
LESS IS MORE
James McCormack
BSc (Pharm), PharmD
Professor
Faculty of Pharmaceutical Sciences
University of British Columbia
Vancouver, BC, Canada
MORE OR LESS
therapeuticseducation.org
medicationmythbusters.com
TO GET A HANDOUT GO HERE
http://therapeuticseducation.org/handouts

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

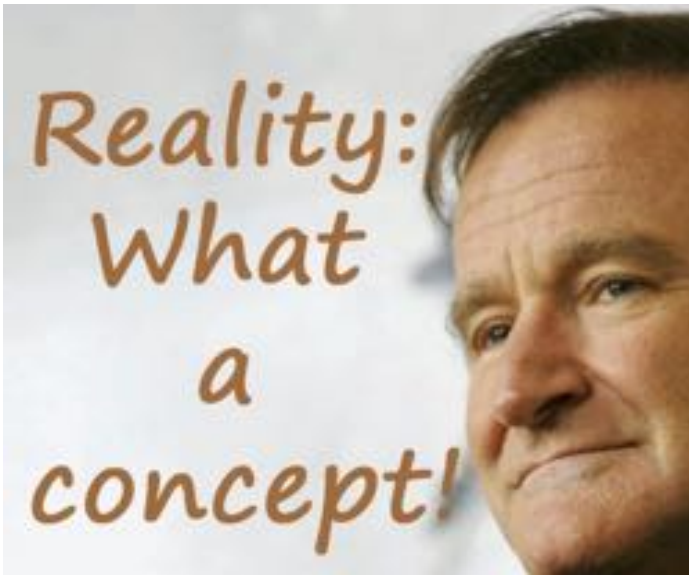
Polypharmacy case

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

The Concept for the Concept

NEVER use what I'm going to say/ recommend on your exams

ALWAYS consider these concepts when you are face-to-face with a real live patient



What Will You Do?

You are approximately 45 y/o

You have been diagnosed “properly” with elevated blood pressure

You have tried non-drug measures for 6 months and still your blood pressure remains elevated

QUESTION

ABOVE what blood pressure would YOU take a drug every day for the next 5 years?

What drug and dose would you start with?

What Will You Do?

You are approximately how old you are

You have been diagnosed “properly” with community acquired pneumonia

QUESTION

What drug, dose and duration would you take?

We need minimally disruptive medicine

The burden of treatment for many people with complex, chronic, comorbidities reduces their capacity to collaborate in their care. **Carl May, Victor Montori**, and **Frances Mair** argue that to be effective, care must be less disruptive

BMJ 2009;339:b2803

The Bullshit Asymmetry

the amount of energy needed
to refute bullshit is an order of
magnitude bigger than to produce it

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

Aldous Huxley

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

BMJ 2000;320:874

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

We are knowledge brokers

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

Mayo Clinic Proceedings 2013;88:56-67

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	1	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 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

CD000023

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 1-10% 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/Ibuprofen 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 ≈ 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

N Engl J Med 1998;338:1397-404

Depression

Patients who respond in the SSRI group ≈ 60%

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

Patients who respond in the placebo group ≈ 45%

6/10 patients will respond to an antidepressant

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

CD007954

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"

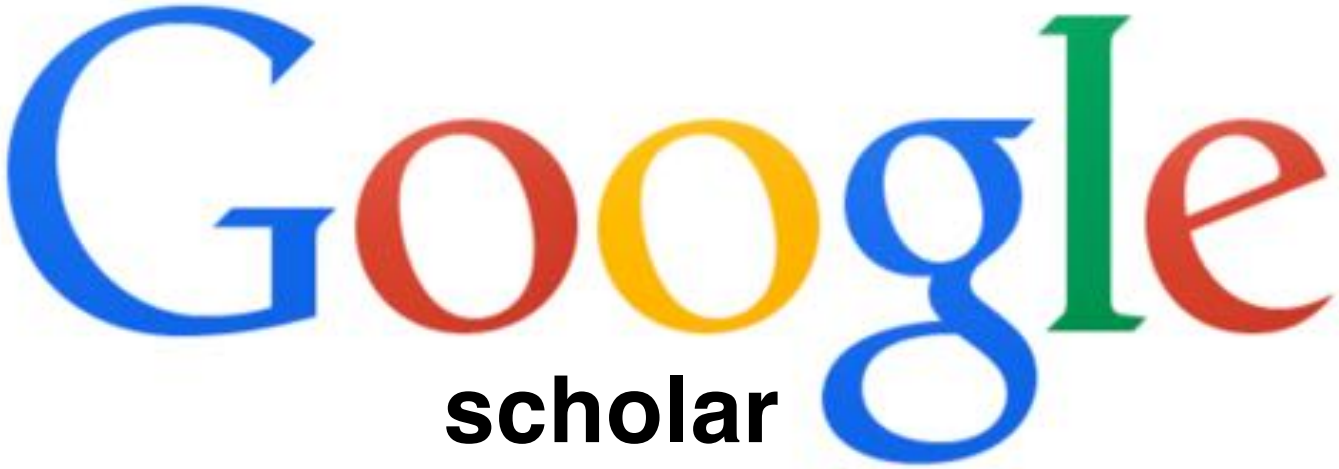
Qualitative descriptor	EU assigned frequency	Mean frequency estimated by participants (n=200)
Very common	>10%	65% (24·2)
Common	1–10%	45% (22·3)
Uncommon	0·1–1%	18% (13·3)
Rare	0·01–0·1%	8% (7·5)
Very rare	<0·01%	4% (6·7)

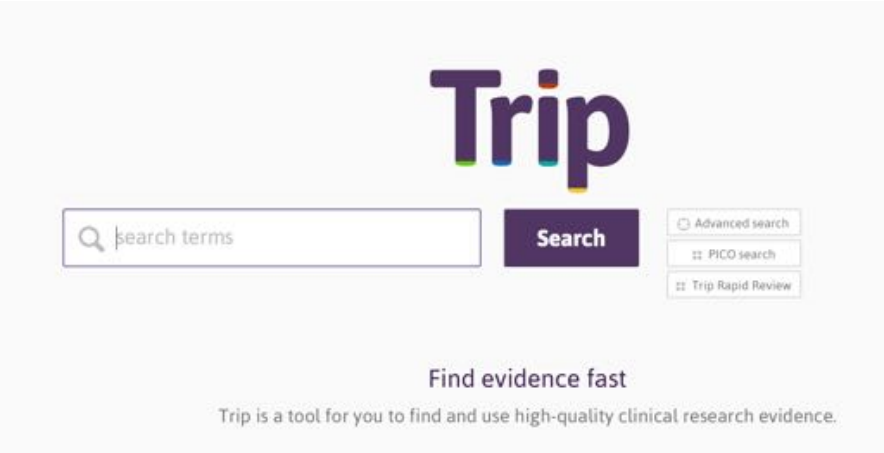
Values are mean (SD).

Lancet 2002;359:853–54

LOVE THEM!

They are my BFF





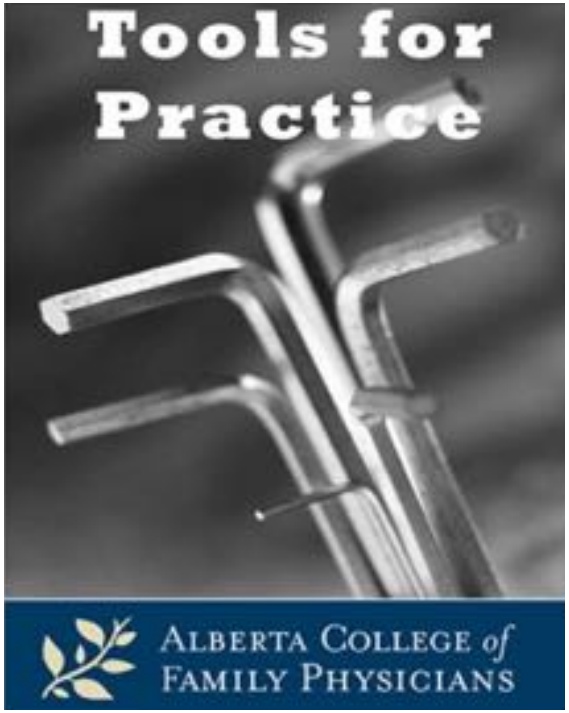
Trip Database - a clinical search tool designed to allow health professionals to rapidly identify the highest quality clinical evidence for clinical practice

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

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)

BLOOD PRESSURE

ALTITUDE (aliskiren)

VALISH, AASK, ACCORD

(aggressive BP lowering)

DIABETES

ACCORD, ADVANCE, VADT

(aggressive A1c lowering)

ROADMAP (olmesartan)

ORIGIN (insulin)

SAVOR-TIMI 53 (saxagliptin)

EXAMINE (alogliptin)

ALECARDIO (aleglitazar)

GENERAL

ACTIVE (irbesartan/afib)

CRESCENDO (rimonabant)

VISTA-16 (varespladib

182,000+ patients

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-C	Class, level
High	<2 mmol/L	Class I, level A
CAD, PVD, atherosclerosis	or	
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"

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	0.8	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

“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 james.mccormack@ubc.ca. For more detailed information and acronym definitions etc see the FAQ. For important calculator caveats click here.

CVD | CHD | Heart Attacks | Strokes | ASCVD

Risk Time Period
10 years

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
120 mmHg is used for baseline risk

Total Cholesterol
3 mmol/L
3 mmol/L is used for baseline risk.
Click to change to mg/dL

HDL Cholesterol
1.3 mmol/L
1.3 mmol/L is used for baseline risk.

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
BP meds (not atenolol/doxazosin)
Statins | Fibrates | Niacin
Ezetimibe | Metformin
Sulfonylureas | Insulins | Glitazones
GLPs | DPP-4s | Meglitinides
ASA

Benefit Estimate Details

Family History of Early CHD
If CHD in men < 55 years, women < 65 years - increase risk by 50%. If no family history - decrease estimates by 33%.

Adjust Overall Risk
100 %
Use to adjust risk based on family history or if patient is at a lower/higher risk than the Framingham cohort. See the FAQ for guidance.

97.6%	No events
2.4%	Baseline events using baseline factors
0.0%	Additional events – "caused" by risk factors over baseline
0.0%	Benefits – will not have an event because of "treatment"
NNT	∞	Number needed to treat

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

http://cvdcalculator.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

BMJ

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 *professor*[1], G Michael Allan *associate professor*[2]

[1]Faculty of Pharmaceutical Sciences, University of British Columbia, BC, Vancouver, Canada V6T1Z3; [2]Department 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

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."

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

CMAJ 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*,

(c) does not, despite any wording to the contrary in any contract of insurance and despite any other enactment, void, impair or otherwise [illegible] with that matter, and

[illegible]

(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 [illegible]

"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 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 - **$$$$$$$$$**

We Are All Individuals

Every patient is an "n of 1" study
Every treatment is an experiment

The Elderly

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

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

CMAJ, January 11, 2011

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 as100 mg
5 mg daily fluoxetine (Prozac)	similar effects to those seen at 20 mg and 40 mg daily
0.25 mg ezetimibe (Ezetrol)	1/40th 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
150 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
1.8 mg colchicine	as effective as 4.8mg for acute gout with less adverse events

Doxepin (Sinequan)

Depression - start 25-50 mg - optimal 75mg -150mg 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

Efficacy and Safety of Three Different Doses of Doxepin in Adults with Primary Insomnia

All three doses worked better than placebo
AND
NO side effects over placebo

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