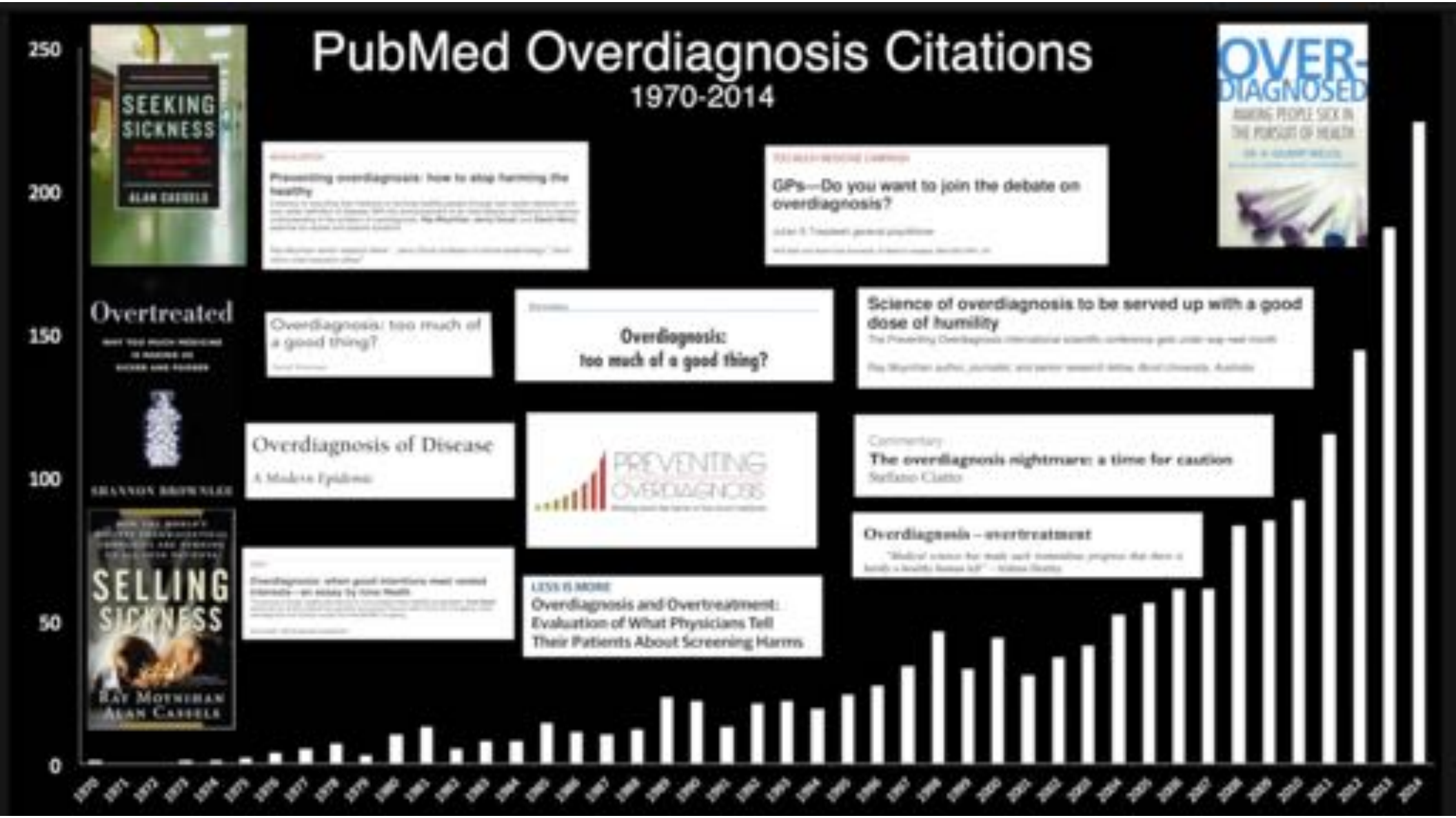
James McCormack
BSc (Pharm), PharmD
Professor
Faculty of Pharmaceutical Sciences
University of British Columbia
Vancouver, BC, Canada

Just a few of the diagnoses that are solely or partially lab-based dependent

Acid-Base Disorders
Acidosis and Alkalosis
Acidosis/Alkalosis
aCL Syndrome
ACS
Acute DIC
Acute Idiopathic Polyneuritis
Acute Inflammatory Demyelinating Polyneuropathy
Acute Kidney Injury
Acute Myocardial Infarct
Acute Renal Failure
AD
Addison Disease
Adrenal Insufficiency
Adrenal Insufficiency and Addison Disease
AKI
Albuminuria
Alcohol dependence
Alcoholism
Allergies
Alzheimer Dementia
Alzheimer Disease
AMI
Anemia
Anencephaly
Angiitis
Angina
Angina pectoris
Ankylosing Spondylitis
Anthrax
Anticardiolipin Antibody Syndrome
Antiphospholipid Antibody Syndrome
Antiphospholipid Syndrome
aPL Syndrome
APLS
APS
ARF
Arteritis
Arthritis
AS
Asthma
Atypical Mycobacteria
Atypical Pneumonia
Autoimmune Diseases
Autoimmune Thyroiditis
Avian Flu
Bacillus anthracis infection
Bacterial Arthritis
Bacterial Vaginosis
Benign Prostatic Hyperplasia
Benign Prostatic Hypertrophy
Biological Warfare
Bioterrorism Agents
Bleeding Disorders
Blood in the urine
Bone Marrow Disorders
Borrelia burgdorferi Infection
Borrelia mayonii Infection
BPH
Breast Cancer
CAH
Cancer
Candidiasis
Carbohydrate Intolerance
Cardiovascular Disease
Celiac Disease
Celiac Sprue
Cervical Cancer
CF
CFIDS
CFS
CHF
Chlamydia
Chronic Fatigue and Immune Dysfunction Syndrome
Chronic Fatigue Syndrome
Chronic Kidney Disease
Chronic Thyroiditis
Circumscribed Scleroderma
Cirrhosis
CKD
Coagulopathy
Cobalamin Deficiency
Colon Cancer
Colorectal Cancer
Community-Acquired Pneumonia
Congenital Adrenal Hyperplasia
Congenital Alactasia
Congestive Heart Failure
Conn Syndrome
Consumption Coagulopathy
Copper Storage Disease
CREST
Crohn Disease
Cushing Syndrome
Cutaneous anthrax
CVD
Cystic Fibrosis
Degenerative Joint Disease
Dehydration
Dermatosclerosis
Diabetes
Diabetes mellitus
Diarrhea
DIC
Diffuse Cutaneous Scleroderma
Diffuse Thyrotoxic Goiter
Disaccharidase Deficiency
Discoid Lupus
Disseminated Intravascular Coagulation
Disseminated Intravascular Coagulopathy
Disseminated Lupus Erythematosus
DJD
Double Pneumonia
Down Syndrome
Drug-induced Lupus
DS
Dysmetabolic Syndrome
Ebola Hemorrhagic Fever
Ebola Virus Disease
Ebola Virus Infection
Encephalitis
End Stage Renal Disease
Endocrine Syndromes
Endocrine System and Syndromes
Epilepsy
ESRD
EVD
Excessive Clotting Disorders
Extraosseous Plasmacytoma
Fibromyalgia
Flu
Folate Deficiency
Folic Acid or B9 Deficiency
Food and Waterborne Illness
Food Poisoning
Fungal Infections
Gastroenteritis
Gluten-Sensitive Enteropathy
Gonorrhea
Gout
Gouty Arthritis
Graves Disease
GSE
Guillain-Barré Syndrome
H1N1
H3N2
H5N1
H7N9
Hashimoto Thyroiditis
HBP
HD
Healthcare-Associated Pneumonia
Heart Attack
Heart Attack and Acute Coronary Syndrome
Heart Disease
Heart Failure
Hematuria
Hemochromatosis
Hemoglobin Abnormalities
Hemoglobin Barts
Hemoglobin C Disease
Hemoglobin E Disease
Hemoglobin S
Hemoglobin Variants
Hemoglobinopathy
Hepatic Disease
Hepatitis
Hepatolenticular Degeneration
Hereditary Persistence of Fetal Hemoglobin
Herpes
Herpes Zoster
High Blood Pressure
HIV
HIV Infection and AIDS
HL
Hodgkin Disease
Hodgkin Lymphoma
Hospital-Acquired Pneumonia
HPFH
HPV
Hughes Syndrome
Huntington Disease
Huntington's Chorea Disease
Hypercoagulable Disorders or States
Hyperparathyroidism
Hypersensitivity
Hypertension
Hyperthyroidism
Hypoparathyroidism
Hypothyroidism
IBD
Icterus
Infectious Arthritis
Infectious Polyneuritis
Infertility
Inflammatory Bowel Disease
Influenza
Influenza A
Influenza B
Inhalation anthrax
Inherited Copper Toxicity
Insulin Resistance
Insulin Resistance Syndrome
Iron Overload Disease
Iron Storage Disease
Jaundice
JIA
JRA
Juvenile Idiopathic Arthritis
Juvenile Rheumatoid Arthritis
Keratoconjuntivitis Sicca
Kidney Disease
Lactase Deficiency
Lactose Intolerance
Landry's Ascending Paralysis
LE
Lead Poisoning
Leukemia
Limited Cutaneous Scleroderma
Linear Scleroderma
Liver Disease
Lobar Pneumonia
Localized Scleroderma
Lower Respiratory Tract Infection
Lung Cancer
Lung Diseases
Lupus
Lupus Anticoagulant Syndrome
Lupus Erythematosus
Lyme Disease
Lymphocytic Thyroiditis
Lymphoma
Malabsorption
Malaria
Malignancy
Malignant tumor
Malnutrition
MDS
ME
Melanoma
Meningitis and Encephalitis
Meningococcal Meningitis
Menopause
Metabolic Syndrome
MG
MI
Morphea
MOTT
MPDs
MPNs
MRSA
MS
Multiple Myeloma
Multiple Sclerosis
Myalgic Encephalomyelitis
Myasthenia Gravis
Mycobacteria other than tuberculosis
Mycoses
Myelocele
Myelodysplasia
Myelodysplastic Syndrome
Myelomeningocele
Myeloproliferative Disorders
Myeloproliferative Neoplasms
Myocardial Infarct
Neonatal Lupus
Nephrotic Syndrome
Neural Tube Defects
Neuropathy
NHL
Non-Hodgkin lymphoma
Non-Small Cell Lung Cancer
Nontuberculous Mycobacteria
Nontuberculous Mycobacteria Infections
NTD
NTM
OA
Obesity Syndrome
Osteoarthritis
Osteoarthrosis
Osteoporosis
Ovarian Cancer
PA
Pancreatic Cancer
Pancreatic Diseases
Pancreatic Insufficiency
Pancreatitis
Parathyroid Cancer
Parathyroid Diseases
PCOS
Pelvic Inflammatory Disease
Peptic Ulcer
PID
Pituitary Disorders
Plasma Cell Dyscrasia
Plasma Cell Myeloma
Plasma Cell Neoplasm
Plasmacytoma
Plasmacytoma of Bone
Pneumonia
Polycystic Ovary Syndrome
Porphyria
Post-infectious Arthritis
Pre-eclampsia
Pregnancy
Pregnancy-induced Hypertension
Presenile Dementia
Primary Aldosteronism
Primary Hyperaldosteronism
Prinzmetal's angina
Prostate Cancer
Protein in urine
Proteinuria
RA
Reactive Arthritis
Reaven Syndrome
Renal Disease, Kidney Failure
Rheumatoid Arthritis
Rheumatoid Spondylitis
Sarcoidosis
SCD
Scleroderma
SEID
Seizure Disorder
Sepsis
Septic Arthritis
Sexually Transmitted Diseases
Sexually Transmitted Infections
Shingles
Sicca Syndrome
Sickle Cell Anemia
Sickle Cell Disease
Sjögren Syndrome
SLE
Small Cell Lung Cancer
Spina bifida
Spinal dysraphism
Spinal Meningitis
SSc
Stable angina
Staph
Staph aureus
Staph Infections
Staph Infections and Methicillin-Resistant Staphylococcus aureus
Staphylococcus aureus
STDs
Stein-Leventhal Syndrome
Sticky Blood Syndrome
STIs
Stomach Flu
Stroke
Subacute Cutaneous Lupus
Swine Flu
Syndrome X
Syphilis
Systemic Exertion Intolerance Disease
Systemic Lupus Erythematosus
Systemic Scleroderma
Systemic Sclerosis
TB
Testicular Cancer
Thalassemia
Thrombophilia
Thyroid Cancer
Thyroid Diseases
Toxemia
Toxic Diffuse Goiter
Travelers' Diseases
Trich
Trichomonas
Trichomoniasis
Trisomy 21
Tuberculosis
Types of Liver Disease
Ulcerative Colitis
Unstable angina
Urinary Tract Infection
UTI
Vaginal Infection
Vaginitis and Vaginosis
Vaginitis/Vaginosis
Variant angina
Vasculitis
VD
Venereal Diseases
Vitamin B12 and Folate Deficiencies
Vitamin B12 Deficiency
Vitamin K Deficiency
Vulvovaginitis
Walking Pneumonia
West Nile Virus
Wilson Disease
WNV
Wound and Skin Infections

“It is commonly thought that laboratory tests provide two-thirds to three-fourths of the information used for making medical decisions. If so, test results had better tell the truth about what is happening with our patients.”

Clinica Chimica Acta 2004;346:3-11


PubMed Overdiagnosis Citations
1970-2014
250
200
150
100
50
0
SEEKING SICKNESS
ALAN CASSELS
Preventing overdiagnosis: how to stop harming the healthy
GPs—Do you want to join the debate on overdiagnosis?
OVER-DIAGNOSED
Overtreated
Overdiagnosis: too much of a good thing?
Overdiagnosis: too much of a good thing?
Science of overdiagnosis to be served up with a good dose of humility
SHANNON BROWNLEE
Overdiagnosis of Disease
A Modern Epidemic
PREVENTING OVERDIAGNOSIS
Commentary
The overdiagnosis nightmare: a time for caution
Stefano Canto
SELLING SICKNESS
RAY MOYNIHAN
ALAN CASSELS
Overdiagnosis – overtreatment
LESS IS MORE
Overdiagnosis and Overtreatment: Evaluation of What Physicians Tell Their Patients About Screening Harms

The Overdiagnosis Problem

It's multifactorial - everyone involved in health care (clinicians, technicians and patients) plays a role

Or in other words - EVERY HUMAN

Overdiagnosis is not just the "lab's" fault - but it is a MAJOR player

Clinical Practice Guidelines - also MAJOR culprits

The Media!

New Rule Grants Patients Direct Access to Lab Results

By Melinda Beck

Feb. 3, 2014 1:05 p.m. ET

Clinical laboratories must give patients access to their own lab-test results upon request, without going through the physician who ordered them, according to a new federal rule announced Monday by the Department of Health and Human Services.

PROBLEM #1

It's typically the same report that goes to health care providers

PROBLEM #2

Many health care providers don't appreciate the key nuances of "lab" tests

MY THESIS

"For much in medicine, we knowingly sell preeminent precision even though we all know in our heart of hearts we can only deliver educated estimates.
I believe most patients would be very understanding about this imprecision if we were just more open about it."
-James McCormack, Pharm D (1959 - hopefully not soon)

"We also CAN'T be precise about the imprecision"

I am speaking in general, and do realise there are always some exceptions

I am presenting concepts

I will be providing ball-park estimates

Two Problems with Faking Precision

FALSE BELIEFS

BELIEF #1 - the good/bad thresholds are relatively black and white

BELIEF #2 -when the numbers change these changes are real

These beliefs can potentially lead to inappropriate feelings
of fear, happiness, frustration, confusion…

Both in patients AND clinicians

Sources of Imprecision

Lab Error

Analytic variation

Biologic variation

Actual LAB errors

Lab Error

0.3%

~60% pre-analytical
~15% analytical
~ 25% post analytical

Table 1. Laboratory errors in stat testing.

Defects: detection steps	Defects found: No.	Defects found: Frequency, %
Preanalytical		
Specimen collected from infusion route	3	1.9
Sample contaminated	1	0.6
Tube filling error	21	13.1
Empty tube	11	6.9
Inappropriate container	13	8.1
Nonrefrigerated sample	3	1.9
Missing tube	5	3.1
Digoxin test timing error	1	0.6
Patient identification error	14	8.8
Request procedure error	12	7.5
Data communication conflict	6	3.8
Physician's request order missed	3	1.9
Order misinterpreted	2	1.3
Check-in not performed (in the Laboratory Information Systems)	4	2.5
Subtotal	99	61.9
Analytical		
Instrument-caused random error	3	1.9
Analytical inaccuracy not recognized	21	13.1
Subtotal	24	15
Postanalytical		
Results communication breakdown	32	20
Lack of communication within laboratory	3	1.9
TAT excessive	2	1.3
Subtotal	37	23.1

Clinical Chemistry 2007;53:1338-42

Dispensing errors ~1-2%

Measurement Landscape

Assuming no pre-analytic issues - timing/labelling etc

Population-based reference intervals

Analytical Variation

Analytic variation

CVA - analytical variation

Biological Variation

Biologic variation

CVI - within subject

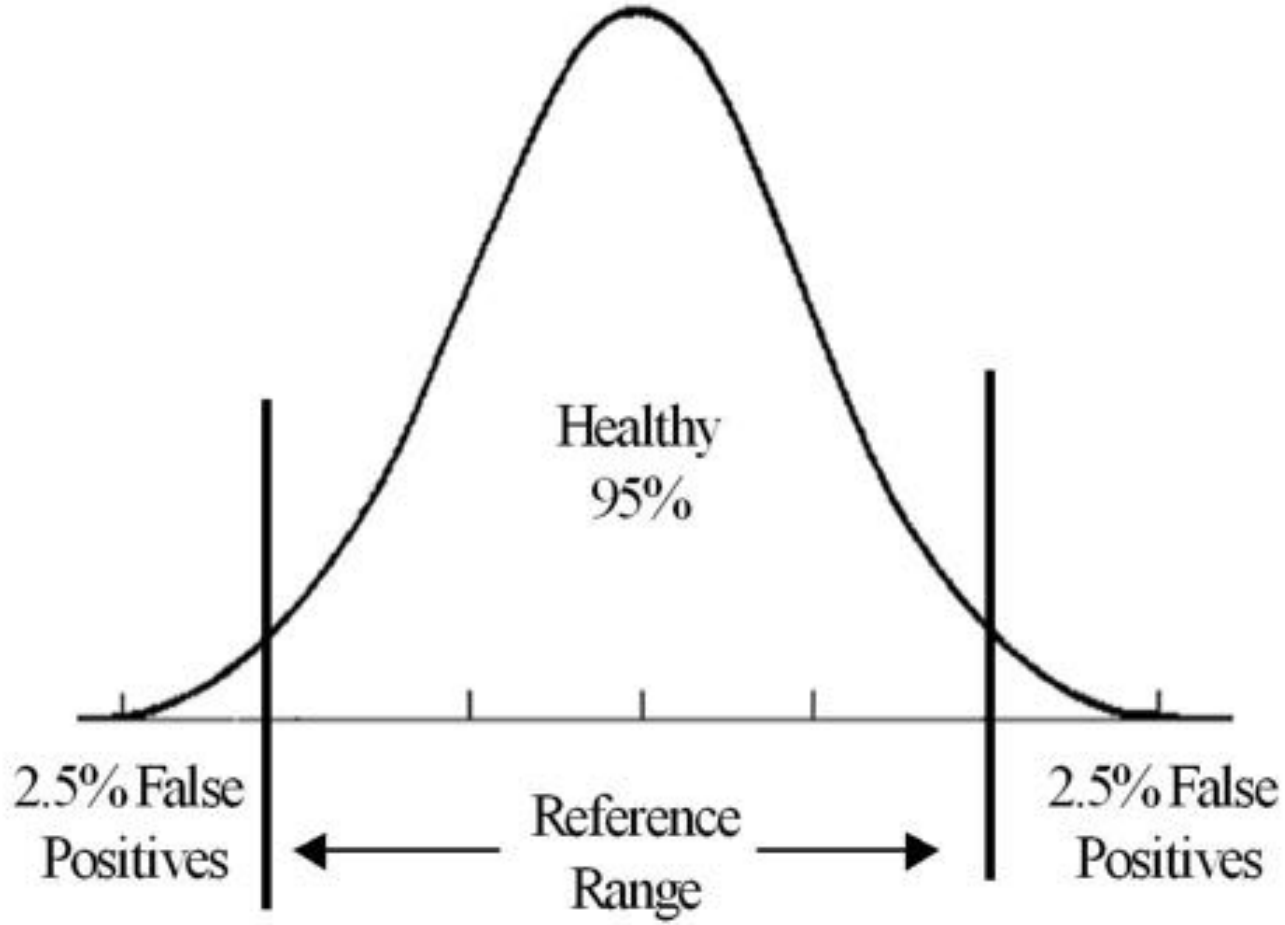
CVG - between subject

Reference change values (RCV)

Population-based reference intervals

Population-based reference intervals

The interval/range where 95% of healthy people fall



Number of Tests Ordered	Probability of at Least One Abnormal Test
1	5%
2	10%
5	23%
10	40%
15	54%
20	64%

Lab results report
exact numbers
BUT
Every test result is
really only a range
that hopefully includes
the true result
+/- 1-2% up to
+/-20-30% or more

YOU CANNOT BE SERIOUS!!
That ball was on the line

When we do tests, typically we are wondering

what are the results NOW, and/or

have they changed from PREVIOUS measurements

Analytic variation

Biologic variation

Every “measurement” will be “different”

Analytic variability

Biologic variability

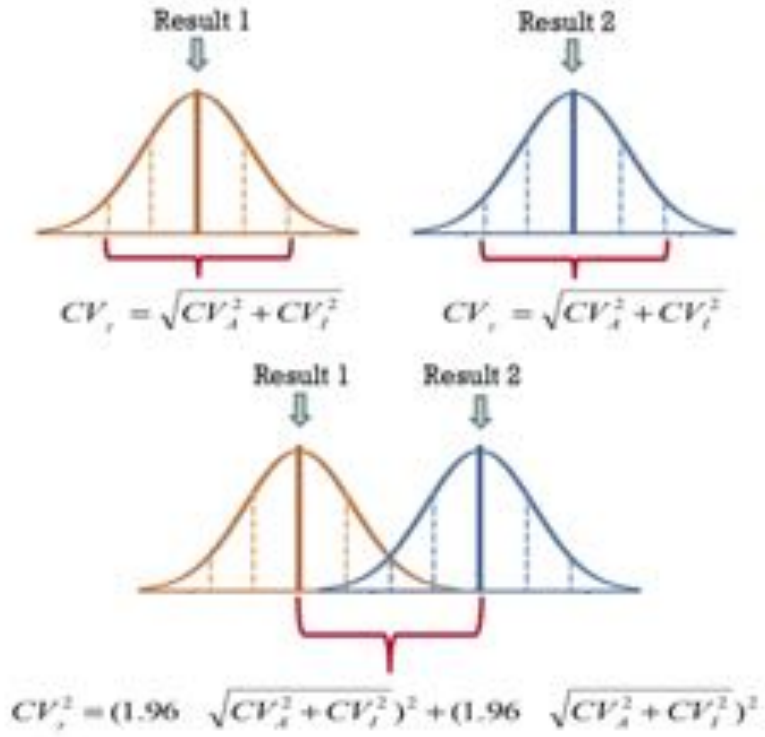
Reference Change Values (RCV)

a tool for assessment of the significance of differences in serial results from an individual

Reference Change Values

Used with SERIAL results to help deal with the analytic imprecision and biologic variation

Coefficients of Variation (total) = analytic PLUS biologic variation



MINIMUM DIFFERENCE between two consecutive results which needs to be EXCEEDED in order for one to state a STATISTICALLY SIGNIFICANT change has taken place

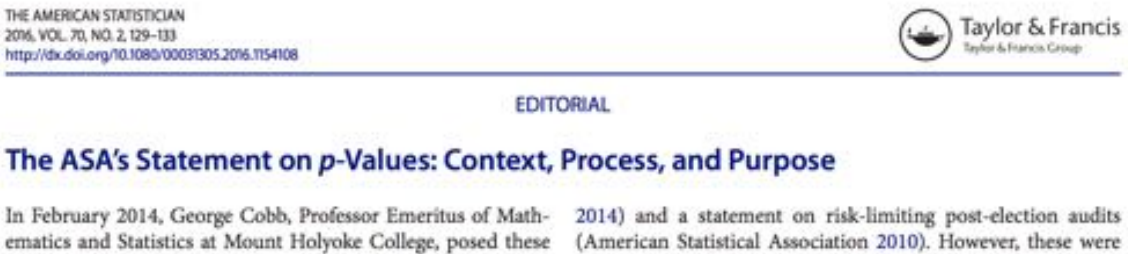
$$RCV = \sqrt{2} * 1.96 * \sqrt{(CV^2_{Analytical} + CV^2_{Intraindividual})}$$

How good, analytically speaking, does a “test” need to be

“The analytical CV (CVA) should be less than one-half the average within-subject biological variation (CVI)”

When it is, the CVA has almost no impact on the RCV - the RCV is pretty much determined by the CVI

Reference change values provide a “p-value” for the differences between two measurements



THE AMERICAN STATISTICIAN
2016, VOL. 70, NO. 2, 129–133
http://dx.doi.org/10.1080/00031305.2016.1154108

Taylor & Francis
Taylor & Francis Group

EDITORIAL

The ASA's Statement on *p*-Values: Context, Process, and Purpose

In February 2014, George Cobb, Professor Emeritus of Mathematics and Statistics at Mount Holyoke College, posed these

2014) and a statement on risk-limiting post-election audits (American Statistical Association 2010). However, these were

“It’s science’s dirtiest secret: The ‘scientific method’ of testing hypotheses by statistical analysis stands on a flimsy foundation.”

“Numerous deep flaws in null hypothesis significance testing.”

“Statistical techniques for testing hypotheses …have more flaws than Facebook’s privacy policies.”

Experts issue warning on problems with P values

Misunderstandings about common statistical test damage science and society

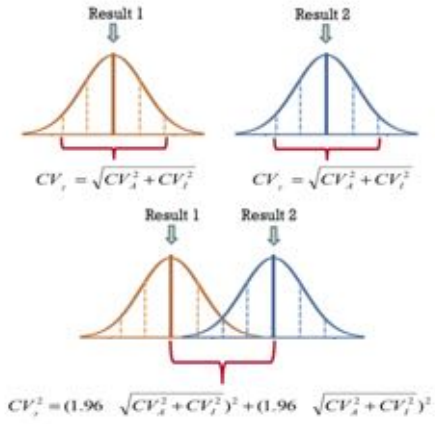
BY TOM SIEGFRIED 10:30AM, MARCH 11, 2016

Reference Change Values

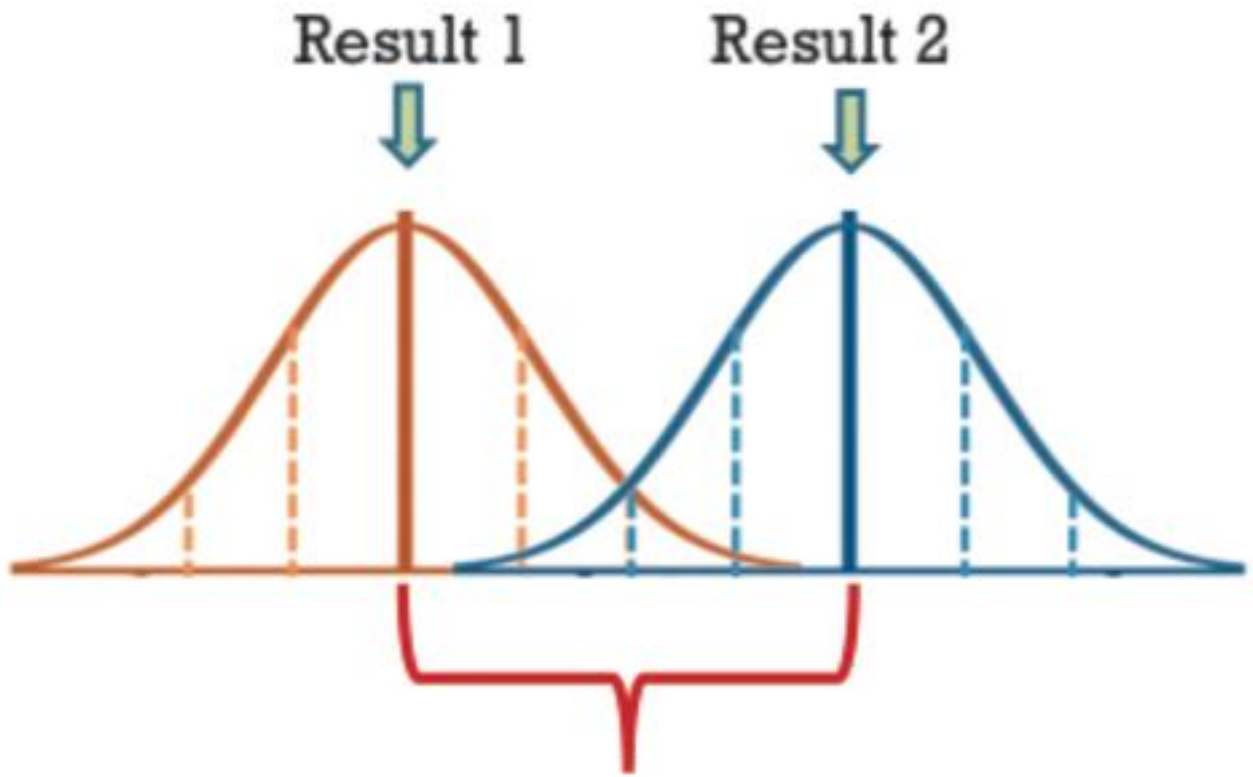
findings of a “significant difference" JUST means we are ruling out that the difference seen is due to chance

NOT

THAT THE MAGNITUDE OF THE DIFFERENCE SEEN IS THE ACTUAL MAGNITUDE OF THE DIFFERENCE



We believe these two results are different



can’t necessarily quantify this difference with any precision

What about multiple measurements?

Table 1. RCV using multiple estimates of the initial and new set points, expressed as a fraction of traditional RCV from two singleton measurements.

		Number of results estimating initial set point				
		1	2	3	4	5
Number of results estimating new set point	1	1.00	0.87	0.82	0.79	0.77
	2	0.87	0.71	0.65	0.61	0.59
	3	0.82	0.65	0.58	0.54	0.52
	4	0.79	0.61	0.54	0.50	0.47
	5	0.77	0.59	0.52	0.47	0.45

with 4 measurements before and 4 afterwards
(vs 1 before and 1 after)
you can lower the RCV by 50%

Annals of Clinical Biochemistry 2016;53:413-4

Lab
Error

Analytic
variation

Biologic variation

This is the problem and it is NOT fixable, it is only KNOWABLE

Bone Density
Cholesterol
Blood pressure
Glucose
Vitamin D

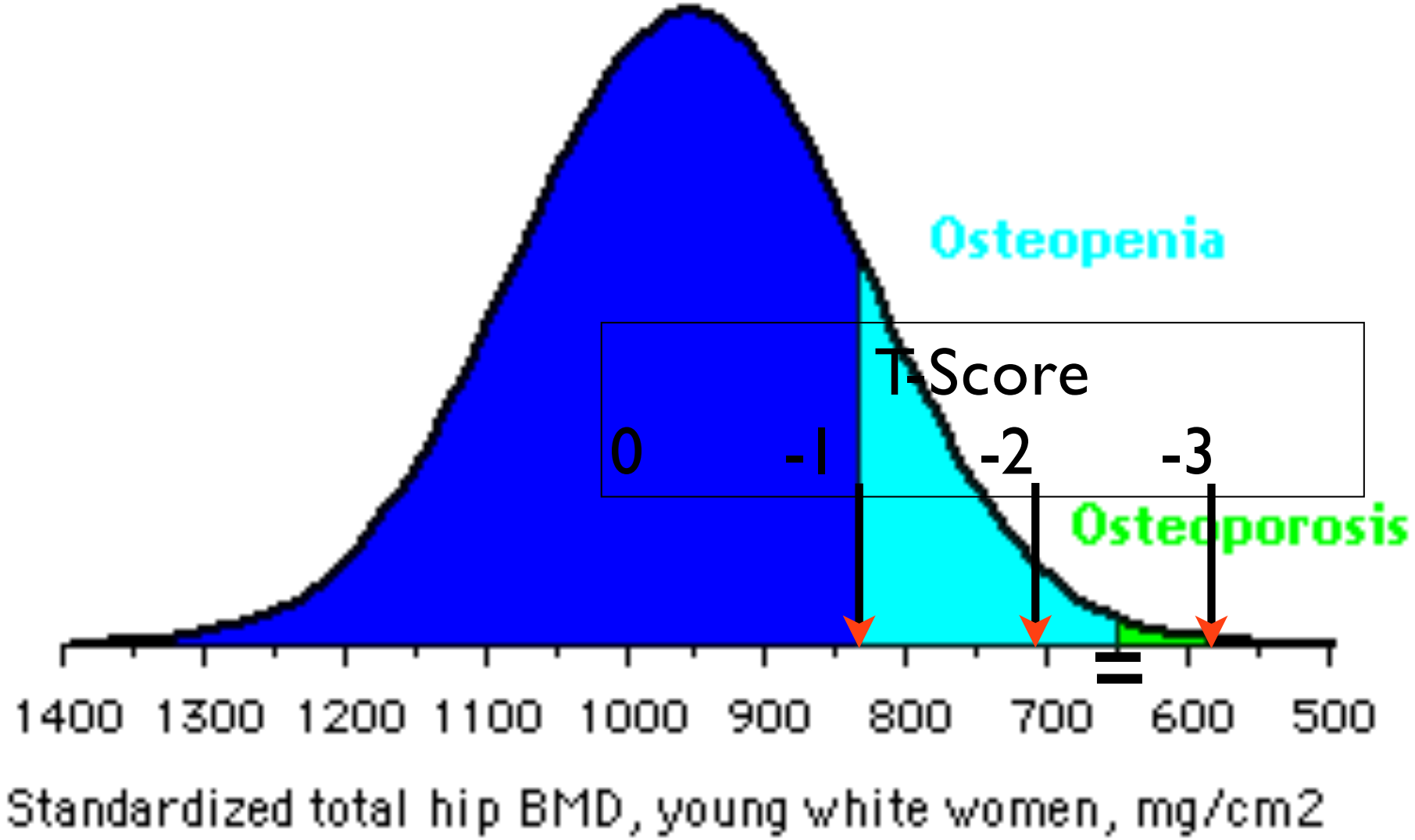
AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE DIAGNOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS **2010**

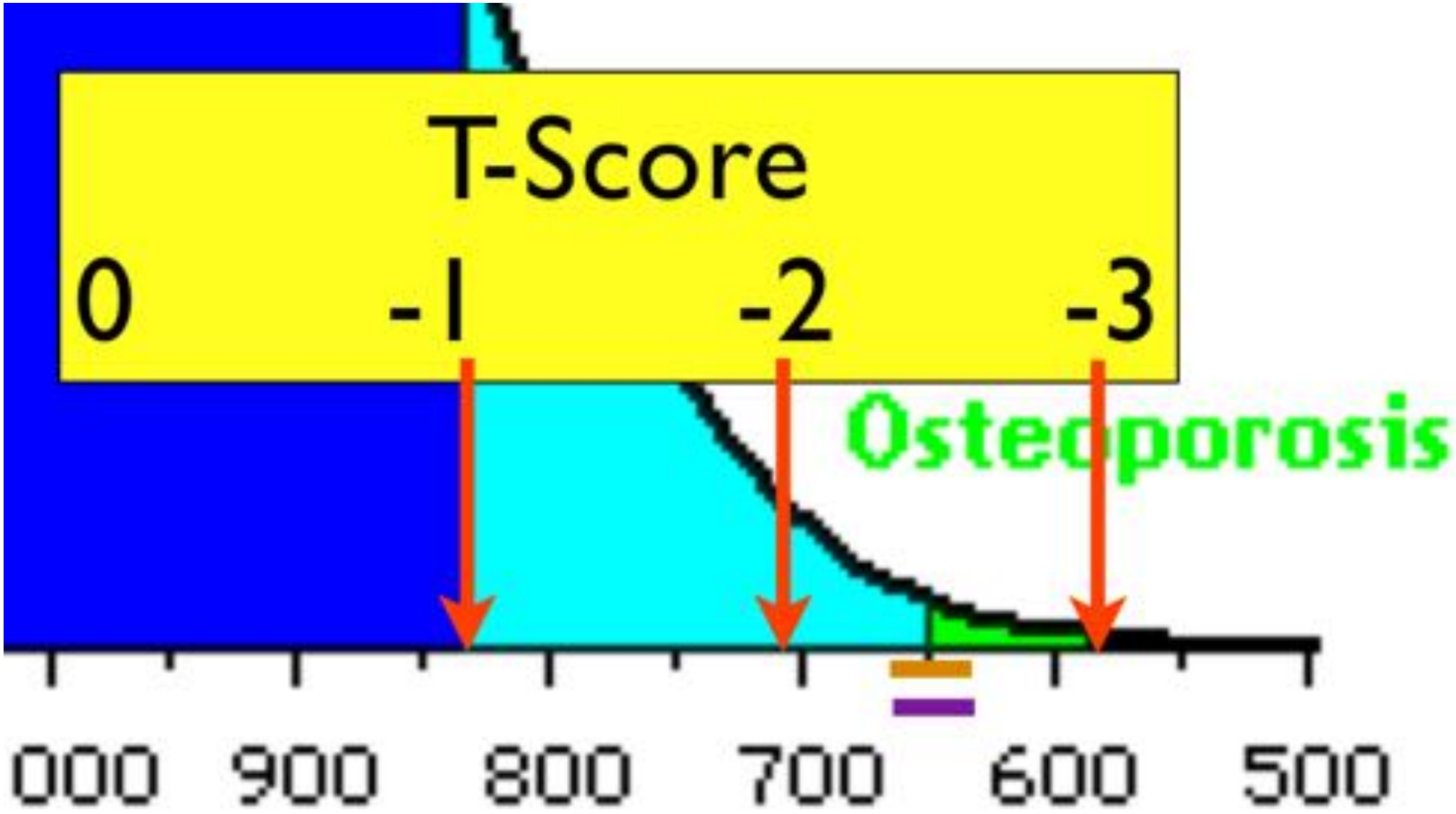
"Obtain a baseline DXA, and repeat DXA every 1 to 2 years until findings are stable. Continue with follow-up DXA every 2 years or at a less frequent interval"

1) Average bone loss per year ~ 0.6%

2) Difference in BMD between drug and placebo - 3 years ~5%

3) BMD measurement precision +/- 2-3%




T-Score
0
-1
-2
-3
Osteoporosis
000
900
800
700
600
500

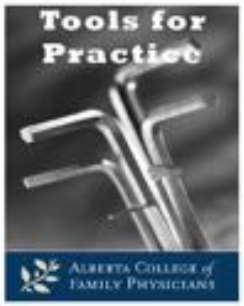
Other Smarter People

Value of routine monitoring of bone mineral density after starting bisphosphonate treatment: secondary analysis of trial data

Katy J L Bell, Andrew Hayen, Petra Macaskill, Les Irwig, Jonathan C Craig, Kristine Ensrud and Douglas C Bauer

BMJ 2009;338;b2266;

"Monitoring BMD in the first 3 years after starting treatment with a bisphosphonate is unnecessary and may be misleading"



Bone Mineral Density – Too much of a good thing?

Clinical Question: Once we have initiated bisphosphonate therapy, how frequently should we check bone mineral density (BMD)?

#32 Christina Korownyk & Michael R. Kolber

"Repeating BMD in the first three years after starting treatment with a bisphosphonate is unnecessary and potentially confusing. The vast majority of patients taking a bisphosphonate will get an adequate increase in BMD after three years and have a reduced fracture risk regardless of BMD changes"

ACP American College of Physicians
Leading Internal Medicine, Improving Lives

2017 CLINICAL GUIDELINE

Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians

2017

"The data do not support monitoring BMD during the initial 5 years of treatment in patients receiving pharmacologic agents to treat osteoporosis."

Other Smarter People

Average bone loss per year ~ 0.6%

Evaluating the Value of Repeat Bone Mineral Density Measurement and Prediction of Fractures in Older Women

The Study of Osteoporotic Fractures

Teresa A. Hillier, MD, MS; Katie L. Stone, PhD; Doug C. Bauer, MD; Joanne H. Rizzo, MS; Kathryn L. Pedula, MS; Jane A. Cauley, DrPH; Kristine E. Ensrud, MD, MPH; Marc C. Hochberg, MD; Steve R. Cummings, MD

Arch Intern Med. 2007;167(2):155-160.

"repeat BMD [8 years] measurement provides little additional benefit as a screening tool"

Arch Intern Med 2007;167:155-60

2016 Canadian Cardiovascular Society Guidelines for the Management of Dyslipidemia for the Prevention of Cardiovascular Disease in the Adult

"In individuals with a modified FRS of 5%-9%, yearly monitoring could be used to evaluate change in risk"

AACE 2017 Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY GUIDELINES FOR MANAGEMENT OF DYSLIPIDEMIA AND PREVENTION OF CARDIOVASCULAR DISEASE

"Lipid status should be re-assessed 6 weeks after therapy initiation and again at 6-week intervals until the treatment goal is achieved."

"While on stable lipid therapy, individuals should be tested at 6-to 12-month intervals"

ARTICLE | Annals of Internal Medicine

Monitoring Cholesterol Levels: Measurement Error or True Change?

Paul P. Glasziou, MBBS, PhD; Les Irwig, MBBS, PhD; Stephane Heritier, PhD; R. John Simes, MBBS, MD; and Andrew Tonkin, MBBS, MD, for the LIPID Study Investigators

Background: Cholesterol level monitoring is a common clinical activity, but the optimal monitoring interval is unknown and practice varies.

Objective: To estimate, in patients receiving cholesterol-lowering medication, the variation in initial response to treatment, the long-term drift from initial response, and the detectability of long-term changes in on-treatment cholesterol level ("signal") given short-term, within-person variation ("noise").

Design: Analysis of cholesterol measurement data in the LIPID

of variation, 7%) to 0.60 mmol/L (23 mg/dL) (coefficient of variation, 11%), but it took almost 4 years for the long-term variation to exceed the short-term variation. This slow increase in variation and the modest increase in mean cholesterol level, about 2% per year, suggest that most of the variation in the study is due to short-term biological and analytic variability. Our calculations suggest that, for patients with levels that are 0.5 mmol/L or more (≥19 mg/dL) under target, monitoring is likely to detect many more false-positive results than true-positive results for at least the first 3 years after treatment has commenced.

Ann Intern Med 2008;148:656-61

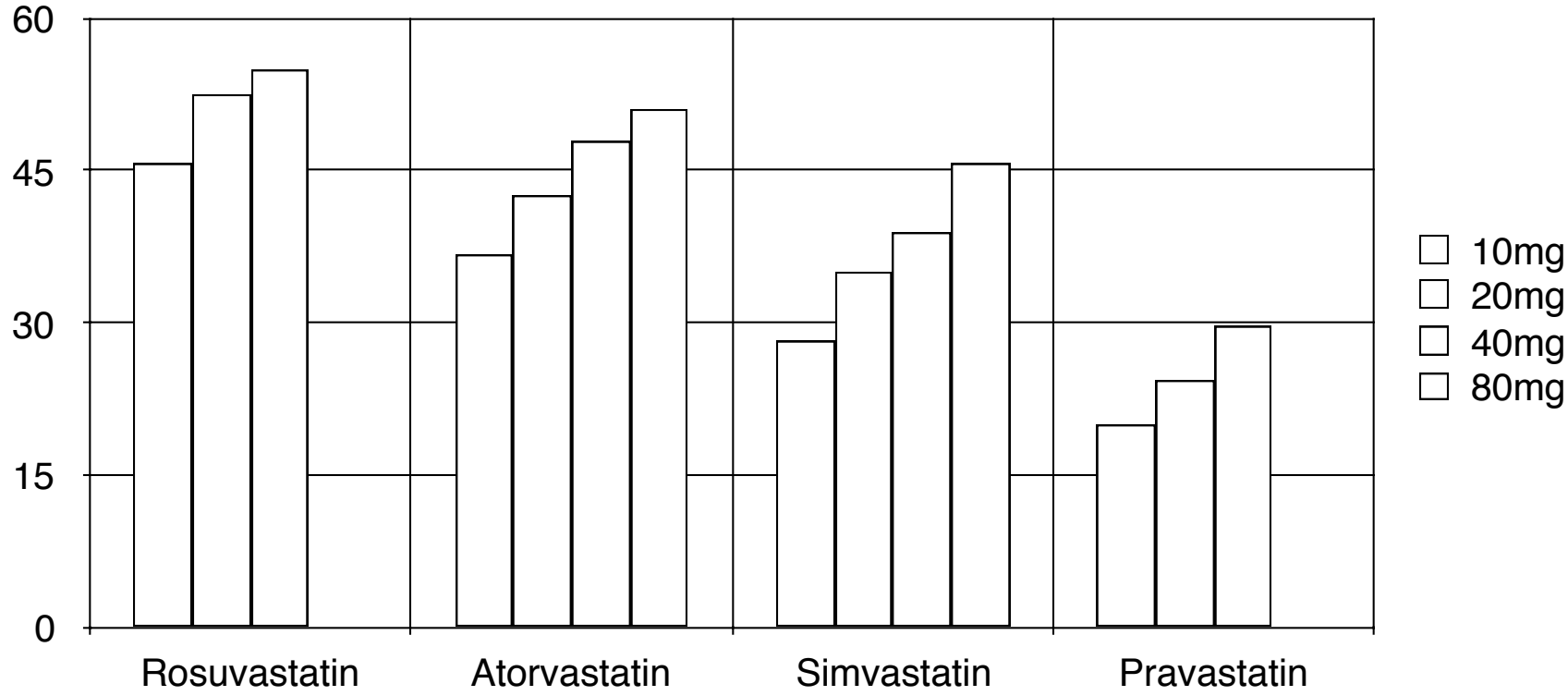
VARIATION
Total chol ~ - 0.80 to 0.80 mmol/L (~30 mg/dL)
LDL chol ~ - 0.5 to 0.5 mmol/L (~20 mg/dL)

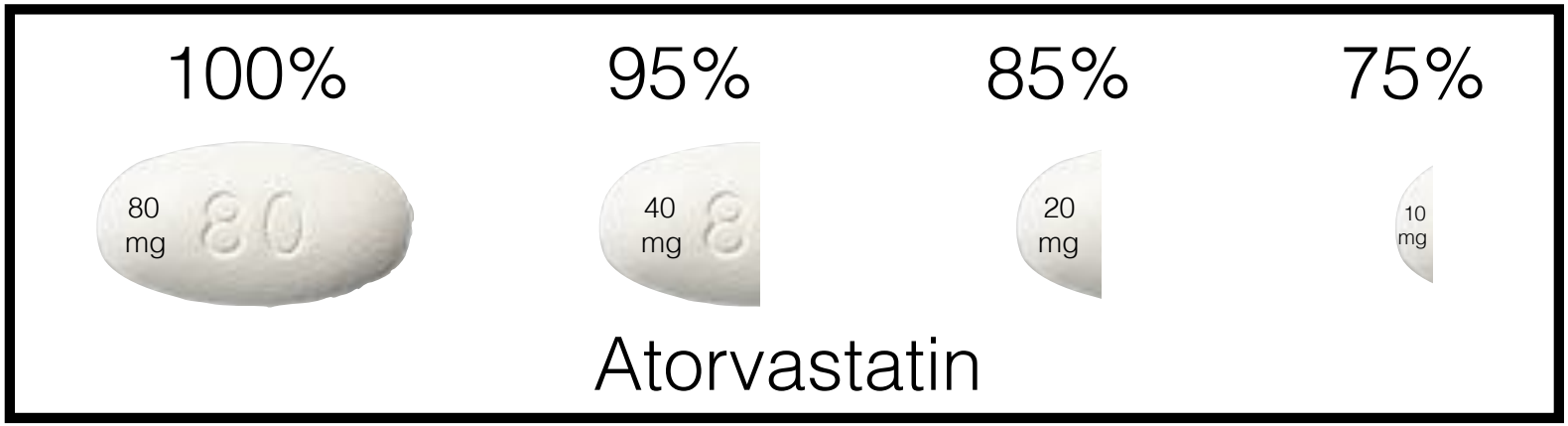
Average increase in cholesterol is 0.5-1%/year

"After initial change only measure every 3-5 years"

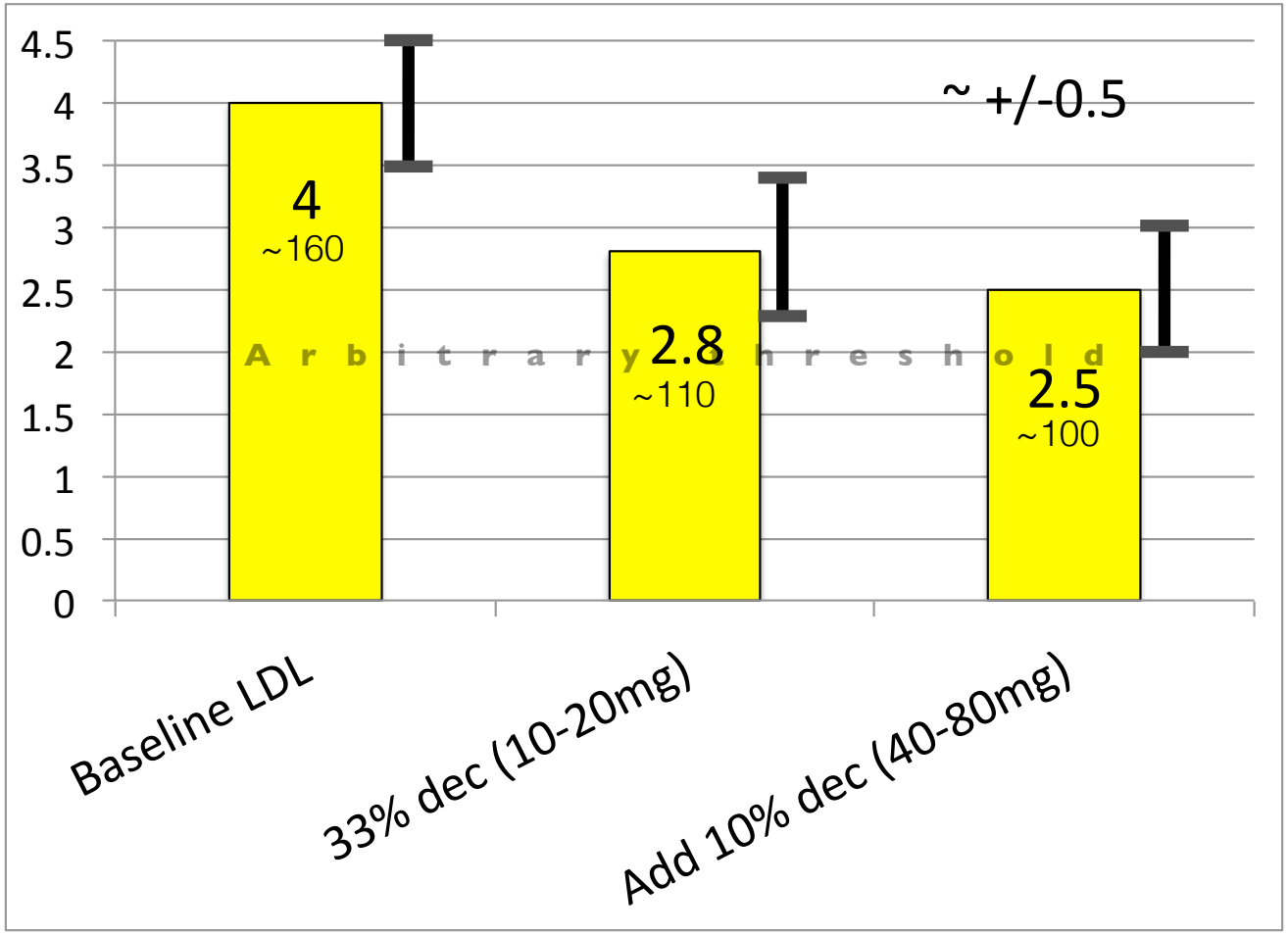
DOSE increases do not lead to proportional EFFECT increases

% reduction in LDL cholesterol





LDL cholesterol - 2 mmol/L ~80mg/dL



RESEARCH

When to remeasure cardiovascular risk in untreated people at low and intermediate risk: observational study

BMJ 2013; 346 doi: http://dx.doi.org/10.1136/bmj.f1895 (Published 3 April 2013)
Cite this as: *BMJ* 2013;346:f1895

"Repeat risk estimation before 8-10 years is not warranted for most people initially not requiring treatment"

Systolic blood pressure

TYPICAL CHANGES SEEN

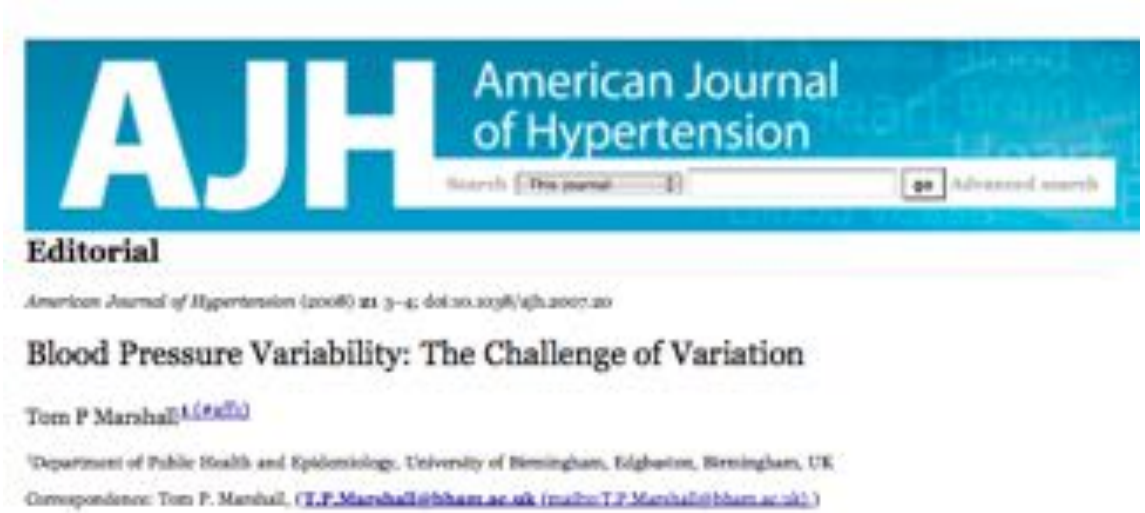
Start medication - avg 9 mmHg ⬇

Increase dose - avg 2-5 mmHg ⬇

Seasonal differences - avg 8 mmHg ⬇ when warm

Age related (per year) - avg 0.5-0.8 mmHg ⬆

Sample size calculation - 40 office measurements before and after treatment to be REASONABLY confident that a 5 mmHg change has occurred



Need changes of at least 10/5 mmHg before you can say there has been a change

Am J Hyper 2008;21:3–4

"clinicians cannot identify individuals who have good or poor responses to drugs"

"coefficients of variation for systolic office, ambulatory, and self-monitored blood pressure, compared at baseline and 6 weeks, were 8.6%, 5.5%, and 4.2% respectively"

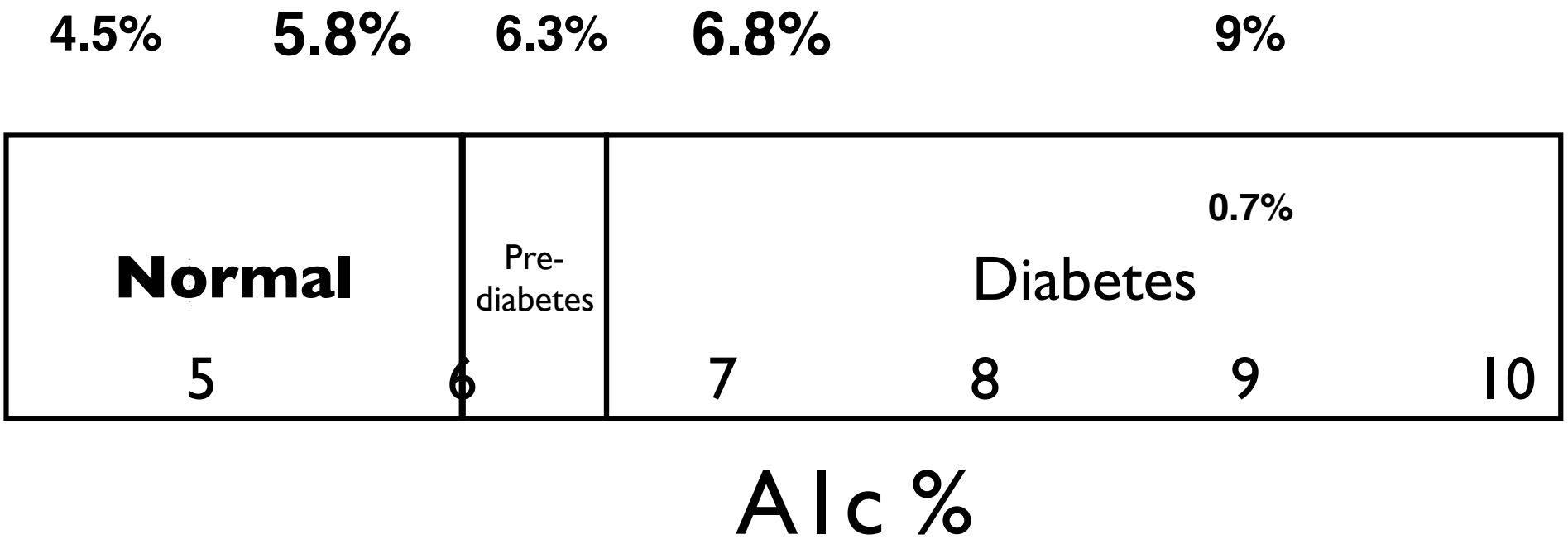
Br J Gen Pract 2010; 60: 675–80

"a single careful blood pressure measurement taken a few months after the start of treatment is not useful for monitoring"

BMJ 2009;338:b1492

Precisely Imprecise

What an A1c result really means



Typical A1c change seen with a medication = 0.7% ⬇

Seasonal variation 0.2-0.5%
Higher in the winter

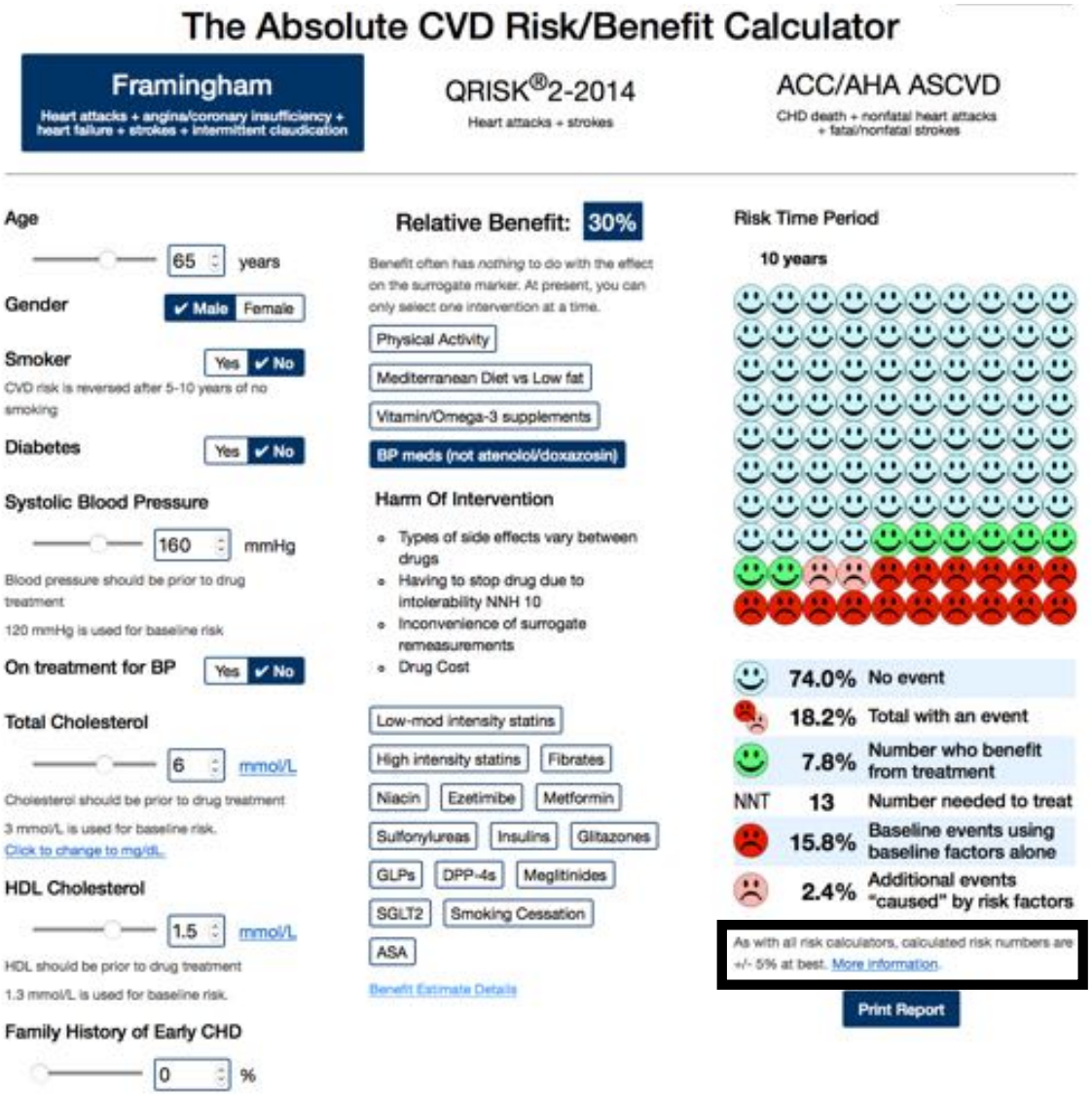
Am J Epi 2004;161:565-74

Yet another IMPORTANT issue for measurements pf glucose, cholesterol, blood pressure and bone density

These are RARELY measures of any disease

They are simply RISK FACTORS

They should be presented in the context of the risk of developing important clinical outcomes - heart attacks, strokes, ESRD etc



Calculate ballpark 10-yr risk of CVD - BP, chol, diabetes
Make estimate of benefit based on the best available evidence
Gives a list of adverse effects to discuss

cvdcalculator.com

BCBiomedical
LABORATORIES LTD.

Cost? $50-60 - 2-3 x the yearly treatment cost


THE GLOBE AND MAIL | NATIONAL

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Provinces struggle with demand for Vitamin D tests

Martin Mittelstaedt

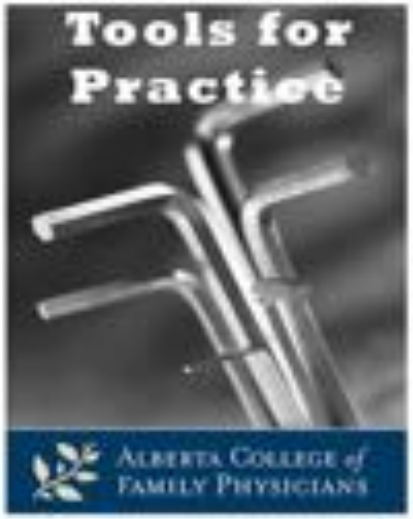
Published on Wednesday, Jan. 06, 2010 6:56PM EST

"the most-ordered hormone assay in the United States"

J Clin Endocrinol Metab
2009;94:1092–3

Adrienne J Lindblad BSP ACPR PharmD, Scott Garrison MD PhD, James McCormack BScPharm PharmD

February 3, 2014



Vitamin D Levels: Vitamin Do or Vitamin Don't

Clinical Question: In adults, what is the evidence to test serum vitamin D levels?

Bottom Line: Routine testing of vitamin D levels is unnecessary. Laboratories often report serum levels between 50 and 75–80 nmol/L as insufficient but this is not supported by consistent or reliable evidence. Additionally, large variability in the test limits interpretation of repeat measurements.

Variability in Measurement

Between lab/Assay variability
"The differences between the mean values for serum 25(OH)D between the laboratories with the highest and lowest values was 38%"
Ost Int 1999;9:394-7

"the mean relative uncertainties...were 19.4%, 16.0%, and 11.3%"
Ost Int 2009 - 9 September 2009 -Online

Within patient variability - 15-20%
"The results of our analyses do not support the view that vitamin D supplements should be given on the basis of measurements of individual 25-OH-vitamin D levels. Conversely, our results indicate that subjects classified as having a sufficient vitamin D status may be diagnosed with vitamin D insufficiency in a subsequent measurement"
Ost Int 1998 8:222–30

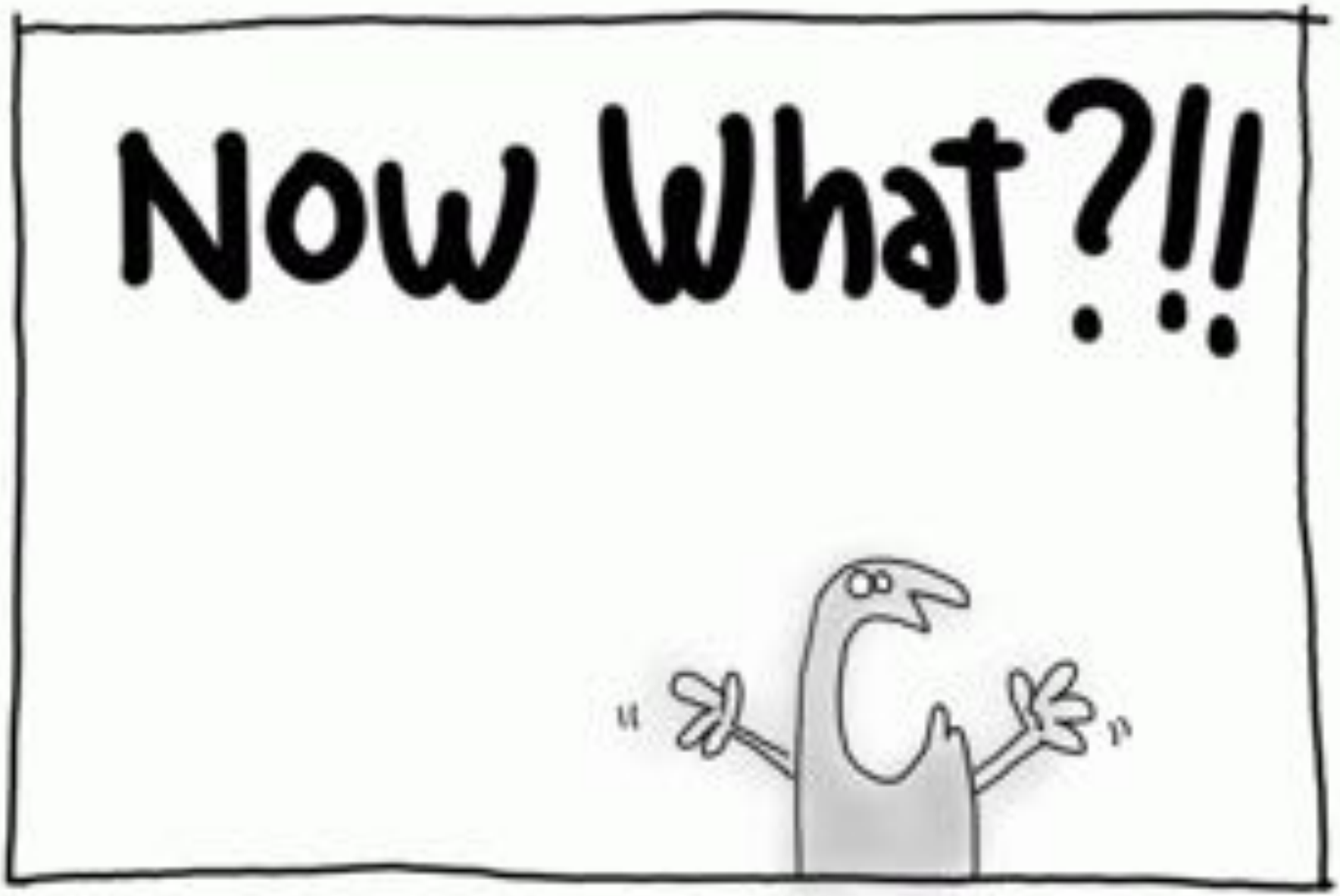
Variability VS Change from Treatment

800 IU raises vitamin D levels by ~ 20 nmol/L

Scand J Clin Lab Invest 2006;66:227–38

This increase is only slightly more than the within-in patient variability (15-20%) in the measurement but we also have analytic variability

*Vitamin D testing is only covered under MSP when the patient is < 19 years or the test is ordered by a specialist. All other vitamin D tests are user paid.


Now What?!!

“The obscure we see eventually.
The completely obvious, it seems,
takes longer.”

Edward R Murrow 1908-1965

The Problem
is
NOT Fixable,
it is
Only
KNOWABLE

Important caveats not discussed

Biological variances are typically from populations - can vary with age etc

Evidence behind the population-based reference intervals

Arbitrary thresholds in “guidelines”

One-sided vs two-sided testing

Not all lab tests are Gaussian/normally distributed

Bayesian approaches - pre-test and post-test probabilities

Point of Care Testing (POCT) is a whole other story

of fear of change/IT/Legal - blah blah blah

Just the facts, Ma'am

Should we…

Openly explain and present lab variability - YES

Openly discuss the potentially black and white things about lab variability - ABSOLUTELY

Continue to use words like low, medium, high, significant - NO, NO, NO, NO

Use a 95% or a 90% or an 85% significance threshold - UNKNOWABLE

Get hung-up on the fact the evidence-base isn't perfect - NO - USE THE BEST AVAILABLE EVIDENCE

Care who is the driver of change - WHOEVER CAN DO IT RIGHT

Report SDs, levels of significance, error bars - IN GENERAL, NO

Discuss the variability or the exceptions to the rule - OF COURSE

Be OK with “ball parking” - WELCOME TO HEALTH CARE

Care if improved lab reporting improves patient outcomes - IT’S REALLY ABOUT DECISIONS AND THE “TRUTH”

Believe it is just the “other” lab’s problem not ours - THAT’S ADORABLE

If I was the boss of “LAB” result reporting

All of this could be done today

Shift from a laboratory perspective to a patient-centered viewpoint

Using BALLPARK estimates

ALWAYS provide the imprecision

Provide MUCH more definitive guidance

Stop using terms like low, medium, high or significant

If they are “risk factor” measurements then they should only be provided with “risk” estimates

Do not do a test without discussion of a pre-test probability and then provide a post-test probability

Make many tests more “inconvenient”?

As much as humanely possible

DO NOT use “flags”, adjectives, or mention SDs, Gaussian distributions, two-sided tests, Z-scores, T-scores, confidence intervals, or p-values.

Not sure if we even need point estimates

Ballpark RCVs

(means you have to see a change of this much to, by definition, rule out chance)

<5%
Chloride
Sodium
Osmolality

5-10%
Albumin
Bone density
Calcium
Haemoglobin
HbA1c
INR
Total protein
Systolic BP

10-20%
Creatinine
Globulins
Glucose
Magnesium
pC02
Potassium
Total cholesterol

20-40%
AST
Alkaline phosphatase
BUN
HDL
LDH
LDL
Phosphorous
Platelets
Rheumatoid factor
Testosterone
Uric acid
WBC

40%-60%
GGT
Neutrophils
PSA
Vitamin D

60% +
ALT
Bilirubin
Folate
Iron
Triglycerides
TSH
Vitamin B12

The magnitude of the imprecision around routinely ordered medical measurements*						
MEASUREMENT	Chloride Sodium Osmolality	Albumin Bone density Calcium Hematocrit Hemoglobin HbA1c INR MCH MCV Total protein Systolic BP	Creatinine Globulins Glucose Magnesium pC02 Potassium PTT Total cholesterol T4	AST Alkaline phosphatase BUN HDL LDH LDL Phosphorous Platelets Rheumatoid factor Testosterone Uric acid WBC	GGT Neutrophils PSA Vitamin D	Aldosterone ALT Bilirubin Folate Iron Lactate Triglycerides TSH Vitamin B12
Approximate +/- range for a single measurement	~1-3%	~3-7%	~7-15%	~15-30%	~30-50%	~>50%
The magnitude of the change required between two serial measurements so one can be reasonably confident there has been a change**	~2-5%	~5-10%	~10-20%	~20-40%	~40-60%	~>60%

* based on the analytic and biologic variation

** also known as the reference change value

Data collated primarily from here - https://www.westgard.com/biodatabase1.htm
but some also taken and confirmed from a few other sources - numbers rounded off for ease of use
James McCormack BSc (Pharm), Pharm D - therapeuticseducation.org

The issue of Analytic/BIOLOGIC variation

	Statins (LDL/total chol)	BP meds (SBP)	Glucose meds (A1c)	Bone density meds (DEXA)
Changes that need to occur to rule out chance (RCV)	LDL ~20-40% Total chol 10-20%	~5-10%	~5-10%	~3-5%
Typical changes per year as one ages	~0.5-1% ⬆	~0.5-8 mmHg ⬆ (~0.5%)	~0.5% ⬆	~0.5% ⬇
Typical changes seen with treatment	10-20 mg ~30% ⬇ Inc dose to 40-80mg ~10% ⬇	Initial dose 7-9mmHg (~5%) ⬇ Increased dose 2-5 mmHg (~2-3%) ⬇	0.7% A1c (~10%) ⬇	5% ⬆ over 3 years

RCV = reference change value

~WHAT CHANGE
IN HEIGHT CAN
YOU PICK UP IF
THE “HOM” RCV WAS…

RCV 2% - 5’11”- 6’1”

RCV 5% - 5’10”- 6’2”

RCV 10% - 5’9” - 6’3”

RCV 20% - 5’6”- 6’6”

RCV 30% - 5’0”- 7’0”

RCV 40% - 4’6” - 7’6”

RCV 60% - 4’0” - 8’0”

6’ TALL

2%

Chloride
Sodium
Osmolality

5%

Albumin
Bone density
Calcium
Haemoglobin
HbA1c
INR
Total protein
Systolic BP

10%

Creatinine
Globulins
Glucose
Magnesium
pC02
Potassium
Total chol

20%

30%

AST
Alk phos
BUN
HDL
LDH
LDL
Phos
Platelets
RF
Testosterone
Uric acid
WBC

40%

GGT
Neutrophils
PSA
Vitamin D

60%

ALT
Bilirubin
Folate
Iron
Triglycerides
TSH
Vitamin B12

“We should stop using clinical practice guidelines when it comes to teaching health care providers - or should we?”

James McCormack, BSc(Pharm), Pharm D
Professor, Faculty of Pharmaceutical Sciences, UBC

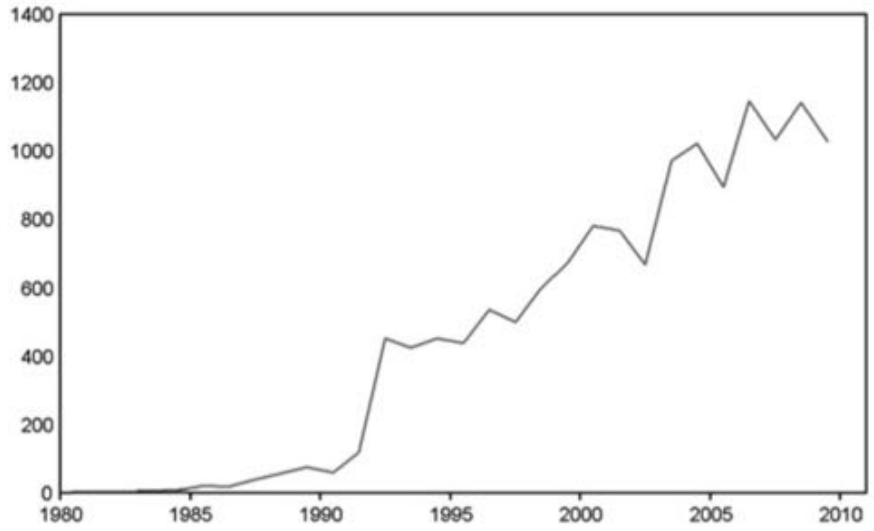


Figure 1 Number of guidelines in PubMed.

What is a Clinical Practice Guideline (CPG)?

The Institute of Medicine definition:

"…statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options”

Clinical Practice Guidelines in Practice and Education

Alfred O. Berg, MD, MPH, David Atkins, MD, MPH, William Tierney, MD

1997 - THE REASONS FOR INTEREST IN QUALITY CLINICAL PRACTICE GUIDELINES

"medical history is littered with clinical practice guidelines that have been fatally incorrect"

"the physician's ability to keep up with the medical literature erodes with each year's burden"

"costly and unexplained variability in medical practice"

"growing demand from patients for greater participation in medical decisions"

J Gen Intern Med 1997;12(Suppl 2):S25–S33

National Guideline Clearinghouse

The Number of Guidelines

Diseases/conditions - 2,983

Treatments/interventions - 7,364

~10,000 guidelines ~10 pages each?

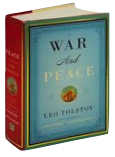
~100,000 pages

500 pages ~ 2 inches

400 inches ~ 33 feet ~10 meters

Highest pole vaulter ~ 20 feet ~ 6 meters

War and Peace is ~1500 pages ~ 70 copies



Wrong guidelines: why and how often they occur

Primiano Iannone,[1] Nicola Montano,[2] Monica Minardi,[3] James Doyle,[3] Paolo Cavagnaro,[4] Antonino Cartabellotta[5]

"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."

EBM 2017;22:1-3

Wrong guidelines: why and how often they occur

Primiano Iannone,[1] Nicola Montano,[2] Monica Minardi,[3] James Doyle,[3] Paolo Cavagnaro,[4] Antonino Cartabellotta[5]

"guideline reliability is largely over-stated, and guidelines still suffer methodological flaws, limited panel composition and conflicts of interests, making their conclusions often untrustworthy. Even when evidence-based methodology is claimed, it is often not fully adopted and the 'evidence-based quality mark' gets misappropriated by vested interests"

EBM 2017;22:1-3

Wrong guidelines: why and how often they occur

Primiano Iannone,[1] Nicola Montano,[2] Monica Minardi,[3] James Doyle,[3] Paolo Cavagnaro,[4] Antonino Cartabellotta[5]

"Furthermore, no official, publicly accountable, reliable, independent and unconflicted rating agency of published guidelines exists."

EBM 2017;22:1-3

Where to find CPGs

Canadian Medical Association Infobase (Canada) - Clinical Practice Guidelines - www.cma.ca/cpgs

National Guideline Clearinghouse (USA) - www.guideline.gov

National Health Service Evidence (UK) - www.evidence.nhs.uk)

Clinical Practice Guidelines Portal (Australia) - www.clinicalguidelines.gov.au

Turning Research Into Practice (TRIP) - www.tripdatabase.com

PubMed - can limit a search to practice guideline

Just do a google search

How to assess CPGs

Appraisal Tools for Clinical Practice Guidelines: A Systematic Review

"the most comprehensively validated appraisal tool is the AGREE II instrument

PLoS ONE 8(12): e82915. doi:10.1371/journal.pone.0082915

Appraisal of Guidelines for Research and Evaluation (AGREE) II

DOMAIN 1. SCOPE AND PURPOSE

DOMAIN 2. STAKEHOLDER INVOLVEMENT

DOMAIN 3. RIGOUR OF DEVELOPMENT

DOMAIN 4. CLARITY OF PRESENTATION

DOMAIN 5. APPLICABILITY

DOMAIN 6. EDITORIAL INDEPENDENCE

OVERALL GUIDELINE ASSESSMENT

How to use CPGs

Is the CPG trustworthy?

Is the CPG applicable to your patient?

Is the CPG setting similar to your practice?

Does the CPG reflect you or your patient's values and preferences?

The Jekyll and Hyde problem with CPGs

Reassessment of Clinical Practice Guidelines

Go Gently Into That Good Night

Terrence M. Shaneyfelt, MD, MPH
Robert M. Centor, MD

of 44 guidelines, 87% of the guideline authors had some form of industry tie.[6]

Other biases are also important. The specialty composi-

often “have a one-size-fits-all mentality and do not build flexibility or contextualization into the recommendations”

“greater concern, however, is that some of these consensus statements are being turned into performance measures”

JAMA 2009;301:868-9

STATEMENT

Rethinking the Role of Clinical Practice Guidelines in Pharmacy Education

Daniel L. Brown, PharmD

Palm Beach Atlantic University Lloyd L. Gregory School of Pharmacy, West Palm Beach, Florida

"CPGs can undermine clinical growth by providing a tempting academic short-cut: memorizing clinical facts rather than learning clinical principles"

Amer J Pharmaceutical Education 2015;79

July 8, 2009

Clinical Practice Guidelines and Scientific Evidence

Francesco Enia, MD

JAMA. 2009;302(2):142-147. doi:10.1001/jama.2009.910

"Rather than endeavor to design a map with an answer for every question, I believe that it would be preferable to educate clinicians to handle clinical reality directly and without filtered advice"

JAMA July 8 2009

Clinical Practice Guidelines and Scientific Evidence

Shyam S. Kothari, MD

"Bombarding students with guidelines for all scenarios … may seem more efficient in the short-term but does little to enhance discriminatory skills and numbs the facility for critical thinking."

JAMA 2009;302:145

Spectrum of Decisions

Immediate life-threatening issues or very "technical" work - surgery, dispensing etc - YES

Guidelines, even policies, are likely very useful

Symptom treatment - SORT OF

Each person is an experiment - need to know just what has the potential to work and the safety

Risk factor interventions - NO

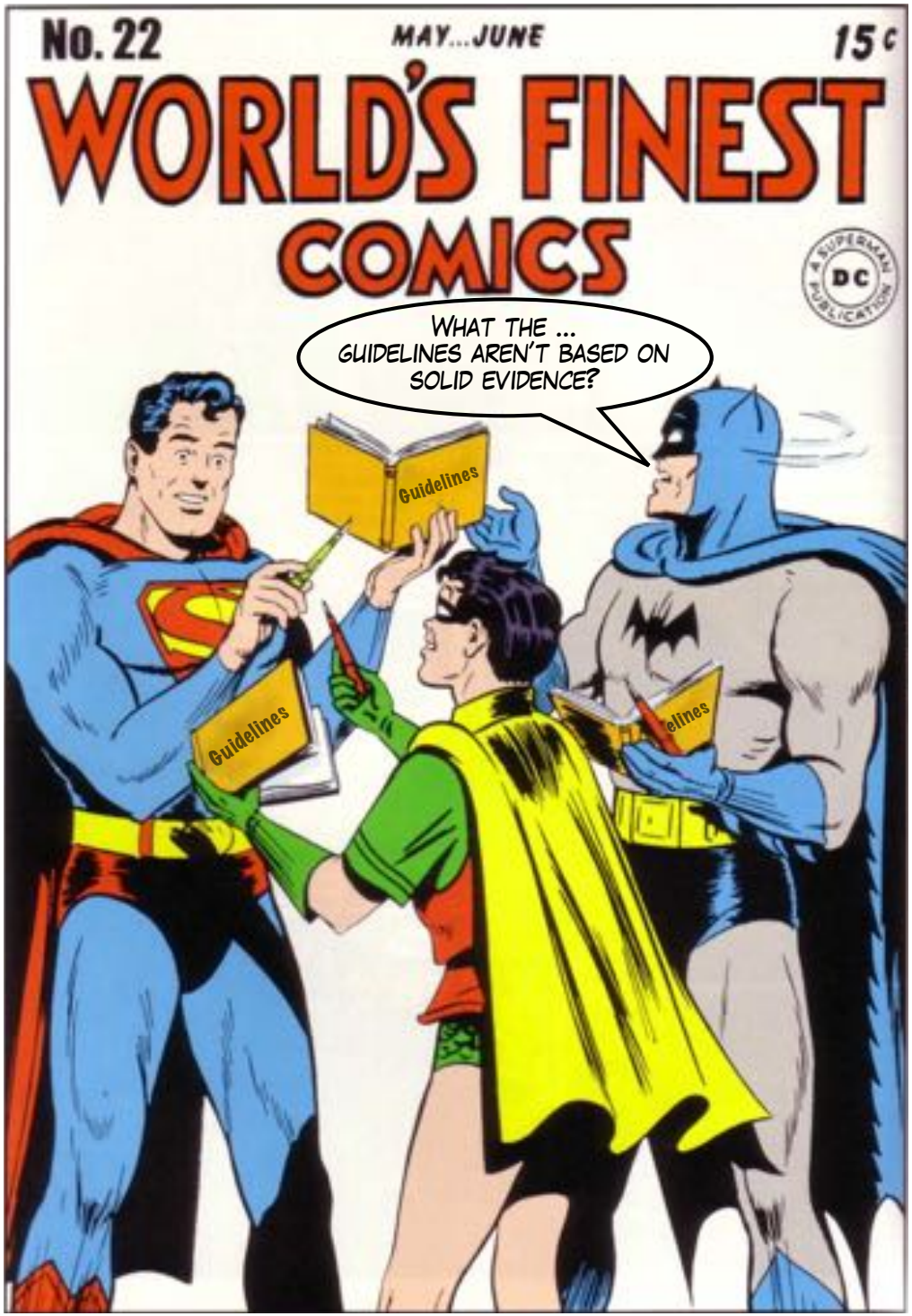
At least not what CPGs are now

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



How evidence-based are CPGs?

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

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Pierluigi Tricoci; Joseph M. Allen; Judith M. Kramer; et al.

JAMA. 2009;301(8):831-841 (doi:10.1001/jama.2009.205)

Analysis of Overall Level of Evidence Behind Infectious Diseases Society of America Practice Guidelines

Dong Heun Lee, MD; Ole Vielemeyer, MD *Arch Intern Med. 2011;171(1):18-22*

Clinical Endocrinology (2013) 78, 183–190 doi: 10.1111/j.1365-2265.2012.04441.x

METHODOLOGICAL ASSESSMENT IN ENDOCRINOLOGY

A comparative quality assessment of evidence-based clinical guidelines in endocrinology

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

BMJQS

The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies

Table 2 Appraisal of Guidelines, Research and Evaluation domain scores of guidelines over time (total sample=608)

	1988–1992 (n=9)	1993–1997 (n=102)	1998–2002 (n=291)	2003–2007 (n=206)	p Value for trend
Domain scores					
Scope and purpose	44	61	60	71	<0.001
Stakeholder involvement	18	38	33	37	0.01
Rigour of development	14	41	43	44	0.003
Clarity and presentation	32	56	55	68	<0.001
Applicability	10	30	18	23	<0.001
Editorial independence	17	30	28	33	0.26

Top Score = 100%

Engaging the right people, quality of evidence appraisal, providing useful tools, and competing interests have not improved in 14 years (1993-2007)

Qual Saf Health Care 2010;19:e58. doi:10.1136/qshc.2010.042077

Recent examples of Guideline **Quality/Rigour**

AGREE II (Appraisal of Guidelines for Research and Evaluation)

is the instrument typically used ***- 207 guidelines***

avg 55% - neuropathic pain - 16 CPGs - range 27%-88% - BMC Anesthesiology 2016;16:12

avg 30% - hypertension - 11 CPGS - range 8%-86% - PLoS ONE 2013 8(1): e53744

avg 32% - asthma - 18 CPGs - range 8%-64% - Chest 2013 144: 390-7

avg 48% - diabetes - 24 CPGs - range 0%-81% - PLoS ONE 2013 8(4): e58625

avg 20% - vancomycin - 12 CPGs - range 4%-73% - PLoS ONE 2013 9(6): e99044

avg 18% - hypertension (China) - 17 CPGs - range 1-36% - BMJ Open 2015;5:e008099

avg 8% - respiratory (China) - 109 CPGs - range 0%-27%- Chest 2015;148:759-766

August 2016

Original Article

Glycemic Control for Patients With Type 2 Diabetes Mellitus

Our Evolving Faith in the Face of Evidence

René Rodríguez-Gutiérrez, MD, MSc; Victor M. Montori, MD, MSc

Evidence since 1998 for
Tight glycemic control (A1c 6.5%-7%) vs less tight (A1c 7%-8.5%)

Endpoints - End Stage Renal Disease/dialysis, renal death, blindness or clinical neuropathy

5 large trials, 8 meta-analyses, 2 follow-up trials

31 estimates of outcomes

- 2 (6%) suggested benefit
- 29 (94%) suggested NO benefit

Endpoints - all-cause mortality, CV mortality, non-fatal MIs, stroke, amputations/ PVD

5 large trials, 10 meta-analyses, 5 follow-up trials

78 estimates of outcomes

- 10 (13%) suggested benefit
- 64 (82%) suggested NO benefit
- 4 (5%) suggested harm

Circ Cardiovasc Qual Outcomes. 2016;9:00-00. DOI: 10.1161

Overall estimates of benefits and harms (micro and macro)

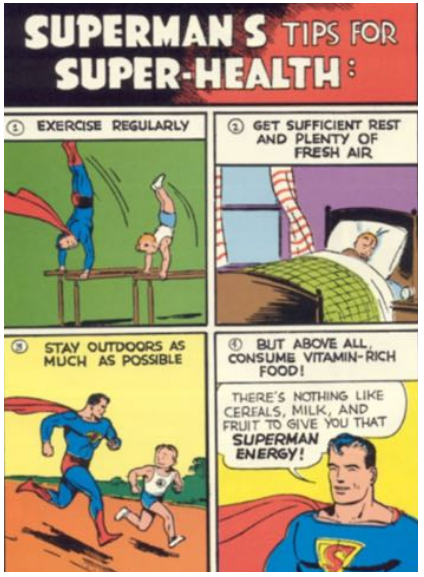
11% of estimates = a benefit

4% of estimates = harm

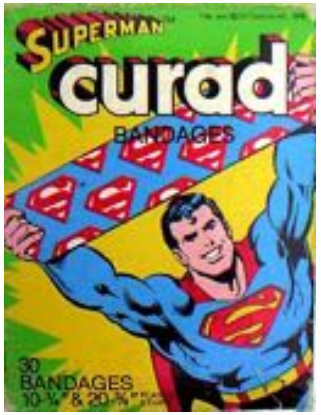
85% of estimates = no benefit

despite this, over the last 10 years -
"practice guidelines and published statements offer a consistent and confident consensus, with 100% of the guidelines and 77% to 100% of the statements in favor of tight glycemic control to prevent microvascular complications"

Circ Cardiovasc Qual Outcomes. 2016;9:00-00. DOI: 10.1161



Who writes/ sponsors guidelines?



Research

Contributors to primary care guidelines

What are their professions and how many of them have conflicts of interest?

G. Michael Allan MD CCFP Roni Kraut Aven Crawshay Christina Korownyk MD CCFP
Ben Vandermeer MSc Michael R. Kolber MD CCFP MSc

176 PRIMARY CARE guidelines in the CMA database

CONTRIBUTORS

54% non–family physician specialists
17% family physicians - 8% if industry sponsored
11% other clinicians
8% non-clinician scientists
6% nurses
3% pharmacists

69% of guidelines didn't report conflicts of interest

Can Fam Physician 2015;61:52-8

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/

Prevalence of financial conflicts of interest among panel members producing clinical practice guidelines in Canada and United States: cross sectional study

~50-80% of panel members on guidelines have financial COIs

BMJ 2011;343:d5621 doi: 10.1136/bmj.d5621

EVIDENCE BASED MEDICINE

Why we can't trust clinical guidelines BMJ;2013:346

Despite repeated calls to prohibit or limit conflicts of interests among authors and sponsors of clinical guidelines, the problem persists. **Jeanne Lenzer** investigates

Adding "value" to clinical practice guidelines

James P. McCormack PharmD Peter Loewen PharmD

5 Canadian Guidelines for
blood pressure, cholesterol, glucose, and bone density

197 PAGES - 90,000 WORDS

99(0.1%) words - relevant to
patients' values and preferences

Can Fam Physician 2007;53:1326-27

Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach

Update to a Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes

Diabetes Care 2015;38:140–149 | DOI: 10.2337/dc14-2441

Diabetes Care
THE JOURNAL OF CLINICAL AND APPLIED RESEARCH AND EDUCATION
January 2015 Volume 38, Supplement 1

Standards of Medical Care in Diabetes—2015

Diabetes Care January 2015

113 PAGES

Looked for info on

- Risk estimation (magnitude)
- Impact of treatment on risk
- Potential harms (magnitude)

"The information presented in these documents is glucose-centric and not organized or presented in a way that could be construed as supporting shared decision making"

Their response

“would like to thank McCormack et al for their thoughtful letter regarding the American Diabetes Association’s Standards of Medical Care in Diabetes”

“agrees that shared decision making is a valuable aspect of diabetes care … that process would be incredibly labor intensive and would make the Standards long and unwieldy”

“Clinical guidelines are the foundation for evidence-based medicine”

Guidelines

Hypertension Canada's 2016 Canadian Hypertension Education Program Guidelines for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension

~11,800 words - 20 pages

Total mention of values and preferences - 0.19% of the words

"Practitioners are advised to consider patient preferences, values, and clinical factors when determining how to best apply these recommendations at the bedside"

"In the absence of Canadian data to determine the accuracy of risk calculations, **avoid using absolute levels of risk** to support treatment decisions"

ACP American College of Physicians — Leading Internal Medicine, Improving Lives

2017 CLINICAL GUIDELINE

Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians

~8,700 words - 27 pages

Benefits

No numbers whatsoever for fracture risk or fracture benefit

Do present info in an appendix - new studies

Harms

2017

28 numeric mentions of side effects

6 absolute numbers

22 relative numbers

One mention of patient preferences

Recommendation 6: *ACP recommends that clinicians should make the decision whether to treat osteopenic women 65 years of age or older who are at a high risk for fracture based on a discussion of patient preferences, fracture risk profile, and benefits, harms, and costs of medications. (Grade: weak recommendation; low-quality evidence)*

ACP American College of Physicians
Leading Internal Medicine, Improving Lives

2017

CLINICAL GUIDELINE

Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians

Recommendations: Recommendation 1: *ACP recommends that clinicians offer pharmacologic treatment with alendronate, risedronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis. (Grade: strong recommendation; high-quality evidence)*

"Evidence is insufficient to determine the comparative effectiveness of pharmacologic therapy or the superiority of one medication over another, within the same class or among classes, for prevention of fractures"

ACP American College of Physicians
Leading Internal Medicine, Improving Lives

2017 CLINICAL GUIDELINE

Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians

2017

"The data do not support monitoring BMD during the initial 5 years of treatment in patients receiving pharmacologic agents to treat osteoporosis."

Patient benefit expectations

Patients' Expectations of the Benefits and Harms of Treatments, Screening, and Tests
A Systematic Review

Tammy C. Hoffmann, PhD; Chris Del Mar, MD, FRACGP

BENEFIT - 88% of study authors concluded that participants **overestimated benefits**

HARM - 67% **underestimated harm**

JAMA Intern Med 2015;175:274-286

Evaluating physician understanding of harms and benefits of common tests and therapies

Paper survey to residents and attending internal medicine physicians
– 18 questions – 117 people responded

	Estimate of benefit in absolute terms						
Green cells are the correct answer	<1%	1 to 5%	5 to 10%	10 to 20%	20 to 45%	45 to 70%	70 to 100%
	Percent of respondents						
Mild HTN 5 years	11	35	28	19	7	1	1
Aspirin with risk factors 5 years	8	32	29	17	8	3	3
Aspirin in CVD 5 years	0	16	29	30	16	8	0
Warfarin Afib 1 year	3	31	29	17	12	8	0
Hip fracture osteoporosis 5 years	3	24	30	24	13	5	0
Death from bleed with PPI 5 years	21	22	20	19	9	9	1
Cancer diagnosis among + screening	4	14	23	35	18	7	0
Major bleeding with ASA 5 years	21	46	21	8	3	0	0
Major bleeding with warfarin 1 year	14	42	30	11	2	2	0
Unneccessary biopsy with screening 10 years	1	9	15	33	26	15	0

79% overestimated benefit

66% overestimated harm

67% were unconfident

JAMA Aug 29 2016

307 subjects using a written questionnaire and interview

Results

Patients	Median acceptable absolute % benefit threshold	% that would take a "safe" drug for 5 years		Absolute % benefit they felt they were getting from their drug	% who wanted to be told percent chance of benefit
		If benefit over 5 years was < 5%	If benefit over 5 years was < 5% AND their MD recommended it		
Post MI patients	20	32	69	70	79
On drugs	20	29	74	68	72
No drugs	30	21	56	-	84

Clin Med 2002;2:527-33

Ability of clinicians to make an estimate of CHD risk

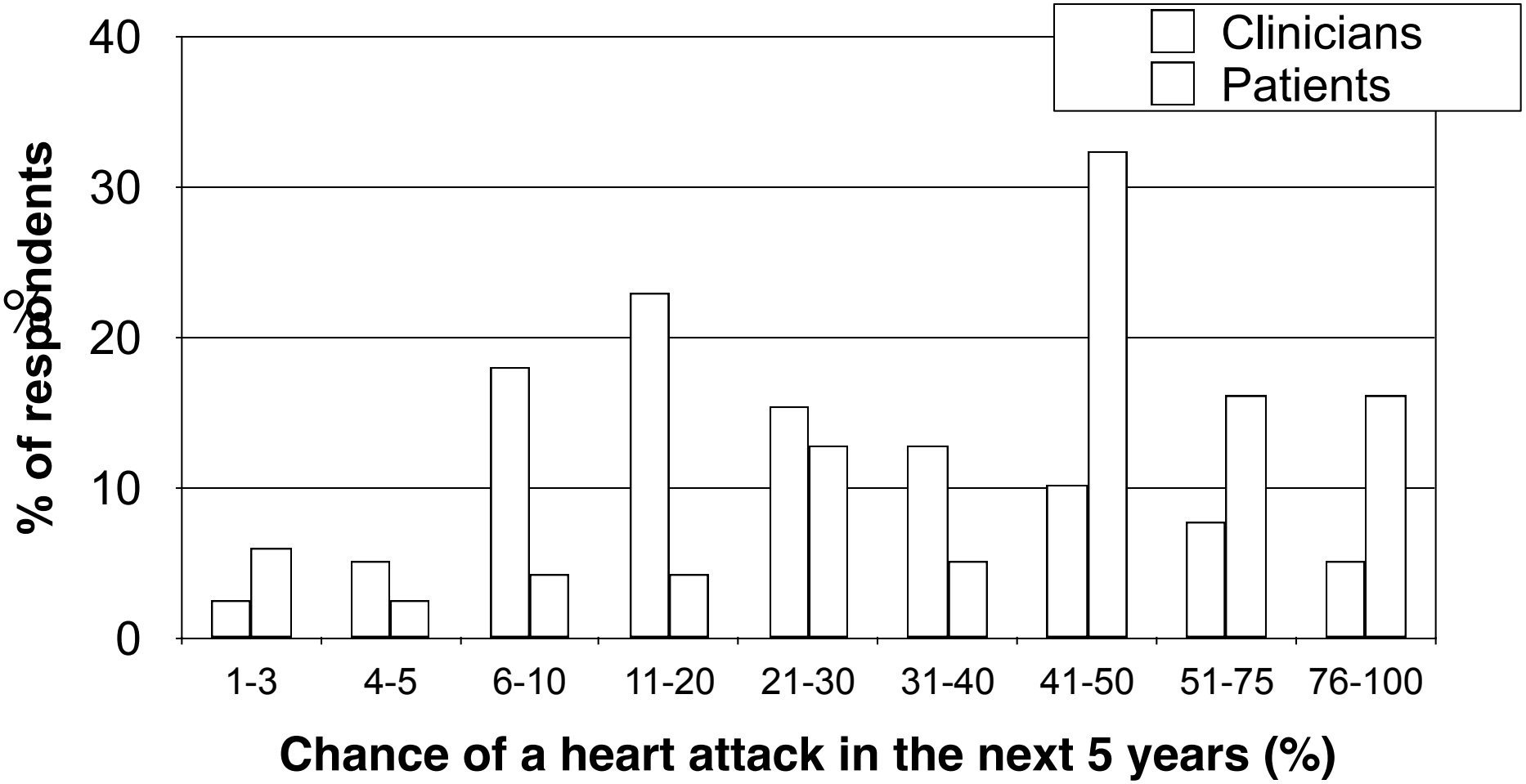
53 residents, 8 fellows, 18 attending physicians

The **mean degree of over-estimation** compared to the Framingham estimate:

low-risk scenarios - **7.8 times**
medium-risk scenarios - **2.8 times**
high-risk scenarios - **1.5 times**

BMC Health Services Research 2003;3:13

What is "High Risk"



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

David K Lewis, Jude Robinson, Ewan Wilkinson

Qualitative study using semi-structured interviews

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

BMJ 2003;327:841

Differing perceptions of intervention thresholds for fracture risk: a survey of patients and doctors

Did NOT ask patients to consider side effects or drug cost, just the dosing regimen, in the decision

"A typical patient in our study required a
50% absolute fracture risk and
50% relative risk reduction (giving an absolute risk reduction of 25%)
before considering long-term drug therapy"

A prominent current guideline …
recommends pharmacologic intervention at thresholds of
10- year risk of 20% for major osteoporotic fracture or
3% for hip fracture

125 (77%) of doctors would recommend treatment
24 (21%) of our patient cohort would consider treatment justified

Osteoporos Int 2012;23:2135–40

20 "NEGATIVE" STUDIES IN A ROW

LIPIDS

AIM-HIGH, HPS2-THRIVE (niacin)

ACCORD (fibrates)

dalOUTCOMES (dalcetrapib)

STABILITY (darapladib)

DIABETES

ACCORD, ADVANCE, VADT

(aggressive A1c lowering)

ROADMAP (olmesartan)

ORIGIN (insulin)

SAVOR-TIMI 53 (saxagliptin)

EXAMINE (alogliptin)

ALECARDIO (aleglitazar)

BLOOD PRESSURE

ALTITUDE (aliskiren)

VALISH, AASK, ACCORD

(aggressive BP lowering)

GENERAL

ACTIVE (irbesartan/afib)

CRESCENDO (rimonabant)

VISTA-16 (varespladib)

182,000+ patients

FINALLY!!!!!

1) EMPA-REG OUTCOME (empagliflozin) -1.6% ARR over 3 years

2) LEADER (liraglutide) - 1.8% ARR over 4years

3) SPRINT (120mmHg vs 140mmHg) - 1.6% ARR (CVD over 3 years but also 1.8% ARI (Kidney)

4) HD, BUT blood pressure measure no benefit

5) TECOS - 1.6% ARR over 2 years (saves YES, BUT $16,000/year

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

BUT!!!!!

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]

"In three quarters of the cancer studies … the majority of patients preferred shared or autonomous decision making. In contrast, this was true for only about half of the studies with non- disease specific study populations"

"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"

Patient Educ Couns (2011), doi:10.1016/j.pec.2011.02.004

THE COURT ACTUALLY LIKES SHARED DECISION-MAKING

Guidelines and the Law

Guidelines and the Law

"As per the Canadian Medical Association Handbook on Clinical Practice Guidelines, guidelines should NOT be used as a legal resource in malpractice cases as "their more general nature renders them insensitive to the particular circumstances of the individual cases."

CJD
Canadian Journal of Diabetes
A Publication of the Professional Sections of the Canadian Diabetes Association
Une publication des sections professionnelles de l'Association canadienne du diabète
CONTENTS: April 2013 ▪ Volume 37 ▪ Supplement 1

CMPA
Empowering
better healthcare

The Bottom Line

Sep 2011

Even an authoritative CPG may NOT be found to be determinative of a standard of care.

It is prudent for physicians to be aware of authoritative clinical practice guidelines relevant to their practices. If a clinical decision may be perceived as being contrary to a recognized and accepted CPG, a physician, where appropriate, may consider the following steps: consult with a colleague or relevant specialist, discuss reasonable treatment options with the patient, and document the patient's consent for the chosen treatment.

If deviating from an established CPG, physicians should consider documenting the rationale for doing so, as well as any discussions with the patient about such variance.

Many courts (UK, US, CA)

"The reasonable-patient standard … requires physicians and other health care practitioners to disclose all relevant information about the risks, benefits, and alternatives of a proposed treatment that an **OBJECTIVE PATIENT** would find material in making an intelligent decision as to whether to agree to the proposed procedure"

JAMA 2016;315:2063-4

OPEN ACCESS Freely available online

PLOS | MEDICINE

Expanding Disease Definitions in Guidelines and Expert Panel Ties to Industry: A Cross-sectional Study of Common Conditions in the United States

2013

Raymond N. Moynihan[1]*, Georga P. E. Cooke[1], Jenny A. Doust[1], Lisa Bero[2], Suzanne Hill[3], Paul P. Glasziou[1]

1 Bond University, Robina, Australia, 2 University of California, San Francisco, San Francisco, California, United States of America, 3 Australian National University, Acton, Australia

Of 16 publications on 14 common conditions, 10 widened and 1 narrowed definitions.

Widen by 3 methods: (i) "pre-disease"; (ii) lowering thresholds; (iii) earlier or new diagnostic methods.

None had rigorous assessment of potential harms of proposed changes.

The average proportion of members with industry ties was 75%; 12/16 chairs had ties.

CONCLUSION:

"research and policy attention might be directed at designing new processes for reviewing disease definitions, free of financial conflicts of interest and informed by rigorous analysis of benefits and harms."

FRAMEWORK CONVENTION ON TOBACCO CONTROL

Guidelines for Guidelines

Guidelines for Guidelines
We've Come a Long Way

GUIDELINES FOR WHO GUIDELINES

Global Programme on Evidence for Health Policy
World Health Organization
Geneva, Switzerland

Guidelines for Guidelines

W.-I. Steudel and K. Schwerdtfeger

Department of Neurosurgery, Saarland University Medical School, Homburg/Saar, Germany

Guidelines for Guidelines: Are They Up to the Task? A Comparative Assessment of Clinical Practice Guideline Development Handbooks

Guidance for updating clinical practice guidelines: a systematic review of methodological handbooks

Robin WM Vernooij[1,2], Andrea Juliana Sanabria[1], Ivan Solà[1], Pablo Alonso-Coello[1*] and Laura Martínez García[1]

There are LOTS of guidelines

Often don't provide a solid synopsis/ systematic review of the best available evidence

Often don't provide sufficient information to do shared-decision-making or even support the concept

Many "conflicts" and ownership issues

Patient expectations are often at odds with guideline recommendations

Legal precedents are leaning in favour of benefit/harm communication

Education and Guidelines

“WHEN ALL ELSE FAILS THERE’S ALWAYS DELUSION”

CONAN O’BRIEN

If all else fails use guidelines BUT…

Education and Guidelines

Obviously inform you that CPG's exist

We all need to discuss up front the limitations and issues of clinical practice guidelines

We need to know how to appraise and integrate the best available evidence

Admit we don't have answers for everything

We need to help you think for yourselves and use common-sense

Need to be allowed to make "mistakes"

It is totally OK to go "against" the guidelines

The Guideline Solution?

What should guidelines contain?

Who should write them?

What should they not contain?

Are there examples of well-done guidelines?

Guidelines should provide
ballpark estimates
of what happens if
you DON’T treat/test/screen
and if
you DO treat/test/screen

Top 20 Primary Care Diagnoses

Hypertension
Hyperlipidemia
Diabetes
Back pain
Anxiety
Obesity
Allergic rhinitis
Reflux esophagitis
Respiratory problems
Hypothyroidism
Visual refractive errors
Osteoarthritis
Fibromyalgia/myositis, neuritis
Malaise and fatigue
Pain in joint
Acute laryngopharyngitis
Acute maxillary sinusitis
Major depressive disorder
Acute bronchitis
Asthma

Risk assessment - diabetes, hyperlipidemia, hypertension

Pain - back pain, osteoarthritis, fibromyalgia/ myositis, neuritis, malaise and fatigue, pain in joint

Psychiatry - anxiety, depression

Infectious - acute laryngopharyngitis acute maxillary sinusitis, acute bronchitis

Pulmonary - asthma, respiratory problems, allergic rhinitis

Other - obesity, GERD, hypothyroidism

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

An Example of a Guideline that Promotes Discussion Rather than Treatment

Simplified lipid guidelines

Prevention and management of cardiovascular disease in primary care

G. Michael Allan MD CCFP Adrienne J. Lindblad ACPR PharmD Ann Comeau MN NP CCN(C) John Coppola MD CCFP
Brianne Hudson MD CCFP Marco Mannarino MD CCFP Cindy McMinis Raj Padwal MD MSc
Christine Schelstraete Kelly Zarnke MD MSc FRCPC Scott Garrison MD PhD CCFP Candra Cotton
Christina Korownyk MD CCFP James McCormack PharmD Sharon Nickel Michael R. Kolber MD CCFP MSc

Can Fam Physician 2015;61:857-67

Reducing Your Risk for Heart Attacks & Strokes

A SHIFT IN THINKING...

What's Changed?

If you asked anyone how to reduce your risk of a heart attack or stroke you'd likely hear them mention the need to lower your cholesterol.

However, many studies have shown improving cholesterol does not always reduce risk of cardiovascular disease (heart attack or stroke). By worrying only about cholesterol we might miss helping the right people because cholesterol is only one risk

CHOLESTEROL ONLY TELLS US PART OF YOUR HEART HEALTH STORY

Medication

Statin therapy should be discussed with all people with moderate to high cardiovascular risk (10% or more). Your healthcare provider can explain your risk and how statins can reduce that risk by 25-35%.

STATINS CAN REDUCE YOUR RISK OF HEART ATTACK AND STROKE BY 25% TO 35%

A low-dose of ASA (Aspirin®) may also be recommended for further risk reduction if you are at high cardiovascular risk (20% or more) or have had a heart attack or stroke. ASA reduces cardiovascular risk by about 12.5% (half or third as effective as statins). Note – ASA can cause bleeding.

What are the side effects of statins?

All drugs come with

Most Common — **1 in every 10 to 20 people – muscle aches or stiffness***

1 in every 10,000

Are statins right for you?

You decide. Speak with your healthcare provider about your risk of cardiovascular disease and the benefits and risks of taking statins. Regardless of your decision, your healthcare provider will support you!

This number is an educated guess of your chances of developing cardiovascular disease in the next 10 years. For example, a 10% risk means you have about a 1 in 10 chance of having a heart attack or stroke in the next 10 years.

What can you do to reduce your risk of heart attack or stroke?

Eat healthy – be active – don't smoke

These lifestyle choices reduce your risk of cardiovascular disease and benefit your overall health.

EXERCISE OR A MEDITERRANEAN DIET CAN REDUCE YOUR RISK OF HEART ATTACK AND STROKE BY 30%

tested?

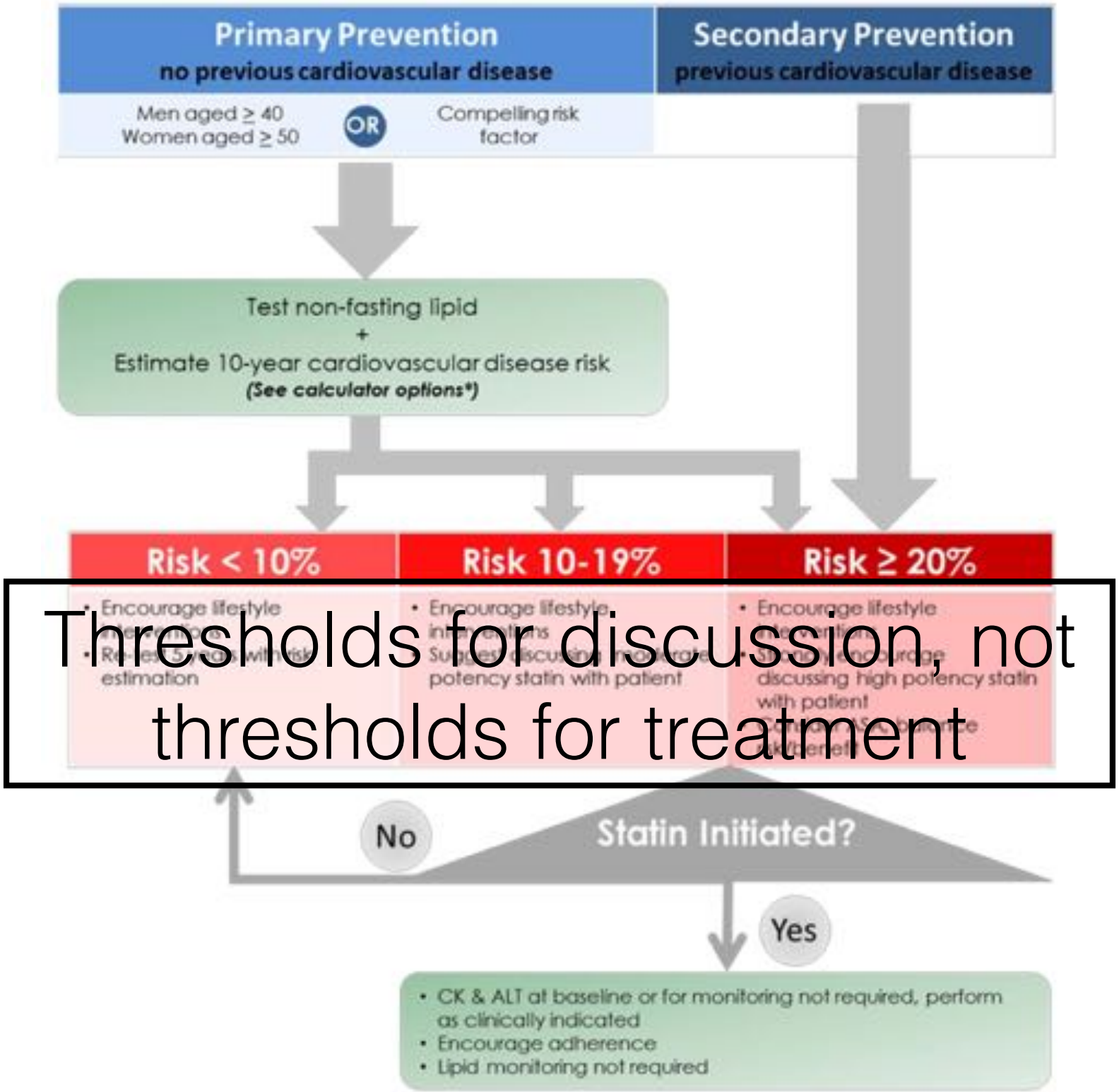
Not taking a statin → You should continue to have your cholesterol tested every 5 years.

Taking a statin → No. Once you have decided to take a statin a cholesterol test is unnecessary – statins help to reduce your cardiovascular risk no matter what your cholesterol level. So knowing your cholesterol level would not change your treatment plan.

Are statins right for you?

You decide. Speak with your healthcare provider about your risk of cardiovascular disease and the benefits and risks of taking statins. Regardless of your decision, your healthcare provider will support you!

Alberta College of Family Physicians
The College of Family Physicians of Canada / Le Collège des médecins de famille du Canada
TOP Toward Optimized Practice



Thresholds for discussion, not thresholds for treatment