Tips for Reaching Escape Velocity Ben Best Pharmacy (BSc Pharm) Physics/Computing Science (BSc) Cryonics Institute Past President Currently Director of Research Oversight Biomedical Research & Longevity Society (formerly named Life Extension Foundation)

Plans for Reaching Escape Velocity

Plan A (mean, average lifespan) Extend lifespan by healthy living Plan B (maximum lifespan) Try current possible rejuvenation strategies ■ Rapamycin + Metformin, NAD+ infusions, eliminate senescent cells (quercetin + dasatinab), GDF11, etc Plan C (maximum lifespan) Promote and conduct rejuvenation research Plan D (maximum lifespan) Cryonics

Plan A is practical, but not as trivial as is commonly believed

- Avoid the most common causes of death
- There is no limit to how healthy you can live
- Healthy living can add at least a decade or two to healthy life without extending maximum lifespan

Avoid the most common causes of death

- Ages 45 to 64
 - Cancer 29.2%
 - Heart disease 20.9%
 - Unintentional injuries 8.4%
 - Chronic lower respiratory diseases 4.1%
 - Chronic liver disease and cirrhosis 4.0%
 - Diabetes 3.8%
 - Stroke 3.3%
- (Source: US CDC Leading Causes of Death for 2016
 -- published July 26, 2018 National Vital Statistics Reports)

Avoid the most common causes of death

- Over age 65
 - Heart disease 25.3%
 - Cancer 21.1%
 - Chronic lower respiratory diseases 6.5%
 - Stroke 6.1%
 - Alzheimer's Disease 5.7%
 - Diabetes 2.8%
 - Unintentional injuries 2.7%
- (Source: US CDC Leading Causes of Death for 2016
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Cancer is rarely not preventable

Only 5-10% of cancer is due to heredity

90-95% of cancer due to lifestyle and environment

- 25-30% due to tobacco
- 30-35% due to diet
- 15-20% due to infections
- nearly 10% due to radiation (including UV light)
 PHARMACEUTICAL RESEARCH 25:2097 (2008)

4-20% due to overweight or obesity
 NEW ENGLAND JOURNAL OF MEDICINE 348:1625 (2003)

Tobacco Smoke

A 50-year study of nearly 35,000 male British MDs showed nonsmokers lived about 10 more years
 BMJ 328:1519 (2004)

 An American study of non-physicians found smokers lose an average 13.2 (male),14.5 (female) years of life.
 MORBIDITY AND MORTALITY WEEKLY REPORT (CDC) 51:300 (2002)

Tobacco Smoke

 Causes nearly all chronic lower respiratory disease (along with air pollution)

Causes a large portion of deaths from cancer and heart disease

In 2005 tobacco smoking caused about one fifth of all deaths in the United States, despite the fact that in 2005 only about one fifth of Americans were smokers
 MORBIDITY AND MORTALITY WEEKLY REPORT (CDC) 63:1108 (2014)

Tobacco smoke IS NOT listed as a cause of death
Diabetes IS listed as a cause of death

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Type 2 Diabetes

The major cause of insulin resistance (pre-diabetes, metabolic syndrome, type 2 diabetes) is obesity
NATURE MEDICINE 18:363 (2012)
Estimated lost years of life due to obesity for American whites is 13 years (men) or 8 years (women)
JAMA 289:187 (2003)

About 80% of diabetic patient deaths are due to atherosclerosis

■ VASCULAR PHARMACOLOGY 57:139 (2012)

Possibly even more underrated than tobacco smoke as a cause of death (much more than 3-4%)

Obesity Leads to Type 2 Diabetes

 In 2014 the WHO estimated 39% of adults to be overweight and 13% to be obese WORLDWIDE !!!
 DIABETES & METABOLISM JOURNAL 42:179 (2018)

In 2017 the Kaiser Family Foundation estimated 70% of American men and 60% of American women to be overweight or obese

 In 2016 OECD (Organization for Economic Cooperation and Development) estimated obesity rates to be

■ United States 40%

■ United Kingdom 26%

■ Spain 17%

Avoid Obesity

Eat less

Exercise more

Eat Less for Better Health

In the 1970s most Americans ate 3 times per day
 By 2006 Americans were eating more snacks with less time between eating, consuming an additional 500 calories per day
 AMERICAN JOURNAL OF CLINICAL NUTRITION 91:1342 (2010)
 Stop snacking !

Skipping breakfast and eating two meals per day can reduce daily calories by at least another 500 calories
 AMERICAN JOURNAL OF CLINICAL NUTRITION 100:539 (2014)

I generally only eat one meal per day and avoid snacking

Eat Less for Better Health

- Eating less is not so difficult when sugars and starches are minimized, and there is no restriction on the amount of protein, fat, and high-fiber foods
 - OBESITY REVIEWS 16:64 (2015)
 - PROCEEDINGS OF THE NUTRITION SOCIETY 74:328 (2015)
- With the above diet, ketones as a source of energy is increased and sugar-energy (as well as insulin) is reduced
- Insulin and glucose promote cancer growth, whereas ketones inhibit cancer
 - INTERNATIONAL JOURNAL OF CANCER 135:1711 (2014)
- Insulin and glucose cause mitochondrial dysfunction, whereas ketones protect mitochondria
 - ENDOCRINOLOGY 152:3638 (2011), JOURNAL OF ENDOCRINOLOGY 233:R15 (2017), NEUROSCIENCE 145:256 (2007)

Eat More Fiber for Better Health
 One study showed a high fiber diet increased insulin sensitivity by 8%

JOURNAL OF NUTRITION 138:439 (2008)

Type 2 diabetics consuming an average of 18 grams of fiber per day for 8 weeks showed a reduction of fasting blood glucose of 15mg/dL

JOURNAL OF THE AMERICAN BOARD OF FAMILY MEDICINE 25:16 (2012)

 A randomized, double-blind, placebo controlled trial of 16 gram/day fiber for 8 weeks was shown to reduce oxidized LDL cholesterol, systolic blood pressure, and insulin (-4.68 pmol/L, reduced insulin resistance)

ATHEROSCLEROSIS 211:630 (2010)

Eat Less for Better Health

More extreme calorie restriction may be too difficult for most people, but evidence from BioSphere participants as well as from practicing members of the Calorie Restriction Society indicate reduced risk factors for cancer, type 2 diabetes and cardiovascular diseases

AGEING RESEARCH REVIEWS

Exercise More

- Low cardiorespiratory fitness is a stronger predictor of death than smoking, high cholesterol, type 2 diabetes, or high blood pressure
 CIRCULATION 134:e653 (2016)
- People with elevated cholesterol and triglycerides who are highly fit, but not taking statins have a substantially lower risk of death than unfit people with elevated cholesterol and triglycerides who take statins
 LANCET 381:394 (2013)
- Increasing insulin resistance is not an inevitable consequence of aging.
 Increasing insulin resistance with age occurs due to increased body fat partly resulting from decreased activity
 - DIABETES 59:89 (2010)
- Endurance exercise will increase insulin sensitivity
 - JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM 96:E1137 (2011)

Brisk Walking

- After age 40 increased brisk walking would extend life expectancy
- Brisk walking time: 75 minutes per week
 Increased life expectancy 1.8 years
 Brisk walking time: 150-299 minutes per week
 Increased life expectancy 3.4 years
 Brisk walking time: 300-499 minutes per week
 Increased life expectancy 4.2 years

PLOS MEDICINE 9:e1001335 (2012)

High Intensity Interval Training

- High Intensity Interval Training (HIIT) can reduce time spent on exercise
- In one study HIIT involving three 20-second bursts of "allout" cycling efforts interspersed with 2 minutes of low effort cycling was compared with 45 minutes of moderate intensity cycling 3 times per week for 12 weeks
 - Insulin sensitivity, cardiorespiratory fitness, and muscle mitochondrial content was the same for both groups despite the fact that moderate cycling took 5 times longer

PLOS ONE 11:e0154075 (2016)

Don't take Statins just Because your LDL Cholesterol is High

- Statins are believed to reduce mortality in persons with history of coronary artery disease, but there is no evidence of benefit for people who simply have high LDL cholesterol
 ARCHIVES OF INTERNAL MEDICINE 170:1024 (2010)
- Cholesterol is an essential component of all cell membranes. Testosterone, estrogen, cortisol, bile acids, and vitamin D are synthesized from cholesterol.
- Nearly one-fourth of the body's cholesterol is in the brain (which is 2% of body weight). Cholesterol is required for synaptic plasticity and is particularly high in myelin around axons in the brain.
 JOURNAL OF NEUROCHEMISTRY 84:1215 (2003)
- LDL cholesterol reduces deaths from infectious diseases by adhering to bacteria and virus, reducing their toxicity
 - ANNALS OF NUTRITION & METABOLISM

Insulin Resistance versus LDL

A study of over 100,000 healthy persons showed insulin resistance highly predictive of cardiovascular disease, but LDL cholesterol was not predictive

- THE PERMANENTE JOURNAL 19:4 (2015)
- A 6.3 year follow-up of 208 healthy persons divided in thirds based on insulin resistance found no age-related disease in the least insulin resistant third, but 18% of those in the most insulin resistant third had at least one of cancer, stroke, high blood pressure, coronary artery disease, or type 2 diabetes
 JOURNAL OF CLINICAL ENDOCRINOLOGY AND METAOLISM 86:3574 (2001)
- Insulin resistance causes endothelial dysfunction, which leads to atherosclerosis
 - ENDOCRINE REVIEWS 28:463 (2007)

LDL Particle Size

Persons with small dense LDL particle size have much more atherosclerosis than persons with large LDL cholesterol
 ATHEROSCLEROSIS, THROMBOSIS, AND VASCULAR BIOLOGY 34:1069 (2014)

- Small, dense LDL enters blood vessel walls more readily and is more easily oxidized and glycated than large LDL
- Diets high in sugar or starch increase small, dense LDL
 AMERICAN JOURNAL OF CLINICAL NUTRITION 83:1025 (2014)
- Insulin resistance increases formation of small, dense LDL
 ACTA DIABETOLOGICA 55:209 (2018)

Elevated Blood Glucose

- Dietary sugar and elevated blood glucose causes insulin resistance
 - THE JOURNAL OF CLINICAL INVESTIGATION 128:545 (2018)
 - ENDOCRINE REVIEWS 28:463 (2007)
- Elevated blood glucose after a meal is an even greater risk for coronary artery disease than insulin resistance
 SCIENTIFIC REPORTS 7:14212 (2017)

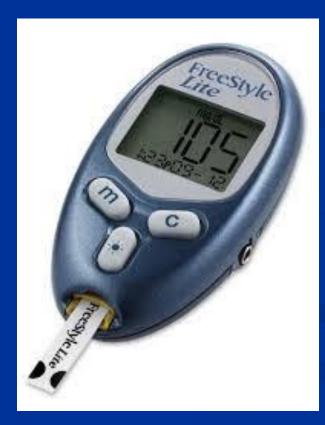
Measuring My Blood Value Responses to Foods for a Healthier Diet

GLUCOSE (blood sugar)
Lower is better (above 50 mg/dL)
TRIGLYCERIDES (FAT)
Can be temporarily high to produce ketones
KETONES (produced from FAT)
Higher is better (not as high as ketoacidosis)
Better fuel than glucose

FreeStyle Lite to measure blood glucose

Values in mg/dL

[milligrams per tenth of a liter (decaLiter)]



CardioChek System to measure blood triglycerides Values in mg/dL (same units as glucose)

[milligrams per tenth of a liter (decaLiter)]



Measuring Ketones

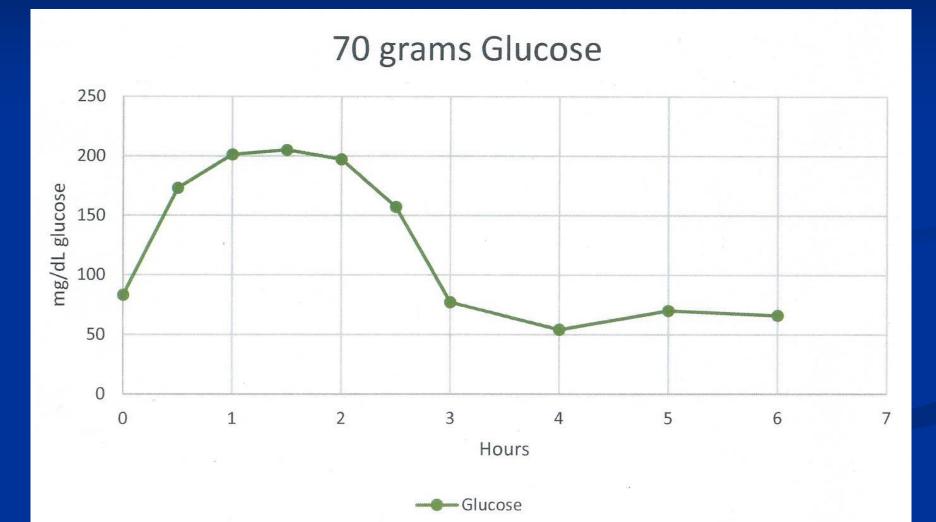


Precision Xtra Blood β-Hydroxybutyrate [mmol/Liter]

Blood glucose after eating is my primary concern

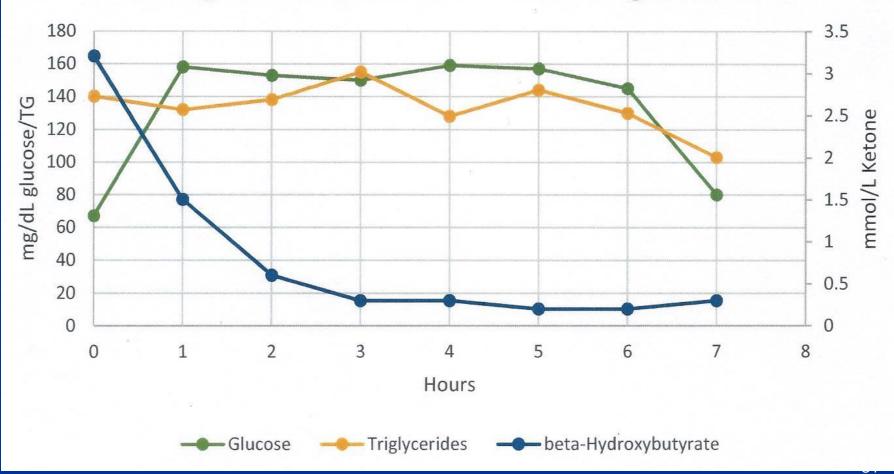
- Blood vessel damage by blood glucose is my major concern, I want my blood glucose after meals to be below 100 mg/dL
- I prefer foods that supply energy from ketones
- Drinking pure glucose is not a good idea, but most soft drinks (and fruit juices) have a comparable effect
- Avoid soft drinks (soda, pop) and fruit juices !!

Oral Glucose Tolerance Test



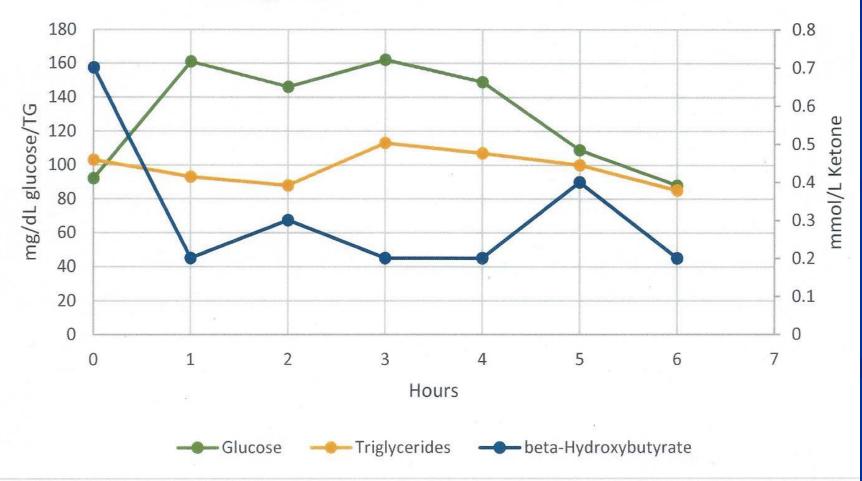
Hamburger Buns (White Bread)

400 grams Trader Joe's Hamburger Buns



100% Whole Wheat Bread

400 grams Whole Wheat Bread

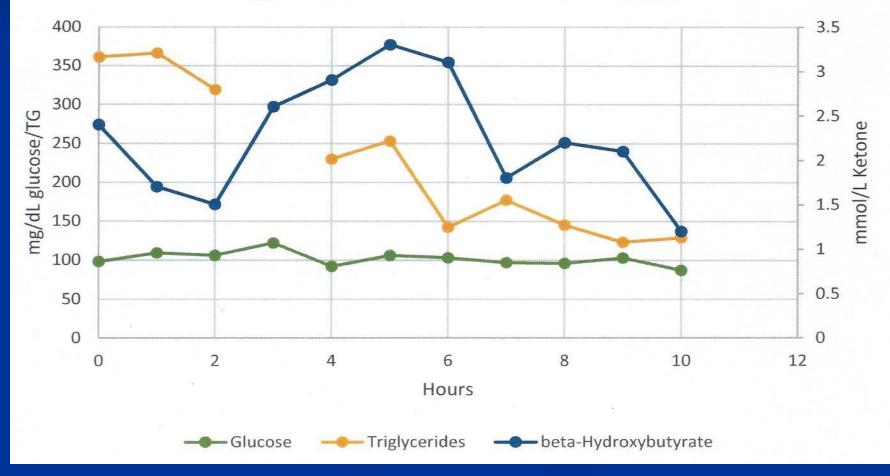


All-fiber (Non-starch Carbohydrate) Noodles



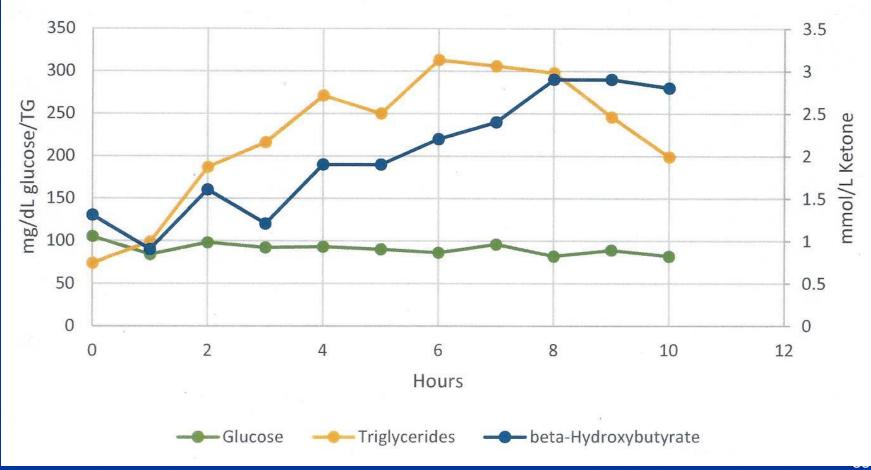
All-fiber (Carbohydrate) Noodles

400 grams Genki Allfiber Noodles

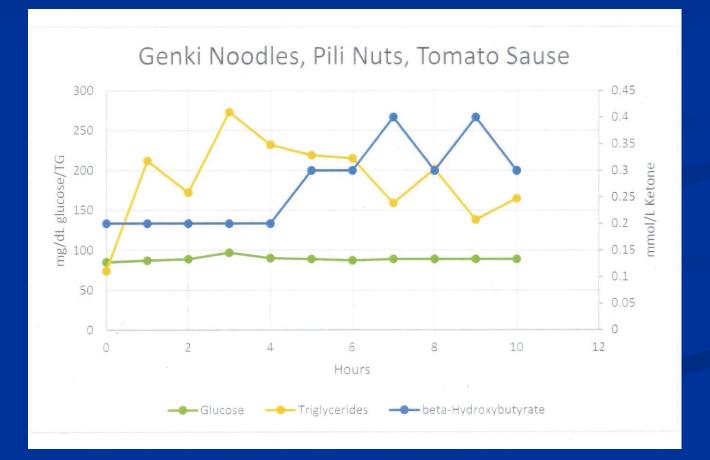


Pili Nuts (80% fat)

400 grams Pili Nuts



452 grams Allfiber Noodles + 156 grams Sprouted Pili Nuts + 425 grams Organic Tomato Sause

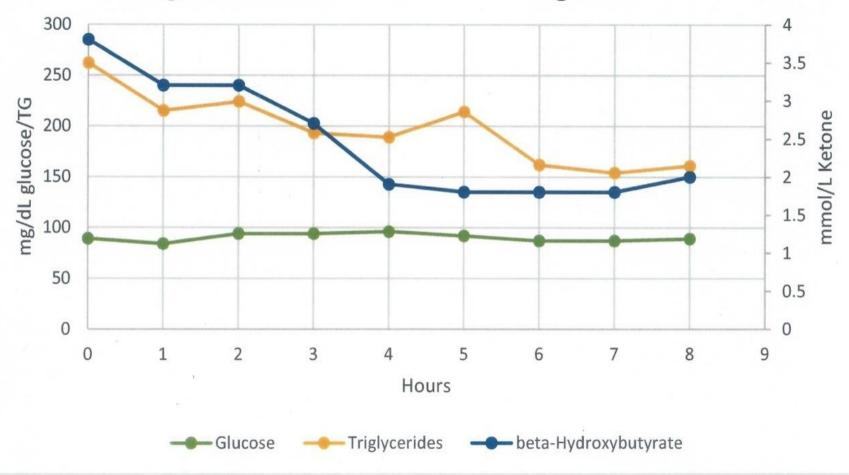


Bagels without starch



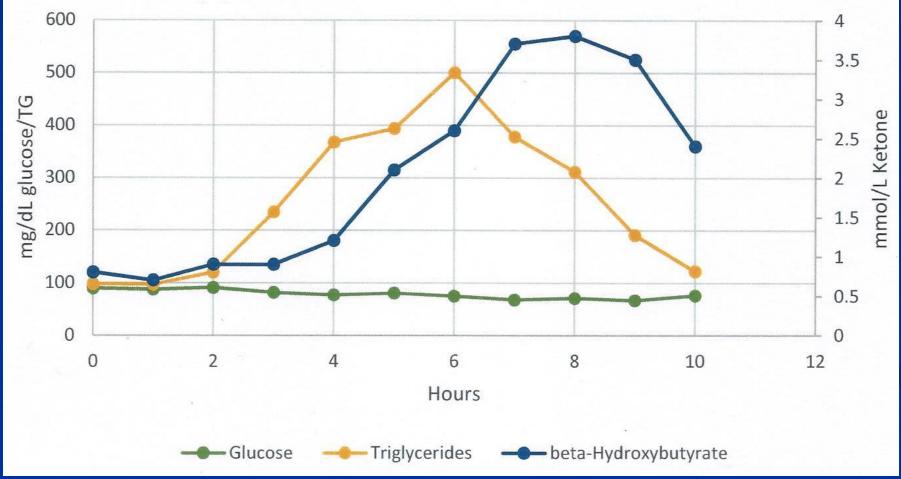
Bagels without starch

400 grams Fox Hill Kitchens Bagelz



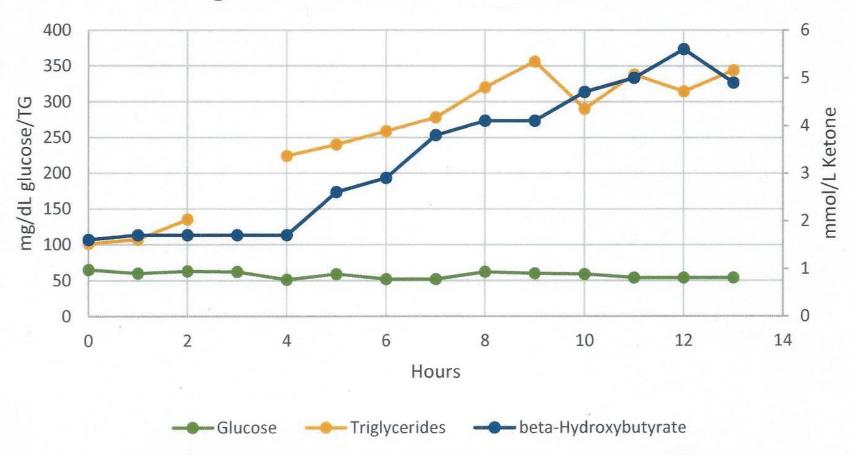
Organic Avocado

400 grams Organic Avocado



Organic Olive Oil (MUFA Oleic Acid)

200 grams Whole Foods 365 Olive Oil



Medium Chain Triglycerides (MCTs)

Plasma beta-hydroxybutyrate (ketone) increases in direct proportion to the amount of MCTs consumed
 ANNALS NY ACADEMY OF SCIENCES 1367:12 (2016)

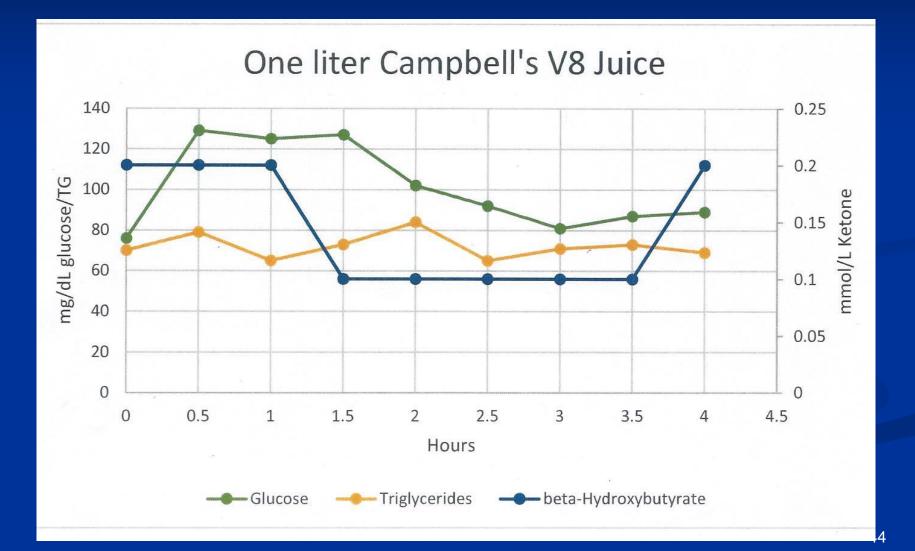
Zenwise MCT Oil 2/3 C8:0 Caprylic Acid 1/3 C10:0 Capric Acid



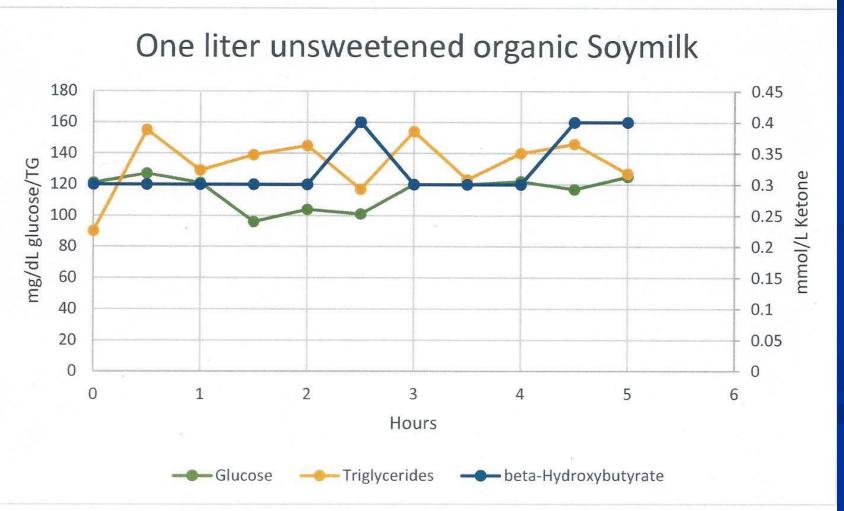
Zenwise MCT Oil 2/3 C8:0 Caprylic Acid 1/3 C10:0 Capric Acid

200 grams Zenwise MCT Oil 250 3.5 3 200 2.5 mg/dL glucose/TG mmol/L Ketone 150 2 1.5 100 1 50 0.5 0 0 0 1 2 3 4 5 6 7 8 9 10 Hours Triglycerides beta-Hydroxybutyrate Glucose

Campbell's V8 Juice

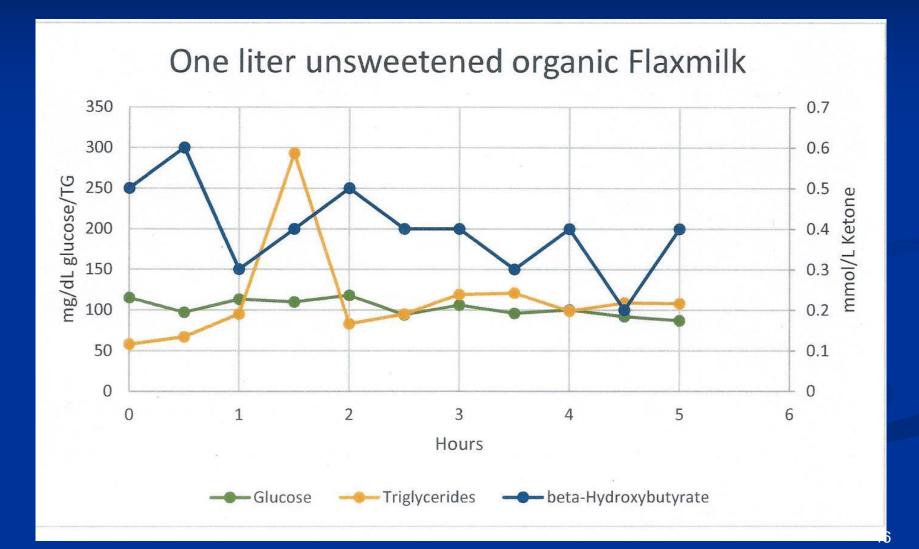


Soymilk

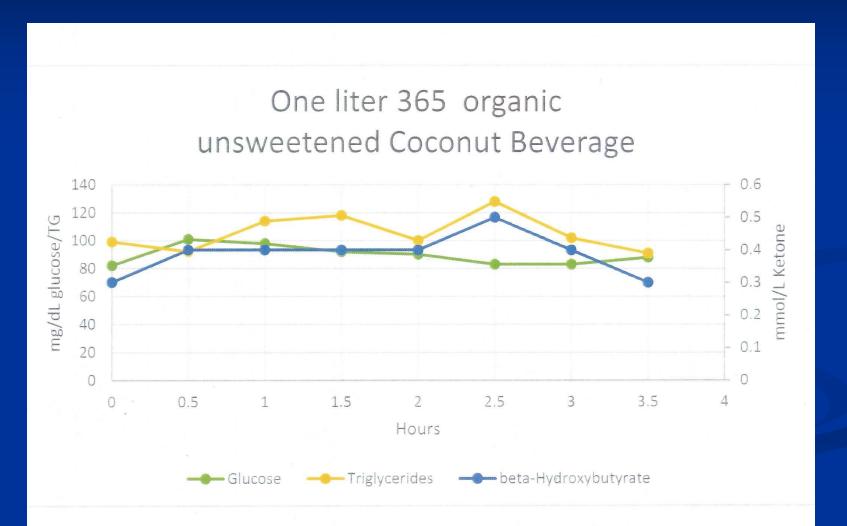


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Flaxmilk



Coconut Beverage



Toxic Metals in Fish Meat

Toxic metals bioaccumulate. Fish that eat fish have more toxic metal than the fish they eat

- THE SCIENCE OF THE TOTAL ENVIRONMENT 506:126 (2015)
- Humans that eat the fish bioaccumulate toxic metal even more
- Mercury causes kidney problems and decreased intelligence
- Methyl mercury levels in human hair are indicative of fish consumption. Men consuming 30 grams of fish or more per day have 56% more hair mercury than men consuming less fish, and 2.4 times the risk of death from coronary heart disease. Women have 3 times the risk.

■ ENVIRONMENTAL HEALTH PERSPECTIVES 115:609 (2007)

Methyl mercury is particularly high in large, long-lived fisheating ocean fish (swordfish, mackerel, tuna, etc.)

Mercury in Fish Meat

- DHA in fish oil is beneficial for the developing brain of a foetus
- Methyl mercury accumulates in brain tissue, and is particularly damaging to the developing brain of a foetus
- Women of childbearing age are warned by medical authorities to eat limited amounts of small fish low on the food chain to gain the benefits of DHA and limit the harm of mercury
 - JAMA 296:1885 (2006)
- Mercury has toxic effects on the nervous system and on immune function
 - JOURNAL OF PREVENTATIVE MEDICINE AND PUBLIC HEALTH 45:353 (2012)
- Mercury binds to the protein in meat, not to the oil
 - JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY 58:2047 (2011)
- I take omega-3 oil supplements and do not eat fish meat
- Toxic metals are not metabolized, accumulating in soft tissues.
 - Not just mercury, but lead, iron, cadmium, etc.
 - Toxic metals accumulated in any form of meat will accumulate in the tissues of humans that eat meat

Persistant Organic Pollutants in Meat

- DDT was banned in the US in 1972, PCBs (PolyChlorinated Biphenyls) were banned in 1979, but these organic substances persist in the environment, bioaccumulate in fat tissue of animals and bioaccumulate in the fat of humans that eat meat
- Nitrates in processed meats (sausages, salami, bacon) have been shown to cause insulin resistance and atherosclerosis.
 - PNAS 75:233 (2017)
- TMAO (TriMethylAmine N-Oxide, unpleasant odor of rotting fish) contributes to atherosclerosis. Intestinal microbiota produce TMAO from meat in meat-eaters, but not in vegetarians who are experimentally fed meat.
 - NATURE MEDICINE 19:576 (2013)
- PCBs substantially increase TMAO formation in the liver
 - JOURNAL OF NUTRITIONAL BIOCHEMISTRY 33:145 (2016)

Vegetarianism and Life Expectancy

- Vegetarianism was studied in a cohort of Seventh Day Adventists (circa year 2000)
- For Adventists practicing vegetarianism longer than 17 years, the average age at death was 86.5
- For Adventists practicing vegetarianism less than 17 years, the average age at death was 82.9
 - AMERICAN JOURNAL OF CLINICAL NUTRITION 78:526s (2003)
 - Neither groups of Adventist vegetarians were tobacco smokers
- Average American life expectancy from birth in the year 2000: was about 77 years
 - PEDIATRICS 108:1241 (2001)
- Some, but not all, of the survival advantage seen in vegans and vegetarians could due to a healthier lifestyle (exercising?)

Seventh-Day Adventists US & Canada NUTRIENTS 6:2131 (2014)

CAUSE OF DEATH	OMNIVORES	VEGETARIANS
CARDIOVASCULAR		
Male	1.00	0.71
Female	1.00	0.99
CANCER	1.00	0.92
ALL CAUSES		
Male	1.00	0.82
Female	1.00	0.93

Women live longer than men Survival advantage of women circa year 2000 ■ Russia 12 years ■ France 7.8 years \blacksquare USA 6.7 years ■ UK 5.3 years ■ India 0.6 years ■ SCIENTIFIC AMERICAN 29:120 (2004) ■ With advancing age, genetics rather than healthy living becomes the predominant determinant of survival AMERICAN JOURNAL OF CLINICAL NUTRITION 78:526s (2003)

Gain at least a couple of decades of healthy life Exercise Restrict all eating, except fiber Restrict eating sugar or starchy foods Don't drink soft drinks or fruit juices Don't eat meat Don't take statins if you have no history of coronary artery disease

Don't smoke