

Men's Health: The Focus on Healthspan and Lifespan

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Agenda

- Traditional category of Men's Health
- The new paradigm of Men's Health – Lifespan and Healthspan
- Men's Health - Lifespan
 - Cardiovascular disease
 - Neurocognitive disorders
 - Urological health
- Men's Health - Healthspan
 - Hormonal health
 - Metabolic disease
 - Mental/Emotional health



“Traditional” Men’s Health

Men’s Health issues/conditions

- Prostate cancer
- BPH/Enlarged prostate
- Sexual dysfunction
- Fertility
- Other urologic issues

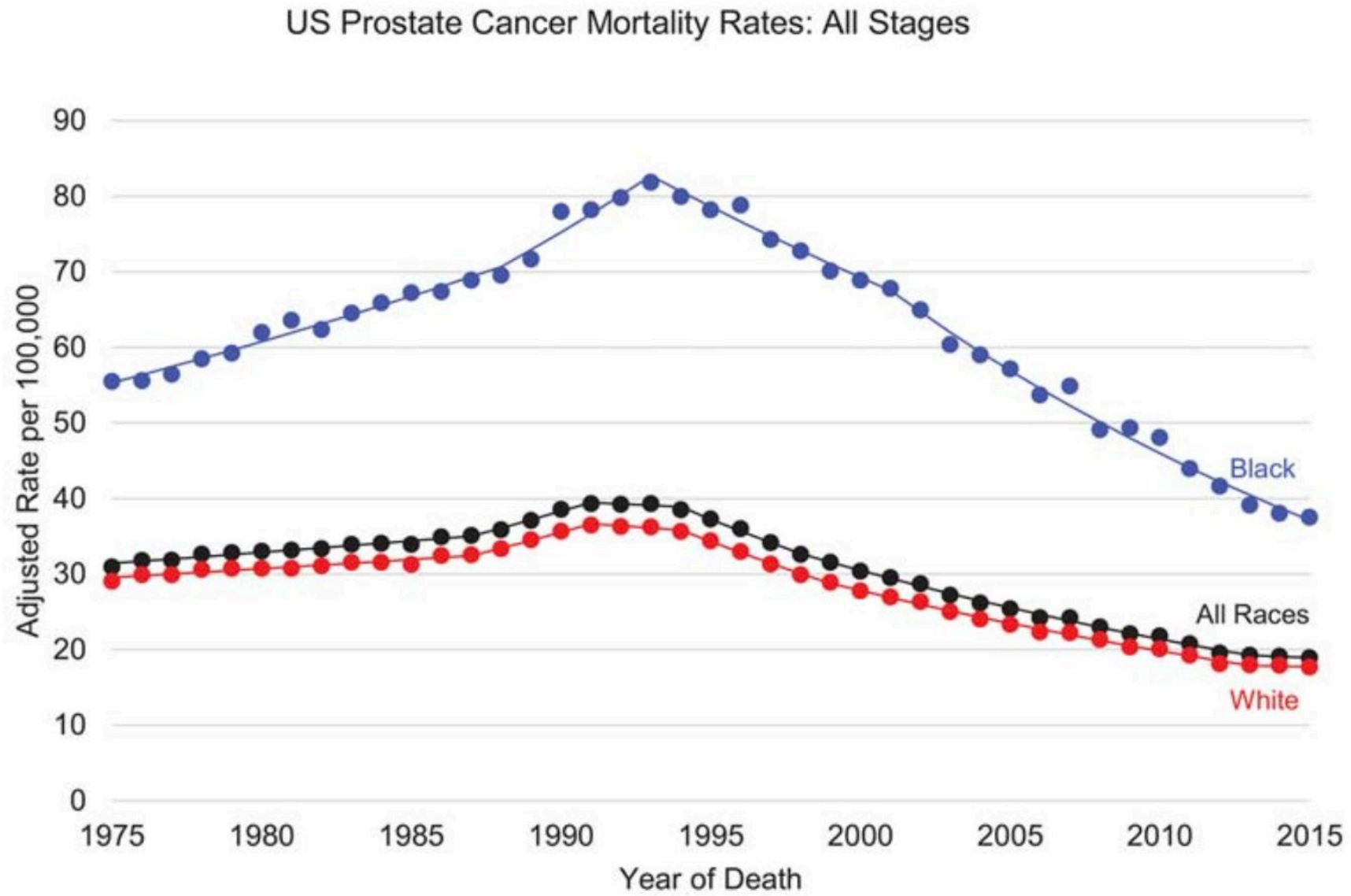


“Traditional” Men’s Health

Prostate cancer

- PSA_v, PSA_d
- mpMRI
- 4Kscore
- Bx + Genetic testing
- Physical exam (DRE)

Figure. Trends in prostate cancer death rates by race in the United States in 1975-2015 (NCHS).





“Traditional” Men’s Health

BPH/Enlarged prostate prevention

- Ultrasound/MRI
- Urodynamic studies
- Physical exam + intake



“Traditional” Men’s Health

Sexual dysfunction

- SHIM questionnaire
- Hormone + biomarker testing
- Physical exam + intake
- Imaging



Anti-Lifespan Diseases

Cardiovascular disease + stroke

Cancer

- Prostate cancer - #2 cancer death

Alzheimer's/Neurocognitive disease

Diabetes

Figure. Percent distribution of the 10 leading causes of death in males: United States, 2019

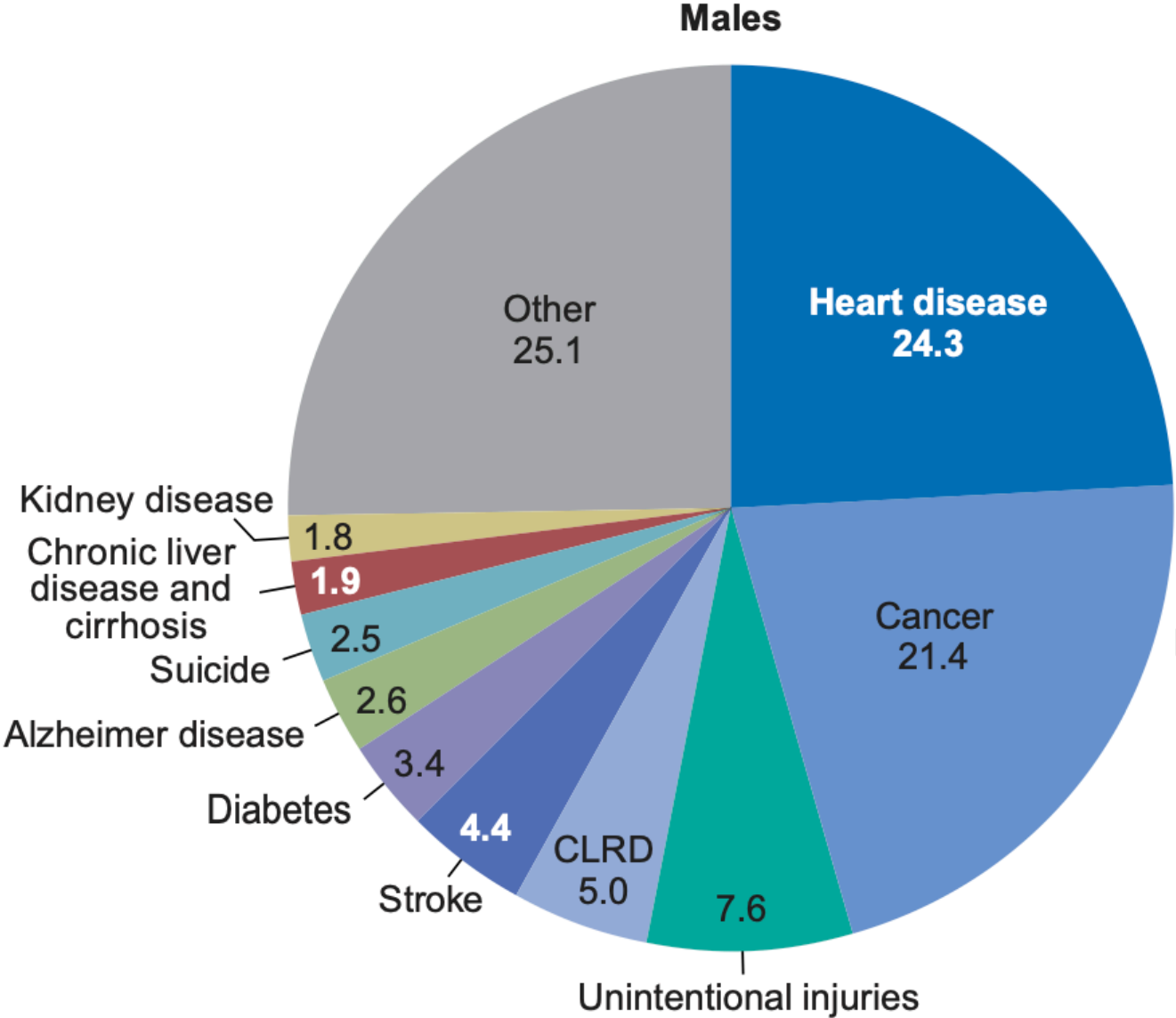
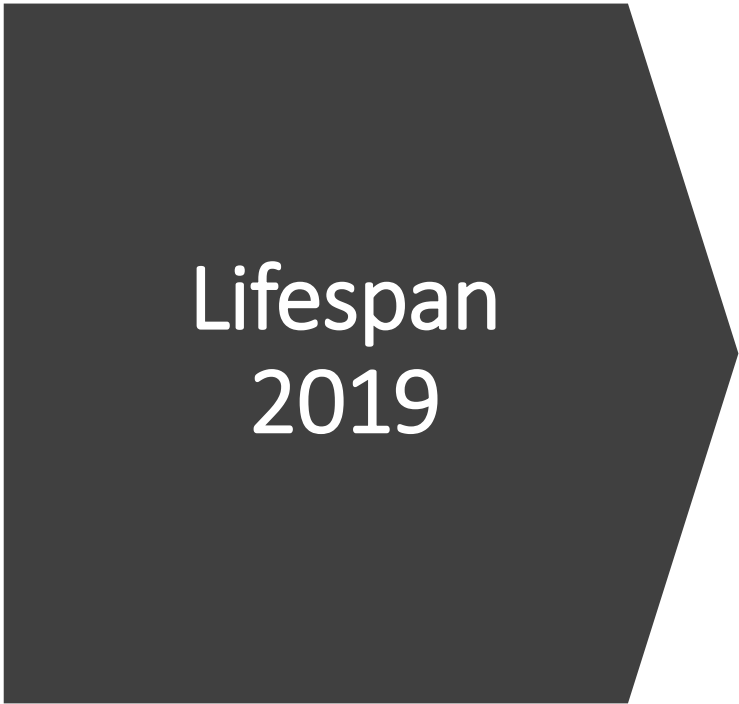
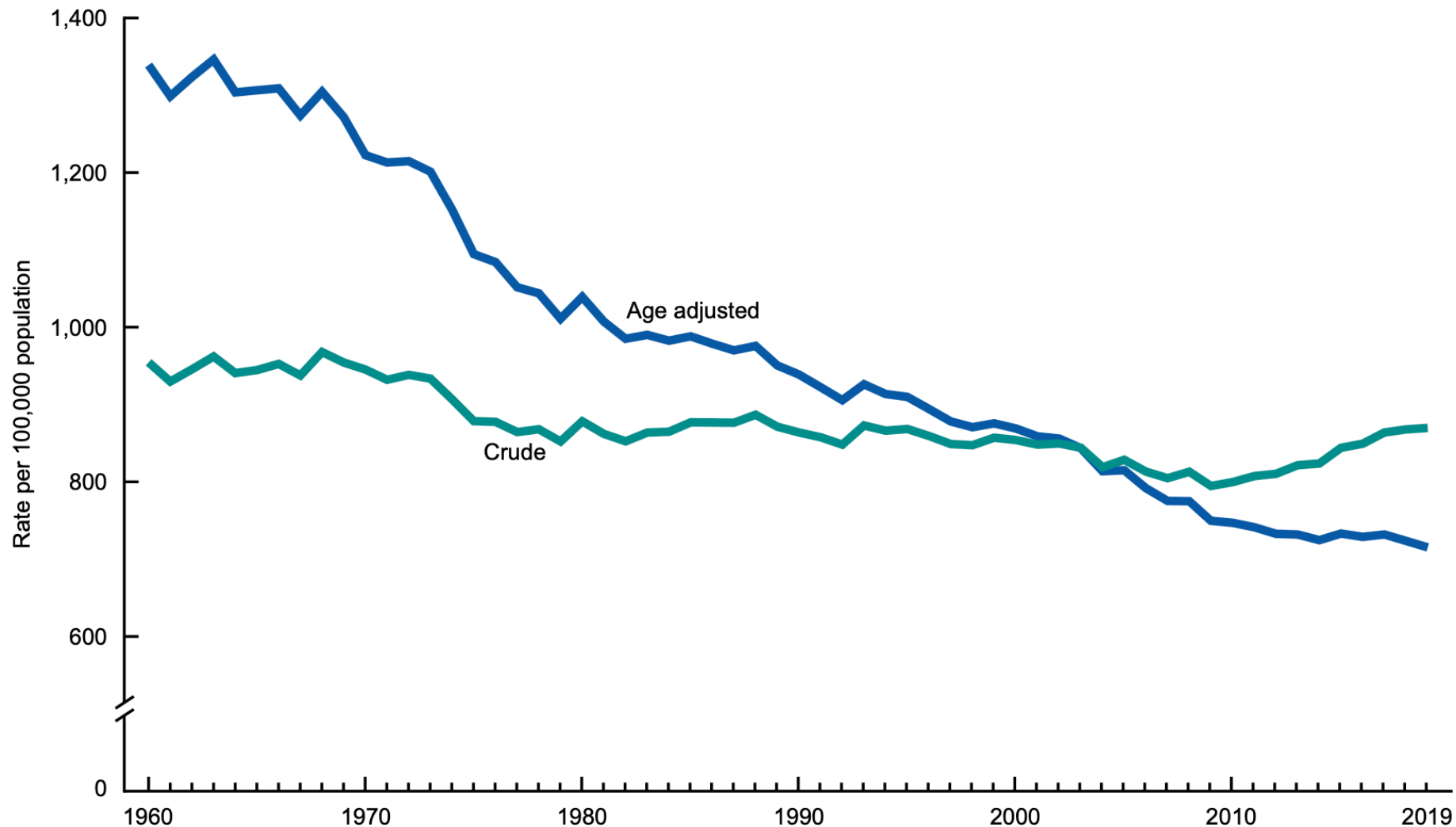


Figure. Crude and age-adjusted death rates: United States, 1960–2019



NOTE: Crude death rates are on an annual basis per 100,000 population; age-adjusted rates are per 100,000 U.S. standard population; see Technical Notes in this report.
SOURCE: National Center for Health Statistics, National Vital Statistics System, Mortality.

Custom Chart for Men, All Races, Ages 30-75 Years

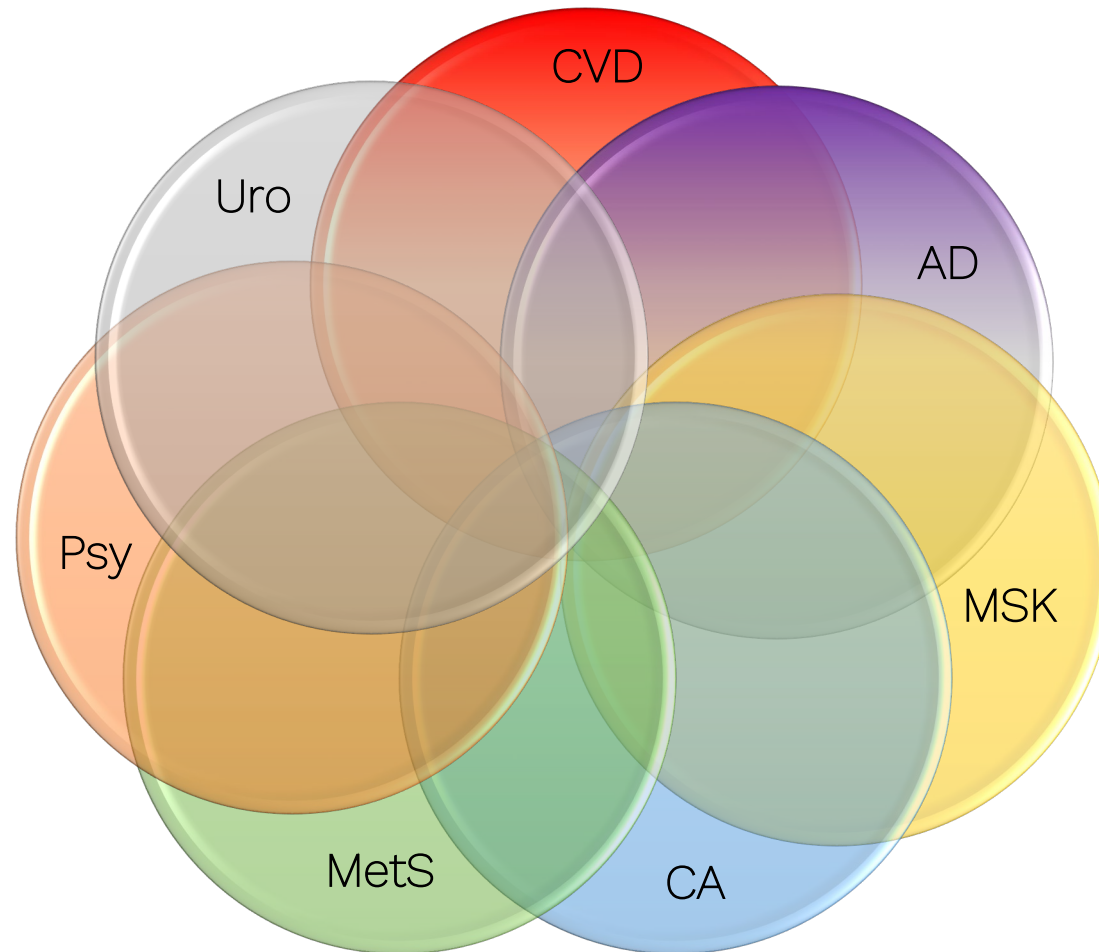
The numbers in each age column tell you the percent of men who will die eventually from...

Cause of Death	Age									
	30	35	40	45	50	55	60	65	70	75
All Causes*	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%
Vascular Disease	33.55%	33.79%	34.01%	34.20%	34.38%	34.58%	34.83%	35.15%	35.61%	36.32%
Coronary Heart Disease	20.82%	20.98%	21.14%	21.28%	21.41%	21.53%	21.67%	21.82%	22.01%	22.34%
Cancer	21.08%	21.24%	21.39%	21.54%	21.65%	21.68%	21.47%	20.92%	19.96%	18.53%
Lung and Bronchus	5.11%	5.16%	5.21%	5.26%	5.32%	5.34%	5.27%	5.09%	4.74%	4.17%
Prostate	2.52%	2.54%	2.57%	2.61%	2.65%	2.72%	2.80%	2.89%	2.96%	3.01%
Colon and Rectum	1.84%	1.85%	1.86%	1.86%	1.84%	1.81%	1.77%	1.70%	1.62%	1.52%
Lung Disease	8.66%	8.73%	8.81%	8.90%	9.02%	9.18%	9.35%	9.51%	9.59%	9.49%
Infection	4.67%	4.69%	4.71%	4.71%	4.72%	4.71%	4.70%	4.70%	4.72%	4.78%
Accidents and Injury	7.12%	6.53%	5.97%	5.45%	4.97%	4.49%	4.07%	3.76%	3.58%	3.49%
Blood Diseases	0.34%	0.34%	0.34%	0.34%	0.34%	0.33%	0.33%	0.33%	0.33%	0.33%
Urinary Tract Disease	2.76%	2.79%	2.81%	2.83%	2.86%	2.90%	2.95%	3.02%	3.09%	3.17%
Gastrointestinal Disease	3.39%	3.39%	3.38%	3.34%	3.26%	3.13%	2.95%	2.75%	2.56%	2.41%
Diabetes^a	3.03%	3.05%	3.06%	3.06%	3.05%	3.02%	2.97%	2.89%	2.76%	2.59%
Neurological Disease	7.34%	7.39%	7.45%	7.52%	7.63%	7.80%	8.05%	8.42%	8.90%	9.46%
Alzheimers Disease	3.68%	3.71%	3.75%	3.81%	3.88%	4.00%	4.19%	4.45%	4.82%	5.31%
Malnutrition and Vitamin Deficiencies	0.27%	0.28%	0.28%	0.28%	0.29%	0.29%	0.30%	0.31%	0.33%	0.35%

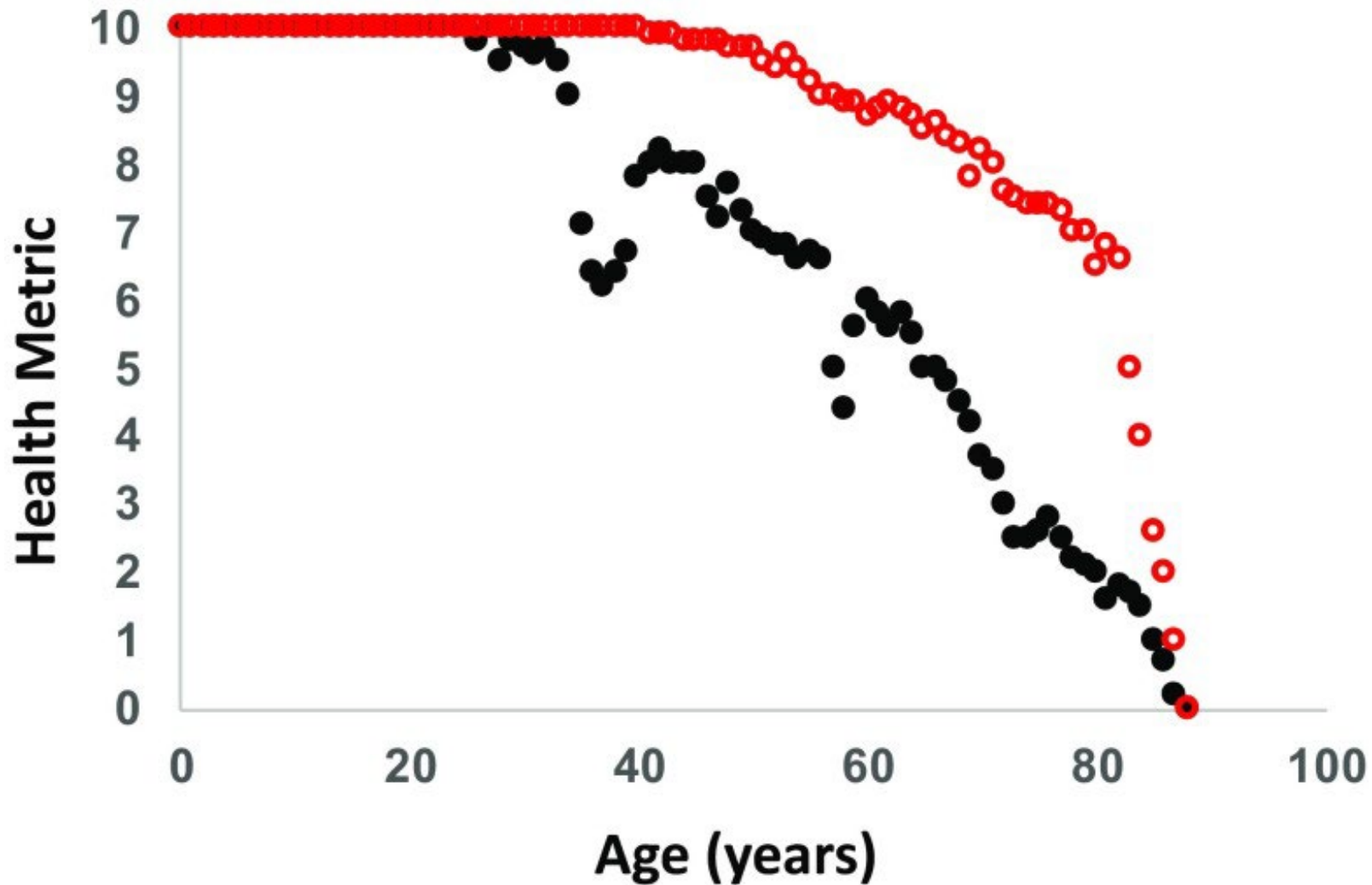
Source: US Mortality Files, National Center for Health Statistics, Centers for Disease Control and Prevention.

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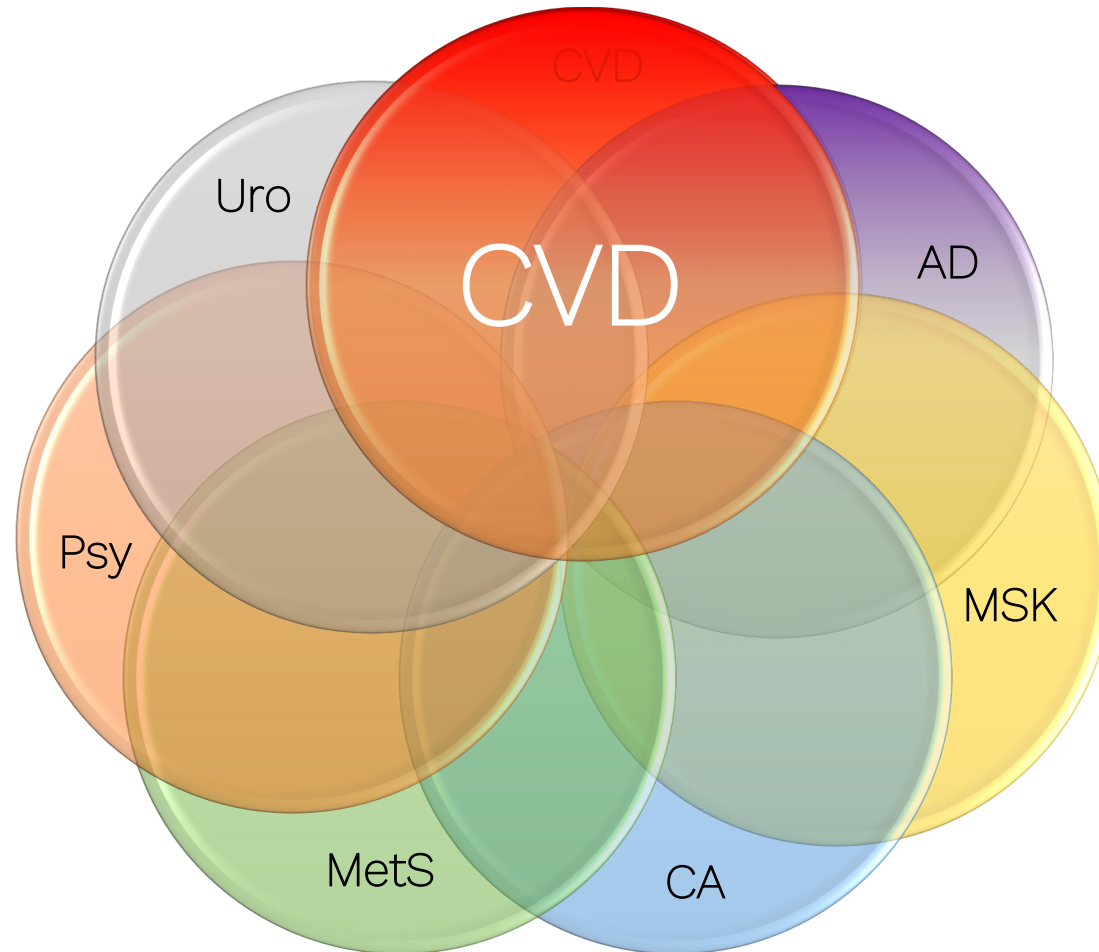
New Paradigm of Men's Health




New Paradigm of Men's Health




New Paradigm of Men's Health





New Paradigm of Men's Health CVD

- Advanced lipid testing
- Apolipoprotein B
- Lipoprotein(a)
- Synthesis and reabsorption Sterols
 - Desmosterol
 - Lathosterol
 - Sitosterol
 - Campesterol
- LDL-P via NMR + Particle size
 - Function of TG, LPL and clearance
- HDL-P + particle size
 - Reverse cholesterol transport
- Oxidized-LDL
- ApoA-I
- Oxidized-PL ApoB



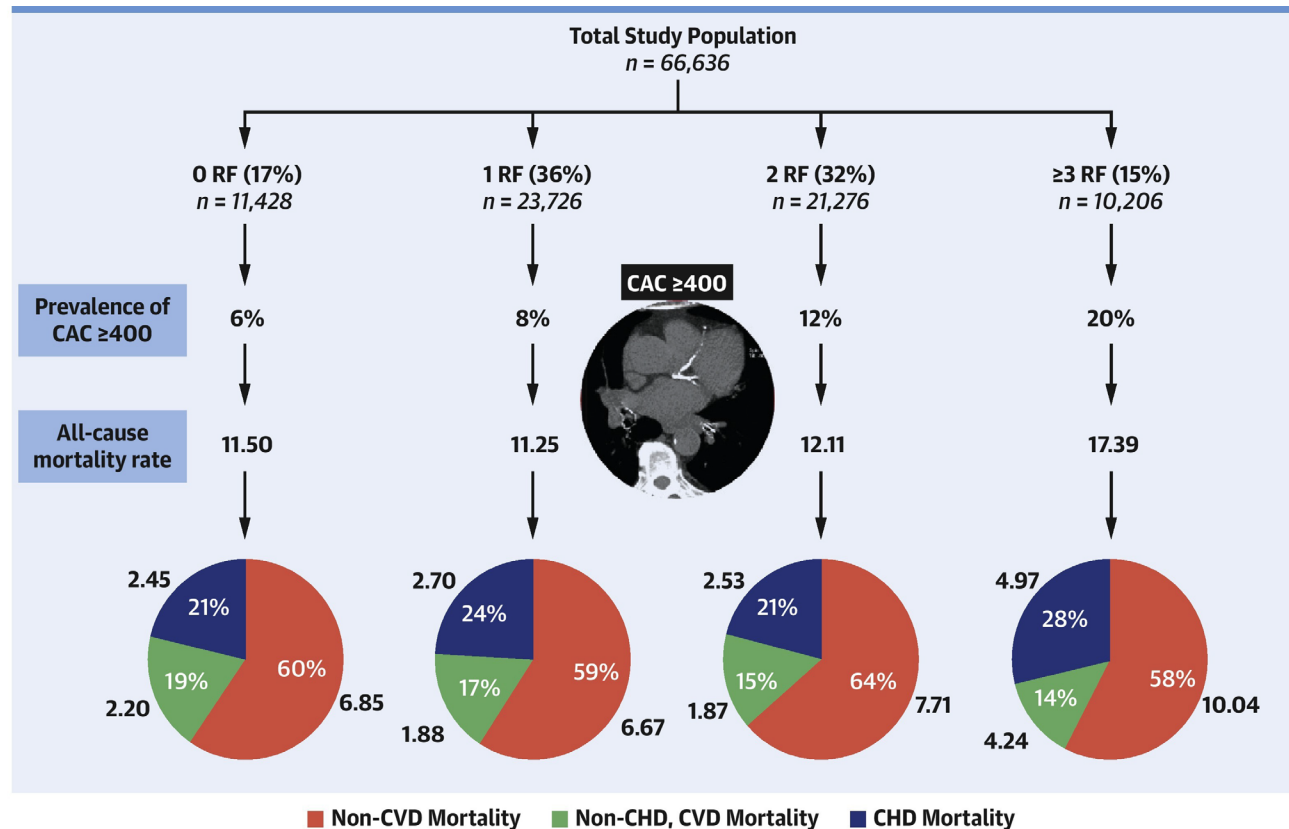
New Paradigm of Men's Health CVD

Cardiovascular disease and stroke

- ApoB containing particles are *necessary* but not *sufficient* in the pathogenesis of atherosclerosis

CT Coronary Calcium Score

- Utilization in risk assessment with and without lipoproteins

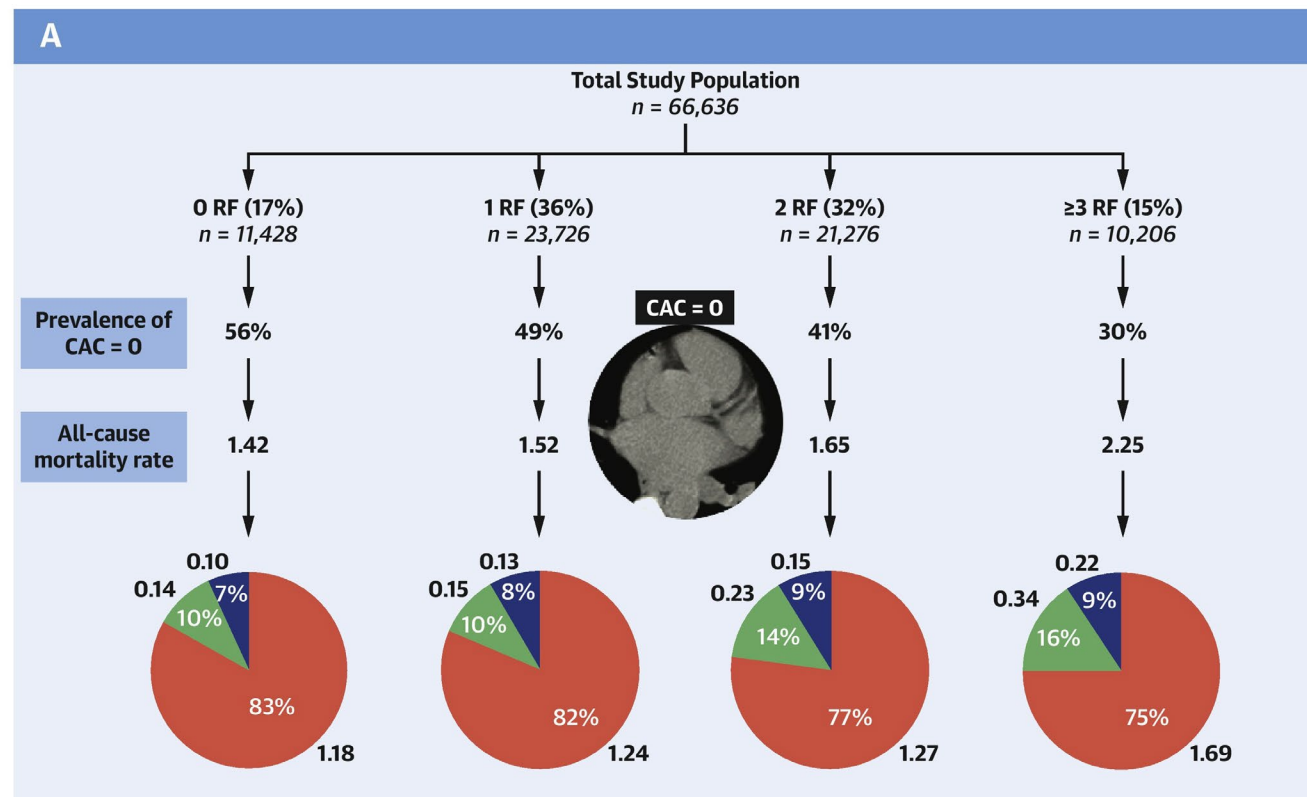


Grandhi, G.R. et al. J Am Coll Cardiol Img. 2020;13(5):1175-86.

CT Coronary Calcium Score

- Utilization in risk assessment with and without lipoproteins

CENTRAL ILLUSTRATION: Mortality Rate (per 1,000 Person-Years) of Participants With CAC



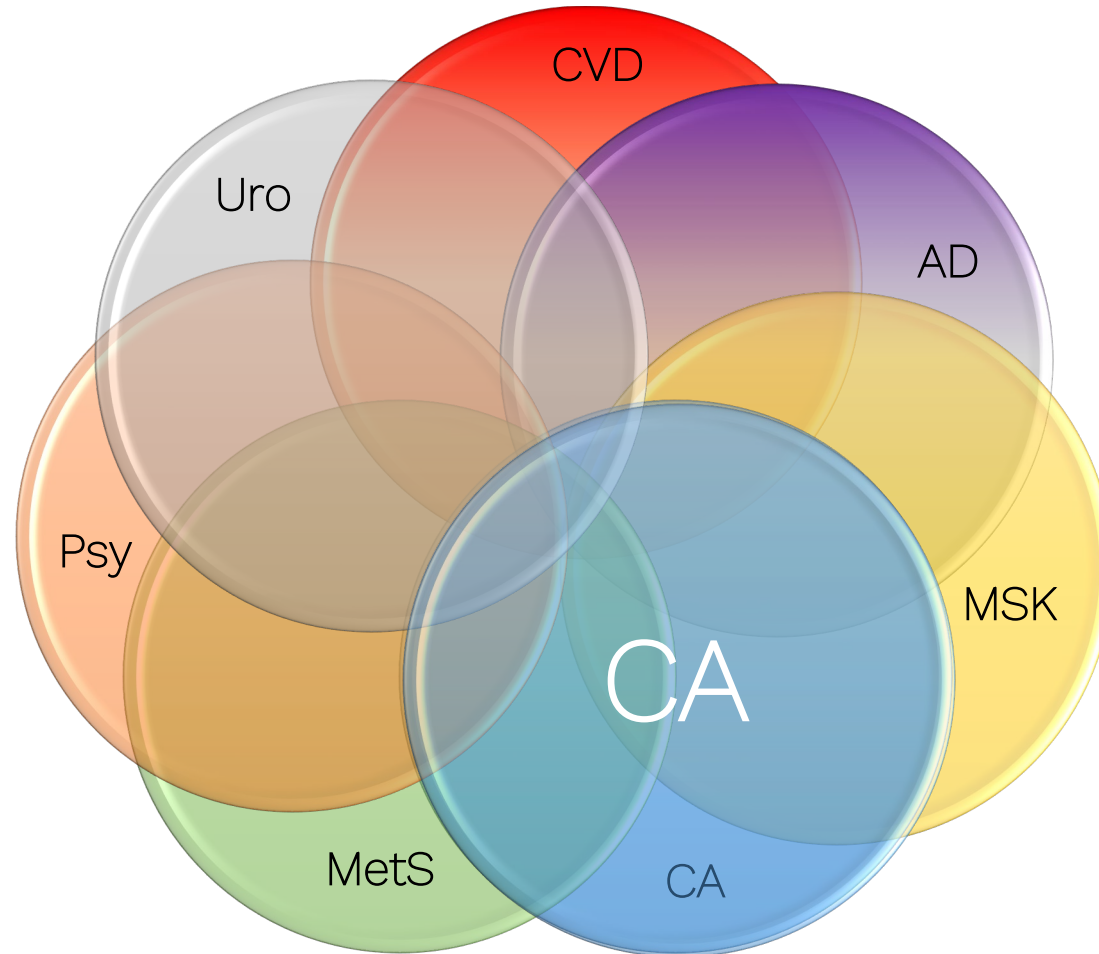
Nutraceuticals

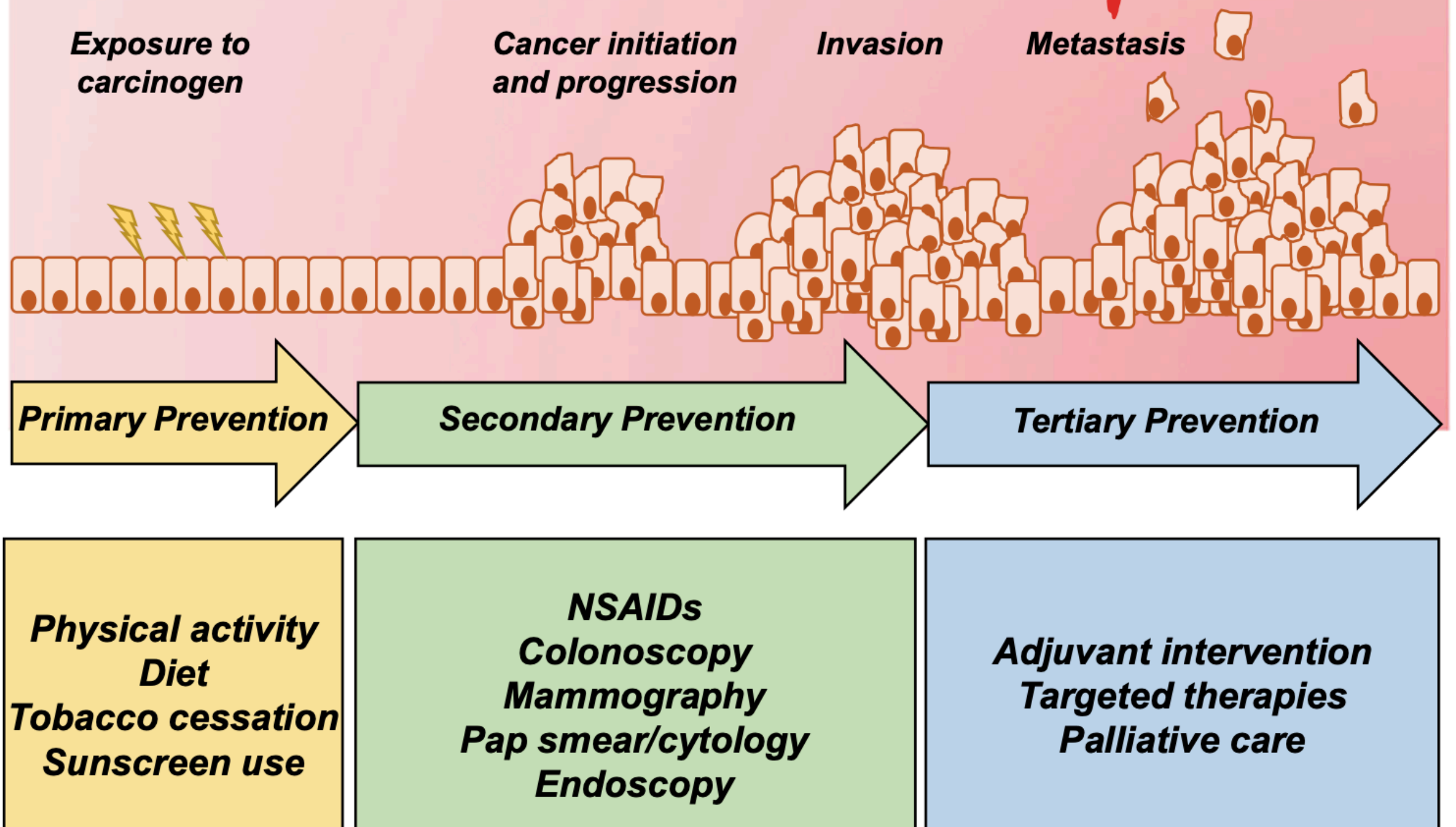
- Red yeast rice
 - Lovastatin
- Berberine
 - LDL-R and PCSK9i
- Bergamot
 - Synergistic with statins
- Omega-3 Fatty Acids (EPA/DHA)
 - REDUCE IT trial
 - Resolvins and Protectins
- Niacin
 - Lp(a) reduction
 - LDL-R and PCSK9i
- Soluble and Insoluble fiber
 - Absorption and reabsorption

Nutrition

- Dietary interventions
 - Driven by basic and advanced lipid testing
 - Saturated fat intake
 - Mechanism of action – LDL-receptors
 - Monounsaturated fat intake
 - Omega-3 fatty acids
- Time restriction and Fasting
- Caloric restriction
- Insulin resistance
 - Targeting triglycerides

New Paradigm of Men's Health





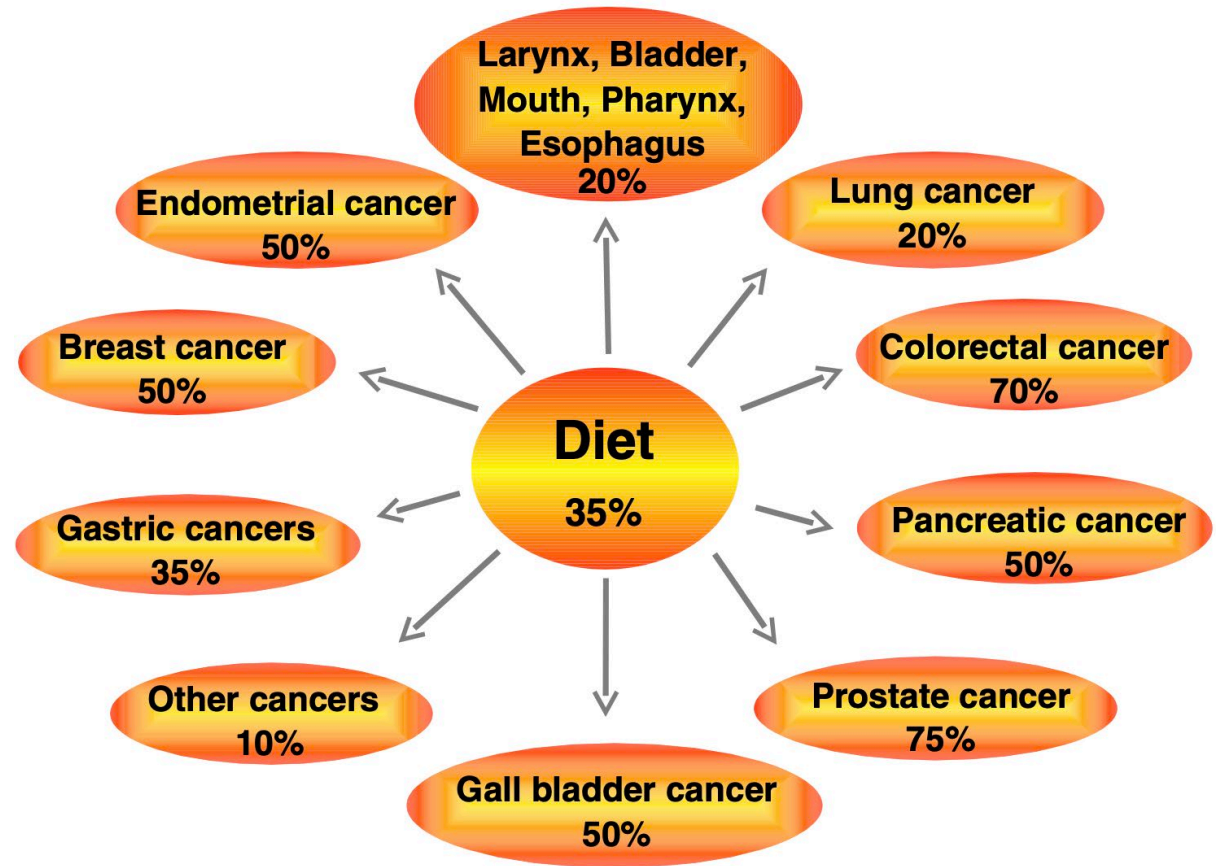
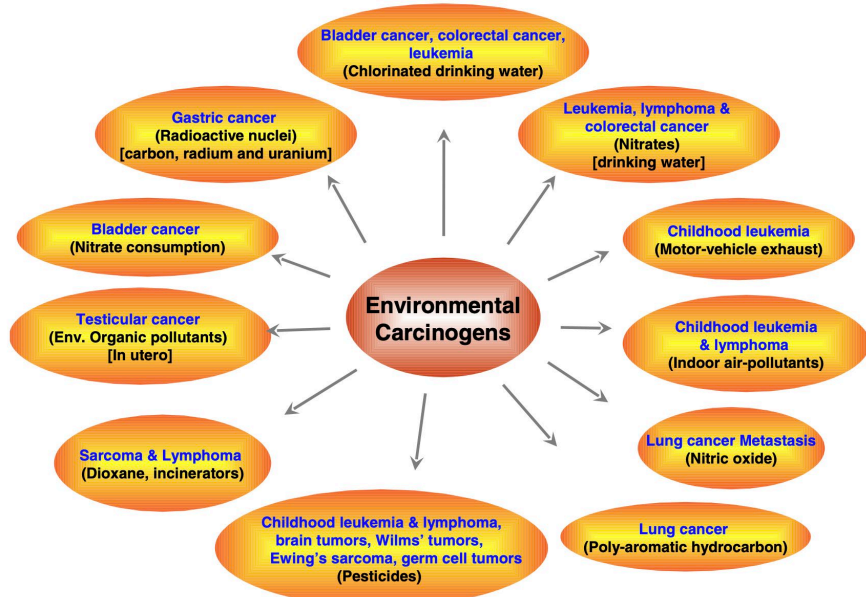
Screening – The Unsung Hero

- 90% of the nation's \$4.1 trillion in annual health care expenditures are for people with chronic and mental health conditions
 - Heart disease and stroke: ~ \$216 billion per year
 - Cancer: ~ \$240 billion by 2030
 - Diabetes ~ \$327 billion in 2017
 - Obesity ~ \$173 billion per year
 - Alzheimer's ~ \$305 billion in 2020
 - Arthritis ~ 303.5 billion in 2013

Screening – The Unsung Hero

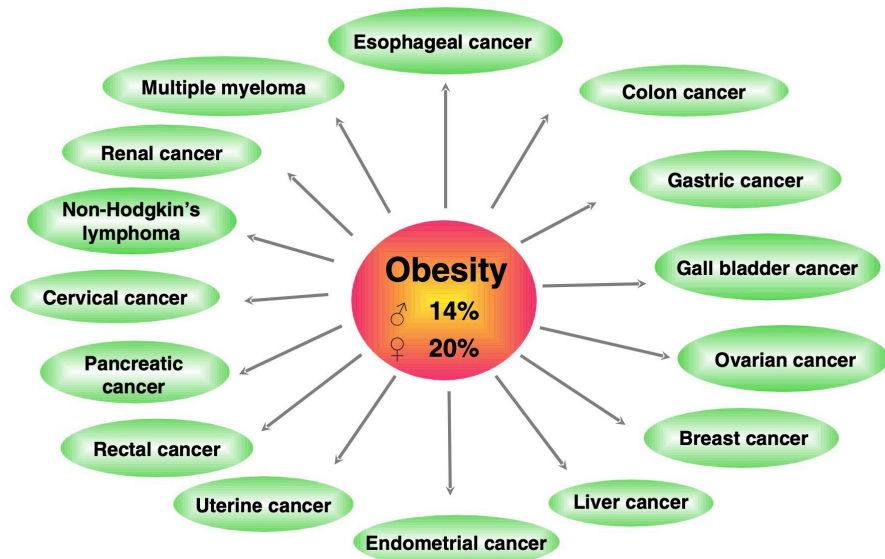
- Primary prevention
 - Direct avoidance or reduction in exposure to known carcinogenic factors
- Secondary prevention
 - Early detection, treatment, or removal of precancerous lesions
- Tertiary prevention
 - Initiated after a diagnosis of cancer to improve quality of life and survivorship

2010-The five most costly and preventable chronic conditions cost the U.S. nearly \$347 billion—30% of total health spending



Cancer deaths (%) linked to diet as reported by Willett
 W. C. Willett. Diet and cancer. *Oncologist*. 5:393-404 (2000) doi:10.1634/theoncologist.5-5-393.

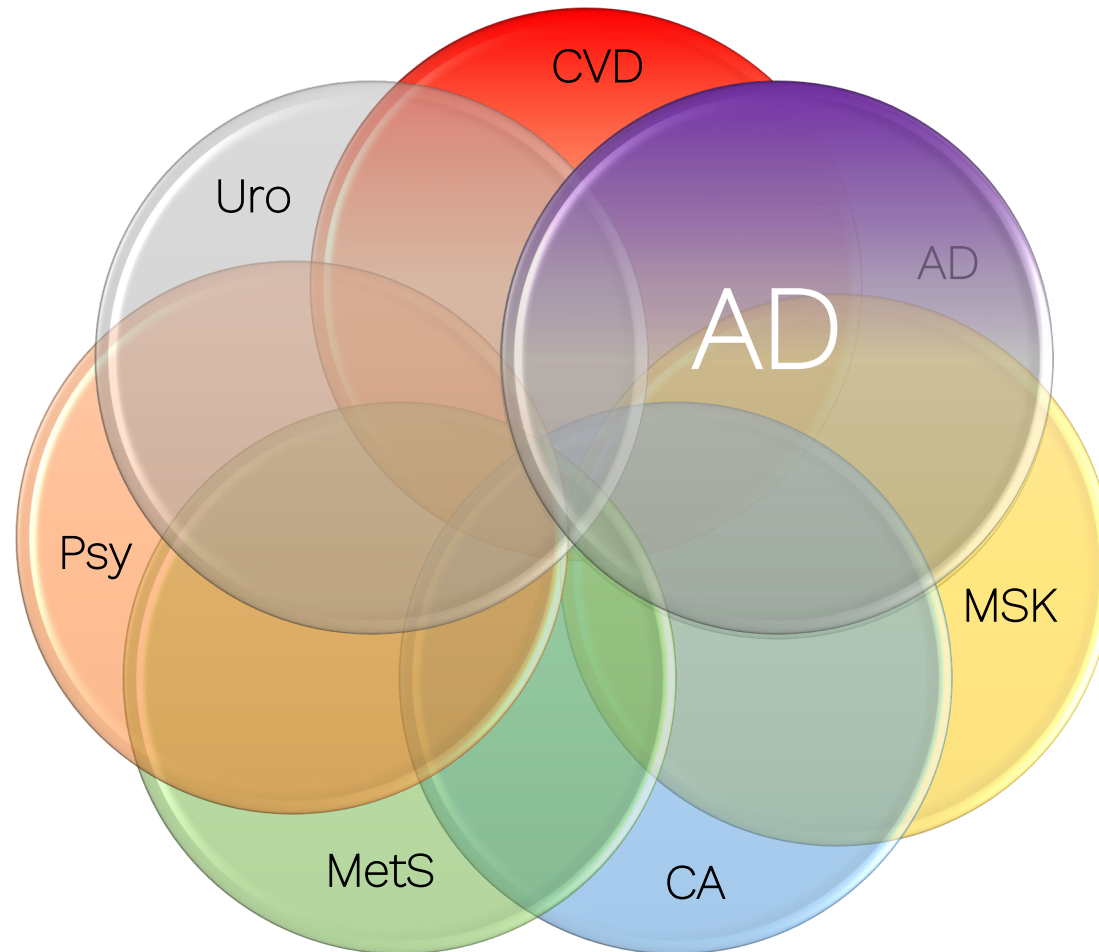
Various cancers that have been linked to obesity. In the USA overweight and obesity could account for 14% of all deaths from cancer in men and 20% of those in women



Various cancers that have been linked to environmental carcinogens. The carcinogens linked to each cancer is shown inside bracket.

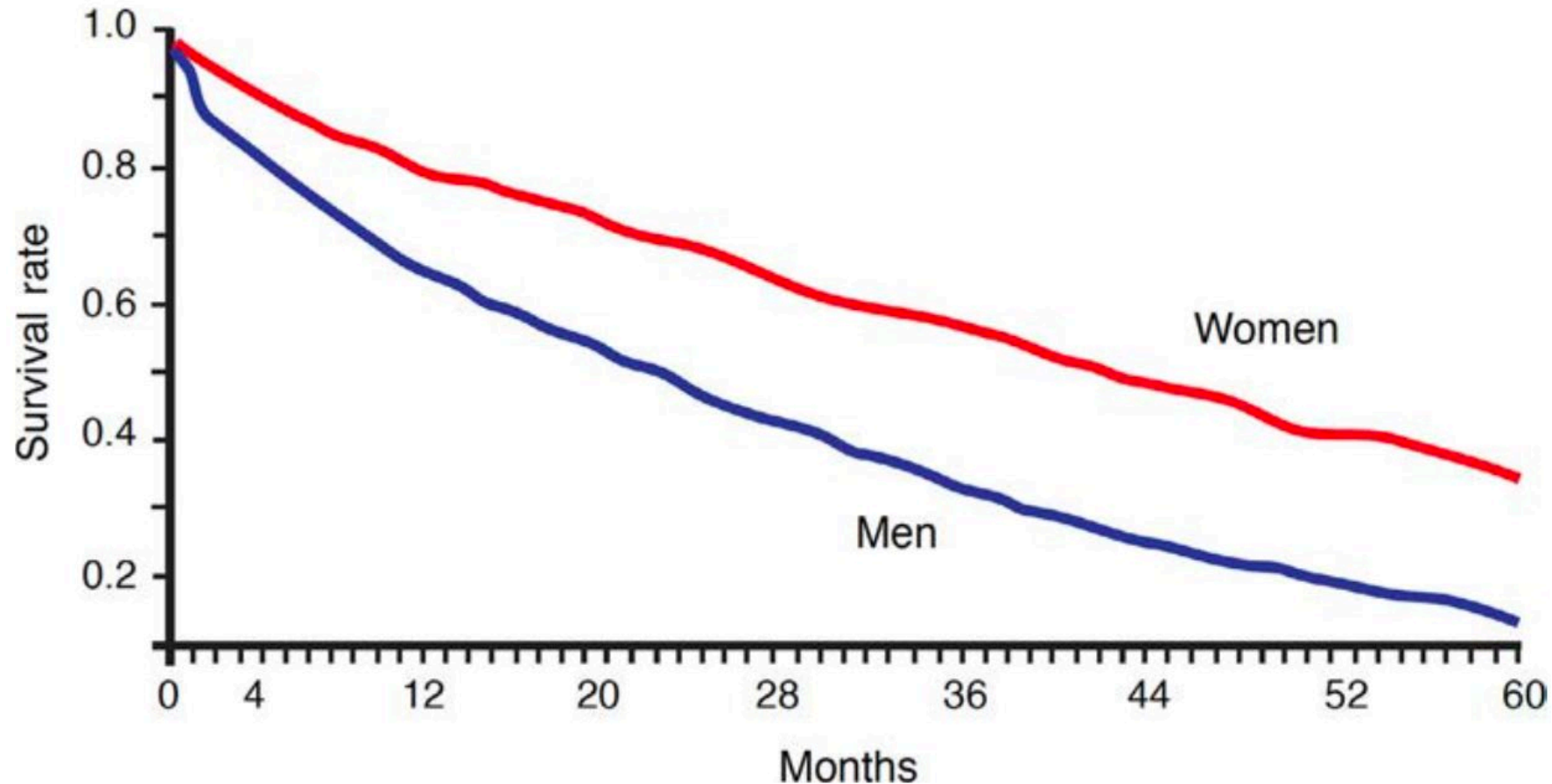


New Paradigm of Men's Health



Alzheimer's Disease

Figure. Women with AD live longer, and men with AD progress to death faster.



Alzheimer's Disease/Cognitive Decline

- 2-fold increased risk in women versus men
- Men have a shorter life span after diagnosis
- Vascular dementia is more common in men
- Lewy body dementia & Parkinson's are more common in men
 - Severity and rate of decline increased in men

Alzheimer's Disease/Cognitive Decline

The solution includes (but not limited to)

- Prevention – Cardio/Neuro/Metabolic-focused
- Screening - Family history, biomarkers, genomics (*ApoE4*, *TOMM40*, *KLOTHO*)

Alzheimer's Disease/Cognitive Decline

Interventions

- Supplementation – Homocysteine, lipids, inflammation
- Stress – Cortisol management and assessment – **DUTCH**
- Socialization and Community
- Exercise - BDNF
- Nutrition – Glycemic control
- Sleep - OSA (PSQI, Epworth, STOP-bang)



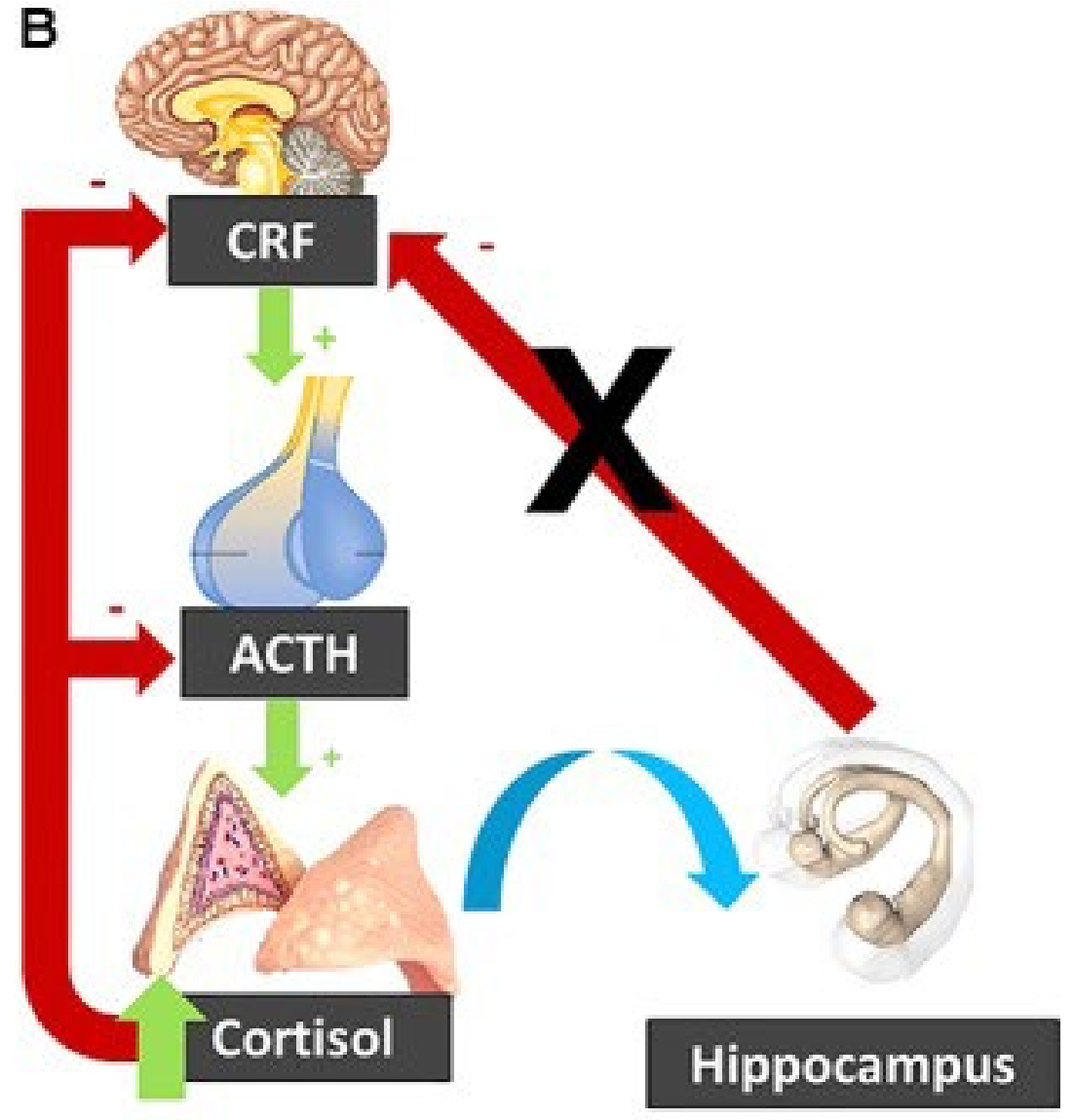
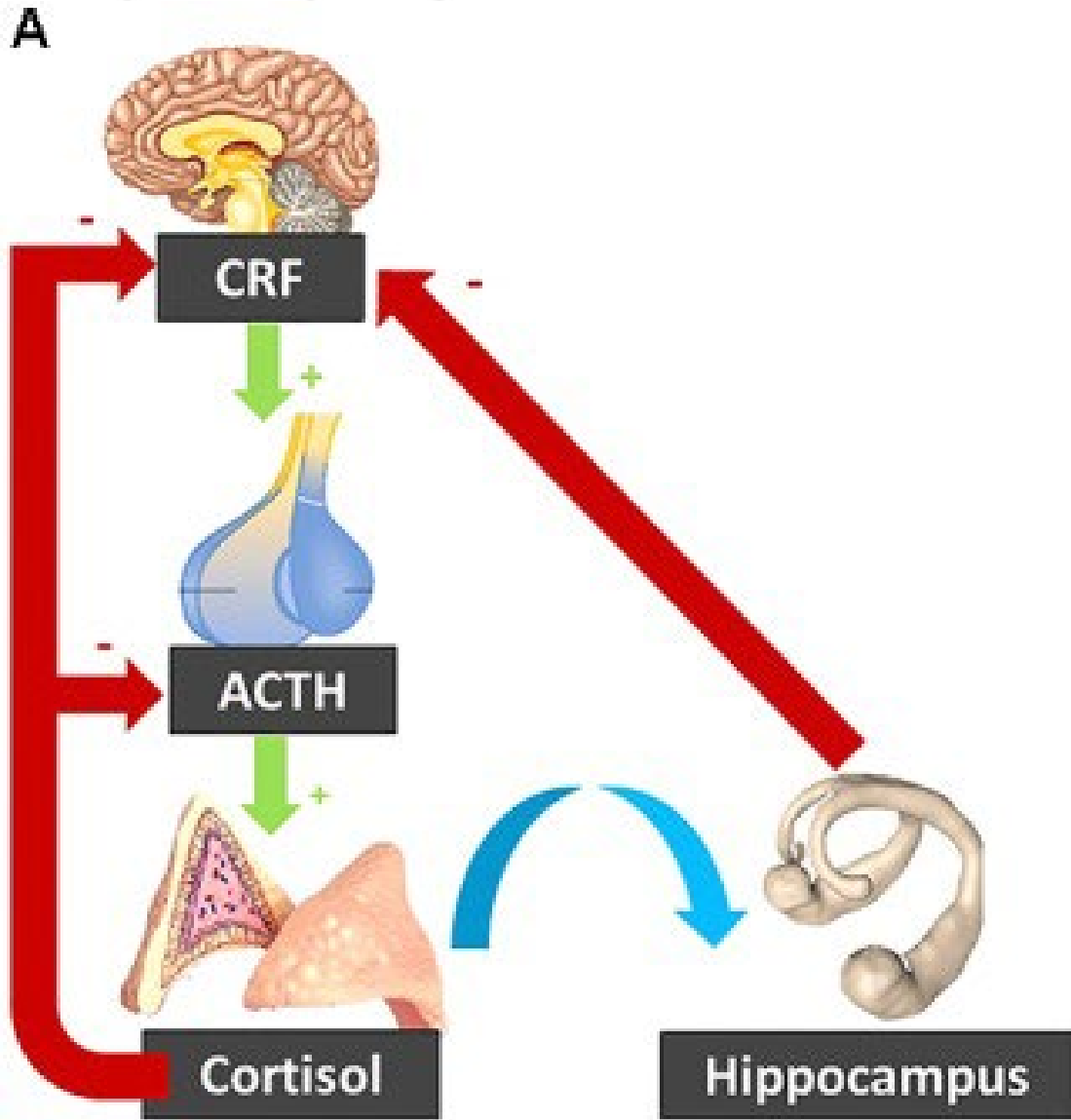
AD and Cortisol

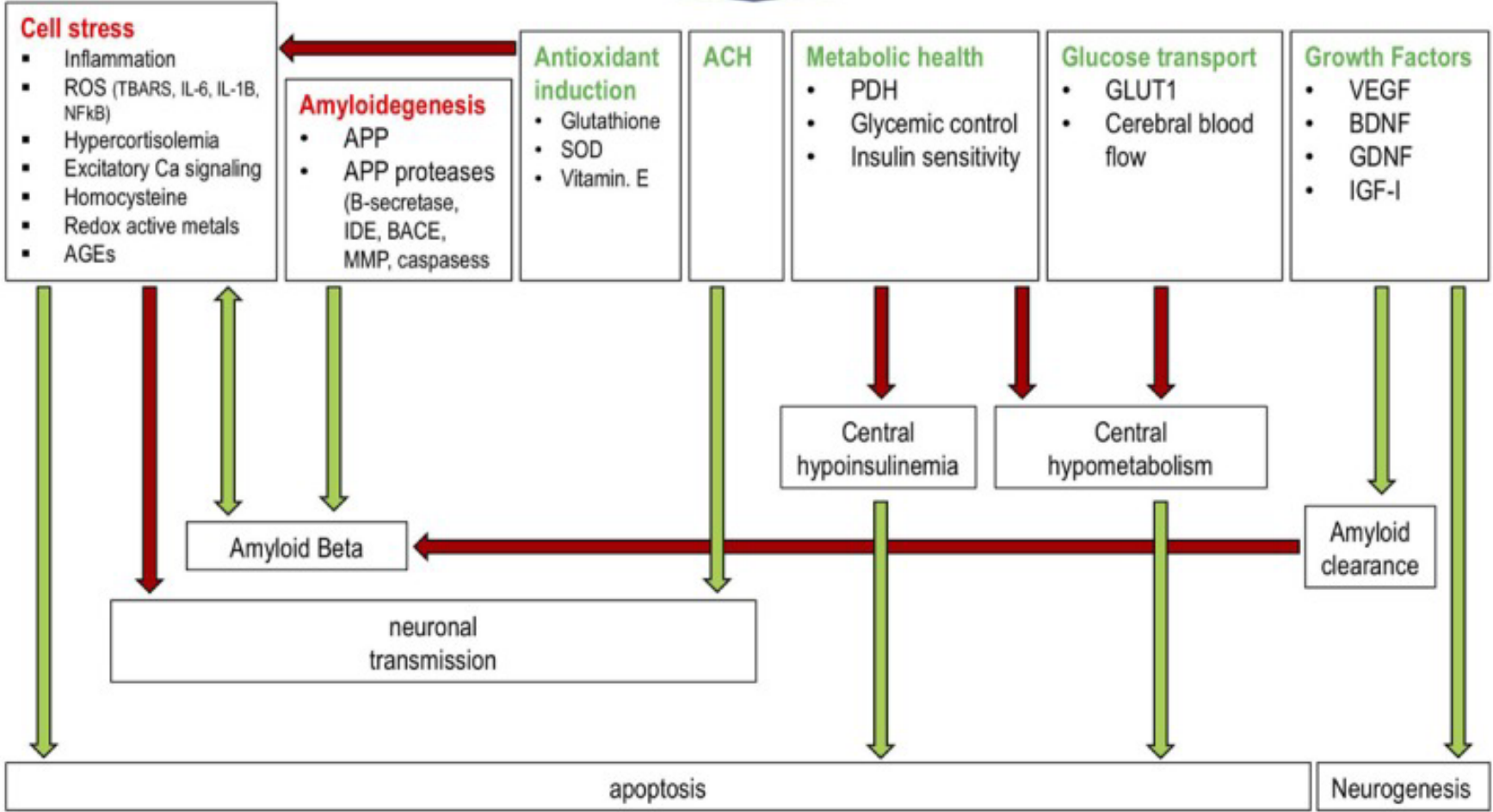
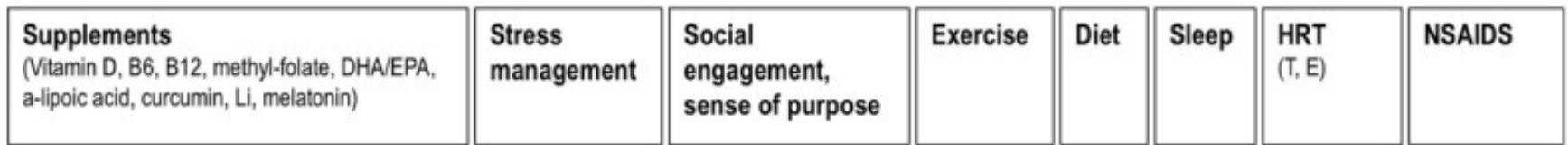
Hypercortisolemia → Hippocampal atrophy

Glucocorticoids stimulate receptors leading to lower BDNF

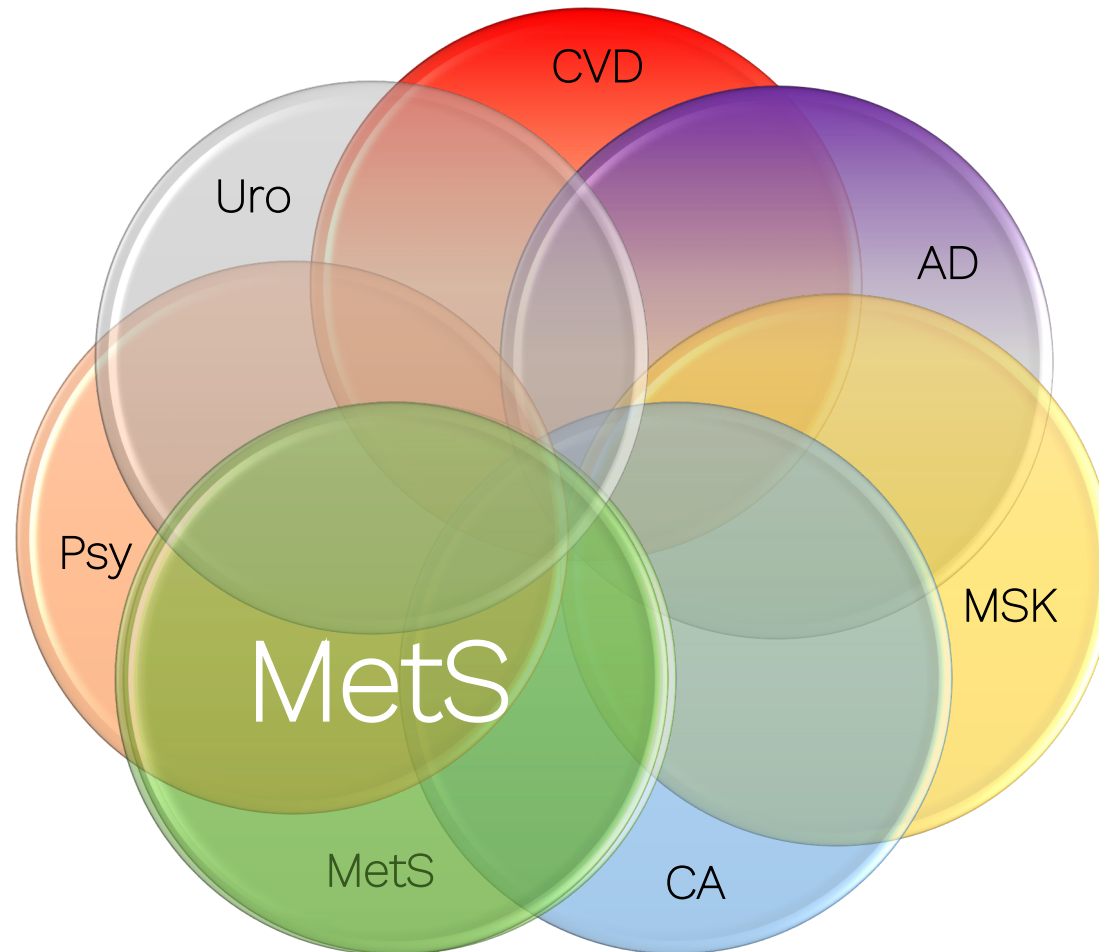
Inflammatory cytokines (IL-1-Beta and IL-6) stimulate HPA axis

... AD and hypercortisolemia is a multi-faceted disease





New Paradigm of Men's Health



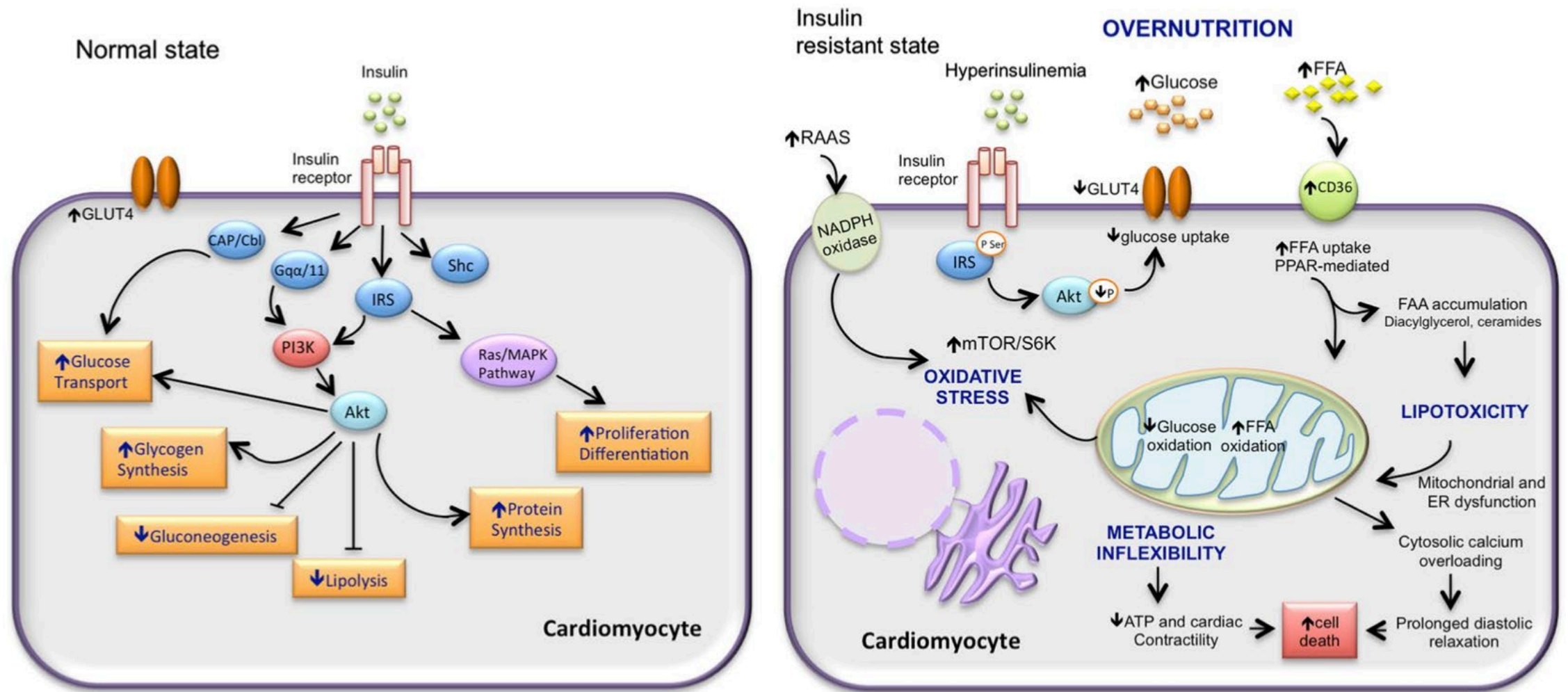
Metabolic Syndrome/Insulin Resistance

The underlying cause of many chronic diseases

- Cardiovascular disease
- Endothelial dysfunction
- Cognitive decline
- Cancer risk
- **Sarcopenia**
- Chronic renal disease
- Diabetes

...All of the above are necessary to prevent for lifespan and healthspan

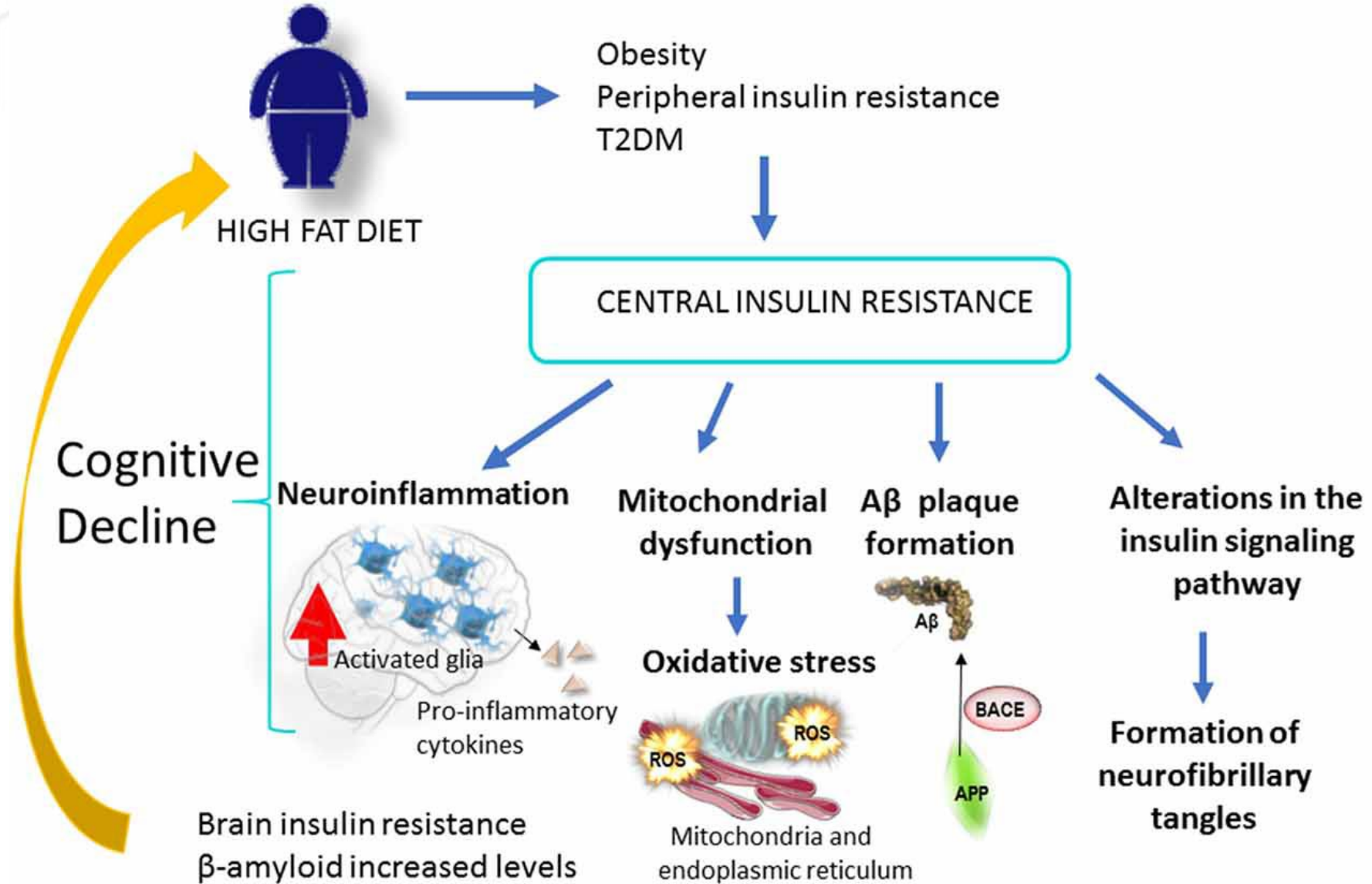
Figure: Mechanisms implicated in the development of diabetic cardiomyopathy.



Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovasc Diabetol*. 2018;17(1):122. Published 2018 Aug 31. doi:10.1186/s12933-018-0762-4a

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Metabolic hypotheses of LOAD





Insulin Resistance

Assessment

- Fasting glucose: <100 mg/dL
- Fasting insulin: <8 mIU/L
- HbA1c%
- CGM: Postprandial glucose in real time
- Oral glucose/insulin tolerance test

Metabolic Syndrome/Insulin Resistance

Interventions

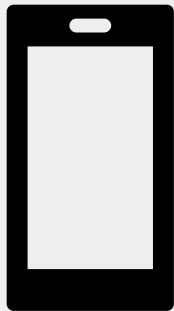
- Nutrition is the #1 tool
- Exercise is a close runner up
- Together they outcompete *any* drug or supplement.





Wrap up

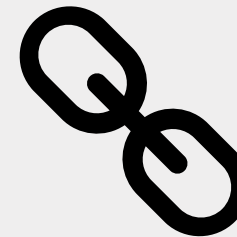
- Men's Health extends beyond urology and endocrinology
- The leading causes of death in men are chronic diseases
- Risk assessment and prevention > reactive medicine



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