LESS IS MORE

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

MORE OR LESS

Dealing with Polypharmacy

therapeuticseducation.org
medicationmythbusters.com

POLYPHARMACY

does NOT= >5 meds

It means taking medications/supplements which

For symptoms

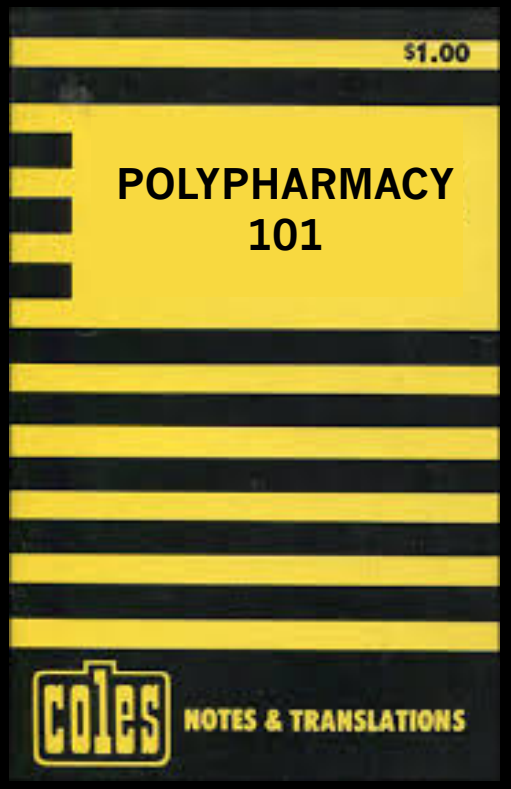
are not providing a complete or clinically important effect or are given at doses larger than is required to achieve that effect

For prevention

if one was fully informed by the best available evidence about benefits and harms one would not take them

STEP 1 - Do a Comprehensive Medication History

UNTIL PROVEN OTHERWISE



The drug and the dose are WRONG!!!!!!

STEP 2 - Prioritize the medications

a)Will it Reduce Symptoms?

Is it actually helping?

b)Will it Reduce the Risk of Future Illness?

Is the size of the effect big enough to justify the potential side effects, costs and inconvenience?

c)Will it Cause Harm?

Are any of their symptoms being caused by their medication?

Prescribing Guides

BEERS

Drug Burden Index

HEDIS

STOPP/START

NEJM 2011;365:2002-12

What causes hospitalizations

Hospitalization for Drug-related Adverse Events

In people ≥65

- Half happened in ≥80
- 66% were unintentional overdoses

67% were:

warfarin (33%), insulins (14%), oral antiplatelet agents (13%), and oral hypoglycemic agents (11%)

Prescribing rules (HEDIS, BEERS) would identify only 1-6% of the problems

N Engl J Med 2011;365:2002-12

STEP 2a - Will it reduce symptoms?

- does it have evidence that it works? - and how big of an effect?
    - sildenafil/PPIs ~ 50% absolute benefit
    - antidepressants, dementia meds ~10% absolute benefit?
- is it actually working in that patient?
- were the symptoms being caused by a medication?

STEP 2b - Will it reduce the risk of future illness?

- does it have evidence that it works? - and how big of an effect - risk tools, benefit estimates
  - ~baseline CVD/fracture risk, ~absolute benefit
- neither you nor your patient will ever know if it works
- is the medication causing any symptoms?

Risk Factors versus Clinical Endpoints

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

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

It's all about figuring out

The Chance
WITH NO TREATMENT

vs

The Chance
WITH TREATMENT

Risk of future illness
CVD risk/benefit

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

EDITORIAL

Challenging treatment thresholds

James McCormack PharmD, Aseem Malhotra MRCP and David Newman MD

National organisations such as NICE or American College of Cardiology (ACC)/American Heart Association (AHA) regularly release cardiovascular disease (CVD) guidelines that recommend lifestyle and medication interventions along with treatment thresholds based either on risk factors or calculated CVD risks.

The release of these recommendations predictably leads to intense debate from healthcare organisations, government, industry, and clinicians on whether or not the recommendations are reasonable. At one extreme the recommendations are typically pilloried as being sufficiently weak to cost lives, while others insist the guidelines have threatened public health through over-medication.

This overwrought debate is rooted, we believe, in the mysterious imperative to provide treatment thresholds, rather than offer a reasonable synopsis of best evidence and its limitations so that patients and clinicians can apply individual values. Such a best-evidence approach would support the increasing call – and need – for shared decision making in professional society guidelines.[1] Moreover, care guided by treatment thresholds largely removes individual preference from the exam room while care explicitly informed by best evidence allows tailoring to a patient's values and priorities.

When it comes to CVD risk factors, some population health advocates justify threshold-based guidelines by estimating how many heart attacks or strokes might be prevented across a population. This approach may be reasonable with vaccination for transmissible diseases, or public health regulations that demonstrate reliable and rapid real world reductions in morbidity and mortality (eg public smoking bans). However, risk factor modification with lifestyle interventions may for some individuals be unacceptably inconvenient, burdensome, or costly. In addition it is neither feasible nor desirable to speculate on a population's values or preferences. Such questions are best left to individuals, as evidenced by one recent survey study demonstrating marked variation in negative values assigned to the act of taking daily pills: some respondents would refuse daily medications even if an inexpensive pill would cause no side-effects and add 10 years to their life.[2] What current guidelines therefore fail to address is the negative value assignments associated with commonly prescribed and recommended healthcare interventions.

Hopefully most clinicians and patients will agree with the principle that information is power. While not all patients will want to take the pills, undergo invasive procedures, or take on lifestyle changes commonly used for risk factor modification, all should have access to basic facts and evidence about the utility of these options.

Lifestyle interventions

Clinicians and patients should know that roughly 80 per cent of CVD can be attributed to modifiable lifestyle factors such as nutrition, physical activity and smoking. Patients should be counselled about the nature and value of a healthy diet – a Mediterranean diet in moderation, with as little processed food as possible, is a cardiovascular intervention tested in randomised trials and shown to reduce CVD events.[3] Patients should know that physical activities, particularly enjoyable ones, can lead to important, lasting health and quality of life benefits.[4] Finally, patients should be counselled and supported to quit smoking. While associated with some costs and inconveniences, these three interventions rarely include significant harm risk, can prolong life, and have the added advantage of substantial non-cardiovascular benefits. Still, the decision to capitalise will remain individual.

Blood pressure	ALTITUDE, VALISH, AASK, ACCORD
Lipid	AIM-HIGH, HPS2-THRIVE, ACCORD, dal-OUTCOMES, RYR-ILITY
Glucose	ACCORD, ADVANCE, VADT, ROADMAP, ORIGIN, SAVOR-TIMI 53, EXAMINE, ALEDAR-DIG, TECOS

Table 1. CVD risk-factor modification studies that showed no overall CVD benefit

Theoretical benefits of risk-factor modification

Let us assume a person's lifetime risk of CVD is that of a male with two CVD risk factors, roughly 50 per cent.[5] Now let us assume that with multiple risk-factor modification we can reduce that risk relatively by 60 per cent, an optimistic assumption. This would shift a person's lifetime risk for CVD from 50 per cent to 20 per cent. In this best-case scenario approximately 30 per cent of individuals benefit, but 70 per cent do not, even despite a lifetime of treatment. This is critical for clinicians and patients to appreciate; not everyone benefits when they reduce CVD risk factors.

Indeed it may be equally important for patients and physicians to understand that over the last five or so years, a number of large, well designed studies have shown either no benefit or harm from interventions (primarily medications) that successfully modified CVD risk factors (see Table 1). Thus not only do a limited percentage of patients benefit, but in the case of risk factor modification with medications the endeavor may not always lead to a change in important clinical outcomes.

A potential solution

Below is an example of using best evidence to construct a script for offering information patients can use. We offer statins as an example, as they have likely been studied more than any risk reduction medication.

Assume a person's lifetime risk of CVD is that of a male with two CVD risk factors - roughly 50% (NEJM 2012;366:321-9)

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

Risk goes from 50% ➡ 20%

30% of individuals BENEFIT

70% DO NOT despite a LIFETIME of treatment

Prescriber September 2015

Risks over short time periods

Assume a 5% (5/100) reduction in CVD over 5 years

~ 1% (1/100) reduction over one year

~ 0.1% (1/1000) per month

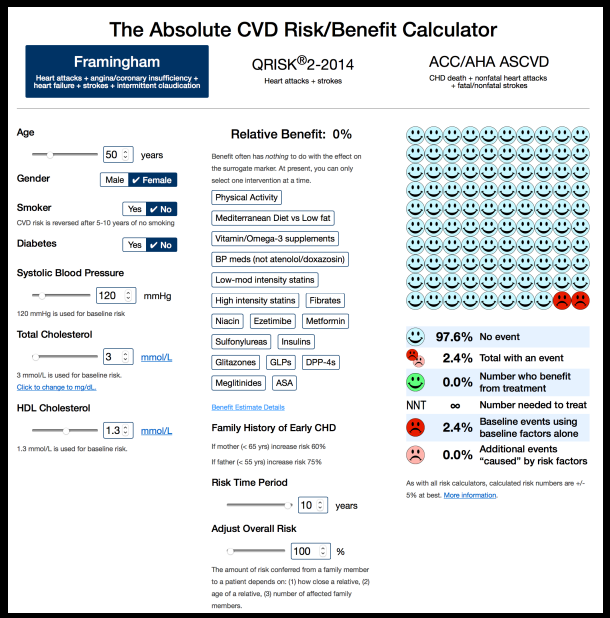
~ 0.02 (1/5000) per week

Patient

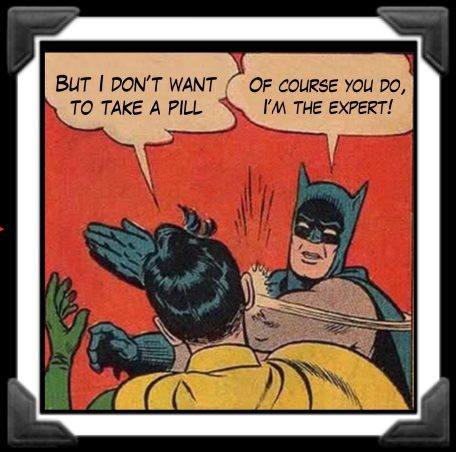
ACTIVITY AND NUTRITION!!!

Measure SBP/chol/glucose

Risk of cardiovascular disease



Patient decision



Treatment
Thiazides
ACE inhibitors
Statins etc

EVIDENCE FOR, AND MAGNITUDE OF, THE reduction in cardiovascular outcomes
SIDE EFFECTS

Repeat measurements?

Reevaluate need

The Absolute CVD Risk/Benefit Calculator

Framingham
Heart attacks + angina/coronary insufficiency + heart failure + strokes + intermittent claudication

QRISK®2-2014
Heart attacks + strokes

ACC/AHA ASCVD
CHD death + nonfatal heart attacks + fatal/nonfatal strokes

Age 50 years

Gender Male ✔ Female

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

Diabetes Yes ✔ No

Systolic Blood Pressure 120 mmHg
Blood pressure should be prior to drug treatment
120 mmHg is used for baseline risk

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

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

Family History of Early CHD 0 %
The amount of additional risk conferred from a family member to a patient depends on: (1) how close a relative, (2) age of a relative, (3) number of affected family members.
If mother (< 65 yrs) increase risk 60%
If father (< 55 yrs) increase risk 75%

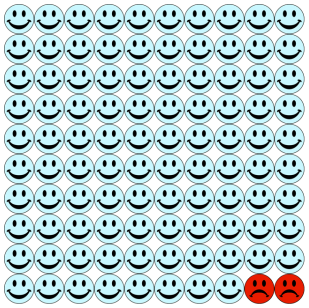
Relative Benefit: 0%

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

- Physical Activity
- Mediterranean Diet vs Low fat
- Vitamin/Omega-3 supplements
- BP meds (not atenolol/doxazosin)
- Low-mod intensity statins
- High intensity statins
- Fibrates
- Niacin
- Ezetimibe
- Metformin
- Sulfonylureas
- Insulins
- Glitazones
- GLPs
- DPP-4s
- Meglitinides
- SGLT2
- Smoking Cessation
- ASA

Benefit Estimate Details

Risk Time Period 10 years



	97.6%	No event
	2.4%	Total with an event
	0.0%	Number who benefit from treatment
NNT	∞	Number needed to treat
	2.4%	Baseline events using baseline factors alone
	0.0%	Additional events "caused" by risk factors

As with all risk calculators, calculated risk numbers are +/- 5% at best. More information.

Switch to "Basic" View

cvdcalculator.com

Oswald Chesterfield Cobblepot
AKA The Penguin
60 years old
Loves birds
Lives a luxurious lifestyle
Relatively inactive
PMH - Conduct disorder
Smoker
A1c 8
BP 150/90 mm/Hg
Total cholesterol 6 (240)
HDL 1 (40)

10 year risk

Framingham (HA, angina, HF, stroke, int claud) = 53%

ASCVD (HA, stroke) = 41%

Bruce Banner
AKA The Hulk
Age 45
Scientist
Easily agitated,
and emotionally withdrawn
SBP 160 mm/Hg
Non-smoker
Non-diabetic
Total cholesterol 4.4 (180)
HDL 1.5 (60)
AM testosterone: 330 nmol/L (N 6.7-29)
Urine catechol: +ve (no urine found)

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AKA The Hulk
Age 45
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Urine catechol: +ve (no urine found)

10 year risk

Framingham (HA, angina, HF, stroke, int claud) = 8%

ASCVD (HA, stroke) = 2%

Wonder Woman
Age 40 (OK she ages well)
BP 120/70 mmHg
Total cholesterol 6.8(270)
HDL 1.6 (65)
LDL 5.0 (200)
Trigs 1
Diet mostly caiman and anaconda (rich in cholesterol)
Non-diabetic
Not a smoker (but still smokin')
PMH: Charles Bonnet Syndrome
(suffers from visual hallucinations that are pleasant: in this case, a jet)
Wears bracelets as a defence but otherwise dresses more than appropriately!

Wonder Woman
Age 40 (OK she ages well)
BP 120/70 mmHg
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Not a smoker (but still smokin')
PMH: Charles Bonnet Syndrome
(suffers from visual hallucinations that are pleasant: in this case, a jet)
Wears bracelets as a defence but otherwise dresses more than appropriately!

10 year risk

Framingham (HA, angina, HF, stroke, int claud) = 2%

ASCVD (HA, stroke) = 1%

Relative risk reductions with different interventions in DM2

	Treat BP	Treat Lipid	Treat Sugar
CVD events	~ 50%	~20-25%	~ 12.5%
Mortality	16%	8%	NSS

Diabetes Care 2010;33(1): S11-61, Ann Intern Med 2008;148:846-54, Lancet 2009;373:1765–72, Lancet 2008; 371:117–25, Ann Intern Med 2003;138:587-92

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."

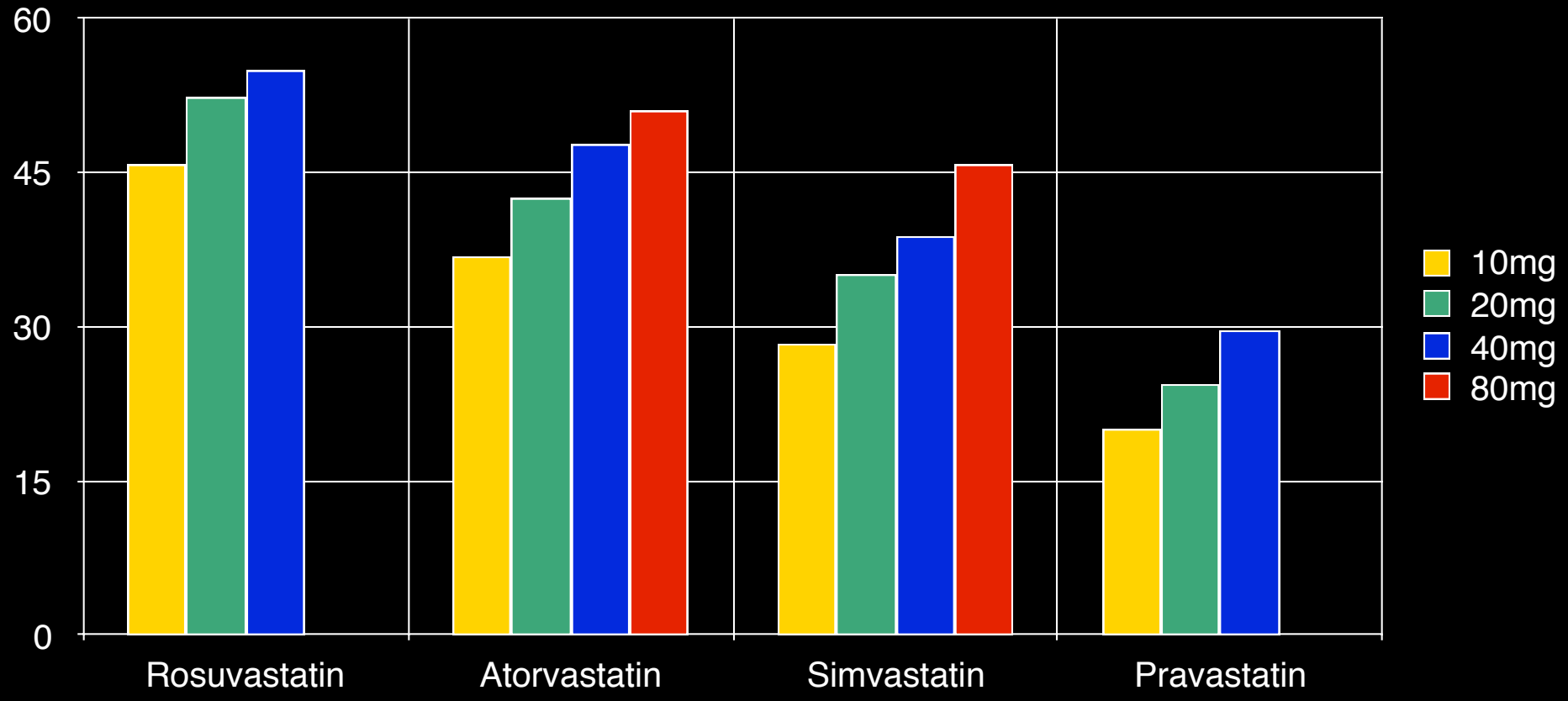
STEP 2c - Realise every medication causes harm

- inconvenience
- labelling
- costs
- SIDE EFFECTS

STEP 3 - Identify if the lowest dose has been determined

- recommended starting doses are typically too high
- 75% of side effects are dose-related
- can’t predict response
- the right dose is the lowest dose that does the job

% reduction in LDL cholesterol



STEP 4 - Let the patient help you

- what ones don’t they like taking?
- which ones do they feel are helping them?
- cost/inconvenience

STEP 5 - Use tricks to get buy-in

THEIR ARGUEMENTS

- I've been on these for years and now you are telling me I don't need them
- But these are for my heart!!
- It's OK, I don't pay for my medications
- But my "insert any specialist" says I need these
- If it ain't broke don't fix it

YOUR ARGUMENTS

- Well your renal function/hepatic function are decreased
- Look what you've been able to do for yourself
- You take control and figure out the dose - you teach me what works
- Your specialist doesn't know you like I do
- We can always restart if we need to

STEP 6 - Use common sense when tapering medications

- if it is causing an important problem just stop it
- most medications could probably just be stopped BUT…
- typically recommend one at a time BUT be realistic
- cutting the dose in half reduces everyone's apprehension
- rebound - psychiatric/CVD medications for symptoms - IHD/blood pressure

The MedStopper Team

James McCormack (UBC)
Rita McCracken (UBC)
Dee Mangin (McMaster U, Hamilton)
Barb Farrell (Bruyère Research Institute, Ottawa)
Robert Rangno (UBC, Emeritus)
John Sloan (Vancouver GP)
Michael Allan (University of Alberta)
Johanna Trimble (patient representative and observer)
Alan Cassels (project administrator)
Keith White (Local GP)
Malcolm MaclureBC Academic Chair in Patient Safety and Professor in the Department of Anesthesiology, Pharmacology and Therapeutics at UBC.
Dan Kim (IHI student)
Robert Yao (IHI student)
Jacqueline Eng (IHI student)
Saaranga Sasitharan (IHI student)

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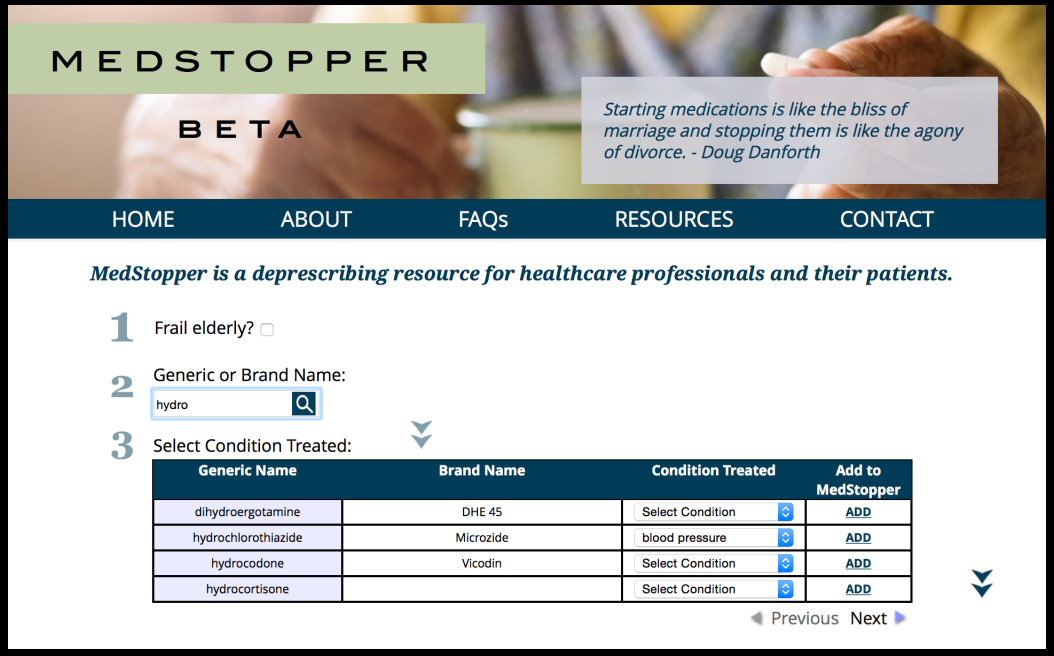
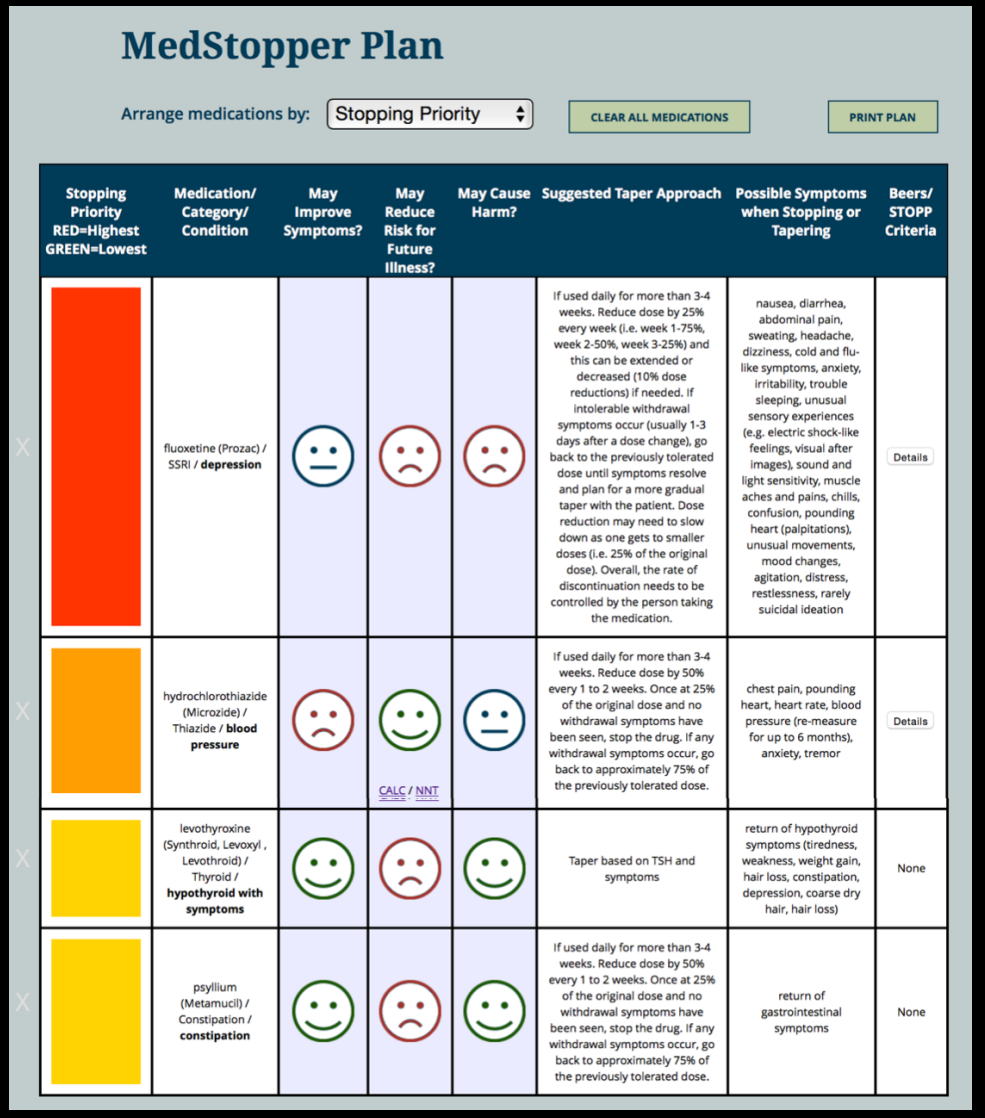
Optimum Prescribing Updates and Support Action-Period Tools (OPUS-APT). KTA grant is “to increase the uptake/application of knowledge by supporting partnerships between researchers and knowledge-users to bridge a knowledge-to-action gap, and in so doing, increase the understanding of knowledge application through the process.”

Participants from BC’s Shared Care Polypharmacy Risk Reduction Initiative and the Institute of Healthcare Improvement (IHI) Open School UBC Chapter

MEDSTOPPER





medstopper.com

You Might Have a Problem if you Find:

- Any drug that was not started at the very lowest dose
- Any drug that has been added without the patient having been given an informed choice
- Any drug that hasn't been re-evaluated "annually"
- Any drug that doesn't make the patient feel better

Med Stopper

A parody of the great Beatles song

Day Tripper

UNFORTUNATELY TOO OFTEN

"Starting a drug is like the bliss of marriage and stopping a drug is like the agony of divorce"


STOP
REALLY
YOU GOTTA
STOP

RL (a Family MD)
Mid -Feb

Her Grandmother - 90 year old very frail female

History of a. fib, hypertension, angina, congestive heart failure, familial tremor, macular degeneration and recently diagnosed with diabetes. Blood sugars running 8-15 prior to treatment

Hb A1C - 8.3

Never smoked

Suffered a compression fracture of a thoracic vertebrae in the fall.

A lung mass not yet diagnosed - elected not to proceed with the bronchoscopy.

Echocardiogram from the fall - not much of anything

Clinically she gets tachycardia and short of breath walking 15 feet

HR 81

BP sitting 139/65

BP standing after 1 minute 154/73 and heart rate 73

20 regular meds/4 PRNs	Improves symptoms	Long term benefit	Potential for harm	Rebound potential	Dose reduction useful	STOP 12 HALF 5
Gliclazide 30mg daily	N	?	+++	Y	Y	STOPPED
Potassium chloride 600mg daily	N	N	+	N	N	STOPPED
Ramipril 10mg daily	?	Y	+++	Y	Y	HALF
Metoprolol 100mg twice daily	?	Y	+++	Y	Y	HALF
Furosemide 40mg daily	Y	Y	++	Y	T	KEPT
Valsartan 160mg daily	?	Y	+++	Y	Y	HALF
Digoxin 0.0625mg daily	N	?	+++	N	Y	STOPPED
Hydromorphone 3mg twice daily	Y	Y	++	Y	T	KEPT
Vitamin D 1000 IU daily	N	?	-	N	N	STOPPED
Calcium 1250mg daily	N	N	+	N	N	STOPPED
B12 250mg daily	N	N	+	N	N	STOPPED
Vitamin C 500mg daily	N	N	-	N	N	STOPPED
Vitalux daily	N	Y	-	N	N	STOPPED
Omega 3s daily	N	N	-	N	N	STOPPED
Warfarin 2mg daily/3mg every other day	N	Y	+++	N	T	KEPT
Atorvastatin 20mg daily	N	Y	++	N	Y	HALF
Zopiclone 3.75mg daily	Y	N	++	Y	Y	HALF
Senosside 12mg daily	Y	Y	+	Y	T	KEPT
Nitro patch 0.4mg qhs	Y	Y	+	Y	T	KEPT
Atrovent	N	N	-	N	Y	STOPPED
Flovent	N	N	+	N	Y	STOPPED
PRN Ativan 0.5 mg sl for anxiety/ SOB	N	N	+	N	Y	STOPPED
PRN Nitro spray	Y	Y	-	N	N/A	-
PRN Hydromorphone 1mg	Y	Y	-	N	N/A	-
PRN Gravol	Y	Y	-	N	N/A	-