



# Longevity in the 21<sup>st</sup> century: When medicine trumps extrapolation

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*Chief Science Officer, SENS Research Foundation, USA  
VP New Technology Discovery, AgeX Therapeutics, USA*

# Longevity in the 21st century:

when medicine trumps extrapolation

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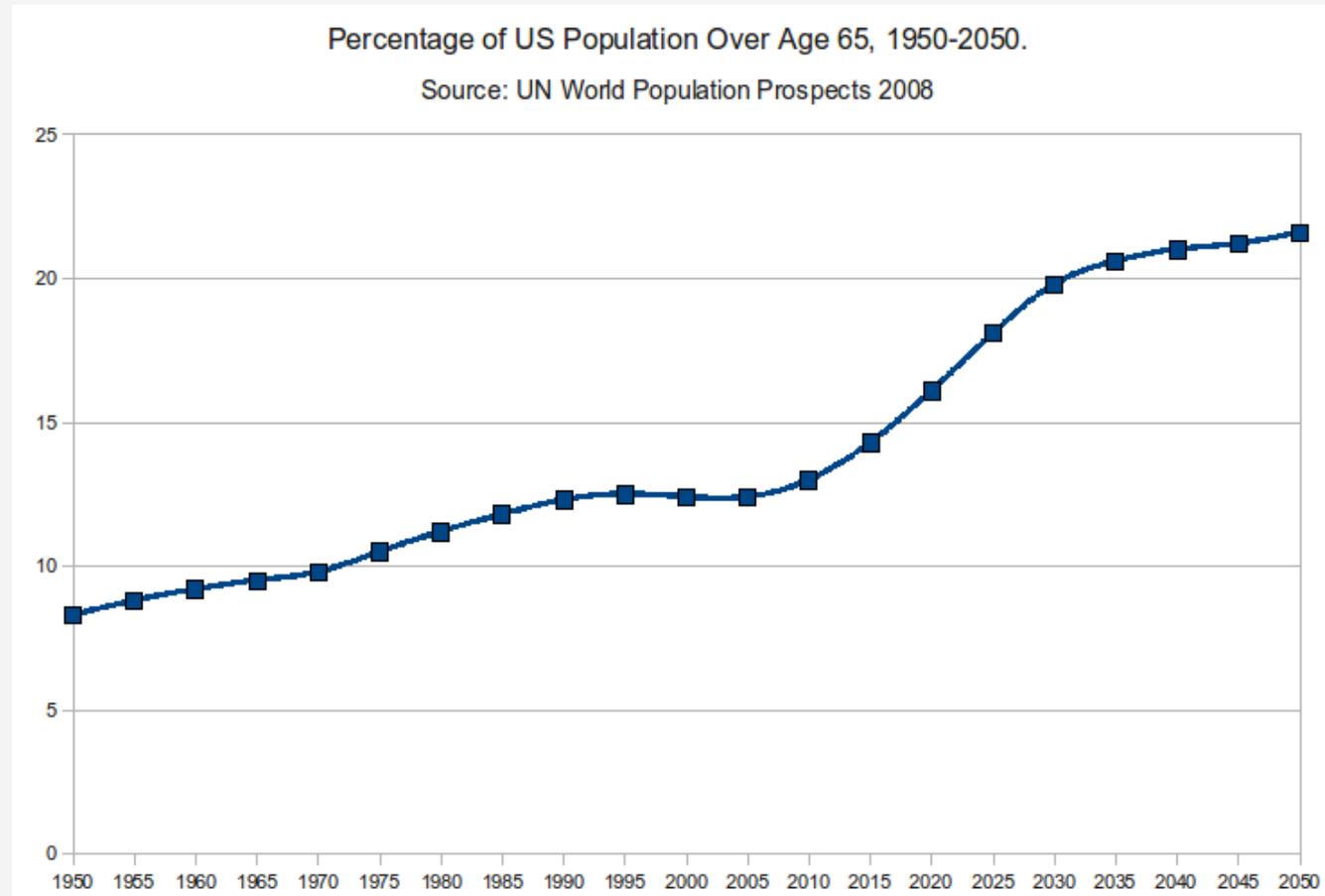
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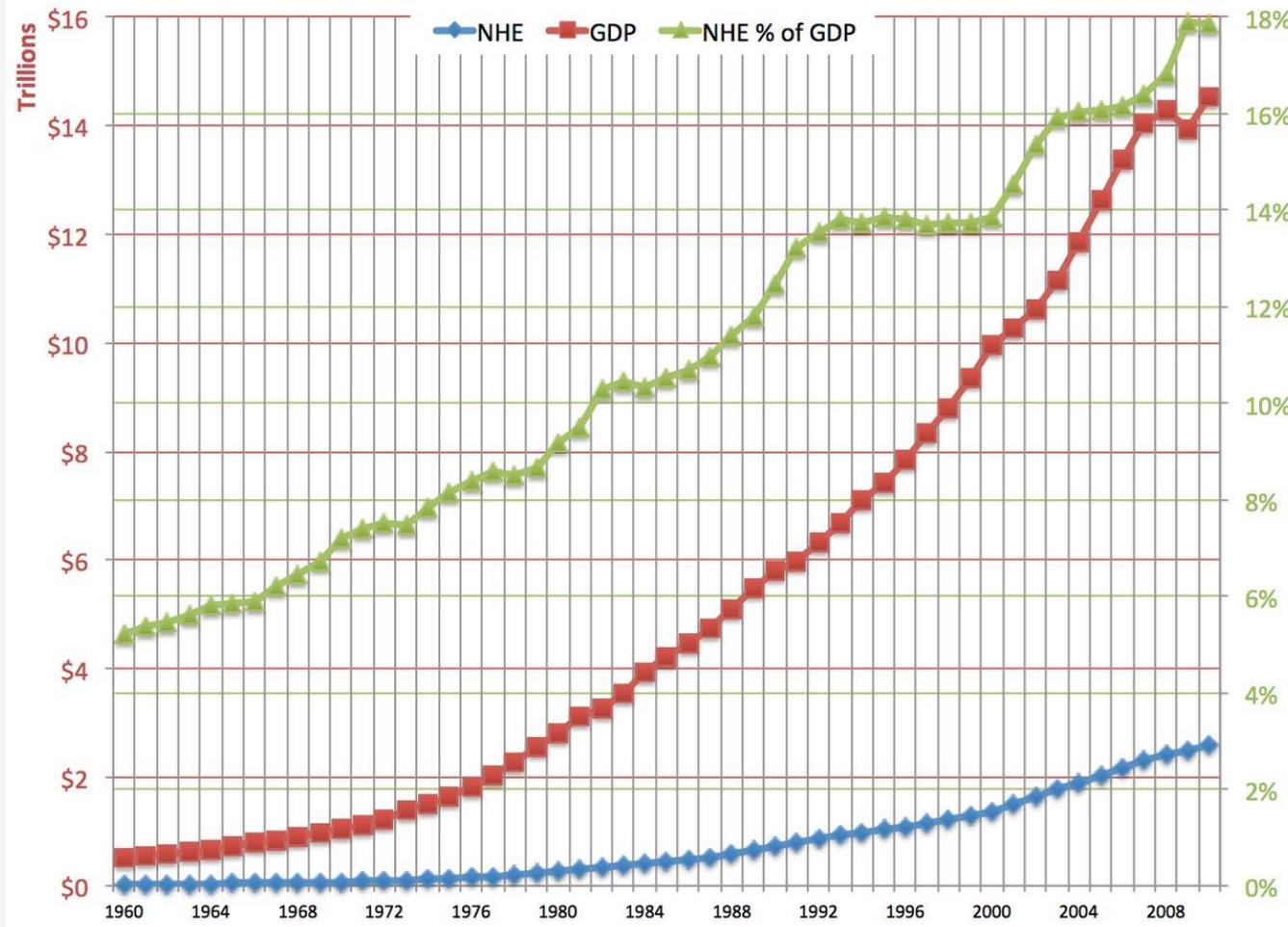
<http://www.sens.org/>

# The aging population



\* Source: [http://esa.un.org/wpp/unpp/panel\\_population.htm](http://esa.un.org/wpp/unpp/panel_population.htm)

# The economics of aging



Source: <http://sambaker.com/econ/classes/nhe10/>

If historical rates continue, US healthcare spending will be 34% of GDP by 2040. Source: <http://www.whitehouse.gov/administration/eop/cea/TheEconomicCaseforHealthCareReform>

In 2010, the US spent \$1.186 trillion on healthcare for people 65+. Source: [http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us\\_dchs\\_2012\\_hidden\\_costs112712.pdf](http://www.deloitte.com/assets/Dcom-UnitedStates/Local%20Assets/Documents/us_dchs_2012_hidden_costs112712.pdf)

# Age-related vs. infectious diseases

- Most infectious diseases have been easily prevented
  - Sanitation
  - Vaccines
  - Antibiotics
  - Carrier control
- Age-related diseases have not. Why not?

# Well, if not impossible, at least intractable?

presbycusis  
osteoporosis  
osteoarthritis  
autoimmunity  
greying hair  
presbyopia  
cataract  
glaucoma  
temporal arteritis  
polymyalgia rheumatica  
wrinkling  
Alzheimer's disease  
Pick's disease  
corticobasal degeneration  
progressive supranuclear palsy  
Parkinson's disease  
multiple system atrophy  
dementia with Lewy bodies  
sarcopenia  
glomerulonephritis  
senile cardiac amyloidosis  
atherosclerosis  
arteriosclerosis  
age-related macular degeneration  
cardiomyopathy  
diastolic heart failure  
cancer  
systemic inflammation  
oxidative stress  
reduced coronary blood flow  
loss of cardiac reserve  
andropause  
thymic involution  
reduced plasma renin activity

reduced light adaptation  
reduced ethanol metabolism  
altered drug pharmacokinetics  
somatopause  
loss of cardiac adaptability  
incontinence  
impaired wound healing  
idiopathic axonal polyneuropathy  
autonomic neuropathy  
arrhythmia  
chronic obstructive pulmonary disorder  
benign prostatic hypertrophy  
menopause  
leukoaraiosis  
stroke  
vascular dementia  
frontotemporal dementia  
immunosenescence  
anosmia  
cachexia  
anorexia of aging  
systolic hypertension  
ageusia  
erectile dysfunction  
orthostatic hypotension  
impaired adaptive beta-cell proliferation  
fibroblast collapse  
anergic T-cell clones  
cellular senescence  
vascular calcification  
impaired transdermal absorption  
impaired thermoregulation  
reduced tactile acuity

impaired pH maintenance  
reduced chemical clearance  
altered dermal immune cell residence and function  
aberrant allergic and irritant reactions  
loss of skin elasticity  
impaired vitamin D synthesis  
reduced renal reserve  
renal cortex atrophy  
gut dysbiosis  
loss of jejunal villus height  
impaired response to vaccination  
impaired thirst  
lentigo senilis  
thinning hair  
impaired proprioception  
impaired balance  
reduced vital capacity  
reduced cardiorespiratory endurance  
impaired sweat response  
impaired blood distribution  
nutrient malabsorption  
diverticular disease  
presbyphagia  
increased reflux  
alveolar loss  
neuronal loss  
senile emphysema  
degenerative disc disease  
joint calcification  
pineal calcification  
aberrant differentiation  
gait instability  
frontal demyelination

# Aging in three words



# What we do these days against aging



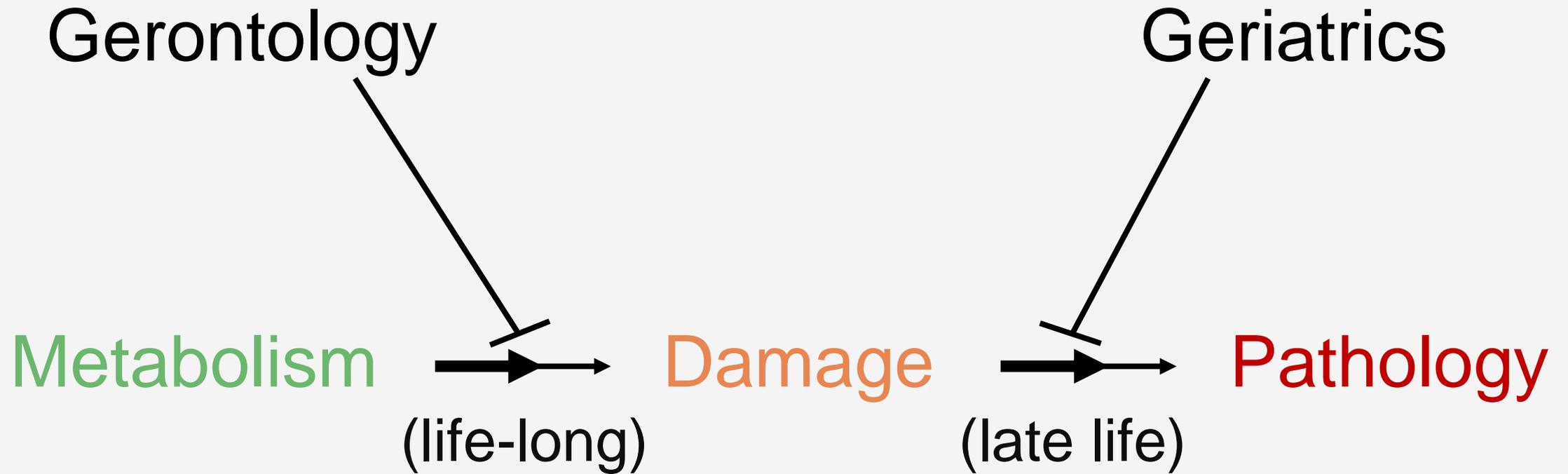
# Diseases and aging: popular view

Diseases			Aging
Communicable	Congenital	Chronic	
Tuberculosis Malaria HIV ...	Tay-Sachs MELAS Li-Fraumeni ...	Alzheimer's Cancer Atherosclerosis ...	Frailty Sarcopenia Immunosenescence ...

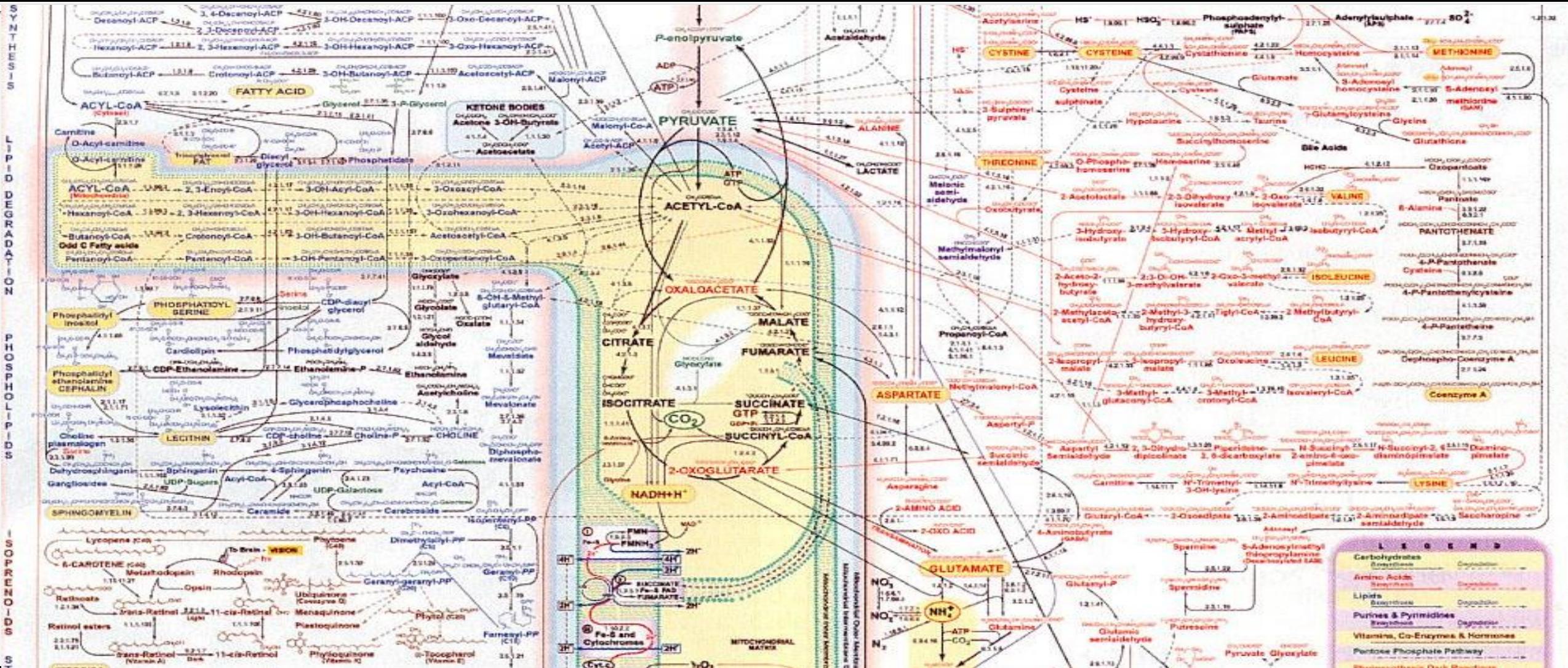
# Diseases and aging: correct view

Diseases		Aging	
Communicable	Congenital	Specific	General
Tuberculosis Malaria HIV ...	Tay-Sachs MELAS Li-Fraumeni ...	Alzheimer's Cancer Atherosclerosis ...	Frailty Sarcopenia Immunosenescence ...

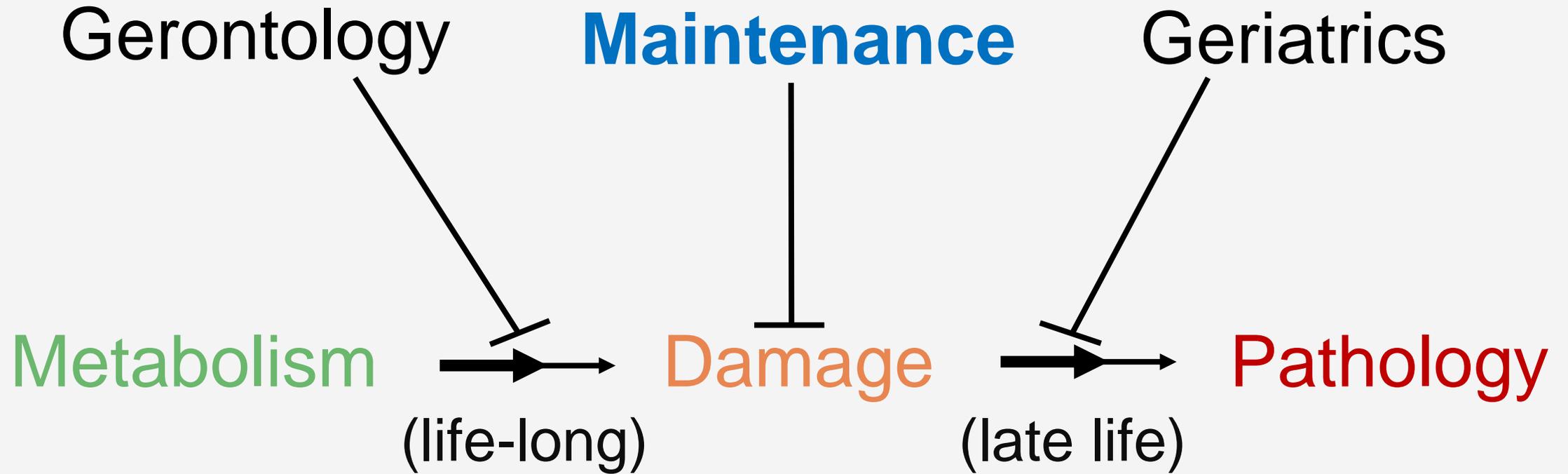
# A more promising alternative?



# Unfortunately...



# A common-sense alternative



# Comparison: car maintenance



# Why is rejuv. biotech so promising?

Aging is a phenomenon of physics, not biology!

Comprehensive preventative maintenance is how we already keep simple machines working as well as when they were built, long beyond their designed lifespan.

The body is far more complex. But wait: how much more complex is its **damage**?

# The “seven deadly things” & their fixes

## Damage type

## The maintenance approach

Cell loss, cell atrophy

Replace, using stem cells

Division-obsessed cells

Reinforce, using telomere control

Death-resistant cells

Remove, using suicide genes etc

Mitochondrial mutations

Reinforce, using backup copies

Intracellular waste products

Remove, using foreign enzymes

Extracellular waste products

Remove, using immune system

Extracellular matrix stiffening

Repair, using crosslink-breakers

**Existence of any 8<sup>th</sup> category is looking increasingly unlikely**

# Things you may be thinking right now

- This guy looks crazy; what do “credentialed” people think about these ideas?
- Even if he’s right, are the consequences for longevity big/near enough to affect my work?
- Even if they are, will society let it happen?

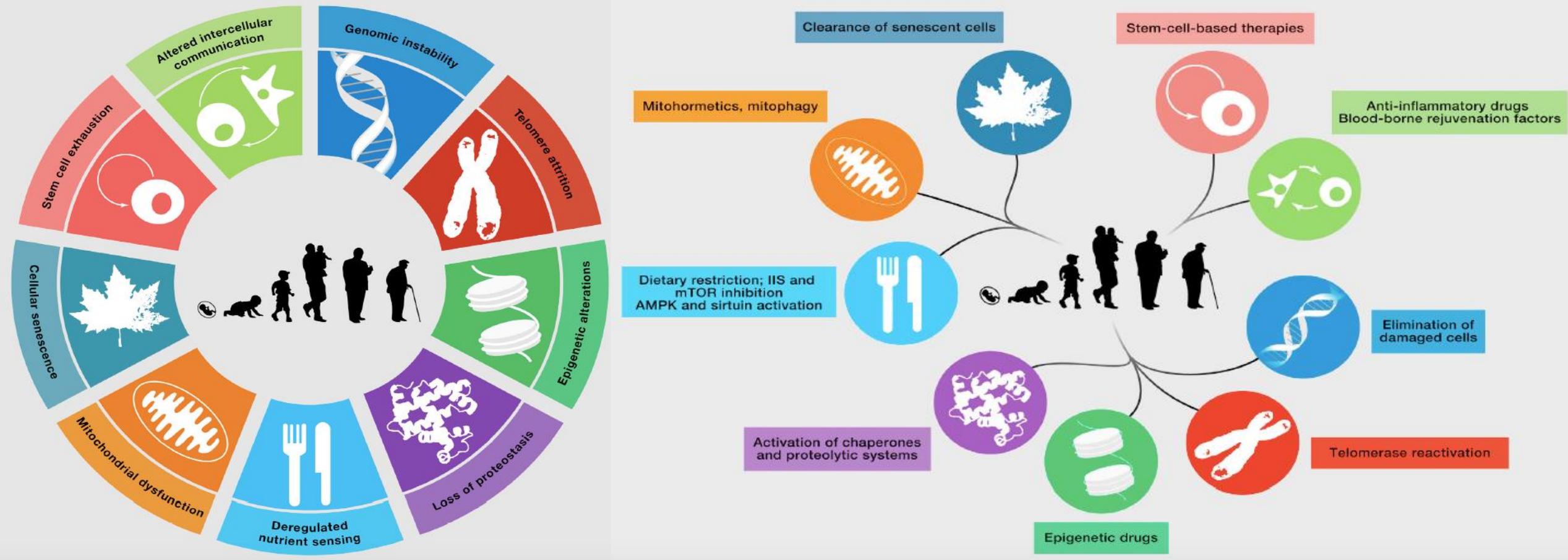
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# Our implementation progress

- Total synthesis of glucosepane, allowing identification of antibodies and degraders (*Science*, 2015)
- Modified bacterial enzyme protects cells from atherogenic oxysterols (*Biotech Bioeng*, 2012)
- Antibodies cleave cardiotoxic amyloid (*J Biol Chem*, 2014)
- Two out of 13 mitochondrial genes successfully relocated to the nucleus (*Nucleic Acids Res*, 2016)

# Cell 153:1194 (2013) – over 2000 citations



# Recent spin-outs from SRF

- LysoClear: reversing macular degeneration
- Antoxerene: clearing senescent cells
- Covalent: clearing transthyretin amyloid
- Arigos: cryopreserving organs for transplant
- Revel: breaking AGE crosslinks vs hypertension
- Underdog: retooling cyclodextrin vs oxidized cholesterol

# Other SENS-aligned startups

- AgeX – funded by Juvenescence and Kizoo among others
- Unity - raised >\$300M before even STARTING its FIRST clinical trial
- Insilico Medicine – funded by Juvenescence and now many others
- Lygenesis – funded by Juvenescence
- BioAge – funding from Andreessen Horowitz and now many others
- Repair Biotechnologies – mostly self-funded so far
- Rejuvenation Tech – funded by YCBio (Y Combinator)
- Elevian – funding from BOLD and others
- NaNotics, AgeCurve, Nuchido, Elastrin, Retrotope, Leucadia, Cleara, Senolytx...
- Total count conservatively >100 by now: see <http://agingbiotech.info/>

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# So... longevity?

- We ***DON'T WORK ON LONGEVITY***, whatever the media may like to tell you
- However, we know that this medicine may increase longevity a lot, I mean really a lot
- We think this is a good thing, even though it will put people like you out of business 😊

# How BIG is the longevity side-benefit?

- Rejuvenation therapies may never be perfect; first-generation may give “only” ~30y extra life
- However, that would buy us time to develop better ones with which to re-rejuvenate the same people, and so on (“**longevity escape velocity**”)
- So...?

# How BIG is the longevity side-benefit?

- Western mortality in the 20s is under  $10^{-3}/y$
- If it didn't rise with age (and in fact it will surely fall with time), most people would live to over 1000
- Period (i.e. "headline") life expectancy will very suddenly become incalculable (literally!)

# How NEAR is the longevity side-benefit?

- This is pioneering technology, so we don't know
- Guess: 50% chance in 20-25y if funding rises soon
- At least 10% chance it'll take >100y
- That's for the therapies I've mentioned today
- They will probably give around 30yr extra life
- LEV will ~certainly be maintained thereafter
- **Everyone will understand the above this decade**

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# Sociological considerations

- Overpopulation?
- Inequality of access?
- Immortal dictators?
- Boredom?
- Pensions collapse?

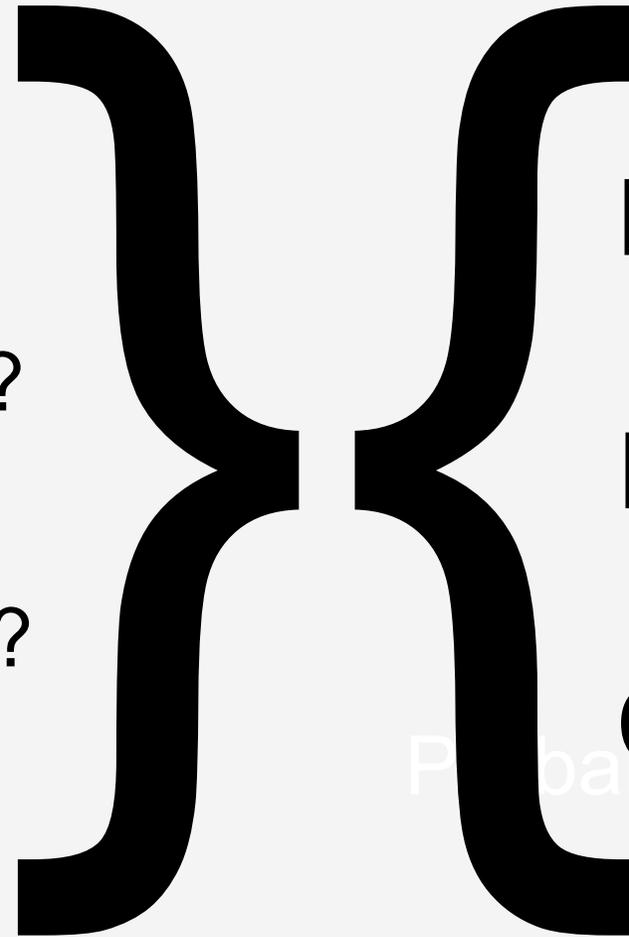
# Sociological considerations

- Overpopulation?
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- Pensions collapse?

# “Ethical” considerations

- Overpopulation?
- Unequal access?
- Immortal dictators?
- Boredom?
- Pensions collapse?
- Etc, etc, etc

happen



Health

Proportion

Choice

Probably won't

# Sociological considerations

- No age-related ill-health
- Elderly *contribute* wealth
- Energy to explore novelty
- Flexible career structure
- Not a burden on your kids

# Learn more

Read the (semi-technical) book.

Available at Amazon and all good book stores.

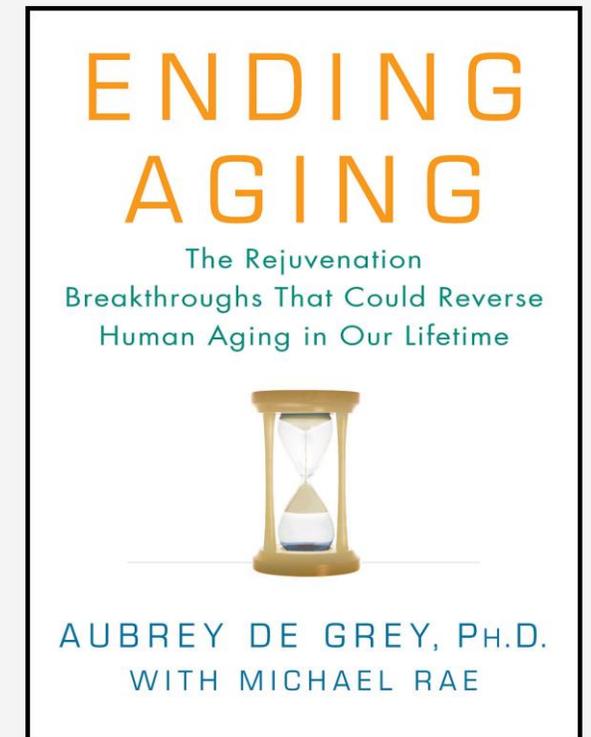
Paperback is cheaper, and has an extra chapter!

Visit us on the web at

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reimagine aging

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