

Lies I Taught In Medical School

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Disclosures:

- Not medical advice
- Opinions are my own and not of UCLA or USC Medical Schools
- Financial:
Revenue from various health longevity ventures and *Lies I Taught In Medical School*







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Conventional Career in Academic Medicine

(Professor academic rank at UCLA and USC)

Practice Medicine:

Daily patients and procedures

Scientific Research:

Laboratory with \$ millions in funding

Authored > 200 peer reviewed papers

President of 2 International Medical Societies

Numerous patents

Teaching:

Authored 13 textbooks in 6 languages

Lectured around the world



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Arthritis (Gout)

Dyslipidemia

Hypertension

Prediabetes

-4 separate diseases were largely unrelated.

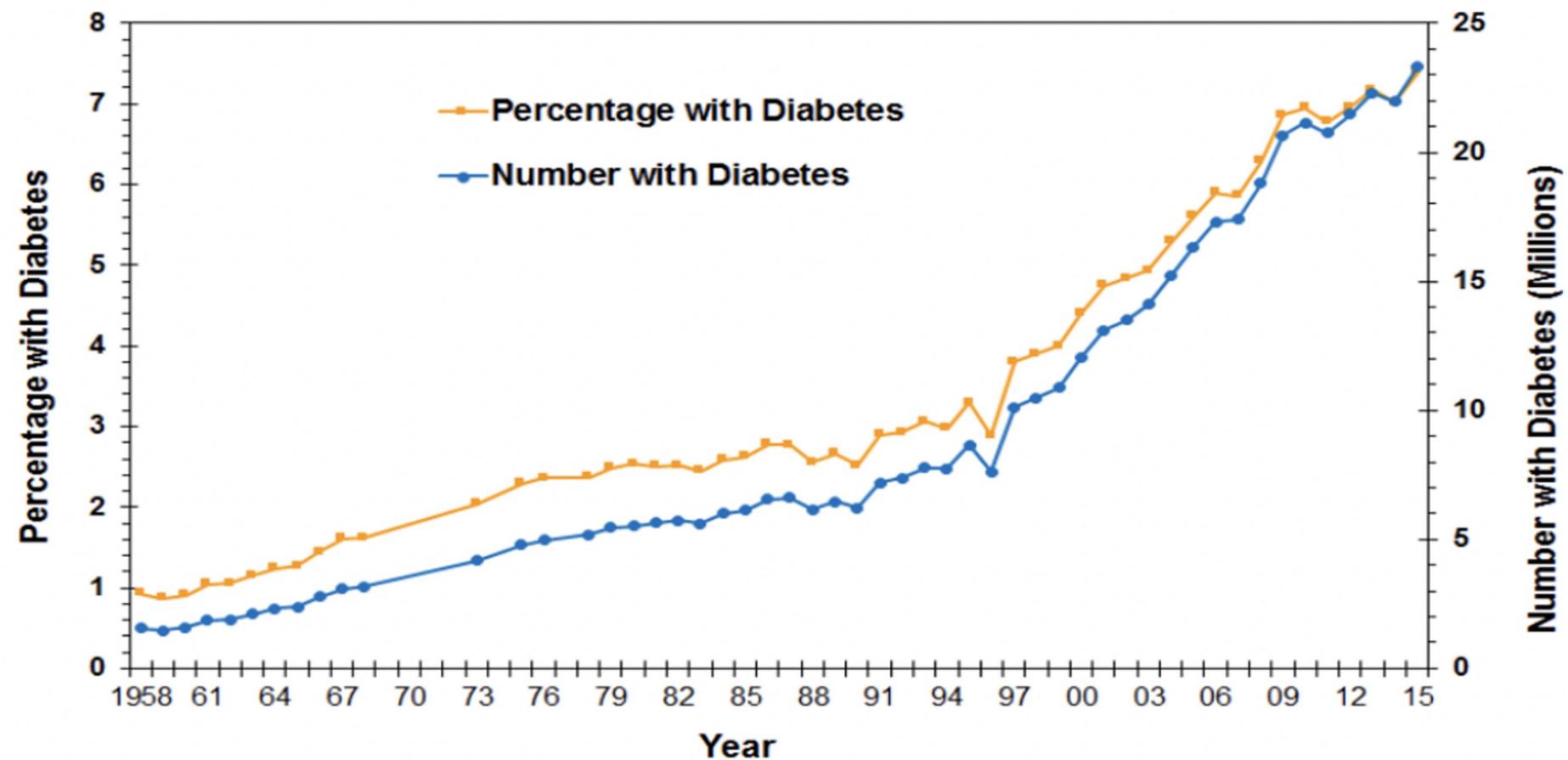
-Drug treatments were not just for symptoms but corrected the underlying diseases.

-Lifestyle worth trying but these diseases best treated with drugs.



The Type 2 Diabetes Epidemic- I wasn't alone

Number and Percentage of U.S. Population with Diagnosed Diabetes, 1958-2015



CDC's Division of Diabetes Translation. United States Diabetes Surveillance System available at <http://www.cdc.gov/diabetes/data>



It's not just fat people who get type 2 diabetes

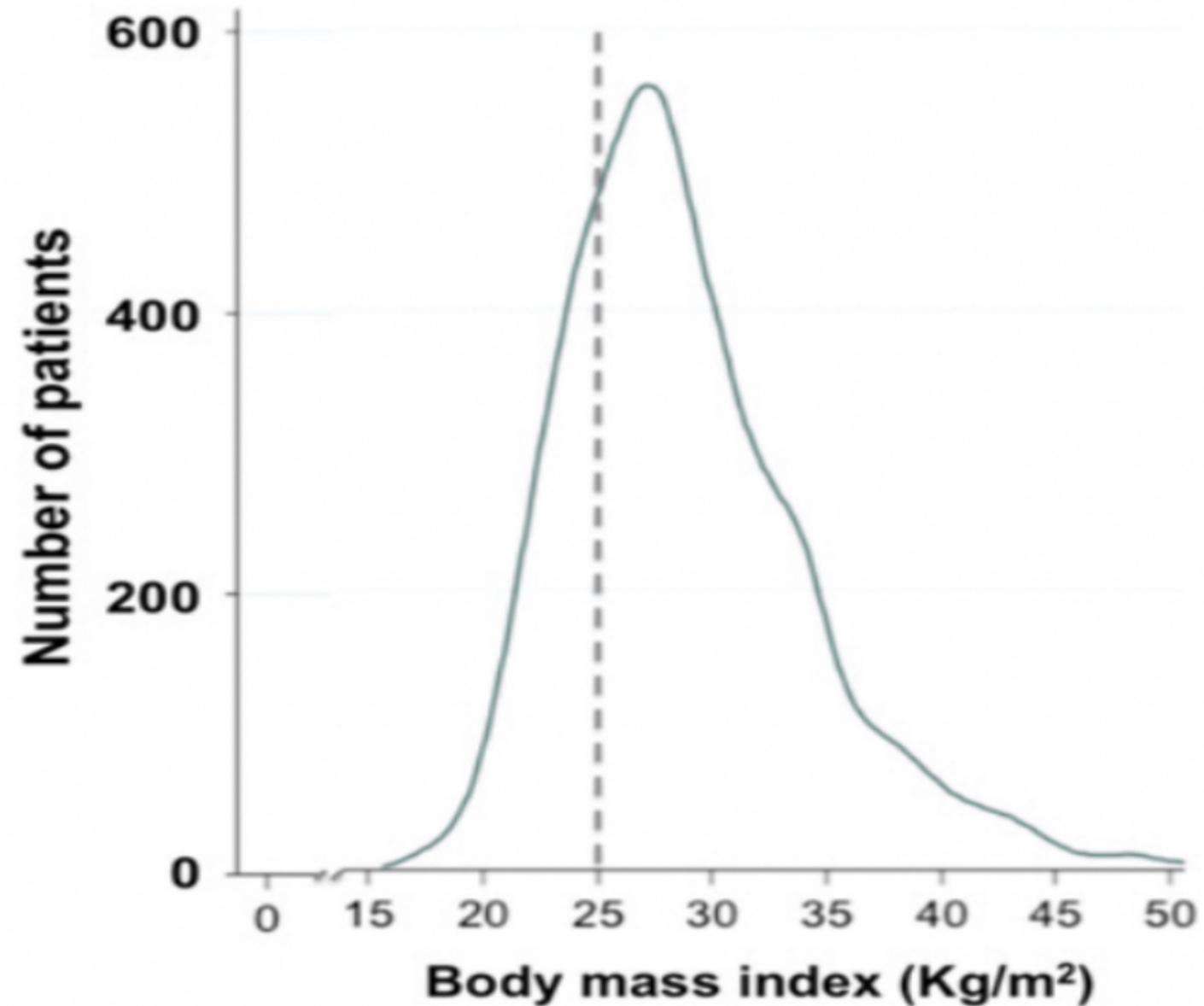
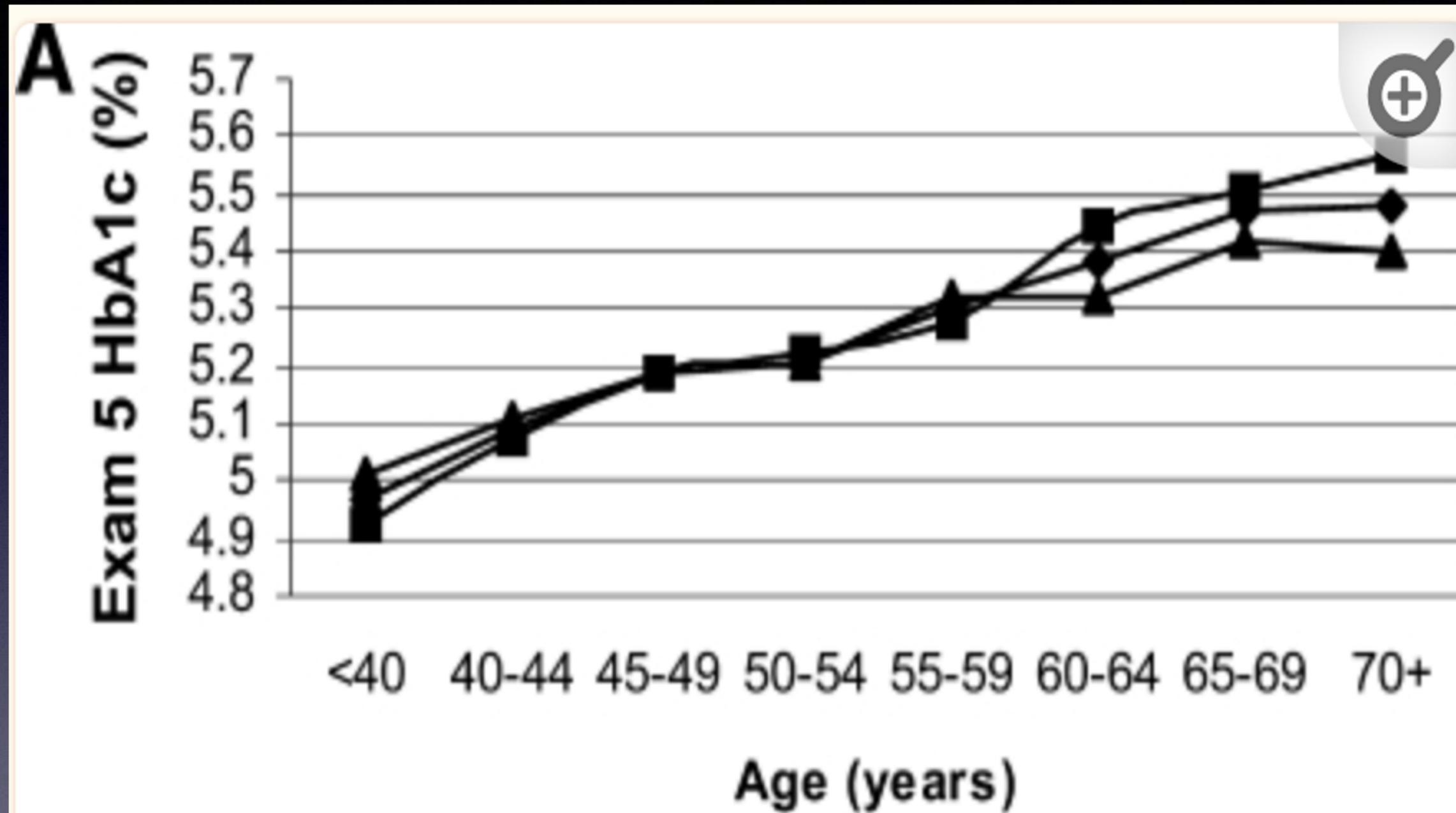


Figure 1 Population BMI distribution frequency plot for the entire 1977-1991 UKPDS cohort with newly diagnosed diabetes



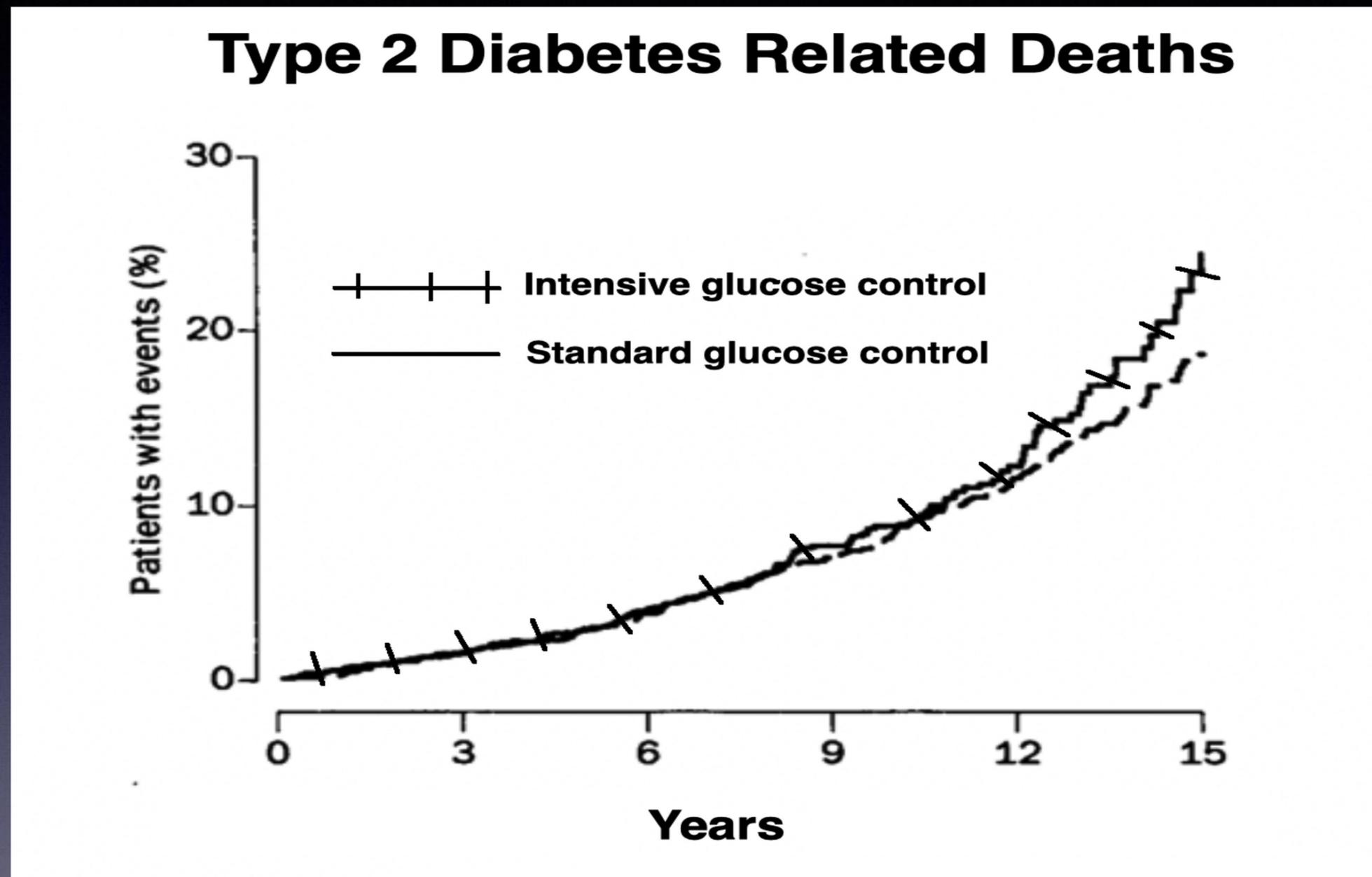
Is Type 2 Diabetes Like Gray Hair?



Pani, Lydie N., Leslie Korenda, James B. Meigs, Cynthia Driver, Shadi Chamany, Caroline S. Fox, Lisa Sullivan, Ralph B. D'Agostino, and David M. Nathan. "Effect of Aging on A1C Levels in Individuals Without Diabetes." *Diabetes Care* 31, no. 10 (October 1, 2008): 1991–96. <https://doi.org/10.2337/dc08-0577>. <https://ncbi.nlm.nih.gov/pmc/articles/PMC2551641/>



Do the drugs at least work?



“Intensive Blood-Glucose Control with Sulphonylureas or Insulin Compared with Conventional Treatment and Risk of Complications in Patients with Type 2 Diabetes (UKPDS 33).” *The Lancet* 352, no. 9131 (September 1998): 837–53. [https://doi.org/10.1016/S0140-6736\(98\)07019-6](https://doi.org/10.1016/S0140-6736(98)07019-6).

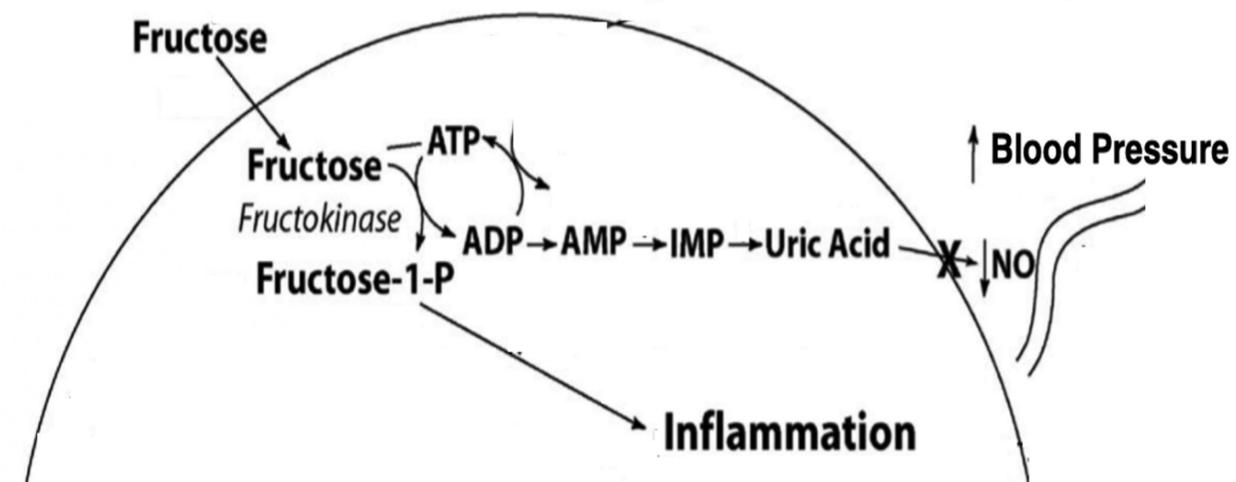


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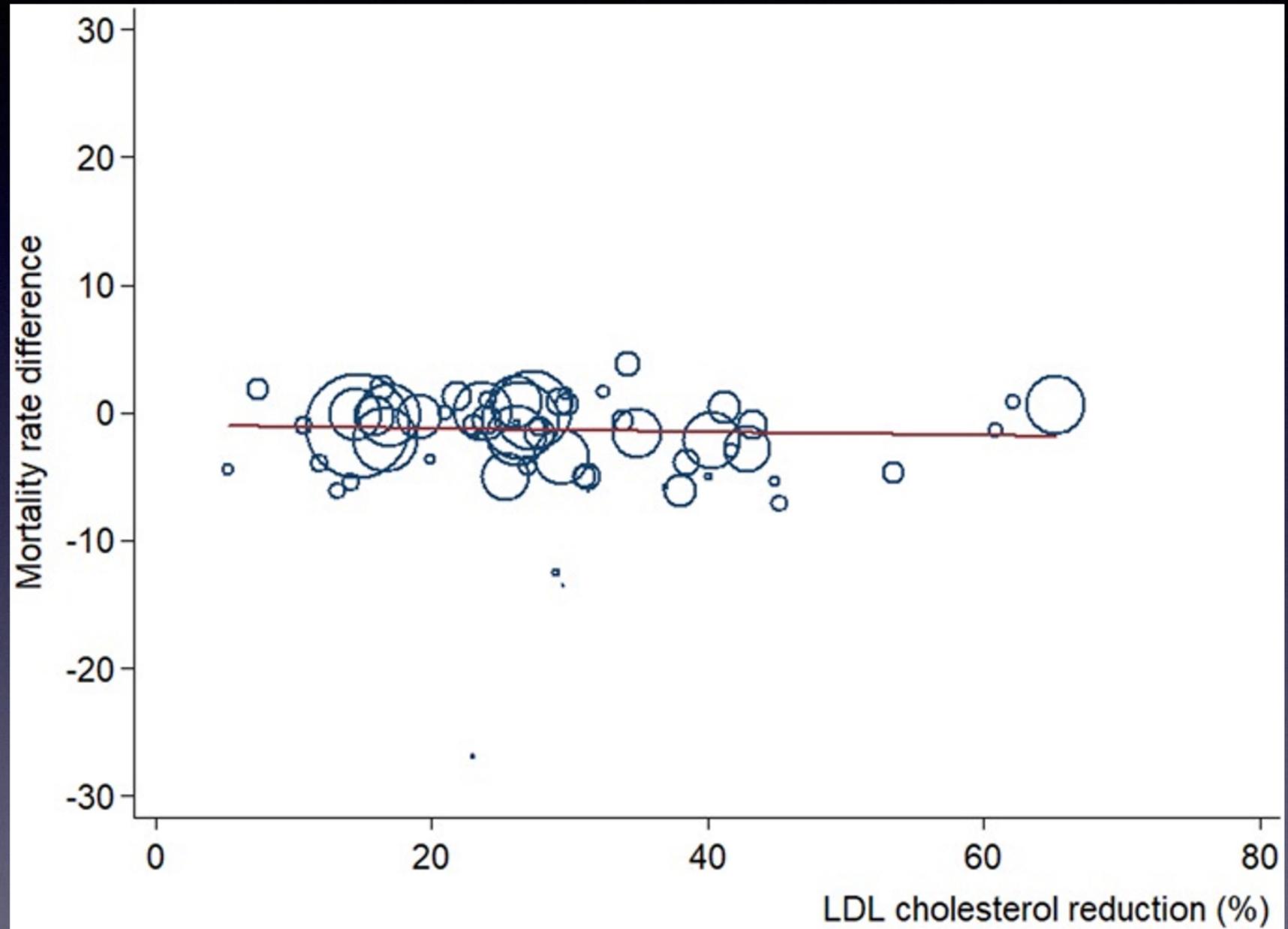
Hypertension- 'Avoid salt and lose weight'



Effects of Fructose on Nitric Oxide and Blood Pressure



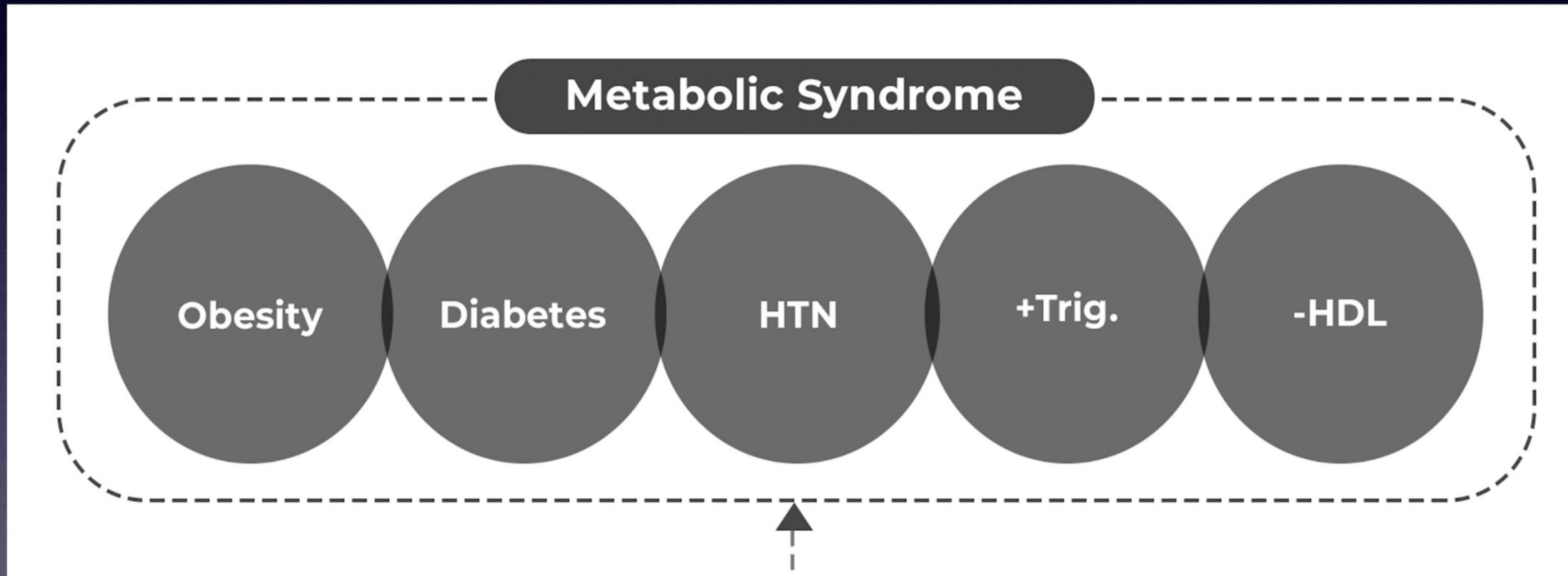
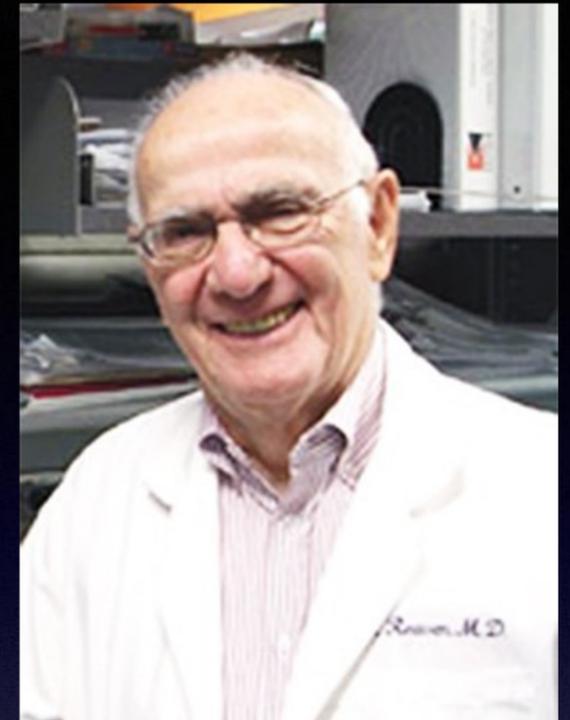
Effect of statins, PCSK9 inhibitors & ezetimibe on all cause mortality.



Ennezat, Pierre Vladimir, Raphaëlle-Ashley Guerbaai, Sylvestre Maréchaux, Thierry H. Le Jemtel, and Patrice François. "Extent of Low-Density Lipoprotein Cholesterol Reduction and All-Cause and Cardiovascular Mortality Benefit: A Systematic Review and Meta-Analysis." *Journal of Cardiovascular Pharmacology* 81, no. 1 (January 2023): 35–44. <https://doi.org/10.1097/FJC.0000000000001345>.



Gerald Reaven MD- Syndrome X



Abstract

Background: Several guidelines for cardiometabolic risk factor identification and management have been released in recent years, but there are no estimates of current prevalence of metabolic health among adults in the United States. We estimated the proportion of American adults with optimal cardiometabolic health, using different guidelines.

Methods: Data from the National Health and Nutrition Examination Survey 2009–2016 were analyzed ($n=8721$). Using the most recent guidelines, metabolic health was defined as having optimal levels of waist circumference (WC <102/88 cm for men/women), glucose (fasting glucose <100 mg/dL and hemoglobin A1c <5.7%), blood pressure (systolic <120 and diastolic <80 mmHg), triglycerides (<150 mg/dL), and high-density lipoprotein cholesterol ($\geq 40/50$ mg/dL for men/women), and not taking any related medication.

Results: Changing from ATP III (Adult Treatment Panel III) guidelines to more recent cut points decreased the proportion of metabolically healthy Americans from 19.9% (95% confidence interval [CI]: 18.3–21.5) to 12.2% (95% CI: 10.9–13.6). Dropping WC from the definition increased the percentage of adults with optimal metabolic health to 17.6%. Characteristics associated with greater prevalence of metabolic health were female gender, youth, more education, never smoking, practicing vigorous physical activity, and low body mass index. Less than one-third of normal weight adults were metabolically healthy and the prevalence decreased to 8.0% and 0.5% in overweight and obese individuals, respectively.

Conclusions: Prevalence of metabolic health in American adults is alarmingly low, even in normal weight individuals. The large number of people not achieving optimal levels of risk factors, even in low-risk groups, has serious implications for public health.

Araújo, Joana, Jianwen Cai, and June Stevens. "Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009–2016." *Metabolic Syndrome and Related Disorders* 17, no. 1 (February 2019): 46–52. <https://doi.org/10.1089/met.2018.0105>.



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TOR

Grow

Repair

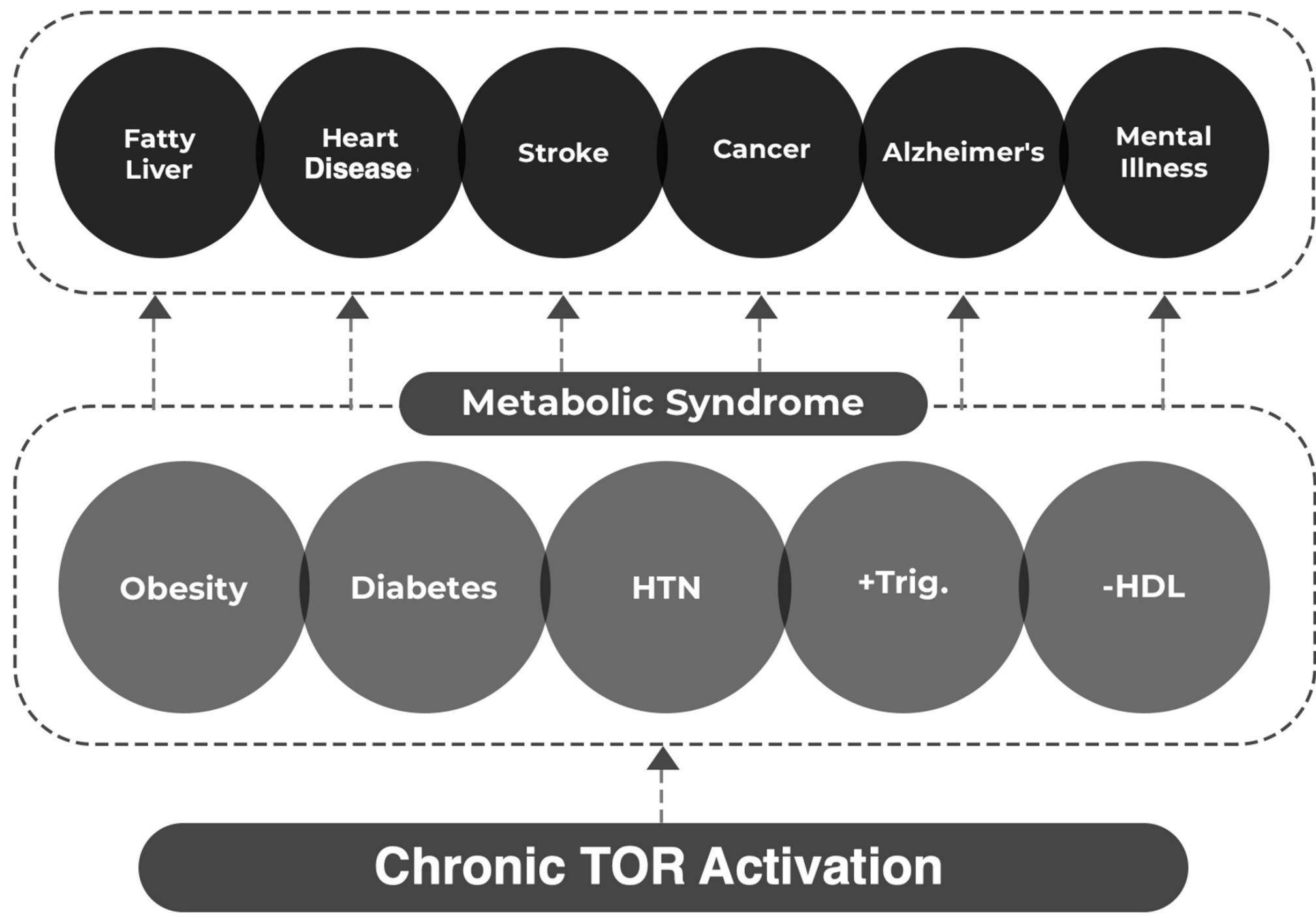


yes

Nutrients?

no

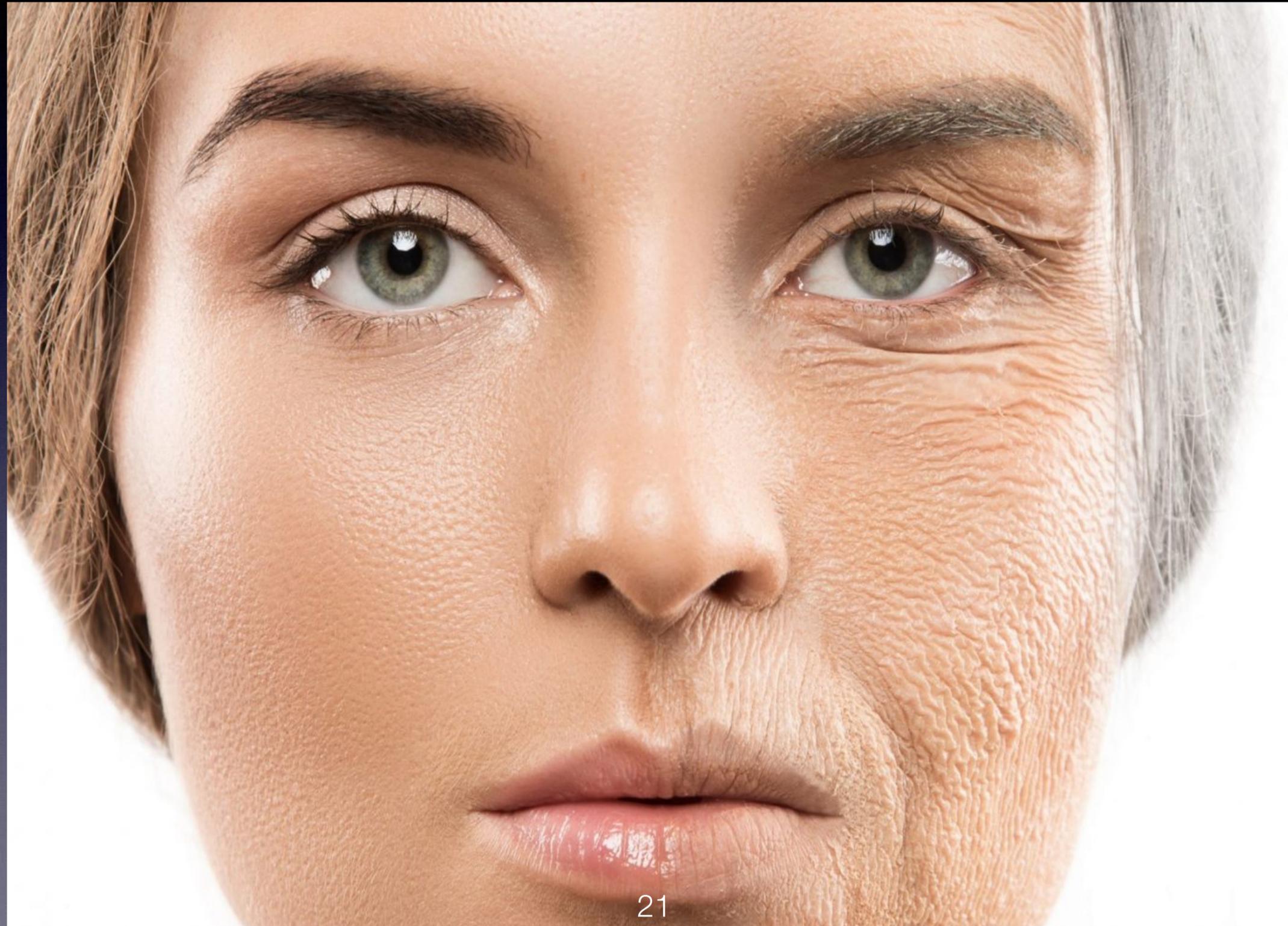




What happens when we turn down TOR?

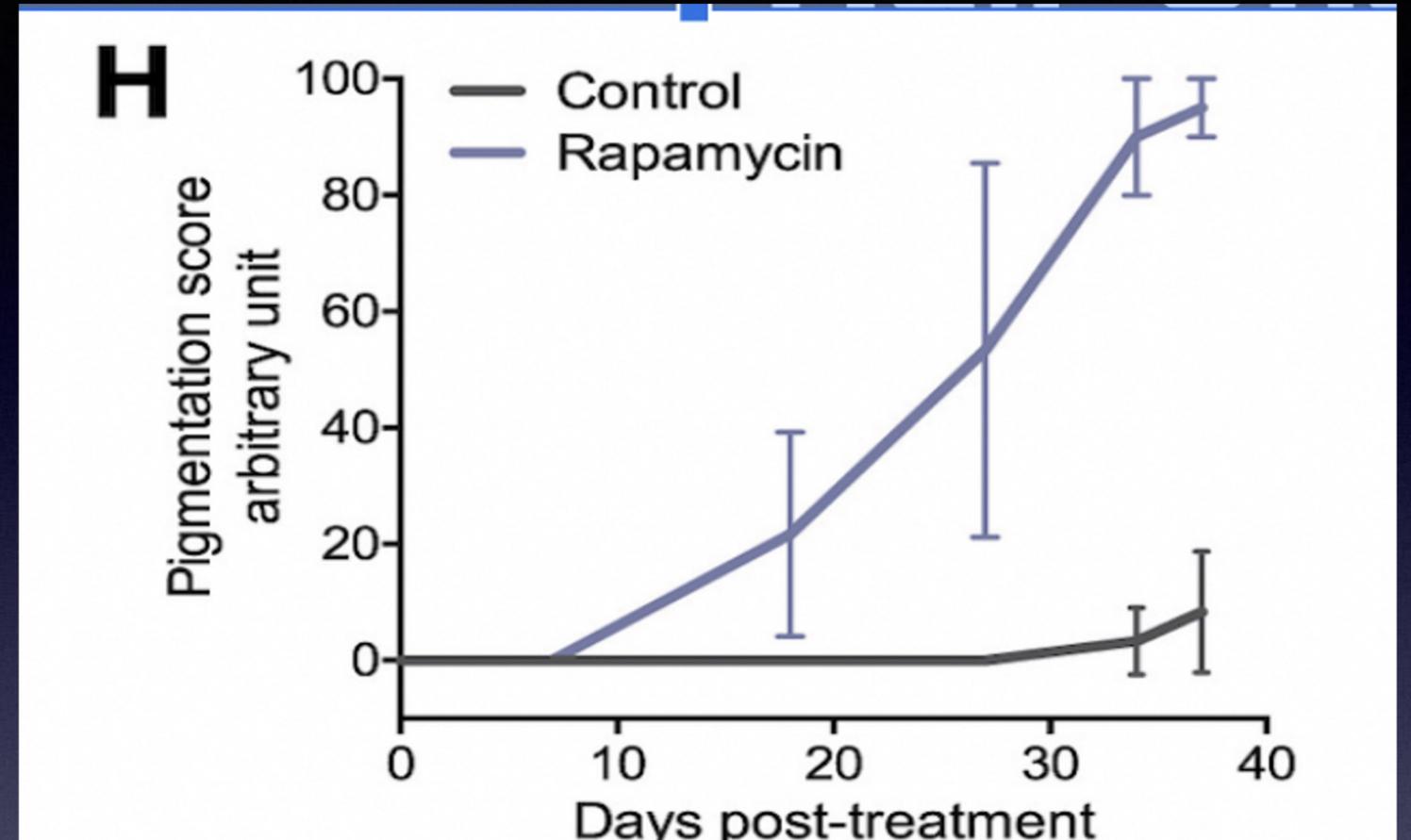
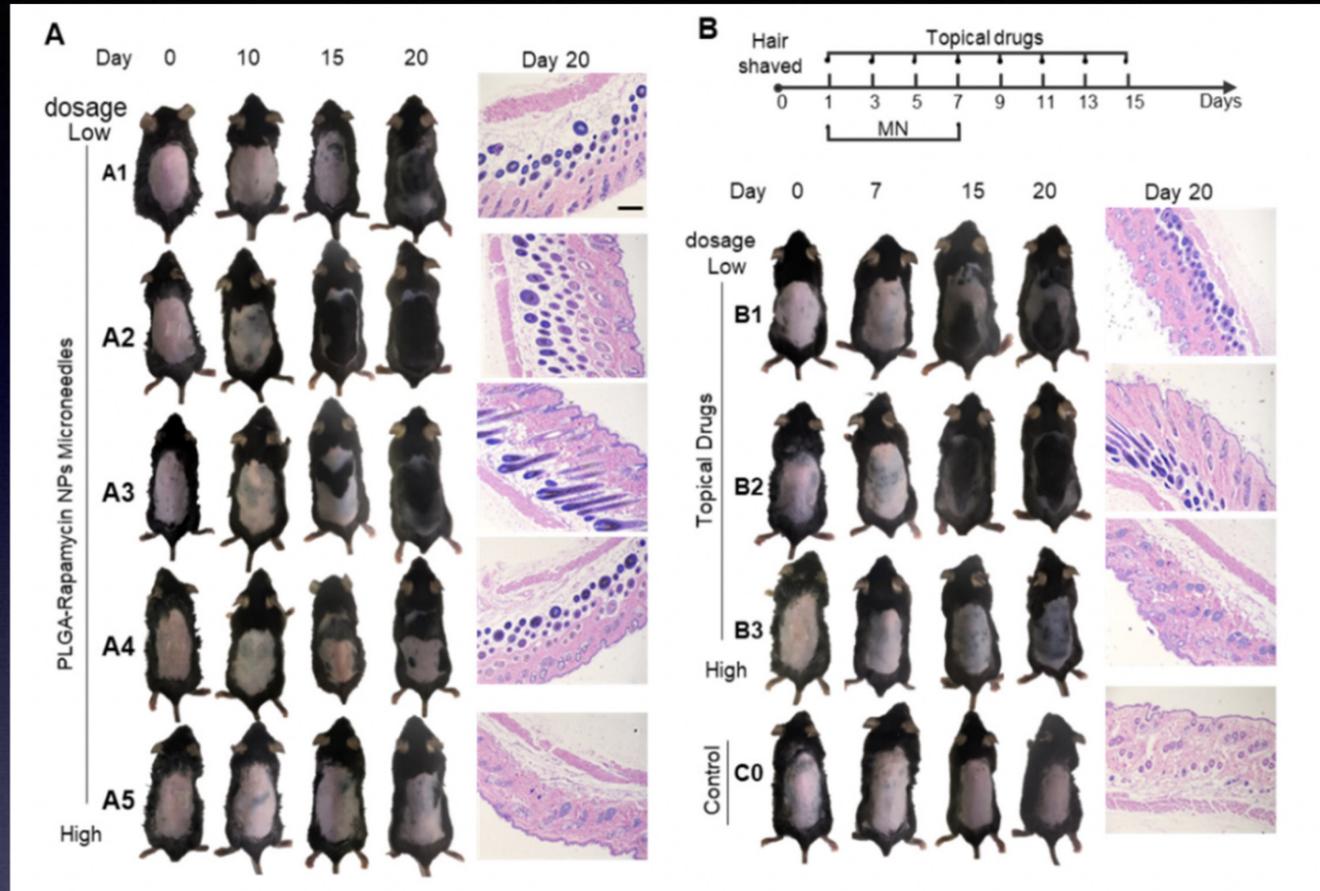


1- Phenotypes of Aging



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Hair Changes



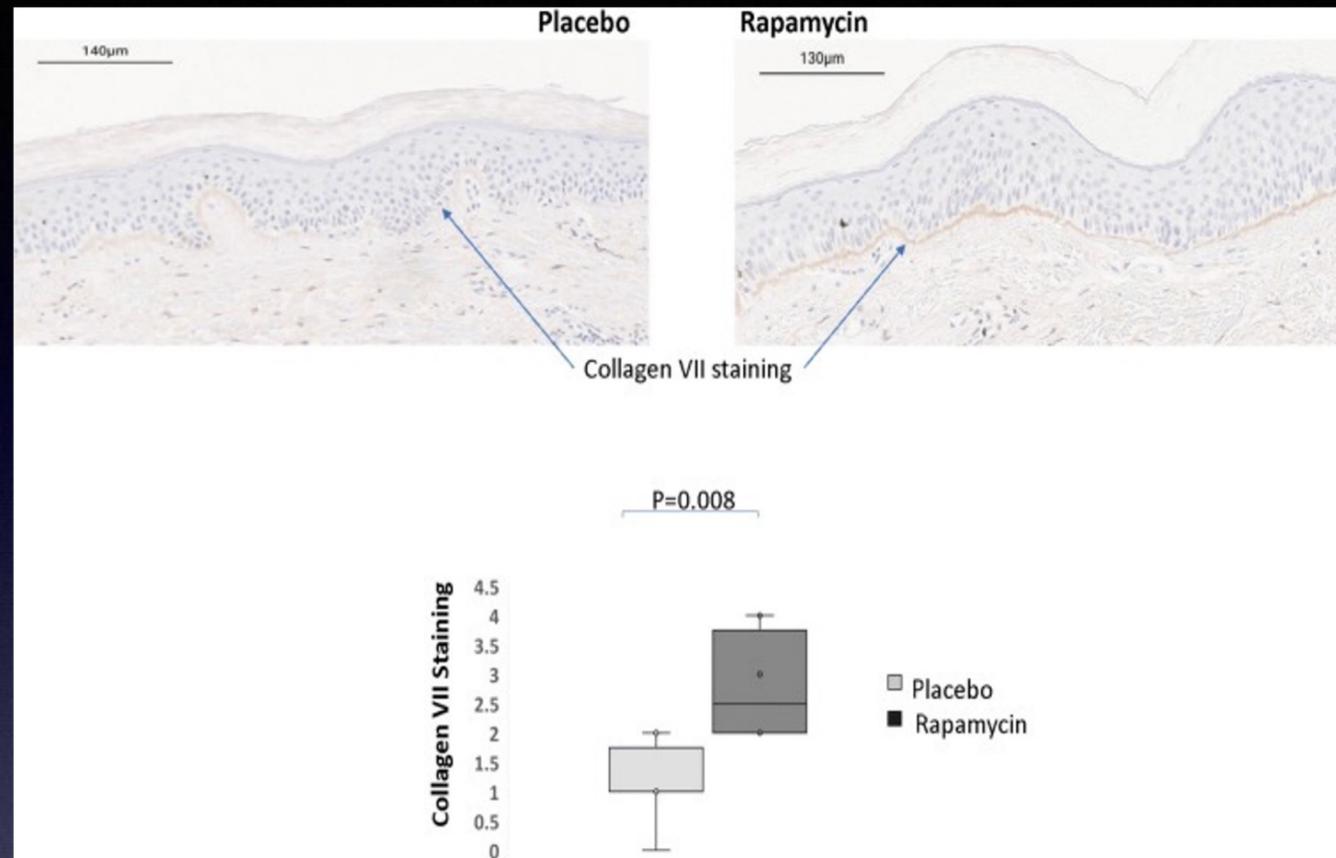
‘Rapamycin (1.6 mM) induces hair regeneration. Male mice were shaved on postnatal day 43 and treated topically every other day. Photographs were taken on day 37 post-treatment.’

Lin, Yali, Ruomei Shao, Tong Xiao, and Shuqing Sun. “Promotion of Hair Regrowth by Transdermal Dissolvable Microneedles Loaded with Rapamycin and Epigallocatechin Gallate Nanoparticles.” *Pharmaceutics* 14, no. 7 (July 4, 2022): 1404. <https://doi.org/10.3390/pharmaceutics14071404>.

Chai, Min, Meisheng Jiang, Laurent Vergnes, Xudong Fu, Stéphanie C. de Barros, Ngan B. Doan, Wilson Huang, et al. “Stimulation of Hair Growth by Small Molecules That Activate Autophagy.” *Cell Reports* 27, no. 12 (June 2019): 3413-3421.e3. <https://doi.org/10.1016/j.celrep.2019.05.070>.



Skin Changes

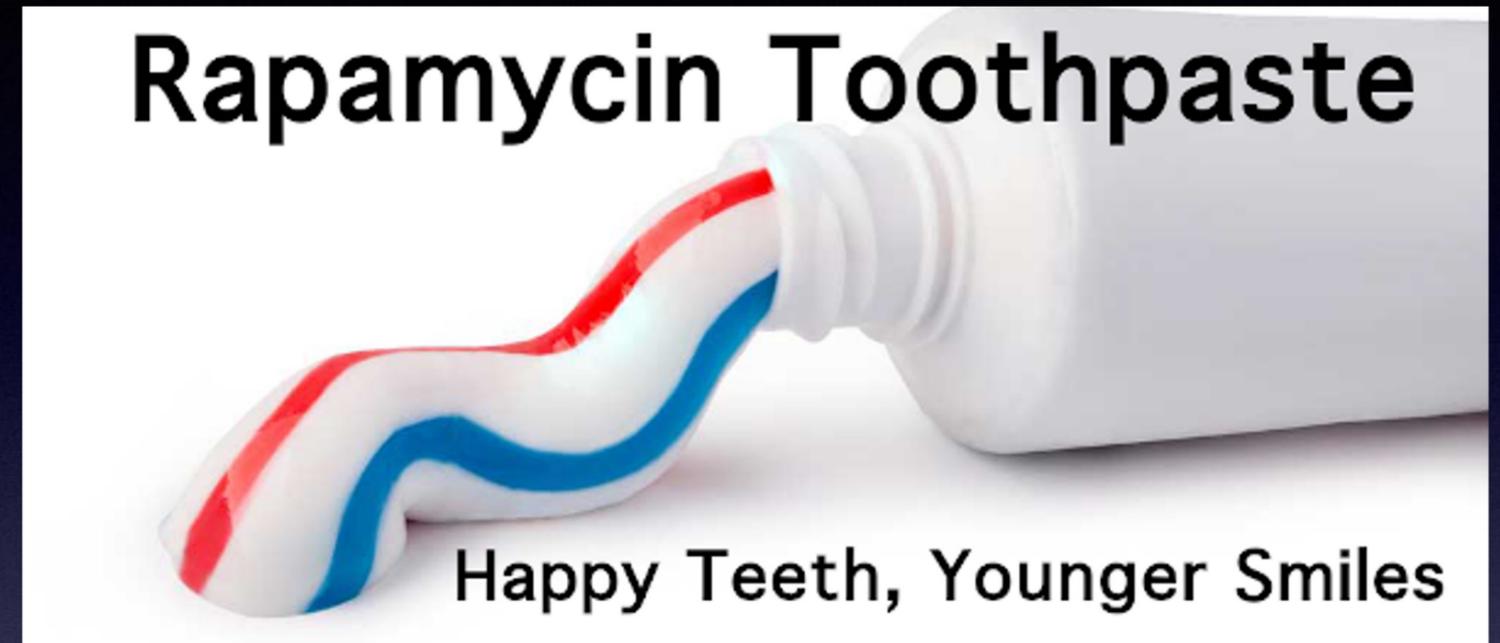
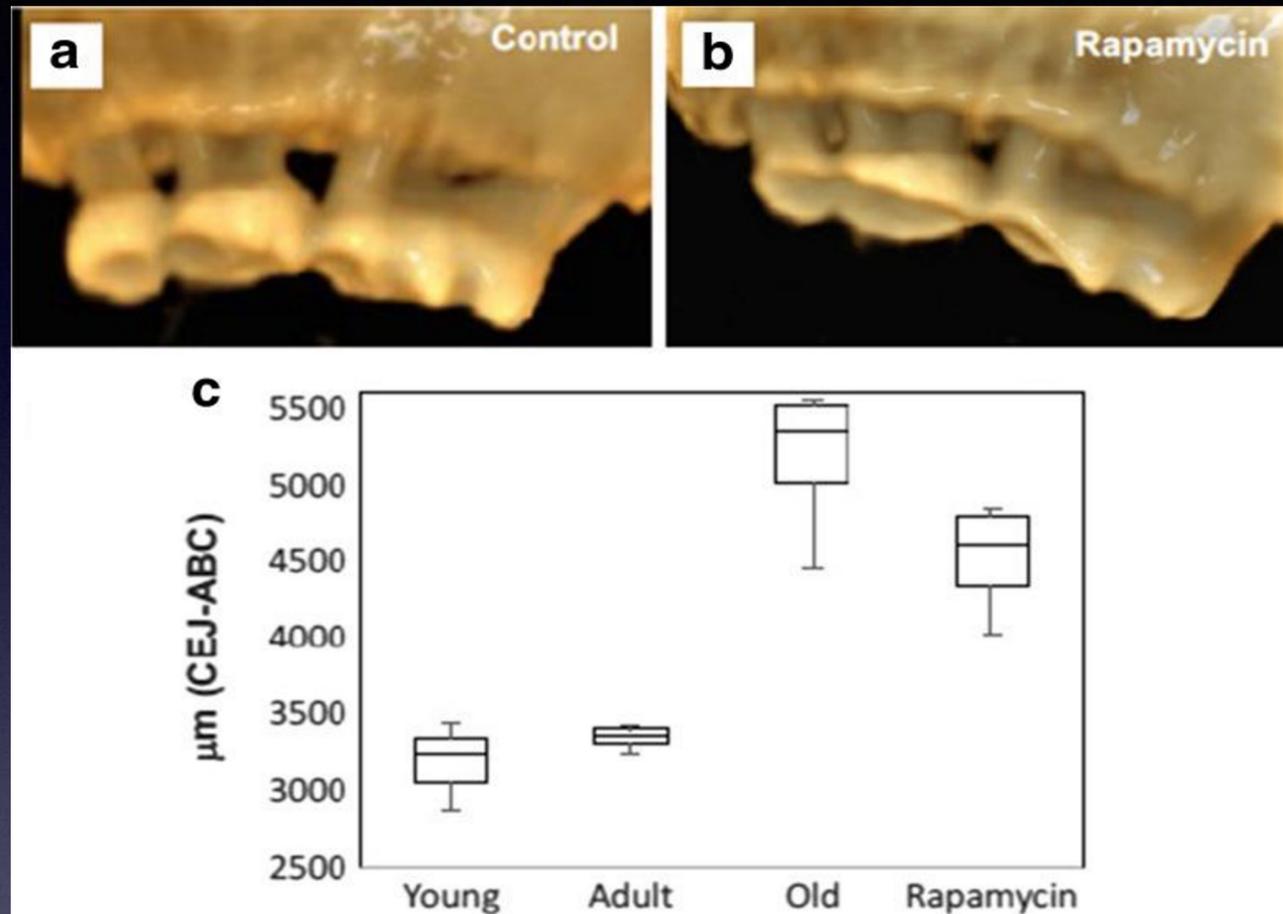


‘Topical rapamycin increases collagen VII in the basement membrane of human skin. Biopsies from patients (n = 6), placebo- and rapamycin-treated skin stained using antibodies specific for the collagen VII protein’

Chung, Christina Lee, Ibiyonu Lawrence, Melissa Hoffman, Dareen Elgindi, Kumar Nadhan, Manali Potnis, Annie Jin, et al. “Topical Rapamycin Reduces Markers of Senescence and Aging in Human Skin: An Exploratory, Prospective, Randomized Trial.” *GeroScience* 41, no. 6 (December 2019): 861–69. <https://doi.org/10.1007/s11357-019-00113-y>.



Periodontal Disease

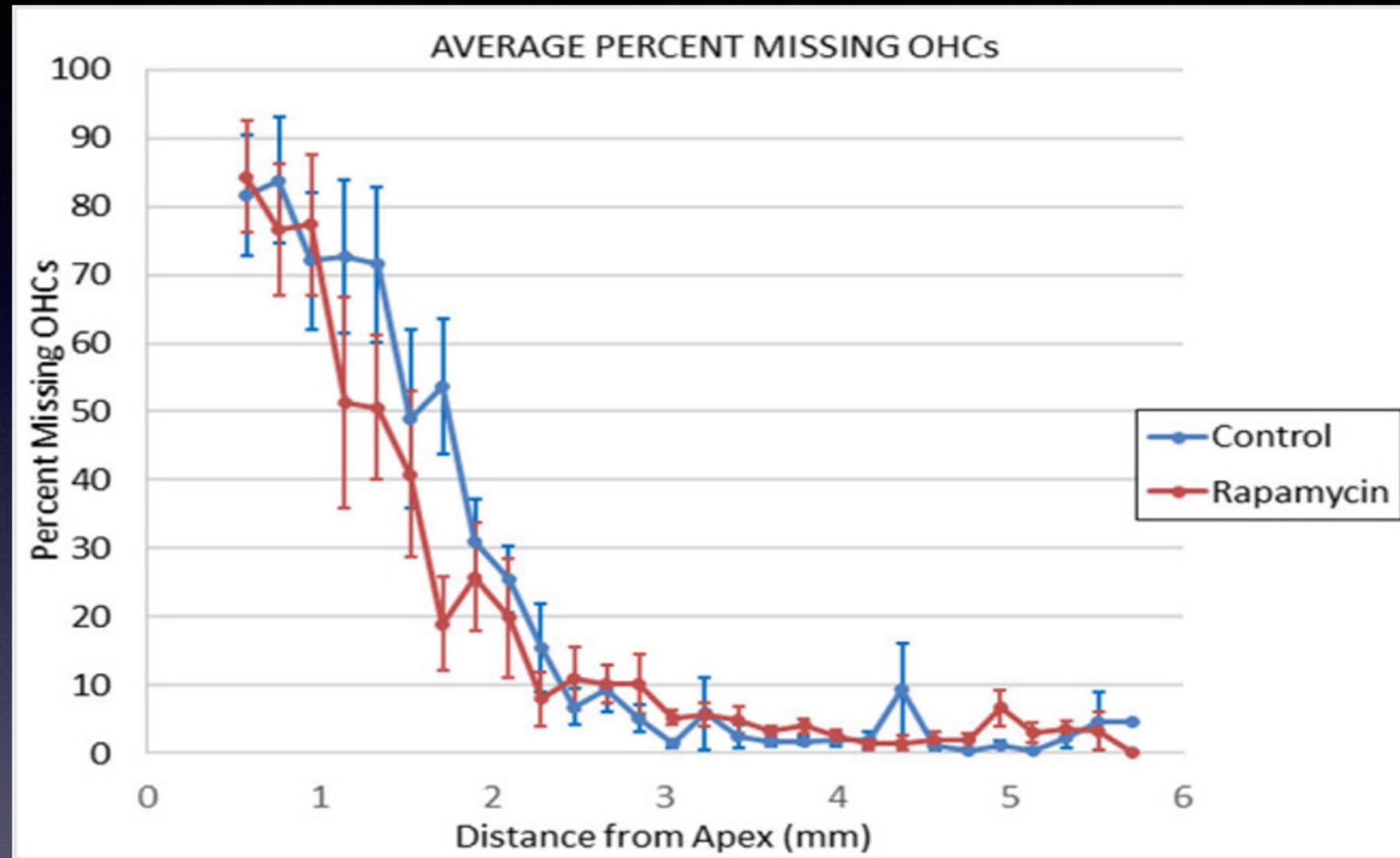


‘A single 8 week treatment with rapamycin attenuates alveolar bone loss in aged C57BL/6JNia mice.’

An, Jonathan Y., Ellen K. Quarles, Surapat Mekvanich, Alex Kang, Anthony Liu, Danielle Santos, Richard A. Miller, Peter S. Rabinovitch, Timothy C. Cox, and Matt Kaeberlein. “Rapamycin Treatment Attenuates Age-Associated Periodontitis in Mice.” *GeroScience* 39, no. 4 (August 2017): 457–63. <https://doi.org/10.1007/s11357-017-9994-6>.



Hearing Loss



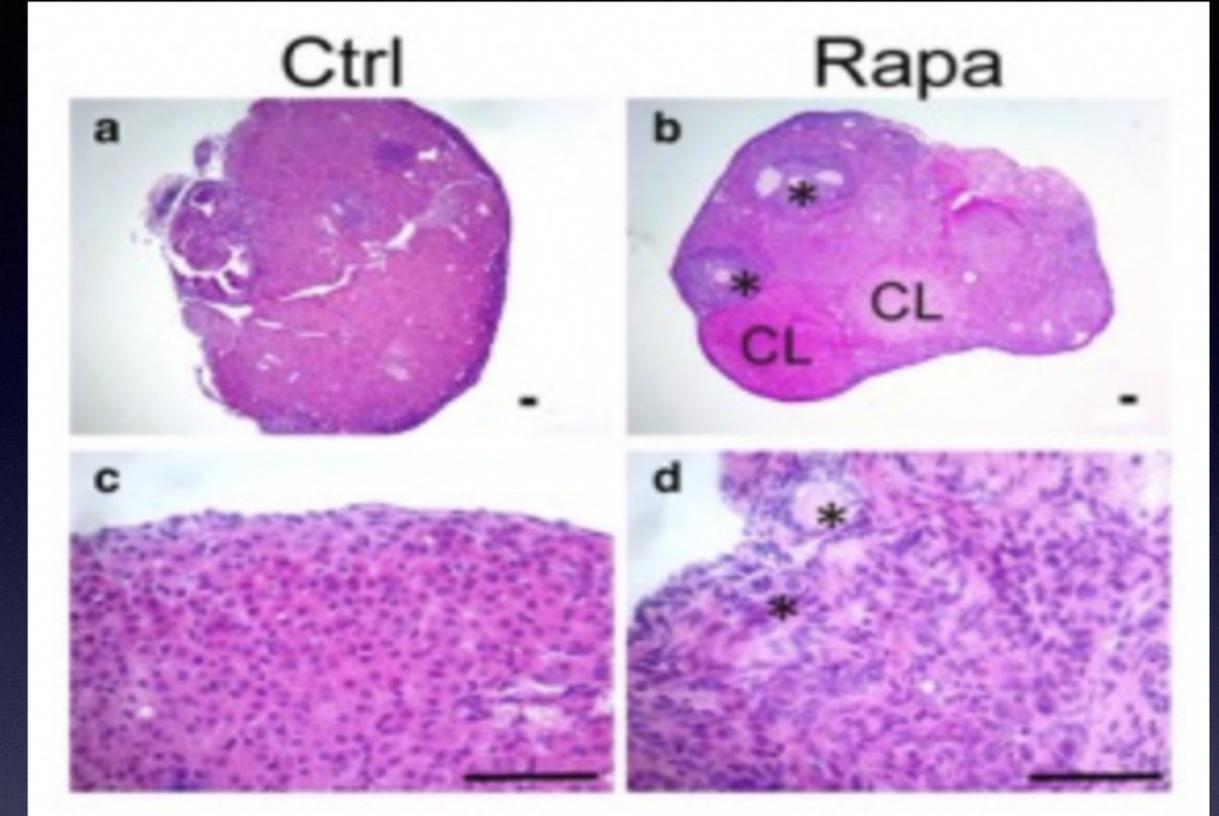
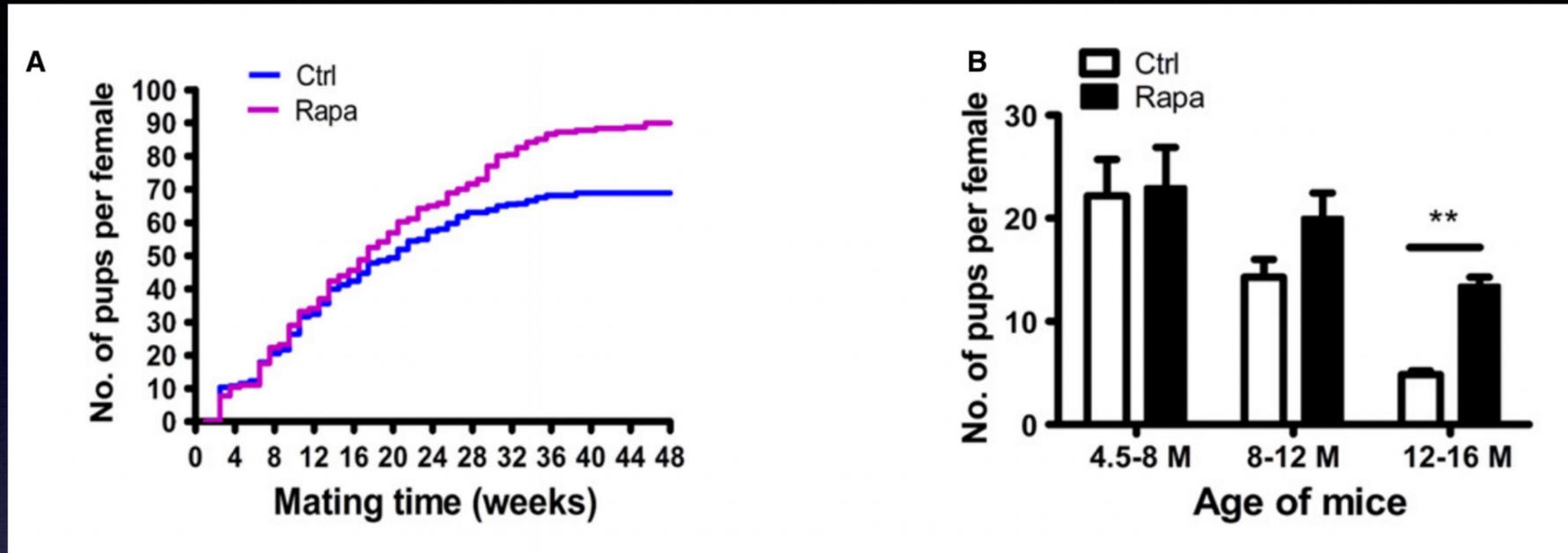
‘Cytochleograms comparing the mean outer hair cell loss across the cochlea spiral at 24 months of age in mice from the group that had rapamycin added to diet at 14 months of age (red line) vs. the control diet’

Liu, Hongyan, Feitian Li, Xuanyi Li, Qianru Wu, and Chunfu Dai. “Rapamycin Ameliorates Age-Related Hearing Loss in C57BL/6J Mice by Enhancing Autophagy in the SGNs.” *Neuroscience Letters* 772 (February 2022): 136493.

<https://doi.org/10.1016/j.neulet.2022.136493>.



Ovarian Failure



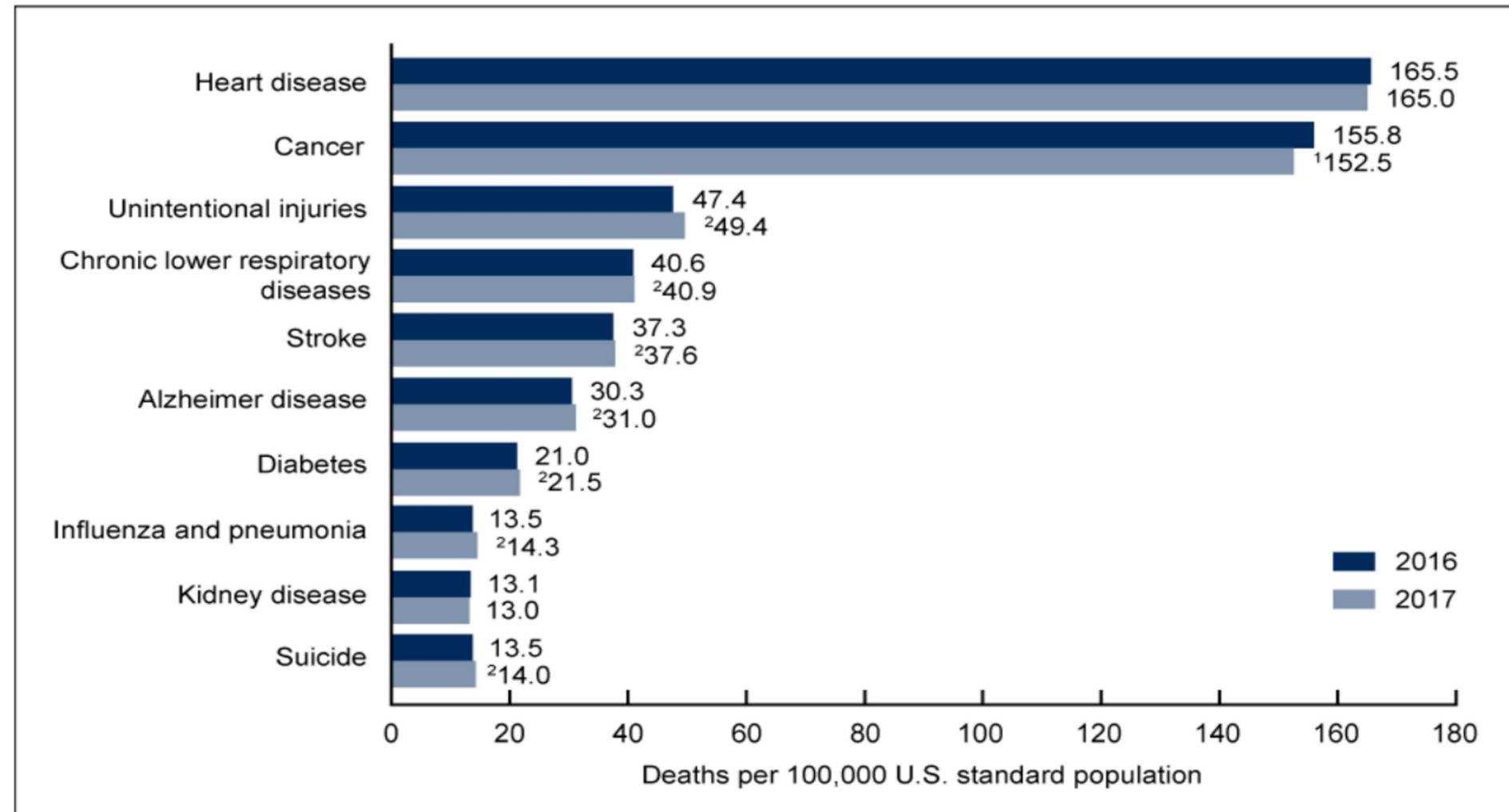
‘Prolongation of fertility in aging females after Rapa treatment (n = 24 for the control group, n = 23 for the Rapa-treated group). (A) Comparison of the cumulative numbers of pups per female in control (blue) and Rapa-treated (purple) groups.’

Dou, Xiaowei, Yan Sun, Jiazhao Li, Jing Zhang, Dandan Hao, Wenwen Liu, Rui Wu, Feifei Kong, Xiaoxu Peng, and Jing Li. “Short-Term Rapamycin Treatment Increases Ovarian Lifespan in Young and Middle-Aged Female Mice.” *Ageing Cell* 16, no. 4 (August 2017): 825–36. <https://doi.org/10.1111/acel.12617>.



2- Diseases of Longevity

Figure 4. Age-adjusted death rates for the 10 leading causes of death: United States, 2016 and 2017



¹Statistically significant decrease in age-adjusted death rate from 2016 to 2017 ($p < 0.05$).

²Statistically significant increase in age-adjusted death rate from 2016 to 2017 ($p < 0.05$).

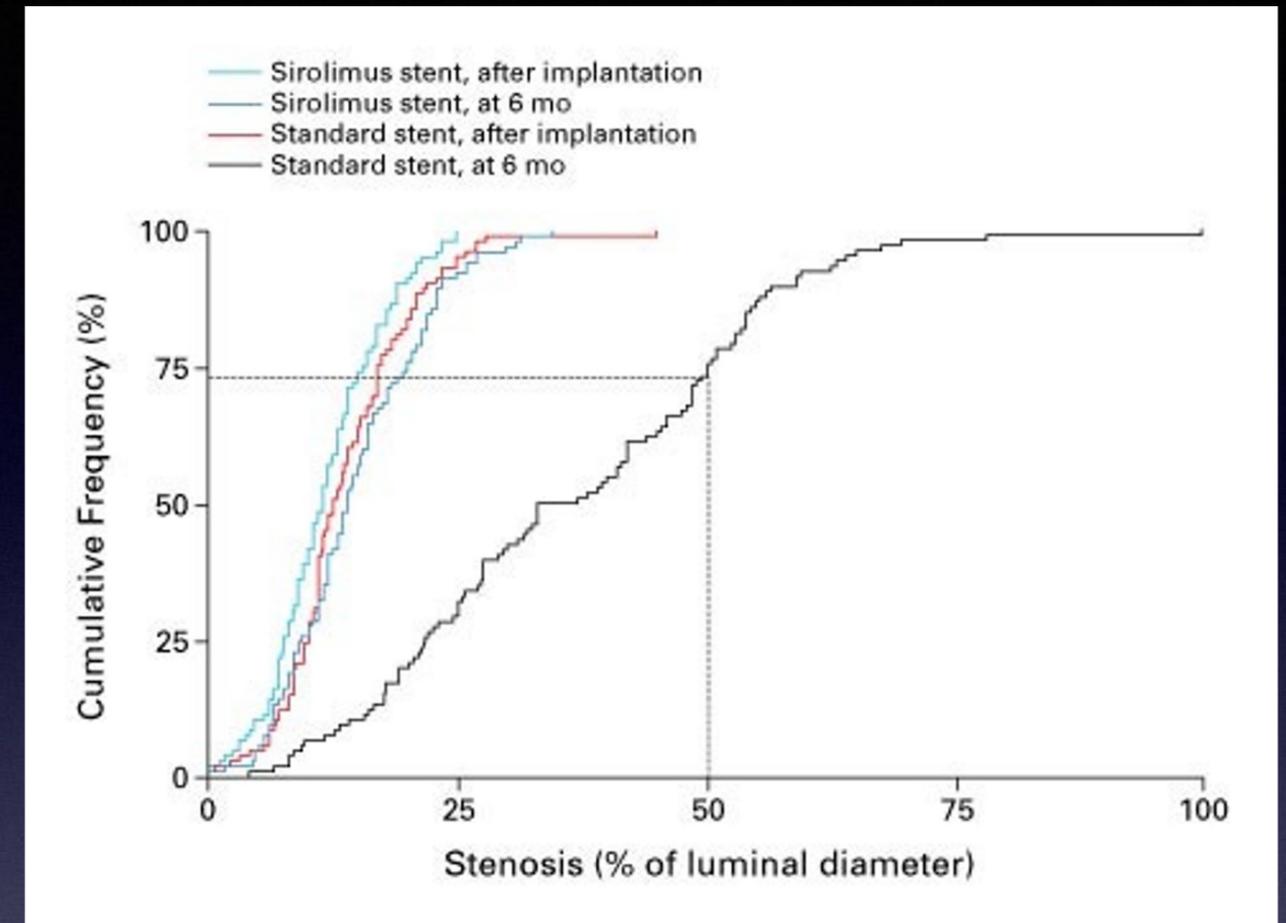
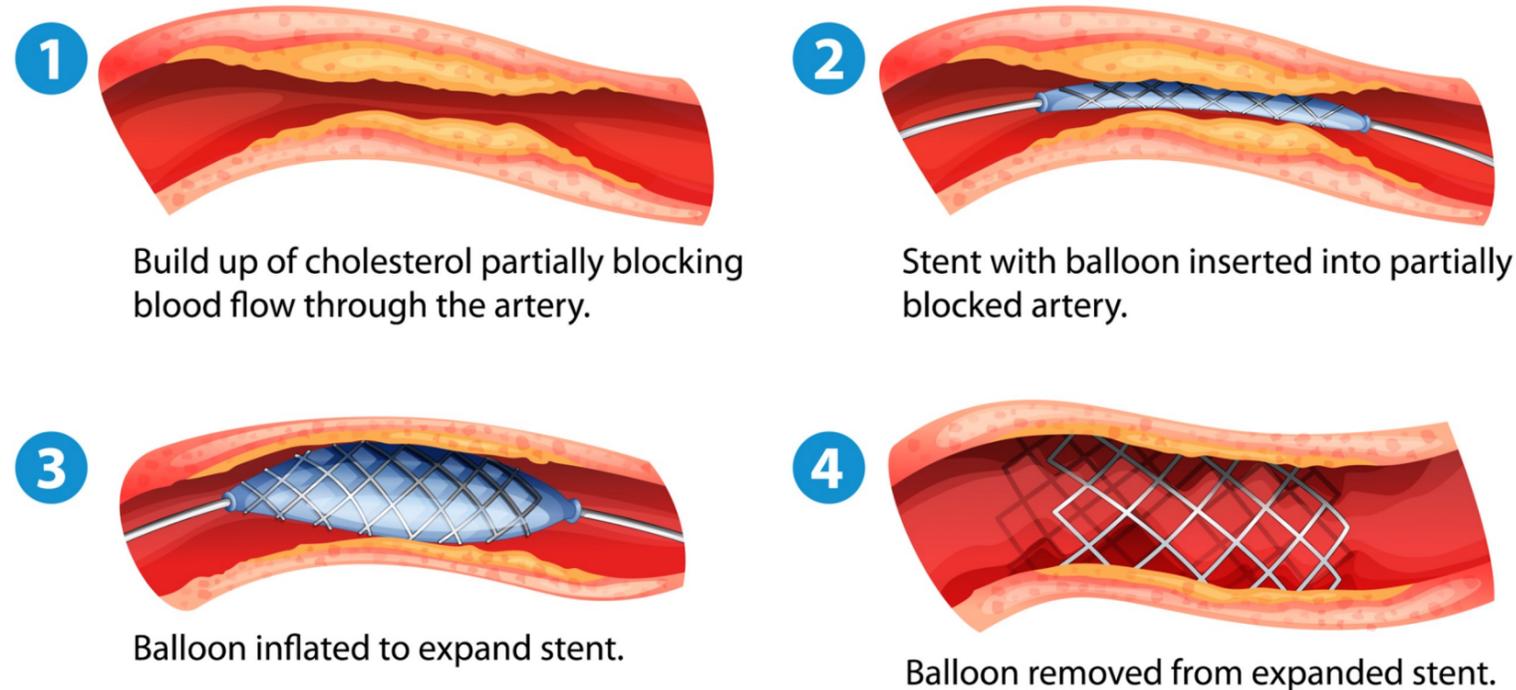
NOTES: A total of 2,813,503 resident deaths were registered in the United States in 2017. The 10 leading causes accounted for 74.0% of all deaths in the United States in 2017. Causes of death are ranked according to number of deaths. Rankings for 2016 data are not shown. Data table for Figure 4 includes the number of deaths for leading causes. Access data table for Figure 4 at: https://www.cdc.gov/nchs/data/databriefs/db328_tables-508.pdf#4.

SOURCE: NCHS, National Vital Statistics System, Mortality.



Cardiovascular Disease (human)

Stent with Balloon Angioplasty



Morice, Marie-Claude, Patrick W. Serruys, J. Eduardo Sousa, Jean Fajadet, Ernesto Ban Hayashi, Marco Perin, Antonio Colombo, et al. "A Randomized Comparison of a Sirolimus-Eluting Stent with a Standard Stent for Coronary Revascularization." *New England Journal of Medicine* 346, no. 23 (June 6, 2002): 1773–80.
<https://doi.org/10.1056/NEJMoa012843>.

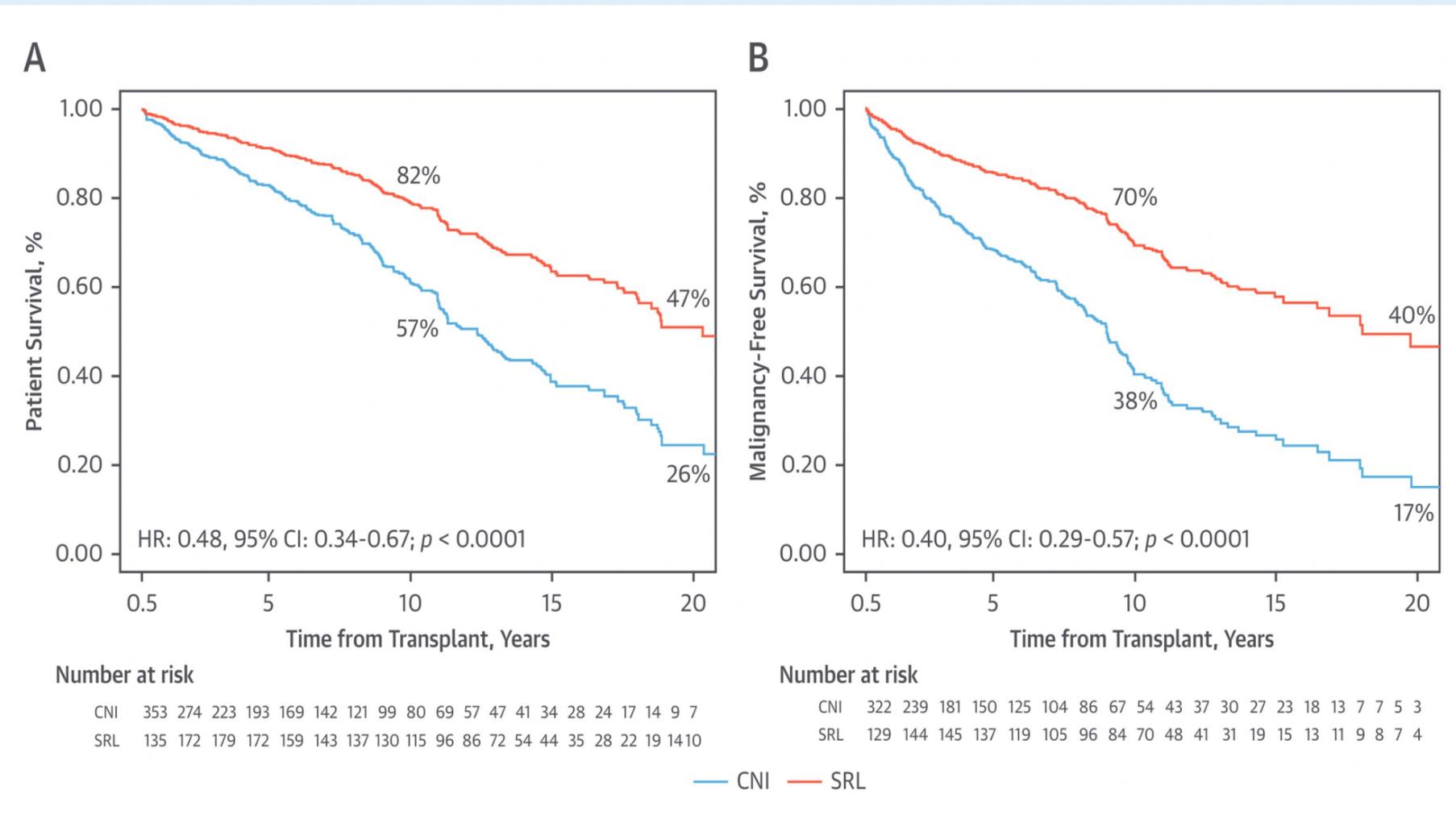
CYPHER Sirolimus-Eluting Coronary Stent Integrated Delivery System - P20026 Apr 2003

SLENDER Sirolimus-Eluting Coronary Stent Integrated Delivery System - P210014 Dec 2021



Cancer (human)

FIGURE 5 Patient Survival and Malignancy-Free Survival Probabilities in HT Recipients Comparing Patients Converted to SRL With Those Maintained on CNI Therapy

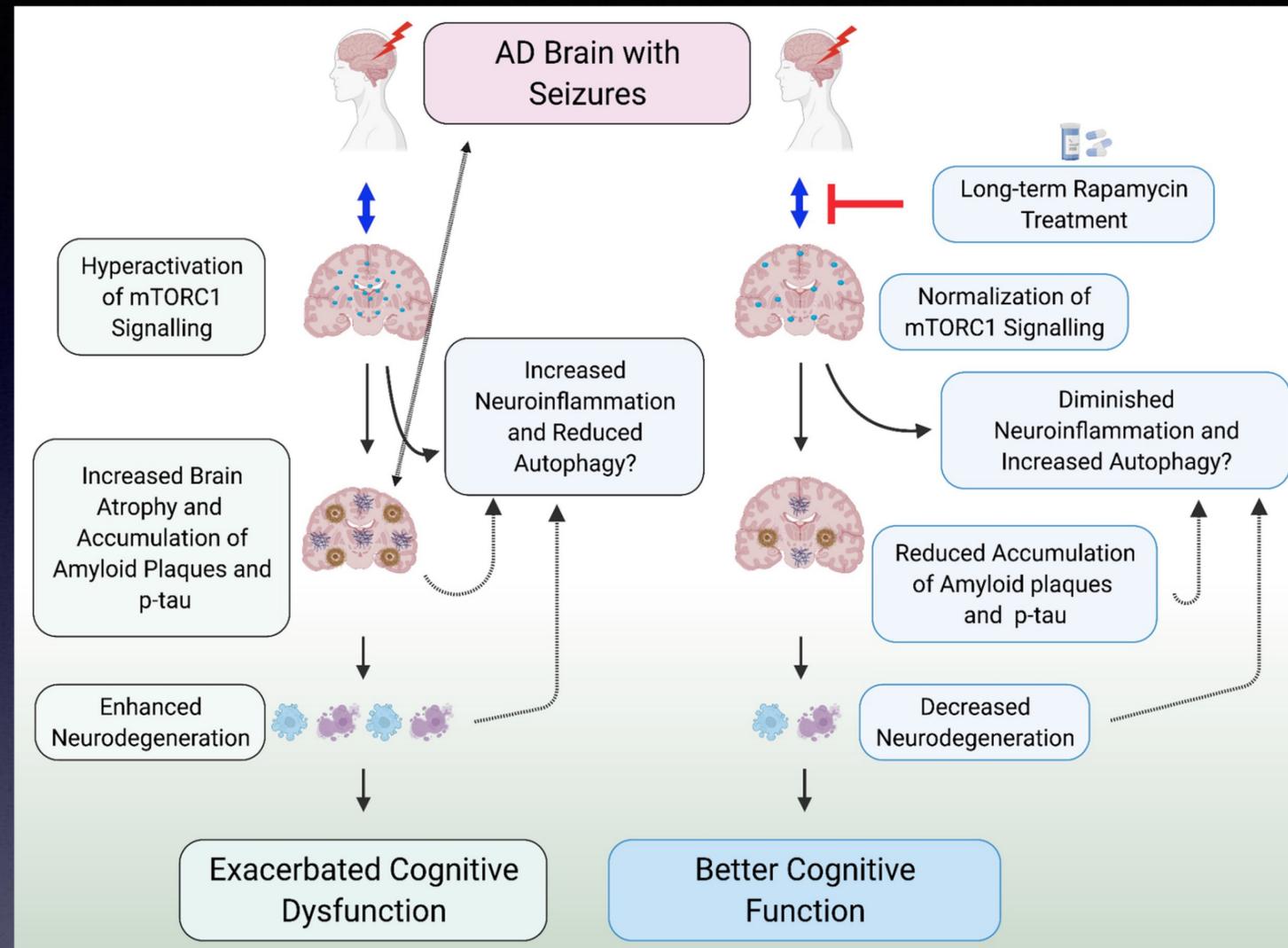
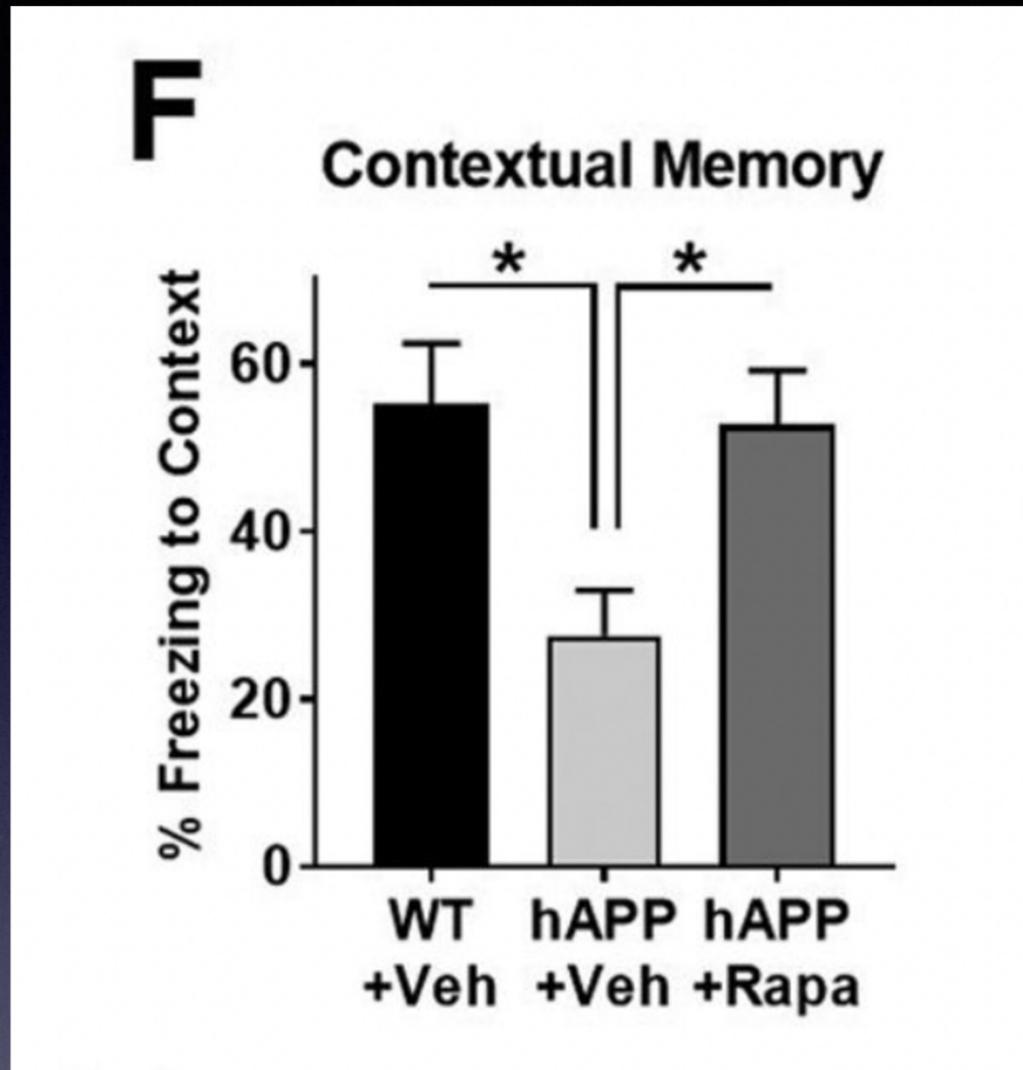


‘(A) Both patient survival and (B) malignancy-free survival were significantly increased among patients who were treated with Rapa(red) compared with CNI maintenance therapy (blue).’

Asleh, Rabea, Alfredo L. Clavell, Naveen L. Pereira, Byron Smith, Alexandros Briasoulis, Hilmi Alnsasra, Walter K. Kremers, et al. “Incidence of Malignancies in Patients Treated With Sirolimus Following Heart Transplantation.” *Journal of the American College of Cardiology* 73, no. 21 (June 2019): 2676–88. <https://doi.org/10.1016/j.jacc.2019.03.499>.



Alzheimer's Disease



‘Hippocampal-dependent contextual memory impairment in 12-month-old hAPP(J20) mice [hAPP(J20) vs WT, $q(16) = 4.19, p = 0.024$] is negated by 2 months of rapamycin treatment [$q(16) = 3.93, p = 0.034$, hAPP(J20) vs hAPP(J20)1rapamycin].’

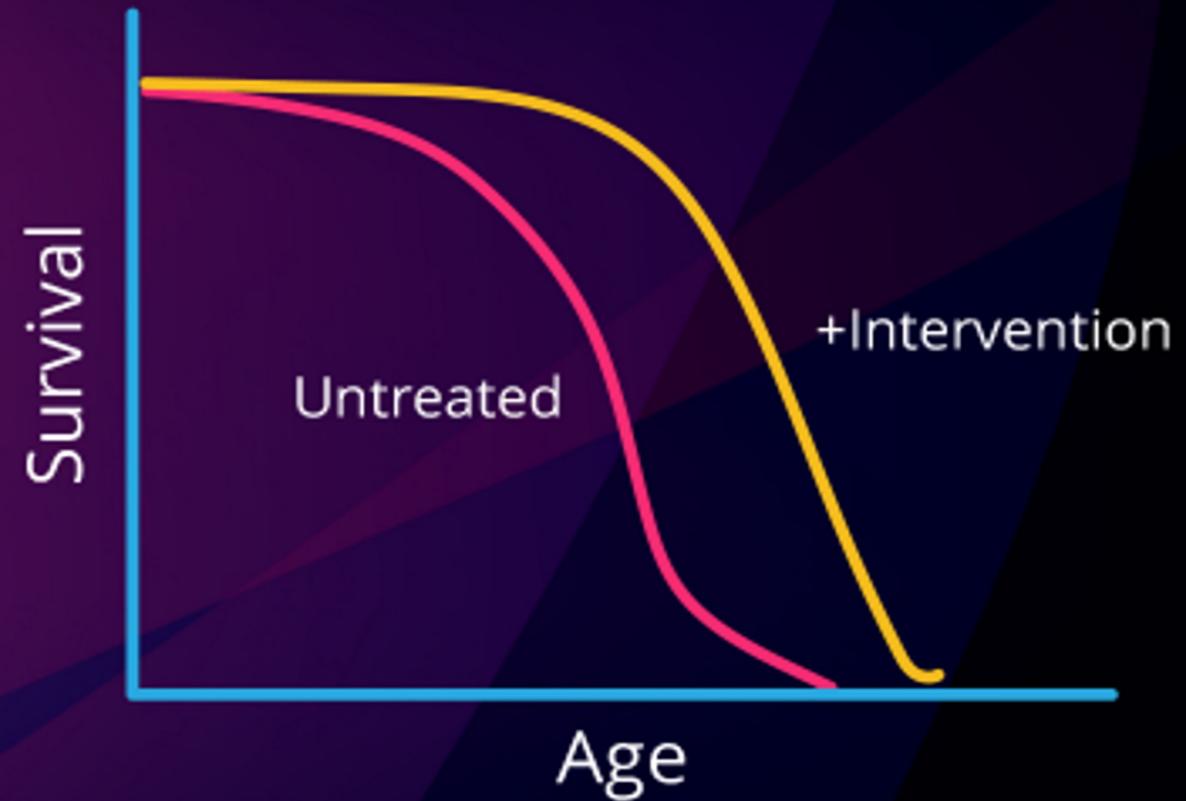
Shetty, Ashok K. “Can Rapamycin Slow down Memory Decline in Alzheimer’s Disease with Seizures?” *Brain* 145, no. 1 (March 29, 2022): 14–16. <https://doi.org/10.1093/brain/awab474>.

Van Skike, Candice E., Stacy A. Hussong, Stephen F. Hernandez, Andy Q. Banh, Nicholas DeRosa, and Veronica Galvan. “MTOR Attenuation with Rapamycin Reverses Neurovascular Uncoupling and Memory Deficits in Mice Modeling Alzheimer’s Disease.” *The Journal of Neuroscience* 41, no. 19 (May 12, 2021): 4305–20. <https://doi.org/10.1523/JNEUROSCI.2144-20.2021>.



3- Longevity Itself

Intervention
Testing
Program



Resveratrol, fish oil, curcumin, MCT oil, oxaloacetic acid, MitoQ, methylene blue, simvastatin, NR, fisetin, ashwagandha, green tea extract, and metformin

<https://www.nia.nih.gov/research/dab/interventions-testing-program-itp/about-itp>

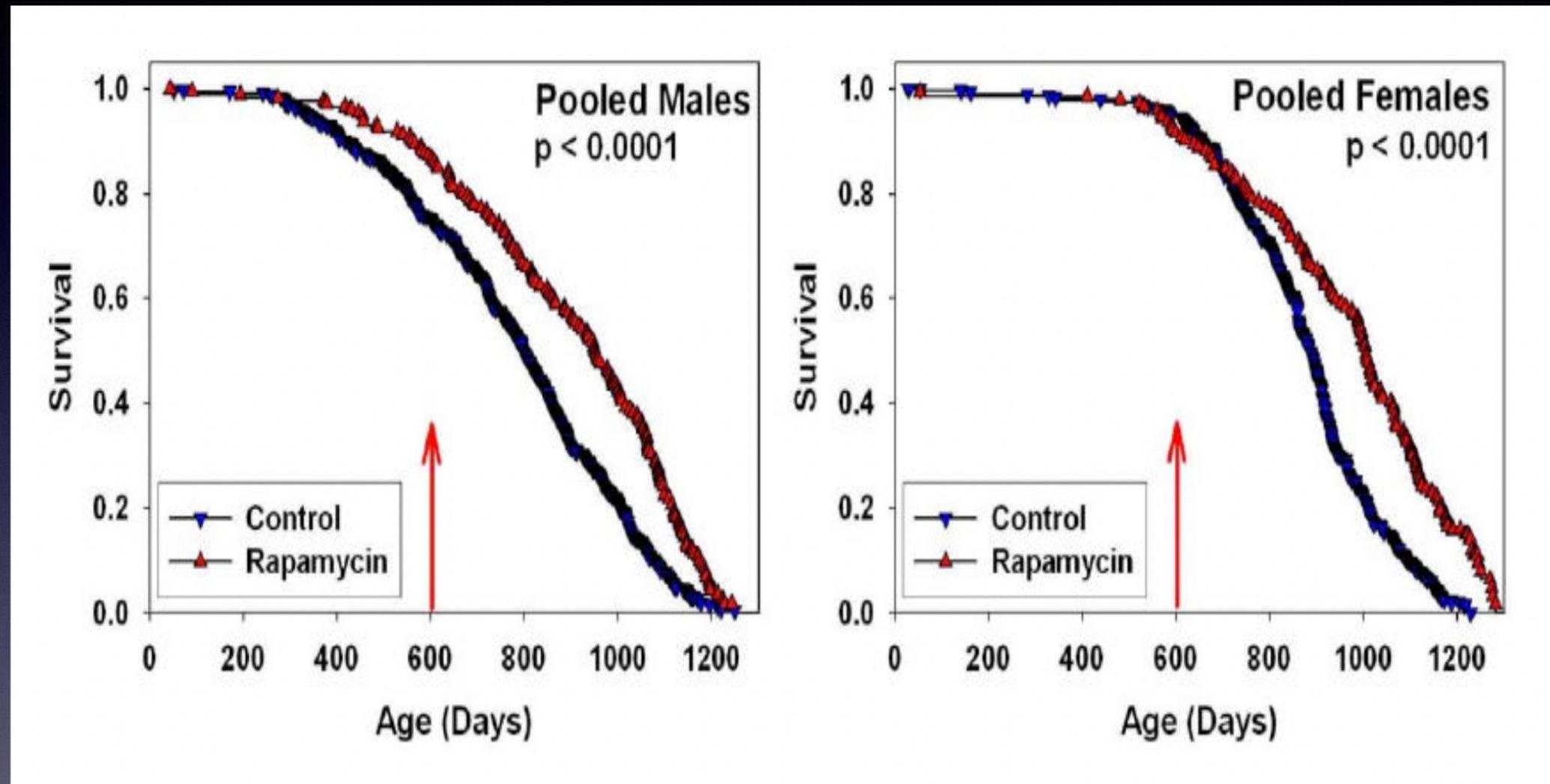


Interventions Testing Program Successes

Compound	Current Use	Life Span Gains
Aspirin	Pain Relief	8% gain – males No gain - females
Acarbose	Diabetes Treatment	22% gain – males 5% gain – females
NDGA	Skin ailments (topical)	8-10% gain – males No gain – females
17- α -estradiol	Hair loss (topical)	12% gain – males No gain - females



Rapamycin at the ITP



‘Survival plots for male (left) and female (right) mice, comparing control mice to those fed rapamycin in the diet starting at 600 days of age, pooling across the three test sites.’

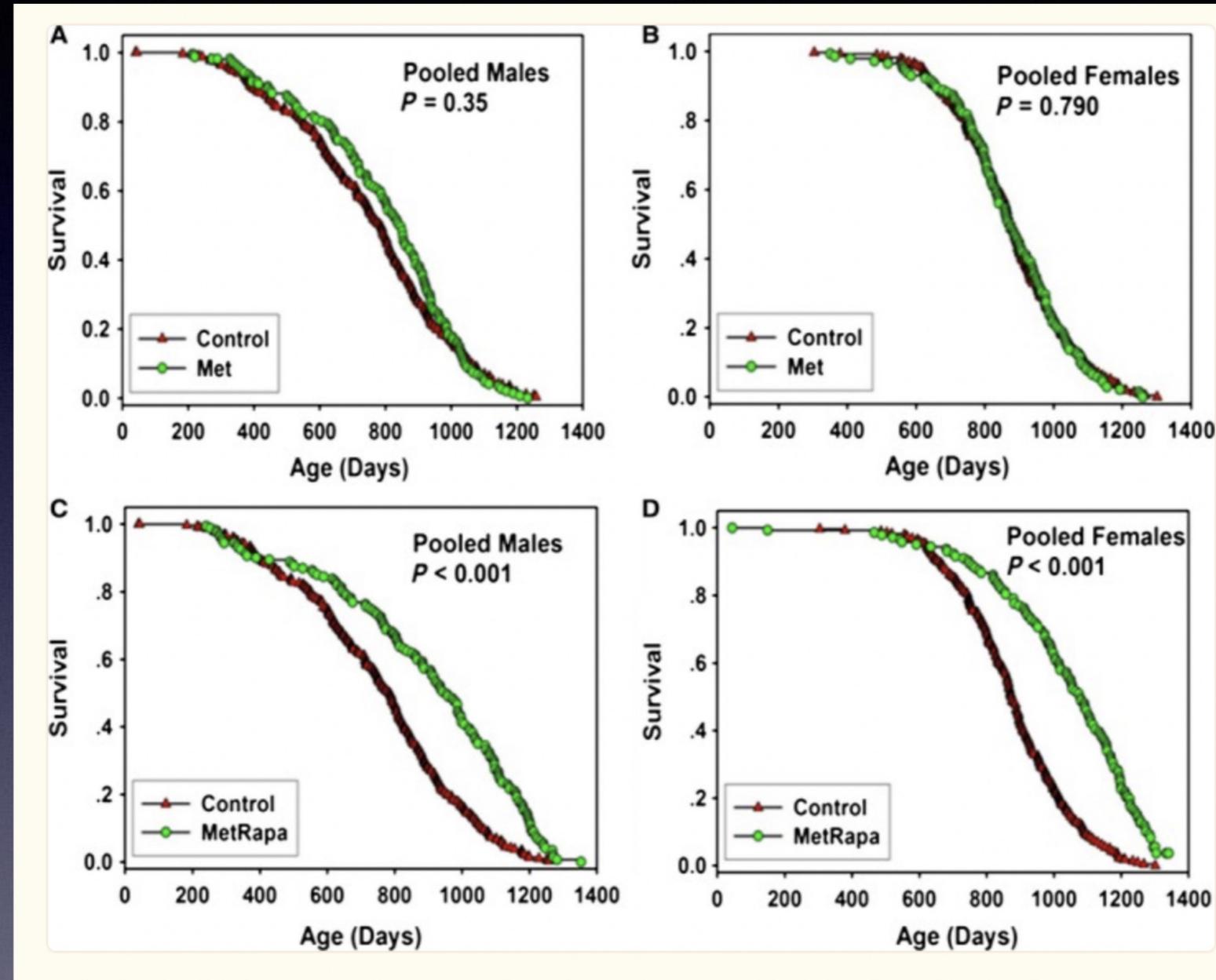
Harrison, David E., Randy Strong, Zelton Dave Sharp, James F. Nelson, Clinton M. Astle, Kevin Flurkey, Nancy L. Nadon, et al. “Rapamycin Fed Late Life Extends Lifespan in Genetically Heterogeneous Mice.” *Nature* 460, no. 7253 (July 2009): 392–95. <https://doi.org/10.1038/nature08221>.



***Is the solution to just take rapamycin
and a few other drugs?***

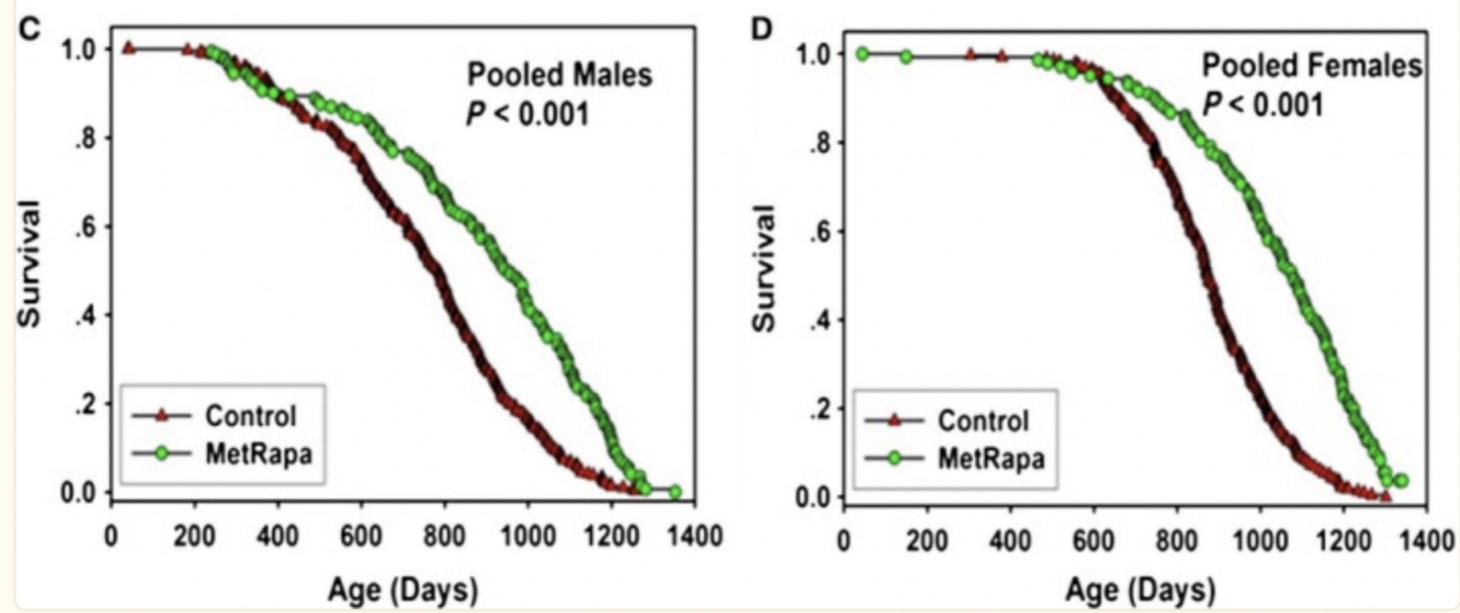


Metformin + Rapamycin (2016)

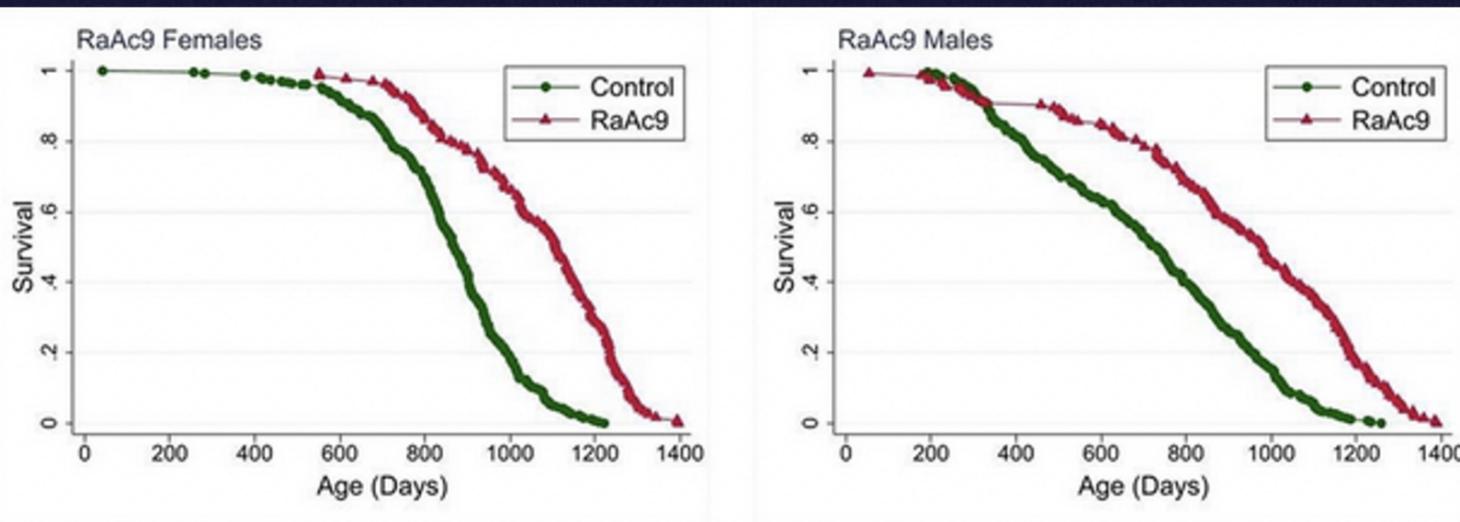


Strong, Randy, Richard A. Miller, Adam Antebi, Clinton M. Astle, Molly Bogue, Martin S. Denzel, Elizabeth Fernandez, et al. "Longer Lifespan in Male Mice Treated with a Weakly Estrogenic Agonist, an Antioxidant, an A-glucosidase Inhibitor or a Nrf2-inducer." *Aging Cell* 15, no. 5 (October 2016): 872–84. <https://doi.org/10.1111/ace1.12496>.





Metformin + Rapamycin (2016)



Rapamycin + Acarbose (2022)

Strong, Randy, Richard A. Miller, Catherine J. Cheng, James F. Nelson, Jonathan Gelfond, Shailaja Kesaraju Allani, Vivian Diaz, et al. "Lifespan Benefits for the Combination of Rapamycin plus Acarbose and for Captopril in Genetically Heterogeneous Mice." *Aging Cell*, September 30, 2022. <https://doi.org/10.1111/acel.13724>.



What happened to me?

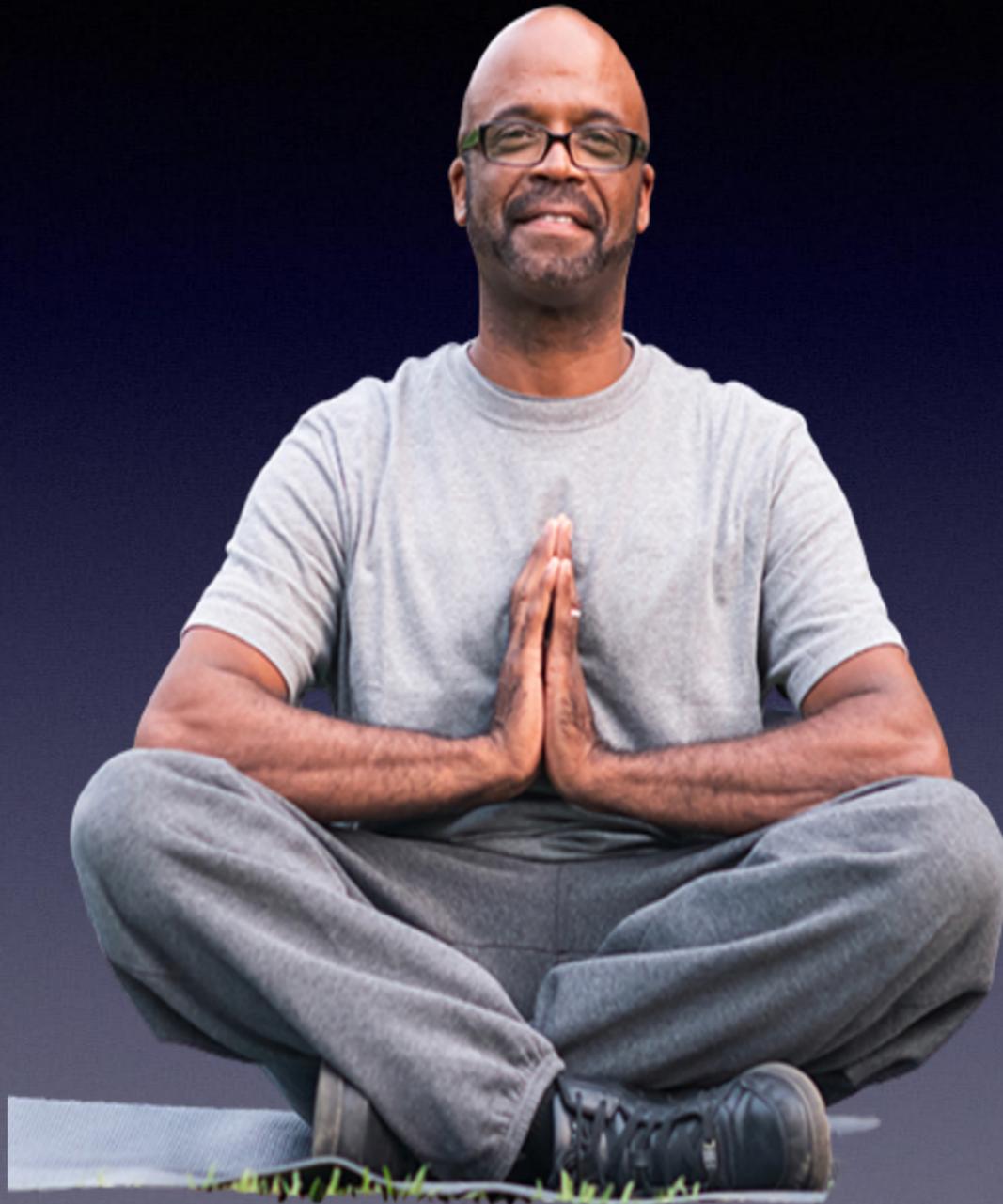
I changed my lifestyle in four key areas:

Nutrition

Sleep

Exercise

Stress



No more
symptoms!

Off all
medications!



FLCCC
ALLIANCE
EDUCATIONAL
CONFERENCE

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Edit profile

Robert Lufkin MD

@robertlufkinmd

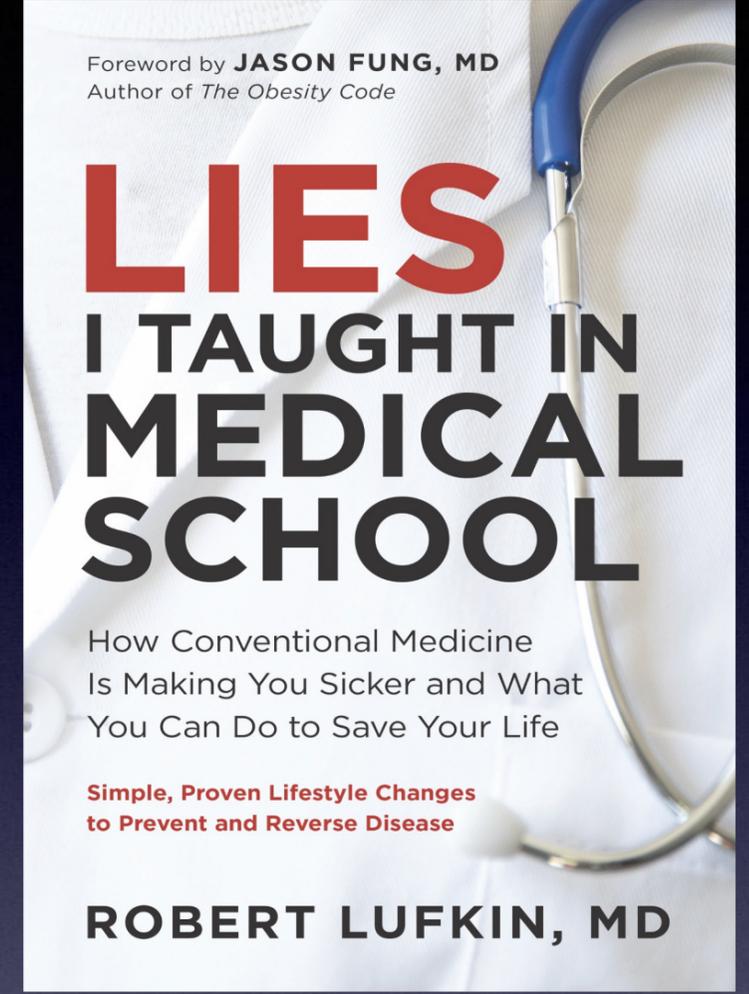
Medical school professor (UCLA & USC) helping people prevent/reverse chronic disease, cultivate consciousness, and live life to the fullest.

Medical & Health California linktr.ee/robertlufkinmd
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A new series by the award winning filmmaker
Charles Mattocks

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THE RACE FOR LONGEVITY

Is a longer, healthier life possible?

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WITH
DR ROBERT LUFKIN



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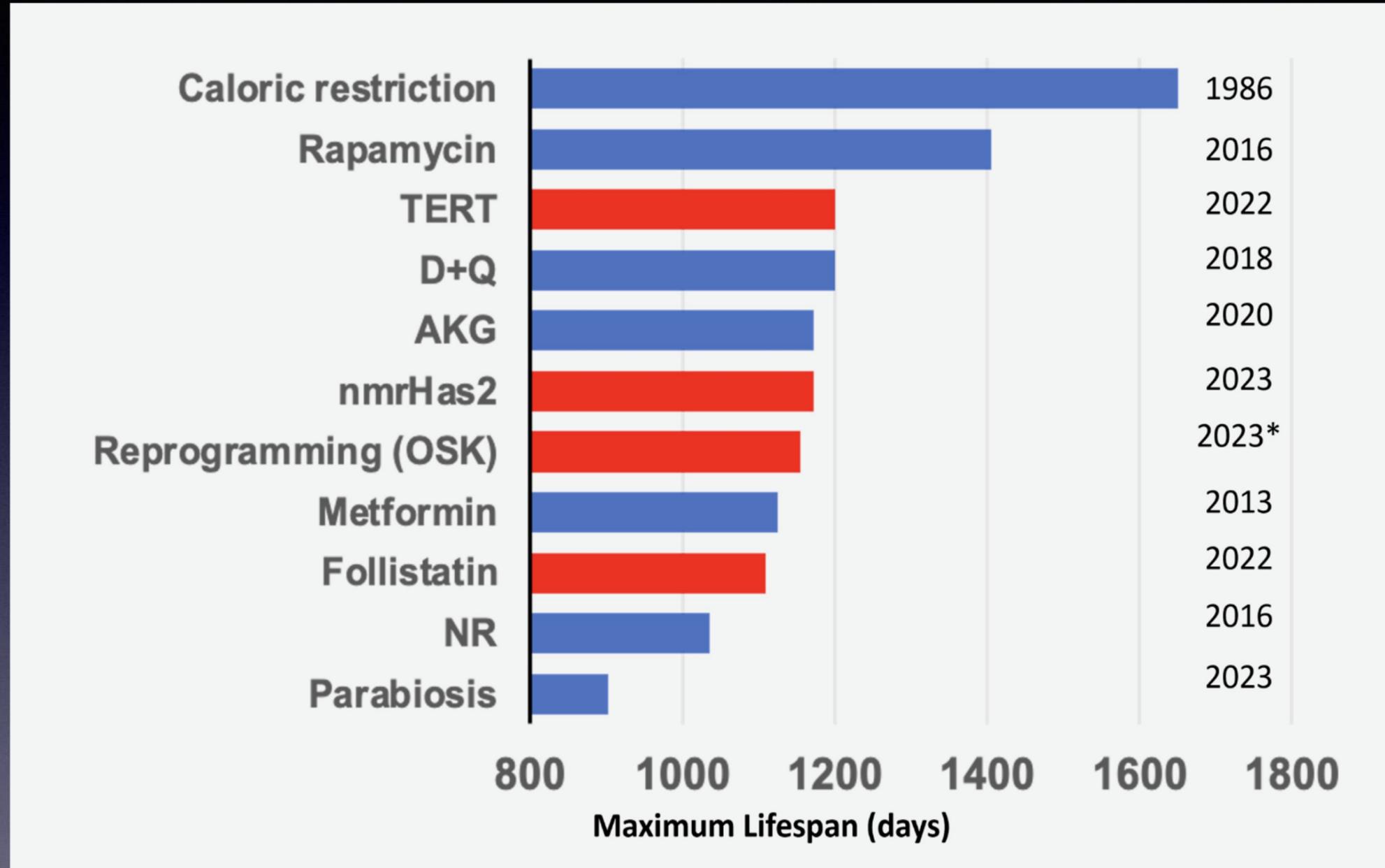
120k Member Managed Care Plan with Innovation Lab



New Graduate Medical Education Program

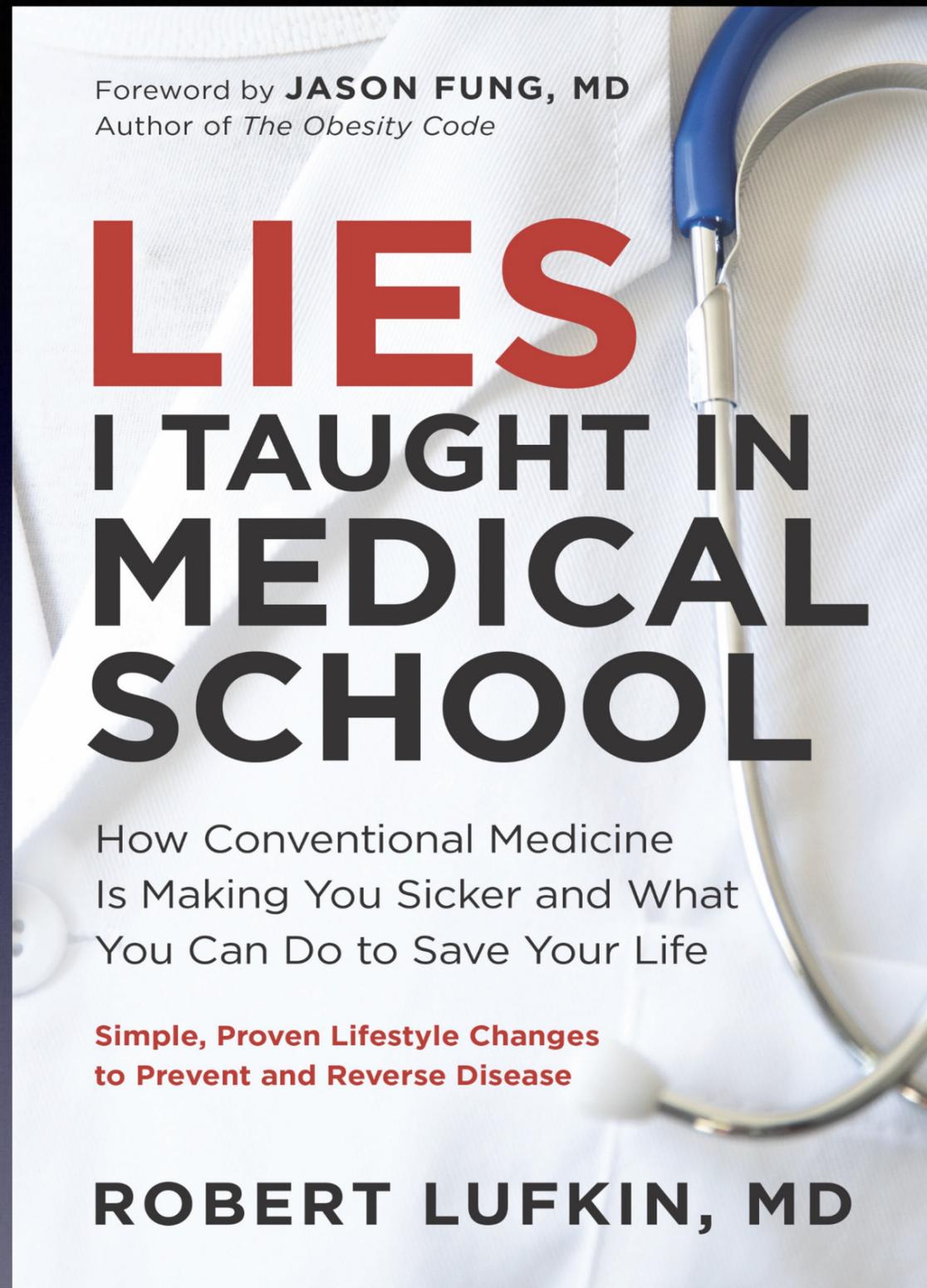


Longevity Progress



Is 80 becoming the new 40?





Sample Chapter

