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therapeuticseducation.org medicationmythbusters.com

77/400

The Agenda

Start by making you the patient

Philosophy - once you "know" the evidence - decision making/doing the right thing/choosing wisely/less is more

The 10 "New" Therapeutic Commandments - evidence, tools, myths

Polypharmacy case

Have fun, engage, ask questions, debate, be open-minded

antibiotics

thiazides

many vaccines

ACE inhibitors

proton pump inhibitors

H2 receptor antagonists

contraceptives

corticosteroids

beta-agonists

insulin

anesthetics

adrenalin

narcotics

chemotherapy

warfarin

300+

medications



The Selection and Use of Essential Medicines

Report of the WHO Expert Committee, 2011 (including the 17th WHO Model List of Essential Medicines and the 3rd WHO Model List of Essential Medicines for Children)



The BMJ

The BMJ Today: Choosing Wisely makes me happy

7 Jul, 14 | by BMJ

Sometimes we all need cheering up on a Monday morning, and today I couldn't recommend more highly this parody of "Happy" by Pharrell Williams, which sings the virtues of the Choosing Wisely campaign.

Featuring some very sprightly OAPs and lyrics such as "antibiotics for a cold will do nothing but make you ill, a routine screen for many things is often overkill," the song perfectly encapsulates the Choosing Wisely campaign, which is building up steam in the USA and Canada.

"Medical science has made such tremendous progress that there is hardly a healthy human left."

Aldous Huxley

World of Optimal Therapy

Patient-Centered **Evidence-Based**

Interprofessional

"Choice is a gift from the patient to the doctor, not the other way around"

Loss Of The Individual

"This kind of utilitarian medicine that treats every individual as identical can easily erode the stature and autonomy of patients"



What this involves

Listening and not interrupting

Eliciting facts and experiences without selective bias

The sharing of knowledge

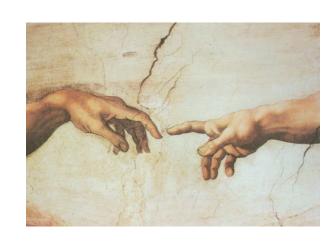
Ultimately a joint process of decision-making

"a physician should order a test only if he or she plans to change therapy as a result"

Susan Ott, MD
Professor
Department of Medicine
University of Washington



Knowing the evidence = Empowerment



Memorise how to do things - difficult and doesn't require you to think

Have an awareness of the evidence - much easier AND requires you to think

Know what isn't known

Patient choice - not wrong or right thing

Approach to prevention is very different than it is to symptom control

Knowing the evidence leads to a far more satisfying practice

Top 10 reasons for MD visits

Skin disorders, including cysts, acne and dermatitis Joint disorders, including osteoarthritis Back problems Cholesterol problems Upper respiratory conditions Anxiety, bipolar disorder and depression Chronic neurologic disorders High blood pressure Headaches and migraines **Diabetes**

Top 10 reasons for MD visits

RISK REDUCTION
Cholesterol problems
High blood pressure
Diabetes

SKIN DISORDERS

Cysts, acne and dermatitis

PAIN CONTROL
Joint disorders, including osteoarthritis
Back problems
Headaches and migraines

PSYCH/NEURO
Anxiety, bipolar disorder and depression
Chronic neurologic disorders

INFECTIOUS DISEASES
Upper respiratory conditions

Describing Benefits

The chance of "X"

WITH NO TREATMENT

The chance of "X"

WITH TREATMENT

Numbers

	Major coronary events (%)			
	Primary	Secondary		
Placebo	5	15		
Statin	4	11		
RRR	20	25		
ARR		4		
NNT	100	25		

Baseline risk RRR, ARR, NNT Difference between groups

Penicillin for sore throat

```
NNT for sore throat at 3 days ~ 6
more effective if Strep + throat swab (RR 0.58 vs 0.78)

NNT for sore throat at 1 week ~ 20
more more effective if Strep + throat swab (RR 0.29 vs 0.73)

Symptoms are shortened by ~ 16 hours

NNH for rash or diarrhoea ~10
~1/40,000 severe allergic reaction
```

Antibiotics for otitis media

NNT for pain at 24 hours ~ ∞? 20?

NNT for pain at 2-3+4-7 days ~ 20

NNT for tympanic membrane perforation ~ 33

NNH for rash/diarrhoea/skinrash ~15

Delayed ABX no difference

CD000219

Flu Shot

- ~ 70-90% effective using antibodies as the diagnosis
- ~ 60% effective if use culture endpoints
- ~ 85% effective nasal spray in children 6 months to 6 years old

Every year I-10% adults get the flu

~ 5% - therefore reduced to 1% - less if unmatched

5-20% per year in children

~10% - therefore reduced to 2%

5% down to 2% (1%) in adults

10% down to 4% (2%) in children

Heartburn

Indication	Outcome	Placebo/no treatment (%)	H2RA (%)	PPI (%)	NNT (PPI vs placebo)
GERD-like symptoms (CD002095)	Heartburn remission	25-40	55	70*	2-3
NSAID ulcer prevention (CD002296)	Clinical ulcers over 6-12 months	0.5-2	No studies	No studies	-
	Endoscopic ulcers at 12 weeks or longer	35	15 high dose H2RA	15	5

^{*}high dose provides approximately a 5% absolute increase in benefit

Pain

The best non-narcotic acute pain killer - dental pain, headache etc

NSAID plus acetaminophen 1000 mg

Naproxen 250 mg/lbuprofen 400 mg

FULL glass of water - lie on right side

Neuropathic pain

post herpetic neuralgia/diabetic neuropathy

Gabapentin

Moderate improvement 43% (G) vs 26% (P) - NNT~6 Substantial improvement 31% (G) vs 17% (P) - NNT~7 dizziness, sedation, confusion, ataxia, peripheral edema - NNH ~8

CD007938

A test of benefit/harm can be made after 1-2 days at a low dose (100-900 mg/day)

Benefit is unlikely to increase with higher doses or longer treatment

Erectile dysfunction

"Successful" attempts in the sildenafil group ≈ 70%

"Patients" who "responded" in the placebo group $\approx 20\%$

7/10 "patients" will "respond" each time to sildenafil

2 of these 7 "responded" not because of the drug - NNB of 2

10% headache, 15% flushing, 10% dyspepsia - <1% stopped drug due to side effects

Depression

Patients who respond in the SSRI group $\approx 60\%$

40% in primary care? Am J Psychiatry 2009; 166:599–607

Patients who respond in the placebo group $\approx 45\%$

6/10 patients will respond to an antidepressant

4-5 of these 6 improved not because of the drug - NNT of 6-7

Accutane/Epuris

10, 20 and 40 mg capsules

Therapeutic Choices - 0.5-2 mg/kg/day for 12-16 weeks 60 kg = 30 to 120 mg/day "Low dose" was considered 0.5 mg/kg/day and there was a cumulative dose of 120-150 mg/kg

Start with 10 mg a day and continue until all lesions are gone and then continue for 2-4 months at 5 mg/day or 10 mg every other day

Australasian J of Dermatol 2013;54:157–62 Indian J Dermatol Venereol Leprol 2010;76:7-13

ORIGINAL ARTICLE

Isotretinoin 5 mg daily for low-grade adult acne vulgaris – a placebo-controlled, randomized double-blind study

Journal of the European Academy of Dermatology and Venereology 2013

Beware of "qualitative quantification"

Qualitative descriptor	EU assigned frequency	Mean frequency estimated by participants (n=200)
Very common	>10%	65% (24·2)
Common	1-10%	45% (22.3)
Uncommon	0.1-1%	18% (13.3)
Rare	0.01-0.1%	8% (7.5)
Very rare	<0.01%	4% (6.7)

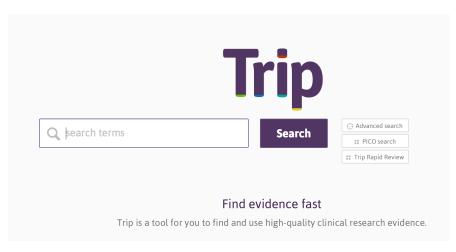
Values are mean (SD).

Lancet 2002;359:853-54

G003le

LOVE THEM!
They are my BFF

GOOGIC scholar



Trip Database - a clinical search tool designed to allow health professionals to rapidly identify the highest quality clinical evidence for clinical practice

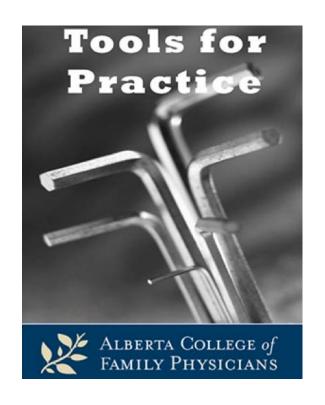


Cochrane Library - full-text access, regularly updated systematic reviews by the Cochrane Collaboration. Includes completed systematic reviews and review protocols in development.

Pubmed-Medline - broadly covers biomedical literature. The indexing data for Medline comes from the US National Library of Medicine.

OvidSP-Embase - indexes biomedical literature, with strengths in pharmaceutical information and the European and Japanese literature

Tools for Practice

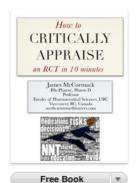


Sponsored by: Alberta College of Family Physicians http://www.acfp.ca/tfp_original.php

Every two weeks: <350 words Evidence-based review of a focused clinical question

Selected articles in: Canadian Family Physician and on PubMed

How to Critically Appraise an RCT in 10 minutes - free iBook



Get Sample

Send a sample of this book to iBooks on your devices that have Automatic Downloads enabled.

This book includes audio, video, and other interactive materials.

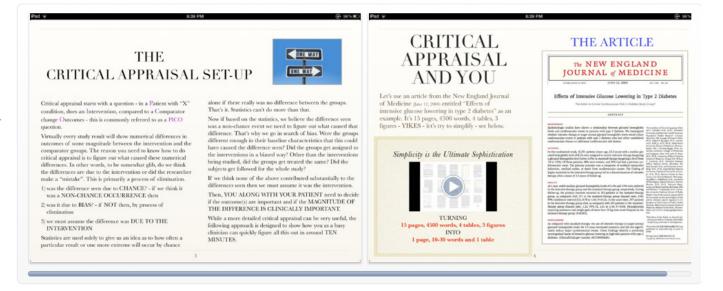
Category: Medical
Published:Jul 04, 2012
Publisher: James McCormack
Seller: Therapeutics Education
Collaboration
Print Length: 17 Pages
Size: 79.1 MB
Language: English

Requirements: This book can only be viewed using iBooks 2 or later on an iPad with iOS 5 or later.

How to Critically Appraise an RCT In 10 Minutes

Description

If the thought of reviewing a clinical study seems like an insurmountable task, this book was developed to show you how to critically evaluate a randomized controlled trial in around 10 minutes.





Outcomes Are Not Created EQUAL Surrogate Markers

Ask yourself: Can a patient feel the outcome?

If No - it is a surrogate marker

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



Risk MARKERS - lots

(risk assessment)

VS
Risk FACTORS - few (treat)

1967

Effects of Treatment on Morbidity in Hypertension

Results in Patients With Diastolic Blood Pressures Averaging 115 Through 129 mm Hg

Veterans Administration Cooperative Study Group on Antihypertensive Agents

Lower BP in patients with average DBP of 121 mmHg - 19 months

Placebo - 70 patients - 27 CVD events - 4 deaths

Drug - 73 patients - 2 events - 0 deaths

2009 Canadian Cardiovascular Society/Canadian guidelines for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease in the adult – 2009 recommendations

TARGETS OF THERAPY

Risk level	Primary target: LDL-0	C Class, level
High	<2 mmol/L	Class I, level A
CAD, PVD, atherosclerosis	or	provide the second
Most patients with diabetes	≥50% ↓ LDL-C	
FRS ≥20%	apoB <0.80 g/L	
RRS ≥20%		
Moderate	<2 mmol/L*	Class IIa, level A
FRS 10% to 19%	or	
LDL-C >3.5 mmol/L	≥50% ↓ LDL-C	
TC/HDL-C >5.0	apoB <0.80 g/L	
hs-CRP >2 mg/L in men		
>50 years and women		
>60 years of age		
Family history and hs-CRP		
modulate risk		
Low	≥50% ↓ LDL-C	Class IIa, level A
FRS <10%		

Level A = recommendation based on evidence from multiple randomized trials or meta-analyses

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

"The Expert Panel was unable to find RCT evidence to support titrating cholesterol-lowering drug therapy to achieve target LDL-C or non-HDL-C levels, as recommended by ATP III"

Effectiveness of Estrogens for Therapy of Myocardial Infarction in Middle-Age Men

JAMA 1963;183:106-12

10 mg versus placebo - over 5 years Cardio/renal event - first 3 months - 22% vs 5% - but mortality lower at 5 years therefore a new trial suggested "Feminizing effect" - 40% vs 30%

The Coronary Drug Project

Initial Findings Leading to Modifications of Its Research Protocol

The Coronary Drug Project Research Group

Terminated early

JAMA 1970;214:1303-13

5 mg versus placebo - over 18 months Definite non-fatal MI - 6.2% vs 3.2% Pulmonary embolism - 1.5% vs 0.4% Excessive shopping - 80% vs 3%

Overdiagnosis/overtreatment

the diagnosis/treatment of a condition which a person fully informed by the best available evidence would not want.

Real "Targets"

FOR RISK REDUCTION

Patient has had the benefits and risks of therapy explained to them and they have made a shared-decision

FOR SYMPTOM CONTROL

Patient has received the least expensive therapy at the lowest dose that effectively controls their symptoms

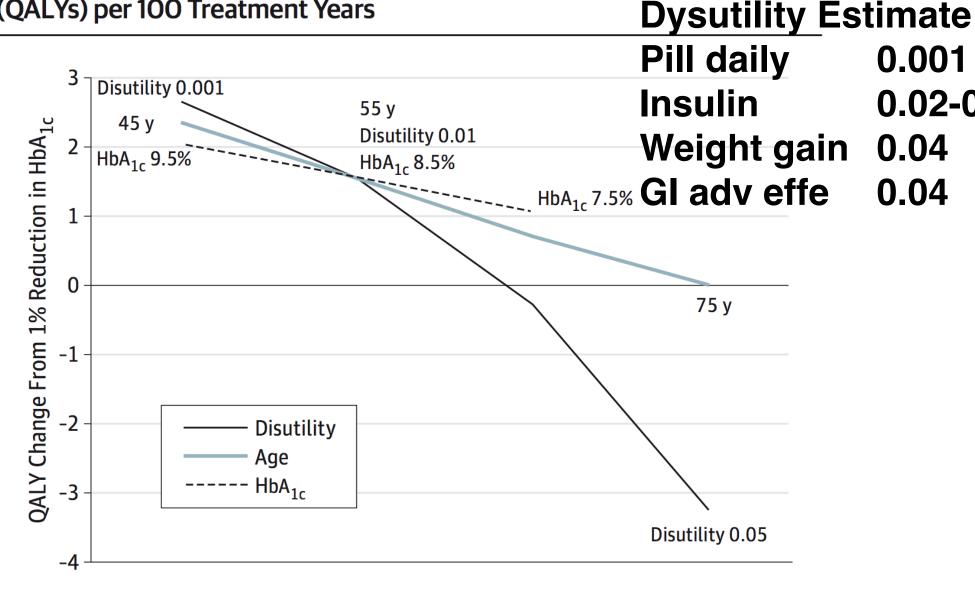
T2DM - Lifetime Treatment Benefits - absolute risk reduction

	Age	ESRD	Vision Loss	Amputation	First MI
Metformin at diagnosis	45	6.5	2.1	2.7	2.6
	55	4.2	1.6	2.2	4.0
	65	2.1	1.0	1.5	3.7
	75	0.7	0.5	8.0	2.7
Switch to Insulin after 10 years	45	1.3	0.4	0.4	1.0
	55	0.7	0.2	0.3	0.8
	65	0.3	0.1	0.2	0.6
	75	0.1	0	0.1	0.3

UKPDS - most optimistic

JAMA Intern Med. doi:10.1001/jamainternmed.2014.2894

Figure 2. Sensitivity Analysis: Changes in Quality-Adjusted Life Years (QALYs) per 100 Treatment Years



0.001

0.04

0.04

0.02-0.12

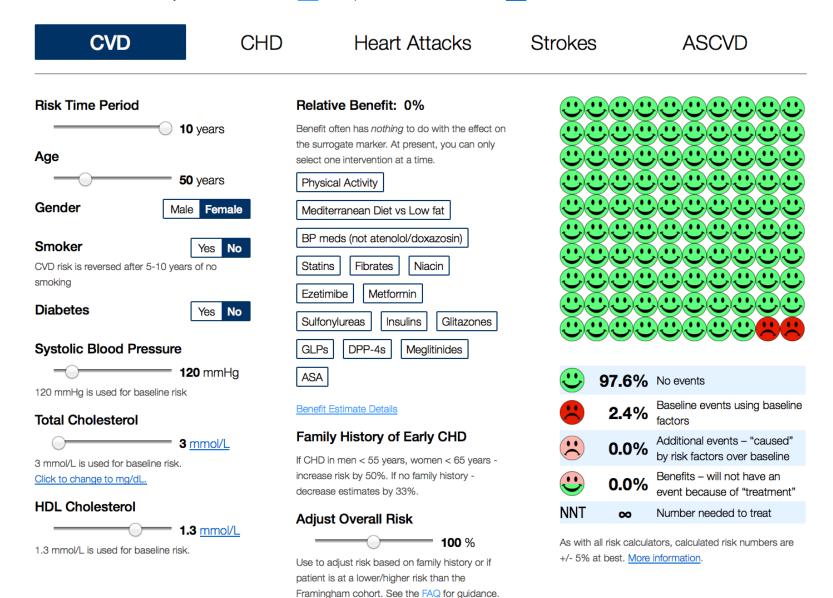
Variability in gains in QALYs from 1% reduction in hemoglobin A_{1c} HbA_{1c}) level for various age, utility, and starting HbA_{1c} values.

"Pre-diabetes could be defined as a risk factor for developing a risk factor."

Yudkin J, Montori V

Cardiovascular Risk/Benefit Calculator

Please provide feedback and suggestions to iames.mccormack@ubc.ca. For more detailed information and acronym definitions etc see the FAQ. For important calculator caveats click here.



http://cvdcalculator.com

SPARC - Stroke Prevention in Atrial Fibrillation Risk Tool

for estimating risk of stroke and benefits & risks of antithrombotic therapy in patients with chronic atrial fibrillation

references/notes

version 6.21, March 2013

Developed by Peter Loewen, ACPR, Pharm.D., FCSHP

peter.loewen@ubc.ca

In your patient with atrial fibrillation, which of the following stroke or bleeding risk factors are present?

. .	
CHADS2 CRITERIA	
CHF/LV dysfunction (diagnosed at any time in the past)	
Hypertension (controlled or uncontrolled)	
Age > 75	
Diabetes (Type I or II) controlled or uncontrolled	_
TIA or stroke at any time in the past	_
CHADS2 SCORE (0-6):0	
CHA2DS2-VASc CRITERIA	
Prior MI, peripheral artery disease, or aortic plaque	
Age 65-75	
Female	
CHA2DS2-VASc SCORE (0-9):0	
HAS-BLED CRITERIA*	
Abnormal renal function	
Abnormal liver function	
History of major bleeding (any cause)	
History of labile INR (time in therapeutic range <60%)	
Current "excess" use of alcohol	
Currently taking antiplatelet drug(s) or NSAID(s)	
HAS-BLED SCORE (0-9)*:0	
*no studies have observed major bleeding in patients with score>5,	

so these must be interpreted as "risk probably >10%".

	PERCENT PER YEAR				
				Major	
	Stroke / I		Bleed		
		CHA2DS2-		HAS-	
THERAPY	CHADS2	VASc	Pop.Avg.	BLED	
NO THERAPY	1.2%	0.7%	0.6%		
ASPIRIN	0.9%	0.5%	1.1%		
ASPIRIN+CLOP	0.7%	0.4%	3.8%		
WARFARIN	0.4%	0.2%	3.8%	1.2%	
DABIGATRAN 110	0.4%	0.2%	3.0%	1.0%	
DABIGATRAN 150	0.3%	0.2%	3.8%	1.2%	
RIVAROXABAN	0.4%	0.2%	3.8%	1.2%	
APIXABAN	0.3%	0.2%	2.6%	0.8%	

http://www.sparctool.com

Watchful Waiting

Many patients want advice and reassurance

Repeat blood pressures, cholesterols, glucose, bone densities - TRICKY but...

"Watchful waiting" - for BPH/prostate related symptoms

Alpha blockers change symptoms

irritative (frequency, nocturia, burning, urgency, or urge incontinence) or obstructive(hesitancy, weak stream, dribbling, incomplete voiding, or retention)

by 3 point on a 35 point scale - considered slightly improved

Upper respiratory tract infections

Scandinavian Prostate Cancer Group Study Number 4 (SPCG-4)

	Radical prostatectomy	Watchful waiting	Control group
Death at 18 years <65	40	66	N/A
Androgen deprevation <65	44	73	N/A
Death at 18 years >65	70	72	N/A
Androgen deprevation >65	41	63	N/A
Distress from erectile dysfunction	48	36	37
Urinary leakage once a day or more	41	H	3
Regular use of protective aid	54	25	8
Nocturia	49	63	42

N Engl J Med 2014;370:932-42

Lancet Oncol 2011; 12:891-99



EDITORIALS

BMJ 2012;344:d7955 doi: 10.1136/bmj.d7955 (Published 2 February 2012)

A prescription for improving antibiotic prescribing in primary care

Comprehensive education programmes can reduce antibiotic prescriptions, but the impact on clinical outcomes is unclear

James McCormack professor¹, G Michael Allan associate professor²

¹Faculty of Pharmaceutical Sciences, University of British Columbia, BC, Vancouver, Canada V6T1Z3; ²Department of Family Medicine, University of Alberta, AB, Edmonton, Canada

"Most community acquired infections still respond to the same antibiotics that have been used for decades and many guidelines still support their use"

Delayed prescriptions

Delayed prescriptions for sore throats and otitis media reduces the use of antibiotics far more than education about inappropriate antibiotic use

Upper respiratory tract infections

93% down to 32% - 14% still get them if you don't initially

prescribe an antibiotic

Urinary tract infections

97% down to 77%

Quality of life comparisons

	QOL utilities
Mild stroke	0.7
Angina	0.64
Diabetic neuropathy	0.66

Comprehensive diabetes care	0.64
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Diabetes Care 2007;30:2478-83

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."



A Publication of the Professional Sections of the Canadian Diabetes Association

Une publication des sections professionnelles de l'Association canadienne du diabète

We Are All Individuals

Every patient is an "n of I" study Every treatment is an experiment



Effect of Statins on Glucose

```
Jupiter study
2 years
Median A I c - 5.8% (placebo) vs 5.9% (rosuvastatin) p=0.001
Newly diagnosed diabetes inc. from 2.4% to 3.0% but
primary CV endpoint dec. from 2.8% to 1.6%
```

345,417 patients
2 years VA
Non-diabetics - FPG inc 0.17 mmol/L (3 mg/dL) more if on a statin vs no statin
0.6 (10) if diabetic

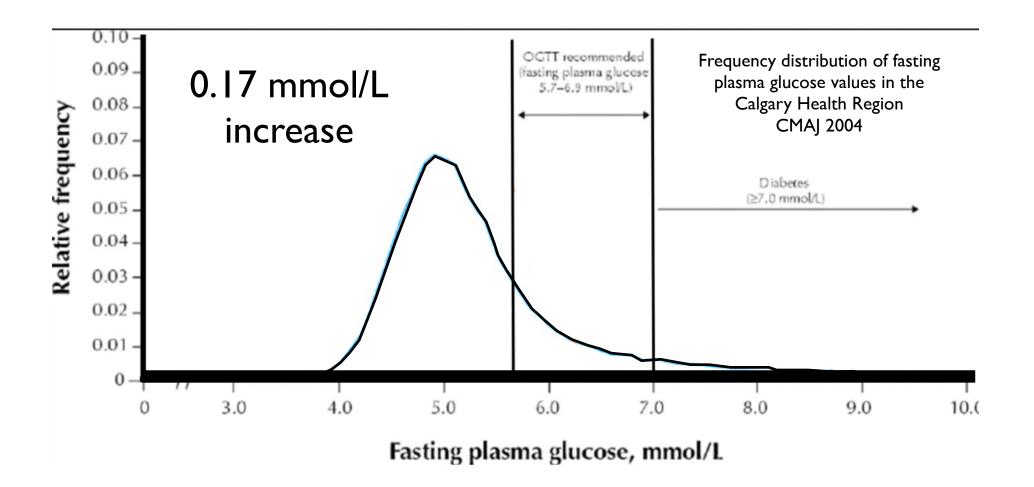
| Investig Med. 2009 Mar;57(3):495-9. doi: 10.231/JIM.0b013e318197ec8b

Effect of Statins on Glucose

TNT and IDEAL studies - statin comparative studies - excluded diabetics from analysis

	New-onset diabetes (%)	CV event (%)
Atorvastatin 10 or simvastatin 20-40mg	6.9	10.7
Atorvastatin 80 mg	7.8	9.2
RR	16% inc	I5% dec
AR	0.9% inc	1.5% dec

JACC 2013;61:148-52



The diagnosis of diabetes is the diagnosis of a SURROGATE condition/marker = HCTZ inc. glucose but dec. CV events

The Elderly

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Consider that renal and liver function are 50% at best Symptoms key!!!
Life expectancy
Statins
```

Aspirin

Warfarin

Heart failure
Inhalers for COPD

CMAJ

ANALYSIS

Is bigger better? An argument for very low starting doses

CMAJ, January 11, 2011,

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

A sample of RCT Evidence

6.25 mg hydrochlorothiazide	first marketed at 50 to 200 mg daily
6.25 mg captopril	25 mg PO TID is still a commonly recommended initial starting dose for hypertension
25 mg sildenafil (Viagra)	effective dose for erectile dysfunction
25 mg sumatriptan (Imitrex)	works as well as 100 mg
5 mg daily fluoxetine (Prozac)	similar effects to those seen at 20 mg and 40 mg daily
0.25 mg ezetimibe (Ezetrol)	I/40th of the recommended initial starting dose provides 50% of the LDL lowering effect
15 mg elemental iron daily	as effective for anemia in the elderly as 50 mg and 150 mg with a lower incidence of side effects
I50 mg daily bupropion (Zyban) 0.5 mg BID varenicline (Champix)	produces the same rate of smoking cessation at one year as 300 mg daily (1.0 mg BID)
10 mg atorvastatin	produces 2/3 of the effect on cholesterol as that seen with an 80 mg (8-fold increase) dose
200 mg ibuprofen (Motrin)	as effective as 400 mg for migraine headache
25 mg ranitidine (Zantac)	as effective as 125 mg for heartburn relief
I.8 mg colchicine	as effective as 4.8mg for acute gout with less adverse events

Doxepin (Sinequan)

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

Doxepin in the Treatment of Primary Insomnia: A Placebo-Controlled, Double-Blind, Polysomnographic Study J Clin Psychiatry 2001;62:453-63

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

INSOMNIA

Sleep 2007; 30: 1555-61

Effictative and the type of the property of th

All three doses worked better than placebo AND

NO side effects over placebo

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

CMA]

EDITORIAL

CMAJ • JANUARY 6, 2009 • 180(1)

Français à la page suivante

Medical errors, apologies and apology laws

Effect of apology on liability

- 2 (1) An apology made by or on behalf of a person in connection with any matter
 - (a) does not constitute an express or implied admission of fault or liability by the person in connection with that matter,
 - (b) does not constitute a confirmation of a cause of action in relation to that matter for the purposes of section 5 of the Limitation Act,
 - to loes not, despite any wording to the contrary in any contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract of insurance and despite any other enactment, void, impair or otherwise affect estimated and contract estimated and c
 - apology-made by-corrion-behalf-of-a-person in
 - (2) Despite any other enactment, evidence of an apology made by or on behalf of a person in connection with any matter is not admissible in any connection with a conn

court as evidence of the fault or liability of the person in connection with that matter"

How to decrease chance of lawsuits

BC has an apology law - So apologise!!!

Put in place something that will prevent the error in the future

Don't be a JERK

If there is negligence - \$\$\$\$\$\$\$\$\$