

How to Live to Be 100

T.W. Wilson, MD, MSc, FRCPC



Objectives

following this presentation the learner will be able to:

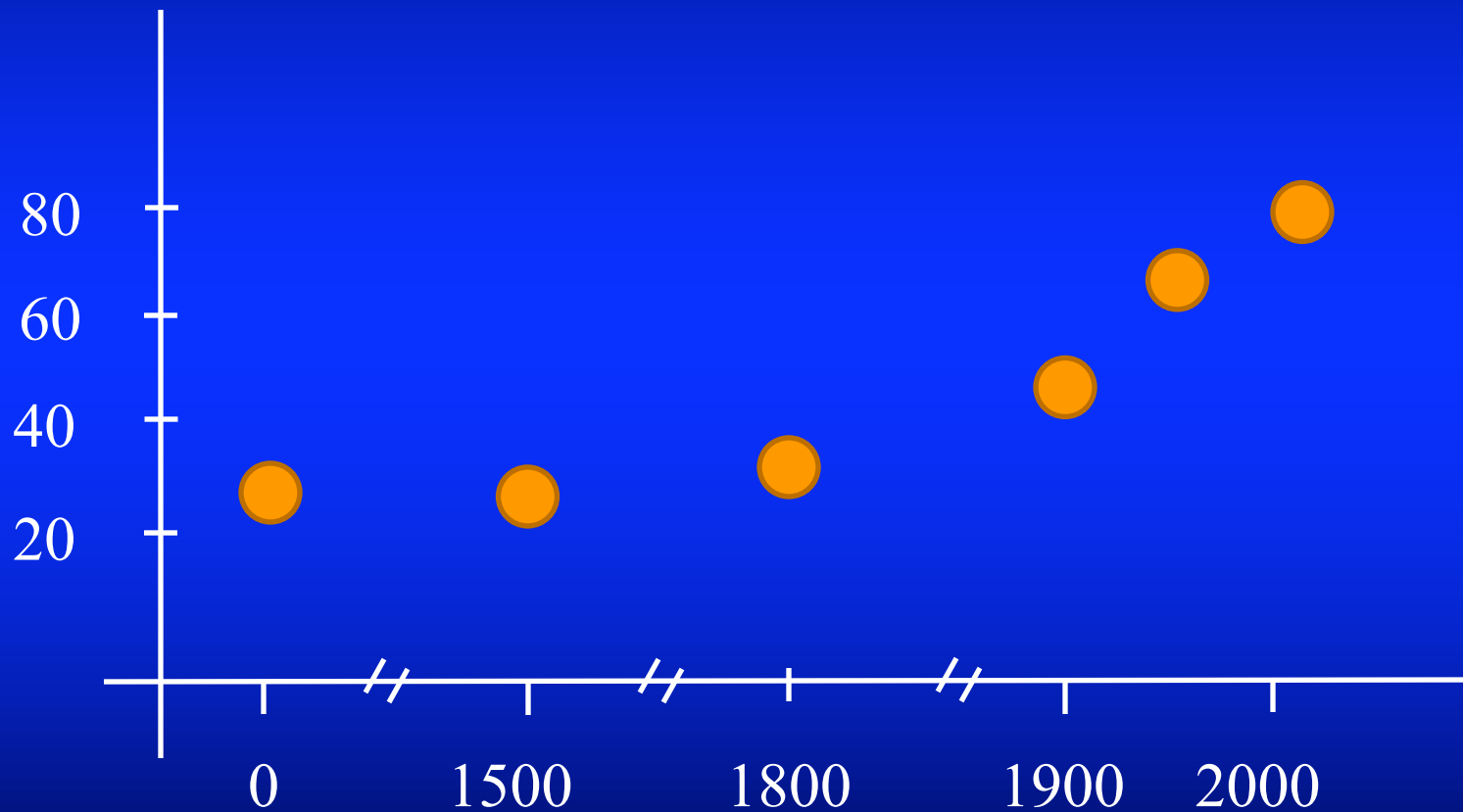
- Appreciate levels of evidence in scientific studies.
- Distinguish between *average* and *maximum* life span.
- Quote the odds of a human being living to 100.
- Quote the relative contributions of genetics and environment on longevity.
- Advise people on diet, vitamin supplementation, exercise and other choices to attain their “rightful” age.

levels of evidence

Quality	What it means	
High	Conclusions will not be changed	“Good” RCT
Moderate	Conclusions could be changed	“bad” RCT; “good” Obs study
Low	Conclusions could be changed	Obs study (cohort, case-control)
Very low	Conclusions likely will be changed	Expert opinion; bad studies

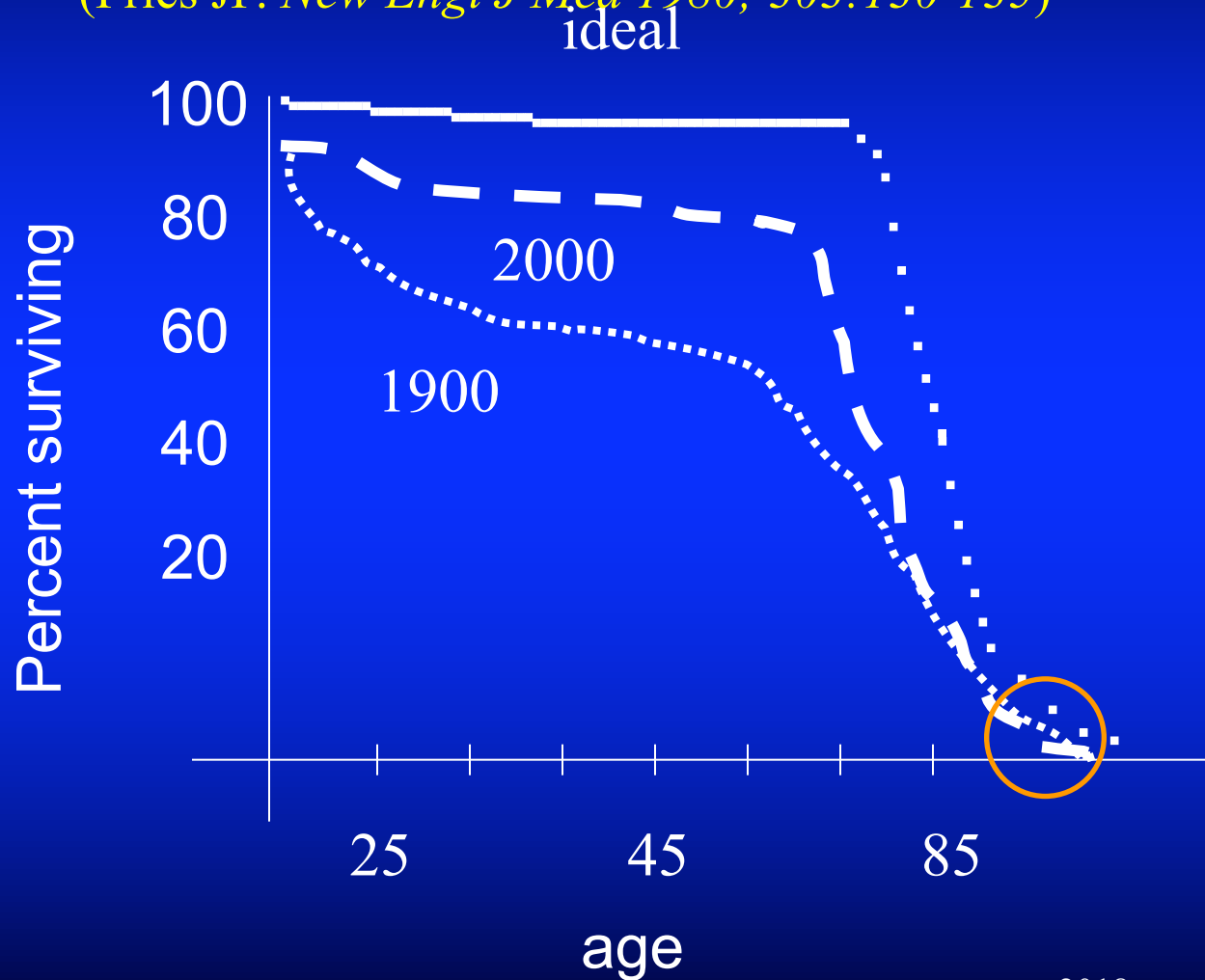
Average Age at Death add line to explain?

<http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/health26-eng.htm>



Maximum Age at Death add line to explain?

(Fries JF. *New Engl J Med* 1980; 303:130-135)



What are the odds of living to 100?

- About 12.5/100000 live births.

Can we increase the odds?



LIVING TO 100 NOW WITHIN SIGHT FOR THOUSANDS OF CANADIANS

Oherström took up computer at the late in life — at the age of 80. Following the death of her husband of 50 years, she moved away from their home in Victoria. Her son, now 60, insisted that she learn how to use one. She already knew how to type (and still remembers how to take short-hand) from her years working as a stenographer and bookkeeper.

"I thought I would be interested — and I was."

Oherström is part of a growing cohort of centenarians that Statistics Canada called at 6,000 in 2011. 84 per

aerobics classes each week in her Vancouver residence. She makes an effort to keep fit and eat right after the earliest decades of her life — as a child of Jewish Russian immigrants in Winnipeg — were spent overweight, unhappy and harbouring suicidal thoughts.

"They say obesity is a disease now, but I say it's an addiction. It's like an alcoholic that can't resist liquor," says the stylish woman with black-rimmed glasses and neatly pulled-back hair. "You've got to fight it. A lot of times I don't feel like go-

ing in on the century mark, it's both unexpected and sought."

"We moved to this apartment when I was 80 and I thought I'd live two more years. I never thought I'd live this long. Quite frankly I often say, 'Look, I'm ready.'"

When it comes to arduous physical work and the value of community, 100-year-old Lillian Gabert tells a tale of being a young wife to a Lutheran pastor near Wetaskiwin, Alta. as the Depression wore on in the '30s. She spent her childhood in and around Edmonton with the

Globe Focus & Books

ANTI-AGING RESEARCH || HOURGLASS FIGURES

First they beat the squares, the war and the patriarchy. Now the baby-boom generation wants to outwit Father Time. Fears of mortality and elder-care burdens are giving science a senior moment as labs investigate how to sustain healthy vigour far into old age. But is cheating frailty and death more than just a dream? Carolyn Abraham reports

The quest for the test tube of youth

Not Thomas Patton was so when he decided that he would not go gently into that good night. He was born in December, 1945, on the eve of the baby boom, and sees it as his bright light not to follow in the orthopedic footsteps of his father's generation — "when you sat in your rocking chair, played checkers, watched TV and then you died."

Mr. Patton, now 69, wants to keep his mind

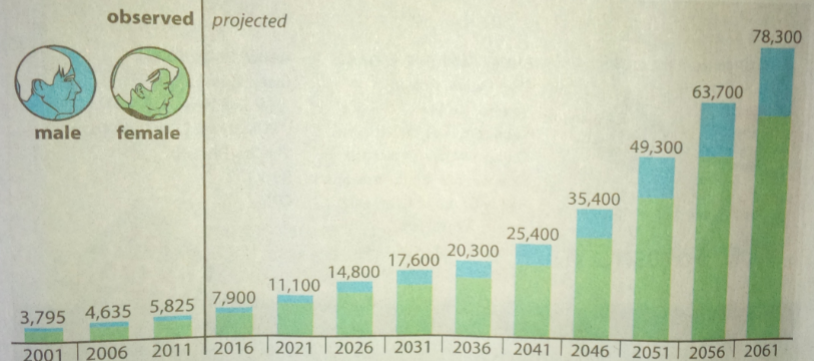


Williams hoped it would be found while they waited on ice. Ponce de Léon thought he'd find it bubbling up from the ground in Florida. And now Mr. Patton, a multimillionaire hungry for science to back up his hopes, has joined the age-old quest to extend the vigour of youth.

His timing couldn't be better. Once considered a fringe field littered with charlatans and quacks, anti-aging research has entered the

Centenarians in Canada

As a result of gains in life expectancy, an increasing number of Canadians are reaching the age of 100. The 2011 Census enumerated 5,825 people aged 100 years and older, compared to 4,635 in 2006 and 3,795 in 2001



Source: Statistic Canada

GRAPHIC: MAGGIE WONG/VANCOUVER SUN

Choose your grandparents wisely



Lifespan heritability

Herskind AM et al. *Hum Genet* 1996; 97: 319-323

- 2872 twin pairs born 1870-1900 (752 MZ, 2120 DZ)
- 99.4% dead, males @ 68-71; females @ 72-74
- Correlation of age at death:
MZ 0.18-0.33
DZ 0.07-0.19
- Proportion of variance due to heredity: **21-26%**
- Others as high as **50%**
- **YOU CAN BEAT YOUR GENES**

Environment: the other 75%



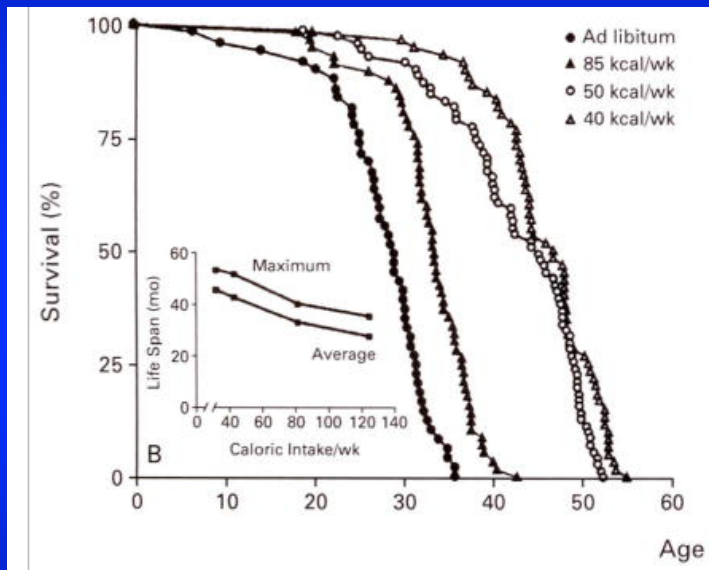
Be Skinny; Live Longer?

(Haq R. *Clin Invest Med* 2003; 26: 116-20)

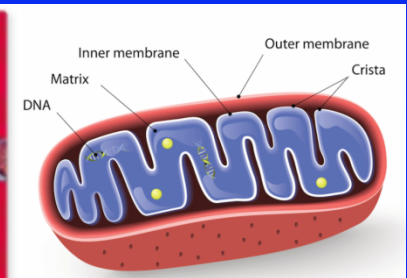
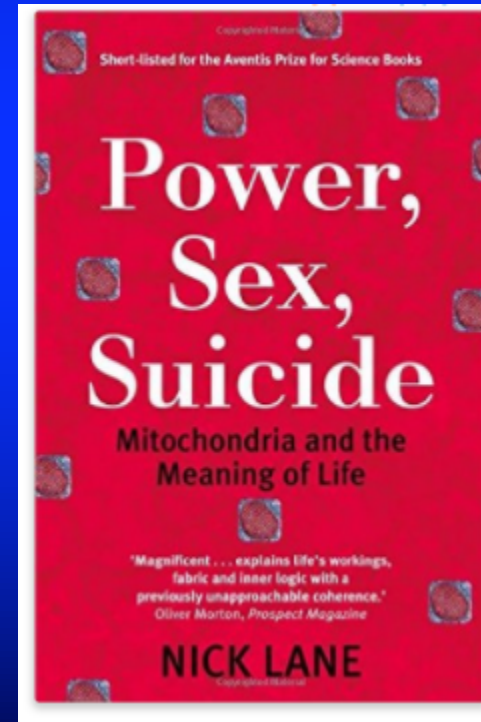
- Reducing calorie intake by 25%-50% prolongs life in yeast, worms, rats, non-human primates.
- Need to have proper protein and vitamin intake

What is the Mechanism?

Weindruch R, Sohal RS *New Eng J Med* 1997; 337: 986-94



A gift from our mothers



Generate energy (good)

Generate reactive oxygen species (bad)

Another Possibility

StarPhoenix 2017-11-04



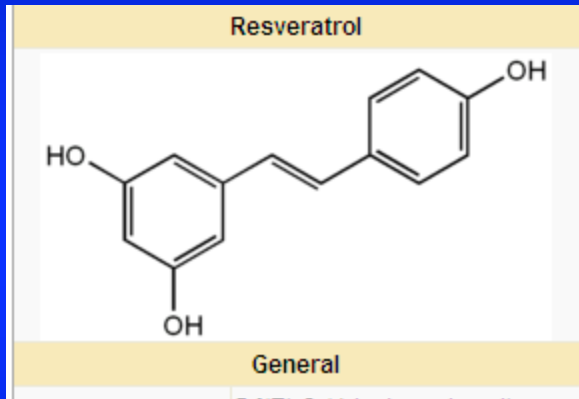
Clinical Trial: No placebo or other control

Another Theory

Di Chistina M et al. 2007 www.sciam.com

- *a gene!!*
- *Sir2* (silent information regulator)
- Found in yeast→humans
- Prevents transcription of redundant genes; cell doesn't expend energy on making useless proteins
- Adding 1 copy to yeast cell ↑lifespan by 30%
- Calorie restriction turns on *Sir2*
- *Resveratrol* (found in red wine) also does

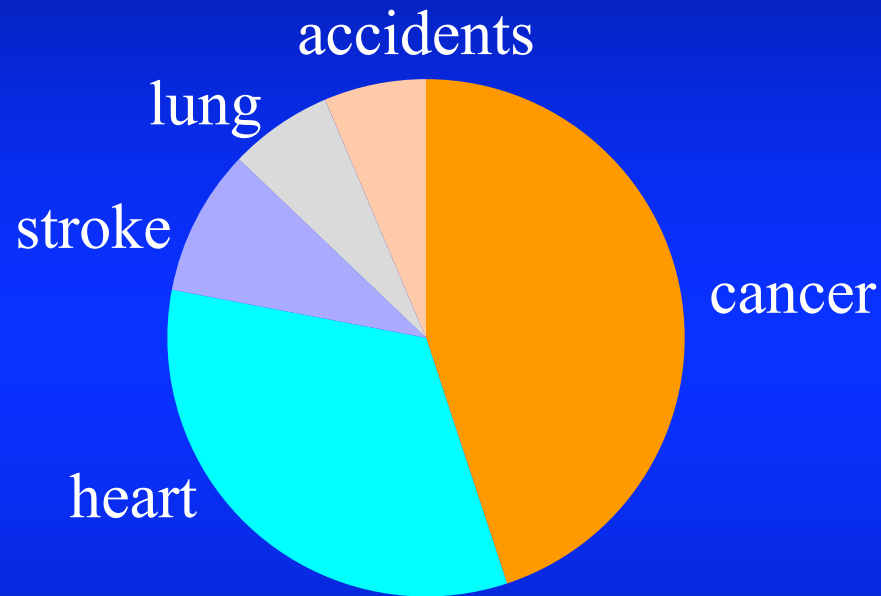
Good News: Resveratrol



- 1.7-6.0 grams/5 oz glass
- also in blueberries, peanuts
- Capsules are 1-500 mg (0.001-0.5 gr)
- clinical trials using up to 5 g
- obese mice lived 15% longer
- also: cancer, dementia prevention, improves athletic performance.

Causes of Death in Canada

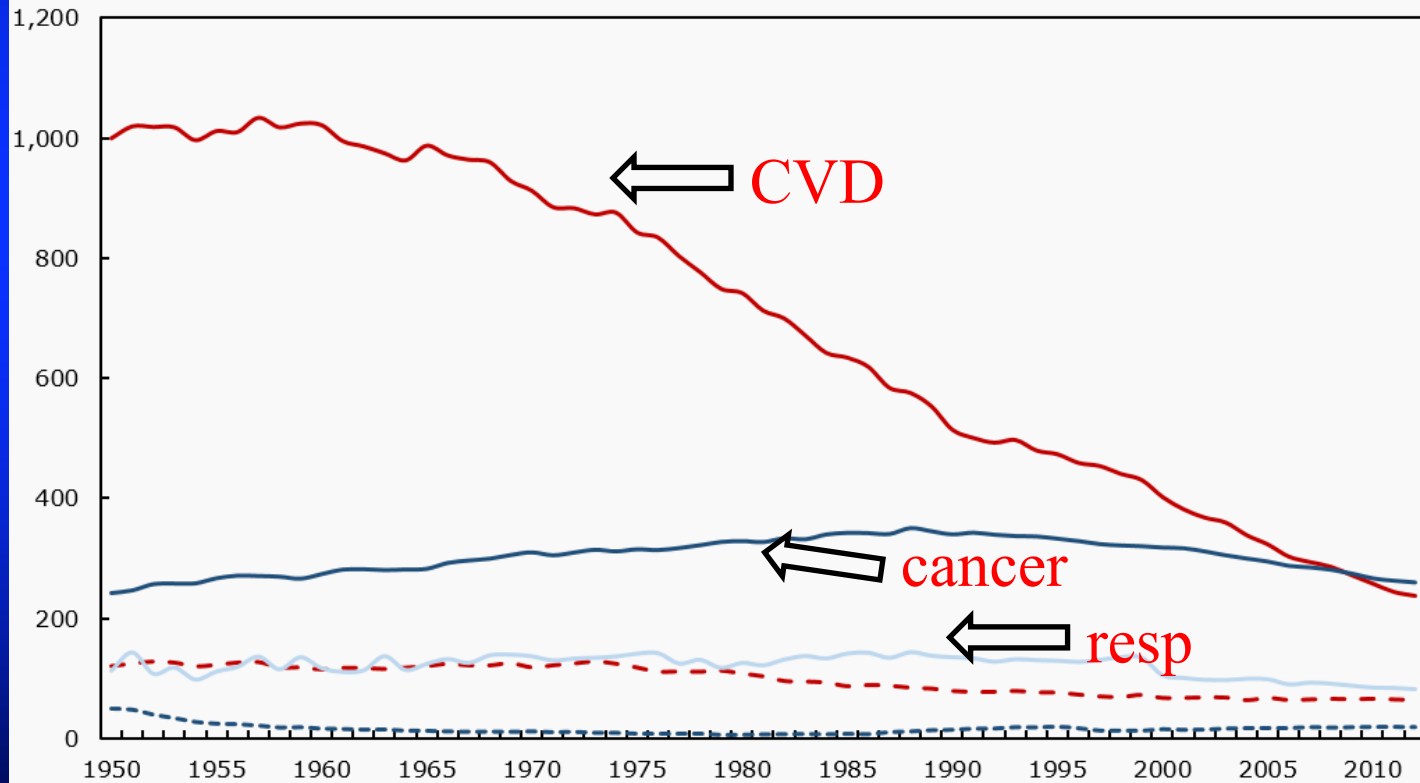
<https://top5ofanything.com/list/72d90ec7/Leading-Causes-of-Death-in-Canada>



Progress!

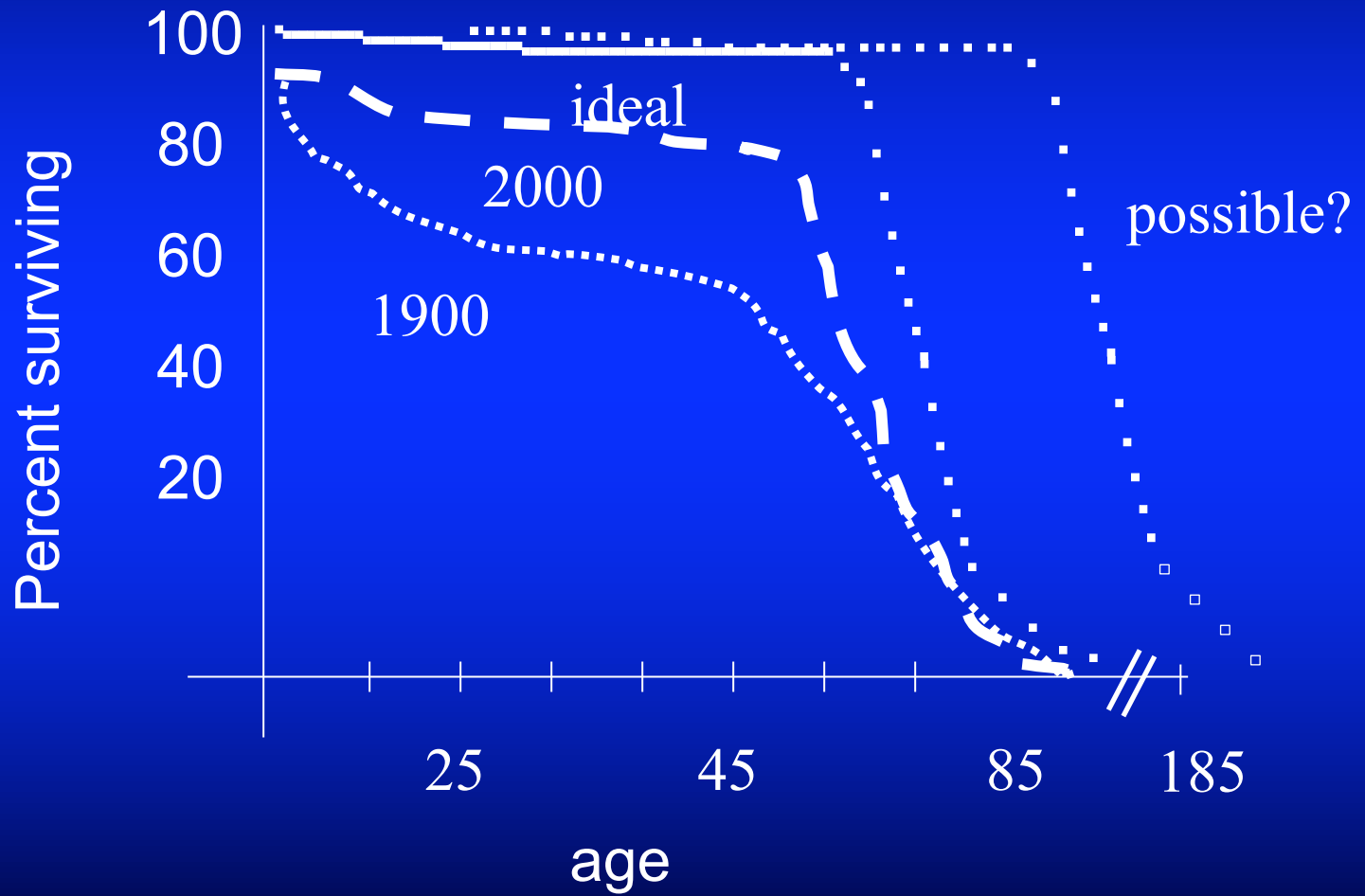
Changes in death rates for selected causes of deaths in Canada, men, 1950 to 2012

rates per 100,000
standard population
(2011)

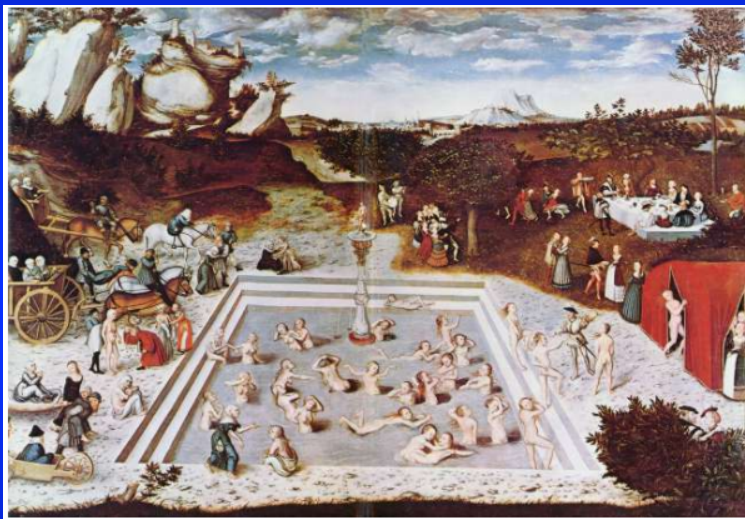


2018

The future



Some possibilities

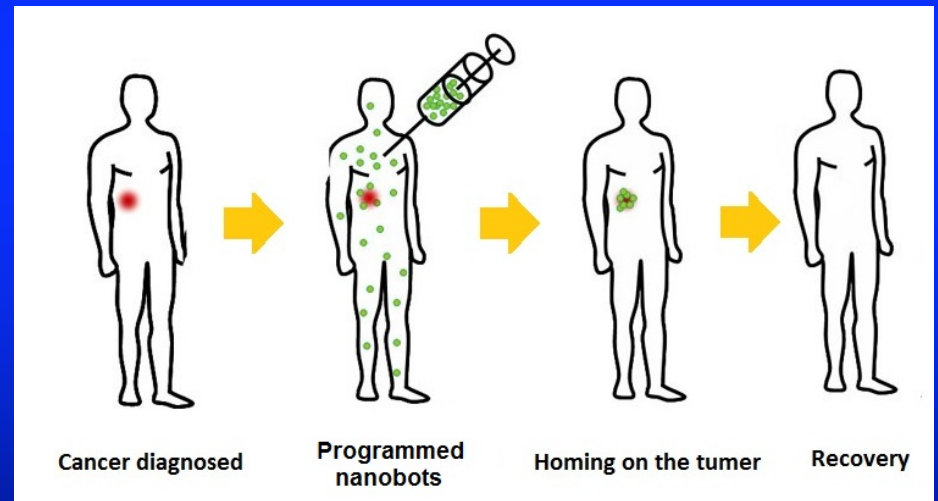


The 1546 painting *The Fountain of Youth* by Lucas Cranach. *Wikimedia Commons*

- Nanobots to root out diseased cells
- Reprogramming DNA
- Senolytics
- Artificial organs (3D printed)
- Uploading your brain to computer
- Cryonics

Nanobots Root Out Cancer Cells

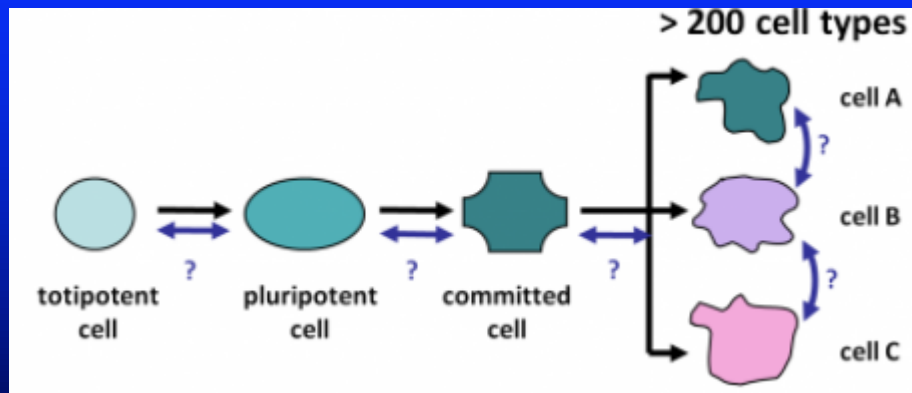
<http://www.iflscience.com/health-and-medicine>



Reprogramming DNA

<https://www.nature.com/articles/nbt.3805>

- Each one of our 1 trillion cells contains all our DNA
- Some DNA (genes) is “turned off” during development to allow specialized cells (brain, muscle, liver etc)
- We can reprogram DNA to recover “lost genes”
- We can build new brain, muscle, liver cells)



3D Organ Printing

Sirota C. Sci. J. Lander Arts and Sci 2016; 10:1

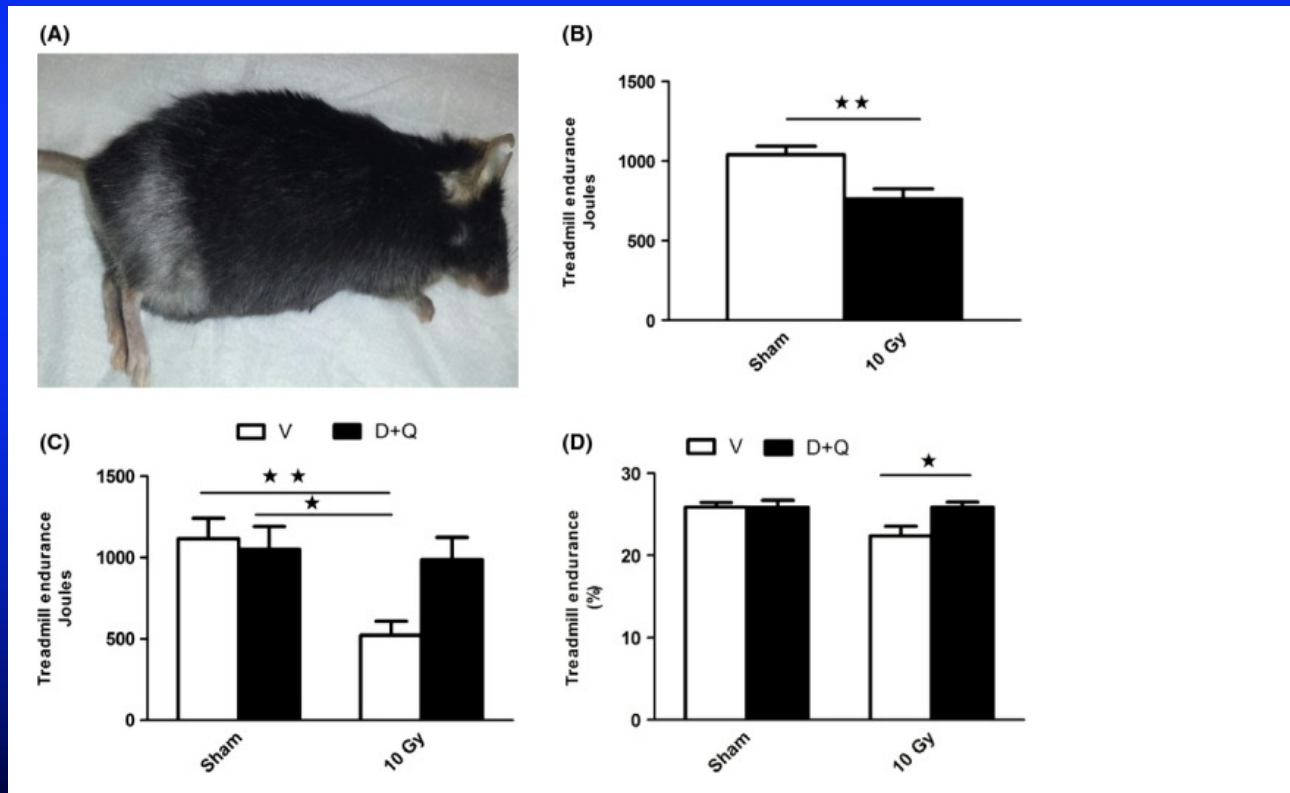
Scan the structure→clone various cell types→assemble the organ



Senolytics

Zhu Y et al. *Aging Cell*; 2015: 644-58.

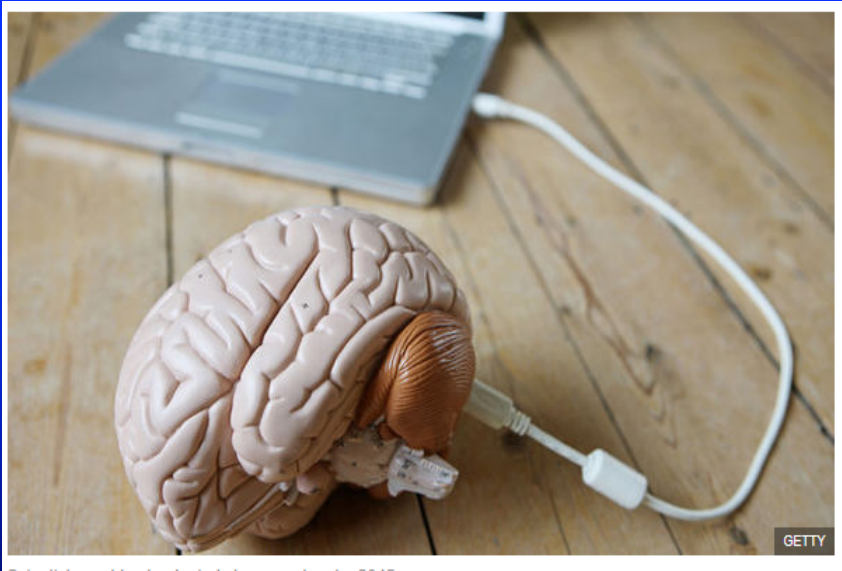
Agents that induce senescent (old, useless) cells to commit suicide.



Uploading the Mind to a Computer

<http://www.bbc.com/news/magazine-35786771>

immortality



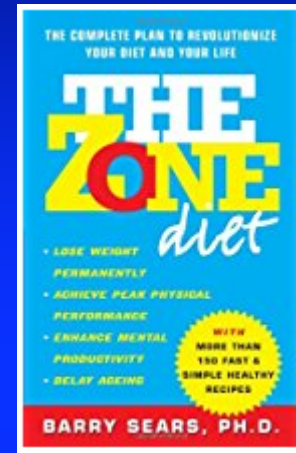
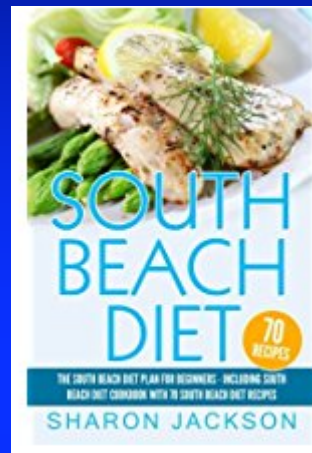
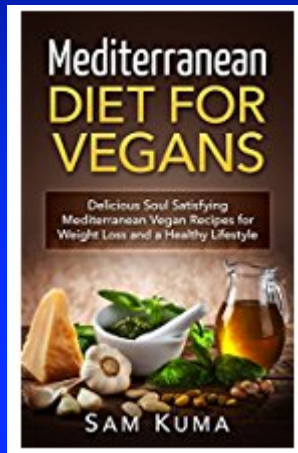
Cryonics

<http://www.cryonics.org/>

- Freeze (-186°C) just before natural death
- Store (\$28K US)
- Thaw, fix whatever is broken



What Should I Eat?



Is Tom Brady's diet — no nightshades or fruit — the secret behind his success?

SHARON KIRKEY | February 7, 2017 2:50 PM ET
More from Sharon Kirkey | @sharon_kirkey



Tom Brady of the New England Patriots holds the Vince Lombardi Trophy after defeating the TIMOTHY A. CLARY/AP/Getty Images Atlanta Falcons 34-28 in overtime during Super Bowl 51 at NRG Stadium on February 5, 2017 in Houston, Texas.

HEART AND STROKE FOUNDATION OF CANADA

- Calories to maintain healthy weight
- Vegetables, fruit, whole grains
- Protein (fish, lean meat, dairy)
- **Avoid** processed, sugary soft drinks

Vitamins!



Observational vs. RCT

- Cohort or Case-control
- Residual confounding
- Never Level 1 evidence (no Gr A rec.)
- “Hypothesis generating”

Vitamin C?

(StarPheonix 27 Oct 2007)

Is your heart dying from chronic scurvy?

(c) 2007 W. Gifford-Jones M.D.
Why is research that could save countless lives unknown to Canadian and U.S. doctors?

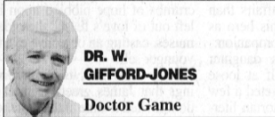
Dr. Sydney Bush, an optometrist in Hull, England, has made an historic discovery. He claims that atherosclerosis (hardening of arteries) can be reversed. His research, which could save millions from heart attack, should have made headlines around the world.

It's been said that the eye is the window to the heart. It's the only part of the body through which doctors can see arteries and veins during an eye examination. This allows doctors to see changes in retinal vessels, the result of aging, hypertension, diabetes and atherosclerosis. And it's been believed for years that blockages in arteries due to cholesterol deposits could not be reversed.

Dr. Bush decided to do more than look into the eye. In 1998, he started to use a technique called CardioRetinometry at his eye clinic in Hull, England. This instrument takes pictures of the retina, the back part of the eye, that transmits images to the brain. These photos have enabled Dr. Bush to observe change in retinal vessels over a course of several years.

CardioRetinometry photos could also pinpoint collections of cholesterol deposits in retinal vessels. Bush states that he could see a fine, white line, similar to a silver wire, running down almost every artery of adults who had high cholesterol.

But a chance encounter occurred that would reshape his thinking about coronary heart disease. While taking photos of the retina, Dr. Bush was also prescribing 3,000



DR. W.
GIFFORD-JONES
Doctor Game

to 10,000 milligrams of vitamin C to treat certain eye problems.

To his surprise he discovered that this amount of vitamin C resulted in changes in retinal arteries. Cholesterol deposits decreased in size, arteries became larger and there was increased blood flow to the retina. Proof this was happening was staring him in the face. And what happens to arteries in the retina also happens to arteries in the heart.

What does all this mean? Few people realize that animals manufacture vitamin C, but humans do not. For instance, goats produce 13,000 milligrams of vitamin C daily. Humans lost this ability during the course of evolution. This is why cats never died of scurvy during voyages to the New World while sailors succumbed to this disease.

Dr. Linus Pauling, two-time Nobel Prize winner, whom I have interviewed, extolled the virtues of vitamin C. He claimed that although humans no longer die from scurvy, they are nevertheless suffering from inadequate amounts of vitamin C.

So why is vitamin C so important in preventing retinal disease and heart attack?

Brick walls are held together by strong mortar and we all know what happens if mor-

tar starts to crumble. Cells, on the other hand, are glued together by collagen and vitamin C is necessary to manufacture and maintain its strength.

Pauling believed that the heart dies from a silent form of scurvy. In effect, inadequate levels of vitamin C weaken collagen, which is not good news for coronary arteries as they face the greatest pressure when the heart beats. The end result is injured arteries and heart attack.

Pauling's theory about coronary attack and now the findings of Dr. Bush compliment each other. Namely, a lack of vitamin C triggers heart attack and an excess of C guards against it.

The great irony is that British physicians, rather than looking at Dr. Bush's research with an open mind, have criticized his work. It may be the old story that new, revolutionary ideas, contrary to current medical thinking, often collect dust.

I've not yet had time to visit Bush's clinic in England. But he has sent me retinal pictures taken before vitamin C was prescribed and those taken following its use. The results are there for everyone to see.

Each year millions of North Americans die from coronary attack. Surely it's time for heart specialists and ophthalmologists to take a look at Dr. Bush's research. They may decide that our heart is not healthy until the eyes say so.

For last week's column on vitamin C see the web site www.mydoctor.ca/gifford-jones.

Observational studies:

4: modest benefit

2: no benefit

RCT:

incl E; no benefit, stones.

**BOTTOM LINE:
TAKE AT MOST
500 MG**

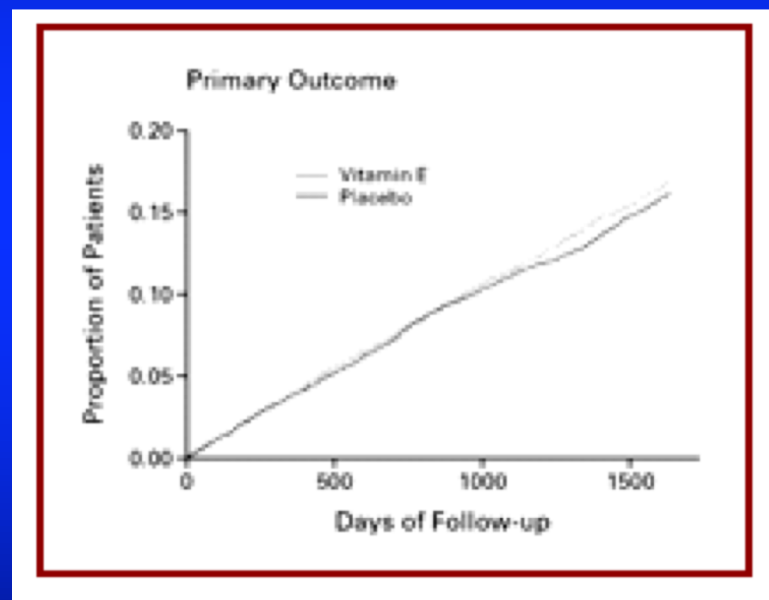
Vitamin E?

(HOPE Study Invest. *N Engl J Med* 2000; 342: 154-60)

Observational studies: 10-33% reduction in CV death

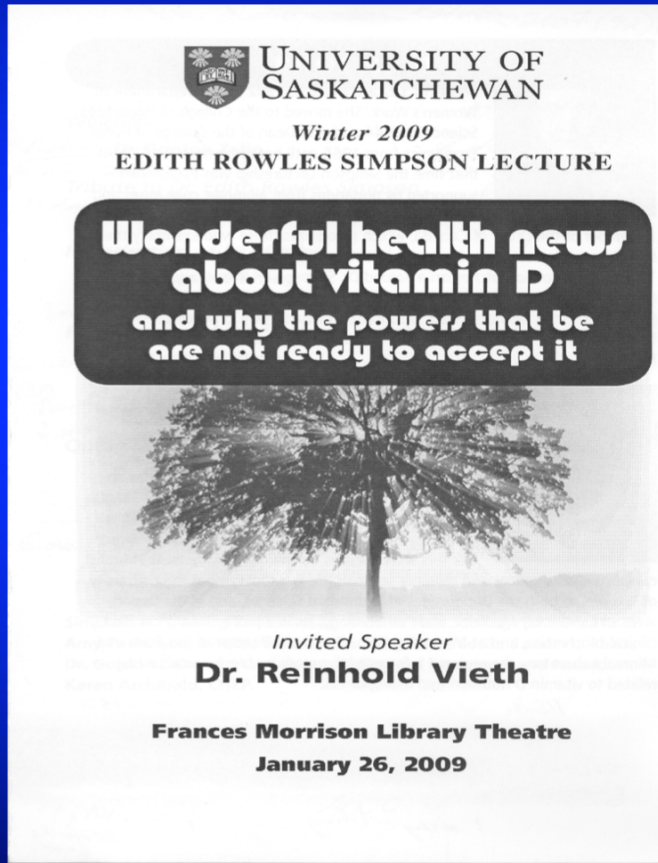
In 2 large trials (including HOPE) vitamin E had no benefit?

In HOPE-TOO, vitamin E caused heart failure.
(<http://www.fhs.mcmaster.ca/pubrel/hope2.htm>, 20 Apr 04)



BOTTOM LINE: DON'T BOTHER UNLESS YOU HAVE NASH.

Vitamin D?



Observational studies: (vs deficient)

7% reduction in death

17% reduction in cancer

30-50% reduction in CVD

RCTs: no effect (so far)

BUT:

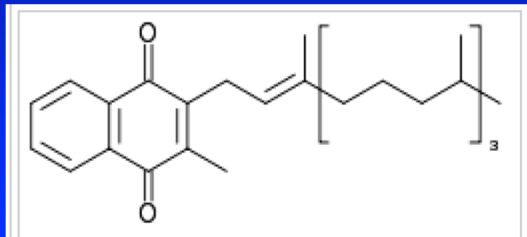
57% of hosp pts are <75 nmol/L

22% are <20 nmol/L

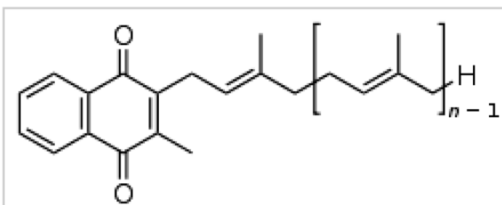
2018

BOTTOM LINE: TAKE 800-2000 UNITS OD.

Vitamin K?



Vitamin K₁ (phylloquinone). Both contain a functional naphthoquinone ring and an aliphatic side chain. Phylloquinone has a phytyl side chain.



Vitamin K₂ (menaquinone). In menaquinone the side chain is composed of a varying number of isoprenoid residues.

Basic science:

Activates factors II, VII, IX, X

Also proteins C and S

Also bone, CV system proteins

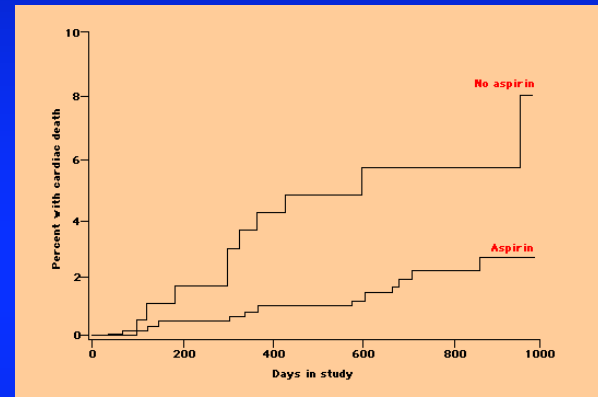
Observational:

High intake improves insulin sensitivity

**BOTTOM LINE: EAT YOUR VEGETABLES
(OR TAKE A MULTIVITAMIN)**

Aspirin?

- aspirin (81-325 mg/day) reduces the risk of all CV events by 13%
- there is a slight risk of bleeding
- **PERSONS AT HIGHER THAN AVERAGE RISK OF CVD (10% IN 10 YEARS) SHOULD TAKE ASPIRIN.**
- **INCLUDES MOST MEN OVER 55 AND MOST WOMEN OVER 65.**



Survival benefit of aspirin after acute coronary syndromes Kaplan-Meier plot of cardiac mortality in 936 patients who were enrolled one to six months after an acute coronary event (acute myocardial infarction or unstable angina) prompting hospital admission. Eighty percent of the patients were regular aspirin users. There was a significant decrease in subsequent cardiac mortality ($p=0.0028$) among regular aspirin users compared to nonusers. (Data from Goldstein, RE, Andrews, M, Hall, WJ, et al for the Multicenter Myocardial Ischemia Research Group, J Am Coll Cardiol 1996; 26:326.)

Almonds?

Jenkins DJ et al *Circulation* 2002; 106: 1327-32

27 people received either:

Almonds (72 gr)

Muffin

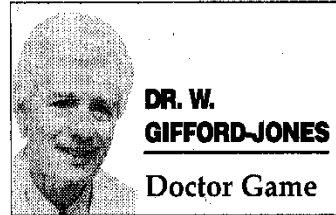
Half and half

Eating almonds eases blood cholesterol level

(c) 2002: W. Gifford-Jones Ltd.

Would you like to lower blood cholesterol without having to use cholesterol-lowering drugs (CLDs)?

In view of the millions of people taking this medication (I've been one of them) you may think this is a nutty suggestion. But if you were to be nuts about almond snacks every day, this would result in a significant drop



... cholesterol (high density lipoproteins HDL).

So if you're not allergic to nuts what effect would these changes

to eat sensibly. And they did not eat oily, highly salted or sugared nuts. The best kind of almond is the dry-roasted one.

I find this research interesting as I'm always looking for non-pill ways of lowering cholesterol.

Since my bypass surgery I have had no problem with taking a baby Aspirin daily. It makes sense to oil the blood platelets, preventing the formation of a clot

Muffin did nothing

Low dose almonds reduced LDL by 4.4%

High dose almonds reduced LDL by 9.4% (cf 20-60% with drugs)

Estrogens?

(WHI Invest. *JAMA* 2002; 288: 321-333)

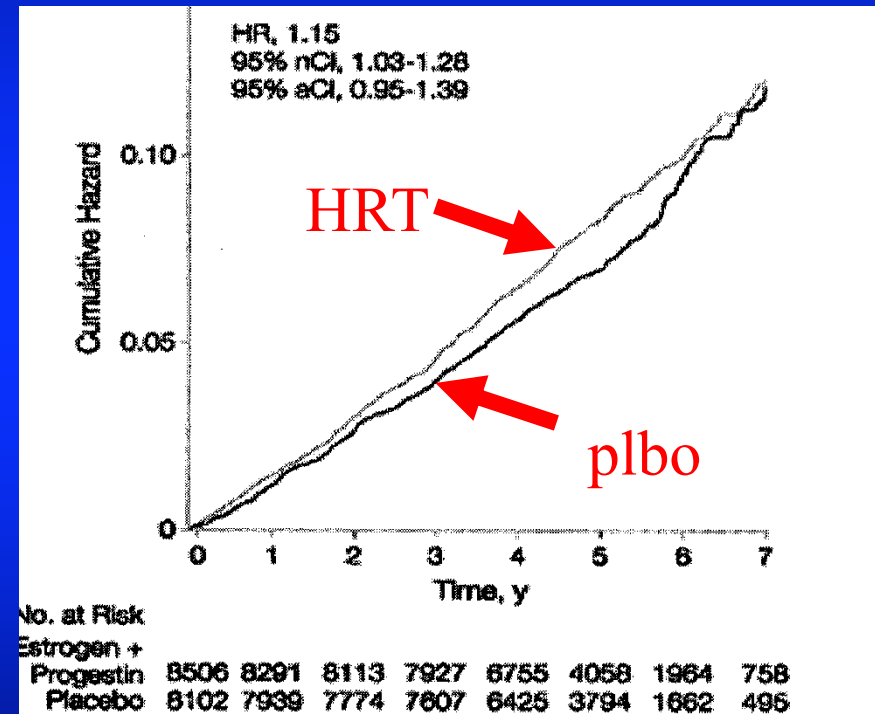
Observational studies:

modest benefit

Randomized

Controlled Trials:

NO BENEFIT.



Testosterone?

Bolona ER et al *Mayo Clin Proc* 2007;82: 22-28

Modest effect on sexual function (including ED)

Body fat ↓6%; lean body mass ↑3%.

Slight ↑ in BMD.

“neutral” (possibly beneficial) effect on CV events.

↑insulin sensitivity

healthier endothelium?

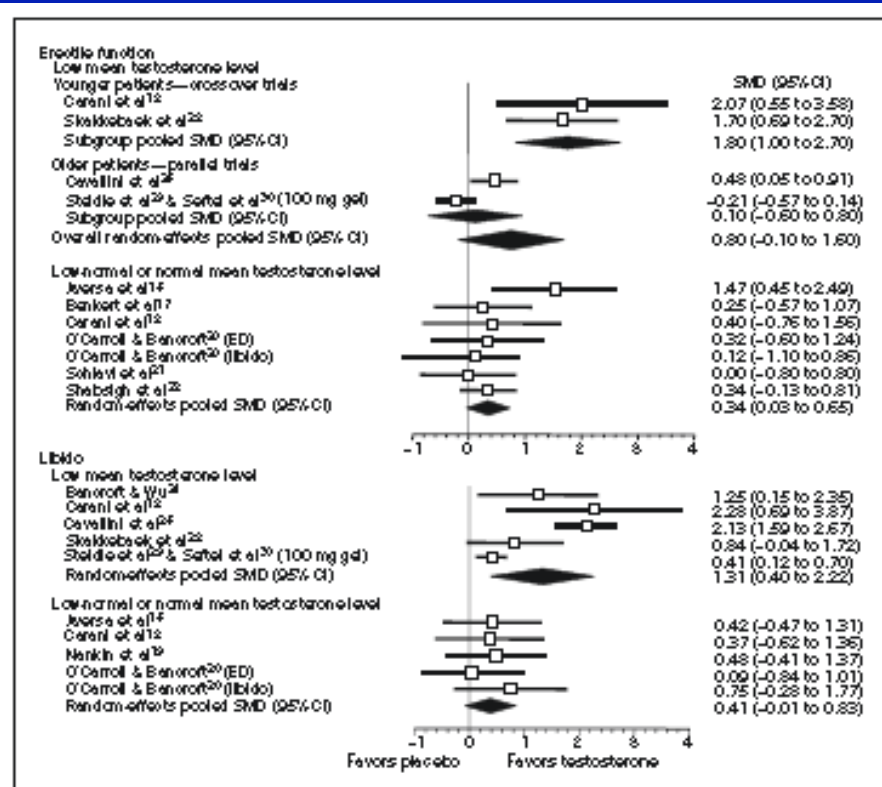


FIGURE 2. Random-effects meta-analysis of testosterone on sexual function (erectile function and libido) by mean testosterone level subgroups. Vertical line indicates no treatment effect; squares and horizontal lines point estimates and associated 95% confidence intervals (CIs) for each study; diamonds: random-effects pooled standardized mean difference (SMD) for each sexual function outcome by level of testosterone, the width representing its 95% CI. Studies are listed in alphabetical order, showing only the 100-mg arm of the trial by Stedje et al.²² We also identified the 2 cohorts (patients presenting with either erectile dysfunction [ED] or low libido) randomized by O'Carroll and Baneroff.²⁰

Growth Hormone?

Nass R et al *Ann Int Med* 2008; 149: 601-11

- Muscle mass and GH decline with age (3.8-7 Kg)
- Giving GH doesn't restore pulsatile profile
- MK 677, ghrelin mimetic, restores pulsatile GH to youthful levels.
- MK 677 25 mg po for 2 yrs increased fat free mass by 1.6 Kg (3%) ((M/F 60-83; n=43)
 - Stimulated appetite
 - Increased fat, but not visceral fat
 - Lowered LDL-C
 - Increased insulin resistance
 - No change in strength

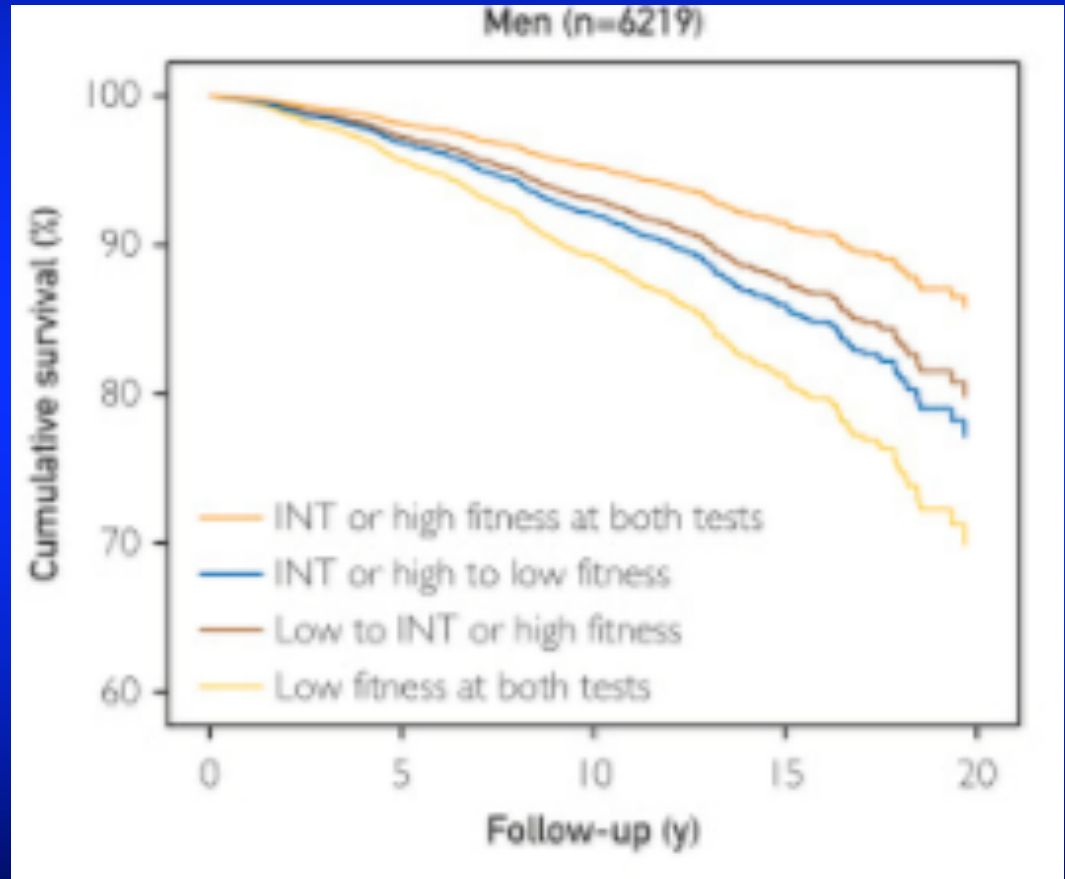
Exercise?



Being Fit is Better

Brawner CA et al. *Mayo Clin Proc* 2017; 92: 383-90

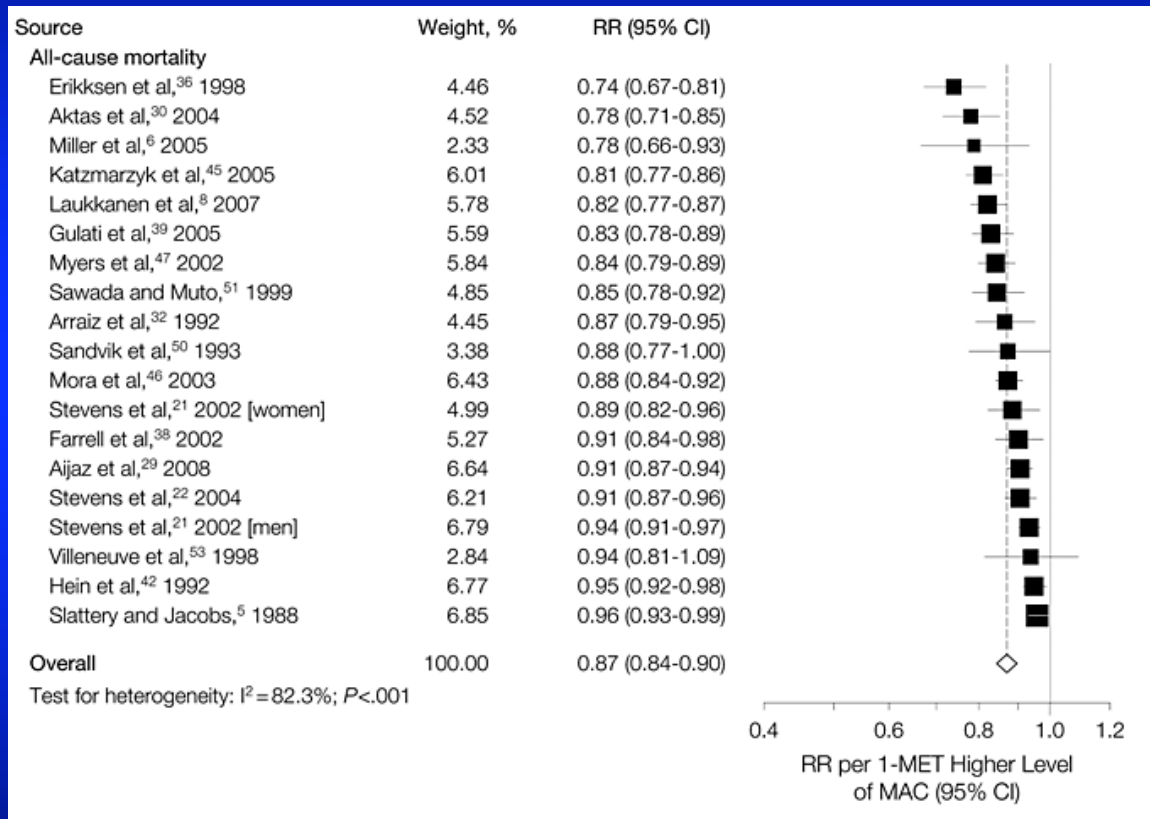
10,854 adults
2 exercise tests,
12 months apart
high \geq 11 METS
low \leq 8 METS



No RCT's But a Metanalysis

(study of studies)

Kodama S et al. *JAMA* 2009; 301: 2024-35



↑ 1 MET =
↑ 1 km/hr
running

How much exercise is enough?

FREQUENCY

“most days”

INTENSITY

moderate

TIME

30 min

TYPE

cardio, strength,
flexibility, balance

What Microsoft Network Says:


2009-02-24

<http://health.msn.com/health-topics/articlepage.aspx?cp-documentid=100233437&page=1>

1. Don't retire
2. Floss every day
3. Move around
4. Eat a fiber rich cereal
5. Get > 6hrs sleep
6. Use whole foods
7. Be less neurotic (!)
8. 7th Day Adventist (community)
9. Creature of habit
10. Stay connected

How Long Will You Live?

https://www.sunlife.ca/ca/Learn+and+Plan/Tools+and+Calculators/Life+expectancy+calculator?vgnLocale=en_CA

 **TELL US ABOUT YOURSELF:**


Gender: Male Female


Current age: 18 years old


Desired retirement age: 65 years old


Height: ft in


Weight: lbs


 **YOUR LIFESTYLE:**

Do you smoke? 

How often do you drink alcohol? 

What's your activity level? 

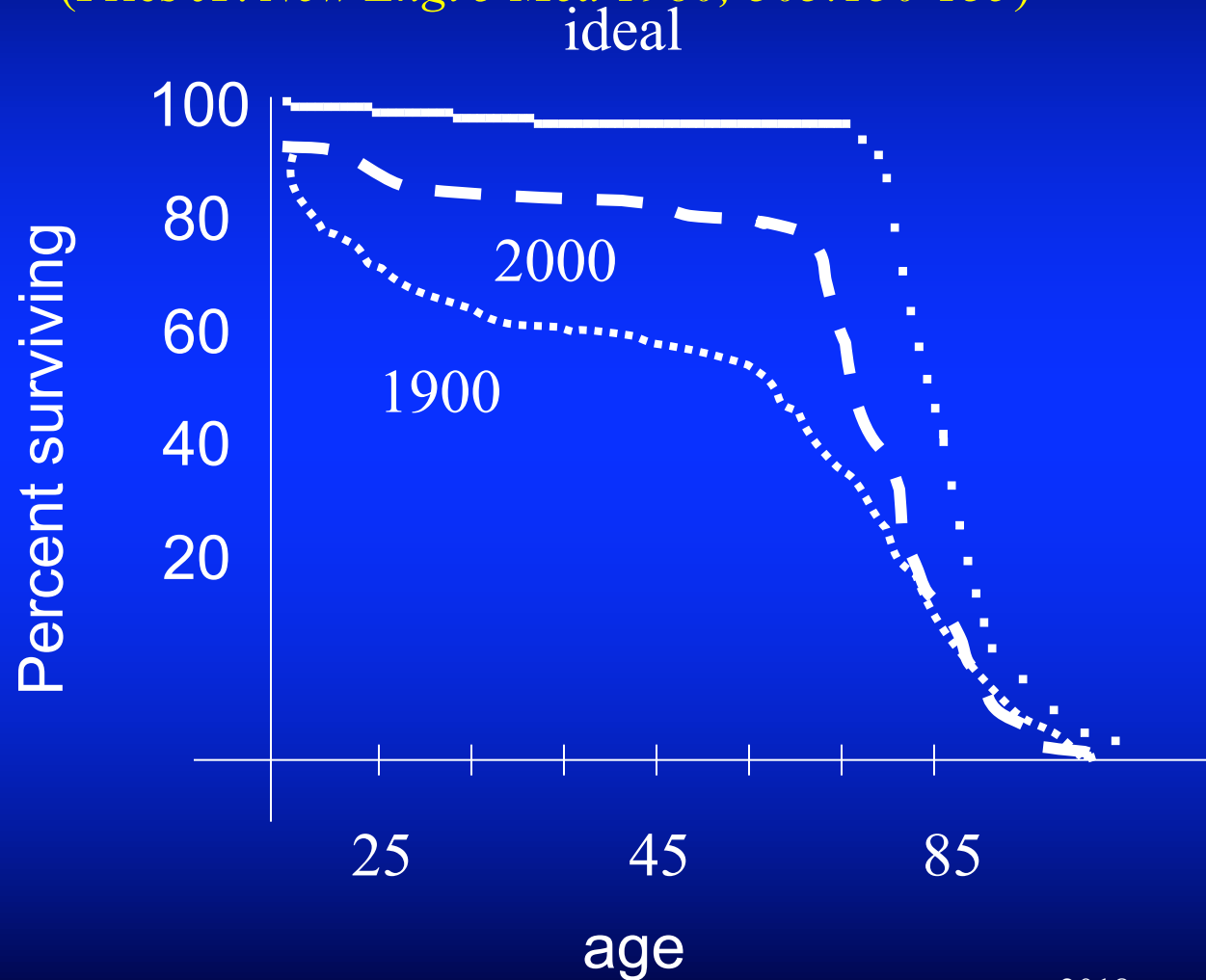
How healthy is your diet? 

How stressed are you? 

CALCULATE YOUR RESULTS

Compression of Mortality

(Fries JF. *New Engl J Med* 1980; 303:130-135)



A problem with “compression of mortality”



- If we don't die “prematurely” of CVD, will we die later of other nasty, more expensive things?
- Since sudden death from CVD is quick, painless and cheap, why are we trying to prevent it?

Will We Have More People with Dementia?

Larson EB et al. *New Engl J Med* 2013; 369: 2773-5

Probably yes, because more people are living longer

BUT

**THE INCIDENCE OF DEMENTIA IS
DECREASING:**

1989-94 8.3%

2008-11 6.5%

(better education; fewer risk factors)

Summary

- Currently, there is no “fountain of youth” pill or diet.
- We can help people attain their “rightful” age by preventing cardiovascular disease and cancer.
- We don’t lead to more disabled people.
- diet, exercise and medication are all important.
- aspirin and multivitamin do more good than harm.

Life is Finite



Small Changes Can Make a Big Difference

