Optimizing Biological Age

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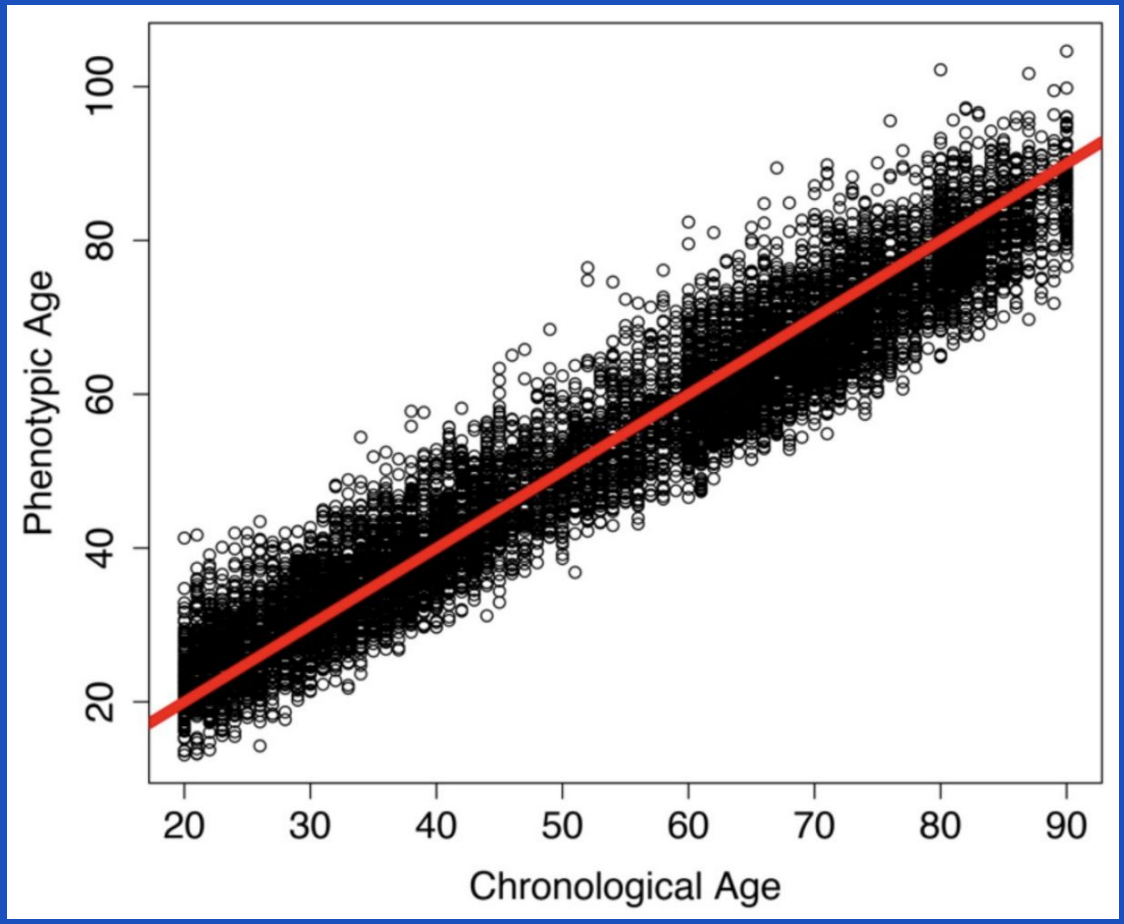
Calculating Biological Age

Variable	
Albumin	Liver
Creatinine	Kidney
Glucose, serum	Metabolic
C-reactive protein (log)	Inflammation
Lymphocyte percent	Immune
Mean (red) cell volume	Immune
Red cell distribution width	Immune
Alkaline phosphatase	Liver
White blood cell count	Immune
Age	

Levine *et al.* 2018



Liu *et al.* 2018

Correlation between the 9 clinical analytes + chronological age = 0.94

Biomarkers derived from NHANES III (n=9,926)

Correlation between the 9 clinical analytes + chronological age = 0.96

Biomarkers derived from NHANES IV (n=11,432)

Phenotypic Age Is Associated With All-Cause Mortality Risk

Mortality category		Number of deaths	Hazard ratio (95% CI)	*z*-Score	*P* value
All-cause	Full sample	871	1.09 (1.08–1.10)	15.03	<0.001
	Those with 5+ years of survival	389	1.08 (1.06–1.10)	7.84	<0.001
	Young adults (20–39 years)	32	1.13 (1.09–1.18)	6.47	<0.001
	Middle aged adults (40–64 years)	247	1.10 (1.08–1.12)	10.29	<0.001
	Older adults (65–84 years)	592	1.08 (1.06–1.09)	10.40	<0.001
Disease-specific	Heart disease	141	1.10 (1.07–1.13)	7.38	<0.001
	Cancer	227	1.07 (1.05–1.09)	6.70	<0.001
	Chronic lower respiratory disease	52	1.07 (1.04–1.11)	4.16	<0.001
	Cerebrovascular disease	56	1.03 (0.98–1.09)	1.26	0.208
	Diabetes	26	1.19 (1.13–1.26)	6.64	<0.001
	Influenza or pneumonia	24	1.12 (1.08–1.16)	6.43	<0.001
	Nephritis/nephrosis	15	1.20 (1.16–1.25)	9.67	<0.001

For every 1 year increase in Phenotypic Age, all-cause mortality risk increases by 9%

Liu *et al.* 2018

Optimizing Biological Age

Have your blood tested for the standard chemistry panel + CBC (~$35) + CRP (~$40)

Calculate Phenotypic Age with the embedded link:
https://michaellustgarten.com/2019/09/09/quantifying-biological-age/

Knowing your biological age is interesting,
but optimizing it is better!

How can we optimize biological age?

How does each analyte change during aging?

What's its association with all-cause mortality risk?

What's my data: Can diet, fitness, or optimization of body composition impact it? (where applicable)

What's My Biological Age?

Blood test measurement 3/8/2020

Def.	Albumin	Creatinine	Glucose	C-reac Protein	Lympocyte	Mean Cell Volume	Red Cell Dist Width	Alkaline Phosphatase	White Blood Cells	Age	Phenotypic Age
Input	4.9	0.97	92	0.37	35	89	12	47	4.7	47	31.61
Units	g/dL	mg/dL	mg/dL	mg/L	%	fL	%	U/L	10^3 cells/µL	years	

15+ years younger than my chronological age, 47y

One way that I'm reducing/maintaining a relatively young biological age is through diet

Every day, with use of a food scale, I track macro- and micro-nutrients, and individual food intake

I blood test 4-6x/year, and accordingly, I look for correlations between my blood test results with my average dietary intake during that period. With enough data, I can have adequate statistical power to identify potentially meaningful correlations

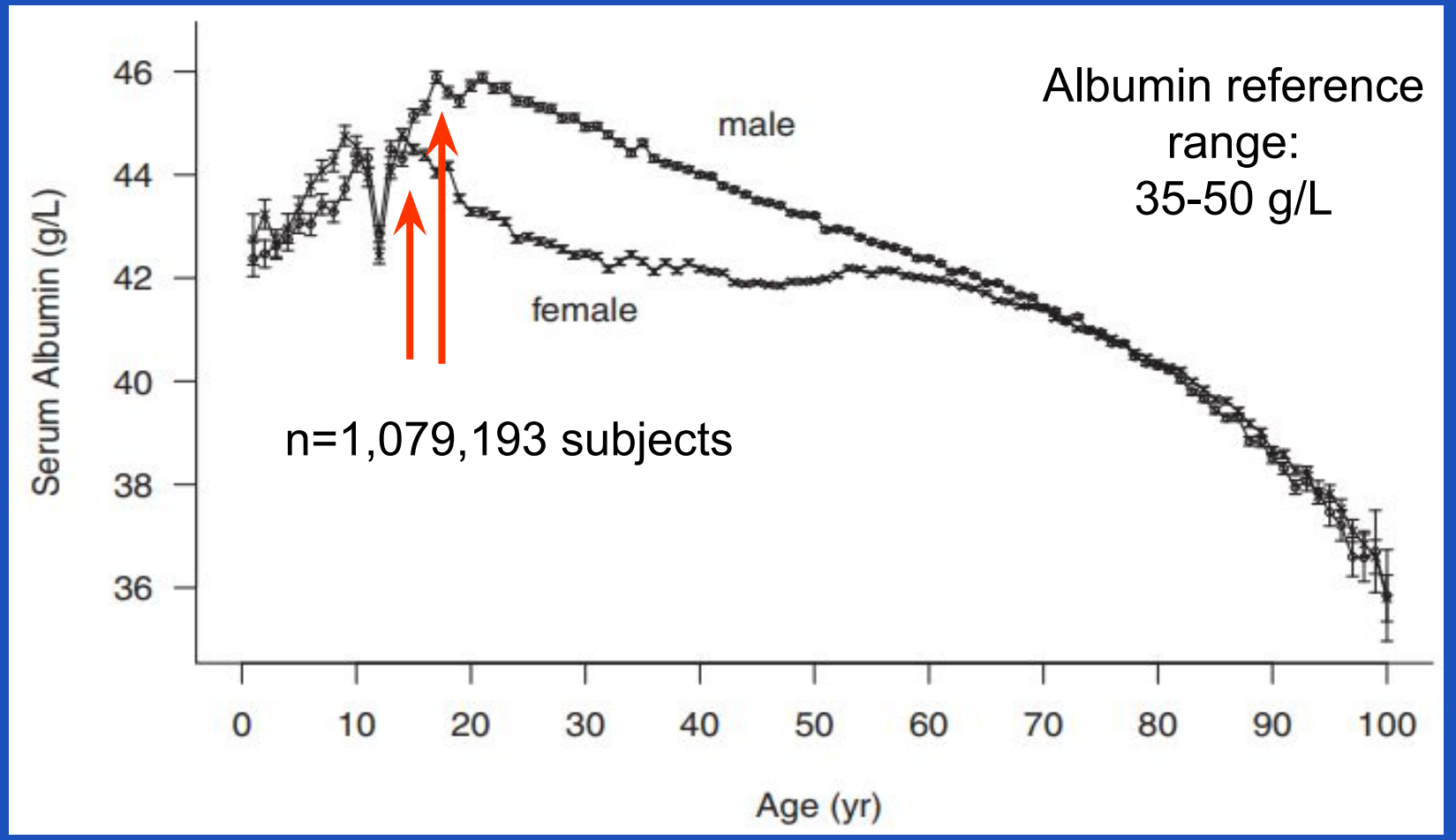
Once I identify correlations between diet with my blood test results, I make dietary changes, and see how it affects my circulating biomarkers

Phenotypic Age Checklist: Reference Range vs. Optimal Range

Variable		Reference Range	Optimal range
Albumin	Liver	35-55 g/L	
Creatinine	Kidney	0.76-1.27 mg/dL	
Glucose, serum	Metabolic	65-99 mg/dL	
C-reactive protein (log)	Inflammation	0-3 mg/L	
Lymphocyte percent	Immune	Not established	
Mean (red) cell volume	Immune	79-97%	
Red cell distribution width	Immune	11.6-15.4%	
Alkaline phosphatase	Liver	39-117 IU/L	
White blood cell count	Immune	3.4-10.8*10^3 cells/μL	
Age			

Levine *et al.* 2018

Albumin Decreases During Aging

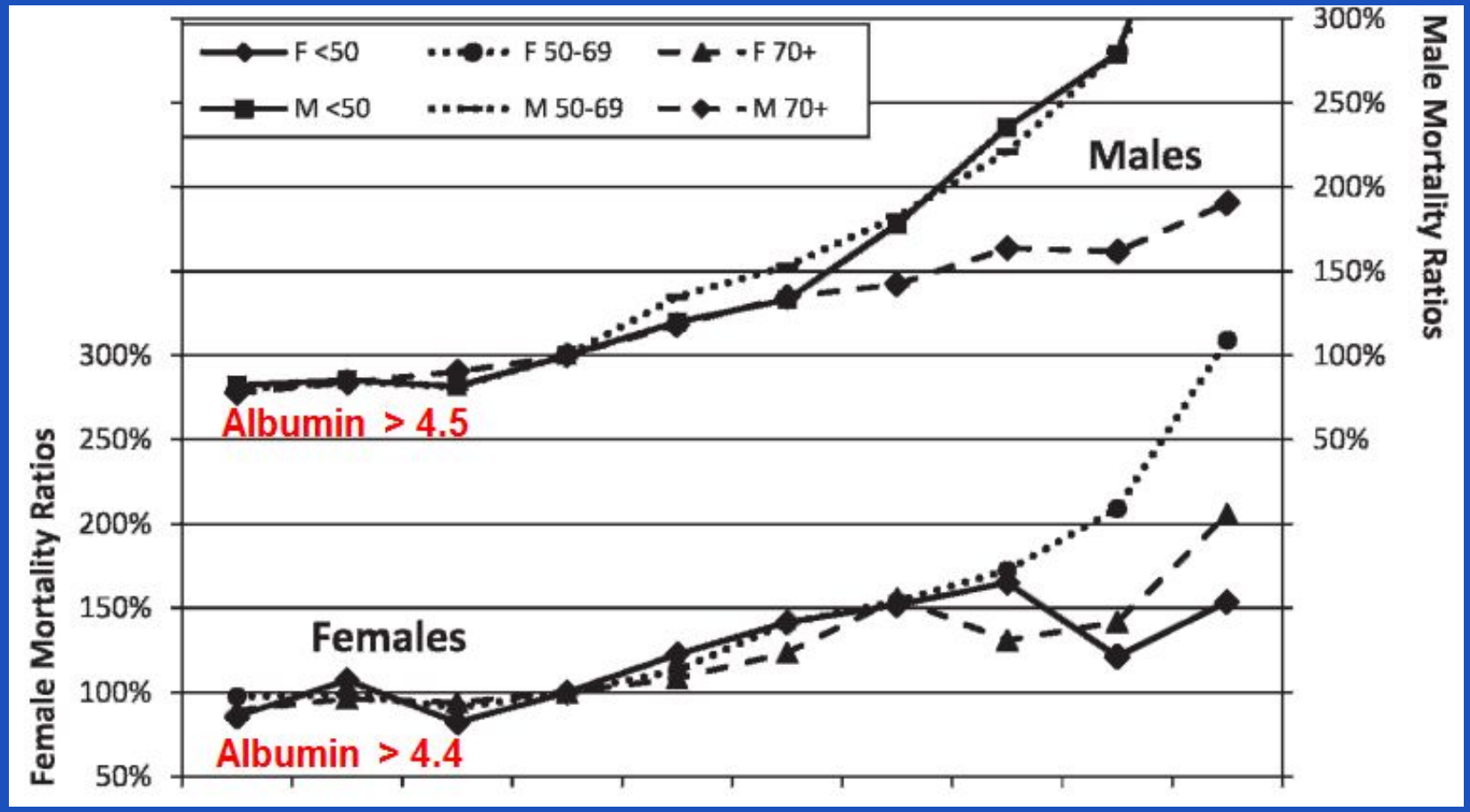


Weaving *et al.* 2016

Higher albumin levels are associated with biologic youth

Higher Albumin Is Associated With A Lower All-Cause Mortality Risk

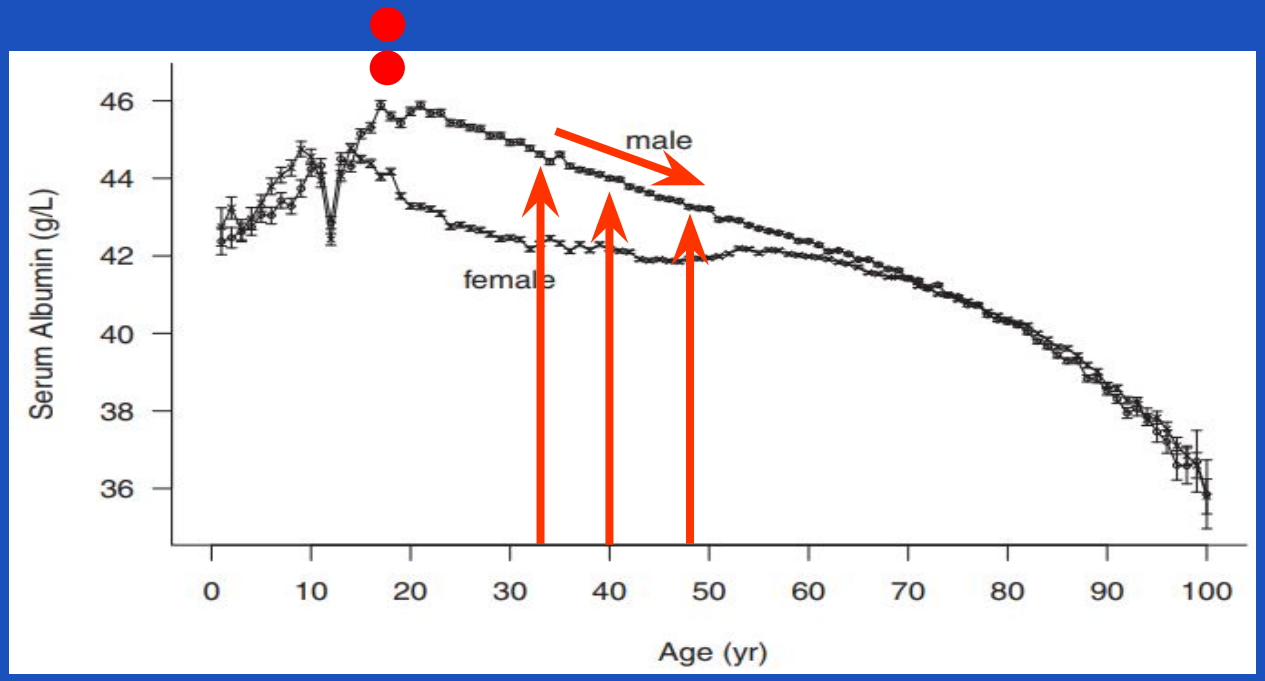
n=1,704,566 subjects



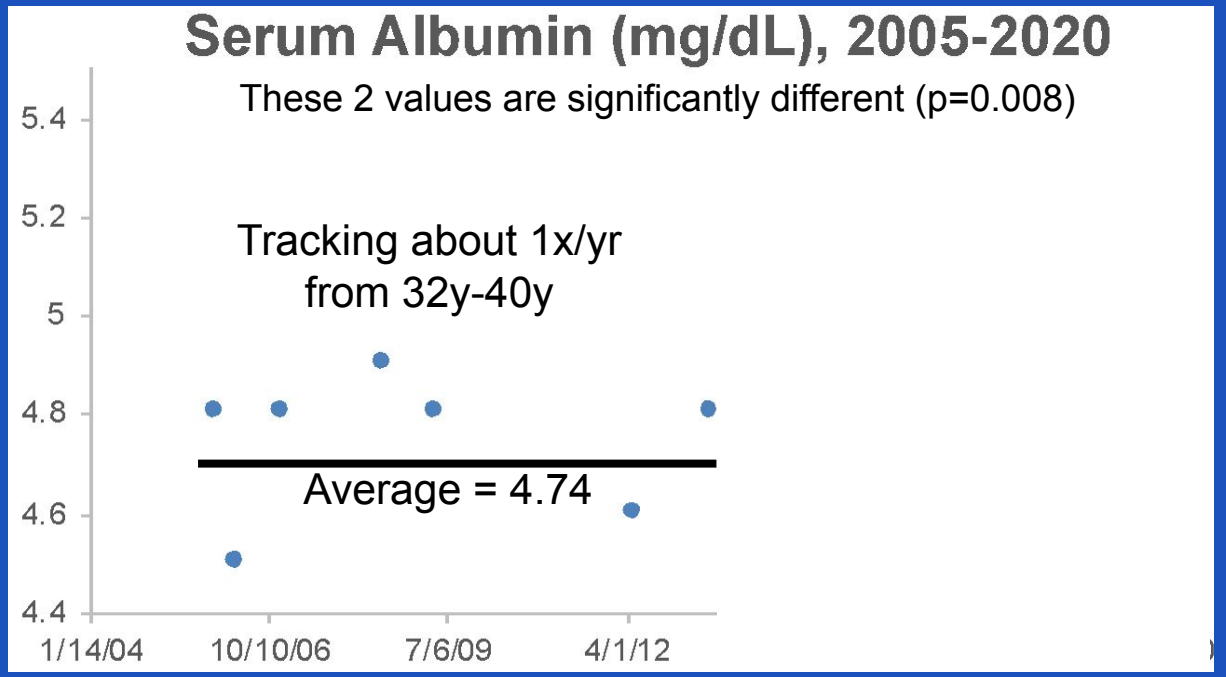
Higher Albumin ⟵ ⟵ ⟵ ⟵ ⟵ Lower Albumin

Fulks *et al.* 2010

Can Albumin Levels Be Optimized?



Weaving *et al.* 2016

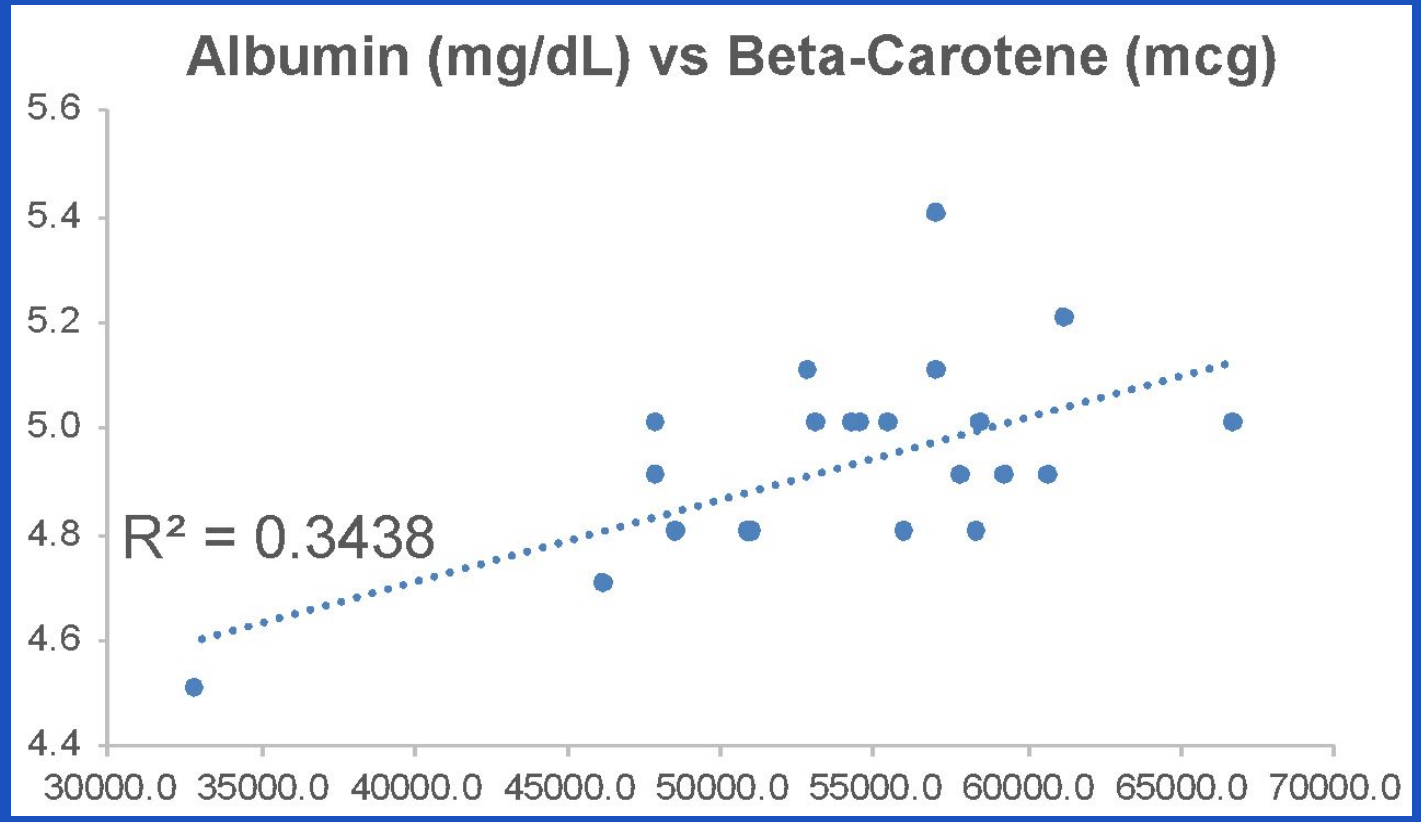


How have I been able to keep my albumin levels high, and to resist the age-related decline?

Started daily dietary tracking in April 2015, n=1800+ days in conjunction with blood testing more often, 4-6x/yr (n=23)

Can diet be used to optimize albumin?

Beta-Carotene Is Positively Associated With Albumin

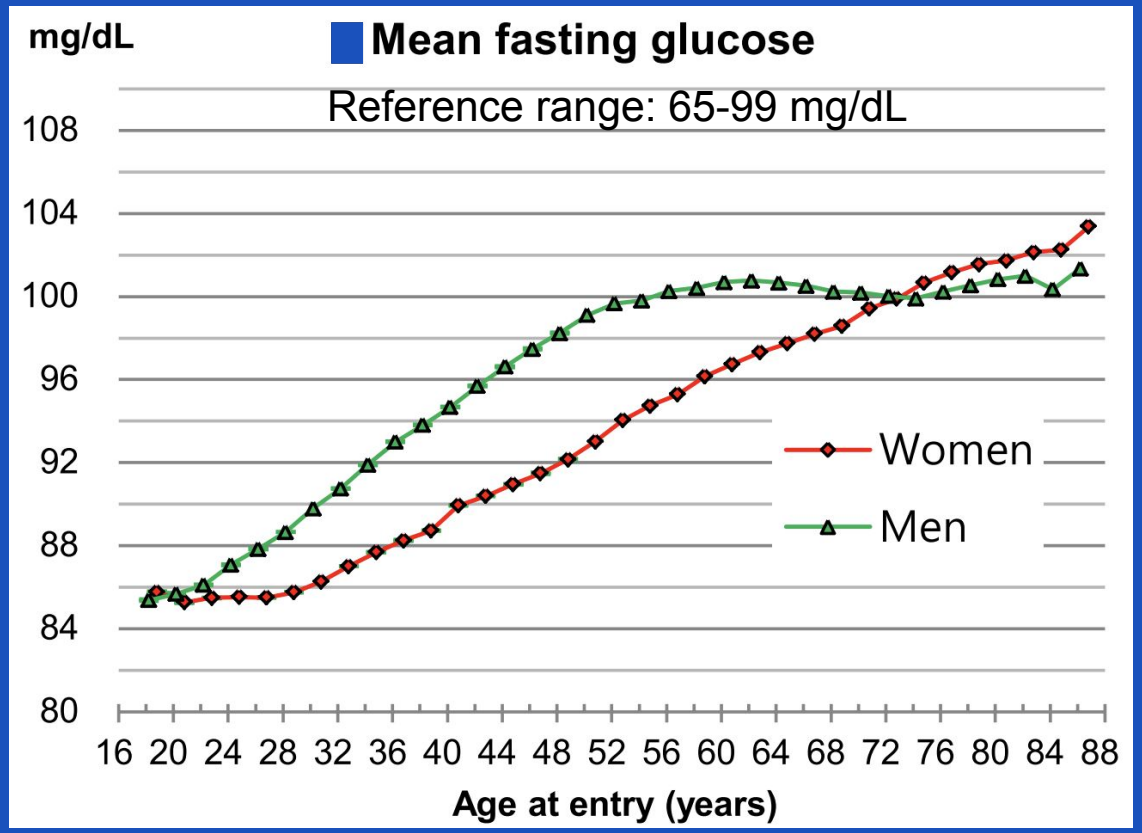


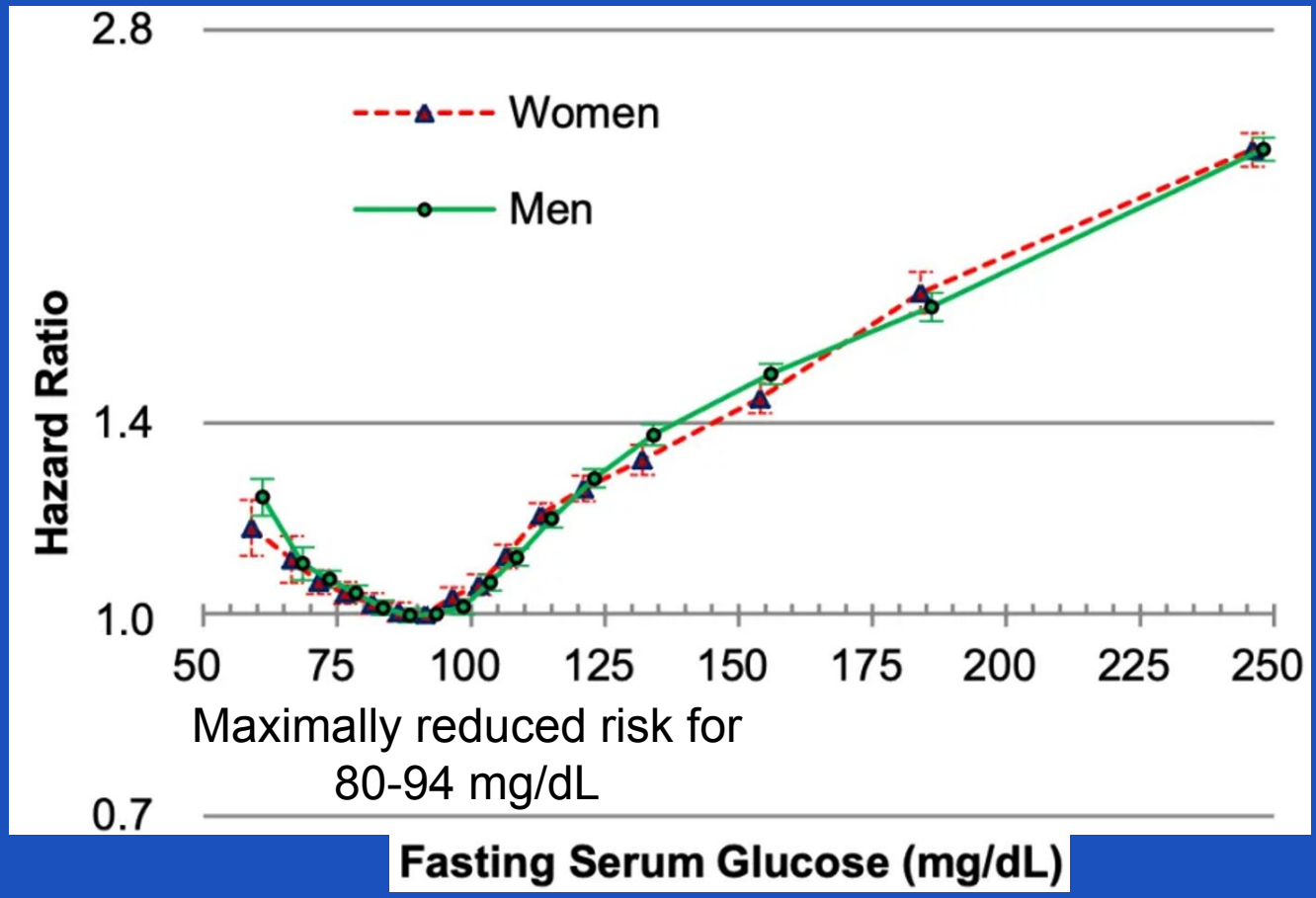
The strongest correlation between my diet with albumin is for Beta-carotene, *r* = ~0.6 (moderately strong)

With the goal of keeping my albumin at close-to-youthful levels, I shoot for 60 mg of beta-carotene per day. Primary sources (for me) are carrots, orange sweet potatoes, red bell peppers, spinach, and parsley.

Glucose Increases During Aging, Which Is Associated With A Higher All-Cause Mortality Risk

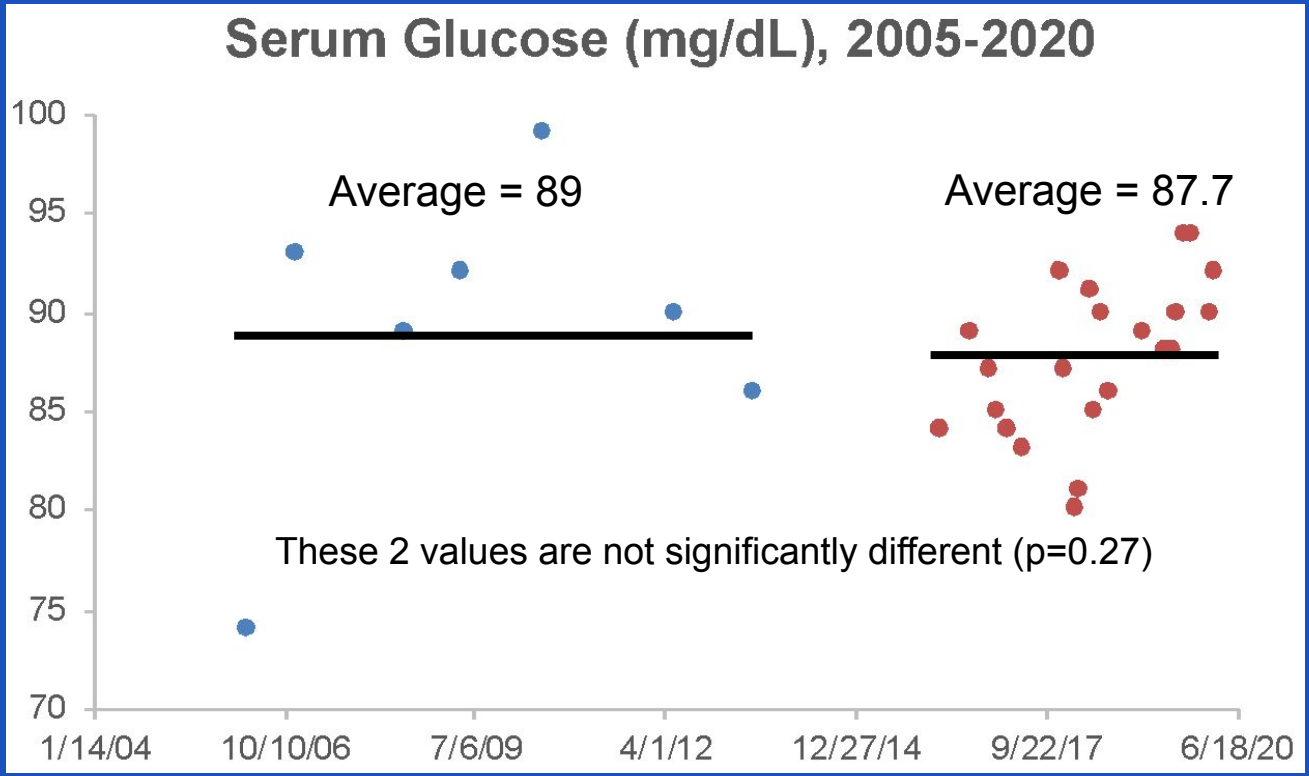
n=12,455,361 subjects





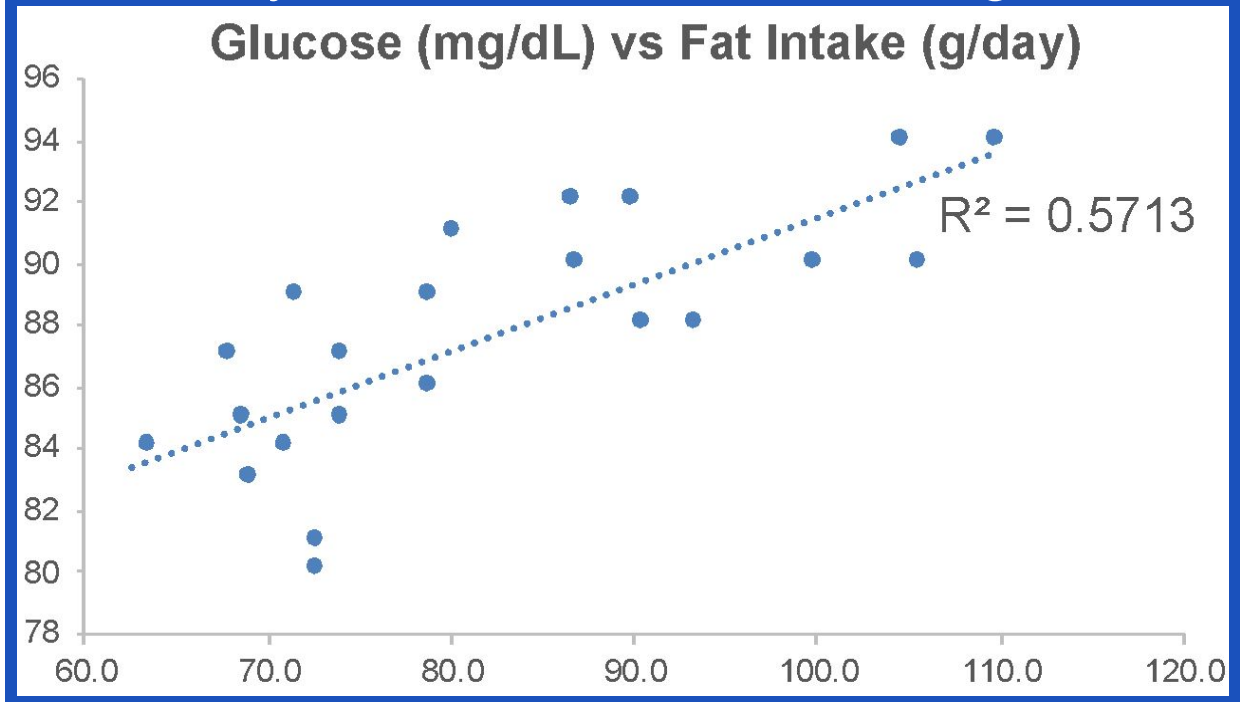
Yi *et al.* 2017

Resisting The Age-Related Increase For Glucose



Reduce my saturated fat intake, keep glucose low? It may not be that simple…

How is my diet correlated with blood glucose?



Strong correlation (r = 0.75) between how much fat I eat/day with glucose levels

Within my fat intake, the correlation between saturated fat with glucose is moderately strong (r = 0.61)

C-Reactive Protein (CRP) Increases During Aging, Which Is Associated With A Higher All-Cause Mortality Risk

Reference Range: 0-3 mg/L

n=1,343

	Age, y						
	20-39	40-49	50-64	65-74	75-84	85 +	P*
CRP, g/L							
Men	1.0 (0.8-1.4)	1.9 (1.1-3.2)	1.8 (1.3-2.5)	2.6 (2.2-2.9)	3.1 (2.6-3.7)	5.4 (3.8-7.9)	< .0001
Women	1.1 (0.8-1.5)	1.1 (0.6-1.8)	2.3 (1.8-2.9)	2.5 (2.2-2.8)	3.0 (2.6-3.5)	3.3 (2.6-4.3)	< .0001

Ferrucci *et al.* 2005

<u>Lower CRP is associated with reduced ACM risk:</u>

< 3 mg/L (Oluleye *et al.* 2013)

< 1 mg/L (Hamer *et al.* 2010, Koenig *et al.* 2008, Kuoppamäki *et al.* 2015)

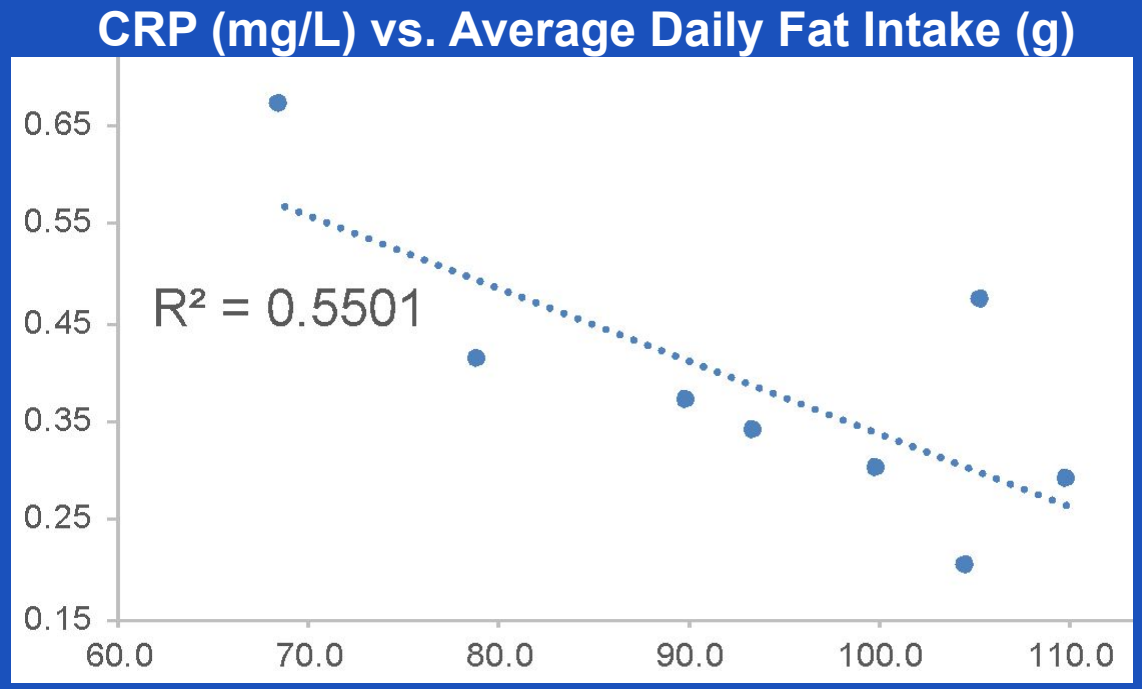
< 0.86, 0.83 mg/L (Shen *et al.* 2019, Laaksonen *et al.* 2014)

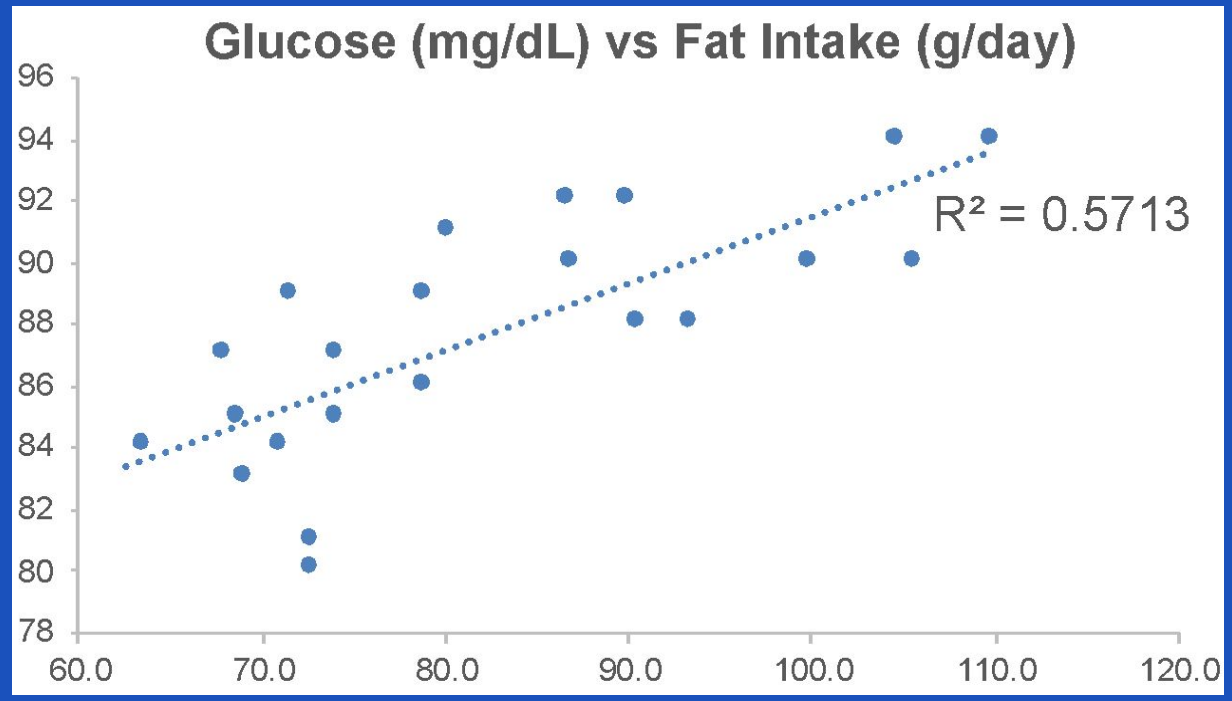
0.5-0.8 mg/L (Zuo *et al.* 2016, Ahmadi-Abhari *et al.* 2013)

< 0.33 mg/L (Shinkai *et al.* 2008, Nisa *et al.* 2016, Makita *et al.* 2009, Arima *et al.* 2008)

For CRP, lower seems to be better; as close to 0 as possible may be optimal

Higher (Saturated Fat) Intake Is Strongly Correlated With Lower CRP But…





Strong correlation (r = 0.74) between how much fat I eat/day with CRP

Within my fat intake, the correlation between saturated fat with CRP is strong (r = 0.76)

Eat more saturated fat (mostly from coconut butter, cacao) to lower CRP?

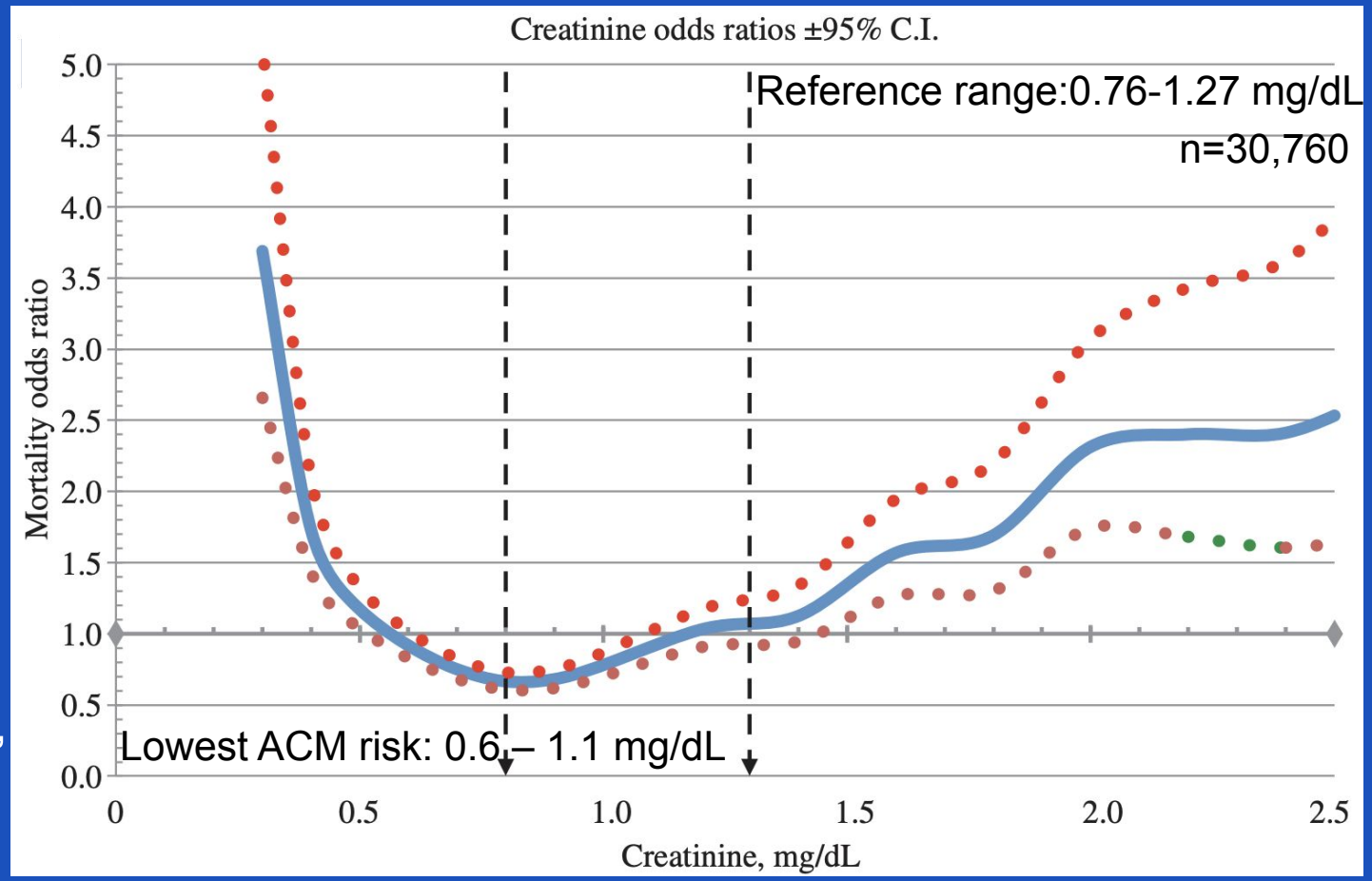
A higher (saturated) fat intake is moderately-strongly correlated with HIGHER glucose levels

This illustrates the constant trial-and-error process of potentially improving 1 variable while making another worse. **Finding the sweet spot is key!**

Creatinine Increases During Aging, Which Is Associated With a Higher All-Cause Mortality Risk

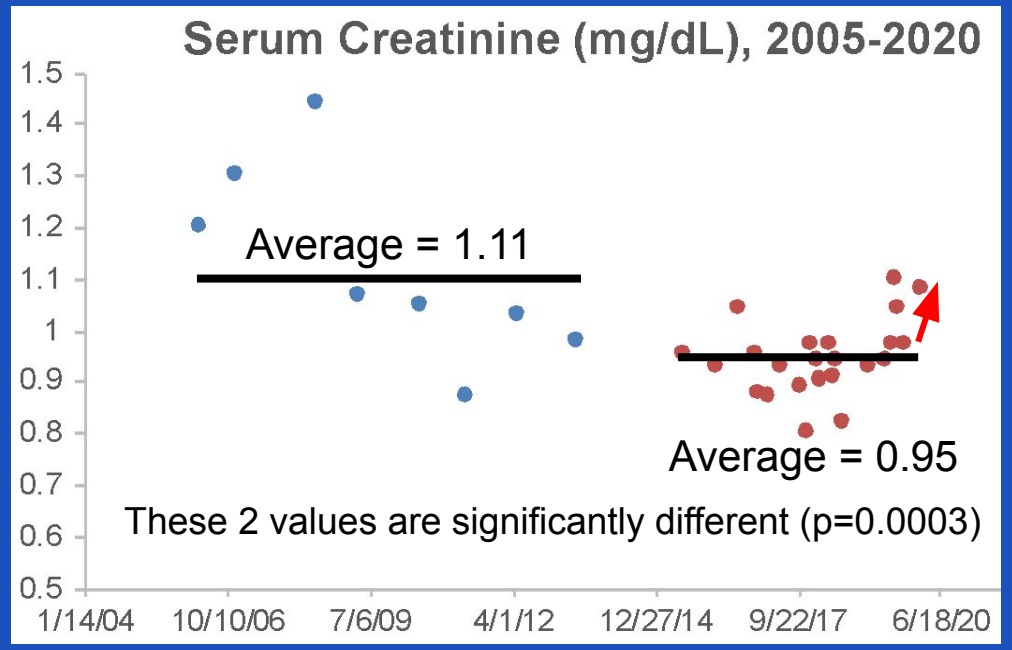
Creatinine increases during aging from 1.05 mg/dL in 30-59 yr olds to 1.14 mg/dL in 60-75 yr olds (n=9,389; Levine 2013)

As creatinine decreases below 0.8 mg/dL, or increases above 0.8 mg/dL, all-cause mortality risk increases

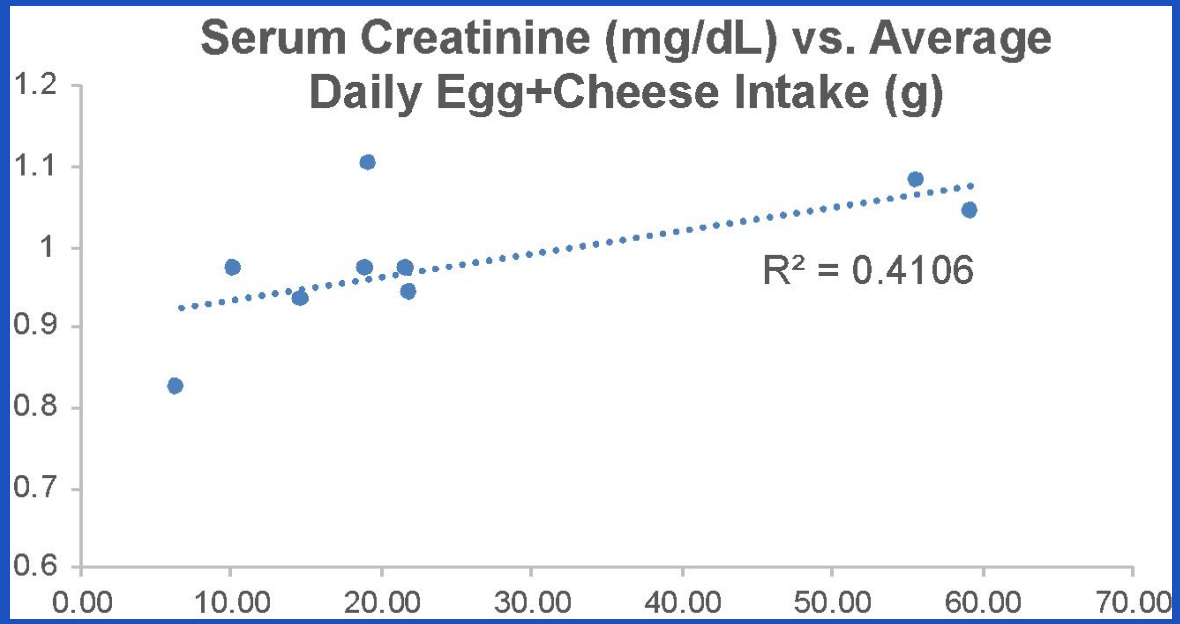


Solinger and Rothman 2013

Resisting The Age-Related Increase For Creatinine



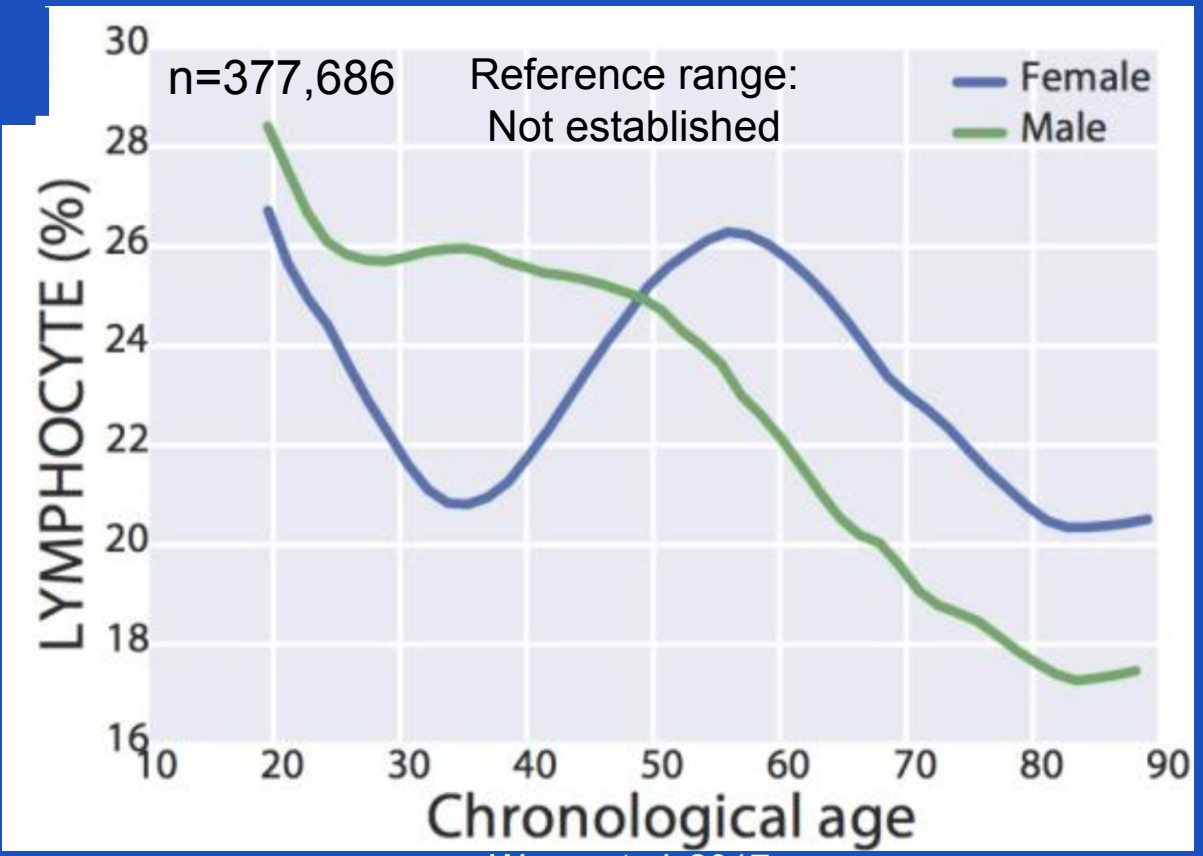
Whereas there was more variability in my data when measuring ~1x/yr, with more often measurements and dietary tracking there is less variability



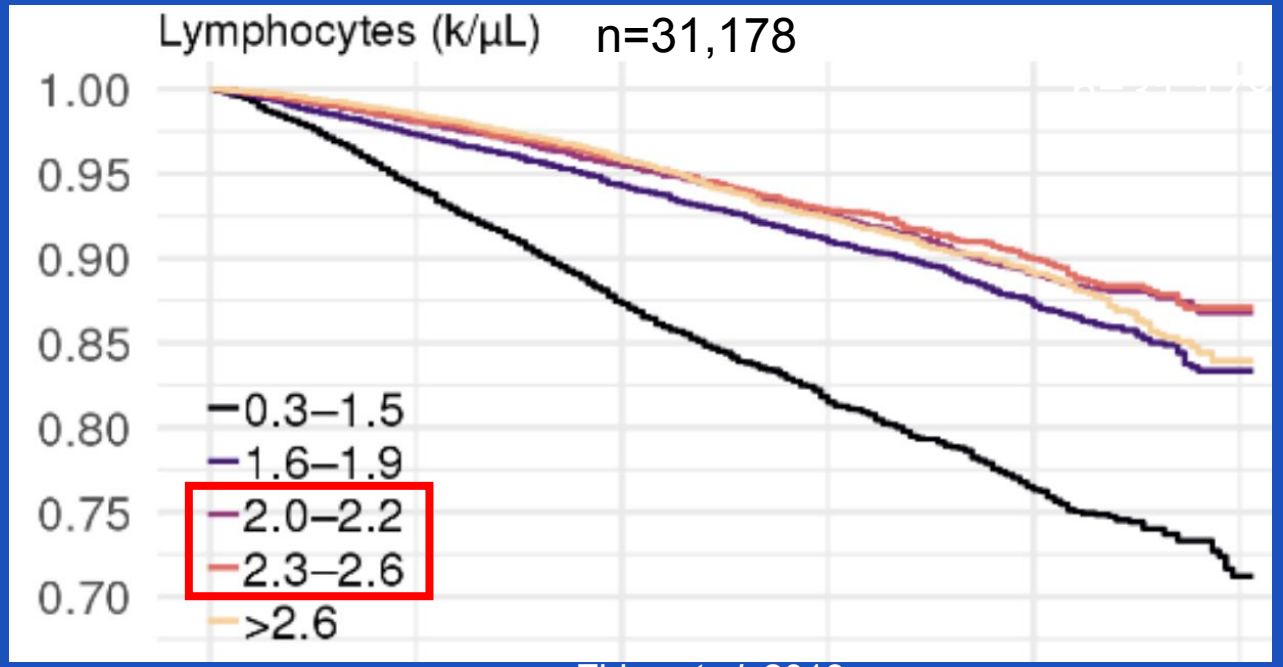
In addition to tracking macro- and micro-nutrient intake, I also track daily food amounts. Although I have less data for that (n=9), there is a moderately strong (*r* = 0.64) correlation between my average daily egg+cheese intake with higher creatinine.

By tracking daily diet and circulating biomarkers, you can identify the dietary pattern that leads to the best biomarker profile

A Higher Lymphocyte % Is Associated With Chronological Youth



Wang *et al.* 2017



Zidar *et al.* 2019

Lowest all-cause mortality risk is associated with 2000-2600*$10^3/\mu L$ lymphocytes

Studies have not investigated the association between lymphocyte % with ACM risk, but what about the association between absolute # of lymphocytes with ACM risk?

Mean Corpuscular Volume Increases During Aging, Which Is Associated With An Increased ACM Risk

Reference range: 79-97%

	Age Group	Sample No.	Mean	± S.E.	Significance
MCV	Young	25 (169)	88.8 (89.2)	0.92 (0.32)	
	Middle-aged	22 (293)	91.3 (91.1)	1.24 (0.26)	$P < 0.005$ ($P < 0.001$)
	Old	37 (301)	92.4 (92.9)	0.66 (0.24)	

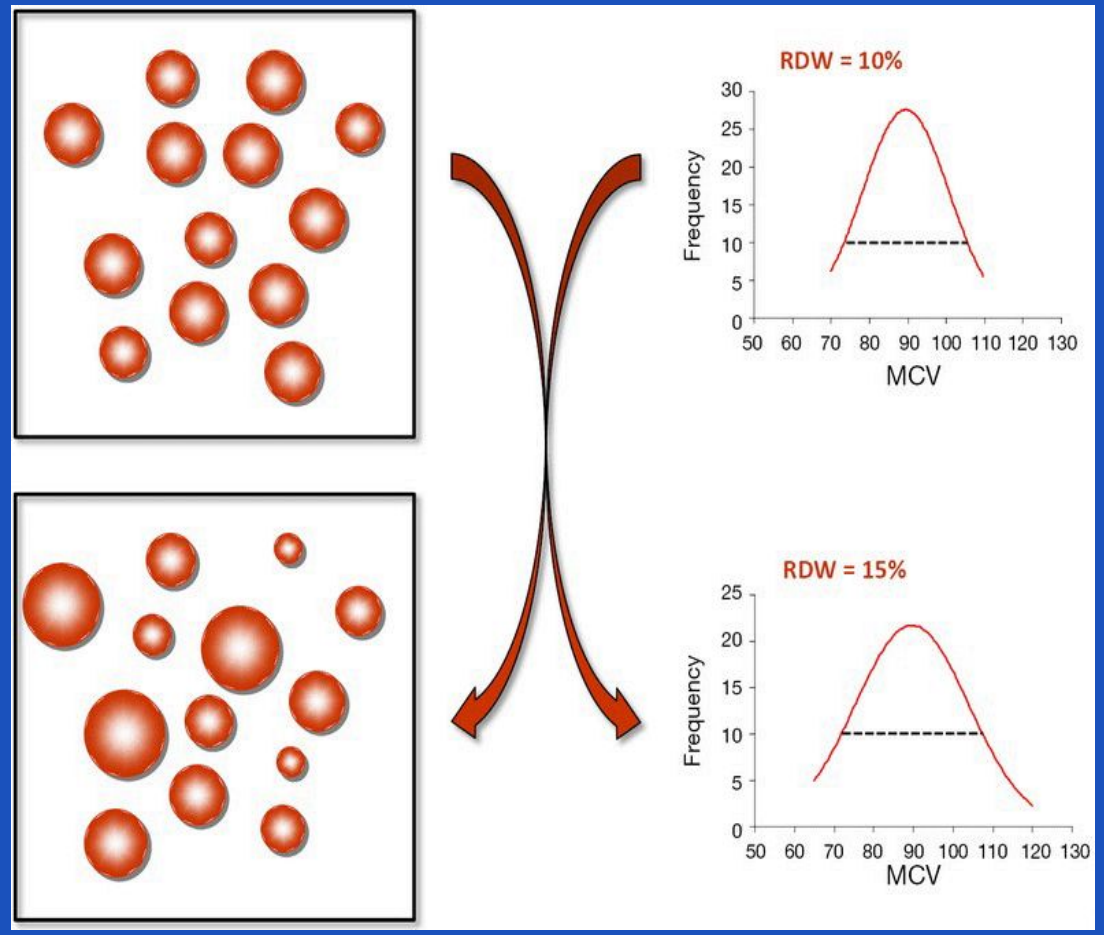
Araki and Rifkind, 1984

n=36,260			HR	95% CI	P_{trend}
	Men				
	All-cause mortality				
	1st quartile	4607	1.06	0.83–1.34	0.003
90.5-93.0%	2nd quartile	4755	1.00	Reference	
	3rd quartile	4722	1.16	0.92–1.45	
>95.8%	4th quartile	4711	1.44	1.15–1.80	
	Women				
	All-cause mortality				
	1st quartile	4322	1.00	0.70–1.43	0.006
89.2-91.6%	2nd quartile	4353	1.00	Reference	
	3rd quartile	4400	1.37	0.96–1.94	
>94.2%	4th quartile	4390	1.55	1.08–2.22	

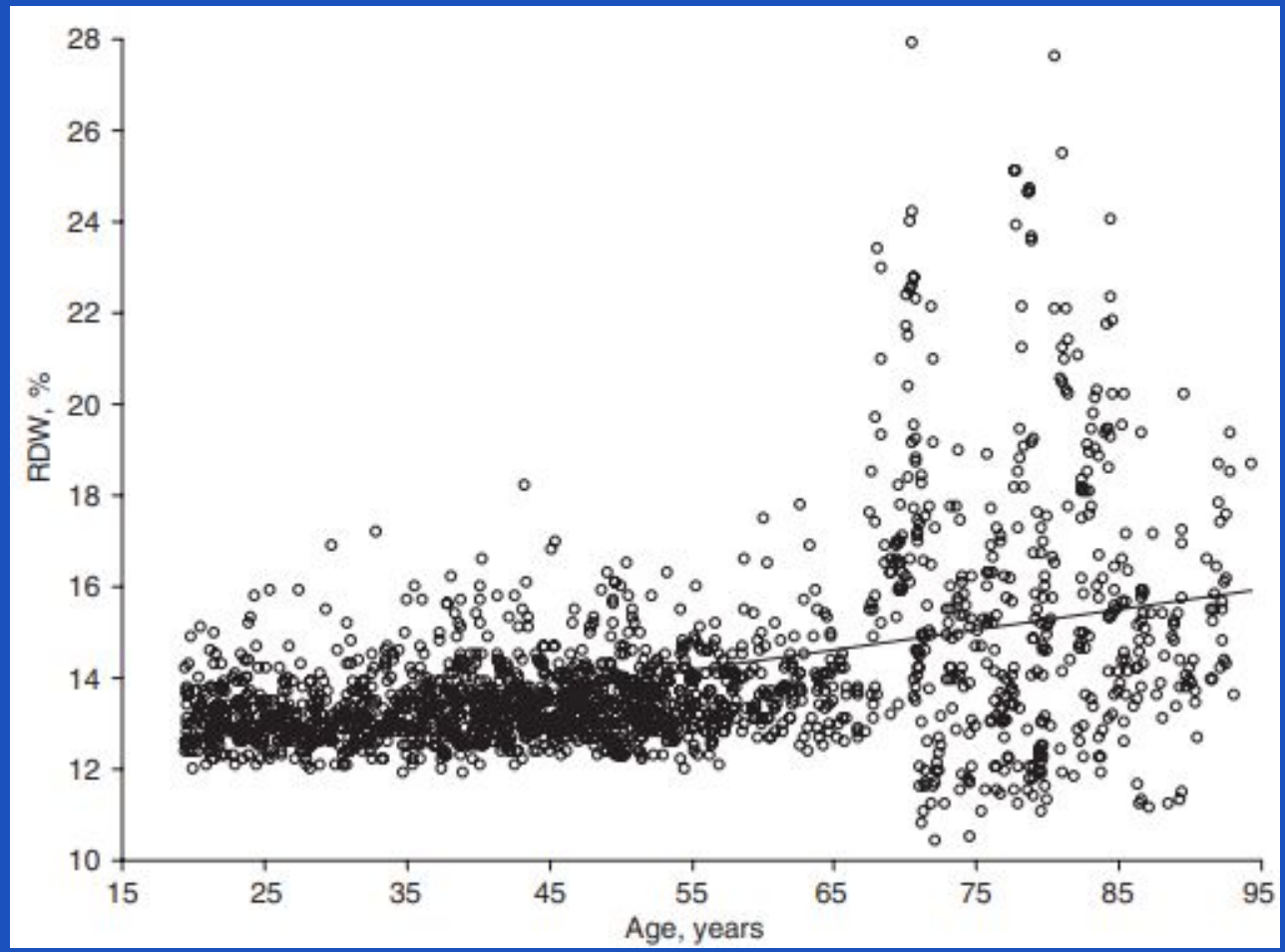
Yoon *et al.* 2016

Red Blood Cell Distribution Width % (RDW%) Increases During Aging

What is the RDW%?

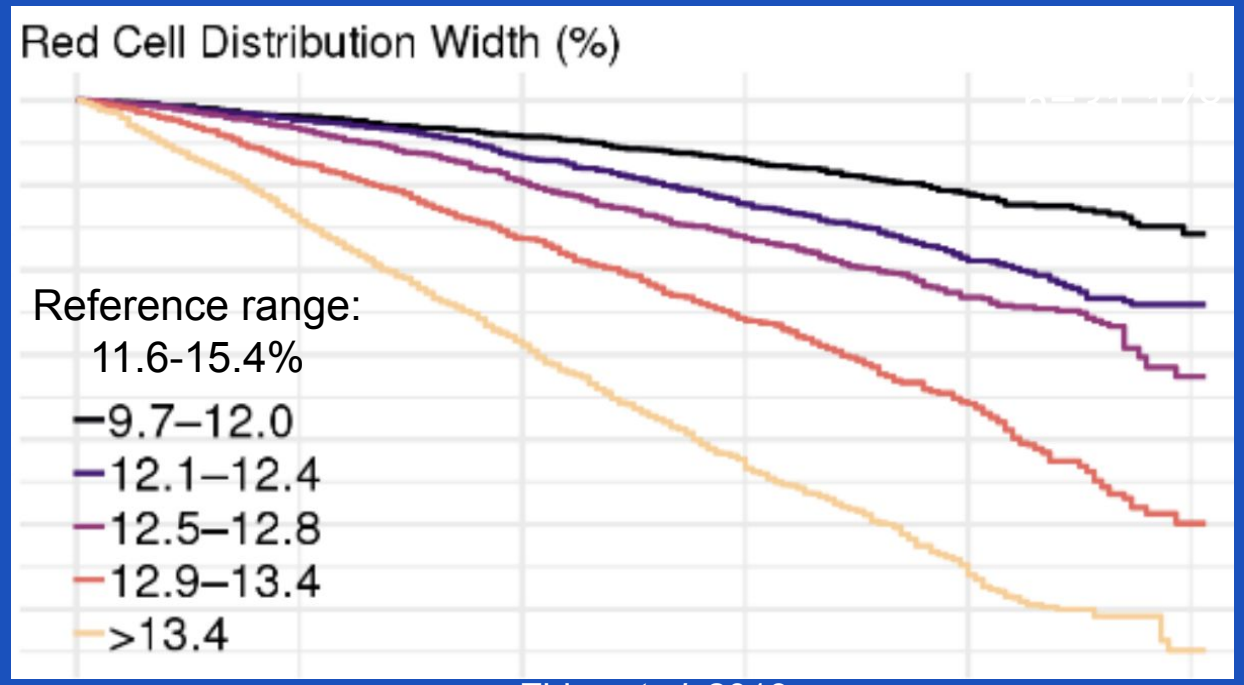


Danese *et al.* 2015

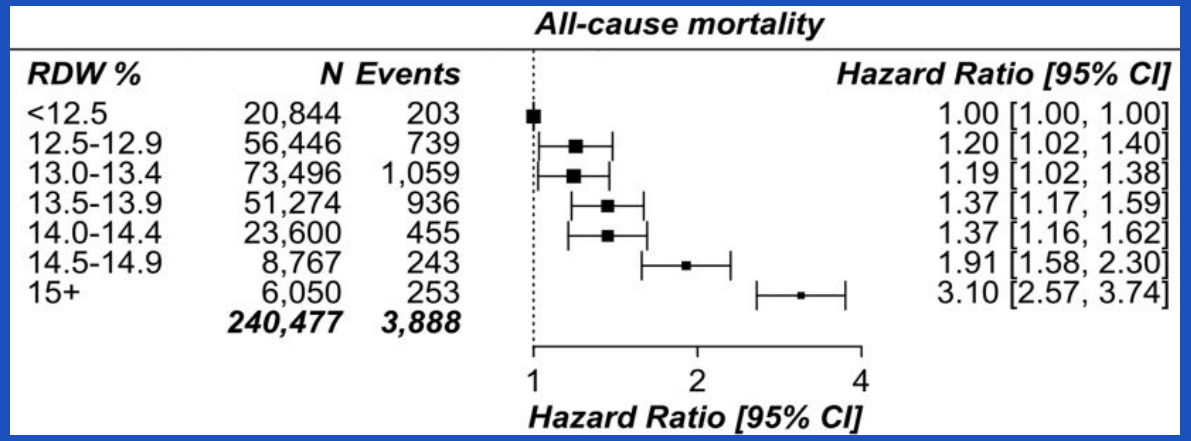


Lippi *et al.* 2014

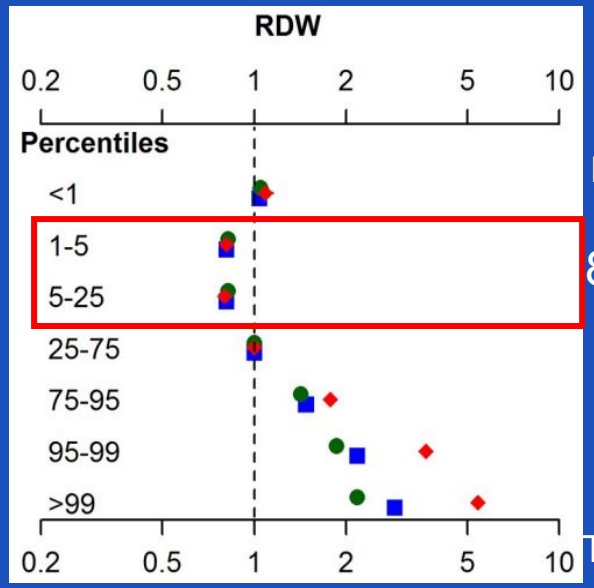
A Higher RDW% Is Associated With An Increased All-Cause Mortality Risk



Zidar *et al.* 2019



Pilling *et al.* 2018



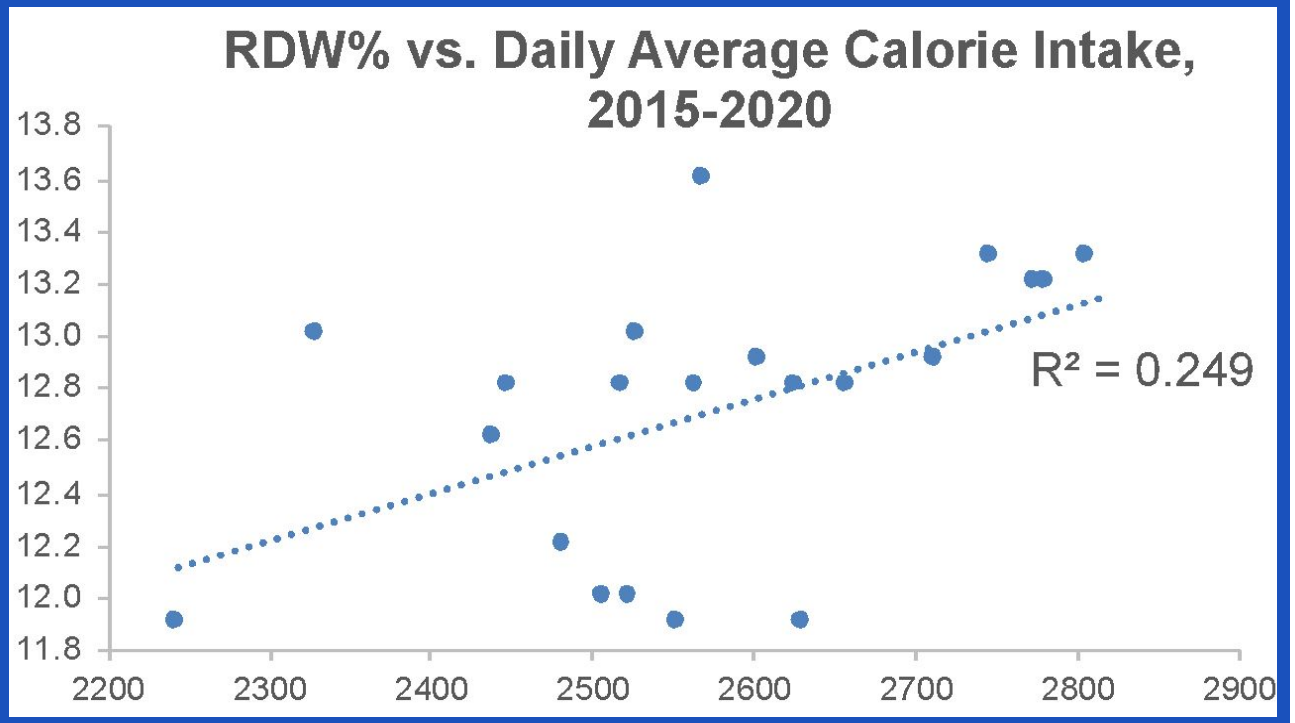
n=3,156,863

8.1 - 12.5%

>13.1%

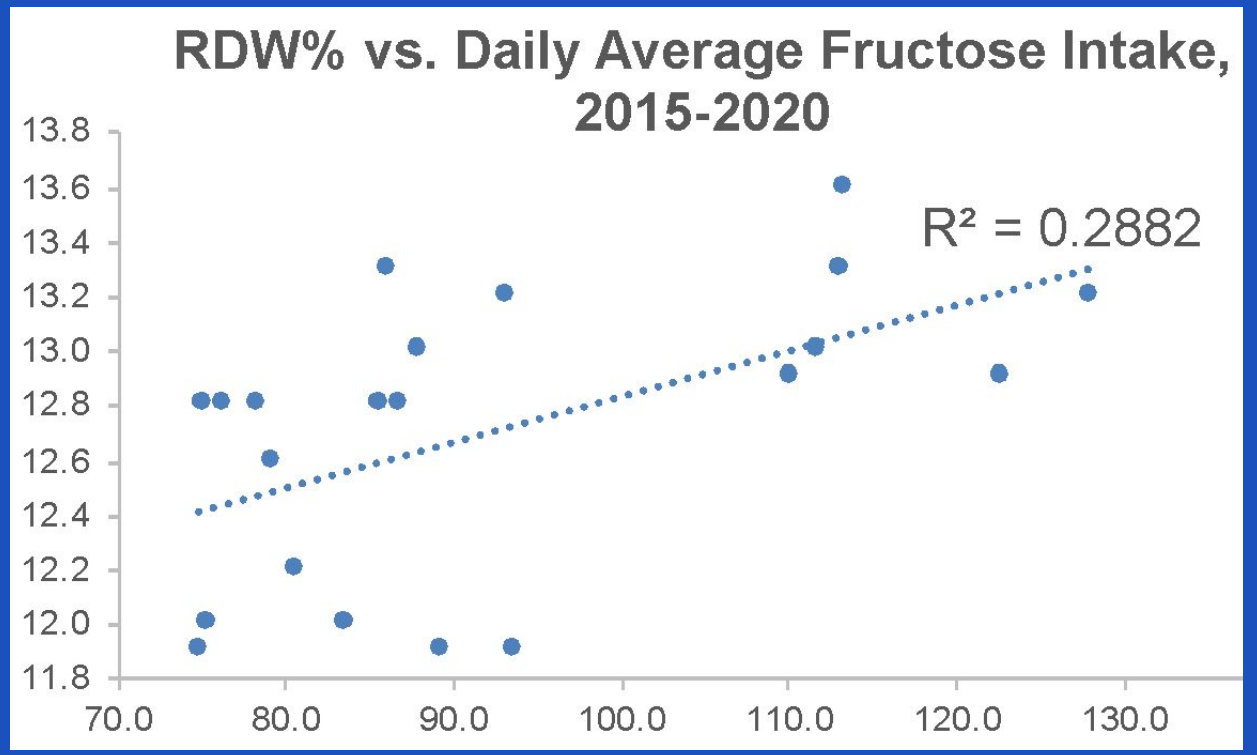
Tonelli *et al.* 2019

Higher Calorie And Fructose Intake Are Correlated with RDW%



Moderately strong correlation (r = 0.5) for average daily calorie intake with RDW%

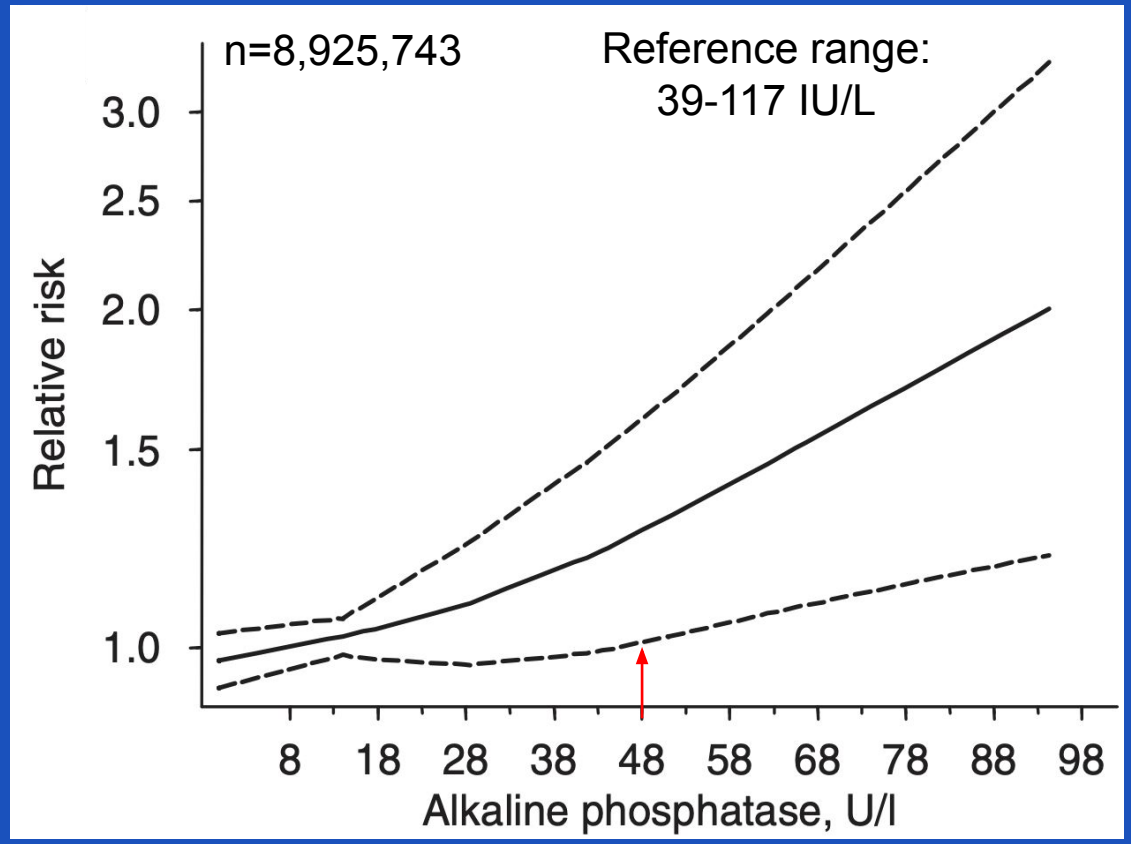
Calories from what, though?



Based on these data, with the goal of optimizing RDW%, I currently aim for ~2500 calories/day, < 70g/day from fructose

Alkaline Phosphatase Increases During Aging, And Higher Values Are Associated With An Increased ACM Risk

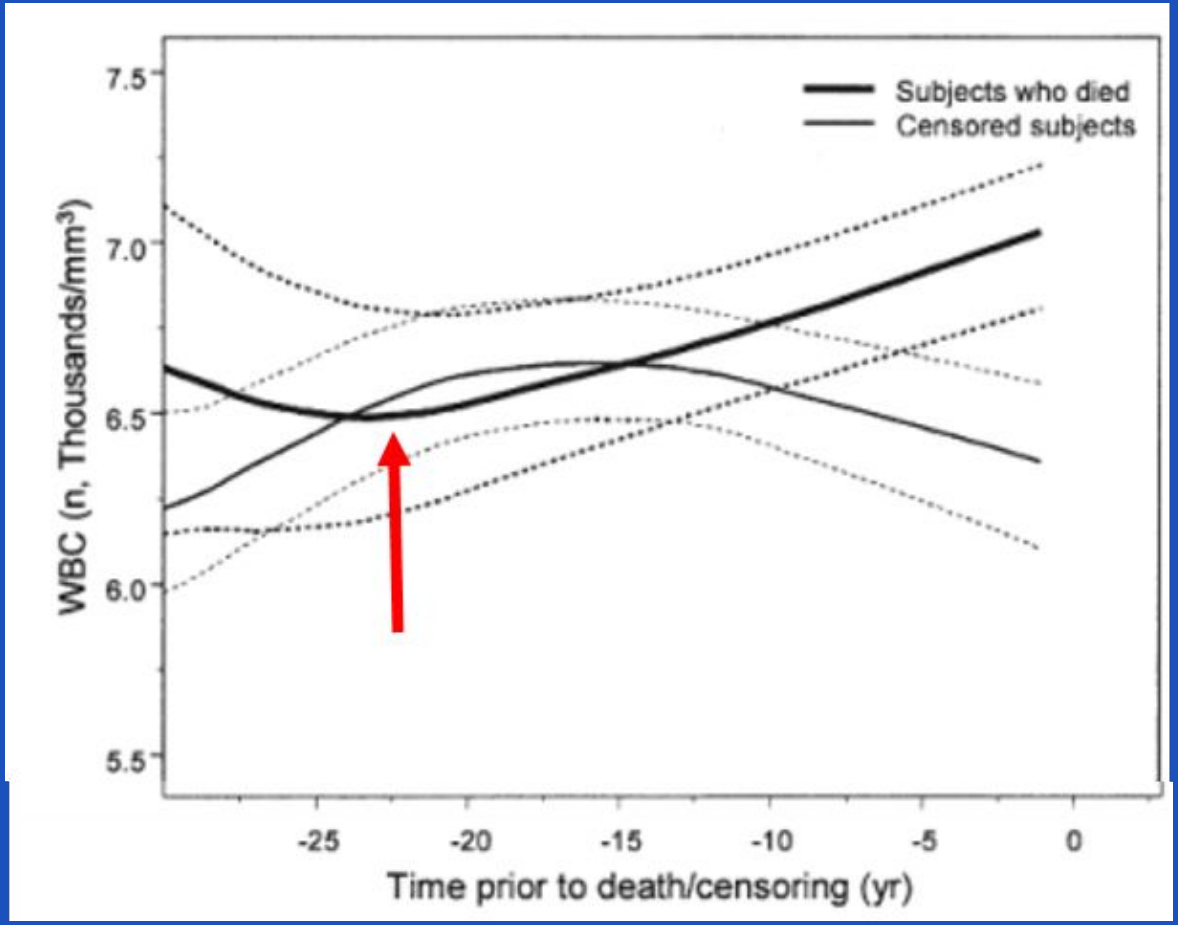
Alkaline phosphatase increases during aging (Levine 2013)

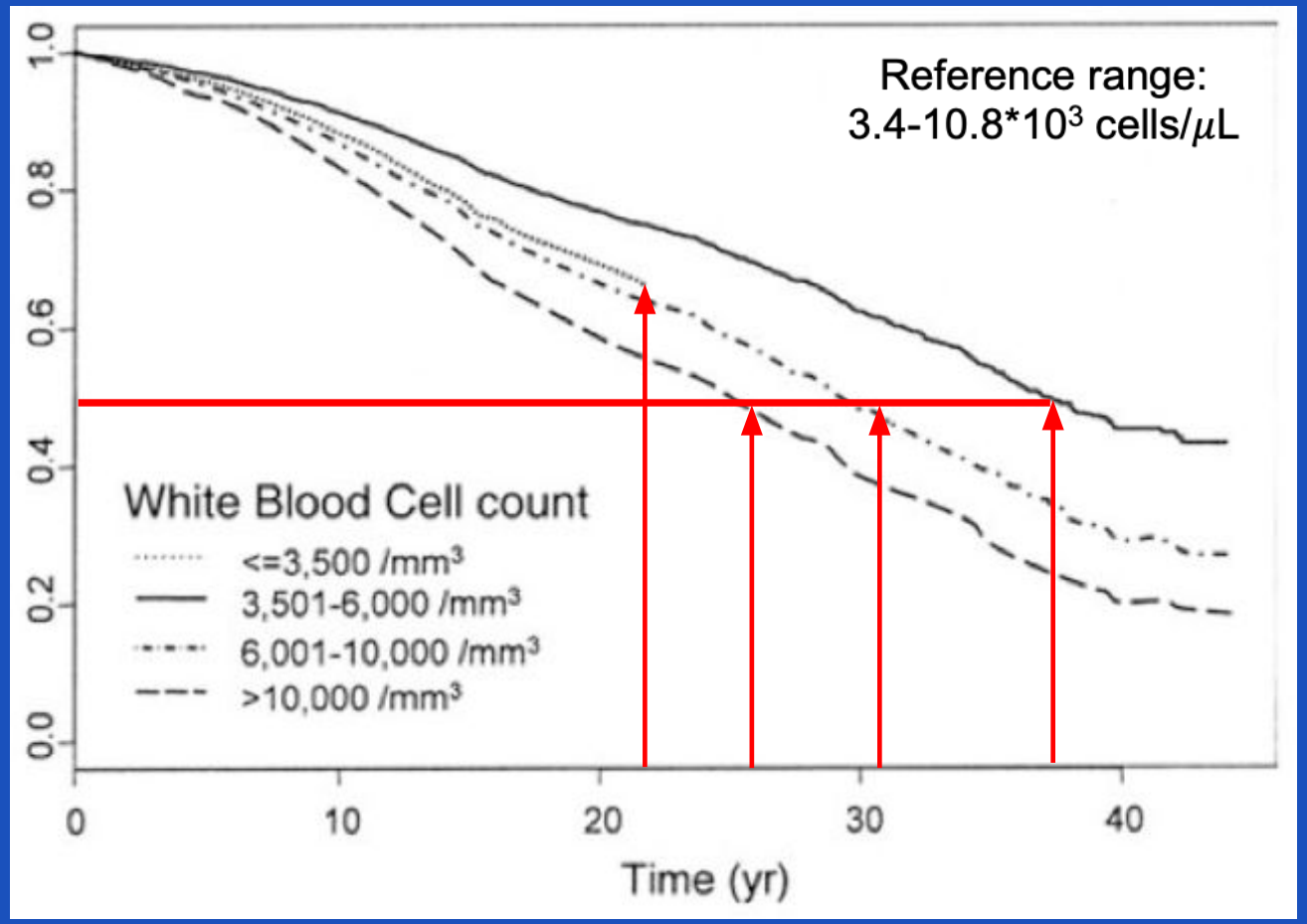


Kunutsor *et al.* 2014

All-cause mortality risk significantly increases above 48 U/L

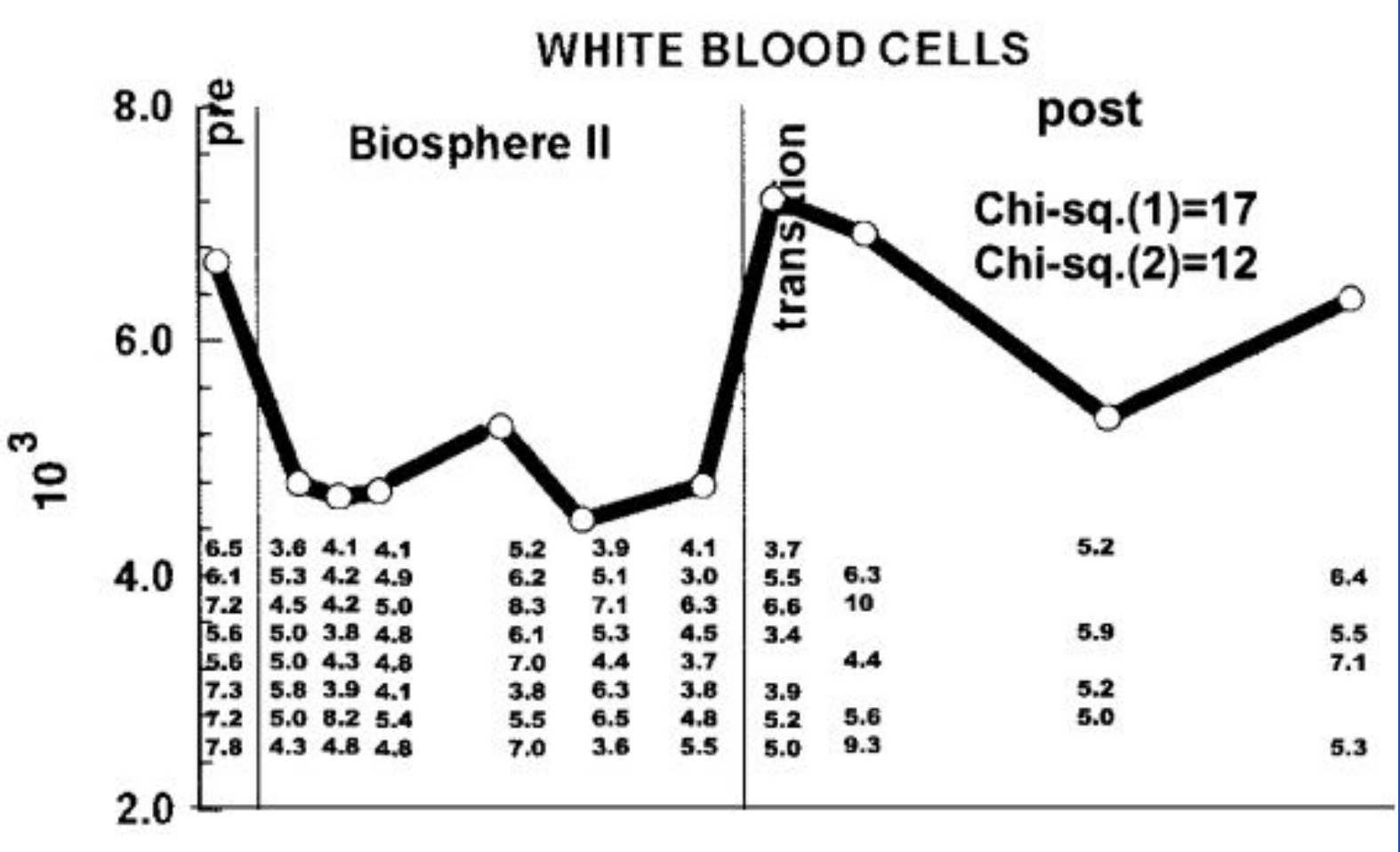
White Blood Cells (WBCs) Increase During Aging, And Higher Values Are Associated With A Shorter Life Expectancy





Ruggiero et al. 2007

White Blood Cells (WBCs) Decrease In Response to Calorie Restriction And Weight Loss



Walford et al. 2002

The correlations for WBCs with my average daily calorie intake and body weight are weak, but CR and BW reduction may result in reduced WBCs for others

Potential Optimal Ranges For Phenotypic Age Variables

Variable	Reference Range	Optimal range
Albumin	35-55 g/L	44, 45 g/L for women, men
Creatinine	0.76-1.27 mg/dL	Higher is better 0.6-1.1 mg/dL
Glucose, serum	65-99 mg/dL	80-94 mg/dL
C-reactive protein	0-3 mg/L	< 0.33 mg/L, lower is better
Lymphocyte percent	Not established	2000-2600*$10^3/\mu L$
Mean (red) cell volume	79-97%	~89-91%, lower found in chronological youth
Red cell distribution width	11.6-15.4%	8.1-12.5%, lower found in chronological youth
Alkaline phosphatase	39-117 IU/L	< 48 IU/L
White blood cell count	3.4-10.8*10^3 cells/μL	3.5-6.0*10^3 cells/μL
Age		

Notes

For more info, I've organized relatively brief literature reviews for each of these 9 biomarkers at https://michaellustgarten.com/2019/11/20/quantifying-biological-age-checklist/

Some biomarkers may be easier to modify than others (Albumin, Glucose, CRP, Creatinine, WBCs vs. Lymphocyte%, MCV, RDW, Alkaline Phosphatase)

Continuous trial-and-error process to find the diet, exercise, and body composition approach that optimizes internal health

Thanks for your attention!

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