

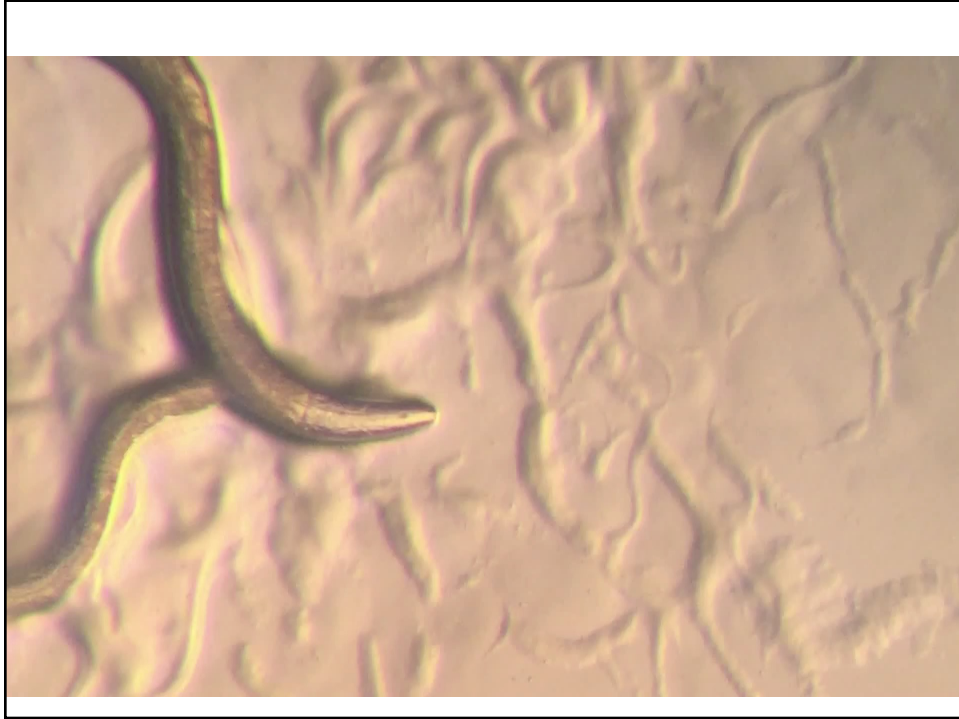
50<sup>th</sup> year HACETTEPE UNIVERSITY  
Faculty of Sport Sciences www.sporbilimleri.hacettepe.edu.tr

# Fiziksel inaktivite: Diyabete Giden Yolun Moleküler Taşları

Dr.Haydar A. Demirel  
Hacettepe Üniversitesi, Tıp Fakültesi Spor Hekimliği Anabilim Dalı  
Spor Bilimleri Fakültesi, Egzersiz ve Spor Fizyolojisi Anabilim Dalı

YAKIN DOĞU ÜNİVERSİTESİ  
DESAM ARAŞTIRMA ENSTİTÜSÜ

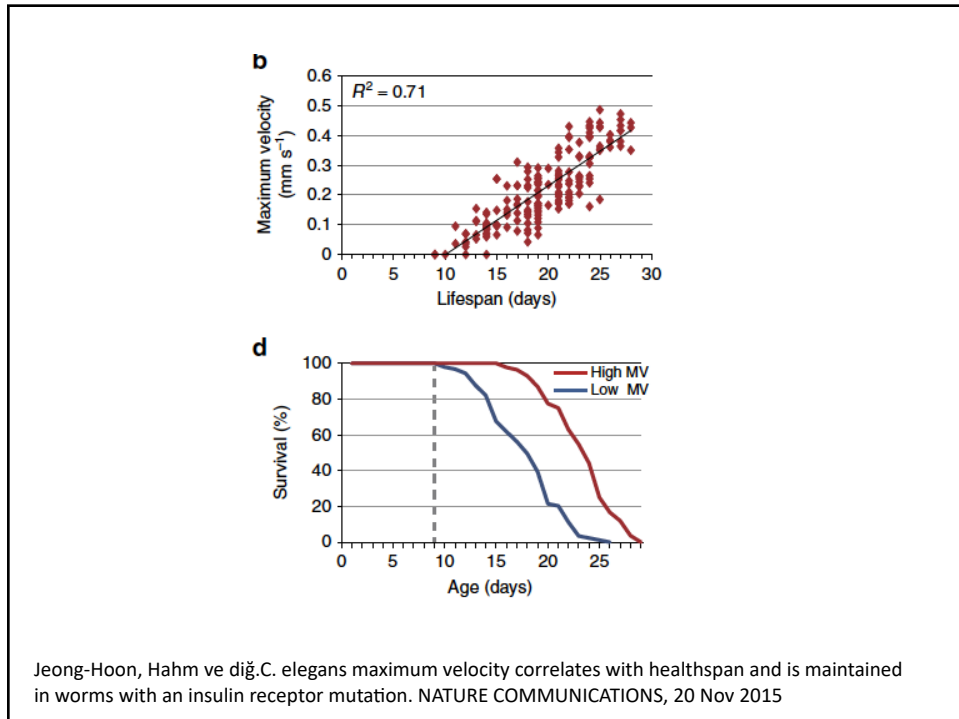
1



2



3



4

## Azrail ne kadar hızlı yürür?

- 1705 Avusturalyalı erkek, yaş  $\geq 70$
- 6 metre yürüme hızı
- 5 yıllık mortalite
- $< 3$  km/saat ölüme daha yakın  $\geq 5$  km/saat yürüyen erkekler hayatta kalmayı başardılar

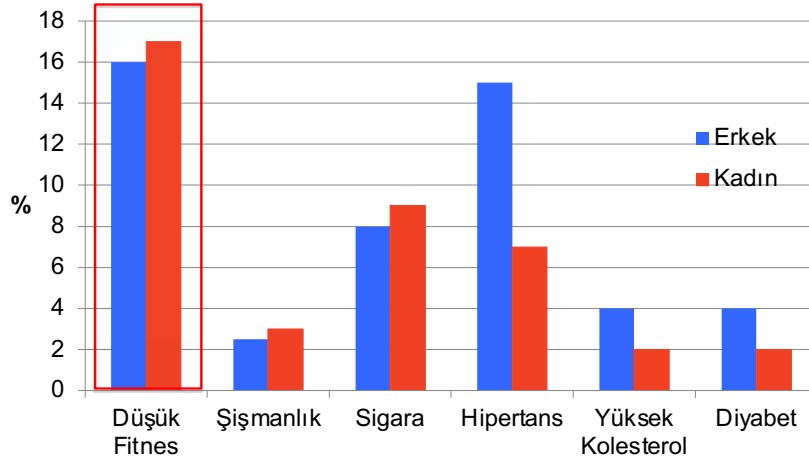


**Azrailin maksimum yürüme hızı 5km/saatin altında! Hızlı yürüyebilmek ölümden korur!**

BMJ 2011;343:d7679 doi: 10.1136/bmj.d7679 (Published 15 December 2011)

5

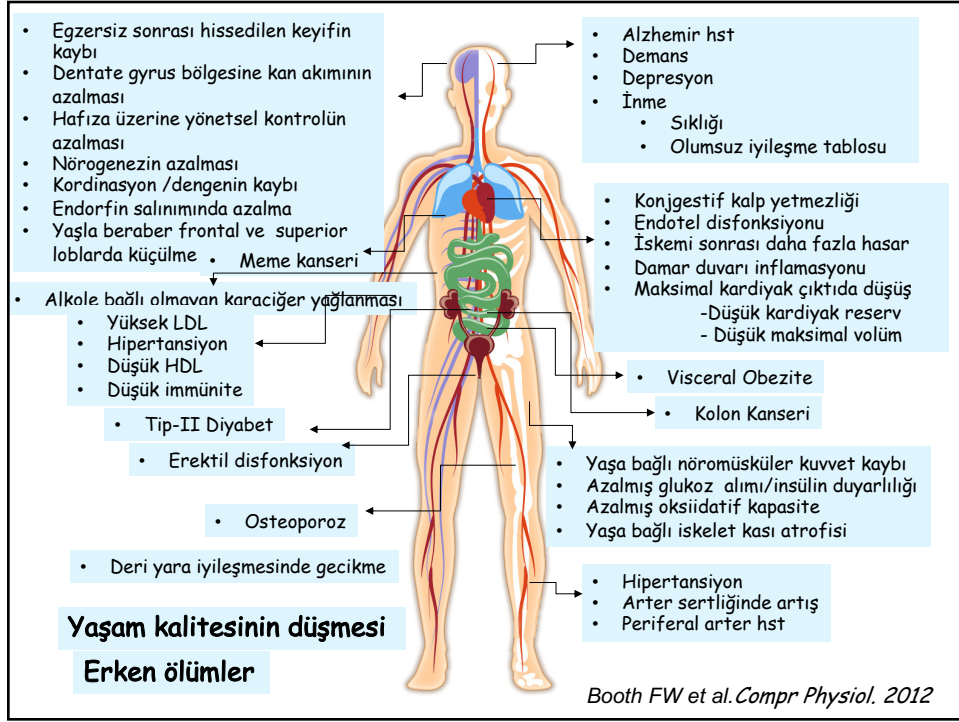
## Kardiyorespiratuar Fitnes ve Mortalite



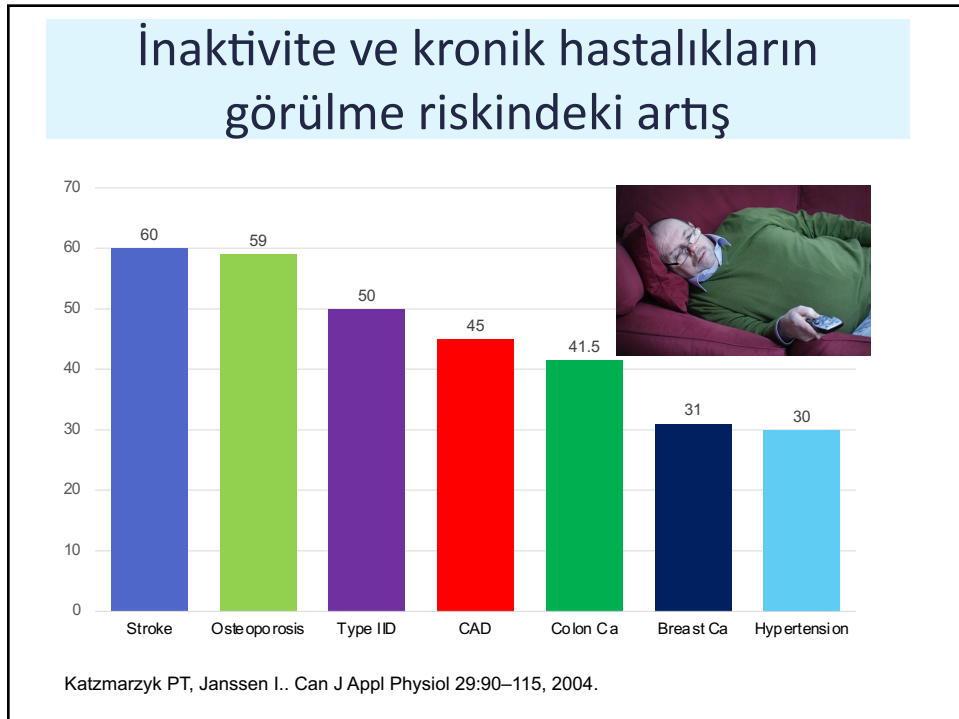
Cooper Institute Aerobics Center Longitudinal Çalışması: 40,842 erkek ve 12,943 kadın

(Blair S.N., Br J Sports Med., 2009)

6

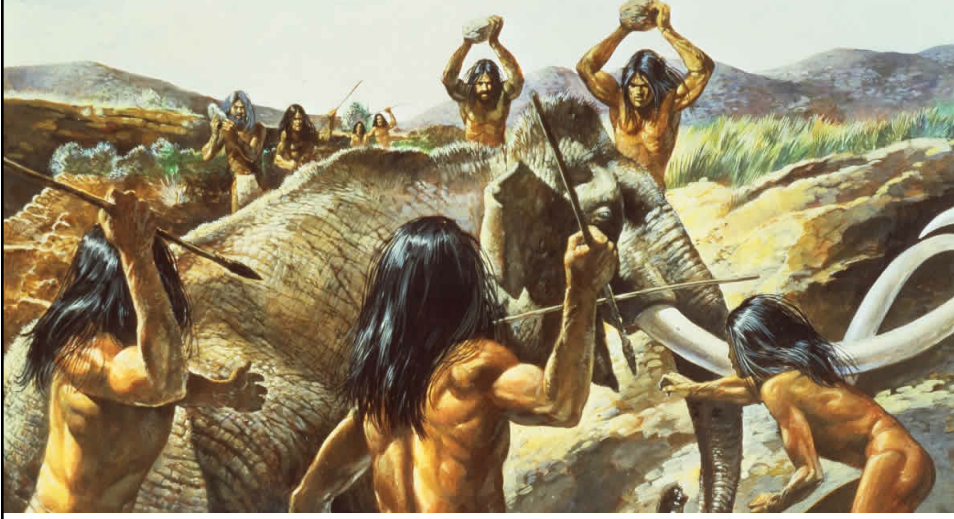


7



8

Hareketli bir yaşama programlandık !



Avcı-toplayıcı toplum: 84.000 kuşak (2.5 milyon yıl)

9

Hareketli bir yaşama programlandık !



10

## Avcı toplayıcı toplum



84.000 kuşak

11

## Aktarılan genler!



12

5  
Australopithecus afarensis

4  
Homo habilis

3  
Homo erectus

2  
klassischer Neanderthaler

1  
moderner Homo sapiens

vor 1 Million Jahren

**E1** Im Gegensatz zu den frühen Hominiden könnte der **Homo erectus** bereits über Ansätze eines Sprachapparats verfügt haben, mit dem er Grundlaute besser modulieren konnte als seine Vorfahren. Der Homo erectus benutzte keilartige Werkzeuge, was ein bestimmtes Maß an abstrakter Denkfähigkeit voraussetzte. Seitdem dürfte die Herausbildung von Lauten und ersten Wörtern einer Protosprache begonnen haben.

**E2** Nachdem der moderne Homo sapiens vor rund 150 000 trat, vollzog sich eine regelrechte kulturelle Revolution: Er feierte und Knochen, stellte Schmuck her und malte. Ob diese geistige Leistung oder Folge der Sprachfähigkeit waren, ist noch unklar. Sapiens bereits eine komplette Sprache mit Wörtern und Grammatik, die er vor etwa 50 000 Jahren von Afrika aus in Europa brachte.

Genlerimiz taş devrinden kalma peki ya alışkanlıklarımız?

Eaton, Konner and Shostak, 1988

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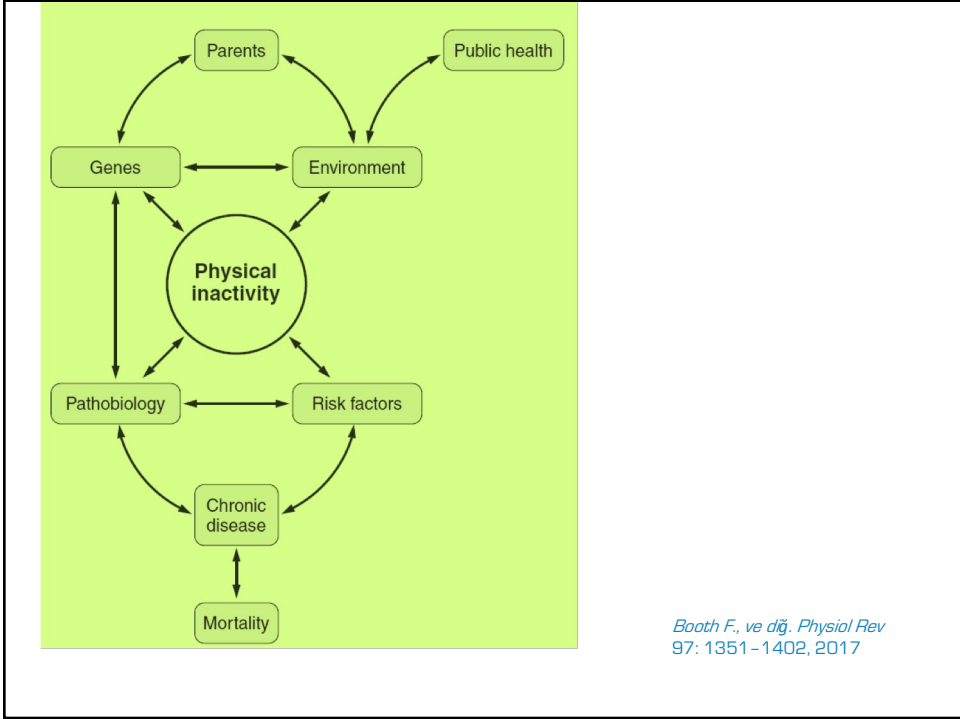
## Endüstri Devrimi

Son yedi kuşak

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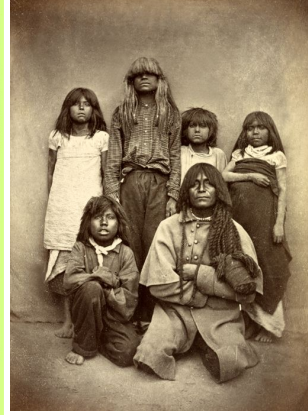
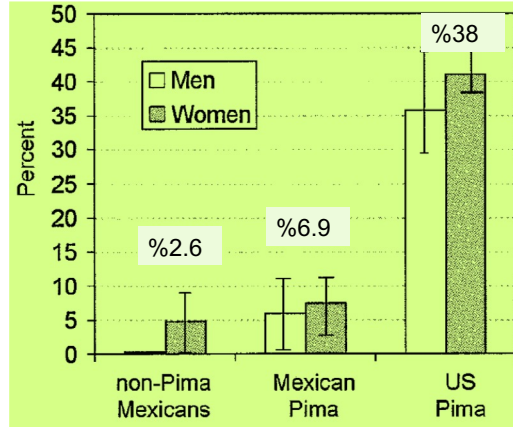


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## Amerikalı ve Meksikalı Pima yerlilerinde T2D

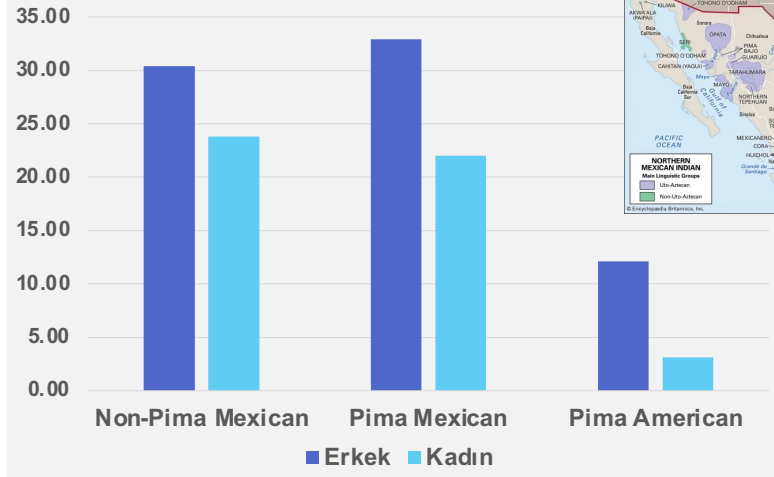
Yaşa göre düzeltilmiş diyabet prevalansı



Schulz, L.O. ve diğ. Diabetes Care 29:1866–1871, 2006

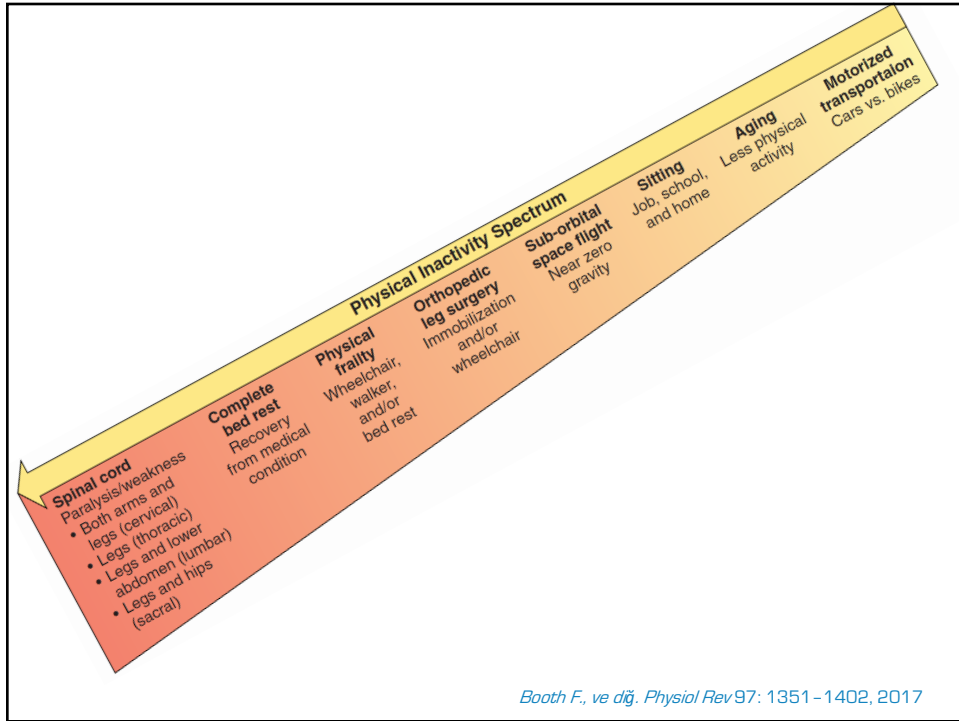
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## Fiziksel aktivite düzeyi



Schulz, L.O. ve diğ. Diabetes Care 29:1866–1871, 2006

18



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### İnsanda inaktivite/azalmış kullanım/immobilizasyon modelleri

The diagram illustrates four models of inactivity and immobilization in humans:

- Computer Work:** A person sitting at a desk in a cubicle, working on a computer, representing sedentary behavior.
- Space Flight:** Astronauts in a microgravity environment, representing a state of near-zero gravity.
- Leg Immobilization:** A person's leg is shown in a cast and immobilized, representing orthopedic leg surgery.
- Medical Examination:** A person lying on a table during a medical examination, representing complete bed rest.

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## Hayvanda azalmış kullanım, kullanmama veya inaktivite modelleri

- Kuyruktan asma
- Ekstremitte immobilizasyonu
- Mekanik ventilasyon
- Spinal kord kesisi
- Tenotomi
- Denervasyon



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## Fiziksel Aktivite Yoksunluğu: Dallas yatak istirahati çalışması, 1966



Fotograf : UT Southwestern Kütüphanesi

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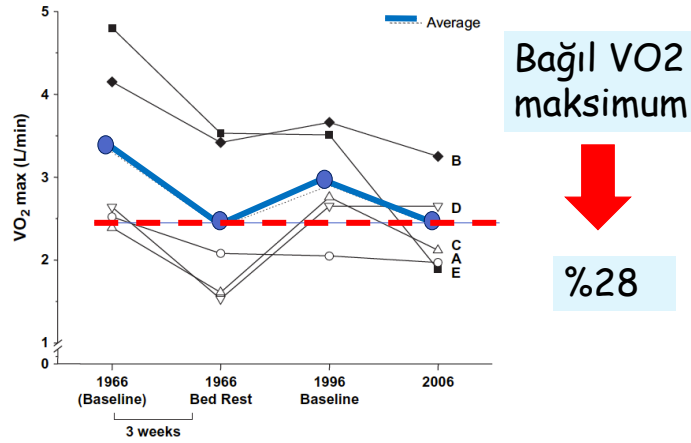
## Dallas yatak istirahati çalışmasının 30. (1996) ve 40.yıl (2006) takibi



Photo: UT Southwestern Library

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## Dallas Yatak İstirahati Çalışması



Saltin et al, 1968 Circulation in McGavock et al. Journal of Gerontology, 2009  
McGuire et al. Circulation. 2001

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## Bir hafta yatak istirahati

- Pik VO<sub>2</sub> %6.4±2.3
- Yağsız kütle 1.4±0.2 kg
- Quadriceps EKA %3.2±0.9
- 1RM %6.9±1.4
- Tüm vücut insülin duyarlılığı %29±5



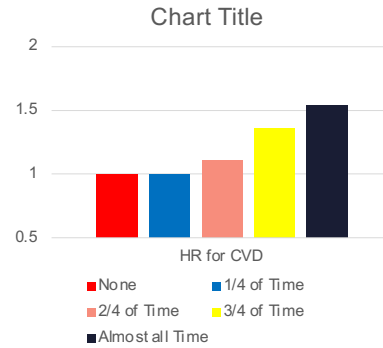
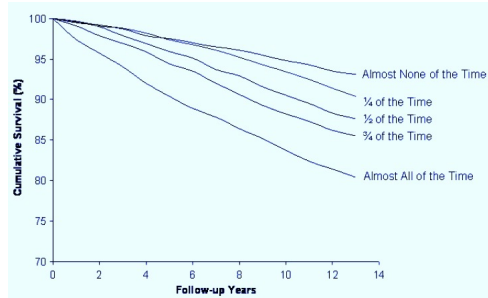
Fotograf: Avrupa Uzay Ajansı

Dirks ML et al. Diabetes. 2016

25

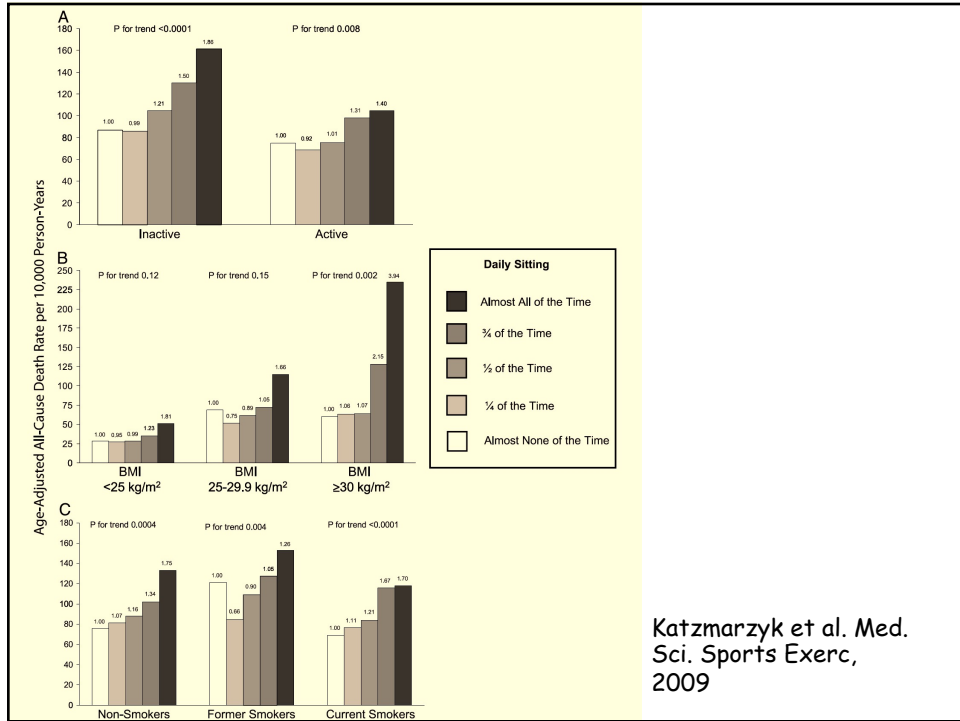
## Oturma süresi ve KVH ve diğer nedenlerle ölüm ilişkisi

18-90yr n=17,013 Total 1832 deaths (759 CVD and 547 Ca)

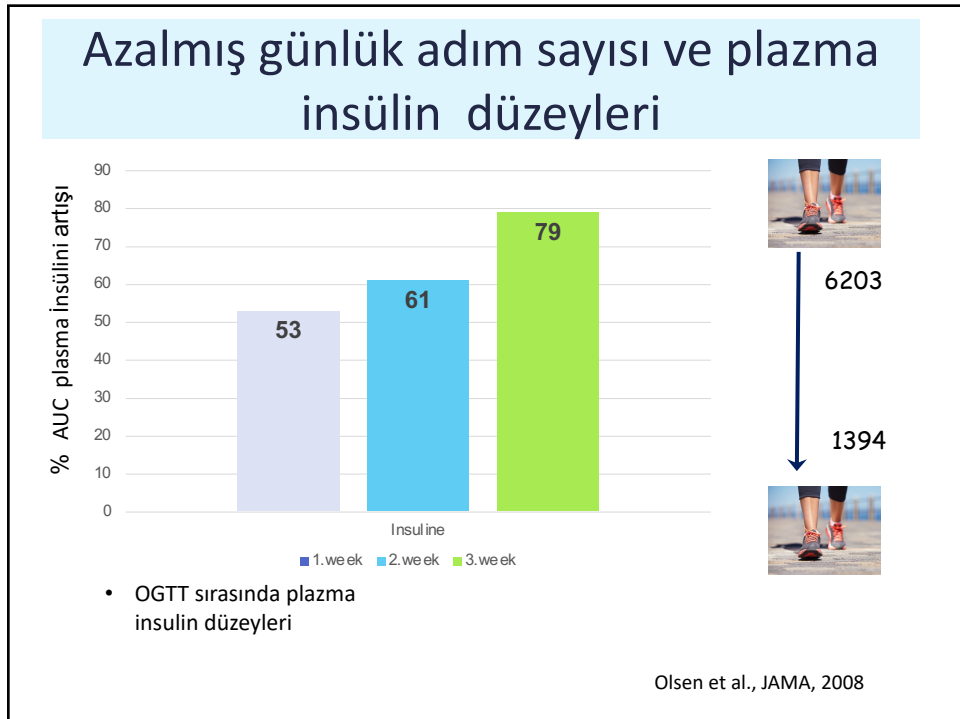


Katzmarzyk et al. Med. Sci. Sports Exerc, 2009

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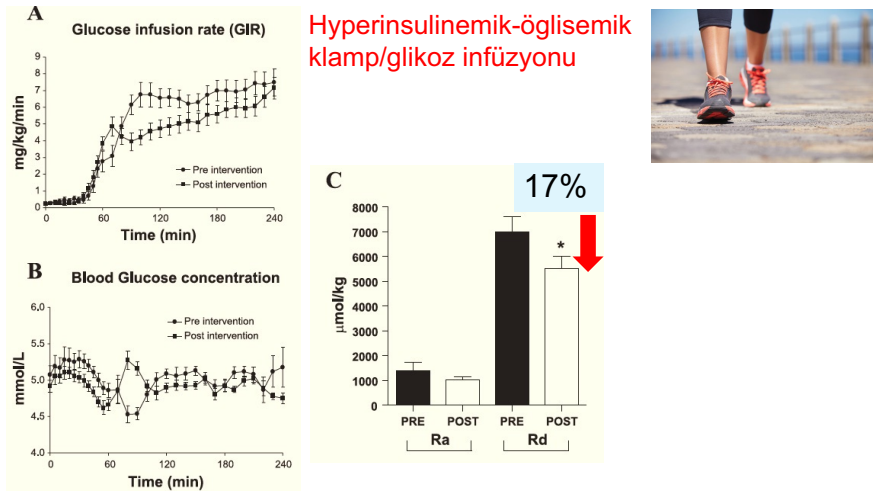
## Günlük adım sayısında 2 haftalık azalma



Krogh-Madse et al. J Appl Physiol 108: 1034-1040, 2010.

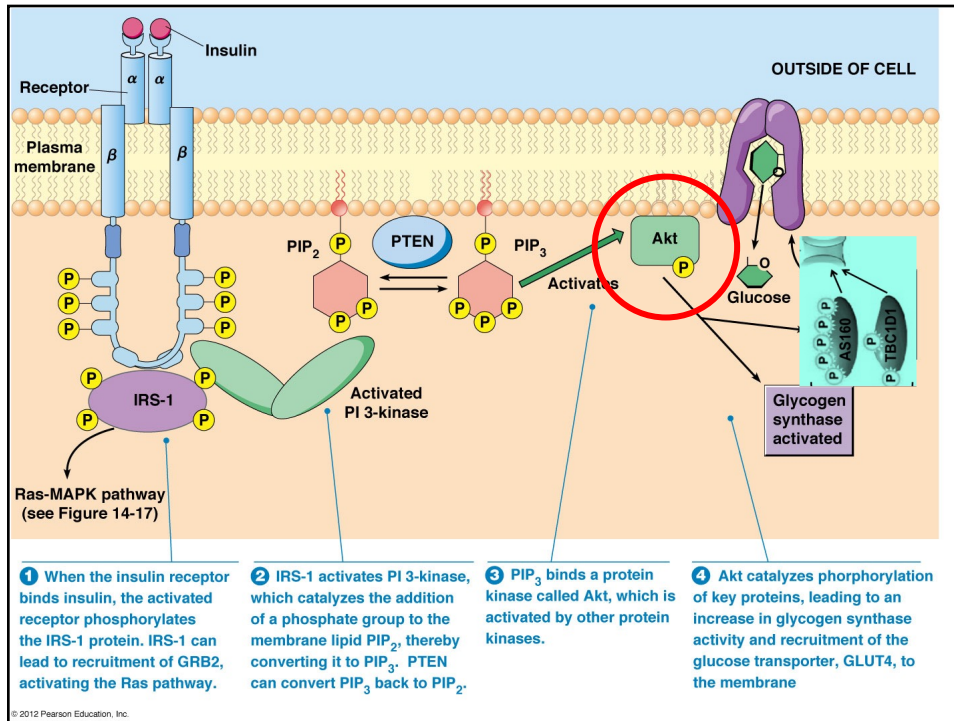
29

## Günlük adım sayısında 2 haftalık azalma: Periferel insülin duyarlılığında azalma

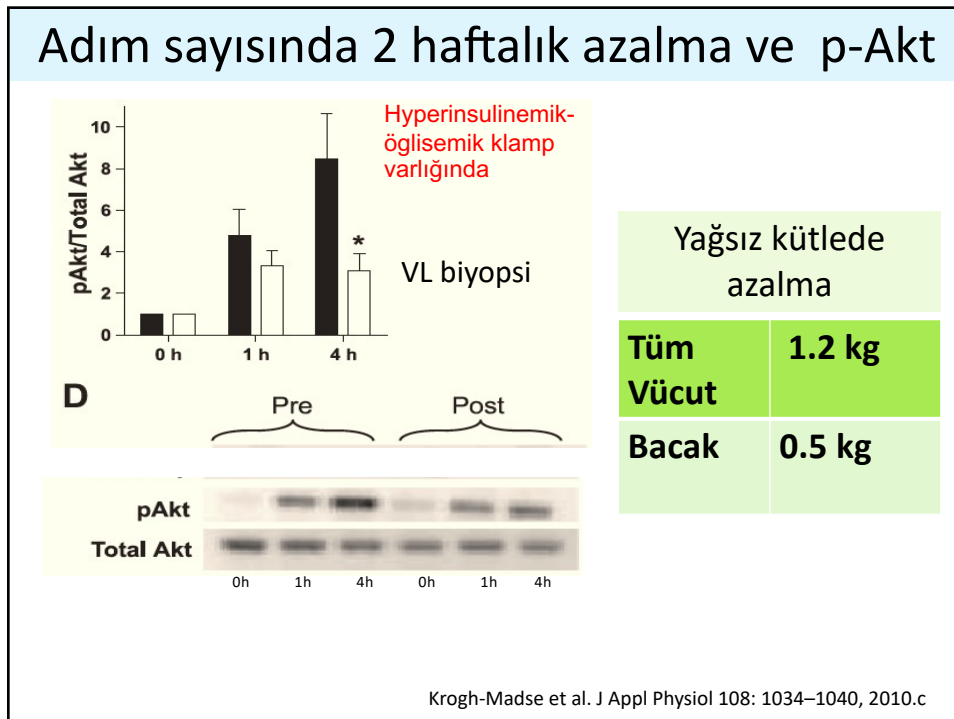


Krogh-Madse et al. J Appl Physiol 108: 1034-1040, 2010.

30



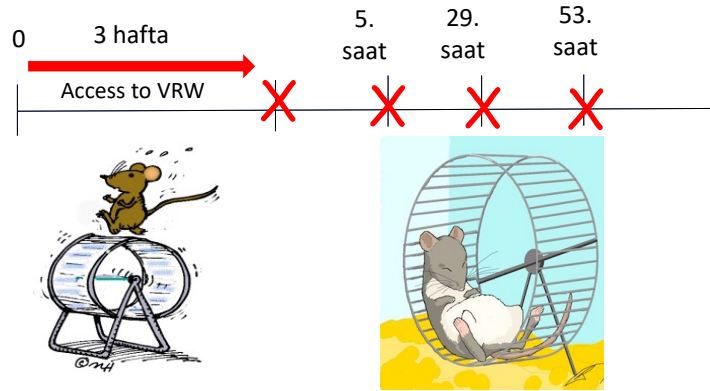
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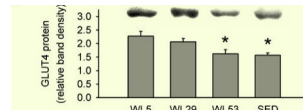
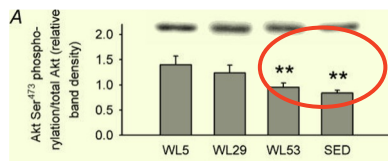
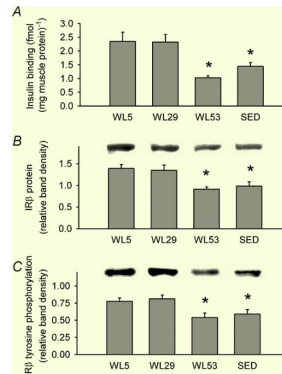
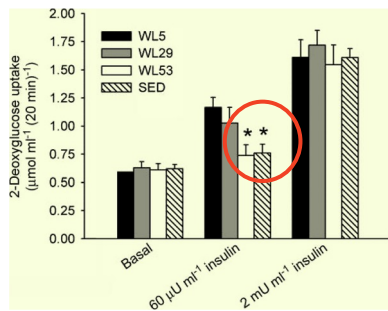


## Gönüllü egzersizin kesilmesi ile sıçanda insulin reseptör sinyalindeki değişiklikler



Kump D ve Booth FW J Physiol. 2005 February 1;562(Pt 3):829-838

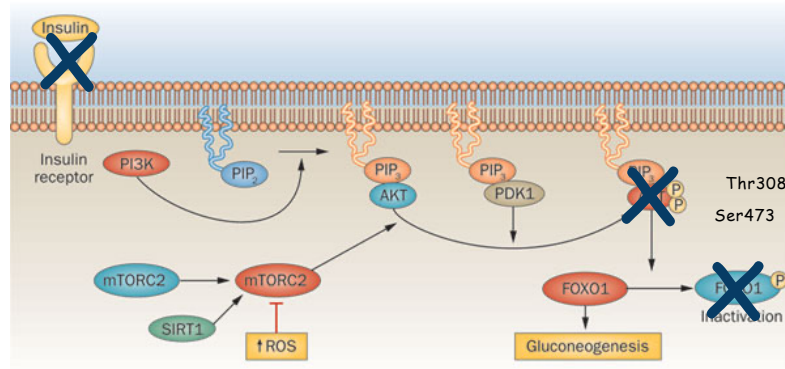
33



Kump D ve Booth FW J Physiol. 2005 February 1;562(Pt 3):829-838

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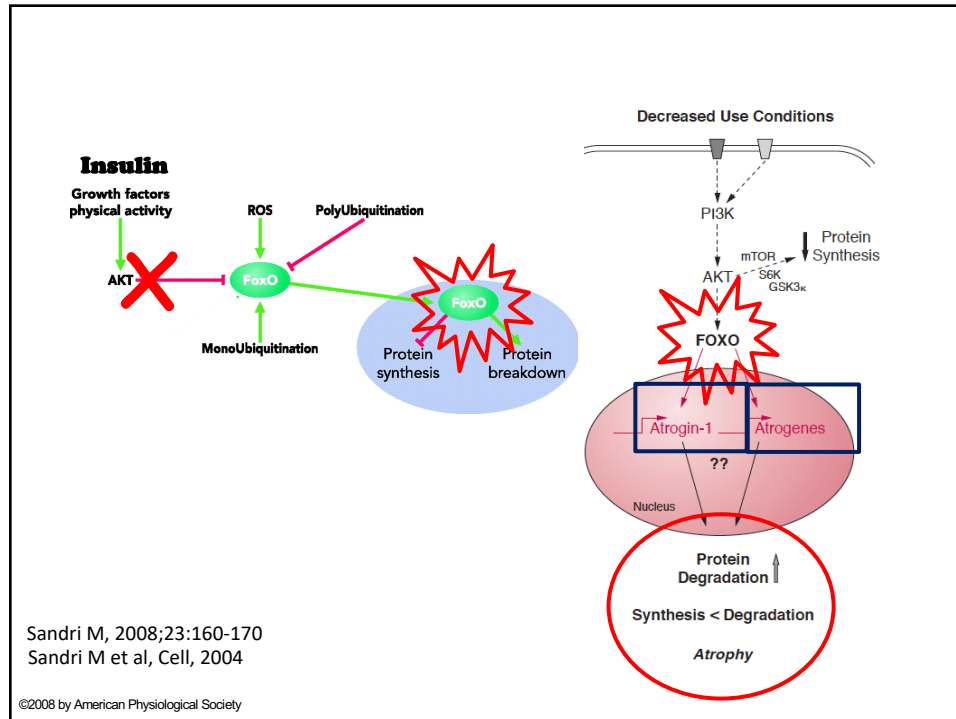
**Figure 1** The complex mTORC2 suppresses gluconeogenesis by phosphorylating and activating AKT



Horio, Y. (2011) Insulin signal meets SIRT1 at AKT  
*Nat. Rev. Endocrinol.* doi:10.1038/nrendo.2011.208

nature  
 REVIEWS ENDOCRINOLOGY

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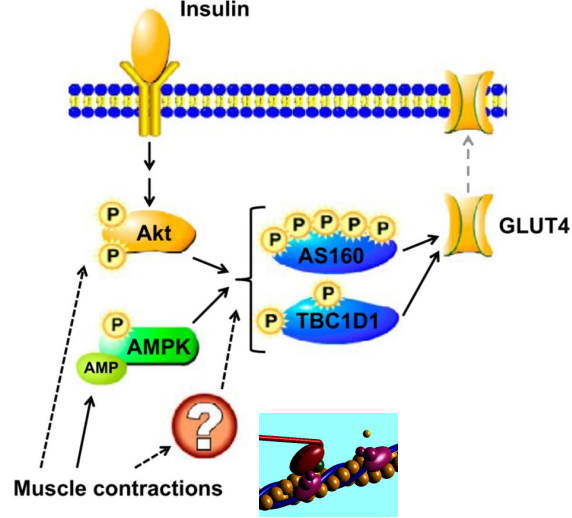


Sandri M, 2008;23:160-170  
 Sandri M et al, Cell, 2004

©2008 by American Physiological Society

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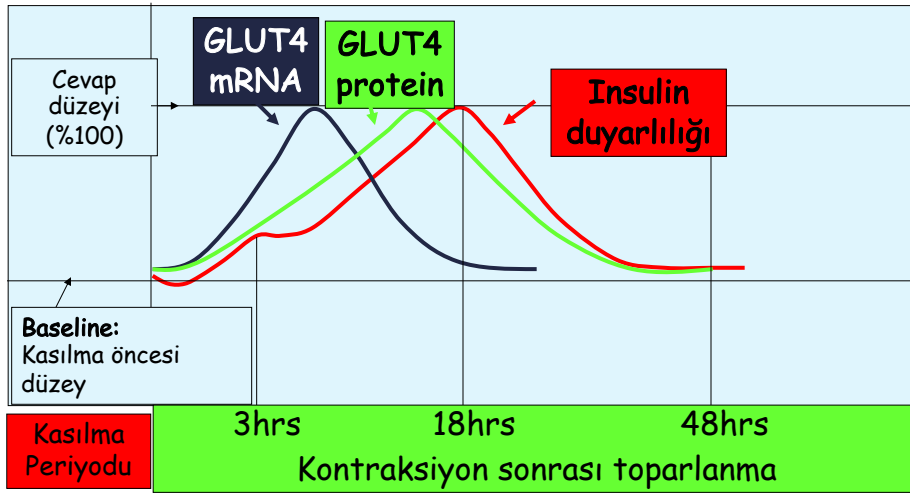
## AMPK fosforilasyonu ve insülin direnci



Vendelbo ve diğ. J Appl Physiol, 2014

37

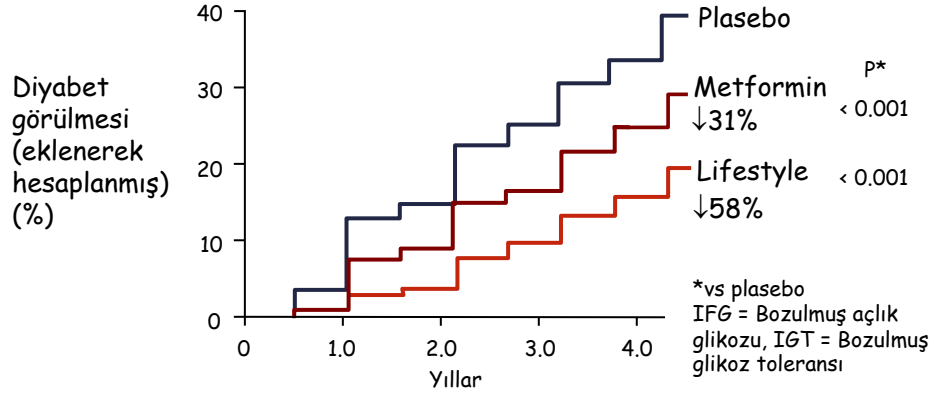
## Kas kontraksiyonu ve GLUT4 ekspresyonu



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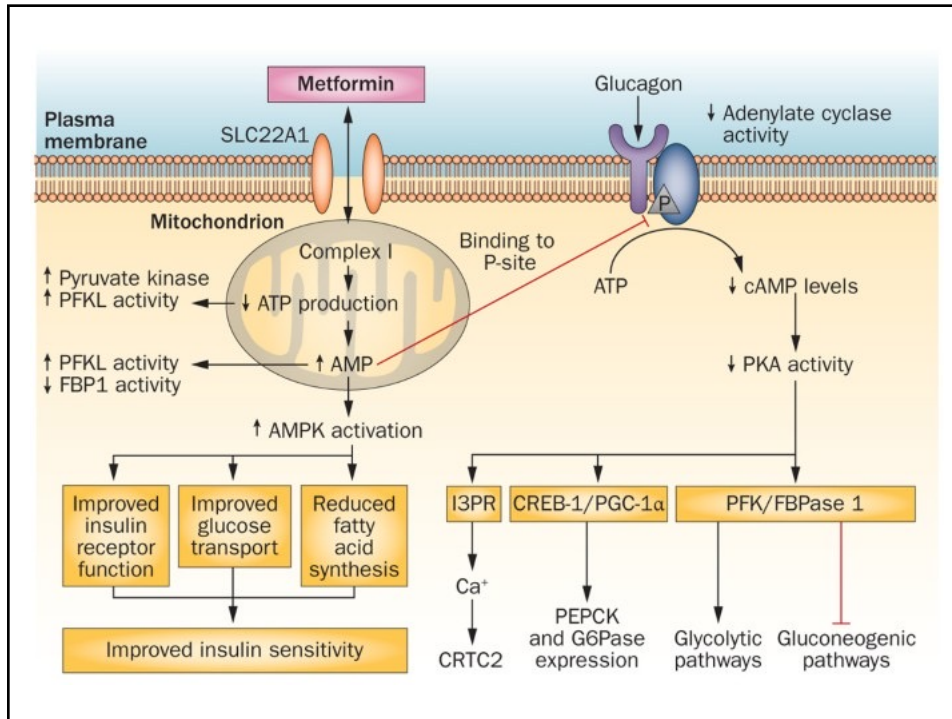
## Amerikan diyabet önleme çalışması

- Egzersiz ve diyet veya Metforminin etkisi,
- N = 3234, Artmış açlık ve yükleme sonrası glikozu pozitif, diyabet yok ( $\leq 125$  mg), ~ 2.8 yıl (1.8-4.6) takip



Diabetes Prevention Program (DPP) Research Group. *N Engl J Med* 2002;346:393-403.

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# TIME

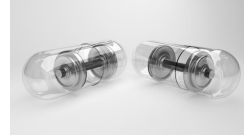


## Exercise Pills May Be In Your Future!

October 12, 2015 | By Mandy Oaklander, Time.com

### The Washington Times

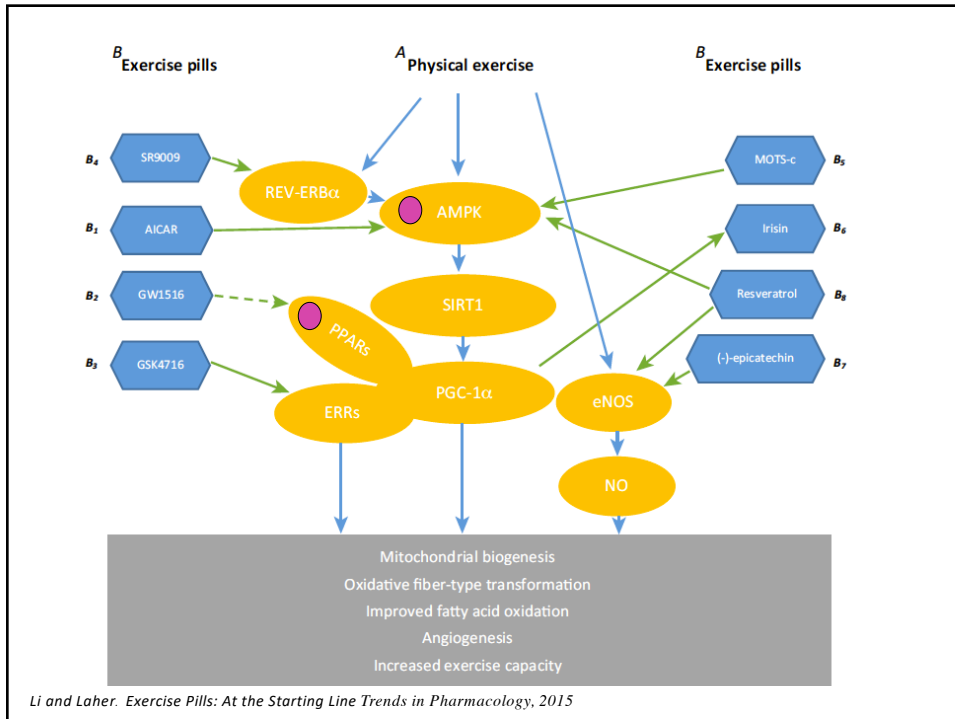
MONDAY, SEPTEMBER 21, 2009 \*\*



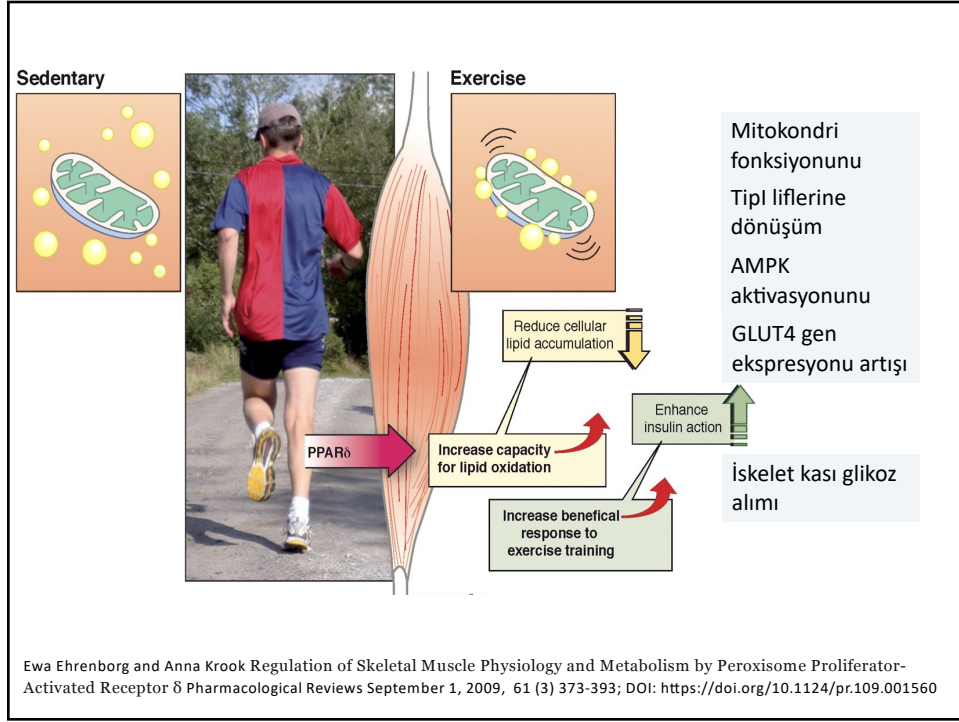
## 'Exercise in a bottle,' scientists working on pill that mimics effects of working out

<http://www.smithsonianmag.com/innovation/scientists-are-working-pill-just-might-replace-exercise-180956910/#ZSc8pO7BWFWDuYh1.99>

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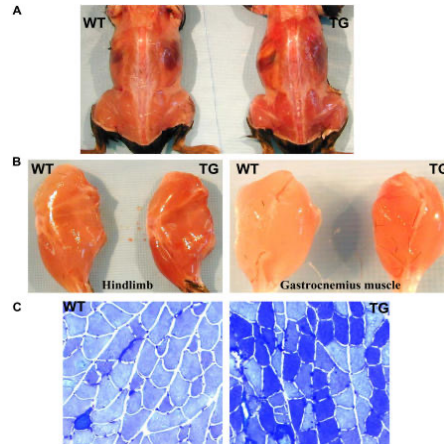
42



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## Maratoncu Fare: PPAR $\delta$ , mitokondri biyogenzinde ana regülatör

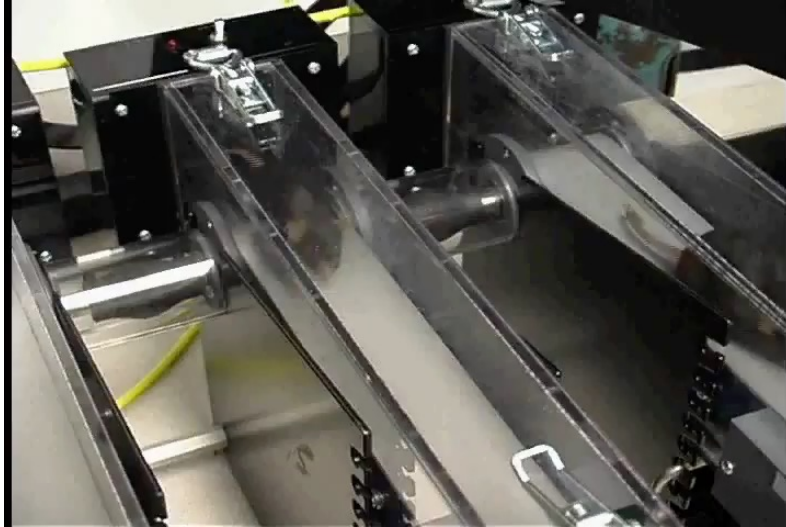
- Yağ metabolizmasını hızlandırıyor
- Tipli kas lifi miktarı 2 katına çıkmış
- Fare normal fareden %92 daha uzun koşmuş



Wang et al. 2004. Regulation of Muscle Fiber Type and Running Endurance by PPAR $\delta$ . Public Library of Science. August 24, 2004

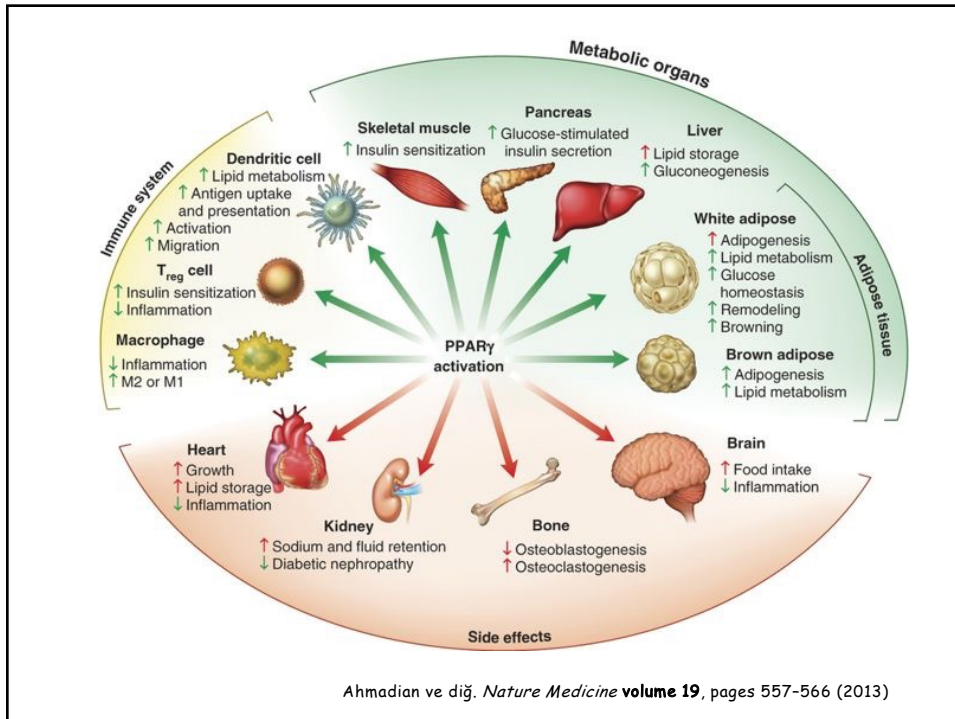
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# GW501516: PPAR $\delta$



Narkar et al. Cell. 2008

45

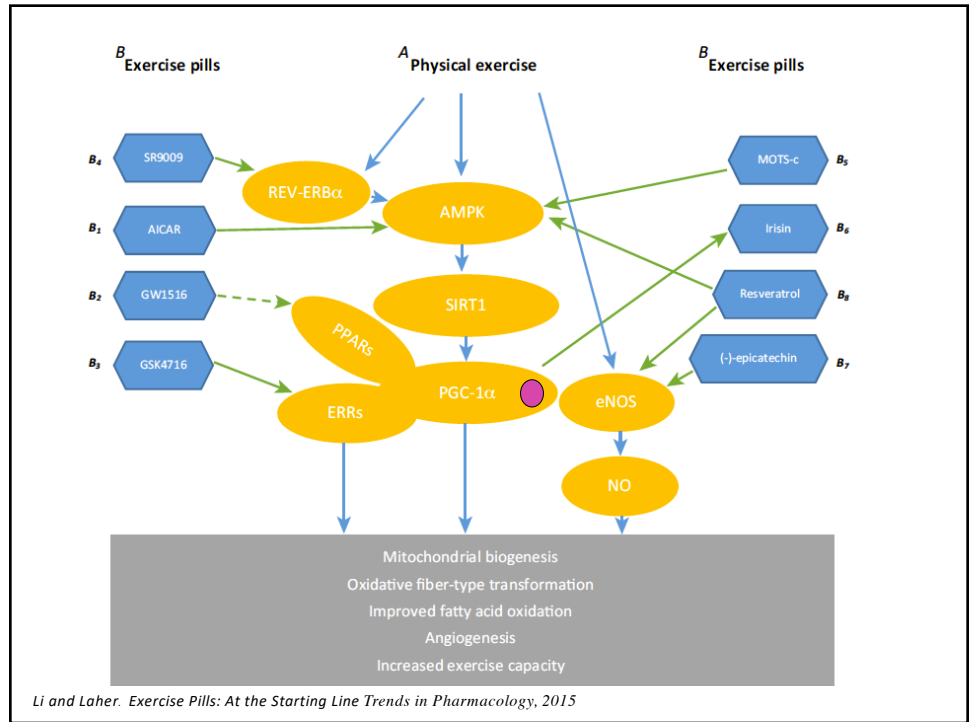


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# AMPK and PPAR $\delta$ Agonists Are Exercise Mimetics

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

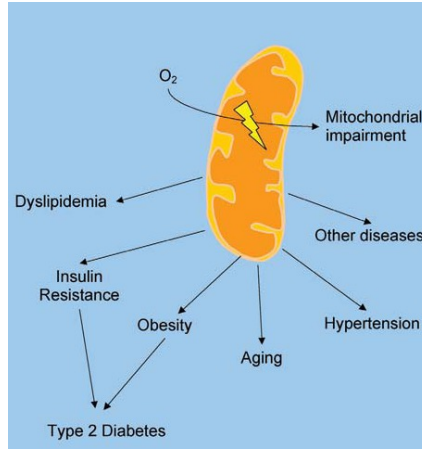
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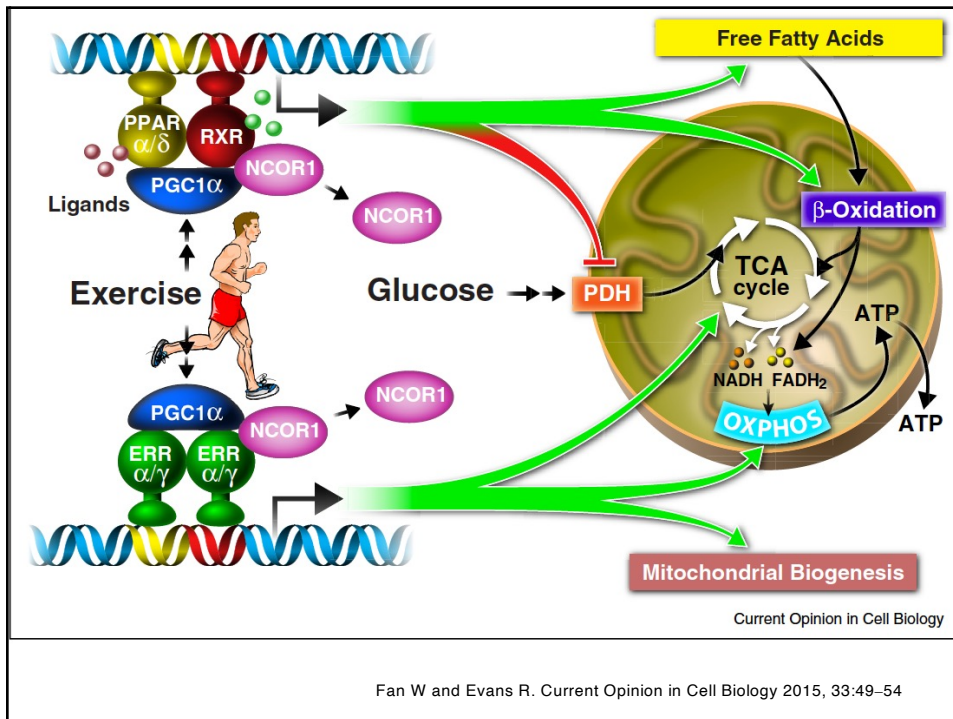


# İnaktivite mitokondri fonksiyonunu bozar!



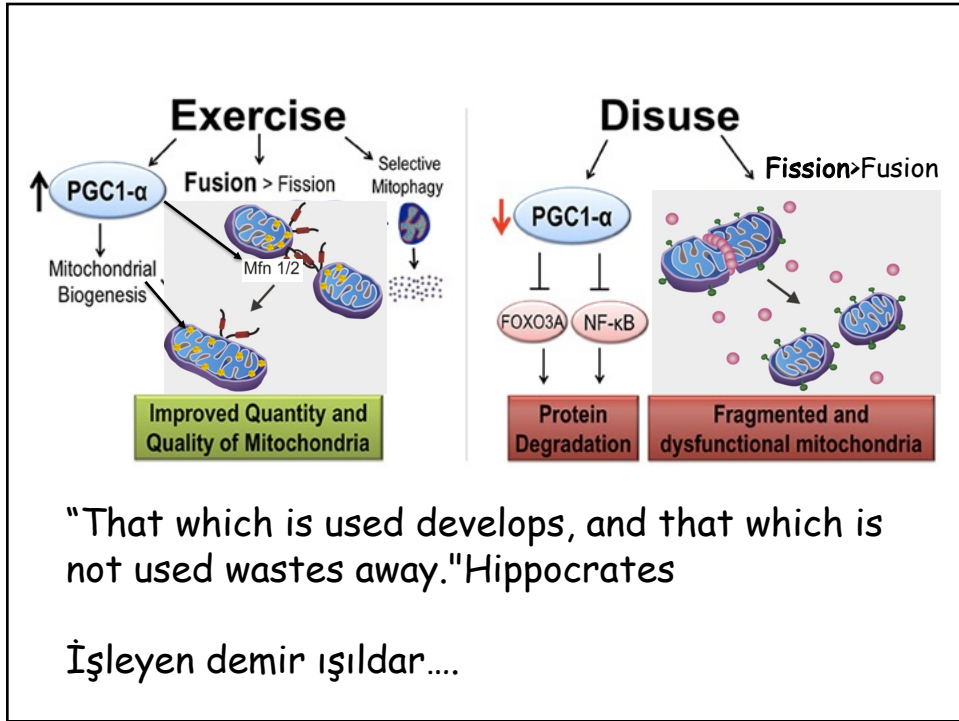
Michele Guescini, Laura Stocchi, Chiara Di Loreto, Cristina Fatone, Pierpaolo De Feo and Vilberto Stocchi. Molecular Modifications Induced by Physical Exercise: A Significant Role in Disease Prevention In: V. Stocchi (ed), *Role of Physical Exercise in Preventing Disease and Improving the Quality of Life* Springer 2007

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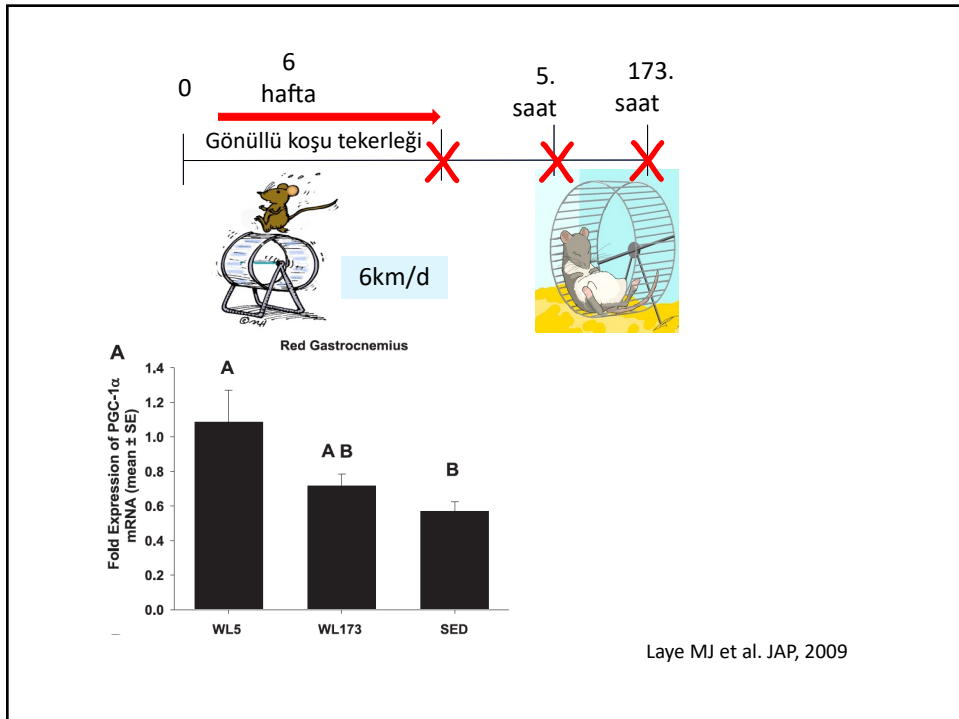


Fan W and Evans R. *Current Opinion in Cell Biology* 2015, 33:49–54

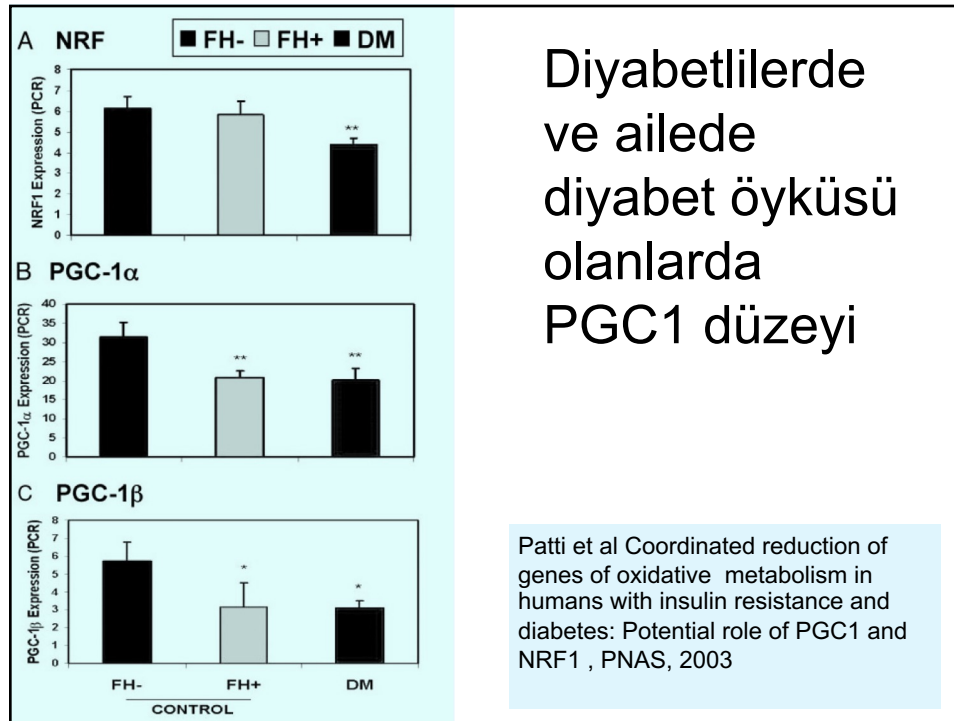
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**TO THE EDITOR: Hot-tub therapy for type 2 diabetes mellitus. 1999 Sep 16;341(12):924-5. Philip L. Hooper, M.D. McKee Medical Center, Loveland, CO 80537**

**Yaş:** 43 -68 years

**Ağırlık:**  $X \pm SD$  ] =104.7  $\pm$  53.2 kg

**Su Sıcaklığı:** 37.8°C - 41.0°C

**Sıcak Uygulama süresi:**

30dk/gün; 6gün/hf; 3 hf

**Oral sıcaklık:** 0.8C artıyor

**Plazma açlık glukoz**

182  $\pm$  37/dl den 159  $\pm$  42 mg/dl  
(P=0.02)

**HbA1C**

% 11.3  $\pm$  3.1 den 10.3  $\pm$  2.6  
(P=0.004)

**Vücut ağırlığı azalışı**

1.7  $\pm$  2.7 kg (P=0.02)

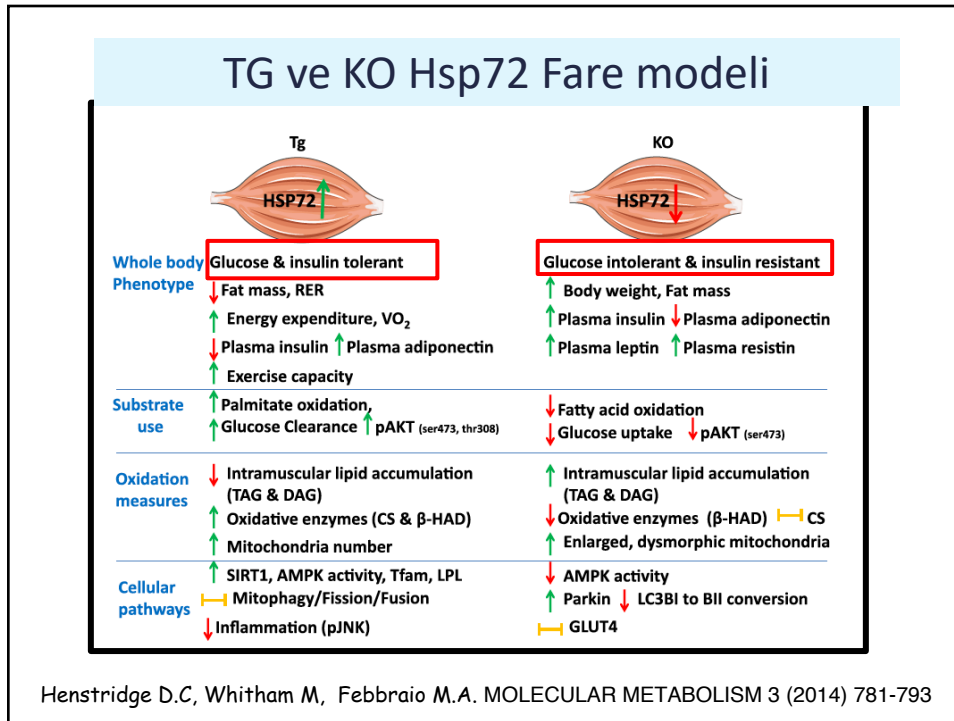
**TABLE 1. CHARACTERISTICS OF THE EIGHT PATIENTS AND RESULTS OF THREE WEEKS OF EXPOSURE TO A HOT TUB.**

AGE	SEX	DURATION OF DIABETES	MEDICATIONS	BODY WEIGHT (BEFORE/ AFTER EXPOSURE)	FASTING PLASMA GLUCOSE (BEFORE/ AFTER EXPOSURE)*	GLYCO-SYLATED HEMOGLOBIN (BEFORE/ AFTER EXPOSURE)†
yr		yr		kg	mg/dl	%
43	M	14	Glyburide, metformin hydrochloride	83.2/80.9	190/186	13.6/12.7
50	M	13	Glyburide, troglitazone, insulin	201.8/199.1	109/66	8.6/7.7
51	M	9	Glyburide, metformin hydrochloride, insulin	175.0/168.2	231/181	12.2/11.1
54	F	9	Metformin hydrochloride, insulin	60.9/61.8	207/156	17.4/14.8
57	F	8	Glipizide, metformin hydrochloride	64.5/64.5	197/155	11.0/11.1
57	M	3	Glyburide, troglitazone	75.0/73.6	165/162	8.6/7.6
63	M	11	Glipizide, metformin hydrochloride	91.8/91.8	158/160	9.1/8.1
68	F	9	Glyburide, metformin hydrochloride, troglitazone	85.5/84.1	197/203	9.5/8.9

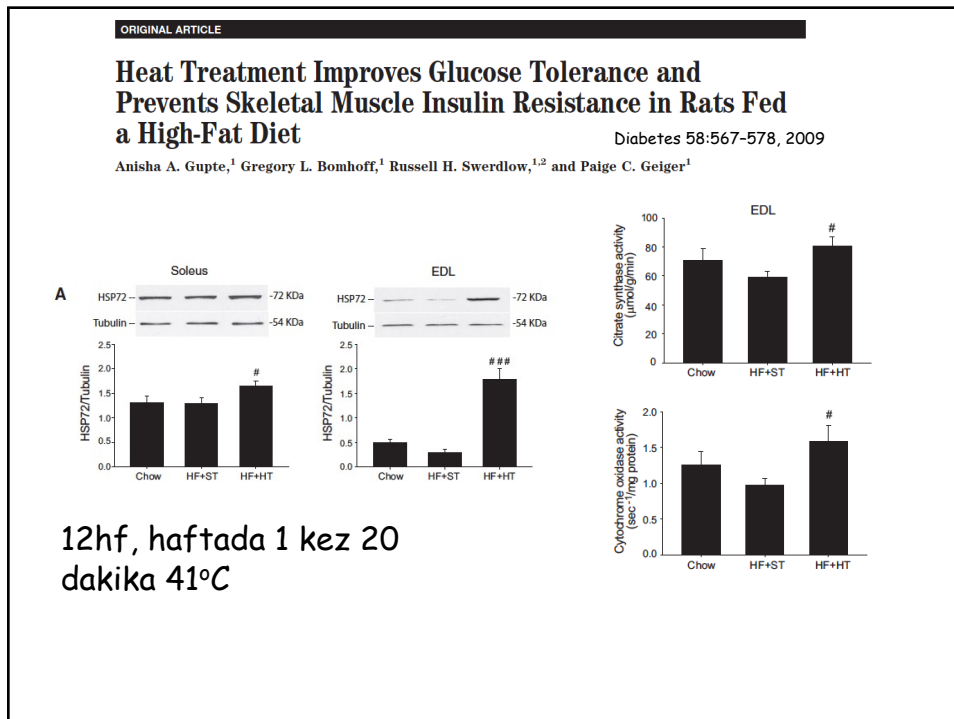
\*To convert the values to millimoles per liter, multiply by 0.05551.

†The normal range was 4 to 8 percent.

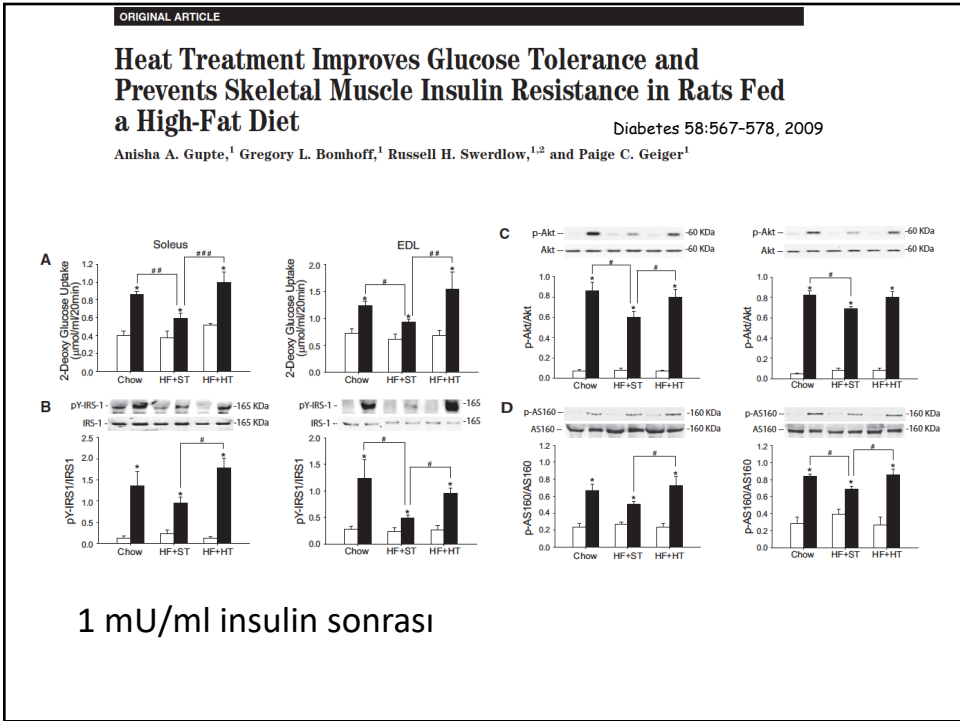
54



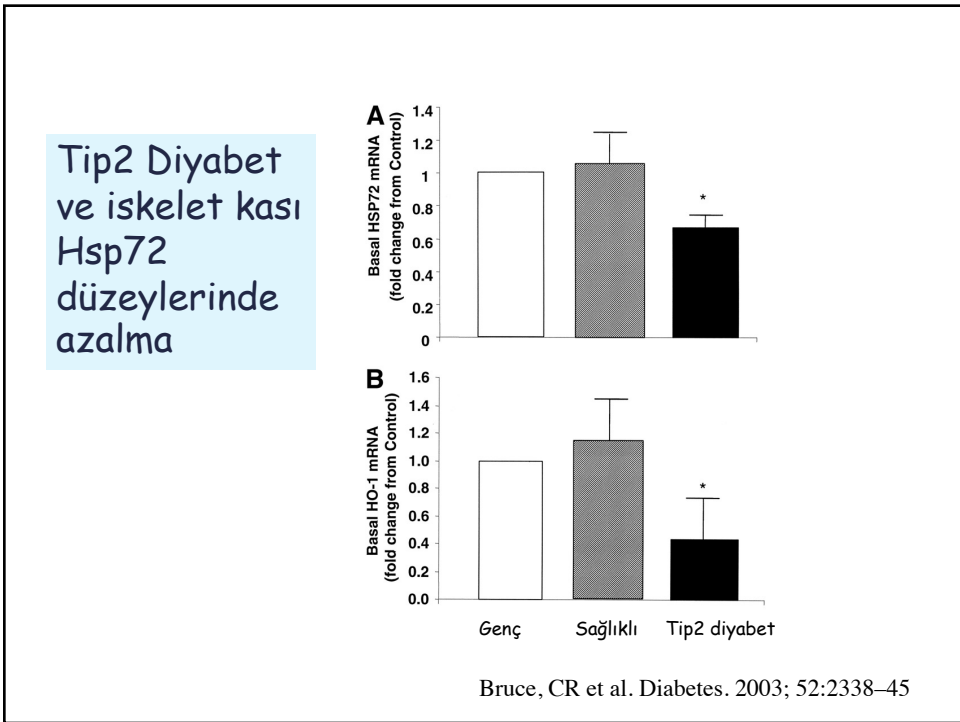
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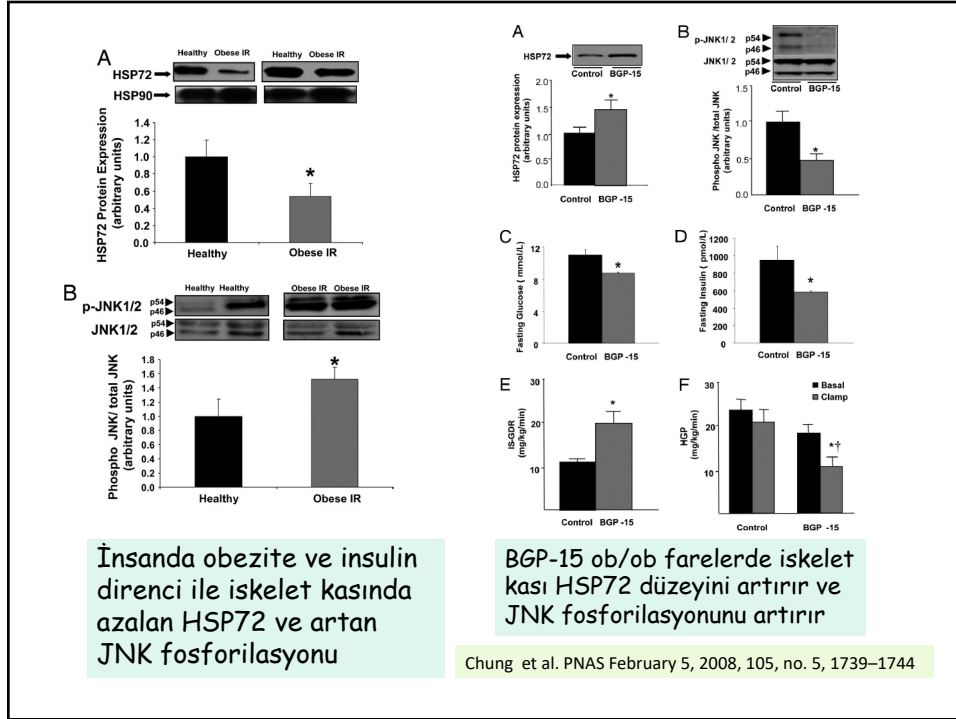
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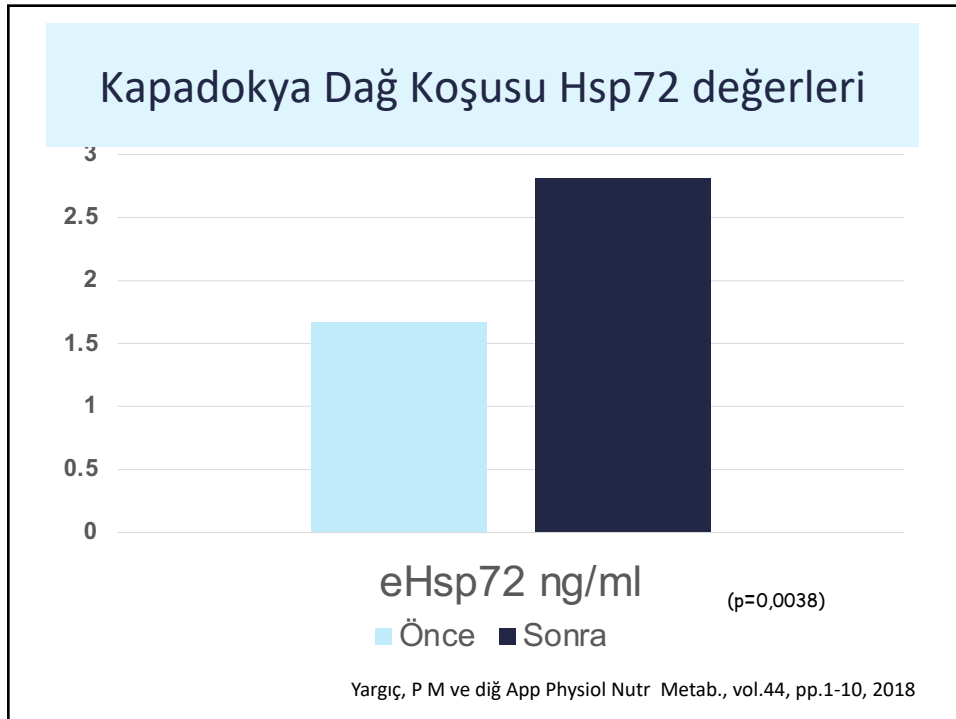
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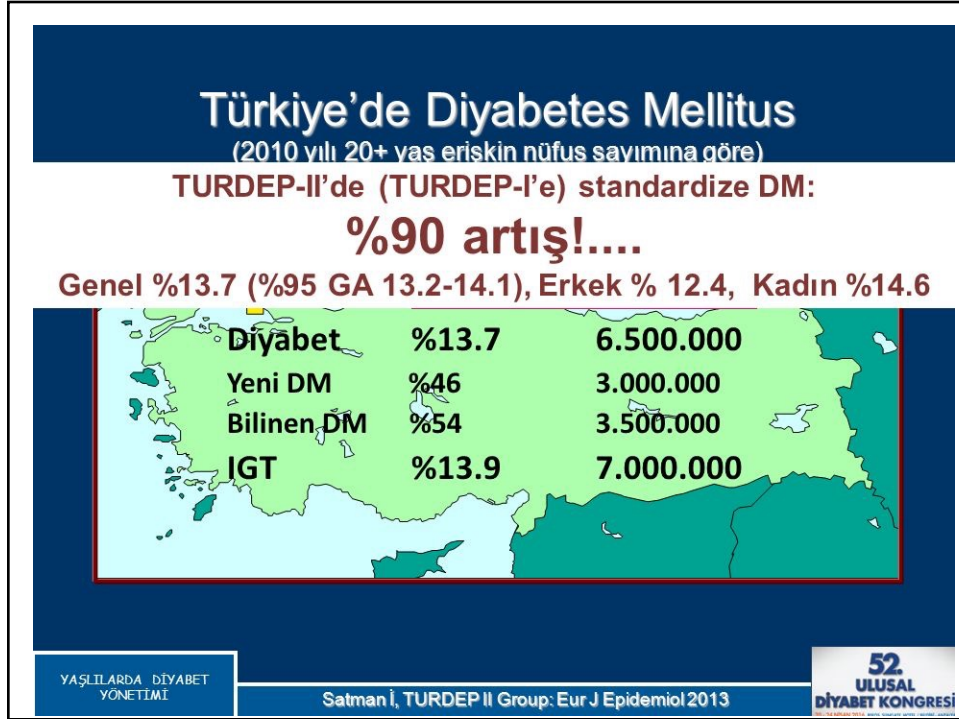
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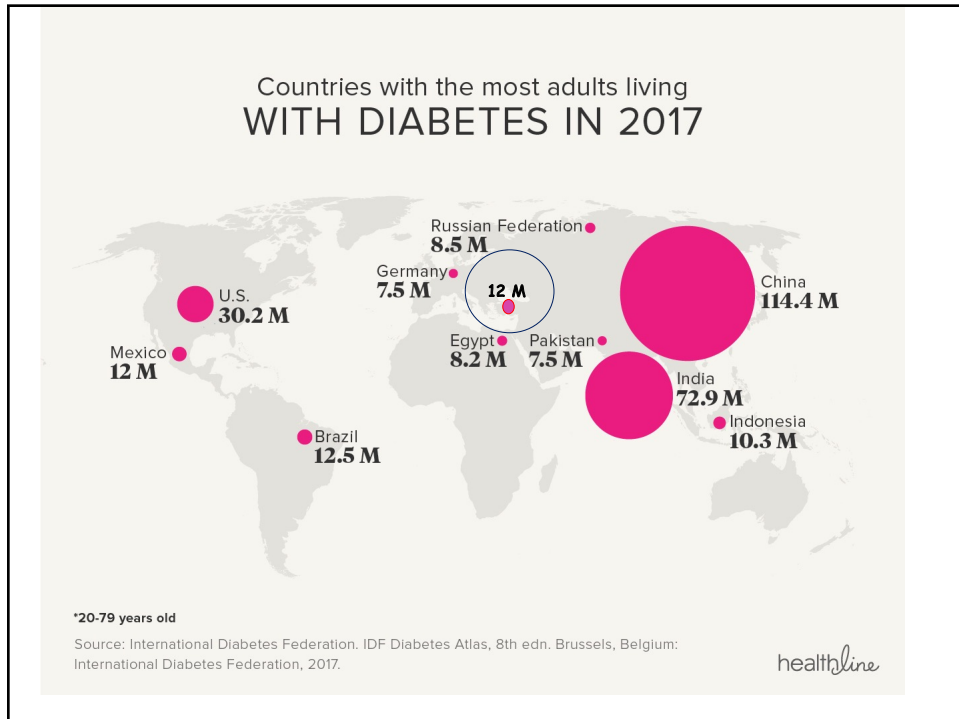
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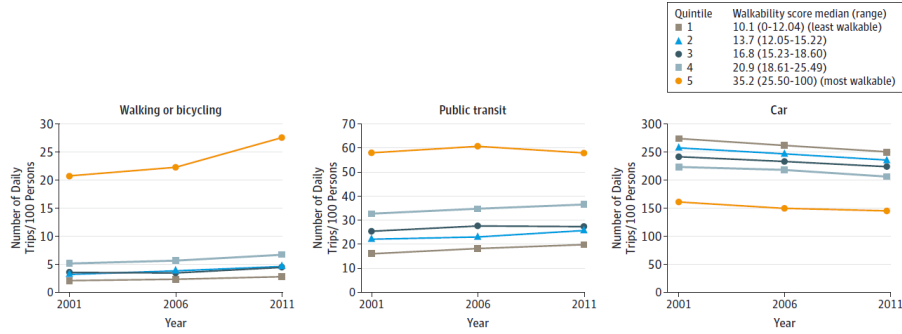


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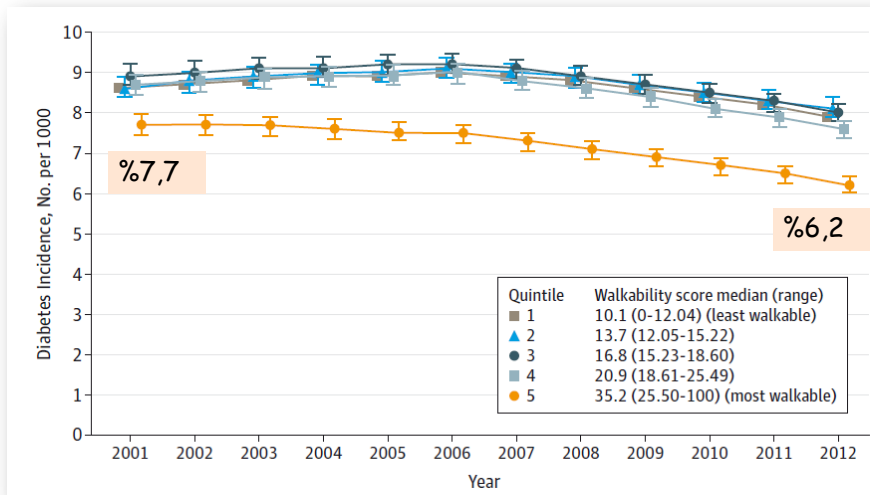
## 12 yıl takip: yürünebilirlik be aktif ulaşım



Creatore M,I ve diğ. JAMA. 2016;315(20):2211-2220. doi:10.1001/jama.2016.5898

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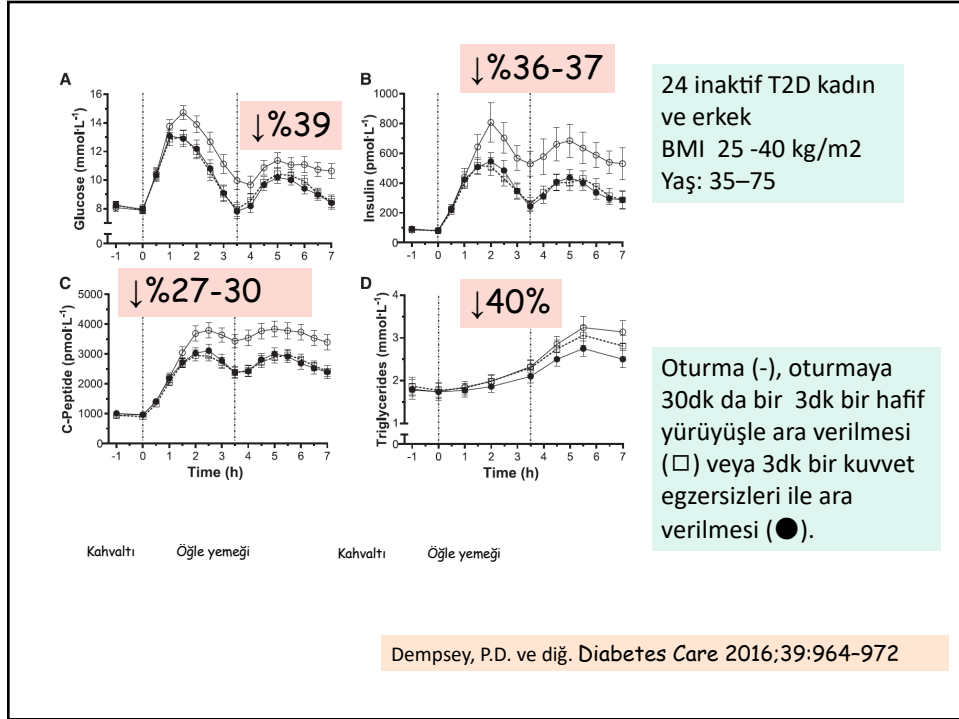
## 12 yıl, yürünebilirlik ve diyabet



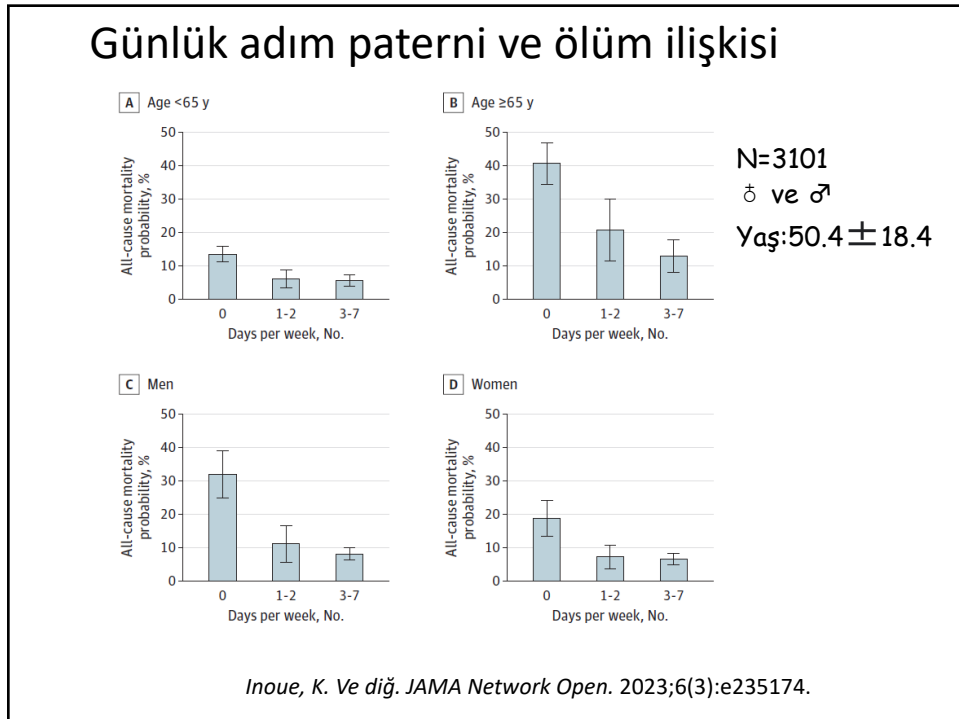
Creatore M,I ve diğ. JAMA. 2016;315(20):2211-2220. doi:10.1001/jama.2016.5898

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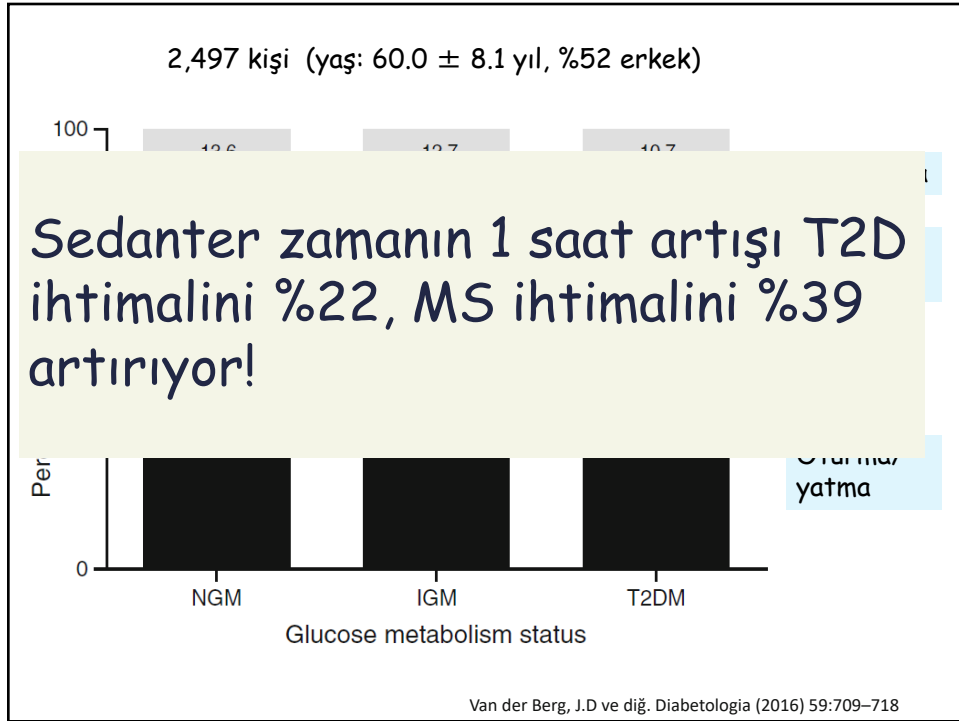




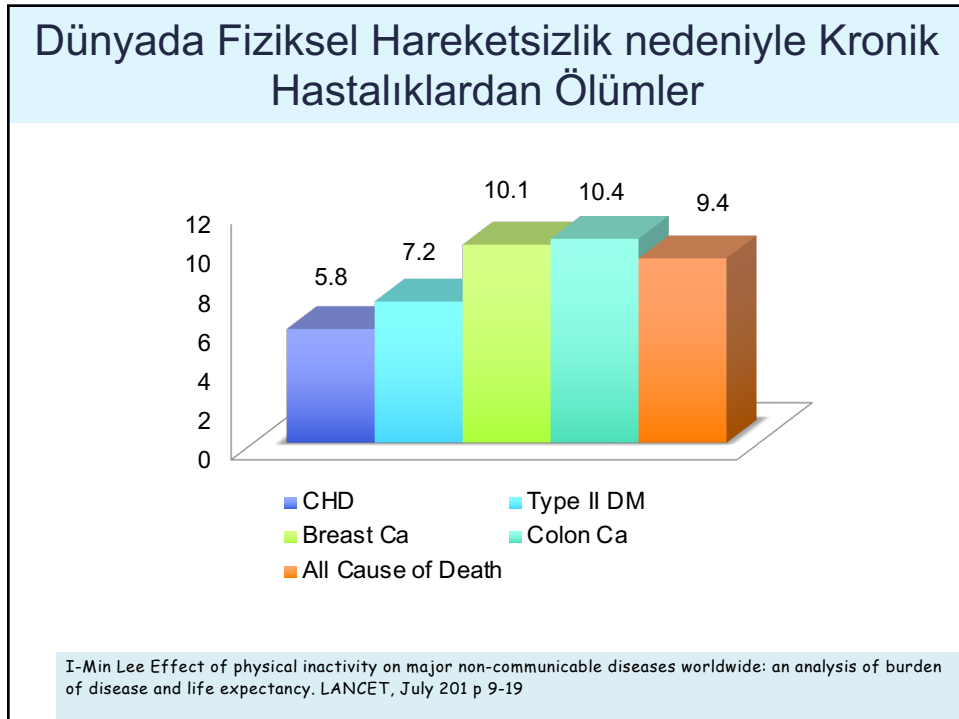
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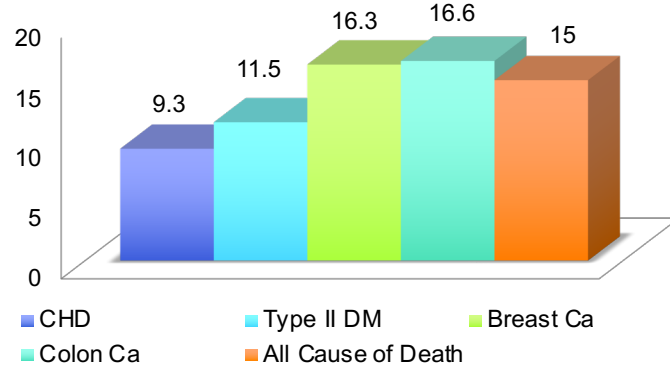


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## Türkiye'de Fiziksel Hareketsizlik nedeniyle Kronik Hastalıklardan Ölümler



*I-Min Lee Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. LANCET, July 201 p 9-19*

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Zamanınız için teşekkür ederim...

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