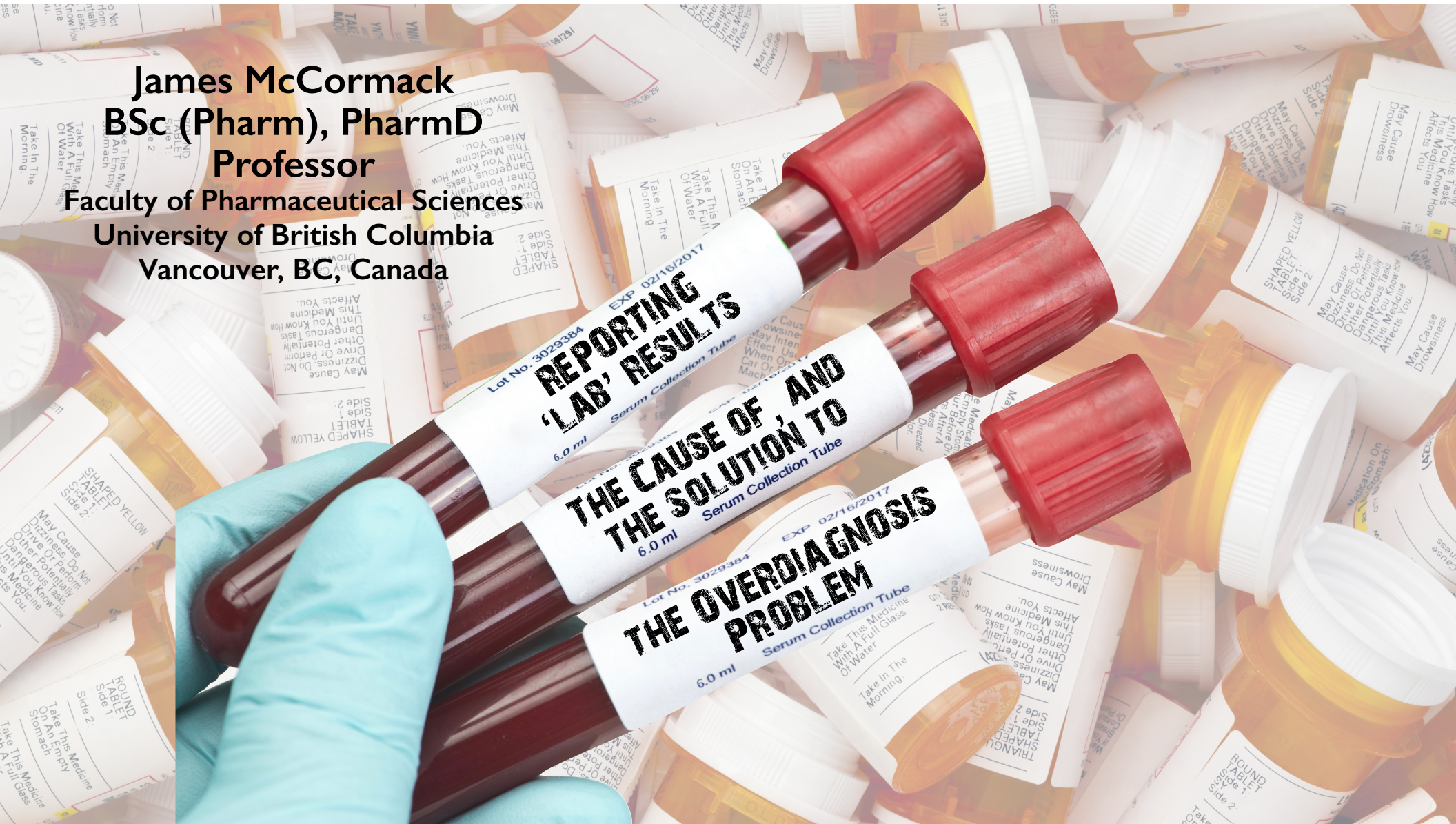


James McCormack
BSc (Pharm), PharmD
Professor
Faculty of Pharmaceutical Sciences
University of British Columbia
Vancouver, BC, Canada



Objectives

- 1) outline the problem of lab test measurement and reporting and some of the ways it contributes to the overdiagnosis problem
- 2) demonstrate with some examples (BP, LDL, glucose)
- 3) hopefully offer some useful tips, and suggestions and simple charts for how to deal with this extremely important and relevant healthcare conundrum
- 4) INTERACTIVE
 - Poll questions - internet access
 - Play with virtual dice - work through a few scenarios

22 February 2020
368:261-302 No 6234 | ISSN 1759-2151



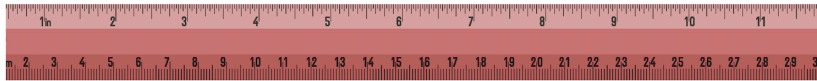
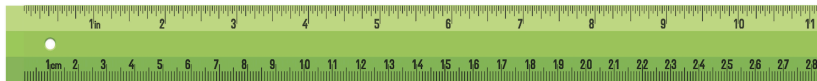
Tamiflu: what have we learnt? p 274

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.



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 <i>i</i>	Biologic variation <i>i</i>	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 *i*

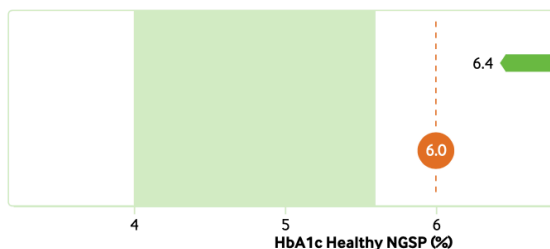
Result 1 7.0

Result 2 6.0

Show ▶

4 View estimates

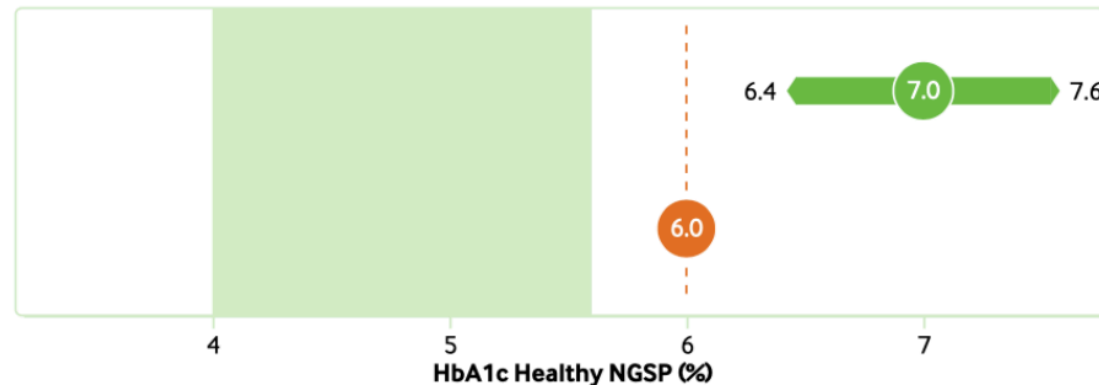
The minimum change required to conclude that two serial measurements are likely "reference change value" (RCV). Arrows to the left and right of your first result show For serial results, measurements can be considered different if the second is outside



Normal range *i*
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

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 *i*

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

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

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

“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.”

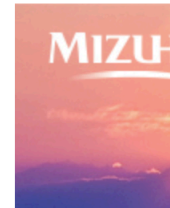
Clinica Chimica Acta 2004;346:3-11

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.	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

CVA - analytical variation

Biological Variation

CVI - within subject

CVG - between subject

Reference change values (RCV)

Analytic
variation

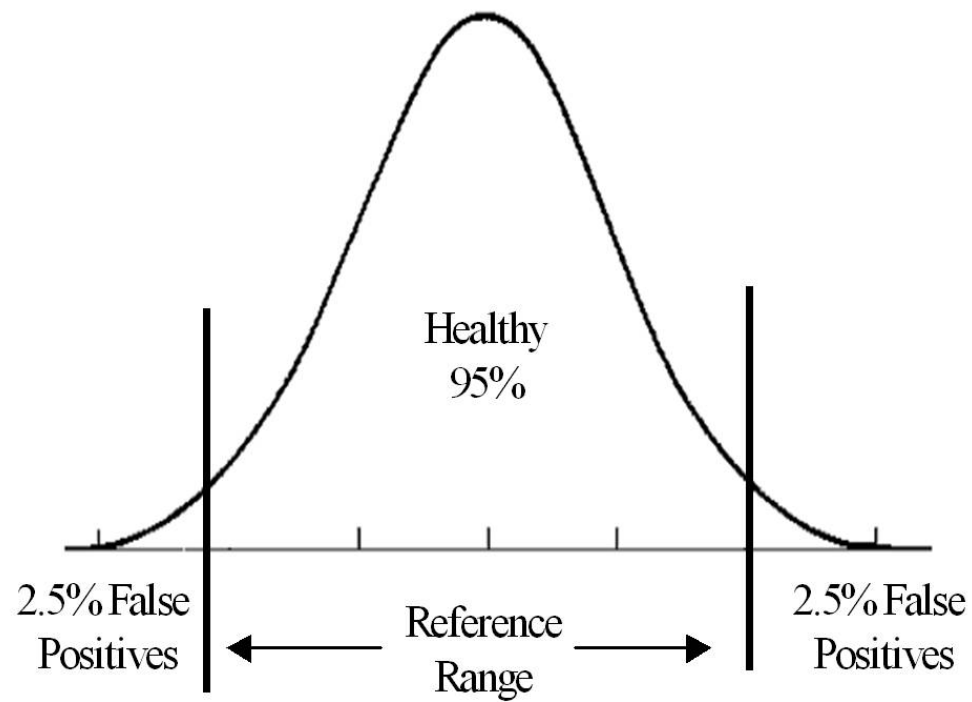
Biologic
variation



Population-based
reference intervals

Population-based reference intervals

The interval/range where 95% of healthy people fall



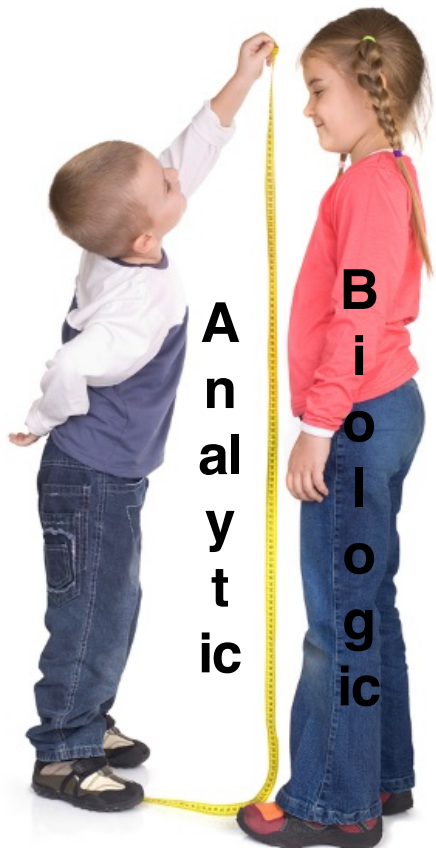
Lab results report
exact numbers
BUT
Every test result is
really only a range
that hopefully includes
the true result
*+/- 1-2% up to
+/-20-30% or more*

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

When we do tests, typically
we are wondering

what are the results NOW, and/or

have they changed from PREVIOUS measurements



A
n
a
l
y
t
i
c

B
i
o
l
o
g
i
c

Analytic
variation

Biologic
variation

Every “measurement” will be “different”

Analytic variability
Biologic variability

Nerd Alert



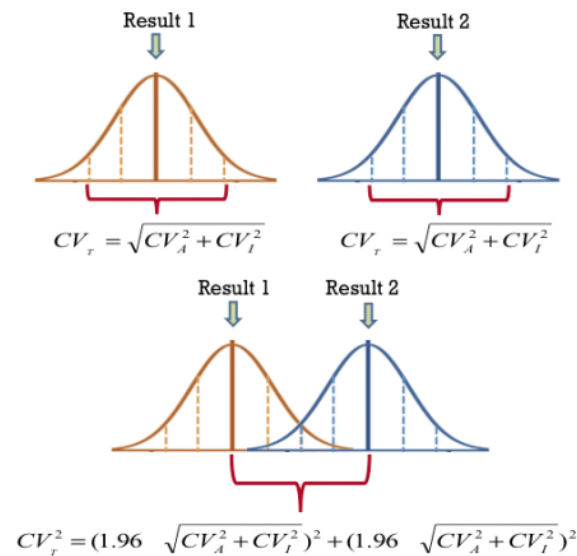
Reference Change Values (RCV)

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

Reference Change Values

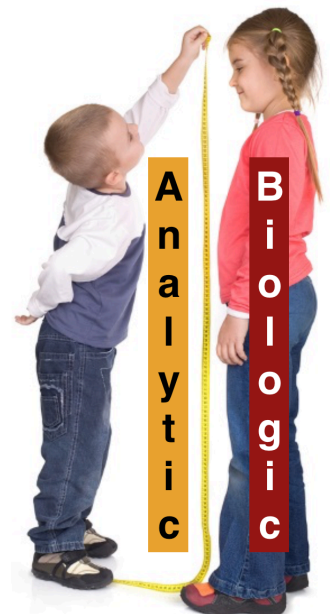
Used with SERIAL results to help deal with the analytic imprecision and biologic variation

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

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



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

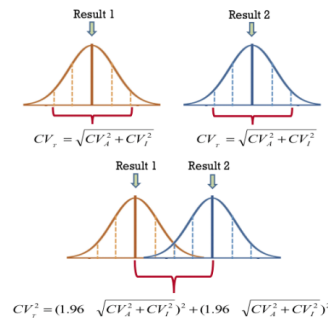


Reference Change Values

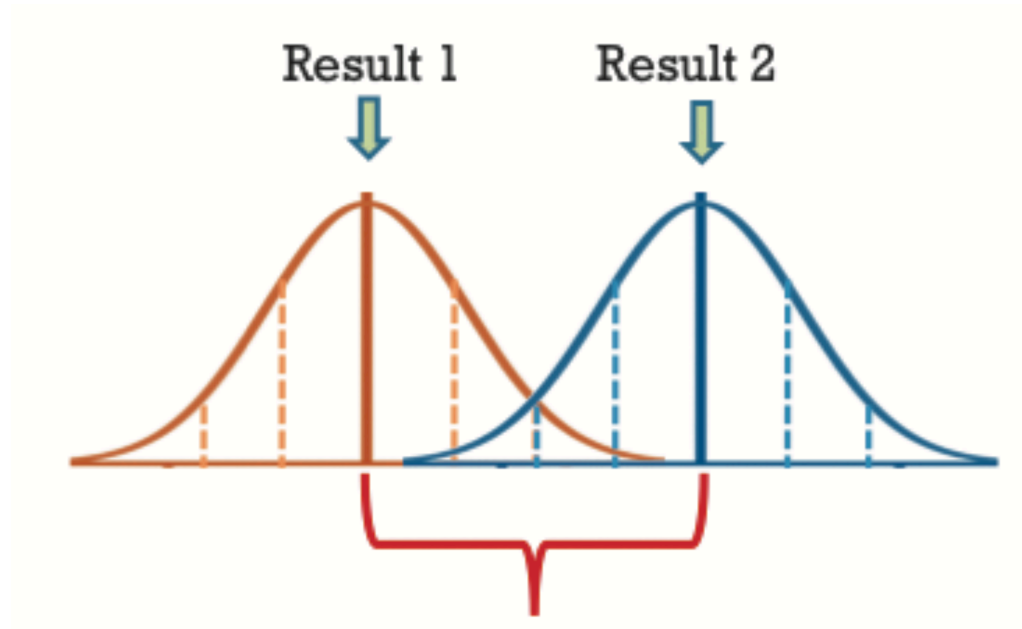
findings of a “significant difference” JUST means we are ruling out that the difference seen is due to chance

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%

Lab
Error

Analytic
variation

Biologic
variation



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

Glucose
Blood pressure
Cholesterol

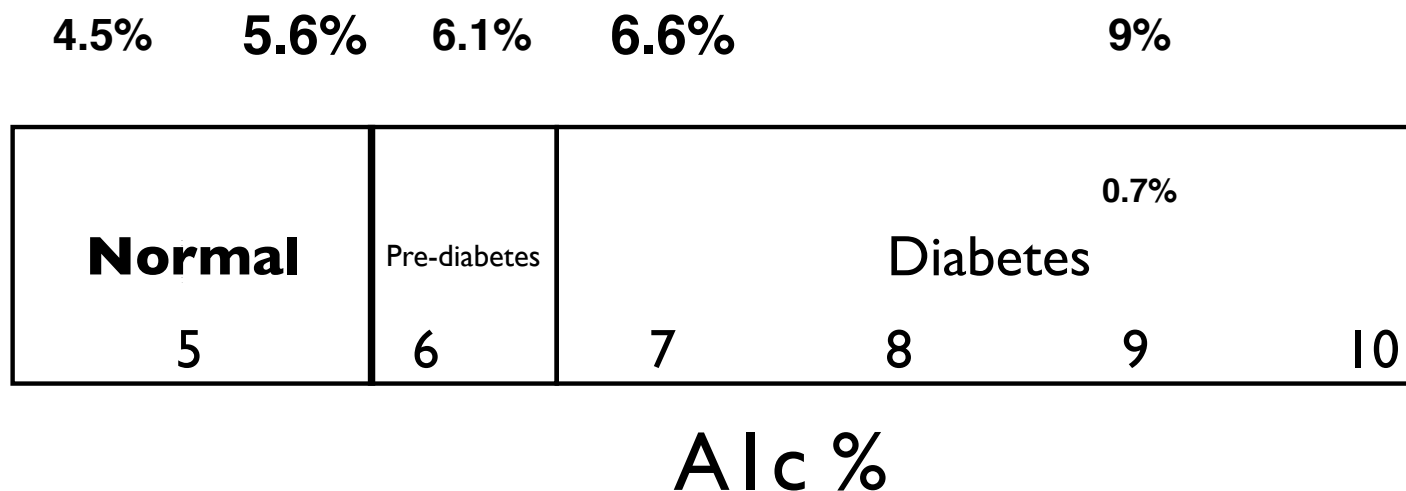




Glucose

Precisely Imprecise

What an A1c result really means



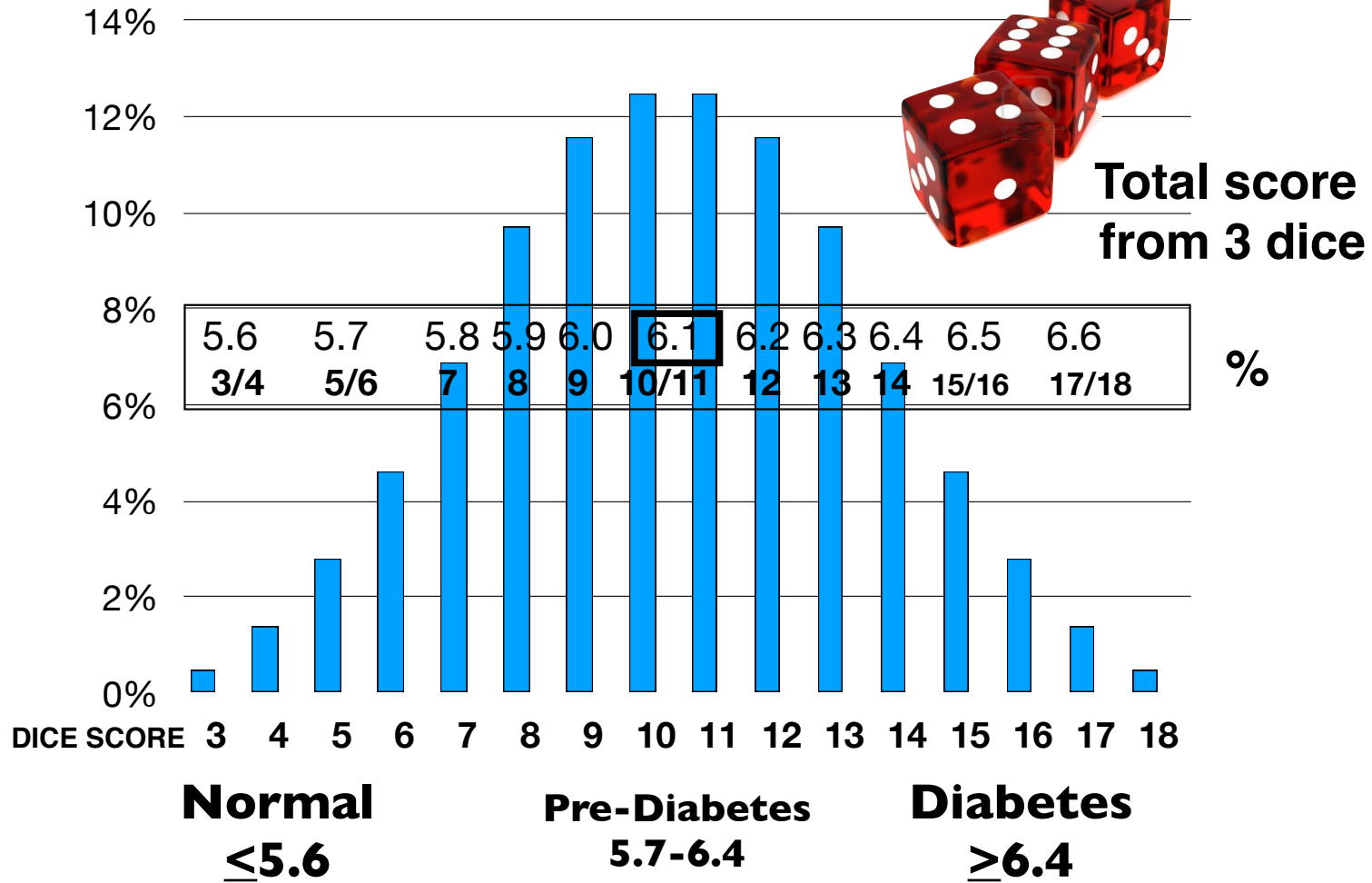
Typical A1c change seen
with a medication
= 0.7% ↓

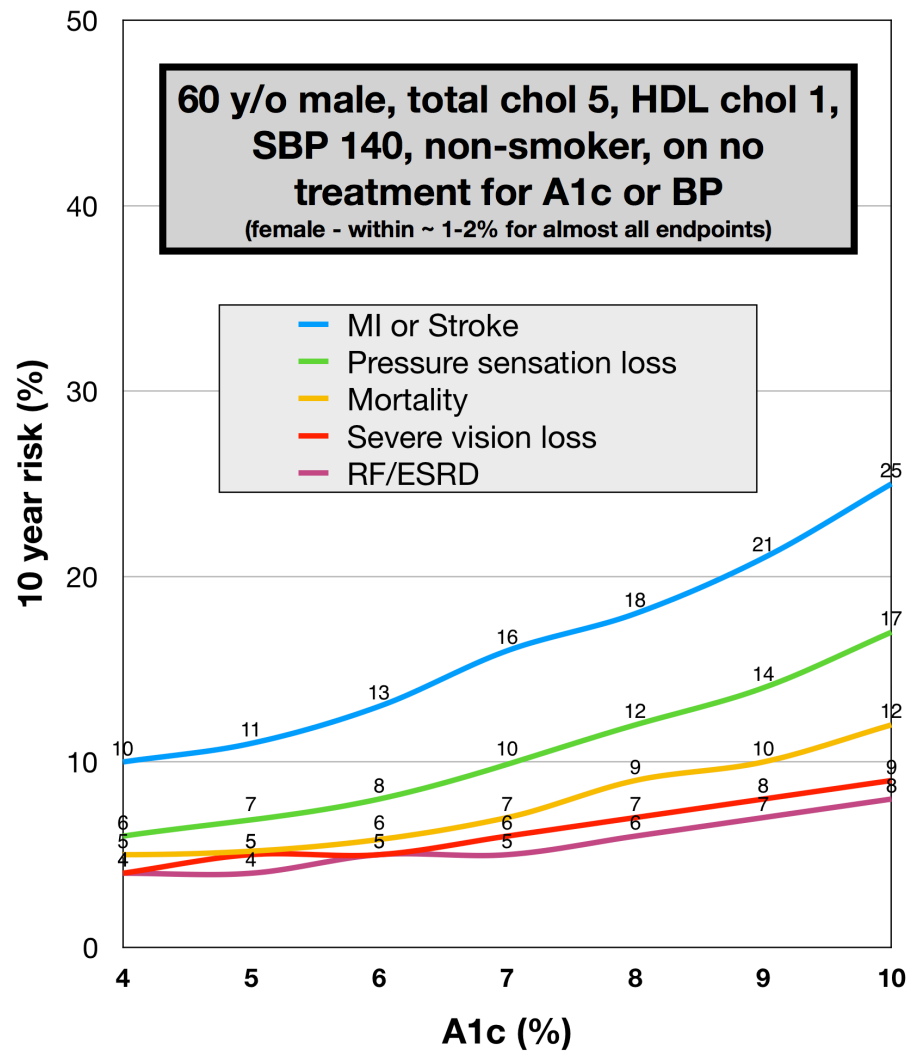
Seasonal variation 0.2-0.5%
Higher in the winter

Am J Epi 2004;161:565-74

A1c %

= True value





T2DM risk
should not
be
categorized
as
YES
or
NO

<https://sanjaybasu.shinyapps.io/recodesi/> - from the ACCORD study



Blood pressure

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

BLOOD PRESSURE

Less than 135/85 “Despite a -4/-3 mmHg greater achieved reduction in systolic/diastolic BP, attempting to achieve “lower targets” instead of “standard targets” did not change total mortality, MI, stroke, CHF, major CV events or ESRD”

Cochrane Review 2009;Issue 3:CD004349

“the oft-cited <140 mm Hg systolic threshold used to define hypertension has admittedly been arbitrarily chosen as a 'compromise' and one could make a strong case for a lower threshold in high-risk patients and a higher threshold in those at lower risk”

“‘treatment’ refers to both lifestyle modifications and pharmacologic therapy”



Editorial

American Journal of Hypertension (2008) **21** 3–4; doi:10.1038/ajh.2007.20

Blood Pressure Variability: The Challenge of Variation

Tom P Marshall¹ ([#aff1](#))

¹Department of Public Health and Epidemiology, University of Birmingham, Edgbaston, Birmingham, UK

Correspondence: Tom P. Marshall, (T.P.Marshall@bham.ac.uk (<mailto:T.P.Marshall@bham.ac.uk>))

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



Cholesterol

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

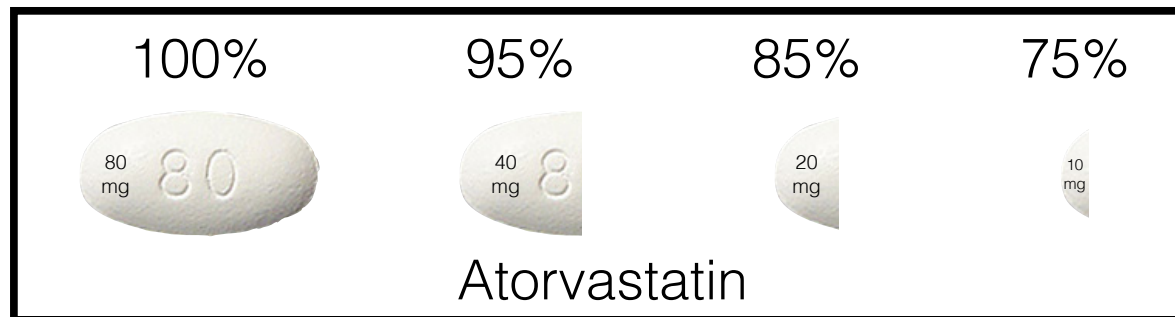
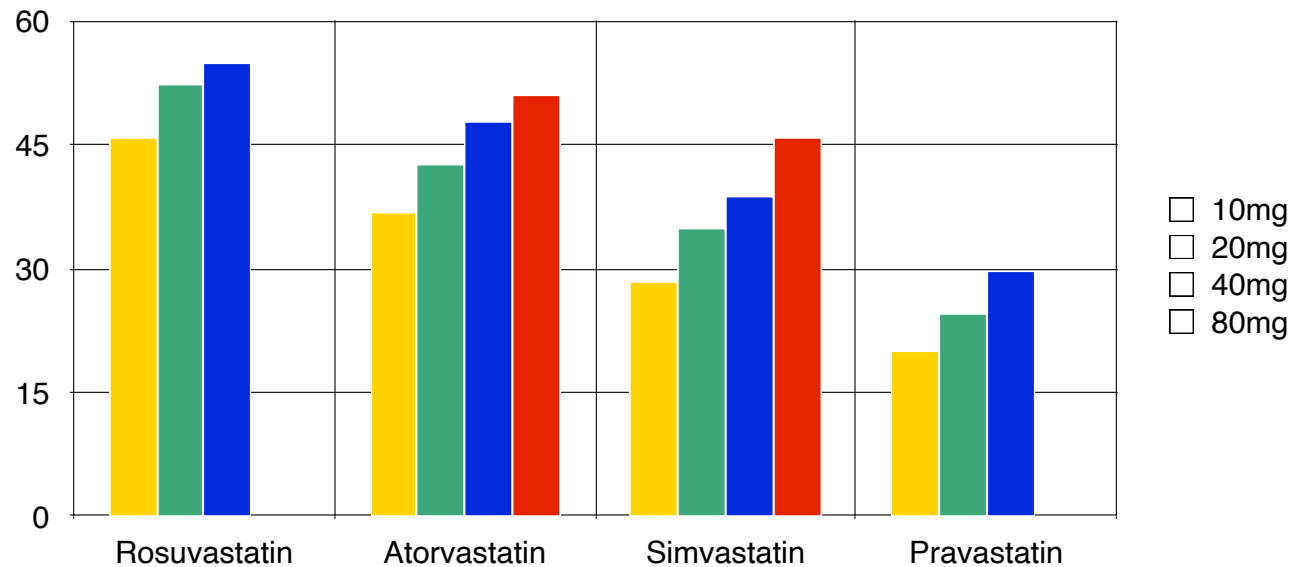
Total chol ~ - 0.80 to 0.80 mmol/L (~30 mg/dL) ~15%

LDL chol ~ - 0.5 to 0.5 mmol/L (~20 mg/dL)

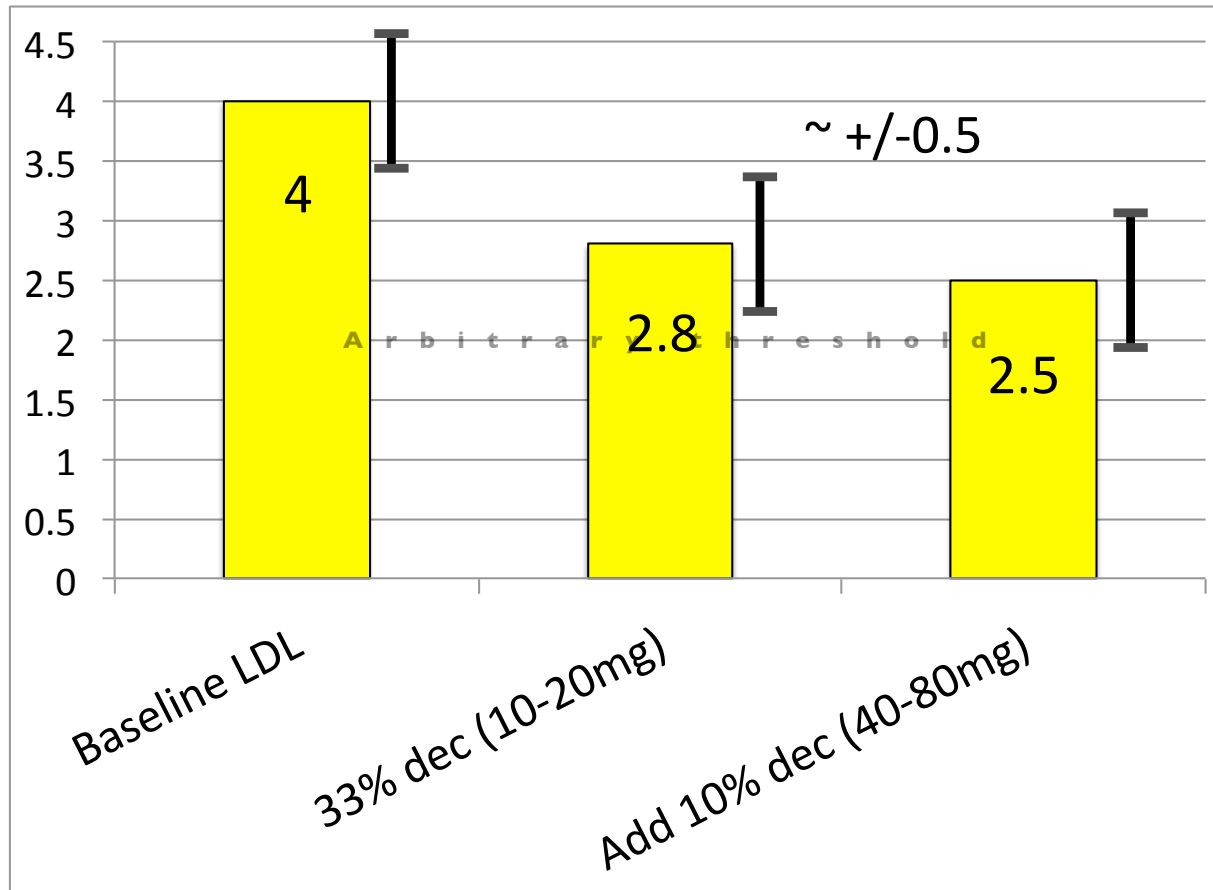
Average increase in cholesterol is 0.5-1%/year

“After initial change only measure every
3-5 years”

DOSE increases do not lead
to proportional EFFECT increases
% reduction in LDL cholesterol

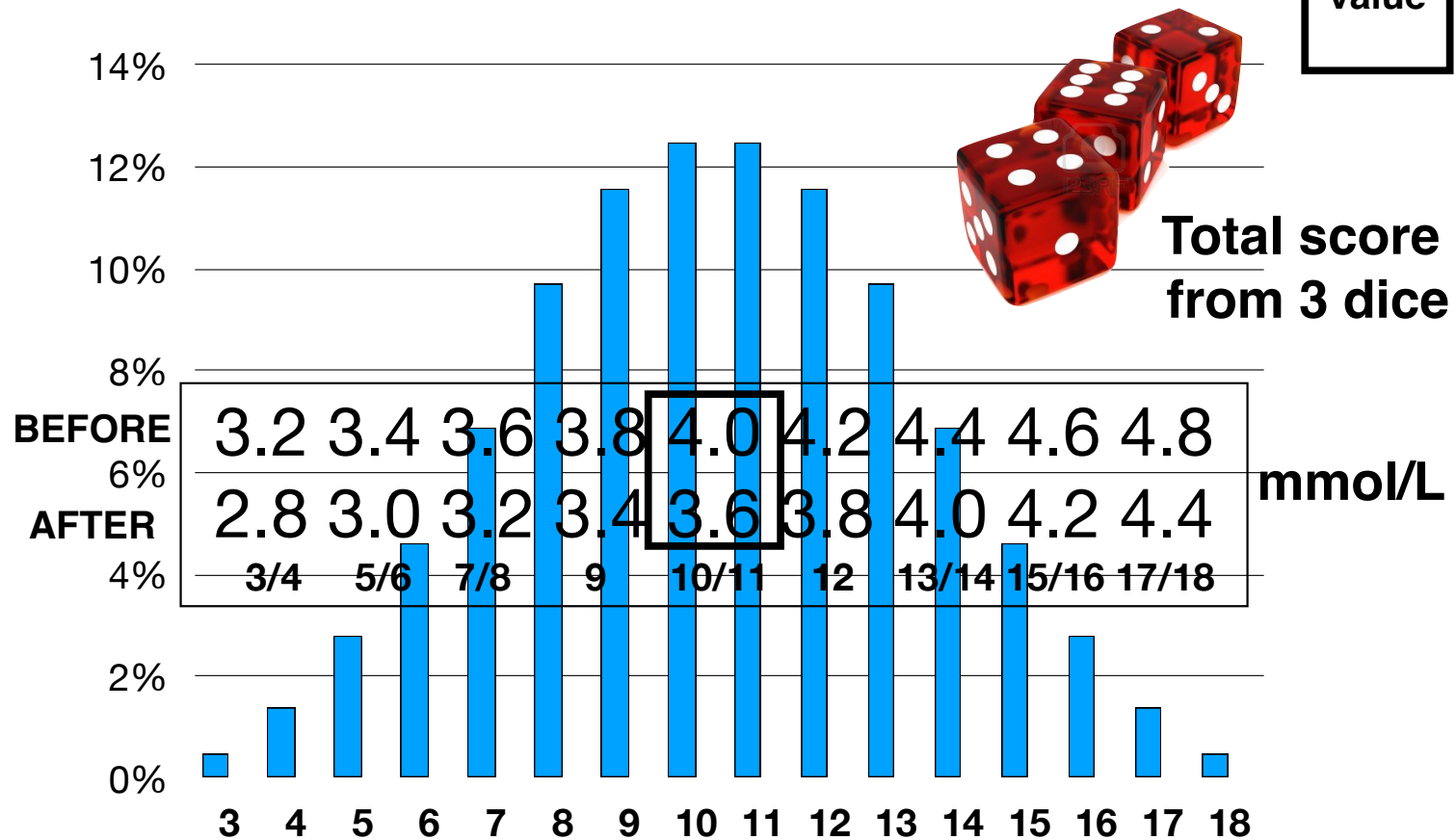


LDL cholesterol - 2 mmol/L ~80mg/dL



LDL mmol/L - medication that lowers LDL by 10%

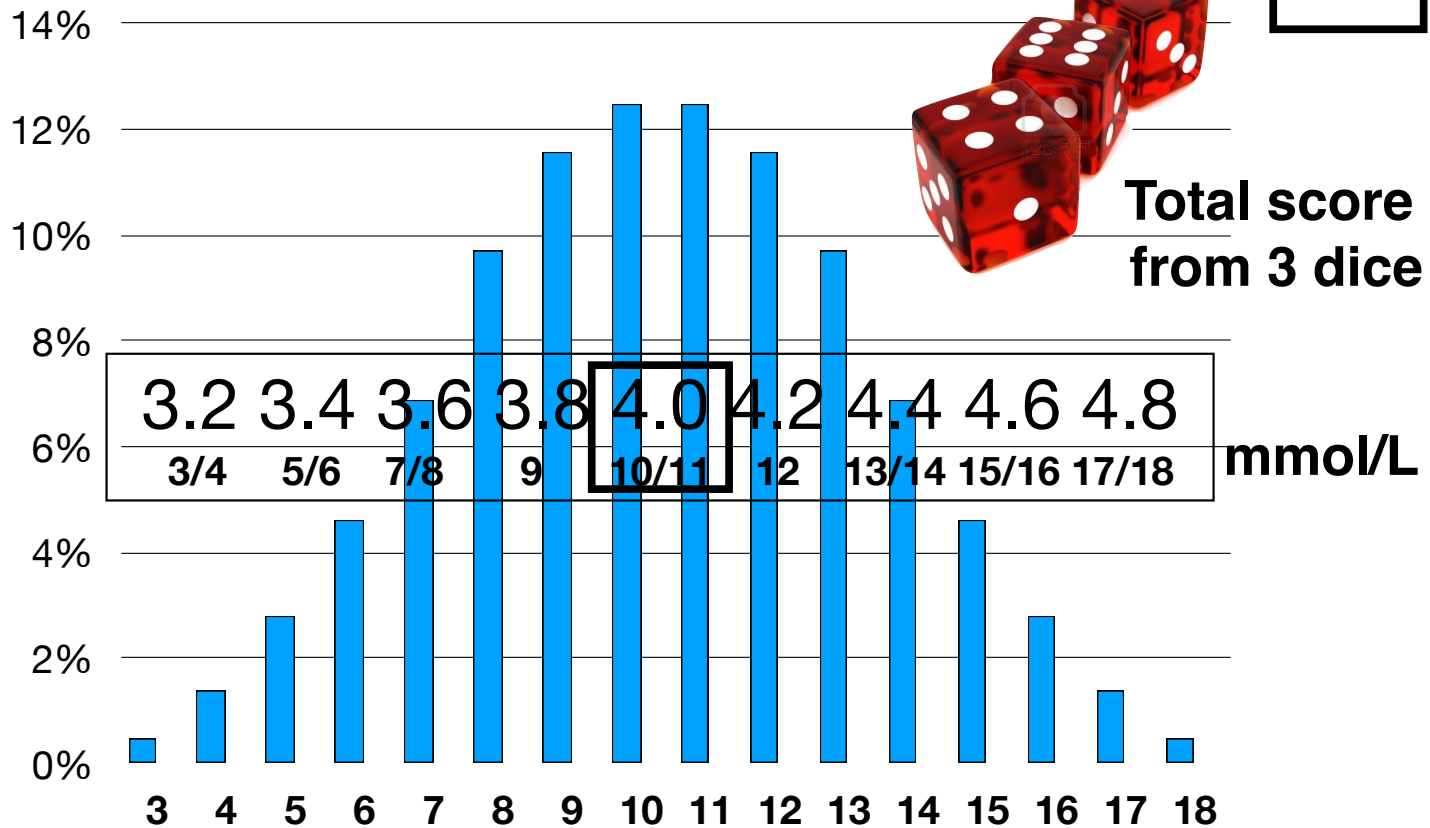
= True value



Trying to get to “target” by increasing the dose

LDL mmol/L - Average increase in cholesterol is 0.5-1%/year

= True
value



When to remeasure

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”

The Absolute CVD Risk/Benefit Calculator

Languages: English (EN)

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

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

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

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

Age years

Gender ☐ Male ☒ Female

Smoker ☐ Yes ☒ No
CVD risk is reversed after 5-10 years of no smoking

Diabetes ☐ Yes ☒ No

Systolic Blood Pressure mmHg
Enter present blood pressure regardless of treatment
120 mmHg is used for baseline risk

On treatment for BP ☐ Yes ☒ No
Click YES if taking blood pressure medication
Only applies if SBP is greater than 120 mmHg

Total Cholesterol mmol/L
Cholesterol should be prior to drug treatment
3 mmol/L is used for baseline risk.
[Click to change to mg/dL.](#)

HDL Cholesterol mmol/L
HDL should be prior to drug treatment
1.3 mmol/L is used for baseline risk.

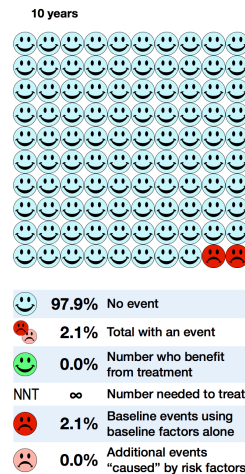
Chronic Kidney Disease ☐ Yes ☒ No
CKD status is not part of the risk algorithm but is used for calculating the benefit of certain therapies

Relative Benefit: 0%

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

[Benefit Estimate Details](#)

Risk Time Period



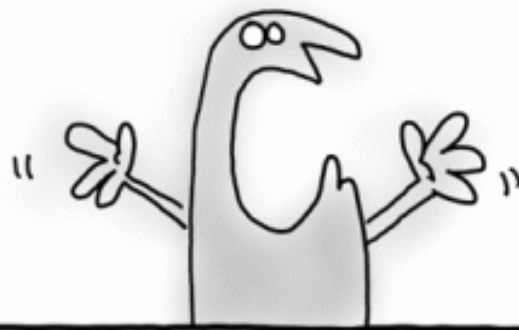
As with all risk calculators, calculated risk numbers are +/- 5% at best. [More information.](#)

[Print Report](#)

Calculate ballpark 5/10-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

Now What?!!



The Problem
is
NOT Fixable,
it is
Only
KNOWABLE

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

Confidence interval (%) around a single measurement = analytic variation

Confidence interval (%) around a single measurement of something that might be ongoing = analytic and biologic variation

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

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Lactate	2-5%	>50%	>50%
Total bilirubin	2-5%	41-50%	>50%
Triglycerides	2-5%	31-40%	>50%



LiveSlides web content

To view

Download the add-in.

liveslides.com/download

Start the presentation.

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 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

Lab Value thoughts

have you first looked at how the patient is clinically doing?

will the result of your test change what you would do?

does a “risk factor” test improve your assessment of risk?

how big a change do you expect from your treatment?

what is the sensitivity and specificity of the test? - pre-test and post-test probability

how long does that change take?

how big a change is needed to be confident a change has occurred?



**When someone
does something
wrong, don't forget
all the things they
did right.**