Health Studies Collegium Foundation

Rethink Health: Predictive Biomarkers

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PERQUE™ Integrative Health,
ELISA/ACT™ Biotechnologies,
RMJH Rx

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THE NEXT BIG THING

Predictive Biomarkers

Ethnic

Geographic

Socioeconomic

Predictive Significance

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High sensitivity

PREDICTIVE BIOMARKERS TESTS

Epigenetics,

Metabolomics &

Microbiomics

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PREDICTIVE BIOMARKERS TESTS

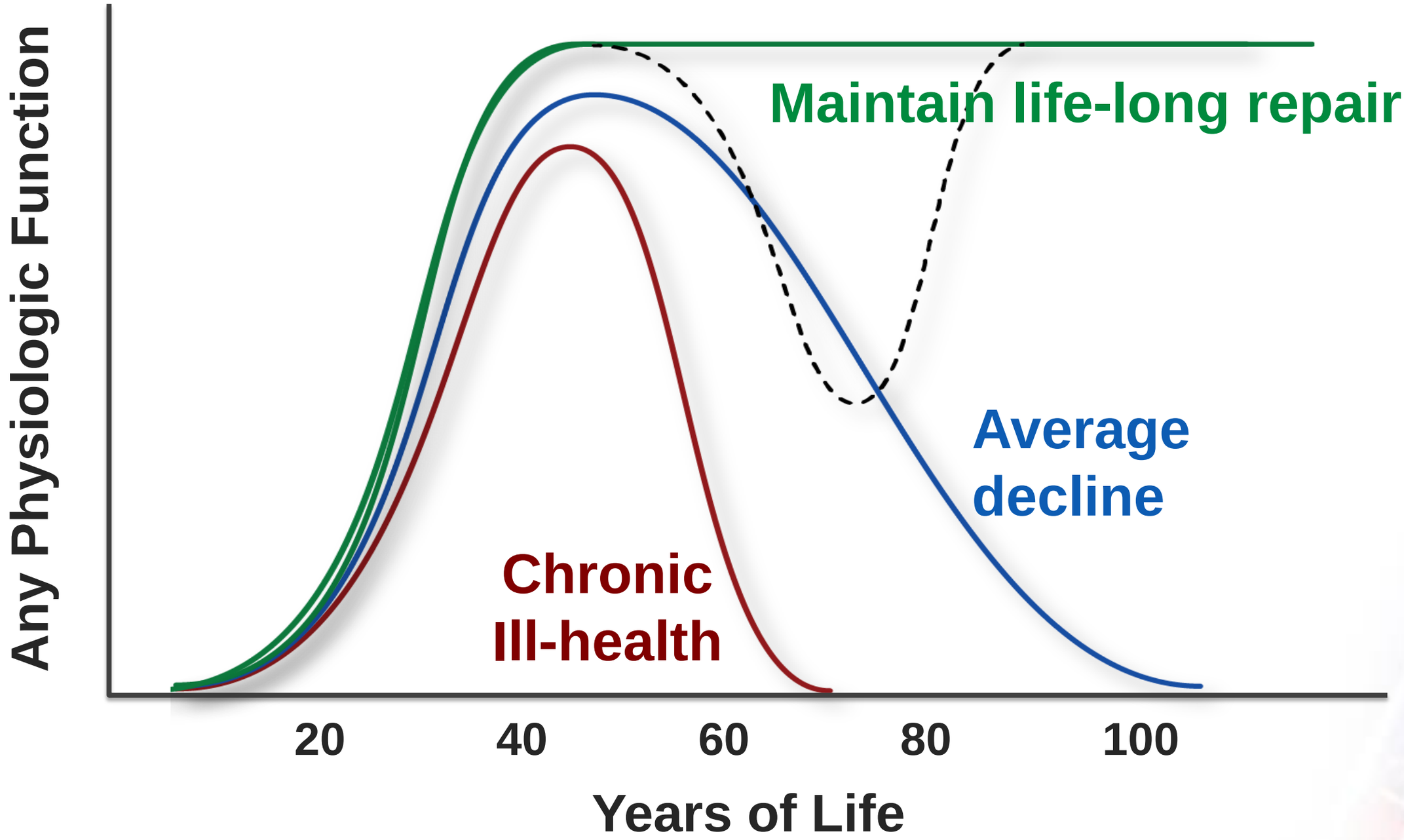
hsPB

All cause morbidity & mortality

Compare therapy outcomes

Therapeutic Biomarkers

Averages deceive; individuals choose



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High Sensitivity Predictive Biomarkers (hsPB)
Personalized, Evidence-Based, Comparative

hsHgb A1c:

Sugar, insulin… **AGEs**

hsCRP:

Inflammation, repair disease

8 oxo-guanine:

Oxidative stress… **ALEs**

hsHomocysteine:

Methylation, detox…**Sulfur**

Omega 3 Index:

Omega 3:6; **EFAs**

hsLRA

Immune Tolerance

Vitamin D:

Cell talk & adhesion

1st AM urine pH:

cell acidosis risk

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Jaffe R, Predictive Biomarkers Provide Evidence for Comparative Effectiveness Research, HSC 90_13:01 Advisory on Predictive Medicine & Health Promotion.

Gruenewald TL, Seeman TE, Ryff CD, Karlamangla A, Singer BH. Combinations of Biomarkers Predictive of Later Life Mortality. *PNAS*, 2006; 103 (38): 14158-14163.

Essential Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Predictive Goal Values
hsHgb A1c (hsHemoglobin A1c)	Sugar / insulin / energy… **AGE**	<5%
hsCRP (hsC-Reactive Protein)	Repair, inflammation immune status	<0.5 mg/L
hsHCY (hsHomocysteine)	Detox, epigenetic, methylation… **Sulfur**	< 6 µmol/L
hsLRA (hsLymphocyte Response Assay)	Immune memory / repair tolerance	No delayed reactions

Elective Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Predictive Goal Values
1st AM Urine pH (acid/alkaline status)	Mineral need & cell acidosis risk	**6.5 – 7.5**
Vitamin D (25-Hydroxy-cholecalciferol)	Vitamin D level (cell communication status)	**50 – 80 ng/mL**
Omega-3 Index (Omega 3:6 EFA ratio)	Omega 3:6 ratio; EFAs	**>8%**
8-OHdG (8-Oxo-Guanine)	Oxidative stress and antioxidant status	**<5 ng/mg creatinine**

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Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Predictive Goal Values
hsHgb A1c (hsHemoglobin A1c)	Sugar/insulin/energy… **AGE**	<5%
hsCRP (hsC reactive protein)	Repair & inflammation immune status	<0.5 mg/L
hsHCY (hsHomocysteine)	Detox, epigenetic, methylation… **Sulfur**	< 6 µmol/L
hsLRA (hslymphocyte response assay)	Immune memory/immune tolerance	No reactions
Ur pH >6º rest (1st AM Urine pH)	Mineral status & cell acid/alkaline balance	6.5 – 7.5
Vitamin D (25-Hydroxy-cholecalciferol)	Cell communication status	50 – 80 ng/mL
Omega-3 Index (Omega 3/6 EFA ratio)	Omega 3:6 ratio; EFAs	**>8%**
8-OHdG (8-Oxo-Guanine)	Oxidative stress/antioxidant nucleus status	**<5 ng/mg creatinine**

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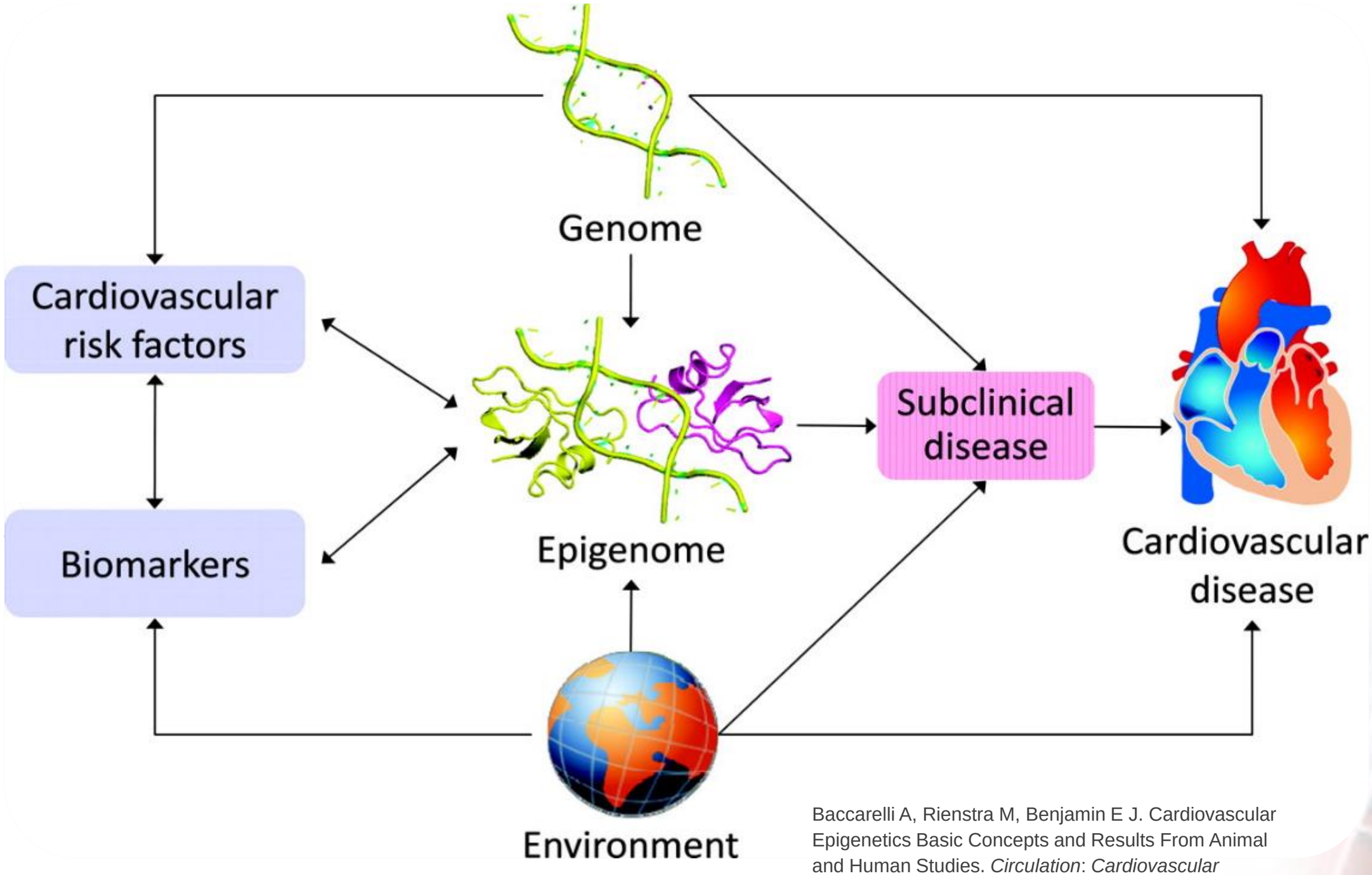
Lifetime Health: 92% choices



Baccarelli A, Rienstra M, Benjamin E J. Cardiovascular Epigenetics Basic Concepts and Results From Animal and Human Studies. *Circulation*: *Cardiovascular Genetics.* 2010; 3: 567-573.

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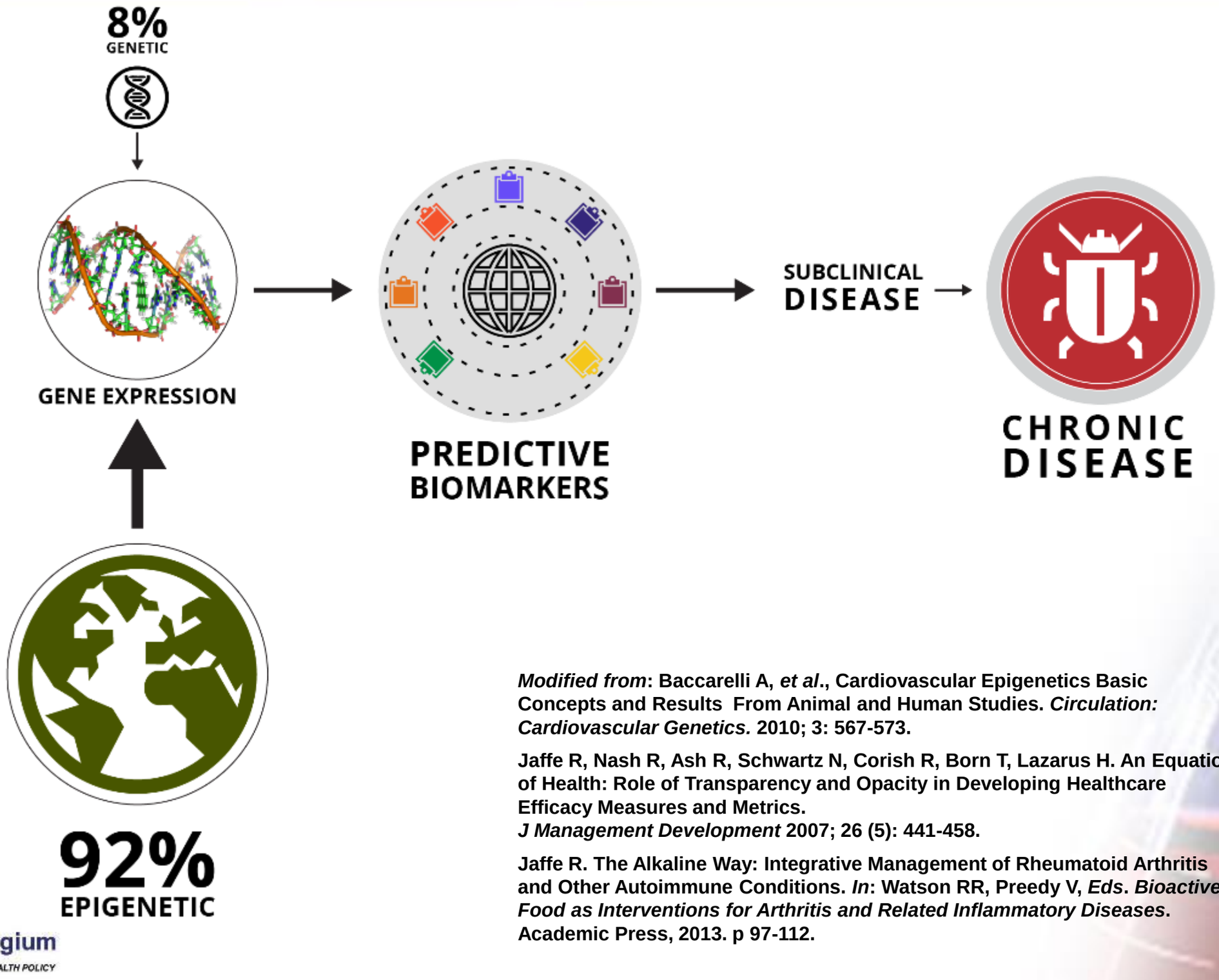
Lifetime Health: 92% choices



***Modified from*: Baccarelli A, *et al*., Cardiovascular Epigenetics Basic Concepts and Results From Animal and Human Studies. *Circulation: Cardiovascular Genetics.* 2010; 3: 567-573.**

Jaffe R, Nash R, Ash R, Schwartz N, Corish R, Born T, Lazarus H. An Equation of Health: Role of Transparency and Opacity in Developing Healthcare Efficacy Measures and Metrics.
***J Management Development* 2007; 26 (5): 441-458.**

Jaffe R. The Alkaline Way: Integrative Management of Rheumatoid Arthritis and Other Autoimmune Conditions. *In*: Watson RR, Preedy V, *Eds*. *Bioactive Food as Interventions for Arthritis and Related Inflammatory Diseases*. Academic Press, 2013. p 97-112.

Predictive Biomarker 1

hsHemoglobin A1c = hsHgb A1c = hsHbA1c

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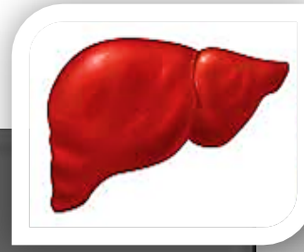
Insulin & Blood Sugar Control

Glucose Production

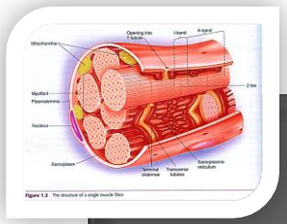


Liver

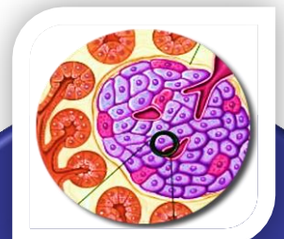
Blood Glucose

Insulin

Glucose Uptake



Muscle:
Fat from sugar
(as energy store);
receptors can be resistant



Pancreatic Islet Cells

Secretion triggers blood glucose

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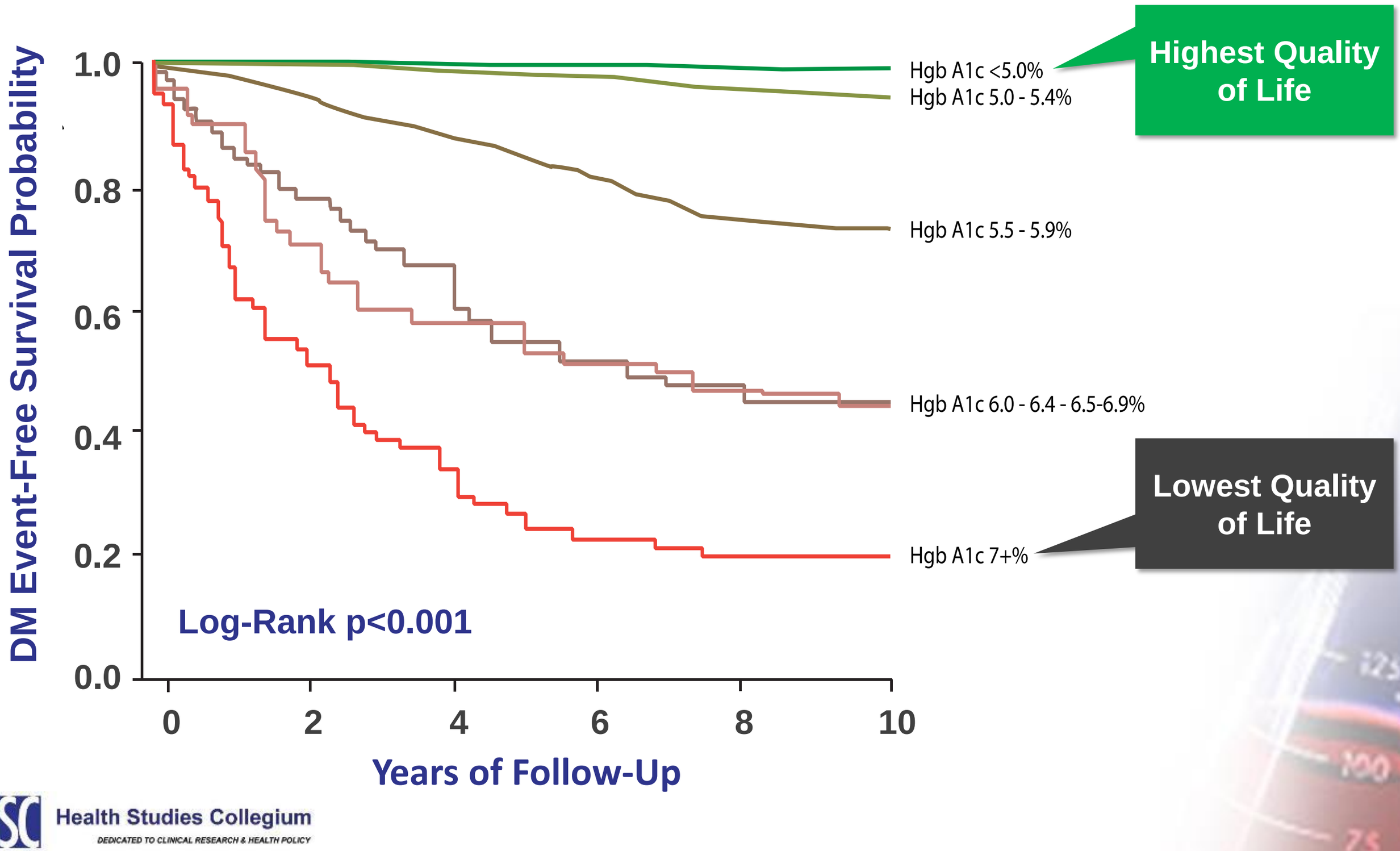
Hgb A1c <5 *is* Predictive Biomarker



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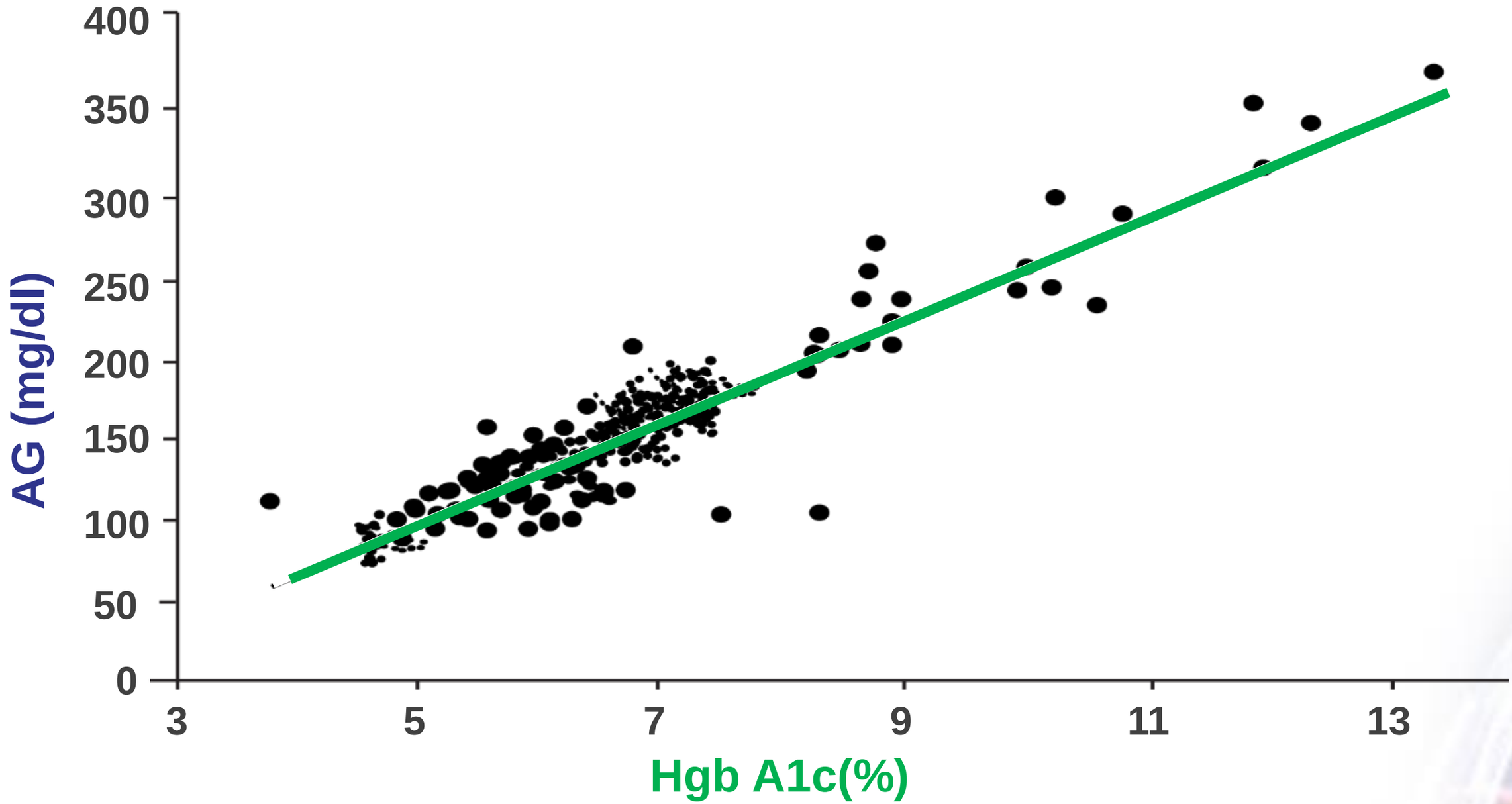
Hgb A1c Predicts AG (Average Glucose; Blood Sugar)



Hinzmann R, Schlaeger C, Tran C T. What Do We Need Beyond Hemoglobin A1c to Get the Complete Picture of Glycemia in People With Diabetes? *Int. J. Med. Sci*. 2012; 9: 665-681

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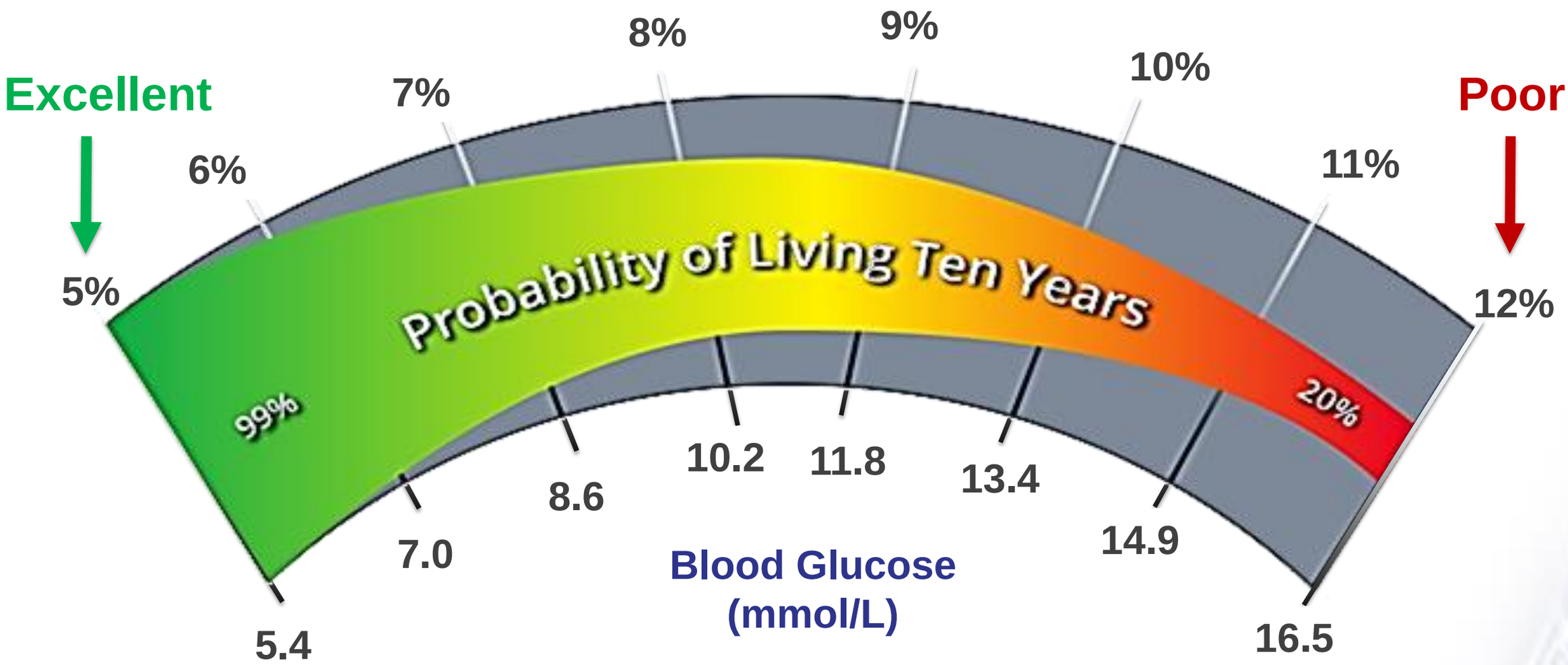
Hgb A1c / HgA1c Predicts Survival



Bunn HF, Haney DN, Gabbay KH, Gallop PM. Further Identification of the Nature and Linkage of the Carbohydrate in Hemoglobin A1c. *Biochem Biophys Res Commun*. 1975; 67(1): 103-109.

Luevano-Contreras C et al, *Dietary Advanced Glycation End-Products and Aging. Nutrients* 2010; 2: 1247-1265.

Hinzmann R, Schlaeger C, Tran C T. What Do We Need Beyond Hemoglobin A1c to Get the Complete Picture of Glycemia in People with Diabetes? *Int J Med Sci* 2012; 9(8):665-681. doi:10.7150/ijms.4520

Gruenewald TL, Seeman TE, Ryff CD, Karlamangla A, Singer BH. *Combinations of Biomarkers Predictive of Later Life Mortality. PNAS,* 2006; 103 (38): 14158-14163.

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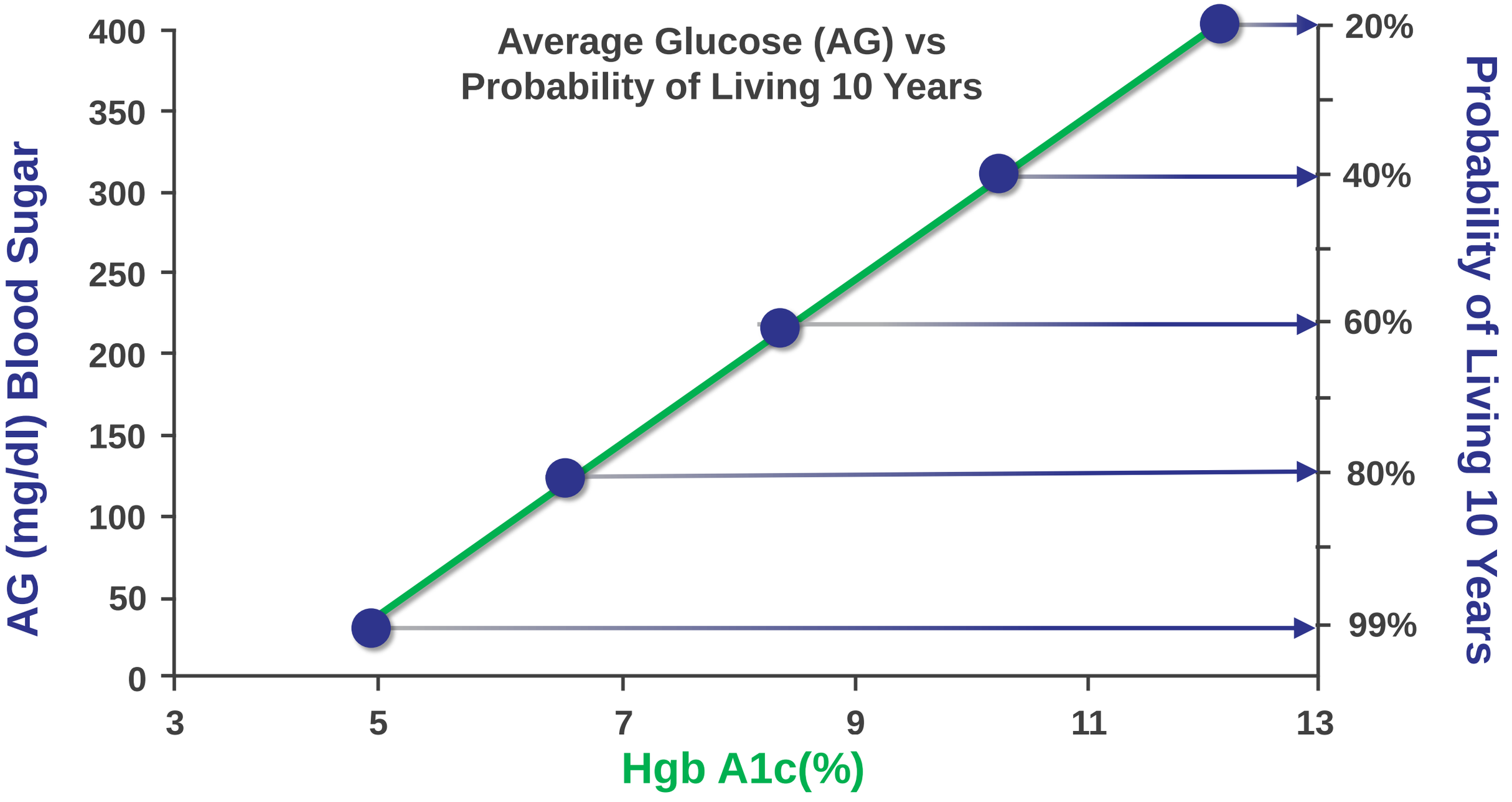
hsHgb A1c
Predictive Biomarker Report



Hardy H et al, Probiotics, Prebiotics and Immunomodulation of Gut Mucosal Defenses: Homeostasis and Immunopathology, *Nutrients*, 2013; 5(6): 1869-1912.

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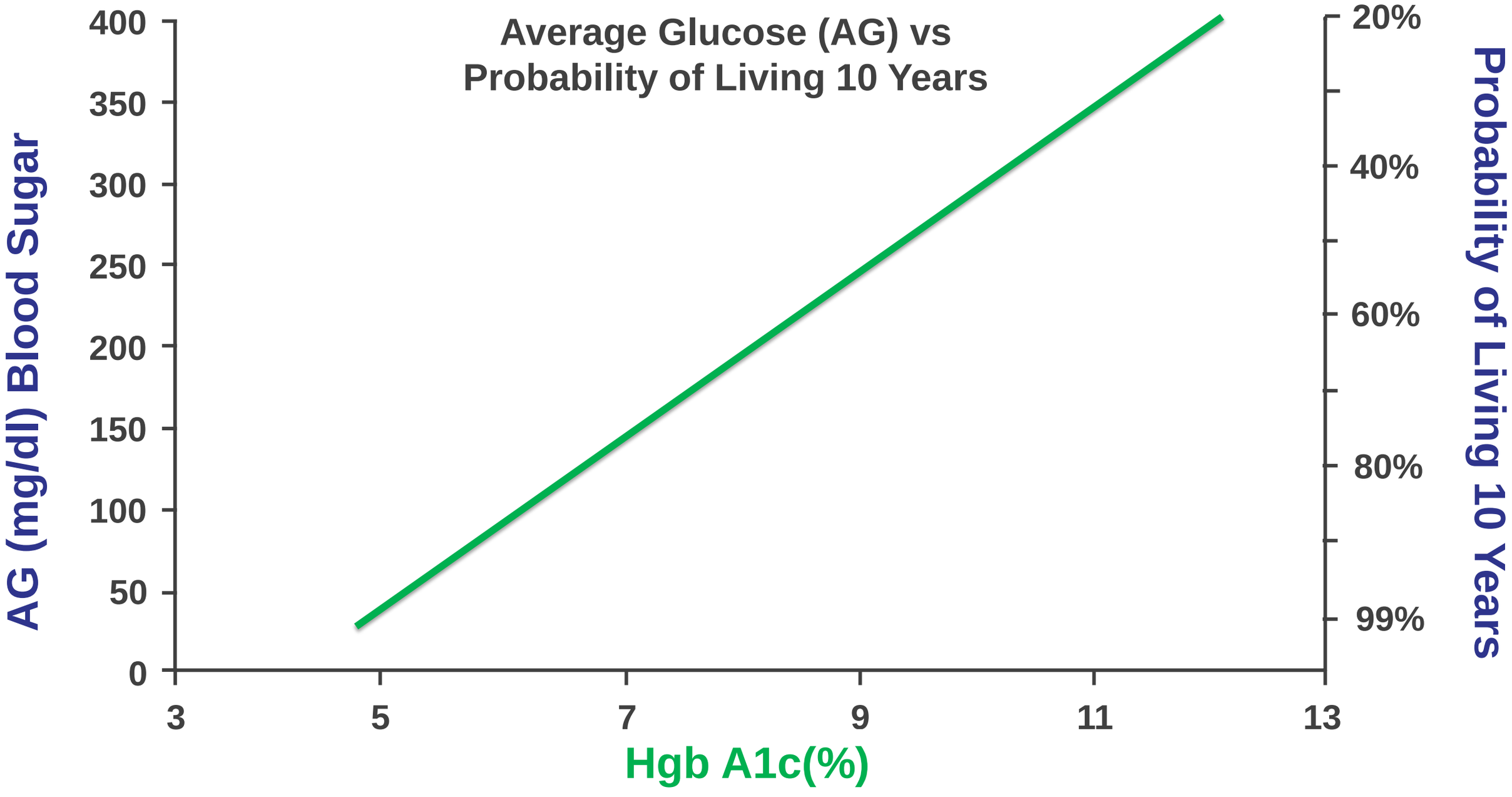
hsHgb A1c
Predictive Biomarker Report



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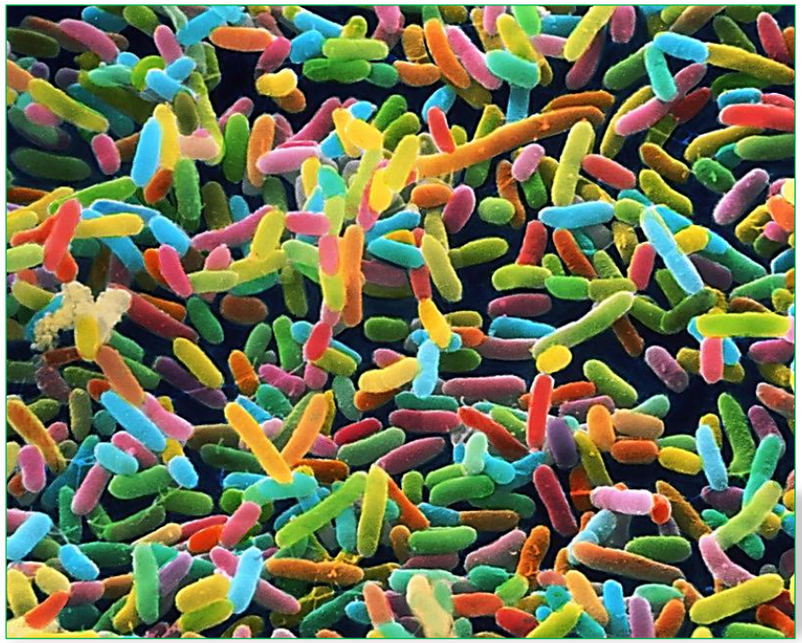
Hgb A1c >5%, Life Habit Solutions

- Immunotolerant Diet
- 40 Component Super Multi

40+ g Fiber

40+ Bn live Probiotics



Hyman M, Mani J, Jaffe R. Diabetes and Insulin Resistance, Food and Nutrients in Primary Care. In: Kohlstadt I, Ed. Advancing Medicine with Food and Nutrients, 2nd Ed., CRC Press, 2012, p 373-390.

Jaffe, R. Diabetes as an Immune Dysfunction Syndrome. In: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions for Diabetes, Academic Press, 2013, p 41-52.

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Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators > actives:

Lagerstroemia Speciosa

- **Standardized corosolic acid, 50 mg***

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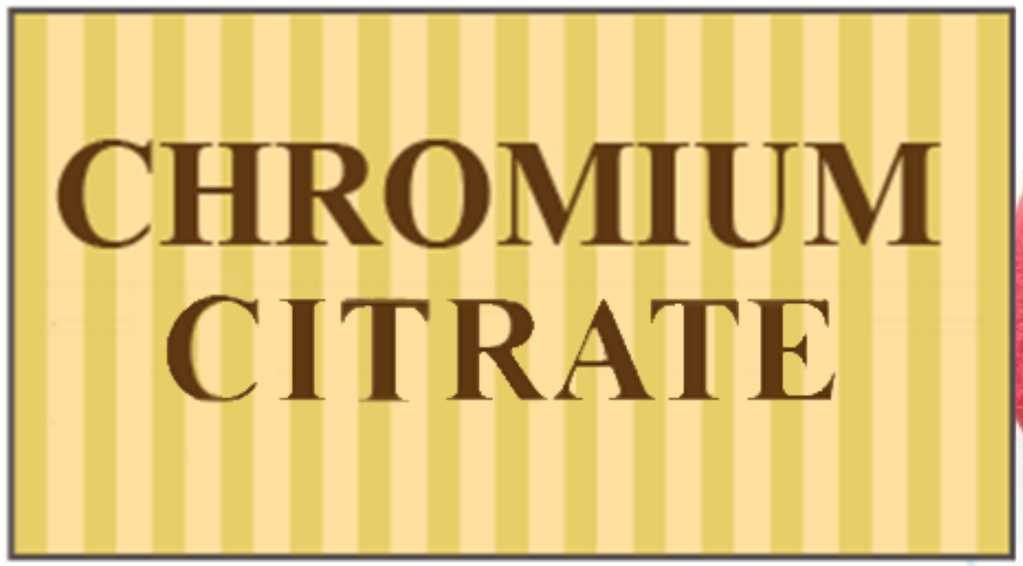
Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators when
more active* forms** are then ***micellized:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***

Chromium as citrate
250 mcg*



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Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators when ***more active* forms** are then ***micellized***:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***

Vanadium as ascorbate 250 mcg*

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Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators when
more active* forms** are then ***micellized:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***
- **French lilac, 150 mg***

French Lilac
150 mg*

Hyman M, Mani J, Jaffe R. Diabetes and Insulin Resistance, Food and Nutrients in Primary Care. In: Kohlstadt I, Ed. Advancing Medicine with Food and Nutrients, 2nd Ed., CRC Press, 2012. p 373-390.

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Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators when
more active* forms** are then ***micellized:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***
- **French lilac, 150 mg***
- **Bitter Melon / Marah, 150 mg***

Bitter Melon / Marah
150 mg*

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Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators when ***more active* forms** are then ***micellized***:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***
- **French lilac, 150 mg***
- **Bitter Melon / Marah, 150 mg***
- **Huckleberry / Bilberry, 100 mg***

Huckleberry / Bilberry 100 mg*

Hyman M, Mani J, Jaffe R. Diabetes and Insulin Resistance, Food and Nutrients in Primary Care. In: Kohlstadt I, Ed. Advancing Medicine with Food and Nutrients, 2nd Ed., CRC Press, 2012. p 373-390.

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Hgb A1c >5%, herbal solutions

Herbal ***symbiotic*** sugar regulators when
more active* forms** are then ***micellized:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***
- **French lilac, 150 mg***
- **Bitter Melon / Marah, 150 mg***
- **Huckleberry / Bilberry, 100 mg***
- **Agnus Castus, 250 mg***

Agnus Castus 250 mg*

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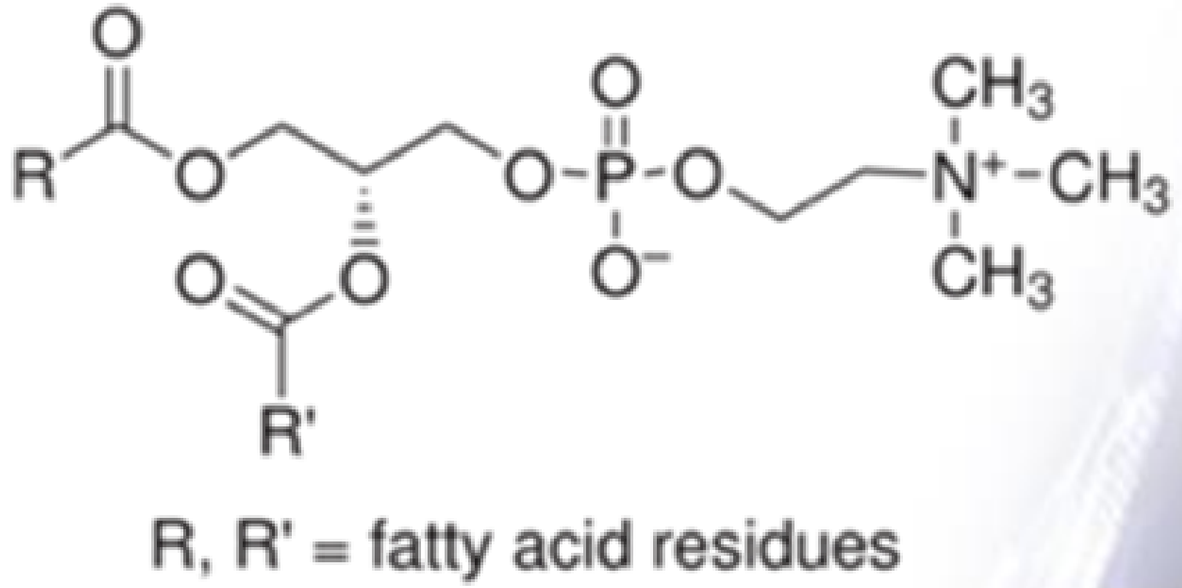
Jaffe, R. Diabetes as an Immune Dysfunction Syndrome. In: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions for Diabetes, Academic Press, 2013. p 41-52.

Hgb A1c >5%, single softgel

Herbal ***symbiotic*** sugar regulators when ***more active* forms** are then ***micellized***:

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***
- **French lilac, 150 mg***
- **Bitter Melon / Marah, 150 mg***
- **Huckleberry / Bilberry, 100 mg***
- **Phosphatidylcholine, 71 mcg***

Phosphatidylcholine
71 mcg*



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Jaffe, R. Diabetes as an Immune Dysfunction Syndrome. In: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions for Diabetes, Academic Press, 2013. p 41-52.

Hgb A1c >5%, Manage AGEs

Herbal ***symbiotic*** glucose/sugar regulators
more active* forms** then ***micellized for 3X greater uptake

- **Standardized corosolic acid, 50 mg***
- **Chromium as citrate, 250 mcg***
- **Vanadium as ascorbate, 250 mcg***
- **French lilac, 150 mg***
- **Bitter Melon / Marah, 150 mg***
- **Huckleberry / Bilberry, 100 mg***
- **Phosphatidylcholine, 71 mcg***

Dose based on
Hgb A1c
or
Blood Sugar
results

Hyman M, Mani J, Jaffe R. Diabetes and Insulin Resistance, Food and Nutrients in Primary Care. In: Kohlstadt I, Ed. Advancing Medicine with Food and Nutrients, 2nd Ed., *CRC Press*, 2012. p 373-390.

Jaffe, R. Diabetes as an Immune Dysfunction Syndrome. In: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions for Diabetes, *Academic Press*, 2013. p 41-52.

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Predictive Biomarker 2

High Sensitivity

C Reactive Protein = hsCRP

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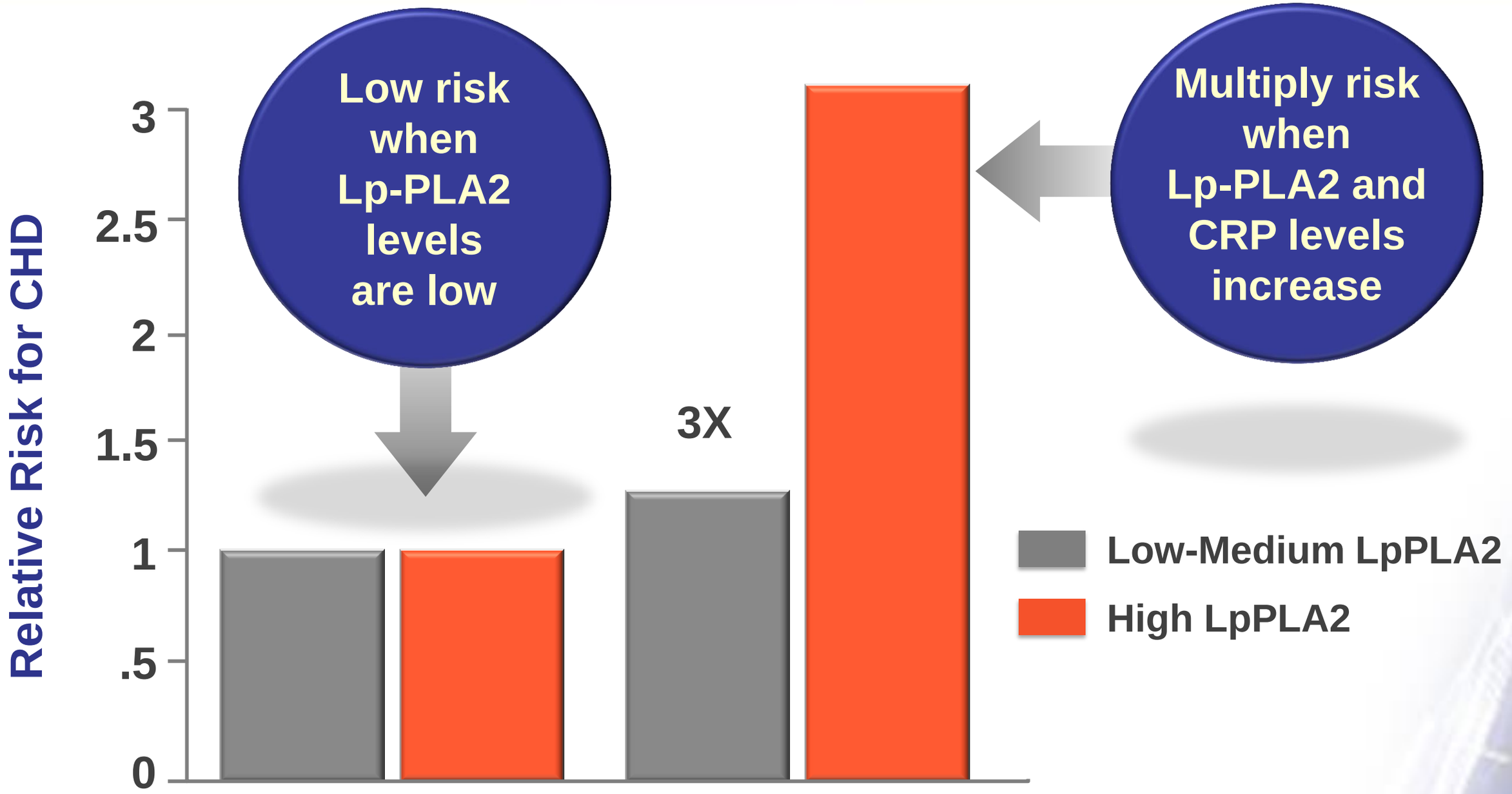
ARIC, Circulation 2004;109:837-842
Interaction of CRP & Lp-PLA2 CHD Risk in ARIC Study



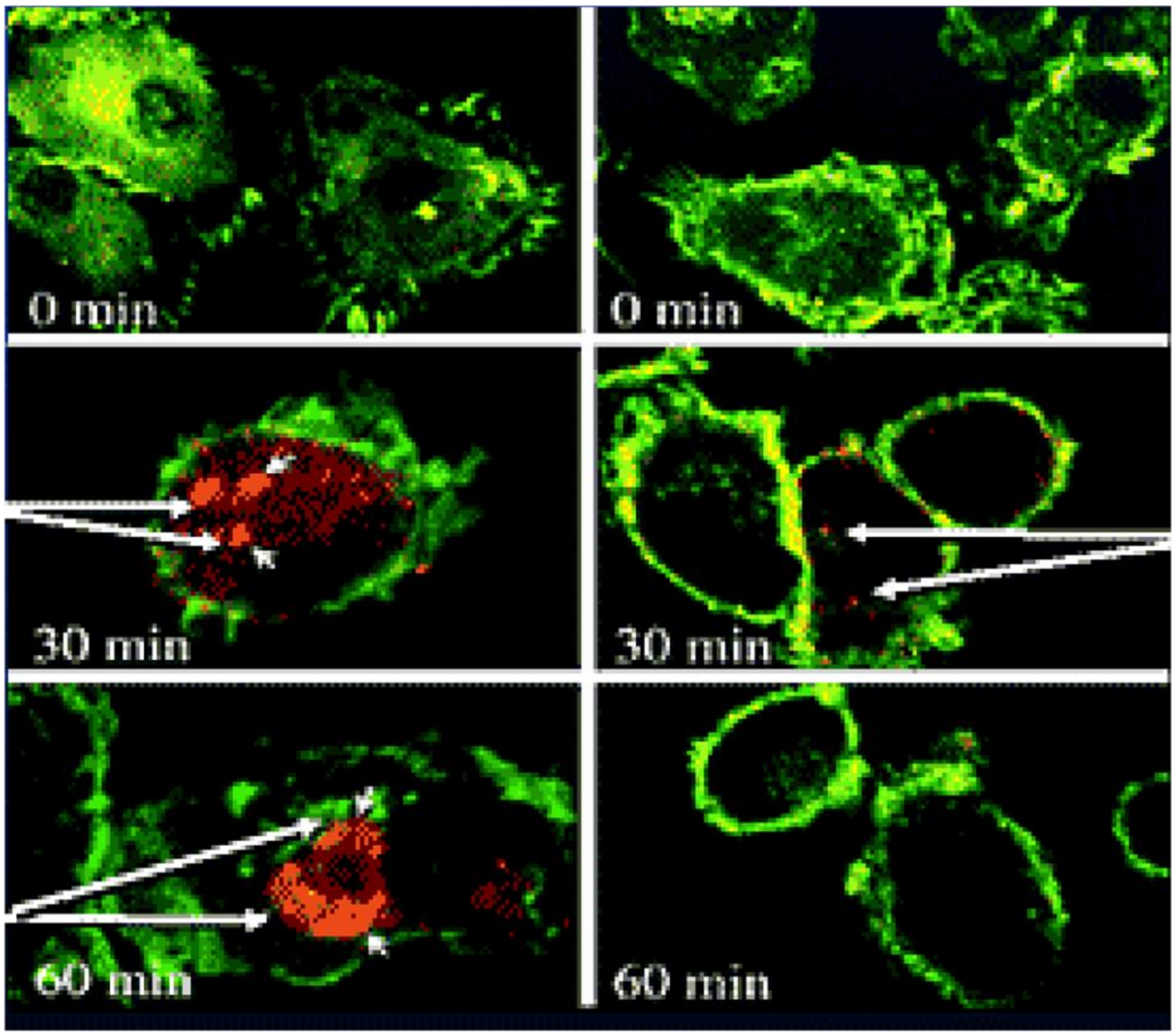
C M Ballantyne, R C Hoogeveen, H Bang, J Coresh, A R Folsom, G Heiss, A R Sharrett, Lipoprotein-Associated Phospholipase A2, High-Sensitivity C-Reactive Protein, and Risk for Incident Coronary Heart Disease in Middle-Aged Men and Women in the Atherosclerosis Risk in Communities (ARIC) *Study Circulation*. 2004; 109: 837-842.

hsCRP *is* Body's Cry For Repair

CRP-Mediated Uptake of LDL by Macrophages

Macrophages incubated with CRP / LDL

Macrophages incubated with LDL alone



LDL Containing Vesicles

Slight dissemination of LDL

LDL vesicles deeper and disseminated within the cytoplasm

No LDL Containing Vesicles

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Adaptedfrom Zwaka TP,, *et al.* Circulation 2001; 103; 1194-1197.
Silva D, Pais de Lacerda A. High-sensitivity C-reactive Protein as a Biomarker of Risk in Coronary Artery Disease, *Rev Port Cardiol*. 2012; 31: 733-745

Predictive Value of Multiple Biomarkers

JUPITER Trial: Rosuvastatin 20 mg in Older, Normolipidemic Subjects w/ ↑ hsCRP, N=17,802

- Men >50, women >60 years old CVD/DM (mean 66)
- **LDL <130 (TC 186, LDL 108, HDL 49, TG 118)**
- **hsCRP >2 mg/L (mean 4.3)**
- BMI 28, BP 134/80, FBG 94, **Hgb-A1C 5.7%**
- Metabolic syndrome 41%
- 13.6% 10-yr CV risk with placebo (intermediate)
- Study stopped early (1.9 years)*

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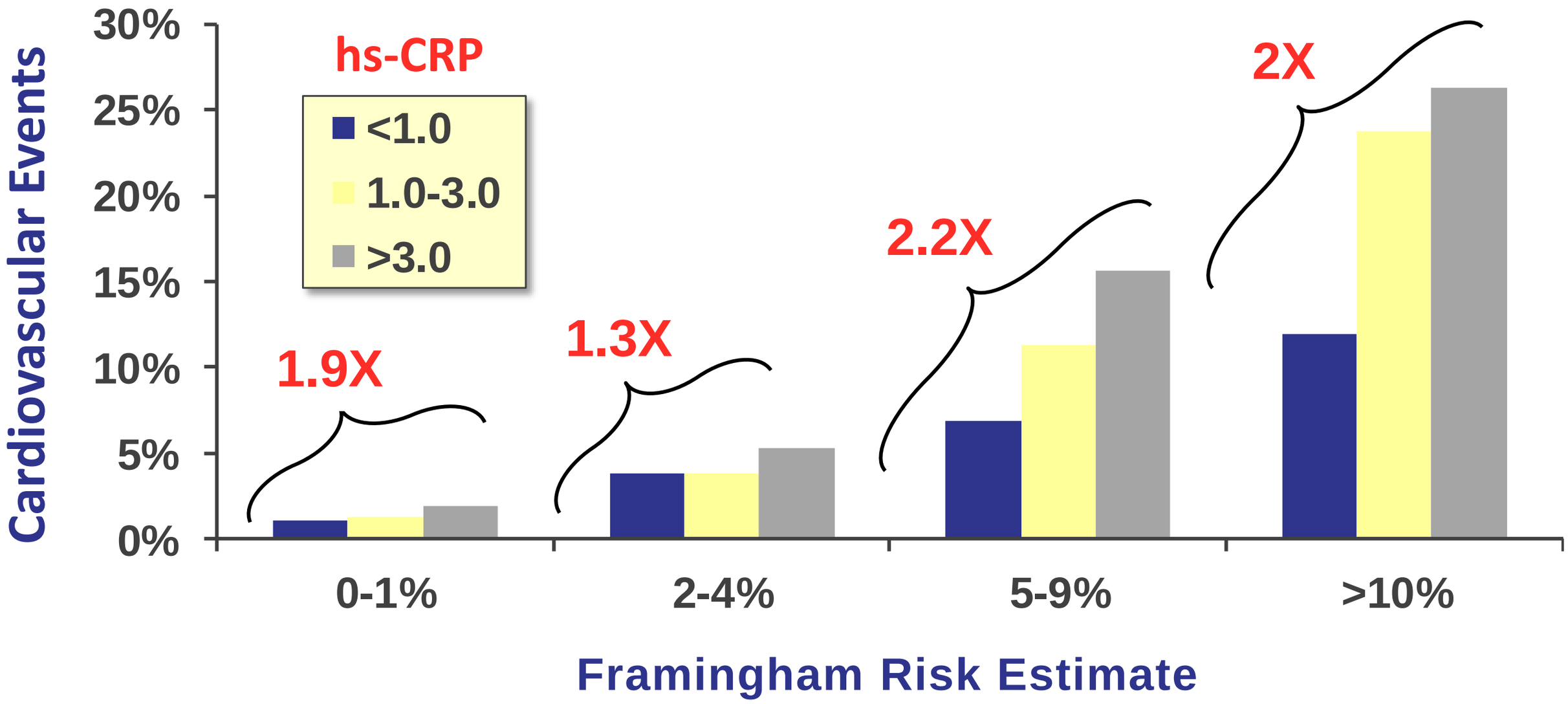
* Ridker PM, The JUPITER Trial Results, Controversies, and Implications for Prevention Circulation: *Cardiovascular Quality and Outcomes*. 2009; 2: 279-285

Support for hsCRP as Predictive Biomarker

Actual Cardiovascular Events vs Framingham Estimate + hs-CRP in WHS



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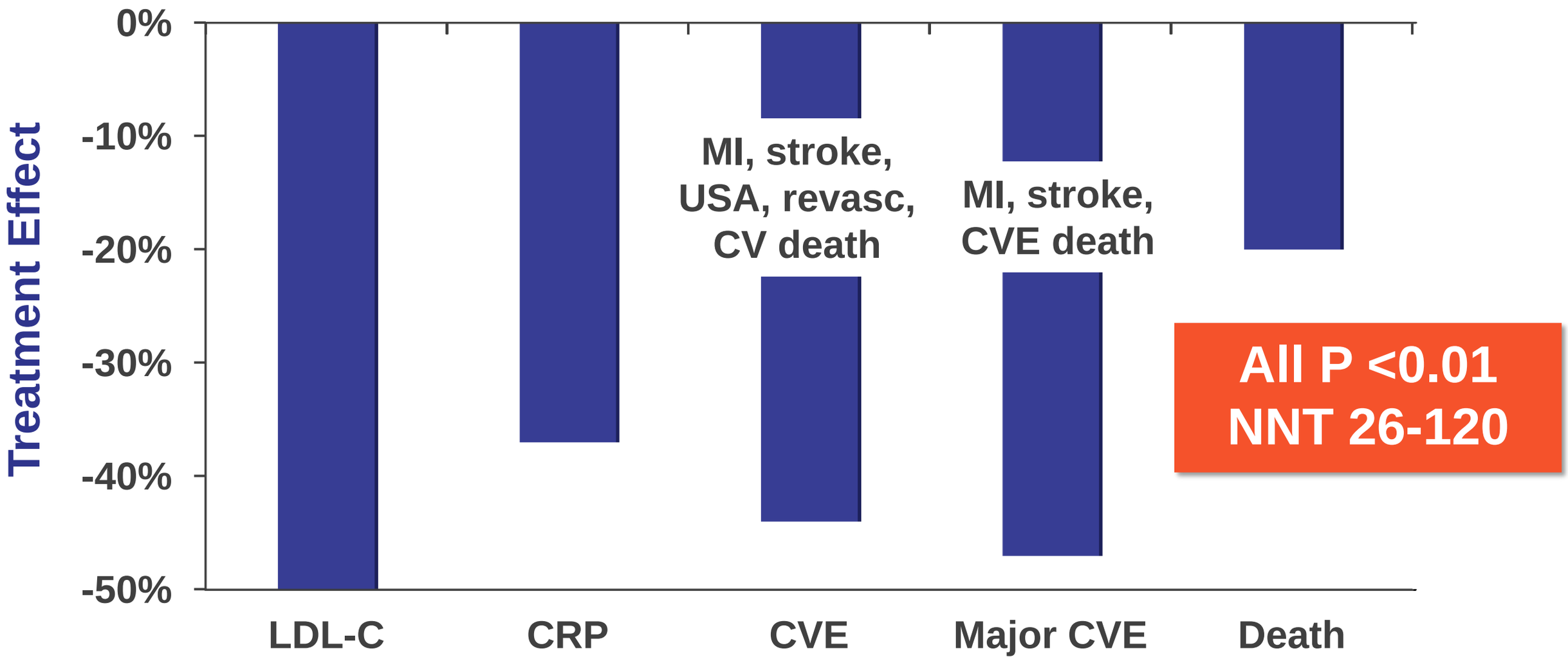
Ridker PM et al, N Engl J Med 2002;347:1557-1565

Predictive Value of Multiple Biomarkers

JUPITER Trial:

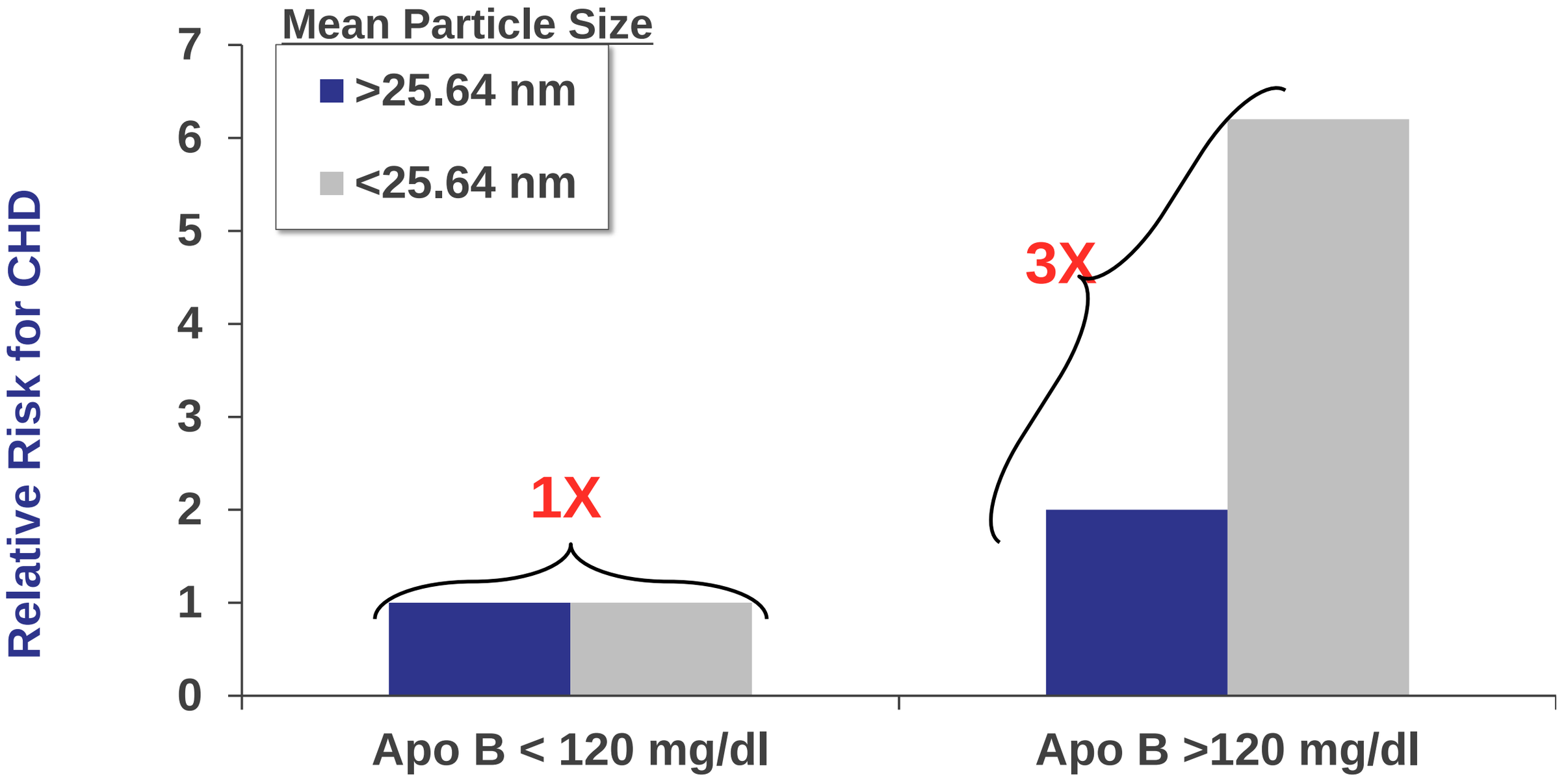
Rosuvastatin 20 mg in Older, Normolipidemic Subjects w/ ↑ hsCRP



* Ridker PM, The JUPITER Trial Results, Controversies, and Implications for Prevention Circulation: Cardiovascular Quality and Outcomes. 2009; 2: 279-285

hsCRP as Predictive Biomarker

CRP, LDL Particle Size and Apo B CHD Risk



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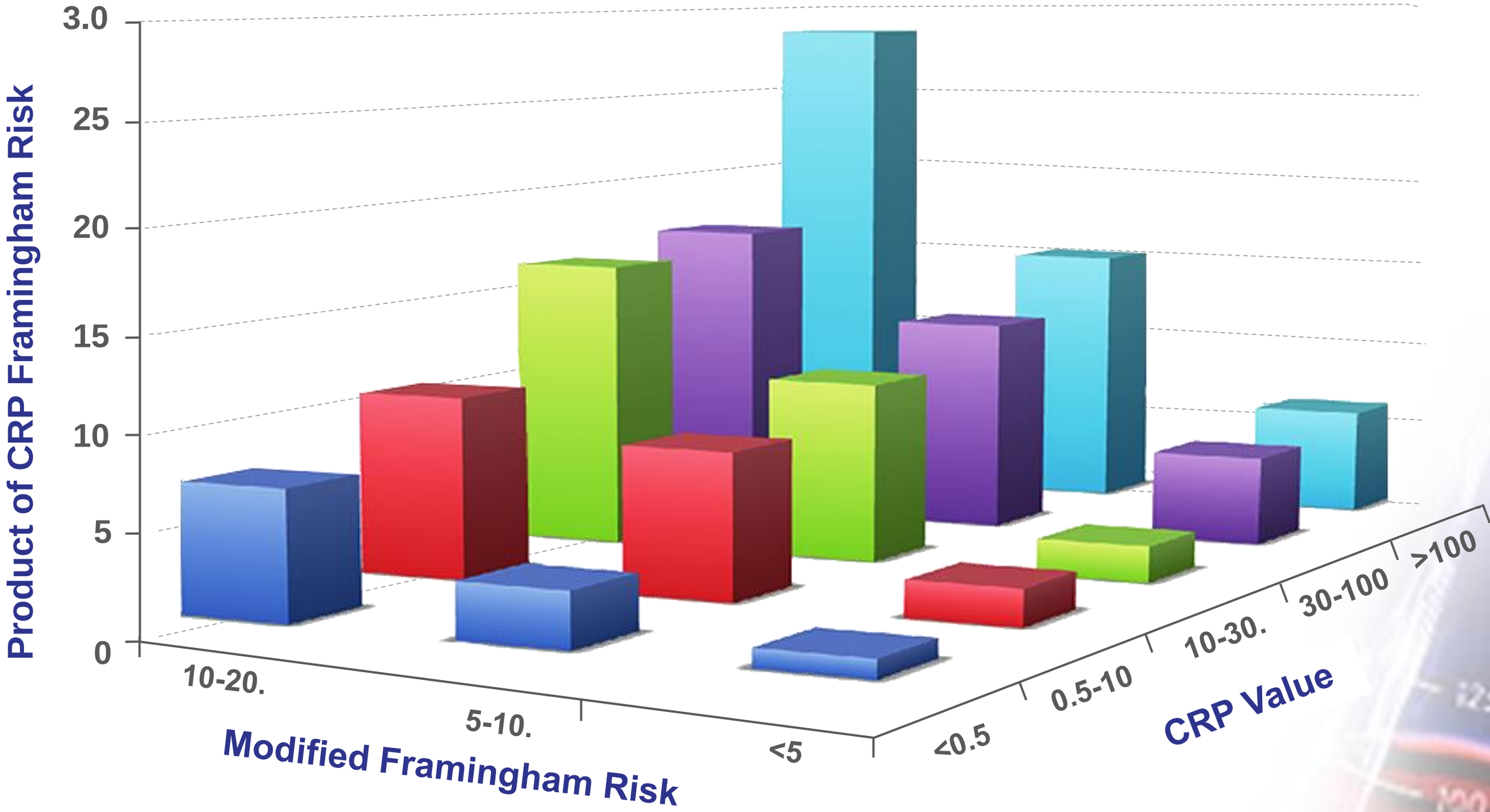
Lamarche B, Tchrnof A, Moorjani S, Cantin B *et a*l, Small, Dense Low-Density Lipoprotein Particles as a Predictor of the Risk of Ischemic Heart Disease in Men: Prospective Results From the Quebec Cardiovascular Study. *Circulation*. 1997; 95: 69-67.

hs-CRP <0.5 *is* Predictive Biomarker

Calculated Framingham 10-Year Risk



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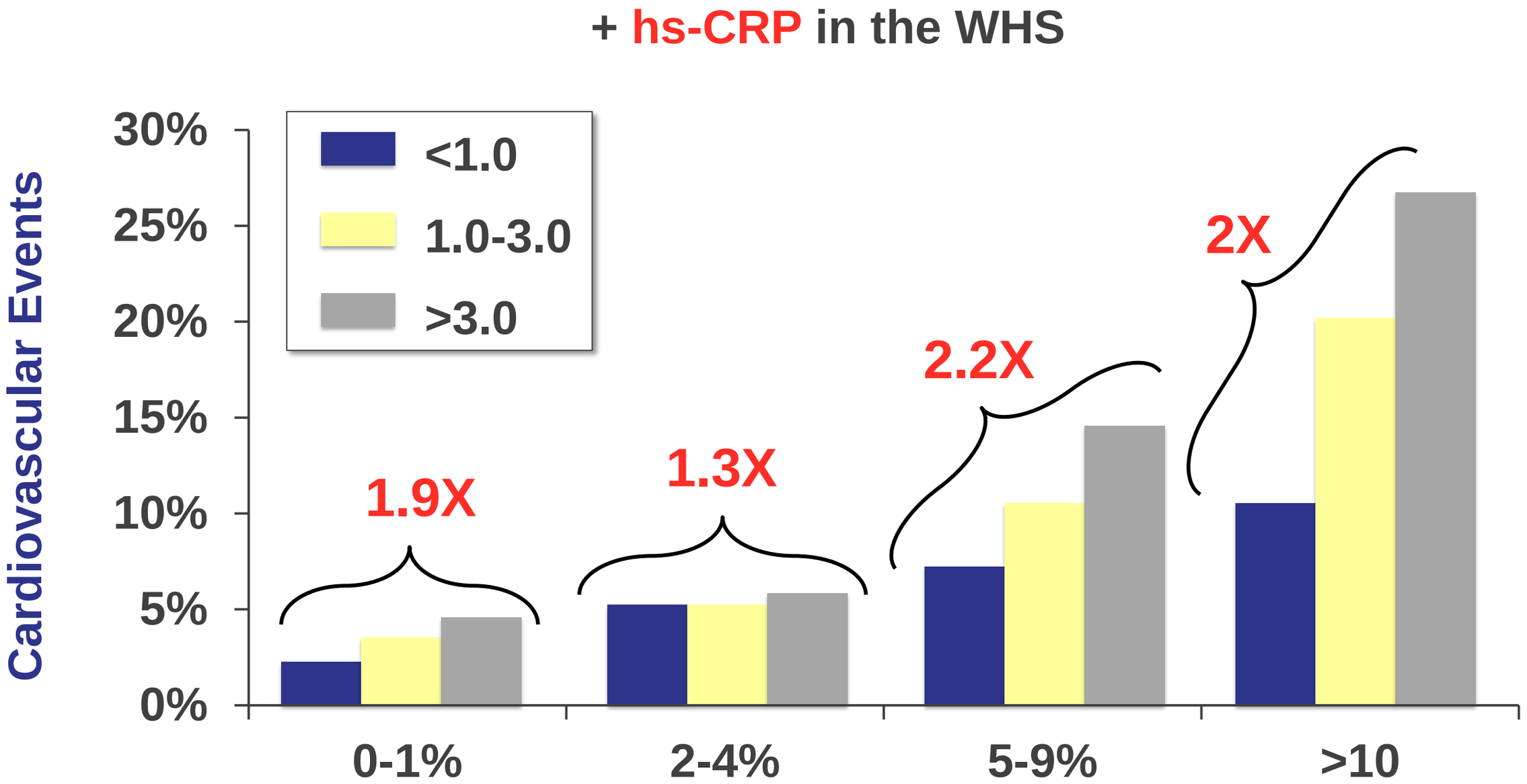
Ridker PM, Wilson PWF, Grundy SM. *Circulation* 2004; 109; 2818-2925

Actual Cardiovascular Events Compared with Framingham Estimate



Ridker PM et al, N Engl J Med, 2002;347:1557

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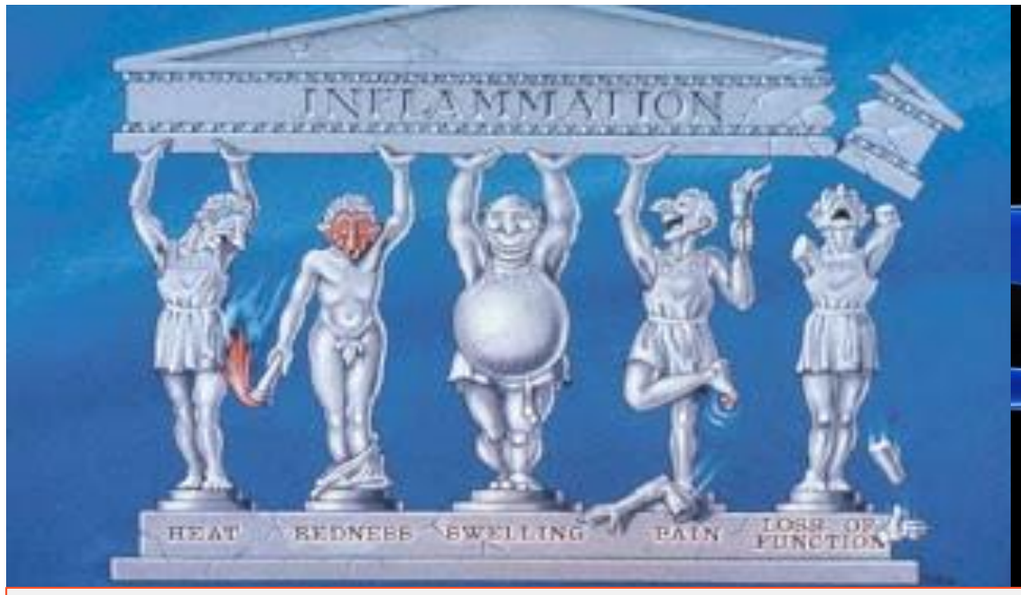
hsCRP Measures Repair Need



Inflammation in pathology =

Repair deficit in physiology

Healthy body repairs w/o **hsCRP**… ‘cry for *help*’

Vavuranakis M, Kariori MG, Kalogeras KI, Vrachatis DA, Moldovan C, Tousoulis D, Stefanadis C. Biomarkers as a Guide of Medical Treatment in Cardiovascular Diseases. *Curr Med Chem*. 2012; 19(16): 2485-2496.

Silva D, Pais de Lacerda A. High-sensitivity C-Reactive Protein as a Biomarker of Risk in Coronary Artery Disease, *Rev Port Cardiol*. 2012; 31: 733-745.

Jaffe R, Mani J. Rethink Health: Inflammation Is Actually Repair Deficit: Using Physiology First to Achieve Better Outcomes, Part 1: Value and Importance of Understanding Inflammation as Repair Deficit. *Townsend Letter for Doctors and Patients*. 2013, Jun (359): 68-74.

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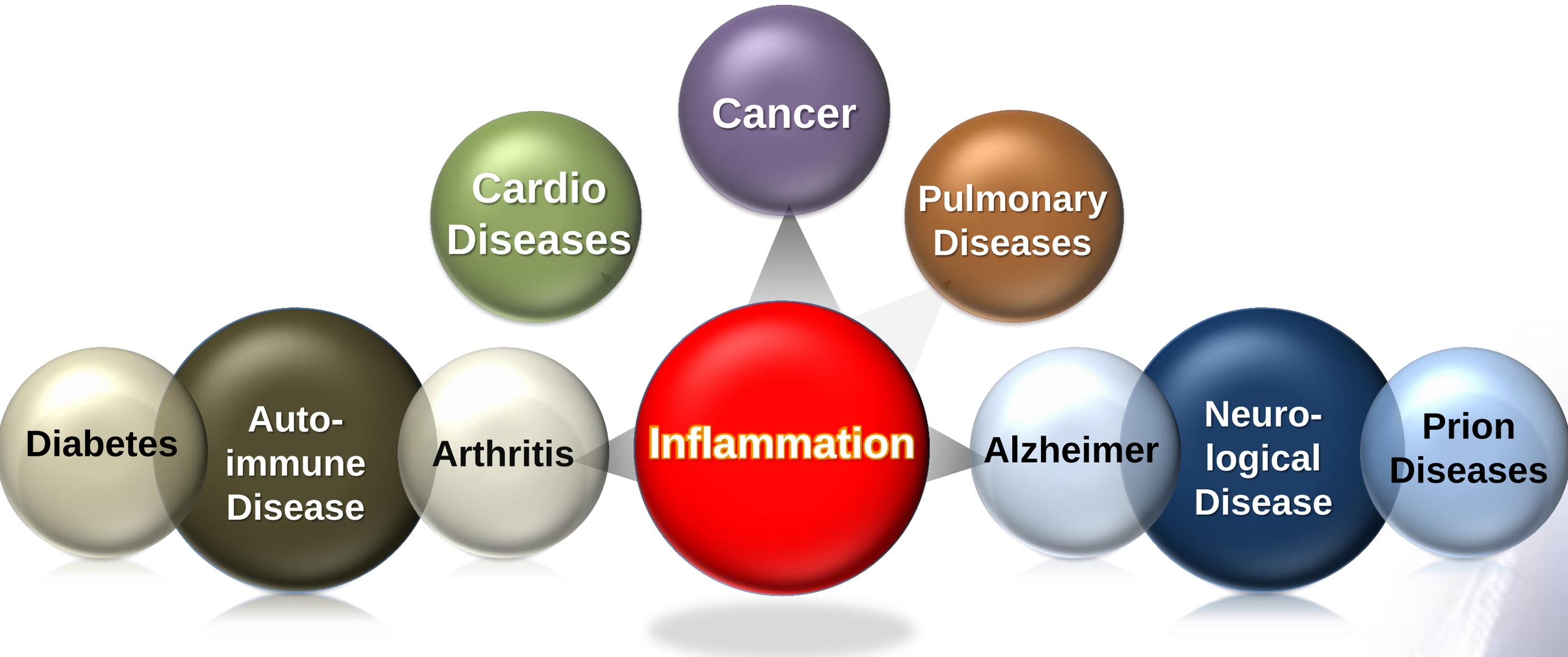
ReThink Systemic Inflammation



Grundy SM, Cleeman JI, Daniels SR, Donato KA *et. al*., Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 2005;112(17):2735-2752.

Kahn R, Buse J, Ferrannini E, Stern M et. al., The Metabolic Syndrome: Time for a Critical Appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2005 Sep;28(9):2289-2304.

Jaffe R, Mani J. Rethink Health: Inflammation Is Actually Repair Deficit: Using Physiology First to Achieve Better Outcomes, Part 1: Value and Importance of Understanding Inflammation as Repair Deficit. *Townsend Letter for Doctors and Patients*. 2013, Jun (359): 68-74.

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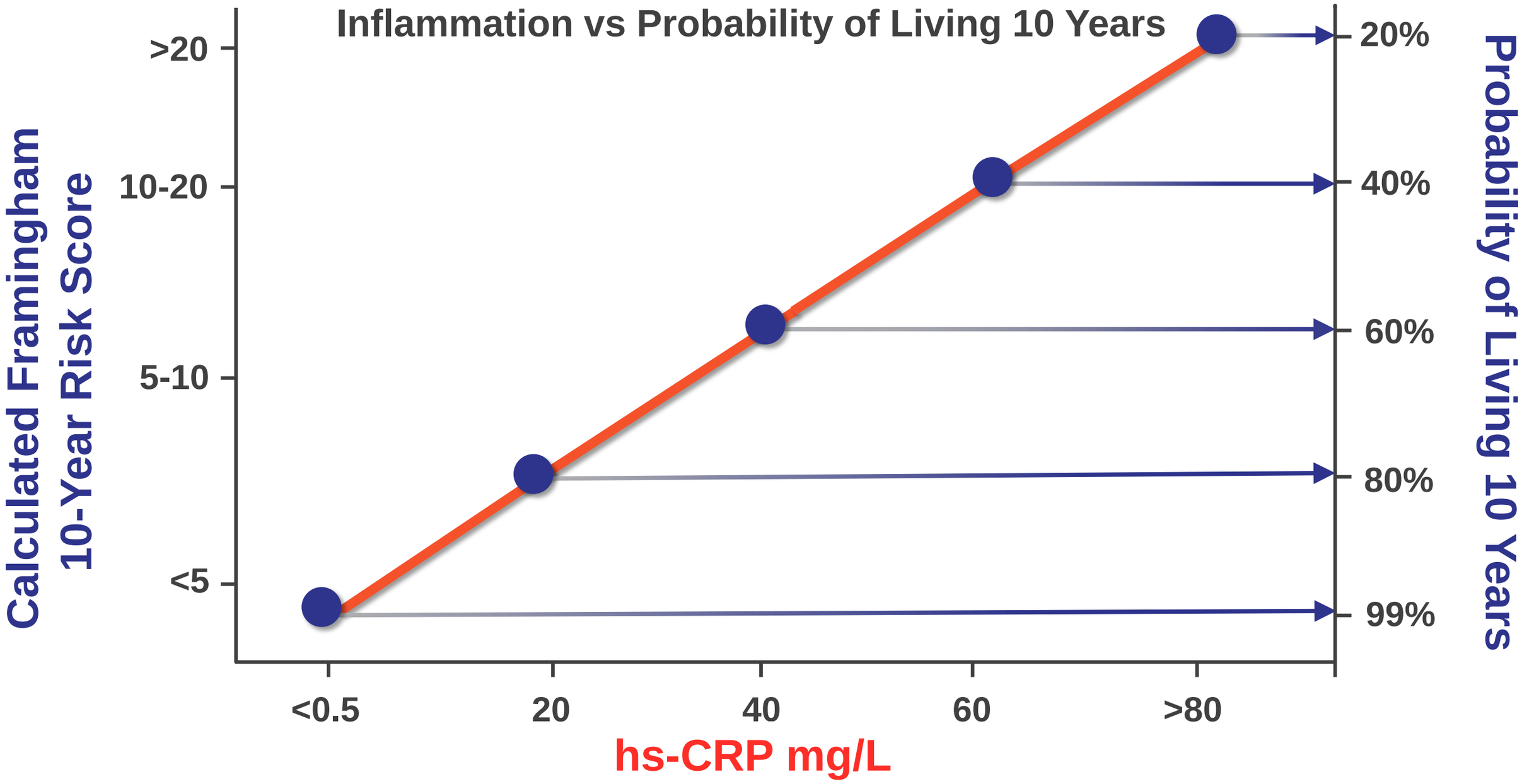
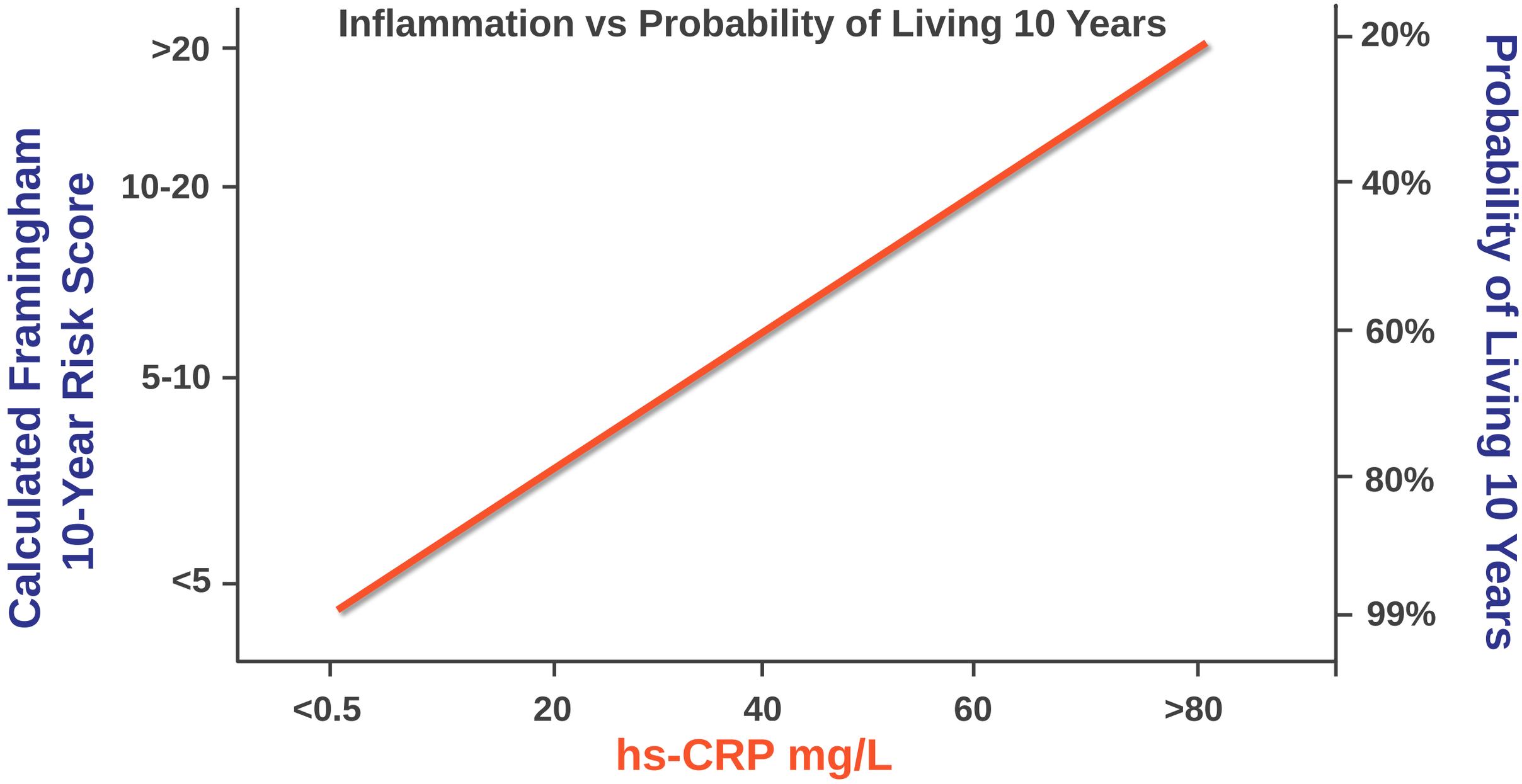
High Sensitivity C-Reactive Protein (hs-CRP)



Nygård O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma homocysteine levels and mortality in patients with coronary artery disease. *New Engl J Med*. 1997; 337(4): 230-236.

High Sensitivity C-Reactive Protein (hs-CRP)



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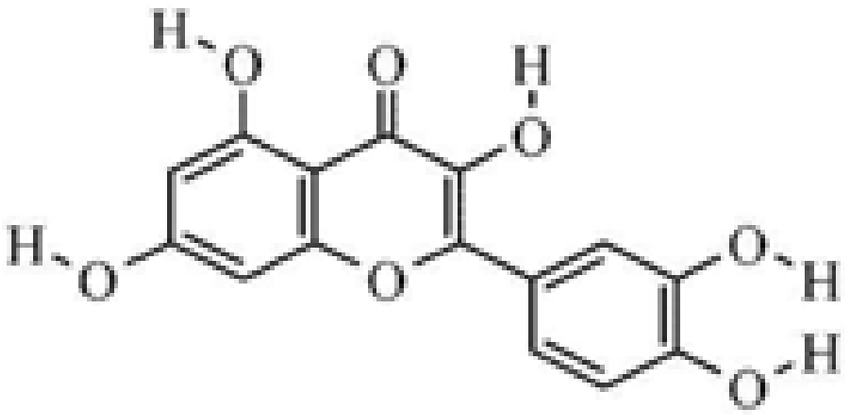
Oxidation Markers as Predictive Biomarkers

Flavonoids & Flavanols



Polyphenolic Ascorbate Synergists

- **Clinical Pearl**: Protect & Activate repair; Recycles cell ascorbate
- Safer, synergistic… anti-histaminic, steroid sparing
- Activate elective protectives, detox, recycling

Middleton E, *et. al*. The Effects of Plant Flavonoids on Mammalian Cells: Implications for Inflammation, Heart Disease and Cancer. *Pharmacol Rev*, 2000; 52: 673-751.

Kim Y J, Park H J, Yoon S H, Kim M J, Leem K H, Chung J H, Kim H K. Anticancer Effects of Oligomeric Proanthocyanidins on Human Colorectal Cancer Cell Line, *S NU-C4 World J Gastroenterol*. 2005; 11(30): 4674-4678.

Jaffe R, Mani J. Clinical Evidence in Favor of Specific Polyphenolics. *In*: Watson RR, Preedy VR, Zibadi S, Eds. Polyphenols in Human Health and Disease, *Academic Press,* 2013: 695-705.

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hsCRP Pro Repair Antioxidant Nutrients

1 Personal C Cleanse

Only 100% l-ascorbate, fully reduced & buffered

2 Dark fruits; super foods

Polyphenolics

3 B methyl cofactors

Balanced Natural Forms

4 BioDetox

Ascorbates & Chlorophyll

5 High sulfur foods

GGOBE

6 Acetylenes & EPA/DHA

Purer, uncontaminated, micellized = better uptake

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Jaffe R, Mani J. Clinical Evidence in Favor of Specific Polyphenolics. *In*: Watson RR, Preedy VR, Zibadi S, *Eds*. Polyphenols in Human Health and Disease, Academic Press, 2013, 695-705.
Jaffe R. Cardioprotective Nutrients. *In*: Watson RR, Preedy VR, *Eds.* Bioactive Food as Dietary Interventions in Cardiovascular Disease. *Academic Press*, 2013. p 103-119.

hsCRP < 0.5 Goal Value

Ascorbates: Personalized need
Ascorbate Calibration: CCLEN.4HSC.ORG

***In vivo* always protective antioxidant;**
100% l-ascorbate, fully reduced & buffered

Recycles tocopherols, lipoate, GSH, taurine,
ALA, NAD, FAD, DNA, cytochromes,
PUFA [Omega 3 & Omega 6],

Sets cell ReDox level: $Fe^{++/+++}$, $Cr^{++/+++/++++++}$,

Quench oxidative damage; trap free radicals

Donates Electrons: ↑ Ascorbate salvages
Cyt C mitochondria battery

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Englard S, Seifter S. The Biochemical Functions of Ascorbic Acid. *Annu Rev Nutr.* 1986; 6: 365-406.

hsCRP
Repair Deficit & Inflammation

Adequate ascorbates, polyphenolics & other antioxidants enhance repair and reduce 'cries' for health such as hsCRP, ferritin, COX2, IL-6, fibrinogen, TNF, alpha 2 macroglobulin…

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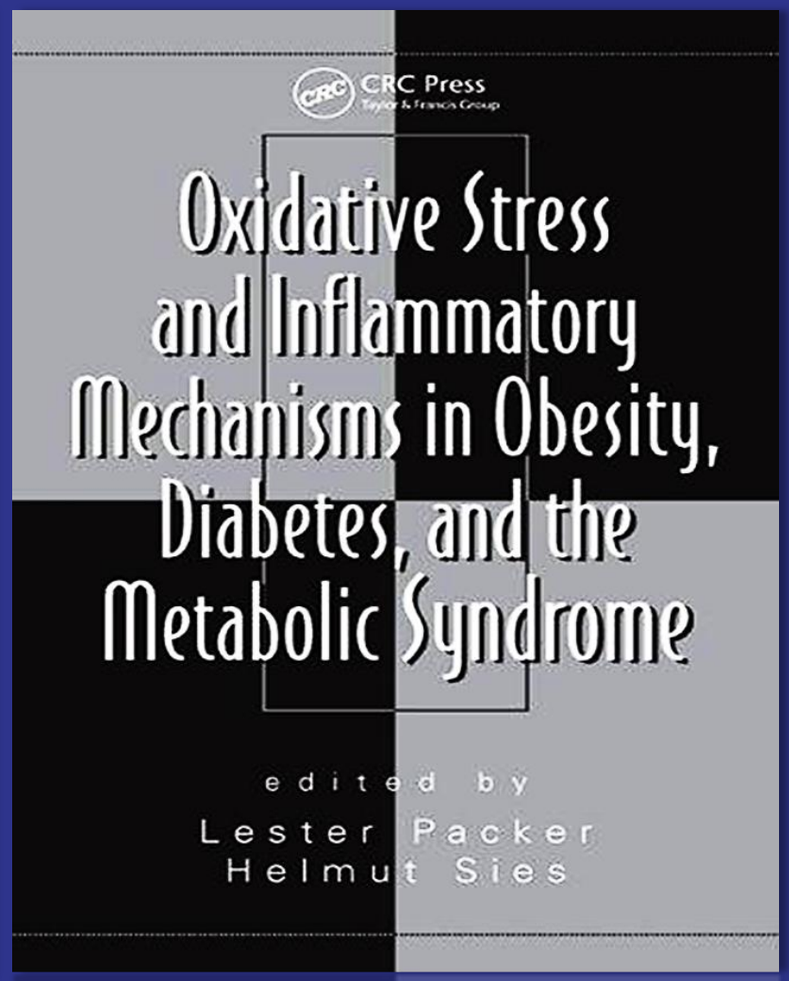
Chronic Inflammation = Chronic Disease = Chronic Repair Deficit

Yet Two Americans every minute have ***avoidable*** coronary events

Chronic Inflammation = Chronic Disease = Chronic Repair Deficit (cont'd)



By 2025 in US:

~ 50 MM Diabetics &
100 MM Pre-diabetics

Source: CDC and AHA

Individual Ascorbate Based on Oxidative Stress

Ascorbate Calibration

± Probiotics, recycled Glutamine, Mg, Polyphenolics

Healthy

- 1.5 grams; ½ tsp
- Every 15 min
- 6 grams / hour

Moderate Ills

- 3 grams; 1 tsp
- Every 15 min
- 12 grams / hour

Chronic Ills

- 6 grams; 2 tsp
- Every 15 min
- 24 grams / hour

* Health Studies Collegium, Joy in Living The Alkaline Way, 20th ed. 1990-2014.

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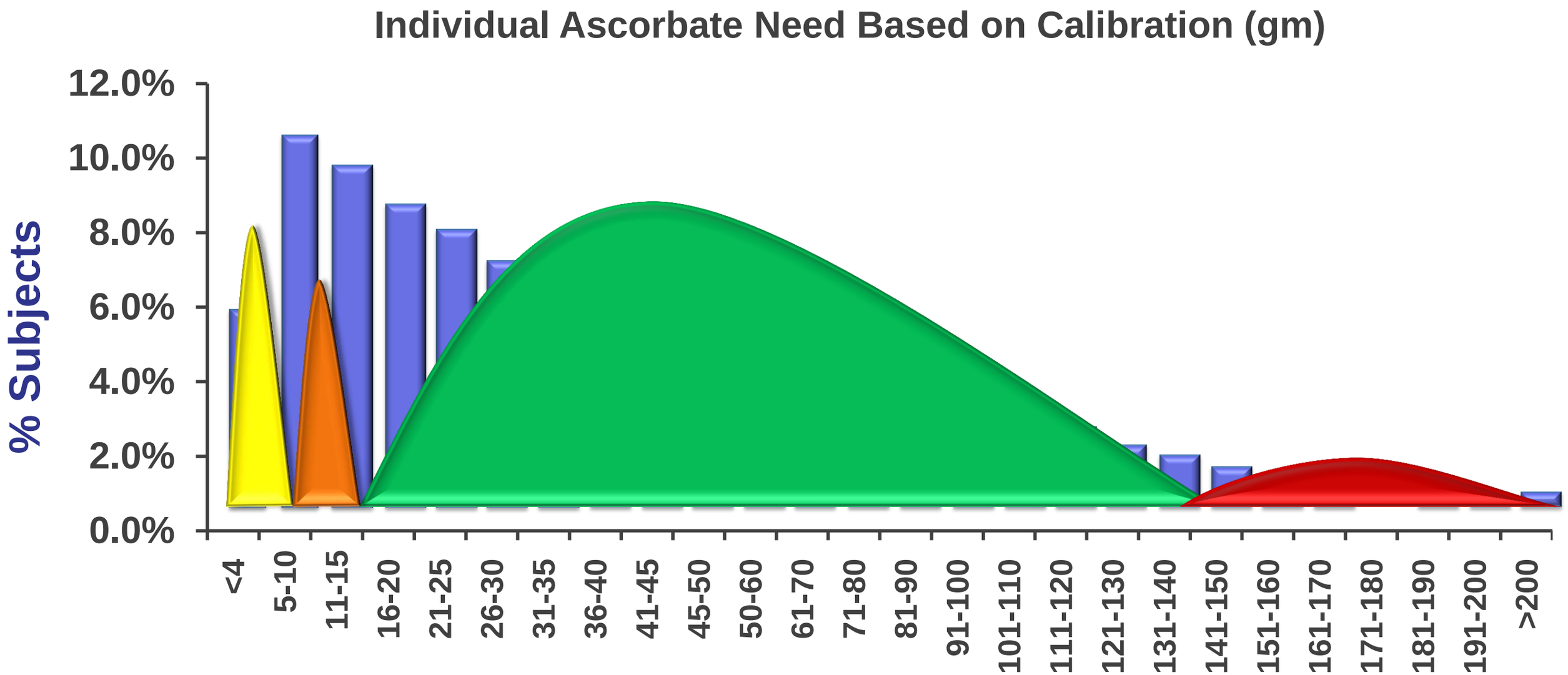
Ascorbate needs from 4-100+ g/day



~5%(185) <4 gm (healthy);

~10% (348) from 5-10 gm (usual)

~80% (2798) from 10-130 gm (walking worried/wounded)

~5% (166) > 130 gm (multiple chronic diseases)

Based on Jaffe Protocol 1987-2008

Jaffe R. Cardioprotective Nutrients. *In*: Watson RR, Preedy VR, Editors Bioactive Food as Dietary Interventions in Cardiovascular Disease. *Academic Press*, 2013, 103-119.

Predictive Biomarker 3

Homocysteine; hsHCY
2-Amino-4-sulfanylbutanoic acid

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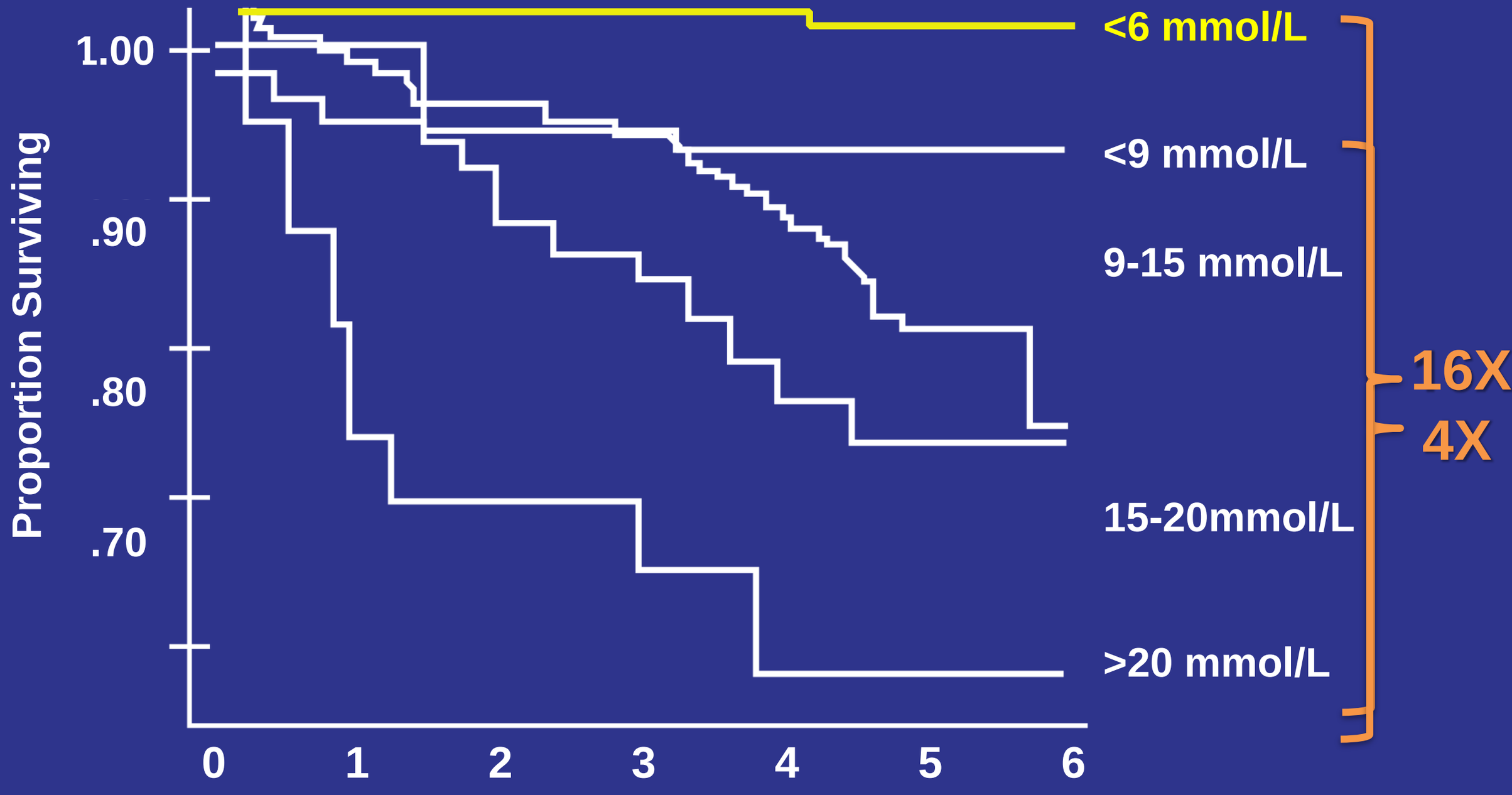
Homocysteine

<6 is Predictive Biomarker



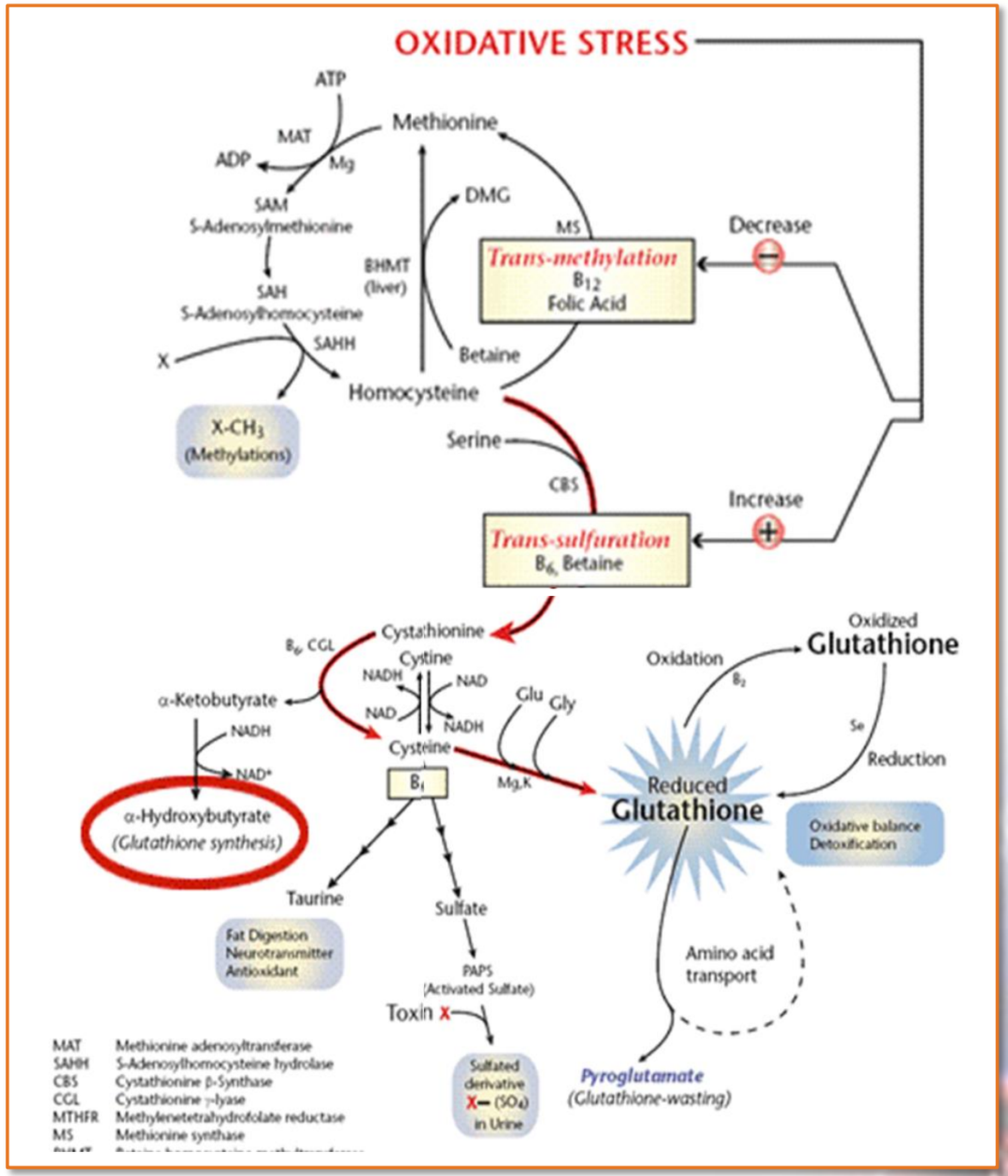
Nygård O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma Homocysteine Levels and Mortality in Patients with Coronary Artery Disease. *NEJM*. 1997; 337(4): 230-236.

Healthy Methylation to move cells

- Oxidation, detoxification, transportation
- Elective protective mode ***or*** survival ***mode*** *for cells*
- Cardiovascular ***&*** stroke ***risk*** cancer, AI & chronic disease

Sulfur aminoacid pools

- ***Often abnormal*** in T21 & ASD



Nimni ME, Han B, Cordoba F. Are we Getting Enough Sulfur in our Diet? *Nutr Metab (Lond).* 2007; 4: 24.

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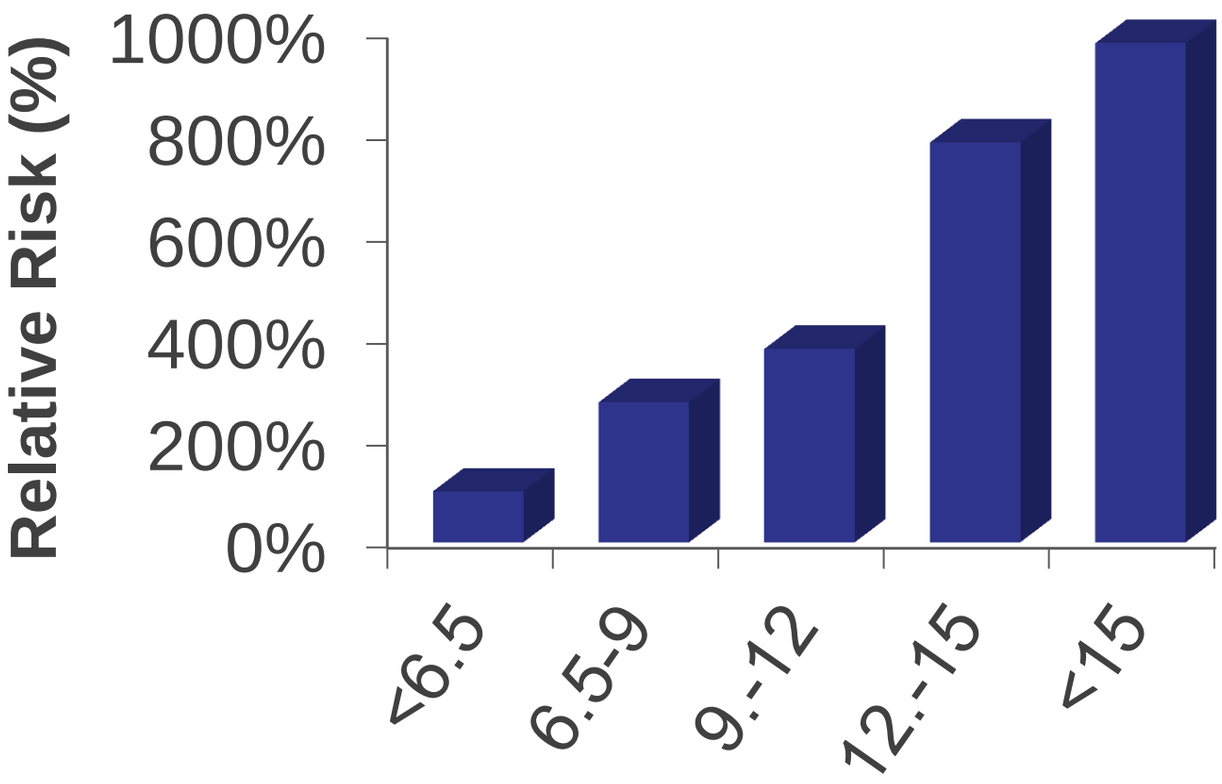
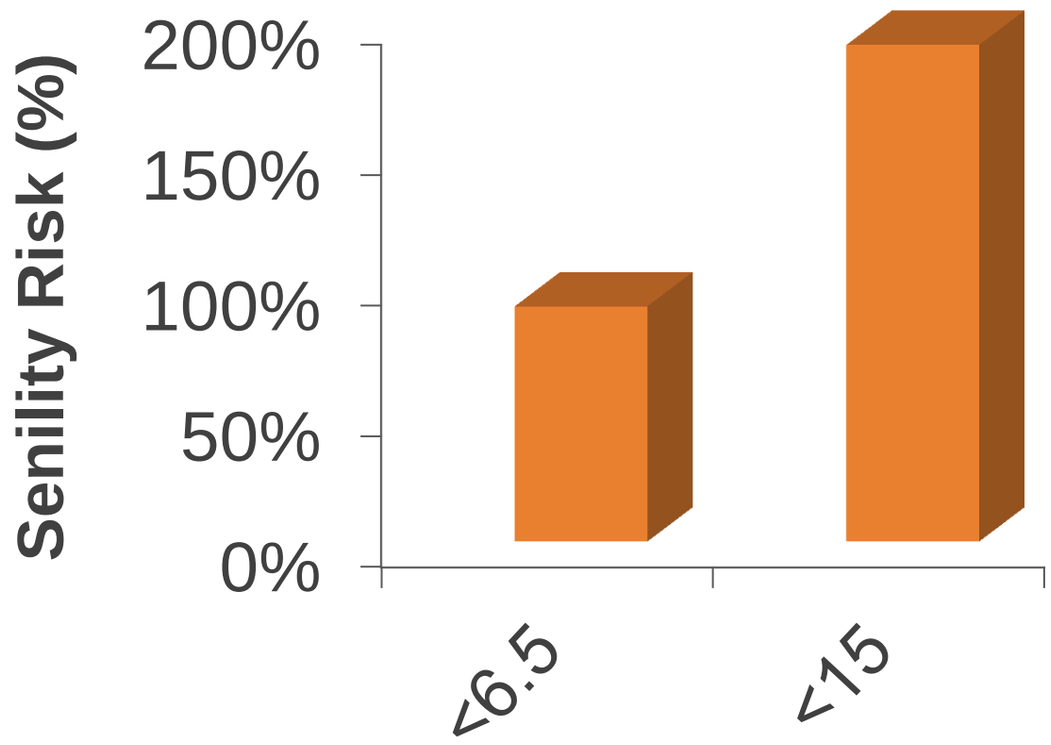
Healthy Methylation:
B Complex, C

Difference in Five-Year Mortality Risk



Relative Risk at Different Homocysteine

Difference in Senility Risk



Relative Risk of Senility in Relation to Homocysteine Levels

Methylation cofactors delivered in lingual dots

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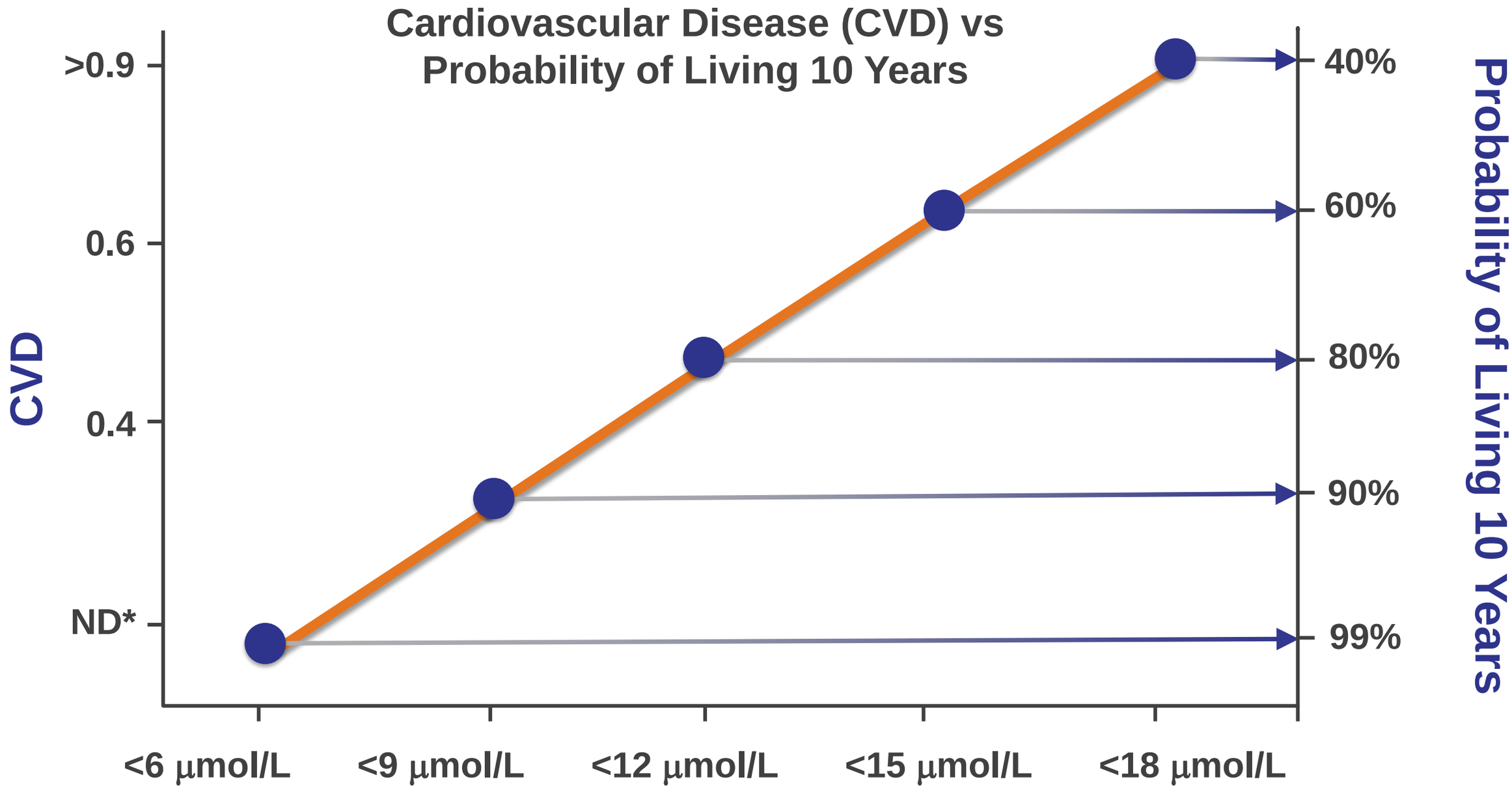
Arch Chem. 2004; 50: 3-32. *Arch Intern Med* 2003; 163: 1933-1937. *NEJM*. 2002; 346: 476-483.

Schroecksnadel K, *et. al*. Hyperhomocysteinemia & Immune Activation. *Clin Chem Lab Med* 2003; 41(11):1438-1443.

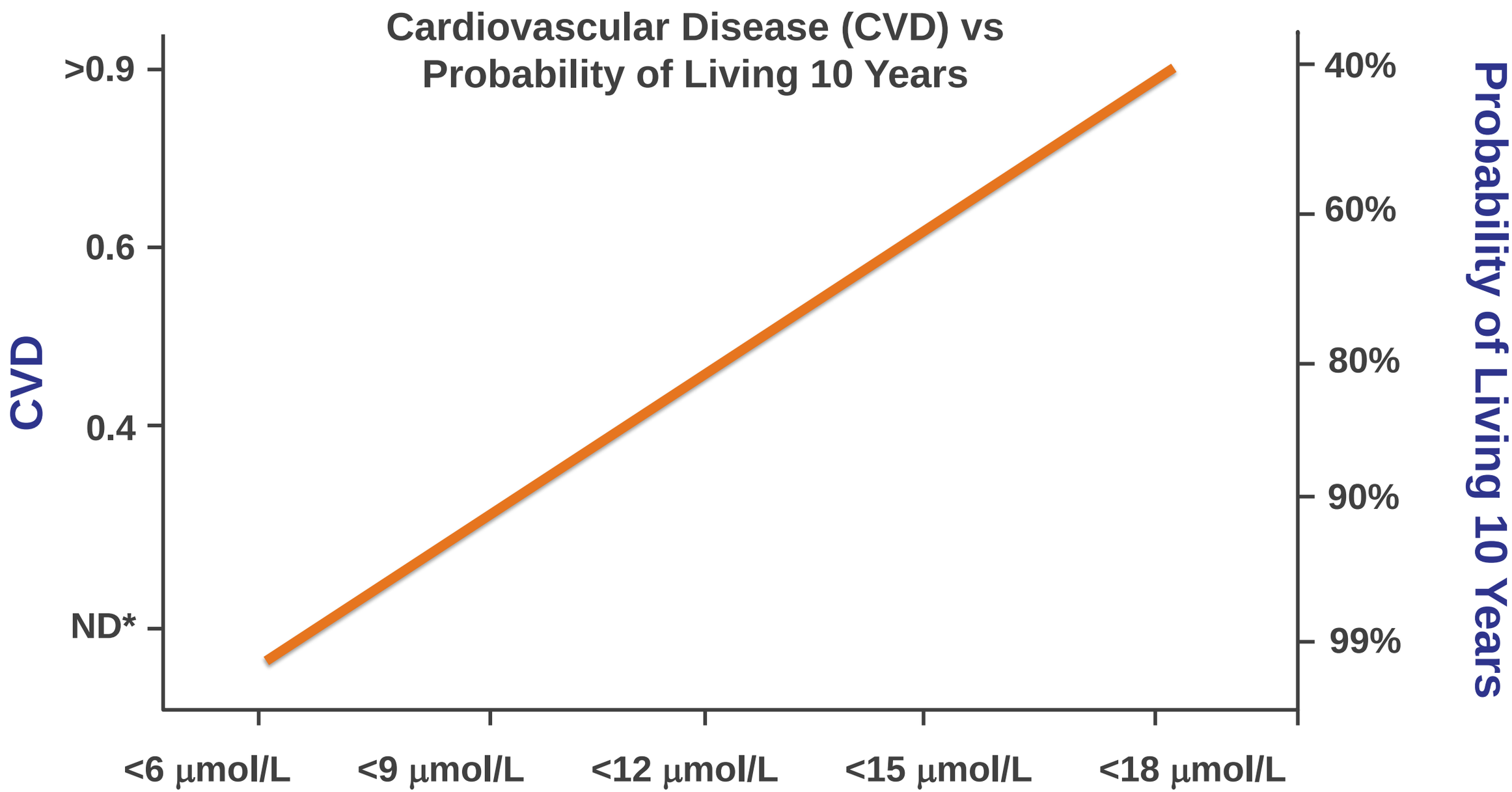
hsHomocysteine



*Essentially Not Detectable.

Nygård O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma homocysteine levels and mortality in patients with coronary artery disease. *New Engl J Med*. 1997; 337(4): 230-236.

hsHomocysteine



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hsHomocysteine Tests

Standard HCY testing methods (EDTA)

- Significant limitations
- Limits clinical application

HCY leaks from RBCs starting *immediately* after draw.

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hsHomocysteine (hsHCY)

hsHCY method eliminates RBC leakage limitations .

Clinical use of hsHCY assays

√ Cost effective
√ Predictive
√ Evidence based
√ Usual and customary

Tan Y & Hoffman RM. A highly sensitive single-enzyme homocysteine assay . *Nature Protocols.* 2008; 3: 1388-1394
Liang G, Jaffe A, Larkin J, Jaffe R. A high sensitivity Homocysteine (hsHomocysteine) test improves a predictive biomarkers sensitivity, specificity, and predictive significance, manuscript in preparation

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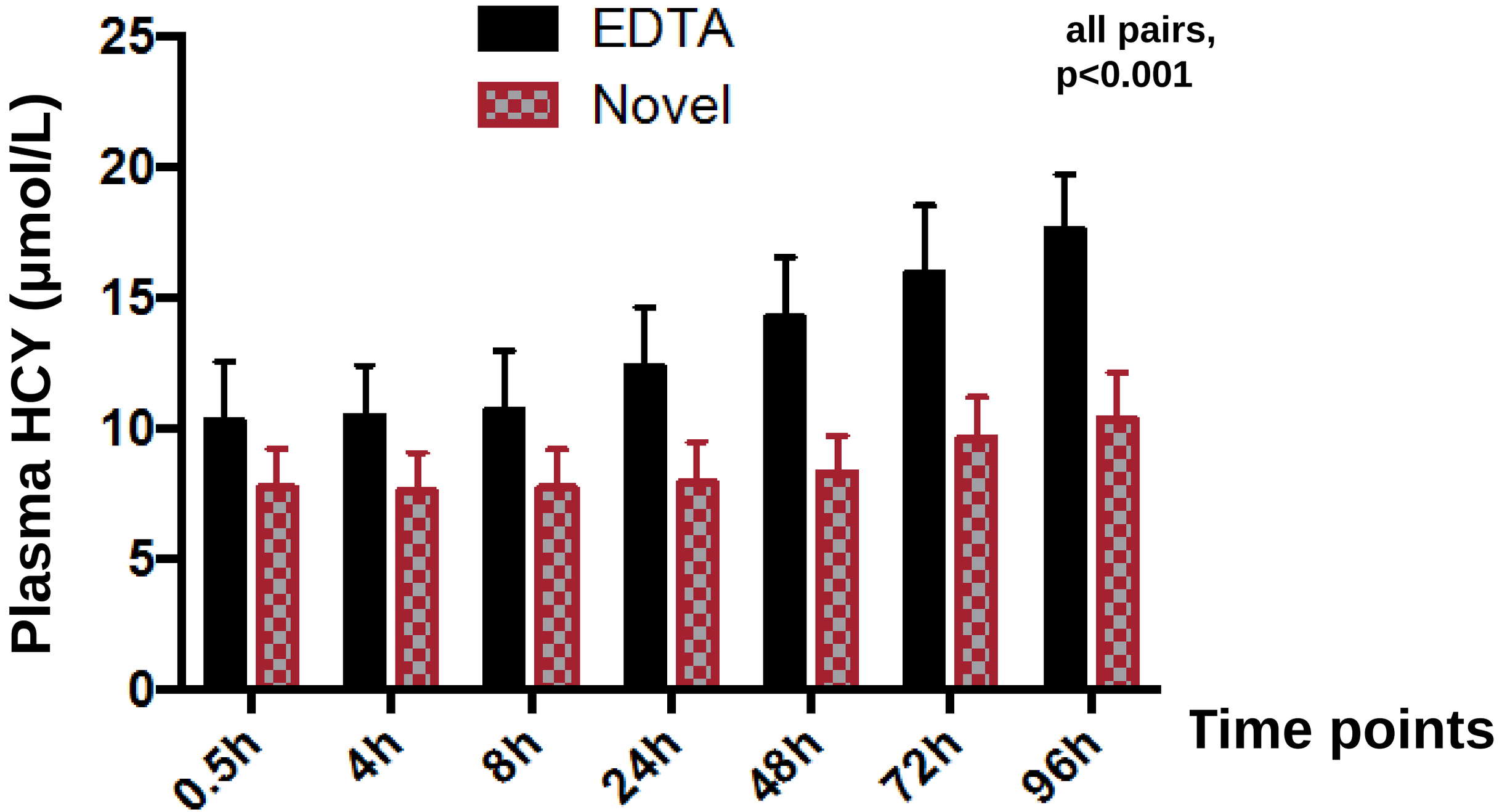
hsHomocysteine

Comparison between novel-plasma & EDTA-plasma



Liang G, Jaffe A, Larkin J, Jaffe R. A high sensitivity Homocysteine (hsHomocysteine) test improves a predictive biomarkers sensitivity, specificity, and predictive significance, manuscript in preparation

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hsHomocysteine (hsHCY)

EDTA specimens release HCY within *minutes* after blood draw.

High Sensitivity Homocysteine (hsHCY) specimen viable for ***days.***

hsHCY…

more reliable, specific, predictive biomarker

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hsHomocysteine < 6µmol/l is goal

Lifely Colors: Carotenoids & B Complex

Targeted Supplementation

For healthy methylation.

- Vitamin B12 (hydroxocobalamin)
- B6
- Mixed natural folates

Lingual dot for optimum uptake

Comprehensive antioxidants

- Pure sylimarin
- CoQ10
- Mixed natural carotenoids
- Mixed natural tocopherols

Micellized in a softgel for increased uptake

Chew B P, Park J S. Carotenoid Action on the Immune Response. *J Nutr.* 2004 Jan; 134(1): 257S-261S.

D'Adamo C R, Miller R R *et a*l. Higher Serum Concentrations of Dietary Antioxidants are Associated with Lower Levels of Inflammatory Biomarkers During the Year After Hip Fracture. *Clin Nutr*. 2012 Oct; 31(5): 659-665

Brady J, Holford P. Homocysteine Revisited the H Factor Solution, BHP, N Bergen, NJ, 2003

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Lifely Colors: Carotenoids & B Complex

Targeted Supplementation

PERQUE Vessel Health Guard
Vitamin B12 (hydroxocobalamin), B6 and mixed natural folates for healthy methylation.

PERQUE Liva Guard Forté
Comprehensive antioxidants with pure sylimarin CoQ10, mixed natural carotenoids micellized in a softgel for increased uptake

Chew B P, Park J S. Carotenoid Action on the Immune Response. *J Nutr.* 2004 Jan; 134(1): 257S-261S.

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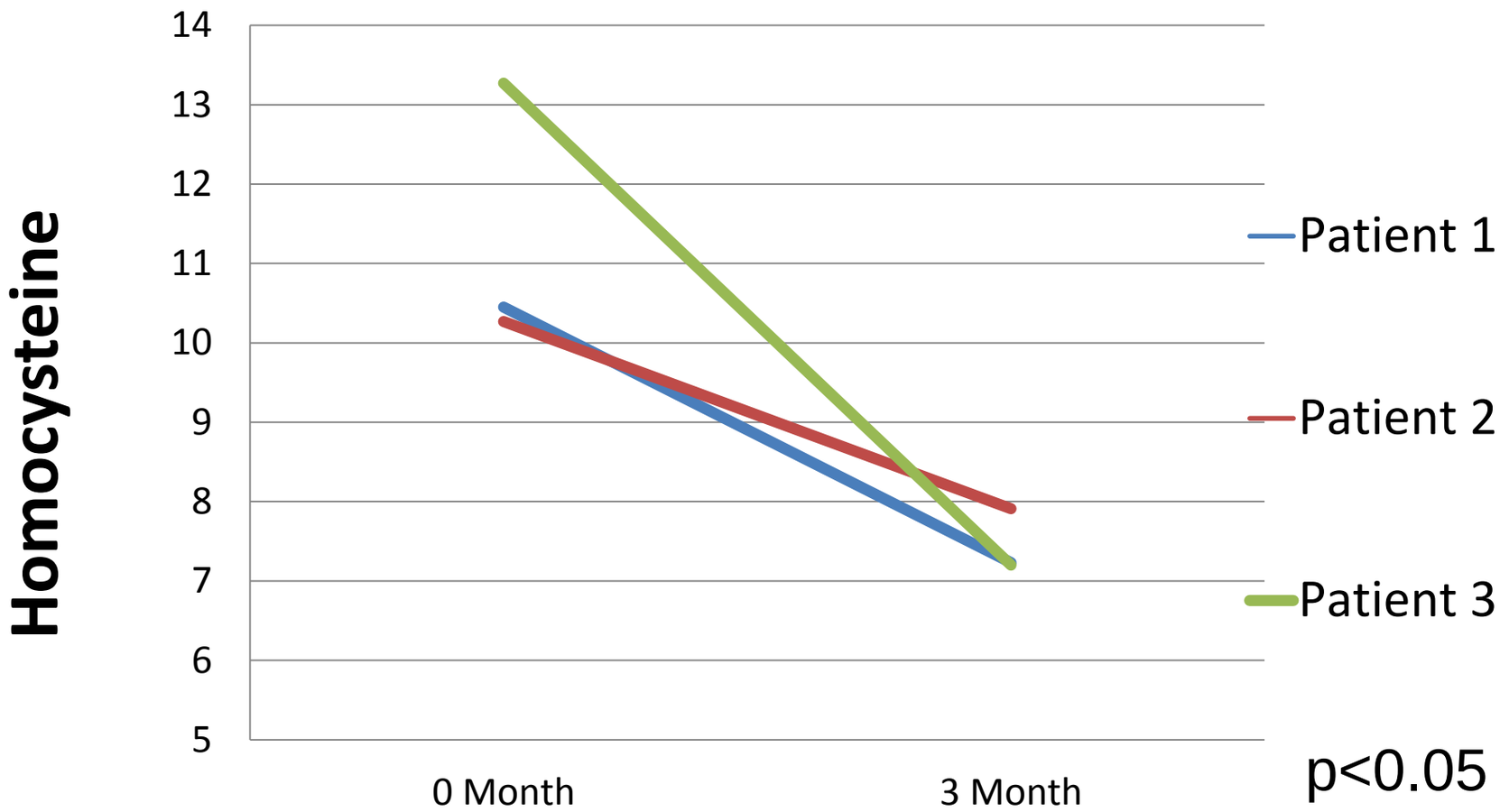
hsHomocysteine < 6µmol/l is goal

Oral injection: hydroxocobalamin B12 + folates + B6

Effect on homocysteine levels: 2 lozenges/day



Genqing Liang, Jamie Larkin,Russell Jaffe Healthier homocysteine levels using oral methylation factors- abstract submitted for publication

Jaffe R, Mani J. Clinical Evidence in favor of specific polyphenolics. *In*: Watson RR, Preedy VR, Zibadi S, Eds. *Polyphenols in Human Health and Disease*, Academic Press, 013, 695-705.

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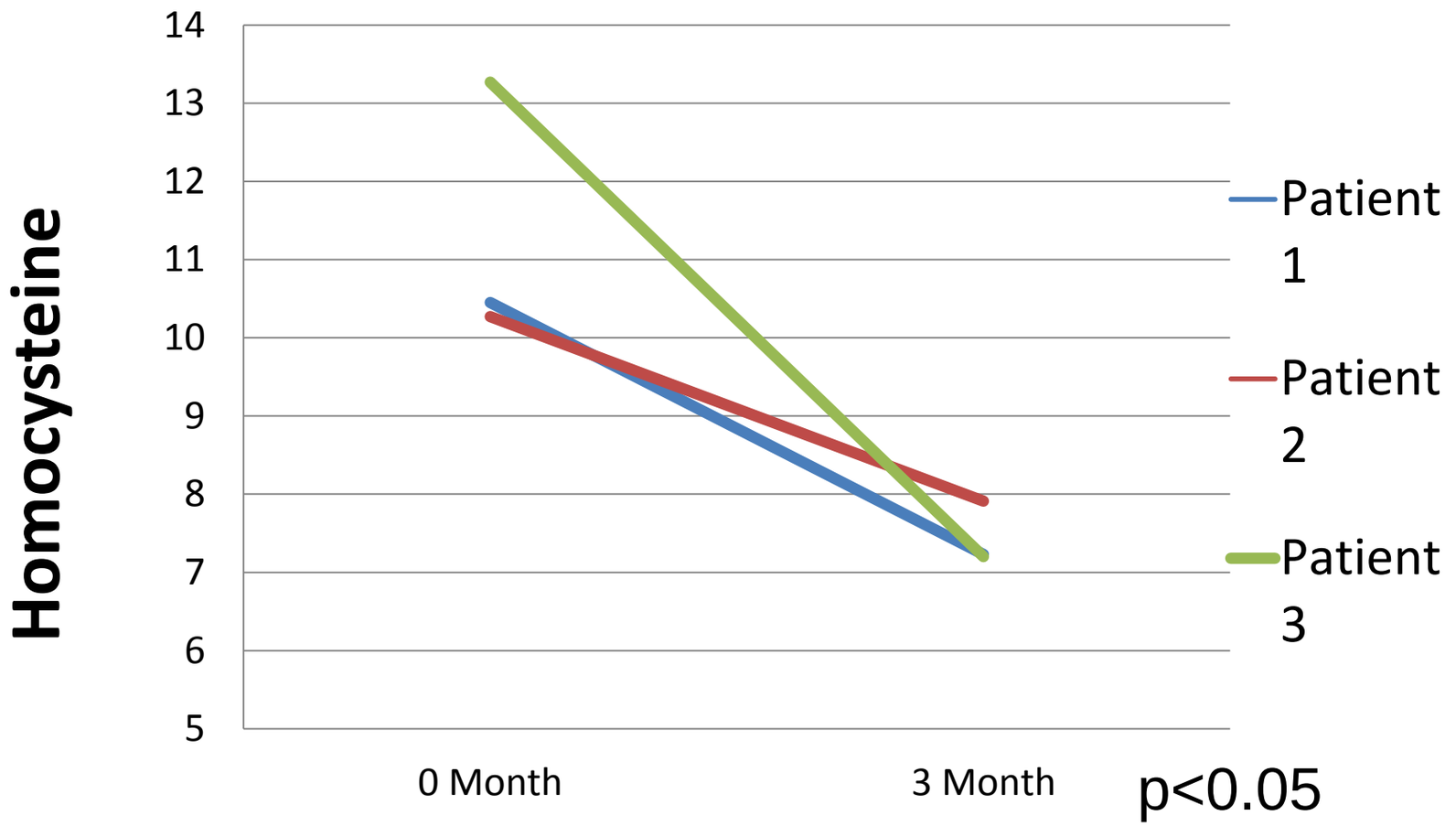
hsHomocysteine < 6µmol/l is goal

PERQUE Vessel Health Guard

Effect on homocysteine levels: 2 lozenges/day



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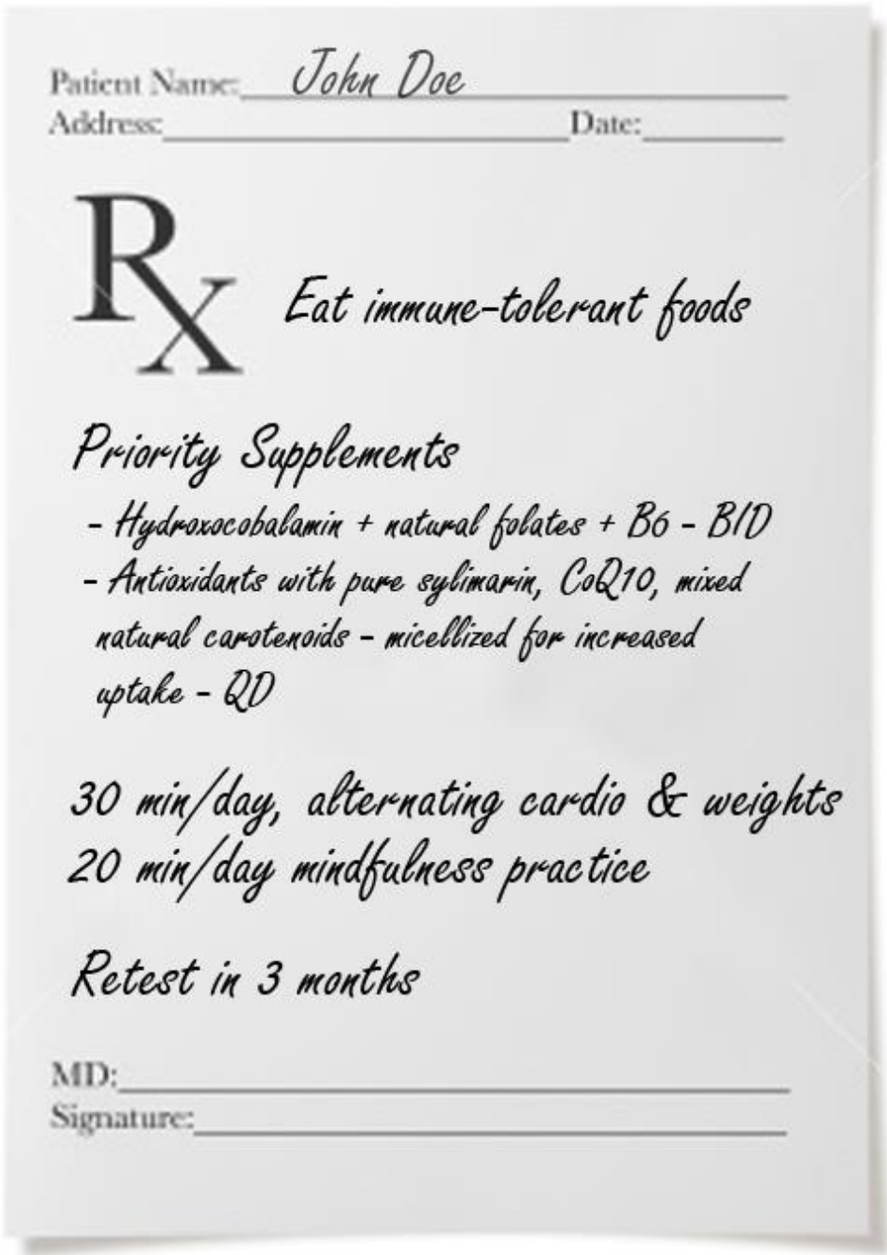
Achieving hsHCY Predictive Goal



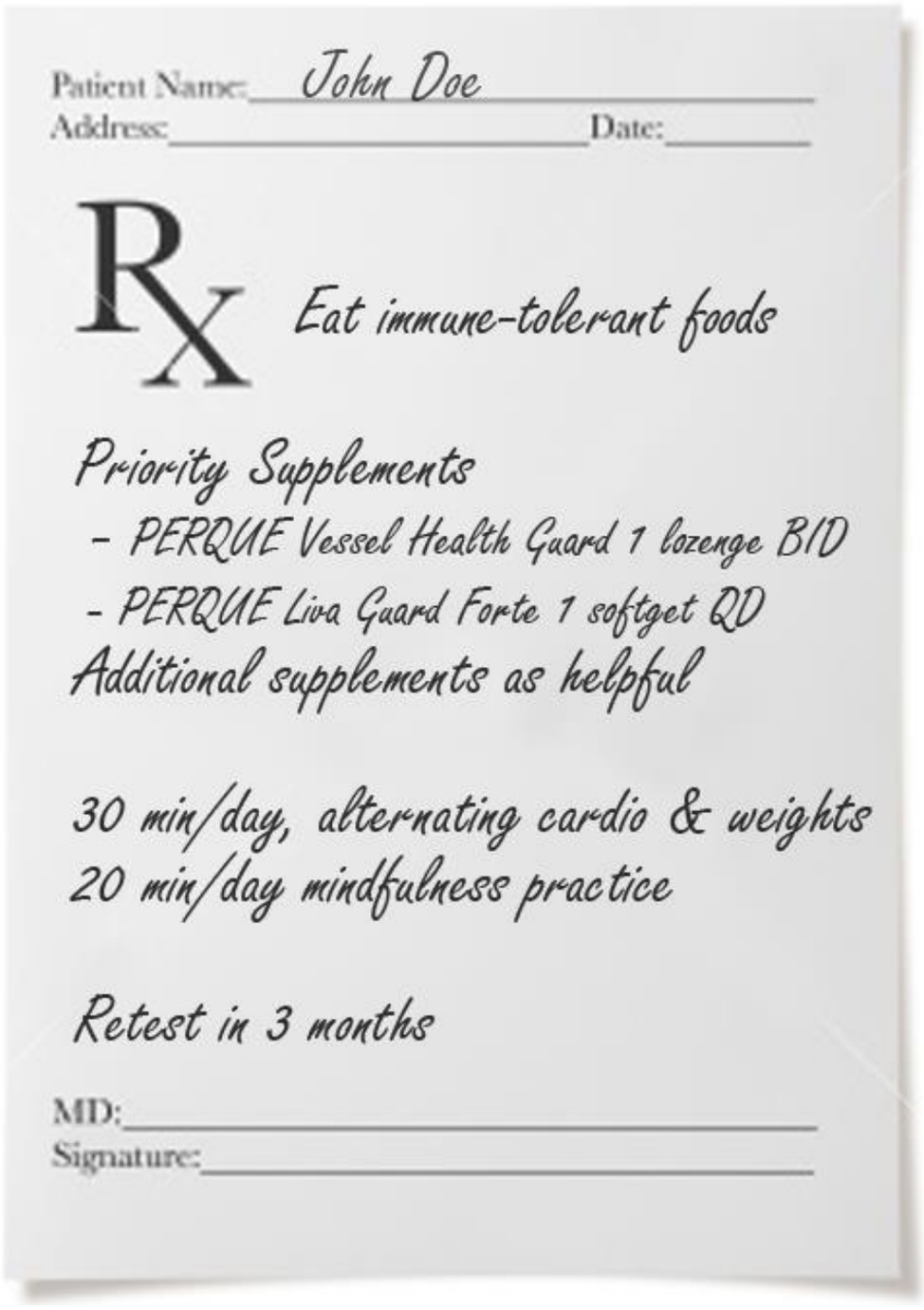
MORE PRIORITY SUPPLEMENTS

Super multi/mineral w/40 actives: 2x day
Buffered ascorbate powder/ tabsules:
Based on C cleanse
Magnesium glycinate/citrate/ascorbate: 2 caps **+**
Choline Citrate: 1 tsp or to keep 1st AM urine pH 6.5-7.5

ADDITIONAL SUPPORT FOR SUSTAINED RESULTS

Quercetin dihydrate+ OPC+ Pomegranate: 2-4 tabs/day
or in a pure whey based powder**:** 2 scoops /day
Recycled l-glutamine with PAK: 6 caps /day
Fermented foods daily or
Multi-strain, live, implantable probiotics: 6-8 caps/day

Achieving hsHCY Predictive Goal



PRIORITY SUPPLEMENTS

PERQUE Vessel Health Guard™: 2x day
PERQUE Liva Guard Forte™ : 1x day
PERQUE Life Guard™ mini Tabsules™: 2x day
PERQUE Potent C Guard™ powder/ tabsules:
Based on C cleanse
PERQUE Mg Plus Guard™ w/ **PERQUE Choline Citrate**: 2 caps + 1 tsp or to keep 1st AM urine pH 6.5-7.5

ADDITIONAL SUPPORT FOR SUSTAINED RESULTS

PERQUE Repair Guard™: 2-4 tabs/day
& PERQUE Whey Guard Repair™: 2 scoops /day
PERQUE Endura PAK Guard™: 6 caps /day
Fermented foods daily or
PERQUE Digesta Guard™: 6-8 caps/day

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Homocysteine < 6µmol/l is goal
Ascorbates, Polyphenolics & Probiotics

1. Super multi/mineral w/40 actives;
√ keep urine sunshine yellow

2. Vitamin C powder and tabsules 100% buffered, fully reduced l-ascorbate w/ K^{+}, Zn^{++}, Mg^{++} & Ca^{++}
√ amount based on 'C Cleanse'

3. Polyphenolics: Quercetin dihydrate + soluble OPC

4. Recycled Glutamine w/PAK

5. Magnesium as glycinate, ascorbate, & citrate w/ **Choline Citrate** to enhance uptake; √ 1st AM urine pH

6. Fermented foods (40 g) and 40-60+ Bn **probiotics** /day

Homocysteine
BioDetox Super Foods

Garlic, ginger, onions, broccoli sprouts, eggs

GGOBE, Sulforaphane, IP6, minerals

Glutamine recycled by PAK cell energy repair

Jaffe, R. Diabetes as an Immune Dysfunction Syndrome. *In*: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions for Diabetes, *Academic Press*, 2013, 41-52.

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hsHomocysteine < 6µmol/l is goal

Lifely Colors: Carotenoids & B Complex





As part of comprehensive liver detox sylimarin, carnitine fumarate, CoQ10, carotenoids micellized softgel

Mixed Natural Carotenoids:

Alpha & Beta Carotene, Astaxanthin, Zeaxanthin, Cryptoxanthin, Lutein, Lycopene

Chew B P, Park J S. Carotenoid Action on the Immune Response. *J Nutr.* 2004 Jan; 134(1): 257S-261S.

D'Adamo C R, Miller R R *et a*l. Higher Serum Concentrations of Dietary Antioxidants are Associated with Lower Levels of Inflammatory Biomarkers During the Year After Hip Fracture. *Clin Nutr*. 2012 Oct; 31(5): 659-665

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hsHomocysteine < 6µmol/l is goal

Lifely Colors: Carotenoids & B Complex

B Complex *balanced* natural forms:





B1, B3, B6, B12

(hydroxocobalamin), Folates, PABA, Inositol, Choline

Chew B P, Park J S. Carotenoid Action on the Immune Response. *J Nutr.* 2004 Jan; 134(1): 257S-261S.

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Keep urine sunshine yellow

Clinical pearl:

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hsHomocysteine < 6µmol/l is goal
Ascorbates ,Quercetin and Probiotics

Super multi/mineral w/40 actives;
√ keep urine sunshine yellow

Vitamin C powder and tabsules 100% buffered, fully reduced l-ascorbate w/ K^{+}, Zn^{++}, Mg^{++} & Ca^{++}
√ amount based on 'C Cleanse'

Polyphenolics: Quercetin dihydrate + soluble OPC

Recycled Glutamine w/PAK

Magnesium as glycinate, ascorbate, & citrate w/
Choline Citrate to enhance uptake;
√ 1st AM urine pH

Fermented foods (40 g) or 40+ Bn **probiotics** /day

hsHomocysteine Solution

< 6µmol/L	Congratulations! Continue and Retest 2x per Year

> 6µmol/L	**<u>Eat & Drink</u>**:
	• ImmunoTolerant Alkaline Way diet
	• **Targeted Supplementation**:
	  • **Vitamin B12 (hydroxocobalamin),** B6 & mixed natural folates for healthy methylation.
	  • **Comprehensive antioxidants** with pure sylimarin CoQ10, mixed natural carotenoids in a micellized softgel for increased uptake
	  • **Super multi/mineral** with 40 active constituents; √ keep urine sunshine yellow
	  • **Vitamin C powder and tabsules** 100% buffered, fully reduced l-ascorbate w/ K^{+}, Zn^{++}, Mg^{++} & Ca^{++} √ amount based on 'C Cleanse'
	  • **Polyphenolics**: Quercetin dihydrate + soluble OPC
	  • **Magnesium** as glycinate, ascorbate, & citrate w/ **Choline Citrate** to enhance uptake; √ 1st AM urine pH
	  • **Fermented foods** and multi-strain, live, healthy implantable **probiotics** daily
	<u>Think & Do</u>
	• 30 minutes alternate days cardio & weight bearing activities
	• 20 minutes every day mindfulness practice

hsHomocysteine Solution

< 6µmol/L	Congratulations! Continue and Retest 2x per Year
> 6µmol/L	**Eat & Drink**: • ImmunoTolerant Alkaline Way diet • **Targeted Supplementation**: **PERQUE Vessel Health Guard** Vitamin B12 (hydroxocobalamin), B6 and mixed natural folates for healthy methylation. **PERQUE Liva Guard Forté** Comprehensive antioxidants with pure sylimarin CoQ10, mixed natural carotenoids micellized in a softgel for increased uptake **PERQUE Life Guard™ mini Tabsules™** Super multi/mineral with 40 active constituents; √ keep urine sunshine yellow **PERQUE Potent C Guard™ powder and tabsules** 100% buffered, fully reduced l-ascorbate w/ K^{+}, Zn^{++}, Mg^{++} & Ca^{++} √ amount based on 'C Cleanse' **PERQUE Repair Guard™ & PERQUE Whey Guard Repair™** Polyphenolics: Quercetin dihydrate + soluble OPC **PERQUE Mag Plus Guard™** Magnesium as glycinate, ascorbate, & citrate w/ **PERQUE Choline Citrate** to enhance uptake; √ 1st AM urine pH Fermented foods or **PERQUE Regularity & Digesta Guard™** [40g or Bn /day] **Think & Do** • 30 minutes alternate days cardio & weight bearing activities • 20 minutes every day mindfulness practice

Predictive Biomarker 4

Immune Tolerance

hsLRA

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Predictive Biomarker 4

Lymphocyte Response Assay hsLRA

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Predictive Biomarker 4

hsLRA

LRA by ELISA/ACT

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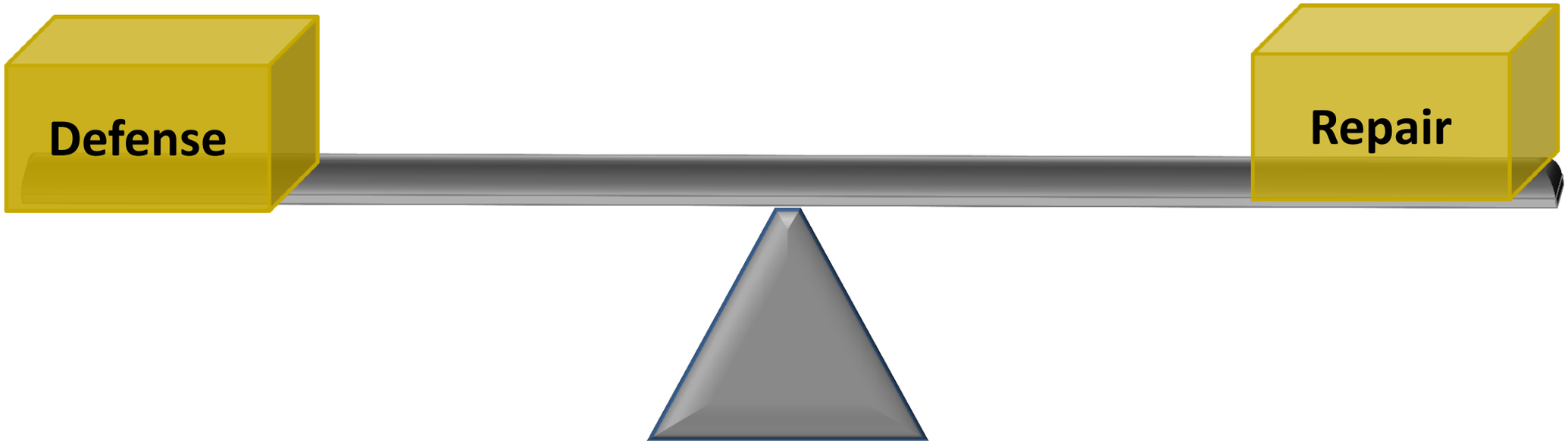
Your Immune System



Here to Defend & Repair

Immune System: IDRS

- Human immune system:
  * Innate: Repair & cancer deletion
  * Adaptive: Defense & Repair

- Over burdened immune system…
  Hidden (delayed) hypersensitivity/allergy
  Compare **<u>delayed</u>** allergy/hypersensitivity tests

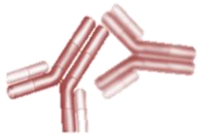
Immune System

Adaptive Immune System
(specific, acquired)
2nd line
Protects / remembers re-exposure

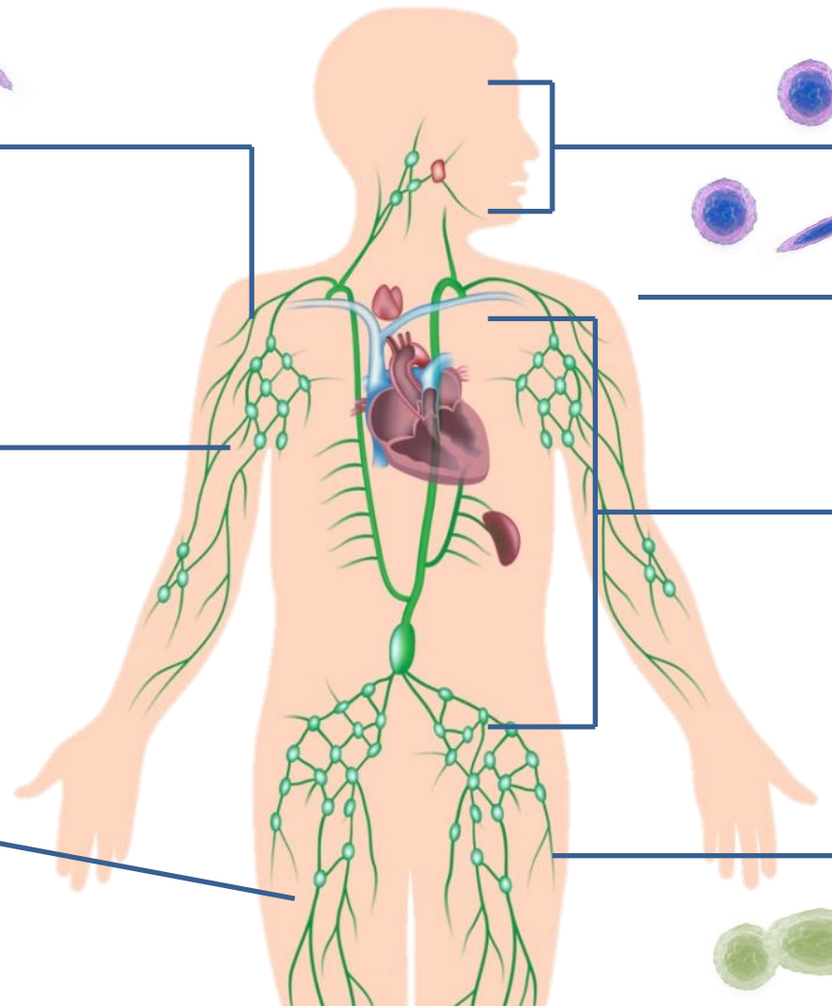
Innate Immune System
(nonspecific, surveillance)
1st line
Engulfs, recycles, renews

B lymphocytes
Defense WBCs

Antibodies



Defense cells:
T lymphocytes



Bacteria-killing substances

Skin protects outside:

Mucous membranes
protects inside

Innate tissue response…
Scavenger cells

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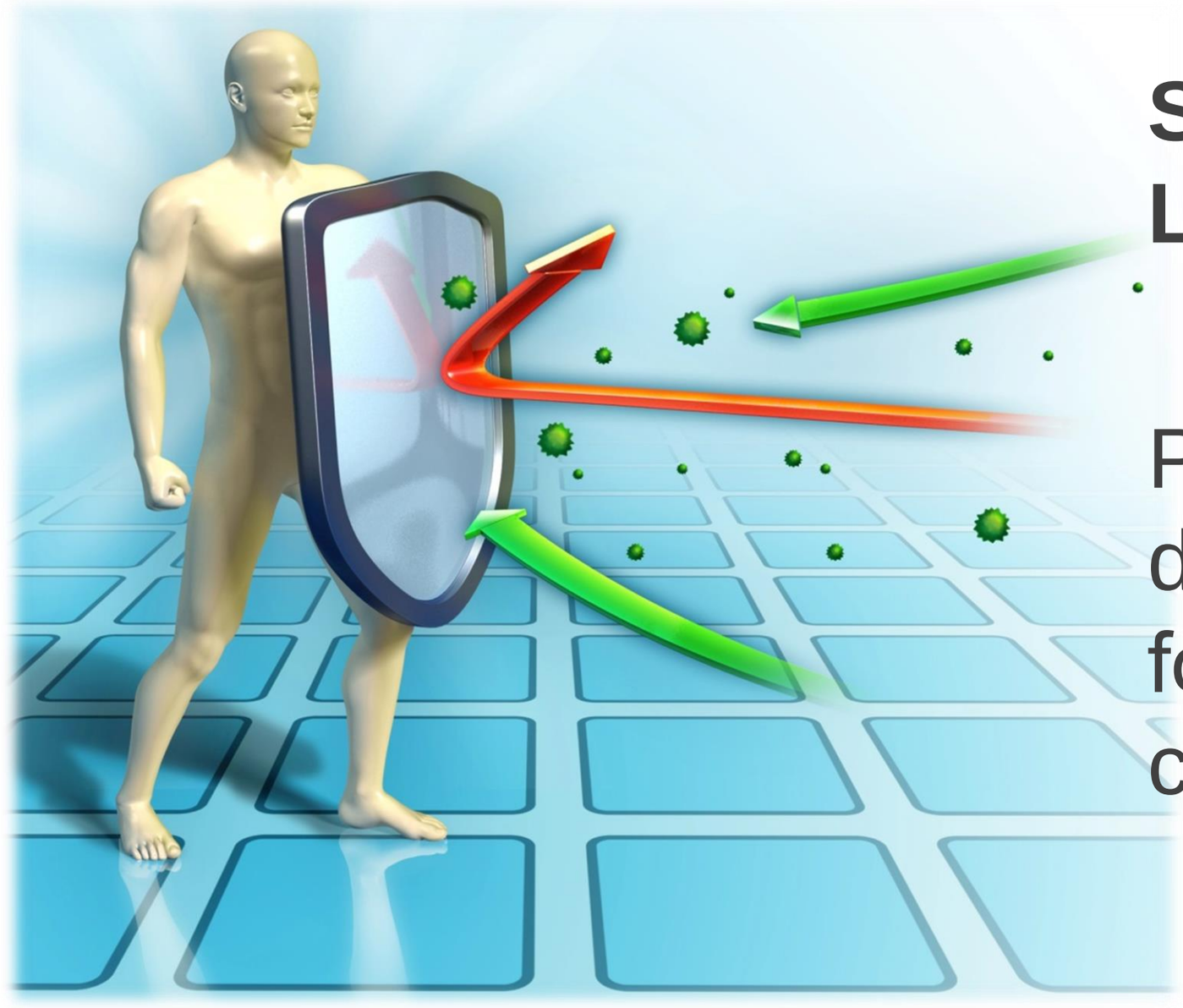
Innate Immune System



Skin, Nose, Mouth, Lungs, GI Tract

Provides immediate defense to anything foreign… repairs & anti-cancer *as able*.

Eliminate foreign invaders *before* they get in

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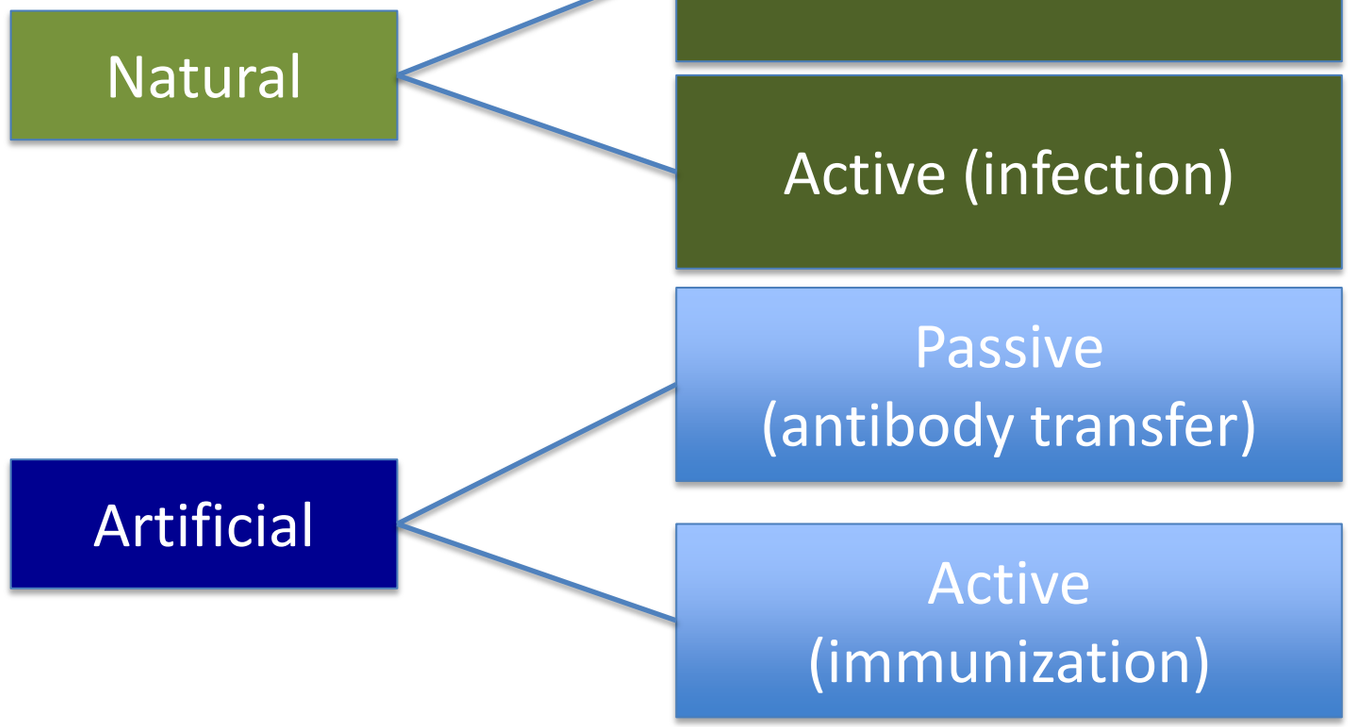
Adaptive Immune System

Adaptive Immune System



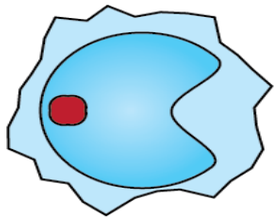
Blood, Lymph & tissue systems

Utilizes memory & antibody mechanism: ***specific***.

Attacks invaders that get inside.

Adaptive Immune Responses

Cell Mediated



T cell

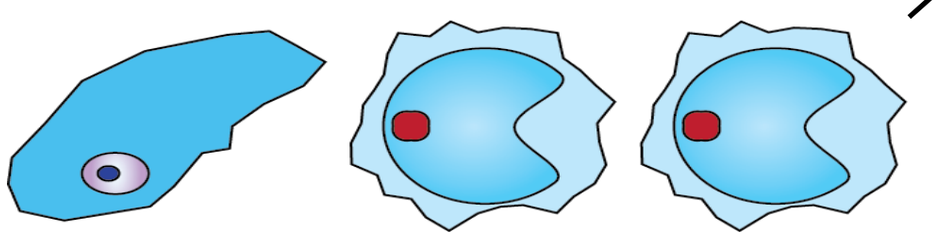
↓

Migrates to lymph nodes

↓

Antigen stimulation

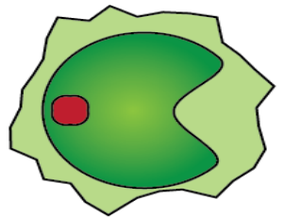
↓



Memory T cell | T cytotoxic cell | T helper cell

Cell-mediated Immunity

Antibody Mediated



B cell

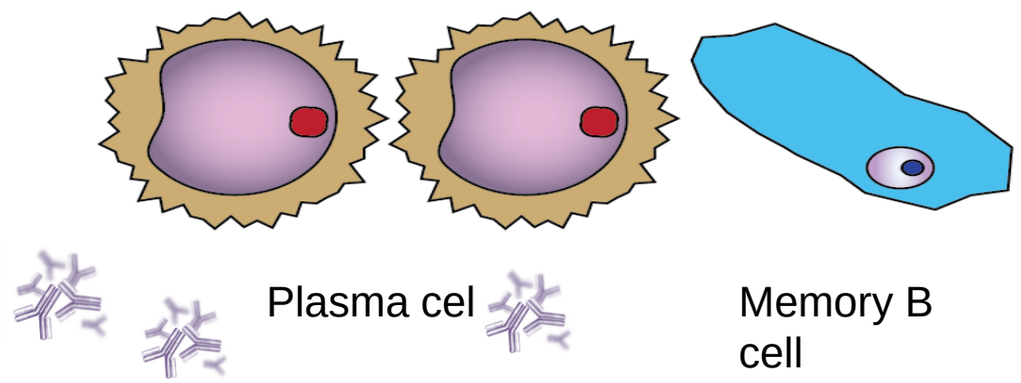
↓

Migrates to lymph nodes

↓

Antigen stimulation

↓



Plasma cel | Memory B cell

Antibody-mediated Immunity

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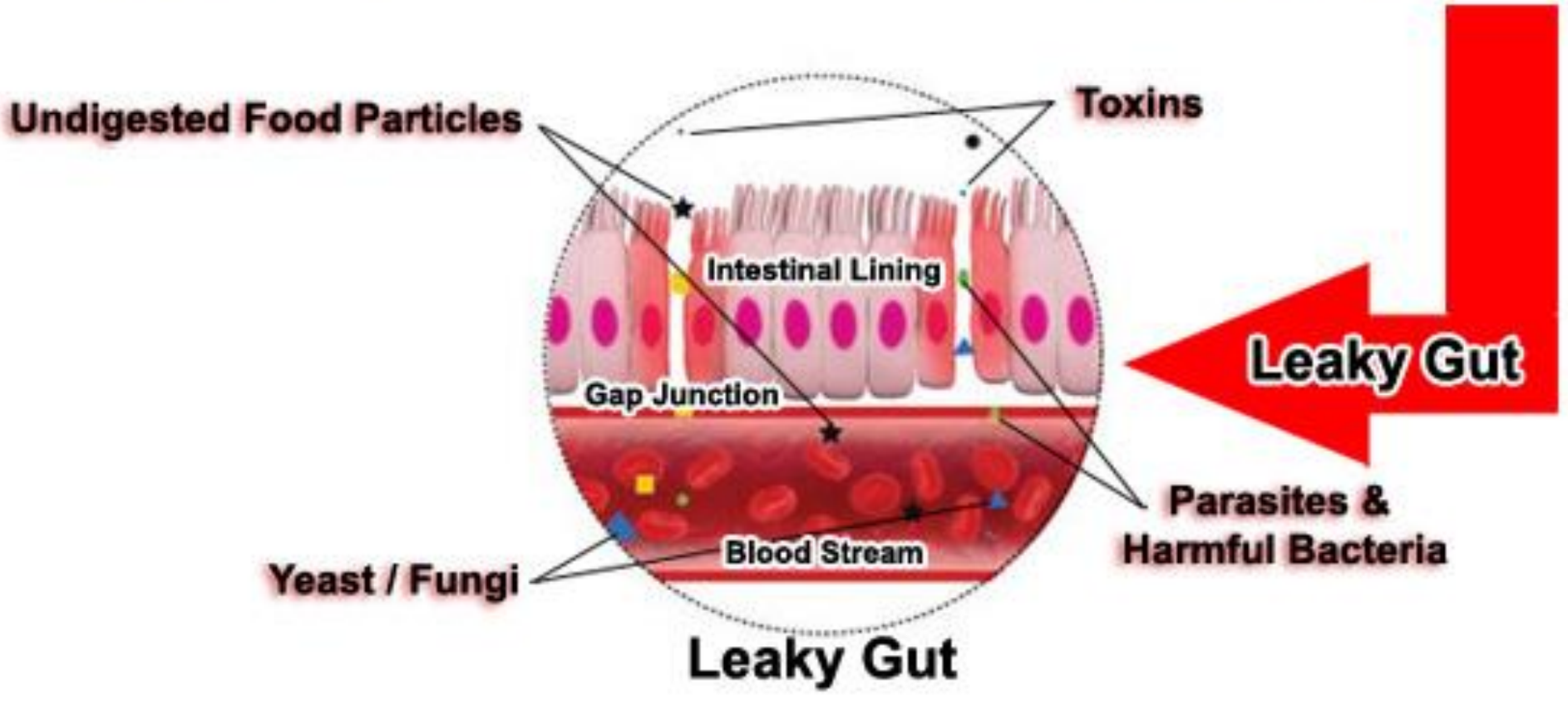
Leaky Gut

75% immune system within gut: Peyer's patchs



Hidden Immune Burdens

Delayed hypersensitivities/allergies hard to find.

Symptoms occur…

3 Hours

to 3 Weeks

After exposure

Symptoms may not even be specific…
immune system burden drains vitality; ache-y

Delayed Hypersensitivity

3 test methods:

- Antibody tests
- Particle size tests
- Lymphocyte response tests

Delayed Hypersensitivity

3 test methods:

- Antibody tests: Static, mis-leading
- Particle size tests: Random, mis-leading
- Lymphocyte response tests: hsLRA <3%!

Antibody Tests

- ELISA/EIA IgG, IgG4, IgA, IgM
- Quantify specific antibodies
  - Good from bad NOT possible
  - Long list items to avoid w/many false positives & false negatives

Particle Size Tests

- Particle size tests (automated cytotoxic):
  - Device measures blood particles

- Detect ***Any*** particle **10 micron in size…**
  not just reactive lymphocytes
  - Lots of 10 μ particles in blood…
    Rouleaux RBC, platelet clumps, granulocyte debris…
  - Low specificity, not predictive
  - Not reproducible

Hodsdon,W Zwickey H Reproducibility and Reliability of Two Food Allergy Testing Methods, Natural Medicine Journal, 2010; 2(3): 8.

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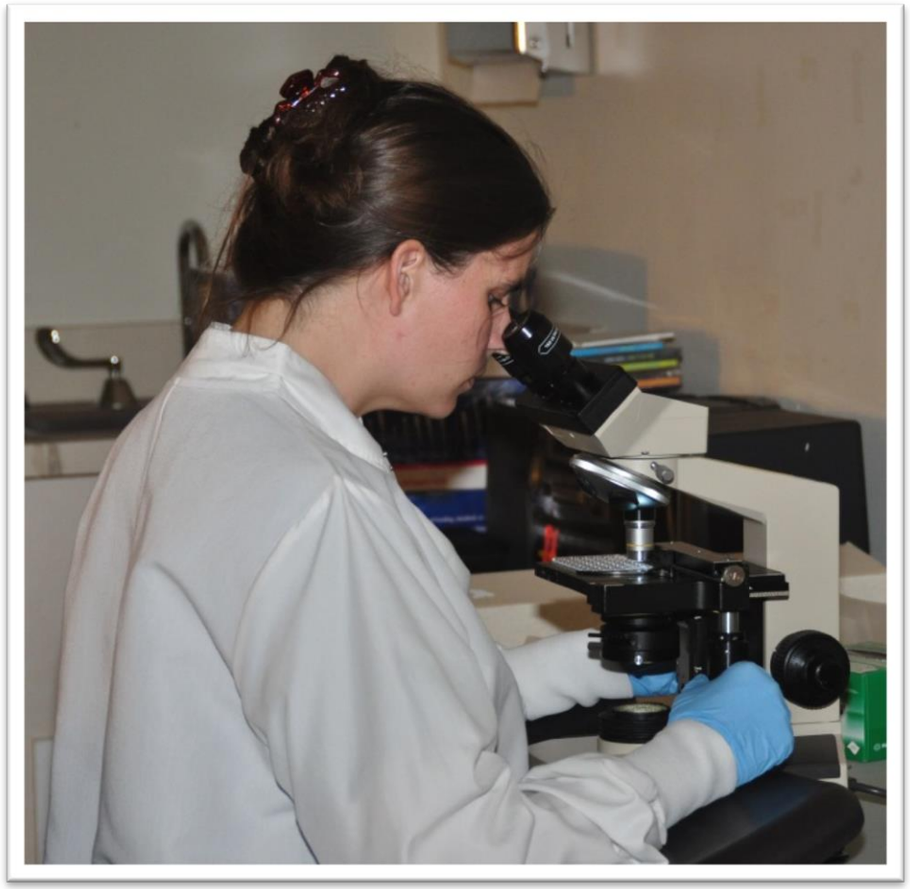
Lymphocyte Response Assays (LRA)

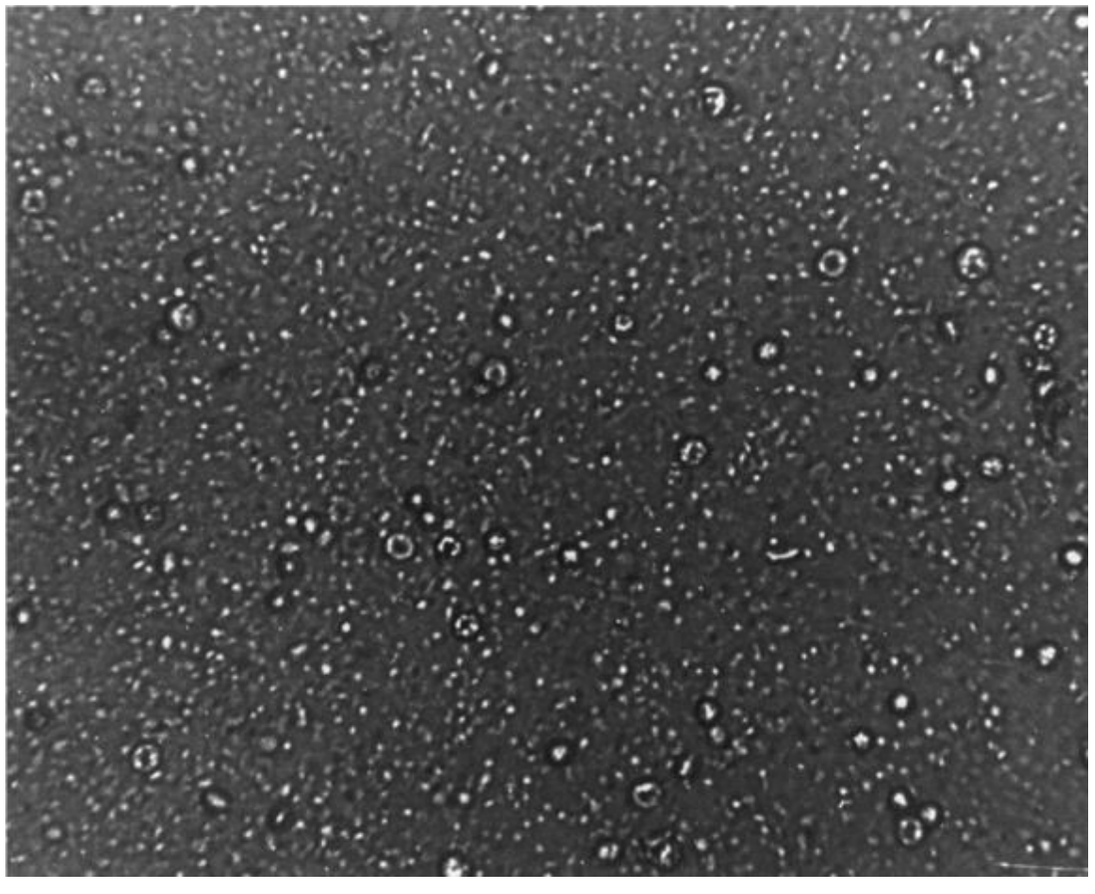
hsLRA (ELISA/ACT™ method)

- Directly observe lymphocytes under conditions similar to body (*ex*-vivo)
- ALL 3 delayed allergy paths
- Advanced method few false positives (<1%)
- Can then detect intolerances (if any)

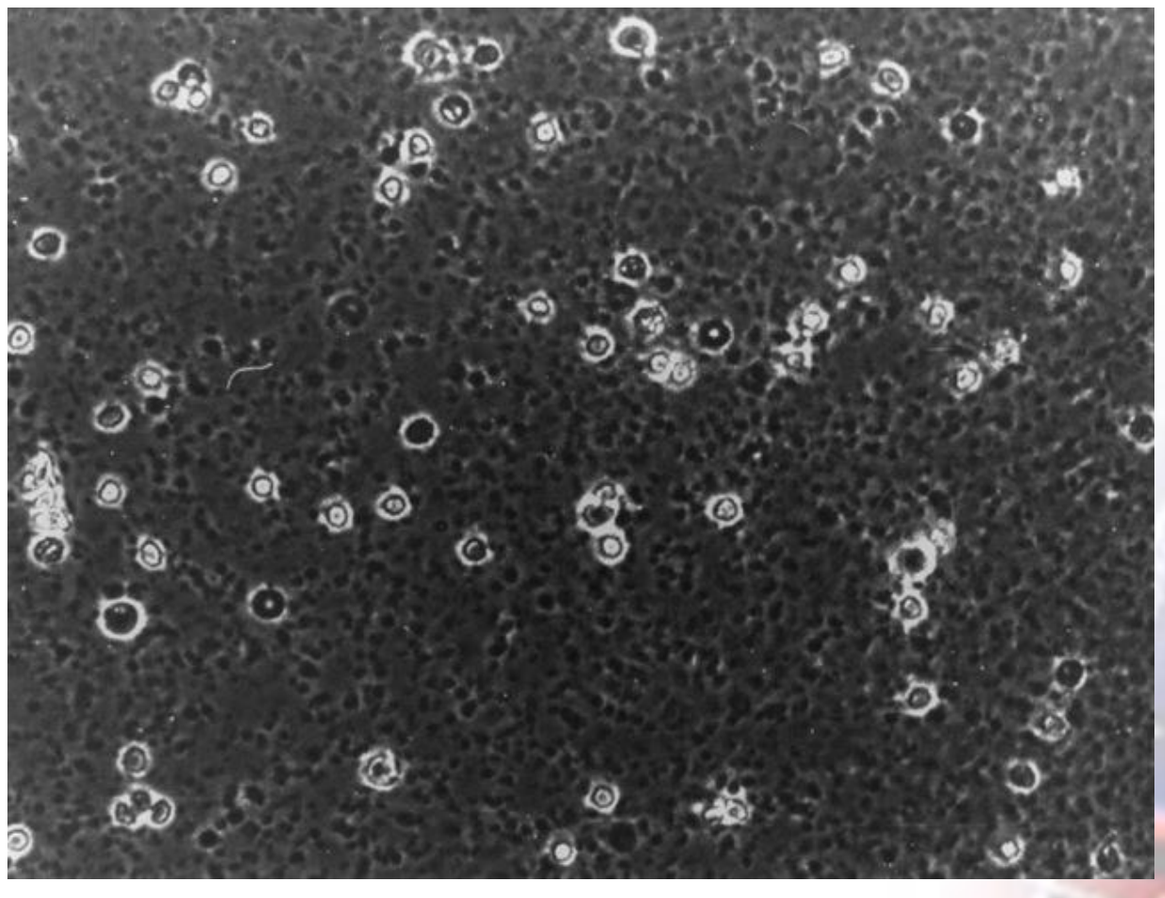


hsLRA by ELISA/ACT

Non-reactive lymphocytes



Reactive lymphocytes



Olympus SC35 Magnification 600x

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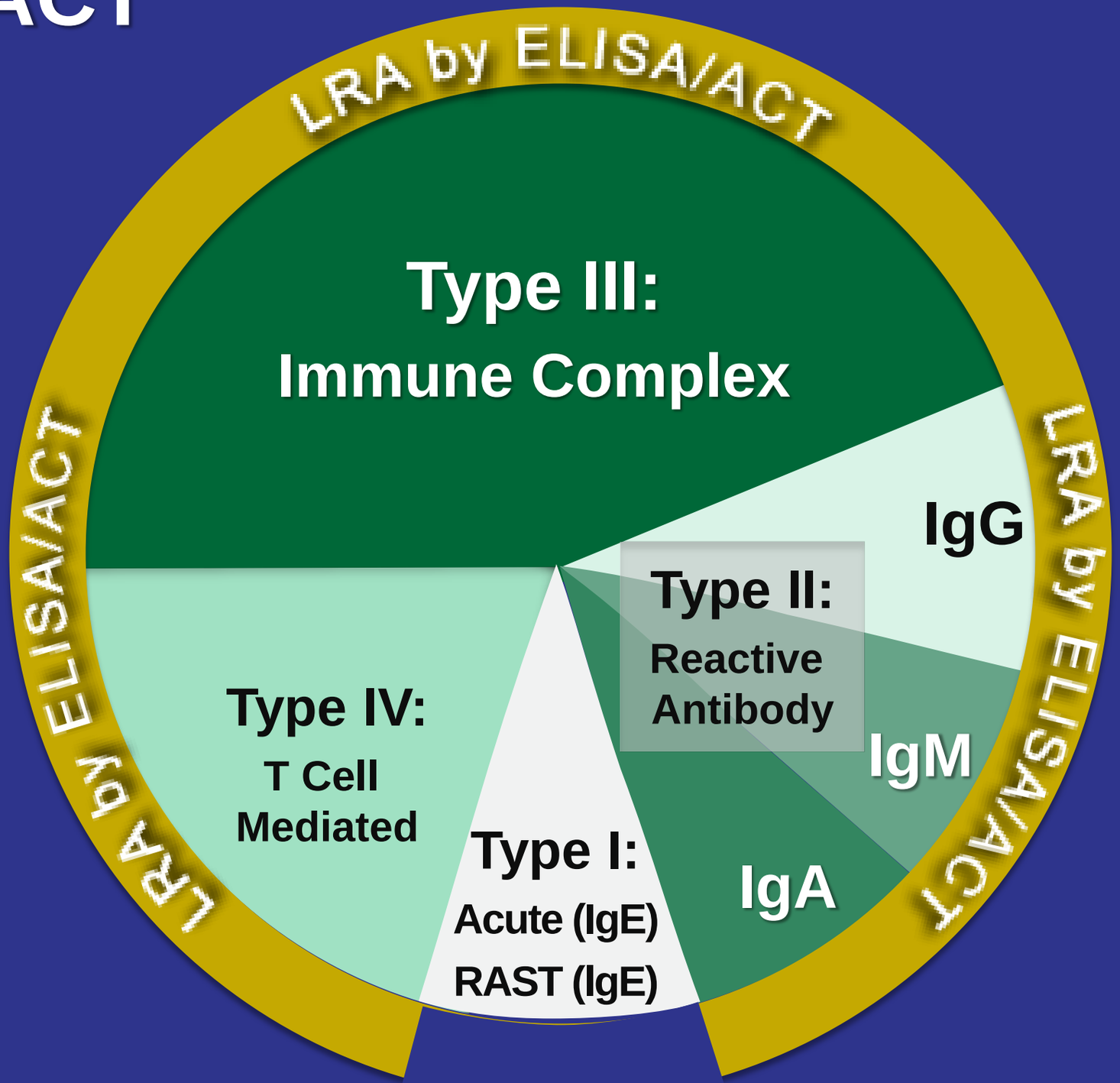
hsLRA by ELISA/ACT

Comprehensive Functional Ex-Vivo



Hyman M, Mani J, Jaffe R. Diabetes and Insulin Resistance, Food and Nutrients in Primary Care. *In*: Kohlstadt I, *Ed*. Advancing Medicine with Food and Nutrients, 2nd Ed., CRC Press, 2012.p 373-390.

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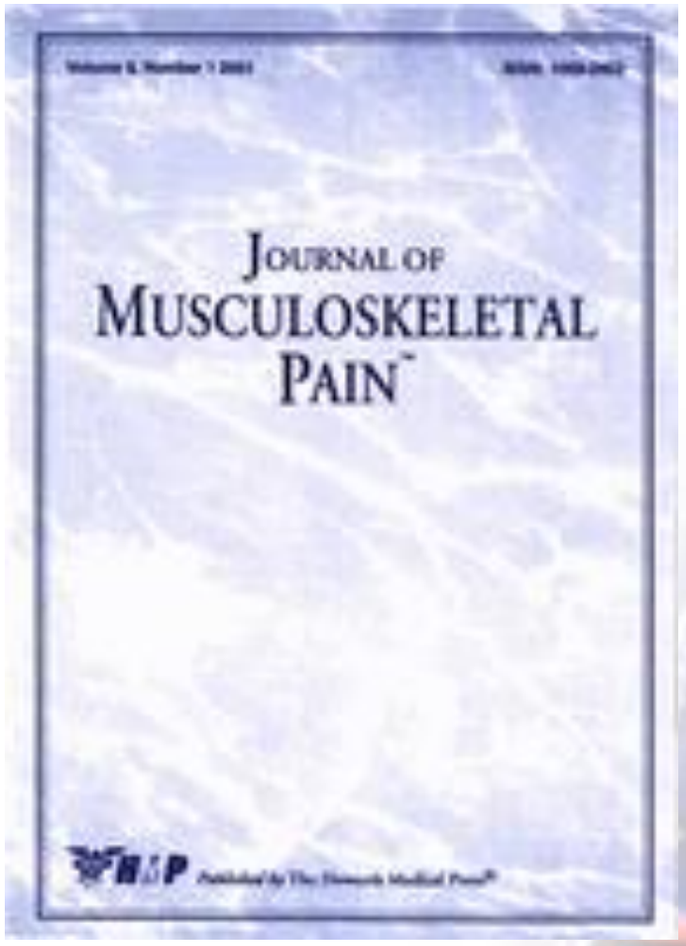
hsLRA: Successful Studies

"A Novel Treatment for Fibromyalgia Improves Clinical Outcomes in a Community-Based Study"

- **50% less pain**
- **70% less depression**
- **50% more energy**
- **30% less stiffness**

70,000+ Cases 30+ years
Patient & Practitioner Testimonials

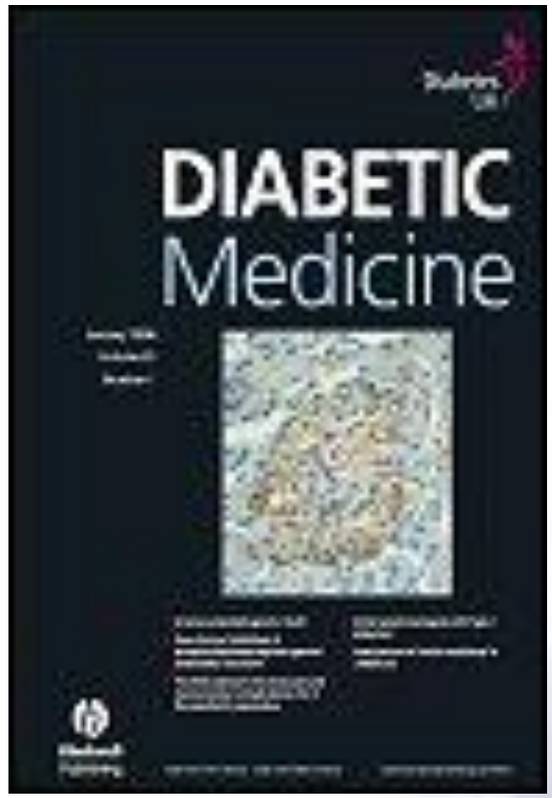


Deuster PA, Jaffe R. A Novel Treatment for fibromyalgia improves Clinical Outcomes in a Community Based Study. *J Musculo Pain.* 1998; 6:133-149.

hsLRA: Successful Studies

Type 1 *and* Type 2 Diabetes

- **Reduction in HgbA1c**
- **Mean reduction in insulin in Type 2**
- **Fewer hypoglycemic episodes**



70,000+ Cases 30+ years
Patient & Practitioner Testimonials

Jaffe R, Mani J, DeVane J, Mani H. Tolerance loss in diabetics: Association with foreign antigen exposure. ***Diabetic Medicine: A Journal of the British Diabetic Association*** **2006 Aug; 23(8): 924-925.**

Candidate Predictive Biomarker 5

Metabolic Acidosis Risk

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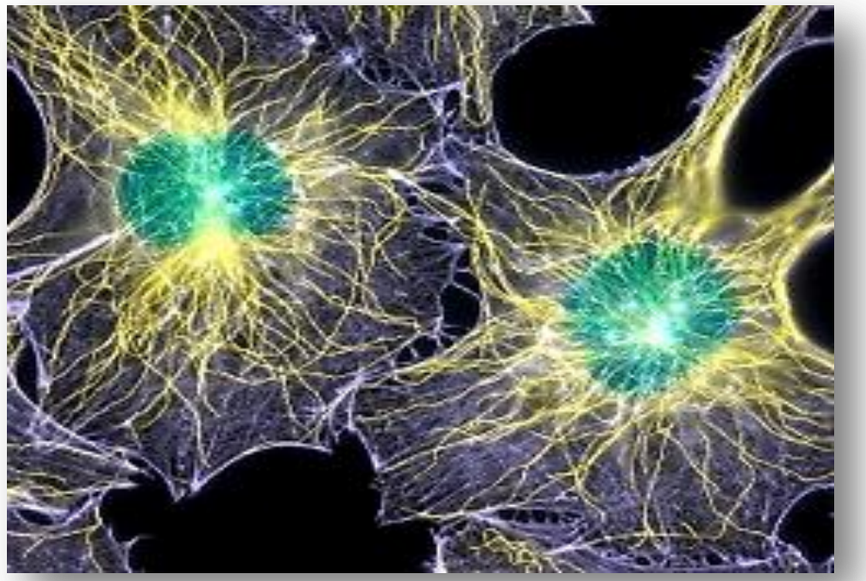
1st AM Ur pH as Predictive Biomarker

- Status: cell acids & minerals
- Enzyme catalysts pH sensitive

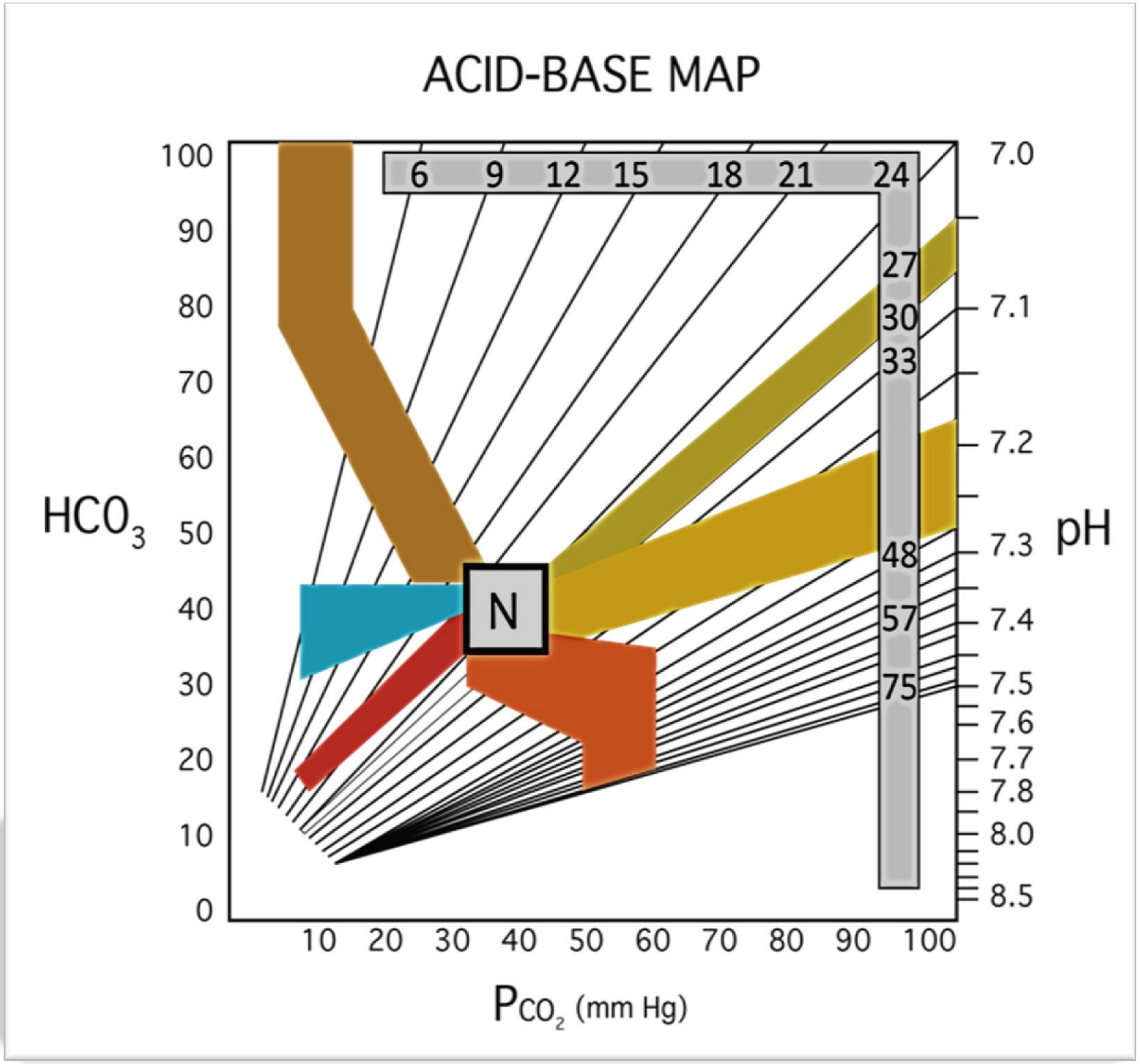


- Protein efficiency >90+% or <10%
- Mg^{++} forgotten electrolyte

Jaffe R. The Alkaline Way in Digestive Health. *In*: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions in Liver and Gastrointestinal Disease. *Academic Press*, 2013, 1-21.

pH: Cells Elective Protection or Survival

Siggaard-Andersen Acid-base Nomogram



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Siggaard-Andersen, O. Therapeutic Aspects of Acid-Base Disorders. Modern Trends in Anaesthesia, Ed. EVANS & GRAY, *Butterworths*, 1967, Vol. 3, 99p.

Urine >6º rest,
Goal Value: pH 6.5-7.5

Excess acid wears you out

Too Acidic (<6.5)

Healthy Repair / Restore Zone

Healthy pH (6.5-7.5)

Catabolic illness tears you down

Too Alkaline (>7.5)

1st urine >6+ hours rest
Ur equilibrates with cells

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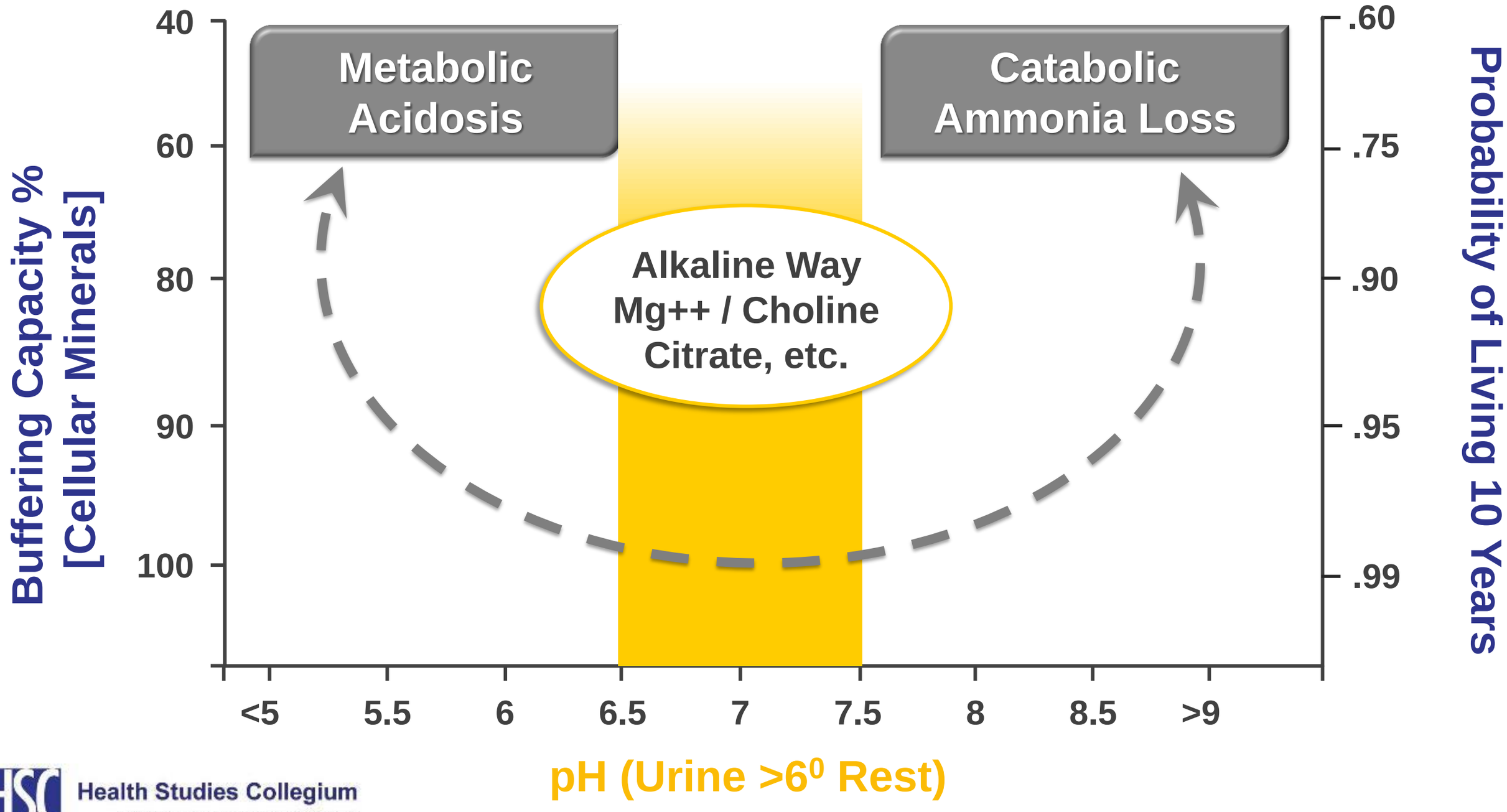
Jaffe R, Mani J. Clinical Evidence in Favor of Specific Polyphenolics. *In*: Watson RR, Preedy VR & Zibadi S, Eds. Polyphenols in Human Health and Disease, *Academic Press,* 2013: 695-705

Metabolic Acidosis Risk

Buffering Mineral Need vs Probability of Living 10 Years



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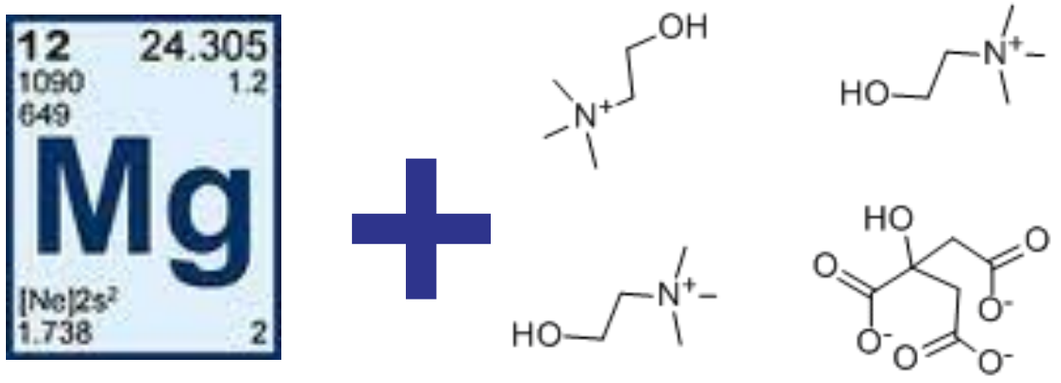
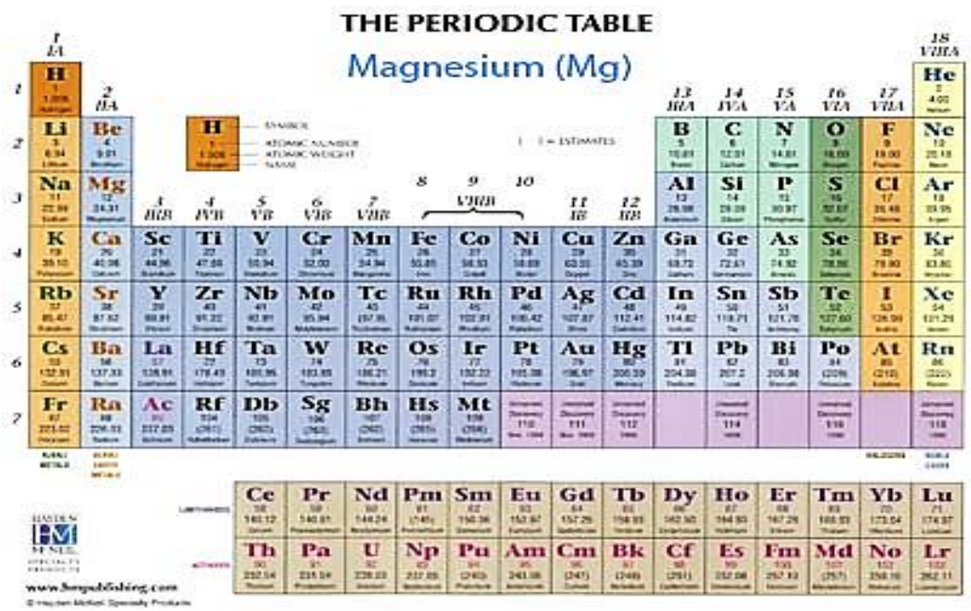
Biomarkers Solutions:
Magnesium, Mg^{++}

Mg uptake block w/
Choline Citrate:
440-880+ Mg/d
elemental **magnesium**

Mg^{++} displaces toxic minerals, protects fats…
Choline → acetylcholine, cholinergic bile Citrate
→ energizes & alkalinizes





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Alkaline Way

Food and Chemical Effects on Acid/Alkaline Body Chemical Balance



MORE ACID
(Consume Less)

Food Category	−−−−	−−−	−−	−
Citrus Fruit Fruit		Cranberry Pomegranate	Plum Prune Tomato	Coconut Fig Guava Persimmon Juice Cherimoya Date Dry Fruit
Bean Vegetable Legume Pulse Root	Soybean Carob	Pea Green, Snow Peanut Legumes (other) Carrot Chick Pea/Garbanzo	Bean Pinto, White, Navy/Red, Aduki, Lima or Mung Chard Split Pea	Bean Fava, Kidney, Black-eyed, String/Wax Spinach Zucchini Chutney Rhubarb
Grain Cereal Grass	Barley *Processed Flour*	Corn Rye Oat Bran	Wheat Semolina, Spelt, teff, Kamut White Rice Buckwheat	Triticale Brown Rice Millet Kasha
Fowl	Pheasant	Chicken	Goose/Turkey	Wild Duck
Meat Game Fish/Shell Fish	Beef Shell Fish (Processed) Lobster	Pork/Veal Mussel/Squid	Lamb/Mutton Game Meat Shell Fish (Whole)	Gelatin/Organs Venison Fish
Egg				Egg, Chicken
Processed Dairy Cow/Human Soy Goat/Sheep	*Processed Cheese* Ice Cream	Casein Cottage Cheese Milk, Soy	Milk; Goat, Cow, Sheep	Cream/Butter Yogurt Cheese; Goat, Sheep
Oil Seed/Sprout Nut	*Cottonseed Oil/Meal* *Fried Food* Hazelnut Walnut Brazil Nut	Oil Chestnut, Palm Kernel Lard Pistachio Seed Pecan	Oil Almond, Sesame, Safflower Tapioca Seitan or Tofu	Oil Canola, Pumpkin Seed, Grape Seed, Sunflower Pine Nut
Beverage Preservative Sweetner Vinegar	*Beer* *"Soda"* *Table Salt* Yeast/Hops/Malt *Sugar*/Cocoa White/Acetic Vinegar	Coffee Aspartame Saccharin Red Wine Vinegar	*Alcohol* Black Tea Benzoate Balsamic Vinegar	*Kona Coffee* *MSG* Honey/Maple Syrup Rice Vinegar
Spice/Herb	Pudding/Jam/Jelly	Nutmeg	Vanilla Stevia	Curry
Therapeutic	*Antibiotics*	*Psychotropics*	*Antihistamines*	

Food and Chemical Effects on Acid/Alkaline Body Chemical Balance



MORE ALKALINE
(Consume More)

Food Category	+	++	+++	++++
Citrus Fruit Fruit	Orange Banana Blueberry Raisin, Grapes Currant Strawberry	Lemon Pear Avocado Apple Blackberry Cherry Peach	Grapefruit Canteloupe Honeydew Olive Mango Citrus Loganberry	Lime Nectarine Raspberry Watermelon Tangerine Pineapple
Bean Vegetable Legume Pulse Root	Brussel Sprout Beet Chive/Scallion Celery/Cilantro Squash Artichoke Lettuce Jicama Turnip Greens	Potato/Bell Pepper Mushroom/Fungi Cauliflower Cabbage Eggplant Pumpkin Collard Greens	Kohlrabi Parsnip/Taro Garlic Asparagus Kale/Parsley Endive/Arugula Jerusalem Artichoke Ginger Root Broccoli	Lentil Brocoflower Seaweed Noril|Kombu|Wakame|Hijiki Onion/Miso Daikon/Taro Root Sea Vegetables Burdock/Lotus Root Sweet Potato/Yam
Grain Cereal Grass	Quinoa Wild Rice Oat			
Fowl				
Meat Game Fish/Shell Fish				
Egg	Egg, Duck	Egg, Quail		
Processed Dairy Cow/Human Soy Goat/Sheep	Ghee Human Breast Milk			
Oil Seed/Sprout Nut	Oil Avocado, Coconut, Olive/Macadamia, Linseed/Flax Seeds (most)	Oil Cod Liver, Primrose Sesame Seed Almond Sprout	Poppy Seed Pepper Chestnut Cashew	Pumpkin Seed
Beverage Preservative Sweetner Vinegar	Ginger Tea *Sulfite* Sucanat Umeboshi vinegar	Green or Mu Tea Rice syrup Apple Cider Vinegar	Kambucha Molasses Soy Sauce	Mineral Water Sea Salt
Spice/Herb	White Willow Bark Slippery Elm Artemesia Annua	Herbs Aloe Vera Nettle	Spices/Cinnamon Valerian Licorice Agave	Baking Soda
Therapeutic	Algae, Blue Green	Sake		Umeboshi Plum

Italicised items are NOT recommended

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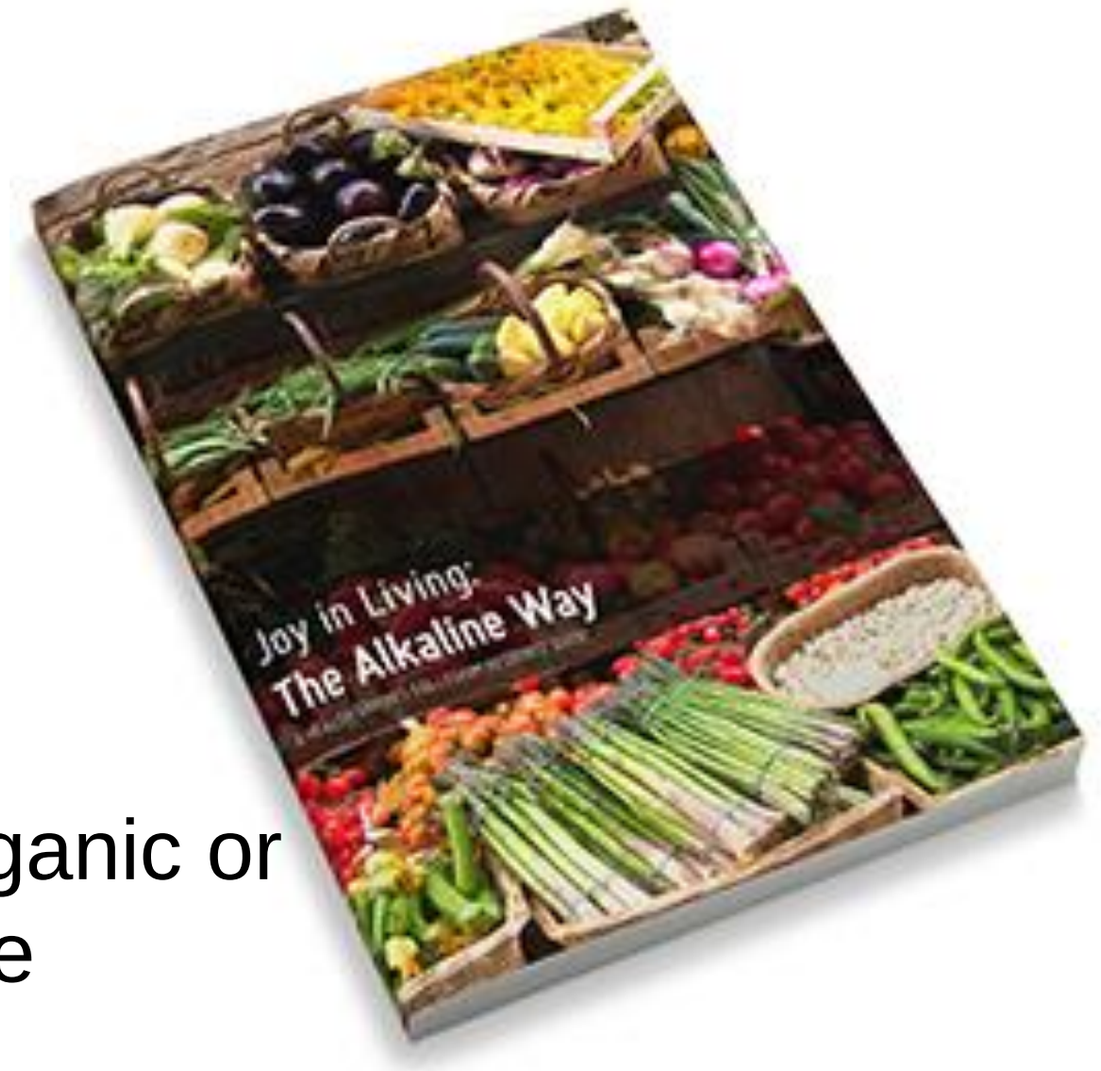
Jaffe R. The Alkaline Way in Digestive Health. *In*: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions in Liver and Gastrointestinal Disease. *Academic Press*, 2013, 1-21.

Alkaline Way brings healthy balance

- Alkalinizing foods & water
- Activity & 1st AM Ur pH
- Mg^{++} w/ Choline Citrate
- Abdominal breathing
- Green light & sunlight
- Eat in harmony with your nature & lifestyle
- Eat locally grown, vine ripened, organic or biodynamically derived, as possible
- Make restorative sleep a priority
- Work muscles & relax in = proportions



Jaffe R. The Alkaline Way in Digestive Health. *In*: Watson RR, Preedy VR, Eds. Bioactive Food as Dietary Interventions in Liver and Gastrointestinal Disease. *Academic Press*, 2013, 1-21.

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Candidate Predictive Biomarker 6

Vitamin D
(25 OH-Cholecalciferol)

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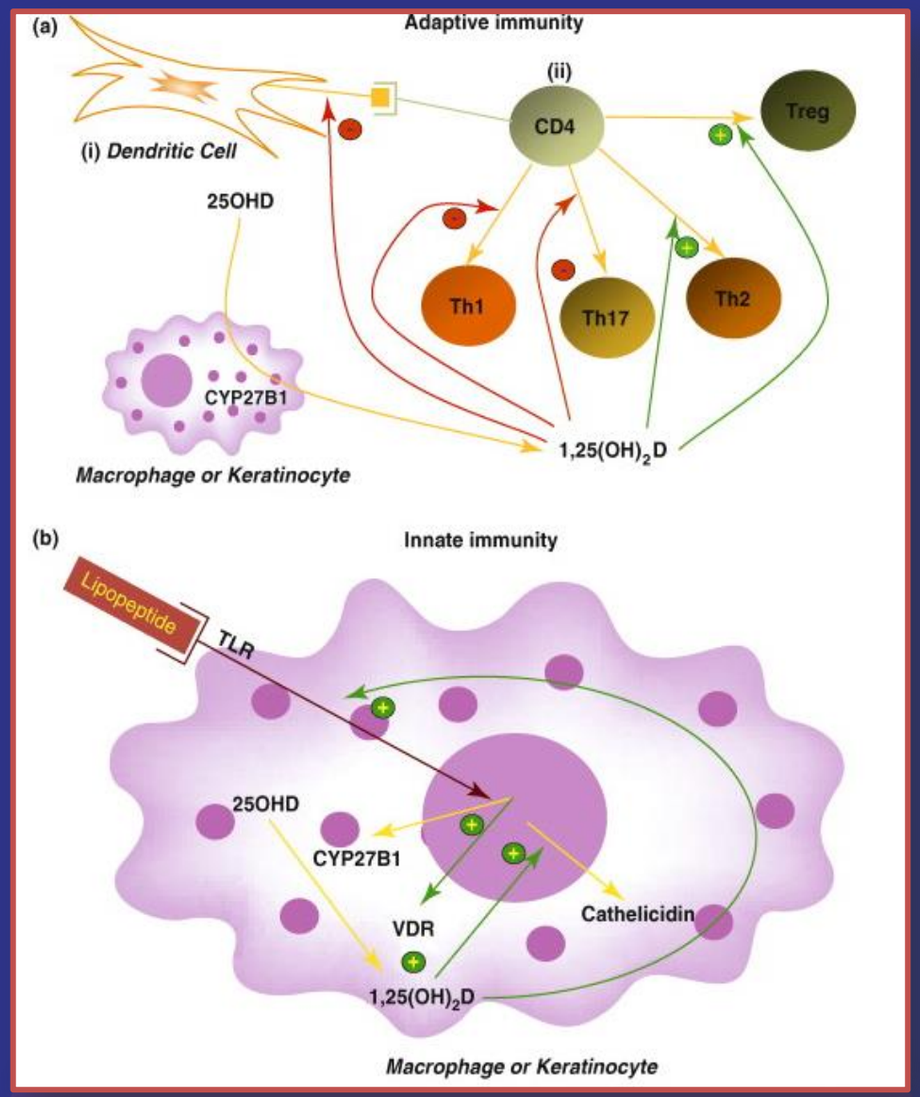
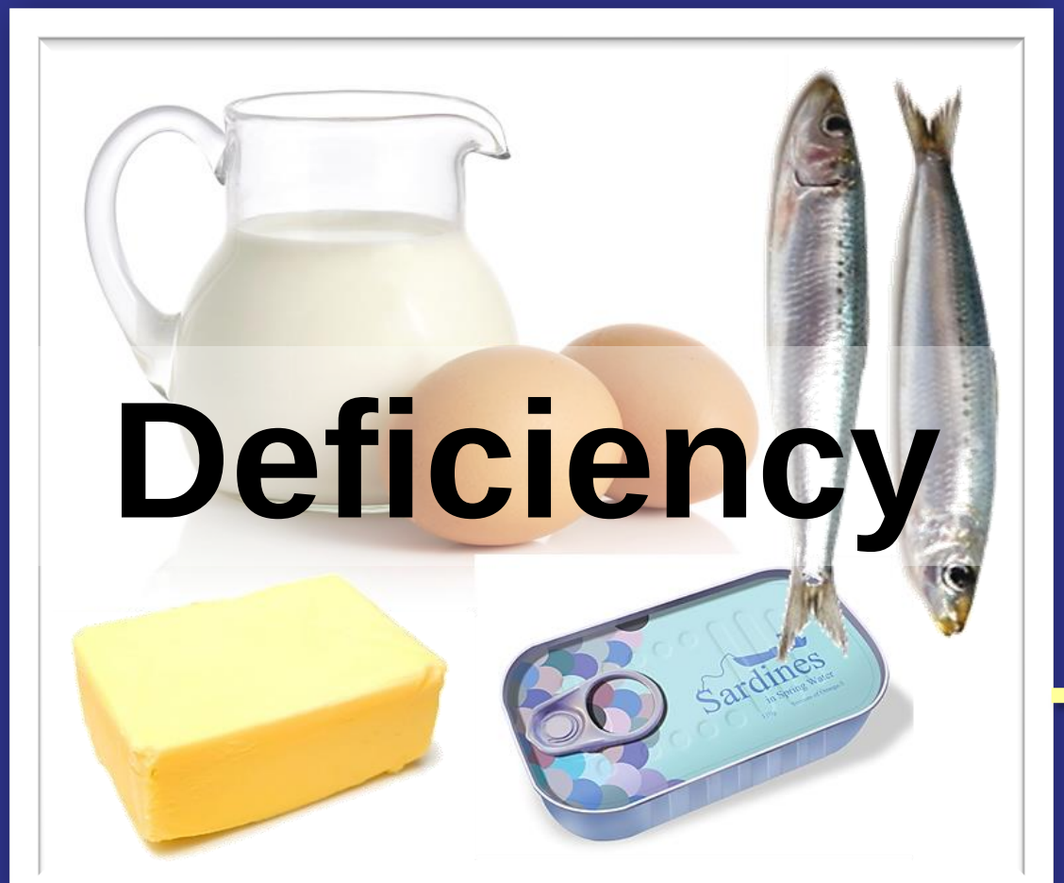
Vitamin D is Primary Biomarker



- Liver & Kidney hydroxylate adhesion molecule between cells
- Communicates enough is enough
- Bone, vessel, & brain health
- Anti-cancer surveillance
  40+ MM poorly absorb D… mucosal uptake!

Vitamin D 50-80 ng/ml Goal Value

500 IU cholecalciferol/drop
in MCT w/Rosemary Oil



hsCRP, IL-10 & Insulin Resistance

Heaney RP. Vitamin D in Health and Disease. *Clin J Am Soc Nephrol*. 2008; 3(5): 1535-1541.
Shute, EV. Proposed Study of Vitamin E Therapy. *Can Med Assoc J.* 1972; 106(10): 1057-1058.

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Candidate Predictive Biomarker 7

Essential Fats:
Omega-3 Index

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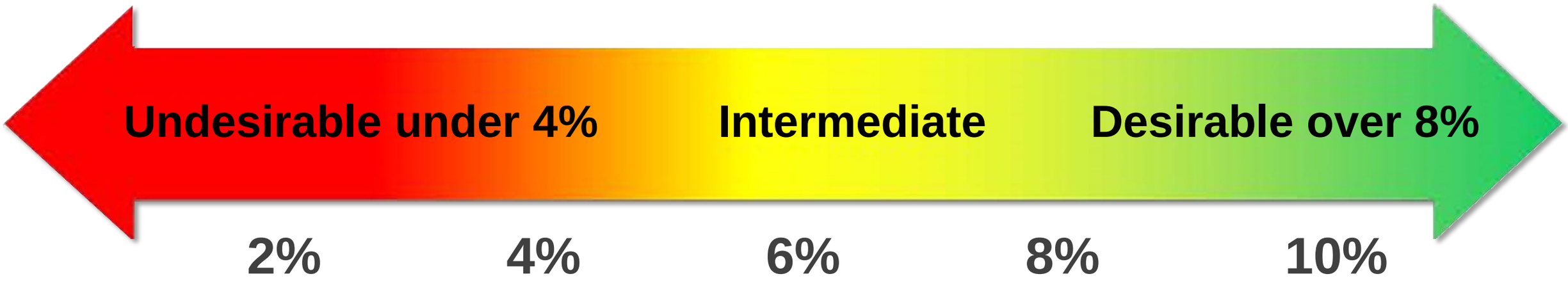
Omega 3 Index >8% Goal Value

SAMPLE RESULT

HS-Omega-3 Index® = 16.4%



Your hsOmega-3 Index is within the target range.
You are advised to maintain your current intake of omega-3 fatty acids.

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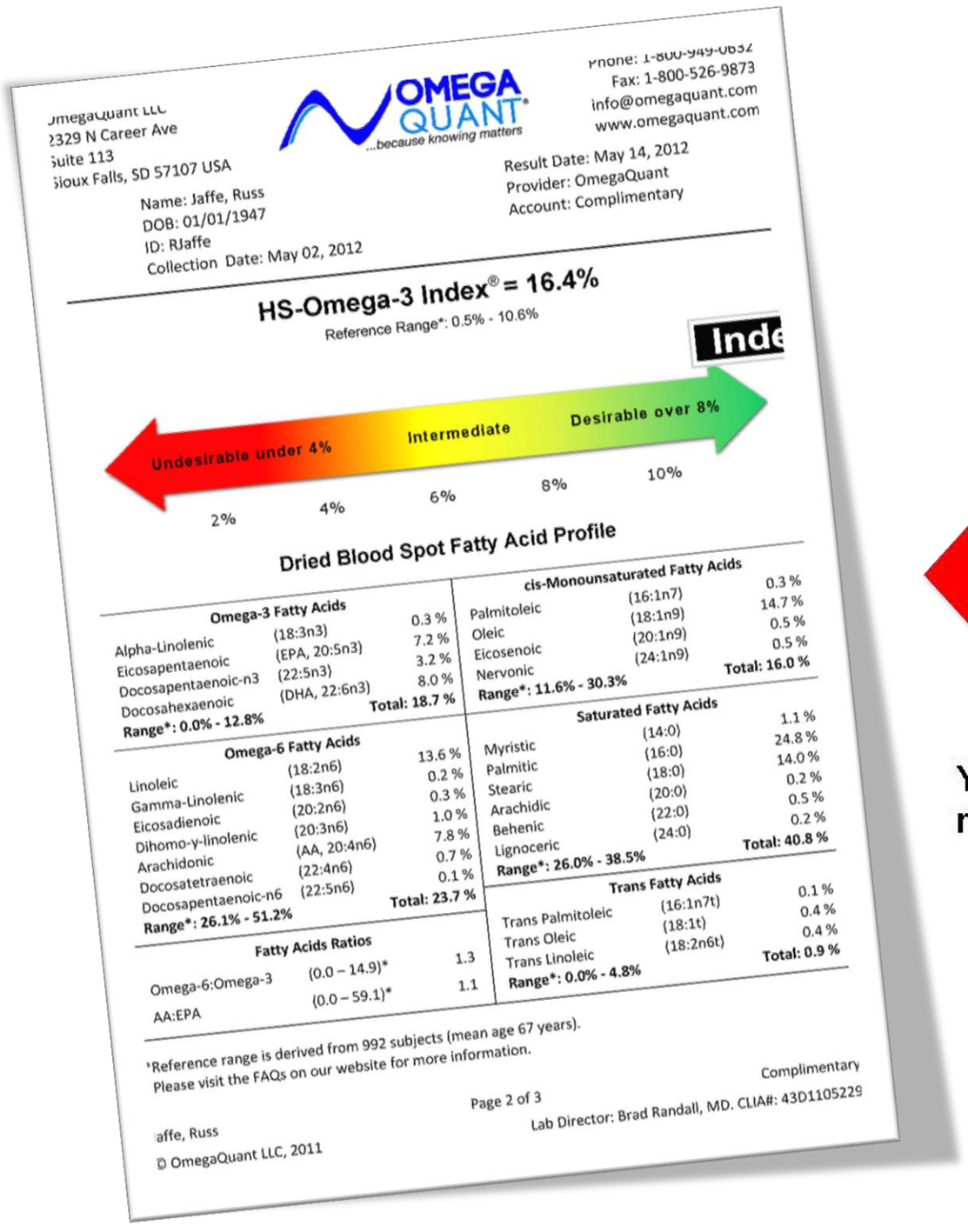
Omega Quant Omega 3 Index



OmegaQuant LLC
2329 N Career Ave
Suite 113
Sioux Falls, SD 57107 USA

OMEGA QUANT ...because knowing matters

Phone: 1-800-949-0632
Fax: 1-800-526-9873
info@omegaquant.com
www.omegaquant.com

Name: Jaffe, Russ
DOB: 01/01/1947
ID: RJaffe
Collection Date: May 02, 2012

Result Date: May 14, 2012
Provider: OmegaQuant
Account: Complimentary

HS-Omega-3 Index® = 16.4%

Reference Range*: 0.5% - 10.6%

Inde

Undesirable under 4% | Intermediate | Desirable over 8%

2% 4% 6% 8% 10%

Dried Blood Spot Fatty Acid Profile

Omega-3 Fatty Acids		
Alpha-Linolenic	(18:3n3)	0.3 %
Eicosapentaenoic	(EPA, 20:5n3)	7.2 %
Docosapentaenoic-n3	(22:5n3)	3.2 %
Docosahexaenoic	(DHA, 22:6n3)	8.0 %
Range*: 0.0% - 12.8%		**Total: 18.7 %**
Omega-6 Fatty Acids		
Linoleic	(18:2n6)	13.6 %
Gamma-Linolenic	(18:3n6)	0.2 %
Eicosadienoic	(20:2n6)	0.3 %
Dihomo-γ-linolenic	(20:3n6)	1.0 %
Arachidonic	(AA, 20:4n6)	7.8 %
Docosatetraenoic	(22:4n6)	0.7 %
Docosapentaenoic-n6	(22:5n6)	0.1 %
Range*: 26.1% - 51.2%		**Total: 23.7 %**
Fatty Acids Ratios		
Omega-6:Omega-3	(0.0 – 14.9)*	1.3
AA:EPA	(0.0 – 59.1)*	1.1
cis-Monounsaturated Fatty Acids		
Palmitoleic	(16:1n7)	0.3 %
Oleic	(18:1n9)	14.7 %
Eicosenoic	(20:1n9)	0.5 %
Nervonic	(24:1n9)	0.5 %
Range*: 11.6% - 30.3%		**Total: 16.0 %**
Saturated Fatty Acids		
Myristic	(14:0)	1.1 %
Palmitic	(16:0)	24.8 %
Stearic	(18:0)	14.0 %
Arachidic	(20:0)	0.2 %
Behenic	(22:0)	0.5 %
Lignoceric	(24:0)	0.2 %
Range*: 26.0% - 38.5%		**Total: 40.8 %**
Trans Fatty Acids		
Trans Palmitoleic	(16:1n7t)	0.1 %
Trans Oleic	(18:1t)	0.4 %
Trans Linoleic	(18:2n6t)	0.4 %
Range*: 0.0% - 4.8%		**Total: 0.9 %**

*Reference range is derived from 992 subjects (mean age 67 years).
Please visit the FAQs on our website for more information.

affe, Russ
OmegaQuant LLC, 2011

Page 2 of 3

Lab Director: Brad Randall, MD. CLIA#: 43D1105229

Complimentary

HS-Omega-3 Index® = 16.4%

Reference Range*: 0.5% = 10.6%

Omega 3 Index

Goal: 8%

Undesirable under 4% | **Intermediate** | **Desirable over 8%**

2% 4% 6% 8% 10%

Your HS-Omega-3 Index is within the target range. You are advised to maintain your current intake of omega-3 fatty acids.

Fatty Acids Ratio		
Omega-6:Omega-3	(0.0 – 14.9*	1.3

Omega 6: Omega 3 Ratio Goal: 1

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Candidate Predictive Biomarker 8

DNA Oxidative Risk: 8-OHdG

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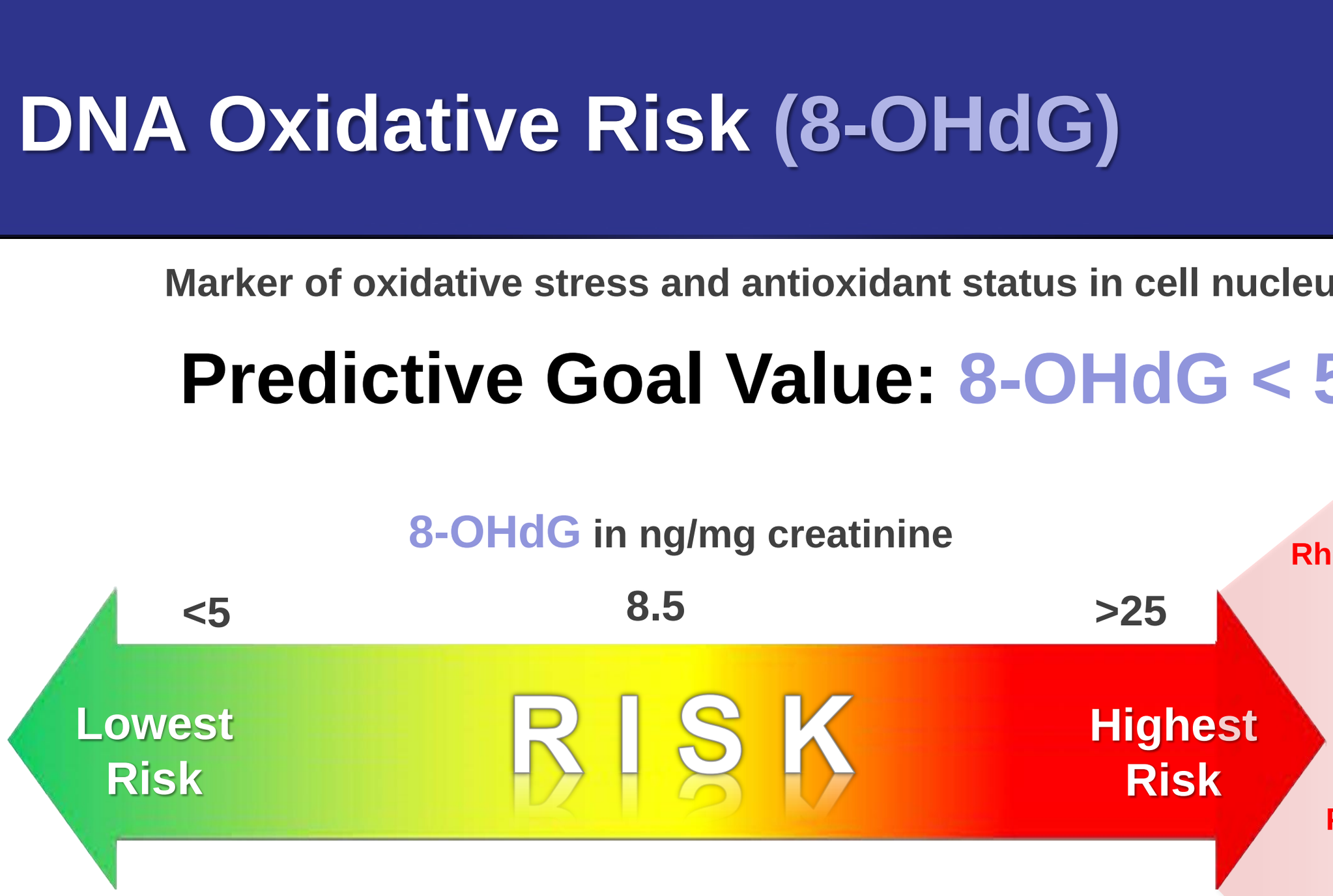
DNA Oxidative Risk (8-OHdG)

Marker of oxidative stress and antioxidant status in cell nucleus

Predictive Goal Value: 8-OHdG < 5

8-OHdG in ng/mg creatinine



Rheumatoid Arthritis

- Inflammatory Bowel Disease
- Parkinson's
- Bladder & Prostate Cancer
- Pancreatitis
- Huntington's
- Alzheimer's

HIGHEST Probability of 10yr Survival

LOWEST Probability of 10yr Survival

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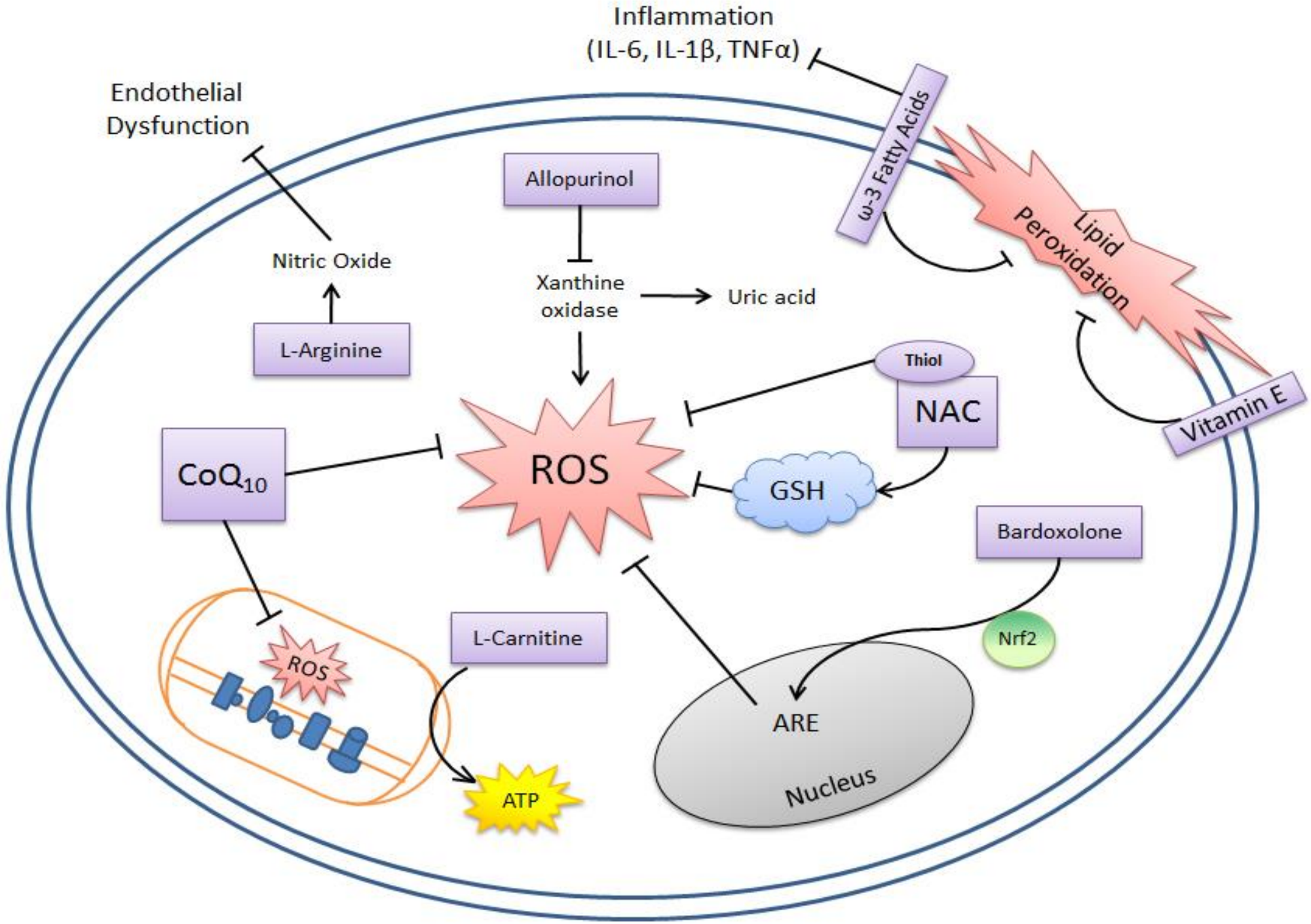
DNA Oxidative Stress (8-OHdG)



Omega-3 Index & 8-Oxoguanine Ur Oxidative Risk; Antioxidants Needed

CoQ10
300-1200 mg/d w/ Tocopherols in Rice Bran Oil

EPA/DHA
3-6+ g/d, nitrogen distilled

Comprehensive Super Multi (40 actives)

Silymarin, l-Carnitine fumarate, Lycopene, Carotenoids

? Liver Detox:

Heaney RP. Vitamin D in Health and Disease. *Clin J Am Soc Nephrol.* 2008; 3(5): 1535-1541.

Shute, EV. Proposed Study of Vitamin E Therapy. *Can Med Assoc J.* 1972; 106(10): 1057-1058.

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Omega 3 Index & 8-oxoguanine are Primary Biomarker Tests

EPA/DHA PUFAs are amplifiers: Cytokines

Omega 3 Index 6:3 Ration; EFAs

8-Oxoguanine reflects DNA oxidative risk

Mg^{++} antioxidant prevents PUFA damage

DNA / RNA translation & transcription

Mabley JG, Pacher P, Deb A, Wallace R, Elder RH, Szabó C. Potential Role for 8-oxoguanine DNA Glycosylase in Regulating Inflammation, FASEB J, 2005 Feb;19(2):290-292.

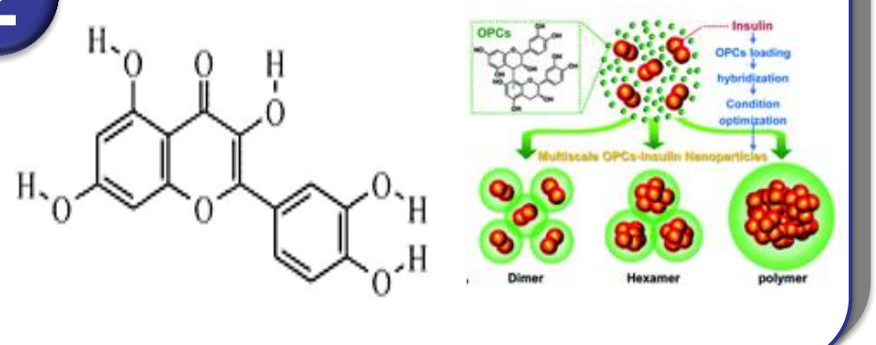
Omega 3 Index & 8-oxoguanine Solutions

Personal Ascorbate Calibration

1

Colorful Super Fruits

2



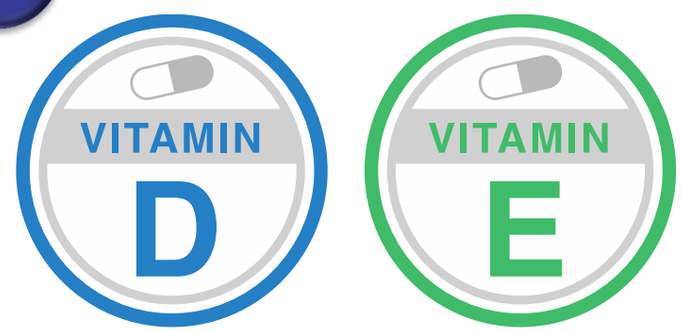
Complex Methyl Cofactors

3

GGOBE Super Foods

4

5



Qualified Predictive Biomarkers
Personalized, Evidence-Based, Comparative

hsHgb A1c:

Sugar, insulin… **AGEs**

hsCRP:

Inflammation, repair disease

8 oxo-guanine:

Oxidative stress… **ALEs**

hsHomocysteine:

Methylation, detox…**Sulfur**

Omega 3 Index:

Omega 3:6; **EFAs**

hsLRA :

Immune Tolerance

Vitamin D:

Cell talk & adhesion

1st AM urine pH:

cell acidosis risk

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Jaffe R, Predictive Biomarkers Provide Evidence for Comparative Effectiveness Research, HSC 90_13:01 Advisory on Predictive Medicine & Health Promotion.

Gruenewald TL, Seeman TE, Ryff CD, Karlamangla A, Singer BH. Combinations of Biomarkers Predictive of Later Life Mortality. *PNAS*, 2006; 103 (38): 14158-14163.

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Hgb A1c:

Sugar, insulin… **AGEs**

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Oxidative stress… **ALEs**

Homocysteine:

Methylation, detox…**Sulfur**

Omega 3 Index:

Omega 3:6; **EFAs**

LRA by ELISA/ACT:

Immune Tolerance

Vitamin D:

Cell talk & adhesion

1st AM urine pH:

cell acidosis risk

Jaffe R, Predictive Biomarkers Provide Evidence for Comparative Effectiveness Research, HSC 90_13:01 Advisory on Predictive Medicine & Health Promotion.

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Metabolic Syndrome:
Predictive Marker Goals

hsLRA Tests Tolerant

Vitamin D 50-80

BP ↓ **Detox** ↑

pH 6.5-7.5

hsHgb A1c <5

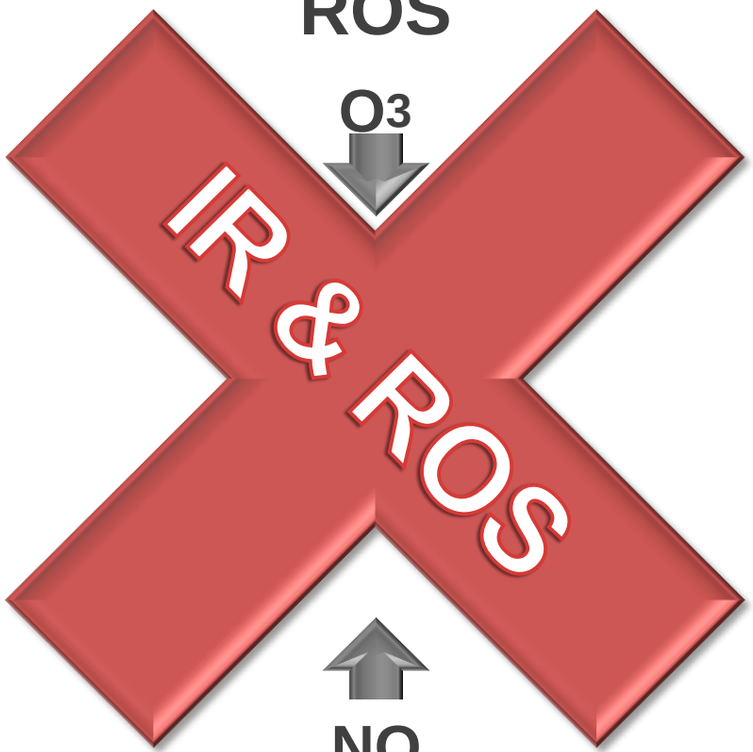
Blood Sugar
Insulin

Prothrombotic PAI-1
'Sticky' Platelets
Fibrinogen

FFA ↓

ROS

O_3 ↓



hsHomocysteine <6

PCOS (Androgenic Hirsutism)
NAFLD (non-alcoholic liver disease)
NASH (non-alcoholic steatohepatitis
Acanthosis Nigricans: **Liver spots**

Omega-3 Index >8
8-oxo-guanine <5

hsCRP <0.5

Abdominal Fat
Oxidized Blood Fats

NO ↓

Endothelial Dysfunction

Insulin ↓ & effective
Organ damage reduced;
promote repair

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Grundy SM, Cleeman JI, Daniels SR, Donato KA *et. al*., Diagnosis and Management of the Metabolic Syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 2005;112 (17):2735-2752.
Kahn R, Buse J, Ferrannini E, Stern M *et. al*., The metabolic syndrome: Time for a Critical Appraisal: Joint Statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2005 Sep;28(9):2289-2304.

Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Predictive Goal Values
hsHgb A1c (Hemoglobin A1c)	Sugar/insulin/energy… **AGE**	<5%
hsCRP (High sensitivity C reactive protein)	Repair & inflammation immune status	<0.5 mg/L
hsHCY (hsHomocysteine)	Detox, epigenetic, methylation… **Sulfur**	< 6 µmol/L
hsLRA	Immune memory/immune tolerance	No reactions
Ur pH >6º rest (1st AM Urine pH)	Mineral status & cell acid/alkaline balance	6.5 – 7.5
Vitamin D (25-Hydroxy-cholecalciferol)	Vitamin D… cell communication status	50 – 80 ng/mL
Omega-3 Index (Omega 3/6 EFA ratio)	Omega 3:6 ratio; EFAs	**>8%**
8-OHdG (8-Oxo-Guanine)	Oxidative stress/antioxidant nucleus status	**<5 ng/mg creatinine**

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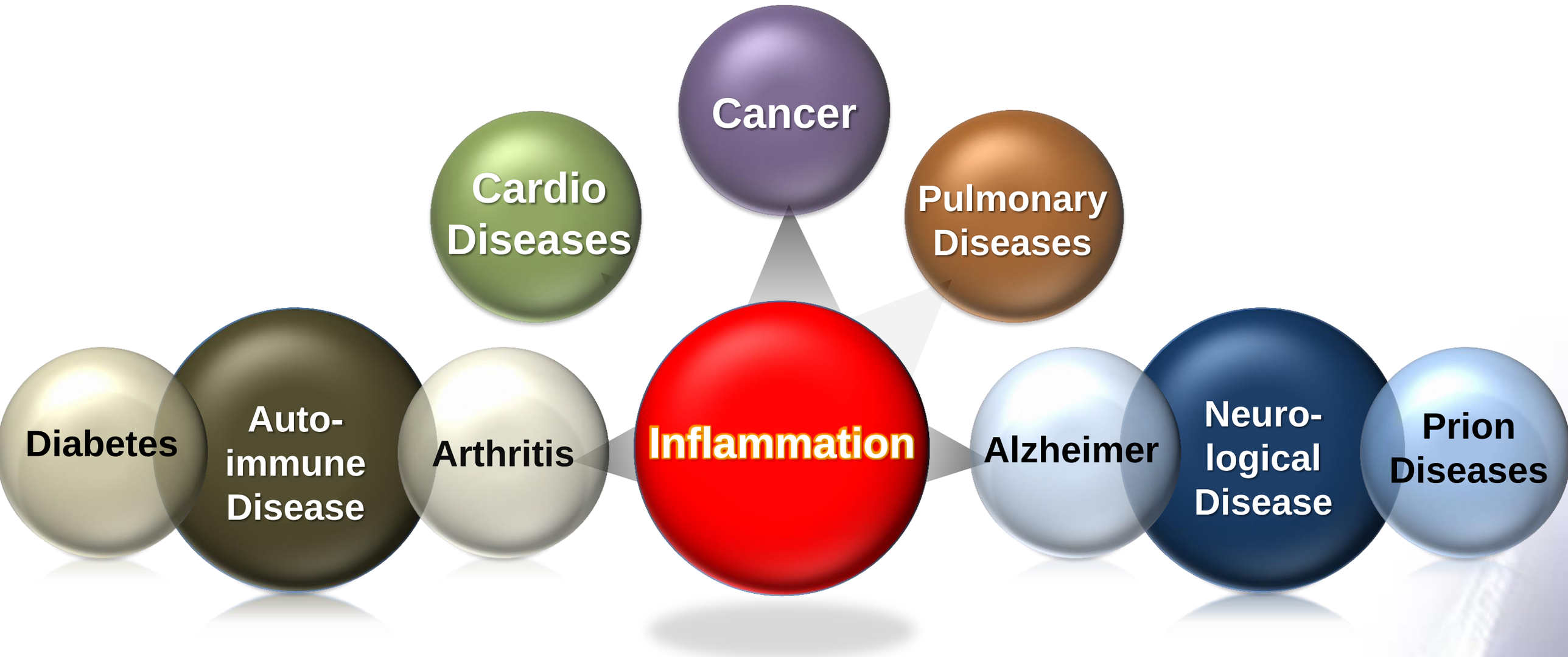
Inflammation Rethought = Remove Repair Blocks



Grundy SM, Cleeman JI, Daniels SR, Donato KA *et. al*., Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*, 2005;112(17):2735-2752.

Kahn R, Buse J, Ferrannini E, Stern M et. al., The Metabolic Syndrome: Time for a Critical Appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2005 Sep;28(9):2289-2304.

Jaffe R, Mani J. Rethink Health: Inflammation Is Actually Repair Deficit: Using Physiology First to Achieve Better Outcomes, Part 1: Value and Importance of Understanding Inflammation as Repair Deficit. *Townsend Letter for Doctors and Patients*. 2013, Jun (359): 68-74.

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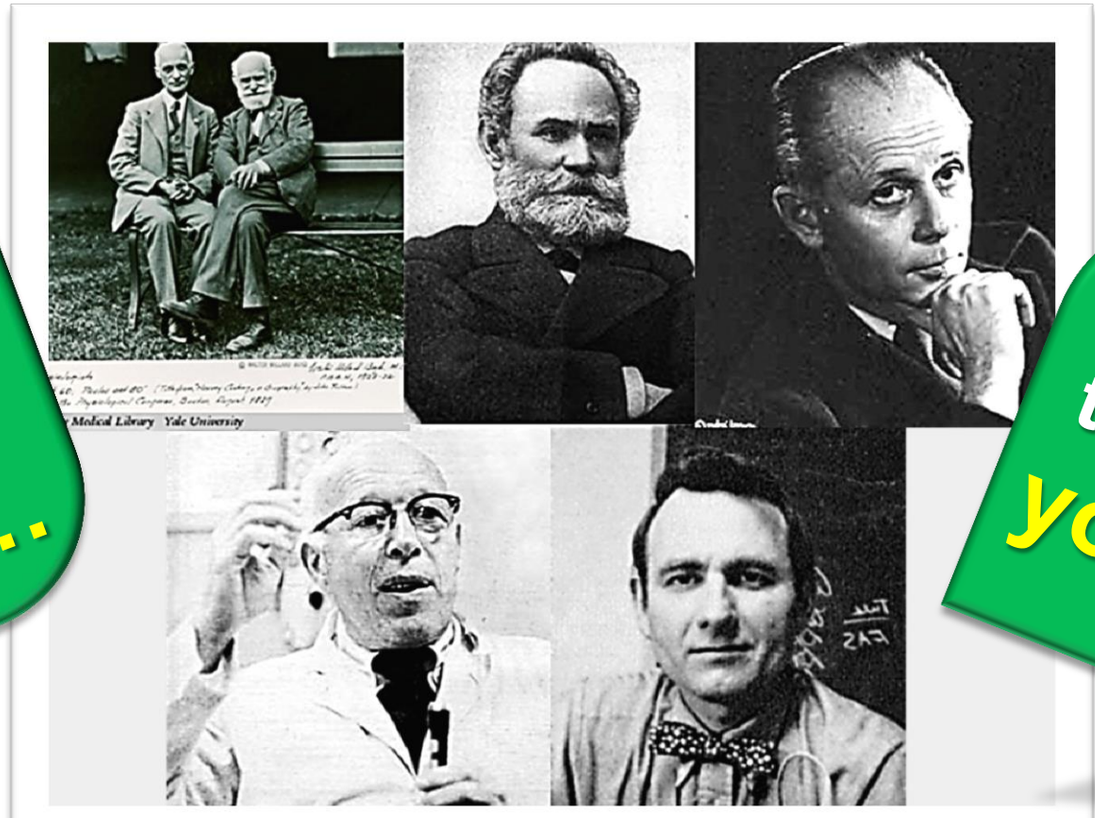
Life: Experience Trumps Theory

Trust experts; Verify in your experience…



Hope, healing touch & go by your results

Governing Systems… Integrative Science

- ±20-40 quality years, personalized risk & resilience now
- Biomarkers of control systems quantified
- Lower costs of care with better outcomes
- Apply what is known; remove obstacles

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Prigogone I, Stengers I. Order Out of Chaos: Man's New Dialogue with Nature, Bantam Books, 1984.

Korzybski A. Science and Sanity: An Introduction to Non-Aristotelian Systems and General Semantics. Institute of General Semantics, 5th Edition, 1994.

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THE NEXT BIG THING

Predictive Biomarkers To Personalize Care:

hsPB

10 year survival…

>99% or < 20%

Use 92% healthier habits

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Essential Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Analysis Laboratory	Specimen Needed	Predictive Goal Values
Hgb A1c (Hemoglobin A1c)	Sugar/ insulin/ energy… **AGE**	ZRT Lab ZRTLab.com	Blood Spot (finger prick)	<5%
hsCRP (High sensitivity C reactive protein)	Repair, inflammation immune status	ZRT Lab ZRTLab.com	Blood Spot (finger prick)	<0.5 mg/L
Homocysteine (cardiovascular risk)	Detox, epigenetic, methylation… **Sulfur**	Quest Diagnostics Questdiagnostics.com	Blood Draw 1 EDTA tube	< 6 µmol/L
LRA by ELISA/ACT™	Immume memory/immune tolerance	**LRA by ELISA/ACT™** ELISAACT.com	Must Use LRA Kit, 4 tubes	No delayed reactions

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Elective Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Analysis Laboratory	Specimen Needed	Predictive Goal Values
1st AM Urine pH (Metabolic acidosis assessment)	Assess mineral need and cell acidosis risk	Self-test. Details available. FUPH.PERQUE.com	**1st Morning Urine** (or after 6 hrs of rest)	**6.5 – 7.5**
Vitamin D (25-Hydroxy-cholecalciferol)	Vitamin D level for cell communication status	ZRT Lab ZRTLab.com	**Blood Spot** (Self collected finger prick	**50 – 80 ng/mL**
Omega-3 Index (Omega 6:3 ratio)	Omega 3:6 ratio; EFAs	Omega Quant omegaquant.com	**Blood Spot** (Self collected finger prick)	**>8%**
8-Oxo-Guanine (8-OHdG)	Oxidative stress and antioxidant status	Doctor's Data, Inc. doctorsdata.com	**Urine** (>6º rest)	**<5 ng/mg creatinine**

Predictive Bio-Marker Tests to Determine Your Functional Age

Test Name	Test Descriptions	Analysis Laboratory	Specimen Needed	Predictive Goal Values
Hgb A1c (Hemoglobin A1c)	Sugar/insulin/energy… **AGE**	ZRT Lab ZRTLab.com	Blood Spot (Self collected finger prick)	<5%
hsCRP (High sensitivity C reactive protein)	Repair and inflammation immune status	ZRT Lab ZRTLab.com	Blood Spot (Self collected finger prick)	<0.5 mg/L
Homocysteine (cardiovascular risk)	Detox, epigenetic, methylation… **Sulfur**	Quest Diagnostics questdiagnostics.com/	Blood Draw 1 tube	< 6 µmol/L
LRA by ELISA/ACT™	Immume memory/ immune tolerance	ELISA/ACT™ Biotechnologies ELISAACT.com	Must Use LRA Kit 4 tubes	No delayed reactions
1st AM Urine pH (Metabolic acidosis assessment)	Assess mineral need and cell acid/alkaline balance	Self-test. Details available at FUPH.PERQUE.com	**1st Morning Urine** (or after 6 hrs of rest)	6.5 – 7.5
Vitamin D (25-Hydroxy-cholecalciferol)	Vitamin D level for cell communication status	ZRT Lab ZRTLab.com	**Blood Spot** (Self collected finger prick	50 – 80 ng/mL
Omega-3 Index (Omega 3/6 ratio)	Omega 3:6 ratio; EFAs	Omega Quant omegaquant.com	**Blood Spot** (Self collected finger prick)	**>8%**
8-Oxo-Guanine (8-OHdG)	Oxidative stress & antioxidant status in cell nucleus	Doctor's Data, Inc. doctorsdata.com	**Urine** 1st morning sample	**<5 ng/mg creatinine**

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THE NEXT BIG THING

Predictive Biomarkers

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Russell Jaffe
MD, Ph.D., CCN

FASCP, FACN, FACAAI, FOCIS, FAMLI, FRSM

Fellow, Health Studies Collegium
rjaffe@4HSC.org

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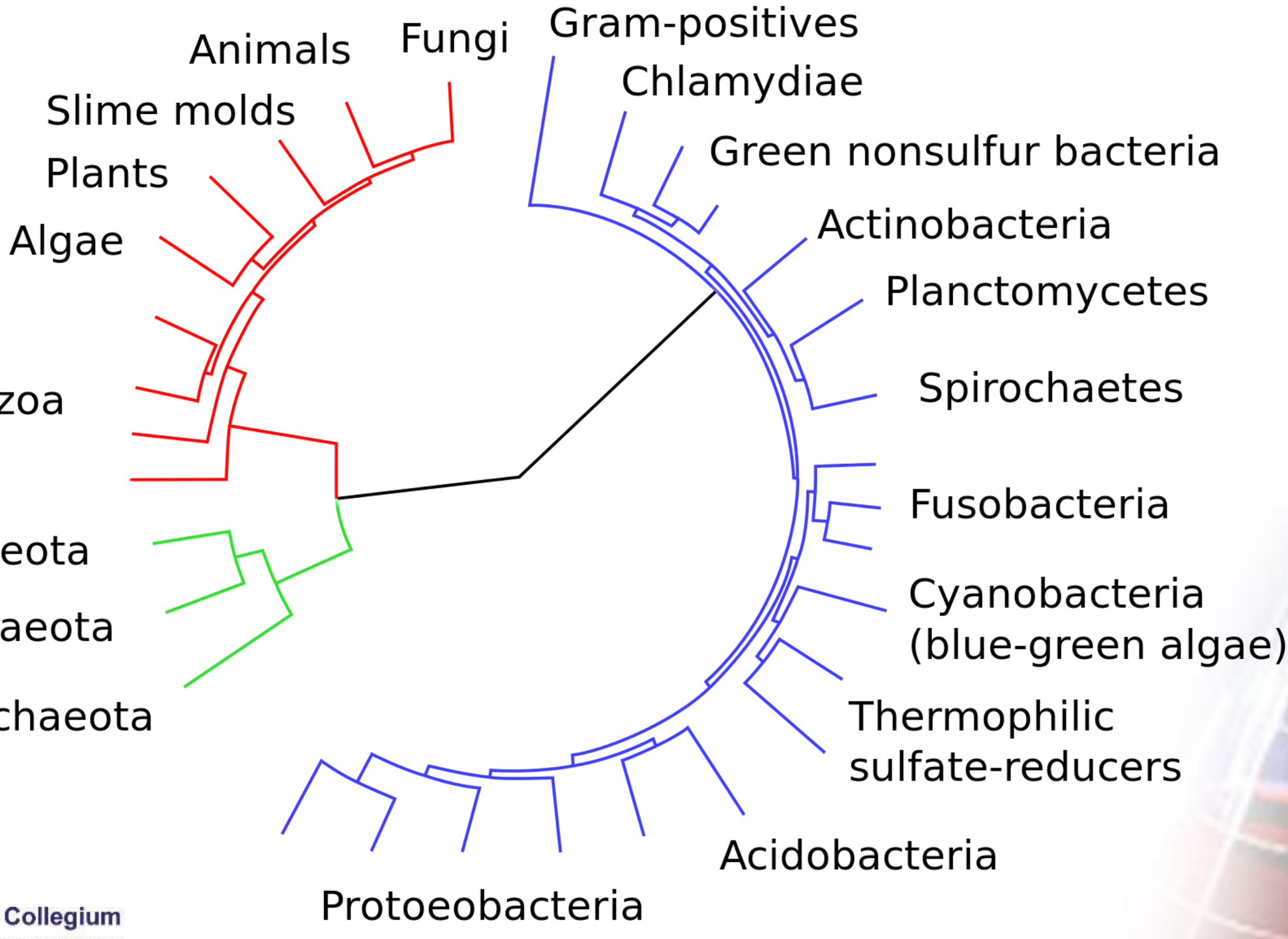
Health Studies Collegium Foundation

Rethink Health: Predictive Biomarkers

Health Studies Collegium

Epigenetics, Microbiome & Predictive Biomarkers



Microbiome & Metabolome: Homeostasis *or* Intolerance

Joel Doré:
http://www.youtube.com/watch?v=T6VZHw-g9tk

Waitzberg D *et a*l, In Gut We Trust,
http://www.ingutwetrust.com.br/videos

Vemocchi P *et a*l, Integration of datasets from different analytical techniques to assess the impact of nutrition on human metabolome. *Frontiers in Cell Infec Micro*, 2012; 2: Article 156.

Shenderov B A, Gut indigenous microbiota and epigenetics. *Micro Ecol Health Dis*. 2012; 23: 17195.

Weichert S, Schroten H, Adam R. The role of prebiotics and probiotics in prevention and treatment of childhood infectious diaseases. *Pediatr Infect Dis J.* 2012 Aug;31(8):859-862.

Hammer H F, Gut Microbiota and inflammatory bowel disease. *Dig Dis* 2011; 29(6): 550-553.

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Predictive Biomarker Tests Objectives

Science reflects social contract

Goal values > *than* usual statistical ranges

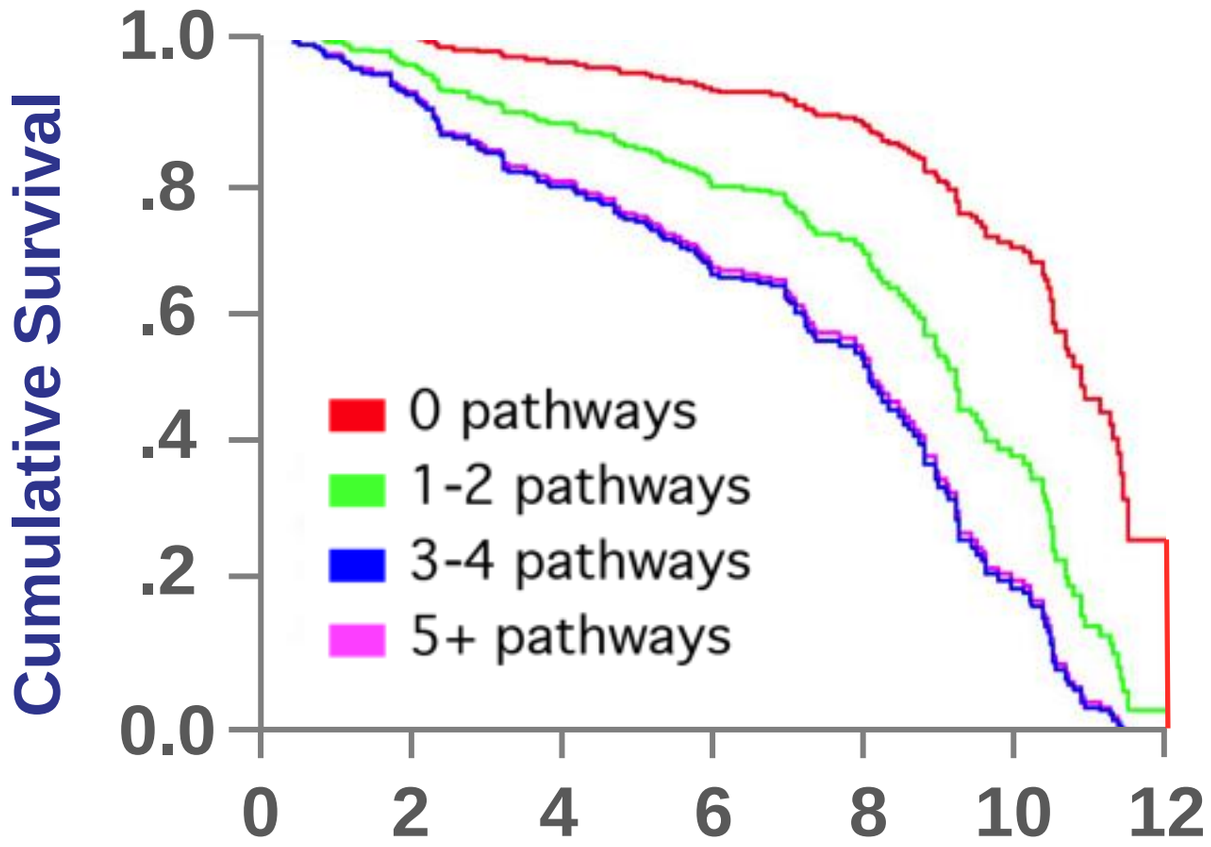
QoLY sacrificed /recoverable

Predictive Biomarker Breakthroughs

- Enhanced health, reduced risk, prosperity
- Overlapping control systems
- Causes 1º; symptoms consequences
- Proactive interventions
- Evidence based approaches to risk
- Personalized care
- Add years to life & life to years; QoLY

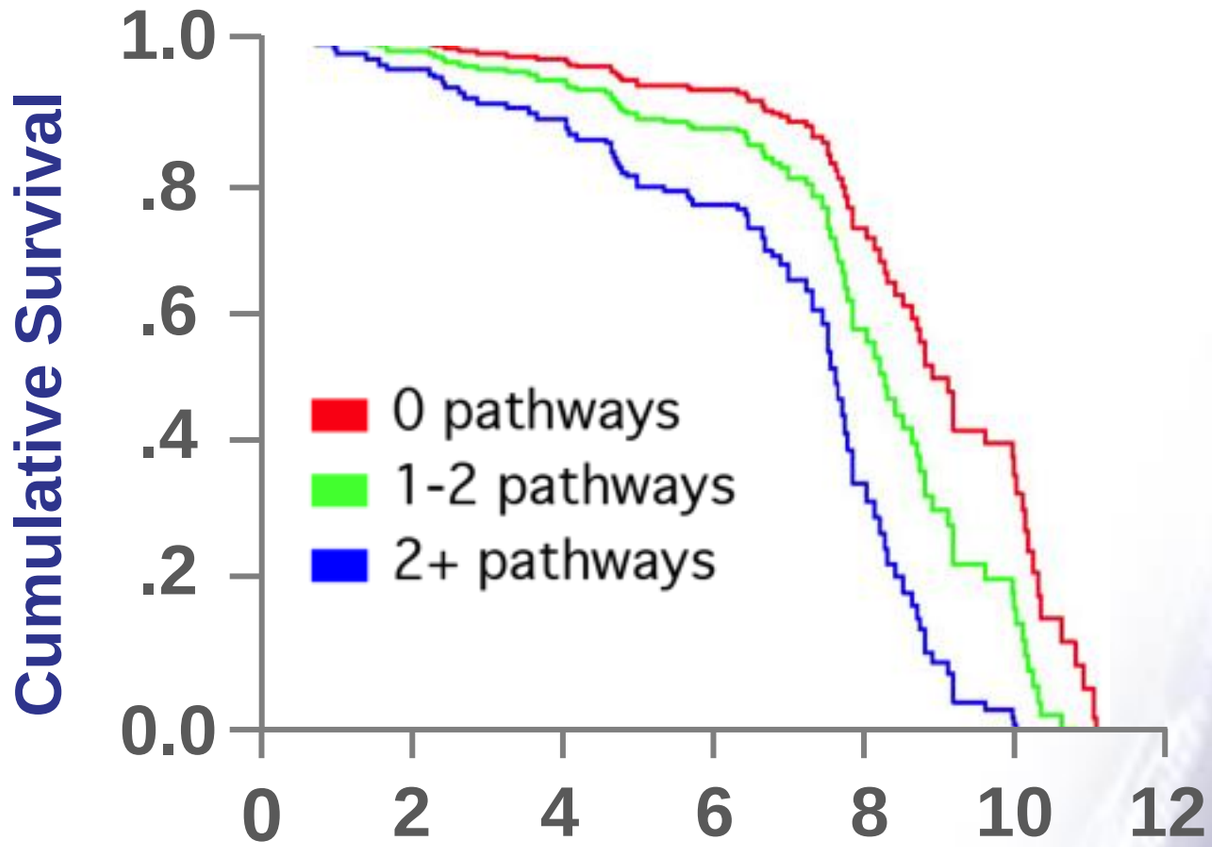
6 Biomarkers Predict Survival:
Hgb A1c, SBP, DBP, hsCRP, IL-6, DHEA

A Men



Time to Death
(Years Since Study Entry)

B Women



Time to Death
(Years Since Study Entry)

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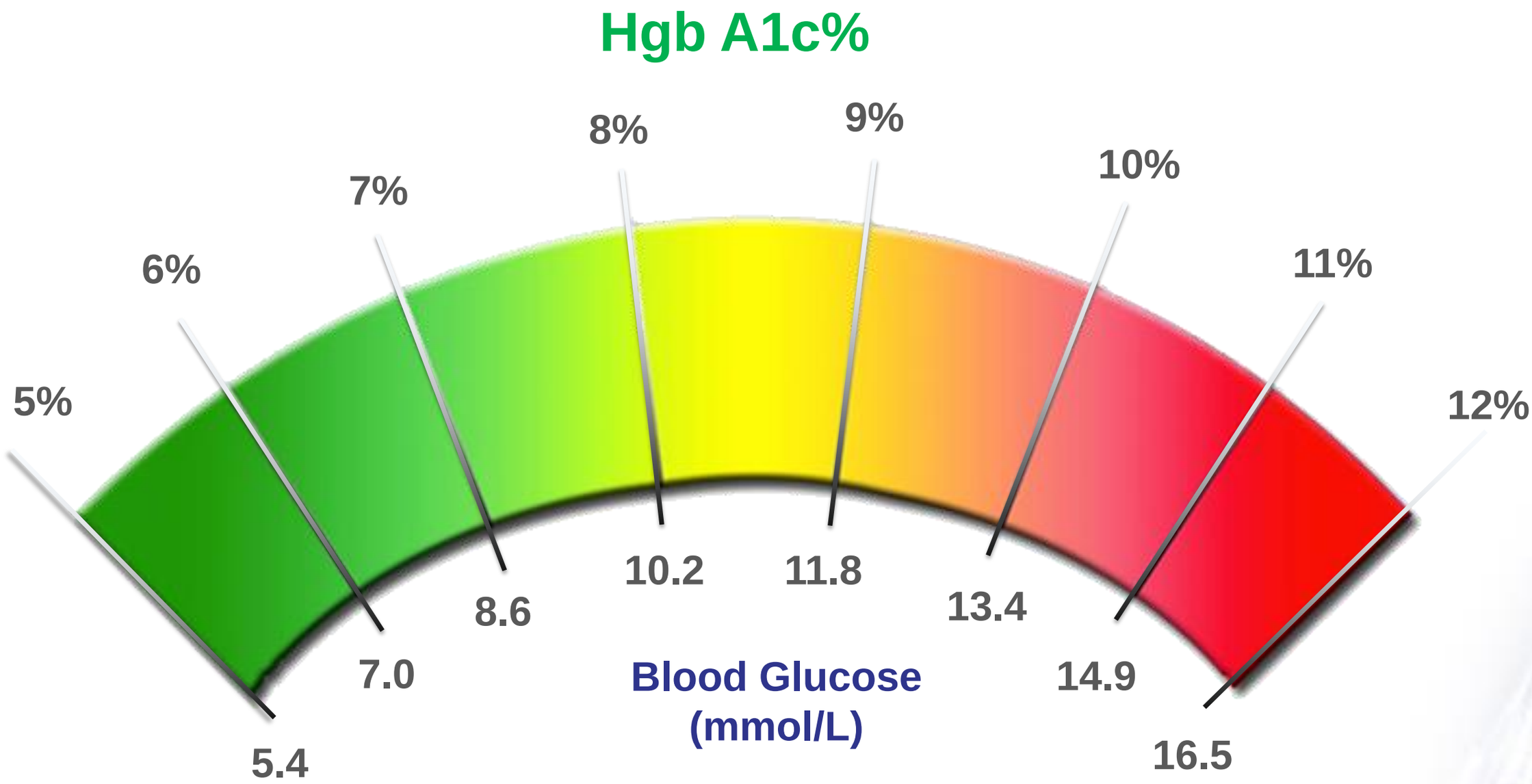
PNAS
Proceedings of the National Academy of Sciences of the United States of America www.pnas.org

Gruenewald T L *et al. PNAS* 2006;103:14158-14163

Hgb A1c Indicates Diabetes Control



Bunn HF, Haney DN, Gabbay KH, Gallop PM. Further Identification of the Nature and Linkage of the Carbohydrate in Hemoglobin A1c. *Biochem Biophys Res Commun.* 1975; 67(1): 103-109.

Hinzmann R, Schlaeger C, Tran C T. What Do We Need Beyond Hemoglobin A1c to Get the Complete Picture of Glycemia in People with Diabetes? *Int J Med Sci* 2012; 9(8):665-681. doi:10.7150/ijms.4520

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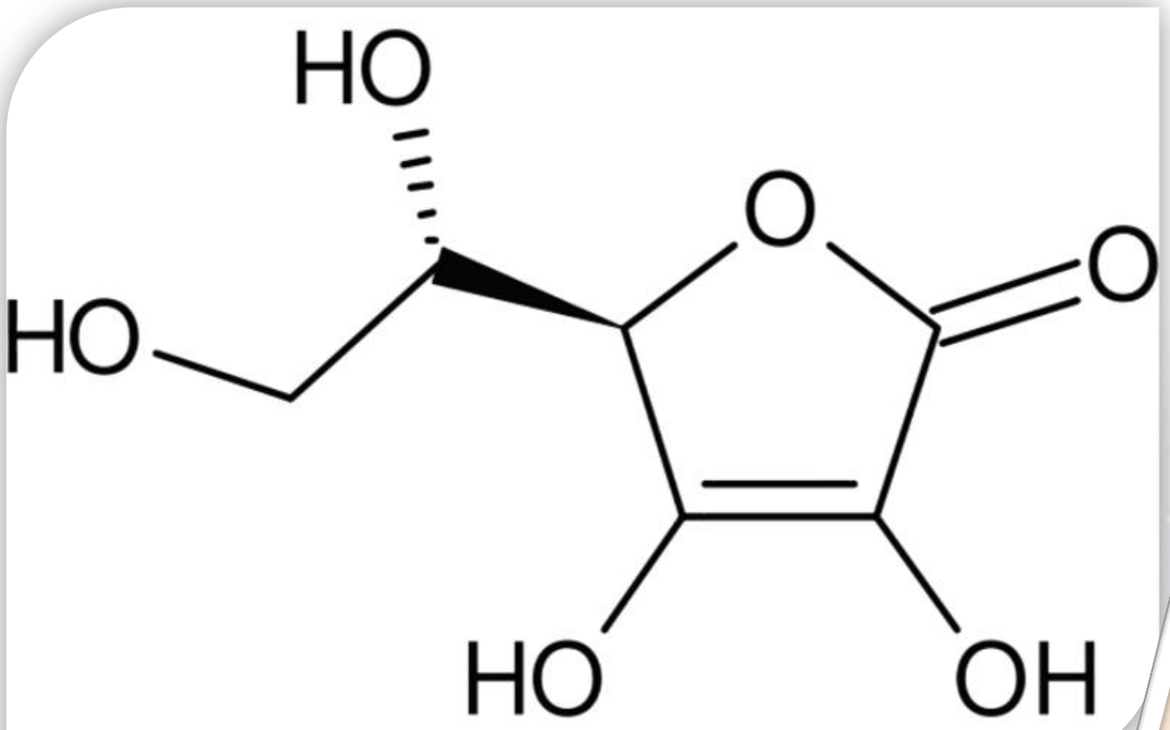
Ascorbate:
Toxic Mineral Excretion

Pump toxins out more safely…



1 gm ascorbate =
1,000,000 mcg;
~0.01% can bind ToxMin =
1,000 mcg ascorbate
binds ~0.1 µmol ToxMin =
~ 10 mcg ToxMin / gm Asc

Daily ToxMin exposure =
~ 2 gm ascorbate/day to
safely protect & excrete

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Understanding… Life as Paradox

Mechanistic, Allopathic View:

Newtonian Mechanics & Reductionism

Intrinsic to TCM, Eclectic, Homeopathy, Ayurveda, Kampo and Hikmet medical systems

Quantum Electrodynamic Non-equilibrium Systems View:

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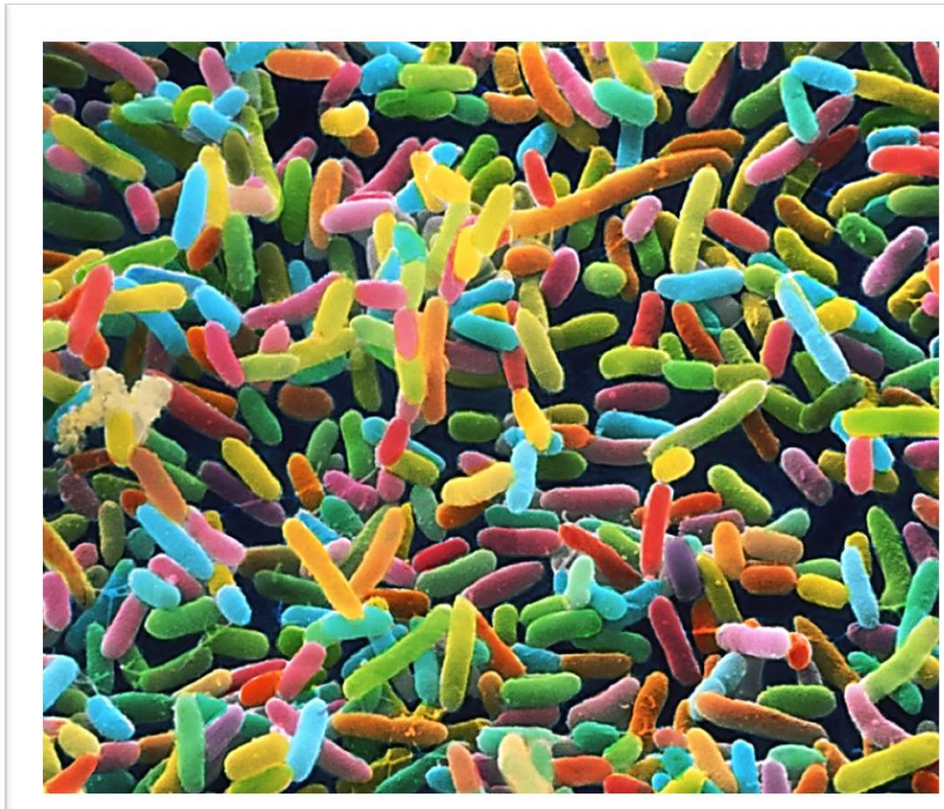
Prigogone I, Stengers I. Order Out of Chaos: Man's New Dialogue with Nature, *Bantam Books,* 1984.
Korzybski A. Science and Sanity: An introduction to Non-Aristotelian Systems and General Semantics, *Institute of General Semantics*, 5th Edition 1994.

Prebiotics, Probiotics, Symbiotics… So…

Probiotics ↓ kids allergy risk



Mammalian Gut Microbiota:

- Immune System
- Autoimmune / Tolerance
- Obesity
- Inflammatory Bowel Disease
- Neurodegenerative Syndromes

Elazab N *et al*., Probiotic Administration in Early Life, Atopy, and Asthma: A Meta-analysis of Clinical Trials, Pediatrics, August 2013. doi: 10.1542/peds.2013-0246

Atarashi K *et al.,* "Treg Induction by a Rationally Selected Mixture of Clostridia Strains from the Human Microbiota," Nature, doi:10.1038/nature12331, 2013.

Isolauri E, Salminen S; Nutrition, Allergy, Mucosal Immunology, and Intestinal Microbiota (NAMI) Research Group Report. Probiotics: Use in Allergic Disorders: A Nutrition, Allergy, Mucosal Immunology, and Intestinal Microbiota (NAMI) Research Group Report. *J Clin Gastroenterol*. 2008 Jul;42 *Suppl* 2:S91-96.

- Alternative version slides starting here

Qualified Predictive Biomarkers
Personalized, Evidence Based, Comparative

Hgb A1c:
Sugar, insulin,
cell energy set point…**AGEs**

hsCRP:
Inflammation, repair ability
reserves **Chronic, degenerative, autoimmune & CVD**

8 oxo-guanine:
Ox stress,
free radical risk; **ALEs**

Homocysteine:
Methylation, detox,
transport…**Sulfur Cycles**

Omega 3 Index:
Omega 3 to 6 ratio;
EFAs

LRA by ELISA/ACT:
hypersensitivity tests
Immune Tolerance

Vitamin D:
Cell talk & adhesion,
enough is enough

1st AM urine pH:
Acidosis risk,
buffering cell minerals

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Gruenewald TL, Seeman TE, Ryff CD, Karlamangla A, Singer BH. Combinations of Biomarkers Predictive of Later Life Mortality. *PNAS*, 2006; 103 (38): 14158-14163.

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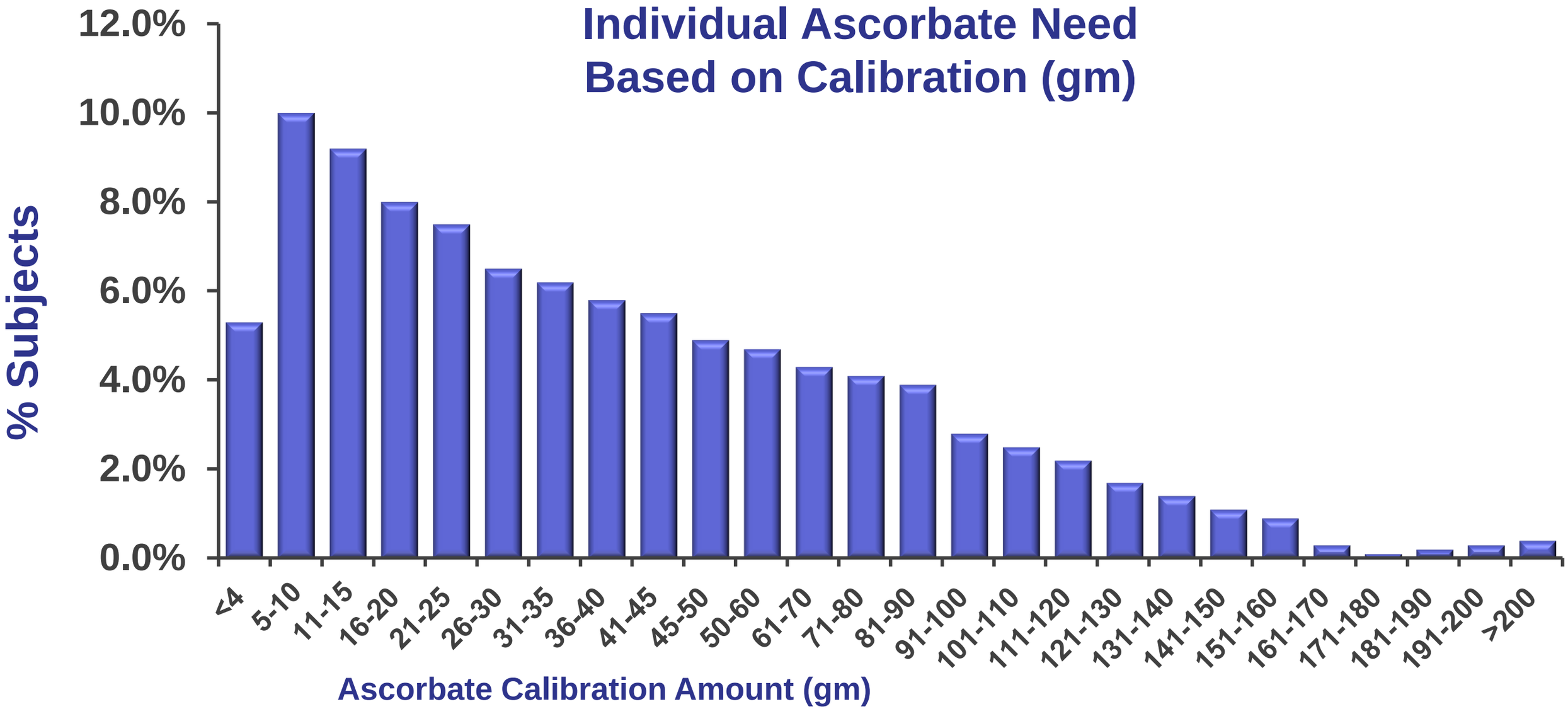
Ascorbate needs from 4-100+ g/day



Jaffe R. Cardioprotective Nutrients. *In*: Watson RR, Preedy VR, Editors Bioactive Food as Dietary Interventions in Cardiovascular Disease. *Academic Press*, 2013. p 103-119.

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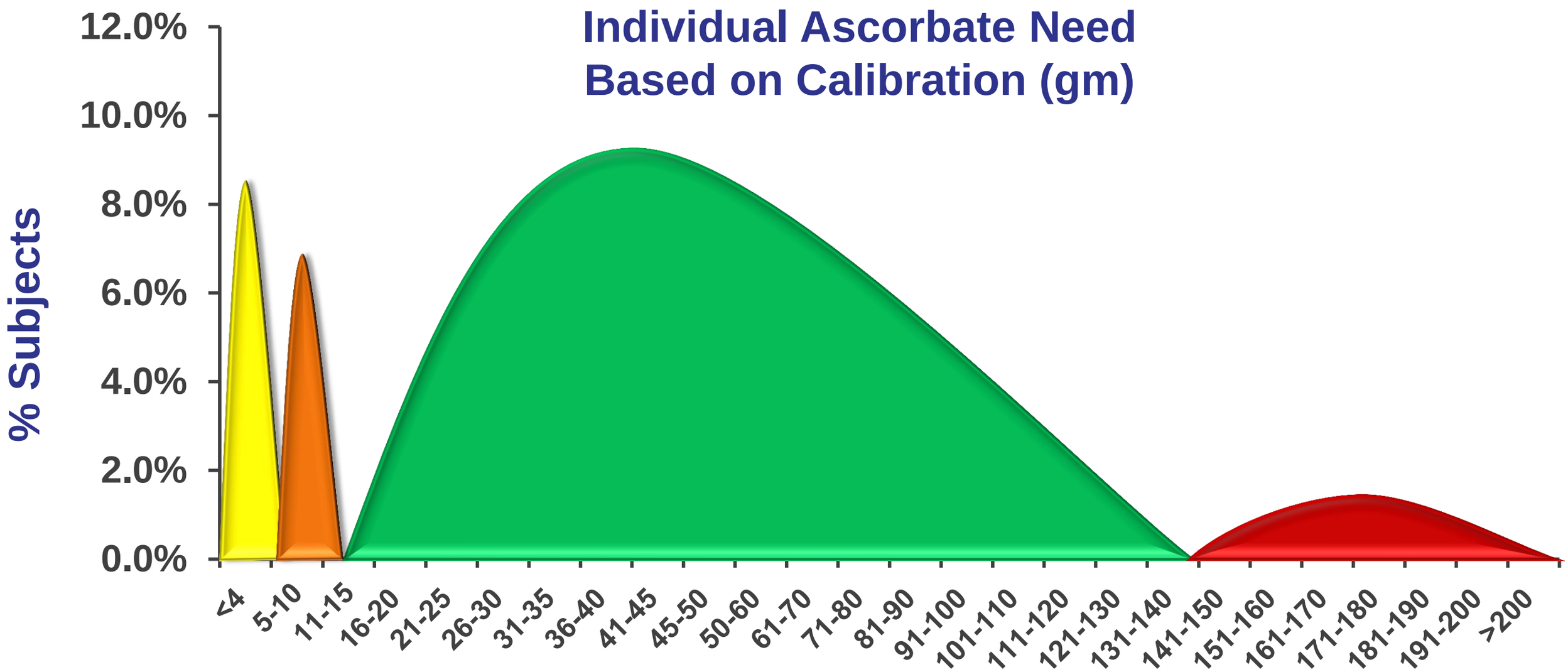
Ascorbate needs from 4-100+ g/day

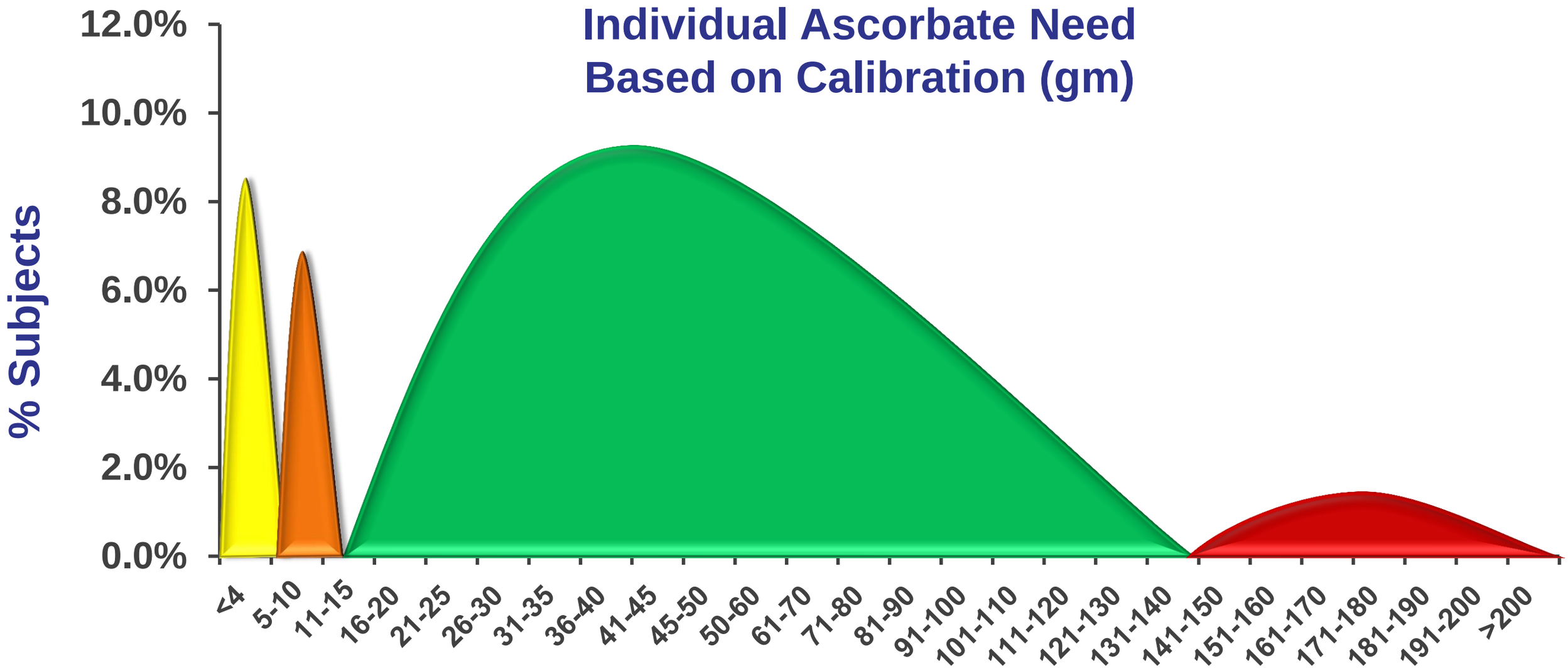


~5% (healthy); ~10% (usual); ~80% (walking worried/wounded); ~5% (multiple chronic diseases)

Based on Jaffe Protocol 1987-2008

Jaffe R. Cardioprotective Nutrients. *In*: Watson RR, Preedy VR, Editors Bioactive Food as Dietary Interventions in Cardiovascular Disease. *Academic Press*, 2013. p 103-119.

Ascorbate needs from 4-100+ g/day



~5% (healthy); ~10% (usual); ~80% (walking worried/wounded); ~5% (multiple chronic diseases)

Based on Jaffe Protocol 1987-2008

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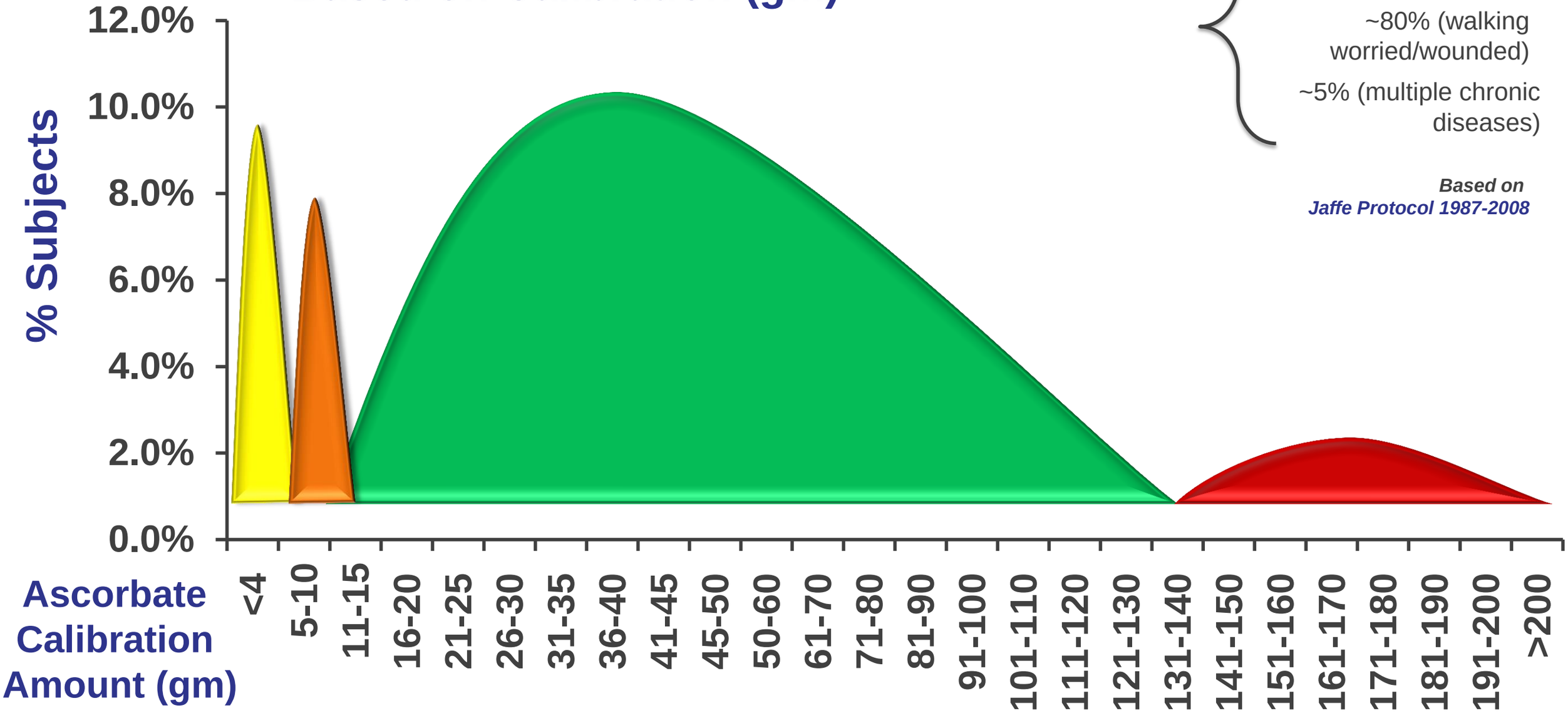
Ascorbate needs from 4-100+ g/day

Individual Ascorbate Need Based on Calibration (gm)



~5% (healthy)

~10% (usual)

~80% (walking worried/wounded)

~5% (multiple chronic diseases)

Based on Jaffe Protocol 1987-2008

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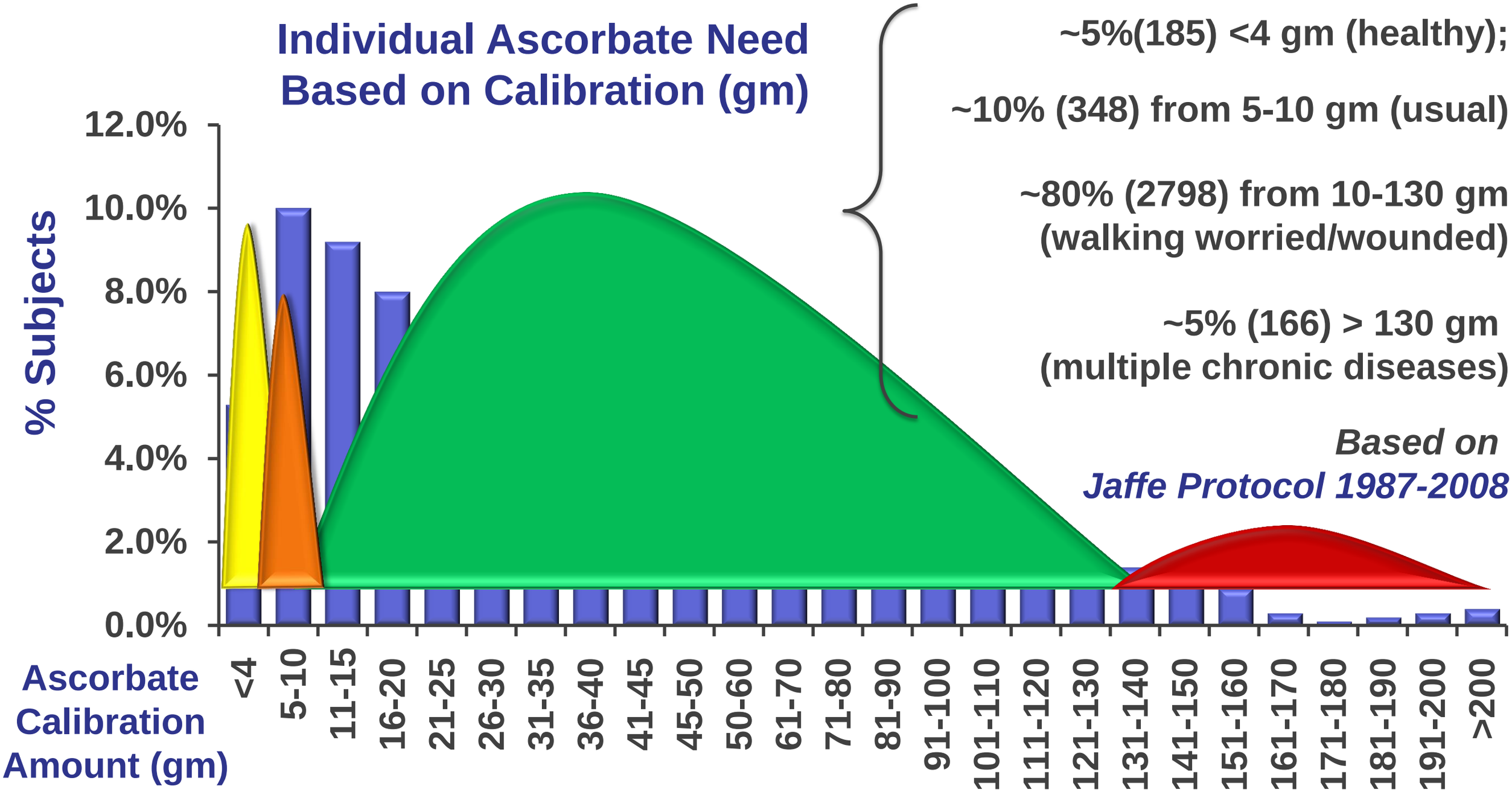
Jaffe R. Cardioprotective Nutrients. *In*: Watson RR, Preedy VR, Editors Bioactive Food as Dietary Interventions in Cardiovascular Disease. *Academic Press*, 2013. p 103-119.

Ascorbate needs from 4-100+ g/day



~5%(185) <4 gm (healthy);

~10% (348) from 5-10 gm (usual)

~80% (2798) from 10-130 gm (walking worried/wounded)

~5% (166) > 130 gm (multiple chronic diseases)

Based on Jaffe Protocol 1987-2008

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