Top 7 Risky Meds in the Elderly

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risk·y
/ˈriskē/

adjective
1. full of the possibility of danger, failure, or loss.

therapeuticseducation.org
mystudies.org
@medmyths

GET HANDOUT HERE
https://therapeuticseducation.org/handouts

Any medication that….

produces an ongoing “side-effect”

has been added without the patient being given an informed choice

was not started at the very lowest dose

you haven’t re-eVALUated annually

doesn’t make your patient, not you, feel better

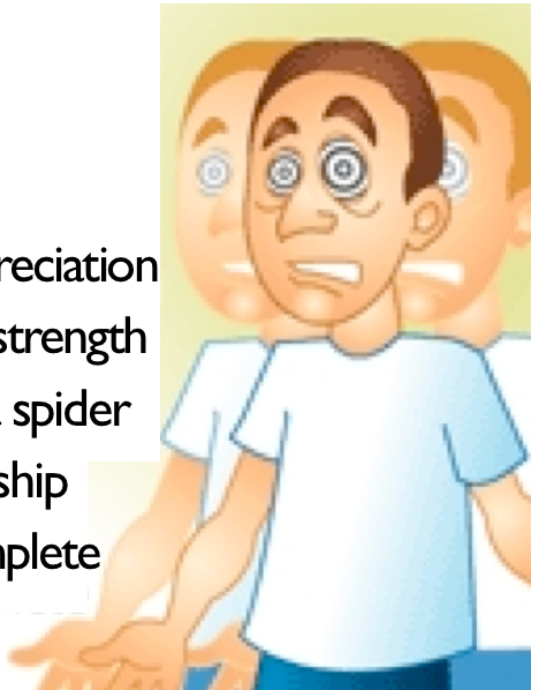
impacts your patient’s ability to buy or do other fun things in life

is any one of the following - stay tuned

1) Any medication that produces an ongoing “side-effect”

MOST COMMON DRUG SIDE EFFECTS

16% Eye poppage
13% Penile lactation
11% Highness
14% Music over-appreciation
21% Proportionate strength and speed of a spider
12% Swedish citizenship
1% Inability to complete “Smile” album



Studies of unsafe prescribing

- Mainly benzodiazepines, antidepressants, antipsychotics, anticholinergics, BP meds, etc.[1]
- Benzodiazepine in age ≥80 associated with falls
  - Perhaps 2.8% increase falls/yr (9% fatal)[2]
- Systematic Rev: 29 studies (28 cohort, 1 RCT)[3]
  - Mainly benzodiazepine, antidepressants, antipsychotics
  - Also BP meds & anti-epileptic (weaker association)
- Med associated with falls[4]
  - Consistent: Sedative/hypnotics, Benzodiazepines, & antidepressants
  - Less consistent: Neuroleptics/antipsychotics & anti-hypertension

1) Arch Intern Med. 2009;169(21):1952-1960. 2) Drugs Aging. 2008;25(1):61-70. 3) J Gerontol A Biol Sci Med Sci. 2007 Oct;62(10):1172-81. 4) Arch Intern Med. 2009;169(21):1952-1960

SLIDE STOLEN FROM MIKE ALLAN

Studies of unsafe prescribing

Systematic review[1]: meds associated with fracture

1.34 (1.24, 1.45) for benzodiazepines (23 studies)

1.60 (1.38, 1.86) for antidepressants (16 studies)

1.54 (1.24,1.93) for antiepileptic drugs (13 studies)

1.59 (1.27, 1.98) for antipsychotics (12 studies)

1.38 (1.15, 1.66) for opioids (six studies).

NSAIDS may also be associated with falls.[2]

1) Drug Safety 2007; 30 (2): 171-184. 2) Drug Safety 2009; 32(6): 489-98.

SLIDE STOLEN FROM MIKE ALLAN

“A drug without a side effect is a drug without an effect”

Bob Rangno circa 1980

All medications can cause side effects

Most side effects are dose-related

In a patient with “symptoms”, suspect their medications

Ask the patient

2) Any medication that has been added without the patient being given an informed choice

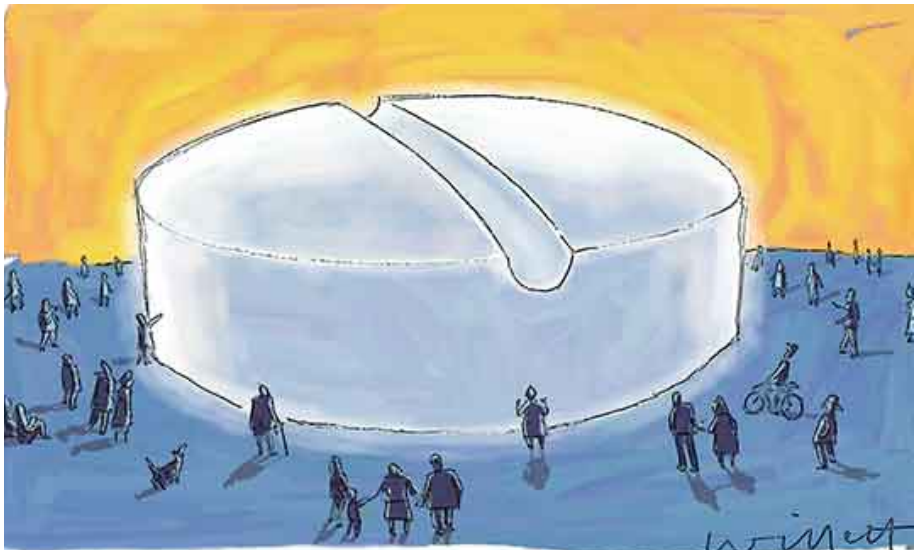
Understanding of the rough numbers

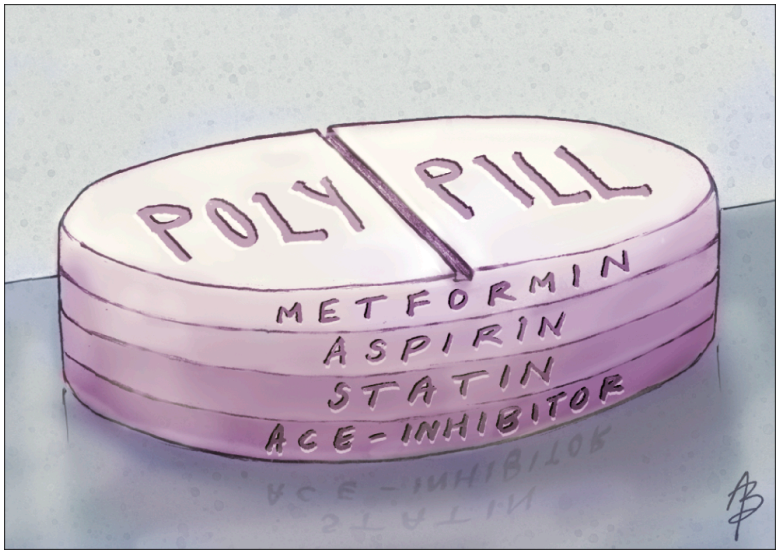
Do the experiment

Re-evaluate

No guilt

Prevention medications





You need to have an agreement agenda NOT an adherence agenda

Intelligent non-adherence

Institutionalised patients!!! - “forced” adherence

How to tell if a medication worked/is working?

Drugs for Prevention

blood pressure, statins, glucose, bone density

YOU really CAN’T

And likely over a lifetime a patient won’t benefit ...

Ballpark absolute benefits (%) for CVD medications

Cardiovascular events	Primary Prevention 5 years		T2DM (glucose) 3-5 years		Secondary prevention 2-3 years
	BP	Statins	Most meds	SGLT2, GLP, metformin?	ACEI, BB, ARB, Statins
Cardiovascular events	2-5	1-2	0	2-5	5-10
Mortality	<1	<1	0	1-2	2-5
RELATIVE BENEFITS	30-50%	25-35%	15%		

mystudies.org, cvdcalculator.com

Annals of Internal Medicine

REVIEW

JUNE 2020 - Ann Intern Med. doi:10.7326/M20-0864

Comparative Effectiveness of Glucose-Lowering Drugs for Type 2 Diabetes

A Systematic Review and Network Meta-analysis

PLACEBO COMPARATORS - 80-100 benefit estimates

α-glucosidase inhibitors
Basal insulin
Basal bolus insulin
DPP-4
GLP-1
Meglitinides
Metformin
Pioglitazone
Prandial insulin
Pre-mixed insulin
SGLT-2
SU

–

Mortality
CVD mortality
MI
Stroke
Hosp HF
Diabetic retinopathy
Amputation
ESRD

1) At low risk - drug naive
43 no evidence/37 no benefit

2) At low risk and on metformin
24 no evidence/60 no benefit/3 benefit/1 harm
GLP - 35% reduction in mortality and MI
SGLT - 45% reduction in MI
SU - 200% increase in retinopathy

3) At increased risk and on metformin
50 no evidence/31 no benefit/6 benefit/1 harm
GLP - 15% reduction in mortality, CVD mortality and stroke
SGLT - 15% reduction in mortality, CVD mortality and 35% reduction in ESRD
Pioglitazone - 40% increase in hosp HF

Insulin and SU all increased hypoglycaemia 2-5 X

Subset analysis in patients >65 - no suggestion of a benefit but only a few classes studied αGI/DPP-4/GLP-1/SU/metformin

Meta-analyses of medications for heart failure - versus placebo

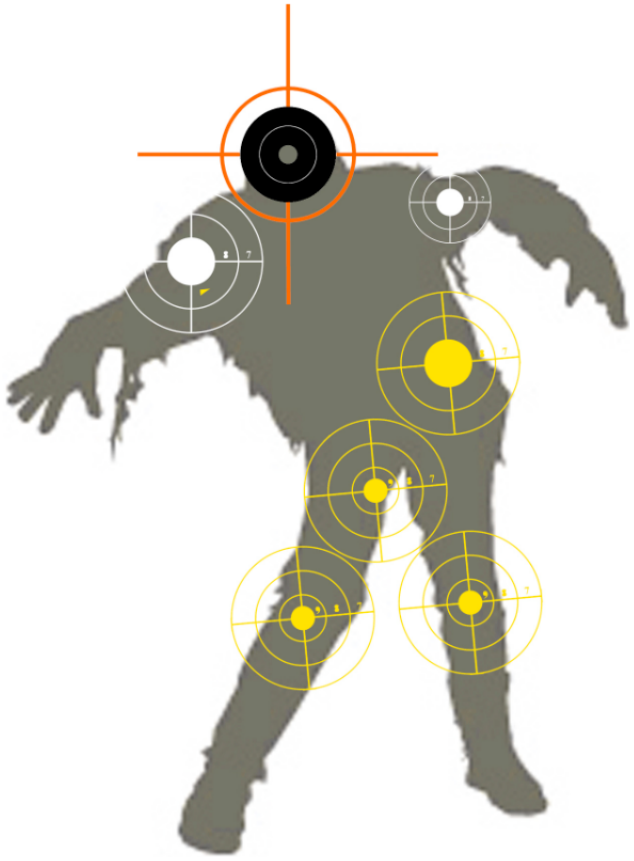
REMEMBER BASELINE - mortality ~15-25% and hospital admission for HF ~15-20%

	Mortality	Hospitalization for HF	
Betablockers 1 year	0.65 (0.53-0.80) ~5% ARR	0.64 (0.53-0.79) ~6% ARR	**Ann Intern Med 2001;134:550-60**
ACEI 3 years	0·80 (0·74-0·87) ~3.5% ARR	0·67 (0·61–0·74) ~5% ARR	**Lancet 2000;355:1575-81**
ARB 2-3 years	0.83 (0.69-1.00) ~3% ARR	0.64 (0.53-0.78) ~9% ARR	**Ann Intern Med 2004;141:693-704**
MRA (spironolactone/eplerenone) 15 months	0.81 (0.75-0.87) ~3.5% ARR	0.76 (0.64-0.90) ~6% ARR	**BMC Cardiovasc Disord 2016;16:246**
Exercise 1 year	~0.9	~0.6	**Open Heart 2015;2:e000163. doi:10.1136/openhrt-2014-000163**

CLASS 2-3 heart failure

	MOST MEDICATIONS (relative reduction)	
Mortality		Mortality
~25% over 2-3 years	**~20% ⬇**	**~20% over 2-3 years**
Hospitalizations for heart failure	MOST MEDICATIONS	Hospitalizations for heart failure
~15% over 2-3 years	**~30% ⬇**	**~10% over 2-3 years**

Target DOSES



Heart failure - if you can get to higher doses

(Absolute differences)

Mortality no difference

OUTCOME	ACEI ~ 2 years	ARB ~ 4 years	BB ~ 1.5 years
Hospitalization for heart failure	No difference	3% less	No difference
Heart failure worsening	5% less	3% less	No difference
Hypotension	3% more	2.5% more	No difference
Dizziness	5% more	Not reported	14% more
Hyperkalemia	2.5% more	3% more	Not reported
Increase SCr	2.5% more	6% more	Not reported
Cough	2.5% less	Not reported	Not reported

PLOS ONE Meta-analysis Feb 28th, 2019

Atrial Fibrillation - benefits/harms

Score	Risk of Stroke/Yr	On ASA ~22% relative benefit	On OAC ~66% relative benefit
Age <65 - 0 RF	0.7%	0.5%	0.2%
<65 - 1 RF 65-74 - 0 RF	1.5%	1.2%	0.5%
<65 - 2 RF 65-74 - 1 RF >75 - 0 RF	2.9%	2.3%	1.0%
<65 - 3RF 65-74 - 2RF >75 - 1RF	4.3%	3.4%	1.4%
<65 - 4RF 65-74 - 3RF >75 - 2RF	6.5%	5.1%	2.1%
<65 - 5RF 65-74 - 4RF >75 - 3RF	10%	7.8%	3.3%
Annual risk of major bleeding	0.5%	1%	2-10%

CVD, Female, CHF, HTN, or T2DM = 1 RF

Previous stroke/ TIA = 2 RF

http://www.sparctool.com

Optimal management of elderly pts with vascular disease (DEBATE)

RCT, f/u 3.4 years 400 patients - avg age 80, all CVD

Usual care (primary care) or specialized care

“Evidence-Based” European CPG for chronic CVD

“it was possible and safe to institute evidence-based cardiovascular treatments and improve risk factors in patients 75 years or older in a pragmatic setting.”

Am Heart J 2006;152:585-92

Outcome

Systolic BP: 7.8 mmHg lower
Diastolic BP: 3.9 mmHg lower
Glucose: 0.55 mmol/L lower
Cholesterol: 0.78 mmol/L lower
LDL: 0.73 mmol/L lower (45% to target)
MEDS: ACE (+30%) & statin (+50%)

PREDICTED BENEFIT
UKPDS risk engine
18% CVD risk
reduced to 14%
NNT = 25

ACTUAL BENEFIT - NONE

IN BOTH GROUPS

Mortality 18%

Stroke 6%

MI/coronary death 16%

NNT = infinite

For T2DM, let's extrapolate the best case example to 10 years

~2% absolute benefit over ~3.5 years - for a few new agents - primarily in secondary prevention

~6% absolute benefit over 10 years

in the best case example at least 94% of people will get no benefit, some will get harm (hypoglycemia, genital infections, Gi disturbance), and all will experience the inconvenience and cost of treating for 10 years

~3500 pills or injections

the new agents cost ~ $12,000 for 10 years, basal insulin ~$4,000, metformin ~$1,200 plus any monitoring costs

NOBODY will feel better because of these treatments

What you should shoot for

Start with really low doses

No hurry

Surrogate markers

Is the benefit because of the effect on the surrogate?

Don't measure obsessively

The most benefit is getting them from really HIGH, not getting to really low

Target Doses

If you can get them to the doses in the studies GREAT but don't sweat it nor let your patients sweat it

75% of side effects are dose-related

Side effects are unacceptable

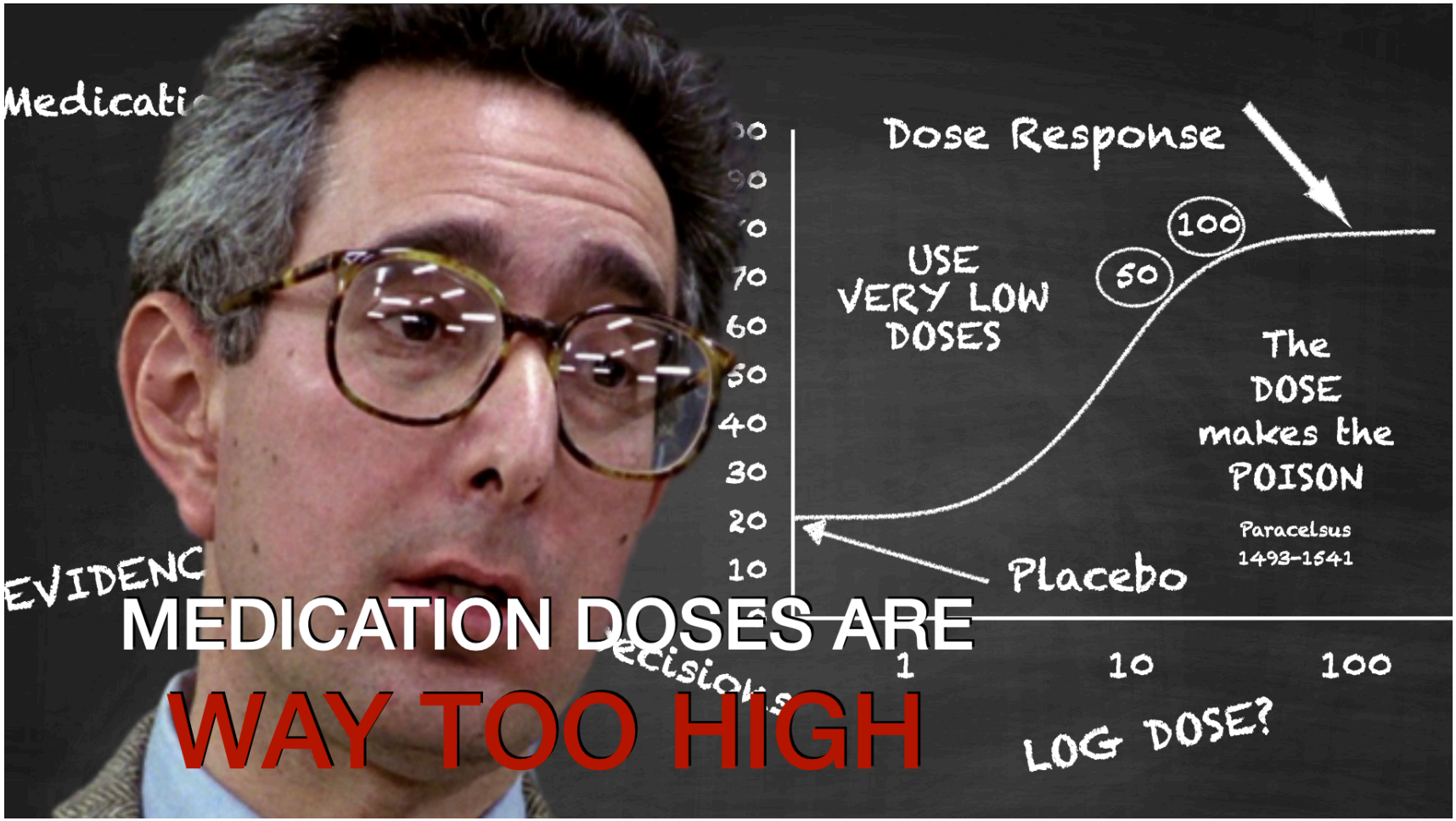
3) Any medication that was not started at the very lowest dose

No hurry

Most standard doses are excessive

DON’T start with low doses

Start with VERY low doses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MEDICATION DOSES ARE
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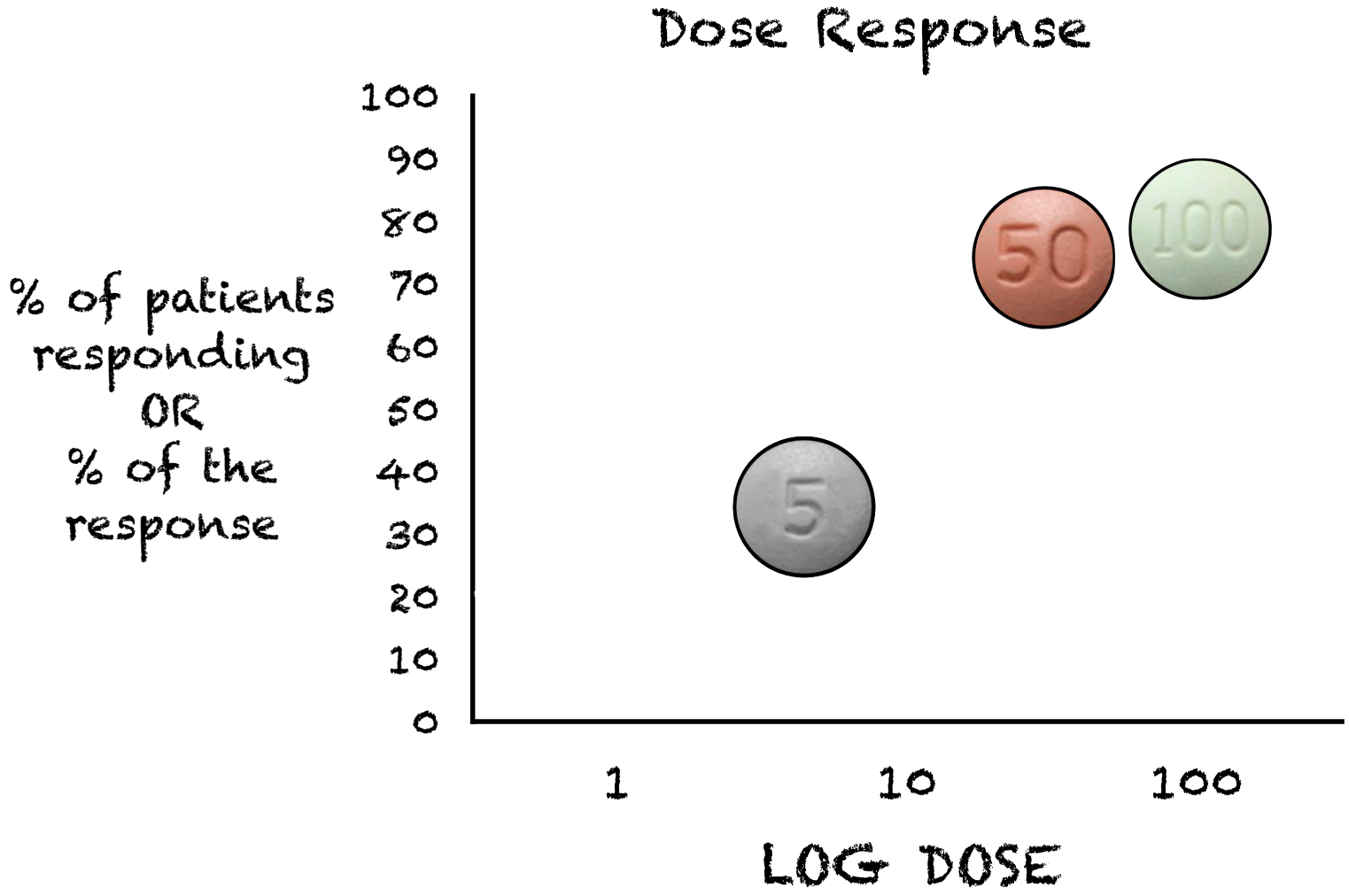
Dose Response
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% of patients responding OR % of the response
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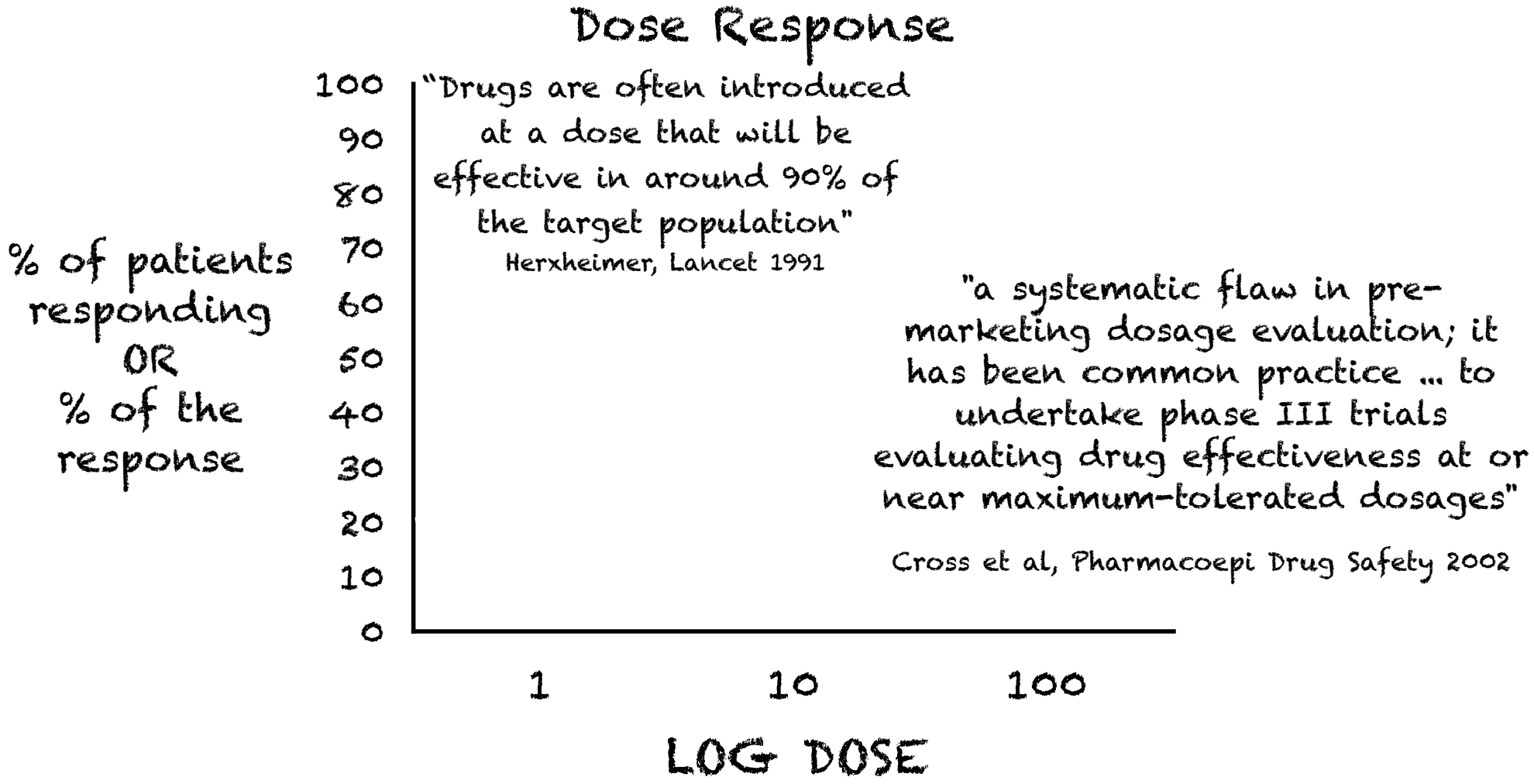


McCormack J. A dose of reality [video clip]. 2020 Mar 21. Available from: URL: https://www.youtube.com/watch?v=lXK2j1Qxb4U.

4) Any medication you haven't re-eVALUated annually

"starting drugs is like the bliss of marriage, stopping them is like the agony of divorce"

Need

Dose

Duration

Guiltless choice

Symptoms

“Depressing” but very empowering concepts

SYMPTOMS

If a patient seems to be getting a benefit from a medication for symptoms they likely aren't

DOSE

If a patient is on a medication they are likely on too high a dose

How to tell if a drug worked/is working?

Drugs for Symptoms

Acute self-limiting symptoms

You really can’t

“Chronic” symptoms - Maybe - with reassessment - Drugectomy or dose reduction

Need to have a rough idea of the response in the placebo group

Symptom NNTs

PPIs, sildenafil - NNT ~2

NSAIDs, opioids - pain NNT ~3-5

Antidepressants - severe depression - NNT ~10

Ipratropium - asthma attack - NNT ~11

Cholinesterase inhibitors - ADAS-Cog >4 - NNT ~10

Sleeping pills - improvement in sleep quality - NNT ~13

Steroids - sore throat - NNT ~3, Bell's palsy - NNT ~10

Antibiotics - acute COPD exacerbation - NNT ~5

Topical antibiotics - bacterial conjunctivitis - NNT ~7

But you need to know what goes on in the placebo group

	If a person has responded, what is the % chance it was the medication	
Response in the placebo group	RCT Benefit 10% - NNT 10	RCT Benefit 20% - NNT 5
0%	~100%	~100%
10%	~50%	~66%
20%	~33%	~50%
30%	~25%	~40%
40%	~20%	~33%

The Placebo Group Effect

NOT the placebo effect and these are ballpark numbers

~0% - general anesthesia

~5% - psychosis

~10% - sildenafil, OCD

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

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

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

~40% - panic disorders

5) Any medication that doesn’t make your patient, not you, feel better

Prevention medications do NOT make people feel better

primary prevention

1-2% (maybe 5%) benefit over 5 years - 98-99% do not

secondary prevention

5-10% benefit over 5 years - 90-95% do not

lab tests

false positives

witch hunt

evidence plus patient values - 1/3 not adherent

Quality of life comparisons

	QOL utilities
Mild stroke	0.7
Angina	0.64
Diabetic neuropathy	0.66

Comprehensive diabetes care	0.64

Diabetes Care 2007;30:2478-83

6) Any medication that impacts your patient's ability to buy or do other fun things in life

Food

Travel

Scotch

Twinkies

Chocolate - the good kind

"newer is better?" - $$

7) Any one of these

Indomethacin

Atenolol

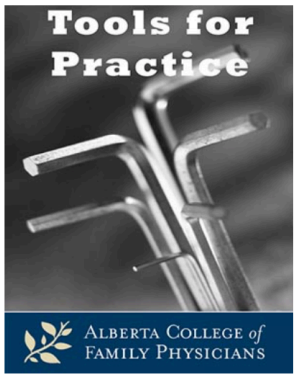
Colace

Digoxin

Antipsychotics

Multivitamins

Drugs that make patients fall down - sedative drugs, blood pressure/glucose lowering drugs



What Are the Risks and Benefits of Stopping Antipsychotics in the Elderly?

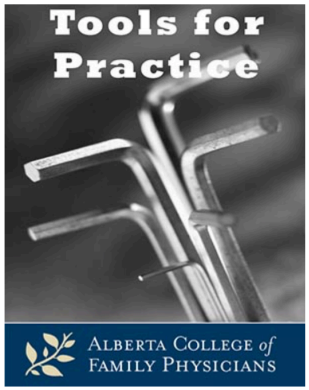
July 4, 2013

<u>Clinical Question</u>: In elderly patients, what are the risks and benefits of stopping long-term antipsychotics (initiated for behavioral concerns)?

<u>Bottom-line</u>: In elderly patients on long-term antipsychotics, withdrawal of antipsychotics in four patients may prevent one death at two years. After discontinuation, neuropsychiatric symptoms appear to vary little, although one study suggests stopping after four months can cause one in four more patients to have a relapse of neuropsychiatric symptoms.

Withdrawal of antipsychotics - for every 4 people, you prevent 1 death and 1 study suggests that 1 in 4 will have a relapse of neuropsychiatric symptoms

Antipsychotics also worsen cognition



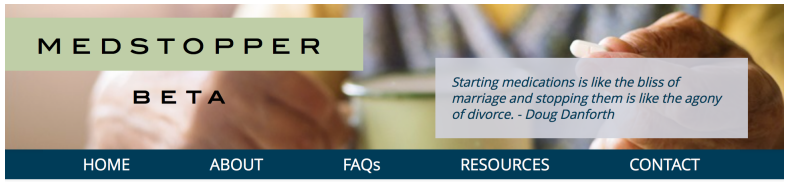
Agitation in Dementia: Are benzos a back-up?

March 2, 2015

<u>Clinical Question</u>: Are benzodiazepines a reasonable pharmaceutical alternative for management of agitation in demented elders?

<u>Bottom-Line</u>: Many trials are old, most are short and/or small, and the results are inconsistent. Benzodiazepines appear, at best, equivalent to antipsychotics in reducing agitation in the short-term, but superior to placebo. If used, they should be stopped as soon as possible due to potential harms.

MEDSTOPPER



MedStopper is a deprescribing resource for healthcare professionals and their patients.

1 Frail elderly? ☐

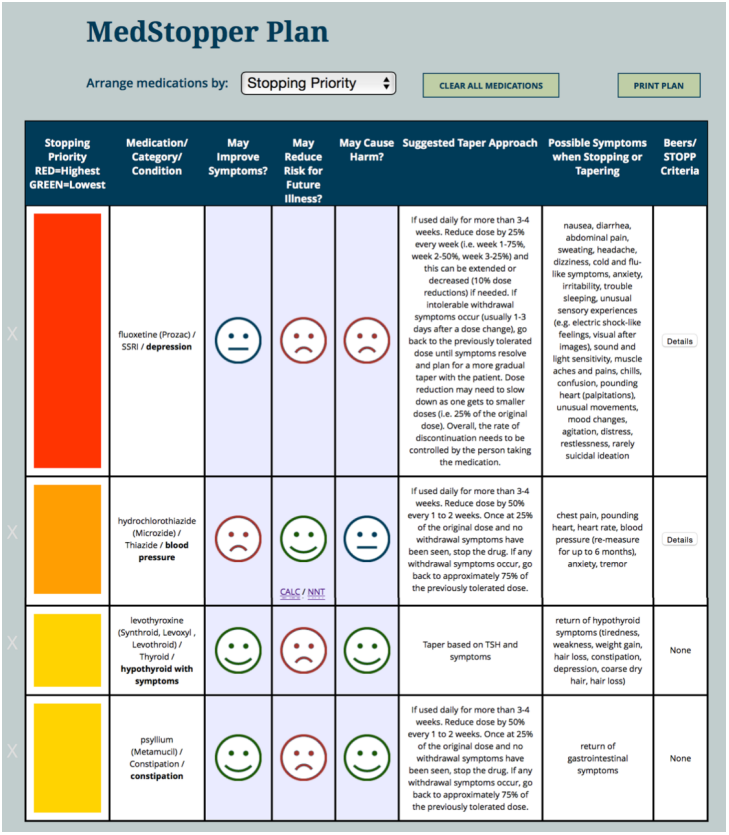
2 Generic or Brand Name:

hydro

3 Select Condition Treated:

Generic Name	Brand Name	Condition Treated	Add to MedStopper
dihydroergotamine	DHE 45	Select Condition	ADD
hydrochlorothiazide	Microzide	blood pressure	ADD
hydrocodone	Vicodin	Select Condition	ADD
hydrocortisone		Select Condition	ADD

Previous Next



MedStopper Plan

Arrange medications by: Stopping Priority

CLEAR ALL MEDICATIONS PRINT PLAN

Stopping Priority RED=Highest GREEN=Lowest	Medication/ Category/ Condition	May Improve Symptoms?	May Reduce Risk for Future Illness?	May Cause Harm?	Suggested Taper Approach	Possible Symptoms when Stopping or Tapering	Beers/ STOPP Criteria
X	fluoxetine (Prozac) / SSRI / **depression**	😐	☹	☹	If used daily for more than 3-4 weeks. Reduce dose by 25% every week (i.e. week 1-75%, week 2-50%, week 3-25%) and this can be extended or decreased (10% dose reductions) if needed. If intolerable withdrawal symptoms occur (usually 1-3 days after a dose change), go back to the previously tolerated dose until symptoms resolve and plan for a more gradual taper with the patient. Dose reduction may need to slow down as one gets to smaller doses (i.e. 25% of the original dose). Overall, the rate of discontinuation needs to be controlled by the person taking the medication.	nausea, diarrhea, abdominal pain, sweating, headache, dizziness, cold and flu-like symptoms, anxiety, irritability, trouble sleeping, unusual sensory experiences (e.g. electric shock-like feelings, visual after images), sound and light sensitivity, muscle aches and pains, chills, confusion, pounding heart (palpitations), unusual movements, mood changes, agitation, distress, restlessness, rarely suicidal ideation	Details
X	hydrochlorothiazide (Microzide) / Thiazide / **blood pressure**	☹	🙂 CALC / NNT	😐	If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	chest pain, pounding heart, heart rate, blood pressure (re-measure for up to 6 months), anxiety, tremor	Details
X	levothyroxine (Synthroid, Levoxyl , Levothroid) / Thyroid / **hypothyroid with symptoms**	🙂	☹	🙂	Taper based on TSH and symptoms	return of hypothyroid symptoms (tiredness, weakness, weight gain, hair loss, constipation, depression, coarse dry hair, hair loss)	None
X	psyllium (Metamucil) / Constipation / **constipation**	🙂	☹	🙂	If used daily for more than 3-4 weeks. Reduce dose by 50% every 1 to 2 weeks. Once at 25% of the original dose and no withdrawal symptoms have been seen, stop the drug. If any withdrawal symptoms occur, go back to approximately 75% of the previously tolerated dose.	return of gastrointestinal symptoms	None

medstopper.com

Stopping medications

if a medication is thought to be causing a serious health issue, just stopping the medication is often the most appropriate step and then monitor for any potential withdrawal issues

some medications (especially those that work on the central nervous system or are for serious conditions) need to be tapered off and the approach very much depends on the specific medication, duration of use dose, and the underlying condition

there is no definitive way to do this as there isn't much evidence to guide tapering medications

it will involve reducing the dose by somewhere between 10% and 50% every few days/ weeks/months, depending on the specific medication, and monitoring to make sure we minimize withdrawal symptoms and if the condition re-appears we make a reassessment


STOP
REALLY
YOU GOTTA
STOP