may involve inhibiting or reversing several fundamental processes of ageing.

World Health Organization

RECOMMENDED LEVELS OF PHYSICAL ACTIVITY FOR HEALTH

5–17 years old

For children and young people of this age group physical activity includes play, games, sports, transportation, recreation, physical education or planned exercise, in the context of family, school, and community activities.
In order to improve cardiorespiratory and muscular fitness, bone health, cardiovascular and metabolic health biomarkers and reduced symptoms of anxiety and depression, the following are recommended:

1. Children and young people aged 5–17 years old should accumulate at least 60 minutes of moderate- to vigorous-intensity physical activity daily.
2. Physical activity of amounts greater than 60 minutes daily will provide additional health benefits.
3. Most of daily physical activity should be aerobic. Vigorous-intensity activities should be incorporated, including those that strengthen muscle and bone, at least 3 times per week.

18–64 years old

For adults of this age group, physical activity includes recreational or leisure-time physical activity, transportation (e.g walking or cycling), occupational (i.e. work), household chores, play, games, sports or planned exercise, in the context of daily, family, and community activities.
In order to improve cardiorespiratory and muscular fitness, bone health and reduce the risk of NCDs and depression the following are recommended:

1. Adults aged 18–64 years should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week, **or** do at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week, **or** an equivalent combination of moderate- and vigorous-intensity activity.
2. Aerobic activity should be performed in bouts of at least 10 minutes duration.
3. For additional health benefits, adults should increase their moderate-intensity aerobic physical activity to 300 minutes per week, **or** engage in 150 minutes of vigorous-intensity aerobic physical activity per week, **or** an equivalent combination of moderate- and vigorous-intensity activity.
4. Muscle-strengthening activities should be done involving major muscle groups on 2 or more days a week.

World Health Organization

RECOMMENDED LEVELS OF PHYSICAL ACTIVITY FOR HEALTH

65 years old and above

For adults of this age group, physical activity includes recreational or leisure-time physical activity, transportation (e.g walking or cycling), occupational (if the person is still engaged in work), household chores, play, games, sports or planned exercise, in the context of daily, family, and community activities.
In order to improve cardiorespiratory and muscular fitness, bone and functional health, and reduce the risk of NCDs, depression and cognitive decline, the following are recommended:

1. Adults aged 65 years and above should do at least 150 minutes of moderate-intensity aerobic physical activity throughout the week, **or** do at least 75 minutes of vigorous-intensity aerobic physical activity throughout the week, **or** an equivalent combination of moderate- and vigorous-intensity activity.
2. Aerobic activity should be performed in bouts of at least 10 minutes duration.
3. For additional health benefits, adults aged 65 years and above should increase their moderate-intensity aerobic physical activity to 300 minutes per week, **or** engage in 150 minutes of vigorous-intensity aerobic physical activity per week, **or** an equivalent combination of moderate- and vigorous-intensity activity.
4. Adults of this age group with poor mobility should perform physical activity to enhance balance and prevent falls on 3 or more days per week.
5. Muscle-strengthening activities should be done involving major muscle groups, on 2 or more days a week.
6. When adults of this age group cannot do the recommended amounts of physical activity due to health conditions, they should be as physically active as their abilities and conditions allow.

World Health Organization

RECOMMENDED LEVELS OF PHYSICAL ACTIVITY FOR HEALTH

Overall, across all the age groups, the benefits of implementing the above recommendations, and of being physically active, outweigh the harms. At the recommended level of 150 minutes per week of moderate-intensity activity, musculoskeletal injury rates appear to be uncommon. In a population-based approach, in order to decrease the risks of musculoskeletal injuries, it would be appropriate to encourage a moderate start with gradual progress to higher levels of physical activity.

November 10, 2015, Vol 314, No. 18

JAMA®
The Journal of the American Medical Association

Exercise Is Medicine At Any Dose?

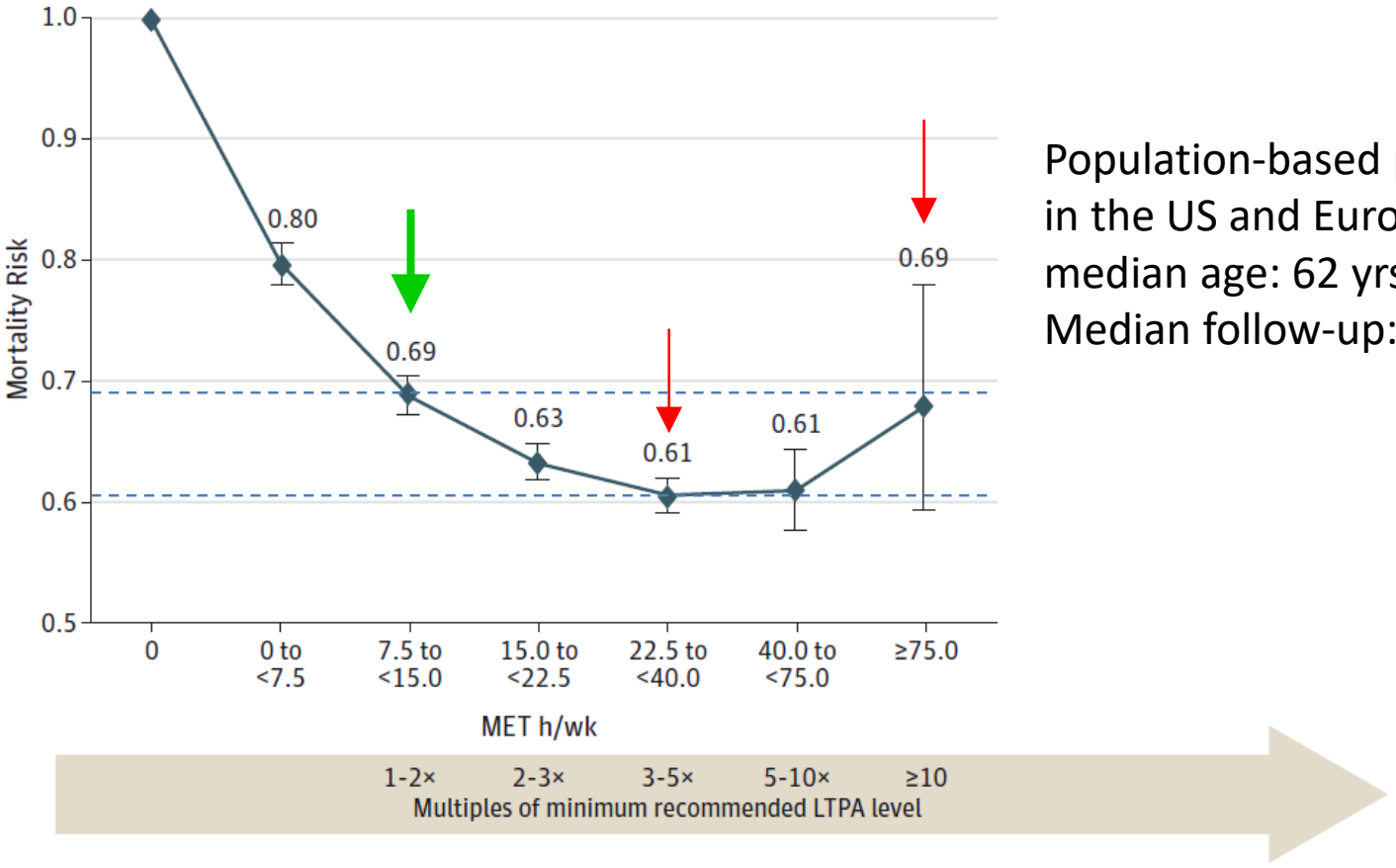
Thijs M. H. Eijsvogels, Paul D. Thompson

JAMA Intern Med. 2015;175(6):959-967. doi:10.1001/jamainternmed.2015.0533

Leisure Time Physical Activity and Mortality

A Detailed Pooled Analysis of the Dose-Response Relationship

Hannah Arem, MHS, PhD; Steven C. Moore, PhD; Alpa Patel, PhD; Patricia Hartge, ScD; Amy Berrington de Gonzalez, DPhil; Kala Visvanathan, MBBS, MPH; Peter T. Campbell, PhD; Michal Freedman, JD, PhD; Elisabete Weiderpass, MD, MSc, PhD; Hans Olov Adami, MD, PhD; Martha S. Linet, MD; I.-Min Lee, MBBS, ScD; Charles E. Matthews, PhD

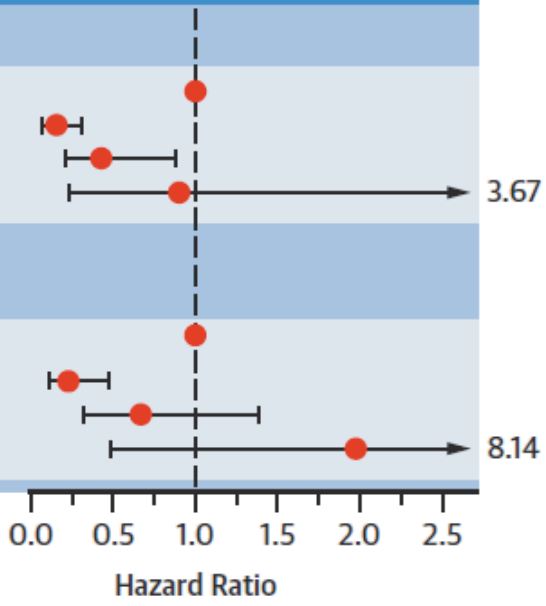


Population-based prospective cohorts in the US and Europe (n=661,137; median age: 62 yrs; range, 21-98 yrs), Median follow-up: 14.2 yrs.

How much exercise is too much?

CENTRAL ILLUSTRATION **Dose of Jogging and Long-Term Mortality**

DOSE OF JOGGING	NO. OF PARTICIPANTS	ALL-CAUSE MORTALITY: DEATHS
Adjusted for age and sex		
Sedentary nonjogger (reference)	413	128
Light jogger	576	7
Moderate jogger	262	8
Strenuous jogger	40	2
Adjusted for age, sex, smoking, alcohol intake, education, and diabetes		
Sedentary nonjogger (reference)	394	120
Light jogger	570	7
Moderate jogger	252	8
Strenuous jogger	36	2



Schnohr, P. et al. J Am Coll Cardiol. 2015; 65(5):411–9.

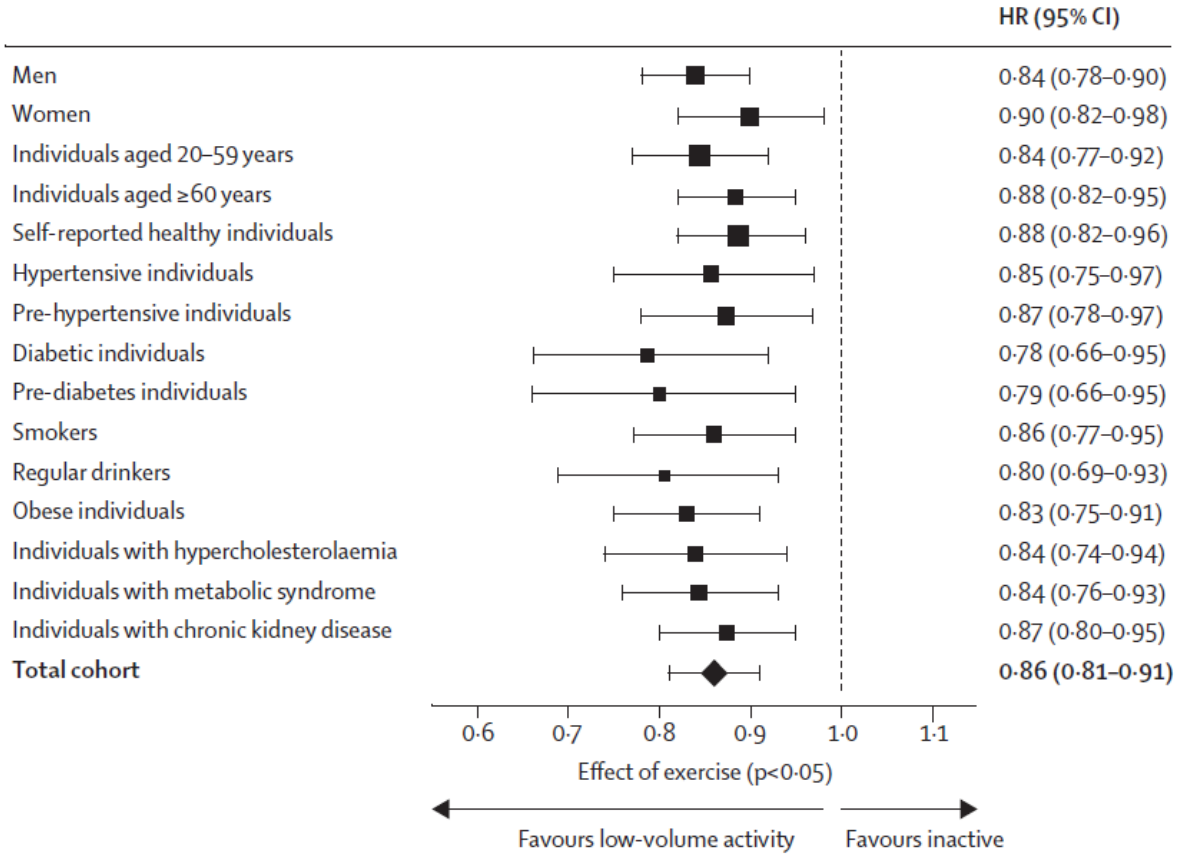
Forest plot indicating all-cause mortality in light, moderate, and strenuous joggers compared with sedentary nonjoggers.

THE LANCET

Vol 378 October 1, 2011

Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study

Chi Pang Wen, Jackson Pui Man Wai*, Min Kuang Tsai, Yi Chen Yang, Ting Yuan David Cheng, Meng-Chih Lee, Hui Ting Chan, Chwen Keng Tsao, Shan Pou Tsai, Xifeng Wu*



n=416,175 individuals
Average follow-up: 8.05 years

15 min a day or 90 min a week of light-to-moderate intensity exercise (3.75–7.49 MET-h) reduce the risk for all-cause mortality by 14% (+3 yrs of life)

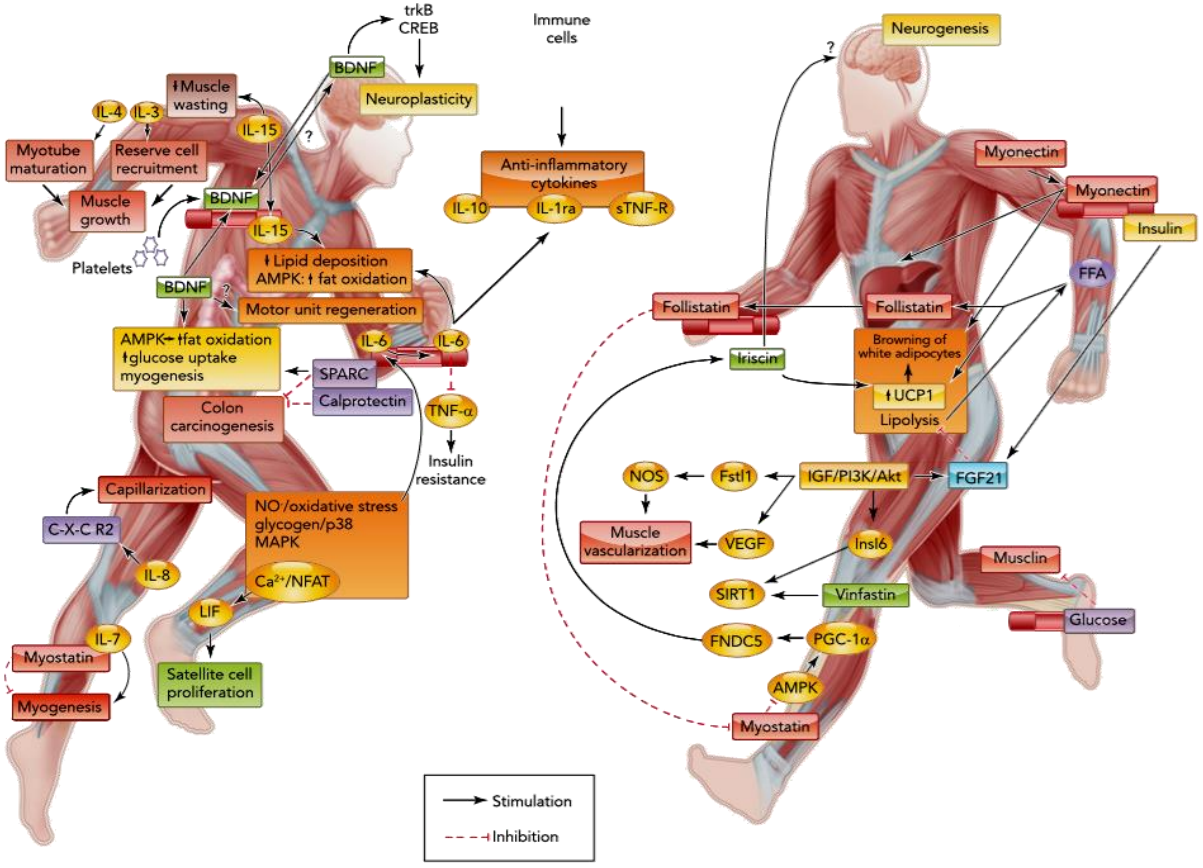
Every additional 15 min of daily exercise beyond the minimum amount of 15 min a day further reduce all-cause mortality by 4%

REVIEWS
PHYSIOLOGY 28: 330–358, 2013; doi:10.1152/physiol.00019.2013

Exercise is the Real Polypill

Carmen Fiuza-Luces,[1,2] Nuria Garatachea,[3] Nathan A. Berger,[4] and Alejandro Lucia[1,2]

	Protective mechanisms of exercise training
1	Improved endothelial function and passivation of atherosclerotic plaques
2	Reduction in systemic inflammation
3	Beneficial effects on the autonomic regulation of cardiovascular function
4	Improvement in cardiovascular risk factor control • Increase in HDL-cholesterol concentrations • Reduction in triglyceride and LDL-cholesterol • Reduction in blood pressure • Reduction in body fat mass • Reduction in insulin resistance and improvement in glucose metabolism
5	Potential anti-thrombotic and anti-platelet effects
6	Heart intrinsic mechanisms • Ischemic preconditioning with reduced myocardial damage during prolonged ischemia • Prevention of reperfusion-induced ventricular arrhythmias
7	Improvement in maximal oxygen uptake (VO_{2max}) • Reduced all-cause and cardiovascular mortality • Improved functional capacity, QoL and ADL performance • Improved pulmonary function • Improved central hemodynamics (cardiac output/stroke volume) • Improved skeletal muscle metabolism (muscle blood flow, O_2 utilization, mitochondrial function)
8	Improvement in skeletal muscle function (resistance training) • Improved muscle mass and strength developed by muscle groups • Improved muscle power (force generation at high contraction speed) • Improved muscle quality, muscle recruitment and connective tissue • Reduction of functional deficits and disease co-morbidity • Improved QoL and IADL performance
9	Improvements in bone mineral density and ultrastructure
10	Improvement of chromosomal function • Improved telomerase enzyme activity • Less reduction in telomerase length
11	Improvement in cognitive function (aerobic and resistance training)



Gremeaux et al., Maturitas. 2012

PHYSIOLOGY 28: 330–358, 2013; doi:10.1152/physiol.00019.2013

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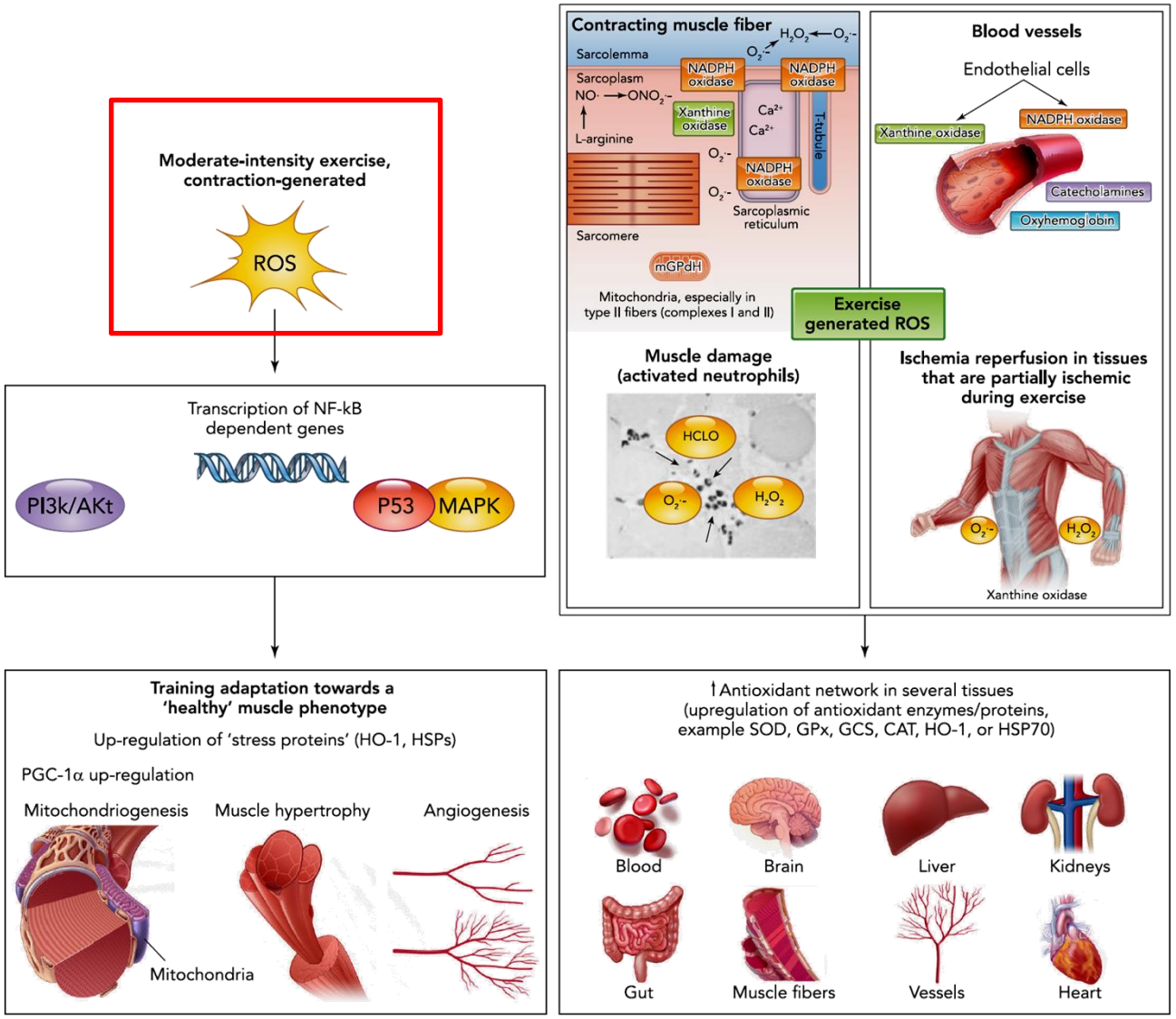


Dose-Response, 12:288–341, 2014
Formerly Nonlinearity in Biology, Toxicology, and Medicine

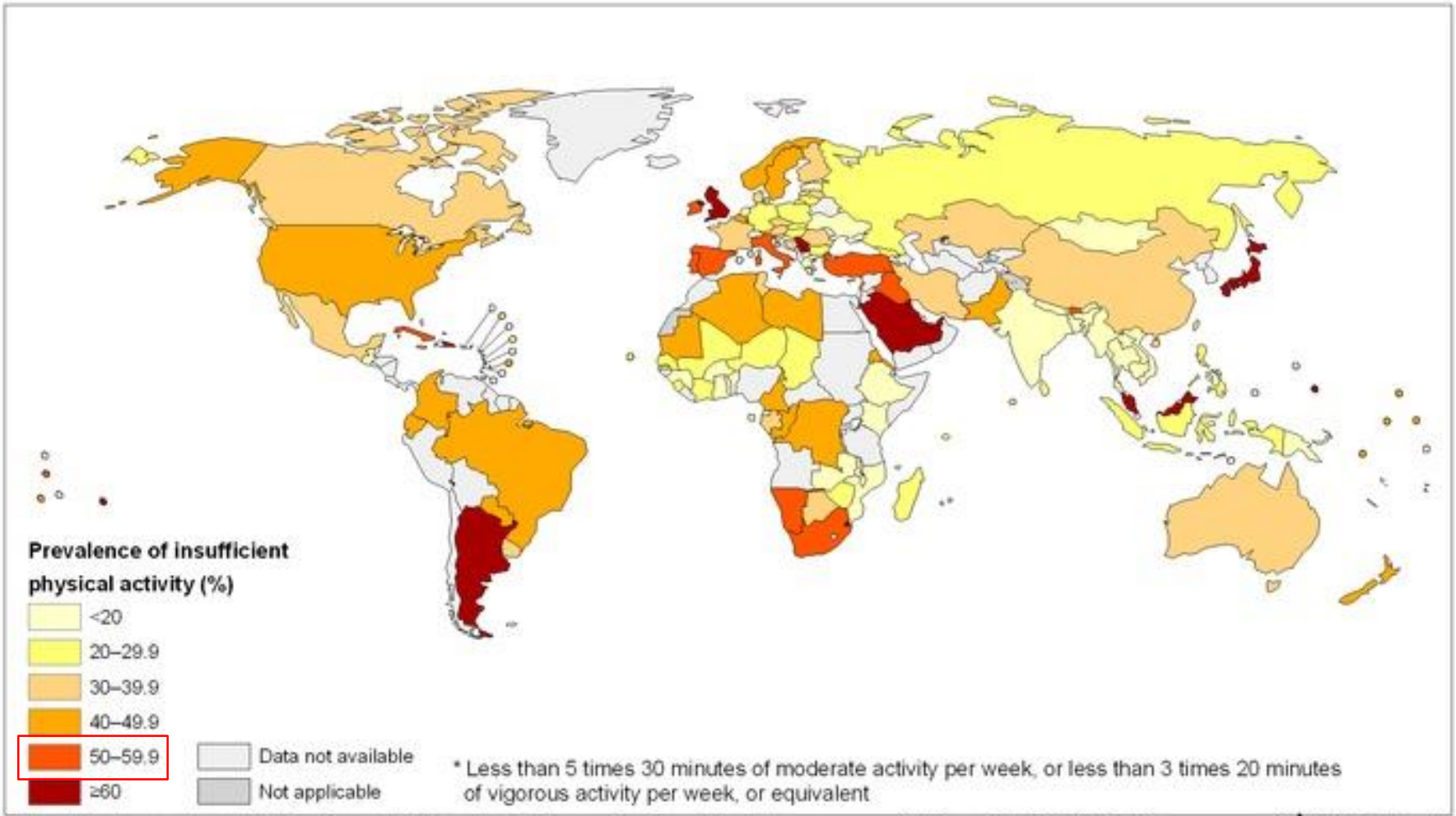
ISSN: 1559-3258
DOI: 10.2203/dose-response.13-035.Ristow

International Dose-Response Society

MITOHORMESIS: PROMOTING HEALTH AND LIFESPAN BY INCREASED LEVELS OF REACTIVE OXYGEN SPECIES (ROS)

Michael Ristow[1,2], Kathrin Schmeisser[2] □ [1] Energy Metabolism Laboratory, ETH Zürich (Swiss Federal Institute of Technology Zurich), Schwerzenbach/Zürich, CH 8603, Switzerland; [2] Dept. of Human Nutrition, Institute of Nutrition, University of Jena, Jena D-07743, Germany

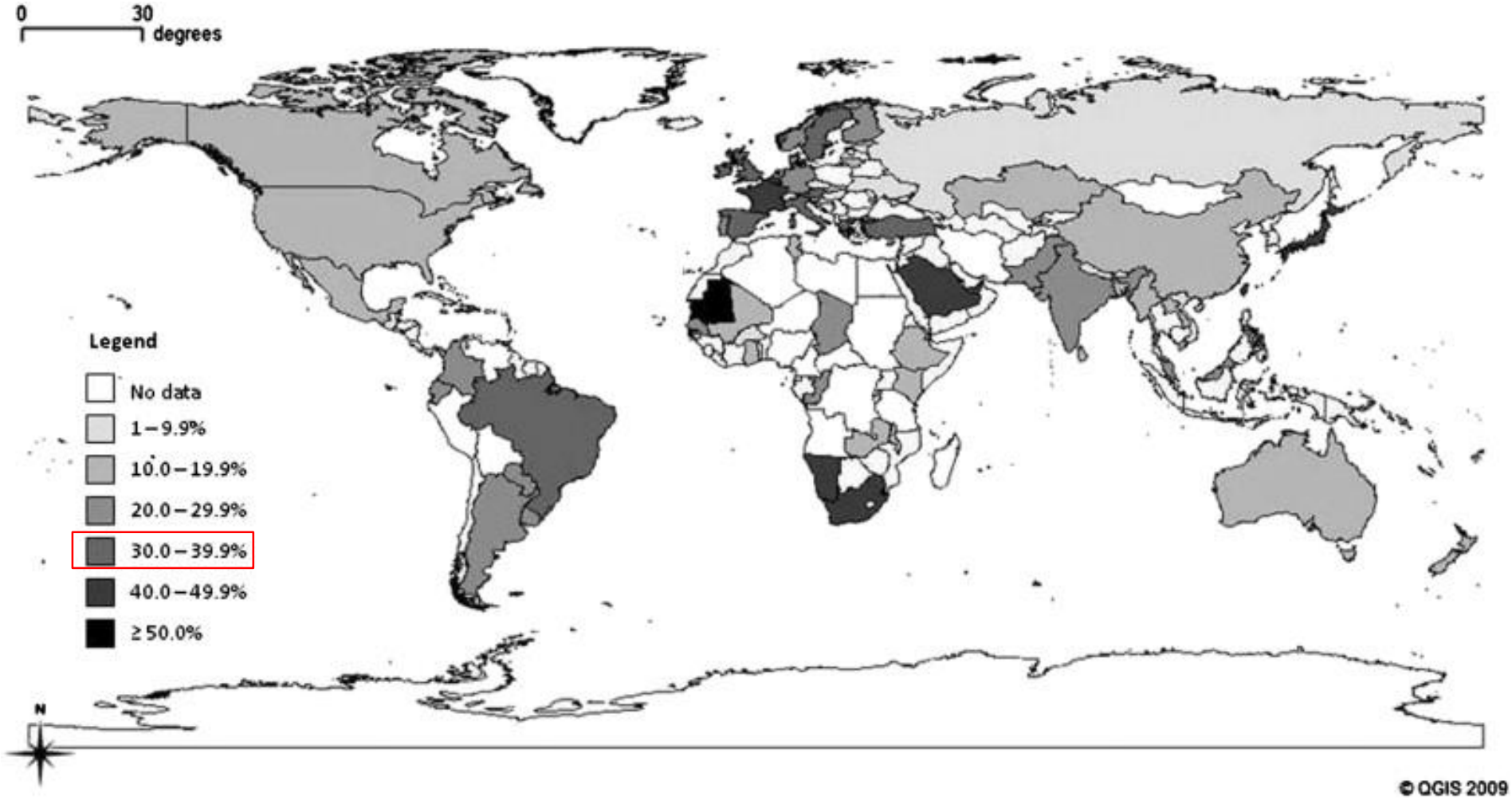
Prevalence of insufficient physical activity*, ages 15+, age standardized
Both sexes, 2008



Data Source: World Health Organization
Map Production: Public Health Information and Geographic Information Systems (GIS)
World Health Organization

World Health Organization

Worldwide prevalence of physical inactivity by country



Dumith et al., Prev Med. 2011

Singapore Med J 2013; 54(10): 581-586
doi:10.11622/smedj.2013203

Barriers to participation in physical activity and exercise among middle-aged and elderly individuals

Maria Justine[1], PhD, PT, *Azliyana Azizan*[1], BPT, *Vaharli Hassan*[2], BPT, *Zoolfaiz Salleh*[1], BPT, *Haidzir Manaf*[1], BSc, PT

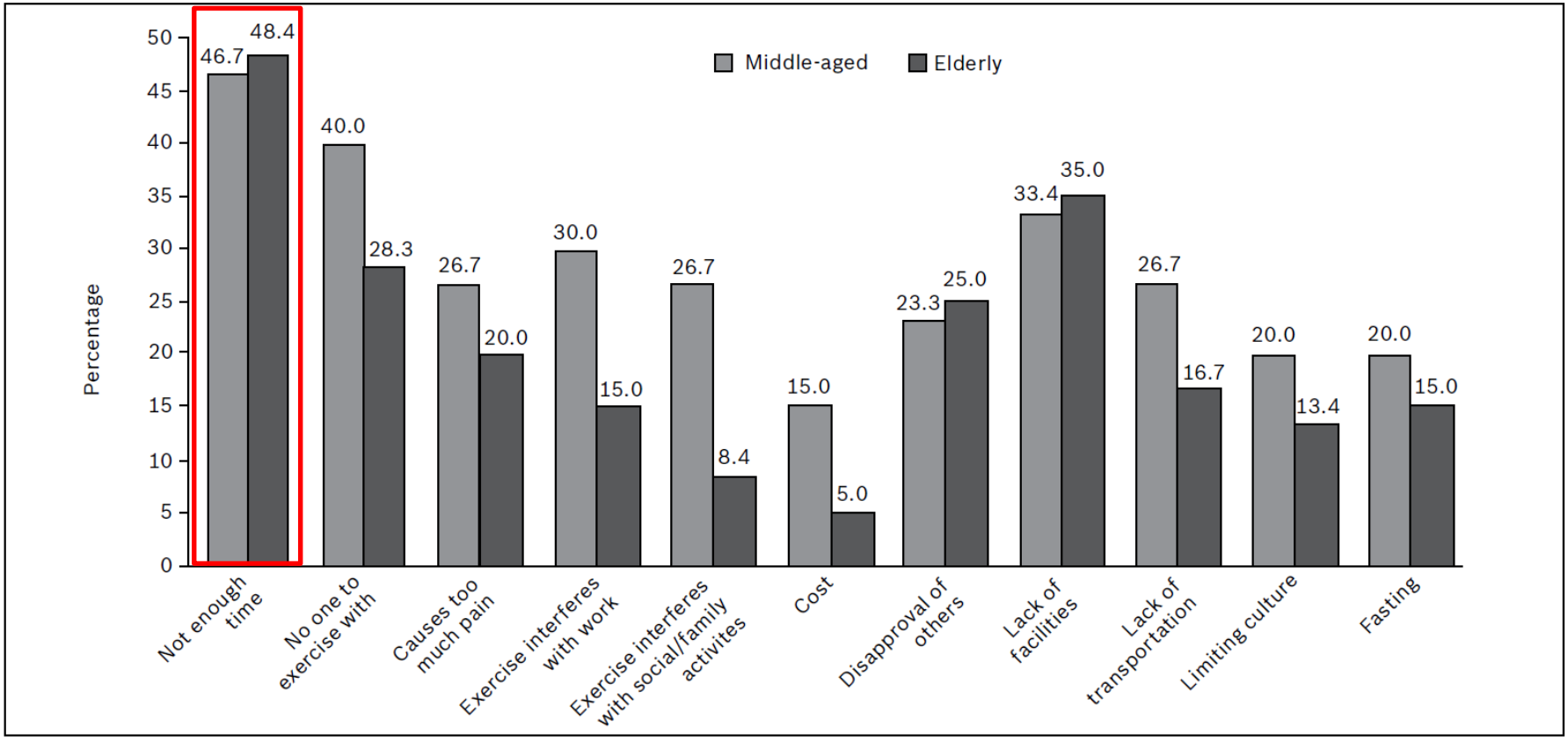


Fig. 1 Graph shows the external barriers to participation in physical activity among middle-aged (n = 60) and elderly (n = 60) respondents.

Singapore Med J 2013; 54(10): 581-586
doi:10.11622/smedj.2013203

Barriers to participation in physical activity and exercise among middle-aged and elderly individuals

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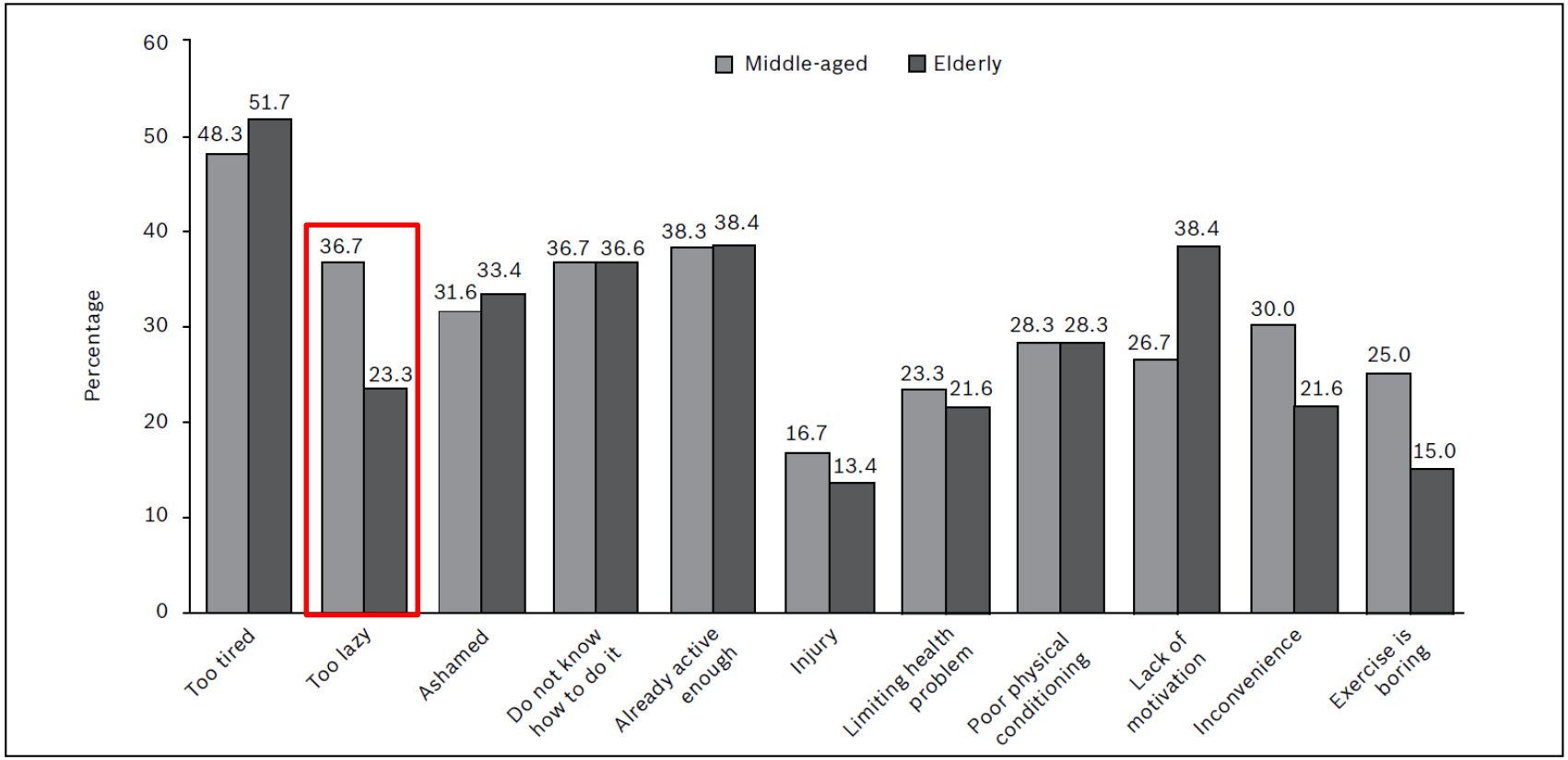
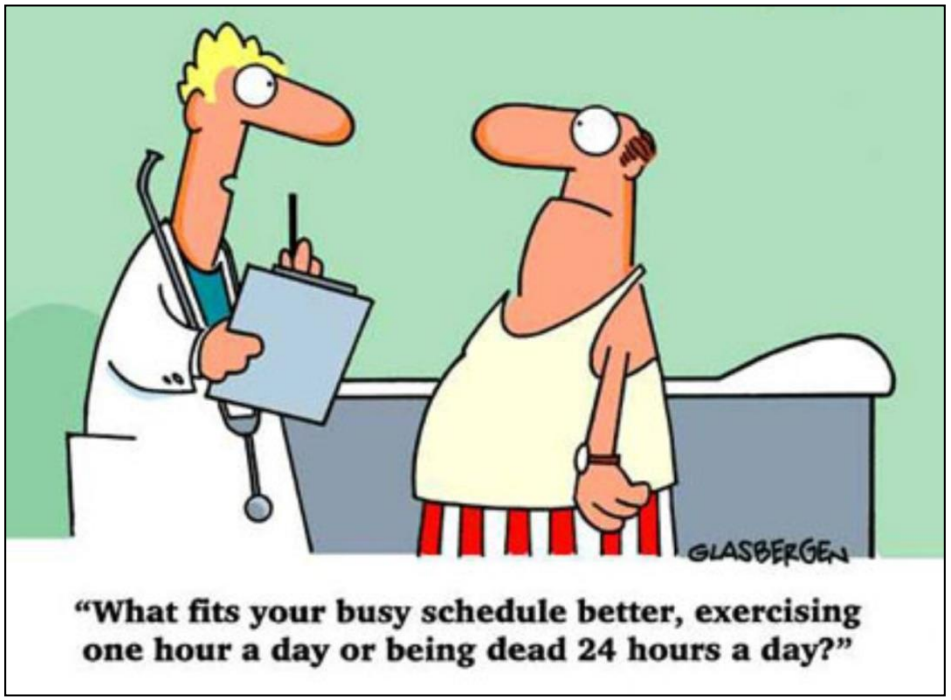


Fig. 2 Graph shows internal barriers to participation in physical activity among middle-aged (n = 60) and elderly (n = 60) respondents.

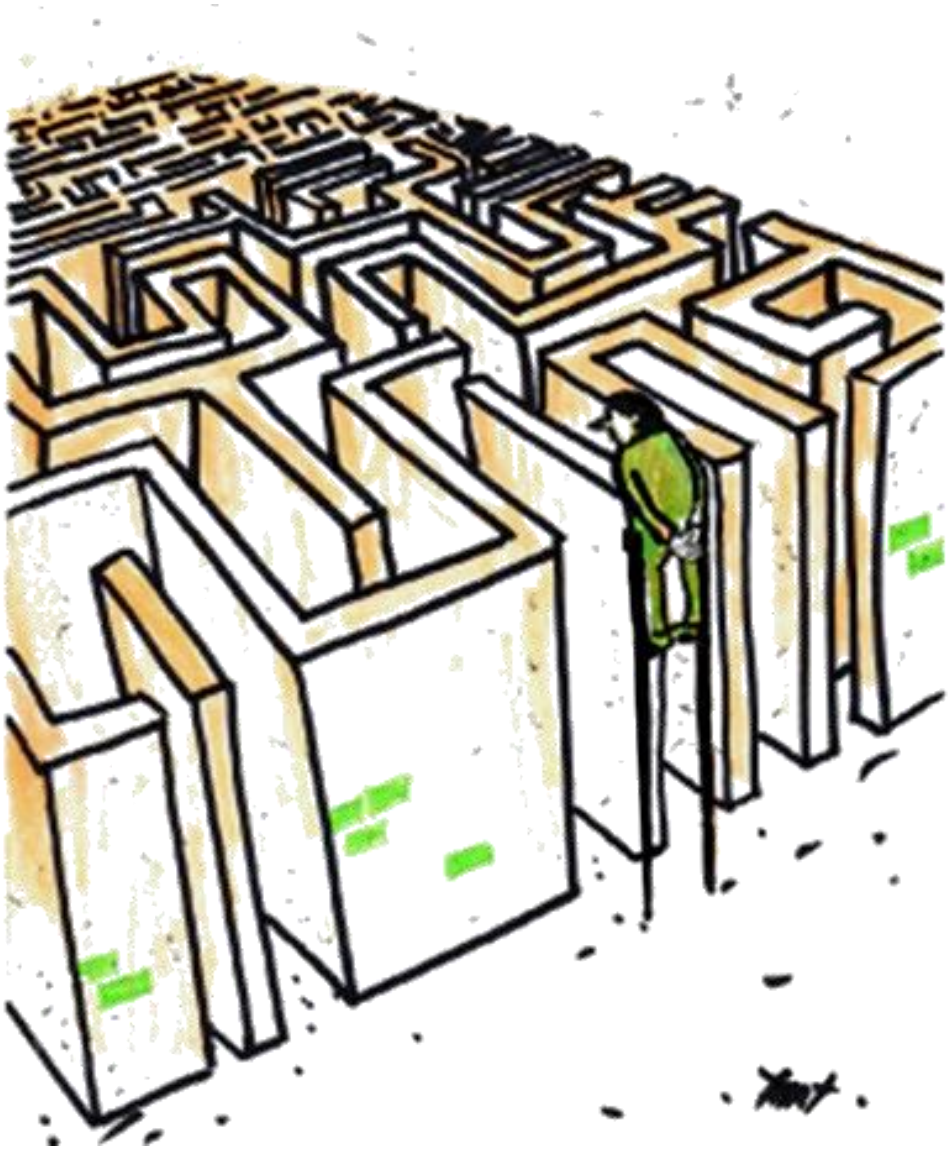
Lack of time is the major barrier to participating in physical activity regardless of age



Poor adherence to exercise prevents long-term benefits

Up to 50% of individuals who begin an exercise program stop within the first 6 months.

Is there a way out?



CLINICAL IMPLICATIONS OF BASIC RESEARCH

The Exercise Pill — Too Good to Be True?

Laurie J. Goodyear, Ph.D.

Am J Physiol Regul Integr Comp Physiol 296: R1071–R1077, 2009.
First published February 11, 2009; doi:10.1152/ajpregu.90925.2008.

Quercetin increases brain and muscle mitochondrial biogenesis and exercise tolerance

J. Mark Davis,[1] E. Angela Murphy,[1] Martin D. Carmichael,[1] and Ben Davis[2]

Biogerontology (2009) 10:423–434
DOI 10.1007/s10522-008-9177-z

RESEARCH ARTICLE

Suppression of the aging-associated decline in physical performance by a combination of resveratrol intake and habitual exercise in senescence-accelerated mice

Takatoshi Murase · Satoshi Haramizu · Noriyasu Ota · Tadashi Hase

Cell *134*, 405–415, August 8, 2008

Cell

AMPK and PPARδ Agonists Are Exercise Mimetics

Vihang A. Narkar,[1] Michael Downes,[1] Ruth T. Yu,[1] Emi Embler,[1] Yong-Xu Wang,[4] Ester Banayo,[3] Maria M. Mihaylova,[2] Michael C. Nelson,[1] Yuhua Zou,[1] Henry Juguilon,[1] Heonjoong Kang,[5] Reuben J. Shaw,[2] and Ronald M. Evans[1,3,*]

ELSEVIER

ScienceDirect

European Journal of Cell Biology 88 (2009) 35–44

European Journal of Cell Biology

www.elsevier.de/ejcb

Sirt1 increases skeletal muscle precursor cell proliferation

Christopher R. Rathbone[a,*], Frank W. Booth[a,b,c], Simon J. Lees[a]

Cell Metabolism

Resource

CellPress

Global Phosphoproteomic Analysis of Human Skeletal Muscle Reveals a Network of Exercise-Regulated Kinases and AMPK Substrates

Nolan J. Hoffman,[1,7] Benjamin L. Parker,[1,7] Rima Chaudhuri,[1] Kelsey H. Fisher-Wellman,[2] Maximilian Kleinert,[2,3] Sean J. Humphrey,[2,6] Pengyi Yang,[2,4] Mira Holliday,[1] Sophie Trefely,[2] Daniel J. Fazakerley,[1] Jacqueline Stöckli,[1] James G. Burchfield,[1] Thomas E. Jensen,[3] Raja Jothi,[4] Bente Kiens,[3] Jørgen F.P. Wojtaszewski,[3] Erik A. Richter,[3] and David E. James[1,5,*]

Cell *134*, 405–415, August 8, 2008

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Four-week administration of the orally active AMPK agonist AICAR induced metabolic genes and enhanced running endurance by 44% in sedentary mice.

DIABETES, VOL. 51, JULY 2002

Long-Term AICAR Administration Reduces Metabolic Disturbances and Lowers Blood Pressure in Rats Displaying Features of the Insulin Resistance Syndrome

Esben S. Buhl,[1] Niels Jessen,[1] Rasmus Pold,[1] Thomas Ledet,[2] Allan Flyvbjerg,[1] Steen B. Pedersen,[3] Oluf Pedersen,[4] Ole Schmitz,[1,5] and Sten Lund[1]

Conclusion

- Physical activity conveys health benefits throughout the life course, across a wide spectrum of intensities.
- Health and longevity benefits of physical activity may be achieved with as little as 15 min a day or 90 min a week of light-to-moderate intensity exercise (e.g., brisk walking).
- Most barriers preventing engagement in physical activity may be overcome through health education campaigns and adequate counseling.
- Exercise mimetics may allow overcoming traditional barriers to long-term adherence to physical activity and grant participation to exercise in population subgroups with social and health limitations.

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Prof. Roberto Bernabei (UCSC, Rome)
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Dr. Matteo Tosato (UCSC, Rome)
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Prof. Christiaan Leeuwenburgh (UFL, USA)
Prof. Matteo Cesari (University of Toulouse, France)

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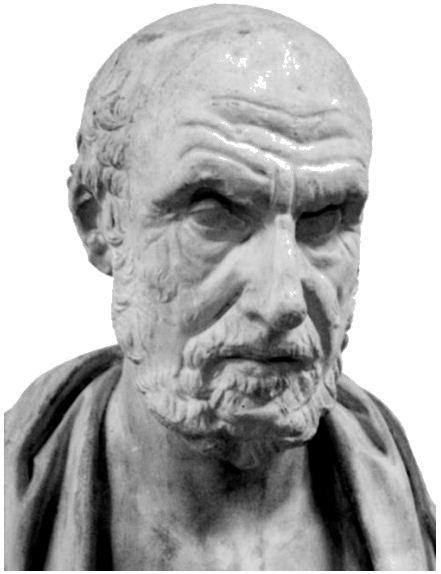
✓Italian Ministry of Education and Research (linea D3.2 2013)
✓“Achille and Linda Lorenzon” Study Center



Hippocrates - 460 BC – 375 BC

"If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have found the safest way to health"

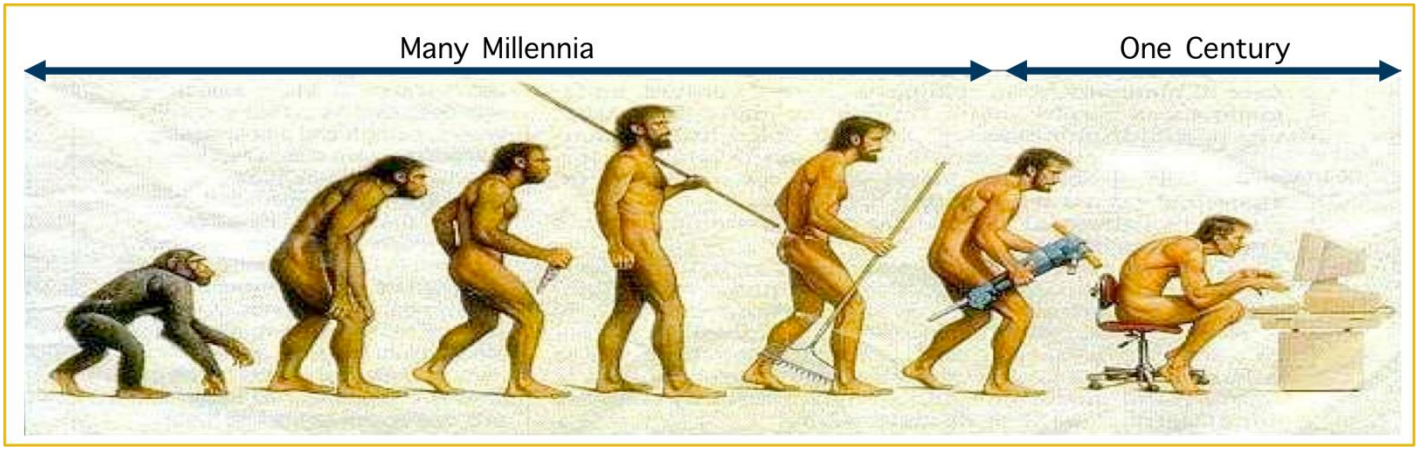
Compr Physiol. 2012 April ; 2(2): 1143–1211. doi:10.1002/cphy.c110025.

Lack of exercise is a major cause of chronic diseases

Frank W. Booth, Ph.D.[1], **Christian K. Roberts, Ph.D.**[2], and **Matthew J. Laye, Ph.D.**[3]

Estimated historical reductions in daily steps by humans.

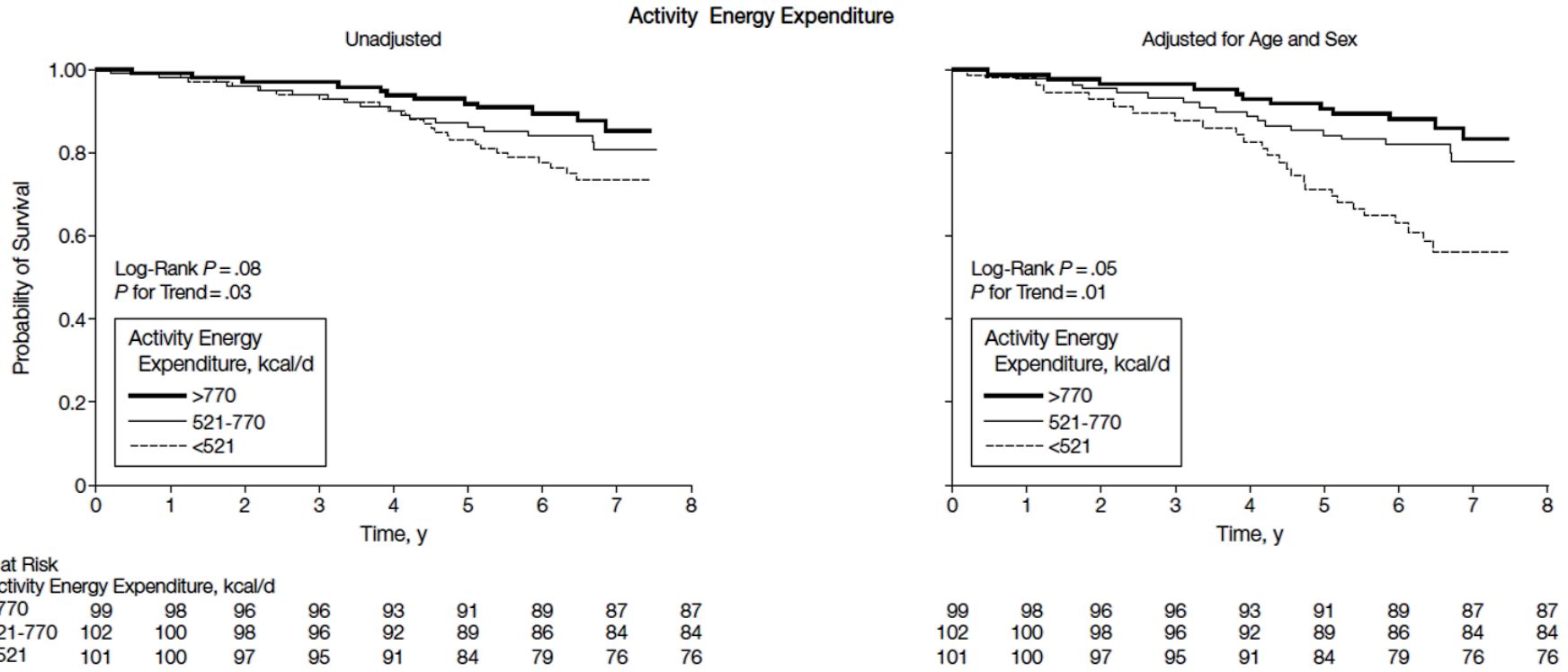
Population	Year	Steps per day		References
Paleolithic	(~20,000 BC)	~13,200–21,120 (men)	~10,560 (women)	(385)
Amish	(2002)	18,425 (men)	14,196 (women)	(27)
Mean of 26 studies	(1966–2007)		7,473 (mainly women)	(63)
Colorado	(2002)	6,733 (men)	6,384 (women)	(573)
US adults	(2010)	5,340 (men)	4,912 (women)	(26)



JAMA, July 12, 2006—Vol 296, No. 2

Daily Activity Energy Expenditure and Mortality Among Older Adults

Manini TM, Everhart JE, Patel KV, Schoeller DA, Colbert LH, Visser M, Tylavsky F, Bauer DC, Goodpaster BH, Harris TB



No. at Risk

Activity Energy Expenditure, kcal/d									
>770	99	98	96	96	93	91	89	87	87
521-770	102	100	98	96	92	89	86	84	84
<521	101	100	97	95	91	84	79	76	76

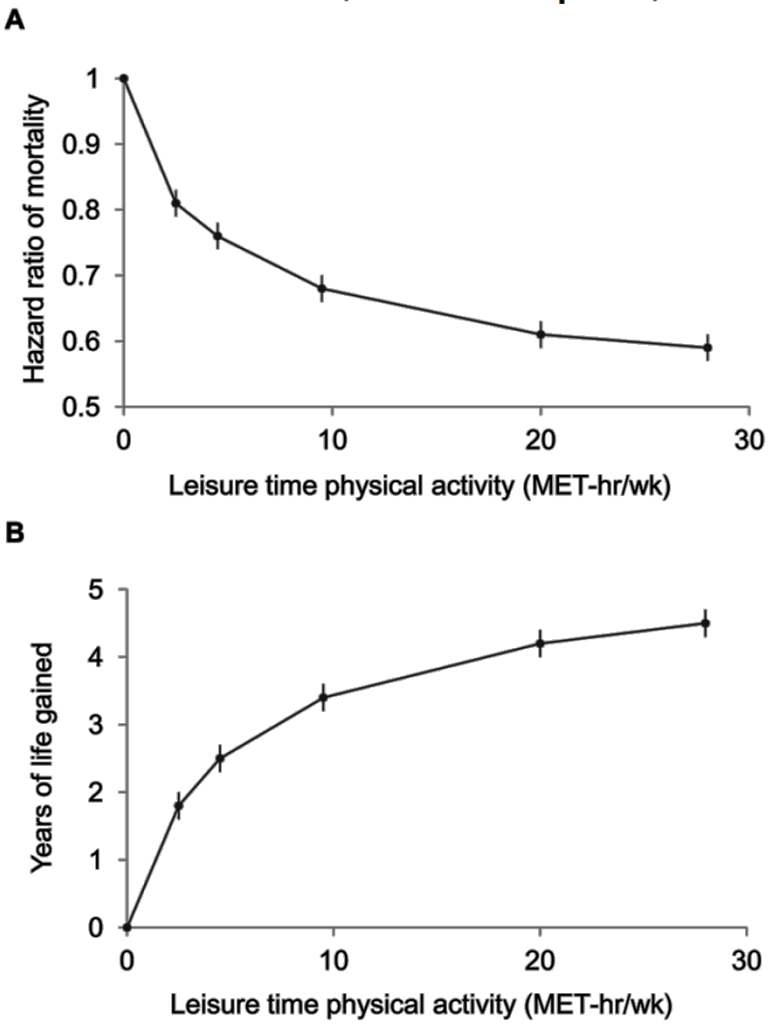
99	98	96	96	93	91	89	87	87
102	100	98	96	92	89	86	84	84
101	100	97	95	91	84	79	76	76

PLoS Med 9(11): e1001335. doi:10.1371/journal.pmed.1001335

PLOS | MEDICINE

Leisure Time Physical Activity of Moderate to Vigorous Intensity and Mortality: A Large Pooled Cohort Analysis

Steven C. Moore[1]*, Alpa V. Patel[2], Charles E. Matthews[1], Amy Berrington de Gonzalez[1], Yikyung Park[1], Hormuzd A. Katki[1], Martha S. Linet[1], Elisabete Weiderpass[3,4,5,6], Kala Visvanathan[7], Kathy J. Helzlsouer[7], Michael Thun[2], Susan M. Gapstur[2], Patricia Hartge[1], I-Min Lee[8]



Pooled analysis of 6 prospective cohort studies (n=654,827; age range: 21-90 yrs); follow-up: 10 yrs.

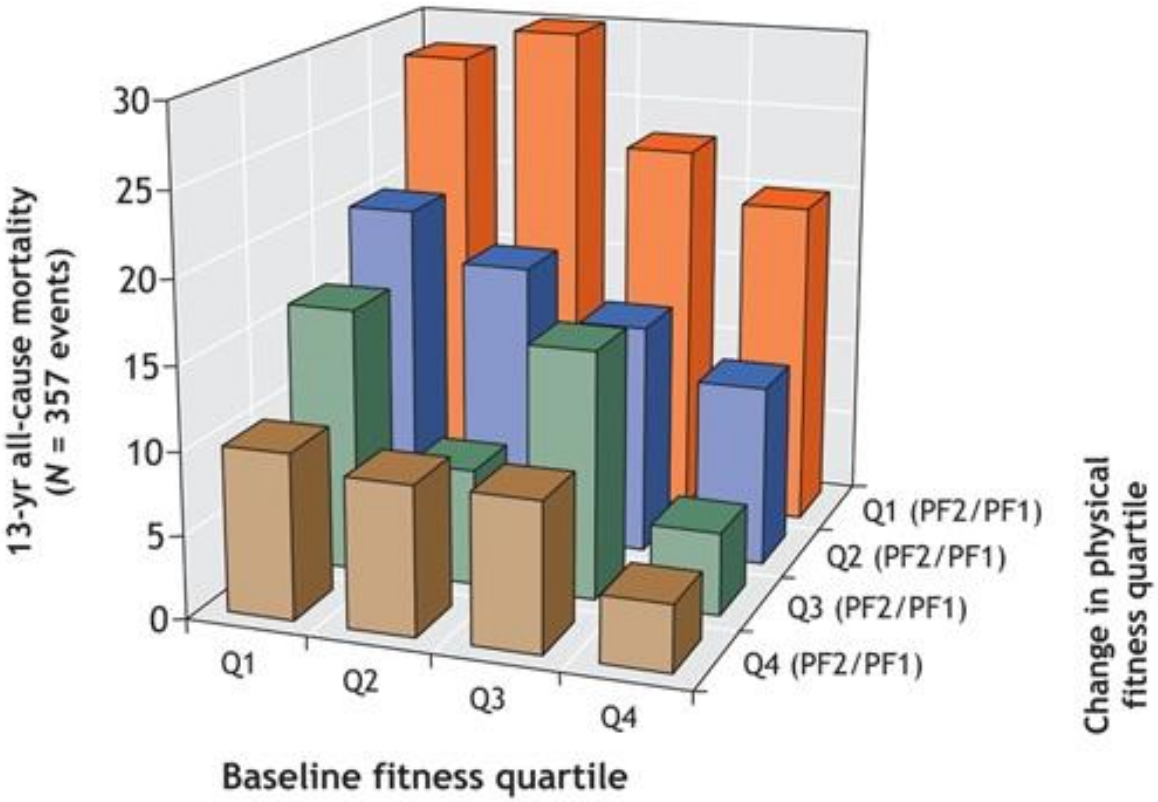
- **Physical activity level of 0.1-3.74 MET-h/wk (brisk walking for up to 75 min/wk): +1.8 yrs.**
- **Physical activity level of 22.5+ MET-h/wk (brisk walking for 450+ min/wk): +4.5 yrs.**

Analyses adjusted for gender, alcohol consumption, smoking status, education, marital status, history of heart disease, history of cancer, and BMI.

Lancet 1998; **352:** 759–62

Changes in physical fitness and changes in mortality

Gunnar Erikssen, Knut Liestøl, Jørgen Bjørnholt, Erik Thaulow, Leiv Sandvik, Jan Erikssen



Definitions

- Physical activity: “bodily movement that is produced by the contraction of skeletal muscle and that substantially increases energy expenditure”.
- Physical exercise: subset of physical activity that involves “planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness”.
- Physical fitness: “a set of attributes that people have or achieve that relates to the ability to perform physical activity”.
- Physical inactivity: absence of physical activity.
- MET (metabolic equivalent): physiological measure expressing the energy cost of a given physical activity (1 MET= energy spent sitting quietly ($[4.184\ kJ]\cdot kg^{-1}\cdot h^{-1}$).

Caspersen et al., Public Health Rep 1985
Guthold et al., Am J Prev Med. 2008

The healthcare providers' perspective…

254 PTs (aged 42± yrs) working in long term care facilities

WHO guideline for PA in 65+

- **84% not familiar with**
- **70% agrees that guideline is useful**
- **75% implementation in LTCF is UNrealistic**
  - *Residents are too old*
  - *Not appropriate for LTCF residents*
  - *Not enough time*
  - *Not enough equipment*

Baert et al., JAMDA 2015

JAMA Intern Med. 2015;175(6):959-967. doi:10.1001/jamainternmed.2015.0533

Leisure Time Physical Activity and Mortality

A Detailed Pooled Analysis of the Dose-Response Relationship

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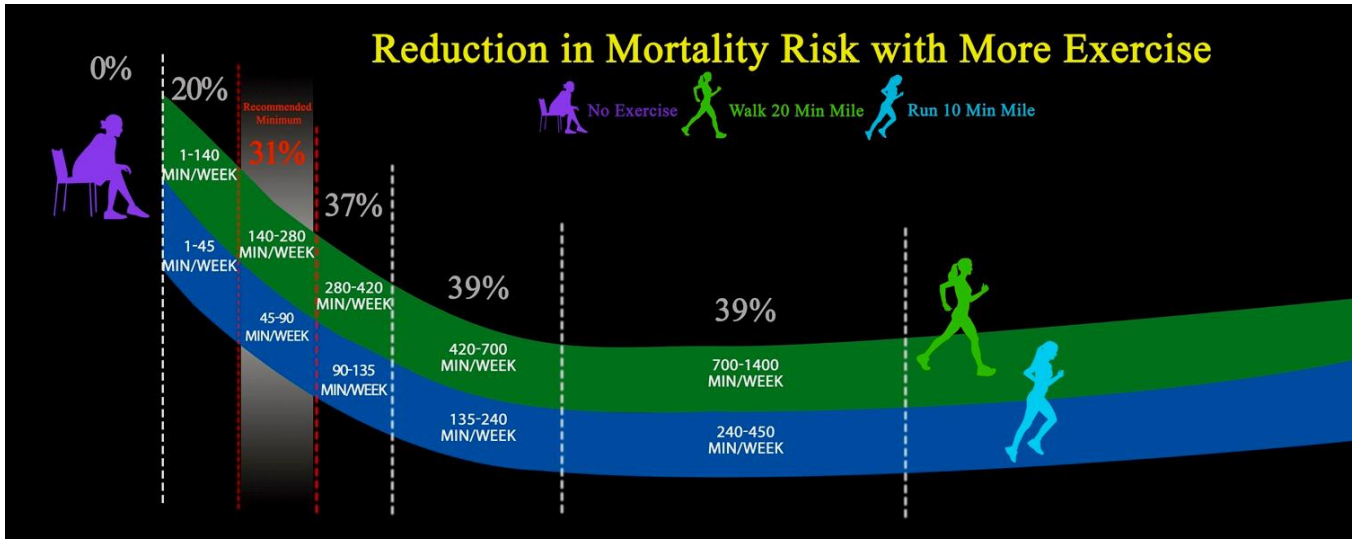
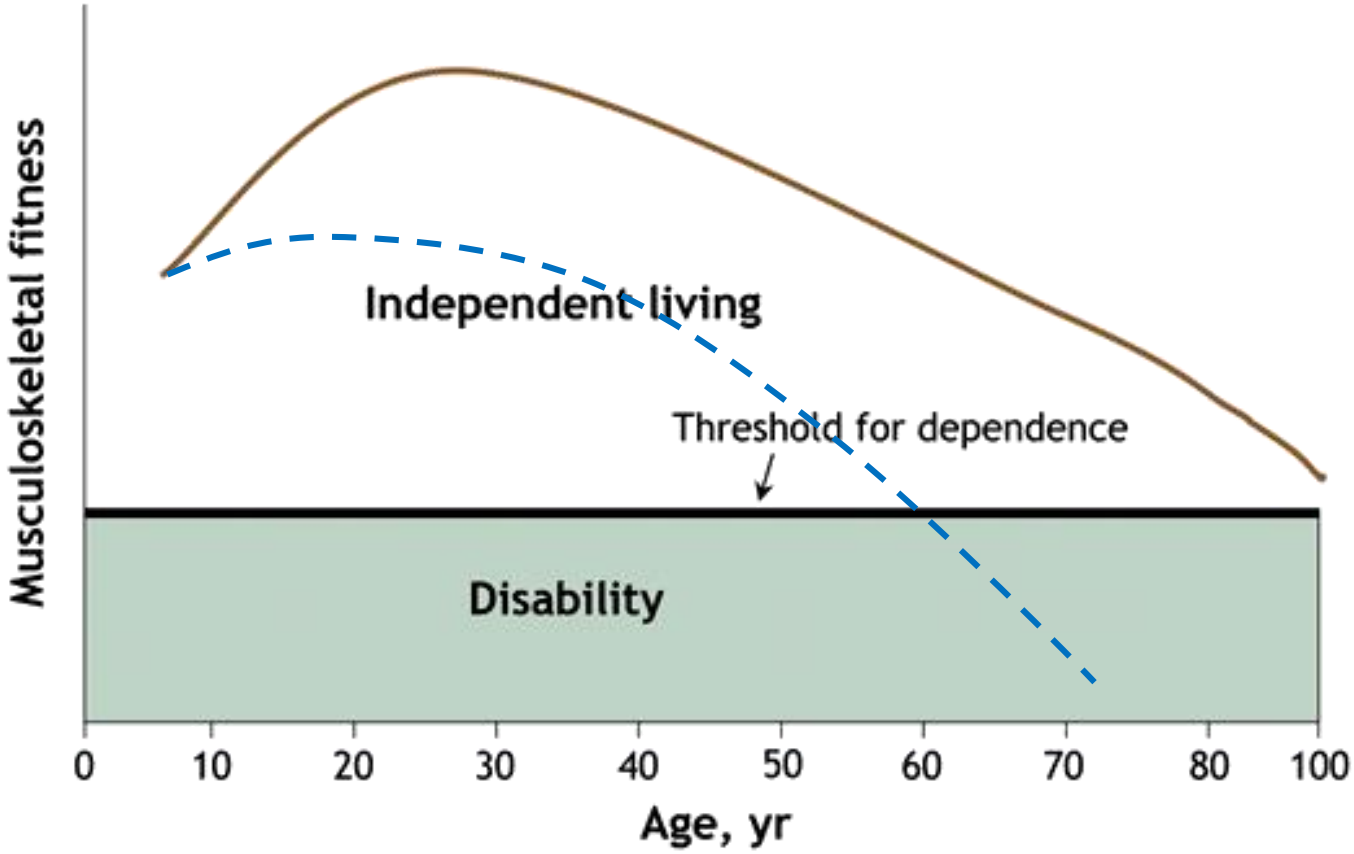
Comparison with Physical Activity Guidelines	**Energy expended (MET h/wk)**	**Example 1:** *Walking (20 min mile or 3 mph)*	**Example 2:** *Biking (leisurely effort)*	**Example 3:** *Swimming (moderate effort)*	**Example 4:** *Running (10 min mile or 6 mph)*
Recommended minimum	7.5	20 minutes per day	45 minutes, 2 days per week	35 minutes, 2 days per week	45 minutes per week
3x minimum	22.5	60 minutes per day	60 minutes, 5 days per week	60 minutes, 3 days per week	45 minutes, 3 days per week
5x minimum	37.5	90 minutes per day	75 minutes, 7 days per week	45 minutes, 7 days per week	60 minutes, 4 days per week
10x minimum	75	180 minutes per day	150 minutes, 7 days per week	90 minutes, 7 days per week	60 minutes, 7 days per week





Musculoskeletal fitness (i.e., muscular strength, muscular endurance, muscular power or flexibility) declines progressively with aging. Many elderly people currently live near or below the functional threshold for dependence. High levels of (or improvements in) musculoskeletal fitness will enhance the capacity to meet the demands of everyday life and allow a person to maintain functional independence for a greater period.

Modified from Warburton et al., CMAJ 2006

EXERCISE AND METABOLISM

Metabolic Signatures of Exercise in Human Plasma

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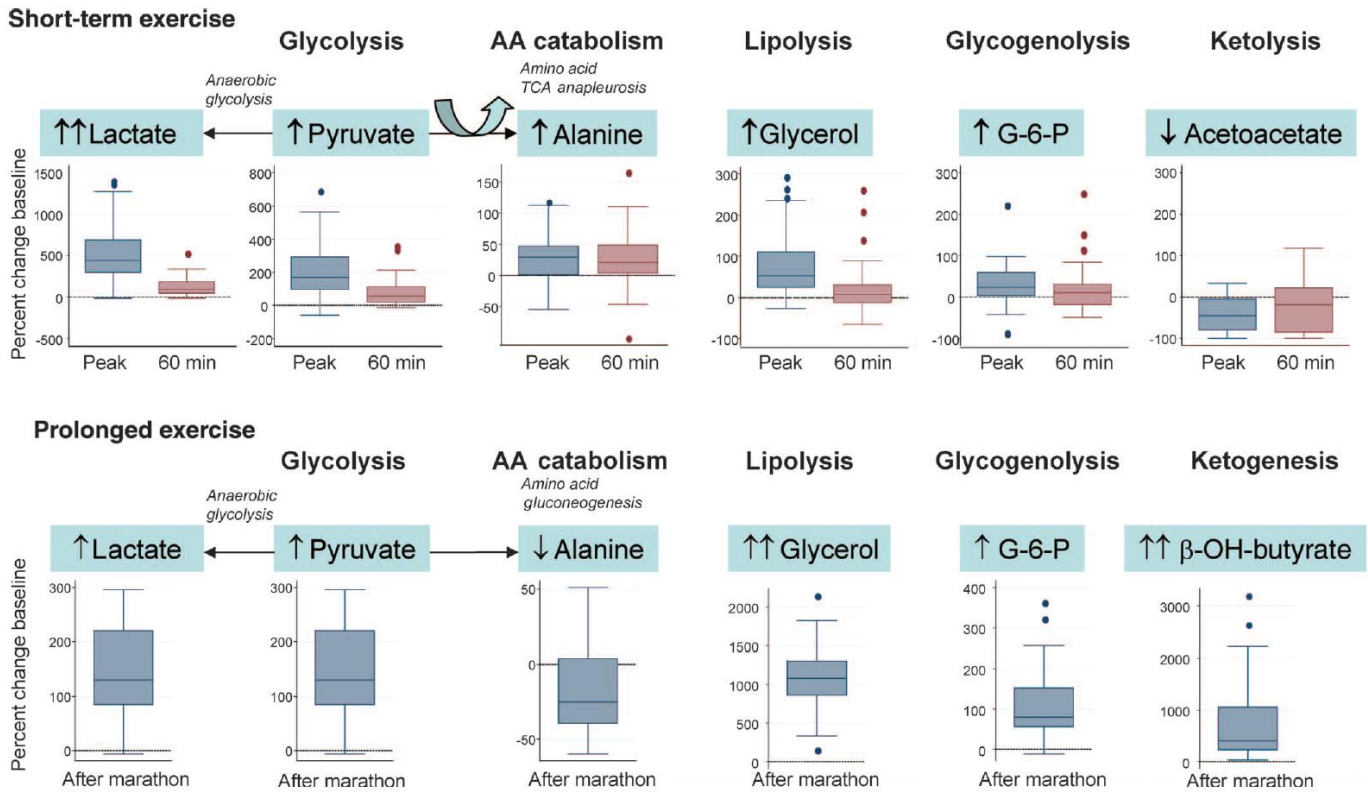

Conflict of interest disclosure

- Consultant for Huron Consulting Group
- Consultant for Novartis
- Co-Leader of Work-Package 8 (analysis of results) of the SPRINTT Project (IMI–JU 115621)

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Exercise Is Medicine At Any Dose?

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There is no known upper limit for moderate-intensity physical activity in healthy individuals, but doses more than 100 minutes a day do not appear to be associated with additional reductions in mortality rates.[5] For vigorous physical activity, low doses are related to large benefits, whereas doses up to 10 times the recommended physical activity levels are not associated with further reductions in mortality rates[5-7]. Some studies suggest an attenuation of health benefits at higher physical activity doses, but methodological flaws may limit the validity of these observations.[1,4] No dose of vigorous physical activity is associated with higher mortality rates than physical inactivity. Physical activity is one of the best modifiable factors for the prevention of noncommunicable diseases and mortality, so it is important for clinicians to keep emphasizing that exercise is medicine.

Physiological mechanisms underlying the effects of exercise on the aging process

	Protective mechanisms of exercise training
1	Improved endothelial function and passivation of atherosclerotic plaques
2	Reduction in systemic inflammation
3	Beneficial effects on the autonomic regulation of cardiovascular function
4	Improvement in cardiovascular risk factor control • Increase in HDL-cholesterol concentrations • Reduction in triglyceride and LDL-cholesterol • Reduction in blood pressure • Reduction in body fat mass • Reduction in insulin resistance and improvement in glucose metabolism
5	Potential anti-thrombotic and anti-platelet effects
6	Heart intrinsic mechanisms • Ischemic preconditioning with reduced myocardial damage during prolonged ischemia • Prevention of reperfusion-induced ventricular arrhythmias
7	Improvement in maximal oxygen uptake ($VO_{2\,max}$) • Reduced all-cause and cardiovascular mortality • Improved functional capacity, QoL and ADL performance • Improved pulmonary function • Improved central hemodynamics (cardiac output/stroke volume) • Improved skeletal muscle metabolism (muscle blood flow, O_2 utilization, mitochondrial function)
8	Improvement in skeletal muscle function (resistance training) • Improved muscle mass and strength developed by muscle groups • Improved muscle power (force generation at high contraction speed) • Improved muscle quality, muscle recruitment and connective tissue • Reduction of functional deficits and disease co-morbidity • Improved QoL and IADL performance
9	Improvements in bone mineral density and ultrastructure
10	Improvement of chromosomal function • Improved telomerase enzyme activity • Less reduction in telomerase length
11	Improvement in cognitive function (aerobic and resistance training)

Gremeaux et al., Maturitas. 2012