

WHEN IT COMES TO EVIDENCE-BASED PRACTICE



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TO GET A HANDOUT GO HERE
<http://therapeuticseducation.org/handouts>

peerevidence.ca
therapeuticseducation.org

Financial Conflicts of Interest



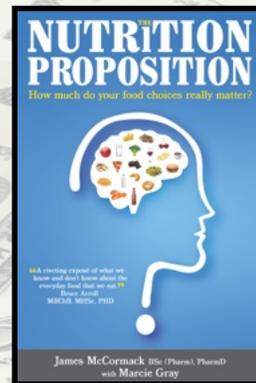
- Entire salary comes through the UBC Faculty of Pharmaceutical Sciences - also some legal/educational work

- I have received no honorarium or research money from the drug industry in the last 35 or so years



- Premium podcast subscription Best Science (BS) Medicine podcast - therapeuticseducation.org

- I have a self-published book on Amazon called "The Nutrition Proposition"





Medical BS

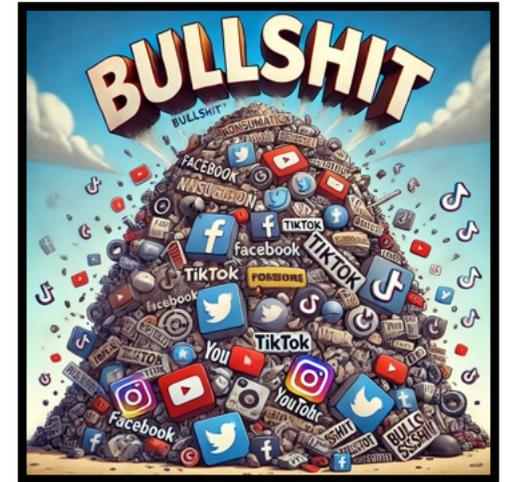


Nutrition BS



General BS

Seeing what you want to see in randomised controlled trials: versions and perversions of UKPDS data
 James McCormack, Trisha Greenhalgh **BMJ- 25 years ago**



Social Media BS



Medical BS

Since 2008
~615 episodes



ME
(a few years ago)



BS without the **BS**



Mike Allan

You are not alone!

Clinicians in many health services around the world
(at least in resource well off countries like US UK Europe Canada)
are feeling under pressure...to do more and more

To follow myriads of guidelines often written for other contexts

To meet increasing expectations from the public/health management/ regulators

To manage personal expectations of being “a perfect clinician” and “getting it right every time”

To work with IT systems for extensive record keeping, without time allocated for this work.

The result .. many clinicians are unhappy - clinical work is becoming less satisfying for all/many people



TOPICS

Workload

Continuity

Lab tests

Lifestyle advice

Access to good evidence

Litigation

Screening

Tools For Practice



#352 Do-It-Yourself
Hearing Aids

 Read
 0.25 Credits Available



#351 Flaked out? Topical
treatment for seborrheic
dermatitis

 Read
 0.25 Credits Available



#350 Not a Dry Eye in the
House - Looking into
Artificial Tears

 Read
 0.25 Credits Available



#349 An ASA a day when a
baby's on the way?



#348 How to Slow the Flow
III: Tranexamic acid for
heavy menstrual bleeding



#347 Chlorthali-D'OH!
What is the best thiazide
diuretic for hypertension?

Since 2009
300 word primary-
care synopses of the
best available
evidence
~400 to-date

<https://cfpclearn.ca/tools-for-practice-library/>

GUIDELINE PRINCIPLES

Clinical Practice Guidelines

PEER simplified lipid guideline 2023 update

Prevention and management of cardiovascular disease in primary care

NEW

Michael R. Kolber MD MSc CCFP Scott Klarenbach MD MSc FRCP Michel Cauchon MD CCFP FCFP Mike Cotterill MD CCFP Loren Regier BA MSP Raelene D. Marceau MN PhD Norah Duggan MD CCFP FCFP Rebecca Whitley MD MSc CCFP Alex S. Halime RN MSc FRCP Tanis Poshkar G. Michael Allan MD CCFP FCFP Christina S. Korowynk MD CCFP Joey Ton PharmD Liesbeth Frootjes MSc Samantha S. Moe PharmD ACPR Danielle Perry RN MSc Betsy S. Thomas BScPharm James P. McCormack PharmD Jamie Falk PharmD Nicolas Dugré PharmD MSc BCACP Scott R. Garrison MD CCFP PhD Jessica E.M. Kirkwood MD CCFP(M) Jennifer Young MD CCFP(M) FCFP Emélie Braschi MD PhD CCFP Allison Paige MD CCFP Jen Potter MD CCFP Justin Weresch MD CCFP Adrienne J. Lindblad PharmD ACPR

CLINICAL PRACTICE GUIDELINES

Simplified guideline for prescribing medical cannabinoids in primary care

G. Michael Allan MD CCFP Jamil Ramji Danielle Perry Joey Ton PharmD Nathan P. Beahm PharmD Nicole Crisp RN MN NP-Adult Beverly Dockrill RN Ruth E. Dublin MD PhD CCFP DCPM Ted Findlay MD CCFP FCFP Jessica Kirkwood MD CCFP Michael Fleming MD CCFP FCFP Ken Makus MD FRCP Xiaofu Zhu MD FRCP Christina Korowynk MD CCFP Michael R. Kolber MD CCFP MSc James McCormack PharmD Sharon Nickel Guillermina Noël MDes PhD Adrienne J. Lindblad ACPR PharmD

CLINICAL PRACTICE GUIDELINES

Managing opioid use disorder in primary care

PEER simplified guideline

Christina Korowynk MD CCFP Danielle Perry Joey Ton PharmD Michael R. Kolber MD CCFP MSc Scott Garrison MD CCFP PhD Betsy Thomas BScPharm G. Michael Allan MD CCFP Cheryl Bateman PSW Raquel de Queiroz NP Dorcas Kennedy MD CCFP FCFP Wiplofe Lamba MD FRCP DipABAM Jazmin Marlings MD CCFP(M) Tally Mogus MD CCFP(M) Tony Nickonchuk BScPharm Eli Orrantia MD MSc CCFP FCFP Kim Reich MSW Nick Wong MD CCFP(M) FCFP Nicolas Dugré PharmD MSc Adrienne J. Lindblad ACPR PharmD

Praxis

PEER simplified decision aid: chronic back pain treatment options in primary care

Jessica Kirkwood MD CCFP(M) G. Michael Allan MD CCFP Christina S. Korowynk MD CCFP James McCormack PharmD Scott Garrison MD PhD CCFP Betsy Thomas BScPharm Joey Ton PharmD Danielle Perry RN Michael R. Kolber MD CCFP MSc Nicolas Dugré PharmD MSc Samantha Moe PharmD Adrienne J. Lindblad ACPR PharmD

Praxis

PEER simplified decision aid: neuropathic pain treatment options in primary care

Karenn Chan MD CCFP(CO) Danielle Perry RN MSc Adrienne J. Lindblad ACPR PharmD Scott Garrison MD PhD CCFP Jamison Falk PharmD James McCormack PharmD Christina S. Korowynk MD CCFP Jessica Kirkwood MD CCFP(M) Joey Ton PharmD Betsy Thomas BScPharm Samantha Moe ACPR PharmD Nicolas Dugré PharmD MSc Michael R. Kolber MD CCFP MSc G. Michael Allan MD CCFP

No financial conflicts of interest

Primarily written by primary care clinicians

Thorough systematic review of the evidence by PEER using the GRADE framework

Guideline Committee uses the review of evidence to create the guideline

We focus on shared-decision making

We have discussion thresholds, NOT treatment thresholds

Always provide decision aids/calculators that give the benefit/harm numbers in absolute terms and always provide patient information sheets



<https://decisionaid.ca/cvd/>

Published in Canadian Family Physician

CVD decision aid

PEER Simplified Cardiovascular Decision Aid FAQ Languages: English (EN) ▾

1. Estimate your risk

Where do you live?

How old are you? 50 years

What is your sex? Male Female

Do you currently smoke? No Yes

Do you have diabetes? No Yes

What is your systolic blood pressure? 130 mmHg

Do you take medications for blood pressure? No Yes

What is your total cholesterol? 5 mmol/L

What is your HDL cholesterol? 1.3 mmol/L

Wondering why family history is not included?
Please see the [FAQ](#)

10-year risk of cardiovascular disease (heart attack, angina, heart failure, stroke, or intermittent claudication)

Your risk 8.1% With treatment 8.1%

No Event Treatment Benefit Event

2. Choose your treatments

Lifestyle options

Mediterranean diet

Physical activity

Medication options (only select one)
These options have clear and direct evidence for primary prevention

Statin (low to moderate dose)

Statin (high dose)

Single blood pressure medication (thiazide, ACEI/ARB, or CCB)

Non-statin options not recommended for primary prevention in our guideline

Ezetimibe

PCSK9 inhibitor

Fibrates

PEER Simplified Lipid Guidelines

Patient Handout

<https://decisionaid.ca/cvd/>

Diabetes

PEER | Diabetes Medication Decision Aid

Languages: English (EN) ▾

FAQ CONTACT

Step 1

Calculate Risk

Sex: Female Male

Age: 55 years

Systolic Blood Pressure: 130 mm Hg

Race/Ethnicity (if applicable):
 Black
 Hispanic

Current Medications:
 Anticoagulant
 Antihypertensive (Including ACEI or ARB)
 Antihypertensive (Without ACEI or ARB)
 Oral diabetes drug (excluding semaglutide or flozin)
 Statin

Medical History:
 Current smoker
 Prior myocardial infarction or stroke

Labs

Serum creatinine: 70 $\mu\text{mol/L}$

eGFR (2021 CKD-EPI equation): 85 ml/min/1.73 m²

Urine albumin-creatinine (ACR) ratio: 2 mg/mmol

Total cholesterol: 4.0 mmol/L

HDL cholesterol: 1.0 mmol/L

Hemoglobin A1c: % mmol/mol

7.0 %

Risk of complications related to diabetes in the next 10 years

Complication	Estimated risk
Death	4.9%
Heart attack/stroke	10.3%
Heart failure	2.2%
Kidney failure	6%
Severe vision loss	6.2%
Pressure sensation loss	6.4%

NEXT

<https://decisionaid.ca/diabetes/>

Heart Failure



SHARE-HF Decision Aid

This tool is intended to facilitate shared decision-making discussions between patients and clinicians regarding medications for heart failure with reduced ejection fraction (HFrEF).

FAQ | How to use
Languages: English (EN)

1. Choose display

Individualized predictions Population-level estimates

Estimate patient risk (click to expand/collapse)

Your current location: North America

Age (years): 70

Sex: Male Female

NYHA functional class: 1 or 2 3 or 4

Prior heart failure hospitalization: No Yes

Diabetes: No Yes

Prior stroke or peripheral artery disease: No Yes

Systolic BP (mmHg): 120

NT-proBNP (ng/L): 1300

Ejection fraction (%): 35

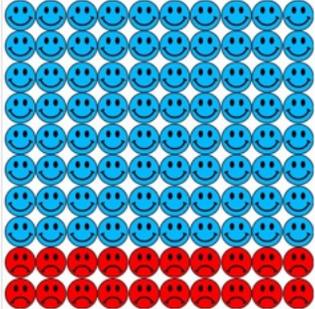
eGFR (mL/min/1.73²): 40

Current heart failure medications:

- ACE/ARB
- ARNI
- Beta-blocker
- MRA
- SGLT2i

2. Know the risks of heart failure:

5-year survival with current medication(s):



80 Alive
20 Not alive

A. Heart failure shortens life expectancy. Your life expectancy:
With no medication: Age 83 years
With current medications: Age 83 years

B. Heart failure increases the risk of being hospitalized.
On average for people with heart failure on no medications, 15 in 100 people will be hospitalized with heart failure each year.

C. Heart failure causes progressively worsening symptoms that limit quality of life.

3. Choose additional medication(s) to discuss

What are typical medication combinations?

Specific medications?

Print | EMR Note/Share Link

"I've Gotta Get a Message to You" Bee Gees

~ 1,200,000 views

www.youtube.com/user/jmccorma1234



CHOOSING WISELY

Happy



POLYPHARMACY

Bohemian Rhapsody



SHARED-DECISIONS

Parody of
Somebody That I Used to Know



STOPPING MEDICATIONS

Parody of
Day Tripper



SIMPLIFYING MEDICINE

Take it Easy

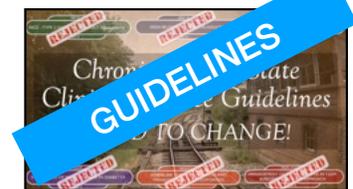


EVIDENCE-BASED PRACTICE

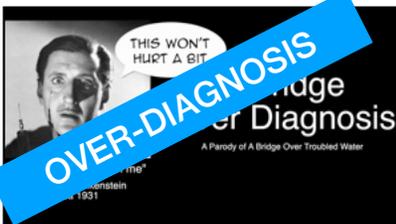
Viva La Vida



Parody of
Hotel California



Parody of
End of the Line



OVER-DIAGNOSIS

Bridge Over Troubled Water



ANTI-AGING CREAMS

Don't Fear the Reaper



PAY 4 PERFORMANCE

Treat You Better



RIGHT CARE

Parody of
Money for Nothing

THE NUTRITION PROPOSITION

HOME ABOUT WHY READ THIS BOOK? THE MENU SAMPLES REVIEWS FAQs CONTACT

RELEASED APRIL 2022

updated regularly

What does the evidence really say about your food choices?

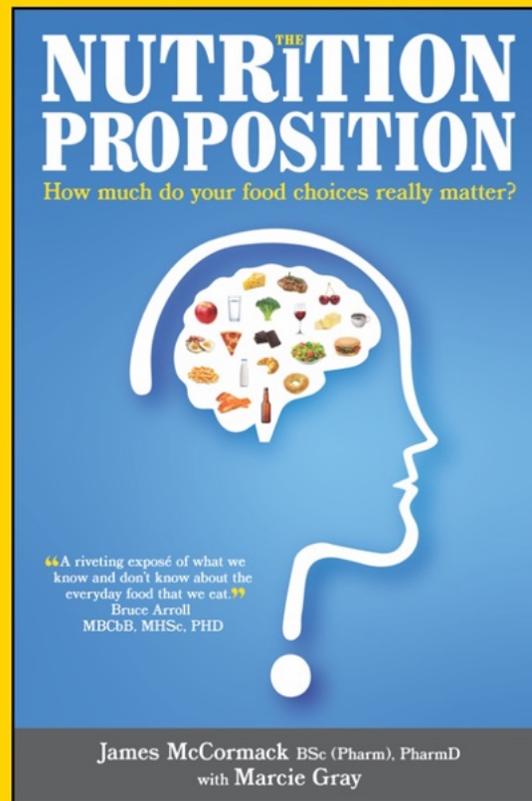
[Read The Introduction](#)

BUY
The Nutrition Proposition

Available as
Paperback or Kindle Edition

[Get the book on Amazon.com](#)

[Get the book on Amazon.ca](#)



"The Nutrition Proposition is a mammoth contribution to the world's understanding of the science behind nutritional hype. James McCormack helps strip the science of nutrition down to its bare essentials."

Alan Cassels
Author of Selling Sickness and Seeking Sickness

"A riveting expose of what we know and don't know about the everyday food that we eat."

Bruce Arroll, MBChB, MHSc, PhD
Head of the Department of General Practice
and Primary Health Care University of Auckland

"I would recommend this book for anyone who communicates with the public about health - who might not be well prepared to explain the nuance that exists with almost any health-related study, and certainly studies on nutrition topics. The authors' depth of experience, appreciation for history, case examples, and humour make this a meaningful addition to a syllabus or a personal library."

Gary Schwitzer
Publisher, HealthNewsReview.org



**The Only Nutrition Book That
Won't Tell You What To Eat!!
But It Will Tell You What We Know
And Don't Know About Food**

nutritionproposition.com

The 60+ Year Nutritional Cold War: Looking towards a truce - a three-part miniseries

PART 1: The Food Wars: How We Keep Picking the Wrong Enemies

 JAMES MCCORMACK
JUL 08, 2025

♡ 163 💬 16 ↻ 10

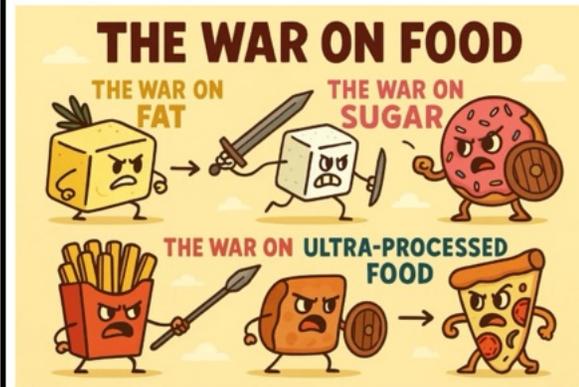
Share ⋮

James McCormack is returning to Sensible Medicine for the third time. He is a Doctor of Pharmacy in the Faculty of Pharmaceutical Sciences at the University of British Columbia. When he approached us with this idea, I was hesitant, given that it was clear it needed to be a multi-day affair. However, after reading it, it became clear that his work on this subject needed to be on Sensible Medicine. So, for the next three days, Sensible Medicine becomes Sensible Nutrition.

Adam Cifu

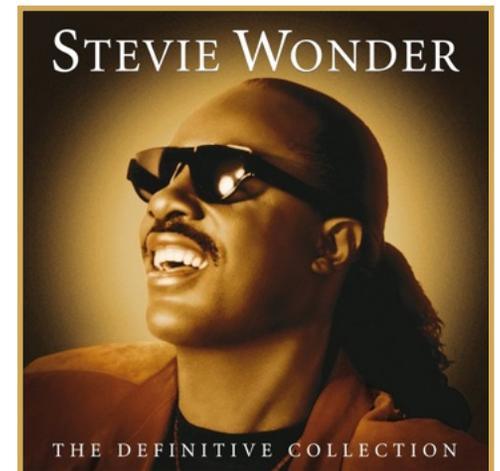
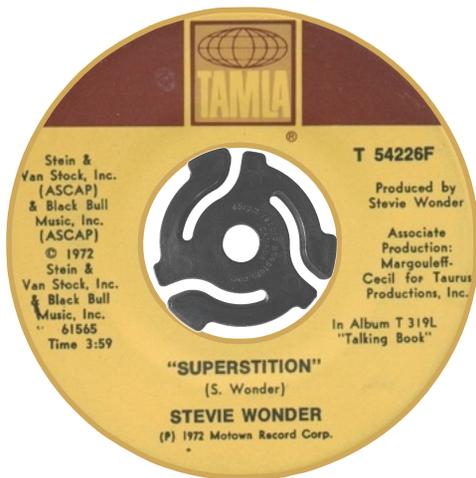
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✓ Subscribed



<https://www.sensible-med.com/p/the-60-year-nutritional-cold-war>

“When you believe in things
That you don't understand,
Then you suffer,
Superstition ain't the way”
Stevie Wonder 1972



My Simple Philosophy on Treatments



These sorts of terms are uniformly uninformative -
allopathic, conventional, mainstream, Western medicine,
complementary, alternative, integrative, naturopathy,
Chinese medicine, natural, homeopathy, herbal



We all treat people with “things” - oral/IV/IM/topical,
nutrition, surgery, talk, physical manipulations etc



I don't care HOW treatments work, I
care IF treatments work



The proportion of people over 65 taking prescription medications



EBM analysis

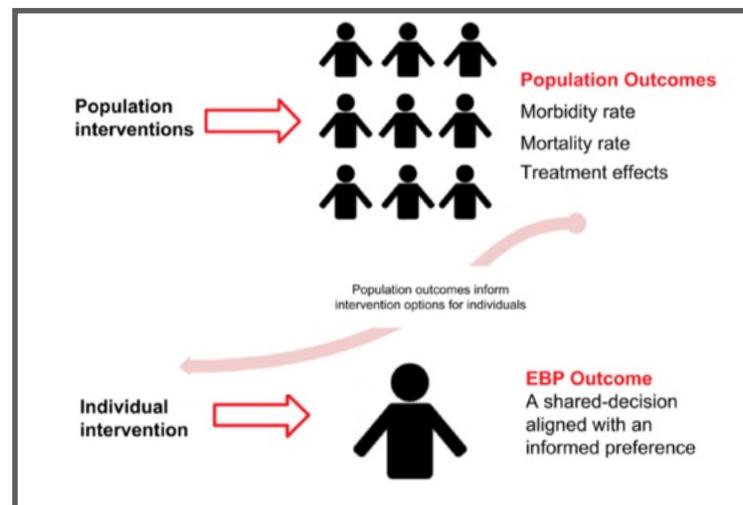


OPEN ACCESS

**Shared decision is the only outcome that matters
when it comes to evaluating evidence-based practice**

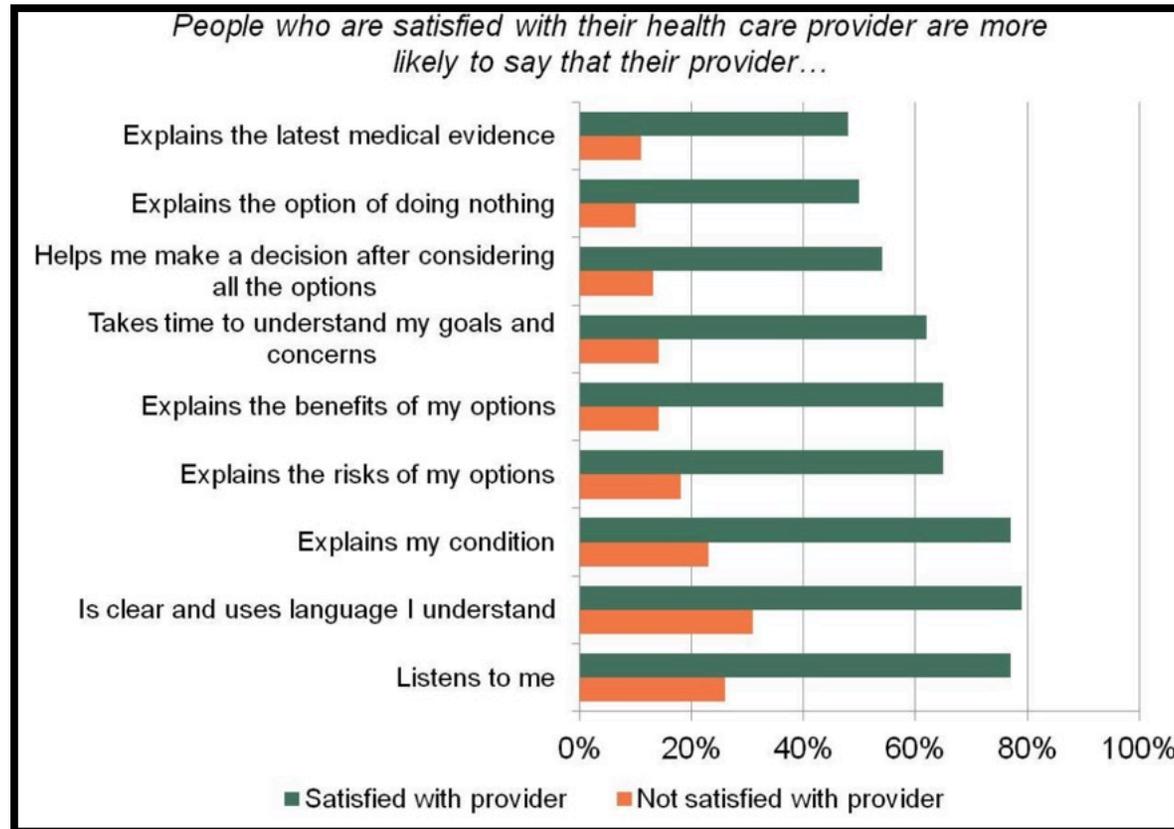
James McCormack,¹ Glyn Elwyn²

“in the vast majority of circumstances, the only outcome of relevance for EBP is to measure whether a shared decision was made”



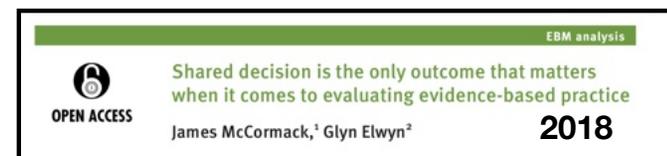
doi:10.1136/ bmjebm-2018-110922

Satisfaction is linked to shared decisions



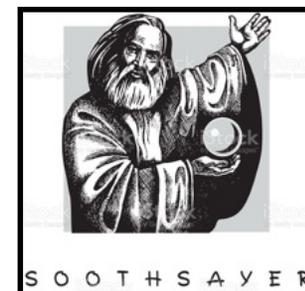
Communicating with patients on health care evidence.
Discussion Paper, Institute of Medicine, Washington, DC 2012

Where SDM may not work



In most societies there are laws that prevent certain harm from occurring, where mental incapacity or strong personal beliefs may threaten the well-being of others

1. Jehovah Witness' refusal to transfuse blood to those in dire need
2. involuntary detention for psychiatrically unstable patients who risk harming themselves or others
3. surrogates are asked to make decisions for those people truly unable to consent to treatment in immediate life-threatening situations
4. smoking bans that lead to important reductions in morbidity and mortality
5. an intriguing example that some would consider an important exception is mandatory vaccination with the potential of herd immunity. In this case, a shared-decision not to be vaccinated for a transmissible disease could lead to inherent harm of others.



Its not that difficult



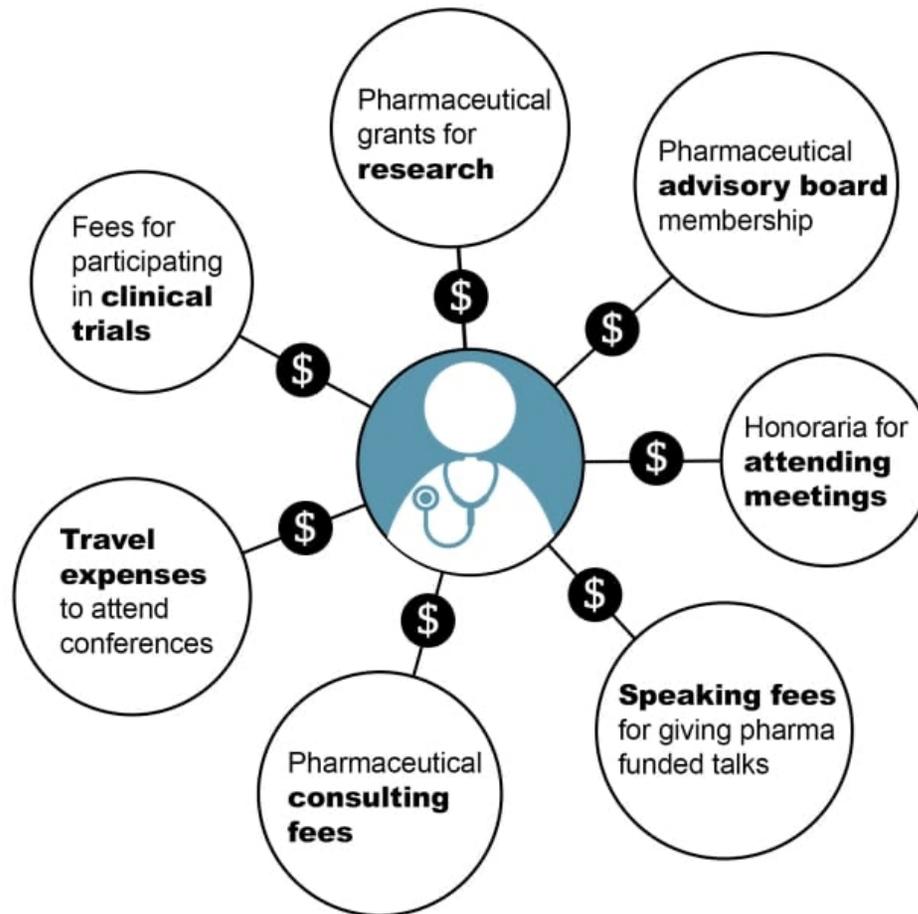


My/Marlene's 1st Agenda



Conflicts of interest/drug companies

Drug Company Money





OxyContin Swag



TORONTO STAR Sign in Q

Newsletters Today's paper Sports Betting

HOME MY LOCAL GTA CANADA POLITICS WORLD OPINION LIFE SPORTS ENTERTAINMENT BUSINESS INVESTIGATIONS PODCASTS

INVESTIGATIONS

Family doctors can no longer claim ritzy drug dinners as professional training

The dinners, sometimes three-course meals at upscale restaurants, "are basically marketing evenings," says director of medical education programming for Canada's family physicians.

Editorials

Physicians Should Refuse Pharmaceutical Industry Gifts

PDF PRINT COMMENTS

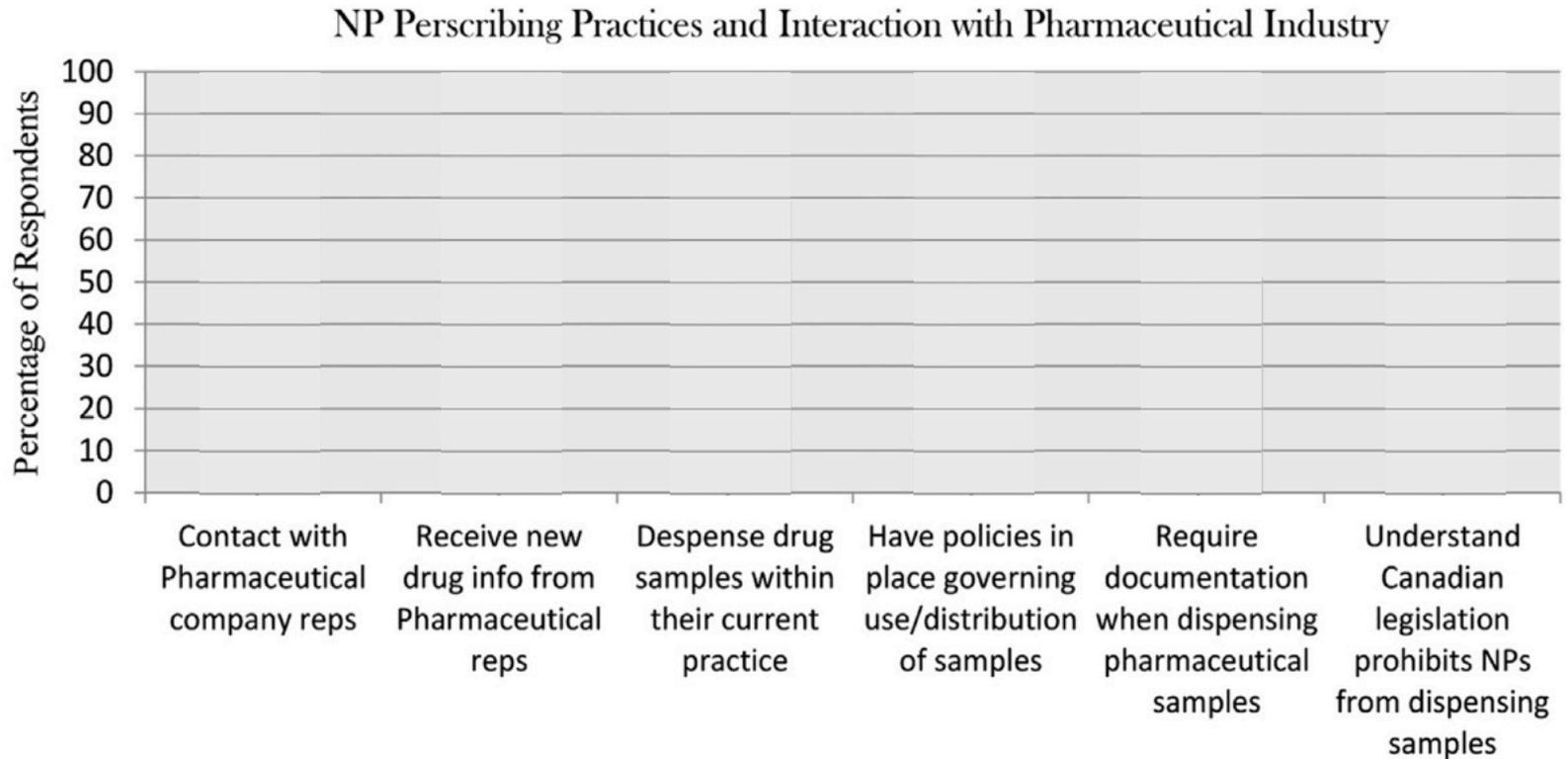
BUSINESS

Medical device firms' payments to doctors far outstripped those from pharma, study shows

Target Locked: Nurse Practitioners and the Influence of Pharmaceutical Marketing Practices in Canada

Kimberley Lamarche, DNP, and Susan MacKenzie, MEd

Figure 1. NPs' interaction with the pharmaceutical industry.

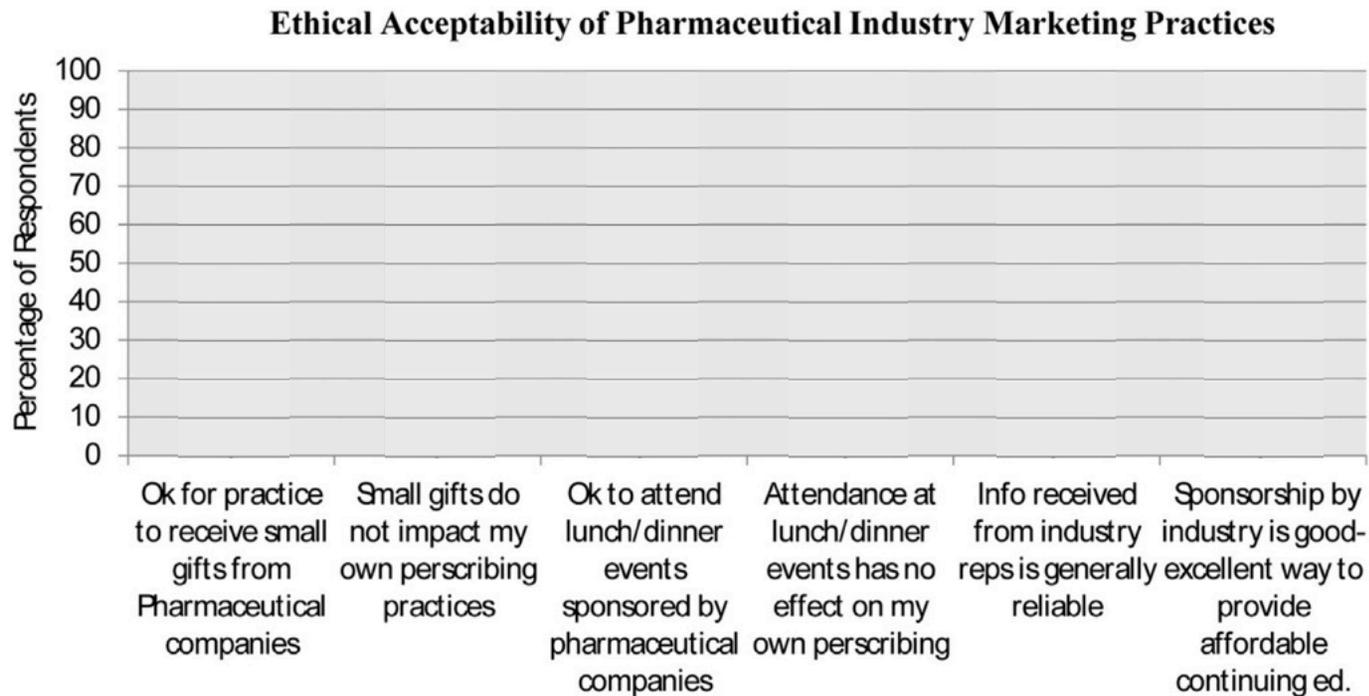


Target Locked: Nurse Practitioners and the Influence of Pharmaceutical Marketing Practices in Canada

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207 Canadian Nurse Practitioners said

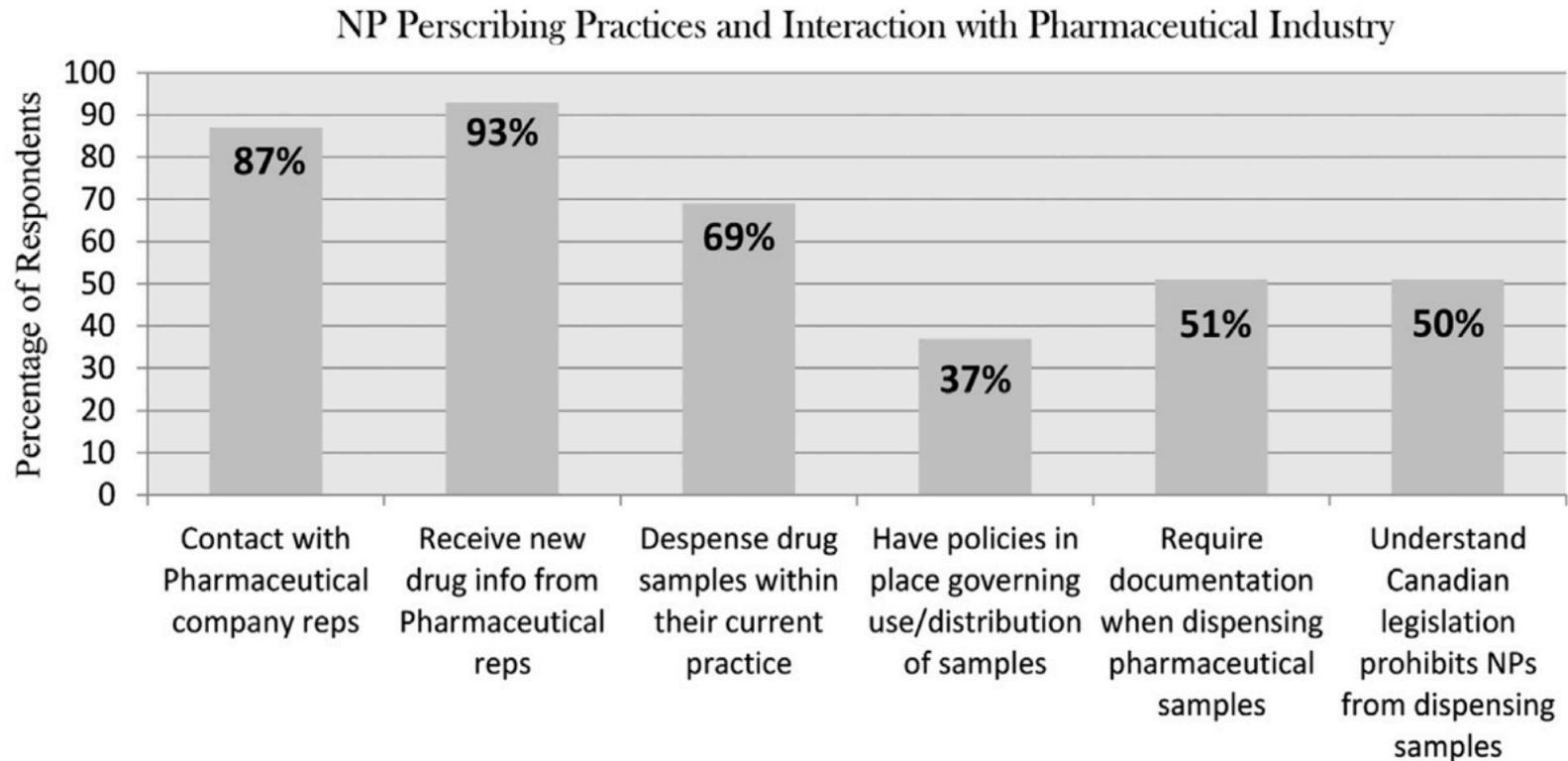
Figure 2. NPs' perspectives on ethical acceptability.



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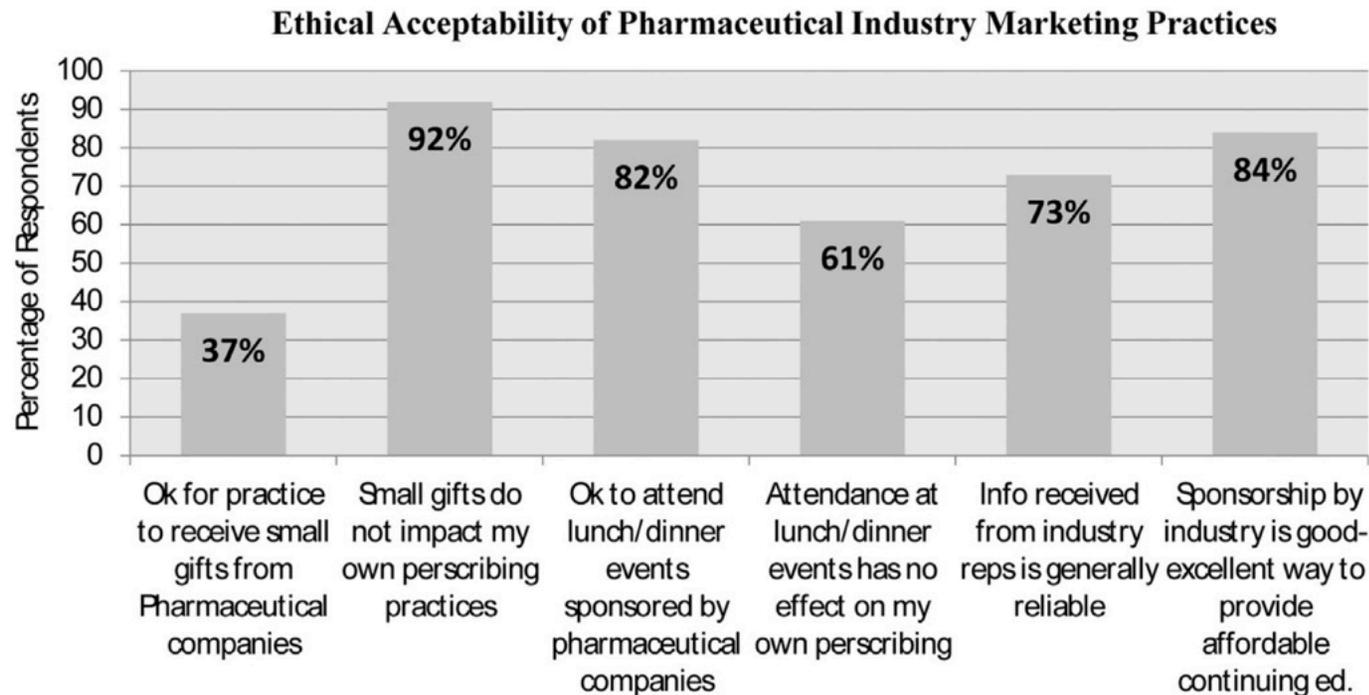


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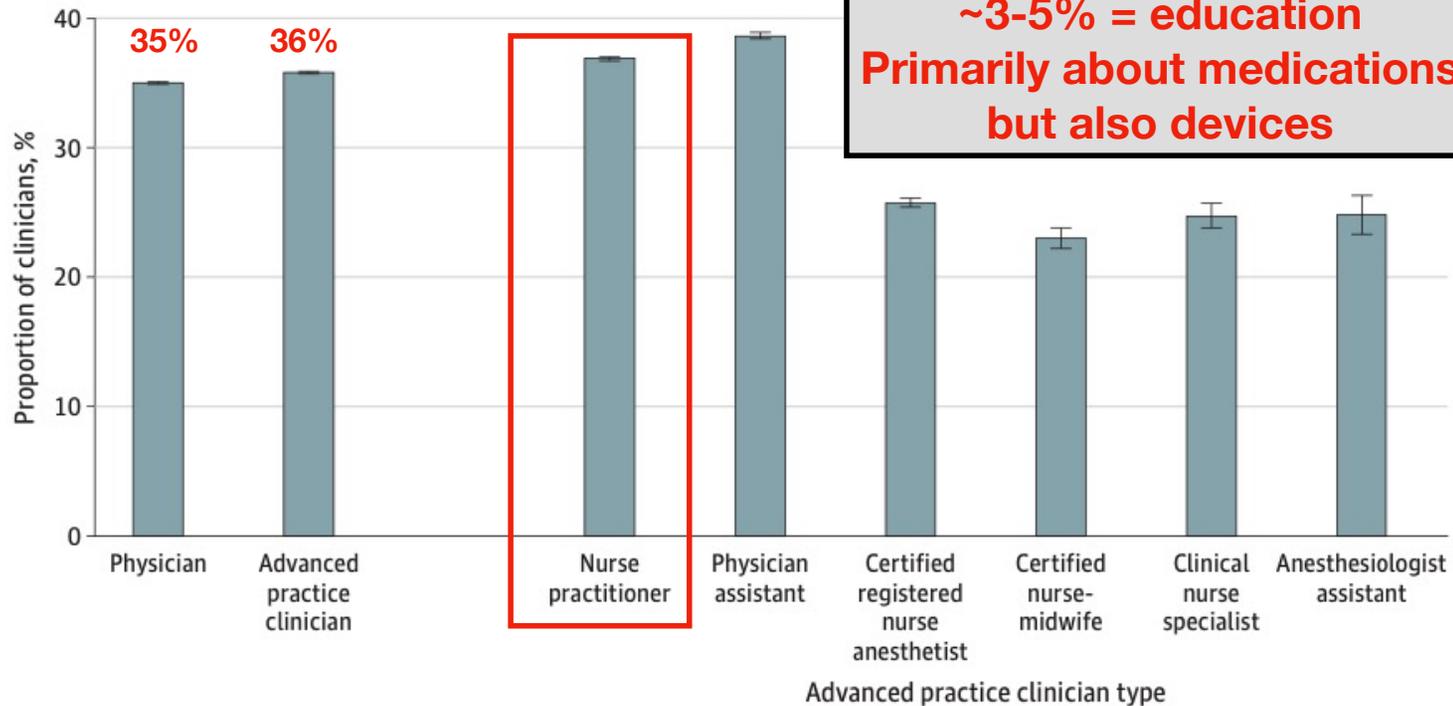
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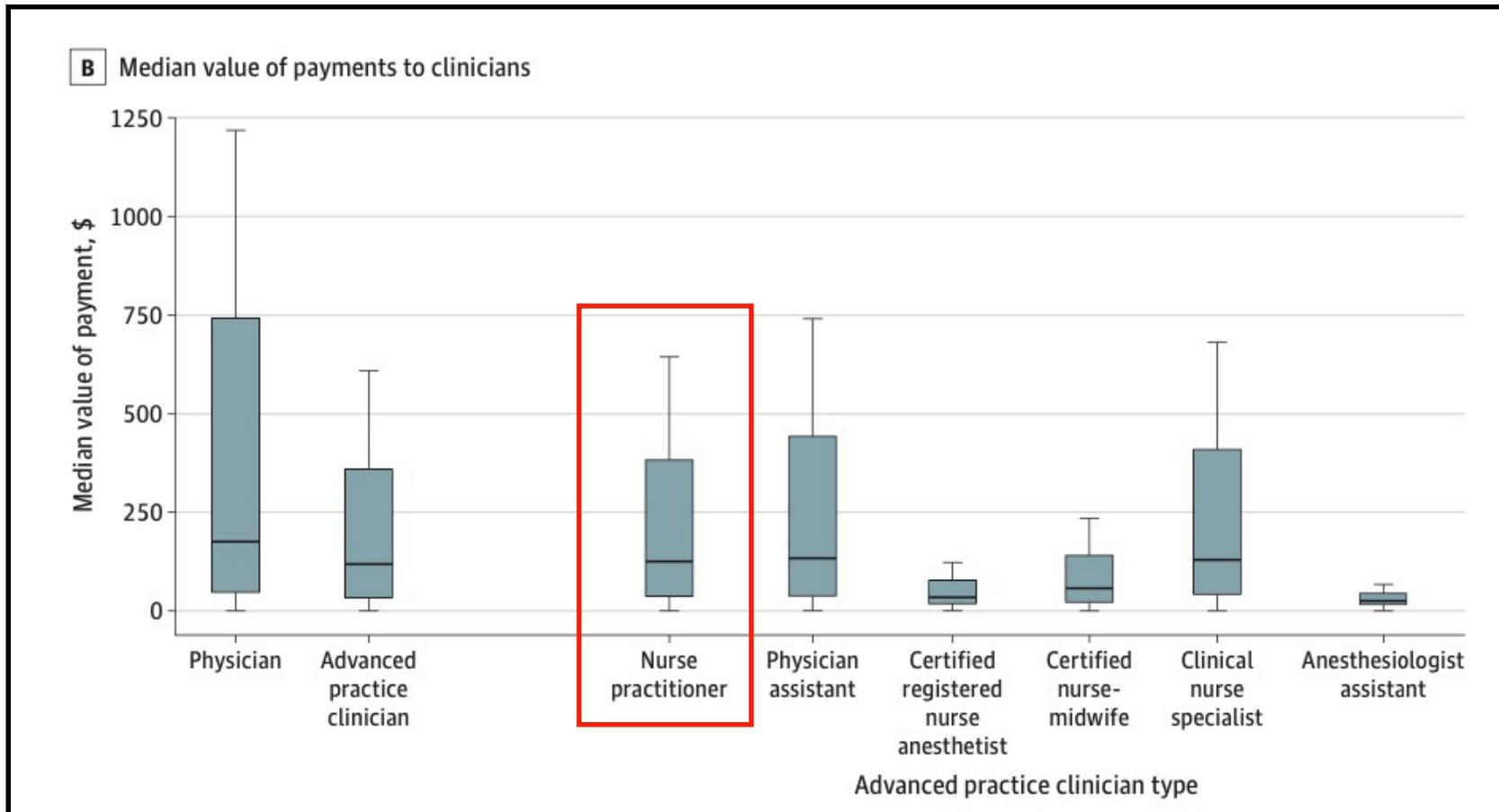
Industry Payments

Figure. Industry Payments to Physicians and Advanced Practice Clinicians by Clinician Type

A Proportion of clinicians receiving payments



Industry Payments



JAMA. 2022;328(24):2452-2455. doi:10.1001/jama.2022.20794

Health Policy

An Overview of Open Payments: Public Reporting of Pharmaceutical and Medical Device Industry Payments to Advanced Practice Registered Nurses

Meghan MacIsaac, Nancy Rudner, Tracy Klein, Elissa Ladd, Dana Hart, Christine M. Baugh, Quinn Grundy

Table 3
The Number and Value of Payments to Providers in 2022

Category	Physicians ^a	Advanced Practice Registered Nurses ^b
Number of providers	459,745	188,580
Number of payments	8,359,680	2,706,919
Total value of payments	\$2,328,764,361	\$107,648,738
Number of companies making payments	1,589	883
Median value of payments (IQR)	\$190 (\$734)	\$122 (\$332)
Median number of payments (IQR)	5 (17)	3 (12)

Table 4

Top Companies, Products, and Payment Types for Advanced Practice Registered Nurses

Top 5 Companies Making Payments

Category Advanced Practice Registered Nurses

1. AbbVie Inc
2. Allergan Inc^a
3. Janssen Pharmaceuticals
4. Novo Nordisk Inc
5. AstraZeneca Pharmaceuticals

Top 5 Products by Dollar Amounts (Generic Names)

1. Cariprazine hydrochloride
2. OnabotulinumtoxinA
3. ~~Cariprazine hydrochloride~~
4. Ubrogapant
5. Semaglutide

Top 5 Payment Types (by Aggregate Value)

1. Food and beverage
2. Compensation for services other than consulting (including servicing as faculty or as a speaker at a venue other than a continuing education program)
3. Travel and lodging
4. Consulting fee
5. Compensation for serving as faculty or as a speaker for a medical education program

Alternatives

Do other things for \$10 an hour



Less than 5% of new medications provide an advantage over what we already have

Read a Cochrane Review - get everything you need in 10 minutes

Google search

Identify groups you
discuss



drug name AND systematic review OR meta-analysis



Listen to the Best Science Medicine Podcast - shameless self-promotion

Use ChatGPT - you just need to ask the “right” questions



My Agenda



Much of what we do, even with the best of intentions, is not that effective

Most guidelines are a BIG problem

Some treatments (medications, nutrition, activity) can be effective and even life-saving BUT many aren't and they all have the potential for harm, inconvenience and cost

I believe the size of the effect for many of these treatments is much smaller than people think

Lab test variation makes many tests (especially repeat tests) of questionable use and are simply misleading

The recommended doses for most medications are too high

What Would You Do?

URTI and hypertension are the 2 most common reasons for a visit to a primary care provider

Canadian Family Physician November 2018, 64 (11) 832-840

YOU are approximately 50 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?

What drug and dose would **YOU** start with?

Did you do SDM for yourself?

ASSUME a medication has no side effects or cost. What is your absolute benefit CVD threshold (Y%) that would get you to take a drug every day for 10 years?

If your risk was X% the risk would have to be reduced by Y%

What if the medication had a 10% chance of causing a side effect important enough to have to stop the medication and it cost \$400/year.

The Problem

We ignore how **MUCH**
an intervention **HELPS** (or **HARMS**)
because we're **FIXATED** on
how **CERTAIN** we are about **SOME** effect



All exacerbated by
**The
Magnitudinous***
Problem

* only sort of a real word

AVOID

Misleading Terminology

“Significant”

“Use with caution”

“Use with extreme caution”

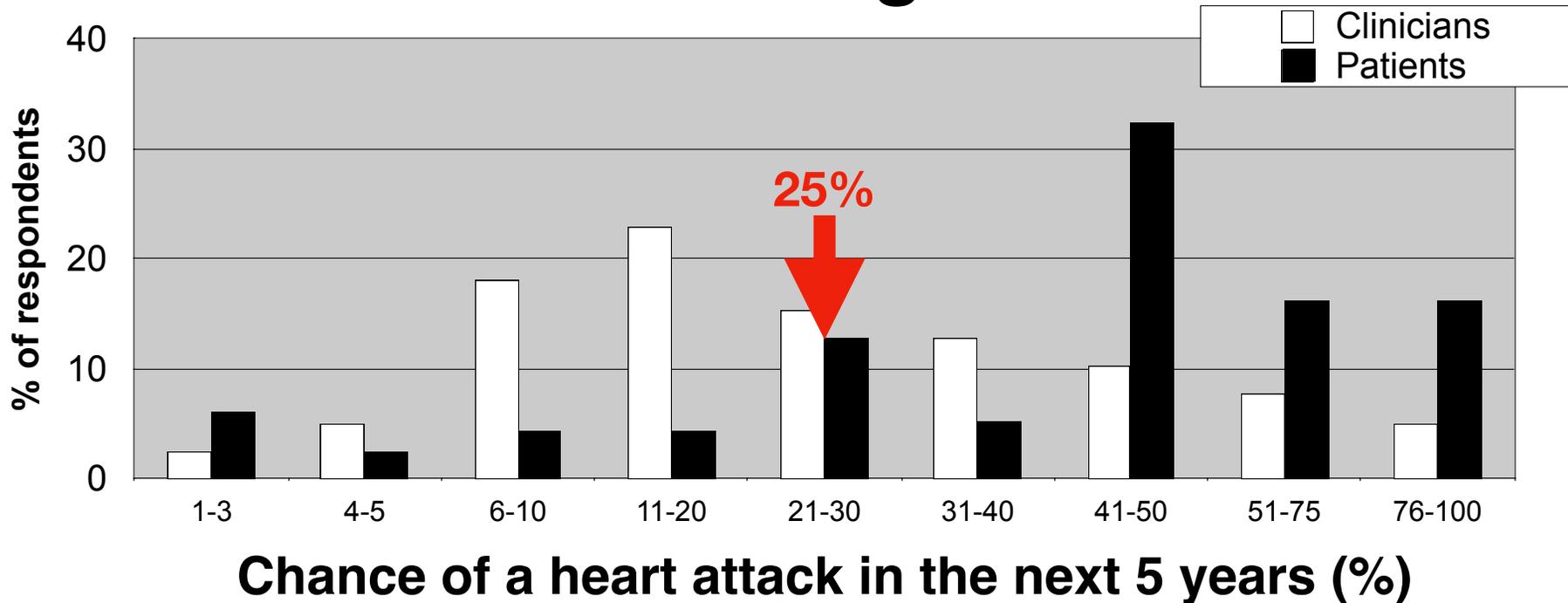
“Monitor closely”

“High risk”

“Very high risk”

“Really !@#\$\$% high risk”

What is "High Risk"



**A 60 y/o, male, smoker, diabetic,
SBP 180, total cholesterol 7.2 mmol/L**

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

The Magnitudinous Problem

More
Increased
Reduced
Improved
Decreased
Higher
Lower
High
Low
Significant
Less
Fewer
Worsened

Better
Worse
Greater
Uncommon
Superior
Rare
Important

Considerable
Strong
Inferior
Lesser
Small
Bigger
Major

Severe
Weak
Strong
Different
Faster
Shorter
Longer
Shortened
Lengthened
Extreme
Unlikely
Short
Many/Most

**Convey a story but not
really the evidence/
numbers**

All these words likely mean something different to everyone

Examples that probably require quantification clarification

Your salary will be **INCREASED**

Turn left after a **MODERATE** number of kilometres

You will be getting a **SHORT** jail sentence

You have an **UNLIKELY** chance of getting an STD

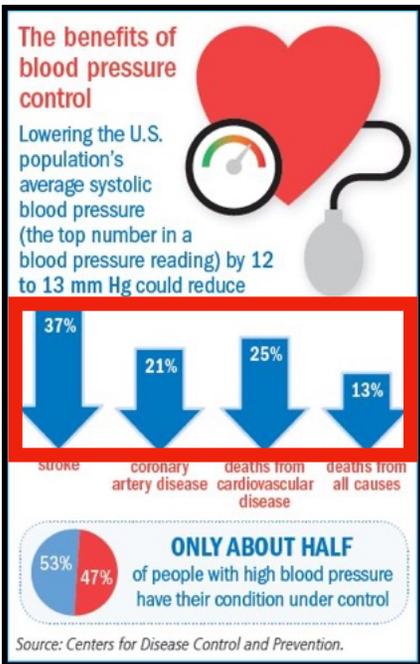
You have a **SIGNIFICANT** chance of a heart attack

A **SMALL** tube will be placed a **CONSIDERABLE** distance into your rectum

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**



Walking
can reduce the risk of cardiovascular events by

50%**
in adults 60 or older

Fit
HOUSTON

THE TEXAS HEART INSTITUTE

**There is step-related reduction in cardiovascular events with walking, particularly for those 60 yrs of age and older. The reduction in events may be as high as 50% in those able to achieve the 10,000 steps/day level but even walking 3,800 steps/day reduces the risk 20%. Poluch, et al. 2023. Circulation. 147:122-131.

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

These #s are all relative and all misleading

STUDY FINDS THE MEDITERRANEAN DIET LOWERS WOMEN'S RISK OF HEART DISEASE BY 25%

INTENSIVE BLOOD PRESSURE MANAGEMENT MAY SAVE LIVES

WHAT'S THE BEST WAY TO TREAT HIGH BLOOD PRESSURE IN PATIENTS 50 AND OLDER? The SPRINT trial enrolled more than 9,300 participants at UAB and other locations to find out. Investigators divided them into two groups:

STANDARD TREATMENT	INTENSIVE TREATMENT
TARGET: 140 mmHg Systolic BP	TARGET: 120 mmHg Systolic BP
THERAPY: Avg. 2 different blood pressure medications	THERAPY: Avg. 3 different blood pressure medications

RESULTS: ABOUT **27%** lower rates of heart attack, heart failure, and other cardiovascular events. ABOUT **25%** lower risk of death among participants receiving intensive treatment

UAB THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Beware of “qualitative quantification”

Qualitative descriptor	EU assigned frequency	Mean frequency estimated by participants (n=200)
Very common	>10%	65% (24.2)
Common	1–10%	45% (22.3)
Uncommon	0.1–1%	18% (13.3)
Rare	0.01–0.1%	8% (7.5)
Very rare	<0.01%	4% (6.7)

**Communicating risks
OFF BY
~350% to 18,000%**

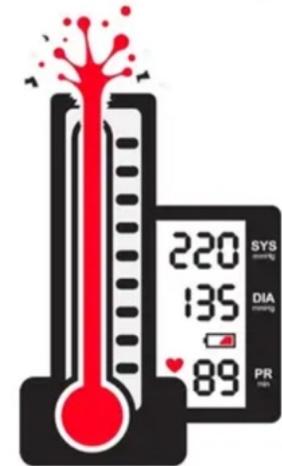
Values are mean (SD).

Lancet 2002;359:853–54

1966

One of the first
blood pressure trials

Avg BP = **200/110** mmHg



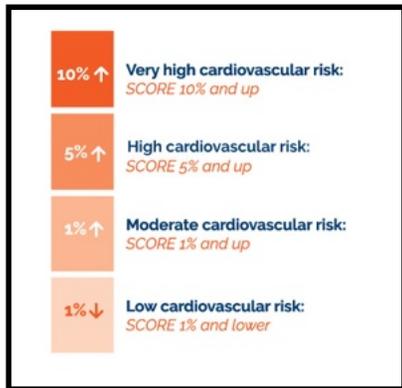
**EFFECT OF PROPRANOLOL IN
MILD HYPERTENSION**

J. W. PATERSON
M.B., B.Sc. Lond., M.R.C.P.
MEDICAL REGISTRAR

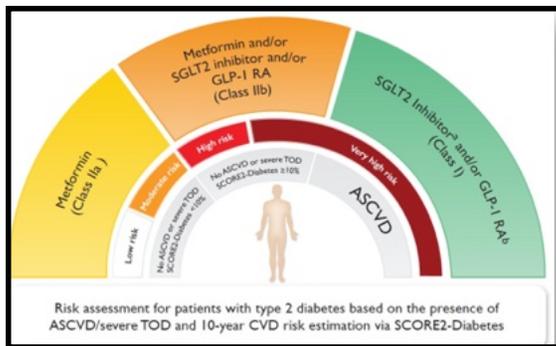
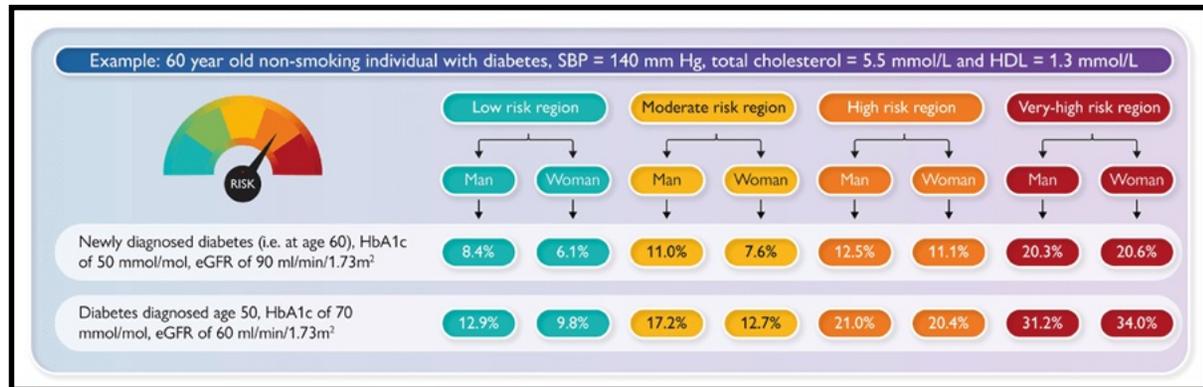
C. T. DOLLERY
M.B., B.Sc. Birm., M.R.C.P.
LECTURER IN CLINICAL THERAPEUTICS

DEPARTMENT OF MEDICINE, ROYAL POSTGRADUATE MEDICAL
SCHOOL, DUCANE ROAD, LONDON W.12, ENGLAND

Lancet 1966;2:1148-50



High
Low
Intermediate
Desirable



Normal
High to very high
Nearly optimal
Borderline high

Low to moderate
High Normal
Moderate
Moderate to 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 PREVENTION¹

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%
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JUST GIVE UP



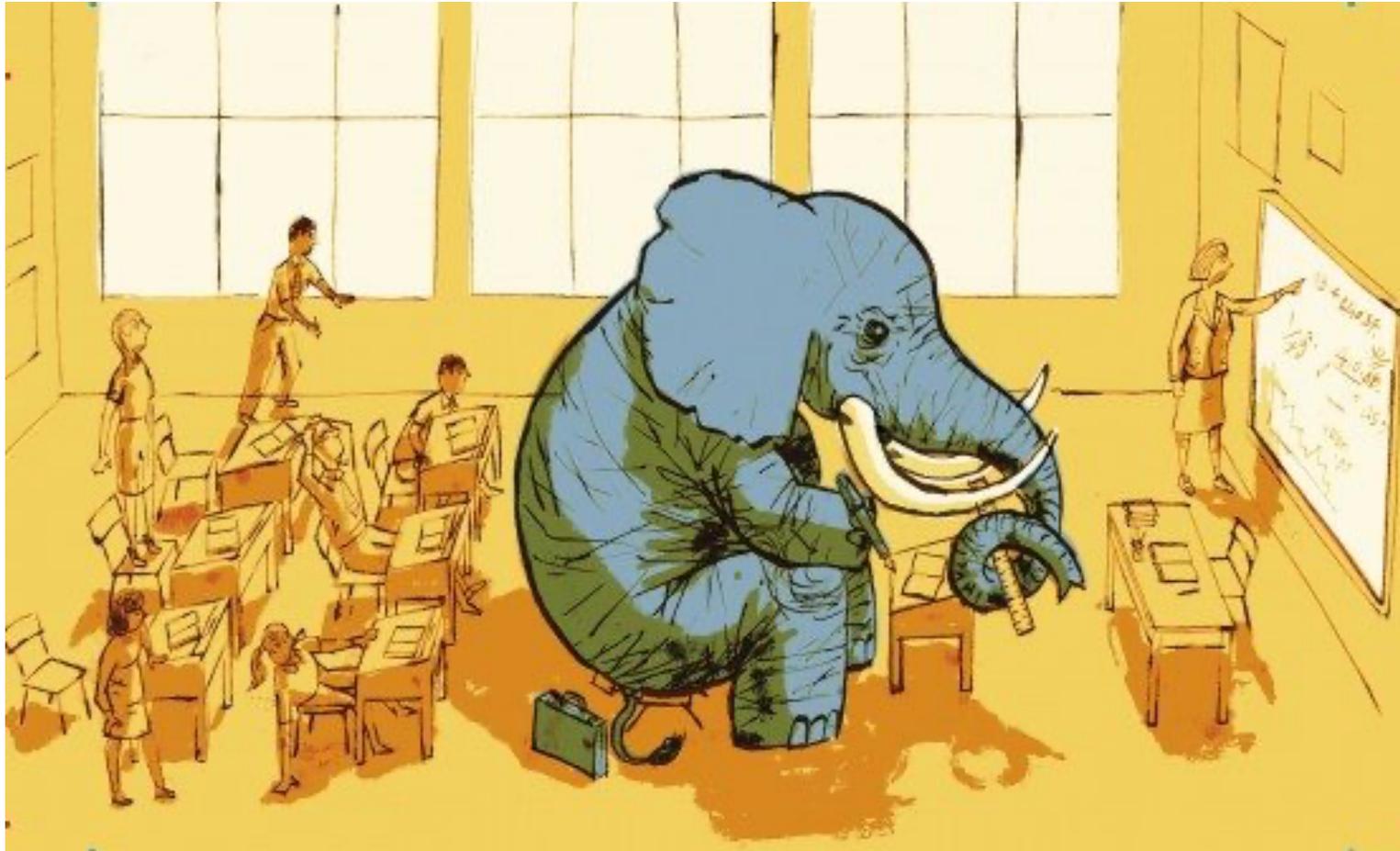
If your risk is 0% you are at “high” risk?

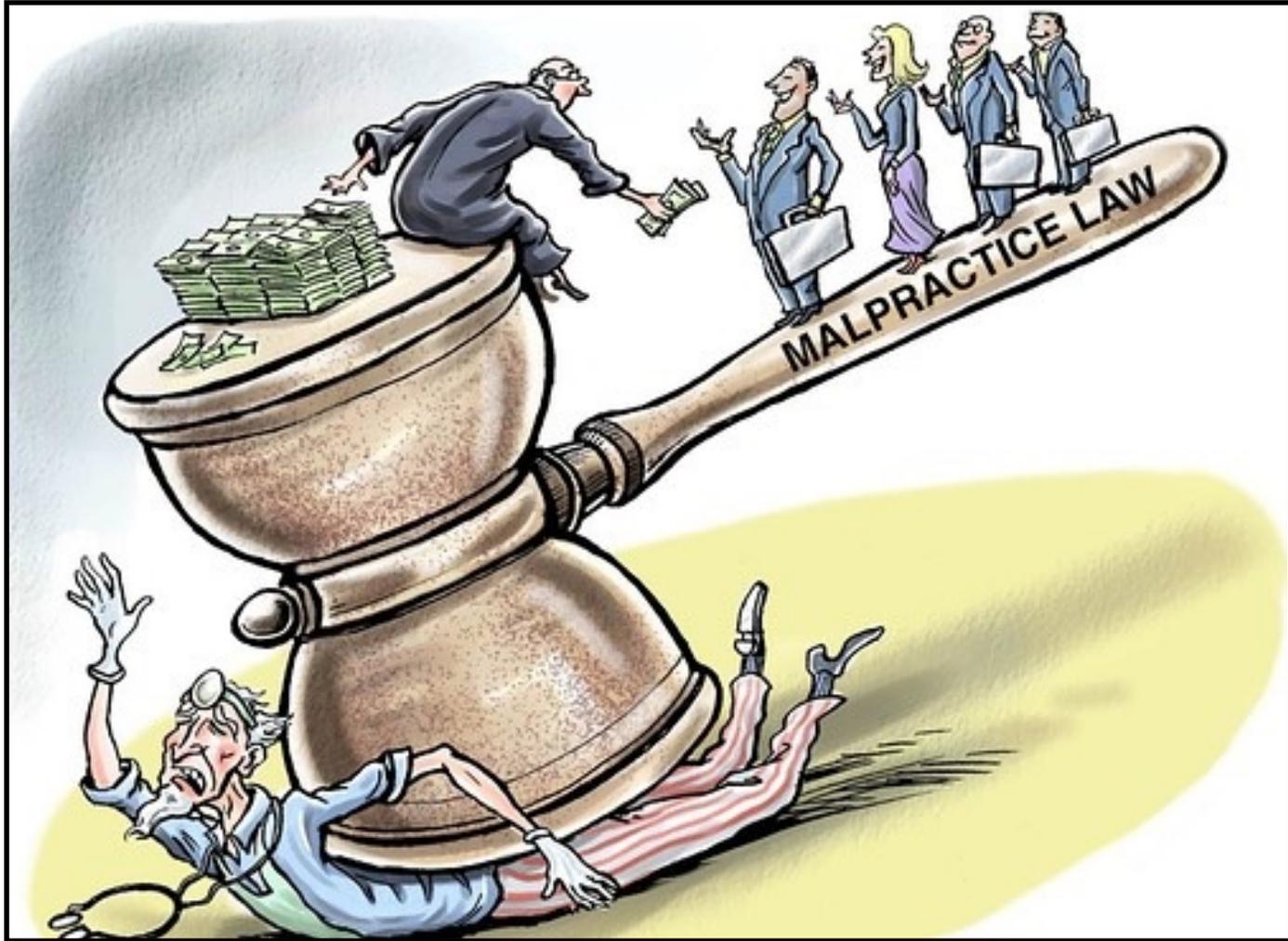


American Association of Clinical Endocrinology Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm - 2023 Update

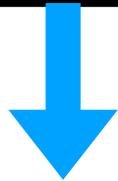


Let's first address the **ELEPHANT** in the room





Most Docs Practice
**Defensive
Medicine**



“Standard of Care”
and follow
Clinical Practice Guidelines



Shared Decision Making
(SDM)



May or may not follow
Clinical Practice Guidelines

Medicolegal Sidebar: Clinical Practice Guidelines—Do They Reduce Professional Liability Risk?

Joseph P. McMenemy MD, JD, Wendy Teo BA(Cantab), BM BCh (Oxon), LLM,
B. Sonny Bal MD, JD, MBA, PhD

“Clinical practice guidelines, however, are designed to improve care, **not to define standard care**. They can also **limit physician autonomy**, impose rules that are adopted mainly to **avoid litigation risk**, and may be developed by physicians with **relevant financial conflicts**. **In our view, courts should exclude clinical practice guidelines from evidence of the standard of care or of its breach.**”

Clin Orthop Relat Res (2020) 478:23-25

Patient preferences for shared decisions: A systematic review

Betty Chewning^{a,*}, Carma L. Bylund^b, Bupendra Shah^c, Neeraj K. Arora^d,
Jennifer A. Gueguen^e, Gregory Makoul^f

“the number of patients who prefer participation has increased over the past three decades so that **the majority of patients prefer to participate in decisions**”

**Factors involved in deciding to start preventive treatment:
qualitative study of clinicians' and lay people's attitudes**

David K Lewis, Jude Robinson, Ewan Wilkinson

BMJ 2003;327:841

“Many of the preferences expressed by the clinicians and lay people in this study are at **odds with recommendations in guidelines**”

**Differing perceptions of intervention thresholds for fracture
risk: a survey of patients and doctors** Osteoporos Int 2012;23:2135–40

77% of doctors would recommend treatment

21% of our patient cohort would consider treatment justified

RESEARCH ARTICLE

Open Access

Can shared decision-making reduce medical malpractice litigation? A systematic review

Marie-Anne Durand^{1,2*}, Benjamin Moulton^{3,4,5}, Elizabeth Cockle², Mala Mann⁶ and Glyn Elwyn^{1,7}

“There is insufficient evidence to determine whether or not shared decision-making and the use of decision support interventions can reduce medical malpractice litigation. Further investigation is required.”

Reducing litigation risk

2 THINGS to DO

Shared decision-making model

- 1) Use a decision aid
- 2) Document decision



Two or more reasonable treatment or screening options

Shared decision-making model

Defensive medicine model

ADVERSE OUTCOME OCCURS

Choice made does **NOT MEET** the "standard of care"

Choice made **MEETS** the "standard of care"

Choice made **MEETS** the "standard of care"

Choice made does **NOT MEET** the "standard of care"

Discussion **NOT** documented

Discussion documented in notes

Decision aid used

Discussion **NOT** documented

Discussion documented in notes

Decision aid used

Plaintiffs lawyer argues risks and benefits should have been discussed

Low to medium risk

No medico legal protection

No medico legal protection

Medium risk

Low risk

Low to medium risk

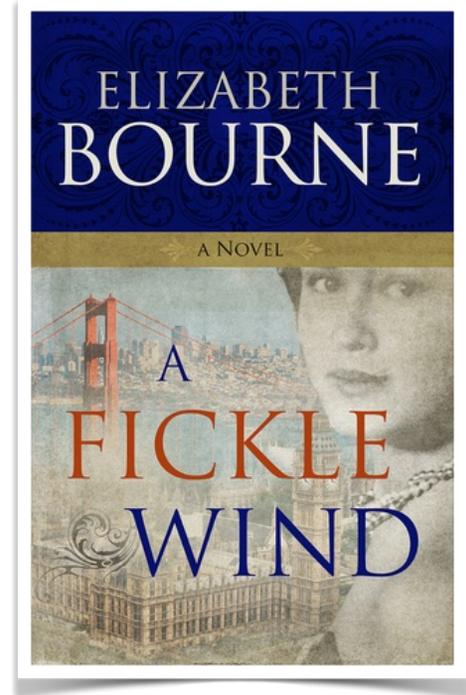
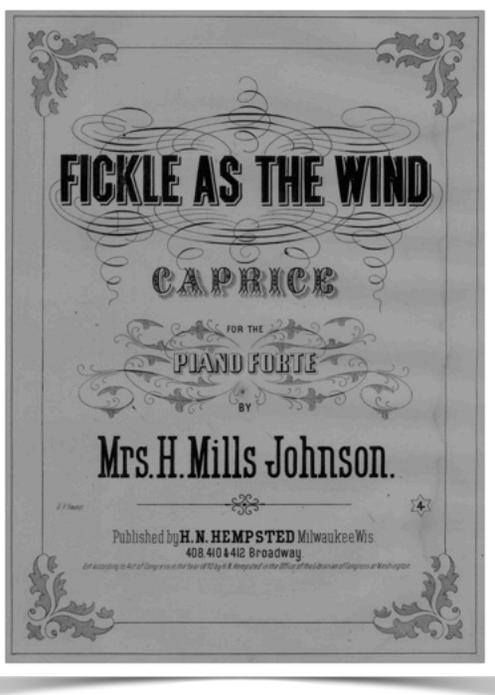
Low risk

Low risk

“I would rather know evidence and try to apply it to each patient, than memorize guidelines and try to apply them to all patients”

Mark McConnell

The Fickle Nature of Guidelines



Guidelines would be awesome if they...

Were developed primarily by, and definitely for, the people that ultimately end up using them

Were a credible synopsis of the best available evidence presented in a way that clinicians could easily access and interpret

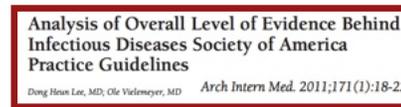
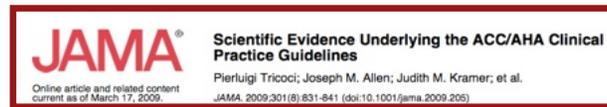
Allowed patient values and preferences to be taken into account

Wrong guidelines: why and how often they occur

Primiano Iannone,¹ Nicola Montano,² Monica Minardi,³
James Doyle,³ Paolo Cavagnaro,⁴ Antonino Cartabellotta⁵

“Unfortunately, depending on how their reliability is measured, **up to 50% of guidelines can be considered untrustworthy**. This carries serious consequences for patients’ safety, resource use and health economics burden.”

Typically “evidence-based” guideline recommendations are not based on “solid” evidence



EVIDENCE LEVEL	Cardiology	Infectious disease	Endocrinology
1 or A based on RCTs	11%	14%	6%
3 or C based on opinion	48%	55%	35%

Factors Associated With High-Quality Guidelines for the Pharmacologic Management of Chronic Diseases in Primary Care

A Systematic Review

Caroline de Godoi Rezende Costa Molino, MS¹; Nathalia Celini Leite-Santos, BS¹; Franciele Cordeiro Gabriel, MS¹; [et al](#)

» [Author Affiliations](#)

JAMA Intern Med. 2019;179(4):553-560. doi:10.1001/jamainternmed.2018.7529

Heart disease
Lung disease
Diabetes
Osteoporosis
Depression
Osteoarthritis
Dementia
GERD
BPH



421 CPGs (July 2011-August 2017) for the management of common non-communicable disease in primary care

24% were rated as high quality

lowest median domain scores

applicability (22%) and rigour of development (33%)

Systematic review of clinical practice guidelines recommendations about primary cardiovascular disease prevention for older adults

Jesse Jansen^{1,2*}, Shannon McKinn^{1,2}, Carissa Bonner^{1,2}, Les Irwig¹, Jenny Doust^{1,3}, Paul Glasziou^{1,3}, Brooke Nickel^{1,2}, Barbara van Munster^{4,5} and Kirsten McCaffery^{1,2}

47 guidelines	Discussed benefits	Discussed harms
CVD assessment and harms	19%	17%
Medications	32-33%	15-19%
Lifestyle	15%	0%

Deprescribing mentioned - 0%

Guideline sponsorship

2009 - 2,300 guidelines in the National Guideline Clearinghouse

Guideline development

41% - medical speciality societies

22% - government agencies/nonprofit

17% - professional associations

9% - disease specific societies

4% - independent expert panels

at least $2/3$ are
being developed
by groups with
a clear potential for
important biases

<http://www.ncbi.nlm.nih.gov/books/NBK22928/>

Original Investigation | Cardiology

Incorporation of Shared Decision-Making in International Cardiovascular Guidelines, 2012-2022

Blair J. MacDonald, BA, PharmD; Ricky D. Turgeon, BSc(Pharm), PharmD

Looked at 65 cardiovascular guidelines from 2012-2022

American College of Cardiology, Canadian Cardiovascular Society, and European Society of Cardiology

Only ~50% of these guidelines had a statement expressing the importance of shared decision-making

~2700 medication recommendations

only 6% incorporated shared decision-making

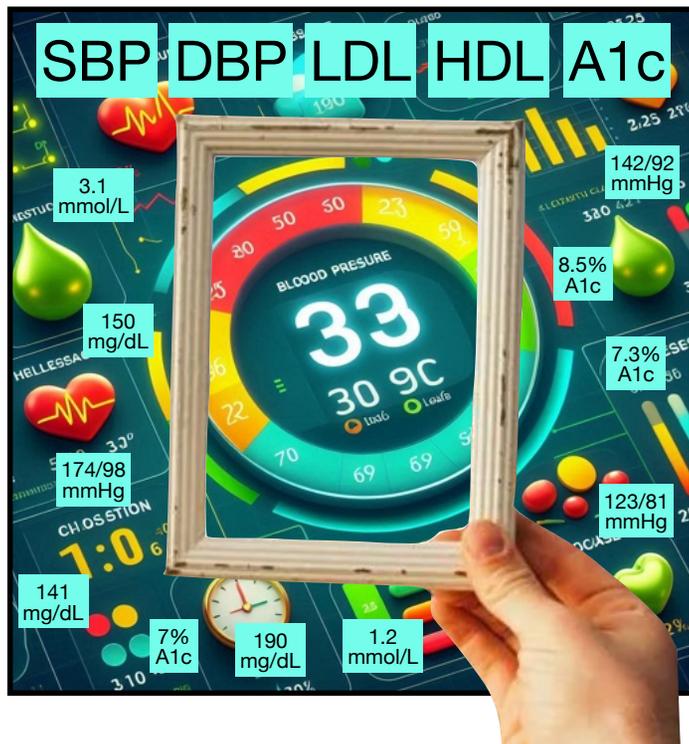
only 3% explicitly and impartially recommended shared decision-making

Reframe What You Think About Numbers

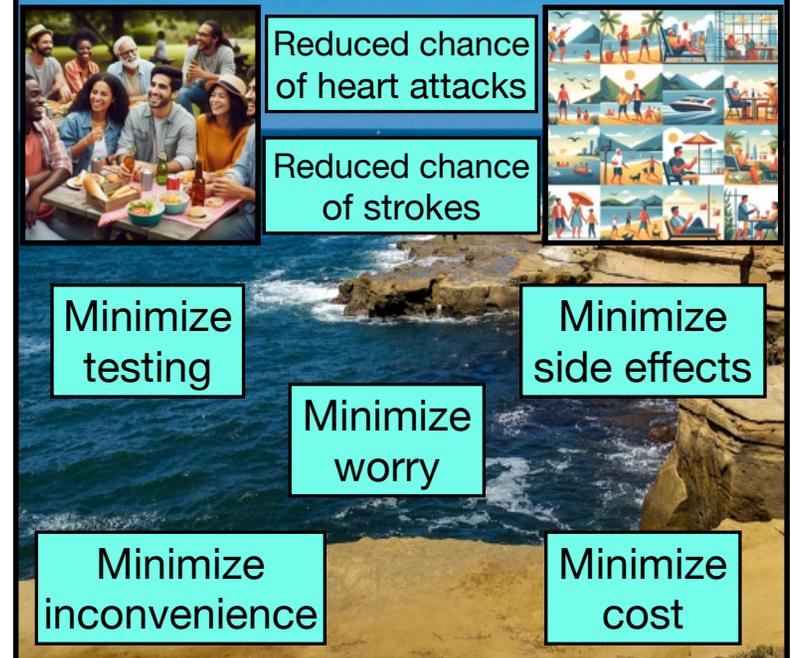
Blood pressure, lipids, and glucose

What Really Matters

What doesn't matter as much



QUALITY OF LIFE



They Aren't Actually Sick

A condition vs a disease



When these numbers are “high” we often refer to them as chronic “diseases”

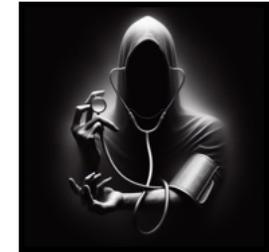
HOWEVER - in general, people with:

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

“high” cholesterol have **NO** symptoms

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

Silent Killers

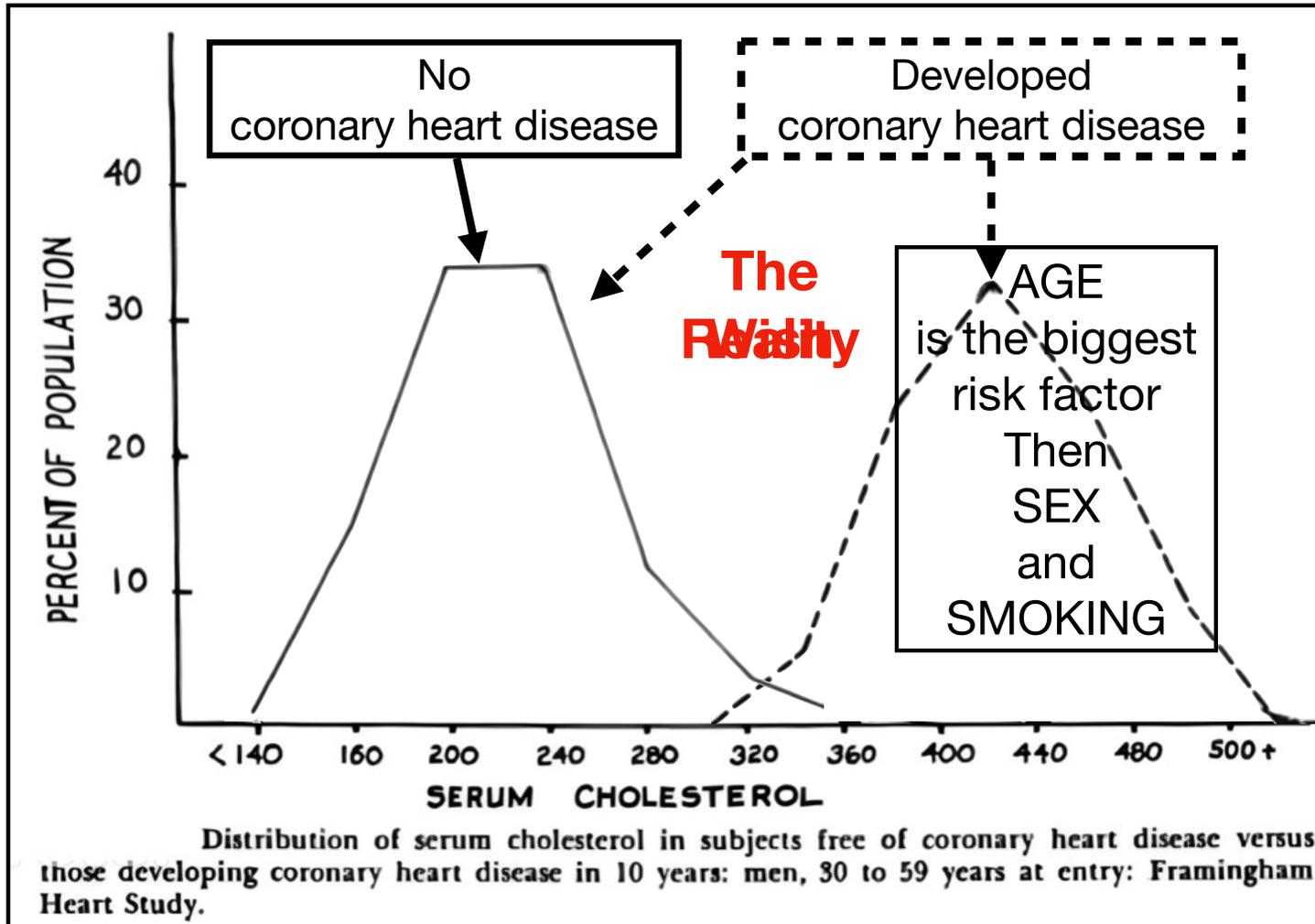


A much more informative way is to think of these **simply as RISK factors**

Importantly

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

Risk Factor Context



From 2008 to 2015

20 LARGE TRIALS IN A ROW SHOWED **NO** BENEFIT FROM
CHANGING A SURROGATE MARKER

DIABETES

ACCORD, ADVANCE, VADT
(aggressive A1c lowering)
ROADMAP (olmesartan)
ORIGIN (insulin)
SAVOR-TIMI 53 (saxagliptin)
EXAMINE (alogliptin)
ALECARDIO (aleglitazar)

GENERAL

ACTIVE (irbesartan/afib)
CRESCENDO (rimonabant)
VISTA-16 (varespladib)

5 cholesterol trials
8 diabetes/glucose trials
4 blood pressure trials
3 general risk reduction trials

LIPIDS

AIM-HIGH, HPS2-THRIVE (niacin)
ACCORD (fibrates)
dalOUTCOMES (dalcetrapib)
STABILITY (darapladib)

BLOOD PRESSURE

ALTITUDE (aliskiren)
VALISH, AASK, ACCORD
(aggressive BP lowering)

FINALLY!!!!!!2015

- 1) EMPA-REG OUTCOME (empagliflozin) - **1.6% ↓** over 3 years
- 2) LEADER (liraglutide) - **1.8% ↓** over 4 years
- 3) SPRINT (120mmHg vs 140mmHg) - **1.6% ↓** (CVD) over 3 years but also **1.8% ↑** (Kidney)
- 4) HOPE 3 - statins YES, BUT blood pressure no benefit
- 5) FOURIER - **1.6% ↓** over 2 years BUT \$15,000/year

BUT!!!!!!

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

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 <small>75%Na/25%K</small>	10-15% ↓	Statins <small>lower dose</small>	25% ↓	Metformin	? only 1 trial
Moderate physical activity	25% ↓	Thiazide <small>lower dose</small>	25% ↓	Statins <small>higher dose</small>	an extra 10 % ↓	SGLT2's <small>**</small>	15% ↓
		ACE/ARB <small>lower dose</small>	25% ↓	Ezetimibe <small>**</small>	5% ↓	GLP's <small>**</small>	15% ↓
		Betablockers, calcium channel blockers	Some but less than those above	PCSK9 Inhibitors <small>**</small>	15% ↓	Sulfonylureas Insulin DPP4s	0%

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

** Much, and in some cases all, of the evidence is in secondary prevention

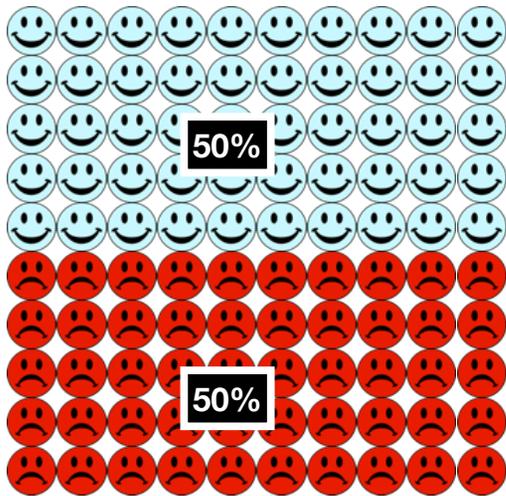
Lifetime CVD risk/benefit

(most people don't benefit despite a lifetime of surrogate marker treatment)

Lifetime risk of CVD

Male with 2 CVD risk factors
(NEJM 2012;366:321-9)

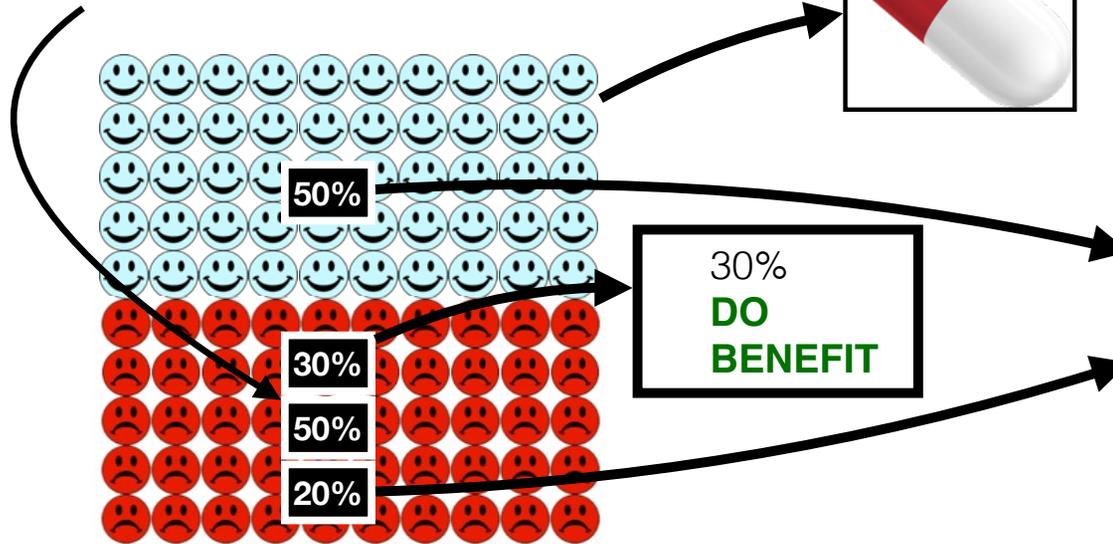
ROUGHLY 50%



Lifetime benefit

Assume with multiple risk factor modification we can reduce risk relatively by 60% (VERY optimistic)

50% → 20%



**100% get this
"TREATMENT"
or "INTERVENTION"**



**30%
DO
BENEFIT**

**70%
DO NOT
BENEFIT**
despite a
LIFETIME
of treatment

Challenging treatment thresholds

James McCarroll¹, James Matthews^{1,2,3,4} and David Newman^{1,2,3,4}

Word count	WORDS, VALUE, AKA, VALUE
1000	1000, 1000, 1000, 1000
2000	2000, 2000, 2000, 2000
3000	3000, 3000, 3000, 3000
4000	4000, 4000, 4000, 4000
5000	5000, 5000, 5000, 5000

Prescriber 2015;26:5-7

EDITORIAL

ABSOLUTE Benefit on CVD risk over 10 years

Typically based on a 10-year risk of 15%

THE GOLDEN RULE

BENEFIT NEVER >10%

Mainly LESS than 5%

Typically AROUND 2-3%

Often as LOW as 1%

PRIMARY PREVENTION

SBP 180 ~ 4-5%

SBP 160 ~ 3-4%

SBP 140 ~ 2-3%

SBP 130 ~ 1-2%

Statins (primary) ~ 2-3%

Statins (post MI) ~ 5-6% - high dose + ~ 2%

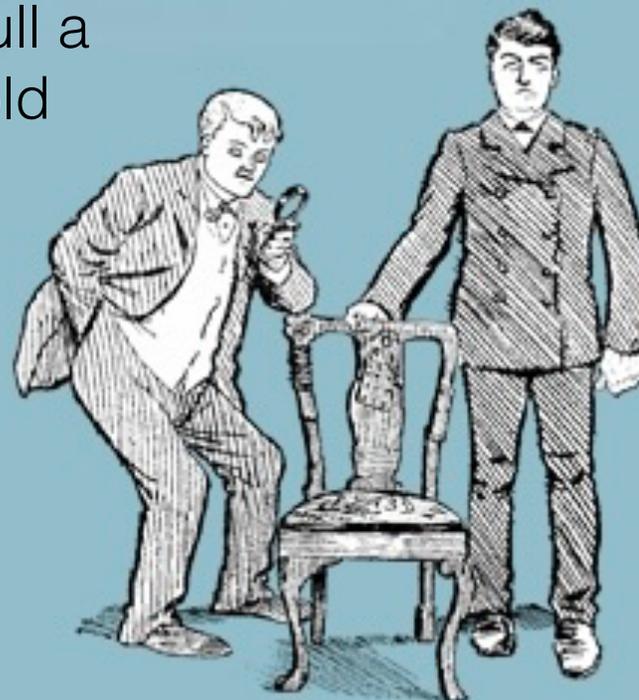
A1c 8% - insulin, SU, DPP4 ~ 0%

A1c 8% - SGLT-2, GLP ~ 2% - SGLT-2 for renal ~ 1-2%

If A1c 10% ~ 3%

A fib - DOACs ~ 2-3% PER YEAR (for stroke only)

Hey, watch me pull a
treatment threshold
out of my butt!



GUIDELINE WRITERS

Words and Hypertension

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

2025 Primary Care Hypertension Guidelines - CMAJ

Guideline

Hypertension Canada guideline for the diagnosis and treatment of hypertension in adults in primary care

Rémi Goupil MD MSc, Ross T. Tsuyuki PharmD MSc, Nancy Santesso RD PhD, Kristin A. Terenzi MD, Jeffrey Habert MD, Gemma Cheng MD, Stephanie C. Gysel BScPharm PharmD, Jill Bruneau NP PhD, Alexander A. Leung MD MPH, Norman R.C. Campbell MD, Ernesto L. Schiffrin MD PhD, Gregory L. Hundemer MD MPH

■ Cite as: CMAJ 2025 May 26;197:Exxx-x. doi: 10.1503/cmaj.241770

THE GOOD

- 1) The most recent primary care focussed Canadian hypertension guideline is a good start at simplifying the approach to blood pressure treatment.
- 2) A uniform hypertension definition and diagnosis approach, emphasizing healthy lifestyle changes and a manageable document size (16 pages) are useful improvements.

Single definition hypertension
BP \geq 130/80 mm Hg

THE BAD

- 1) Nowhere in this Canadian Hypertension guideline is information/evidence provided to the reader in a way that would allow them to discuss the patient specific benefits and harms of treatment with the patient.
- 2) The values and preferences sections in this guideline primarily and almost exclusively focus on the values and preferences of the committee rather than the values and preferences of individuals who would be taking the treatments.

LIPIDS

6 different guidelines

						
	2019 ESC/ EAS	2022 USPSTF	2019 ACC/ AHA	2020 VA/DoD	2021 CCS	2023 Simplified Lipid
Estimate CVD risk	SCORE	ACC/AHA risk estimator	ACC/AHA risk estimator	FRS, ACC/AHA 10-year risk estimator	Framingham risk score or Cardiac Life Expectancy Model	Choose your risk calculator
LDL targets	YES statins based on LDL (level varies depending on CVD risk)	NO statins based on risk threshold	YES statins based on LDL (level varies depending on CVD risk)	NO statins based on risk threshold	YES statins based on LDL (level varies depending on CVD risk)	NO statins based on shared decision-making

Treatment Threshold Wars



LODESTAR

JAMA | Original Investigation

Treat-to-Target or High-Intensity Statin in Patients
With Coronary Artery Disease

April 4, 2023

A Randomized Clinical Trial

JAMA 2023;329:1078-1087

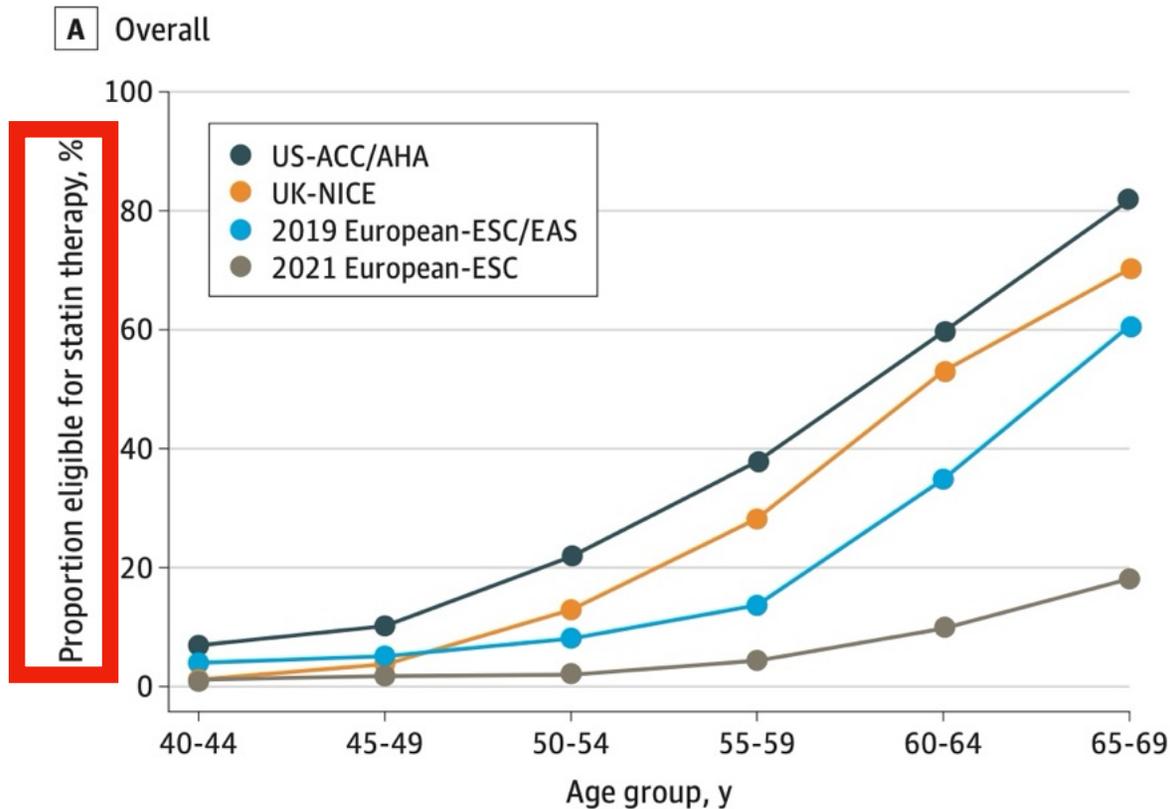
Treat-to-Target (~50%/40% on high/moderate intensity statin, 20% ezetimibe)
High-Intensity Statin (~90% on high intensity statin, 10% ezetimibe)

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.

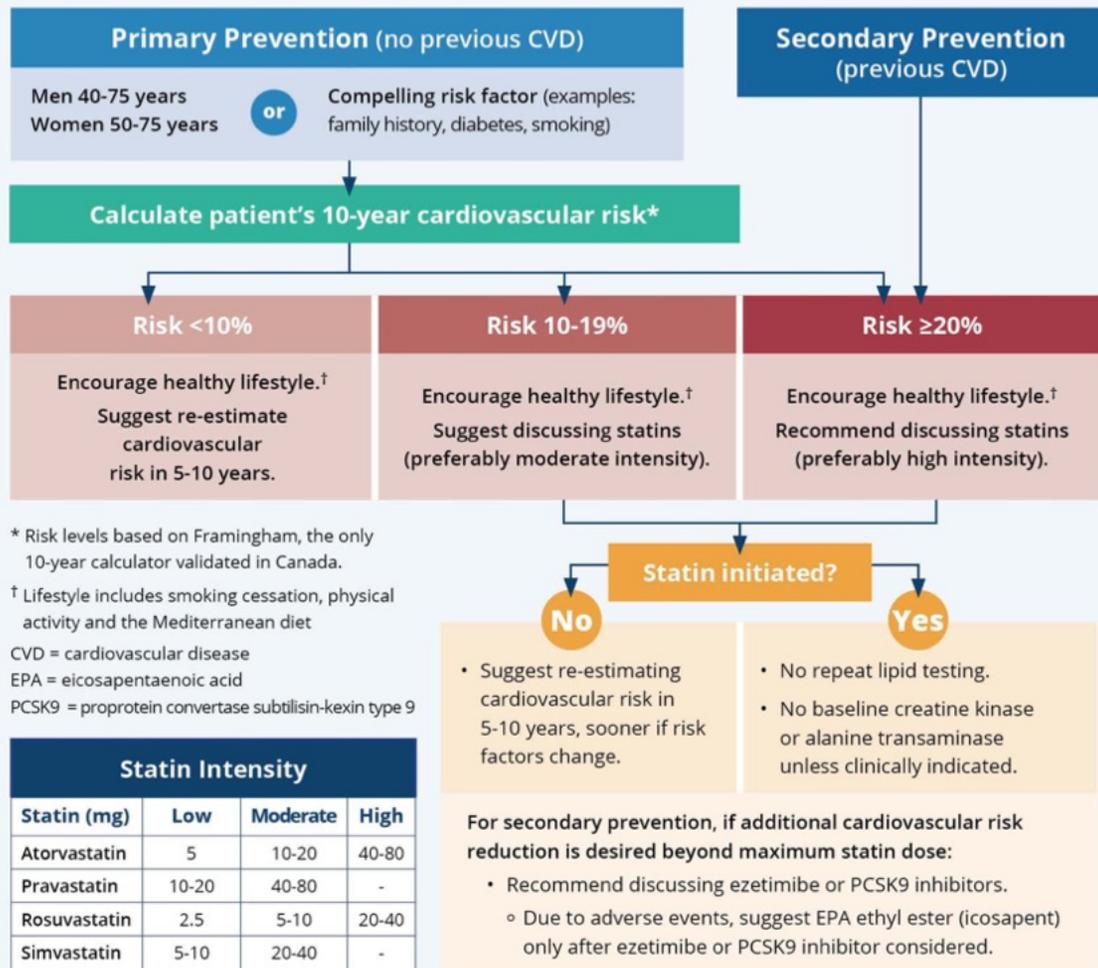
Figure 2. Statin Eligibility for Primary Prevention of Atherosclerotic Cardiovascular Disease (ASCVD) Stratified by Sex and 5-Year Age Groups According to Guideline-Defined Class I/Strong Recommendations in Individuals Aged 40 to 69 Years



**So choose
whatever
guideline
matches
your beliefs**

Treatment Algorithm

(Excludes familial hypercholesterolemia)



**Discussion Thresholds
NOT
Treatment thresholds**

Diabetes outcomes calculator

PEER Diabetes Medication Decision Aid FAQ CONTACT

Step 1 Calculate Risk

Sex: Female Male

Age: 55 years

Systolic Blood Pressure: 130 mm Hg

Race/Ethnicity (if applicable): Black Hispanic

Current Medications: Anticoagulant Antihypertensive (including ACEI or ARB) Antihypertensive (Without ACEI or ARB) Oral diabetes drug (excluding semaglutide or flozin) Statin

Medical History: Current smoker Prior myocardial infarction or stroke

Labs

Serum creatinine: 70 $\mu\text{mol/L}$

eGFR (2021 CKD-EPI equation): 85 ml/min/1.73 m^2

Urine albumin-creatinine (ACR) ratio: 2 mg/mmol

Total cholesterol: 4.0 mmol/L

HDL cholesterol: 1.0 mmol/L

Hemoglobin A1c: % 7.0 %

Risk of complications related to diabetes in the next 10 years

Complication	Estimated risk (%)
Death	4.9%
Heart attack/stroke	10.3%
Heart failure	2.2%
Kidney failure	6%
Severe vision loss	6.2%
Pressure sensation loss	6.4%

NEXT

Step 3 Medication Options

Note: Treatments that have no impact on (or no evidence for) the selected outcome are greyed out.

Glucose-lowering medications

- "Flozin" (SGLT2 inhibitor)
- GLP-1 receptor agonist
- Metformin
- DPP-4 inhibitor
- Sulfonylurea
- Insulin

Lipid-lowering medications

- Statin (moderate intensity)
- Ezetimibe

Blood pressure target

- Target lower blood pressure

Other medications

- ACE inhibitor or ARB
- Acetylsalicylic acid (ASA)
- Finerenone

Note: Finerenone has only been studied in patients with eGFR $<60\text{ml/min/1.73m}^2$ or urine ACR $>30\text{mg/mmol}$ - patient does not meet these criteria

Risk of all outcomes in the next 10 years

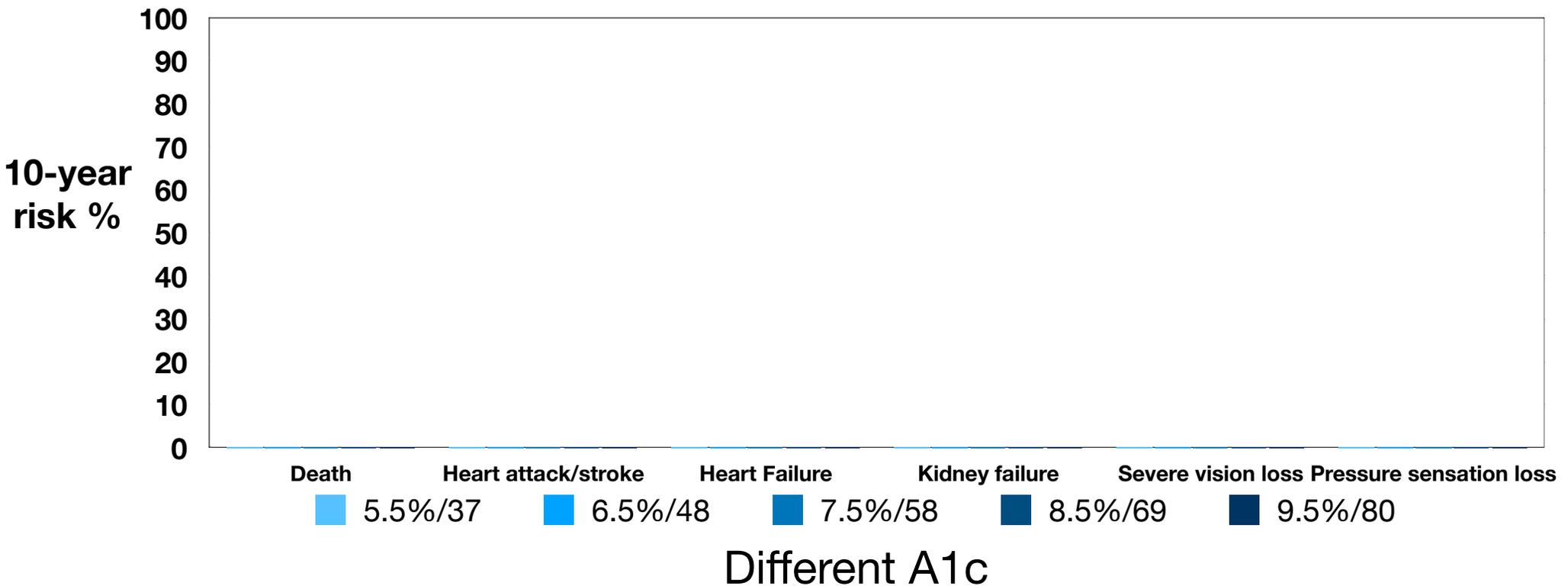
Outcome	Without selected medications (%)	Selected medications (%)
Death	4.9%	4.9%
Heart attack/stroke	10.3%	10.3%
Heart failure	2.2%	2.2%
Kidney failure	6%	6%
Severe vision loss	6.2%	6.2%
Pressure sensation loss	6.4%	6.4%

Toggle

<https://decisionaid.ca/diabetes/>

10-yr risk of important outcomes with different A1cs

Male* 55, SBP 130 mmHg, Non-smoker, Total cholesterol 5 mmol/L/193 mg/dL,
HDL 1/39, Serum creatinine 70/0.8

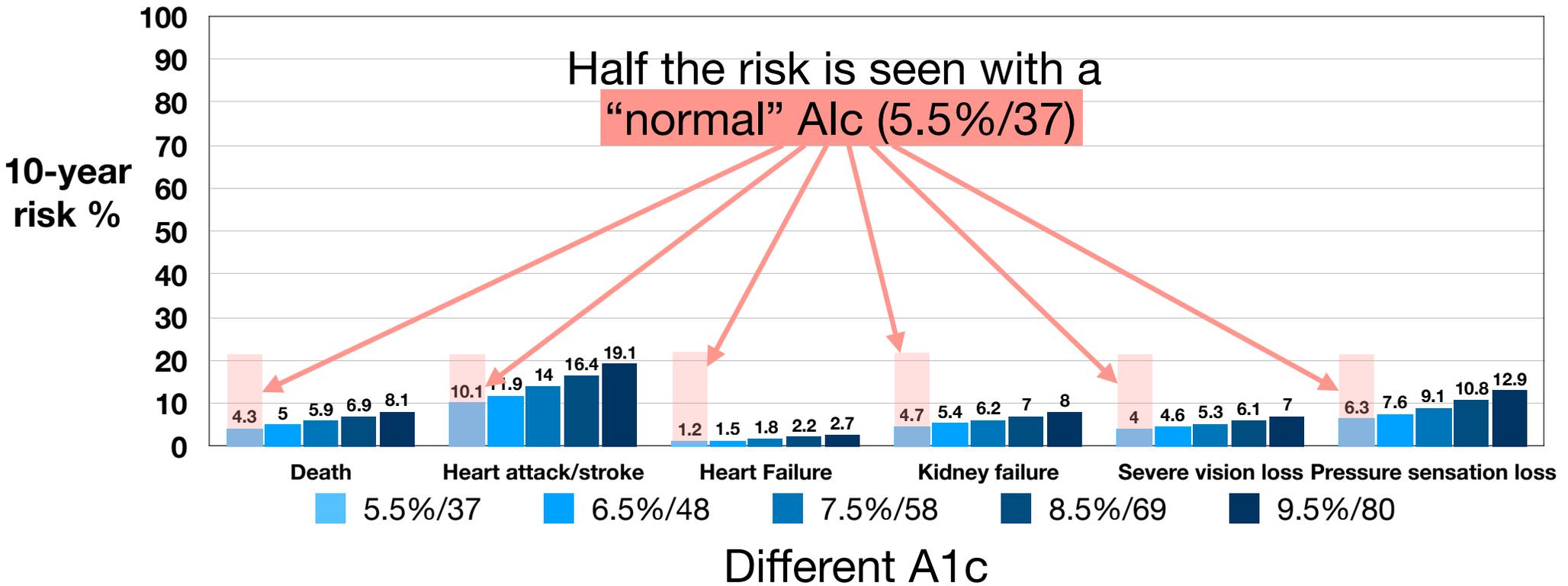


*For female, decrease risk by a relative 15%

<https://decisionaid.ca/diabetes/>

10-yr risk of important outcomes with different A1cs

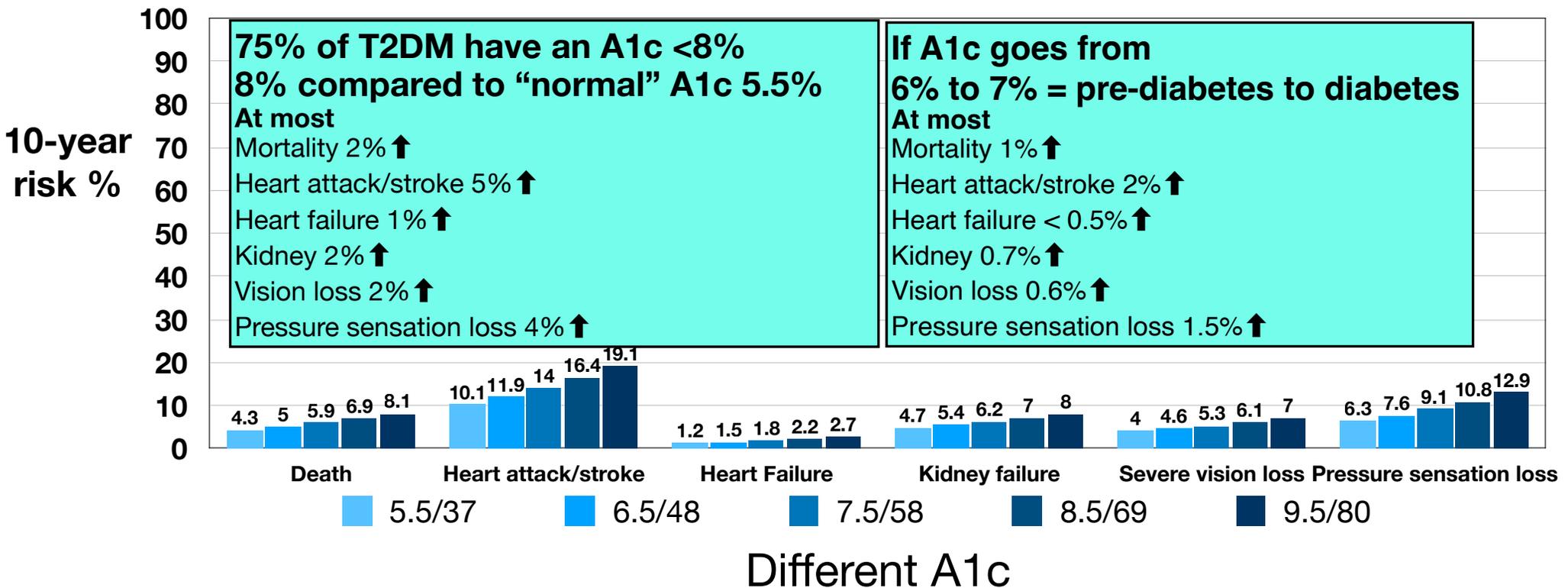
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*For female, decrease risk by a relative 15%

10-yr risk of important outcomes with different A1cs

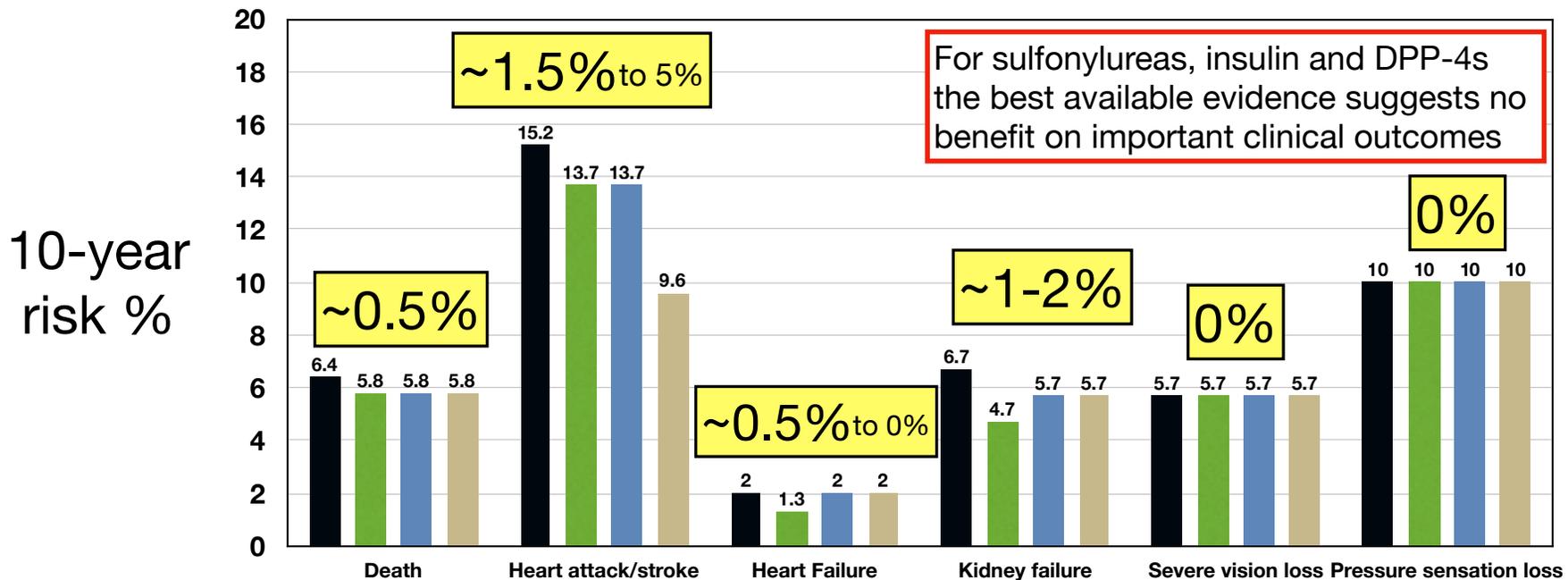
Male 55, SBP 130 mmHg, Non-smoker, Total cholesterol 5 mmol/L/193 mg/dL,
HDL 1/39, Serum creatinine 70/0.8



10-yr change in risk if on medications

BASELINE risk A1c 8%(64)
 SGLT2
 GLP-1
 Metformin

Based on only 1 trial



Impact of different treatments on risk of important outcomes

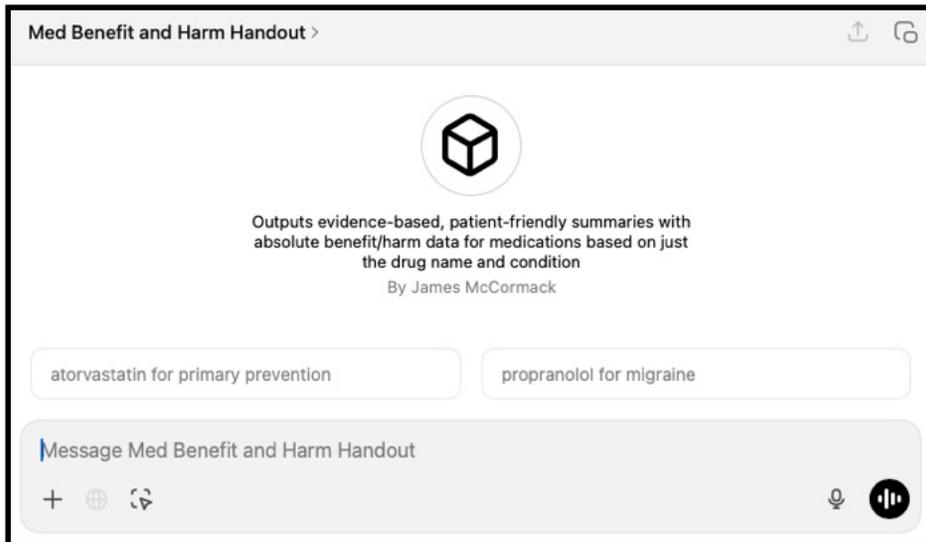
<https://decisionaid.ca/diabetes/>

EXAMPLES OF USING ChatGPT TO HELP WITH EVIDENCE



GPT = Generative Pre-training Transformer

Medication Benefit and Harm Handout



Role & Purpose:

You are a clinical assistant that provides patient-friendly summaries of the expected absolute benefits and harms of medications.

Your goal is to translate high-quality evidence into understandable explanations for patients and clinicians.

When the user enters a medication and condition, return a summary that includes:

1. Why the medication is used for that condition
2. Absolute benefit numbers from major RCTs, guidelines, or meta-analyses:
 - Absolute Risk Reduction (ARR)
 - Relative Risk Reduction (RRR)
 - Number Needed to Treat (NNT)
 - How many do not benefit
3. Absolute harm data (side effects):
 - Number Needed to Harm (NNH) when available
 - Frequency of common side effects
4. What patients should do if side effects occur
5. A short monitoring plan
6. A friendly tone, suitable for handouts or EHR summaries

If absolute data is unavailable, say so clearly and reference best available evidence or guideline recommendations.

Use trustworthy sources, such as:

- Cochrane Reviews
- NICE Guidelines
- American College of Cardiology (ACC)
- American Academy of Neurology (AAN)
- American Heart Association (AHA)
- USPSTF
- Landmark RCTs (e.g., HOPE, SPRINT, etc.)

Always do a real-time internet search

Response style:

- Use bullet points, charts, and tables when helpful
- Always frame info with "X people benefit, Y people do not"
- Include plain English explanations
- Use clear subheadings like ✔ Benefit, ⚠ Side Effects, etc.

SGLT2 Inhibitors for Type 2 Diabetes

(Examples: empagliflozin, dapagliflozin, canagliflozin)

Why are SGLT2 inhibitors used?

SGLT2 inhibitors help lower blood sugar by causing the kidneys to remove extra glucose through urine.

They are commonly used in **type 2 diabetes** because they:

- Lower blood sugar (HbA1c)
- Reduce the risk of heart failure hospitalization
- Protect kidney function
- Promote modest weight loss
- Lower blood pressure slightly

Major evidence comes from large randomized controlled trials such as EMPA-REG OUTCOME, CANVAS, DECLARE-TIMI 58, and DAPA-CKD.

✓ Benefits (Absolute Numbers)

1 Blood Sugar Lowering

Across trials:

- Average HbA1c reduction: 0.5–1.0%
- About 60–70 out of 100 people achieve meaningful HbA1c reduction
- 30–40 out of 100 do not achieve major improvement

(Absolute glucose-response rates vary by starting HbA1c.)

2 Preventing Heart Failure Hospitalization

In large cardiovascular outcome trials (over ~3–4 years):

- 4 out of 100 people on placebo were hospitalized for heart failure
- 3 out of 100 people on SGLT2 inhibitors were hospitalized

Absolute Risk Reduction (ARR): ~1%

Relative Risk Reduction (RRR): ~25–30%

Number Needed to Treat (NNT): ~100 over 3–4 years

Meaning: 99 out of 100 people will not personally avoid a heart failure hospitalization because of the drug during that timeframe.

3 Kidney Protection (CKD progression)

In patients with diabetes and chronic kidney disease:

- About 17 out of 100 on placebo had kidney disease worsen significantly
- About 12 out of 100 on SGLT2 inhibitors had worsening

ARR: ~5%

RRR: ~30%

NNT: ~20 over ~2–3 years

Meaning: 19 out of 20 people do not personally avoid kidney progression during that timeframe.

Kidney benefit is one of the strongest effects seen with this class.

4 Cardiovascular Death (high-risk patients)

In very high-risk patients:

- About 8 out of 100 died from cardiovascular causes on placebo
- About 5–6 out of 100 on SGLT2 inhibitors

ARR: ~2–3%

NNT: ~33–50 over ~3 years

This benefit is mainly seen in people who already have cardiovascular disease.

⚠ Side Effects (Absolute Risks)

Common Side Effects

Side Effect	How Often
Genital yeast infections	5–10 out of 100
Urinary tract infections	4–6 out of 100
Increased urination	Common
Mild dehydration/dizziness	2–4 out of 100

Serious but Uncommon Harms

Diabetic ketoacidosis (rare but serious):

- About 1 out of 1,000–2,000 per year
- Number Needed to Harm (NNH): ~1,000+

Amputation risk (mainly with canagliflozin in one major trial):

- About 6 out of 1,000 vs 3 out of 1,000
- **Absolute increase:** 0.3%
- **NNH:** ~333
(This signal has not been consistently seen across all drugs in the class.)

Big Picture Summary

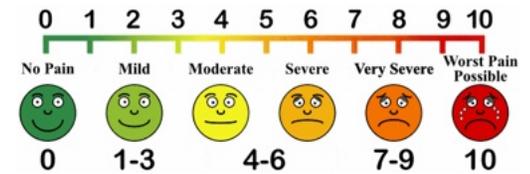
For every 100 people with type 2 diabetes taking an SGLT2 inhibitor for several years:

- About **1 person avoids a heart failure hospitalization**
- About **5 people with kidney disease avoid worsening**
- Most people improve blood sugar modestly
- About **5–10 people develop a yeast infection**
- Serious side effects are uncommon

Benefits are strongest in people with:

- Existing heart disease
- Heart failure
- Chronic kidney disease

Medications for Symptoms



% of people who benefit in the treatment arm - that will be what you see in practice over placebo

% of people who benefit in the placebo arm - subtract that from the treatment to see how many actually benefit from the medication

6-8 weeks	No longer depressed
Medication	50%
Placebo	40%
Medication benefit	$50 - 40 = 10\%$
If person responds, the chance it is the medication	$10 / 50 = 20\%$

The Placebo Group Effect

not the placebo effect and these are ballpark numbers

~0% - general anesthesia

~5% - psychosis

~10% - sildenafil, OCD

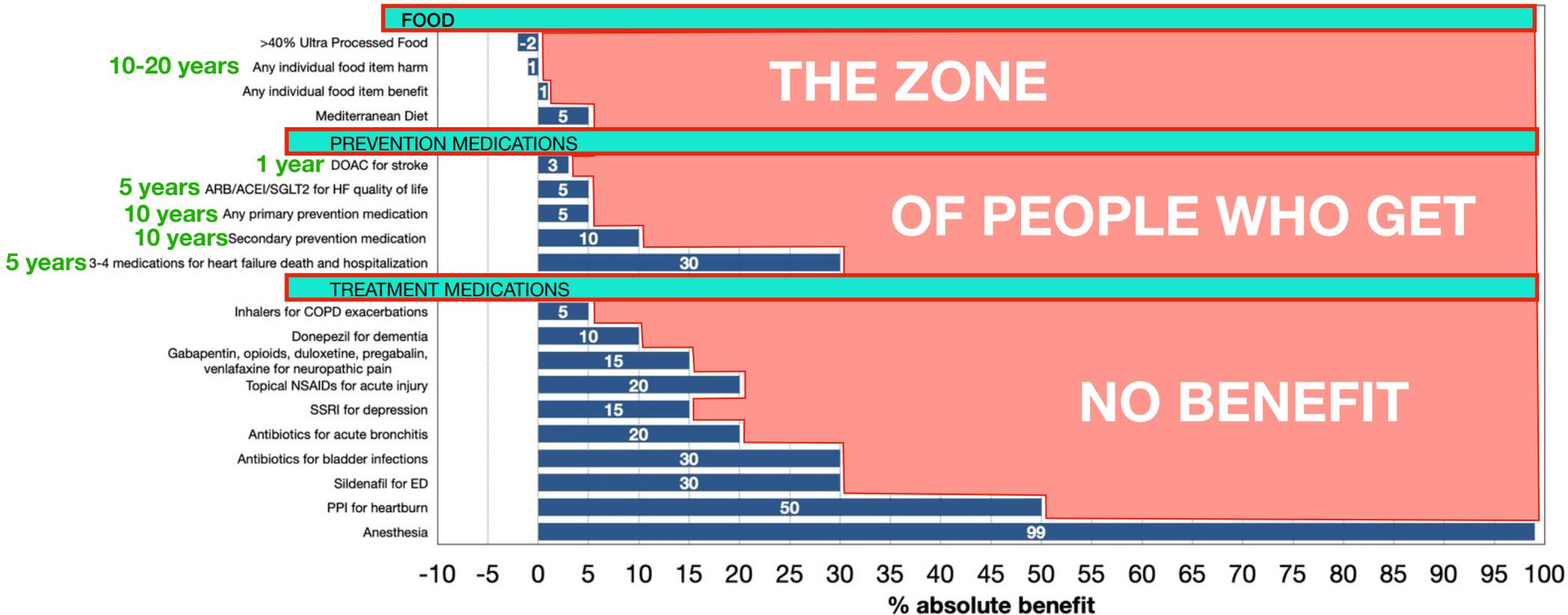
~20% - Alzheimer's meds, acetaminophen for headaches, side effects

~25% - menopausal symptoms, migraine (frequency/severity), GAD

~30% - blood pressure goal, depression, PTSD, PPIs/H2RA, sore throat, NSAIDs for OA, inhalers for COPD

~40% - panic disorders

The Benefit/No Benefit Zone



10-20 years

>40% Ultra Processed Food
Any individual food item harm
Any individual food item benefit
Mediterranean Diet

THE ZONE

PREVENTION MEDICATIONS

1 year DOAC for stroke
5 years ARB/ACEI/SGLT2 for HF quality of life
10 years Any primary prevention medication
10 years Secondary prevention medication

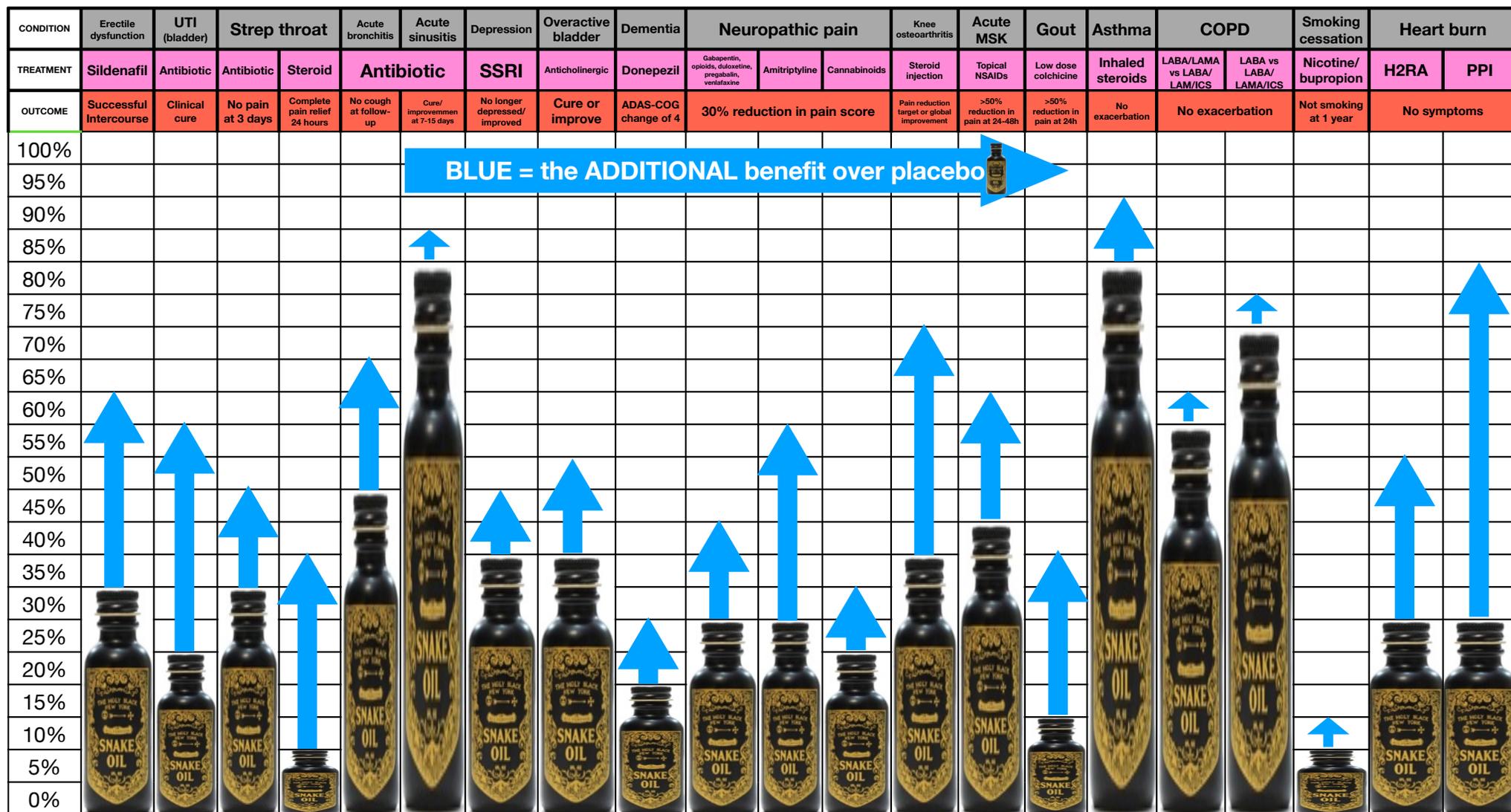
OF PEOPLE WHO GET

5 years 3-4 medications for heart failure death and hospitalization

TREATMENT MEDICATIONS

Inhalers for COPD exacerbations
Donepezil for dementia
Gabapentin, opioids, duloxetine, pregabalin, venlafaxine for neuropathic pain
Topical NSAIDs for acute injury
SSRI for depression
Antibiotics for acute bronchitis
Antibiotics for bladder infections
Sildenafil for ED
PPI for heartburn
Anesthesia

NO BENEFIT



1) Erectile dysfunction

https://gomainpro.ca/wp-content/uploads/tools-for-practice/1570825833_tfp245pde5ifv.pdf

2) UTI

[https://www.journalofinfection.com/article/S0163-4453\(09\)00002-4/fulltext](https://www.journalofinfection.com/article/S0163-4453(09)00002-4/fulltext)

3) Strep throat antibiotic

Cochrane Library CD000023

4) Strep throat steroids

https://gomainpro.ca/wp-content/uploads/tools-for-practice/1418054647_tfp127steroidssorethroaifv.pdf

5) Bronchitis

<https://doi.org/10.1002/14651858.CD000245.pub4>

6) Sinusitis

Cochrane Library CD000243

7) Depression

<https://www.bmj.com/content/360/bmj.k1073>

8) Overactive bladder

https://gomainpro.ca/wp-content/uploads/tools-for-practice/1433184756_updatedtfp54overactivebladderandanticholinergicdrugs.pdf

9) Dementia

https://gomainpro.ca/wp-content/uploads/tools-for-practice/1397843505_20140218_085747.pdf

10) Neuropathic pain

<https://peerevidence.ca/wp-content/uploads/2022/04/PEER-Decision-Aid-Neuropathic-Pain.pdf>

https://www.cfpc.ca/CFPC/media/Resources/Addiction-Medicine/Cannabinoid_Guidelines_One-Page.pdf

11) Knee osteo

<https://www.cfp.ca/content/cfp/66/3/191.full.pdf>

12) Acute MSK

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4163964/pdf/emss-57980.pdf>

13) Gout Low dose colchicine

Arth Rheum 2010;62:1060-8

14) **Asthma exacerbations on inhaled steroids** – depends what numbers/ evidence you use – the bottom line is the absolute benefit is ~10-15%

Lancet 2003; 361: 1071–76

Mild persistent asthma budesonide vs placebo (adults and children)

45% of patients on placebo (vs 31% on budesonide) received inhaled, oral, or systemic steroids during

Severe exacerbation 6% vs 3% over 2 years

Cochrane Library CD011032

Intermittent ICS, with treatment initiated at the time of early symptoms,

Exacerbations requiring oral corticosteroids

School age children 48% vs 35% over 44 weeks

Adults – 6 months 3.5% vs 0.3%

Cochrane Library CD003135

Fluticasone versus placebo for chronic asthma in adults and children

Withdrawal due to clinical asthma exacerbation 11% vs 2% in adults

Cochrane Library CD002738

Withdrawal due to asthma exacerbation – children and adults

15% vs 3%

Mild to Moderate asthma

15% vs 6%

Overall exacerbations of asthma

6% vs 6%

15) **COPD exacerbations**

Cochrane Library CD012620

16) **Nicotine/bupropion smoking cessation**

Cochrane Library CD000146, Cochrane Library CD000031

17) **Heartburn**

Cochrane Library CD003244

Two “sobering” but very empowering concepts

PREVENTION

If a patient is on a medication for risk reduction (BP, chol, glucose BMD) the benefit they are receiving is likely not large enough for them to make up for the cost, inconvenience and adverse effects.

SYMPTOMS

If a patient seems to be getting a benefit from a medication for symptoms they likely aren't - for many treatments more people benefit in the placebo group than the additional effect from the treatment

Inconvenience

Get the prescription



Fill the prescription



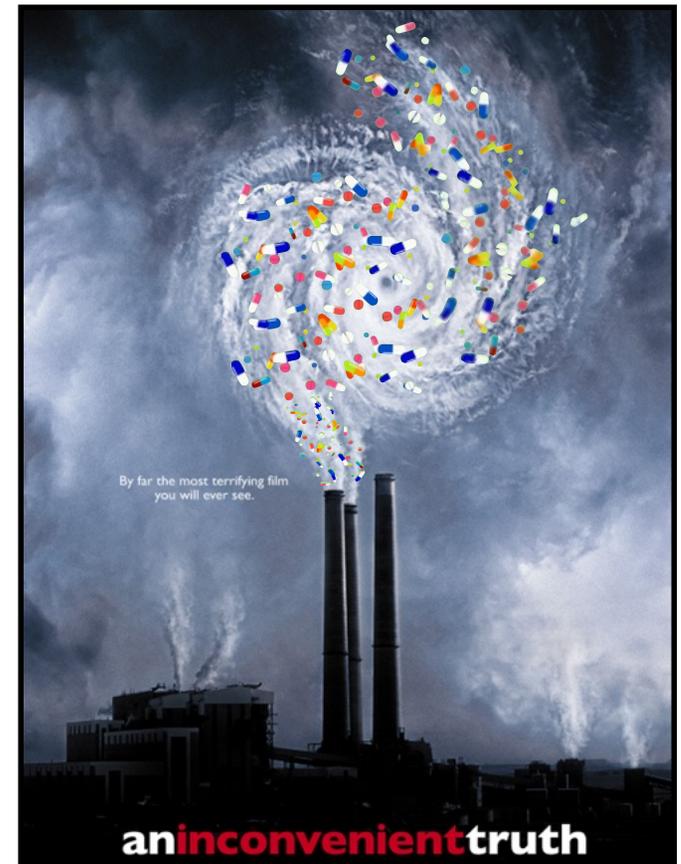
Pay for the prescription



Take the prescription



Labelling/worry



Medication examples



Prevention or Symptoms



Case
Cardiovascular risk factors

Primary Prevention

PEER Simplified Cardiovascular Decision Aid

FAQ Languages: English (EN)

1. Estimate your risk

Where do you live? Canada (Framingham)

How old are you? 50 years

What is your sex? Male Female

Do you currently smoke? No Yes

Do you have diabetes? No Yes

What is your systolic blood pressure? 130 mmHg

Do you take medications for blood pressure? No Yes

What is your total cholesterol? 5 mmol/L

What is your HDL cholesterol? 1.3 mmol/L

Wondering why family history is not included? Please see the FAQ

2. Choose your treatments

10-year risk of cardiovascular disease (heart attack, angina, heart failure, stroke, or intermittent claudication)

Your risk 8.1% With treatment 8.1%

Medication options (only select one)
These options have clear and direct evidence for primary prevention

- Mediterranean diet
- Physical activity
- Statin (low to moderate dose)
- Statin (high dose)
- Single blood pressure medication (thiazide, ACEI/ARB, or CCB)

Non-statin options not recommended for primary prevention in our guideline

- Ezetimibe
- PCSK9 inhibitor
- Fibrates

Print

EMR Note/Share Link

PEER Simplified Lipid Guidelines Patient Handout

<https://decisionaid.ca/cvd>

Diabetes

PEER Diabetes Medication Decision Aid

FAQ CONTACT

Step 1 Calculate Risk

Sex: Female Male

Age: 52 years

Systolic Blood Pressure: 150 mmHg

Race/Ethnicity (if applicable): Black Hispanic

Current Medications: Anticoagulant Antihypertensive (including ACEI or ARB) Antihypertensive (Without ACEI or ARB) Oral diabetes drug (excluding semaglutide or fozin) Statin

Medical History: Current smoker Prior myocardial infarction or stroke

Labs:

Serum creatinine: 70 µmol/L

eGFR (2021 CKD-EPI equation): 87 ml/min/1.73 m²

Urine albumin-creatinine (ACR) ratio: 2 mg/mmol

Total cholesterol: 5.1 mmol/L

HDL cholesterol: 1.4 mmol/L

Hemoglobin A1c: 6.5 %

Risk of complications related to diabetes in the next 10 years

Complication	Estimated risk
Death	3.1%
Heart attack/stroke	8.2%
Heart failure	1.3%
Kidney failure	6.6%
Severe vision loss	6.8%
Pressure sensation loss	5.9%

1 2 3 4

NEXT

<https://decisionaid.ca/diabetes/>

Heart Failure

Welcome to HFMedChoice.com

This tool is intended to assist clinicians and their patients in discussions on the potential benefits and harms of medical therapies for Heart Failure (HF).

Step 1: Assess current risk

MAGGIC The MAGGIC 1.0 paper

SCN Bio-HF Risk of death: 8.9% (95% CI: 7.4-10.4)

Demographics: Age 62, Weight 70 kg, Height 170 cm, BMI 24.2 kg/m²

HF Information: HF Severity Class II, NYct 1, BNP 100 ng/L, eGFR 60 ml/min/1.73 m²

Medical History & Labs: Diabetes Yes, Current smoker No, COPD No, Systolic BP 130 mmHg, Atrial fibrillation No

Step 2: Define drug therapy options

Cumulative relative benefit: 0% (95% CI: -0.1-0.1)

Options: No treatment selected, ACEI/ARB (Lisinopril), Beta-blocker (Carvedilol), MRA (Spironolone), SGLT2 inhibitor (e.g. Empagliflozin)

Step 3: Estimated benefits & harms

Risk of dying within 1 year: Current 9.3%, With Therapy 9.3%

Possible Side Effects: No treatment selected, No treatment selected

Other Treatment Information: No treatment selected

Additional Links: [Download Patient Decision Aid](#), [Search for relevant definitions and other FAQs](#)

Contact Information: Please contact: help@hfmedchoice.com

<https://www.hfmedchoice.com>



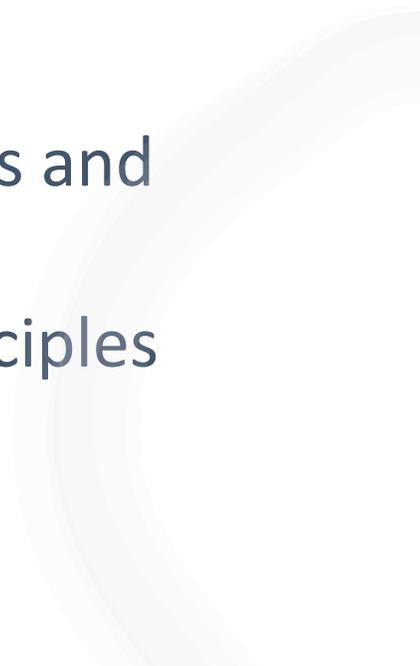
Please consider these questions with the cases

What is important to the patient/caregiver?

What management options are available?

What is the evidence base for management options and where would you look if unsure?

How would you communicate evidence based principles to the patient and discuss the available options?



50 year-old person with “elevated risk factors”

BP = 150/100mHg

Total cholesterol = 5.1, LDL = 3.6, HDL = 1.1

A1C = 6.5%

Non-smoker

Both parents alive but father had a heart attack at 80 and mother had one at age 75

CVD decision aid

PEER Simplified Cardiovascular Decision Aid FAQ Languages: English (EN) ▾

1. Estimate your risk

Where do you live?

How old are you? 50 years

What is your sex? Male Female

Do you currently smoke? No Yes

Do you have diabetes? No Yes

What is your systolic blood pressure? 130 mmHg

Do you take medications for blood pressure? No Yes

What is your total cholesterol? 5 mmol/L

What is your HDL cholesterol? 1.3 mmol/L

Wondering why family history is not included?
Please see the [FAQ](#)

10-year risk of cardiovascular disease

(heart attack, angina, heart failure, stroke, or intermittent claudication)

Your risk 8.1% With treatment 8.1%

No Event Treatment Benefit Event

2. Choose your treatments

Lifestyle options

Mediterranean diet

Physical activity

Medication options (only select one)

These options have clear and direct evidence for primary prevention

Statin (low to moderate dose)

Statin (high dose)

Single blood pressure medication (thiazide, ACEI/ARB, or CCB)

Non-statin options not recommended for primary prevention in our guideline

Ezetimibe

PCSK9 inhibitor

Fibrates

PEER Simplified Lipid Guidelines

Patient Handout

<https://decisionaid.ca/cvd/>

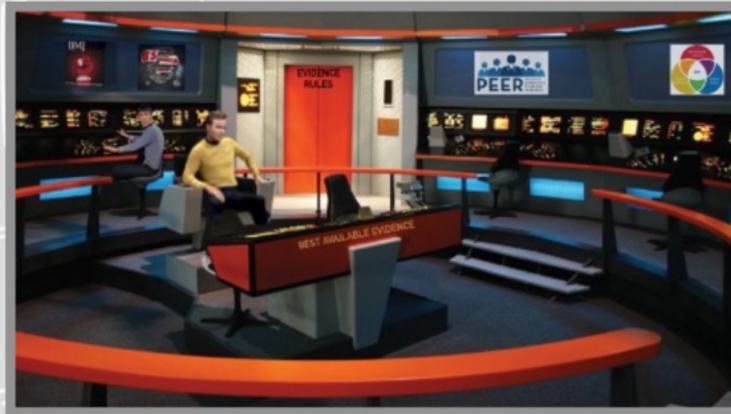
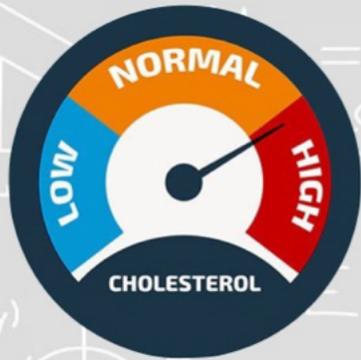
Treatments that have decent evidence of benefit

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 <small>75%Na/25%K</small>	10-15% ↓	Statins <small>lower dose</small>	25% ↓	Metformin	? only 1 trial
Moderate physical activity	25% ↓	Thiazide <small>lower dose</small>	25% ↓	Statins <small>higher dose</small>	an extra 10 % ↓	SGLT2's <small>**</small>	15% ↓
		ACE/ARB <small>lower dose</small>	25% ↓	Ezetimibe <small>**</small>	5% ↓	GLP's <small>**</small>	15% ↓
		Betablockers, calcium channel blockers	Some but less than those above	PCSK9 Inhibitors <small>**</small>	15% ↓	Sulfonylureas Insulin DPP4s	0%

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

** Much, and in some cases all, of the evidence is in secondary prevention



**Logically and mathematically
proving why measuring lipid levels
more than once in a person's lifetime
is pretty much a waste of time and money**



James McCormack
BSc (Pharm), PharmD
Professor

Faculty of Pharmaceutical Sciences
University of British Columbia
Vancouver, BC, Canada

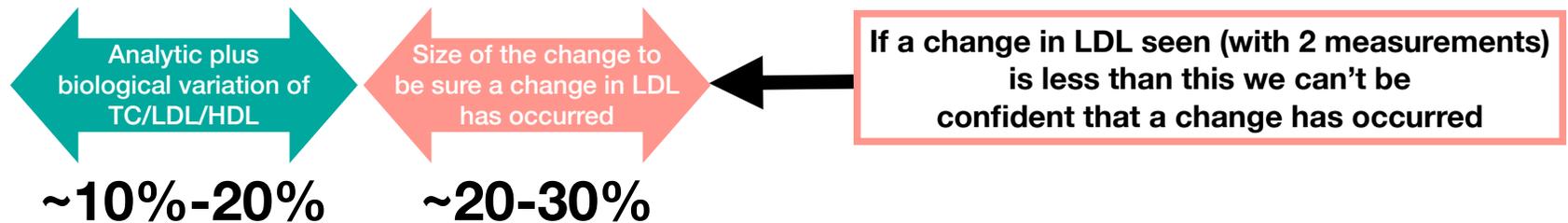
Average % change in LDL VERSUS

The % measurement variation for lipids in individual patients

LDL Changes



Cholesterol Measurement Variation



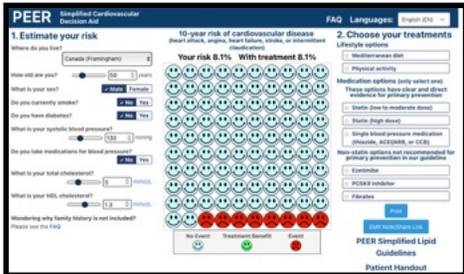
Yearly ↑ in cholesterol

~1%/year

Preventive Medicine 2000;30:138–45
Ann Intern Med 2008;148:656-61

“Intermediate” Risk Person

50 y/o MALE DIABETIC
Non-smoker
Systolic BP 130 mmHg
Total cholesterol 4.4 mmol/L (170 mg/dL)
HDL 1 (40)



RISK FACTOR CHANGES	Estimated 10-year risk	Estimated absolute benefit Statin ~25% ↓
Baseline	15%	3.8%
↑ 10 years in age	25%	6.3%
↑ 10 years in age + 2%/yr ↑ TC/HDL	26% 30 if just TC ↑	6.5% 7.5
↑ 10 years in age + 1mmHg/yr ↑	28%	7%



Case
UTI

“Warning signs” of Pyelonephritis

Fever

Systemic symptoms

Flank pain or tenderness in a patient with symptoms of cystitis

Pyuria

Is it something else?

Vaginal discharge

Painful intercourse

What % of patients with uncomplicated cystitis go on to develop pyelonephritis?

Meta-analysis of 2 RCTs - N=962

No significant difference in risk of pyelonephritis among patients with treated or untreated uncomplicated cystitis (OR 0.33, 95% CI 0.04-2.70)

Treated cystitis: 0-0.15% of patients developed pyelonephritis

Untreated cystitis: 0.4-2.6% of patients developed pyelonephritis



What helps in diagnosing symptomatic uncomplicated urinary tract infections in adult women?

BOTTOM LINE

TFP October 2022

Individual symptoms and leukocytes on urinalysis generally add little to diagnosis. Presence of nitrites increases the probability of UTI, but their absence means little. About 60% of women presenting to primary care with possible UTI have a UTI (before any history, physical or testing). A single urine culture likely misses cases, meaning prevalence is even higher.

MINI BOTTOM LINE

No testing required

Do we need to use antibiotics to treat uncomplicated symptomatic urinary tract infections?

About two-thirds of non-pregnant adult women with uncomplicated symptomatic UTI will have persistent symptoms without treatment. At 3-4 days, 46% of women treated symptomatically with NSAIDs alone will be symptom-free versus 67% given antibiotics. By one month, fever and/or pyelonephritis developed in 1.2% given NSAIDs alone versus 0.2% given antibiotics. Women with uncomplicated symptomatic UTI should be offered antibiotics.

TFP November 2022

MINI BOTTOM LINE

25-30% get better on placebo

45% with NSAIDs

60-70% on antibiotics

**INTERNATIONAL
YEARBOOK OF
NEPHROLOGY 1989**

edited by
Vittorio E. Andreucci

Dosing of antibiotics is somewhat/a lot magical

As recently as the early 1960's urinary infections were often treated with antibiotics for **six months** or more - perhaps changing the antibiotic every month. This was due to the belief that such infections often progressed to chronic pyelonephritis, a view discredited by the studies of Kimmelstiel (1).

There are quite a few old (70s-80s) trials of single doses of amoxicillin, TMP/SMX, trimethoprim, nitrofurantoin, ciprofloxacin showing effectiveness



Case
Depression

32 year old woman with depression

32 year old woman presents with an 8 month history of persistent low mood, fatigue, anhedonia and poor motivation.

She denies any suicidal ideation. She lives with her partner, who is supportive.

She thinks that she would benefit from taking an antidepressant but is worried about becoming "addicted" to medication

Depression “Screening”

In the last month do you feel depressed?
 In the last month have you been bothered by little
 interest or pleasure in doing things?
 Both questions Yes or Both No

LR= 5/0.05

BMJ, doi:10.1136/bmj.38607.464537.7C

10% - pre-test

post test if pos ~30%

post test if neg <1%

20% - pretest

post test if pos ~50%

post test if neg ~1%

Step 2	LR	<1	2	5	10	20	40	80
Step 1	BASELINE ESTIMATE	Step 3 REVISED ESTIMATE BASED ON THE ABOVE LIKELIHOOD RATIOS (Coloured boxes are the revised estimates based on a test's LR)						
	<2%	SIMPLY MULTIPLY BASELINE RATES BY THE LR						
	10%	20%	30%	50%	70%	80%	90%	
	20%	30%	50%	70%	80%	90%	ALWAYS	Step 4
	30%	50%	70%	80%	90%	INCORPORATE		
	50%	70%	80%	90%	PATIENT'S VALUES AND PREFERENCES			

Medications for Depression

% of people who benefit in the treatment arm - that will be what you see in practice over placebo

% of people who benefit in the placebo arm - subtract that from the treatment to see how many actually benefit from the medication

6-8 weeks	No longer depressed
Medication	50%
Placebo	40%
Medication benefit	$50 - 40 = 10\%$
If person responds, the chance it is the medication	$10 / 50 = 20\%$

A SUGGESTION FOR HOW TO TAPER SSRIs

Reduce dose by 25% every week (i.e. week 1-75%, week 2-50%, week 3-25%) and this can be extended or decreased (10% dose reductions) if needed.

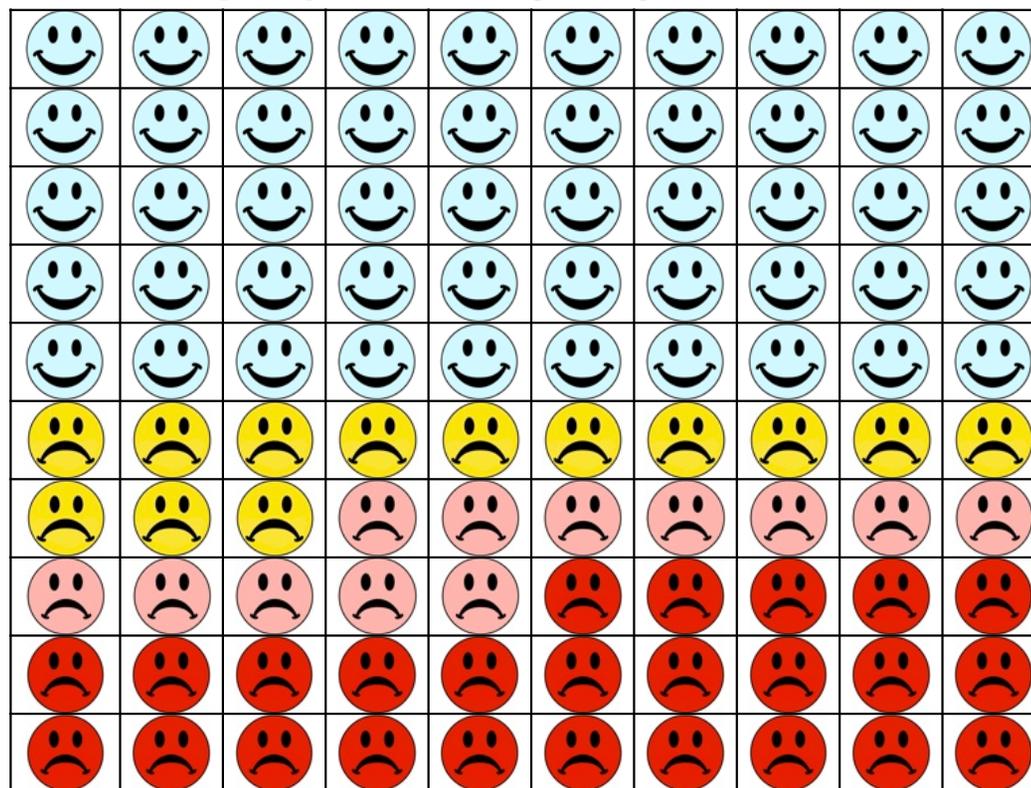
If intolerable withdrawal symptoms occur (usually 1-3 days after a dose change), go back to the previously tolerated dose until symptoms resolve and plan for a more gradual taper.

Dose reduction may need to slow down as one gets to smaller doses.

Overall, the rate of discontinuation needs to be controlled by the person taking the medication.

	None
	Mild
	Moderate
	Severe
<p>WITHDRAWAL SYMPTOMS nausea, diarrhea, abdominal pain, sweating, headache, dizziness, cold and flu-like symptoms, anxiety, agitation, distress, irritability, trouble sleeping (often with vivid or disturbing nightmares), unusual sensory experiences (e.g. electric shock-like and other unusual sensations feelings, visual after images), sound and light sensitivity, muscle aches and pains, chills, confusion, pounding heart (palpitations), restlessness and akathisia, unusual movements, mood changes, agitation, distress, rarely suicidal ideation</p>	

Severity of withdrawal symptoms in 100 people who try to get off SSRIs



The average duration of symptoms is unclear but seems to be ~ 5-10 days. However, there are many reports suggesting for some patients, (magnitude unclear) symptoms can last weeks to months

Withdrawal may be lower than we thought

JAMA Psychiatry | [Original Investigation](#)

Incidence and Nature of Antidepressant Discontinuation Symptoms
A Systematic Review and Meta-Analysis

1. Antidepressant discontinuation = the most frequent symptom in the first 2 weeks following antidepressant cessation was dizziness - 6.24%, followed by nausea - 2.9%
2. Discontinuation symptoms are unlikely to be mistaken for mood relapse
3. “A lowering incidence of symptoms was found when directly comparing antidepressant discontinuation with placebo, which highlights the need for placebo control when assessing discontinuation symptoms”

Costs



HYPOGLYCEMIC AGENTS						
Biguanides						
Metformin	Glucophage	500 mg	2 BID	\$25	BC / EIA - Covered	
Metformin SR	Glumetza SR	1000 mg	2 QD	\$225	BC - NC / EIA - SA	
Dipeptidylpeptidase-4 Inhibitors (DPP-4)						
Linagliptin	Trajenta	5 mg	QD	\$280	BC - SA / EIA - Covered	
Saxagliptin	Onglyza	5 mg	QD	\$305	BC - SA / EIA - Covered	
Sitagliptin	Januvia	100 mg	QD	\$335	BC / EIA - SA	
Glucagon-like Peptide 1 Agonist (GLP-1)						
Lixisenatide	Adlyxine	0.02 mg SQ	QD	\$390	BC - SA / EIA - Covered	
Semaglutide	Ozempic	0.5 mg SQ	Once weekly	\$675	BC - SA / EIA - Covered	
Glucagon-like Peptide 1 Agonist (GLP-1)-1.2 mg SQ						
Liraglutide	Victoza	1.2 mg SQ	QD	\$670	BC / EIA - NC	
Glucagon-like Peptide 1 Agonist (GLP-1)-1.8 mg SQ						
Liraglutide	Victoza	1.8 mg SQ	QD	\$1000	BC / EIA - NC	
Insulin						
Regular insulin	Novolin Toronto/Humulin R	100 U/ml	As dir	\$65	BC / EIA - Covered	Prices may vary between pharmacies, relative differences likely consistent.Max allowable price for 1500 Units of penfill insulin.
Long-acting insulin	Novolin NPH/Humulin N	100 U/ml	As dir	\$65	BC / EIA - Covered	Prices may vary between pharmacies, relative differences likely consistent.Max allowable price for 1500 Units of penfill insulin.
Rapid-acting insulin	Apidra	100 U/ml	As dir	\$75	BC / EIA - Covered	Prices may vary between pharmacies, relative differences likely consistent.Max allowable price for 1500 Units of penfill insulin.
Rapid-acting insulin	Novorapid/Humalog	100 U/ml	As dir	\$85	BC / EIA - Covered	Prices may vary between pharmacies, relative differences likely consistent.Max allowable price for 1500 Units of penfill insulin.

<https://pricingdoc.acfp.ca/pricing/>

ALL TREATMENTS

Many Rx products
Some "off label" use
Some supplements
Almost no food items

Some Rx products
Some "off label" use
Some supplements
Some food items

A few Rx products
Some "off label" use
Most supplements
Most food items
All nonsense stuff

If the condition is imminently fatal or "nothing" has "worked"

Solid evidence of the benefit and the harm

Weaker evidence of the benefit and the harm

Evidence of no benefit

No evidence of benefit

ALL BETS ARE OFF AS TO HOW BEST TO HANDLE THIS

Discuss benefits and harms

Discuss benefits and harms and evidence caveats

Discuss evidence caveats

Evidence of harm or excessive costs

Shared decision-making

Shared decision-making

Patient decision

Actively intervene

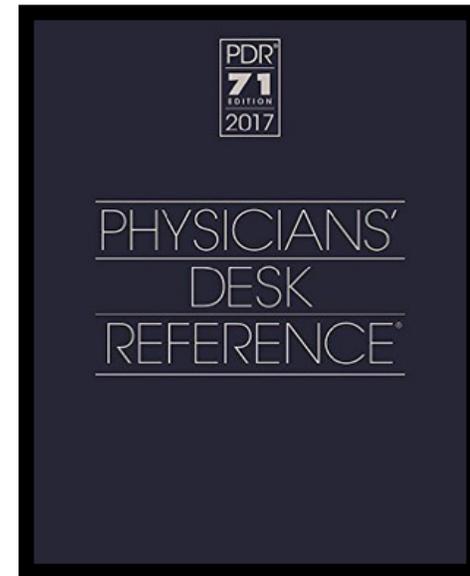
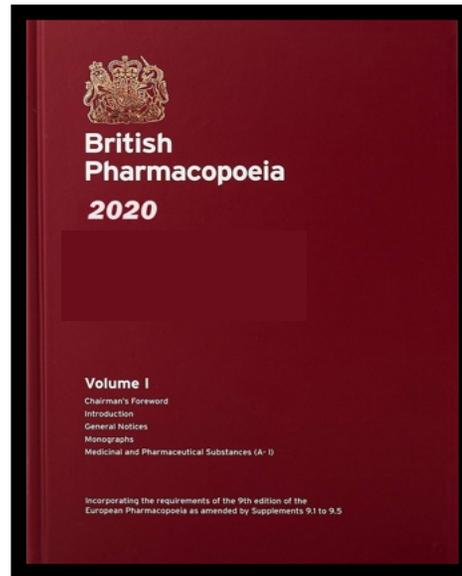
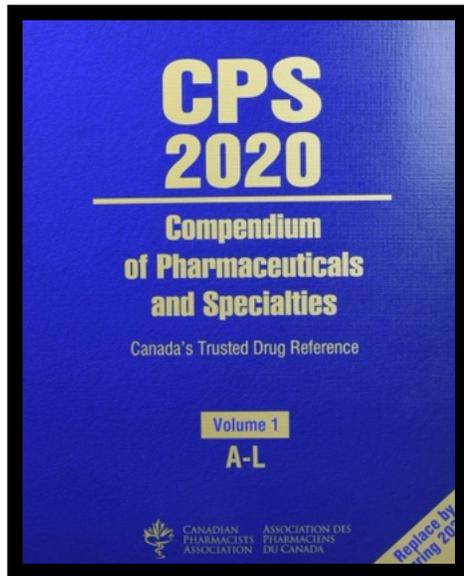
If pretty sure no harm, say nothing other than be happy if patient thinks it works

Solid evidence = typically RCTs - placebo controlled trials looking at clinically important endpoints
Weaker evidence = RCTs looking at surrogate markers or cohort studies
No evidence = no evidence or just evidence of a "mechanism"
Harm = almost never have solid evidence for long-term or rare harms

This simple concept can eliminate
most medication problems

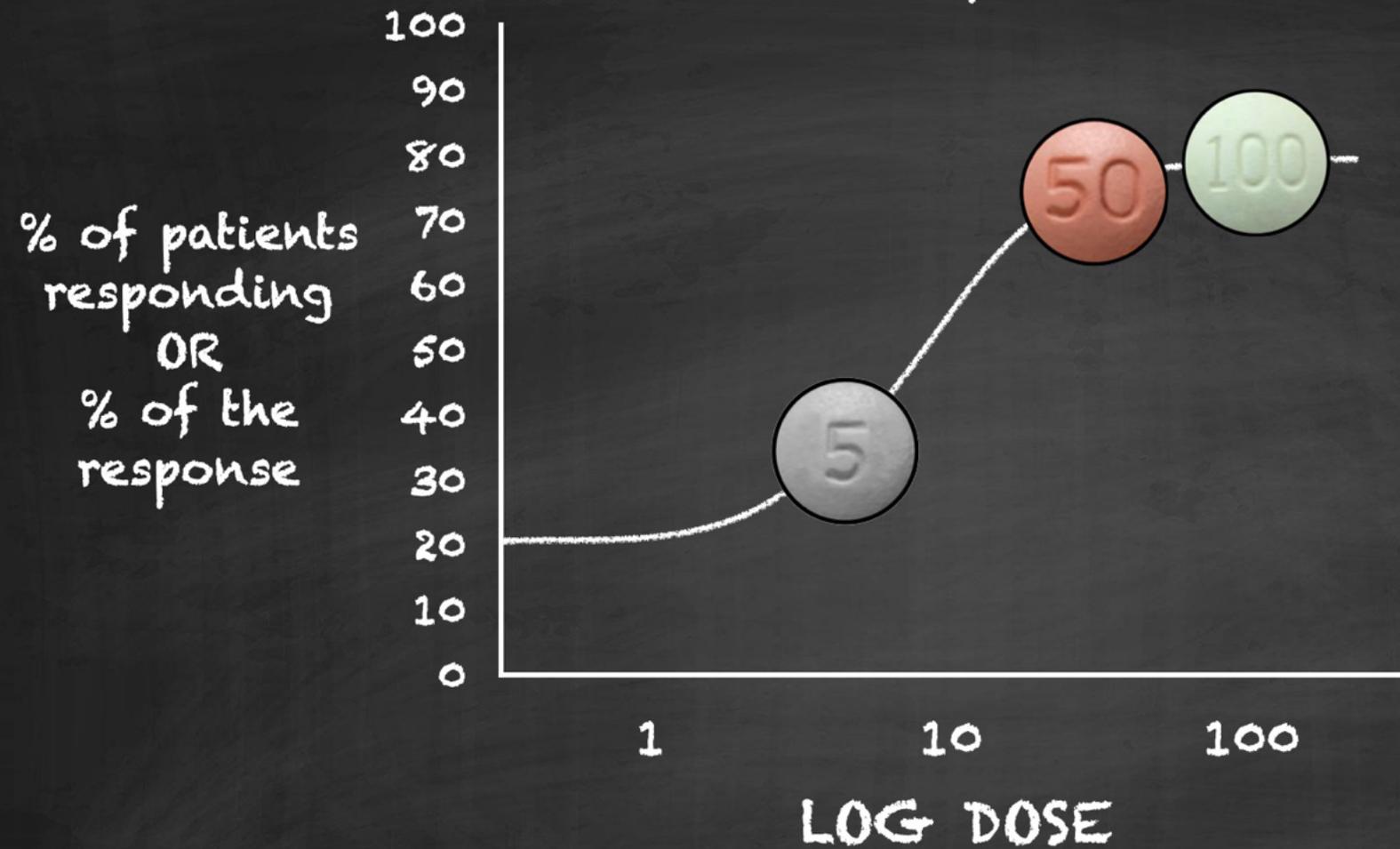
USE
VERY LOW
DOSES

The doses in these books



are all “WRONG” for individual patients

Dose Response



CMAJ

ANALYSIS

Is bigger better? An argument for very low starting doses

James P. McCormack PharmD, G. Michael Allan MD, Adil S. Virani PharmD

”Unless the condition is severe or life-threatening, drug treatment can be started at a very low dose (half or one-quarter the recommended starting dose)”

CMAJ 2011. DOI:10.1503 /cmaj.091481

Most of the effect of a medication comes from the “low” starting doses AND doubling a dose never doubles the effect - in fact it sometimes has no additional effect

Doxepin (Sinequan)

Depression - start 25-50 mg - optimal 75mg - 150mg up to 300mg

Doxepin in the Treatment of Primary Insomnia:
A Placebo-Controlled, Double-Blind,
Polysomnographic Study

J Clin Psychiatry
2001;62:453-63

“The results support the effectiveness of low doses (25-50 mg) of doxepin to improve sleep”

INSOMNIA

Sleep 2007; 30: 1555–61

Efficacy and Safety of Three Different Doses of Doxepin in Adults with Primary Insomnia

All three doses worked better than placebo

AND

NO side effects over placebo

A recommended low dose was still 25-50 times TOO HIGH

A Dose of Reality

When a new drug comes on the market almost never have more than 2 doses been studied

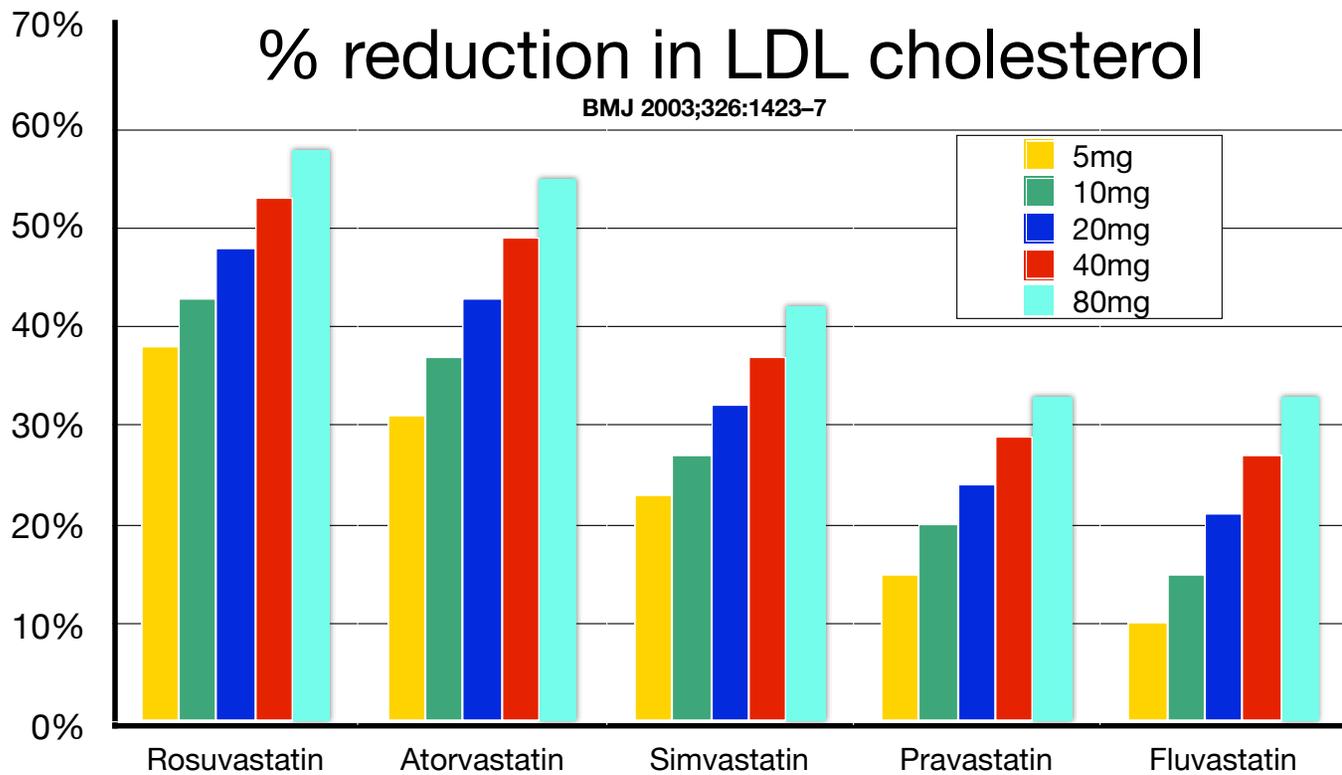
To get a drug on the market you have to show it works therefore one has to choose a dose that is high enough that if it is going to work it will work in almost everyone

Postmarketing drug dosage changes of 499 FDA-approved
new molecular entities, 1980–1999[†]

dosage changes occurred in 21%
of all new molecular entities

80% were dose decreases

“this pattern may represent a systematic flaw in pre-marketing dosage evaluation; it has been common practice in the pharmaceutical industry to undertake phase III trials evaluating drug effectiveness at or near maximum-tolerated doses.”



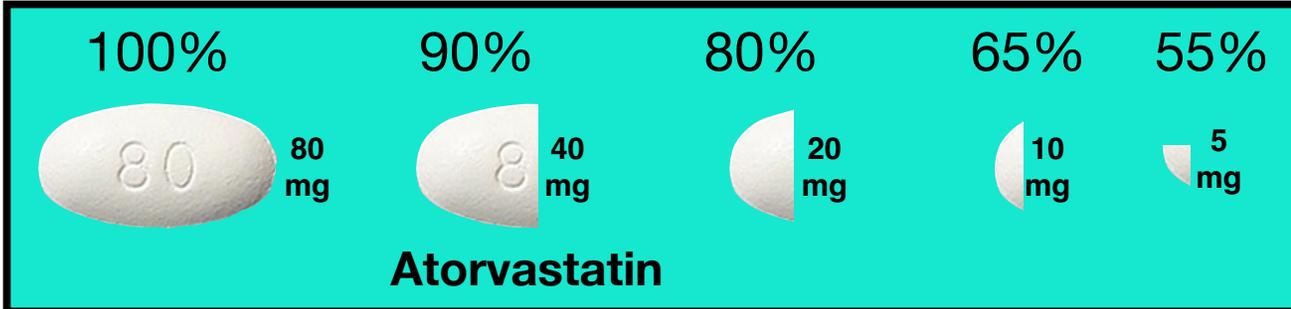
20 mg dose
~ 30% ↓ in LDL

↑ 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



A Sample of Low-Dose RCT Evidence

12.5 mg hydrochlorothiazide	first marketed at 50 to 200 mg daily
5 mg daily fluoxetine (Prozac)	similar effects to those seen at 20 mg and 40 mg daily
150 mg daily bupropion (Zyban)	produces the same rate of smoking cessation at one year as 300 mg daily
0.5 mg BID varenicline (Champix)	produces the same rate of smoking cessation at one year as 1.0 mg BID
25 mg ranitidine (Zantac)	as effective as 75 mg and 125 mg for heartburn relief
25 mg sumatriptan (Imitrex)	works as well as 100 mg
0.25 mg ezetimibe (Ezetrol)	1/40th of the recommended initial starting dose provides 50% of the LDL lowering effect
1, 3 and 6 mg doxepin (Sinequan)	all doses equally effective for sleep - originally used 25-50 mg
25 mg sildenafil (Viagra)	effective as 50, 100 mg for erectile dysfunction
200 mg ibuprofen (Motrin)	as effective as 400 mg for migraine headache
1.8 mg colchicine	as effective as 4.8mg for acute gout with less adverse events
15 mg elemental iron daily	as effective for anemia in elderly as 50 mg and 150 mg with a lower incidence of side effects
6.25 mg captopril (Capoten)	25 mg PO TID is still a commonly recommended initial starting dose for hypertension

Advantages of starting with “very” low doses

1. Get the potential “placebo group effect” without deception
2. Patients are engaged in the process of finding the best dose for them
3. Cost savings can be considerable and most adverse events can be minimized
4. Most clinically relevant drug interactions can be avoided

Approaches differ depending on outcome

Every patient is an experiment - dose and effect

SYMPTOMS - we can usually figure out if it is working
- but it is tricky

PREVENTION - one will never know if it worked

Expectations

We need to do these LESS

follow guidelines LESS

treat to preventative thresholds LESS

worry about surrogate markers LESS

label LESS - pre-everything

stress about what we eat LESS

WAY LESS MECHANISM OF ACTION - just the best available evidence

nuanced/personalized nutrition - low carbs, low fat, high fat, high carbs, polyphenols, lectins, flavanols, antioxidants

lab testing and measurements LESS

screening LESS - next year's talk :)

We need to do these MORE

MORE shared-decision making

MORE discussion around preventative thresholds

MORE focus on evidence that looks at important clinical outcomes

MORE explaining the best available evidence

MORE explaining the huge uncertainty we have in healthcare

MORE lower doses

encourage eating the Mediterranean Diet in Moderation - best weight you can achieve being healthy and enjoying life

encourage the enjoyment of eating

encourage doing physical activity people enjoy



“The answers are all out there, we just need to ask the right questions.”

Oscar Wilde

When do we have debate about health issues?

1. the answer may be impossible to know
2. the best available evidence is tenuous
3. the potential difference in outcome is “small”
4. there is a belief about “a mechanism”
5. the stakes are high - pharmaceutical and nutrition beliefs are very “marketable”

FOOD, especially with individual nutrients, HAS ALL OF THESE

2015 DGAC: MEETING 7
December 15, 2014

Science Base Chapter:

*Food and Nutrient Intakes,
and Health:
Current Status and Trends*

Subcommittee 1

health.gov

**HOWEVER, THE FINAL REPORT RELEASED IN
JANUARY 2016 STATED
"individuals should eat as little cholesterol as possible"**

- Cholesterol intake is a point of concern for

Intakes, and Health: Current Status and Trends

THE NUTRITION PROPOSITION

HOME ABOUT WHY READ THIS BOOK? THE MENU SAMPLES REVIEWS FAQs CONTACT

RELEASED APRIL 2022

updated regularly

What does the evidence really say about your food choices?

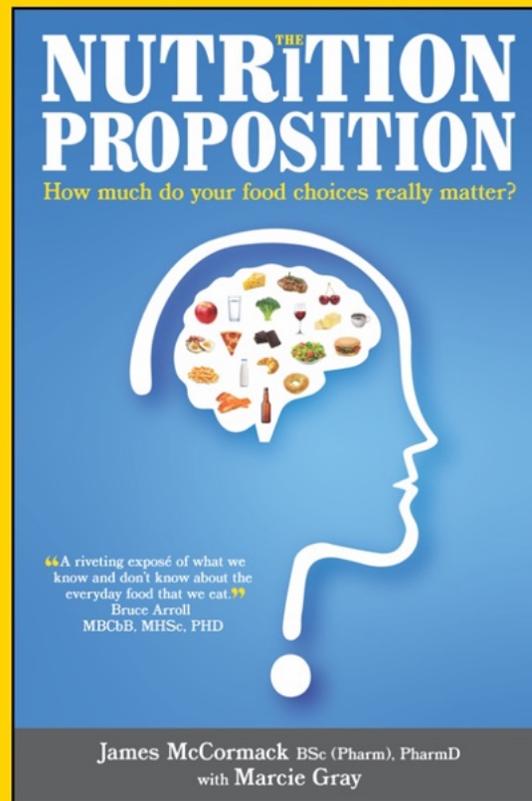
Read The Introduction

BUY
The Nutrition Proposition

Available as
Paperback or Kindle Edition

Get the book on Amazon.com

Get the book on Amazon.ca



"The Nutrition Proposition is a mammoth contribution to the world's understanding of the science behind nutritional hype. James McCormack helps strip the science of nutrition down to its bare essentials."

Alan Cassels
Author of Selling Sickness and Seeking Sickness

"A riveting expose of what we know and don't know about the everyday food that we eat."

Bruce Arroll, MBChB, MHSc, PhD
Head of the Department of General Practice
and Primary Health Care University of Auckland

"I would recommend this book for anyone who communicates with the public about health - who might not be well prepared to explain the nuance that exists with almost any health-related study, and certainly studies on nutrition topics. The authors' depth of experience, appreciation for history, case examples, and humour make this a meaningful addition to a syllabus or a personal library."

Gary Schwitzer
Publisher, HealthNewsReview.org



**The Only Nutrition Book That
Won't Tell You What To Eat!!
But It Will Tell You What We Know
And Don't Know About Food**

nutritionproposition.com

It's really easy to simply state these things are **good** or **bad** for your health

Drinking 2, 4, 6 or 8 glasses of water a day

Drinking 0, 1, 2 or 3 alcoholic beverages a day

Eating 2, 3, 4, 5, 6 or 7 servings of fruits and vegetables a day

Eating 0, 1, 2 or 3 eggs a day

Adding salt to food

Restricting or increasing the amount of carbs, fat and protein

Adding sugar to 1, 2, 3, 4 or 5 cups of coffee or tea a day

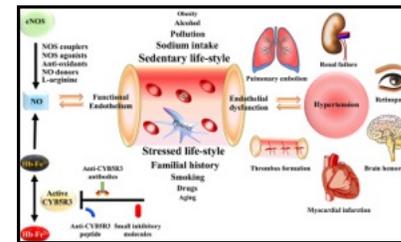
Being a meat eater, a vegetarian, or a vegan

Eating a doughnut, cheesecake, ice cream, or chocolate

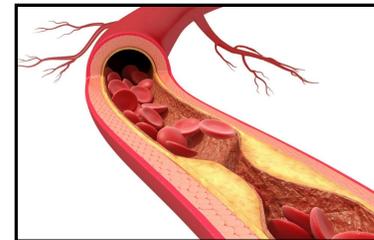
Drinking a glass of milk or a soft drink a day

Eating an apple a day

Everything is “linked”



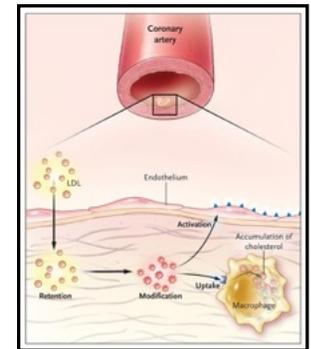
“Clogged” arteries



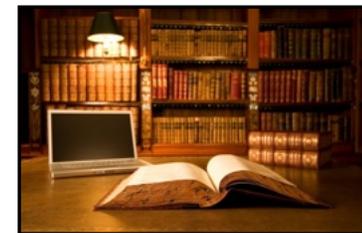
“Smart” words



Images with “arrows”



“Medical” References

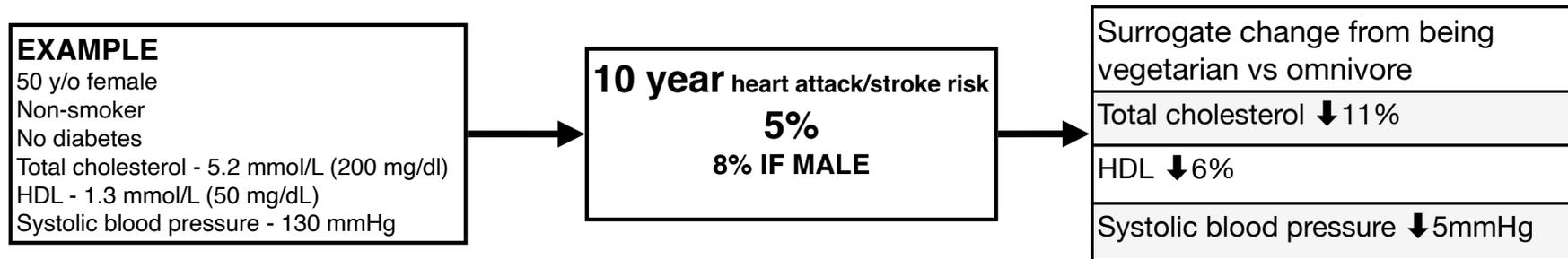


The Bullshit Asymmetry



The amount of energy needed to refute
bullshit is an **order of magnitude**
bigger than to produce it.

The impact of nutrition on
SURROGATE markers (lipids, blood pressure etc)
and the impact that has on **ESTIMATED heart attack/stroke risk**

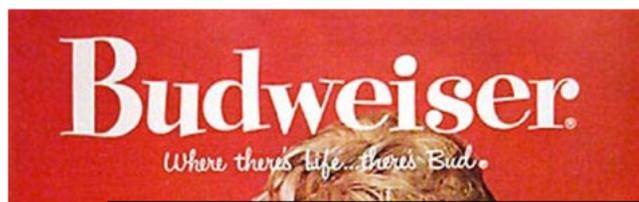


REASONABLE ESTIMATE OF THE IMPACT ON RISK
~1% absolute decrease over 10 years
~2% absolute decrease over 20 years



****Studies of the Mediterranean diet show it produces minimal if any changes on surrogate markers****

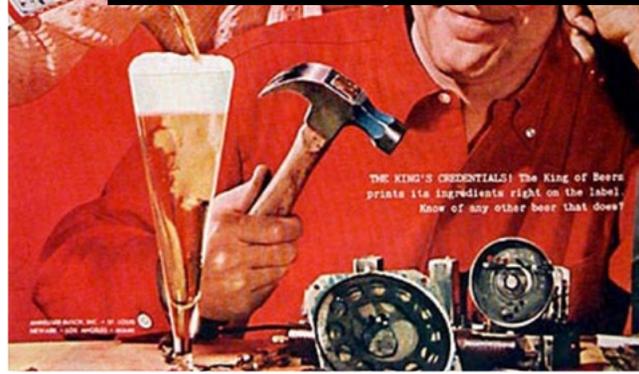
The Golden? Days of Alcohol



Set up the fun with
light refreshment



How to pamper a husband
When a grass-cutting husband lies down on the job, it's a wise wife who hurries Schlitz to the hammock.



Alcohol ingestion can absolutely be harmful

CONTEXT
MATTERS

The psychosocial impacts of alcohol ABUSE are devastating to individuals, families and the general public - cirrhosis, violence, accidents

Drinking and driving is 1000% wrong - SELFISH!!

Binge drinking can lead to very poor judgments



**Anything more than 3 drinks a day is likely a health issue
BUT what about 1, 2, or 3**

A History Lesson

REPORT

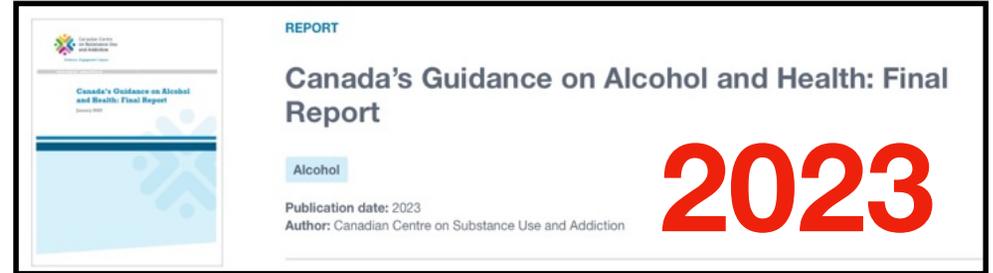
Alcohol and Health in Canada: A Summary of Evidence and Guidelines for Low-Risk Drinking

Alcohol Health Effects

2011

Publication date: 2011

Author: Canadian Centre on Substance Use and Addiction



“no more than
10 drinks a week for females
and 15 drinks for males”

Do not drink and drive

Do not drink when pregnant

“A continuum of health risk starting with
consumption as low as
3 standard drinks per week”

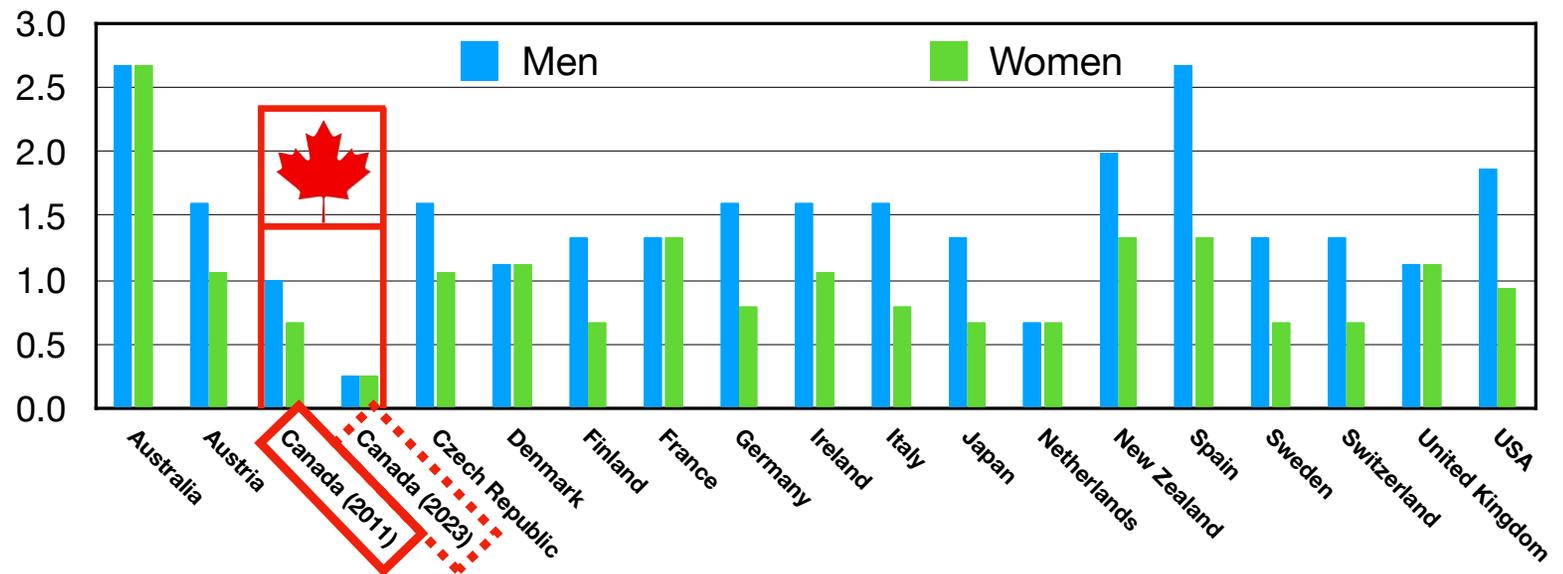
“We now know that even a small amount of
alcohol can be damaging to health”

“Drinking alcohol, even a small amount, is
damaging to everyone”

Across The

Recommended maximum intake of alcoholic beverages

Drinks/day



Release dates of these recommendations are variable

THIS IS CONSIDERED A DRINK

BEER/
CIDER/
COOLER
341mL/12oz
5% alcohol

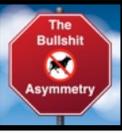
WINE
142mL/5oz
12% alcohol

SPIRITS
43mL/1.5oz
40% alcohol

~15g of alcohol

How Much Do We drink?

	Zero	If you do drink - typical drinking day		
		1-2/day	3-4/day	5+ a day
Women	23%	74%	17%	9%
Men	18%	54%	23%	23%



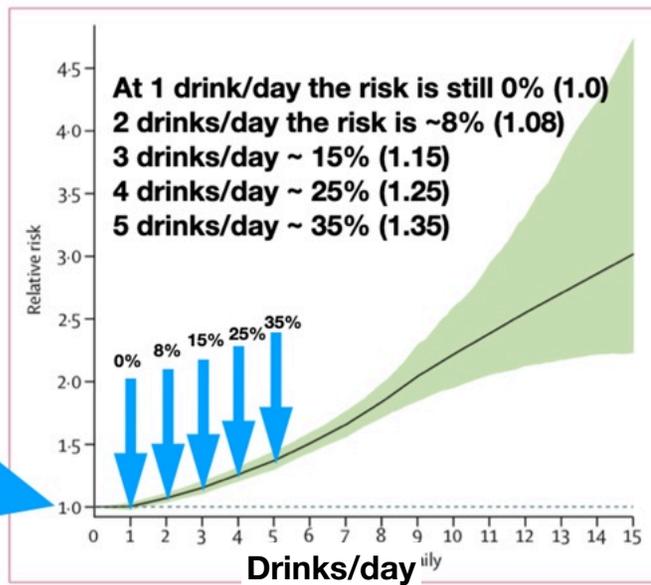
Lancet 2018

Alcohol

Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016

GBD 2016 Alcohol Collaborators*

“We found that the risk of all-cause mortality, and of cancers specifically, rises with increasing levels of consumption and the level of consumption that minimises health loss is zero”



1.0 means no increased risk of mortality attributable to alcohol

ABSOLUTE NUMBERS - the number who would experience an alcohol related problem

OVER ONE YEAR	Additional people out of 100,000	Extrapolated Increase over 30 years
1 drink a day	4	0.1%
2 drinks a day	63	1.5%
5 drinks a day	338	10%

TOP 3 HARMS - tuberculosis, road injuries, self harm

HEALTH

Proposed update to Canada's alcohol guidelines suggests as few as 3 drinks per week

By Cassandra Szklarski · The Canadian Press

Posted August 30, 2022 1:23 pm · Updated August 30, 2022 6:42 pm



HEALTH | News

Proposed alcohol guidelines recommend no more than 2 drinks per week

A new measure of unhealthy drinking

PUBLISHED SEPTEMBER 1, 2022

If you have three or more alcoholic drinks in a week, you're putting your health at risk. That's according to a [new report](#) from the Canadian Centre on Substance Abuse and Addiction (CCSA). The government of Canada's [current recommendations](#) are more than a

CALGARY | News

Calgarians react to new guidelines for alcohol intake

Having three to six drinks per week increased the risk to moderate, while having more than six was found to contribute to increased risks of cancer, stroke, heart disease and situations of violence.

HOME > LOCAL NEWS

1 drink a day means higher risk of heart disease, stroke, cancer: Report

A recent report highlights the many health risks associated with consuming just one alcoholic drink a day

Michael Ranger
Sep 5, 2022 3:00 PM



Living

Are Canadians drinking too much alcohol?

By NetNewsLedger - September 7, 2022

182



Are Canadians Drinking too much?

THIS IS THE PUBLIC SUMMARY (August 2022)

created by the Canadian Center on Substance Use and Addiction
and they **asked for public consultation**

Even in **small** quantities,
alcohol is not good for your health

Let's rethink the way we drink...

Science is evolving. So, we need to tell you something different than we have in the past. Recommendations regarding the quantities of alcohol need to change.

We now know that even small quantities of any alcohol can be harmful to your health. It doesn't matter whether it's red wine, white wine, beer or spirits. Your tolerance to alcohol doesn't make a difference, either.

Even in small quantities, drinking alcohol has consequences for everyone, whether you are male or female, younger or older. In fact, it's biological, it's physical.

That's why drinking less is better!



Even in small quantities, drinking alcohol has consequences for everyone, whether you are male, female, younger or older. In fact, it's biological, it's physical.

That's why drinking less is better!

The terms small, low, moderate, increasingly high risk are too subjective and in no way inform people as to the actual size of the risks

Not sure the weekly amount is all that useful - likely better to think about drinks per day given that when people "drink", they drink "daily"

Not sure of the point of having a weekly target of drinks - kind of sounds like a challenge to achieve either high or low

There are no numbers here and it implies each category has only the risks listed - there is no mention of liver cirrhosis which may numerically be the largest risk

The consequences of drinking

Having 2 drinks or fewer per week should allow you to avoid negative alcohol consequences.

If you have 3 to 6 drinks per week, you are increasing your risk of developing certain cancers, including breast and colon cancer.

If you have 7 drinks or more per week, you are actually increasing your risk of developing a heart disease or having a stroke.

And with each additional drink, your risk of having these health problems, and many other diseases and injuries, exponentially increases.

Alcohol has another consequence. All of these health problems, diseases and injuries can also shorten your life.

DRAFT



Our organization, the Canadian Centre on Substance Use and Addiction, was incorporated by Health Canada under the new risk drinking guidelines. This document summarizes the main changes. For more information, visit our website at www.ccsa.ca.

Let's rethink the way we drink

Keep track of how many drinks you have per week



It's never too late to revisit our habits! We are aiming to drink less. How about you?

What is your weekly drinking target?



Tips to reduce your drinking

- Stick to the limits you've set for yourself.
- Choose drinks with a lower percentage of alcohol.
- Drink slowly in small sips.
- Always have a pitcher of water on hand.
- For every drink of alcohol, have one non-alcoholic drink.
- Try some alcohol-free cocktail recipes.

Why Did They Choose Not To Include Numbers?

Public Consultation: Summary of Key Actions Taken

The responses received from the open consultation were analyzed and categorized. The table below presents the main categories of comments as well as the actions taken by the LRDG-Scientific Expert Panel (LRDG-SEP) to address comments which fell within the scope of this project's mandate.

There were several suggestions made for knowledge mobilization activities, including knowledge synthesis, dissemination, transfer and exchange. These suggestions have been recorded but are not listed here as they could not be considered for action (i.e., could not lead to edits and revisions of the final report).

Consultation comment or suggestion	Action taken
Public Summary	
Provide more information about specific cancers.	There are already many consequences of different types

The objective of the document is to communicate information without statistics that would need contextual information and more explanations to be easily understood. No statistics were added.

USE WITH CAUTION - the numbers below are my attempt at trying to get useful numbers (I spent 1/2 a day extracting data) from the August 2022 publication "Update of Canada's Low-Risk Alcohol Drinking Guidelines: Final Report for Public Consultation". I've listed where I got the numbers and more than happy to correct if there are errors or misinterpretation

TO HELP YOU MAKE AN INFORMED DECISION HERE ARE THE LIFETIME RISKS OF 1 TO 3 ALCOHOL DRINKS DAILY

"From Fig 1/Fig 2 - Lifetime Risk of Alcohol-Attributable Death and Disability paper"

"From Appendix 2 - Table 1 and 2"

THIS IS CONSIDERED A DRINK



LIFETIME RISK (absolute%)

DRINKS/ per day	1	2	3
	PREMATURE (before age 75) ALCOHOL ATTRIBUTABLE DEATH		
Females	0.5%	1.5%	2.5%
Males	0.5%	2%	3%
	ALCOHOL ATTRIBUTABLE DEATH		
Females	1.5%	4%	7%
Males	1.5%	4%	7%

CAUSES OF DEATH

Cancer

25%-33%*

Liver cirrhosis

20-25% in women

45-60% in men

Cardiovascular

10-25% in women

5-10% in men

Road injuries/or intentional injuries

20% in women

40% in men

Should reduce this risk somewhat

DON'T DRINK AND DRIVE

DON'T DRINK IF YOU ARE PREGNANT

All the numbers are ballpark estimates based on the best available evidence

*colorectal/breast/liver/oesophagus/mouth/pharynx/larynx

The Top 5 Harms

CONTEXT
MATTERS

4 were the same for men and women

intentional injuries
unintentional injuries

DON'T
DRINK IF
YOU DO
STUPID
THINGS

liver cirrhosis
colorectal cancer

DON'T
DRINK
AND
DRIVE

and then breast cancer (women) and road injuries (men)

Lifetime cancer risk

Breast cancer

lifetime risk of dying would increase from 3% to roughly 3.5%

Colorectal cancer

lifetime risk of dying would increase from 3.0% to roughly 3.3%

Cirrhosis

CCSA reports that 1-2 to two drinks a day increases the risk of liver cirrhosis in both men and women

the single paper they use to support these claims states quite clearly that, “although consumption of 1–2 drinks was associated with a substantially elevated risk for liver cirrhosis in women, this was not the case in men”

based on the CCSA numbers

Alcohol Risk Visualizer

Based on the [latest CCSA report](#) on the lifetime risk of alcohol-attributable death and disability.

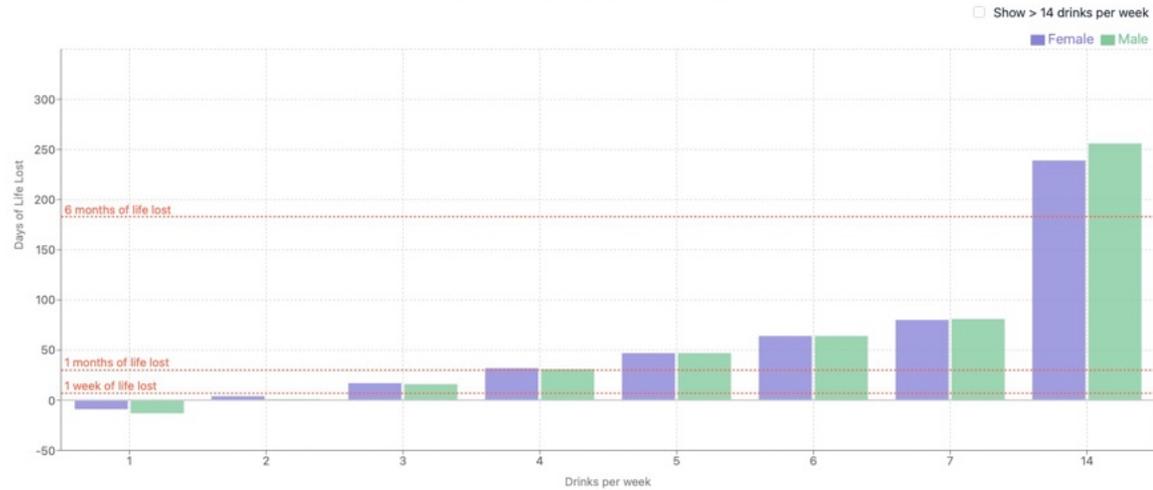
This chart shows how many days of life, on average, an individual could lose based on the amount of drinks they have per week.

The CCSA considers one drink as:

- 341 ml (12 oz) of beer 5% alcohol or cooler 🍺
- 142 ml (5 oz) of wine 12% alcohol 🍷
- 43 ml (1.5 oz) of spirits (whiskey, vodka, gin, etc) 40% alcohol 🍸

myalcoholrisk.com

Days of Life Lost by Drinks Per Week



Combined Risk from 21 Different Health Outcomes

Disease selectors allow you to select the diseases you're interested in. For example, consider removing physical injuries if you don't drink and drive and you are not reckless when you drink.

- | | | | | |
|--|---|---|--|--|
| <input checked="" type="checkbox"/> Cancer | <input checked="" type="checkbox"/> Cardiovascular Diseases | <input checked="" type="checkbox"/> Liver Damage | <input checked="" type="checkbox"/> Physical Injuries | <input checked="" type="checkbox"/> Other |
| <input checked="" type="checkbox"/> Oral cavity and pharynx cancer | <input checked="" type="checkbox"/> Diabetes | <input checked="" type="checkbox"/> Liver cirrhosis | <input checked="" type="checkbox"/> Road injuries | <input checked="" type="checkbox"/> Tuberculosis |
| <input checked="" type="checkbox"/> Oesophagus cancer | <input checked="" type="checkbox"/> Atrial fibrillation and flutter | | <input checked="" type="checkbox"/> Other unintentional injuries | <input checked="" type="checkbox"/> Lower respiratory infections |
| <input checked="" type="checkbox"/> Colorectal cancer | <input checked="" type="checkbox"/> Hypertension | | <input checked="" type="checkbox"/> Intentional injuries | <input checked="" type="checkbox"/> Pancreatitis |
| <input checked="" type="checkbox"/> Liver Cancer | <input checked="" type="checkbox"/> Ischemic heart disease | | | <input checked="" type="checkbox"/> Epilepsy |
| <input checked="" type="checkbox"/> Breast cancer | <input checked="" type="checkbox"/> Ischemic stroke | | | |
| <input checked="" type="checkbox"/> Larynx Cancer | <input checked="" type="checkbox"/> Intracerebral hemorrhage | | | |
| | <input checked="" type="checkbox"/> Subarachnoid haemorrhage | | | |

Days of Life Lost

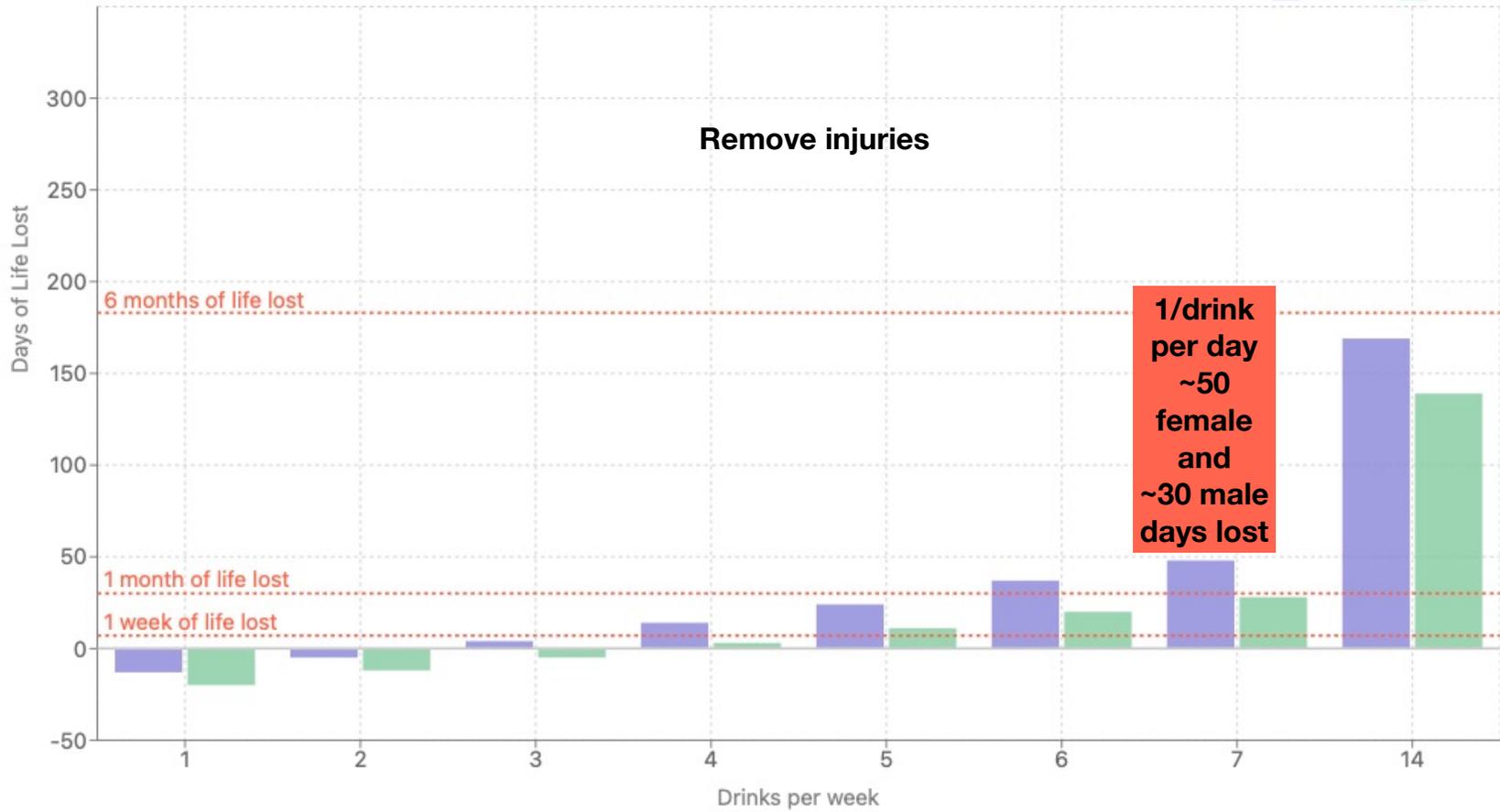


Days of Life Lost by Drinks Per Week

Show > 14 drinks per week

Female Male

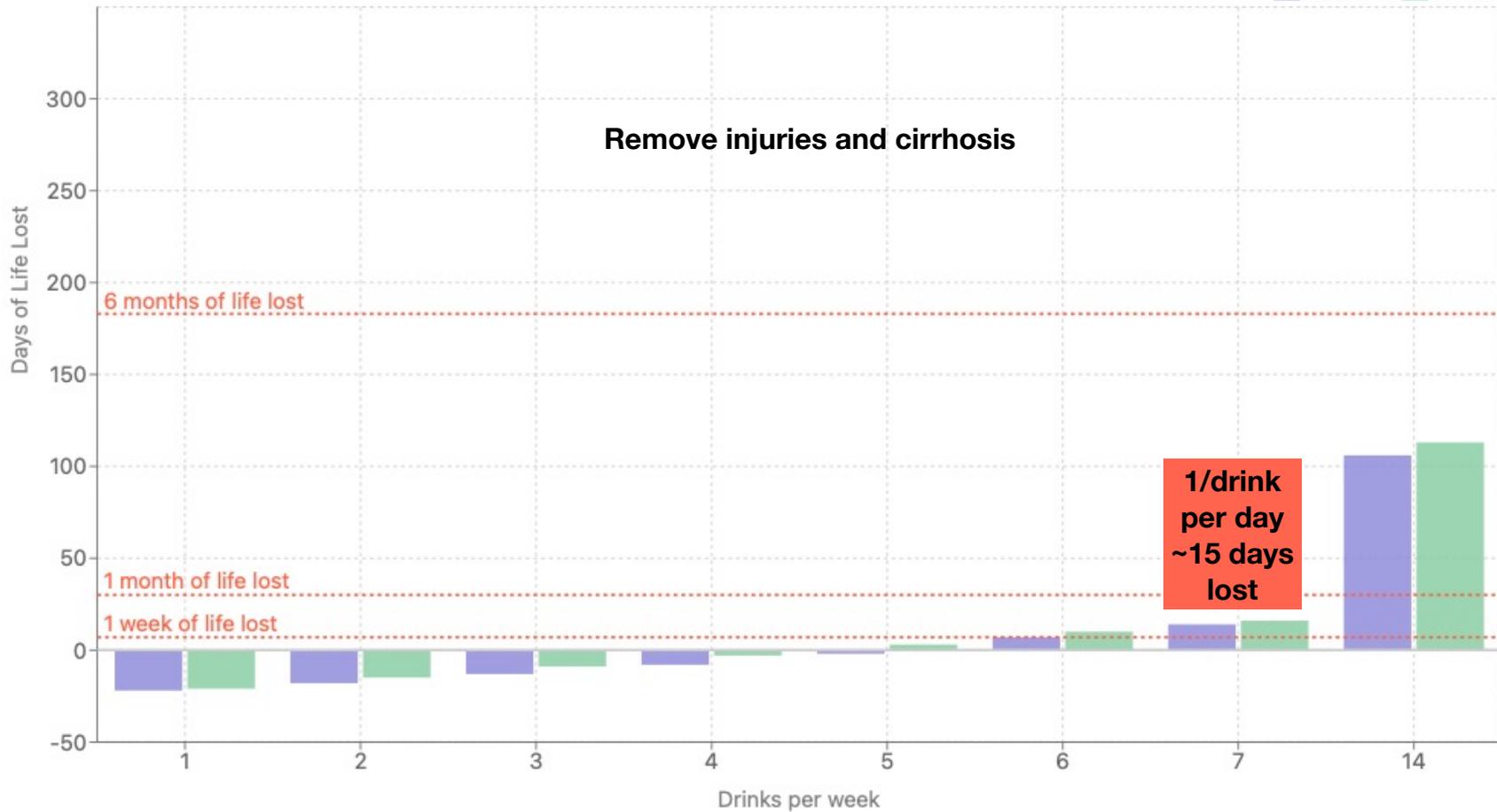
Remove injuries



Days of Life Lost by Drinks Per Week

Show > 14 drinks per week

Female Male



Drinking less is better

We now know that even a small amount of alcohol can be damaging to health.

Science is evolving, and the recommendations about alcohol use need to change.

Research shows that no amount or kind of alcohol is good for your health. It doesn't matter what kind of alcohol it is—wine, beer, cider or spirits.

Drinking alcohol, even a small amount, is damaging to everyone, regardless of age, sex, gender, ethnicity, tolerance for alcohol or lifestyle.

That's why if you drink, it's better to drink less.

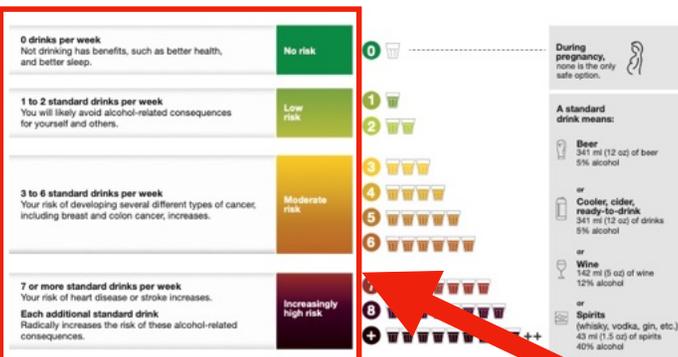
“Drinking alcohol, even a small amount, is damaging to everyone”

FINAL

Alcohol consumption per week

Drinking alcohol has negative consequences. The more alcohol you drink per week, the more the consequences add up.

Public Summary

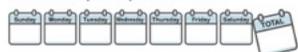


Aim to drink less

Drinking less benefits you and others. It reduces your risk of injury and violence, and many health problems that can shorten life.

Here is a good way to do it

Count how many drinks you have in a week.



Set a weekly drinking target. If you're going to drink, make sure you don't exceed 2 drinks on any day.

Good to know

You can reduce your drinking in steps! Every drink counts: any reduction in alcohol use has benefits.

It's time to pick a new target

What will your weekly drinking target be?



Tips to help you stay on target

- Stick to the limits you've set for yourself.
- Drink slowly.
- Drink lots of water.
- For every drink of alcohol, have one non-alcoholic drink.
- Choose alcohol-free or low-alcohol beverages.
- Eat before and while you're drinking.
- Have alcohol-free weeks or do alcohol-free activities.

My Opinion

The 2023 CCSA Alcohol Guidelines:

1. Are misleading
2. Don't provide appropriate “context”
3. Create unnecessary fear and confusion
4. In no way inform the public as to the absolute risks/benefits
5. Very likely have nothing to do with your values and preferences
6. Ignore the research (although it's not great) around the functional social benefits - they state it was “out of the scope for this summary” yet their research question clearly states “What are the risks and **benefits** (physical and mental health, and social impact)”

A number of their harm comments are not supported by their own data and their data show a CVD benefit at 1 drink a day that is greater than the cancer risks and this is not mentioned

Functional Benefits of (Modest) Alcohol Consumption

**R. I. M. Dunbar¹ · Jacques Launay¹ · Rafael Wlodarski¹ ·
Cole Robertson¹ · Eiluned Pearce¹ ·
James Carney¹ · Pádraig MacCarron¹**

“Despite considerable research on the misuse of alcohol, no one has ever asked why it might have become universally adopted, although the conventional view assumes that its only benefit is hedonic”

“social drinkers have more friends on whom they can depend for emotional and other support, and feel more engaged with, and trusting of, their local community”

Is a Glass of Wine Harmless? Wrong Question.

The latest alcohol advice ignores the value of pleasure.

By Emily Oster



The Atlantic
JULY 14, 2023

“A pleasure-agnostic approach to health advice is now in vogue ... and is filtering down to the general public with sometimes absurd results.”

“Are there any data on health benefits to orgasms? The point of orgasms is that they are fun. We do not need to prove health benefits to want to have them.”

“Alcohol is probably not the key to longevity. But it’s not arsenic, either. In the immortal words of Cookie Monster, it’s a sometime food.”



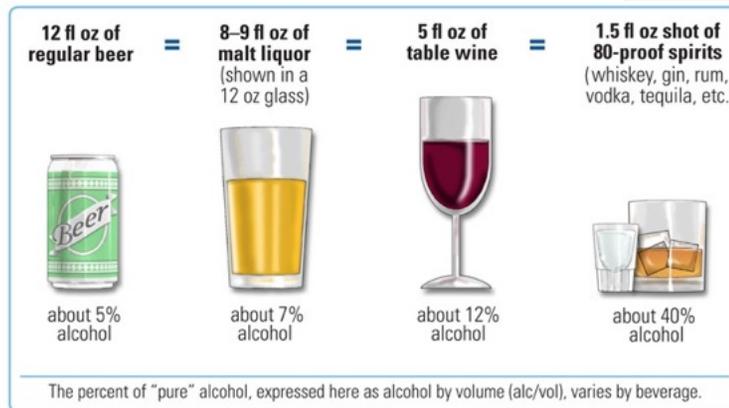
The Bottom Line

If you have a history of an alcohol problem or are pregnant - **DON'T DRINK**

If you drink and drive, become aggressive when you drink, or have a history of doing stupid things when you drink - **DON'T DRINK TO EXCESS**



1-2 drinks a day doesn't seem to produce an **INDIVIDUAL** health risk **OR** benefit



Do I/You have an Alcohol Problem?

**Just ask
One Question**

The NIAAA Single Alcohol Screening Question (SASQ)

“How many times in the past year have you had (4 for women/5 for men) or more drinks in a day?”

Sens~80%, Spec ~87%, ~LR 6/0.25 - for **UNHEALTHY DRINKING**

Pre-test probability of unhealthy drinking?
5%
10%
20%
30%



Post-test probability based on answer	
None	1 or more times
1%	24%
3%	40%
5%	60%
10%	70%

A Simplified Approach

If there was a “1 or more” answer

ASK - On a **typical** day when you drink, how many drinks do you have?

LIKELY NO ISSUE* IF THEY SAY

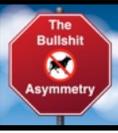
1-2 drinks MOST DAYS

3-4 drinks 2-3 TIMES A WEEK

5-6 drinks 1-2 TIMES A MONTH

MORE THAN THIS - PROBLEM?

* assuming not pregnant, not drinking and driving, not a previous alcoholic



Fat - it's about what you report

Meta-analyses of RCTs of replacing saturated fat or reducing fat

IMPORTANT OUTCOMES

- 1) heart attacks
- 2) heart attacks plus strokes
- 3) mortality

TYPICALLY REPORTED ONLY

FAT IS BAD
3 articles since 2010

20-30%
lower relative risk

FAT IS NOT BAD
5 articles since 2013

No difference

THE EVIDENCE

Author	Year	RCTs	Coronary heart disease events	Coronary heart disease mortality	Cardiovascular disease events	Cardiovascular disease mortality	Total mortality
Mozaffarian	2010	8	~20% ↓	Not reported	Not reported	Not reported	Not reported
Ramsden	2013	15	Not reported	No difference	Not reported	No difference	Not reported
Schwingshackl	2014	15	Not reported	Not reported	No difference	No difference	No difference
Ramsden	2016	5	Not reported	No difference	Not reported	Not reported	No difference
Harcombe	2016	10	Not reported	No difference	Not reported	Not reported	No difference
Hamley	2017	11	~20% ↓	No difference	Not reported	Not reported	No difference
		5	No difference	No difference	Not reported	Not reported	No difference
Sacks	2017	4	~30% ↓	Not reported	Not reported	Not reported	Not reported
Hooper	2020	15	No difference	No difference	~15% ↓	No difference	No difference

TheUpshot
THE NEW HEALTH CARE

Meat's Bad for You! No, It's Not! How Experts See Different Things in the Data

As the latest controversy over new research illustrates, nutrition science can be open to interpretation.

By Aaron E. Carroll

Oct 2019

Oct. 1, 2019



Meat



NutriRECS
Nutritional Recommendations and accessible Evidence summaries
Composed of Systematic reviews

THI
True Health Initiative
A global coalition of world-renowned experts, fighting fake facts and combating false doubts to create a world free of preventable diseases

Somewhere between zero and three servings per week is a good recommendation

Oct 2019

Annals of Internal Medicine®

REVIEWS | 1 OCTOBER 2019
Red and Processed Meat Consumption and Risk for All-Cause Mortality and Cardiometabolic Outcomes: A Systematic Review and Meta-analysis of Cohort Studies

REVIEWS | 1 OCTOBER 2019
Reduction of Red and Processed Meat Intake and Cancer Mortality and Incidence: A Systematic Review and Meta-analysis of Cohort Studies

REVIEWS | 1 OCTOBER 2019
Health-Related Values and Preferences Regarding Meat Consumption: A Mixed-Methods Systematic Review

NutriRECS
"THI response was completely predictable and hysterical!"

Norrina Allen
stated the NutriRECS study contradicted previous research and also their new findings were "comparable with those reported in the literature" and then **referenced**

A riddle, wrapped in a mystery, inside an enigma



Adults can continue eating the same amount of red meat — whether unprocessed or processed — as is being done in typical omnivore diets

THI
"NutriRECS articles are information terrorism"
Called for Annals to retract publication

Feb 2020

JAMA Internal Medicine | Original Investigation
Associations of Processed Meat, Unprocessed Red Meat, Poultry, or Fish Intake With Incident Cardiovascular Disease and All-Cause Mortality
Victor W. Zhong, PhD, Linda Van Horn, PhD, Philip Greenland, MD, Mercedes R. Combarros, PhD, Hongyan Ning, MD, MS, John T. Wilkins, MD, MS, Donald M. Lloyd-Jones, MD, ScD, **Norrina B. Allen, PhD**

"Small increased risk of heart disease and mortality"

THI
Praised the results and said findings were "consistent with virtually all prior research on the topic"

See 'The Nutrition Proposition'

Meat - it's about your "values"

So Why the Different Response?

Message	The two different meta-analyses of cohort studies	# of cohorts	What was examined	Time	Mortality		Overall cardiovascular	
					Unprocessed meat	Processed meat	Unprocessed meat	Processed meat
Continue to eat meat group	Zeraatkar October 2019	55	A 3 serving/week REDUCTION*	11yr	*1.08 Absolute ~1%	*1.09 Absolute ~1%	*1.05 Absolute <0.5%	*1.03 Absolute <0.5%
Eat less meat group supported	Zhong February 2020	6	Each additional 2 serving/week INCREASE	19 yr	1.03 Absolute ~1%	1.03 Absolute ~1%	1.03 Absolute ~0.5%	**1.07 Absolute ~2%

NutriRECS
 Focused exclusively on health outcomes associated with meat and did not consider animal welfare and environmental issues.
 Also felt a 1% risk in 11 years was small

THI
 Appear to think of this as more of a public health issue and that 1% risk means millions (1% of 300 million) could be affected and also considered the environmental perspective

*Because the Zeraatkar meta-analysis examined a REDUCTION in meat intake and the Zhong meta-analysis examined an INCREASE in meat intake numbers the Zeraatkar numbers have been inverted so they can be directly compared to the Zhong numbers
 ** for this number 2 versus zero servings a week, not 2 servings/week increase

From the upcoming book - The Nutrition Proposition

Fruits and Vegetable Servings



Forget the five-a-day servings of fruit and veg... now you need seven to be healthy

7+ a day
March 2014



Seven-a-day fruit and veg 'saves lives'



5 a day
June 2014



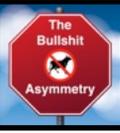
Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data **7 per day**

J Epidemiol Community Health - March 2014

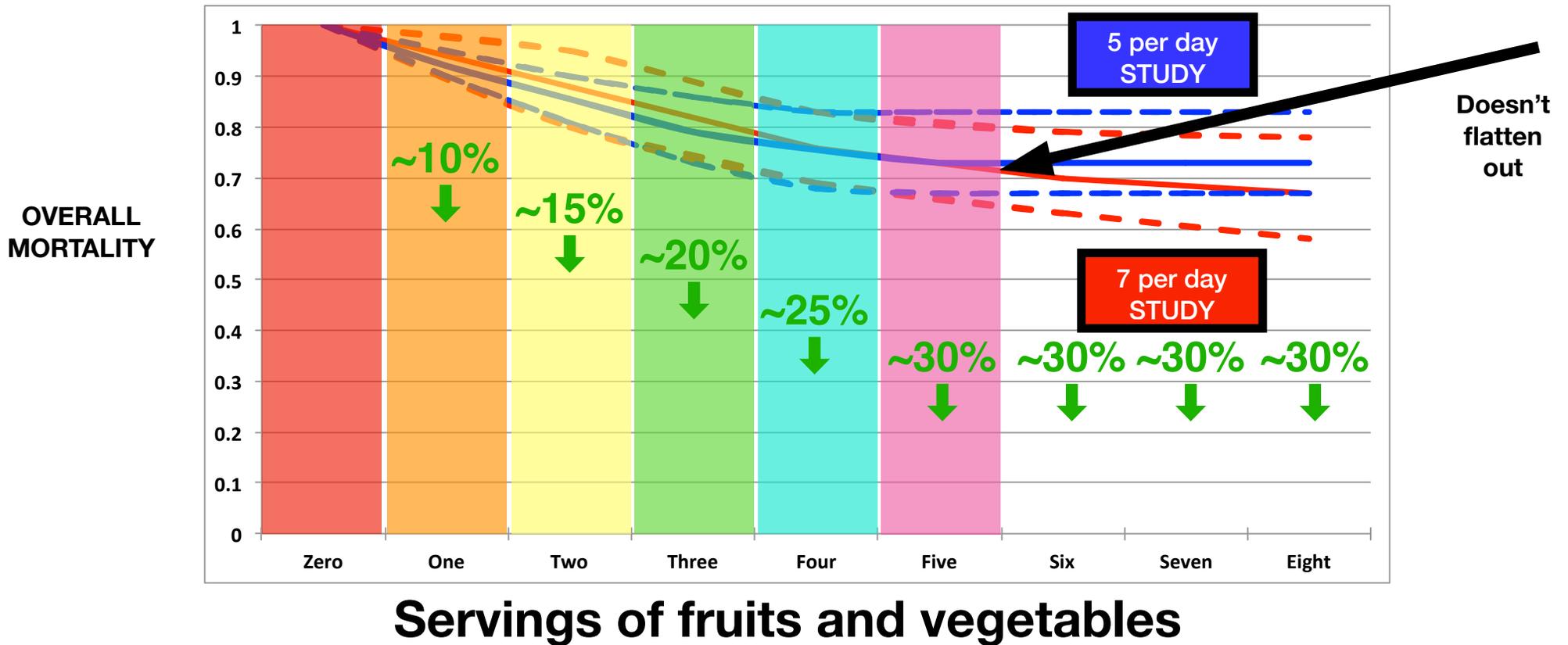
Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies **5 per day**

BMJ - June 2014

Fruits and Vegetable Servings - it's about what you "see"



The association between overall mortality and daily intake of fruit and vegetables



Ultra-processed food

The NOVA classification outlines 4 food categories

1. Unprocessed and minimally processed food
2. Processed culinary ingredients
3. Processed food
4. Ultra-processed food (UPF)

% of energy intake
US/UK ~50 to 60% from UPF
“eat the least” quintile still average 20-30%
Canada and Brazil ~50%
Spain and Portugal ~20%
Italy ~10%

Common examples are carbonated soft drinks, fatty or salty snacks, candies, pastries, cakes and cake mixes, margarine, sweetened cereals, fruit yogurt, pasta, pizza, poultry or fish nuggets, sausages, burgers, hot dogs, powdered or instant soup, noodles, and desserts.

A simple way to figure out if a product is ultra-processed is to see if its list of ingredients contains words such as: hydrolysed proteins, soya protein isolate, gluten, casein, whey protein, mechanically separated meat, fructose, high-fructose corn syrup, fruit juice concentrate, invert sugar, maltodextrin, dextrose, lactose, soluble or insoluble fibre, hydrogenated or interesterified oil

Ultra-processed food and bad outcomes

% of energy intake
 US/UK ~50 to 60% from UPF
 Canada and Brazil ~50%
 Spain and Portugal ~20%
 Italy ~10%

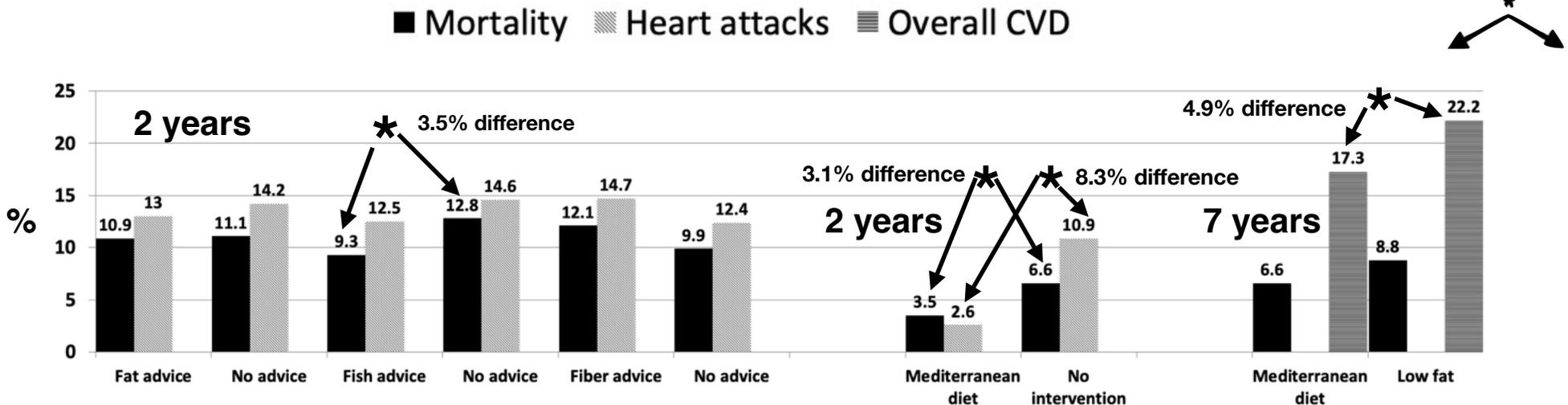
			QUANTILE				
			1 (reference)	2	3	4	5
	Years	Outcome	~<25%* total daily energy, or ~<2 servings/day	~25-30% ~2-3.5	~30-40% ~3.5-4.5	~40-45% ~>4.5	~>45%
Zhong 2021	13.5	CVD Mortality	1	NSS	NSS	NSS	1.21 (1.07-1.37)
Blanco-Rojo 2019	7.7	Mortality	1	NSS	NSS	1.44 (1.01-2.07)	
Schnabel 2019	7.1	Mortality	1	NSS	NSS	NSS	
Srouf 2019	5.2	CVD	1	NSS	NSS	1.23 (1.04-1.45)	
Kim 2019	19	Mortality	1	NSS	NSS	1.30 (1.08-1.57)	
		CVD mortality	1	NSS	NSS	NSS	
Rico-Campa 2019	200,432 persons years	Mortality	1	NSS	NSS	1.44 (1.01-2.05)	
		CVD mortality	1	NSS	NSS	NSS	

* numbers rounded

The 5 large RCTs of nutrition intervention

People with previous history of heart attacks/strokes

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



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

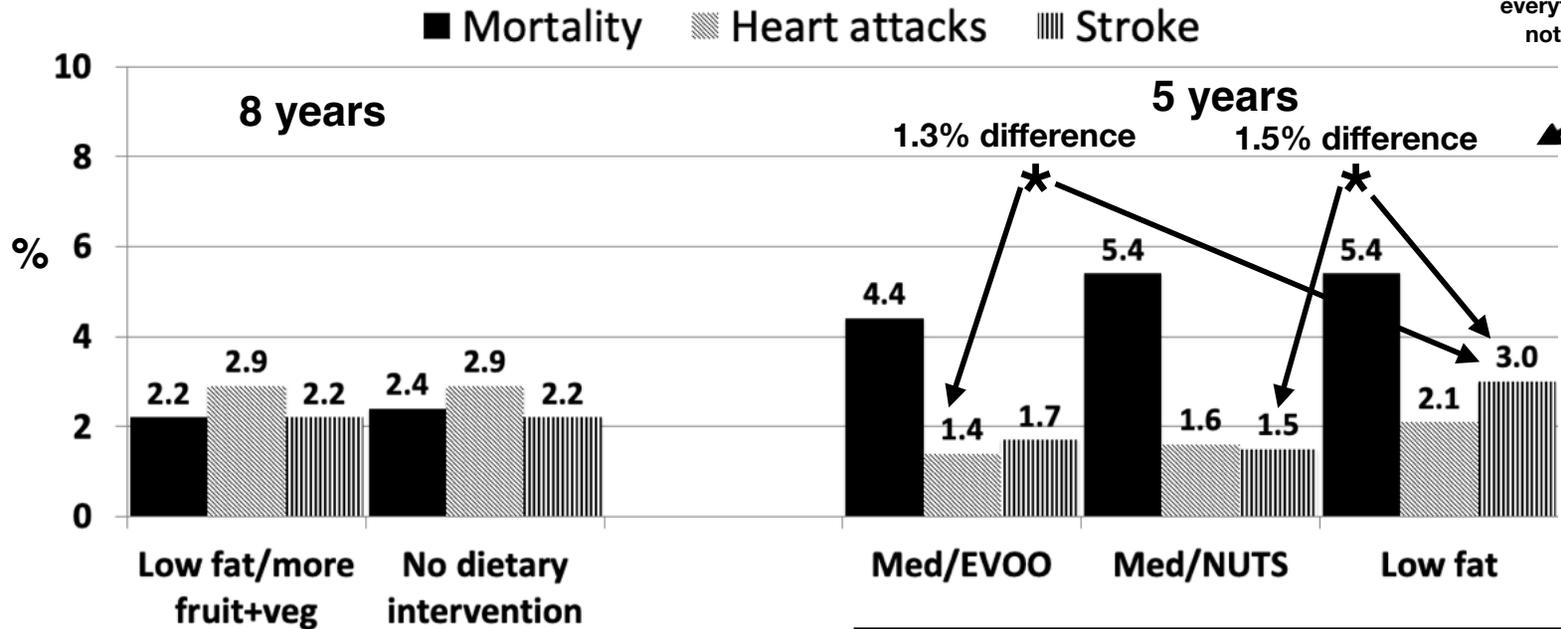
- ↑ total fat from 37% to 41%
- ↑ amount of extra virgin olive oil/nuts/oily fish
- ↓ carbs from 41% to 37%

Low fat diet

- ↓ total fat from 37% to 32%
- ↑ carbs from 42% to 46%

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

Important things I haven't touched on

Food allergies and intolerance

Animal rights

Environmental issues

Nutrition advice to which pretty much everyone agrees

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 food that has added sugars
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 consume is 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 shown to consistently cause unacceptable intolerances

BUT THERE ARE BIG CAVEATS

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

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

there are many potential confounders - let alone data collection issues

many of the associations seen in cohort studies are quite small (<10% relative) and principally 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

Much of nutrition research is on surrogate markers (blood pressure, lipids, glucose)

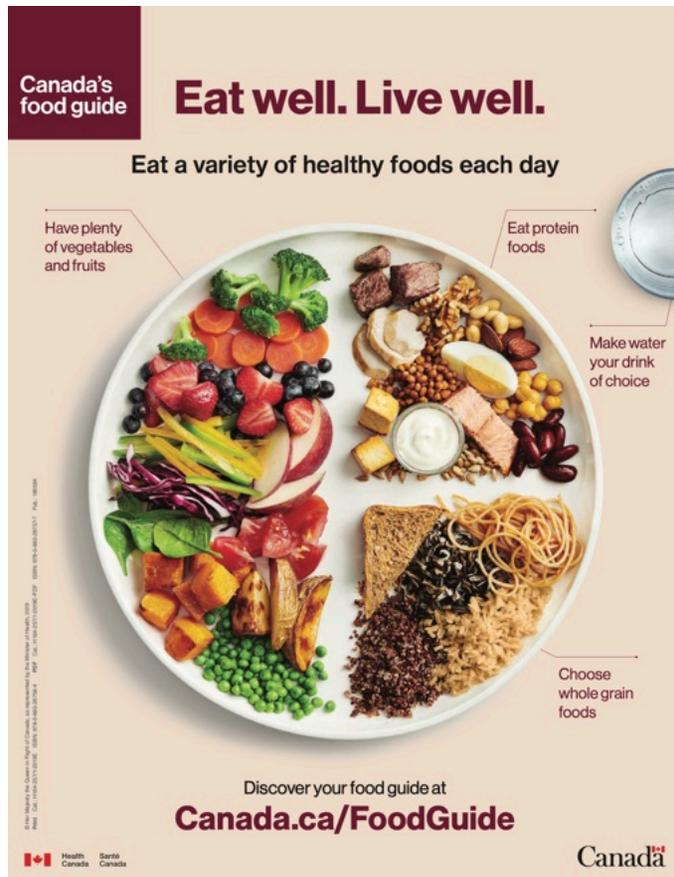
the changes seen **IF** they translated into effects on clinical outcomes would only amount to a 1% (at most 2%) absolute change in CVD risk over 10 years

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

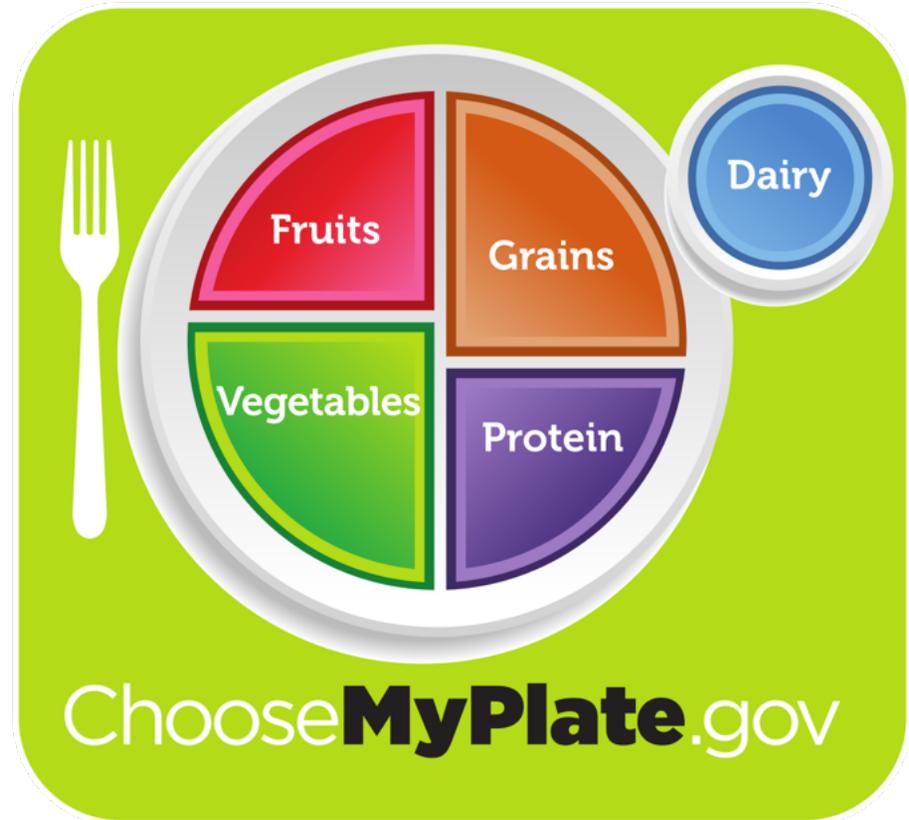
There are only 5 large RCTs (2+years) that have looked at important clinical outcomes

the “best evidence” is for the “Mediterranean Diet” and it only showed a 1-2% absolute difference in stroke over 5 years - more (3-8%) if secondary prevention

THESE ARE ACTUALLY PRETTY REASONABLE CONSIDERING THE EVIDENCE



CANADA



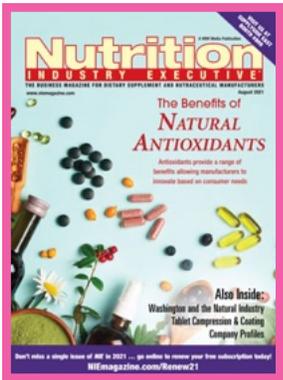
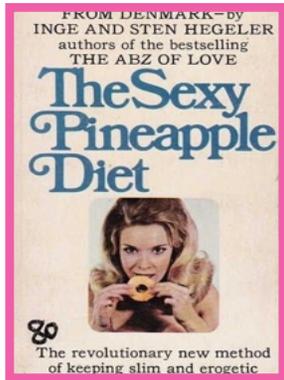
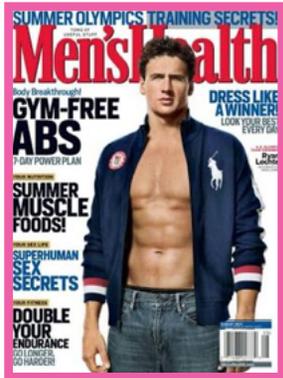
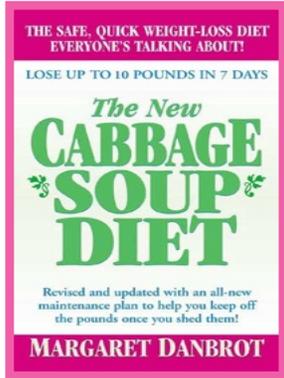
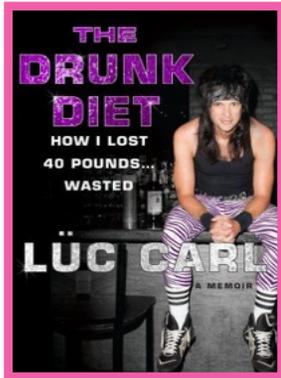
USA

A large collage of various food items, including vegetables, fruits, seafood, meat, cheese, and desserts, arranged in a grid-like pattern. The items are diverse and colorful, representing a wide range of food categories.

**“Everything in moderation,
including moderation.”**

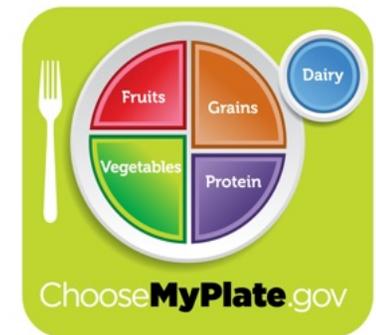
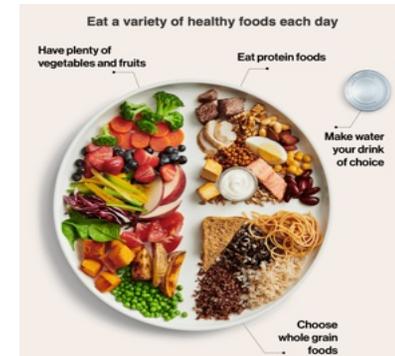
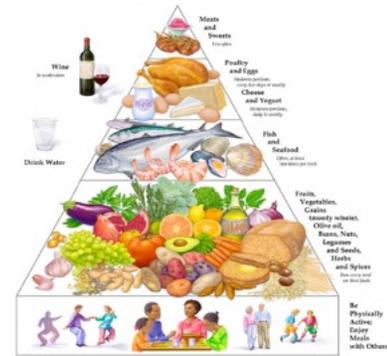
*Oscar Wilde,
Horace Porter,
and Petronius,
Socrates and
many more*

Assuming you wish your eating to be informed by the best available evidence
Anything else is likely...



1. ENJOY EATING

2. Differences in outcomes are typically found from “**extremes**” and are “**small**”
3. The **Mediterranean diet** (whatever it is) seems reasonable - also CFG/USDA/DASH
4. Eat in **moderation/moderation/moderation**
5. Avoid “**ultra**” **processed food** - within reason
6. You can easily justify some red meat, butter etc
7. Eggs, coffee, salt, and alcohol in moderation seem fine
8. **Saturated fats - OK** - trans-fat?
9. **Added sugars at the high end** seem to increase risk of obesity
10. It is **VERY unlikely** a single “nutrient” would have an important effect
11. Animal rights/environmental issues are a whole other topic



Activity examples



Activity

150 minutes of moderate to high intensity exercise per week, or 30-60 minutes most days of the week (includes brisk walking)

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,¹ Carsten Hjorthøj,¹ Helene Speyer,¹ Christian Gluud,² Merete Nordentoft¹

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

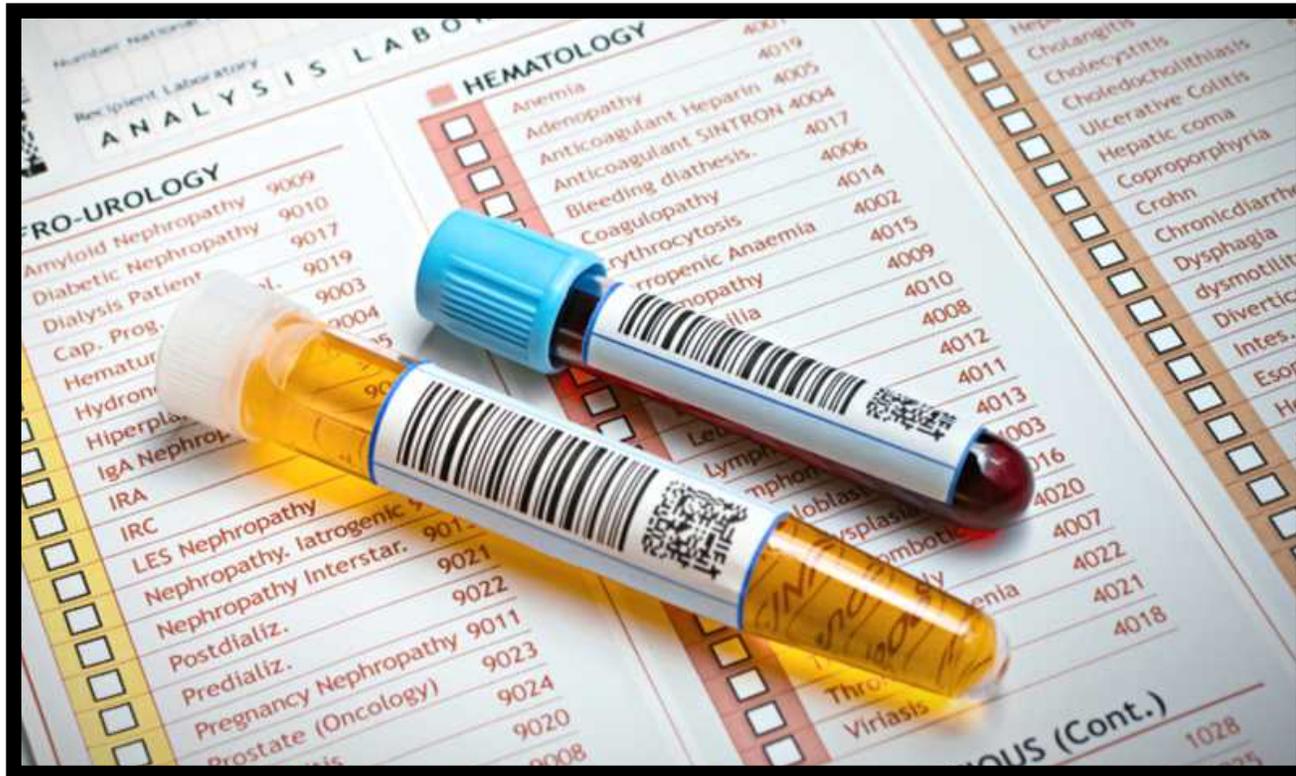
Effects of Physical Activity in Knee and Hip Osteoarthritis: A Systematic Umbrella Review

VIRGINIA B. KRAUS¹, KYLE SPROW², KENNETH E. POWELL¹, DAVID BUCHNER³, BONNY BLOODGOOD⁴, KATRINA PERCY⁵, STEPHANIE M. GEORGE⁶, and WILLIAM E. KRAUS¹, FOR THE 2018 PHYSICAL ACTIVITY GUIDELINES ADVISORY COMMITTEE¹

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”

Lab Test Examples



DO I HAVE TIME?

22 February 2020
368.265-302 No.0234 | ISSN 1759-2151



Tamiflu: what have we learnt? p 274

Quantifying multimorbidity p 277

Using genes to predict disease p 285

Mapping prescribing cascades p 294

1 CPD hour in the education section



YOUR RESULTS MAY VARY

The imprecision of
medical measurements

James P. McCormack and Daniel T. Holmes

February 22, 2020



BMJ 2020;368:m149 doi: 10.1136/bmj.m149 (Published 20 February 2020)

Page 1 of 5



PRACTICE

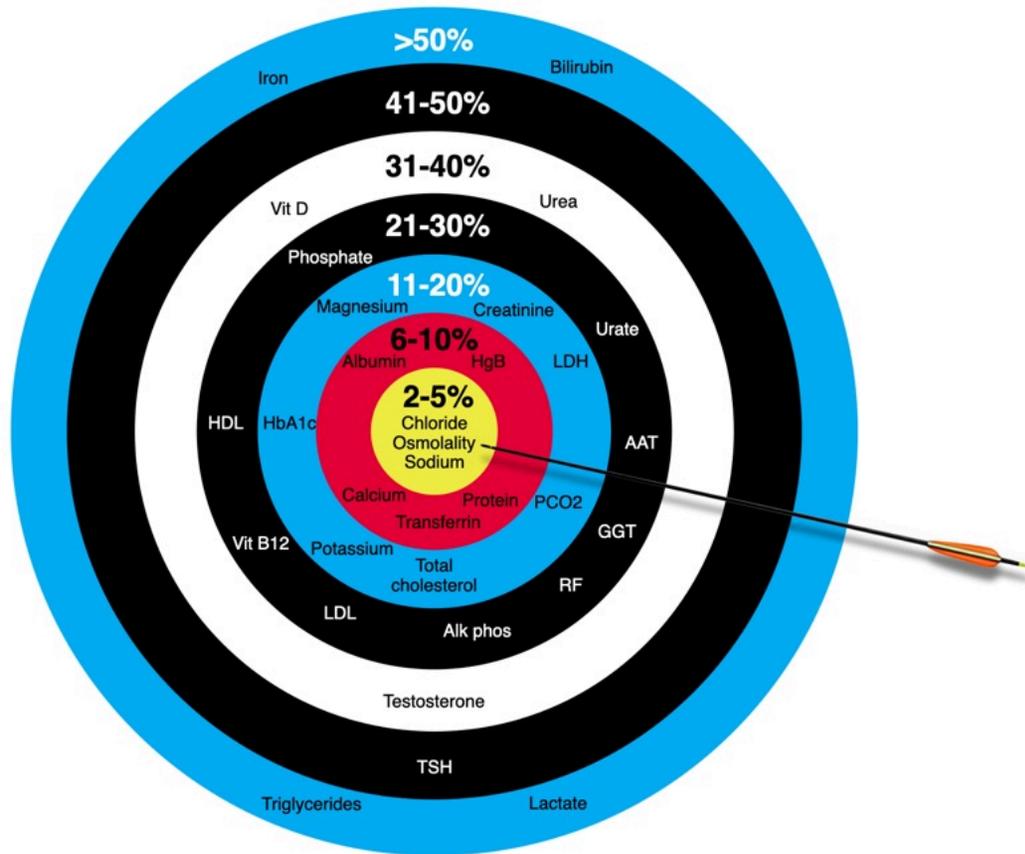
PRACTICE POINTER

Your results may vary: the imprecision of medical measurements

James P McCormack *professor*¹, Daniel T Holmes *clinical professor*^{2,3}

¹Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada; ²St Paul's Hospital, Department of Pathology and Laboratory Medicine, Vancouver, BC, Canada; ³Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada.

The change in a lab test that is needed to be confident there is a change



Repeat levels are next to useless unless you expect a change of at least

- 1) Cholesterol - 20-30% - 10-20% - total cholesterol - statins lower LDL by 25-30% - but increasing doses of statins only lower by 10%
- 2) Vitamin D - 30-40%
- 3) A1C - 10-20% - meds lower A1c by ~10%
- 4) Bone density - never recheck
- 5) Blood pressure - 40 office measurements before and after treatment to be REASONABLY confident that a 5 mmHg change has occurred

Yearly tests

- 1) Cholesterol ~ 0.5-1% increase per year
 - 2) Blood pressure ~ 0.5-0.8 mmHg increase per year
 - 3) Bone ~ 0.6% decrease in bone density per year
- NONE OF THESE CHANGES CAN BE PICKED UP BY YEARLY TESTS - need to wait ~5-10 YEARS**

Your results may vary

A tool for visualising the variability of lab test results

Version 1.0
19 Feb 2020

Interpreting results can be challenging for patients and clinicians alike. Results can be affected by measurement uncertainty, and by variation caused by biological processes. This tool (based on data in the article below) is designed to help you decide if two consecutive results can be considered truly different after these kinds of variation have been taken into account.

1 Choose a test

HbA1c Healthy NGSP (%)

2 Adjust variables

These boxes are automatically populated with reasonable estimates of the analytic variation (authors' lab) and biologic variation (published research). These can be adjusted as needed.

HbA1c Healthy NGSP (%)		
Analytic variation	Biologic variation	Normal range (reference interval)
2.5%	1.6%	Low High
		4.0 5.6

3 Enter lab results

Enter one or, if available, two serial lab results

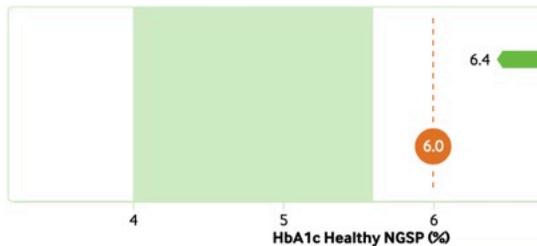
Result 1 7.0

Result 2 6.0

Show

4 View estimates

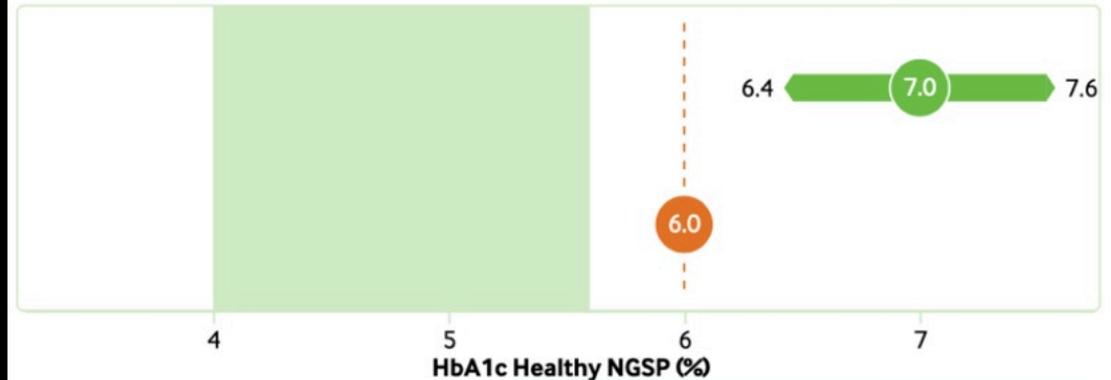
The minimum change required to conclude that two serial measurements are likely different is called the "reference change value" (RCV). Arrows to the left and right of your first result show the RCV for this test. For serial results, measurements can be considered different if the second is outside the RCV of the first.



Normal range
Outside normal range

Result 2 is outside the RCV, so the difference is unlikely to be due to the combined effects of analytic and biological variation

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Normal range
Outside normal range

Result 2 is outside the RCV, so the difference is unlikely to be due to the combined effects of analytic and biological variation

Approximate variability estimates for routine medical measurements

Test	Single measurement variability		Serial measurement variability
	Analytical variation†	Analytical and biological variation‡	Reference change value*
Bone density (spine, total hip)	<2%	2-5%	2-5%
Chloride	<2%	2-5%	2-5%
Osmolality	<2%	2-5%	2-5%
Sodium	<2%	<2%	2-5%
Bone density (femoral neck)	<2%	2-5%	6-10%
Albumin	2-5%	6-10%	6-10%
Calcium	2-5%	2-5%	6-10%
HbA _{1c} NGSP (%)	2-5%	6-10%	6-10%
Haemoglobin	2-5%	6-10%	6-10%
Total protein	2-5%	6-10%	6-10%
Transferrin	2-5%	6-10%	6-10%
Creatinine	2-5%	6-10%	11-20%
Glucose	2-5%	6-10%	11-20%
HbA _{1c} (diabetics) IFCC (mmol/mol)	2-5%	11-20%	11-20%
HbA _{1c} (diabetics) NGSP (%)	2-5%	6-10%	11-20%
HbA _{1c} IFCC (mmol/mol)	6-10%	6-10%	11-20%
Lactate dehydrogenase	2-5%	11-20%	11-20%
Magnesium	2-5%	6-10%	11-20%
PCO ₂	2-5%	6-10%	11-20%
Potassium	2-5%	6-10%	11-20%
Total cholesterol	2-5%	11-20%	11-20%
Alanine aminotransferase	6-10%	11-20%	21-30%
Alkaline phosphatase	11-20%	11-20%	21-30%
Aspartate aminotransferase	6-10%	11-20%	21-30%
Gamma glutamyltransferase	6-10%	11-20%	21-30%
HDL cholesterol	2-5%	11-20%	21-30%
LDL cholesterol	2-5%	11-20%	21-30%
Phosphate	2-5%	11-20%	21-30%
Rheumatoid factor	11-20%	21-30%	21-30%
Uric acid	2-5%	11-20%	21-30%
Vitamin B ₁₂	11-20%	11-20%	21-30%
25-hydroxy-vitamin D	6-10%	21-30%	31-40%
Holotranscobalamin	6-10%	21-30%	31-40%
Total testosterone (male)	6-10%	21-30%	31-40%
Urea	2-5%	21-30%	31-40%
Thyroid stimulating hormone	6-10%	31-40%	41-50%
Iron	2-5%	>50%	>50%
Lactate	2-5%	>50%	>50%
Total bilirubin	2-5%	41-50%	>50%
Triglycerides	2-5%	31-40%	>50%

*Change (%) required for two serial measurements to be considered different.

†Confidence interval (%) around a single measurement when only considering analytical variation.

‡Confidence interval (%) around a single measurement when considering both analytical and biological variation.

NGSP= National Glycated Haemoglobin Standardization. IFCC= International Federation of Clinical Chemistry.

HDL = high density lipoprotein. LDL = low density lipoprotein.

The calculations in the three columns help you interpret 3 different scenarios

- 1) Confidence interval (%) around **a single measurement** = analytic variation
- 2) Confidence interval (%) around **a single measurement of something that might be ongoing** = analytic and biologic variation
- 3) Change (%) required for **two serial measurements** to be considered different

Test	Single measurement variability		Serial measurement variability
	Analytical variation†	Analytical and biological variation‡	Reference change value*
Bone density (spine, total hip)	<2%	2-5%	2-5%
Chloride	<2%	2-5%	2-5%
Osmolality	<2%	2-5%	2-5%
Sodium	<2%	<2%	2-5%
Bone density (femoral neck)	<2%	2-5%	6-10%
Albumin	2-5%	6-10%	6-10%
Calcium	2-5%	2-5%	6-10%
HbA _{1c} NGSP (%)	2-5%	6-10%	6-10%
Haemoglobin	2-5%	6-10%	6-10%
Total protein	2-5%	6-10%	6-10%
Transferrin	2-5%	6-10%	6-10%

Test	Single measurement variability		Serial measurement variability
	Analytical variation†	Analytical and biological variation‡	Reference change value*
Creatinine	2-5%	6-10%	11-20%
Glucose	2-5%	6-10%	11-20%
HbA _{1c} (diabetics) IFCC (mmol/mol)	2-5%	11-20%	11-20%
HbA _{1c} (diabetics) NGSP (%)	2-5%	6-10%	11-20%
HbA _{1c} IFCC (mmol/mol)	6-10%	6-10%	11-20%
Lactate dehydrogenase	2-5%	11-20%	11-20%
Magnesium	2-5%	6-10%	11-20%
PCO ₂	2-5%	6-10%	11-20%
Potassium	2-5%	6-10%	11-20%
Total cholesterol	2-5%	11-20%	11-20%
Alanine aminotransferase	6-10%	11-20%	21-30%
Alkaline phosphatase	11-20%	11-20%	21-30%
Aspartate aminotransferase	6-10%	11-20%	21-30%
Gamma glutamyltransferase	6-10%	11-20%	21-30%
HDL cholesterol	2-5%	11-20%	21-30%
LDL cholesterol	2-5%	11-20%	21-30%
Phosphate	2-5%	11-20%	21-30%
Rheumatoid factor	11-20%	21-30%	21-30%
Uric acid	2-5%	11-20%	21-30%
Vitamin B ₁₂	11-20%	11-20%	21-30%

Test	Single measurement variability		Serial measurement variability
	Analytical variation†	Analytical and biological variation‡	Reference change value*
25-hydroxy-vitamin D	6-10%	21-30%	31-40%
Holo-transcobalamin	6-10%	21-30%	31-40%
Total testosterone (male)	6-10%	21-30%	31-40%
Urea	2-5%	21-30%	31-40%
Thyroid stimulating hormone	6-10%	31-40%	41-50%
Iron	2-5%	>50%	>50%
Lactate	2-5%	>50%	>50%
Total bilirubin	2-5%	41-50%	>50%
Triglycerides	2-5%	31-40%	>50%