HIGH blood pressure/cholesterol/glucose

NOW WHAT?

Let’s Make it as
Simple as Possible - but not Simpler

And also remove most of the fear

What Would You Do?

You are approximately 45 y/o

You have been diagnosed “properly” with elevated blood pressure

You have tried non-drug measures for 6 months and still your blood pressure remains elevated

QUESTION

ABOVE What Blood Pressure Would YOU Take A Drug Every Day For The Next 5 Years?

The Overlying Concept

Objectives

1. Reframe “High” Numbers as Risk Factors, Not Diseases
Explain that high BP, cholesterol, or glucose are risk factors — not diagnoses that demand automatic treatment — and that the decision to start therapy should primarily depend on a patient’s absolute risk and preferences.

2. Use Absolute Numbers to Set Realistic Expectations
Translate relative risk reductions into absolute risk reductions and NNTs to appreciate the benefit of treatment over 5–10 years.

3. Balance Benefits Against Treatment Burden
Highlight the hidden costs of treatment — daily pills, side effects, lab visits, cost, and worry — and include these burdens when discussing options with patients.

4. Choose Medications Wisely
- Start with low doses
- Prioritize medications proven to reduce clinical events (not just surrogate marker numbers)
- Use generics and pill-splitting where appropriate to lower cost

5. Support True Shared Decision-Making
Present options neutrally, involve patients in choosing between lifestyle changes, medications, or watchful waiting, and document and respect the patient’s choice — even if it means “doing less.”

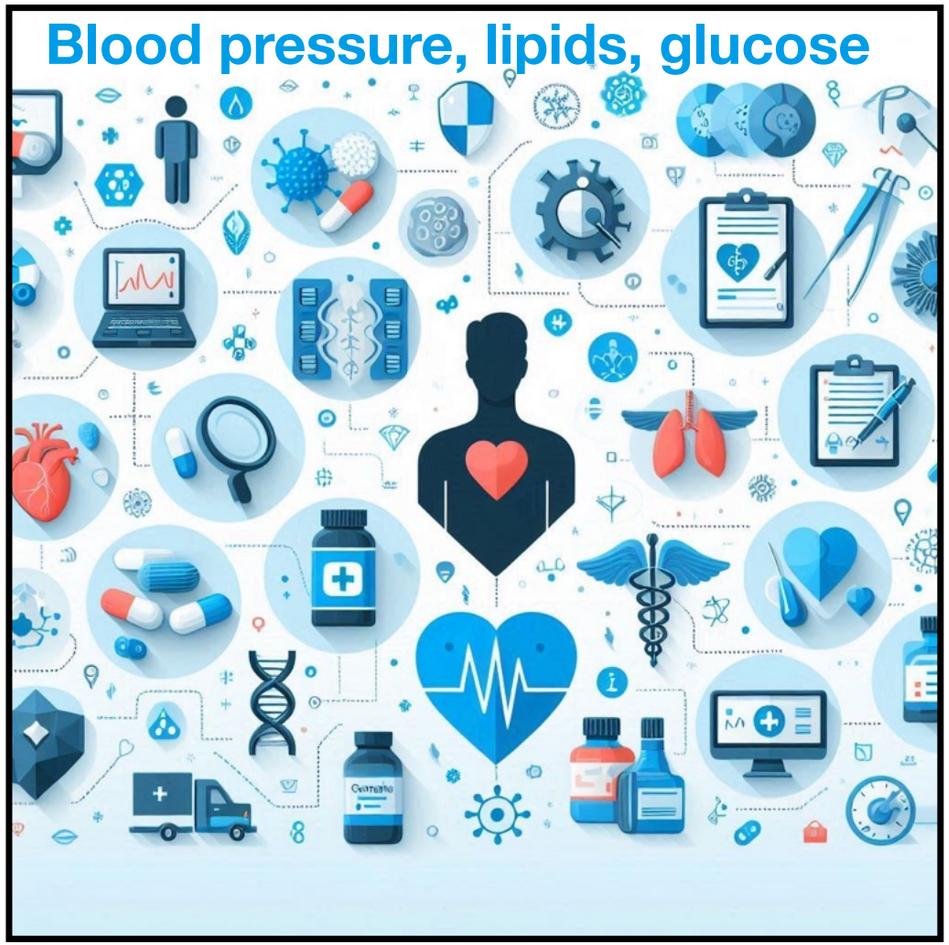
THREE PARTS

Best Available Evidence

A SHARED DECISION

Feels Like There Is A Lot To DO

Drugs, Treatments, Testing, Doctor visits, Labs



Feels Like There Is A Lot To Worry About

Risk, Worry, Fear, Heart attacks, Strokes, Death, Quality of Life

Dealing with blood pressure, lipids (cholesterol) and glucose (diabetes)

Can be a LOT simpler than you might think

MY GOAL FOR YOU

GREATER understanding

LESS worry

LESS monitoring

LOWER doses

FEWER side effects

LOWER cost

The realization that it's all **YOUR Patient's** decision, **NO ONE ELSE'S**

The BENEFIT of treatment may be quite a bit LESS than what YOU or YOUR patient might think

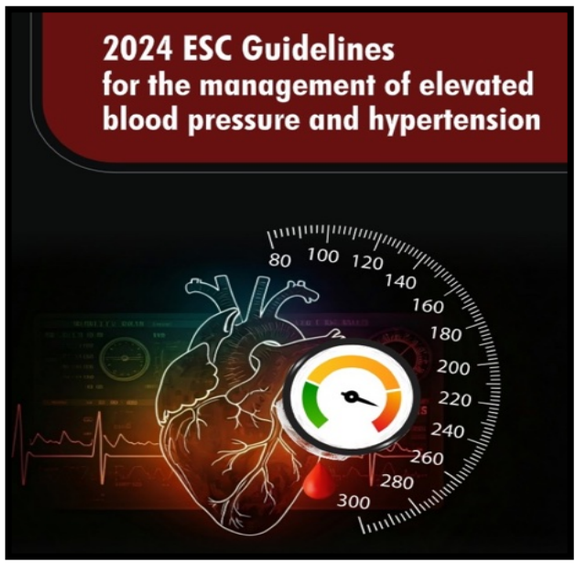
Patients and clinicians typically overestimate the benefit of treating
HIGH blood pressure/cholesterol/glucose

NOT BY JUST A LITTLE BIT - often by more than 10 times the actual benefit

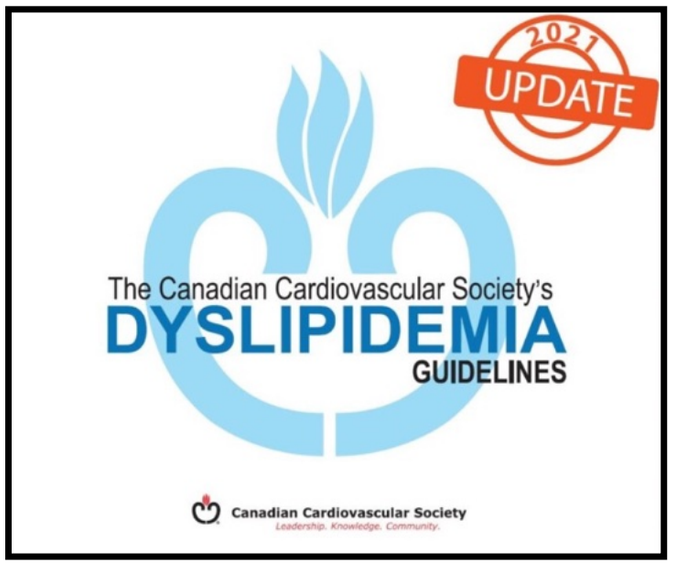
At least 50% of people, if **they knew** the actual benefit, **wouldn't consider taking a medication** to treat their
HIGH blood pressure/cholesterol/glucose
And that probably includes YOU as well

Guidelines Have a Bit of a Problem

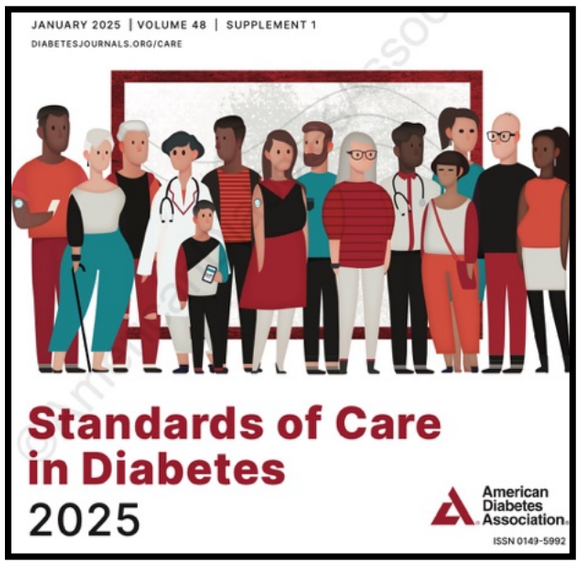
BLOOD PRESSURE



LIPIDS



GLUCOSE



They all talk about taking into account patient preferences BUT then say things like…

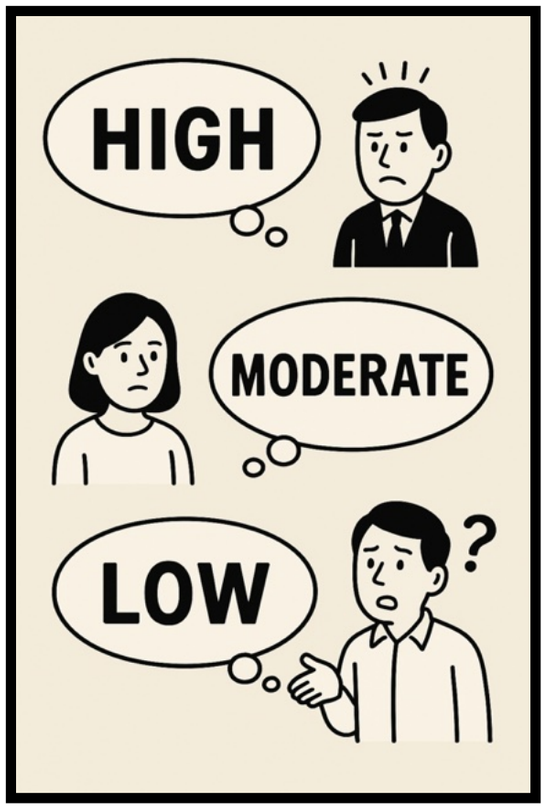
“medications should be started without delay”

“starting treatment is recommended irrespective of risk”

“recommend treatment initiation for all high or intermediate risk patients”

“immediate drug treatment in all patients”

“Words” are a big part of the problem



’Very High,’ ‘High’, ‘Moderate’, ‘Mild,’ and ‘Low’ may sound precise, but in risk communication, they’re **more poetry than data—open to interpretation** and prone to **miscommunication**

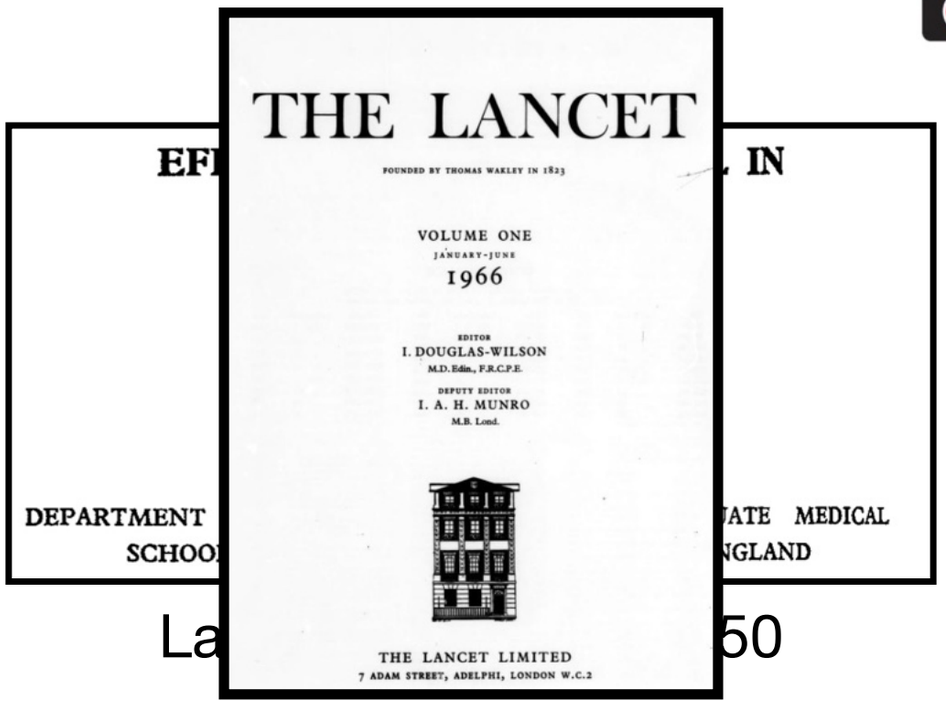
Avoid these words as much as possible

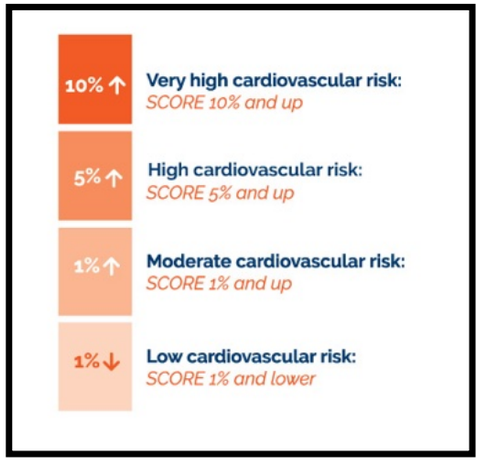
(Unless you always follow up with ballpark numbers)

1966

A study which treated people with average blood pressures of

200/110 mmHg



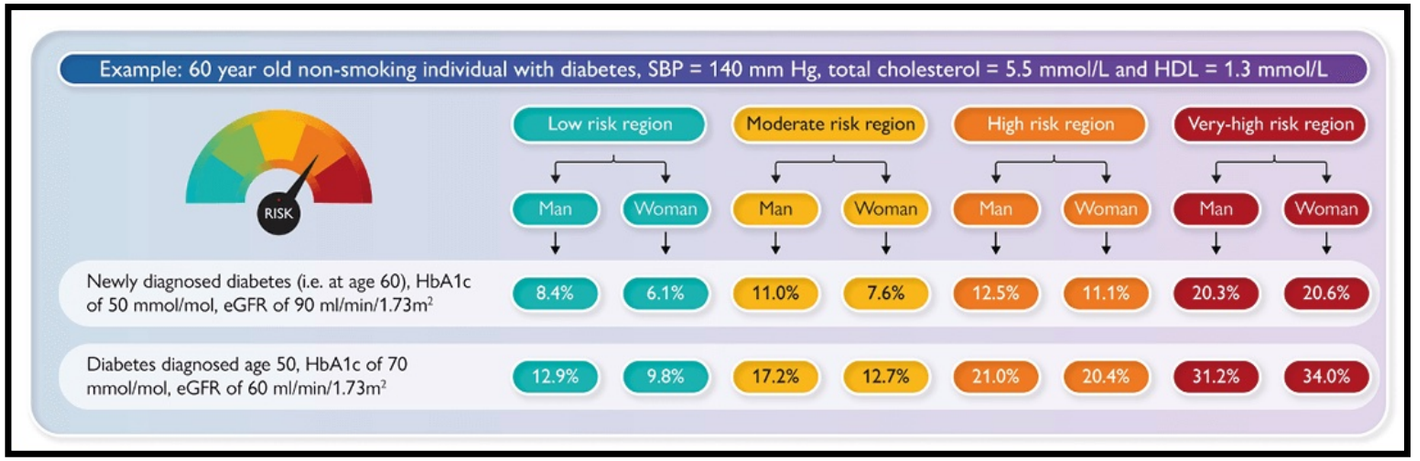


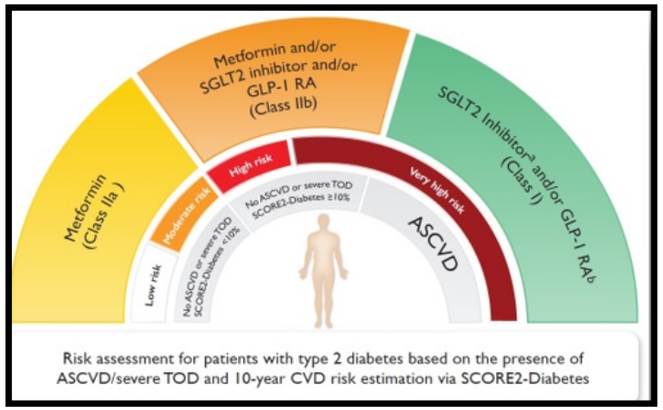
High

Low

Intermediate

Desirable





Normal

High to very high

Nearly optimal

Low to moderate

High Normal

Moderate

Moderate to high

Borderline high

Optimal

Very high

Blood Cholesterol Levels and Heart Disease Risk

Total Cholesterol Level	Category
Less than 200 mg/dL*	Desirable
200-239 mg/dL	Borderline High
240 mg/dL and above	High
LDL Cholesterol Level	**Category**
Less than 100 mg/dL	Optimal (Ideal)
100-129 mg/dL	Nearly Optimal
130-159 mg/dL	Borderline High
160-189 mg/dL	High
190 mg/dL and above	Very High

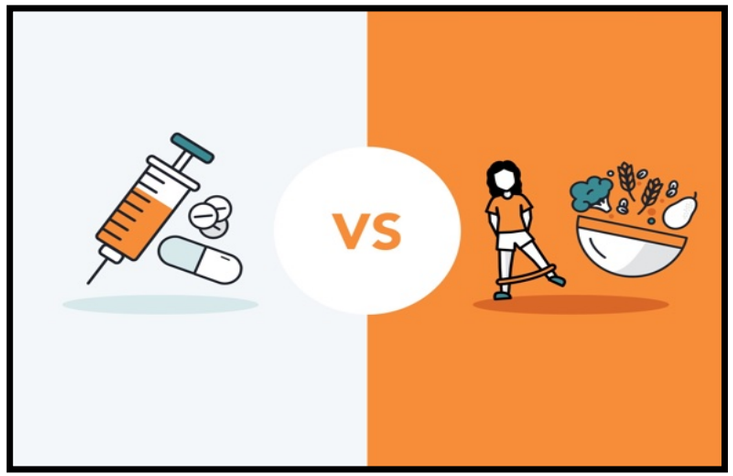
Other risk factors, asymptomatic organ damage or disease	Blood pressure (mmHg)			
	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP ≥180 or DBP ≥110
No other RF		Low risk	Moderate risk	High risk
1–2 RF	Low risk	Moderate risk	Moderate to high risk	High risk
≥3 RF	Low to moderate risk	Moderate to high risk	High risk	High risk
OD, CKD stage 3 or diabetes	Moderate to high risk	High risk	High risk	High to very high risk
Symptomatic CVD, CKD stage ≥ 4 or diabetes with OD/RFs	Very high risk	Very high risk	Very high risk	Very high risk

PRIMARY PREVENTION†		
Low-Risk* **FRS <10%**	**Intermediate-Risk*** **FRS 10-19.9% and** LDL-C ≥3.5 mmol/L **or** Non-HDL-C ≥4.2 mmol/L **or** ApoB ≥1.05 g/L **or** Men ≥50 yrs and women ≥60 yrs with one additional risk factor: low HDL-C, IFG, high waist circumference, smoker, or HTN **or** with presence of other risk modifiers: hsCRP ≥2.0 mg/L, CAC >0 AU, family history of premature CAD, Lp(a) ≥50 mg/dL (100 nmol/L)	**High-Risk*** **FRS ≥20%**

Words and Hypertension

			
Guideline Differences	**2017/2015 ACC/AHA**	**2023 ESH**	**2025 Canada**
Hypertension Definition	≥ 130/80	≥ 140/90	≥ 130/80
Optimal		<120/80	
Normal	< 120/80	120–129/80–84	
High normal (used to be prehypertension)		130–139/85–89	
Elevated	120–129/<80		
Stage 1/Grade 1	130–139/80–89	140–159/90–99	
Stage 2/Grade 2	≥ 140/90	160–179/100–109	
Grade 3		≥ 180/110	

Confusing Press Messages



Even ChatGPT gets the problem!

A Shared Decision = a decision between a patient and their health care provider

When asked how guidelines discourage a shared-decision

Chat GPT said:

How Guidelines **Discourage** Shared Decision-Making

- Use of **Universal Targets** (e.g., BP <130/80, LDL <70 mg/dL) as Defaults Without Nuanced Discussion
- **Strong Language Like "Should"** Instead of "Could," Which Pressures Patients Toward One Path
- **Minimal Discussion of Trade-offs**, Risks vs. Benefits in Terms That Matter to Patients
- **Heavy Focus on Population-Based Data** Instead of Individualized Risk Calculators

How Guidelines Could **Improve** Shared Decision-Making

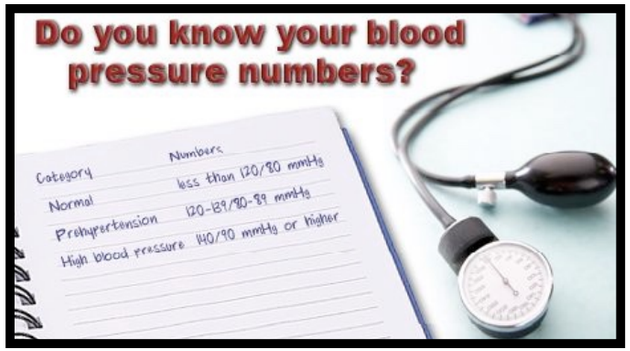
- **Use Absolute Risk Reduction Data → Let patients see how much a treatment actually benefits them**
- **Provide Options, Not Directives** → Instead of "should take statins," say "you could benefit by X%"
- **Acknowledge Individual Values** → Some patients may prefer avoiding medications despite minor benefits
- **Emphasize Quality of Life Over Strict Targets** → Some patients prioritize avoiding side effects over strict control

Empowering **YOU** with information that is specific to **YOUR** patient and thereby allowing **THEM** to make a decision

Know
THE RISK
THE BENEFIT

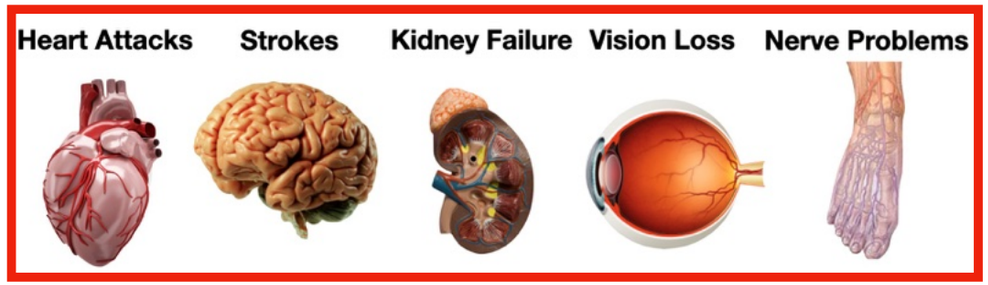
Make
A DECISION

WE ARE TOLD TO KNOW YOUR NUMBERS!



****BUT THERE ARE OTHER NUMBERS THAT ARE MUCH MORE IMPORTANT TO KNOW****

The chance of



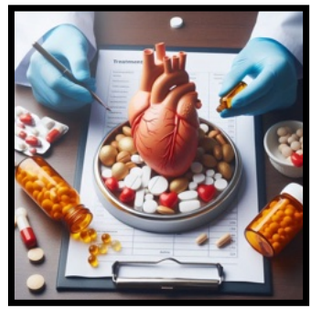
getting these things

LOTS of people are “HIGH”

Roughly*

1 in 4 to 5 - have “high” blood pressure (hypertension)
- 1 in 2 have “pre-hypertension”

1 in 4 to 5 - have “high” cholesterol (lipids)



1 in 10 to 20 - have “high” glucose (type-2 diabetes)
- 1 in 3 have “pre-diabetes”

*depends somewhat on the country and the definition

34 BLOOD PRESSURE

Hydrochlorothiazide
Chlorthalidone
Indapamide
Furosemide
Spironolactone
Amiloride
Ramipril
Enalapril
Lisinopril
Perindopril
Cilazapril
Losartan
Valsartan
Candesartan
Irbesartan
Telmisartan
Amlodipine
Nifedipine
Felodipine
Diltiazem
Verapamil
Metoprolol
Atenolol
Bisoprolol
Propranolol
Carvedilol
Doxazosin
Prazosin
Terazosin
Clonidine
Methyldopa
Aliskiren
Hydralazine
Minoxidil

27 DIABETES

Metformin
Glyburide
Glipizide
Glimepiride
Repaglinide
Nateglinide
Pioglitazone
Rosiglitazone
Sitagliptin
Saxagliptin
Linagliptin
Alogliptin
Liraglutide
Exenatide
Dulaglutide
Semaglutide
Canagliflozin
Dapagliflozin
Empagliflozin
Acarbose
Miglitol
Insulin lispro
Insulin aspart
Regular insulin
NPH insulin
Insulin glargine
Insulin detemir

19 LIPIDS

Atorvastatin
Rosuvastatin
Simvastatin
Pravastatin
Lovastatin
Fluvastatin
Pitavastatin
Ezetimibe
Cholestyramine
Colestipol
Colesevelam
Alirocumab
Evolocumab
Fenofibrate
Gemfibrozil
Niacin
Eicosapentaenoic acid (EPA)
Docosahexaenoic acid (DHA)
Bempedoic acid

There are over 80+ medications

(and many other combination products)

used for blood pressure lipids diabetes

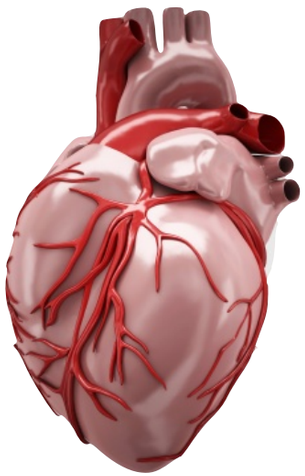
*At least **15** of these medications have decent evidence they provide*

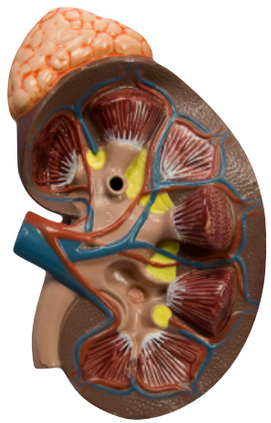
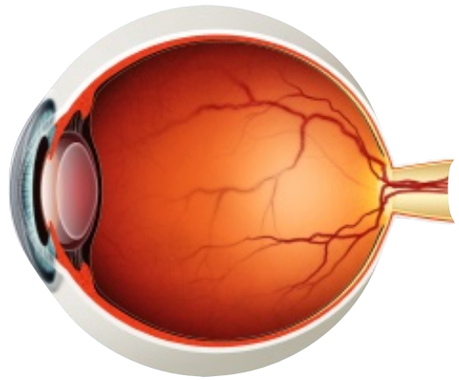
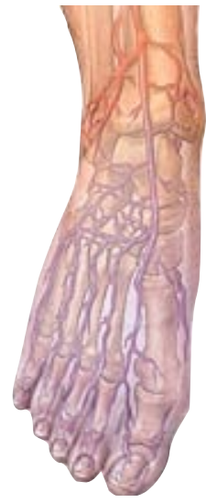
no benefit

on important outcomes

What is KEY to know is, what happens to the chance of these bad outcomes…

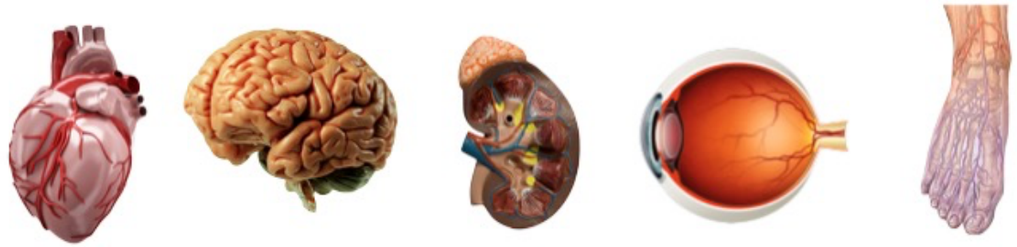
Heart Attacks **Strokes** **Kidney Failure** **Vision Loss** **Nerve Problems**



… and if we treat blood pressure/cholesterol/glucose numbers with medications then, what is the risk?

The Chance of Getting Problems With These



****THESE ARE THE NUMBERS YOU NEED TO KNOW ABOUT****

Risk Factors

Blood pressure, lipid, and glucose numbers

are simply

a measure of 3 Risk Factors

Some call these conditions chronic diseases - but this is misleading

OTHER key Risk Factors

Age, Smoking, Sex, and Family History

RISKS - death/heart attacks/strokes/kidney problems

Do Not Scare ➡ INFORM

Risk Factor(s)

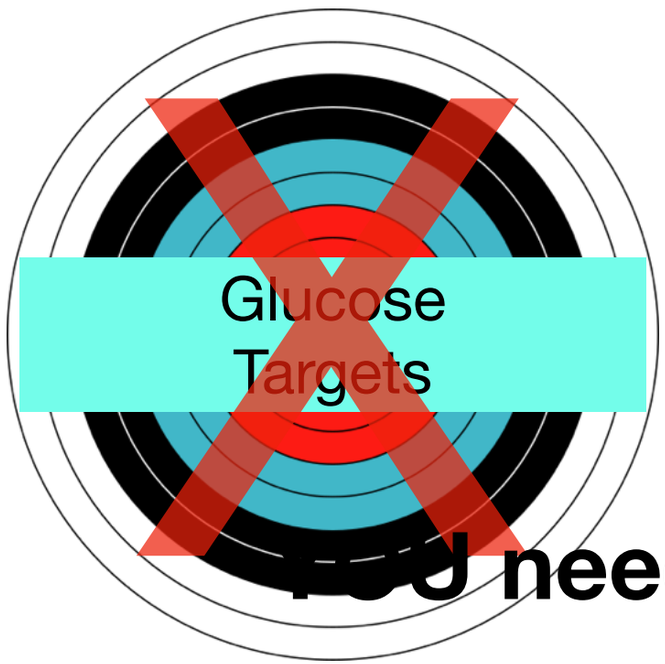
How much do they impact the risk of a bad outcome such as a heart attack or stroke?

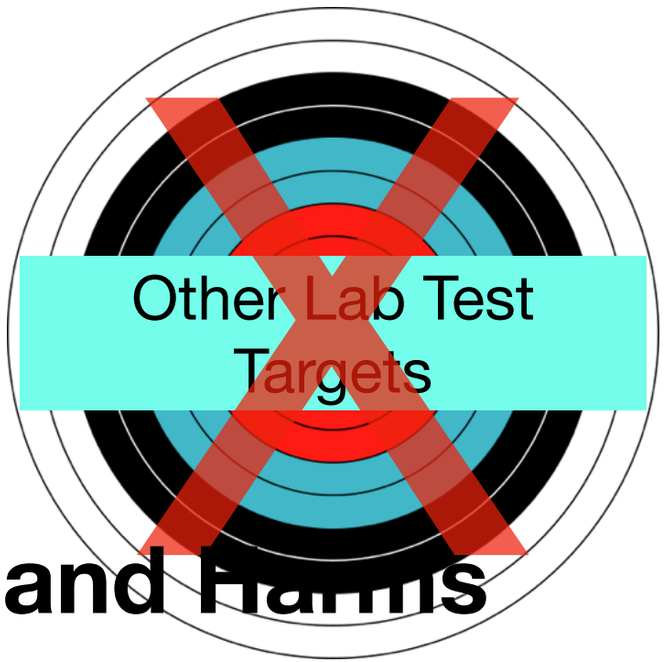
How much would treatment ⬇ the risk?

What are the harms and costs?

The ultimate decision is up to YOUR patient, and YOU should support an informed decision!

YOUR Target



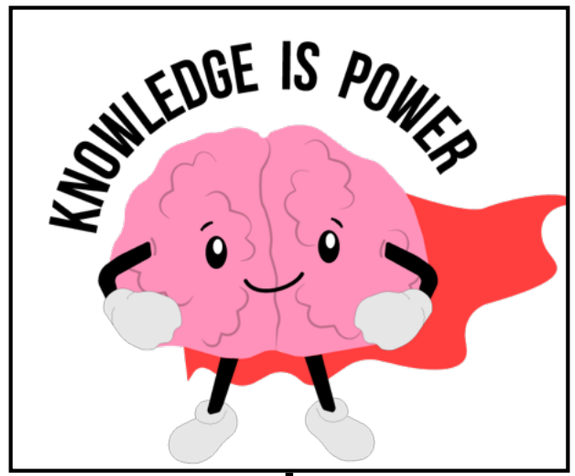


YOU need to know the Benefits and Harms

Helping your patient better understand their health issues

Better health literacy is associated with

- better health status
- less frequent use of health services
- shorter hospital length of stay
- lower mortality
- less unhealthy behaviors (smoking, lower physical activity etc)

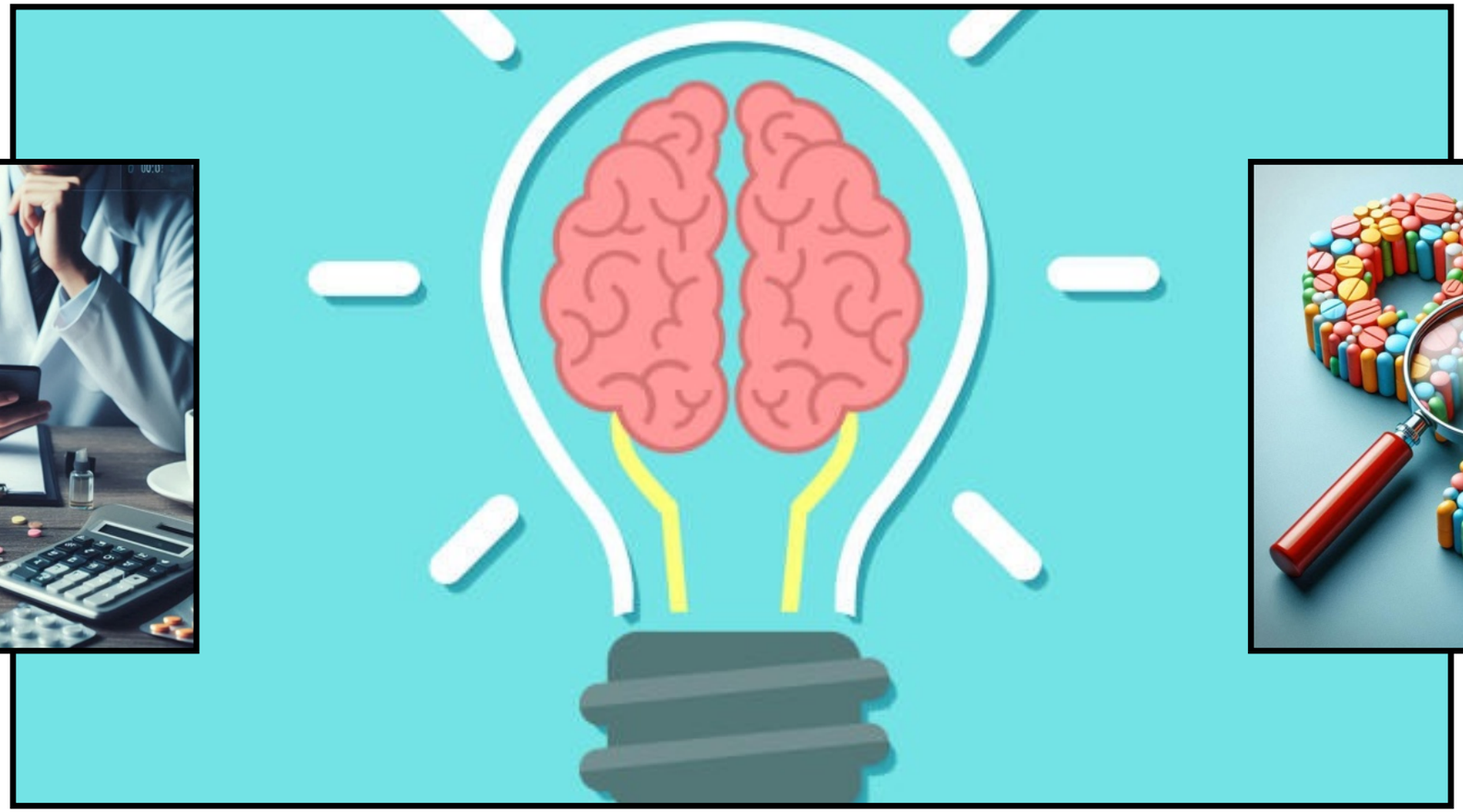


Once it is applied

PLoS One. 2022 Jul 15;17(7):e0271524. doi: 10.1371

Getting Smarter

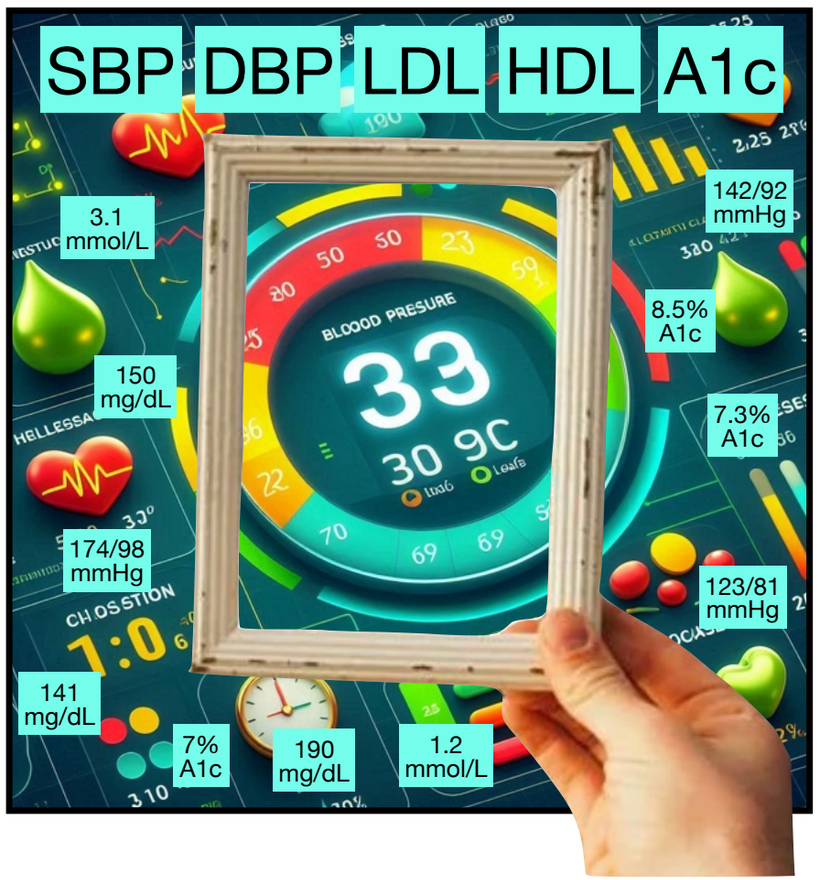
about the numbers, the risks, the potential benefits, the harms…



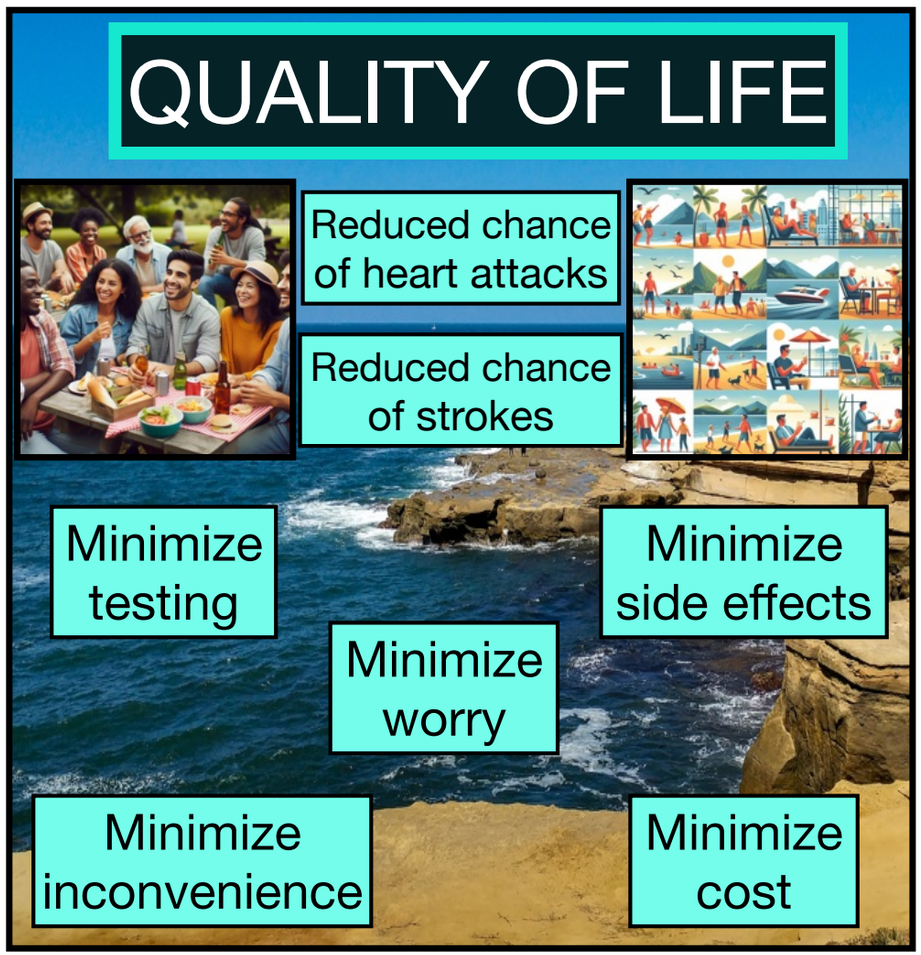
Reframe What YOU Think About THE Numbers

Blood pressure, lipids, and glucose

What doesn't matter as much



What Really Matters



They Aren’t Actually Sick

A condition vs a disease

When BP/chol/glucose numbers are “high” we often refer to them as chronic “diseases”

HOWEVER - in general, people with:

Silent Killers

“high” blood pressure have **NO** symptoms

“high” cholesterol have **NO** symptoms

Type 2 diabetes (“high” glucose) - most have **NO** symptoms (unless glucose is really high then one might experience peeing more frequently, increased thirst, feel tired, recurrent skin/bladder infections)

A much more informative way is to think of these **simply as RISK factors**

Importantly

1) it’s difficult to make a person with no symptoms feel better
2) if a person’s blood pressure and/or cholesterol and/or glucose was ZERO, they would be DEAD

YOU might think with “high” numbers the biggest risk is

A
heart
attack
or a
stroke

These risks are definitely important

BUT…

The ONLY GUARANTEED RISK is Treatment Burden

TREATMENT BURDEN AFFECTS EVERYONE

Health care visits

Dietary restrictions

Taking pills

Side effects

Lab visits

Measuring

Worrying

Costs

Inconvenience

Risk Markers

Risk markers

Risk markers - there are **100s** of cardiovascular risk markers

Things we can see or measure that have been shown in studies to be **associated** with the risk of a bad outcome (death/heart attack/stroke etc)

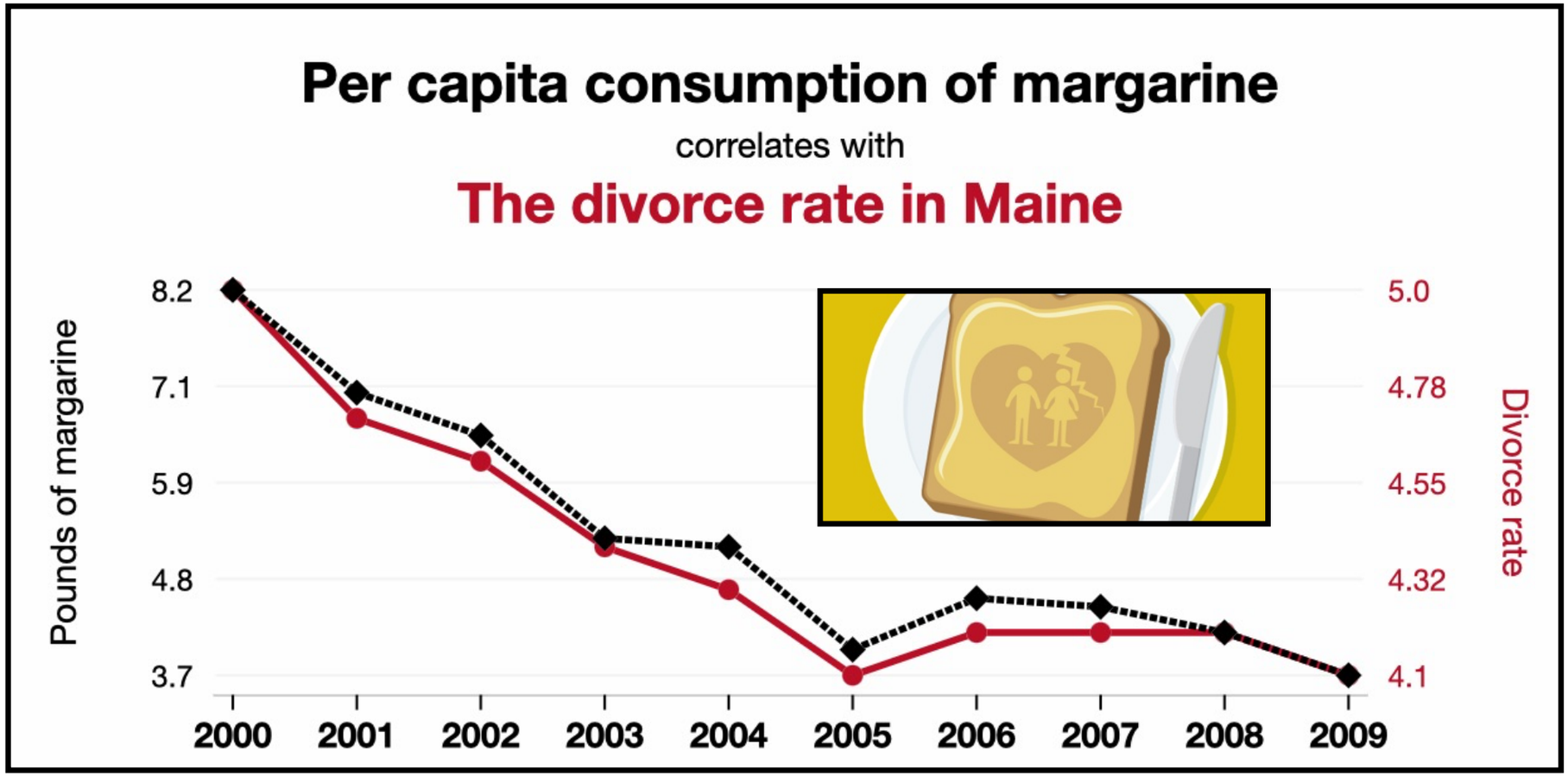
REAL EXAMPLES - smoking, cholesterol, blood pressure, snoring, not having siestas, living in Scotland, high levels of phobic anxiety, being scrupulous about keeping appointments, slow beard growth, and ear canal hair have **ALL** been shown to be **ASSOCIATED** with cardiovascular disease

TYPICALLY - for risk markers like blood pressure/cholesterol/glucose when these numbers are **higher,** they ARE **associated** with an ⬆ cardiovascular risk

HOWEVER - simply finding an **association** doesn't mean that a specific risk marker is a **CAUSE** of that bad outcome

If you study **LOTS** of large populations
you will find **MANY** associations

An example of an association with NO causation



Risk “marker” vs Risk “factor”

Risk factor

If modifying a particular **risk marker** ➡ changes the chance of important clinical outcomes (heart attacks/strokes) then a risk marker is often shifted into being called a potentially modifiable **risk factor**

Blood pressure, lipids and glucose = risk factors - **modifiable**

AGE, sex = risk factors - **non-modifiable**

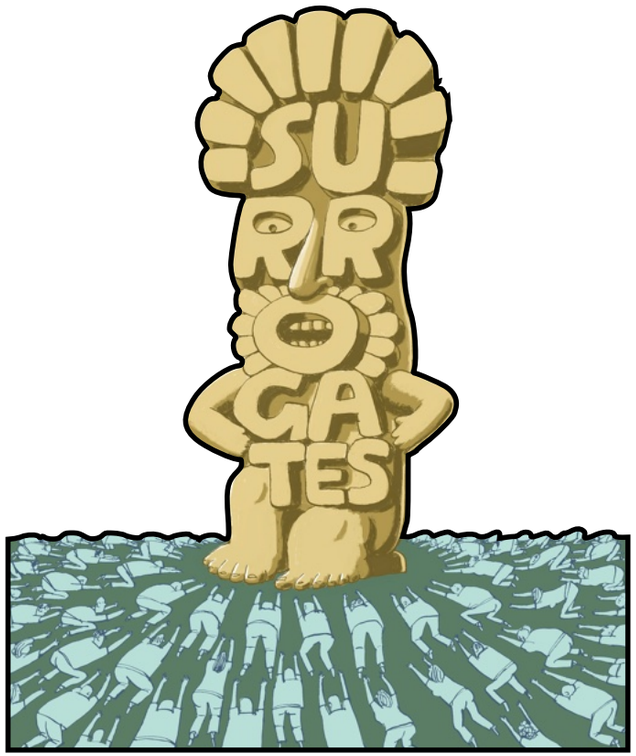
A number of risk factors are also referred to as **SURROGATE MARKERS**

BUT NONE OF THIS MEANS THERE IS A **DEFINITIVE THRESHOLD** OR THAT THERE ARE SPECIFIC **BLACK and WHITE GOOD/BAD NUMBERS**

Risk factors/Surrogate markers VS IMPORTANT Clinical Outcomes

THE IDOLATRY OF THE SURROGATE

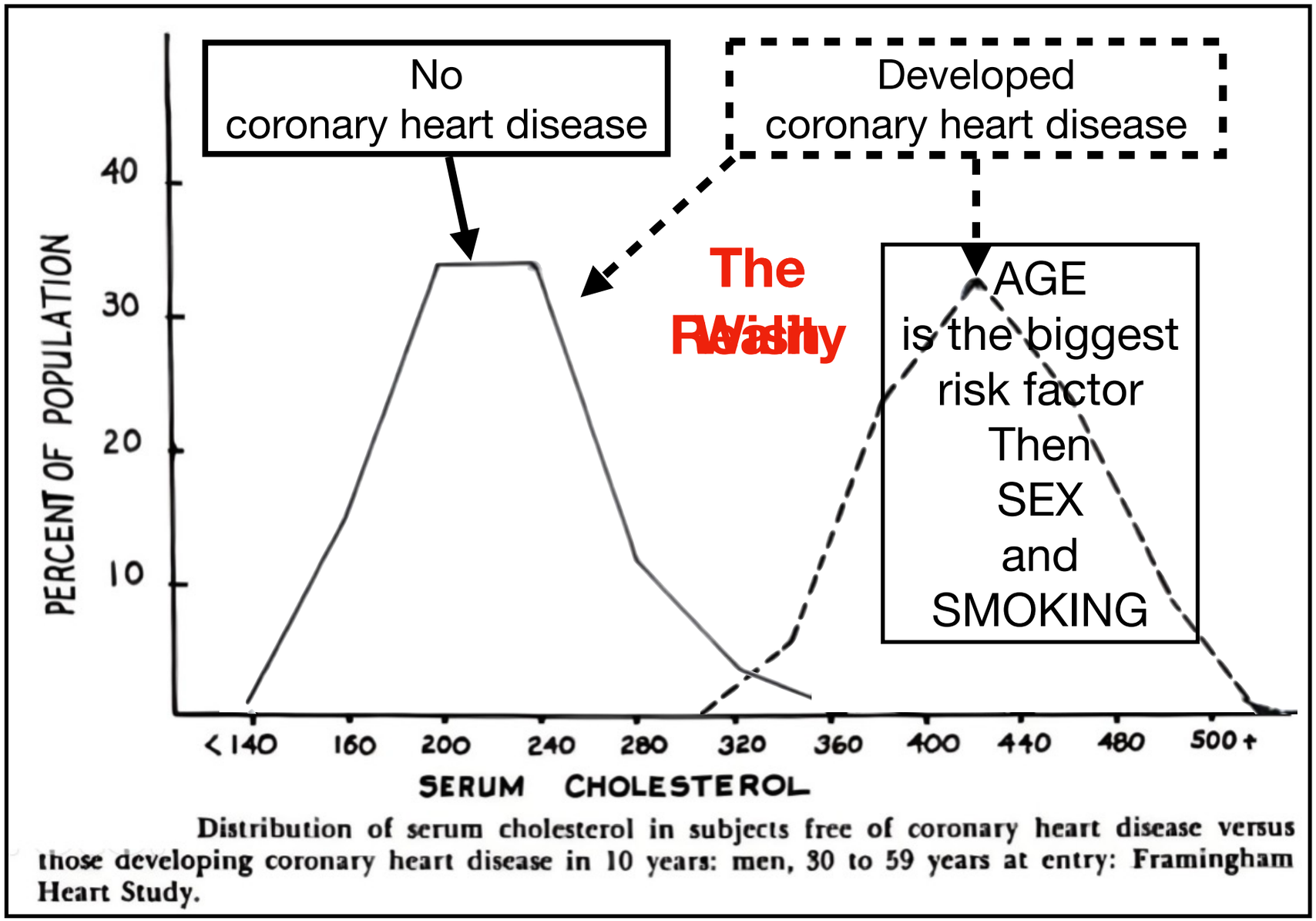
Easier to measure surrogate outcomes are often used instead of patient important outcomes such as death, quality of life, or functional capacity when assessing treatments. **John Yudkin, Kasia Lipska, and Victor Montori** argue that our obsession with surrogates is damaging patient care



BMJ 2011;343:d7995

LESS IMPORTANT Risk factors/Surrogate Markers	IMPORTANT Clinical Outcomes
You CAN'T FEEL THESE Treating these always have the potential for side effects, inconvenience and cost - all of which typically lower your quality of life	You CAN FEEL THESE AND If we can reduce the risk of these in you that could improve your quality of life
blood pressure/ lipids/ glucose (diabetes)	death, heart attacks, heart failure, angina, strokes, transient ischemic attack, coronary artery bypass, stenting, blindness, amputation, kidney failure/dialysis

Risk Factor Context

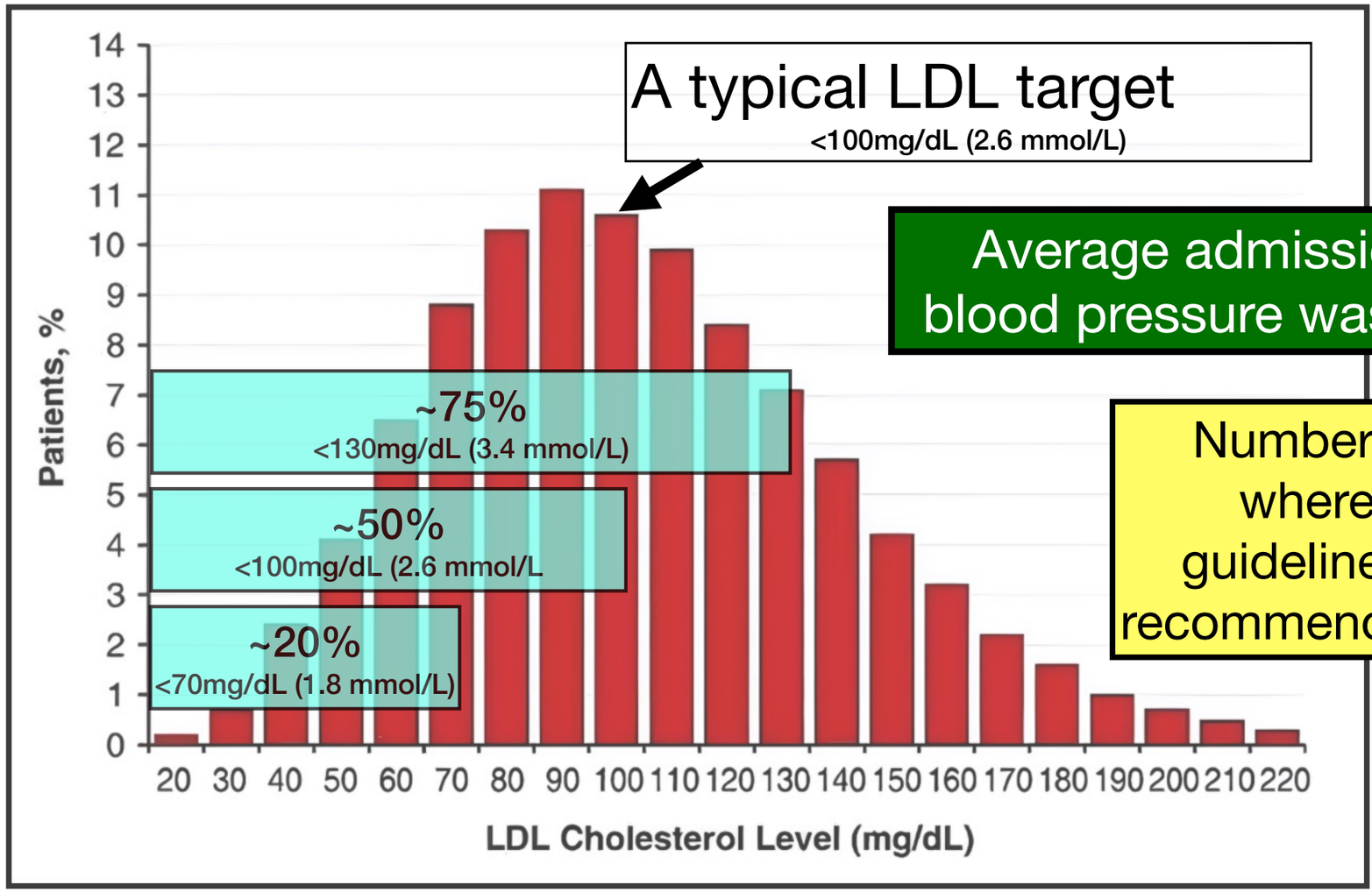


Distribution of serum cholesterol in subjects free of coronary heart disease versus those developing coronary heart disease in 10 years: men, 30 to 59 years at entry: Framingham Heart Study.

Ann Intern Med 1964;61:888-99

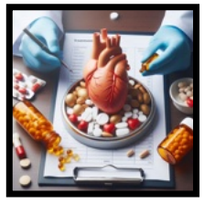
The association between cholesterol and heart disease

Risk factor #s for people who get hospitalized for heart attacks/bypass/stents



Am Heart J 2009;157:111-7.e2

Lifetime Risk of Fatal and Non-fatal Cardiovascular Events in a 45 y/o



Major risk factors after AGE

1. current smoker
2. untreated systolic blood pressure >160 mmHg
3. untreated total cholesterol > 240 mg/dL (6.2 mmol/L)
4. diabetes

	MALE	FEMALE
2 or more major risk factors	**50%** 30% die of CVD	**30%** 20% die of CVD
1 major risk factor	**40%** 20% die of CVD	**20%** 10% die of CVD

These numbers are still WAY TOO HIGH
BUT **"most" people** (>50%) with
2 or more risk factors
WON'T get CVD over a lifetime

N Engl J Med 2012;366:321-9

Does ⬇ a Risk Factor ⬇ The Risk of Important Clinical Outcomes?

FACT

To get a blood pressure/cholesterol/diabetes medication on the market just have to show it ⬇ the risk factor - you don't have to have evidence that it ⬇ clinically important outcomes

IN GENERAL

⬇ BP/chol/glucose numbers does ➜ a ⬇ in the risk of important clinical outcomes

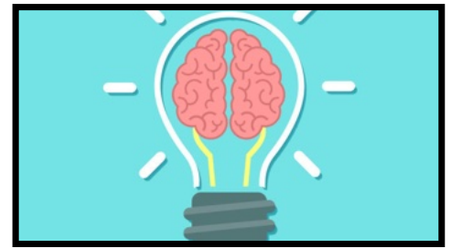
BUT there are **WAY** to **MANY** examples when clinically important benefits did not occur

MEDS - **2-3 blood pressure medications**, **most diabetes medications marketed before 2015, and 2-3 classes of lipid/cholesterol lowering medications**

Personally, I would only use treatments proven to reduce clinical endpoints

FOOD - **most food items** that have been shown to ⬇ risk factors almost **never have evidence** that they ⬇ clinically important outcomes

2008-2015 was a bad stretch



Between **2008-2015** there were **20* large clinical trials** published in major medical journals of **treatments** that **lowered surrogate markers** **(blood pressure, lipids, glucose)**

All 20 trials showed NO cardiovascular benefit - and some showed harm

During that **7 year** period **NOT a SINGLE trial** was published showing a clinical benefit as a result of changing a surrogate marker

***The 20 Large Clinical Trials**

ACCORD, ADVANCE, VADT, ROADMAP, ORIGIN, SAVOR-TIMI 53, EXAMINE, ALECARDIO, ACTIVE, CRESCENDO, VISTA-16, AIM-HIGH, HPS2-THRIVE, ACCORD (fibrates), dalOUTCOMES, STABILITY, ALTITUDE, VALISH, AASK, ACCORD (blood pressure)

Things improved somewhat after that

SUCCESSES

2015 EMPA-REG OUTCOME (empagliflozin) - **~3%** ⬇ mortality/heart failure over 3 years

2015 SPRINT (120mmHg vs 140mmHg) - **1.6%** ⬇ CVD over 3 years but also **1.8%** ⬆ kidney issues

2016 LEADER (liraglutide) - **1.8%** ⬇CVD over 4 years

2016 HOPE 3 - statins **YES**, BUT blood pressure **NO** benefit

2017 FOURIER - **1.6%** ⬇CVD over 2 years BUT **$15,000/year**

But still failures can occur

2017 ACCELERATE (evacetrapib) - increased HDL (130%), reduced LDL (40%) - no CVD benefit

We always need to large clinical trials!!

KEY Concepts to Appreciate

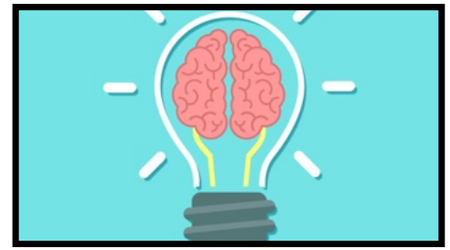
1) ⬇ A RISK FACTOR (blood pressure/lipids/glucose) DOES NOT GUARANTEE THERE WILL BE A ⬇ IN THE RISK OF IMPORTANT CLINICAL OUTCOMES

It very much depends what you did to change the risk factor

2) WHEN THERE IS A ⬇ IN THE RISK OF IMPORTANT CLINICAL OUTCOMES (heart attacks/ strokes etc) THE MAGNITUDE OF THE ⬇ IS OFTEN FAR LESS THAN YOU MIGHT THINK

REMEMBER the majority of people will not get CVD - if you weren't going to get CVD in the first place then one gets **NO benefit** - but one does get a lifetime of worry and treatment

Summary



KEY POINTS

Association does not necessarily = causation

Studies have shown for the most part a clear **association** between blood pressure, lipids and glucose, and an increased risk for heart attacks, strokes and other clinical outcomes.✓✓✓✓

At least half of the people with a heart attack have “normal” blood pressure and cholesterol

However, what the risk of a real disease/outcome is KEY

Death, heart attacks, strokes, kidney problem etc ??

Health Risk Numbers

What Is The Risk?

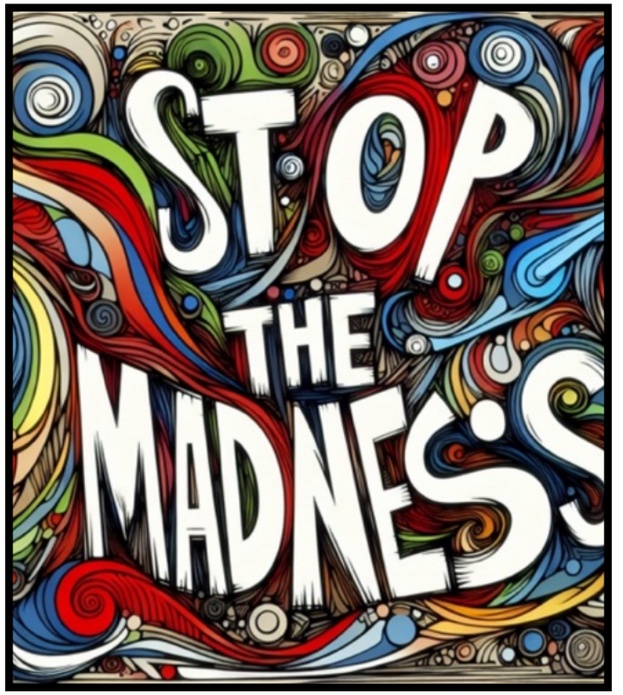
Heart attack/stroke

If you are telling someone they have “HIGH” blood pressure/ cholesterol/ glucose

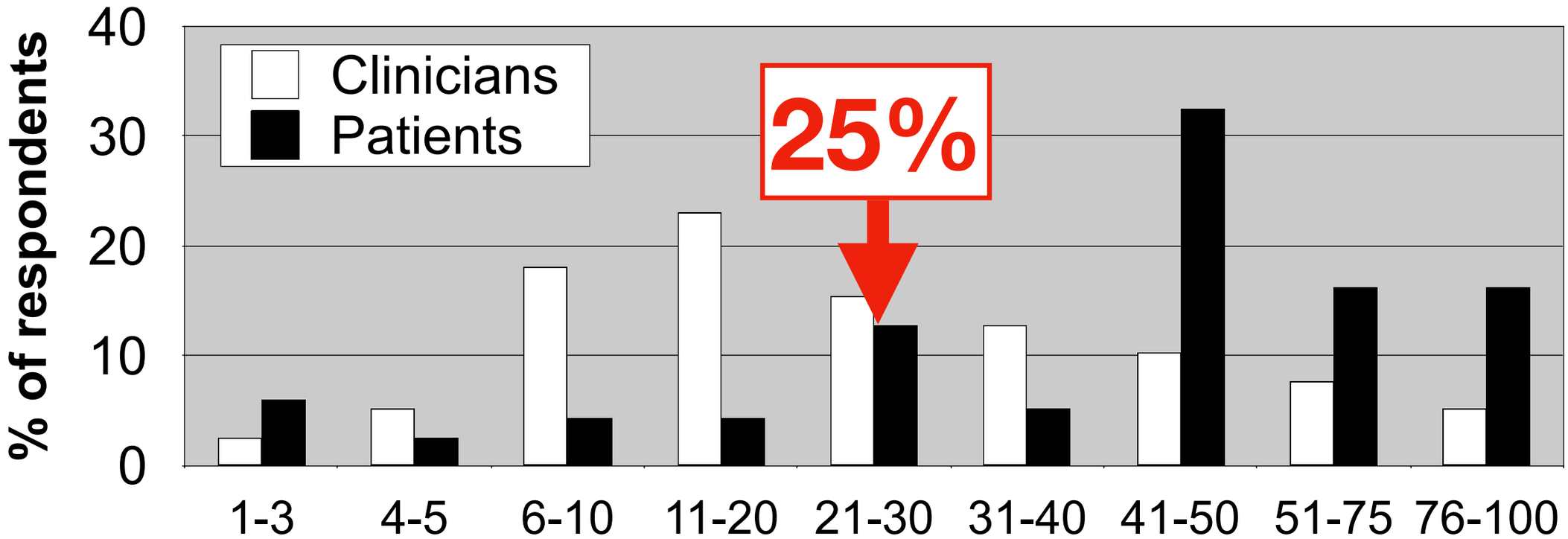
KNOWING THE RISK SHOULD **ALWAYS** BE **STEP #1**

Words DON'T accurately convey risk - PERIOD!

- low risk
- moderate risk
- high risk
- very high risk
- extremely high risk
- "how are you still alive" risk



What is "High Risk"

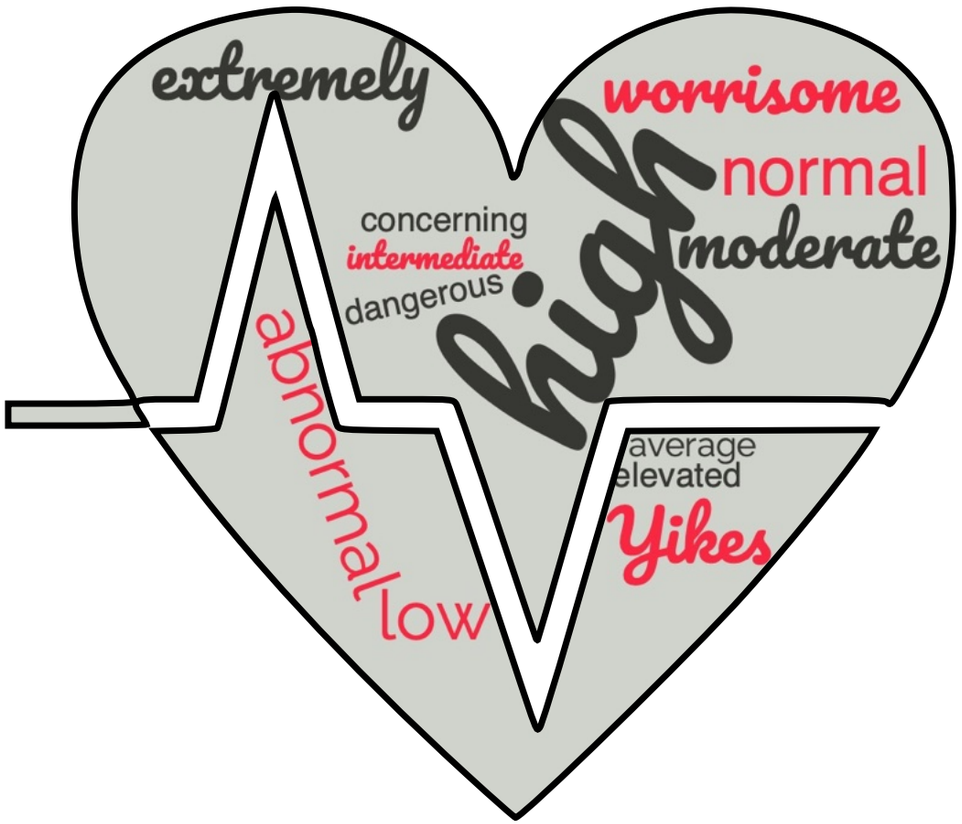


Chance of a heart attack in the next 5 years (%)

A 60 y/o, male, smoker, diabetic,
SBP 180 mmHg, total cholesterol 280mg/dL or 7.2 mmol/L

5-year risk of heart attack PLUS stroke is at most ~ 25%

Risk words are a “big” problem

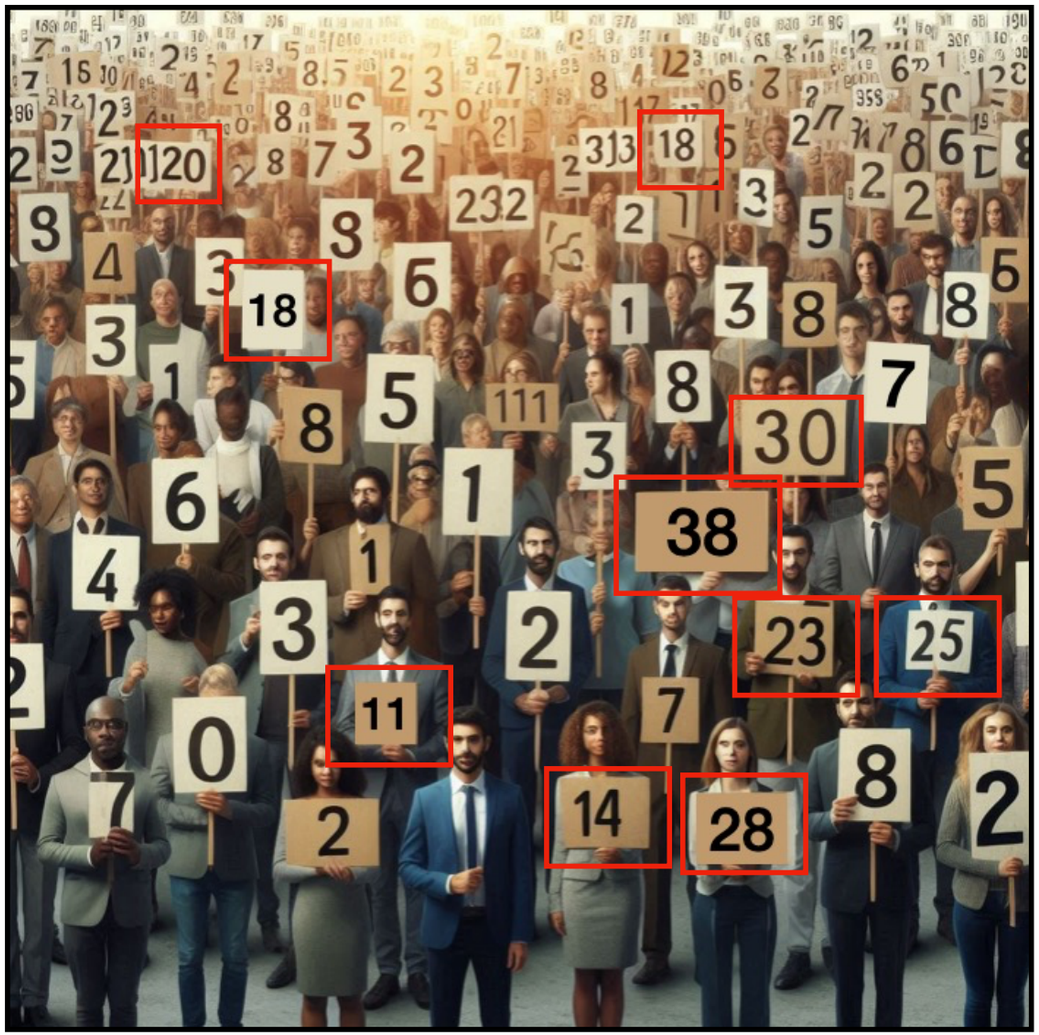


These types of words
do NOT inform you as to
YOUR actual risk

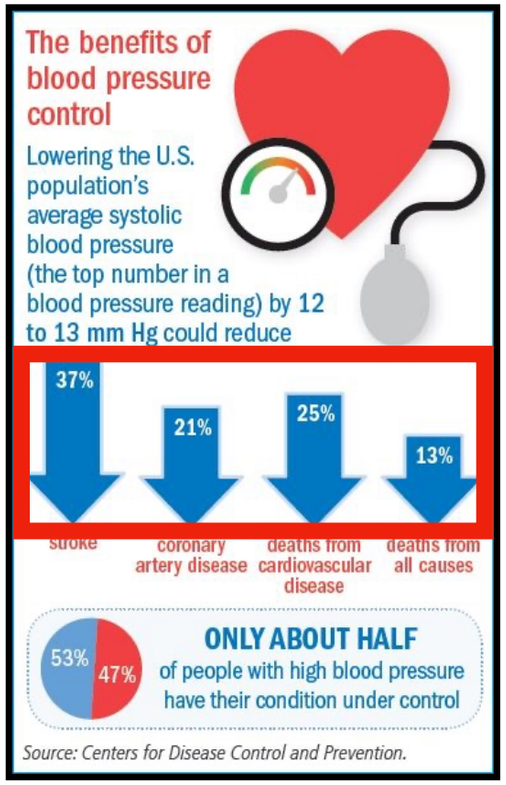
Heart attacks?
Strokes?

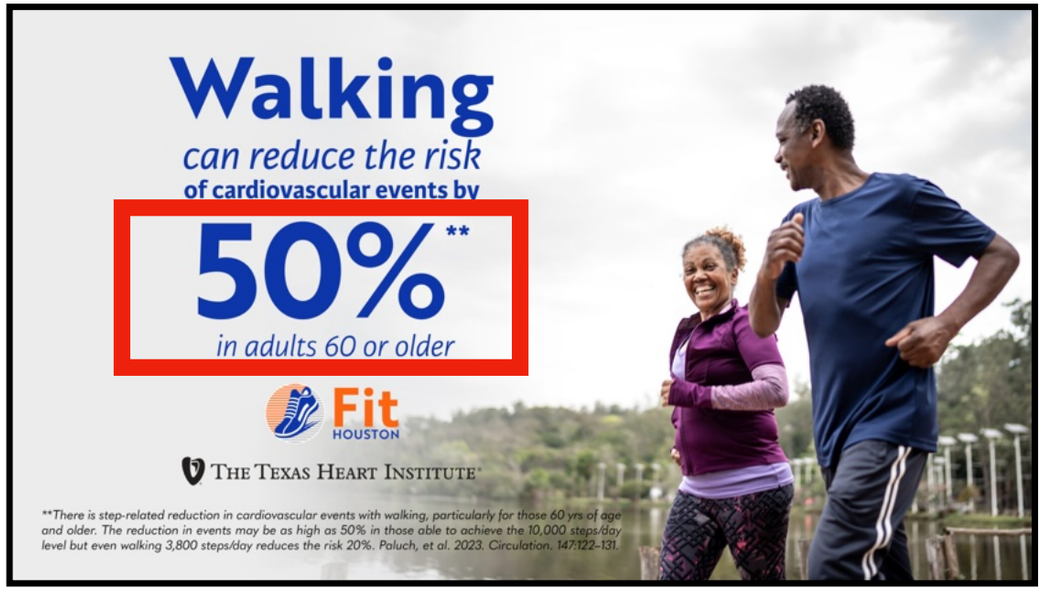
1%?	**1 year?**
5%?	**5 years?**
10%?	**10 years?**
15%?	**20 years**
20%?	**Ever?**

Numbers are essential, BUT they can also be misleading



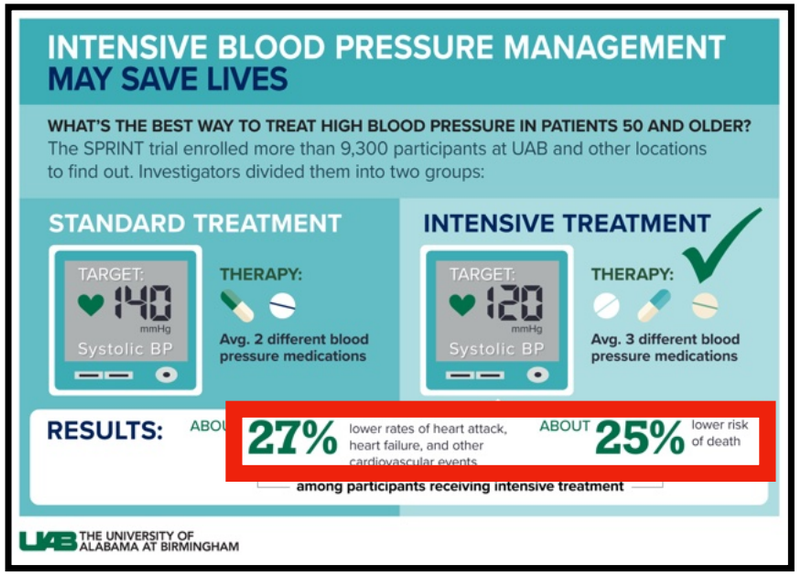
When you see/hear CVD benefit **NUMBERS** **greater** than **10%** these can be **misleading** unless they are put into the **proper context**





NONE of these are **DRUG COMPANY** ads!

These #s are all misleading



!IMPORTANT!

How BIG was the difference?

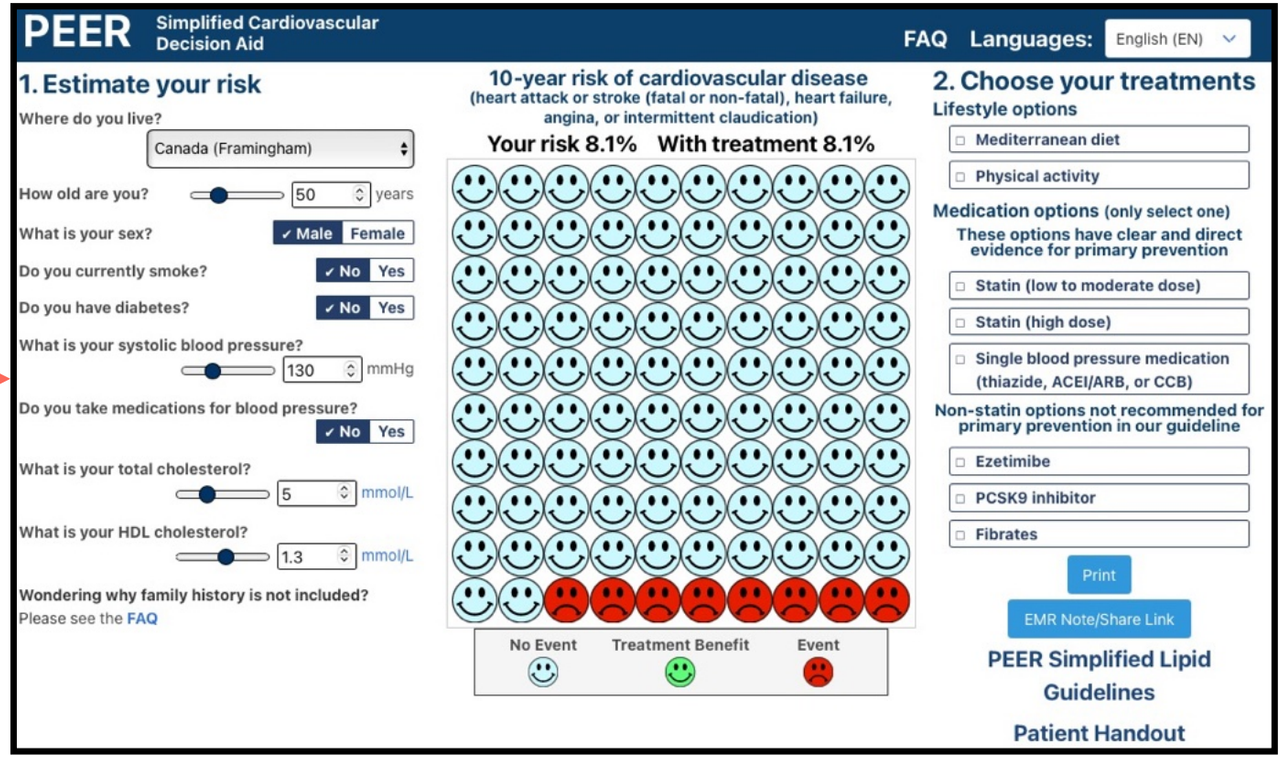
REMEMBER If you hear that ANYTHING is beneficial or harmful and the number is ≥10% this is almost always a RELATIVE number

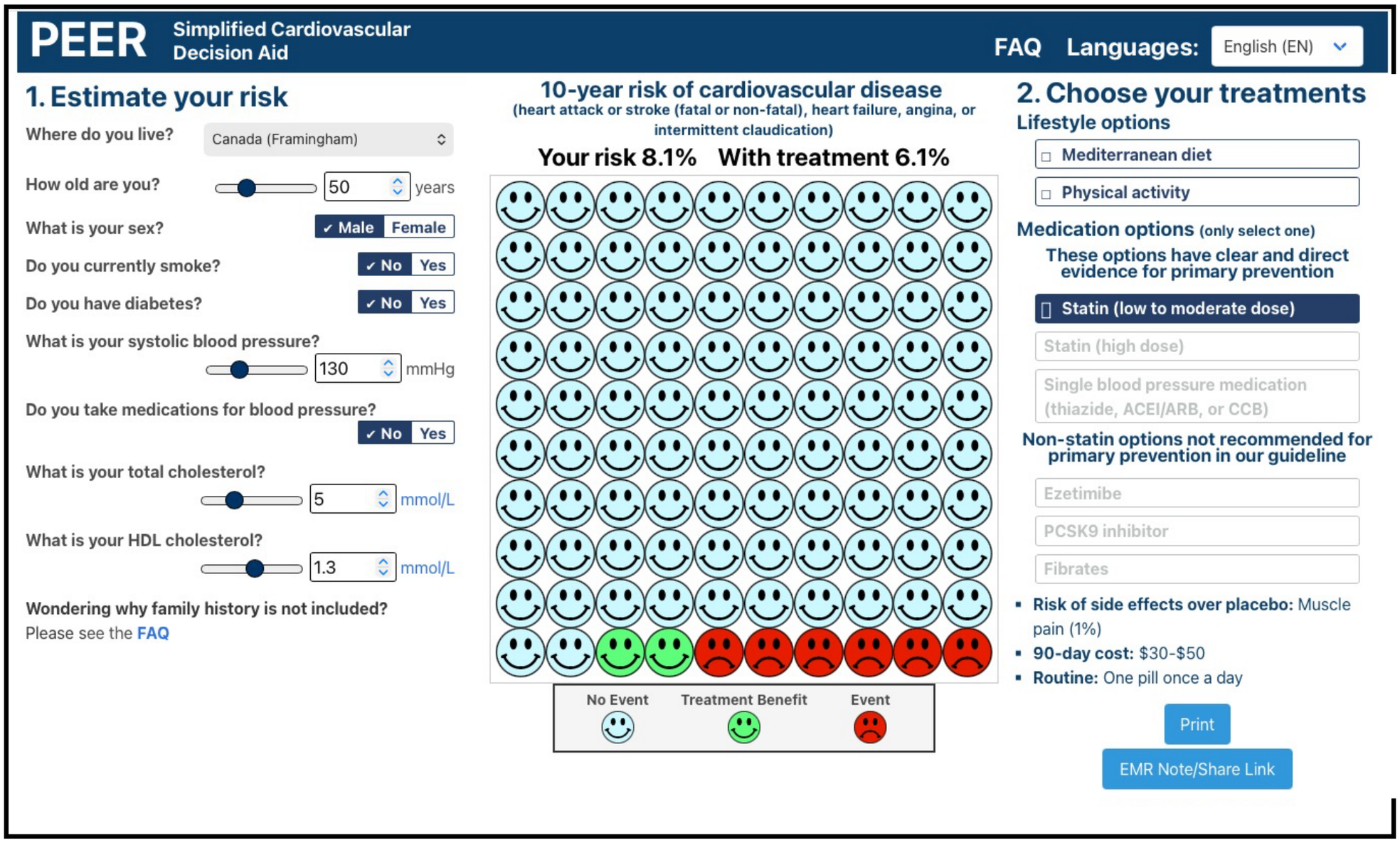
MONEY #s VS MEDICAL RESEARCH #s

MONEY	Units - dollars	MEDICAL RESEARCH	Units - risk of an outcome such as a heart attack
Pre-sale price	$10	Baseline risk	10% over 10 years
SALE SIGN	30% off	RELATIVE BENEFIT	30% reduction/benefit
New price	$7	New risk	7%
Absolute savings	$3	Absolute risk reduction	3%
Relative price	$7 / $10 = 70% of original price	Risk ratio or point estimate	7% / 10% = 0.70 or 70% of original risk

ABSOLUTE NUMBERS
3% BENEFIT AND 97% GET NO BENEFIT

There are better ways to explain risks/benefits/harms





https://decisionaid.ca/cvd/

Treatments that have decent RCT evidence of benefit

in people who have never had a cardiovascular event

Lifestyle and their relative benefits*		Medications and their relative benefit*					
Lifestyle	Heart attack/ stroke benefit	**Blood pressure**	Heart attack/ stroke benefit	**Lipids**	Heart attack/ stroke benefit	**Glucose**	Heart attack/ stroke/kidney benefit
Mediterranean diet	30% ⬇	Salt substitute 75%Na/25%K	10-15% ⬇	Statins lower dose	25% ⬇	Metformin	? only 1 trial
Moderate physical activity	25% ⬇	Thiazide lower dose	25% ⬇	Statins higher dose	an extra 10 % ⬇	SGLT2's	15% ⬇
		ACE/ARB lower dose	25% ⬇	Ezetimibe	5% ⬇	GLP's	15% ⬇
		Betablockers, calcium channel blockers	Some but less than those above	PCSK9 Inhibitors	15% ⬇	Sulfonlyureas, Insulin, DPP4s	0%

*Regardless of their effect on the specific risk factor - all numbers are rounded

Simply apply the
estimated RELATIVE benefit
to the
estimated ABSOLUTE baseline risk

10% risk - 25% benefit - NEW risk = 7.5%
So 2.5% benefit - 97.5% no benefit

20% risk - 30 % benefit - NEW risk = 14%
So 6% benefit - 94% no benefit

“But 10 years isn’t enough”

- some people will say that 10 years is not long enough
- but 10 years is a long time to treat
- risk calculator estimates typically over-estimate the risk
- for 20 years then roughly double the risk - but even that is an overestimate
- lifetime risk - with 2 risk factors MALE - 50% FEMALE - 30%
- we only delay death, NEVER prevent it

Actual
Side Effects

Worrying
about
Side Effects

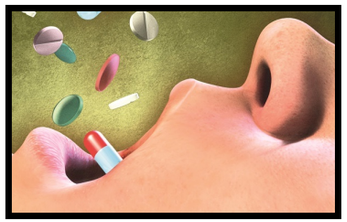
Inconvenience

Get the prescription

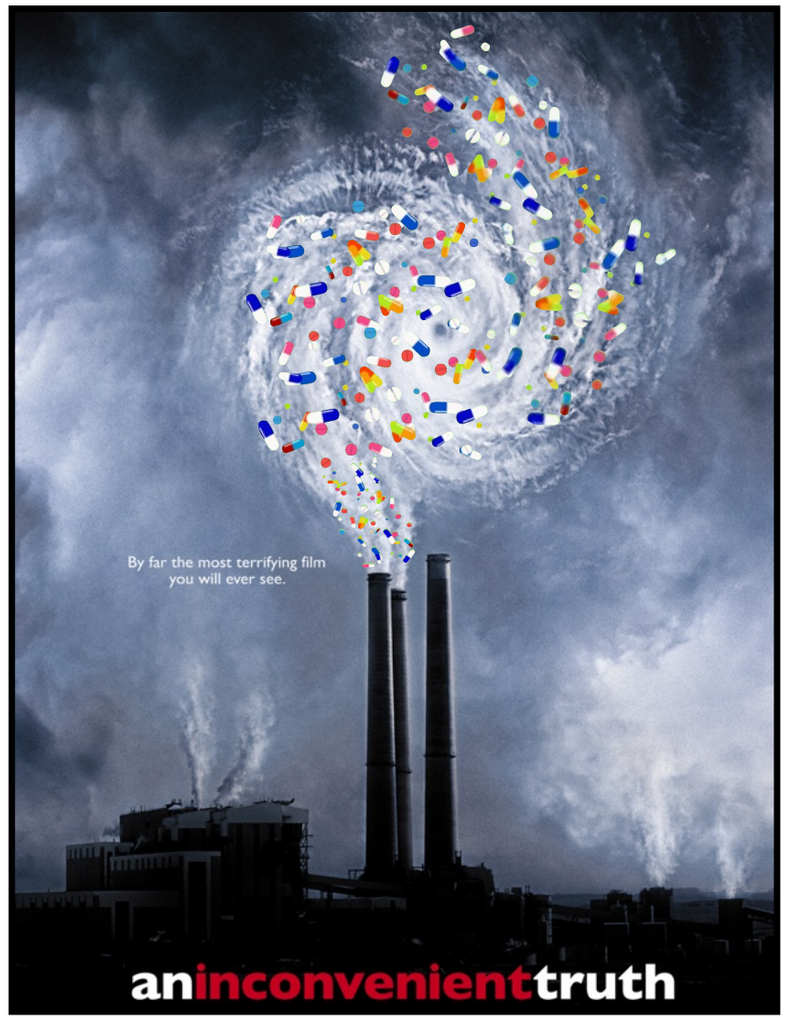
Fill the prescription

Pay for the prescription

Take the prescription



Labelling/worry



Monitoring adds to the…

complexity

worry

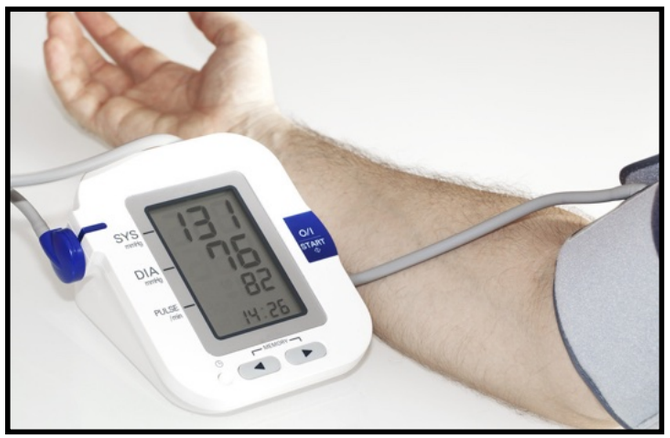
inconvenience

Glucose

24 hour monitoring

Lipids/cholesterol

Blood pressure



Continuous monitoring

Costs

Lifestyle

Nutrition

Activity

Are obviously “important”

Nutrition

An incredible amount of BS

HARVARD HEALTH BLOG

10 superfoods to boost a healthy diet

April 13, 2020

HARVARD UNIVERSITY

NOT A SINGLE REFERENCE

https://www.gousto.co.uk/blog/top-10-superfoods

In 2015 alone - 36% rise in the number of food and drink products launched globally featuring the terms “superfood”, “superfruit” or “supergrain”.

https://www.mintel.com/press-centre/food-and-drink/super-growth-for-super-foods-new-product-development-shoots-up-202-globally-over-the-past-five-years

SUPERFOODS?

Classification of the groups of superfoods by the number of times that were mentioned in selected web pages.

Group of Superfoods	Number of Times Mentioned				
	First Page	Second Page	Any Time	Past Year	Total Mentions
Leafy greens and cruciferous vegetables	122	32	108	46	154
Whole grain cereals, seeds and cereals	71	33	67	37	104
Berries	65	25	65	25	90
Fish and seafood	44	17	37	24	61
Other fruits	41	16	33	24	57
Nuts	46	6	34	18	52
Legumes	33	14	25	22	47
Spices and herbs	22	10	20	12	32
Fermented foods	23	6	14	15	29
Teas and infusions	13	5	9	9	18
Fats and oils	12	4	7	9	16
Other vegetables and plant-based foods [1]	87	23	59	51	110
Other animal-based foods and other [2]	14	7	12	9	21

[1] Miscellaneous group of 19 plant-based foods. [2] Miscellaneous group of 7 animal-based foods.

SUPERMAN

Foods 2023;12(3):546. doi:10.3390/foods12030546

The 5 large trials of nutrition intervention

NO PREVIOUS HISTORY OF HEART ATTACK/STROKE

Women's Health Initiative 2006 - 46,000 women - 8 years

PREDIMED 2018 - 7500 people, 57% female - 5 years

HISTORY OF HEART ATTACK/STROKE

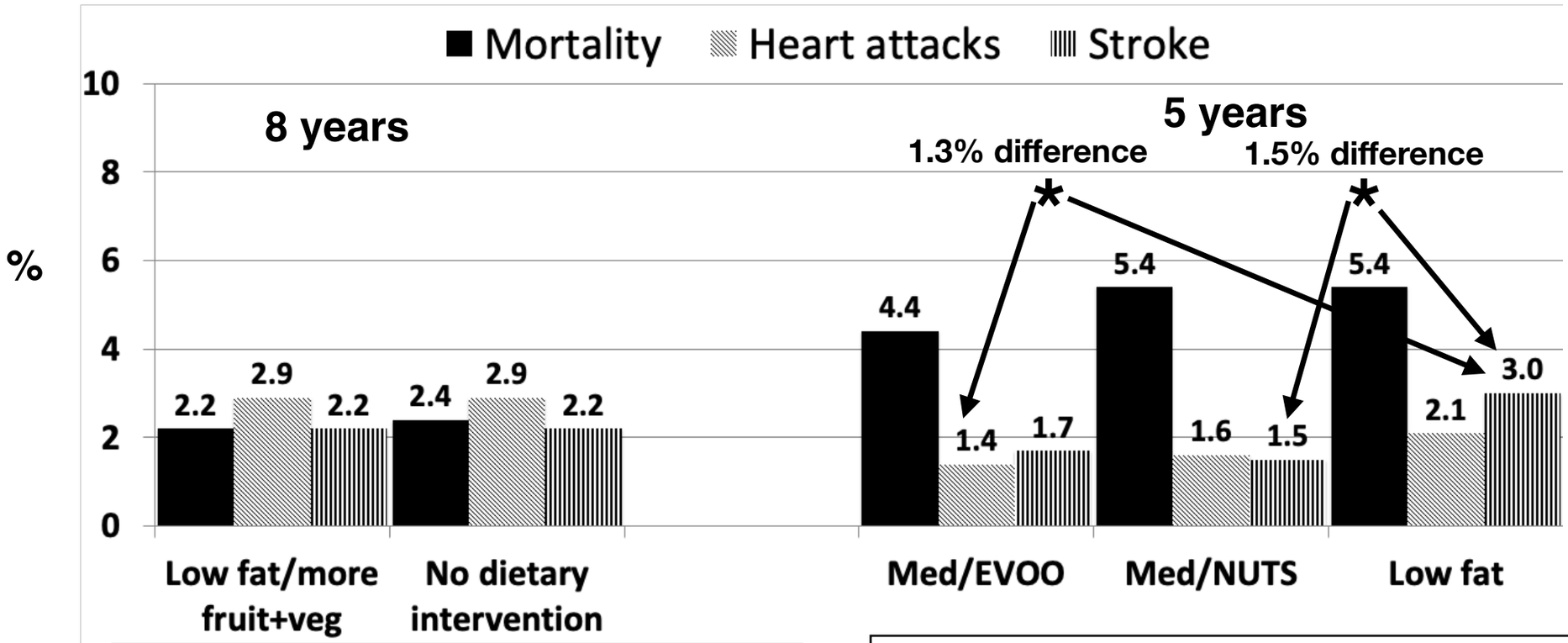
DART 1989 - 2,000 men - 2 years

LYON 1994 - 600 people, 10% female - 2 years

CORDIOPREV 2022 - 1000 people, 17% female - 7 years

People with NO previous history of heart attacks/strokes

these numbers were reported as statistical different, everything else was not statistically different



2006 - WHI - USA
48,835 subjects, 100% female,
62 y/o, 7% smokers

ACTUAL NUTRITIONAL CHANGES MADE

~10% ⬇ in energy from fat
⬆ one more serving a day of vegetables/fruit
~1.4 ⬇ in servings a week of meat

2018 - PREDIMED - Spain
7447 subjects, 57% female,
62 y/o,14% smokers

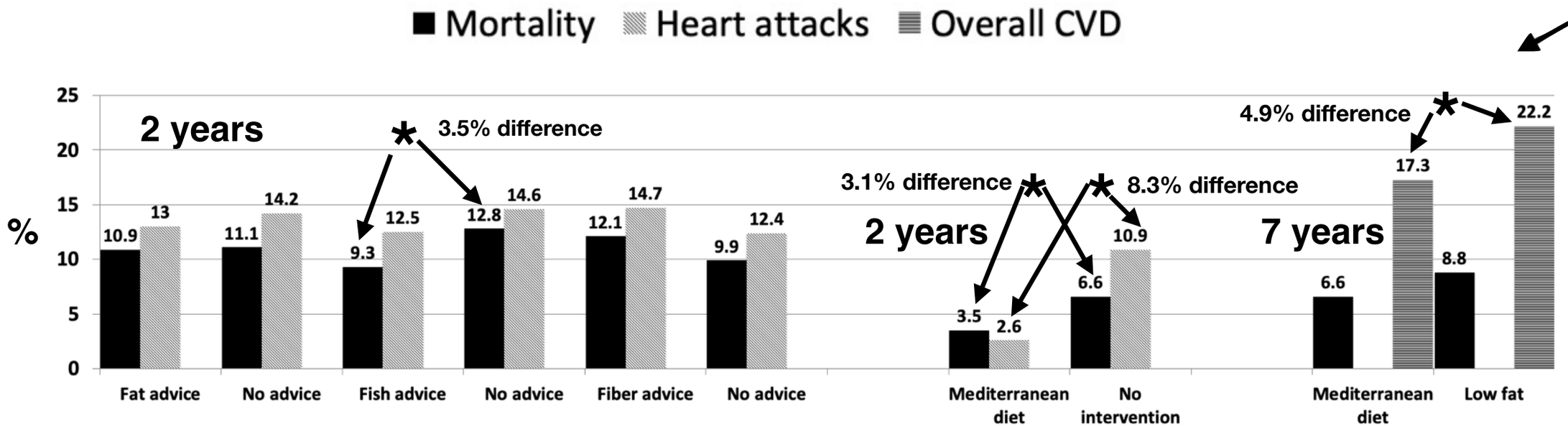
ACTUAL NUTRITIONAL CHANGES MADE

⬆ weekly servings of fish (by 0.3 servings) and legumes (by 0.4 servings)
used 1 litre/week of extra virgin olive oil
or took 30 gm of mixed nuts/day

The 5 large RCTs of nutrition intervention

these numbers were reported as statistical different, everything else was not statistically different

People with previous history of heart attacks/strokes



1989 - DART - Wales 2033 subjects, 100% male, 56 y/o, 62% smokers
ACTUAL NUTRITIONAL CHANGES MADE
⬆ fibre intake from ~10g/day to ~20g/day ⬆ polyunsaturated/saturated fat ratio from ~0.4 to ~0.8 fish intake - ⬆ EPA from ~0.7g/week to ~2.4g/week ⬇% fat energy from ~35 % to ~32%

1994 - Lyon - France 605 subjects, 90% male, 53 y/o, ~15-20% smokers
ACTUAL NUTRITIONAL CHANGES MADE
⬌ polyunsaturated/saturated fat ratio ⬇ cholesterol 318 mg/day vs 217 mg/day ⬇ calories ~2100 vs ~1900 ⬇ saturated fat ~12% of total calories vs ~8% significantly ⬆ intake of bread, fruit, and margarine; and a ⬇ intake of butter, cream, meat, ham, sausage, and offal

2022 - CORDIOPREV - Spain 1002 subjects, 83% male, 60 y/o, ~10% smokers
ACTUAL NUTRITIONAL CHANGES MADE
Med diet ⬆ total fat from 37% to 41% ⬆ amount of extra virgin olive oil/nuts/oily fish ⬇ carbs from 41% to 37% **Low fat diet** ⬇ total fat from 37% to 32% ⬆ carbs from 42% to 46%

Systematic review and network meta-analysis of randomised controlled trials.

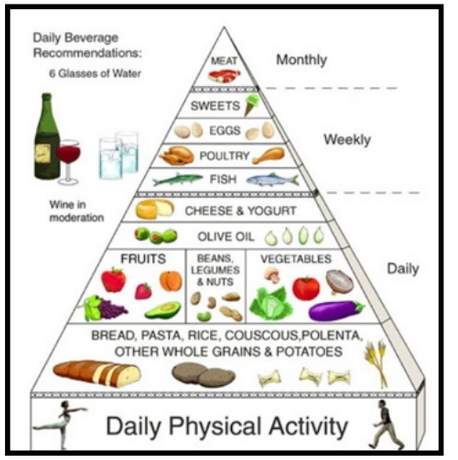
All numbers are absolute differences - over 5 years

BASELINE RISK	**5-10% 5-year CVD risk**				**20-30% 5-year CVD risk**			
Dietary programme *v* minimal intervention (usual or no/ minimal advice)	**All cause mortality**	**Cardiovascular mortality**	**Stroke**	**Non-fatal myocardial infarction**	**All cause mortality**	**Cardiovascular mortality**	**Stroke**	**Non-fatal myocardial infarction**
Mediterranean	2% ⬇	1% ⬇	1% ⬇	2% ⬇	4% ⬇	4% ⬇	2% ⬇	4% ⬇
Low fat (20-30% of diet)	1% ⬇	No difference		1% ⬇	2% ⬇	No difference		2% ⬇
Very low fat (10-20% of diet)	No difference							
Modified fat (⬆ polyunsaturated fat/⬇saturated fat)	No difference							
Combined low fat-low sodium	No difference							
Ornish (<10% fat)	No difference							
Pritikin (<10% fat)	No difference							
Low carb	**NO TRIALS**							

BMJ 2023;380:e072003 http://dx.doi.org/10.1136/ bmj-2022-072003

By far the best, if not the only, nutrition RCT evidence for cardiovascular outcomes (heart attacks/strokes) comes from the

Mediterranean Diet -⬇CVD ~30%



Med Diet is approximately the same as the

DASH Diet

Most national food guides

DASH

US

Canada

Low fat diet - minimal evidence of cardiovascular benefit

Low carb diet - NO evidence one way or the other

AS WITH EVERY DIET
Eat in "**moderation**"

Weight perspective - all about moderation if any effect on risk factors

BUT THERE ARE BIG CAVEATS

Almost all the nutrition "benefits and harms" evidence comes from cohort studies

real possibility of important publication bias because 100s to 1000s of researchers are looking at 100s of different databases

many potential confounders - let alone data collection issues

many associations seen in cohort studies are quite small (<10% relative) and only seen when you compare "lots quantiles" to "not much at all quantiles"

in general - single cohorts - unless that is all you have - should not be used as solid evidence

A lot of nutrition research is based on surrogate marker (blood pressure, lipids, glucose) impact

the changes seen **IF** they translated into effects on clinical outcomes would only amount to a 1% (at most 2%) absolute change in CVD risk over 10 years

in general - single RCTs of surrogates - should not be considered high quality evidence

There are only 5 large RCTs (2+years) that have looked at important clinical outcomes

the "best evidence" is for the "Mediterranean Diet" and even that only showed a 1 to 2% absolute ⬇ in stroke over 5 years in people without a history of CDV - and a bigger decrease (⬇3 to 8%) for people with a history of CVD

Nutrition advice to which pretty much everyone agrees

But the magnitude of the effect is “smaller than you may think”

based on the Best Available Evidence

1. Eat a greater percentage of whole foods (food that has not been overly processed or refined as little as possible)
2. Eat more vegetables
3. Eat less added sugar
4. Eat more whole grains
5. **Eat in a style that fits your food preferences, tolerances, and lifestyle**
6. **Eat in a style you can sustain**
7. **When it comes to weight, how much you eat is really the KEY issue**
8. The “best” weight is the weight you are when living the healthiest life you can enjoy
9. Avoid any food that has, for you, been properly shown to cause unacceptable intolerances

Activity

Aerobic Activity Examples

Moderate-intensity

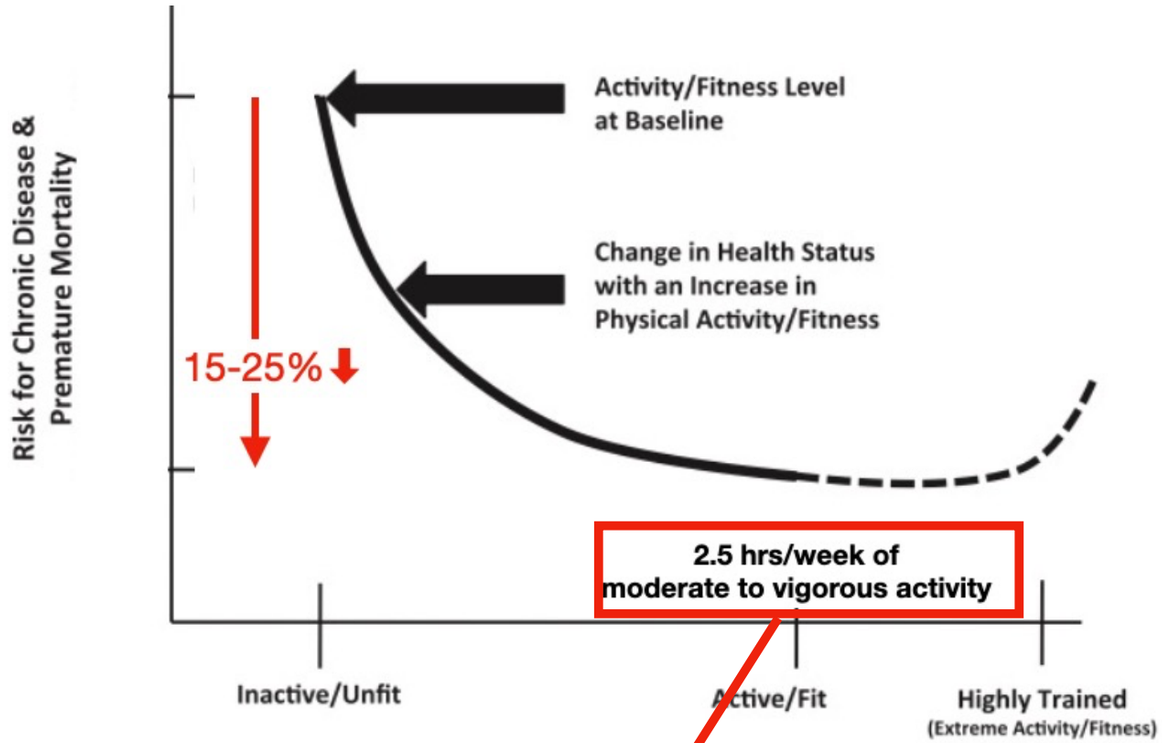
brisk walking - at least 4 km/2.5 miles/hour
water aerobics
ballroom or social dancing
gardening
doubles tennis
biking - slower than 15 km/10 miles/hour

Vigorous-intensity

hiking uphill or hiking with a heavy backpack
running
swimming laps
vigorous aerobic dancing
heavy yard work such as continuous digging or hoeing
singles tennis
biking - 15 km/10 miles/hour or faster
jumping rope

https://www.heart.org/en/healthy-living/fitness/fitness-basics/aha-recs-for-physical-activity-in-adults

There is NO specific activity THRESHOLD
BUT…



Curr Opin Cardiol 2017, 32:000 – 000

~1hr/week of vigorous
and/or
~4-5hr/week of moderate activity

Summary Table: Total Steps vs. Health Outcomes

Daily Steps	Associated Benefit
~2,300	Reduced cardiovascular death risk Harvard Health
~3,800–3,900	Lower all-cause mortality & dementia risk Marie Harvard Health kumc.edu uclahealth.org
~4,000–5,000	General health gains; threshold beyond sedentary levels New York Post hsph.harvard.e- uclahealth.org
~6,000–8,000	Benefits plateau for older adults sph.unc.edu The University New York Post
~8,000–10,000	Plateau benefits for younger adults sph.unc.edu uclahealth.org New York Post
10,000+	Strong across-the-board benefits (cardio, dementia, chronic illness) kumc.edu uclahealth.org Harvard Health

Final Take (with a wink)

The "10,000 steps" myth is fading—but the truth is way more encouraging. Even under **4,000 steps a day can move the needle** on major health risks. The major gains come early, and the payoff plateaus between **6,000–8,000 for older adults** and **8,000–10,000 for younger ones**. And remember: **quantity** beats **intensity** when counting your steps.

ChatGPT

Activity Evidence

Exercise for secondary prevention (RCTs)

Death at 4 years - NNT= 32

Heart failure admissions at 2 years - NNT = 14

Similar to medications?

Tools for Practice #145


Exercise for patients with major depression: a systematic review with meta-analysis and trial sequential analysis

Jesper Krogh,[1] Carsten Hjorthøj,[1] Helene Speyer,[1] Christian Gluud,[2] Merete Nordentoft[1]

BMJ Open 2017;7:e014820.

"There is currently no evidence in favour of exercise for patients with depression with a view to ameliorate depressive symptoms"

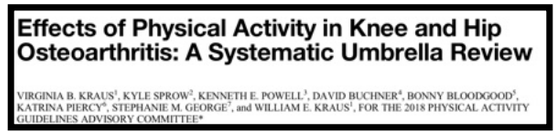
Low vs high risk for bias issue

Exercise for primary prevention (Cohorts)

Going from inactivity to current recommendations

CVD - RR = 0.83 (0.77-0.89)

J Am Heart Assoc. 2016;5:e002495 doi: 10.1161/JAHA.115.002495


Effects of Physical Activity in Knee and Hip Osteoarthritis: A Systematic Umbrella Review

VIRGINIA B. KRAUS[1], KYLE SPROW[2], KENNETH E. POWELL[3], DAVID BUCHNER[4], BONNY BLOODGOOD[5], KATRINA PIERCY[6], STEPHANIE M. GEORGE[7], and WILLIAM E. KRAUS[1], FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE*

Medicine & Science in Sports & Exercise 2019;51:1324-39

"Physical activity decreases pain, improves physical function and HRQoL among people with hip and/or knee OA relative to less active adults with OA"

Blood Pressure

Therapeutic Class	Generic	Common Canadian brand(s)	Typical starting dos	Usual dose range
FIRST LINE				
Thiazide-type diuretics	Hydrochlorothiazide	Various generics (formerly HydroDIURIL/Esidrix)	12.5–25 mg qAM	12.5–50 mg/day
	Chlorthalidone	Generics; (Thalitone in some markets)	12.5 mg qAM	12.5–25 mg/day
	Indapamide	Lozide (indapamide) / generics	1.25 mg qAM	1.25–2.5 mg/day
COULD BE FIRST LINE				
ACE inhibitor	Ramipril	Altace / generics	2.5 mg	2.5–10 mg/day
	Perindopril	Coversyl / generics	2–4 mg	4–8 mg/day
	Enalapril	Vasotec / generics	5 mg	5–40 mg/day (divided)
	Lisinopril	Prinivil/Zestril / generics	5–10 mg	10–40 mg/day
	Cilazapril	Inhibace / generics	1 mg	1–5 mg/day
	Fosinopril	Monopril / generics	10 mg	10–40 mg/day
	Trandolapril	Mavik / generics	1 mg	1–4 mg/day
ARB	Losartan	Cozaar / generics	25–50 mg	50–100 mg/day
	Valsartan	Diovan / generics	80 mg	80–320 mg/day
	Irbesartan	Avapro / generics	150 mg	150–300 mg/day
	Candesartan	Atacand / generics	8 mg	8–32 mg/day
	Telmisartan	Micardis / generics	40 mg	40–80 mg/day
	Olmesartan	Olmetec / generics	20 mg	20–40 mg/day
NEXT LINE				
CCB (dihydropyridine)	Amlodipine	Norvasc / generics	2.5–5 mg	5–10 mg/day
	Nifedipine XL	Adalat XL / generics	30 mg	30–90 mg/day
	Felodipine	Plendil / generics	2.5–5 mg	5–10 mg/day
CCB (non-DHP)	Diltiazem (CD/TZ)	Cardizem/Tiazac / generics	120–180 mg	120–360 mg/day
	Verapamil SR	Isoptin SR / generics	120–180 mg	120–360 mg/day
Beta-blocker	Metoprolol (IR/SR)	Generics (Lopresor SR formerly)	25–50 mg	50–200 mg/day
	Bisoprolol	Monocor / generics	2.5–5 mg	2.5–10 mg/day
	Atenolol	Tenormin / generics	25–50 mg	50–100 mg/day
	Propranolol (LA)	Inderal-LA / generics	60–80 mg	80–240 mg/day
	Carvedilol	Coreg / generics	6.25 mg BID	6.25–25 mg BID
Add-on for hypokalemia prevention				
Potassium-sparing	Amiloride	Generics	5 mg	5–10 mg/day
	Triamterene	Generics (often in combos)	50 mg	50–100 mg/day
Difficult to control and for hypokalemia				
Mineralocorticoid receptor antagonists	Spironolactone	Aldactone / generics	12.5–25 mg	12.5–50 mg/day
	Eplerenone	Inspra	25 mg	25–50 mg BID
If fluid overload is an issue				
Loop diuretics	Furosemide	Lasix / generics	20–40 mg	20–160 mg/day (divided)
	Torsemide	Demadex / generics	2.5–5 mg	2.5–20 mg/day
PRETTY MUCH DON'T USE				
Alpha-1 blocker	Doxazosin	Cardura / generics	1 mg HS	1–8 mg/day
	Prazosin	Minipress / generics	1 mg BID	2–5 mg BID/TID
	Terazosin	Hytrin / generics	1 mg HS	1–10 mg/day
Central alpha-2 agonist	Clonidine	Catapres / generics	0.1 mg BID	0.1–0.3 mg BID
Central agent	Methyldopa	Aldomet / generics	250 mg BID	250–500 mg BID/TID
Direct vasodilator	Hydralazine	Apresoline / generics	10–25 mg TID	25–100 mg TID/QID
	Minoxidil	Loniten / generics	2.5–5 mg	5–40 mg/day
Direct renin inhibitor	Aliskiren	Rasilez / Tekturna (availability variable)	150 mg	150–300 mg/day

Canadian Blood Pressure Meds

Getting the real BP#s

How much does the BP impact the estimated CVD risk?

How much do treatments change BP?

SBP

How much do treatments reduce CVD risks?

What are the harms of treatment?

How often do you have to re-measure BP?

Reducing the “pressure” of high blood pressure

GOAL = Make it as
Simple as Possible - but not Simpler

What is the “real” SBP

White Coat Hypertension (WCH)

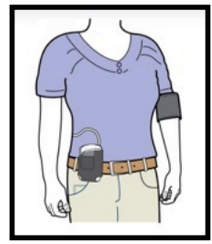
10-30% of people with elevated office BP have “WCH”

WCH = when you get a higher blood pressure reading in the health care providers office than one does at home

Most (but not all) studies have shown that WCH is **NOT** associated with an increased risk of cardiovascular events and/or mortality

Hypertens Rep. 2024 May 18. doi: 10.1007/s11906-024-01309-0

KEY MESSAGE - risk should be based on what the SBP is **“at HOME”** - so likely best to use HOME numbers to estimate CVD risk - either 24-hr ambulatory or home measurements



Home measurements - no absolute rule - for ~ 1 week take 2 measurements in both the **morning** and **evening** separated by **1 minute -** then roughly **average** all the numbers over the week and consider that **YOUR SBP**

2) Meds That Increase BP - daily use of ibuprofen, naproxen and acetaminophen

3) Primary Aldosteronism ~ 10% - as high as 10-30% if resistant hypertension

Drug-Induced ⬆ Blood Pressure

Prescription Drugs:

NSAIDs, including coxibs

Corticosteroids and anabolic steroids

Oral contraceptive and sex hormones

Vasoconstricting/sympathomimetic decongestants

Calcineurin inhibitors (cyclosporin, tacrolimus)

Erythropoietin and analogues

Monoamine oxidase inhibitors (MAOIs)

Midodrine

Other substances:

Alcohol, Licorice root, Stimulants including cocaine, Salt.

How much do “lifestyle” treatments lower SBP?

Intervention	SBP mmHg
Diet and weight control	-6.0
Reduced sodium intake	-5.4
Reduced alcohol intake (if heavy)	-3.4
DASH diet	-11.4
Physical activity	-3.1
Relaxation techniques	-5.5
Increased potassium intake	-3.5

→ ~5 mmHg

NIH and NICE May 2011

Average person consumes between 3,000 and 3,500 mg of sodium (Na) = ~1.5 teaspoons of salt

Decrease Na/Salt by 1/3

⬇ sodium by ~1800 mg/day	SBP
High blood pressure	⬇5 mmHg
“Normal”	⬇2.5 mmHg

BMJ 2013; 346 doi: https://doi.org/10.1136/bmj.f1325

Salt substitutes also ⬇ SBP by 5 mmHg

Heart 2022;108:1608–1615. doi:10.1136/heartjnl-2022-321332

100% NaCl

3/4
75%

+ 1/4
25%

100% KCl

= Pretty much don’t have to worry about the amount of salt

~80%+ people have no taste issues with 75/25 salt Clin Hypertens 2016;22:18

Effect of alcohol reduction on BP

Amount of regular alcohol use	Reduction in alcohol consumption by 50% 1-104 weeks
2 or fewer drinks a day	**No effect on blood pressure**
3 drinks a day	⬇1/1 mmHg
4-5 drinks a day	⬇3/2 mmHg
6+ drinks a day	⬇6/4 mmHg

Meta-analysis - 36 trials 2017 Roerecke

Blood pressure treatments and their relative benefit on cardiovascular disease

Medication Examples

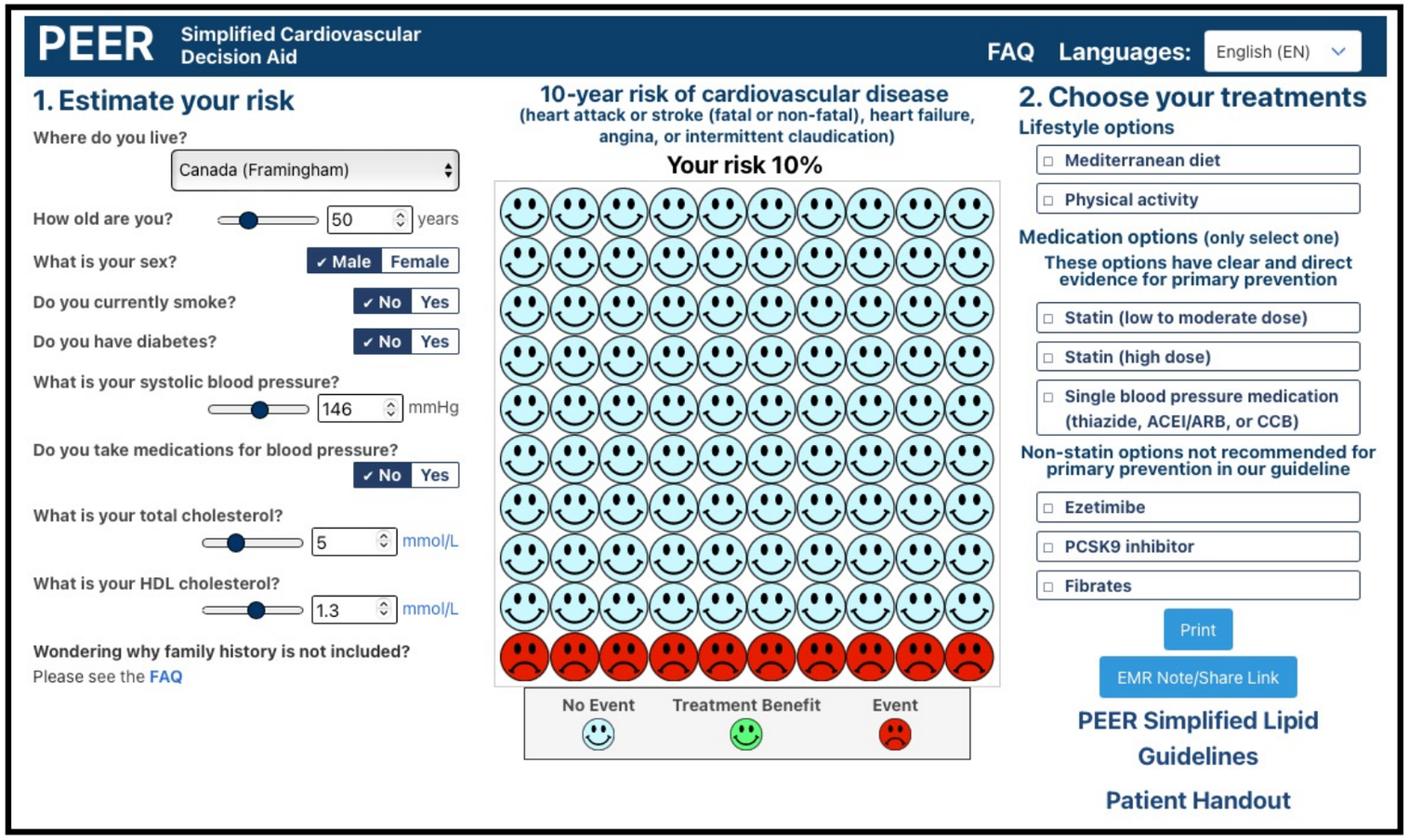
Thiazide	**BRAND NAME**
Hydrochlorothiazide	Hydrodiuril
Chlorthalidone	Hygroton
ACE inhibitor	
Indapamide	Lozide
Ramipril	Altace
Lisinopril	Zestril
Perindopril	Coversyl
Enalapril	Vasotec
ARB	
Losartan	Cozaar
Candesartan	Atacand
Valsartan	Diovan
Telmisartan	Micardis
Losartan	Cozaar
Olmesartan	Benicar

		Heart attack/ stroke benefit
1st	Salt substitute 75%Na/25%K	**10-15%⬇**
2nd	Thiazide lower dose	**25%⬇**
3rd	ACE/ARB lower dose	**25%⬇**
Others	Betablockers, calcium channel blockers	Some but less than those above

There are also a number of combination products

Thiazide/ACE
Thiazide/ARB

If use generic medications and/or combos and/or split tablets
Cost should be
<$150/year



Let's say the risk of a cardiovascular event is

10% over the next 10 years

IMPORTANT

An Example of the Numbers

	Relative benefit	**10% BASELINE** 10-year risk of a heart attack or stroke	# of people who get a benefit from 10 years of "treatment"	# of people who get **NO** benefit from 10 years of "treatment"
Salt substitute	10-15% ⬇	Revised Risk ~8-9%	1-2%	98-99%
add 1 BP medication	25% ⬇	Revised Risk ~6-7%	3-4%	96-97%

If **BASELINE** risk was **5%** then cut these numbers in **HALF**

If **BASELINE** risk was **20%** then **DOUBLE** these numbers

HARMS

VERY MUCH DOSE DEPENDENT

~10%? don't "tolerate" a particular medication at standard doses

Hypotension is likely the most important risk

Thiazides/Diuretics

TOXICITY

Hypotension

Hypokalemia

Gout

Hyperglycemia?

Hypomagnesemia

Hypercalcemia

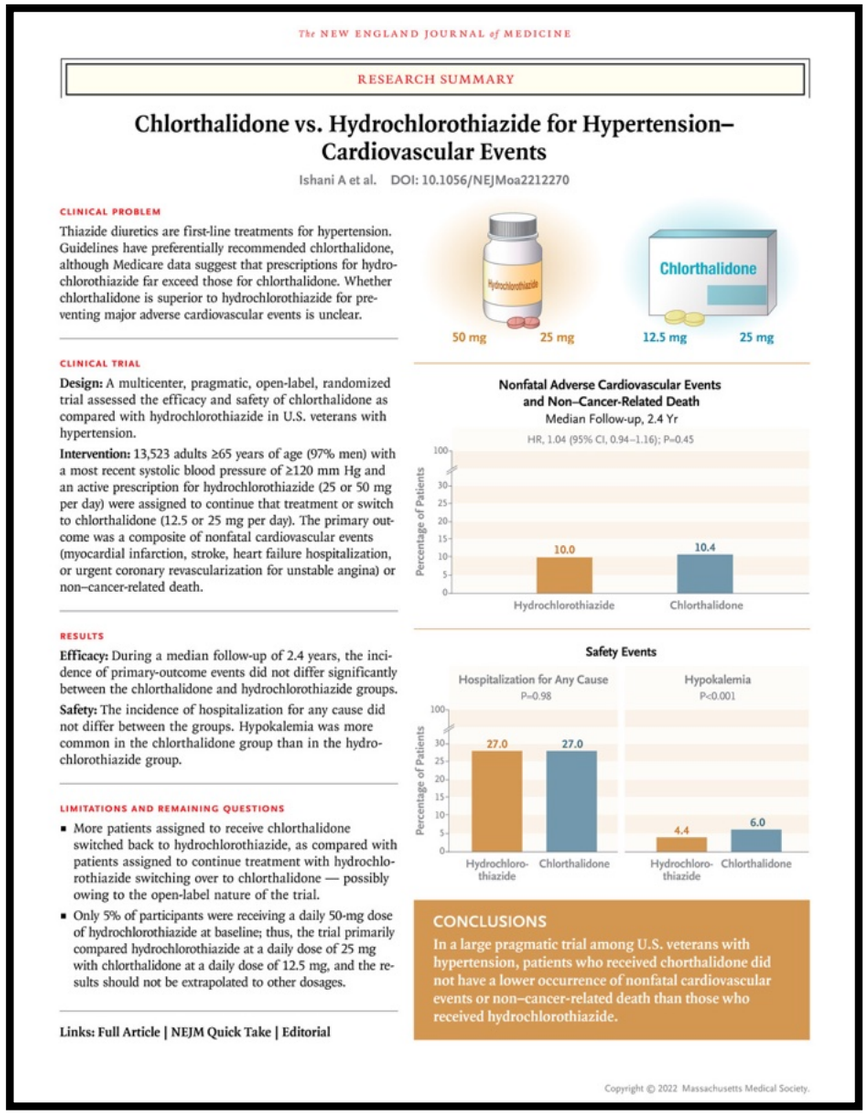
Hyperlipidemia

Blood dyscrasias

Photosensitivity

Gynecomastia (spironolactone)

NEJM 2022 - Pragmatic trial
13,500 people - 2.5 years
25mg HCTZ vs 12.5mg chlorthalidone



The NEW ENGLAND JOURNAL of MEDICINE

RESEARCH SUMMARY

Chlorthalidone vs. Hydrochlorothiazide for Hypertension–Cardiovascular Events

Ishani A et al. DOI: 10.1056/NEJMoa2212270

CLINICAL PROBLEM

Thiazide diuretics are first-line treatments for hypertension. Guidelines have preferentially recommended chlorthalidone, although Medicare data suggest that prescriptions for hydrochlorothiazide far exceed those for chlorthalidone. Whether chlorthalidone is superior to hydrochlorothiazide for preventing major adverse cardiovascular events is unclear.

CLINICAL TRIAL

Design: A multicenter, pragmatic, open-label, randomized trial assessed the efficacy and safety of chlorthalidone as compared with hydrochlorothiazide in U.S. veterans with hypertension.

Intervention: 13,523 adults ≥65 years of age (97% men) with a most recent systolic blood pressure of ≥120 mm Hg and an active prescription for hydrochlorothiazide (25 or 50 mg per day) were assigned to continue that treatment or switch to chlorthalidone (12.5 or 25 mg per day). The primary outcome was a composite of nonfatal cardiovascular events (myocardial infarction, stroke, heart failure hospitalization, or urgent coronary revascularization for unstable angina) or non–cancer-related death.

RESULTS

Efficacy: During a median follow-up of 2.4 years, the incidence of primary-outcome events did not differ significantly between the chlorthalidone and hydrochlorothiazide groups.

Safety: The incidence of hospitalization for any cause did not differ between the groups. Hypokalemia was more common in the chlorthalidone group than in the hydrochlorothiazide group.

LIMITATIONS AND REMAINING QUESTIONS

- More patients assigned to receive chlorthalidone switched back to hydrochlorothiazide, as compared with patients assigned to continue treatment with hydrochlorothiazide switching over to chlorthalidone — possibly owing to the open-label nature of the trial.
- Only 5% of participants were receiving a daily 50-mg dose of hydrochlorothiazide at baseline; thus, the trial primarily compared hydrochlorothiazide at a daily dose of 25 mg with chlorthalidone at a daily dose of 12.5 mg, and the results should not be extrapolated to other dosages.

Links: Full Article | NEJM Quick Take | Editorial

Nonfatal Adverse Cardiovascular Events and Non–Cancer-Related Death
Median Follow-up, 2.4 Yr

Safety Events

CONCLUSIONS

In a large pragmatic trial among U.S. veterans with hypertension, patients who received chorthalidone did not have a lower occurrence of nonfatal cardiovascular events or non–cancer-related death than those who received hydrochlorothiazide.

NO DIFFERENCE

HCTZ - 10% vs Chlorthalidone -10.4%

Composite of nonfatal myocardial infarction, stroke, heart failure resulting in hospitalization, urgent coronary revascularization for unstable angina, and non–cancer-related death

Low potassium ~1.5% ⬆ in chlorthalidone vs HCTZ

6% vs 4.4%

ACE Inhibitors

CONTRAINDICATIONS

Intolerance or allergic reaction to ACE inhibitors

Pregnancy

Rapidly worsening renal failure

Severe hypotension

Bilateral renal artery stenosis, unilateral renal artery stenosis in a patient with one kidney

TOXICITY

Acute renal failure - esp if volume depleted

Hyperkalemia

Hypotension

Dry cough -5-20%

Rash, mucosal ulcerations

Angioedema

Angiotensin II receptor antagonists

CONTRAINDICATIONS

Intolerance or allergic reaction to ARBs

Pregnancy

Rapidly worsening renal failure

Severe hypotension

Bilateral renal artery stenosis, unilateral renal artery stenosis in a patient with one kidney

TOXICITY

Acute renal failure - esp if volume depleted

Hyperkalemia

Hypotension

Angioedema - reported??

Betablockers

CONTRAINDICATIONS

Asthma or chronic bronchitis with bronchospasm

Raynauds

Intermittent claudication?

Bradycardia, atrio-ventricular conduction defects

TOXICITY

Fatigue

Bradycardia, decreased exercise capacity

Asthma

CNS effects

Cold extremities

Calcium channel blockers

CONTRAINDICATIONS

Severe left ventricular dysfunction (EF< 20-30%)

Second- or third-degree AV block or sick sinus syndrome (unless a functioning ventricular pacemaker is in place)

Wolff-Parkinson-White syndrome

Wide-complex ventricular tachycardia

TOXICITY

Hypotension

Headache

Bradycardia (verapamil)

Dizziness or lightheadedness

Exacerbation of congestive heart failure (verapamil)

Constipation

Peripheral edema

Heart burn

IMPORTANT

How much do medications lower blood pressure?

"**Most (70%) of the blood pressure lowering effect** can be achieved with the **lowest recommended dose of the drugs.**"

1/8-1/4 max dose - ⬇SBP ~ 5 mmHg	60-70%
1/2 max dose - ⬇SBP ~ 7 mmHg	90%
Max dose - ⬇SBP ~ 8 mmHg	100%

Blood pressure lowering efficacy of angiotensin converting enzyme (ACE) inhibitors for primary hypertension (Review)

Heran BS, Wong MMY, Heran IK, Wright JM

Blood pressure lowering efficacy of angiotensin receptor blockers for primary hypertension (Review)

Heran BS, Wong MMY, Heran IK, Wright JM

Blood pressure-lowering efficacy of monotherapy with thiazide diuretics for primary hypertension (Review)

Musini VM, Nazer M, Bassett K, Wright JM

Blood pressure-lowering efficacy of antihypertensive drugs and their combinations: a systematic review and meta-analysis of randomised, double-blind, placebo-controlled trials

Nelson Wang, Abdul Salam*, Rashmi Pant, Amit Kumar, Rupasvi Dhurjati, Faraidoon Haghdoost, Kota Vidyasagar, Prachi Kaistha, Hariprasad Esam, Sonali R Gnanenthiran, Raju Kanukula, Paul K Whelton, Brent Egan, Aletta E Schutte, Kazem Rahimi, Otavio Berwanger, Anthony Rodgers*

484 trials including 104,176 participants

Single med at standard dose ⬇ SBP by 8·7 mm Hg

each doubling in dose conferred an additional ⬇ of 1·5 mm Hg

2 meds at standard doses 14·9 mm Hg ⬇

each doubling of doses of both drugs conferred an additional ⬇ of 2·5 mm Hg

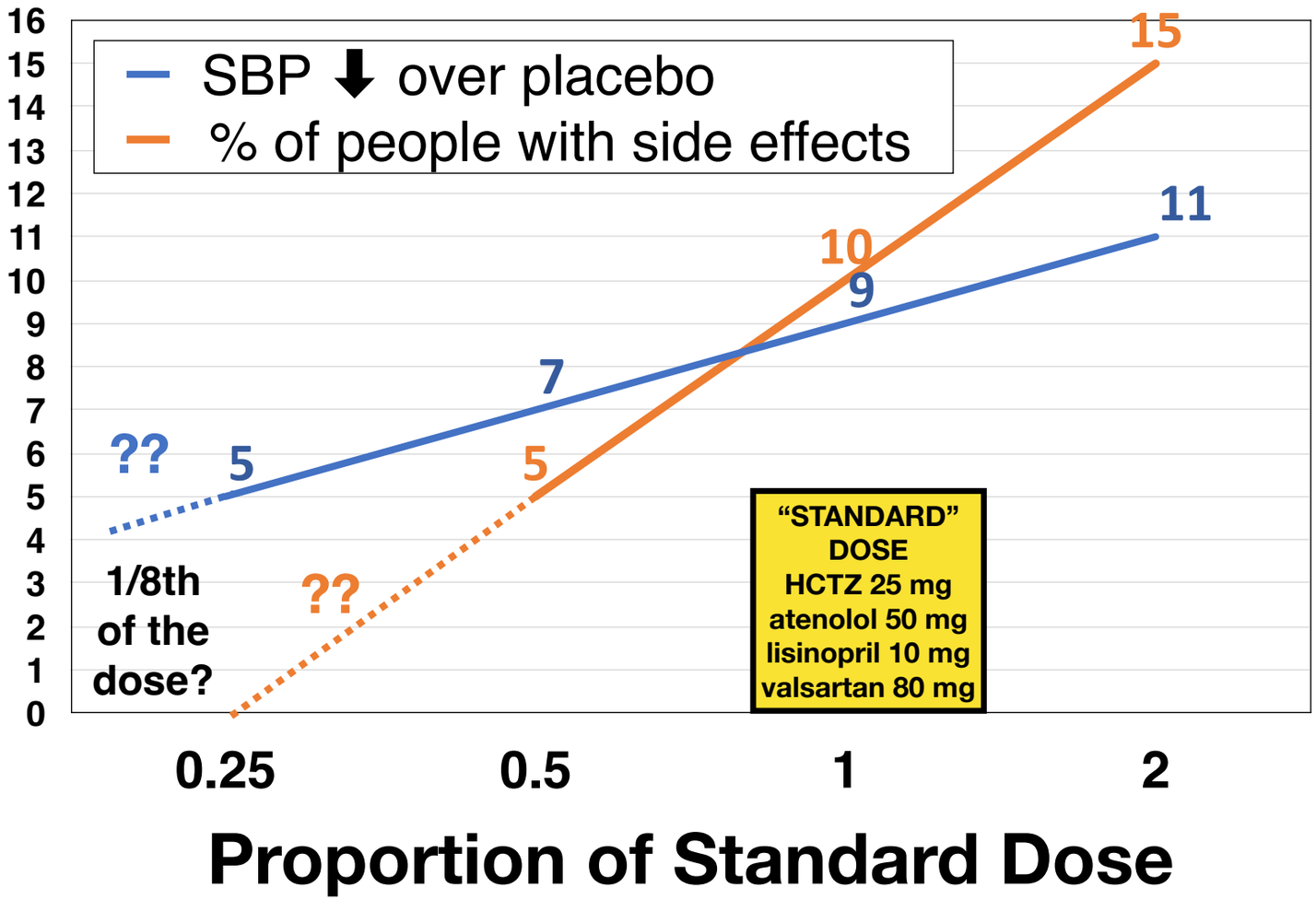
Half standard doses gave 70% of the effect

Lancet 2025;406:915–25

IMPORTANT

Average SBP decrease over placebo and % with side effects on different amounts of a "standard dose" - each increment is a doubling of the dose

mmHg⬇ and % of people with side effects



ADAPTED FROM

BMJ. 2003 Jun 28;326(7404):1427.doi: 10.1136/bmj.326.7404.1427

All measurements have variation

	# of measurements	The Measurement Variation	If you “average” 150 mmHg all you can say is your SBP is somewhere between these ranges
Office	3 at each of 2 visits, 6 weeks apart	~+/- 10 mmHg*	140-160 mmHg
Ambulatory	continuous over 24h	~+/- 10 mmHg**	140-160 mmHg
Home monitored	1 week of 3-4 daily	~+/- 8 mmHg	142-158 mmHg

* to get to ~+/-5 mmHg - 10-13 measurements are required
** because only a single day

“attempting to **fine-tune drug doses** is probably **pointless**”
“**40 office blood pressure measurements** are required both before and after a prescription to be reasonably confident of **detecting a TRUE reduction of 5 mmHg**.”

British Journal of General Practice 2010;60:675–680

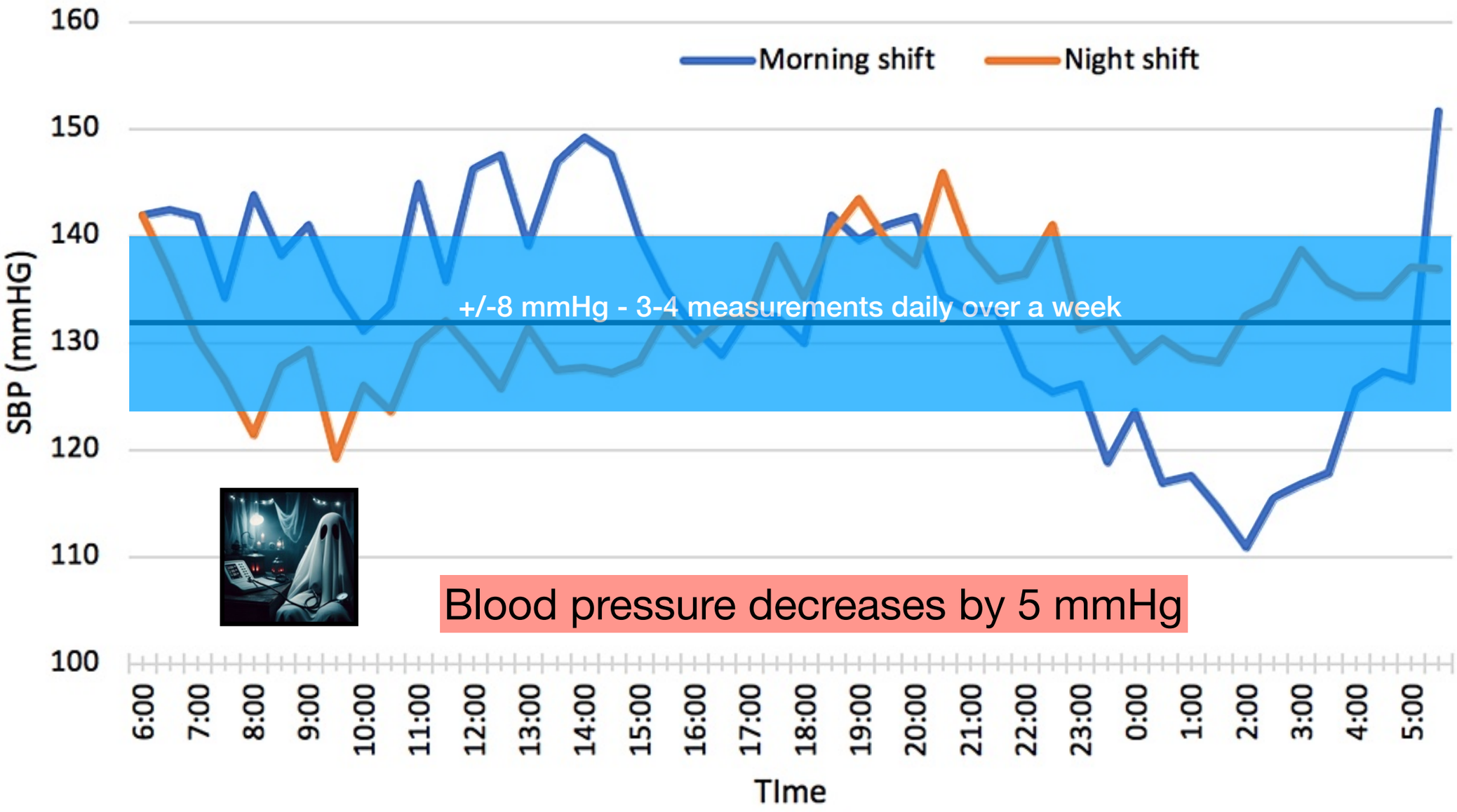
IMPORTANT

Most “treatments” reduce systolic blood pressure on average by ~5 mmHg.

So unless you are using a properly calibrated machine and doing dozens of measurements at the same time of the day both before and after making a change and then averaging them over weeks, you can’t fine-tune.*

In other, words most of the changes you see are simply the “GHOSTS” of measurement variation

*Now, if you combined multiple interventions over time - eg 2 low-dose medications and lowered salt intake, lost 10kg and became physically active etc - and you see over time your SBP has dropped from say ~150 mmHg on average down to 125 to 130. With this large an average change you can likely say some of these things are responsible for the drop but you can’t figure out at all which “worked”


160
150
140
130
120
110
100
SBP (mmHG)
Morning shift
Night shift
+/-8 mmHg - 3-4 measurements daily over a week
Blood pressure decreases by 5 mmHg
6:00
7:00
8:00
9:00
10:00
11:00
12:00
13:00
14:00
15:00
16:00
17:00
18:00
19:00
20:00
21:00
22:00
23:00
0:00
1:00
2:00
3:00
4:00
5:00
TIme

The BP ⬇ numbers are fairly consistently simple

salt ⬇ or K^+ substitution ⬇ SBP by ~5 mmHg

1 drug at 1/4 to 1/2 of the standard dose ⬇ SBP by ~ 5 mmHg

2 drugs at 1/4 to 1/2 dose ⬇ SBP by ~10 mmHg

Adding a low dose 2nd medication = **DOUBLE** the effect on BP from what you would get from **DOUBLING** the dose

“placebo group” ⬇ SBP by ~5 mmHg

But don’t worry too much about the BP effect

Have these things been shown to ⬇ cardiovascular risk

BP measurement

Office	~+/- 10 mmHg*
Ambulatory	~+-10 mmHg**
Home monitored	~+-8 mmHg

“Initial BP changes after pharmacological BP lowering are **NOT informative for gauging individual treatment response**”

“BP measures made before and after treatment initiation should **NOT be the principal driver for clinical decision making**”

Hypertension. 2023;80:608–617. DOI: 10.1161/HYPERTENSIONAHA.122.20458

“the news is that probably **we do not have to trust too much on the initial blood pressure response to antihypertensive drugs as a measure of the long-term successful prevention of cardiovascular disease** in patients with hypertension.”

Hypertension. 2023;80:1180–1182. DOI: 10.1161/HYPERTENSIONAHA.123.20701

Target Shooting

Getting to a target 150, 140, 130, or 120?

This is TRICKY - for decades 140 mmHg was “the target and often it would be stated it should be 150 for the “elderly” because of concern for lowering BP too far and causing harm.

All BP guidelines recommend specific target blood pressures and they vary the targets based on age, diabetes, and other existing medical conditions of the person.

IMPORTANTLY and **FRUSTRATINGLY** guidelines often vary a lot from each other

Systolic Targets for age 60-69

150 mmHg

2020 U.S. Department of Veterans Affairs/U.S. Department of Defense

140 mmHg

2022 American Academy of Family Physicians
2022 National Institute for Health and Care Excellence
2020 International Society of Hypertension

130 mmHg

2021 European Society of Hypertension Council
2017 American College of Cardiology/American Heart Association

Systolic Targets for age 70-79

150 mmHg

2020 U.S. Department of Veterans Affairs/U.S. Department of Defense

140 mmHg

2022 American Academy of Family Physicians
2022 National Institute for Health and Care Excellence
2020 International Society of Hypertension
2021 European Society of Hypertension Council

130 mmHg

2017 American College of Cardiology/American Heart Association

120 mmHg

2020 Hypertension Canada

Getting to a target 150, 140, 130, or 120?

So it seems guidelines can't agree so obviously the evidence isn't all that clear

Over the last 20 years

~5-6 decent trials have looked at the impact of attempting to get systolic blood pressures under 130 mmHg and also 120 mmHg

In general, in the attempt to get people to these lower targets people needed to take ~1 extra medication on top of what they were already taking

Overall, getting "lower" has led to an additional 10-15% relative benefit. Hypertension Research 2019;42:483–95

However one trial (SPRINT) in 2015, reported a 25% benefit and that is the trial that guidelines use to justify lower targets.

The SPRINT trial is **THE MAIN DRIVER** of the get to 120 mmHg recommendation

A Randomized Trial of Intensive versus Standard Blood-Pressure Control

The SPRINT Research Group*

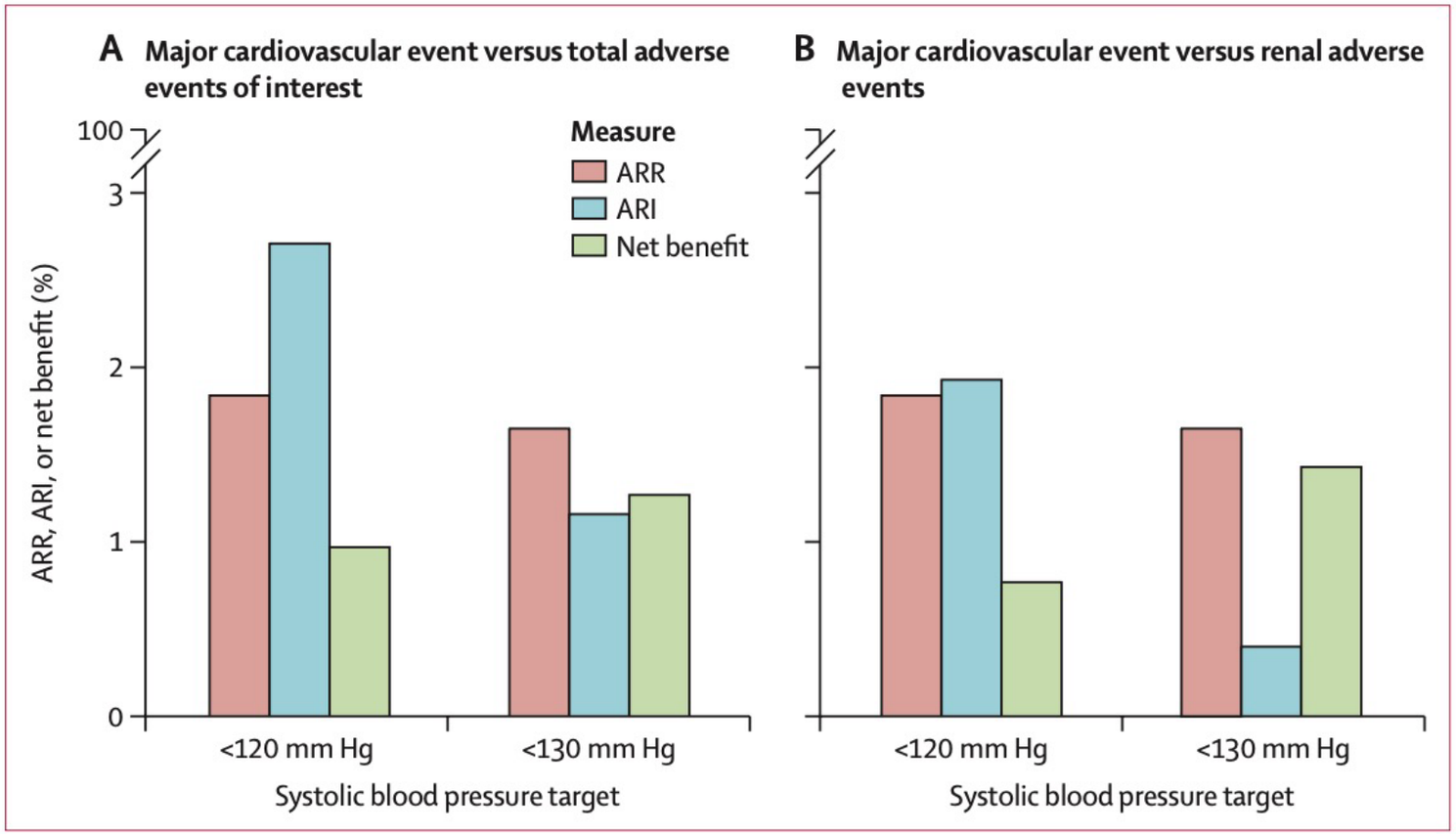
All the Important Results from SPRINT - over 3 years

	Number of meds required	Monitoring required	Myocardial infarction, acute coronary syndrome, stroke, heart failure, or death from cardiovascular	Acute kidney injury or acute renal failure	Serious adverse events (low blood pressure/low electrolytes) classified as possibly or definitely related to the intervention
Get to 140 mmHg Actually got to 135			6.8%	2.6%	2.5%
Get to 120 mmHg Actually got to 122	On average these people took 1 more medication	4-5 more office 4-5 visits required	5.2%	4.4%	4.7%
LOWER VS HIGHER			1.6%* ⬇	1.8% ⬆	2.2% ⬆

* 5.2% is **25%** lower than 6.8% - remember #s greater than 10% can be misleading without context

N Engl J Med 2015;373:2103-16

Net benefits of intensive versus standard blood pressure control in trials with different systolic blood pressure targets (<120 mm Hg and <130 mm Hg) - OVER 3 years



(A) Major cardiovascular events versus total adverse events of interest, weighted at 1·0:3·1.

(B) Major cardiovascular events versus renal adverse events, weighted at 1·0:1·8.

Total adverse effects = hypotension, syncope, injurious fall, arrhythmia, angio-oedema and renal adverse events

Renal adverse effects = acute kidney injury, renal failure, end-stage renal disease or dialysis, a reduction of 50% or more in estimated glomerular filtration rate in patients with chronic kidney disease at baseline, or a reduction of 30% or more in estimated glomerular filtration rate to <60 mL/min per 1·73 m^2 in patients without chronic kidney disease at baseline.

Lancet 2025;406:1009–19

$ Costs $

Use the lowest cost blood pressure medications?
Use the lowest cost medication within a class?
Split higher dose pills - higher doses typically the same price as lower doses

No-Brainer Bottom Lines

regardless of approach - target/fire and forget

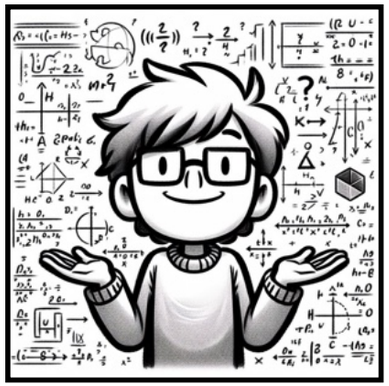
It’s hard to make an asymptomatic person feel better

There is RARELY any urgency to treating risk factor numbers number blood pressures in the 160 mmHg range

Given all the “DIFFERENT” guidelines it seems no one has the “correct answer” for the true target

When possible, discuss risk of a bad CVD outcome and the potential CVD benefits with patients

GOALS - 1/4 to 1/2 “normal” doses of the lowest priced medications and **ZERO SIDE EFFECTS**



A Simple Approach

If it was me

REGARDLESS OF THE NUMBERS

Eating - healthy food - Mediterranean Diet? - if ≤2 alcohol drinks a day wouldn't worry

Activity - do things they enjoy - "moderate" activity is all that is required for CVD benefit

ELEVATED OFFICE BP **- maybe don't measure? - REMEMBER the risk is BP "at home"**

Rule out white coat hypertension - ambulatory or home measurements - 20/10 diff?

IF TRULY "HYPERTENSIVE"

3/4  + 1/4 

a) Salt substitute (75%Na/25%K?) if acceptable - ~80%+ people no issue Clin Hypertens 2016;22:18

b) Then start 6.25mg HCTZ - wouldn't ⬆ the dose

c) If baseline was 160+? then add a low dose ACE/ARB 1/8 or 1/4 of the manufacturer's maximum recommended dose

d) Measure blood pressure if symptoms suggestive of hypotension

Lipids

Therapeutic Class	Generic	Common Canadian brand(s)	Typical starting dose	Usual dose range
FIRST LINE				
Statin	Atorvastatin	Lipitor / generics	10–20 mg	10–80 mg/day
	Rosuvastati	Crestor / generics	5–10 mg	5–40 mg/day
	Simvastatin	Zocor / generics	10–20 mg	10–40 mg/day
	Pravastatin	Pravachol / generics	20–40 mg	10–80 mg/day
	Lovastatin	Mevacor / generics	20 mg	20–80 mg/day
	Fluvastatin	Lescol / generics	40 mg	20–80 mg/day
NEXT				
Cholesterol absorption inhibitor	Ezetimibe	Ezetrol / generics	10 mg	10 mg/day
PCSK9 inhibitor	Evolocumab	Repatha	140 mg SC q2wk or 420 mg monthly	—
	Alirocumab	Praluent	75–150 mg SC q2wk	—
Omega-3 (EPA)	Icosapent e	Vascepa	2 g BID with meals	4 g/day
MAYBE				
ACL inhibitor	Bempedoic	Nexletol; + ezetimibe = Nexlizet/Nustendi*	180 mg	180 mg/day
siRNA (PCSK9)	Inclisiran	Leqvio	284 mg SC at 0, 3 months, then q6 months	—
DON'T USE				
Bile acid sequestrant	Colesevelan	Lodalis	3.75 g/day (single or divided)	3.75 g/day
	Cholestyran	Questran / generics	4 g daily	4–24 g/day (divided)
Fibrate	Fenofibrate	Lipidil / generics	145 mg	48–160 mg/day
	Bezafibrate	Bezalip / generics	400 mg	200–400 mg/day
	Gemfibrozil	Lopid / generics	600 mg BID	600 mg BID
Niacin (ER)	Niacin	Niaspan (availability varies)/generics	500 mg HS	1–2 g HS

Canadian Lipid Meds

Measuring the correct lipids

How much do lipids impact estimated CVD risk?

How much do treatments change lipids?

LDL

cholesterol

Also HDL, VLDL
ApoB, Lp(a) etc

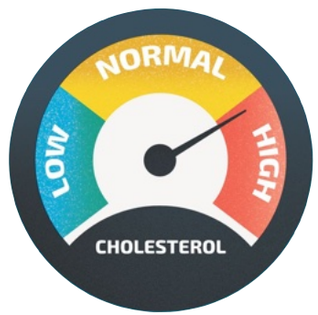
How much do treatments reduce CVD risks?

What are the harms of treatment?

How often do you have to re-measure your lipids?

The MAIN Reasons “Cholesterol” is Measured

1. To use in conjunction with other risk factors (age, blood pressure, diabetes etc) when making an **assessment of a person’s cardiovascular risk**

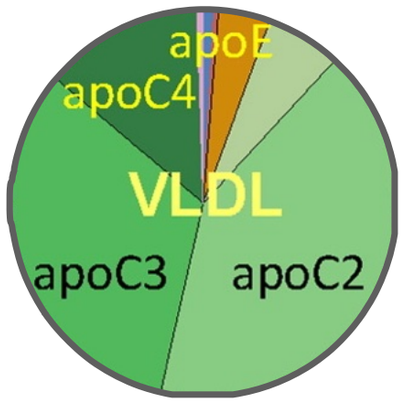


2. To see if a specific **treatment (meds, food, activity) has changed a person’s cholesterol**

GOAL = Make it as
Simple as Possible - but not Simpler

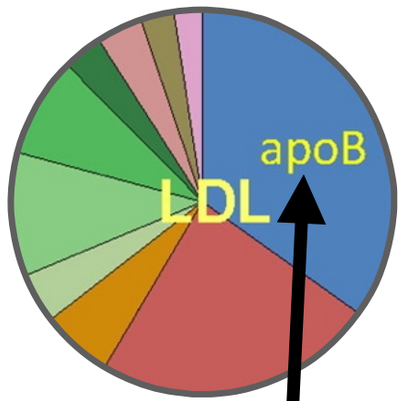
All the Different Lipids

Journal of Proteomics 2014;106:181-190

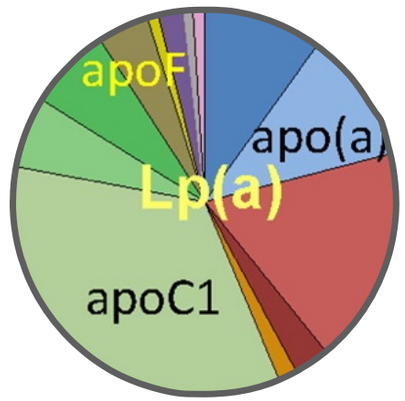


VLDL

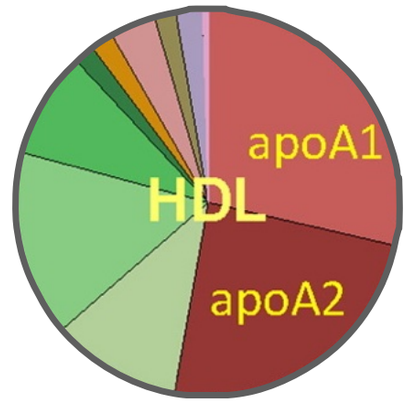
AKA triglycerides



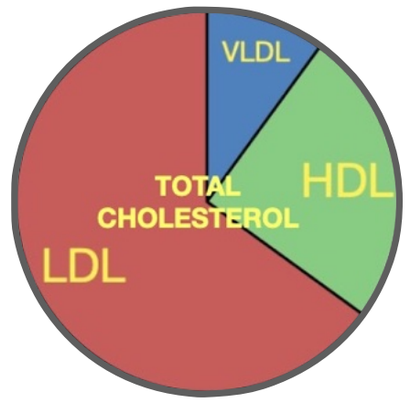
LDL



Lp(a)



HDL



Total cholesterol

Many guidelines use this as a target - associated with increased CVD risk

Some guidelines suggest measuring this and use it as a target

Some guidelines use this as a target

The only 2 measurements needed to make a decent 10-yr CVD risk estimate

A Typical Lipid Panel

Total cholesterol

LDL

HDL

Triglycerides

Other terms - Non-HDL cholesterol = Total cholesterol minus HDL

LIPIDS - 6 different guidelines

	2019 ESC/ EAS	2022 USPSTF	2019 ACC/ AHA	2020 VA/DoD	2021 CCS	2023 Simplified Lipid Guidelines
LDL targets	YES	NO	YES	NO	YES	NO

Treatment Threshold Wars

Some lipid guidelines recommend

Specific thresholds or % reductions for LDL and other lipid markers

Sounds very "logical"

Sounds very "evidence-based"

Targets often vary between guidelines

Evidence is far from conclusive

"To date, no clear target to which LDL-C or non HDL-C or ApoB levels should be lowered is clearly identified in RCTs" Can J Car 2021;37:1129–1150

"The Task Force is aware of the limitations of some of the sources of evidence and accepts that RCTs have not examined different LDL-C goals systematically" European Heart Journal (2020) 41, 111188

Target shooting = definitely more complicated and confusing and requires more testing and possibly more worry

EIther Treat-to-Target or simply giving a High-Intensity Statin

JAMA | Original Investigation

Treat-to-Target or High-Intensity Statin in Patients With Coronary Artery Disease
A Randomized Clinical Trial **LODESTAR**

High Intensity = rosuvastatin 20 mg/atorvastatin 40 mg
High Intensity = double the moderate dose

LDL 50-70 mg/dL (1.3 - 1.8 mmol/L)

What the authors said

Conclusions

Among patients with CAD, a treat-to-target LDL-C strategy of 50 to 70 mg/dL as the goal was noninferior to a high-intensity statin therapy for the 3-year composite of death, MI, stroke, or coronary revascularization. These findings provide additional evidence supporting the suitability of a treat-to-target strategy that may allow a tailored approach with consideration for individual variability in drug response to statin therapy.

NO difference
between the groups

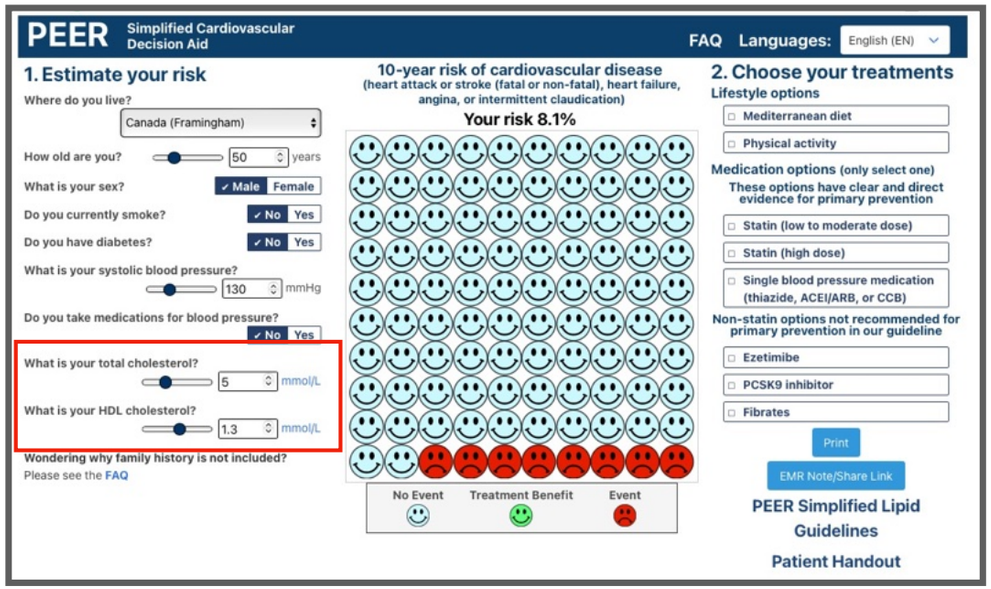
????**BUT**????

Supports a

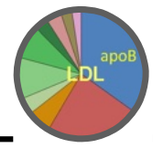
treat-to-target strategy

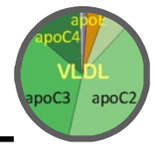
April 4, 2023
JAMA 2023;329:1078-1087

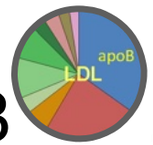
Estimating your 10-year CVD risk using your lipid numbers

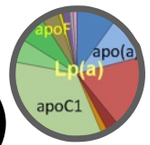


Risk Calculators Don't Use

LDL 

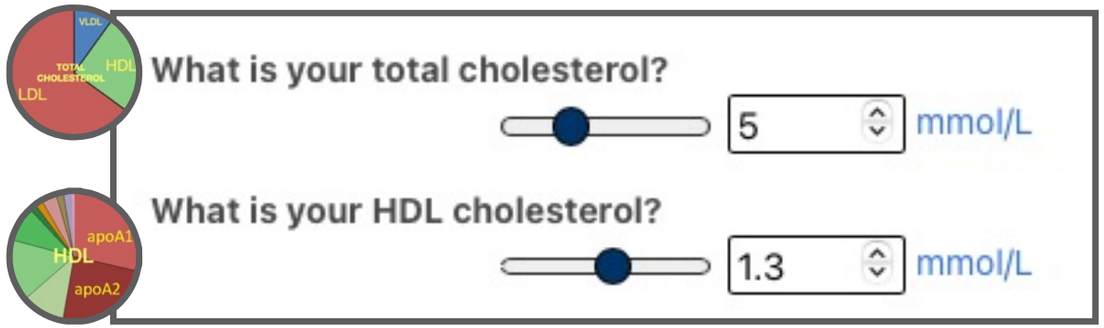
, VLDL 

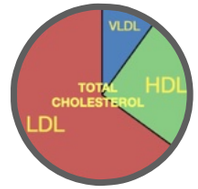
, ApoB 

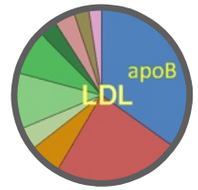
, or Lp(a) 

"Adding Lp(a) or apo B does not meaningfully improve cardiovascular risk prediction above standard risk factors (age, sex, blood pressure, total cholesterol/HDL, diabetes, smoking)"

https://cfpclearn.ca/tfp343/



Most of total cholesterol is LDL 

ApoB is one of the main parts of LDL 

So Total Chol, LDL and ApoB measurements concentrations are highly correlated

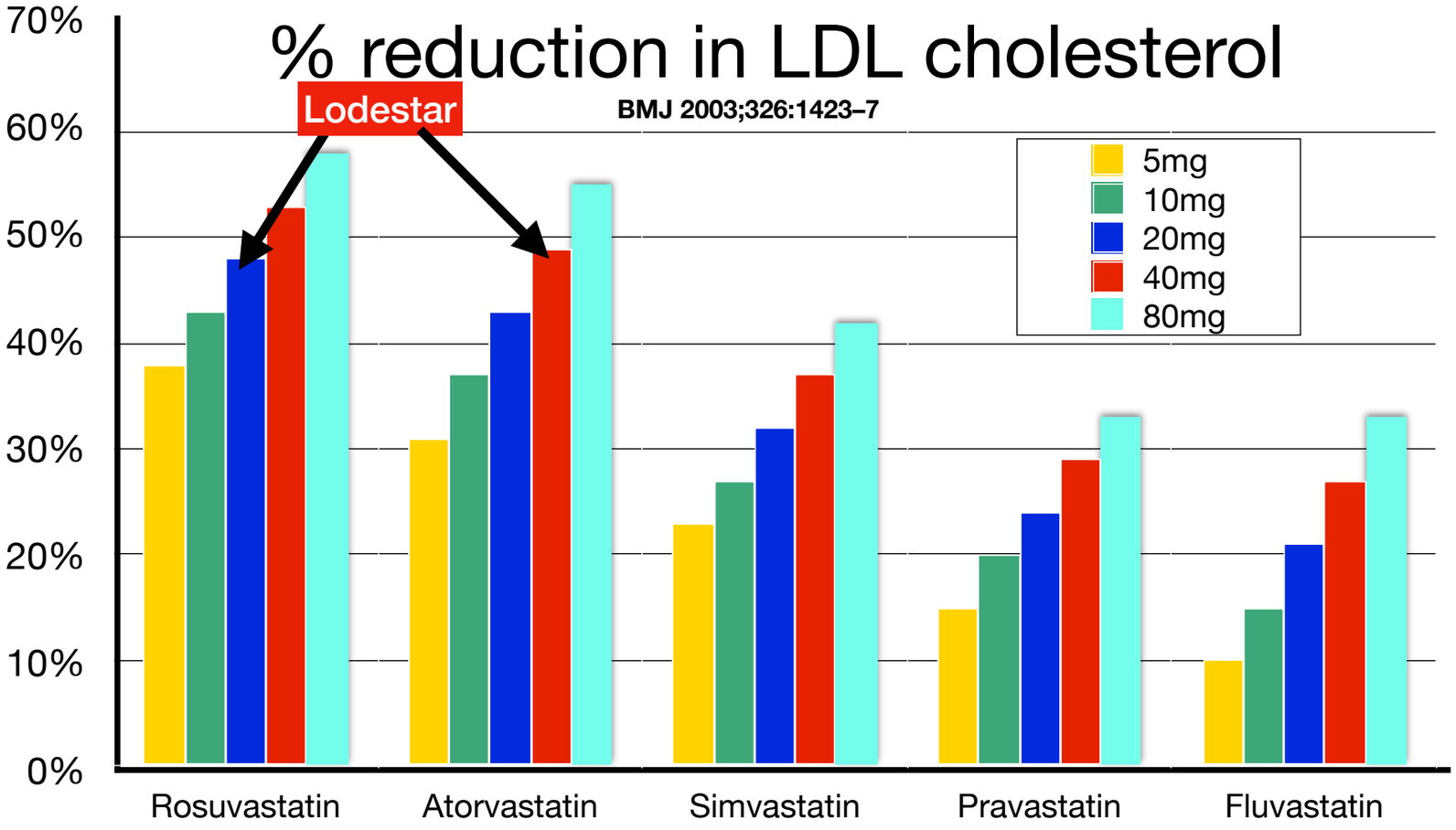
Medication Examples

Statins	**BRAND NAME**
Atorvastatin	Lipitor
Fluvastatin	Lescol
Lovastatin	Mevacor
Pravastatin	Pravachol
Rosuvastatin	Crestor
Simvastatin	Zocor
Pravastatin	Pravachol
Ezetimibe	Ezetrol
PCSK9s	
Evolocumab	Repatha
Alirocumab	Praluent

Lipid Medications and their relative benefit		
	Lipids	Heart attack/ stroke benefit
1st	Statins lower dose typically 10-20 mg	25% ⬇
2nd	Statins higher dose typically 40-80 mg	an extra 10 % ⬇
3rd	Ezetimibe	5% ⬇ minimal evidence if you have never had a heart attack
4th	PCSK9 Inhibitors	15% ⬇ minimal evidence if you have never had a heart attack

For **statins** and **ezetimibe**, if use generic medications and/or combos and/ or split tablets
Cost should be **<$150/year**

For PCSK9s the costs are **$6,000-7,000/ year**

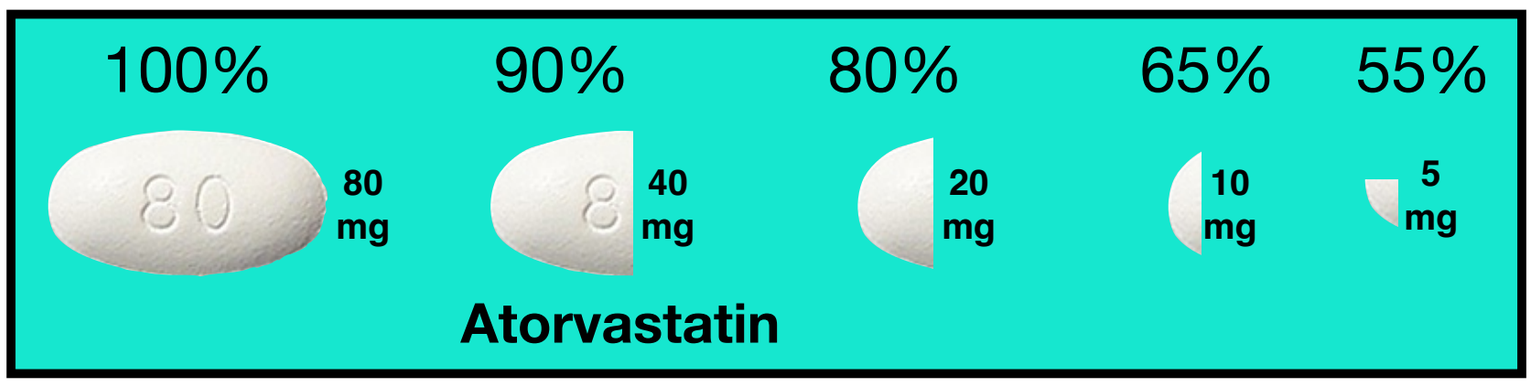


20 mg dose
~ 30% ⬇ in LDL

⬆ **40-80 mg dose**
get an extra ~ 10% ⬇ in LDL

20 mg dose of either rosuvastatin or atorvastatin
~ 85-90% of people get at least a 30% or more reduction in LDL

Increasing to 40 or 80 mg
only gets another 5% of people past that 30%



European Heart Journal – Cardiovascular Pharmacotherapy (2016) 2, 212–217 doi:10.1093/ehjcvp/pvw006

Average % decrease in LDL* from medications
VS
The % measurement variation for LDL in individual people

1) LDL Changes

-30% ⬇

Average % change in LDL with 10-20 mg of a STATIN (lower dose)

-10% ⬇

Additional % change in LDL by INCREASING STATIN DOSE to 40-80 mg (higher dose)

Additional % change in LDL by adding EZETIMIBE

-15% ⬇

Additional % change in LDL by adding a PCSK9

-50% ⬇

+1% ⬆

Average change per year in cholesterol

-10% -20% -30% -40%

2) Cholesterol Measurement Variation

A Single LDL Measurement

Analytic + biological measurement variation of LDL

~+/- 10%-20%

Size of the change to be sure a change in LDL has occurred

~+/- 20-30%

Two Serial LDL Measurements If a change in LDL seen is less than this we can't be confident a change in LDL has occurred

*Total cholesterol and ApoB similar issues

We Remeasure to See if Lipids Have Changed

-15% THE CHANGE YOU NEED TO SEE +15%

⬆/year= ~1-2%

INCREASE STATIN DOSE

10%⬇

ADD EZETIMIBE

15%⬇

1) as we get older
2) dietary changes
3) if we give a medication
4) if we increase the dose
5) if we add another medication

Math - Cholesterol Risk Messages

Increasing age is **BY FAR** is the **“biggest” risk factor - 80-90% OF THE CHANGE IN RISK**

Even if cholesterol increases a lot **(2%/yr)** over the next **10 years** the impact of that change on the estimated absolute CVD risk is no more than **1-3%** and the impact that additional risk has on the estimated **10-year absolute benefit** from a statin is **<0.5%**

BOTTOM LINE - once you know a person’s cholesterol, measuring it again 5-10 years later **WILL NOT** contribute to any treatment decisions **BECAUSE ⬆AGE** is the risk issue

Higher doses and adverse effects

62 trials, 120,000 participants, followed for an average of 4 years

Statin	Muscle symptoms	Muscle disorders	Liver dysfunction	Renal insufficiency	Diabetes	Eye conditions
Atorvastatin	Not more with higher doses	Not more with higher doses	~2x⬆* 80mg!	Not more with higher doses	Not more with higher doses	Not more with higher doses
Fluvastatin			Not more with higher doses			
Lovastatin						
Pitavastatin						
Pravastatin						
Rosuvastatin						
Simvastatin						

BMJ 2021;374:n1537

*Liver dysfunction included a rise in liver enzymes to more than three times the upper limit of normal and other diagnosed liver disorders
Risk of increases in liver enzymes ⬆ from 0.5% (lower dose) to 1% (higher dose)
Risk of severe liver damage overall is ~ 1 in 17,000
https://journals.sagepub.com/doi/epub/10.1177/23247096211014050

IMPORTANT

An Example of the Numbers

	Relative benefit	**10% BASELINE** 10-year risk of a heart attack or stroke	# of people who get a benefit from 10 years of "treatment"	# of people who get **NO** benefit from 10 years of "treatment"
Statins lower dose typically 10-20 mg	25% ⬇	Revised Risk ~7-8%	2-3%	97-98%
Statins higher dose typically 40-80 mg	an extra 10 % ⬇	Revised Risk ~6-7%	3-4%	96-97%
Ezetimibe	5% ⬇ minimal evidence if you have never had a heart attack	Revised Risk ~6-7%	3-4%	96-97%
PCSK9 Inhibitors	15% ⬇ minimal evidence if you have never had a heart attack	Revised Risk ~5-6%	4-5%	95-96%

If your **BASELINE** risk was **5%** then cut these numbers in **HALF?**

If your **BASELINE** risk was **20%** then **DOUBLE?** these numbers

Conclusion

What interventions have been shown⬇ cardiovascular risk?

How **BIG** is the ⬇?

Numbers are REALLY Important

Reducing the burden of treating blood pressure and lipids

Simple MAIN messages

1. **Know the cardiovascular risk**
2. **Know the potential benefit**
3. **You will never know if the patient benefitted**
4. **You will always cause inconvenience**
5. **Always start with low doses - there is almost never a hurry**
6. **Use medications that have been shown to lover CVD risk not just the risk factor**
7. **Use low doses**
8. **Cut the tablets when possible - often “10mg/20mg/40mg+ tablet is a similar price - so cut a “40mg”**
9. **Realise that a lot of the surrogate changes you see are the “ghost” of measurement variation**

Treatments that have decent evidence of benefit

in people who have never had a cardiovascular event

Lifestyle and their relative benefits*		Medications and their relative benefit*					
Lifestyle	Heart attack/ stroke benefit	**Blood pressure**	Heart attack/ stroke benefit	**Lipids**	Heart attack/ stroke benefit	**Glucose**	Heart attack/ stroke/kidney benefit
Mediterranean diet	30% ⬇	Salt substitute 75%Na/25%K	10-15% ⬇	Statins lower dose	25% ⬇	Metformin	? only 1 trial
Moderate physical activity	25% ⬇	Thiazide lower dose	25% ⬇	Statins higher dose	an extra 10 % ⬇	SGLT2's	15% ⬇
		ACE/ARB lower dose	25% ⬇	Ezetimibe	5% ⬇	GLP's	15% ⬇
		Betablockers, calcium channel blockers	Some but less than those above	PCSK9 Inhibitors	15% ⬇	Sulfonlyureas, Insulin, DPP4s	0%

*Regardless of their effect on the specific risk factor and all numbers are rounded