

Inactivity Physiology

Marc Hamilton, Ph.D.

Professor

Pennington biomedical

Baton rouge, Louisiana, USA

My Goal For Inactivity Physiology

To discover a potent solution for millions of people who can't (or won't) exercise.



Well beyond expectations

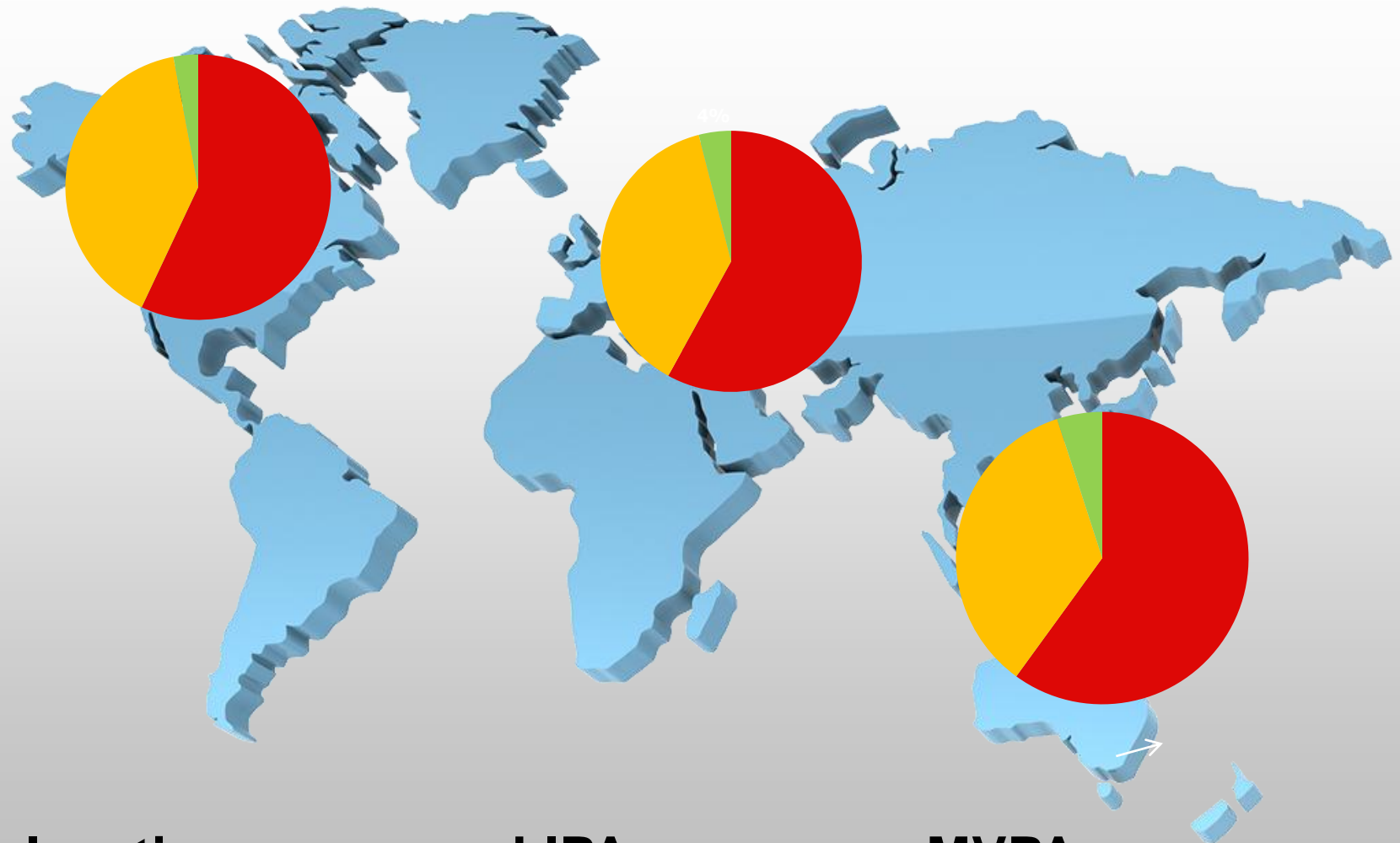
YOU can have a huge impact



Revolutionary, not evolutionary.

Professor A Bauman

An Increasingly Inactive World



Inactive



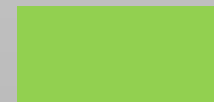
muscular inactivity

LIPA



Low Intensity

MVPA



Moderate + vigorous

Inactivity Physiology Explained Simply

Some of the most potent mechanisms at the root cause of chronic disease are caused by inactivity (generally sitting) because the body needs frequent muscular activity.

See - ESSR, 2004 & Diabetes, 2007



Simple But Profound Rationale-
Cells receive input from their environment
every minute of every day.



A Key Conclusion To Never Forget!

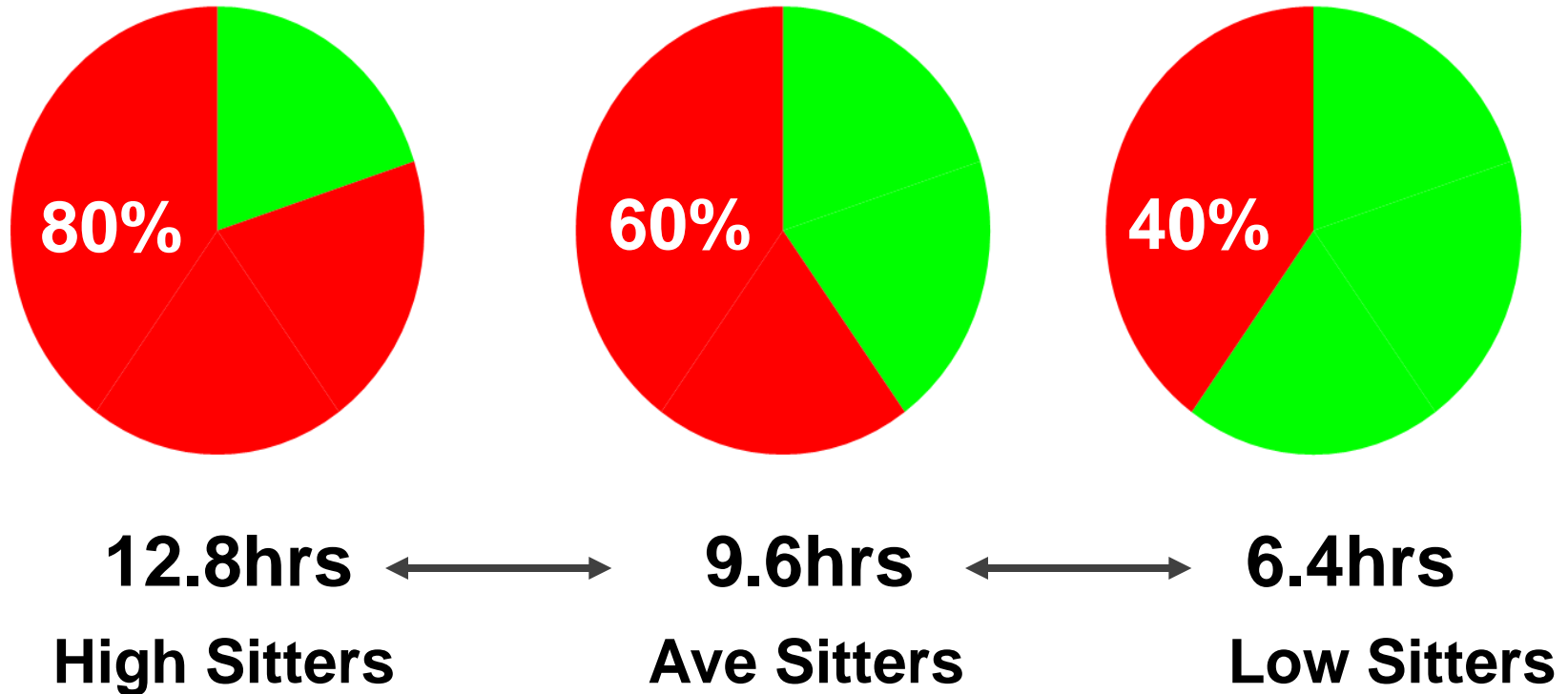
Saying that people spend too many hours each day being sedentary (mostly sitting) is actually **the same as saying** people don't spend enough hours each day being active.

The body naturally needs a large daily duration of muscular contractile activity, and practically that is mostly **Low-Intensity Physical Activity**).

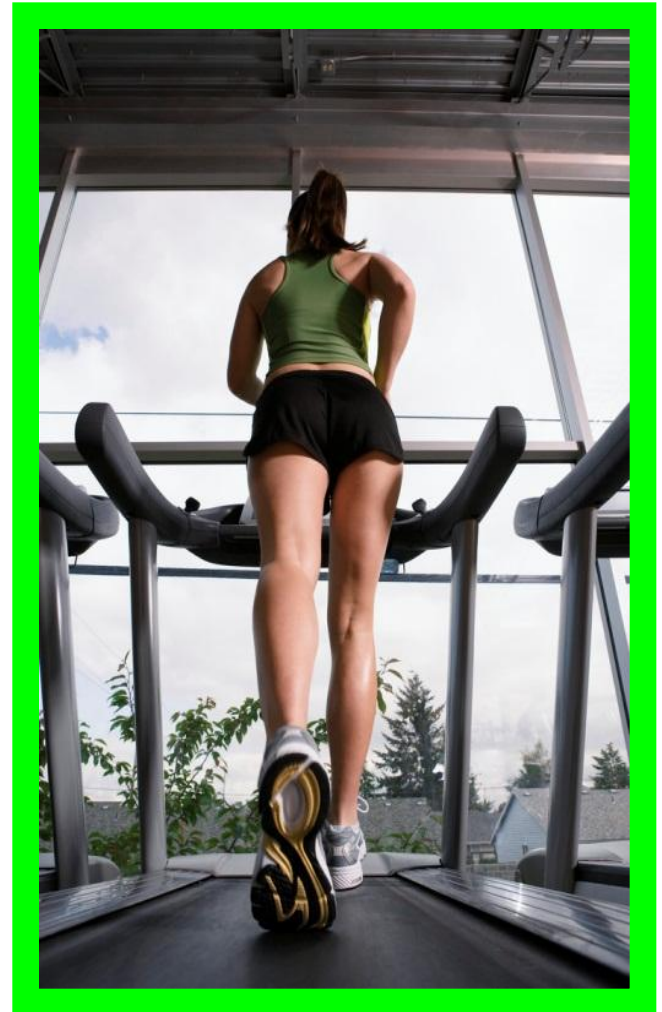


2 SIDES OF THE SAME COIN:

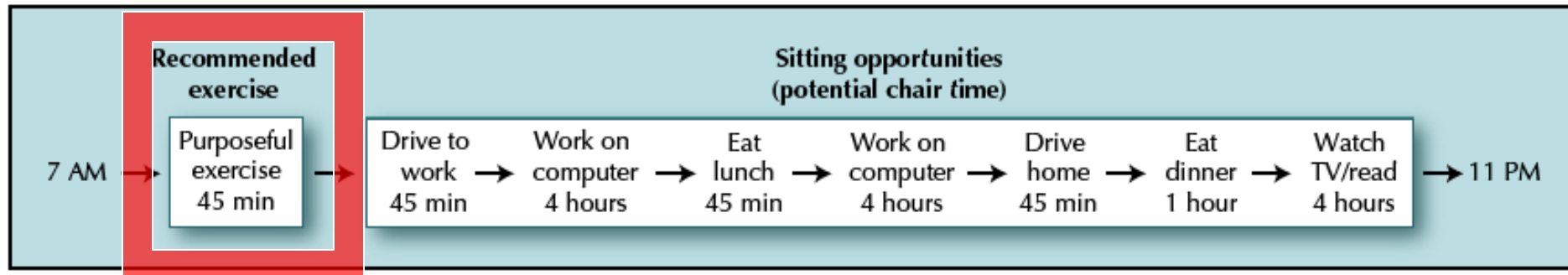
Sedentary time and Low-Intensity Physical Activity



30 min is $\frac{1}{48}^{\text{th}}$ of one day



Are you an “exercising couch potato”?



Hamilton et al. *Too Little Exercise and Too Much Sitting: Inactivity Physiology and the Need for New Recommendations on Sedentary Behavior*

Current Cardiovascular Risk Reports, 2008

A sobering thought about the historical focus on *Moderate-Vigorous Physical Activity* in public health recommendations:

< 5% of the people do them!



“Exercise” (moderate activity for 150 min/week) has always been a very rare behavior, despite many excellent public health efforts.

Objective NHANES data: accelerometry (Troiano MSSE 2008)

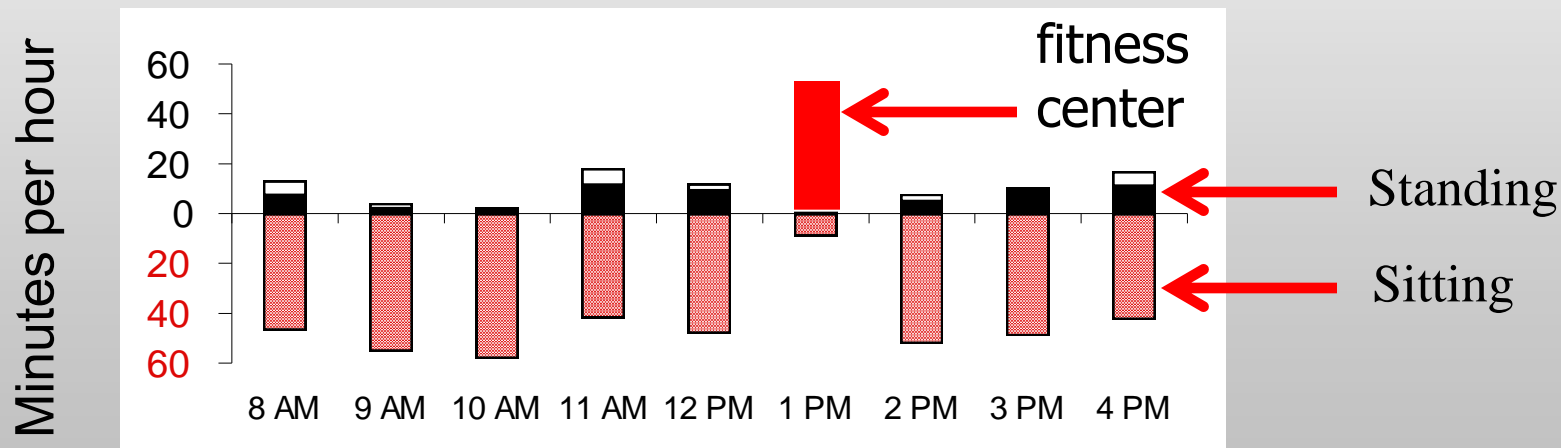
20-59 year olds	$3.5 \pm 0.3 \%$
>60 years	$2.4 \pm 0.4 \%$

Subjective data: self-reported surveys (Kruger MSSE 2007)

28% Americans report 150 min/week MVPA

Even in the minority of people who achieve the recommended 150 min/week of moderate activity...

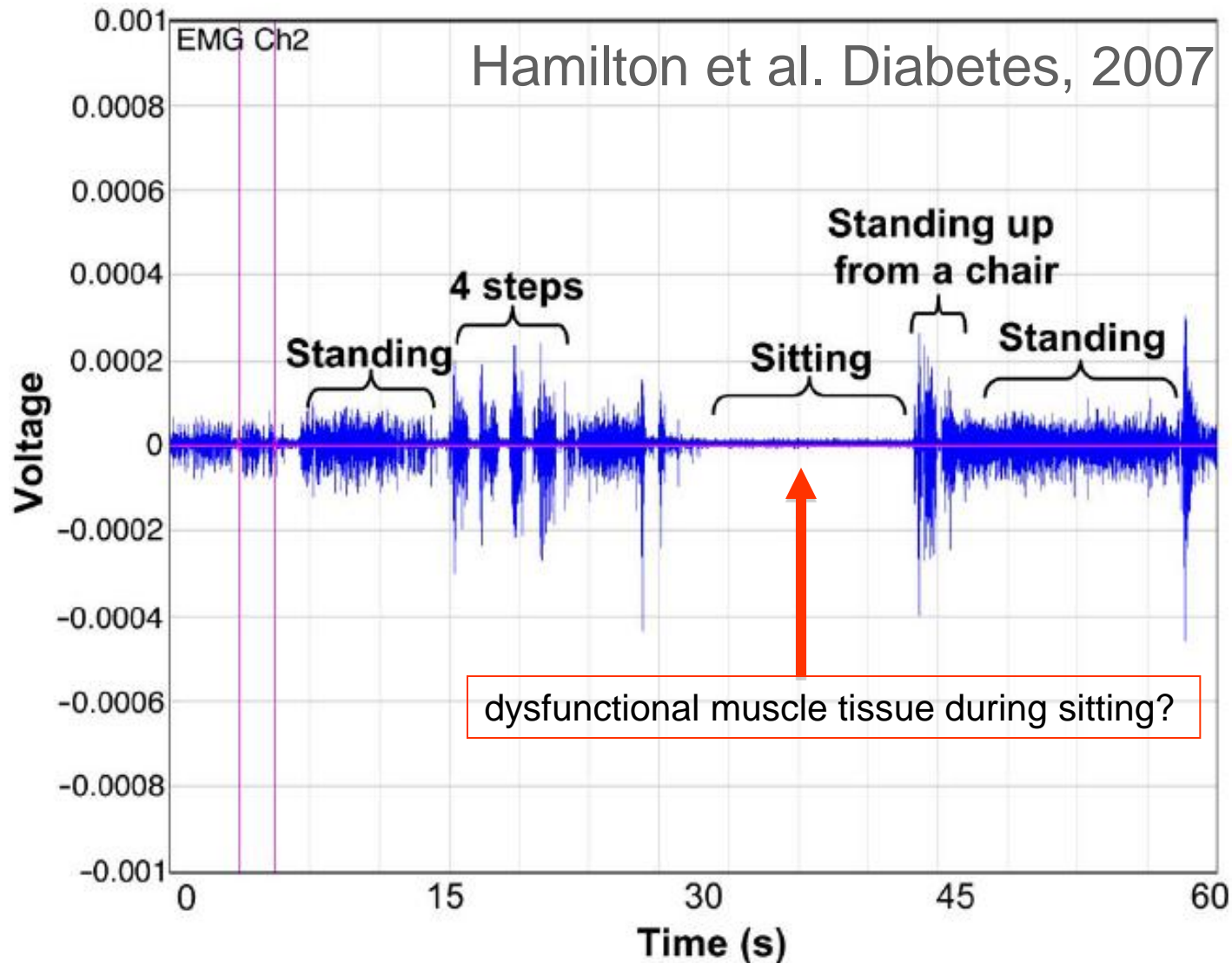
...this still leaves ~16 hrs, ~**1400 minutes** of each waking day with physical inactivity!!!



Flat-line signals alert to dysfunctional tissue

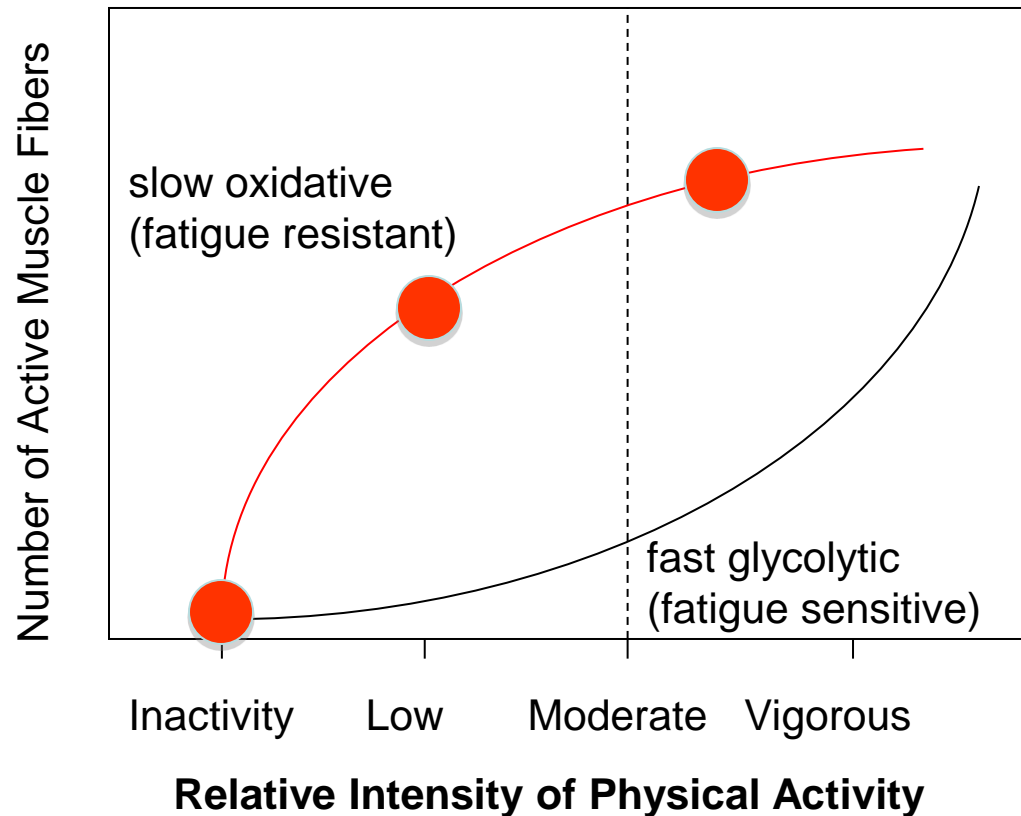


Inactivity Physiology focuses on the benefits of *large durations of intermittent muscular contractile activity* during **Low-Intensity Physical Activity (LIPA)** instead of sitting inactive



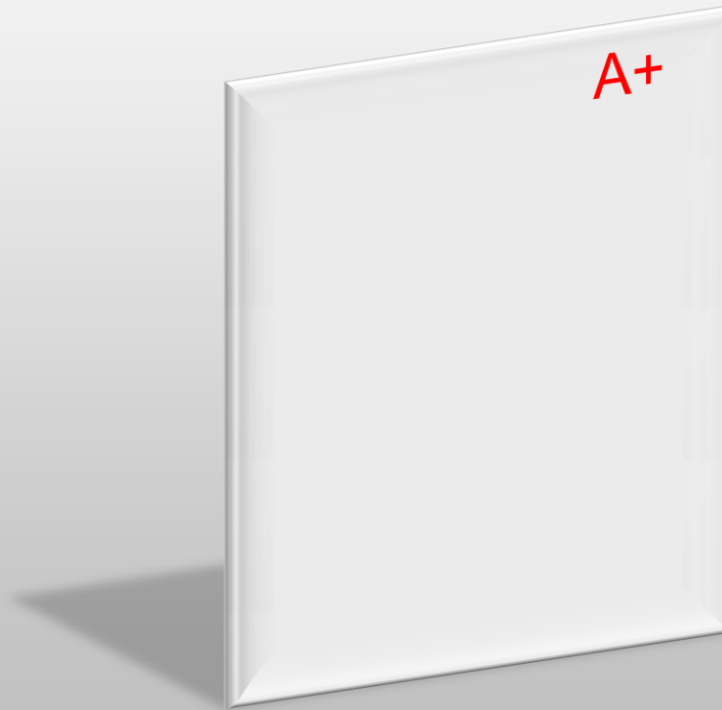
Understanding Why LIPA is Non-Fatiguing & Abundant

Skeletal Muscle Fiber Type Recruitment



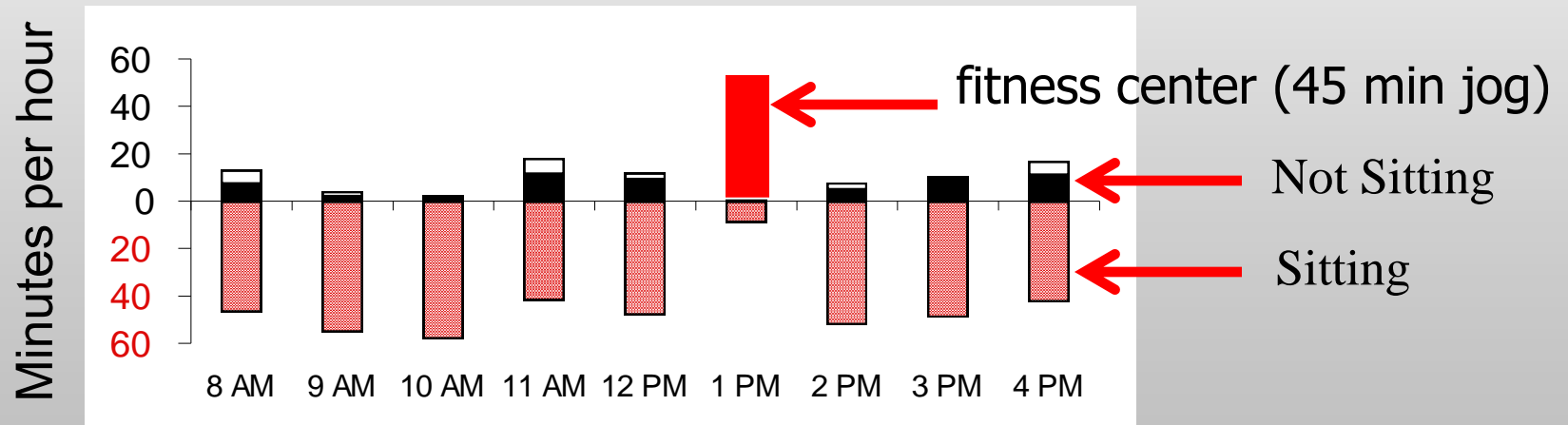
Hamilton and Owen, **Sedentary Behavior and Inactivity Physiology (2012)**. In *Physical Activity and Health*, 2nd edition.

Congratulations, you are now ready for a test!



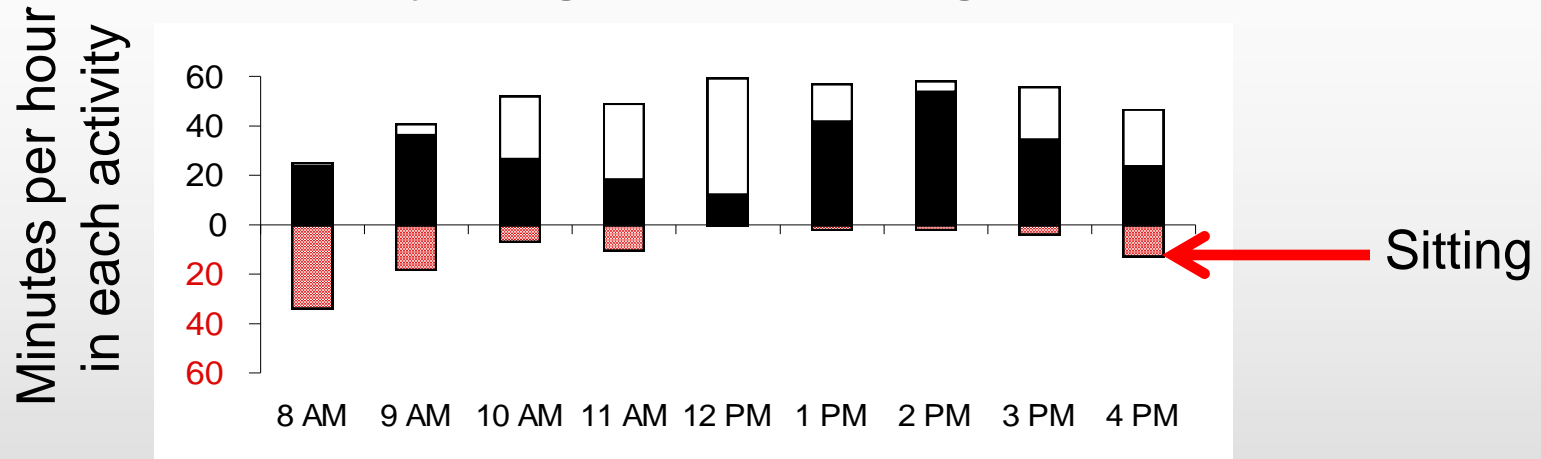
A FUN POP QUIZ

Is it odd to you that this person (who is very sedentary every hour of the day) is categorized by experts as “very *physically active*”?

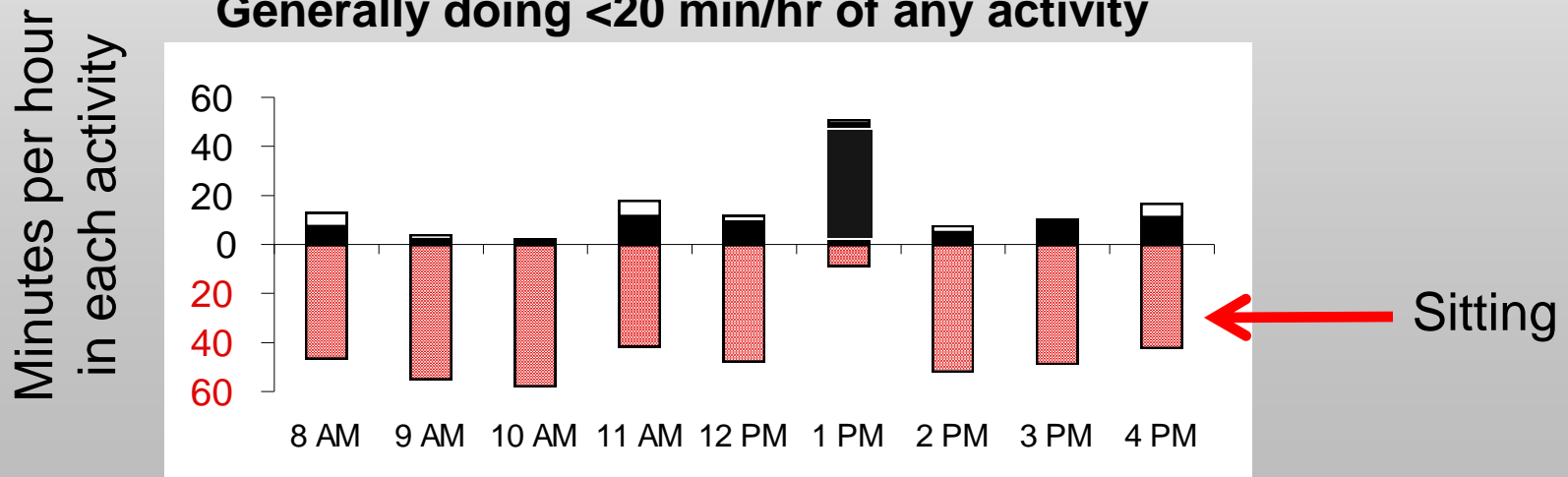


Who ACTUALLY spends more time in physically activity?

Generally doing ~45 min/hr doing LIPA



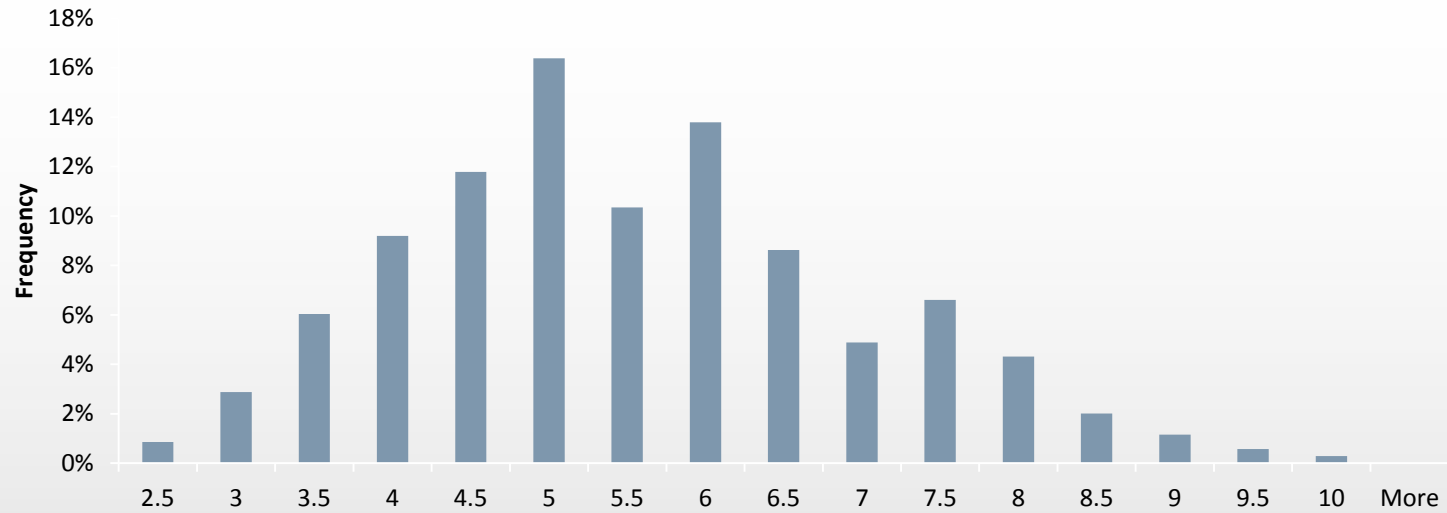
Generally doing <20 min/hr of any activity



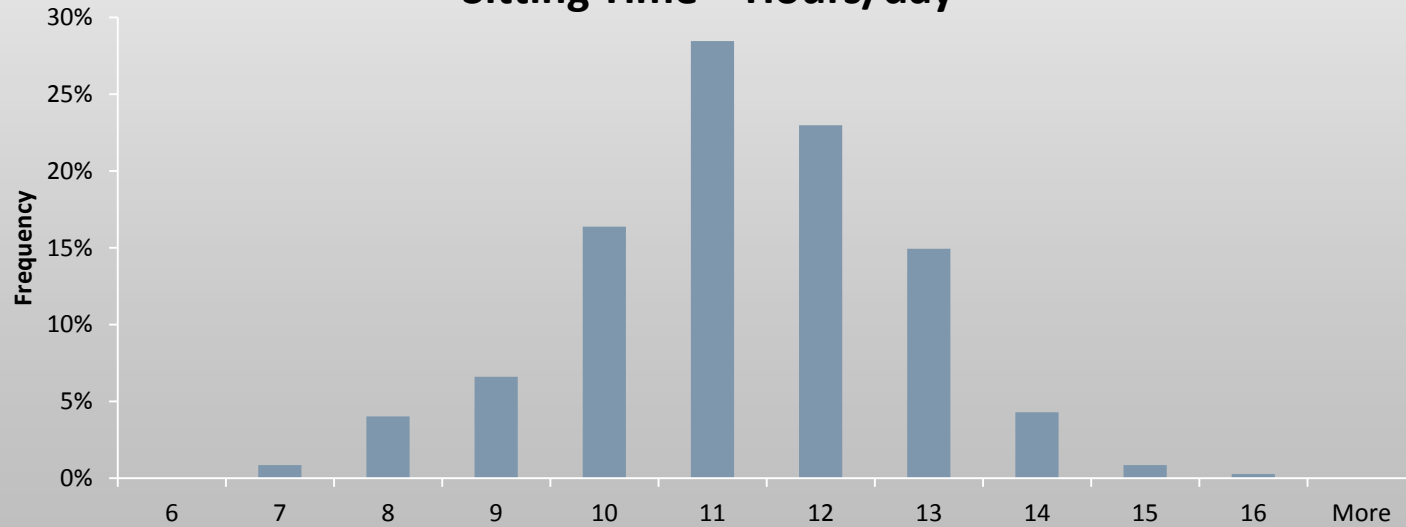
How much time do people in modern societies sit, or alternatively do upright activities?



Total Non-Sitting Time – Hours/day



Sitting Time – Hours/day



Zderic, Hamilton, and Hamilton

Are exercisers less sedentary?



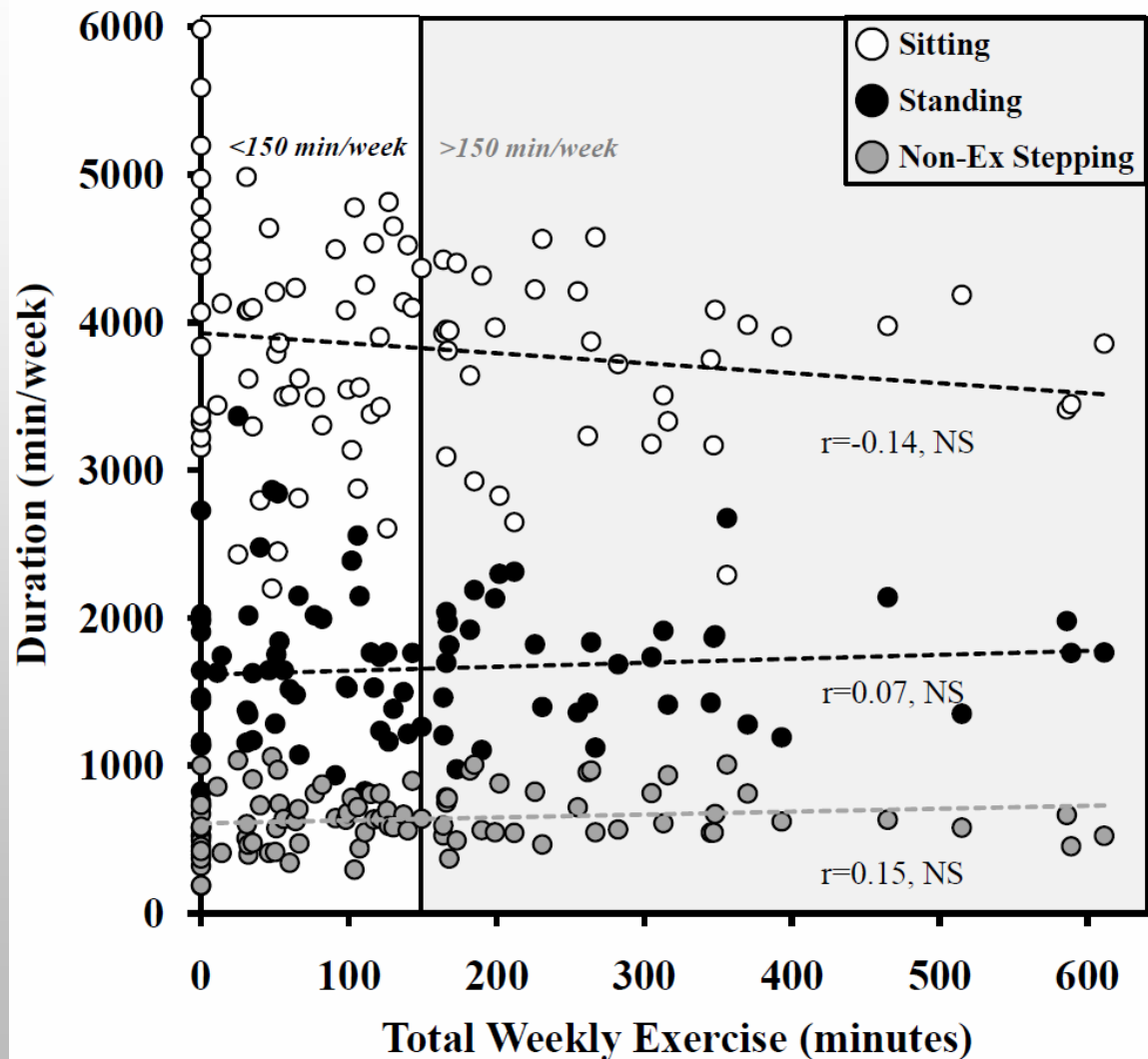
Total weekly sedentary time and LIPA is NOT less in women who do a large amount of moderate intensity walking

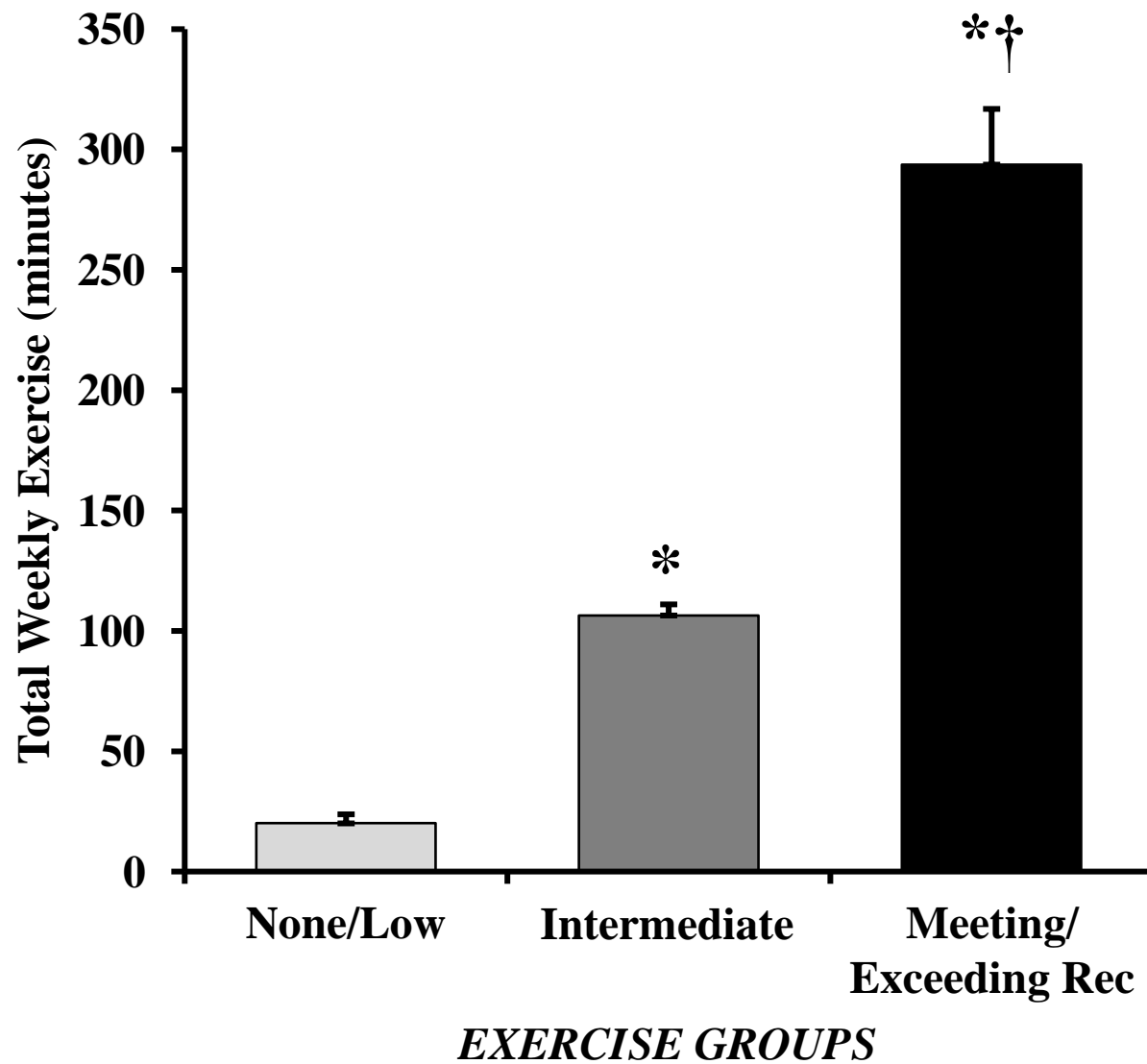


Evidence that women meeting physical activity guidelines do not sit less: An observational inclinometry study.

Craft and Hamilton Int J Behav Nutr Phys Act. 2012

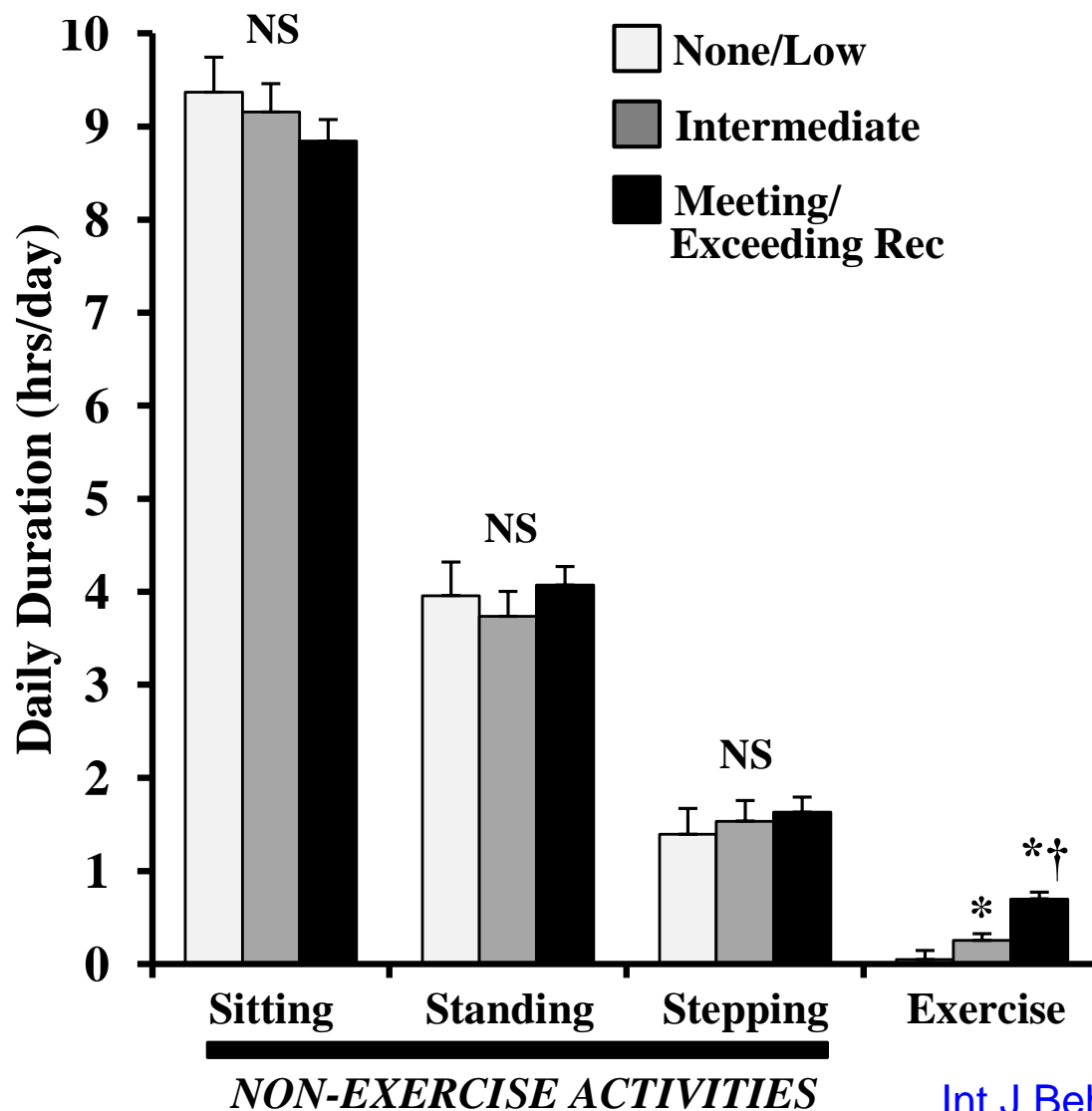
Regardless how much time was spent doing moderate activity there was the same sedentary time and total physical activity.



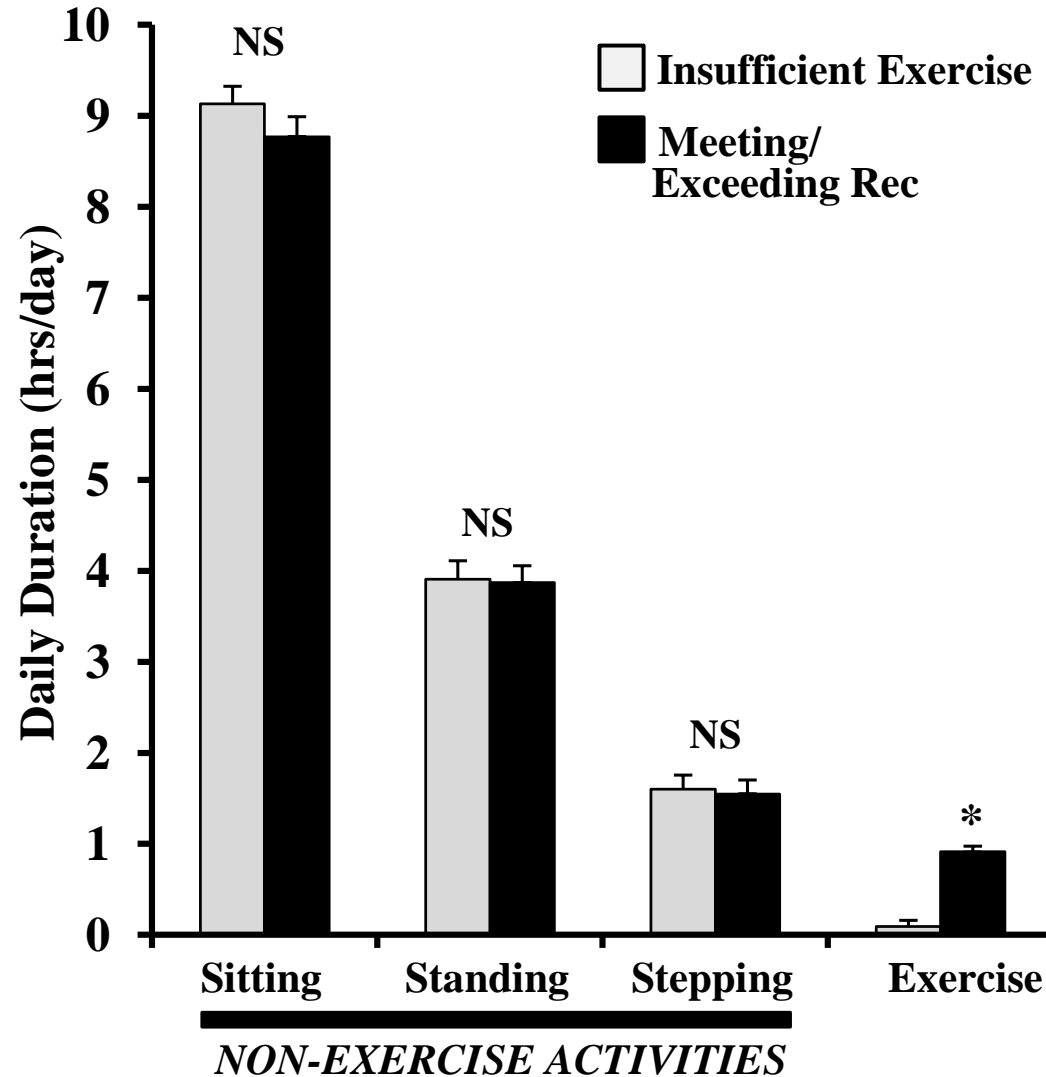


Exercisers are not less sedentary (sit less) than people who do not exercise

Exercisers sit just as much as people who don't exercise



Exercisers are not less sedentary (sit less) even on the days they exercise



Inactivity Physiology Concepts

1. Humans naturally require a large amount of ***time*** in physical activity throughout the whole day for good health.



ESSR, 2004

Diabetes, 2007

Current Cardiovascular Risk Reports, 2008

Inactivity Physiology Concepts

1. Humans naturally require a large amount of *time* in physical activity throughout the whole day for good health.
2. Saying that people need to reduce sedentary *time* is physiologically the same as saying we don't have enough hours each day doing *any* physical activity (i.e. *muscular inactivity*).

ESSR, 2004

Diabetes, 2007

Current Cardiovascular Risk Reports, 2008

Inactivity Physiology Concepts

1. Humans naturally require a large amount of *time* in physical activity throughout the whole day for good health.
2. Saying that people need to reduce sedentary *time* is physiologically the same as saying we don't have enough hours each day doing *any* physical activity (i.e. *muscular inactivity*).
3. **THE GOOD NEWS! NOVEL SOLUTIONS FOR HEALTH PROMOTION ARE ON THE HORIZON.** There are some VERY POTENT health promoting effects of LIPA, even in obese or unfit people who can't (or won't) do MVPA.

ESSR, 2004

Diabetes, 2007

Current Cardiovascular Risk Reports, 2008

New Solutions For People Who Can't or Won't Do More MVPA

- There is a need for a potent solution for **ALL** people, regardless of health status, age, wt, etc. to benefit from **much** more muscular physical activity (LIPA).



INACTIVITY PHYSIOLOGY STUDIES

The Early Years 1998-2003

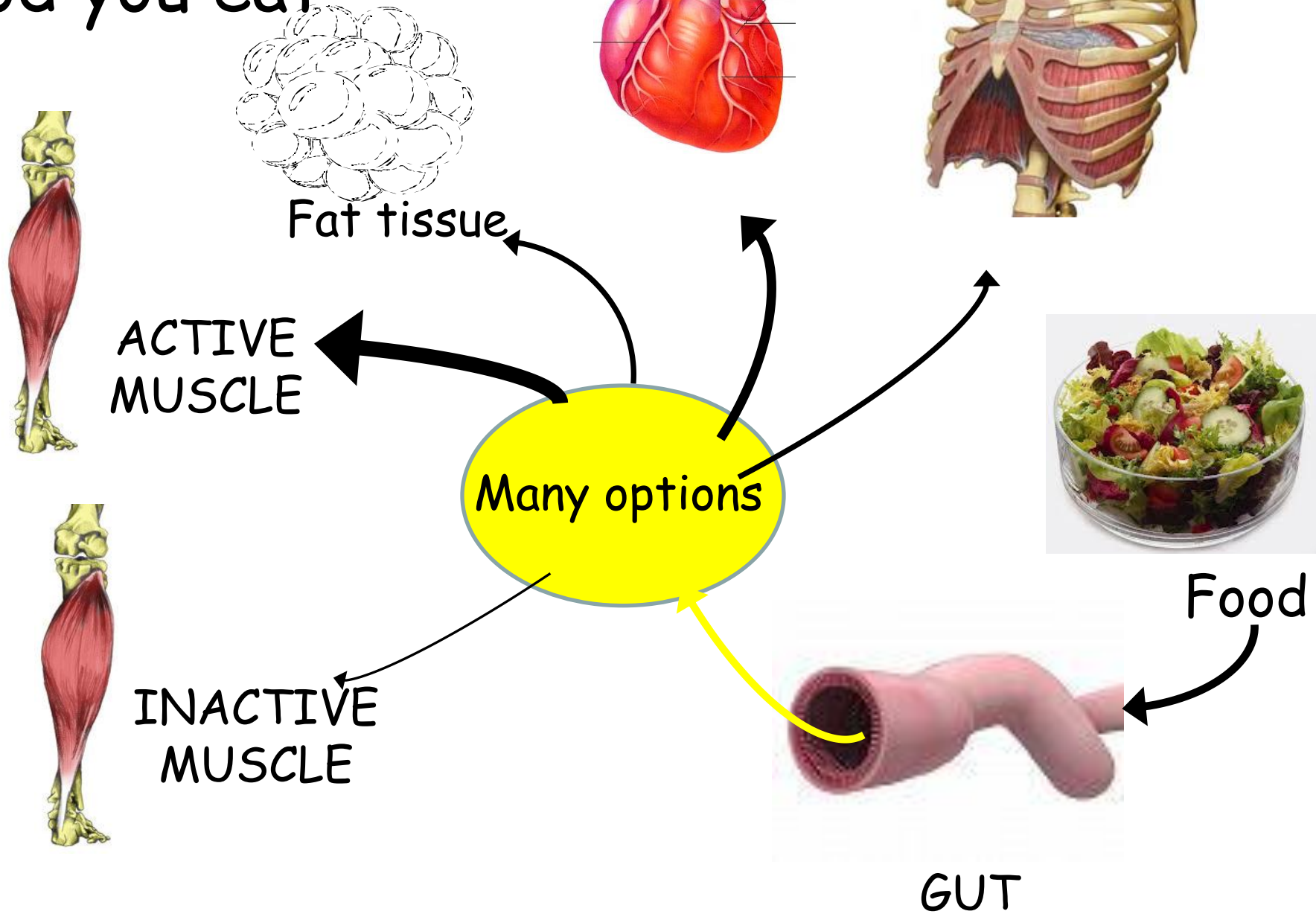
Exercise Physiology versus Inactivity Physiology: An Essential Concept for Understanding Lipoprotein Lipase Regulation

Marc T. Hamilton,^{1,2} Deborah G. Hamilton,¹ and Theodore W. Zderic¹

¹Department of Biomedical Sciences and ²Dalton Cardiovascular Research Center, University of Missouri-Columbia, Columbia, MO

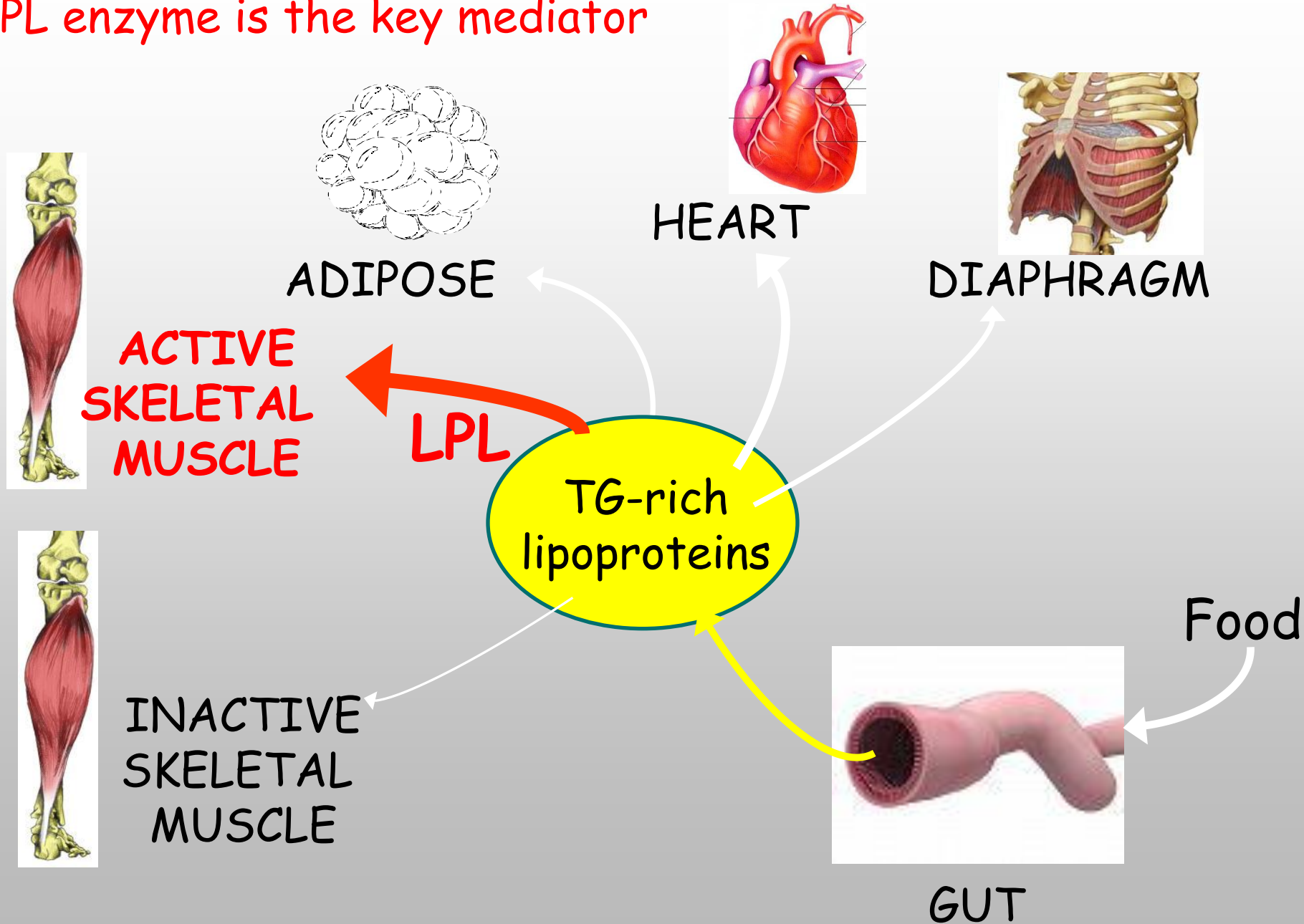
HAMILTON, M.T., D.G. HAMILTON, and T.W. ZDERIC. Exercise physiology versus inactivity physiology: An essential concept for understanding lipoprotein lipase regulation. *Exerc. Sport Sci. Rev.*, Vol. 32, No. 4, pp. 161–166, 2004. Some health-related proteins such as lipoprotein lipase may be regulated by qualitatively different processes over the physical activity continuum, sometimes with very high sensitivity to inactivity. The most powerful process known to regulate lipoprotein lipase protein and activity in muscle capillaries may be initiated by inhibitory signals during physical inactivity, independent of changes in lipoprotein lipase messenger RNA. Key Words: dose response, coronary heart disease (CHD), transcription, posttranslational, signaling, sedentary, aging

Traffic patterns of food you eat



Plasma Lipid Traffic

LPL enzyme is the key mediator



Inactivity Powerfully Shuts Off Lipoprotein Lipase

“The body’s vacuum for fatty lipoproteins in the vasculature becomes unplugged”

Hamilton et al. *American Journal of Physiol (Endoc Metab)* 1998

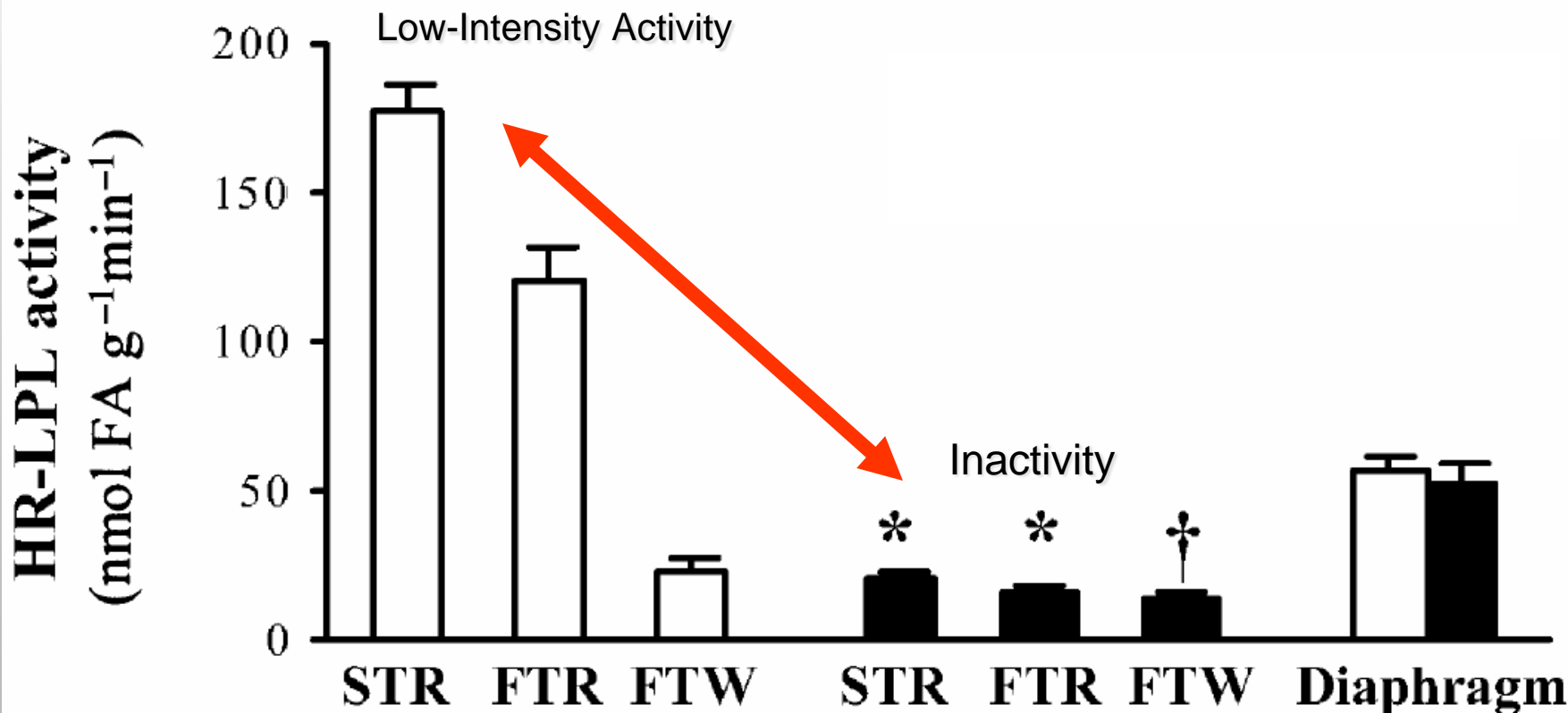
Bey and Hamilton, *J Appl Physiol* 2001

Bey and Hamilton, *J Physiol (Lond)* 2003

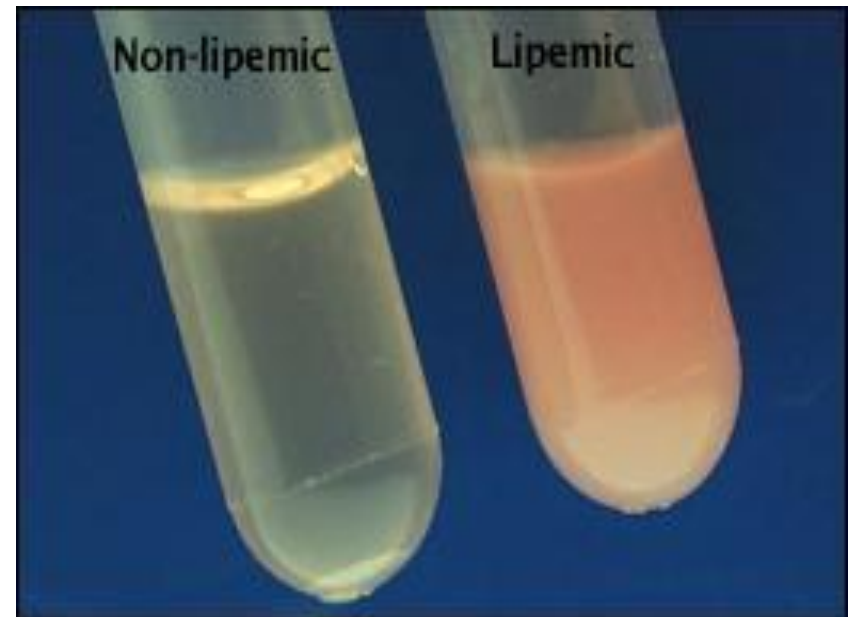
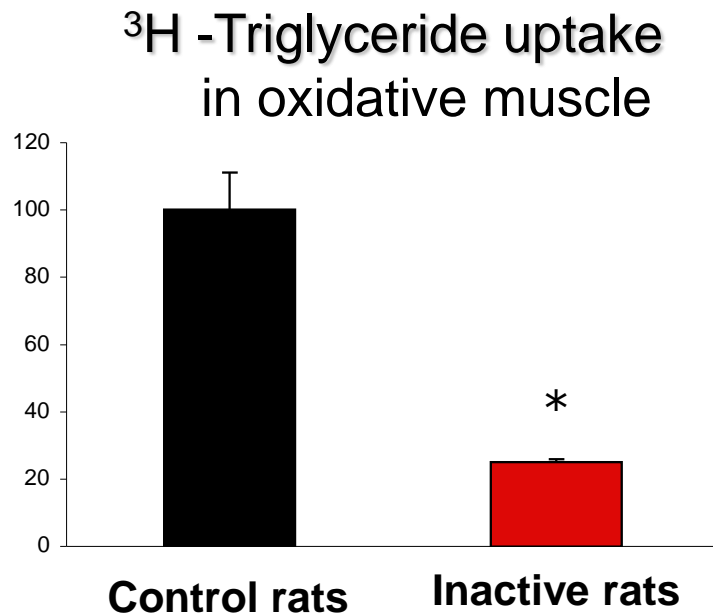
Zderic and Hamilton, *J Appl Physiol* 2007

Suppression of skeletal muscle lipoprotein lipase activity during physical inactivity: a molecular reason to maintain daily low-intensity activity

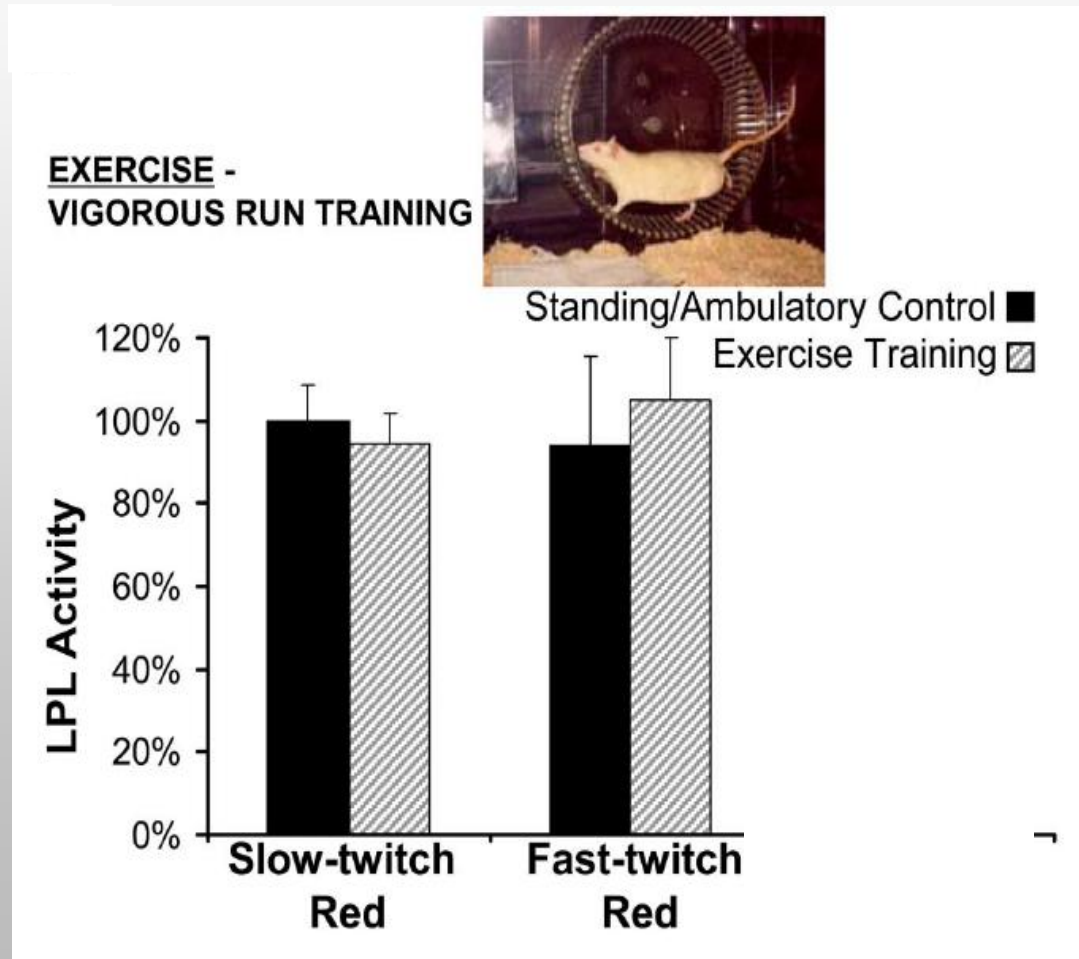
Lionel Bey and Marc T. Hamilton



Lipoprotein metabolism is stalled during inactivity



Run training does NOT have the same potency



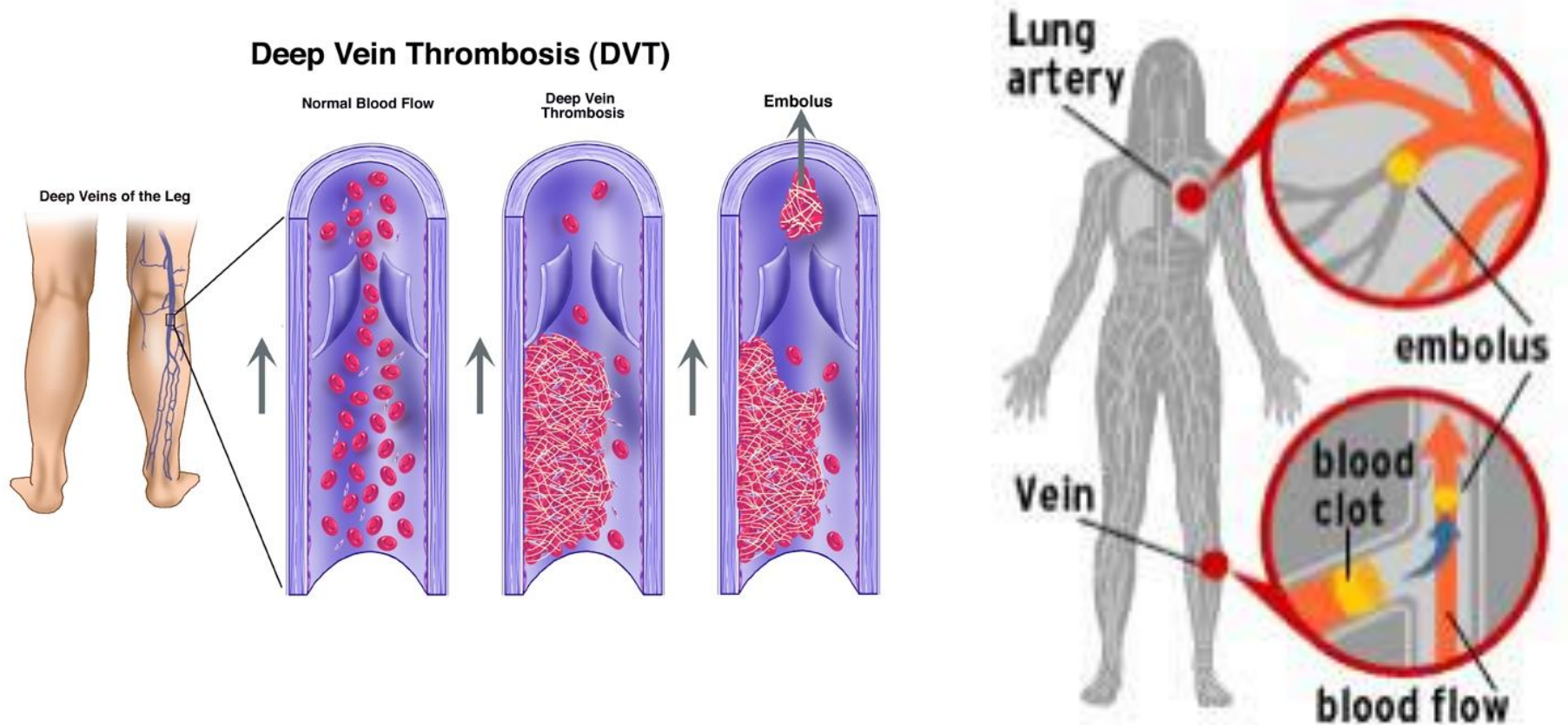
Hamilton et al. *Am. J. Physiol*, 1998

The Specificity Principle

The signals harming the body during physical inactivity are specific and distinct from exercise.

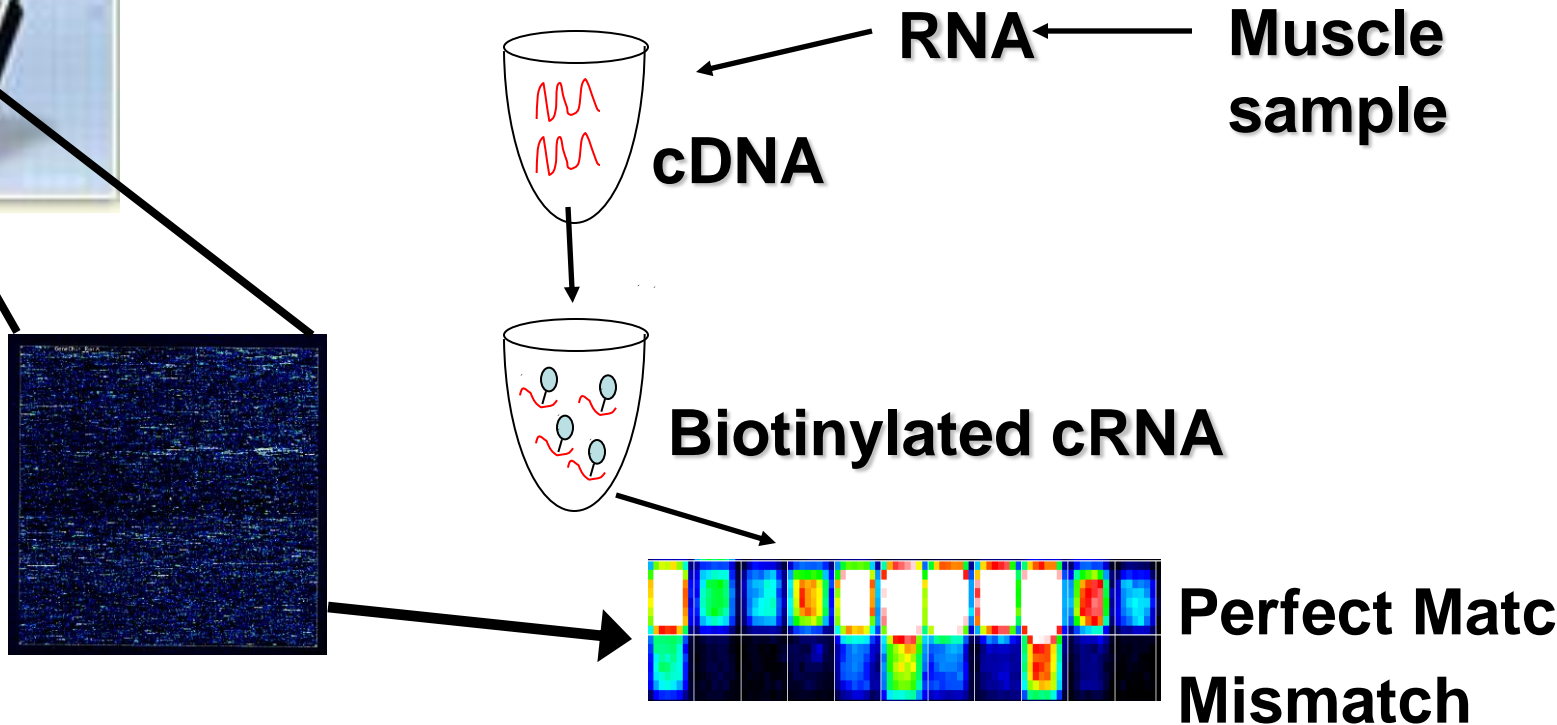
(one reason why “too much sitting is not the same as too little MVPA”)

Inactivity Physiology is opening doors for a novel solution to the elusive and dangerous condition of deep venous thrombosis (DVT)



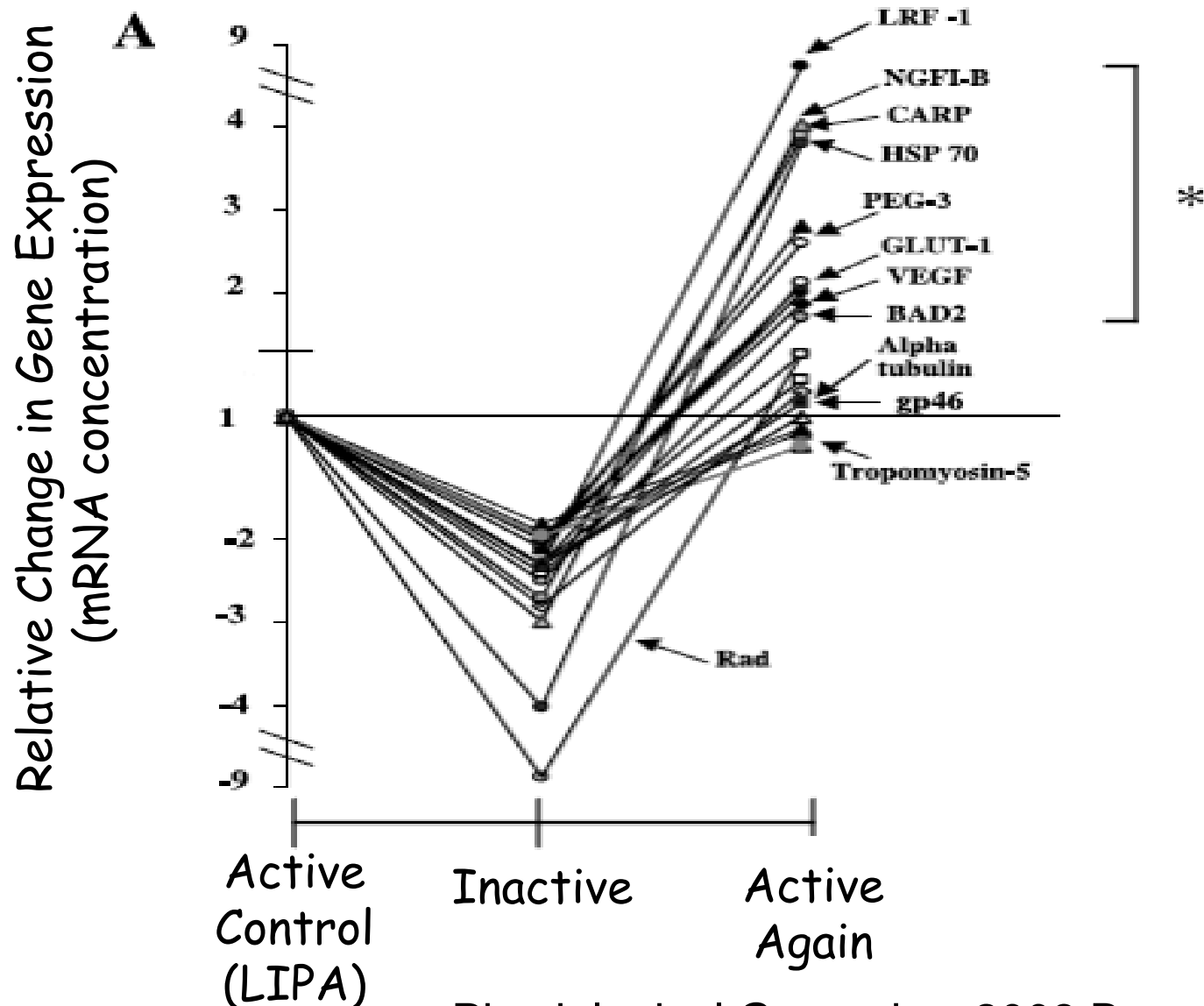
Too much sitting can cause DVT – not too little exercise

Inactivity-Responsive Genes



~980,000 oligonucleotide probes for ~33,000 genes

The Homeostasis for Expression of Hundreds of Genes is Rapidly Disturbed By Contractile Inactivity



Identification of hemostatic genes expressed in human and rat leg muscles and a novel gene (LPP1/PAP2A) suppressed during prolonged physical inactivity (sitting)

Theodore W Zderic* and Marc T Hamilton*

Zderic and Hamilton, 2012

HEMOSTATIC GENE EXPRESSION IN SKELETAL MUSCLE

COAGULANT FUNCTIONS

Coagulation factor VIII

Coagulation factor VII

Vitamin K epoxide reductase complex

von Willebrand factor (vWF)

Tissue factor

Gamma-glutamyl carboxylase

⋮

ANTI-COAGULANT FUNCTIONS

LPP1

Platelet-activating factor acetylhydrolase

Annexin A5

Tissue factor pathway inhibitor

Protein C receptor

⋮

FIBRINOLYTIC FUNCTIONS

Annexin A2

Tetranectin

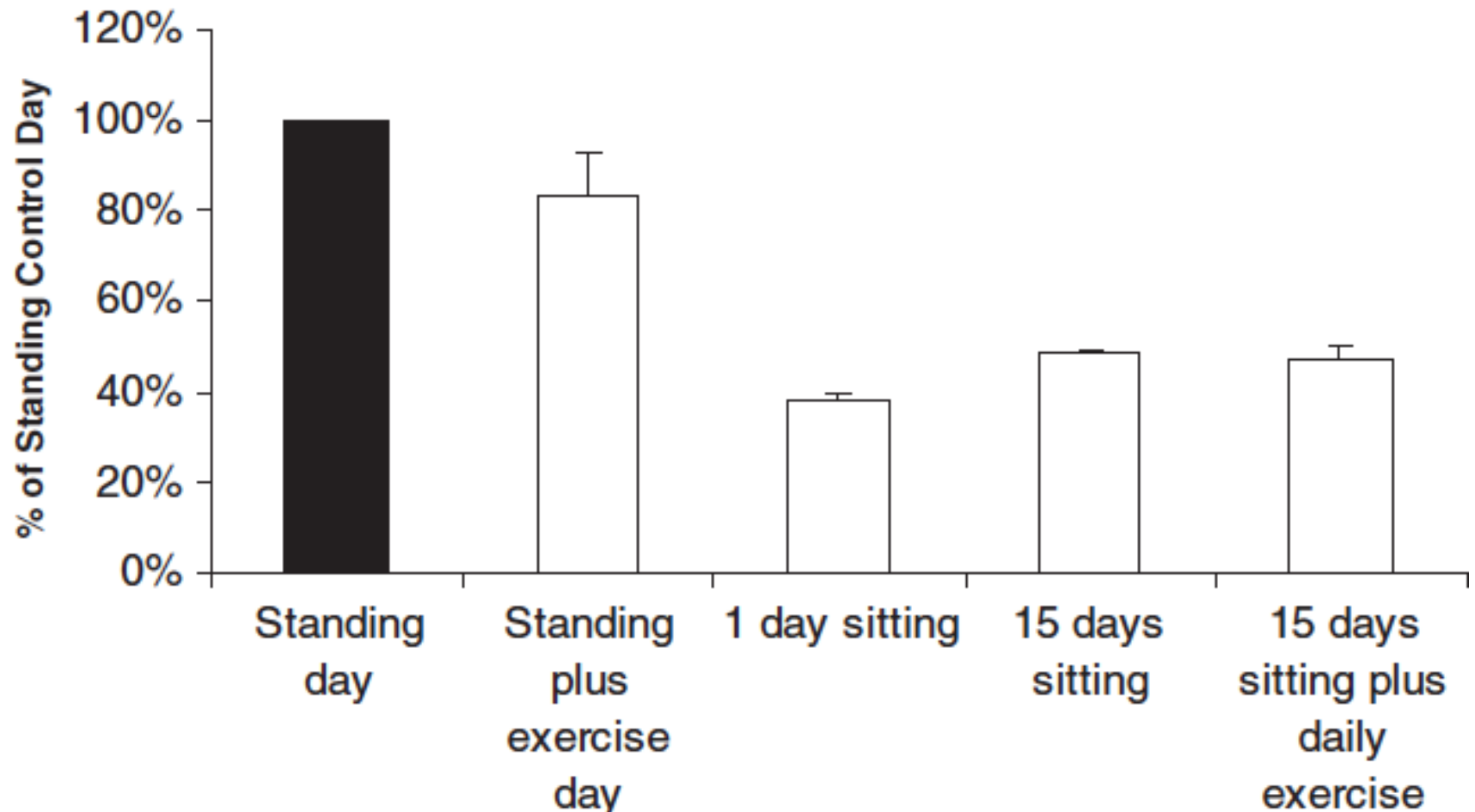
Tissue plasminogen activator

Urokinase plasminogen activator

⋮

LPP1 !

LPP1 is Suppressed During Sitting & Resistant to Exercise



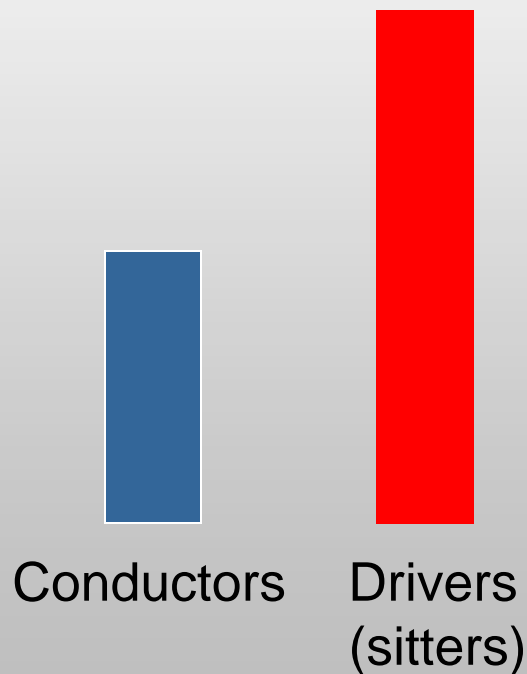
“The dire concern for the future may rest with growing numbers of people unaware of potentially insidious dangers of sitting too much.”

Hamilton Diabetes 2007

In 2004 and 2007, **We Reinterpreted** the Classical Vocational Studies by Morris (c 1953)



Death From CHD
middle age men



Hamilton, Hamilton, Zderic ESSR, 2004
Hamilton, Hamilton, Zderic Diabetes, 2007

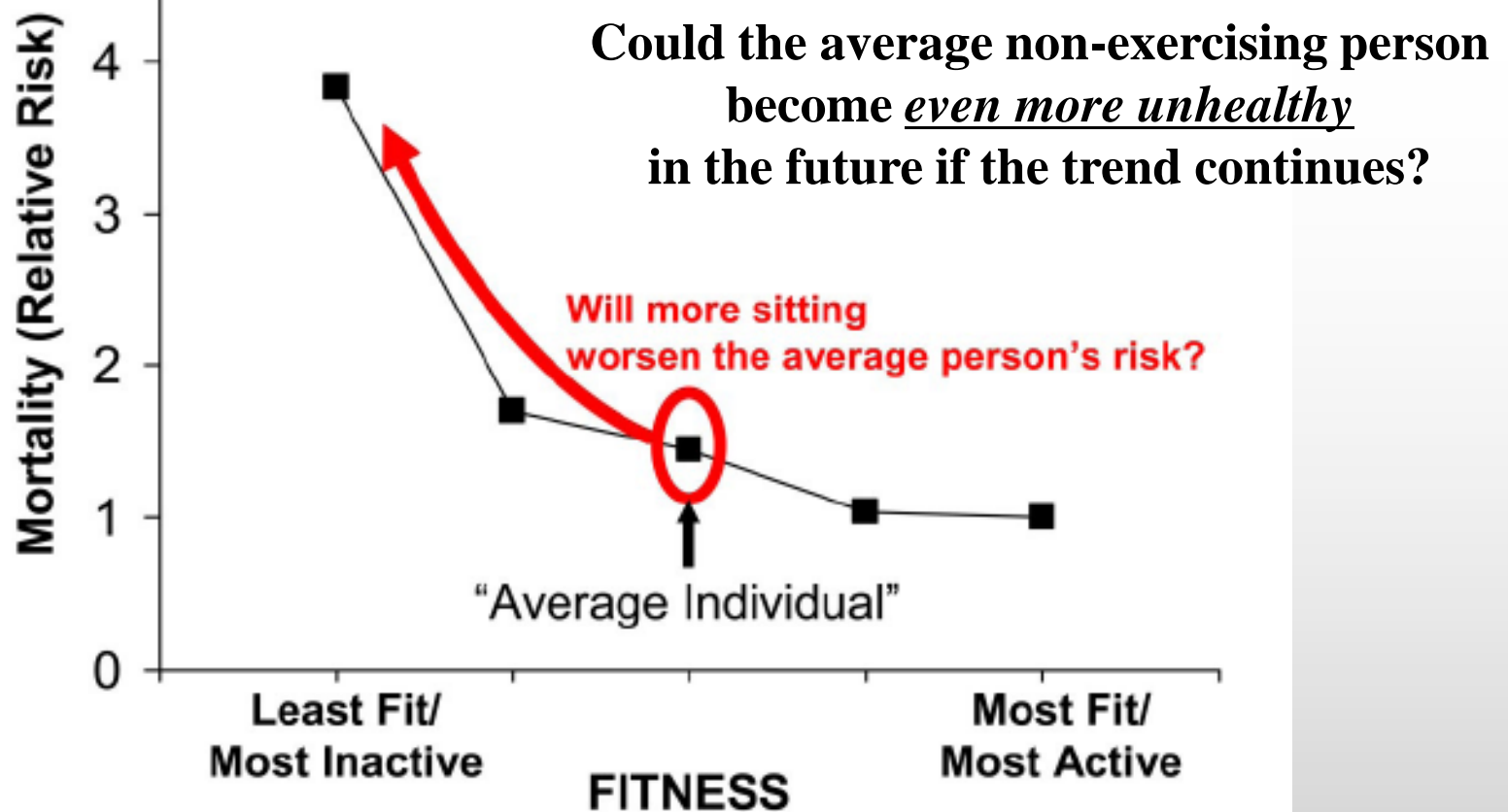
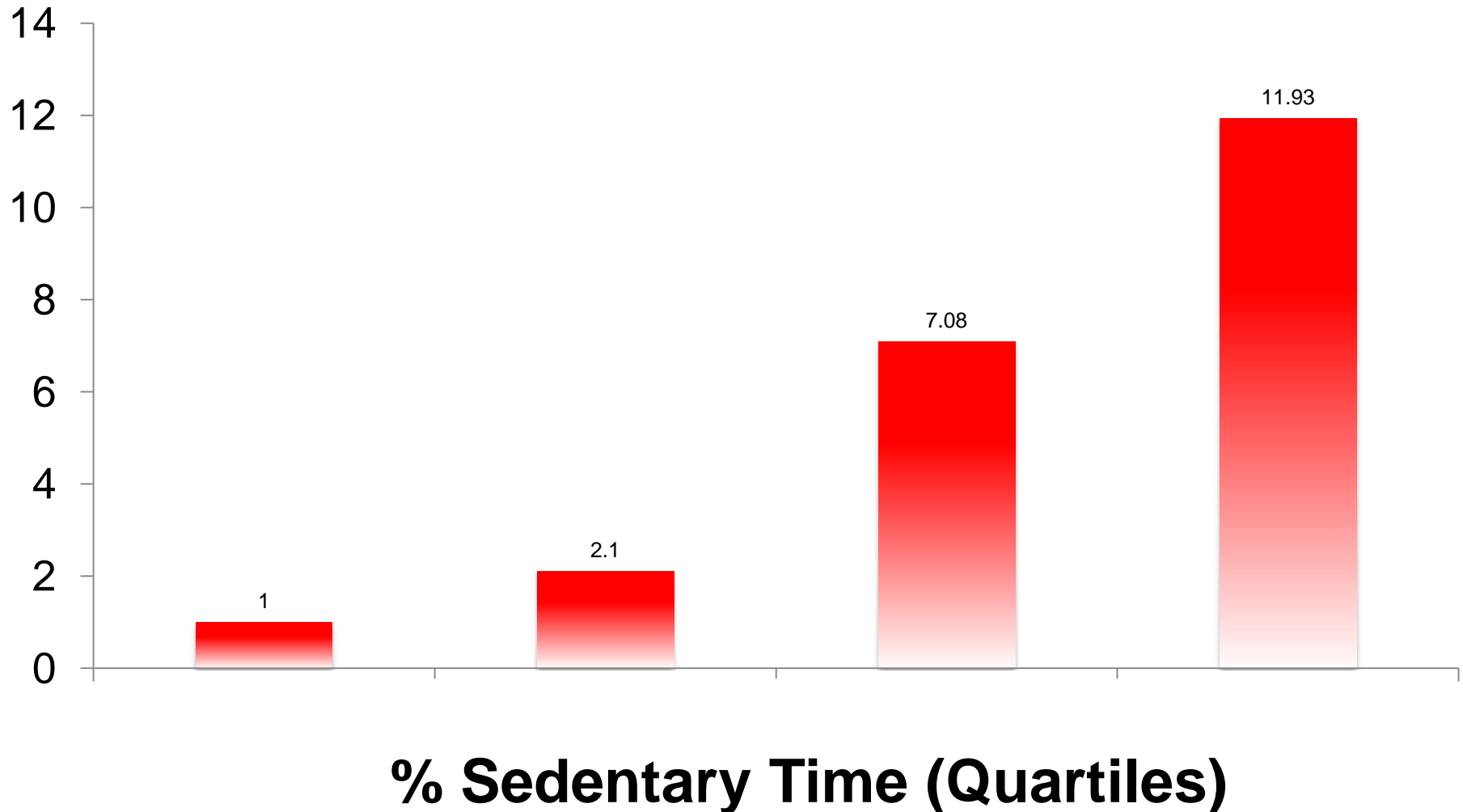


FIG. 1. A major question raised by the inactivity physiology paradigm is whether the typical person who already does not perform structured exercise regularly will have increased risks of metabolic diseases in the coming years as a result of too much sitting. The red circle shadows the median of 13,344 middle-aged men and women (adapted from ref. 86). As described in the text, the majority of people in the general population already do not follow the prescription for enough moderate-vigorous exercise. It logically follows that in people who already do not exercise, it is impossible for higher rates of age-adjusted metabolic syndrome, type 2 diabetes, obesity, and CVD over the coming years to be caused by further exercise deficiency. Inactivity physiology is a discipline concerned with the future of people who may be sitting too much. (Please see <http://dx.doi.org/10.2337/db07-0882> for a high-quality

Mortality From Recent Studies

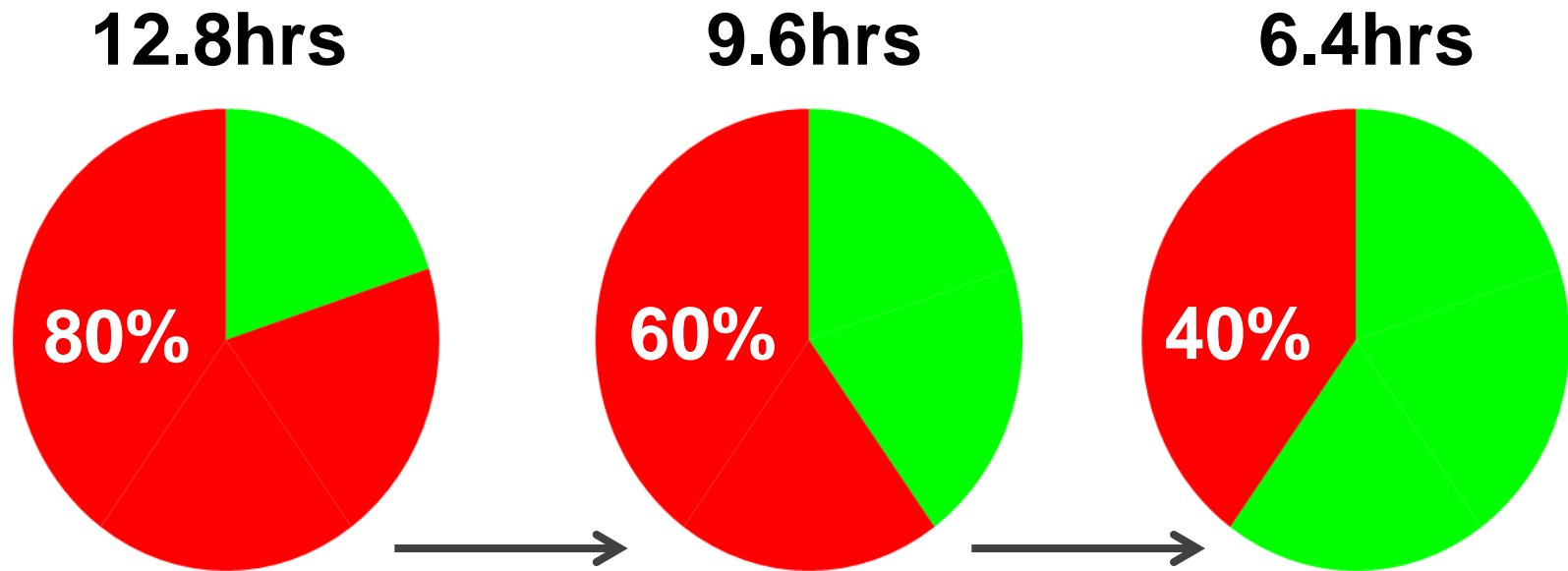
■ Mortality Hazard Ratio in 1,906 persons >50 yrs of age (averaging 63.8 ± 10.5 yrs) from accelerometry (adjusted for age, gender, race/ethnicity, education) Koster et al, PLoS One, 2012



Re-Activating the Human Lifestyle in a VERY sedentary world



Reducing total sedentary time by LIPA



Everyone Benefits - Even the norm is too much. And data shows effects are so rapid they don't require changes in weight or fitness.

How Can This Be Achieved?

That is the holy grail of healthy lifestyles!



Concluding Points

Inactivity physiology is a new field seeking solutions in ways never studied before.

When someone says “sedentary” stop them. It is more productive to look to the other side of the same coin for LIPA.

Encourage you peers to think positively – write about one day soon solving the problems now caused by too little LIPA time instead of “too sedentary”.

The Inactivity Physiology Paradigm

Plasma triglyceride metabolism in humans and rats during aging and physical activity
Int J Sports Nutr and Exer Metab, 2001

Inactivity Physiology vs. Exercise Physiology: An Essential Concept to Understand Lipoprotein Lipase Regulation
ESSR, 2004

The Role of Low Energy Expenditure and Sitting on Obesity, Metabolic Syndrome, Type 2 Diabetes, and Cardiovascular Disease
Diabetes, 2007

Too Little Exercise and Too Much Sitting: Inactivity Physiology and the Need for New Recommendations on Sedentary Behavior
Current Cardiovascular Risk Reports, 2008

Sedentary Behavior and Inactivity Physiology. In: Physical Activity and Health
2nd edition, C. Bouchard, S.N. Blair, and W. L. Haskell (Eds.), 2012