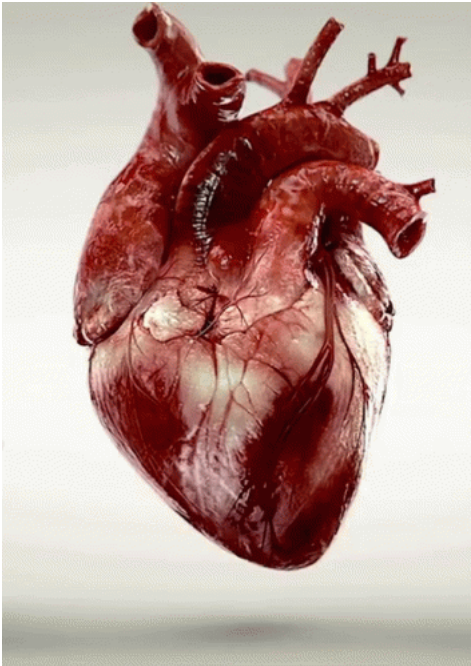


# **ALL THE EVIDENCE YOU NEED WHEN IT COMES TO CARDIOVASCULAR RISK REDUCTION**

It's Just a Numbers Game And So Much More



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University of British Columbia, Vancouver, BC



# Risk definitions...

Risk markers - associated with a bad outcome - 100s

Risk factors - potentially modifiable risk markers ~5

Risk behaviors - smoking, nutrition, activity

Risk of disease - CVD, MI, strokes, blindness, ESRD

Risk of treatment - harms, costs

Risk of overdiagnosis - inconvenience, labelling, worry

# Risk Factors versus Clinical Endpoints

“a risk factor/marker is a variable associated with an increased risk of disease”

Not As Important	Very Important
blood pressure	symptoms
cholesterol	heart attacks
glucose/diabetes	strokes
bone density	heart failure
heart rate	death
CRP	dialysis
proteinuria	amputation
family history	fractures
age	blindness
gender	revascularization
race	angina
FEV1	TIA's



# “Non-traditional” Risk Factors

C-reactive protein

ankle–brachial index

leukocyte count

fasting blood glucose

periodontal disease

carotid intima–media thickness

coronary artery calcification score on CT

homocysteine

lipoprotein(a)

“There is at present no  
place for adding  
additional risk factors to  
the present risk  
prediction models”

Circulation 2013;127:1948–56

*This one might have some use*

## EVALUATION

CLASSIFICATION OF BLOOD PRESSURE (BP)*			
CATEGORY	SBP mmHg	DBP mmHg	
Normal	<120	and <80	
Prehypertension	120–139	or 80–89	
Hypertension, Stage 1	140–159	or 90–99	
Hypertension, Stage 2	≥160	or ≥100	

# GUIDELINES

All these thresholds are ARBITRARY

### For all patients with diabetes:

- A1c < 7.0%
- BP < 130/80 mmHg
- Smoking cessation
- Physical activity (goal: 150 minutes of moderate-intensity exercise per week)
- Healthy body weight
- Healthy diet

Table 1. Recommended targets for glycemic control

	A1C* (%)	preprandial PG (mmol/L)	2-hour postprandial PG (mmol/L)
Type 1 and type 2 diabetes	≤7.0	5.0–10.0 (5.0–8.0 if A1C targets not being met)	5.0–10.0 (5.0–8.0 if A1C targets not being met)

Total Cholesterol (mg/dL)		LDL Cholesterol (mg/dL)	
<200	Desirable	<100	Optimal
200–239	Borderline High	100–159	Near optimal/above optimal
≥240	High	≥160	Borderline High
		≥189	High
		≥200	Very High



CLINICAL GUIDELINES | 6 MARCH 2018

## **Hemoglobin A<sub>1c</sub> Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: A Guidance Statement Update From the American College of Physicians**

“Clinicians should aim to achieve an HbA<sub>1c</sub> level

**between 7% and 8% in most patients** with type 2 diabetes”



**Because of harms - primarily internists**

## **CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY ON THE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM – 2018 EXECUTIVE SUMMARY**

**An A1C level of  $\leq 6.5\%$  is considered optimal** if it can be

achieved in a safe and affordable manner, but higher targets may be appropriate for certain individuals and may change for a given individual over time.”

**Because of benefits - primarily endocrinologists**

Guideline Differences	 American College of Cardiology/American Heart Association (ACC/AHA)			 European Society of Cardiology/European Society of Hypertension (ESC/ESH)		
	Systolic (mm Hg)	and/or	Diastolic (mm Hg)	Systolic (mm Hg)	and/or	Diastolic (mm Hg)
Level of blood pressure (BP) defining hypertension						
Office/Clinic BP	≥ 130		≥ 80	≥ 140		≥ 90
Daytime mean	≥ 130		≥ 80	≥ 135		≥ 85
Nighttime mean	≥ 110		≥ 65	≥ 120		≥ 70
24-hour mean	≥ 125		≥ 75	≥ 130		≥ 80
Home BP mean	≥ 130		≥ 80	≥ 135		≥ 85
BP targets for treatment	< 130/80 mm Hg			Systolic targets < 140 mm Hg and close to 130 mm Hg		
Initial Combination Therapy	Initial single-pill combination therapy in patients > 20/10 mm Hg above BP goal			Initial single-pill combination therapy in patients ≥ 140/90 mm Hg		
Hypertensive requiring intervention	> 130/80 mm Hg			≥ 140/90 mm Hg		

JACC 2019;73:3018–26

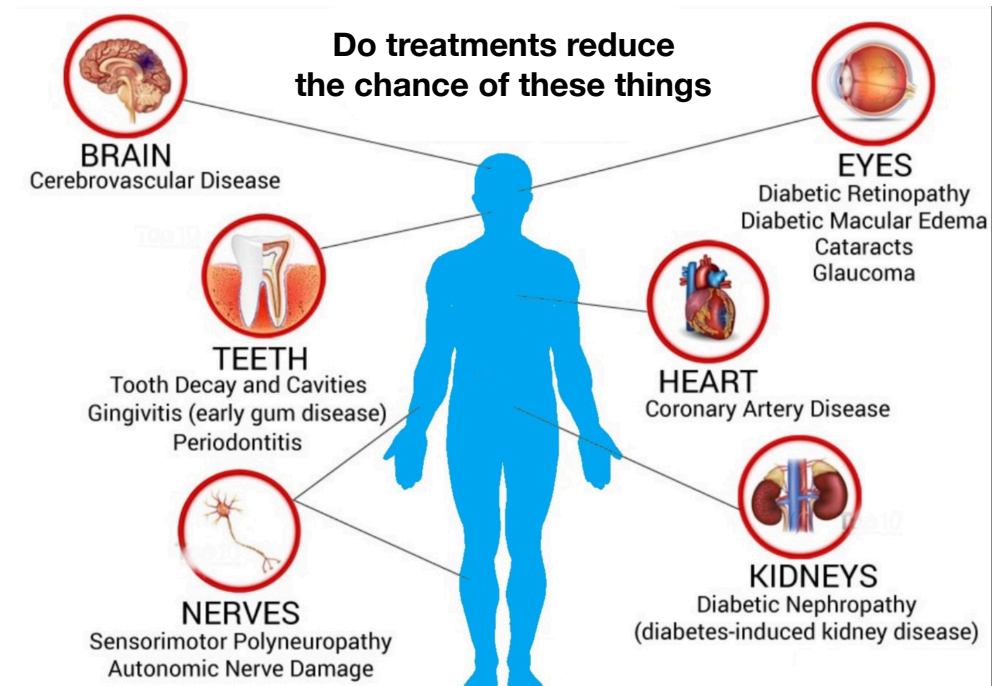
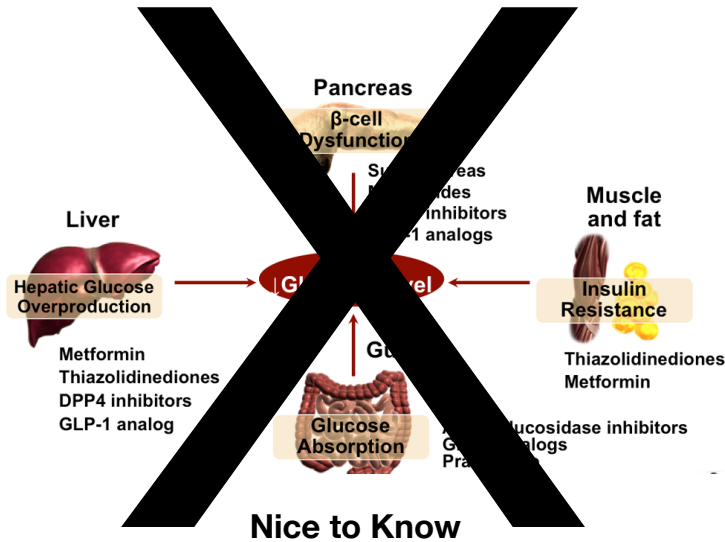
# Treatment thresholds are rather arbitrary

- Not based on patient preferences

- Not based on cost/benefit

- Seem to be primarily emotionally-based

# ~~How~~ Does It Work?



**Absolutely !@#\$\$% Crucial to Know**

# 20 “NEGATIVE” STUDIES IN A ROW

**From 2008-2015**

## LIPIDS

AIM-HIGH, HPS2-THRIVE (niacin)

ACCORD (fibrates)

daIOUTCOMES (dalcetrapib)

STABILITY (darapladib)

## DIABETES

ACCORD, ADVANCE, VADT

(aggressive A1c lowering)

ROADMAP (olmesartan)

ORIGIN (insulin)

SAVOR-TIMI 53 (saxagliptin)

EXAMINE (alogliptin)

ALECARDIO (aleglitazar)

## BLOOD PRESSURE

ALTITUDE (aliskiren)

VALISH, AASK, ACCORD

(aggressive BP lowering)

## GENERAL

ACTIVE (irbesartan/afib)

CRESCENDO (rimonabant)

VISTA-16 (varespladib)

**182,000+ patients**



# FINALLY, STARTING IN 2015...

- 1) EMPA-REG OUTCOME (empagliflozin) ~1.5% ARR (CVD) over 3 years
- 2) LEADER (liraglutide) ~ 2.5% ARR over 4 years
- 3) SPRINT (120mmHg vs 140mmHg) ~ 1.5% ARR (CVD) over 3 years but also ~1.5% ARI (Kidney)
- 4) HOPE 3 (statins) YES, BUT blood pressure no benefit
- 5) FOURIER (evolocumab) ~1.5% ARR over 2 years BUT \$15,000/year
- 6) DECLARE-TIMI 58 (dapagliflozin) ~1% ARR (CVD) over 4 years
- 7) HARMONY (albiglutide) ~ 2% ARR (CVD) over 2.5 years

## BUT!!!!

ACCELERATE (evacetrapib) -  $\uparrow$  HDL (130%),  $\downarrow$  LDL (40%) - no CVD benefit  
TECOS (sitagliptin) - no benefit over 3 years - 0.5% ARI (diabetic eye disease)  
CARMELINA - (linagliptin) - no benefit over 2 years



# Evidence Issues That Influence My Thoughts

Many well designed trials show that just because a treatment ↓ a risk factor doesn't guarantee that CVD risk will by necessity be ↓

In fact, there are a number of trials where the risk factor is ↓ but CVD risk goes ↑

Therefore, without well-designed trials it is very much unknown what impact these treatments will have on CVD risk

# Conditions requiring risk assessment

The main ones are hypertension, cholesterol, glucose/diabetes, atrial fibrillation

Figure out

CVD risk

Potential CVD benefit

Potential harms, costs and inconveniences

# Risky Relative Adjectives

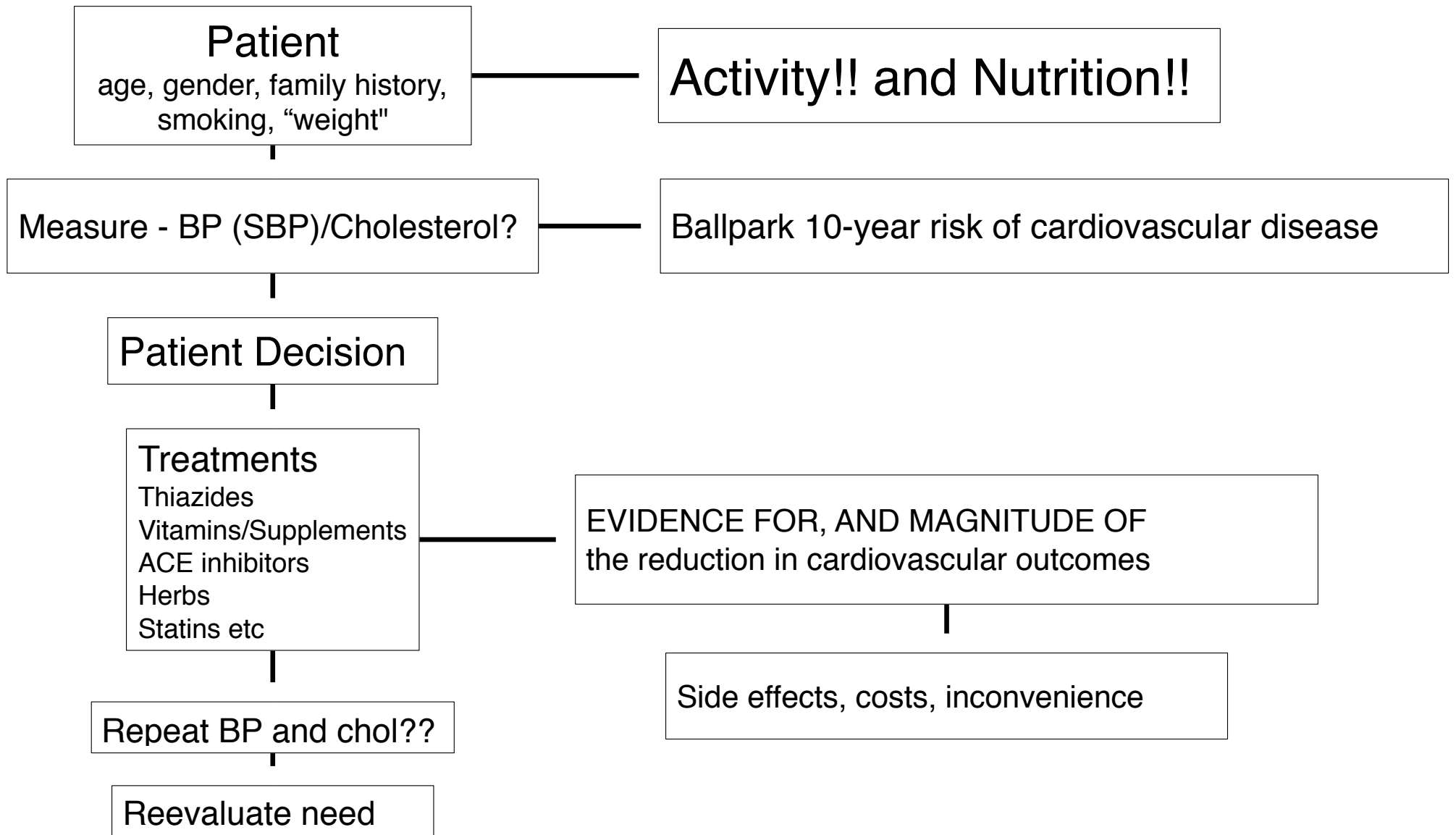
HOW

low is low

moderate is moderate

high is high



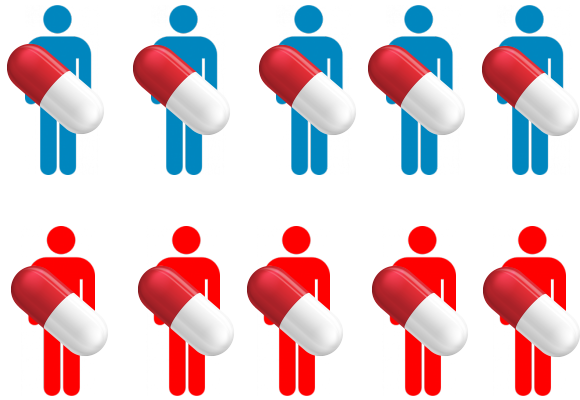


Based on the  
best available evidence  
(primarily RCTs/MAs - and sometimes cohort data)  
here are the CVD numbers  
you need to know

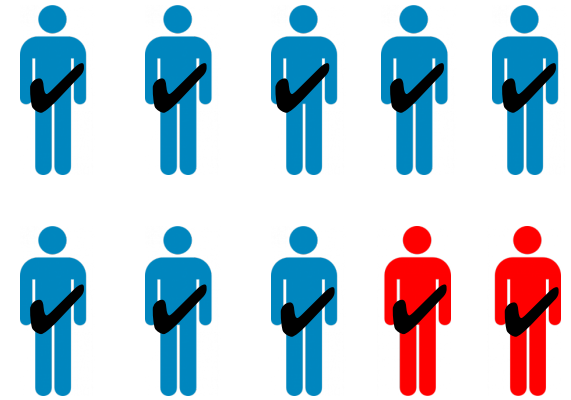


At most, 30% of people will benefit from a lifetime of CVD risk factor modification - but you have to treat ALL of them - 100%

No CVD



60%  
OFF



50% of males with  
2 or more risk factors  
will develop heart disease  
over a lifetime

CVD

**3 out of 10 benefit = 30%**

BASELINE  
10 YEAR  
CVD RISK

RELATIVE  
TREATMENT  
BENEFIT

NEW  
10 YEAR  
CVD RISK

ABSOLUTE  
TREATMENT  
BENEFIT

10%

7%

10% minus 7% = 3%

97% NO BENEFIT

30% relative benefit

20%

14%

20% minus 14% = 6%

94% NO BENEFIT

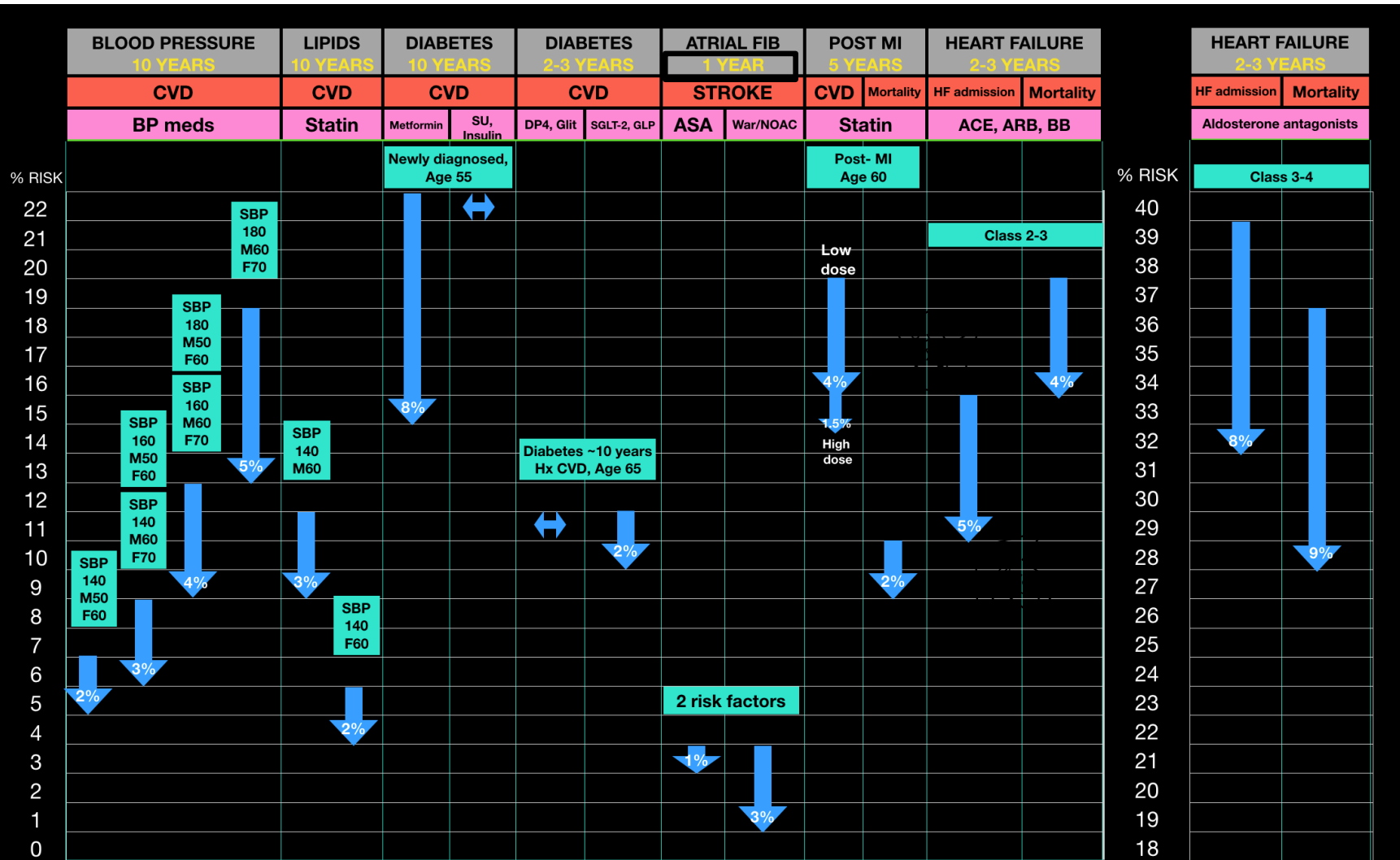


## BALLPARK RELATIVE % BENEFITS FOR CARDIOVASCULAR PREVENTATIVE TREATMENTS

	Lifestyle	Cholesterol	Blood pressure	Glucose	A fib	Heart failure
RRR%	Cardiovascular events				Stroke	Mortality
100	Stopping smoking (obviously no RCTs) CVD but also cancer and lung issues					
95						
90						
85						
80						
75						
70						
65					Warfarin/NOACS	
60						
55						
50			Blood pressure diabetes			
45						
40						
35		Statins		Metformin?		
30	Mediterranean diet		Blood pressure			
25	Physical Activity plus QOL				Aspirin	ACEI, BB, Aldo antag
20						
15		PCSK9 Monoclonal antibodies		SGLT2, GLP		
10		Aspirin				
5		Ezetimibe				
0		Fibrate, niacin		DPP4, SU, insulin, glitazone		

cvdcalculator.com, sparctool.com

## BALLPARK ABSOLUTE % BENEFITS FOR PREVENTATIVE TREATMENTS



cvdcalculator.com, sparctool.com

It's all about figuring out  
The *Ballpark* Chance  
WITH NO TREATMENT  
vs  
The *Ballpark* Chance  
WITH TREATMENT



Oswald Chesterfield Cobblepot

AKA The Penguin

60 years old

Loves birds

Lives a luxurious lifestyle

Relatively inactive

PMH - Conduct disorder

Smoker

A1c 8

BP 150/90 mm/Hg

Total cholesterol 6 (240)

HDL 1 (40)



Languages: English (EN)

## The Absolute CVD Risk/Benefit Calculator

**Framingham**  
US Data, 10 Year Risk  
Heart attacks + angina/coronary  
insufficiency + heart failure +  
strokes + intermittent claudication

**QRISK®2-2014**  
UK Data, 10 Year Risk  
Heart attacks + strokes

**ACC/AHA ASCVD**  
US Data, 10 Year Risk  
CHD death + nonfatal heart attacks  
+ fatal/nonfatal strokes

**PREDICT**  
New Zealand Data, 5  
Year Risk  
Heart attacks + angina + heart  
failure + strokes/TIAs + peripheral  
vascular disease

Age

years

Gender

☐ Male ☒ Female

Smoker

☐ Yes ☒ No

CVD risk is reversed after 5-10 years of no smoking

Diabetes

☐ Yes ☒ No

Systolic Blood Pressure

mmHg

Enter present blood pressure regardless of  
treatment

120 mmHg is used for baseline risk

On treatment for BP

☐ Yes ☒ No

Click YES if taking blood pressure medication

Only applies if SBP is greater than 120 mmHg

Total Cholesterol

mmol/L

Cholesterol should be prior to drug treatment

3 mmol/L is used for baseline risk.

[Click to change to mg/dL.](#)

HDL Cholesterol

mmol/L

HDL should be prior to drug treatment

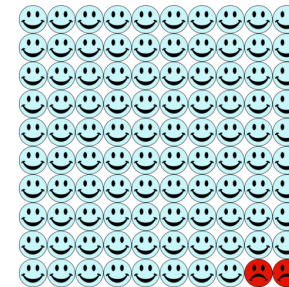
Relative Benefit: 0%

Benefit often has *nothing* to do with the effect on  
the surrogate marker. At present, you can only  
select one intervention at a time.

[Benefit Estimate Details](#)

Risk Time Period

10 years



	97.9%	No event
	2.1%	Total with an event
	0.0%	Number who benefit from treatment
NNT	∞	Number needed to treat
	2.1%	Baseline events using baseline factors alone
	0.0%	Additional events "caused" by risk factors

As with all risk calculators, calculated risk numbers are +/-  
5% at best. [More information.](#)

cvdcalculator.com



Bruce Banner  
AKA The Hulk

Age 45

Scientist

Easily agitated,  
and emotionally withdrawn

SBP 160 mm/Hg

Non-smoker

Non-diabetic

Total cholesterol 4.4 (180)

HDL 1.5 (60)

AM testosterone: 330 nmol/L (N 6.7-29)

Urine catechol: +ve (no urine found)





Bruce Banner

AKA The Hulk

Age 45

Scientist

Easily agitated,  
and emotionally withdrawn

SBP 160 mm/Hg

Non-smoker

Non-diabetic

Total cholesterol 4.4 (180)

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AM testosterone: 330 nmol/L (N 6.7-29)

Urine catechol: +ve (no urine found)

10 year risk

Framingham (HA, angina, HF, stroke, int claud) = 7%

ASCVD (HA, stroke) = 2%



### 10 year risk

Framingham (HA, angina, HF, stroke, int claud) = 64%

ASCVD (HA, stroke) = 41%

Smoker - stop ~15% absolute

A1c 8 ?

BP 150/90 mm/Hg ~ 30-50% RR

Total cholesterol 6 (240) ~ 25% RR

HDL 1 (40)



### 10 year risk

Framingham (HA, angina, HF, stroke, int claud) = 7%

ASCVD (HA, stroke) = 2%

SBP 160 mm/Hg ~ 30% RR

Non-smoker

Non-diabetic

Total cholesterol 4.4 (180) ~ 25% RR

HDL 1.5 (60)



# Type 2 Diabetes

“The disease who must not be named”

Feeling Fatigued or Irritable? There's a 1 in 4 Chance You **Suffer**  
from Diabetes...

10 Things You Should Eat If You Are **Suffering** From  
Diabetes

It is NOT a disease

It is a RISK Factor

**Suffering** from diabetes? Here's some  
good news for you

**Suffering** from diabetes? Fight it like your favourite B-  
town celebs

Medication Class	Medication
Insulin	Insulin
Biguanides	Metformin
	Phenformin
Sulfonylureas	Tolbutamide
	Chlorpropamide
	Glyburide/ glibenclamide
	Gliclazide
	Glipizide
	Glimepiride
Glitazones	Rosiglitazone
	Pioglitazone
Meglitinides	Repaglinide
	Nateglinide
Other	Acarbose
	Aleglitazar
GLP's	Exenatide
	Dulaglutide
	Albiglutide
	Lixisenatide
	Liraglutide
	Semaglutide
DPP4's	Sitagliptin
	Saxagliptin
	Linagliptin
	Alogliptin
	Omarigliptin
Gliflozins	Dapagliflozin
	Empagliflozin
	Canagliflozin
	Ertugliflozin

# All the large RCTs evaluating the impact of glucose lowering medications on CVD Outcomes

RCTs evaluating the impact of medications on CVD outcomes in T2DM						
YEAR	NAME		MEDICATION	RESULT	OUTCOME CHANGED	ABSOLUTE DIFFERENCE/TIME
1970	UGDP	SU	tolbutamide (Orinase)	NEGATIVE	CVD mortality	↑8%/5 years
1971		BG	phenformin (DBI)	NEGATIVE	Mortality	↑ 6%/5-8 years
1976		SU	tolbutamide (Orinase)	NEGATIVE	Fatal MI	↑ 5%/5 years
1982		IN	insulin	NEUTRAL		
1998	UKPDS 33/34	IN,SU	insulin, chlorpropamide, glyburide/glibenclamide, glipizide	NEUTRAL		
1998		IN,SU,BG	metformin, insulin, chlorpropamide, glyburide/glibenclamide, glipizide	NEUTRAL except POSITIVE for metformin	Mortality MI	↓7%/11 years ↓ 6%/11 years
2003	STOP-NIDDM	OTH	acarbose (Precose)	POSITIVE	MI	↓ 1.5%/3 years
2005	PROACTIVE	GLIT	pioglitazone (Actos)	POSITIVE	MI	↓ 1.5%/3 years
2007	RECORD	GLIT	rosiglitazone (Avandia)	NEGATIVE	Heart failure	↑ 1%/4 years
2012	ORIGIN	IN	insulin	NEUTRAL		
2013	EXAMINE	DPP4	alogliptin (Nesina)	NEUTRAL		
2014	SAVOR-TIMI 53	DPP4	saxagliptin (Onglyza)	NEGATIVE	Heart failure	↑ 1%/2 years
2014	ALECARDIO	OTH	aleglitazar	NEUTRAL		
2015	ELIXA	GLP	lixisenatide (Adlyxin)	NEUTRAL		
2015	TECOS	DPP4	sitagliptin (Januvia)	NEUTRAL		
2015	EMPA-REG	GLIF	empagliflozin (Jardiance)	POSITIVE	Mortality Heart failure	↓ 2.5%/3 years ↓ 1.5%/3 years
2016	SUSTAIN 6	GLP	semaglutide (Ozempic)	POSITIVE	Combined outcome	↓ 2%/2 years
2016	LEADER	GLP	liraglutide (Victoza)	POSITIVE	Mortality Combined outcome	↓ 1%/4 years ↓ 2.5%/4 years
2017	CANVAS	GLIF	canagliflozin (Invokana)	POSITIVE	Combined outcome Heart failure Amputations	↓ 2%/3.5years ↓ 1%/3.5 years ↑ 1%/3.5 years
2017	EXSCEL	GLP	exenatide (Byetta)	NEUTRAL		
2017	ACE	OTH	acarbose (Procoese)	NEUTRAL		
2017	Omarigliptin	DPP4	omarigliptin	NEUTRAL		
2018	HARMONY	GLP	albiglutide (Tanzeum)	POSITIVE	Combined outcome	↓ 2%/2 years
2018	CARMELINA	DPP4	linagliptin (Tradjenta)	NEUTRAL		
2018	DECLARE-TIMI 58	GLIF	dapagliflozin (Farxiga)	POSITIVE	Combined outcome (primarily heart failure)	↓ 1%/4 years
2019	REWIND	GLP	dulaglutide (Trulicity)	POSITIVE	Combined outcome Renal outcomes	↓ 1.5%/5.4 years ↓ 2.5%/5.4 years
2019	PIONEER 6	GLP (oral)	semaglutide (Ozempic)	POSITIVE	CVD mortality Mortality	↓ 1%/1.5 years ↓ 1.5%/1.5 years
2019	CREDENCE	GLIF	canagliflozin (Invokana)	POSITIVE	Combined CVD outcome Combined renal outcome outcomes	↓ 2.5%/2.6 years ↓ 3%/2.6 years

# Overall Evidence for T2DM

5 trials - increased CVD

11.5 trials - no effect on CVD

11.5 trials - decreased CVD - typically 1-3% absolute reduction in CVD over 2-5 years

# Activity

## 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 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



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

Jesper Krogh,<sup>1</sup> Carsten Hjorthøj,<sup>1</sup> Helene Speyer,<sup>1</sup> Christian Gluud,<sup>2</sup> Merete Nordentoft<sup>1</sup>

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

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

VIRGINIA B. KRAUS<sup>1</sup>, KYLE SPROW<sup>2</sup>, KENNETH E. POWELL<sup>1</sup>, DAVID BUCHNER<sup>3</sup>, BONNY BLOODGOOD<sup>4</sup>, KATRINA PERCY<sup>5</sup>, STEPHANIE M. GEORGE<sup>1</sup>, and WILLIAM E. KRAUS<sup>1</sup>, 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”

**U.S. Dietary Guidelines: An Evidence-Free Zone**

2016

Steven E. Nissen, MD

“a detailed review of the new guidelines confirms a disturbing reality: the nearly complete absence of high-quality randomized, controlled clinical trials (RCTs) studying meaningful clinical outcomes for dietary interventions. The report repeatedly makes recommendations based on observational studies and surrogate end points, failing to distinguish between recommendations based on expert consensus rather than high-quality RCTs. Unfortunately, the current and past U.S. dietary guidelines represent a nearly evidence-free zone”

## Secondary prevention

### EFFECTS OF CHANGES IN FAT, FISH, AND FIBRE INTAKES ON DEATH AND MYOCARDIAL REINFARCTION: DIET AND REINFARCTION TRIAL (DART)

2033 men post MI randomized to receive/not to receive advice on 3 dietary factors:  
a reduction in fat intake and an increase in the ratio of polyunsaturated to saturated fat  
an increase in fatty fish intake  
an increase in cereal fibre intake

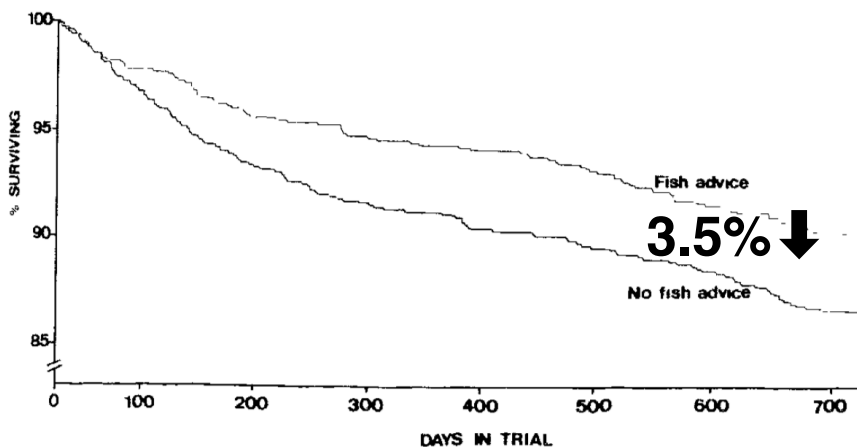


Fig 2—Survival: fish advice.

Fat - no effect

Fibre - no effect

Fish - no effect on CHD but a  
29% ↓ in mortality

## Mediterranean diet in secondary prevention of coronary heart disease - Lyon Diet Heart Study

27 months - 605 patients <age 60 with a previous MI in the last 6 months - 90% male

one group advised in a one-hour session (with a couple of follow ups) to adopt a diet of more bread, more root vegetables, more fish, less beef, lamb and pork (replaced with poultry), no day without fruit; and butter and cream replaced with margarine - also used rapeseed, and olive oils in salad

### Results

Weight, cholesterol, lipoproteins and blood pressure were not statistically different between groups

Lancet 1994;343:1454-9

# Mediterranean diet in secondary prevention of coronary heart disease

	<b>Total mortality (%)</b>	<b>Cardiovascular deaths (%)</b>	<b>Non-fatal MI's (%)</b>	<b>Total primary endpoints (%)</b>
<b>Dietary intervention</b>	3.5	1.0	1.7	2.6
<b>No dietary intervention</b>	6.6	5.3	5.6	10.9
<b>Relative risk reduction</b>	47	81	NSS	76
<b>Absolute risk reduction</b>	3.1	4.3		8.3
<b>Number needed to treat</b>	32	23		12

Lancet 1994;343:1454-9



## Women's Health Initiative Randomized Controlled Dietary Modification Trial - “low fat”

48,835 postmenopausal women (62 y/o) - 4% prev CVD - 8.1 years

1) lower fat intake to 20% of their total calories, and to eat five or more fruit/vegetable servings and six or more grain servings a day

2) asked not to make any dietary changes

led to ~10% reduction in energy from fat and one more serving a day of vegetables/fruit

no statistical difference in CHD, CVD, stroke, breast cancer, colorectal cancer

JAMA 2006;295:629-642, 643-54, 655-66

Primary Prevention of Cardiovascular Disease  
with a Mediterranean Diet PREDIMED - 5 years,  
67 y/o, 58% male, 48% T2DM

	<b>Total mortality (%)</b>	<b>Myocardial infarction, stroke, and death from cardiovascular causes (%)</b>	<b>MI (%)</b>	<b>Stroke (%)</b>
<b>Control “Low fat”</b>	5.4	5.7	2.1	3.0
<b>Mediterranean diet** - EVOO - 1 liter/week</b>	4.4	3.6*	1.4	1.7*
<b>Mediterranean diet** - NUTS (30 gm of mixed nuts per day)</b>	5.4	4.0*	1.6	1.5*

\*\*increased weekly servings of fish (by 0.3 servings)  
and legumes (by 0.4 servings)

\* statistical different from control  
N Engl J Med 2018; 368:1279-90

## Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease (Review)



**Cochrane  
Library**

Cochrane Database of Systematic Reviews

79 RCTs - 112,000 subjects

“Moderate- and high-quality evidence suggests that increasing EPA and DHA has little or no effect on mortality or cardiovascular health (evidence mainly from supplement trials)”

“Low-quality evidence suggests ALA may slightly reduce CVD event risk, CHD mortality and arrhythmia.”

# REDUCE-IT Icosapent - 5 years

8179 pts - Icosapent 2gm BID vs placebo

Trig 216 mg/dL, on statin, mean age 64, 71% male, 58% DM, 71% past CVD

## **Outcome**

Trigs - 20% lower - LDL - 7% higher

All CVD: 17.2% vs 22%, HR 0.75 (0.68-0.83), NNT 21

Stroke, MI or CVD death: 11.2% vs 14.8%, HR 0.74, NNT 28

Death (all cause): HR 0.87 (0.74-1.02)

AFib: 5.3% vs 3.9%, NNH 72

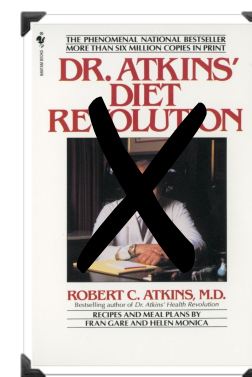
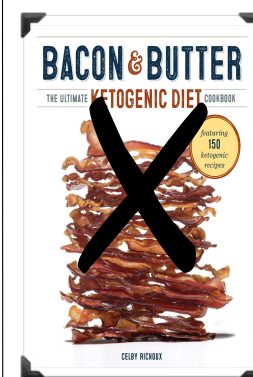
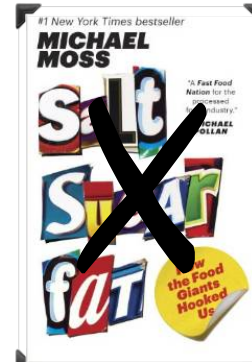
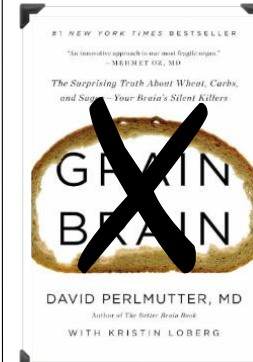
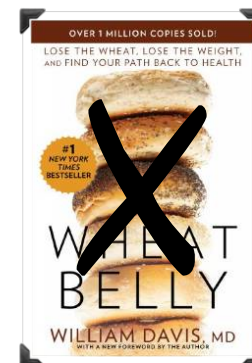
**All the evidence around the debate between**  
**Low Fat** = <~30% of total energy intake  
**Low Carb** =<~20% of total energy - ketogenic = <10%

Surrogate Marker Endpoints NOT AS IMPORTANT AS				Clinically Relevant Endpoints MUCH MORE IMPORTANT				LEVELS OF EVIDENCE IN HEALTH CARE WE USE TO FIGURE OUT WHAT WORKS
LDL cholesterol	HDL cholesterol	Glucose	Decrease weight	Reducing risk of heart attacks/ strokes/cancer		Reducing risk of dying		
LOW FAT ↓LDL~ 5% more than LOW CARB	LOW CARB ↑HDL~10% more than LOW FAT	LOW CARB ↓glucose ~3% more than LOW FAT	LOW CARB ↓weight ~3% more than LOW FAT	NONE		NONE		
Many RCTs for both including head-to-head comparisons see above SR/MA for findings				LOW FAT 1 trial - 49,000 women No benefit seen over 8 years “Mediterranean” diet ↓ CVD by 1-2% more than low fat over 5 years	LOW CARB No trials	LOW FAT 1 trial - 49,000 women No benefit seen over 8 years	LOW CARB No trials	Randomized Controlled Trials
Not really needed as we have lots of randomized controlled trials of surrogate markers				Only higher TRANS FAT intake consistently associated with increased CVD, other “fats” no effect	LOW CARBS associated with no effect on CVD	Only higher TRANS FAT intake consistently associated with increased mortality, others no effect	LOW CARBS associated with increased mortality	Cohort Studies
LOTS, IN FACT WAY TOO MUCH Just see above evidence or, in this case, lack thereof, for either side of the debate to be as definitive as they are								Expert Opinion

Ability of the evidence to ascertain cause and effect

HIGH

LOW



# Nutrition advice which pretty much everyone agrees with

A greater % of whole foods food that has been overly processed or refined as little as possible

More vegetables specifically

Less added sugar

Less refined grains

Choose an eating style that fits your food preferences, health goals, lifestyle

Most importantly, choose an eating style you can sustain



Make ballpark estimates of CVD risk

Make treatment recommendations  
based on the best available  
evidence

Allow the patient to participate in the  
decision - shared-decision!!

Languages: English (EN)

## The Absolute CVD Risk/Benefit Calculator

**Framingham**  
US Data, 10 Year Risk  
Heart attacks + angina/coronary  
insufficiency + heart failure +  
strokes + intermittent claudication

**QRISK®2-2014**  
UK Data, 10 Year Risk  
Heart attacks + strokes

**ACC/AHA ASCVD**  
US Data, 10 Year Risk  
CHD death + nonfatal heart attacks  
+ fatal/nonfatal strokes

**PREDICT**  
New Zealand Data, 5  
Year Risk  
Heart attacks + angina + heart  
failure + strokes/TIAs + peripheral  
vascular disease

Age

50 years

Gender

Male ☒ Female

Smoker

Yes ☒ No

CVD risk is reversed after 5-10 years of no smoking

Diabetes

Yes ☒ No

Systolic Blood Pressure

120 mmHg

Enter present blood pressure regardless of  
treatment

120 mmHg is used for baseline risk

On treatment for BP

Yes ☒ No

Click YES if taking blood pressure medication

Only applies if SBP is greater than 120 mmHg

Total Cholesterol

3 mmol/L

Cholesterol should be prior to drug treatment

3 mmol/L is used for baseline risk.

[Click to change to mg/dL.](#)

HDL Cholesterol

1.3 mmol/L

HDL should be prior to drug treatment

Relative Benefit: 0%

Benefit often has *nothing* to do with the effect on  
the surrogate marker. At present, you can only  
select one intervention at a time.

Physical Activity

Mediterranean Diet vs Low fat

Vitamin/Omega-3 supplements

BP meds (not atenolol/doxazosin)

Low-mod intensity statins

High intensity statins

Fibrates

Niacin

Ezetimibe

Metformin

Sulfonylureas

Insulins

Glitazones

GLPs

DPP-4s

Meglitinides

SGLT2

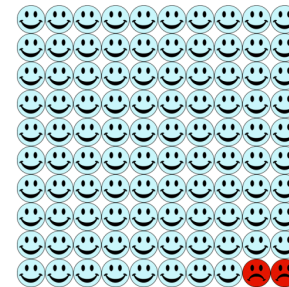
Smoking Cessation

ASA

[Benefit Estimate Details](#)

Risk Time Period

10 years



97.9% No event

2.1% Total with an event

0.0% Number who benefit  
from treatment

NNT ∞ Number needed to treat

2.1% Baseline events using  
baseline factors alone

0.0% Additional events  
"caused" by risk factors

As with all risk calculators, calculated risk numbers are +/-  
5% at best. [More information.](#)

cvdcalculator.com



# ~Relative Benefits

Blood pressure medications ~30%

Activity ~25% - secondary prevention

“Nutrition” ~30% - secondary prevention

Statins ~25-35%

PCSKP ~15% - secondary prevention

Glucose medications ~0-30%

1 or more interventions ~additive???

The absolute benefit  
depends  
on baseline risk -  
but remember that  
even with the  
best case example  
only 30% will  
benefit from  
a lifetime of treatment

## Treatments WITH NO clinical trial evidence around CVD risk

- individual nutrients
- most aspects of nutrition
- all supplements (Omega 3s?)
- all vitamins
- all herbs

## Treatments WITH clinical trial evidence showing NO CVD risk benefit

- a number of medications that lower cholesterol, blood pressure and many that lower glucose