Carbs: The Staff of Life,
or
The Stuff of Death?

Edwin Cox, M.D.

Carbs: What are they?

What are we talking about here?

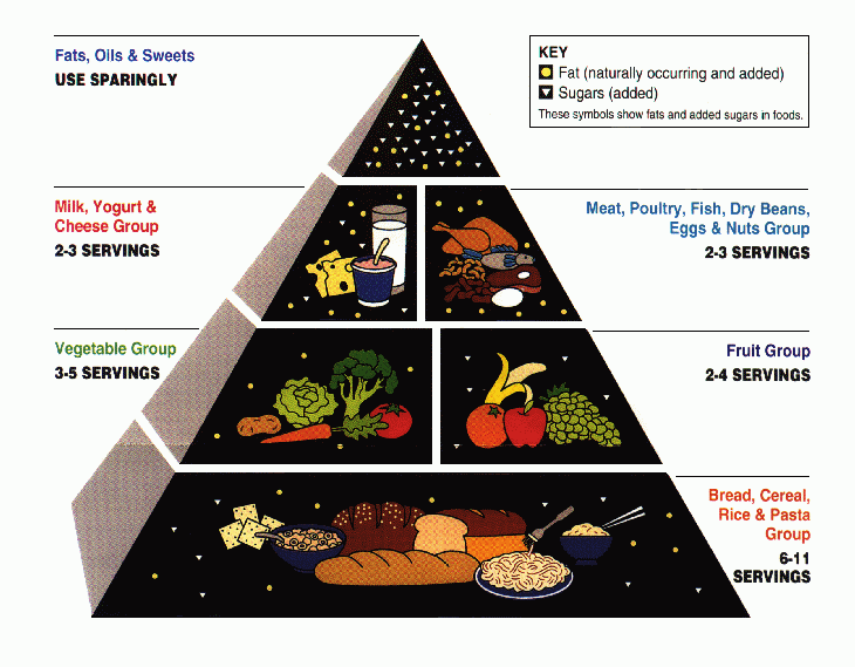
- Foods made up mainly of carbohydrates, one of the 3 macronutrients

Fruits and vegetables are carbohydrates, aren't they?

- Yes, but when they mention "carbs", people are usually referring to foods made from grains and white potatoes

Grains and potatoes have concentrated calories – starch - whereas fruits and vegetables are largely water and indigestible carbohydrates ("fiber") with few calories

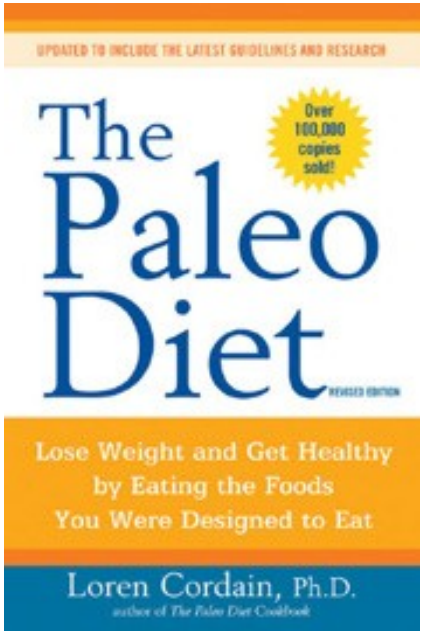
Pyramid, or Paleo?
Both can't be right!?!



USDA Food Pyramid

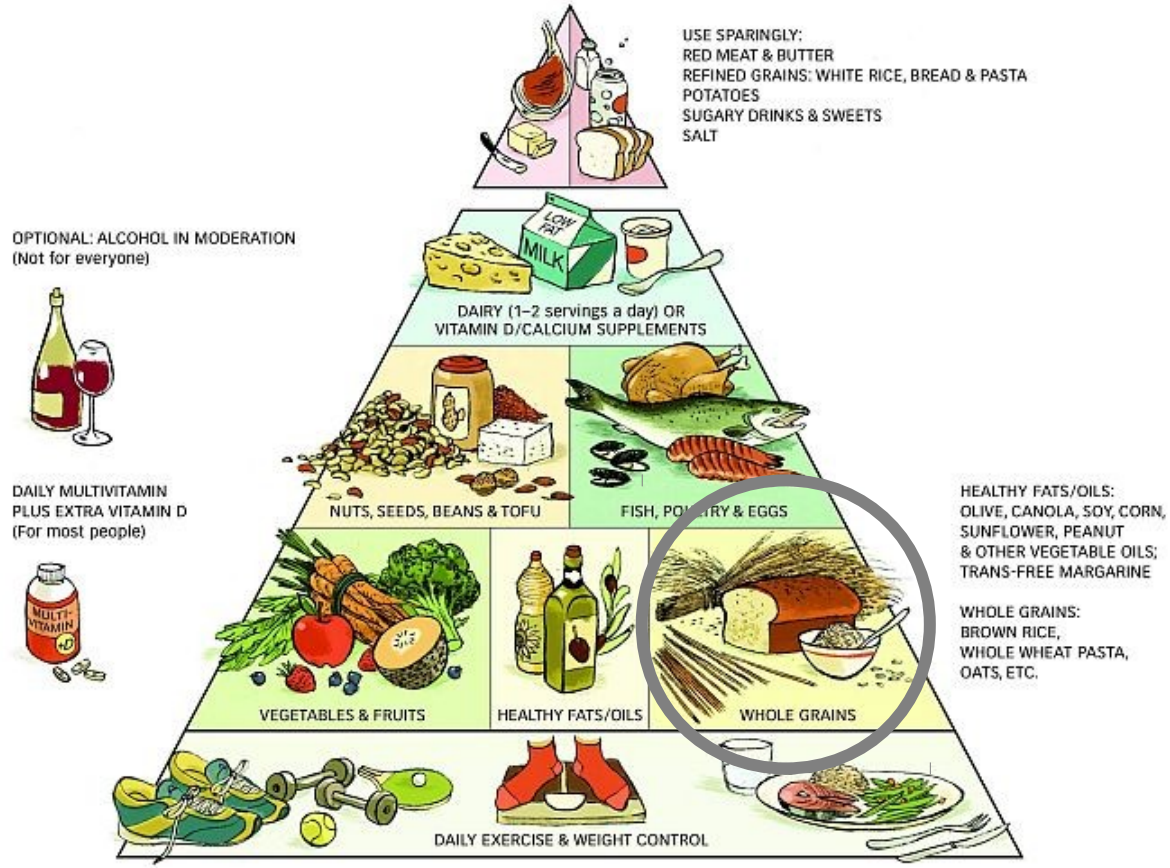
Get 6-11 servings of grain foods a day

Avoid fats like the plague



Avoid carbs like the plague: Atkins, Paleo, Grain Brain, Wheat Belly, Against All Grain, ...

Carbs: The foundation



Actually, both are right, sort of

Carbs *are* beneficial, **but only those from whole grains**

Carbs *are* harmful, **but only those from sugars, starches and refined grains**

What's the difference?

- **FIBER**
- Abundant in whole grains; missing in sugars, starches and refined grains

Grain = starch + fiber

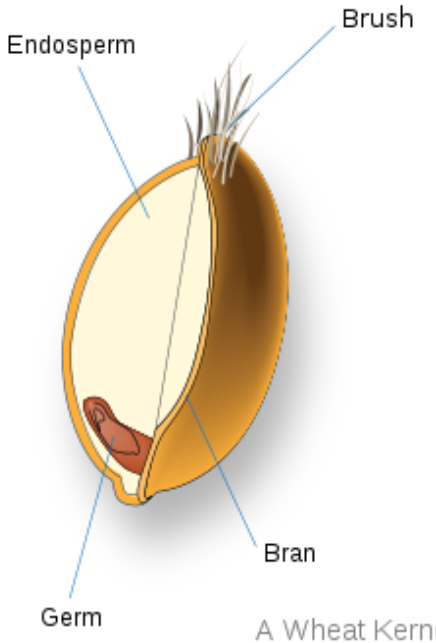
Grains are the seeds of grasses

Whole grain is the intact kernel

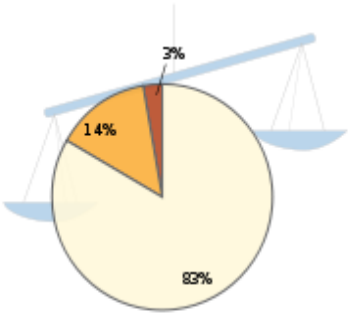
- Endosperm
- Bran
- Germ

"Refining" is separating the endosperm (starch plus gluten) from the germ and bran (fiber, vitamins, minerals, fat, protein)

Refining actually robs the kernel of much of its nutritional value, leaving calories and little else in the "refined" flour



A Wheat Kernel



Composition by Weight

	Carb./g	Protein/g	Fat/g	Fiber/g	Iron (% daily req.)	Others
Bran	63	16	3	43	59	vitamin Bs
Endosperm	79	7	0	4	7	
Germ	52	23	10	14	35	vitamin Bs omega-3/6 lipids

Nutritional Value (per 100g)

Refined grain

Refined grain is starch and elastic proteins (gluten) derived from the endosperm

Refined grain flour, AKA white flour, is used in the vast majority of familiar products

- White bread, white pasta, cakes, pies, cookies
- White rice is also refined – stripped of coating

Refined grains have long shelf life – resist going rancid

Foods made from refined flour are white, light, delectable and easily digestible

Virtue of refined flour is a vice

"Highly refined flours owe most of their good keeping quality to the fact that the nutriment they provide is too incomplete for the growth of animals, including vermin and insects"! - Ancel Keys

Refined flour is so depleted of nutrients that Federal law **requires** that it be "enriched" by adding iron and vitamins (thiamine, niacin, riboflavin, folic acid)

Enriched flour is still nutritionally deficient – no fiber!

It's all about the fiber

I'll be making the point that **fiber** is the key to understanding the proper role of carbs

It is fine to eat as much carbs as you want that are whole-grains and other fiber-bearing foods (vegetables, fruits)

- 6 servings a day of whole-grains
- 4+ servings a day of fruits and vegetables

Reserve sugar, starches and refined grains for treats, in very limited amounts

- When I say starches other than grains, I'm mainly talking about white potatoes
- When I say refined grains, I'm talking about white bread, white rice, refined breakfast cereals and sweet baked goods made with white flour

Are refined grains, sugar and starches directly harmful?

If you consume *mostly* simple carbs - white bread, white rice, potatoes, and/or sugar-sweetened beverages - are they *directly* harmful?

Maybe, maybe not. But it doesn't matter!

The fact is, you will only eat just so much total carbs

If you eat mostly simple carbs, you automatically reduce the amount of fiber you consume, and deprive yourself of **dietary fiber that is extraordinarily beneficial to health!**

The real harm of simple carbs: fiber deficiency!

Stated differently, *dietary fiber deficiency is harmful!*

Fiber deficiency may be the #1 dietary risk that most Americans face!

- Average US fiber consumption is less than half the amount that provides optimal protection against cancer, diabetes and heart disease

Consuming mostly simple carbs precludes your getting desirable amounts of fiber

Carbs and weight gain

The ponderous question:

- "Won't I gain weight by eating carbs?"

The answer comes from:

- Nurses Health Study & Health Professionals Followup Study
- 117,992 men and women
- FFQ, weight taken every four years, up to 24 years
- Weight gain in each four year period correlated with increase in number of servings of each food group in that interval

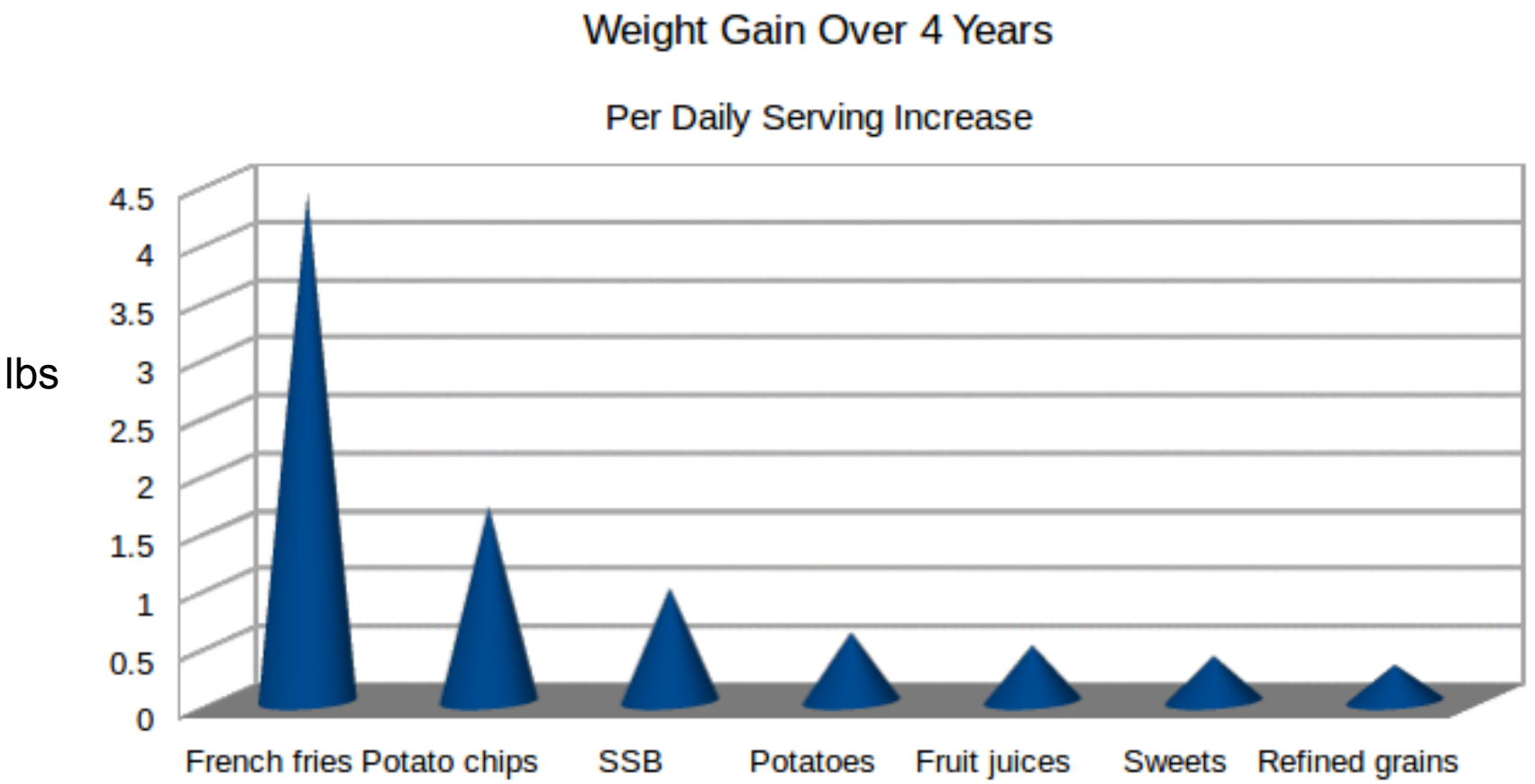
Carbs and weight gain

Won't I gain weight by eating carbs?

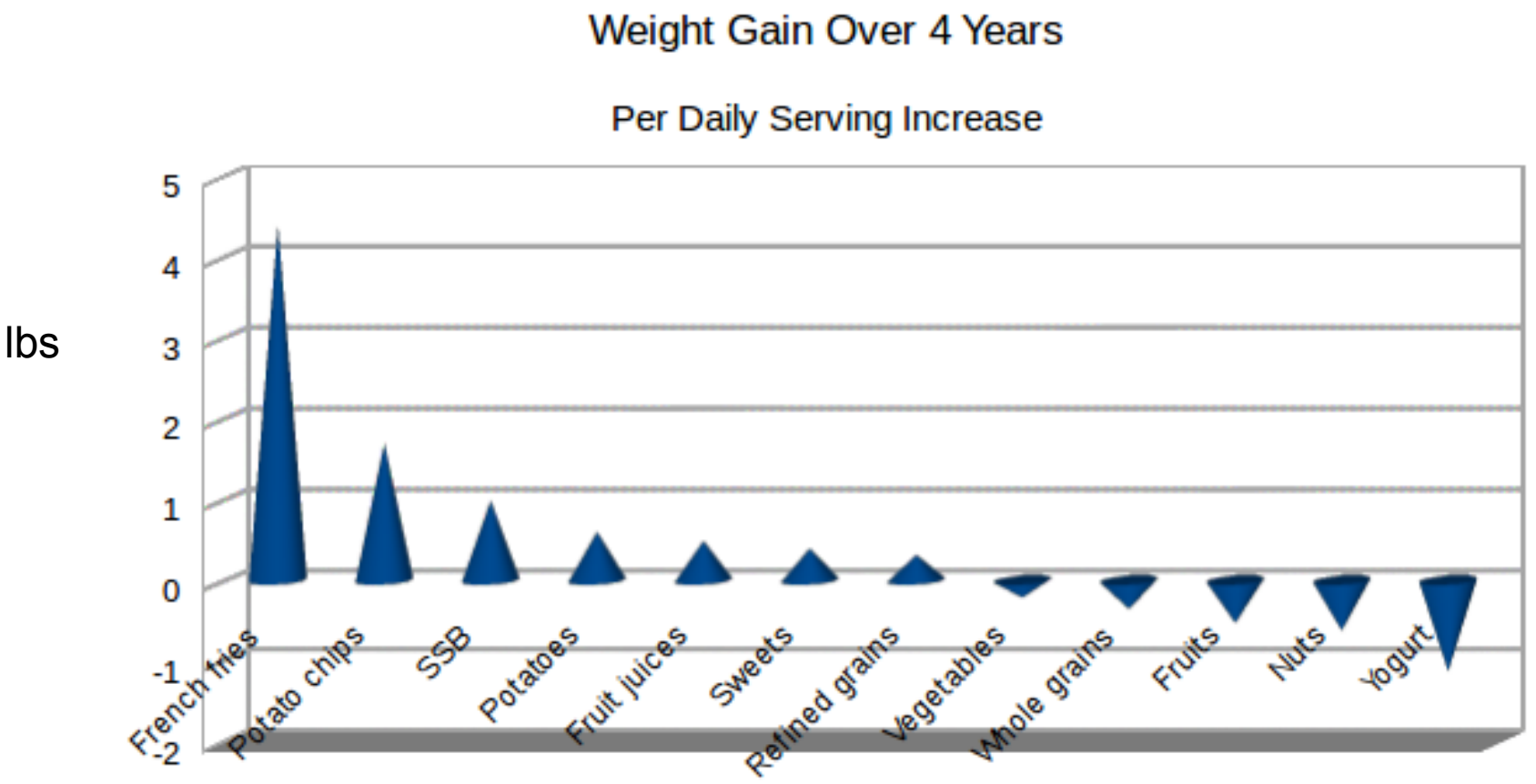
A Comparison of Different Methods for Evaluating Diet, Physical Activity, and Long-Term Weight Gain in 3 Prospective Cohort Studies[1–3]

Jessica D Smith,[4,6]* Tao Hou,[5] Frank B Hu,[4,5,7] Eric B Rimm,[4,5,7] Donna Spiegelman,[5] Walter C Willett,[4,5,7] and Dariush Mozaffarian[6]

Carbs and weight gain



Carbs and weight gain



P<0.002 for all

Carbs and weight gain

Won't I gain weight by eating carbs?

Yes, **BUT ONLY IF** you eat potato chips, french fries, refined grains, and sweets

- Also with sugar-sweetened beverages, including 100% fruit juices

Eating more **whole grain** foods is associated with **weight loss**!

Bottom line on carbs

The issue is not how much carbs, it's **which** carbs

Relying on low quality carbs is not a good idea; they can be deleted

But, if you avoid all carbs - whole grains in particular - you won't be doing yourself any favor

You will fail to get the grain-based fiber that is vitally important to health

- We will get to the evidence for that claim later in the presentation

Low-carb diets have their place

The very-low-calorie (low-carb) ketogenic diet, VLCKD, **as a short-term intervention**, is remarkably safe and effective for durable "weight loss" (mobilization of excess fat)

- This is NOT the popular Keto Diet, whose name is a riff off medically useful ketogenic diets validated in clinical trials

Very-low-carb, high-fat ketogenic diet is necessary to treat some difficult epilepsy cases

Maintenance low-carb diets are otherwise **ill-advised**, based on the data from large observational studies that we will review shortly

What are carbohydrates?

Chemical definition

- Compounds made up of single sugars, small clusters of sugars, or large chains of sugars

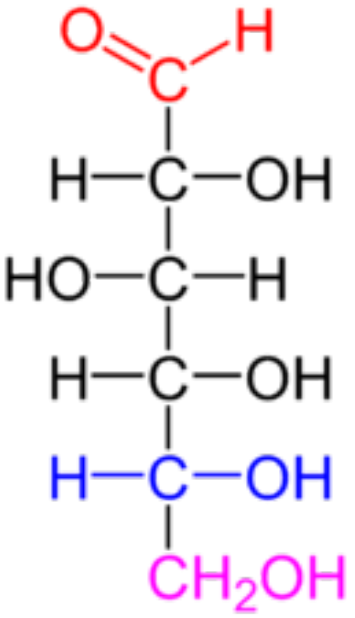
Nutritional definition

- Sugars
- Starches
- Fiber

Dietary definition

- The main ingredient of many plant-based foods, especially grains, fruits and vegetables
- Absent from animal-based foods other than dairy, which may have lactose

Sugar



Roses are red, violets are blue, sugar is sweet, and so are you!

Why do we associate these concepts?

- Both stimulate the reward center of the brain
- Both can be distorted to create addiction

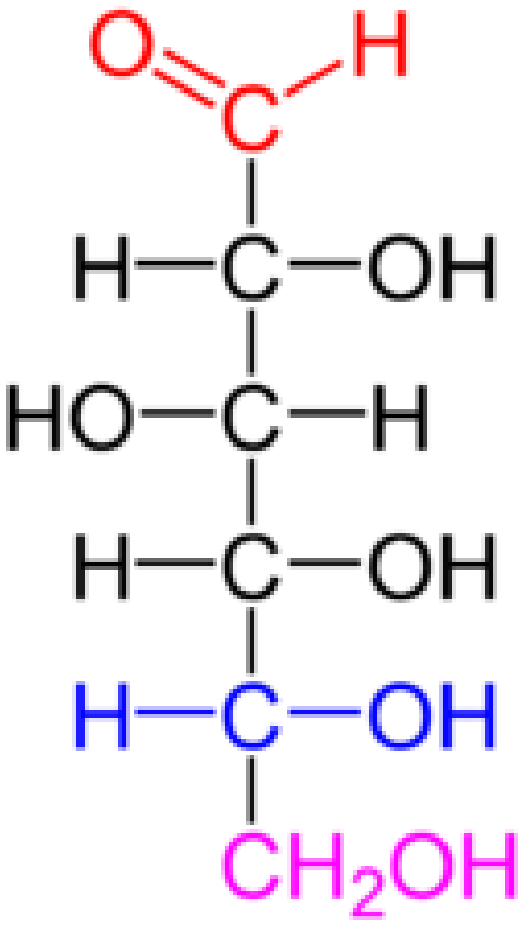
Take it from the top: Sugars

Simple sugars are the fundamental building block of carbohydrates

All carbohydrates are chains and clusters of simple sugars (tech name: monosaccharides)

Glucose is the poster child of a simple sugar

Other simple sugars important for humans are fructose and galactose



Glucose digestion

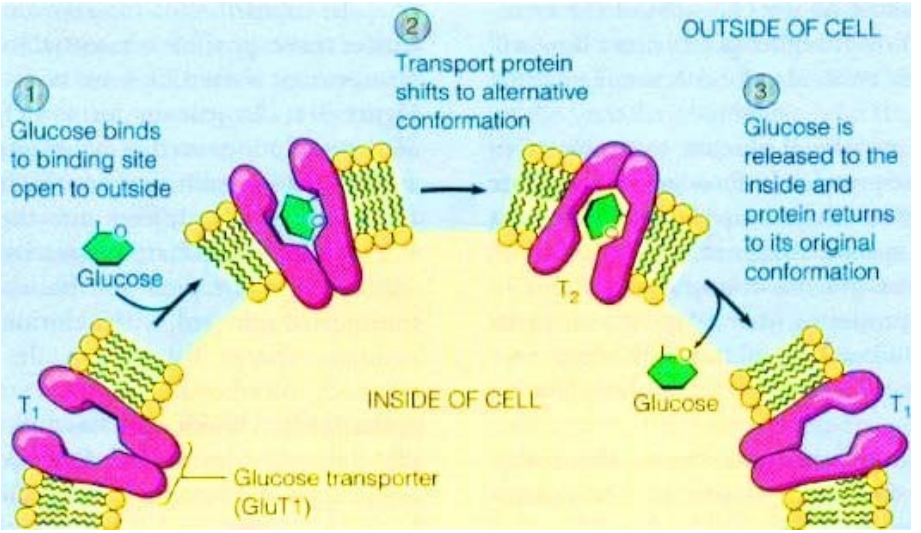
Suppose we consume pure glucose

- Present as such in honey, corn syrup

Passes down the esophagus, through the stomach and into the small intestine (SI)

There it is absorbed by SI lining cells (enterocytes) by glucose transporter GLUT and on into the blood stream

GLUT acts like a lock on a canal to pass glucose from outside to inside

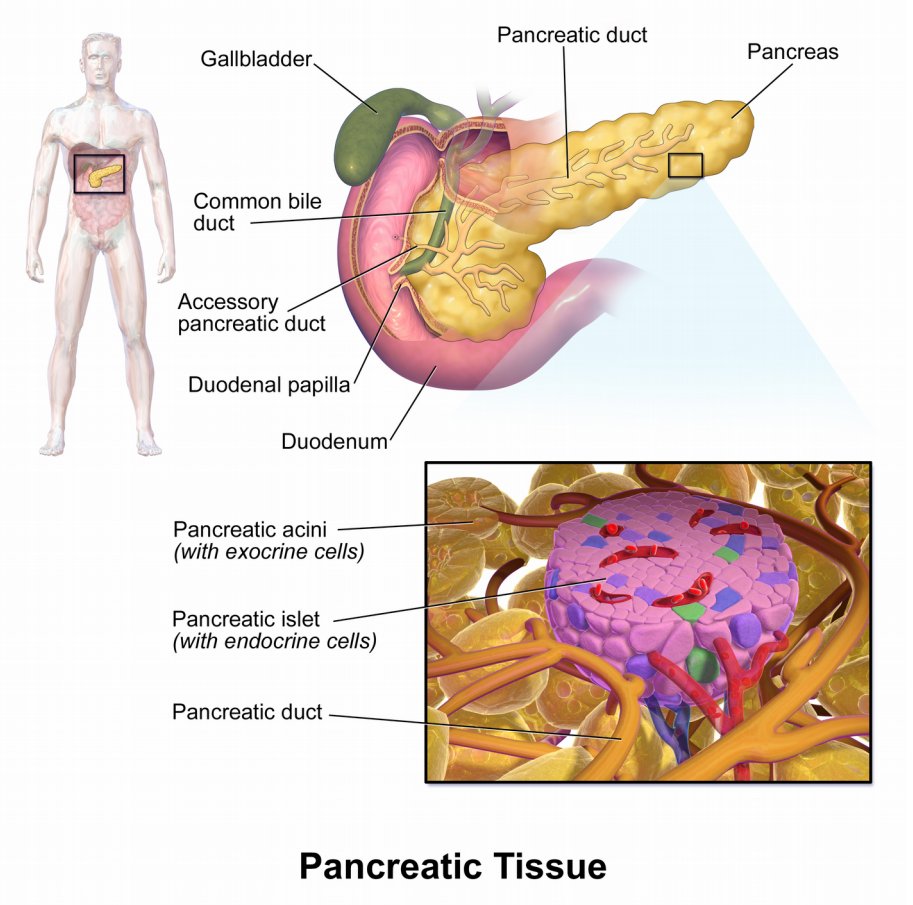


Pancreas: crucial digestive organ

Nestled in the duodenum (first part of SI)

Secretes amylase, lipase and protease into duodenum (exocrine)

Secretes insulin and glucagon into blood from islands of tissue studded within pancreas (endocrine)



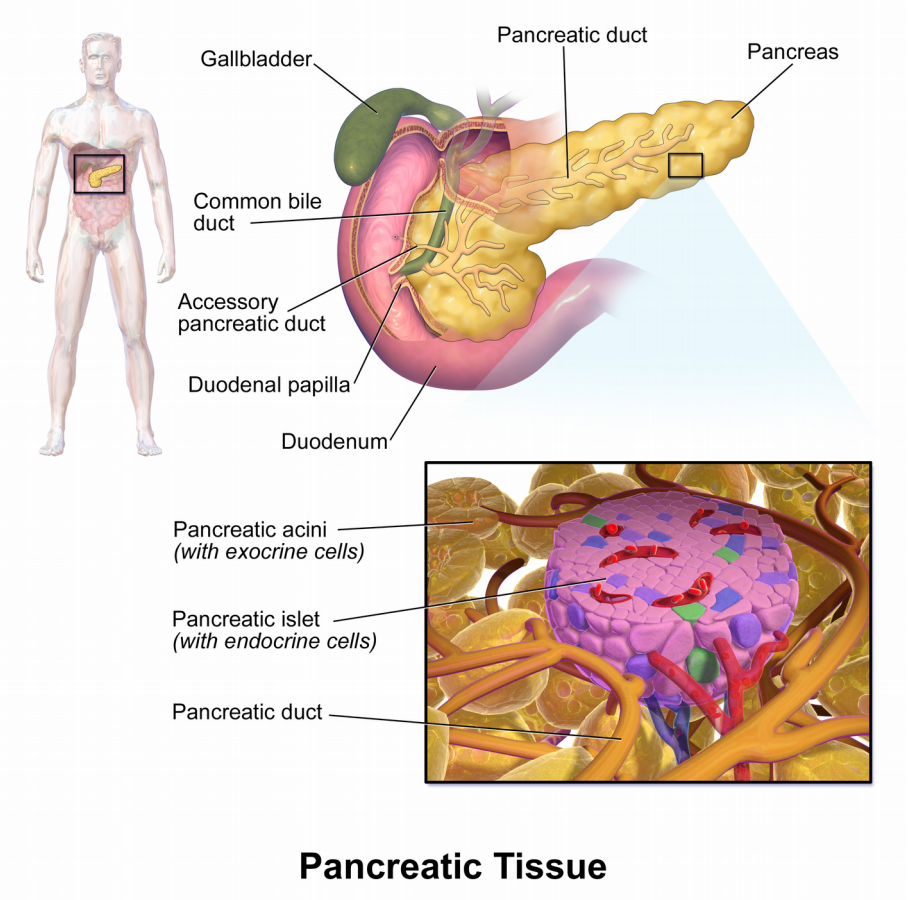
Pancreatic Tissue

Rising Glucose → Insulin release

Blood passes through pancreas

Islets within pancreas contain specialized cells for regulating glucose

Rising glucose level stimulates insulin secretion from pancreatic islet beta cells into the blood



Pancreatic Tissue

Glucose and insulin

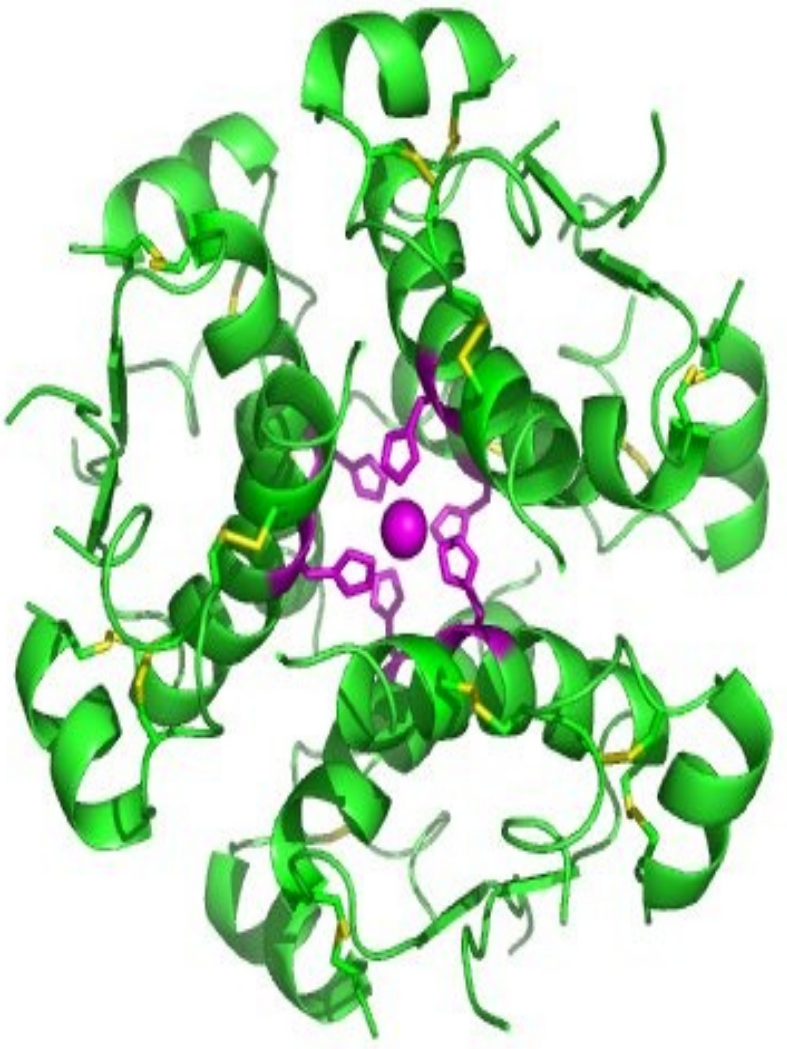
Insulin is the master control molecule to regulate blood glucose level

Polypeptide (i.e., protein) of 51 amino acids in its monomer active form

Diagram shows storage hexamer (six units) form; greater stability

Monomer secreted by pancreas islet cells in response to rising glucose

Signals liver, muscles and fat cells to remove glucose from blood



Insulin effect on fat and muscle

Insulin binds to insulin receptor on liver, fat and muscle cells

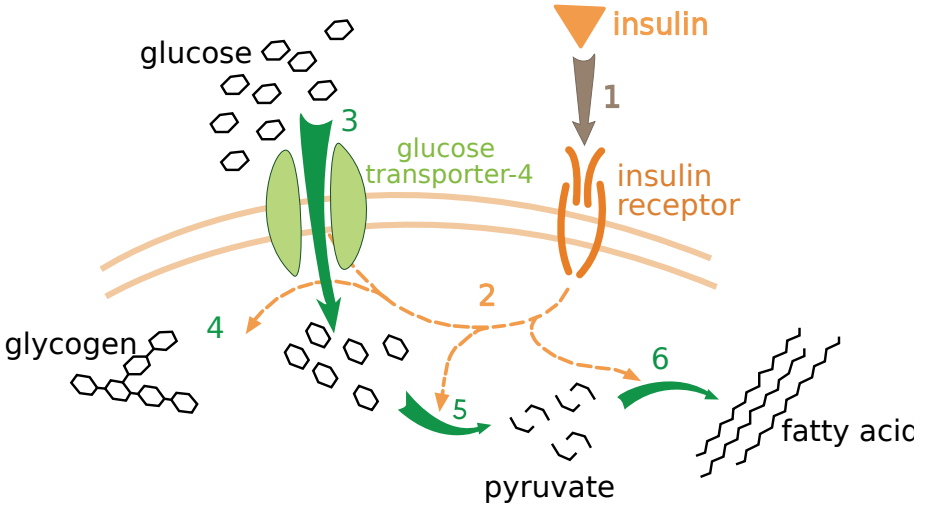
Activates glucose transporter to promote glucose uptake

Removing glucose from blood lowers glucose level

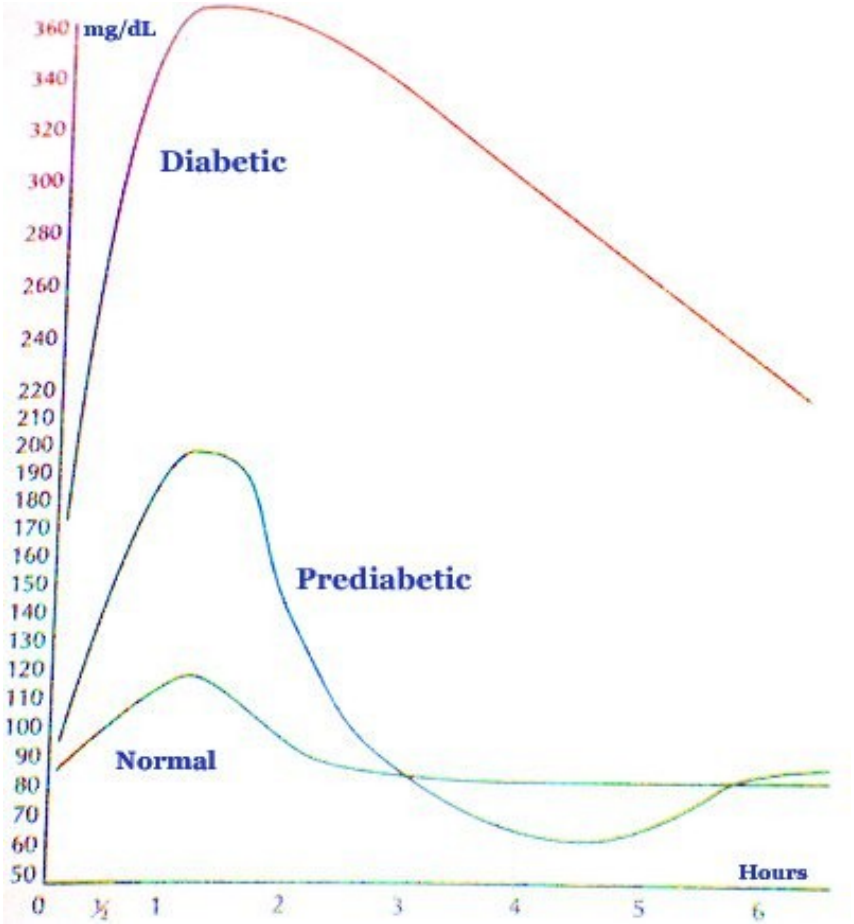
Glucose is converted into glycogen for storage in liver

Glucose is converted into fatty acid for storage in fat cells

Glucose is used as the energy supply in muscle and brain



Blood glucose following a meal

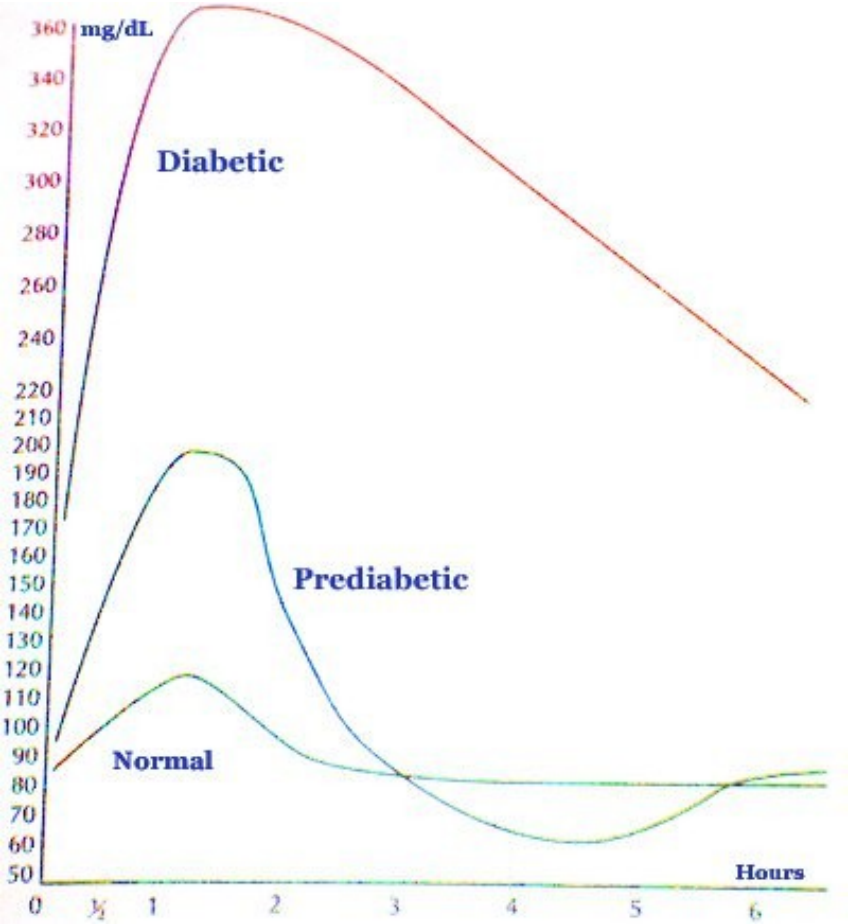


Normal individual has a modest increase in blood glucose, peaking about one hour and returning to normal in two to three hours

Hyperglycemia

Refers to blood glucose values that rise substantially above those in healthy individuals after a meal, or remain elevated after digestion is complete

Hyperglycemia is the defining characteristic of diabetes mellitus and prediabetes



Diabetes mellitus Type I

Type I diabetes is complete failure of insulin secretion by the pancreatic islet cells

- Immune system destroys islet cells
- Previously referred to as "juvenile diabetes"

Requires administration of insulin by injection

Prevention: No known means of prevention

Diabetes mellitus type II

Type II diabetes is insufficient insulin secretion by pancreas relative to the metabolic need for it

- Caused by chronic oversupply of dietary energy – and protein!
- Earliest result is abnormal glucose tolerance, advancing to pre-diabetes, then full-blown diabetes
- Obesity, hypertension added to hyperglycemia = "metabolic syndrome"
- Cholesterol and triglyceride abnormalities foretell increased risk of CHD, CVD

Treated initially with diet and oral medication, but "exhaustion" of pancreatic islets may eventually require insulin

Previously referred to as "adult-onset diabetes"

Prevention: Nearly 100% preventable and reversible with early detection and proper dietary intervention

Effects of hyperglycemia

Persistent blood sugar elevation is associated with dramatic increase in cardiovascular (and other) diseases

- Suspected that the elevated blood glucose itself was strong contributor to vascular disease
- Even slightly elevated blood glucose levels, not high enough to make a diagnosis of diabetes, can be harmful over time

Mechanism of hyperglycemia effects

Sugars attach to proteins at random locations

- Degrades function and viability of protein
- Process known as *glycation*
- Speed and extent are a function of blood sugar level
- Fructose and galactose much more active in glycation at a given level, but their levels are much lower except when consumption is exceptionally high (for example, lactose in milk)
- Result known as AGE (advanced glycation end-products)
- Participates in causation of vascular disease

Quantifying hyperglycemia: A1c

A measure for quantifying the degree and duration of glucose elevation was needed

Effects of elevation are related to both height of glucose elevation as well as its duration

Exposure of tissues to high glucose levels over time can be estimated by amount of glycation in red blood cell hemoglobin (glycated hemoglobin, or Hb A1c)

- Standard test for monitoring diabetes control

Carbohydrates

Links and chains of sugars

The links are monosaccharides (simple sugars, primary sugars)

- The basic building blocks
- Glucose is the most important monosaccharide

The chains

- Disaccharides – two links
- Oligosaccharides – 3-10 links
  - Soluble fiber such as fructans
- Polysaccharides - >10 links
  - Starches
  - Insoluble fibers such as lignin and cellulose

Primary sugars

There are many primary sugars (monosaccharides, simple sugars)

Only three are important from nutrition and metabolism viewpoint

Glucose

- Breakdown of starches; breakdown of complex sugars

Fructose

- Fruits are the classical source

Galactose

- Milk is the main source

Disaccharides

Disaccharides consist of two simple sugars (monosaccharides) linked together

They are sweet, thus also known as sugars

Important disaccharides

- Sucrose: Glucose-Fructose – cane sugar or table sugar
- Lactose: Glucose-Galactose – milk sugar
- Maltose: Glucose-Glucose – released in breakdown of starch in making beer or during digestion of starch

Disaccharides must be broken down into their primary sugars for absorption

- Enzymes cleave disaccharides into simple sugars

Enzymes: Matchmakers of Life

Living compounds are built up of smaller building blocks

- Proteins from amino acids, carbohydrates from sugars, DNA from bases

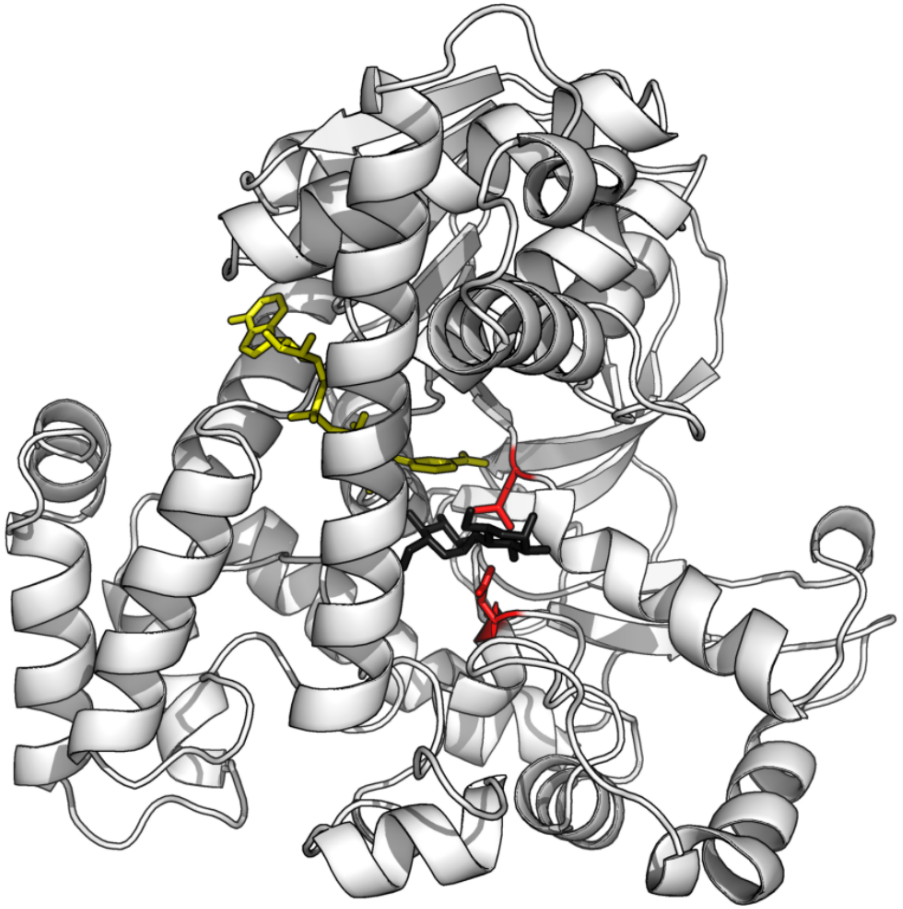
Building blocks don't automatically combine – they must be helped

- Align in proper configuration
- Apply force to combine – think "snap beads"

Enzymes are big molecules that grab onto smaller molecules, line them up, and mash them together

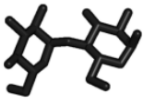
Enzymes also promote the reverse – separating a larger molecule into two or more building blocks

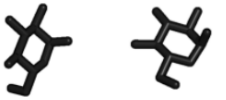
Enzymes as Matchmaker



Alpha-glucosidase

Maltose substrate





Glucose products

Digestion of disaccharides

Lactase is a special enzyme for splitting lactose (milk sugar) into glucose and galactose

Sucrase splits sucrose (table sugar) into glucose and fructose

Maltase splits maltose into two molecules of glucose

Monosaccharides, including glucose from amylase breakdown of starches, are absorbed directly by the small intestinal lining

Lactase deficiency (LD)

If you lack lactase, lactose will pass through undigested

- Microbiome may use it

Intestinal symptoms can occur, such as diarrhea, cramping and pain, in LD individuals after consuming milk products containing lactose

- This condition referred to as "lactose intolerance"

Some cheeses have insignificant amounts of lactose, due to its being consumed during fermentation

- LD individuals may tolerate such cheeses without symptoms

Lactase deficiency: a misnomer

Actually, lactase **normally** disappears after infancy in humans

- Lactase *persistence* after childhood is actually the "abnormal" (mutant) condition!

Lactase persistance is much more common in some regions, especially where milk consumption is high (Scandinavia)

Is lactase persistence good or bad for us?

- Could be good where milk is an abundant food source
- Bad if milk has adverse health consequences
  - In the dairy lecture, we will see data from Sweden strongly suggesting adverse effects suspected to arise from lactose

Nutritional Role of Sugars

Sugar as we know it today is a modern invention

- Ancestors got small amounts in fruits, accompanied by fiber
- Sucrose produced from cane and beets by elaborate industrial process is a recent development - unnatural
- High-fructose corn syrup – ditto – cheaper

Provides fuel – GOOD!

Taste yummy and give us a "high" - GOOD!

Nutritional Role of Sugars

But...

There is no nutritional requirement for sugar

- No micronutrients in sugars; a nutrition-free food

Sugar displaces valuable fiber-containing carbs – BAD!

Sugar is incompletely satiating – can't tell when to stop, thus unwittingly consume excess calories – BAD!

Sugar stimulates the brain's reward center, leading to addictive consumption in susceptible individuals – BAD!

Sugar – Yummy, but BAD! BAD! BAD!

Sugar-sweetened beverages

SSB make up a high percentage of total sugar consumption and overall energy intake

Amount consumed can be measured with relatively good accuracy – helpful in studies

Now sweetened almost exclusively with HFCS (previously sucrose)

Made up of approximately equal amounts of glucose and fructose

Sugary drinks and CHD

Sweetened beverage consumption and risk of coronary heart disease in women[1–4]

Teresa T Fung, Vasanti Malik, Kathryn M Rexrode, JoAnn E Manson, Walter C Willett, and Frank B Hu

Fung *et al* Am J Clin Nutrition 2009

Sugary drinks and CHD - NHS

Nurses Health Study

- 88,520 women ages 34-59
- No pre-existing CHD, stroke, CVD, or diabetes
- Detailed, repeated dietary histories
- Detailed accounting for confounding variables
- Follow-up of 24 years, during which 3,105 cases were observed (MI or death from CVD)

Characteristics of SSB drinkers

More smoking

Less physical activity

Less fruits and vegetables

More calories

Lower diet quality score

In other words, overall less healthy behavior

Sugary beverage and CHD

Those drinking two or more SSB per day had 93% increase in CHD

- Even 1 up to 2 SSB per day had 51% increase

Taking risk factors into account, rates of CHD remained significantly higher

- Increased 27% for 1-2 SSB, 39% for 2+

Sugary drinks and CHD

Woman drinking two or more SSB (sugar-sweetened beverages) a day were at nearly double risk of heart attack or cardiac death

Risk remained 39% higher even after accounting for other contributing factors

Fruit drinks were as bad as colas

Even one SSB was associated with a 27% increased risk

Artificial sweeteners trended toward increased risk at 2 or more servings a day but not statistically significant

Sugar consumption and mortality

Sugars and risk of mortality in the NIH-AARP Diet and Health Study[1–4]

Natasha Tasevska, Yikyung Park, Li Jiao, Albert Hollenbeck, Amy F Subar, and Nancy Potischman

American Journal of Clinical Nutrition 2014

Sugars and mortality

NIH-AARP Diet and Health Study

Subjects: 353,751 (58% men)

Followup: 13 years

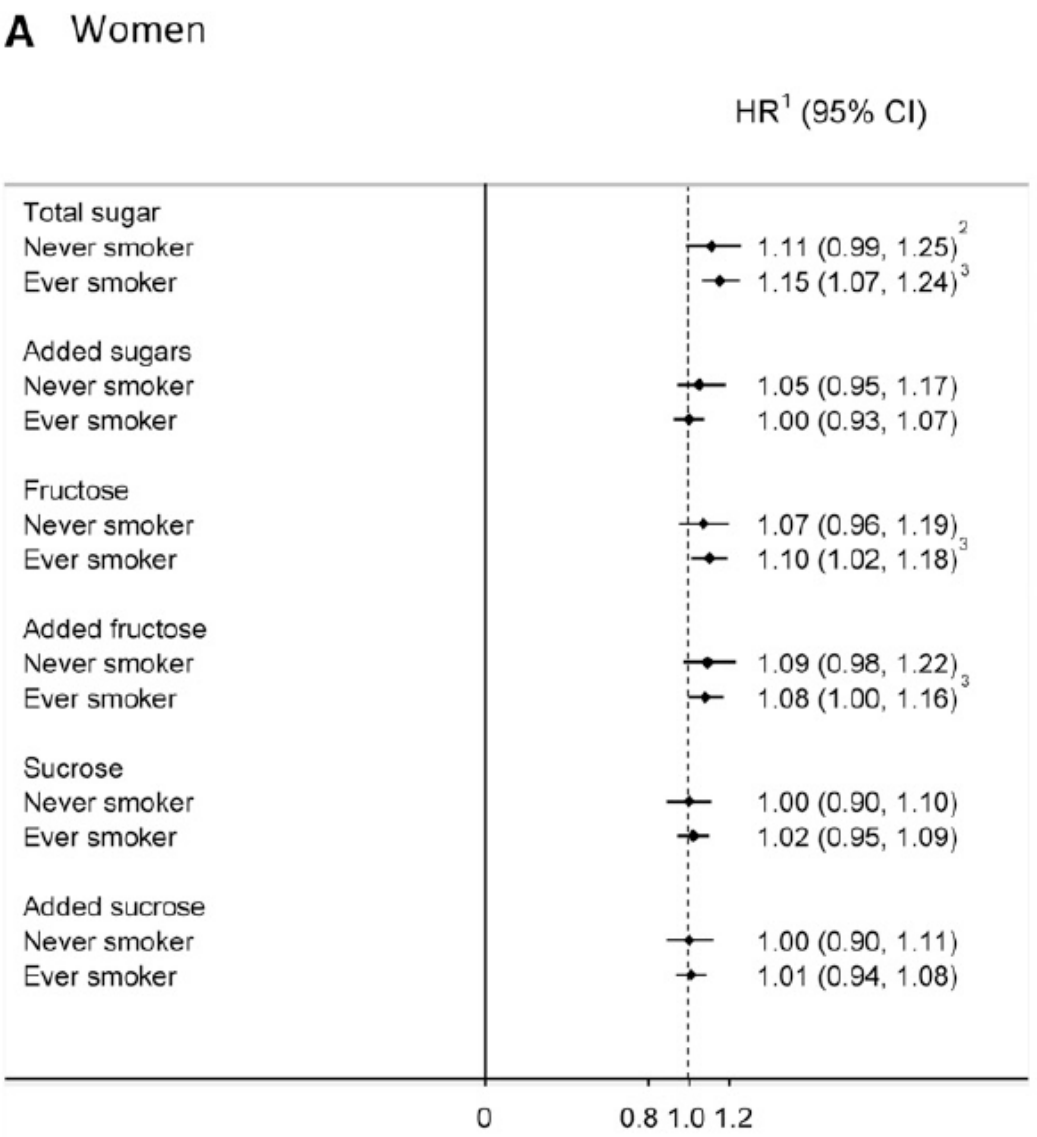
Outcome (death): 43,679 (12%)

Causes of death: Cancer 41%, cardiovascular 25%

Sugars and all-cause mortality

	Women			
	Sugars from solid foods		Sugars from beverages	
	$HR_{Q5\ vs\ Q1}$	*P*-trend	$HR_{Q5\ vs\ Q1}$	*P*-trend
All-cause[2]				
Total sugars	0.99 (0.94, 1.06)	0.85	1.05 (1.00, 1.11)	0.0008
Added sugars	0.89 (0.83, 0.93)	<0.0001	1.09 (1.03, 1.15)	<0.0001
Fructose	0.96 (0.90, 1.01)	0.10	1.09 (1.03, 1.15)	<0.0001
Sucrose	0.91 (0.86, 0.96)	<0.0001	1.07 (1.02, 1.13)	0.0007

Sugars and all-cause mortality



Sugars and all-cause mortality

NIH-AARP conclusions:

Increased mortality associated with increased fructose intake but not sucrose

Increased mortality associated with sugar intake from beverages

Measurement of sugar intake is imprecise

- Computed relative risks likely *understate* the true relative risk
- Example: A true RR of 2.0 could be observed as RR 1.20

Sugars and all-cause mortality

Perhaps most surprisingly, the NIH-AARP study fails to indict sugar as a *major* killer!

Risk ratios are modest at their worst

Amount of added sugar in foods, as opposed to beverages, actually appears to be a beneficial factor!

Starches

Starches are the polysaccharides found in "fruits" of plants

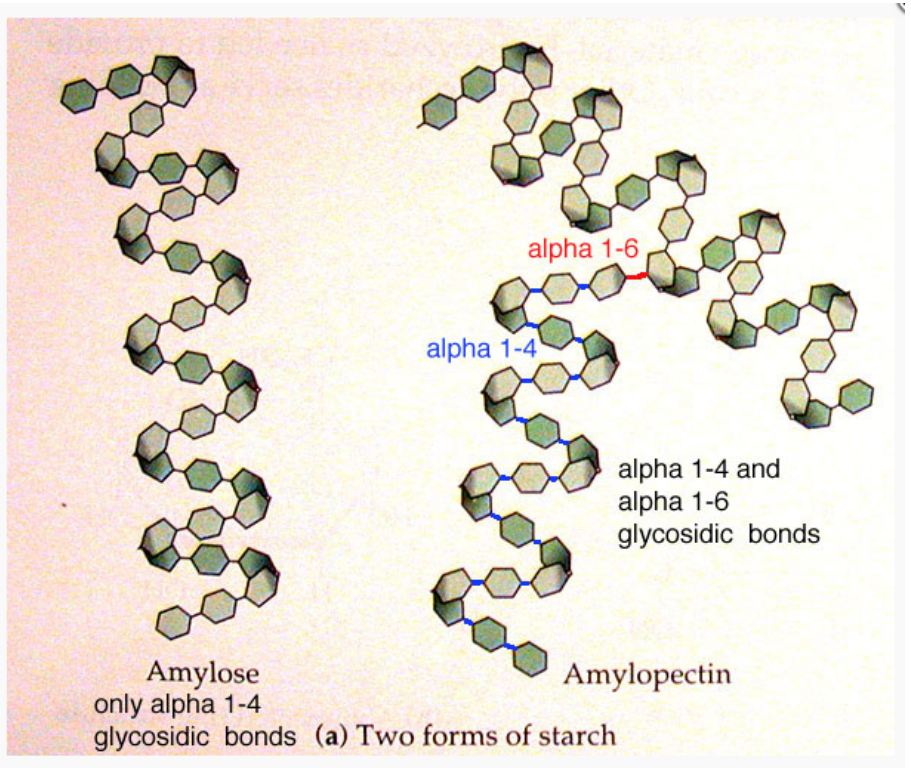
- Store energy for reproducing

Each starch molecule is typically a chain of thousands of glucose links

The chain curls up into a helix for compact storage

The glucose molecules are inaccessible for undergoing chemical reactions until they are freed from the chain

In some starches, the chain branches every so often, making side chains



Starches

Two main classes of starches are amylopectin and amylose

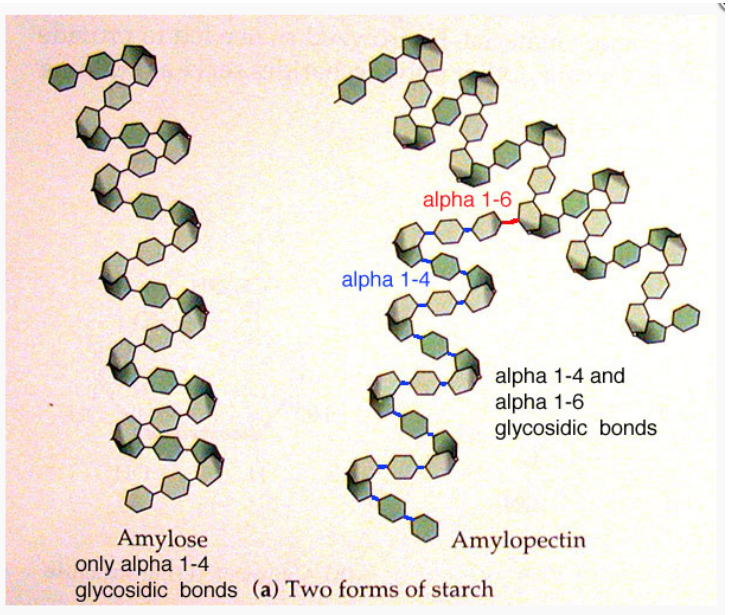
Amylopectin (70-80% of starch) is highly branched and is digested rapidly, into maltose and glucose

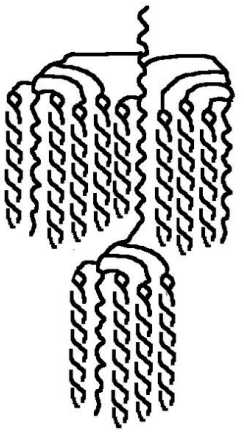
Amylose (20-30% of starch) is an unbranched helix, digested slowly, into maltose and oligosaccharides

- "Resistant starch"

Different strains of plants have different proportions of amylose and amylopectin

- For example, high-amylose rice has more amylose relative to amylopectin





Amylopectin

Digestion of starches

Amylase is the enzyme that cleaves amylose and amylopectin into mono-, di- and oligosaccharides

Amylase is secreted in saliva and in pancreatic juices

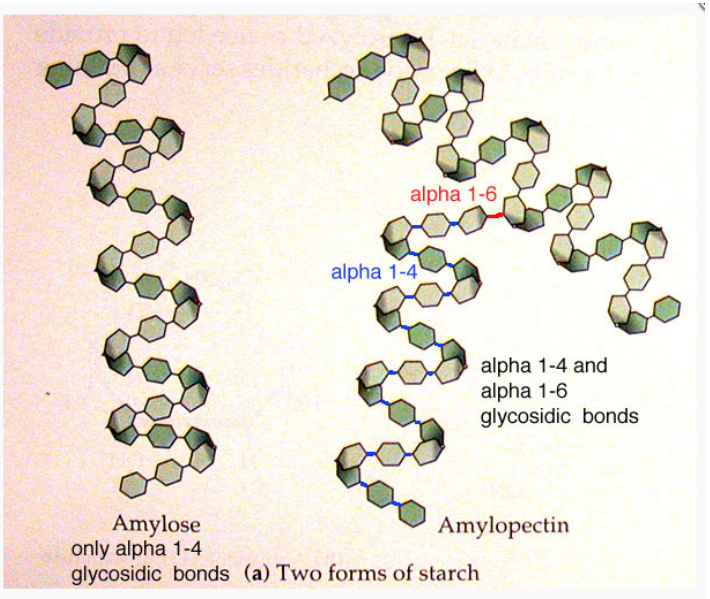
Amylopectin (70-80% of starch) is digested rapidly

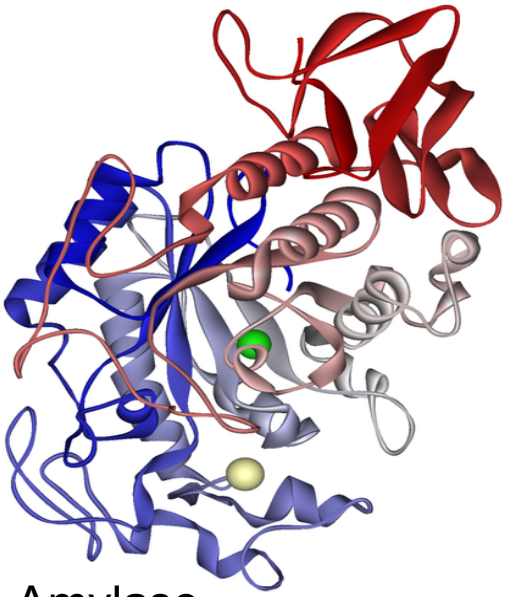
- High glycemic index – rapid rise in blood glucose and insulin

Amylose (20-30% of starch) is digested slowly

- Low glycemic index – more slowly absorbed, with slower rise in blood glucose and insulin

Sugars released are absorbed in small intestine





Amylase

Fiber: Residual Carbohydrates

Oligo- and polysaccharides that cannot be digested pass into the colon, referred to as "fiber"

- Misnomer, since many are small molecules and not literally strands of material implied by the name

In the colon, bacteria consume some of them

- Important, beneficial byproducts are produced

The remainder passes into the stool unchanged

Types of dietary fiber

- Insoluble fiber
  - Cellulose, hemicellulose, lignins, others
  - Passes out of colon intact, binds bile salts, adds bulk to stool
- Soluble fiber
  - Feedstock for intestinal micro-organisms ("gut microbiome")
  - Products of fermentation include many compounds that are beneficial to the colon and body: short-chain fatty acids providing energy, immune signaling, psychoactive compounds

Soluble fiber

- Fructans (polymers of fructose)
  - Inulin (chickory, Jerusalem artichoke, many others)
  - Fructose oligosaccharides (FOS)
- Pectin (polymers of glucuronic acid)
  - Apples, citrus peels
- Raffinose (trisaccharide galactose-glucose-fructose)
  - Legumes, leafy vegetables
  - Bacteria digest, produce gas
  - Alpha-galactosidase (Beano) splits to galactose and sucrose
- Alginic acids
  - Algae

Sources of dietary fiber

- Whole grains
  - Wheat, barley, quinoa, rice, corn, aramanth, ...
  - Fiber is in the bran, the hull of the kernel
  - Processed grains have the fiber removed
- Fruits
- Vegetables
- Pulses (AKA legumes, beans)
- Nuts
- Seeds

Fiber ca. 1960's knowledge

- Useful for treating constipation, irritable bowel, and similar intestinal problems
- Adjunct for lowering cholesterol level by removing bile salts before they recirculate
- Psyllium seed (Metamucil) was the main preparation recommended; inulin, dextran
- Fruits and vegetables contain substantial amounts of fiber, and we know they are good for us
- Fiber slows intestinal absorption, reducing glucose spikes and resulting insulin spikes
- Beans are "good for the heart", but are hard to digest and bring on undesirable side effects ("the musical fruit")

Fiber ca. 2016 knowledge

- Fiber feeds our gut microbiome
  - The human "meta-organism": human + microbiome
  - Gut microbiome considered by some to be an endocrine organ
  - Food for our microbiome given the name "prebiotics"
- The quality of what we feed our microbiome is a key determinant of how well it functions on our behalf
  - More about the microbiome and its functions in a later session

Vegetarianism and fiber

- The emergence of the vegetarian diet and its apparent health benefits focused attention on fiber
  - Seventh Day Adventists were major adherents of vegetarian diets
  - Longevity was somewhat greater in Adventists than the general population
  - Loma Linda University, in the heart of California Adventist population, began systematic study of disease incidence and mortality relative to diet in 1950s with the support of the NIH
  - Fiber is a major aspect of plant-based foods

Fiber and mortality

- Early studies linked high fiber intake to lower rates of metabolic diseases (diabetes) and coronary heart disease
  - Reports in 1970s by Hugh Trowell and Denis Burkett about African Bantu, in contrast to Westerners
- First studies to go beyond effects of fiber on heart disease to effects on overall mortality emerged around 2000
  - Scottish Heart Health Study
  - Zutphen Study (Netherlands)
  - Israeli study
  - All showed inverse relation between amount of fiber consumed and mortality, i.e., lower mortality with increasing dietary fiber
- NIH-AARP Study
  - Largest, most detailed to date

Fiber & mortality: NIH-AARP

Dietary fiber intake and mortality in the NIH-AARP Diet and Health Study

Yikyung Park, Sc.D[1], **Amy F. Subar, Ph.D.**[2], **Albert Hollenbeck, Ph.D**[3], and **Arthur Schatzkin, MD**[1]

[1]Nutritional Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD

[2]Division of Cancer Control and Population Sciences, National Cancer Institute, Rockville, MD

[3]AARP, Washington, DC

Park et al Arch Int Med 2011

Fiber & mortality: NIH-AARP

Invitation to participate went to half a million AARP members in 6 states and two metro areas responding to questionaire in 1995-96

219,123 men & 168,999 women eligible, ages 50-71

Follow-up 9 years avg.

Excluded: existing cancer, heart disease, diabetes, stroke

Food frequency questionaire – 124 items

Lifestyle data: Smoking, exercise, personal and family medical history, HRT, BMI, alcohol, ASA, education

Fiber & mortality: NIH-AARP

Cases

- Men: 5,248 CVD & 8,244 cancer deaths
- Women: 2,417 CVD & 4,917 cancer deaths

Deaths per 100,000 from all-cause, CVD & cancer (age-adjusted)

- Men: 991, 258, 406
- Women: 716, 153, 311

Table 1

Selected characteristics of study participants by categories of dietary fiber intake

	Men			Women		
	Dietary fiber intake			Dietary fiber intake		
	Quintile 1	Quintile 3	Quintile 5	Quintile 1	Quintile 3	Quintile 5
Median dietary fiber intake (g/day)	12.6	19.4	29.4	10.8	17.0	25.8
Age at baseline [a]	61	62	62	61	62	62
White, non-Hispanic (%)	92	94	91	90	91	88
College and post college (%)	38	47	53	24	32	37
Married (%)	82	87	84	42	47	45
Excellent, very good health (%)	55	62	70	50	58	65
Body mass index [a]	27.3	27.2	26.4	26.8	26.6	25.6
Vigorous physical activity, ≥3 times/wk (%)	35	49	64	27	42	58
Former smoker (%)	50	55	54	33	38	41
Current smoker (%)	22	9	4	28	12	6
Current menopausal hormone therapy use (%)	-	-	-	41	47	47
Alcohol (g/day)[a]	27	19	9	12	5	3
Red meat (g/1,000 kcal)[a]	47	40	25	38	30	18
Total energy intake (kcal/day)[a]	2,019	2,084	1,969	1,565	1,573	1,524

[a]Mean values

Fiber & mortality: NIH-AARP

Men and women who consumed more fiber

- more educated
- rated their general health higher
- smoked less
- consumed less alcohol
- ate less red meat
- lower BMI

Multivariable analysis done to adjust for the impact of these factors and isolate the specific prognostic contribution of fiber

Mortality vs. Fiber Consumption

	1	2	3	4	5
Fiber (g/d)	12.6	16	19.4	24.4	29.4
Number	43825	43825	43825	43825	43825
Deaths expected	5278	5278	5278	5278	5278
Deaths observed	5278	4292	3898	3453	3205
Observed / expected	100%	81%	74%	65%	61%

Men who averaged 29.4 grams of fiber a day had a 39% lower mortality than those averaging only 12.6 grams!

Even after accounting for other healthy habits of high fiber eaters, the fiber itself is strongly associated with longevity

Table 2

Relative risks and 95% confidence intervals of total death for quintiles of dietary fiber intake in men and

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P trend
Men (median intake, g/day)	12.6	16.4	19.4	22.9	29.4	
Death (n)	5278	4292	3898	3453	3205	
Mortality rate[a]	1391	1081	957	824	747	
Age-adjusted	1.00	0.77 (0.74–0.81)	0.68 (0.66–0.71)	0.59 (0.56–0.61)	0.53 (0.51–0.56)	<0.001
Multivariate I[b]	1.00	0.90 (0.86–0.93)	0.86 (0.82–0.89)	0.78 (0.75–0.82)	0.75 (0.72–0.79)	<0.001
Multivariate II[c]	1.00	0.94 (0.90–0.98)	0.90 (0.86–0.94)	0.82 (0.78–0.87)	0.78 (0.73–0.82)	<0.001
Smoking status[d]						
Never smokers (n=3877)[e]	1.00	0.96 (0.86–1.08)	0.96 (0.86–1.08)	0.84 (0.74–0.95)	0.81 (0.71–0.93)	<0.001
Former smokers (n=10777)	1.00	0.91 (0.86–0.97)	0.87 (0.82–0.93)	0.81 (0.76–0.87)	0.76 (0.70–0.82)	<0.001
Current smokers (n=4502)	1.00	0.99 (0.91–1.07)	0.96 (0.88–1.06)	0.85 (0.76–0.95)	0.82 (0.70–0.95)	0.003
Body mass index[f]						
<25 (n=6307)	1.00	1.00 (0.93–1.08)	0.95 (0.87–1.03)	0.86 (0.78–0.94)	0.82 (0.74–0.92)	<0.001
25–<30 (n=8961)	1.00	0.93 (0.87–0.99)	0.92 (0.86–0.99)	0.82 (0.76–0.89)	0.79 (0.72–0.86)	<0.001
≥30 (n=4148)	1.00	0.86 (0.78–0.94)	0.79 (0.71–0.87)	0.78 (0.70–0.87)	0.74 (0.65–0.84)	<0.001

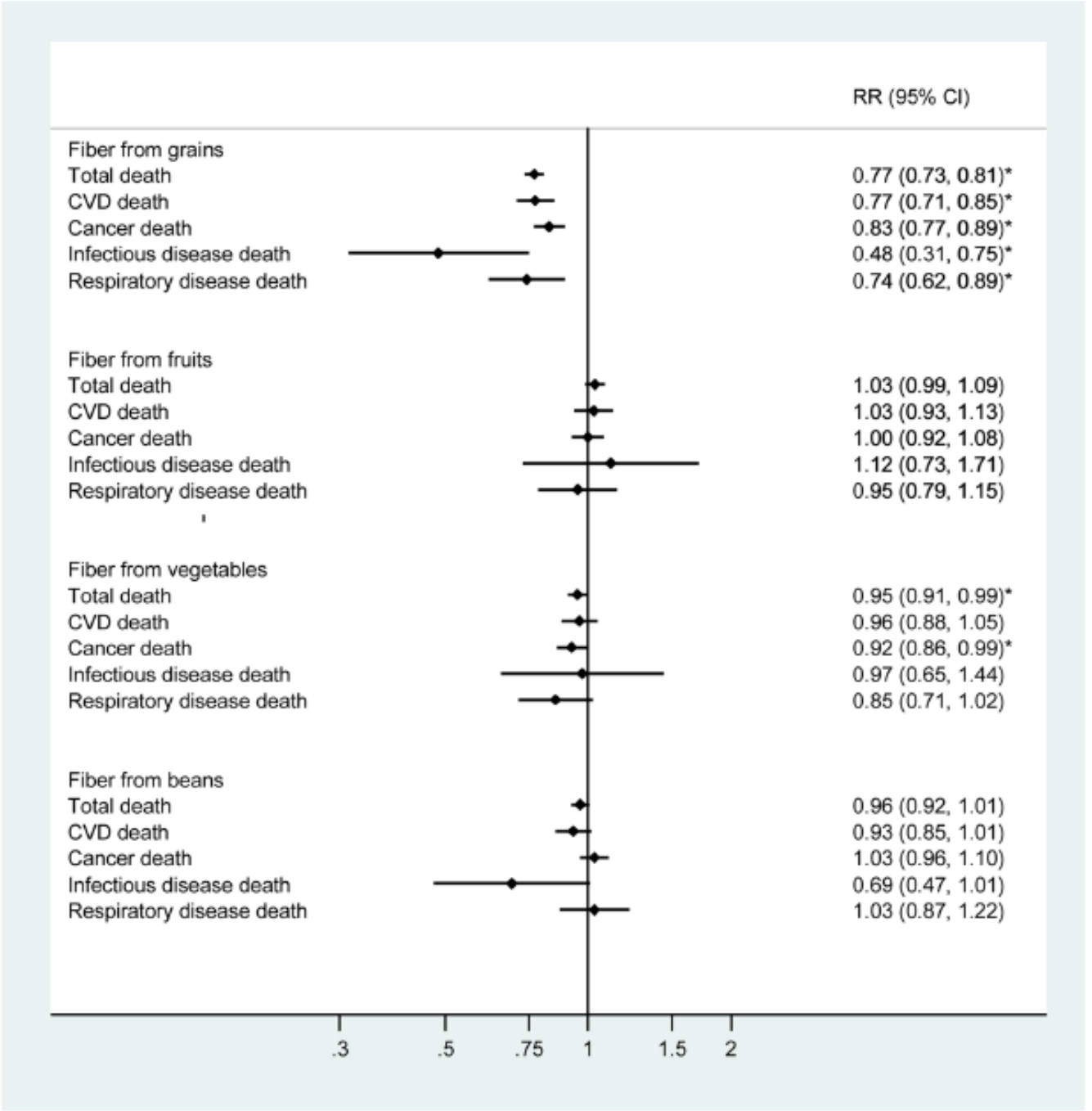
Which fiber is best?

Grains? Fruits? Vegetables? Legumes?

Conventional wisdom is that fiber from fruits, vegetables and beans is associated with the best outcomes

What does the data say?

A. men



* P-trend <0.05

Which fiber is best?

Grain fiber is associated with lower all-cause mortality, as well as specific mortality from cancer, cardiovascular disease, respiratory disease and infectious diseases

Fruit, vegetable and legume fiber had minor and statistically insignificant relationships with these outcomes

Grains (cereals)

"Cereal grains are grown in greater quantity and provide more food energy worldwide than any other crop" - Wikipedia

Corn, rice and wheat are the leading types, at 1016, 745, and 713 million metric tonnes of production annually

Corn is mostly used for animal feed, so rice and wheat are the main grains used for human consumption

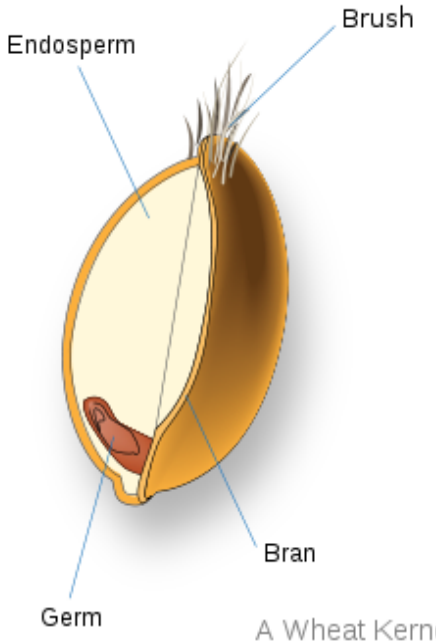
Grains are fruits

"Fruit" in this context refers to the part of a plant responsible for reproduction

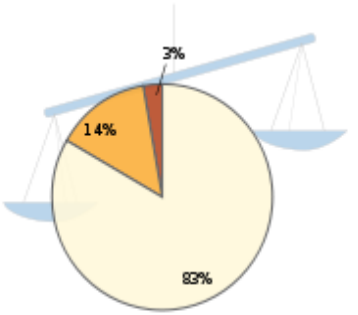
Endosperm is the starch in cereals that provides fuel as a plant germinates, before it can gather energy through photosynthesis

The fruit is the part that is readily used for animal nutrition

Grinding, cooking, etc. partially disrupt the starch to make it more digestible



A Wheat Kernel



Composition by Weight

	Carb./g	Protein/g	Fat/g	Fiber/g	Iron (% daily req.)	Others
Bran	63	16	3	43	59	vitamin Bs
Endosperm	79	7	0	4	7	
Germ	52	23	10	14	35	vitamin Bs omega-3/6 lipids

Nutritional Value (per 100g)

Grain use history

Humans were hunter-gathers until civilization brought agriculture

Planting & harvesting grains gave more certainty and used less time & effort

- Freed up labor for construction, etc.

Refining wheat to remove germ and bran was developed BCE, but was so labor intensive that only wealthy families could afford it

- White baked goods were a status symbol

Industrial revolution brought white flour to the masses

- White flour foods became dominant
- Whole grain cereals and baked goods were "off the table"

We have come full circle: whole grains are back among the cognoscenti

What is whole grain?

Grain

- Small, hard, dried seeds, with or without their attached hull or fruit layers, harvested for human consumption
- Cereals and pulses (legumes, "beans")

Whole

- In contrast to refined grains, where the starchy endosperm is used exclusively after separation from the germ and bran
- May refer to grinding and using the entire grain, or separating the components and putting them back together in the end product
- Is the whole greater than the sum of its parts?

Examples of whole grain

Table 3 Examples of whole grain foods and flours

Amaranth
Barley
Buckwheat
Corn *(whole cornmeal, popcorn)*
Millet
Oats *(oatmeal)*
Qinoa
Rice *(brown rice)*
Rye
Sorghum *(or milo)*
Teff
Triticale
Wheat *(varieties include spelt, emmer, farro, einkorn, Kamut®, durum; forms include bulgur, cracked wheat, and wheatberries)*
Wild rice

When consumed in a form retaining the bran, germ, and endosperm components. Source: The Whole Grains Council (http://www.wholegrainscouncil.org).

Whole grain: + and -

Advantages

- Fiber from bran – improves blood cholesterol profile, digestive regularity
- Vitamins, protein & fat from germ
- Phytosterols, other possible "goodness"
- Slows absorption of carbs; lowers glycemic index

Disadvantages

- Goes rancid sooner; shorter shelf life
- ? less digestible (bloating, abdominal cramps)

Whole grain: legal definition

Each country has its own definition of what the content must be to be labeled "whole grain"

- In Canada, product may have 70% of germ removed and still be labeled WG

"100% whole grain" means just that

NIH-AARP
Whole Grain & Mortality

Huang *et al. BMC Medicine* (2015) 13:59
DOI 10.1186/s12916-015-0294-7

BMC Medicine

RESEARCH ARTICLE Open Access

Consumption of whole grains and cereal fiber and total and cause-specific mortality: prospective analysis of 367,442 individuals

Tao Huang[1], Min Xu[1], Albert Lee[2], Susan Cho[3] and Lu Qi[1,4*]

NIH-AARP WG & Mortality

Subjects: 367,442 (44% female, 50-71 yrs)

Followup: 14 yrs (1995-2009)

Deaths: 11,283 CVD; 19,043 Ca; 3,796 respiratory; 371 diabetes; 922 infection; 5,223 other (46,067 total, 12.5%)

Food frequency questionaire: 124 items calibrated by 24 hour food recall

Covariates: Age, sex, BMI, physical activity, cigarette smoking, education, marital status, alcohol intake, hormone replacement, consumption of red meat, fruits, vegetables

NIH-AARP WG & Mortality

One serving of whole grain defined as 1 oz. (28 gm)

Average intake from quintile 1 to quintile 5 was 0.13, 0.30, 0.47, 0.69 and 1.20 servings per day, respectively

NIH-AARP WG & Mortality: Risk factors

	Quintile 1 (lowest WG)	Quintile 5 (highest WG)
Physical activity, vigorous or moderate	41%	55%
Current smoking	21%	8%
Obesity	23%	17%
Alcohol	33 g/d	9 g/d
Red meat	3.1 servings/d	1.7 servings/d

Those who consume more WG exercise more, consume less red meat, smoke less, and have less obesity, all associated with lower mortality

NIH-AARP WG & Mortality

	Unadjusted		Adjusted	
	Relative risk	% change	Relative risk	% change
All causes	0.61	-39	0.83	-17
Cardiovascular	0.60	-40	0.83	-17
Cancer	0.61	-39	0.85	-15
Diabetes	0.37	-63	0.52	-48*
Respiratory	0.45	-55	0.89	-11*
Infection	0.57	-43	0.77	-23*
Other	0.72	-28	0.86	-14*

Mortality for quintile 5 (highest) vs. quintile 1 (lowest) level of **whole grain** consumption

P<0.0001, except * 0.02<p<0.0009

NIH-AARP WG & Mortality

	Relative risk	% Change	p
All causes	0.94	-6	0.002
Cardiovascular	0.95	-5	0.19
Cancer	0.93	-7	0.025
Diabetes	0.57	-43	0.029
Respiratory	1.03	+3	0.67
Infection	0.89	-11	0.54
Other	0.98	-2	0.54

Mortality for quintile 5 (highest) vs. quintile 1 (lowest) level of **whole grain** consumption after accounting for **cereal fiber**

NIH-AARP WG & Mortality: Conclusions

Whole grain intake is strongly inversely associated with mortality: all causes, cardiovascular disease, cancer, diabetes, respiratory disease, infection and other

Association attenuated – but not abolished - after accounting for better lifestyle factors correlated with WG consumption: fewer smokers, greater physical activity, more desirable BMI, less red meat consumption

NIH-AARP WG & Mortality: Conclusions

Whole grain intake association with mortality is markedly attenuated after adjusting for quantity of cereal fiber (except for diabetes)

This finding suggests that the mechanism of the beneficial effect of WG intake on mortality is mainly by way of its fiber content (except for diabetes)

NHS-HPFS WG & Mortality

JAMA Intern Med. 2015 March ; 175(3): 373–384. doi:10.1001/jamainternmed.2014.6283.

Whole Grain Intake and Mortality: Two Large Prospective Studies in U.S. Men and Women

Hongyu Wu, PhD[1], **Alan J. Flint, MD, ScD**[1], **Qibin Qi, PhD**[2], **Rob M. van Dam, PhD**[3], **Laura A. Sampson, RD**[1,4], **Eric B. Rimm, Sc.D**[1,4,5], **Michelle D. Holmes, MD, DrPH**[4,5], **Walter C. Willett, MD, DrPH**[1,4,5], **Frank B. Hu, MD, PhD**[1,4,5], and **Qi Sun, MD, ScD**[1,4]

NHS-HPFS WG & Mortality

	Subjects	Years F/U	Deaths
Nurses Health Study	74,341	26	15,106
Health Professionals Followup Study	43,744	24	11,815

Food frequency questionaire

- Intake of WG according to dry weight
- Serving = 1 oz = 28 g

Covariates: Medical history, BMI, lifestyle (smoking, physical activity), alcohol, alternative healthy eating index

NHS-HPFS WG & Mortality: Risk Factors

	NHS		HPFS	
	Quintile 1 (lower WG)	Quintile 5 (higher WG)	Quintile 1 (lower WG)	Quintile 5 (higher WG)
Whole grain (g/d)	4	36	6	53
Smoking %	37	15	18	4
Alcohol (g/d)	9	5	15	8
Physical activity (MET-hr/wk)	11	16	18	26
Alternative Healthy Eating Index	43	50	46	55

Those who consume higher amounts of WG are less likely to smoke cigarettes, exercise more, eat healthier foods and consume less alcohol

NHS-HPFS WG & Mortality Results

	NHS	HPFS	Pooled
Unadjusted			
All cause	0.49	0.62	0.54
Cardiovascular	0.46	0.58	0.52
Cancer	0.60	0.67	0.63
Adjusted			
All cause	0.88	0.95*	0.91
Cardiovascular	0.86	0.84	0.85
Cancer	0.99*	0.95*	0.97*

Mortality relative risk for quintile 5 (highest WG) vs. quintile 1 (lowest WG)

P<0.002 except * p>0.05

NHS-HPFS WG & Mortality: Bran and germ

Analysis for cardiovascular death in relation to total bran intake and total germ intake

No relationship between total germ intake and CVD mortality

Relative risk for CVD mortality was 0.80 for quintile 5 (highest) vs. quintile 1 (lowest) of total bran consumption in NHS and HPFS, $p<0.001$

NHS-HPFS WG & Mortality: Conclusions

There is a significant inverse relationship between amount of whole grains consumed and mortality, especially cardiovascular disease mortality

No relation was found between cancer mortality and WG consumption level after adjusting for risk factors (for example, cigarette smoking)

Bran, but not germ, consumption level was also inversely related to cardiovascular mortality

WG & Mortality Meta-analysis

Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: systematic review and dose-response meta-analysis of prospective studies

Dagfinn Aune,[1, 2] NaNa Keum,[3] Edward Giovannucci,[3, 4, 5] Lars T Fadnes,[6] Paolo Boffetta,[7] Darren C Greenwood,[8] Serena Tonstad,[9] Lars J Vatten,[1] Elio Riboli,[2] Teresa Norat[2]

BMJ 2016; 353:i2716

WG & Mortality Meta-analysis

Studies: 45 cohorts – 20 EU, 16 US, 9 Asia

Subjects: 245,012-705,253

Events: 100,726 deaths; 34,346 cancer cases, 26,243 CVD cases, 7,068 CHD cases, 2,337 CVA cases

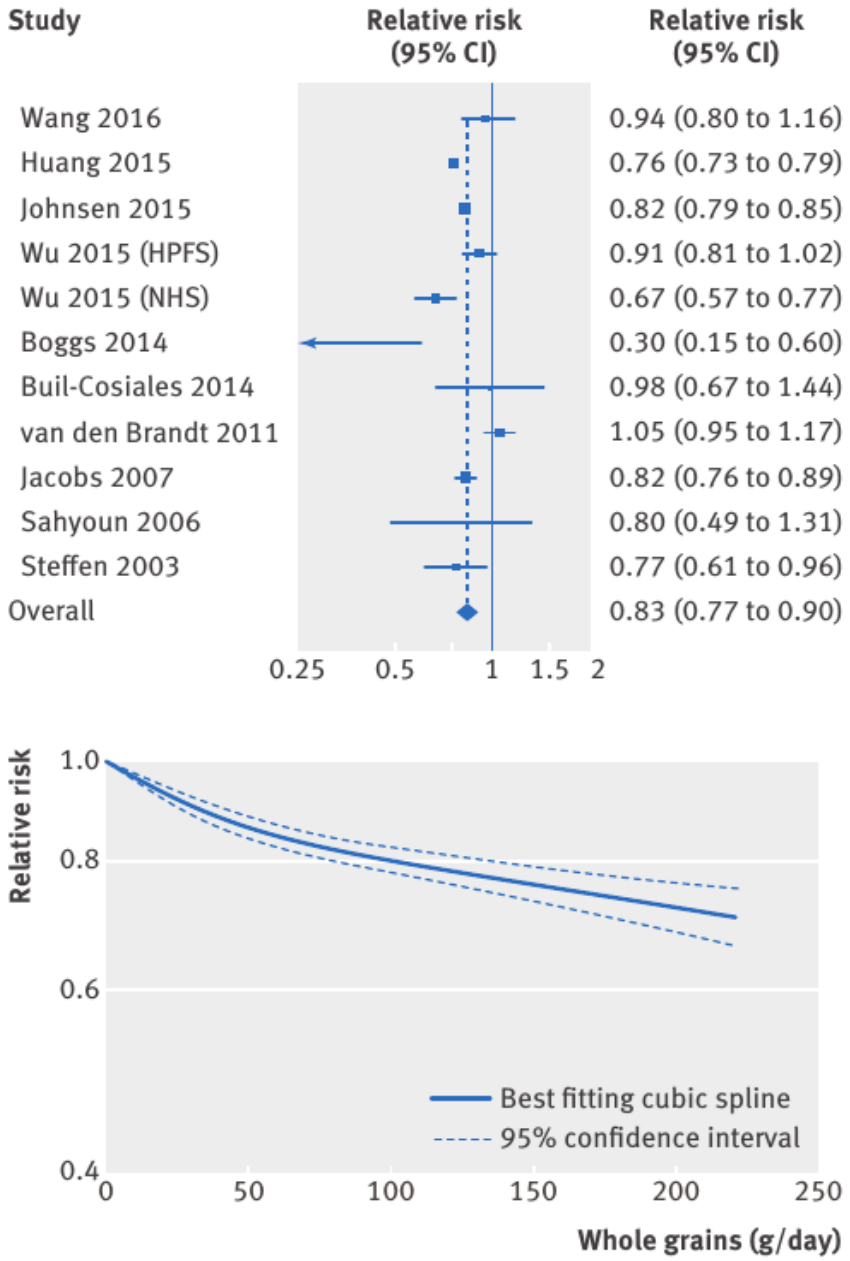


Fig 6 | Forest plot for consumption of whole grains (per 90 g/day) and risk of all cause mortality, with graph illustrating non-linear response

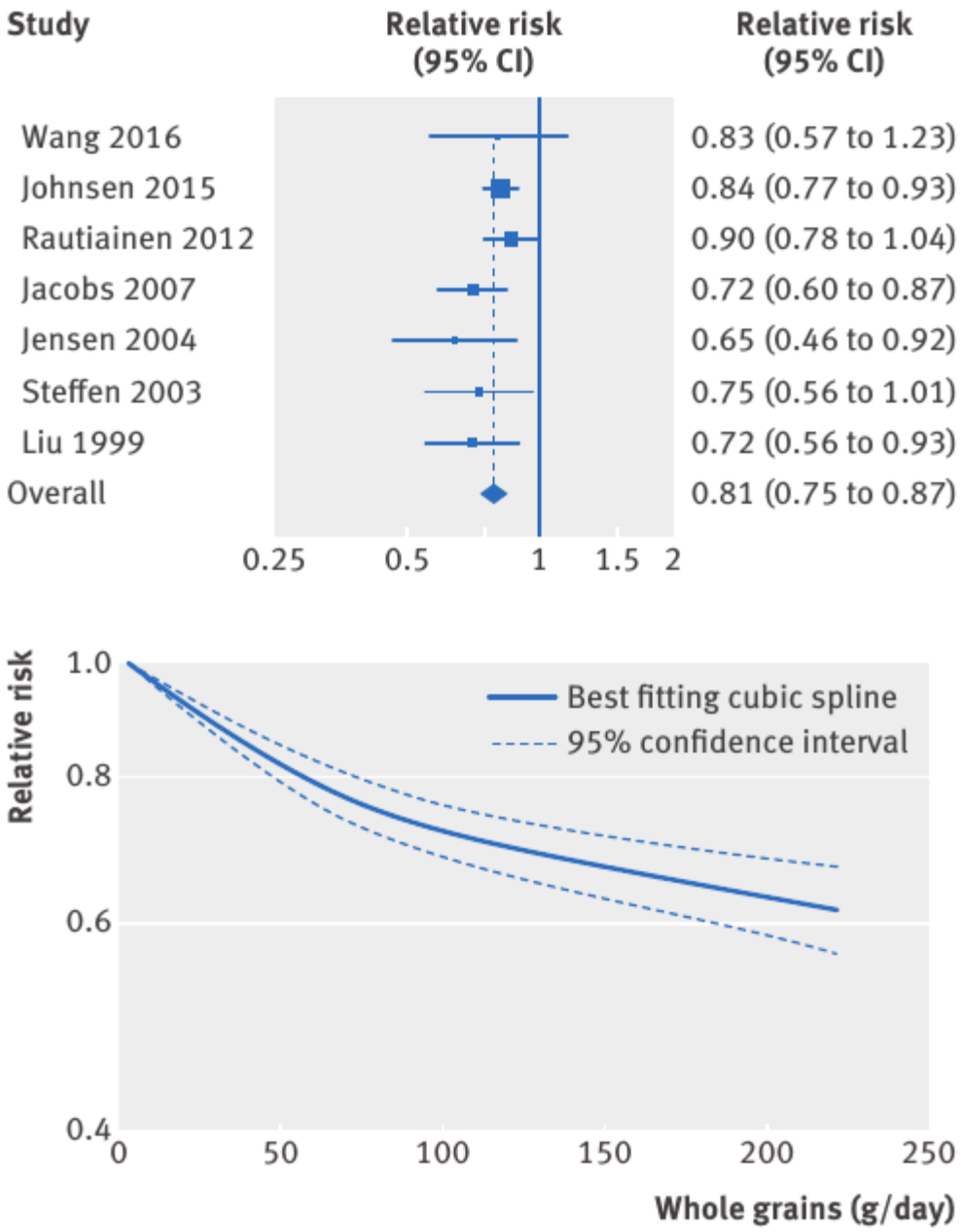


Fig 2 | Forest plot for consumption of whole grains (per 90 g/day) and risk of coronary heart disease, with graph illustrating non-linear response

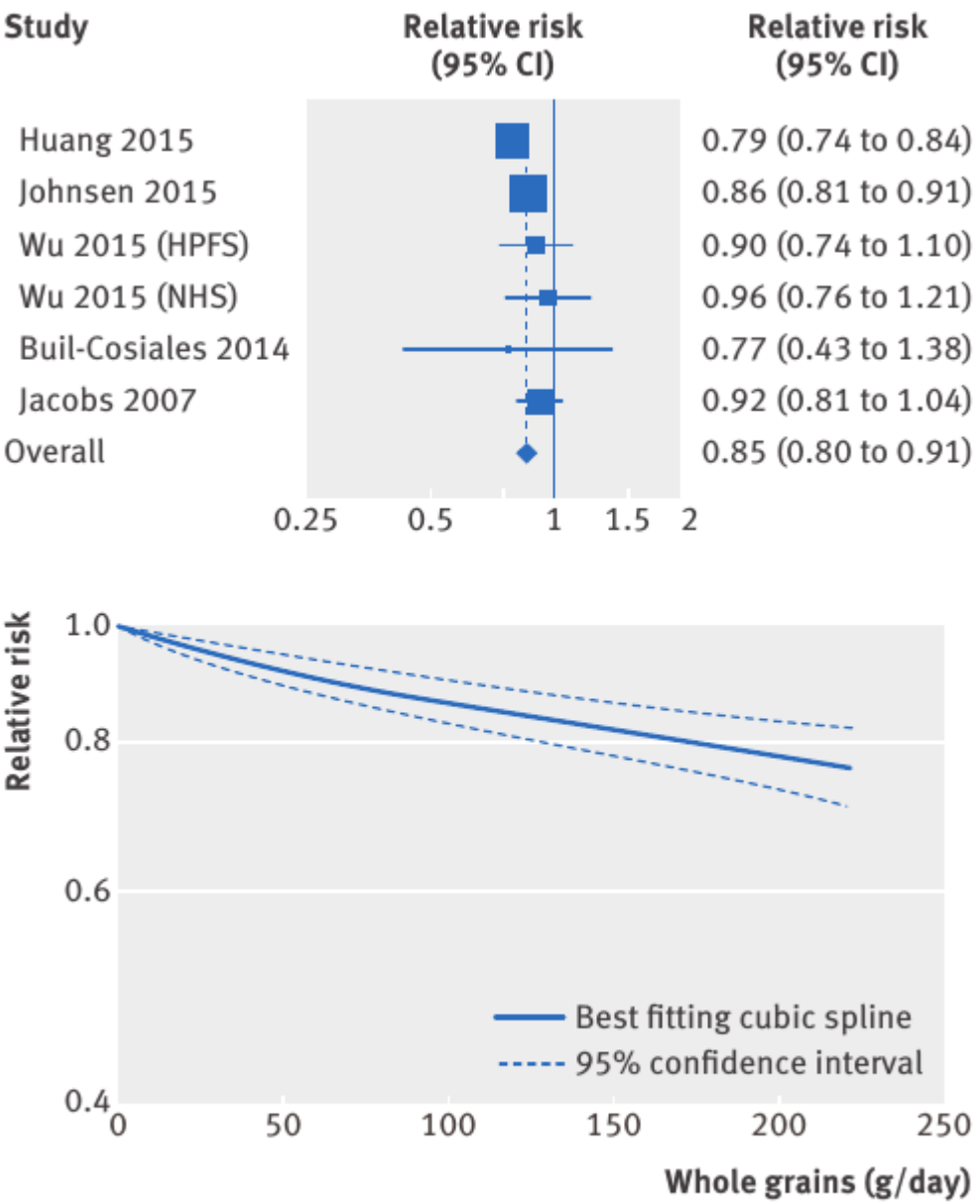


Fig 5 | Forest plot for consumption of whole grains (per 90 g/day) and risk of total cancer, with graph illustrating non-linear response

Whole grain & CVD: Mechanisms

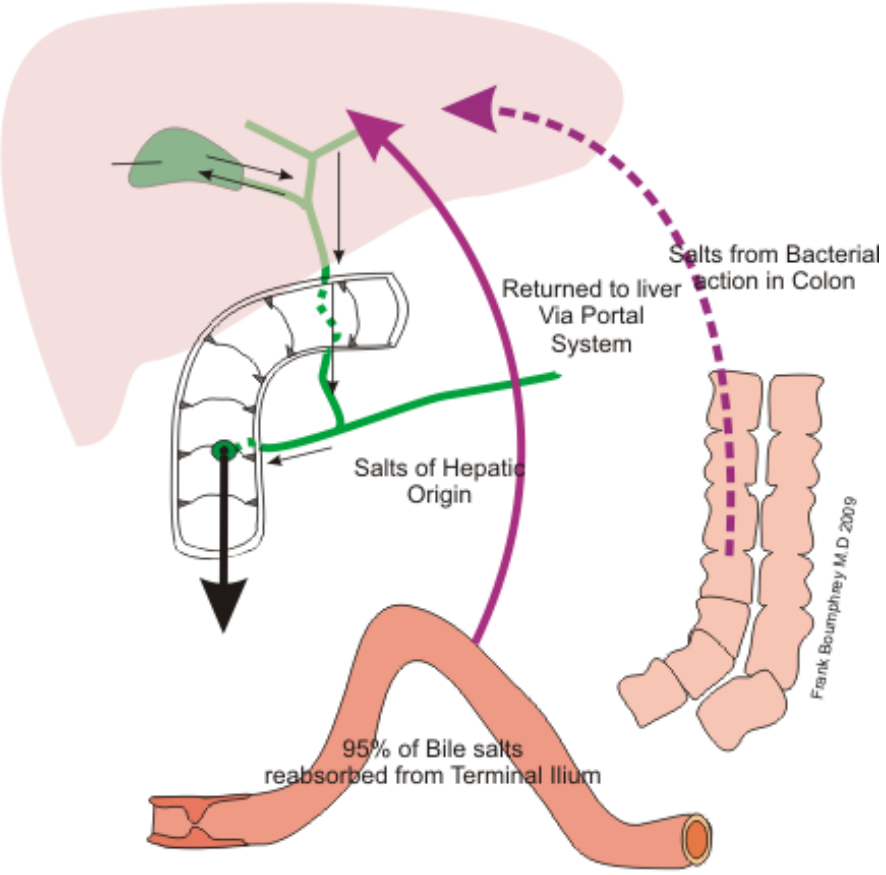
Glucose absorption and metabolism

- Lower GI/GL; reduced insulin response, exposure to elevated glucose level
- Reduces insulin resistance, diabetes, metabolic syndrome

Whole grain & CVD: Mechanisms

Fiber

- Binding of bile salts in intestine, causing greater loss in stool and interrupting enterohepatic bile circulation
- Reduces amount of cholesterol available for LDL synthesis
- More favorable lipid pattern
- Feeds the microbiome, which provides many services



Enterohepatic circulation of Bile salts

Whole grain & CVD: Mechanisms

Improved endothelial cell function

Phytosterols

Antioxidents

Lower blood pressure

Lower homocysteine

Whole grains & health: Conclusions

Increasing whole grain consumption has been correlated with lower rate of all cause mortality, CVD, primarily CHD, in men and women, cancer, respiratory, infectious and other death

Effectiveness seems concentrated in whole grain breakfast cereals and bran; brown rice and wheat germ to lesser extent

Short-term feeding studies demonstrating effect on CVD markers negative thus far

Fiber is the major contributor to health benefits of WG

Dose-response relation of lower mortality maintained out to 210 gm/d (7 servings) for most specific causes, as well as all cause mortality

Whole grains: Recommendations

Make whole grain breakfast cereal a regular feature in your diet

Fiber content is a major benefactor, so should be maximized

Select whole grain products with an eye on their glycemic index

- Not as easy as it sounds, since GI/GL data on U.S. products not easy to come by
- However, in general, it seems certain foods, such as pasta, are relatively low GI, especially if cooked *al dente*

Whole grains: Recommendations

No health outcome basis on which to limit dietary whole grain intake; on the contrary, the more the better, up to seven servings a day

Finding Whole Grain Foods

THE BASIC STAMP

THE 100% STAMP

Whole Grains I Eat

Post Great Grains Raisin, Dates and Pecans Cereal

Uncle Ben's Whole Grain Brown Rice

Ronzoni Healthy Harvest Spaghetti

Arnold Country 100% Whole Wheat Bread

Crunchmaster Five-Seed Multi-Grain Crackers

Wheat Thins Whole Grain Original

Fiber Rule of 10%

We get about 1000 calories / day from carbs (50% of 2000 Kcal)

That's 250 g of carbs (1000 g / 4 cal per g)

We're aiming for 25 g of fiber / day

25/250 is 10%

If we eat carbs where fiber is 10% or more of total carbs, we will get 25 g of fiber / day

- White pasta has 2 g fiber, 40 g total carb per serving → 5% fiber
- Whole grain pasta has 5 g fiber, 40 g carb per serving → 12.5% fiber
- Whole grain pasta contributes a good share, white pasta not so much

Data needed is on Nutrition Facts label on package

Gluten

Gluten – protein in wheat and some other grains; responsible for elasticity of dough

Celiac disease and related diseases

- A disease due to immune cross-reactivity to gluten
- Celiac disease when the prominent symptoms are intestinal
- Dermatitis herpetiformis when skin is primarily involved
- Gluten ataxia when nervous system is primarily involved
- Cured / prevented by avoidance of gluten-containing foods, adhering to gluten-free diet

Gluten intolerance

Some individuals do not have celiac disease but don't tolerate gluten-containing foods

- Is it the gluten, or is gluten just a companion?
- Fiber is probably responsible for many; gluten is the scapegoat

Certain influential medical writers have promoted the idea that gluten is globally bad for health

- Based on anecdotes, not solid science

Response by the public, fanned by food producers, to prefer gluten-free foods, despite unproven benefits

Risks: Insufficient dietary fiber, extra expense

The wrap on carbs

Grain based foods are readily available, inexpensive, and provide good fuel

However, it is all too easy to rely on refined carbs and sugars, resulting in deficiency of vital dietary fiber

You will obtain much benefit by making sure you get at least 25 grams or more of fiber a day, with much of it from grain foods

This, in turn, is accomplished by reading Nutrition Facts labels and choosing whole grain foods and others with at least 10% of total carbs present as fiber

The benefit comes from feeding your inner garden – your intestinal microbiome – which in turn provides you with many valuable nutrients