

DEPRESCRIBING

HERMAN®

by Jim Unger



"I feel a lot better since I ran out of those pills you gave me."


- Britt Simmons, M.D, C.C.F.P.
- ACFP Feb. 26, 2015

Faculty/Presenter Disclosure

- **Faculty: Britt Simmons**
- **Relationships with commercial interests:**
 - **Grants/Research Support:** Not applicable
 - **Speakers Bureau/Honoraria:** Not applicable
 - **Consulting Fees:** Not applicable
 - **Other:** Not applicable

DEPRESCRIBING?

- Defined as:
 - Tapering, stopping, discontinuing, or withdrawing drugs, with the goal of managing polypharmacy and improving outcomes
- Because of the longitudinal nature of the doctor/ patient relationship, family physicians are uniquely positioned to assist



- “ANY NEW SYMPTOM IN AN ELDERLY PATIENT SHOULD BE CONSIDERED A DRUG SIDE EFFECT UNTIL PROVEN OTHERWISE”

- Dr. J. Avorn- Geriatrician



Deprescribing Benefits

- Studies found drug withdrawal has little or no harms, and major benefits in mobility (reduced fall risk), and cognition (delirium prevention)
- Studies examining outcomes showed no differences in functional outcomes, hospital readmissions or mortality (short duration)

Deprescribing Benefits

- MOBILITY- potential improvement
- COGNITION- potential improvement, less delirium
- FALLS- less falls
- QUALITY OF LIFE- improvement
- HARMS?- little or none if done with mindfulness



Deprescribing Benefits

- Polypharmacy and CNS drugs increase fall risk by about 50%
- Withdrawal of psychotropic drugs reduced falls by 66%
- Avoiding benzos in elderly could reduce hip fractures by 10% - Australian study
- In a trial to reduce polypharmacy, global assessment scale improved 88% and in most, cognitive scores improved

Deprescribing Benefits on QOL

- Mean age 82.8 years
 - 61% > 3 co-morbidities
 - Mean 4.9 drugs withdrawn
 - 2% restarted
 - Successful withdrawal in 81%
 - 14% died, mean age 89
 - No attributable deaths/ events
 - 88% reported global improvement in health
 - Antihypertensives, nitrates, diuretics, statins, oral hypoglycemics, PPIs...
- Arch Int Med 2010; 170(18):1648-54

Case 84 yr old male

- Lives independently; travels
- BPH- Bx. x2 1990's Proscar, Flomax
- HTN- 140/80s HCTZ 25 mg., Norvasc
- OTC- Vit E, D, Calcium, MVI, "Brain Boost", Glucosamine
- Sleep- Zopiclone 7.5 mg PRN
- Cardiology consult after high calcium score on CT adds ASA, bisoprolol for BP, Lipitor (Lipids normal and no CAD/ MI)

Case 84 yr old male

- GP recommends meds bubble pak for travel so then using Zopiclone daily
- Presents with falls and cognitive decline
- MOCA 16/30 CT Head- atrophy, white matter
- 120s/70s HR low 50s
- Pedal edema 2+ and “sore” feet
- Considering lodge or assisted living
- GP reluctant to change as Cardiology and CPG recommendations

Clinical Practice Guidelines



Problems with CPGs

- CPGs typically focus on a **SINGLE DISEASE** but elderly usually have multiple co-existing medical conditions
 - 1 in 4 seniors have > 3 conditions
 - Seniors with 1-2 conditions take 3-4 meds
 - Seniors with 3+ conditions take 6+ meds

Problems with CPGs

- The evidence supporting guidelines may NOT have been OBTAINED FROM OLDER PATIENT populations with their multiple co-morbidities
 - Only 9% of cancer drug trial patients > 75 years
 - But 43% of cancer patients are > 75 years
 - Br J Hosp Med 2010;71(12):678-81
 - 40% of CHF clinical trials limited inclusion of seniors
 - Arch Int Med 2011;171(6):550-6



Problems with CPGs

■ ADVERSE EVENTS vs. BENEFITS

- Adverse events are evaluated with less rigor and precision than are benefits in most RCTs

■ OUTCOMES vs. QUALITY OF LIFE

- CPGs focus on biomedical outcomes
- Maintaining a good quality of life and independence was indicated as the most important health outcome by nearly 80% of 357 seniors
 - Arch Int Med 2011;171(20):1854-8



CPGs- Time Until Benefit

- Life expectancy may not be considered
 - Patients may have a life expectancy that is shorter than the time to benefit from therapy
 - Holmes et al: Arch Int Med 2006
 - Limitations of prognostic tools & measures
- Time until benefit vs. time until harm
- Goal Setting
 - Short term (<1 yr)
 - Medium term (1-5 yr)
 - Long term (>5 yr)
- Consider the “Goals of Care” vs. “Standard of Practice”



Problems with Primary Care CPGs

- Written by Specialists 3:1 over FPs
- 2/3 had no conflict of interest statement, those that did showed Specialists more likely to have conflict
- 196 Primary Care guidelines on CMA site:
 - 20 had no information on authors
 - 176 remaining- 54% written by specialists
- 40% of guidelines sponsored by industry and more likely written by specialists

Seniors and Medications

- Success of modern medicine comes with a cost of increased morbidity
- RCTs show we can manage conditions to reduce complications & premature mortality
- Multimorbidity- 1/2 people over 65 have 3+ conditions and 1/5 have 5+
- Results in medication prescribing and resultant risk of polypharmacy, ADRs, interactions, even underprescribing

Seniors and Medications

- Seniors account for approximately:
 - 15% of the population
 - 25% of doctor visits
 - 40% of retail drug sales
 - 28-40% of medication prescriptions in Canada (depending on the province)

Seniors & Numbers of Medications

Table 7: Percentage of Seniors on Public Drug Programs, by Number of Drug Classes and Jurisdiction, Selected Jurisdictions,* 2012

Number of Drug Classes Claimed	P.E.I.	N.S.	N.B.	Ont.	Man.	Sask.	Alta.	B.C.	FNIHB	Total
<5	46.5%	29.2%	27.9%	29.1%	40.5%	36.4%	35.9%	47.8%	16.8%	34.1%
5–9	40.0%	41.0%	42.2%	38.8%	38.7%	40.8%	40.8%	36.8%	29.5%	38.8%
10–14	10.3%	20.7%	20.9%	21.3%	14.9%	17.0%	16.9%	11.8%	26.1%	18.5%
15+	3.2%	9.1%	9.0%	10.9%	5.9%	5.9%	6.4%	3.7%	27.6%	8.6%
Average Number of Drug Classes	5.6	7.7	7.7	7.9	6.4	6.7	6.8	5.6	11.1	7.2

Note

* Nine jurisdictions submitting claims data to the NPDUIS Database as of March 2013: Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia and First Nations and Inuit Health Branch.

Source

National Prescription Drug Utilization Information System Database, Canadian Institute for Health Information.



Seniors Have Altered Pharmacokinetics

- Absorption
 - Passive absorption changes little with age
 - Drugs that alter GI motility affect absorption
- Distribution
 - Reduction in lean body mass
 - Protein-binding reduced as albumin declines
- Metabolism
 - Reduced hepatic enzymes and blood flow
- Excretion
 - Decline in renal functional reserve and lower creatinine production due to muscle mass

Seniors and Medication Harms

- 1 in 4 hospitalized for med-related problems
- 10% of all admissions in this group
- 30-55% deemed preventable
- On 5+ drugs, 1 in 3 suffer an ADR every 12 months; ¼ deemed preventable
- Up to 18% of inpatient deaths in part from ADRs
- 44% inpatients at discharge have at least 1 unnecessary drug

Seniors and Medications

- Polypharmacy in older people associated with increased risk of impaired physical, cognitive function, institutionalization and death
- Reducing drugs has positive outcomes. Study of over 70 yr old showed $\frac{1}{2}$ of meds can be stopped, with only 2% needing restart. Overall improved cognition and global health.
- Withdrawal rarely assoc with adverse events
- Falls and cognitive impairment frequent ADR, yet often attributed to aging process

Seniors & Medications Interactions

- Theoretically, risk increases exponentially with number of drugs:
 - 5 drugs have 10 possible 1 to 1 interactions
 - 10 drugs have 45 possible
 - 15 drugs have 105 possible...
- Drug-drug Interactions:
 - 13% interaction rate seniors on 2 meds
 - 82% interaction rate when on 6 or more meds
 - Approx 100% when on 8 or more meds

Goldberg; Am J Emerg Med 1996



Seniors & Medications Adherence

- Seniors Medication Adherence:
 - Estimated true rate of adherence < 50%
 - 1/2 of prescriptions in community improperly taken
 - Number of meds stronger predictor of nonadherence than advancing age; more # meds = higher % nonadherence

Seniors and Beers Drugs

Table 9: Rate of Use of Drugs From Beers List* Among Seniors on Public Drug Programs by Jurisdiction, Selected Jurisdictions,† 2012

Jurisdiction	Percentage of Senior Claimants With Any Beers Use	Percentage of Senior Claimants With Chronic Beers Use	Percentage of Senior Claimants Using Multiple Beers Drugs
P.E.I.	28.6%	15.9%	7.2%
N.S.	45.4%	29.0%	16.1%
N.B.	51.7%	34.2%	21.7%
Ont.	37.6%	21.9%	11.3%
Man.	40.3%	25.8%	13.4%
Sask.	38.1%	20.6%	12.4%
Alta.	41.2%	24.0%	14.6%
B.C.	38.0%	19.6%	12.2%
FNIHB	49.9%	28.3%	20.9%
Total	38.9%	22.4%	12.4%

Notes

* AGS Beers Criteria 2012 Updated Version, with modifications to make the measure of potentially inappropriate use more applicable to the Canadian market (see Appendix B).

† Nine jurisdictions submitting claims data to the NPDUIS Database as of March 2013: Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia and First Nations and Inuit Health Branch.

Source

National Prescription Drug Utilization Information System Database, Canadian Institute for Health Information.

Seniors Rate of Use - Beers Drugs

Table 10: Top 10 Chemicals From Beers List,* by Rate of Use Among Seniors on Public Drug Programs, Selected Jurisdictions,† 2012

Chemical	Common Uses	Rate of Use Among Beers Users	Rate of Use Among All Senior Claimants
Lorazepam	Anxiety, insomnia	23.5%	9.1%
Nitrofurantoin	Urinary tract infection	14.2%	5.5%
Amitriptyline	Depression	8.2%	3.2%
Glibenclamide	Diabetes	6.8%	2.7%
Clonazepam	Anxiety, seizures	6.5%	2.5%
Conjugated Estrogens	Symptoms of menopause	6.2%	2.4%
Quetiapine	Schizophrenia, bipolar disorder	6.0%	2.3%
Zopiclone	Insomnia	5.9%	2.3%
Oxazepam	Anxiety, irritability, agitation	4.4%	1.7%
Indomethacin	Fever, pain	4.3%	1.7%

Notes

* AGS Beers Criteria 2012 Updated Version, with modifications to make the measure of potentially inappropriate use more applicable to the Canadian market (see Appendix B).

† Nine jurisdictions submitting claims data to the NPDUIS Database as of March 2013: Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Manitoba, Saskatchewan, Alberta, British Columbia and First Nations and Inuit Health Branch.

Source

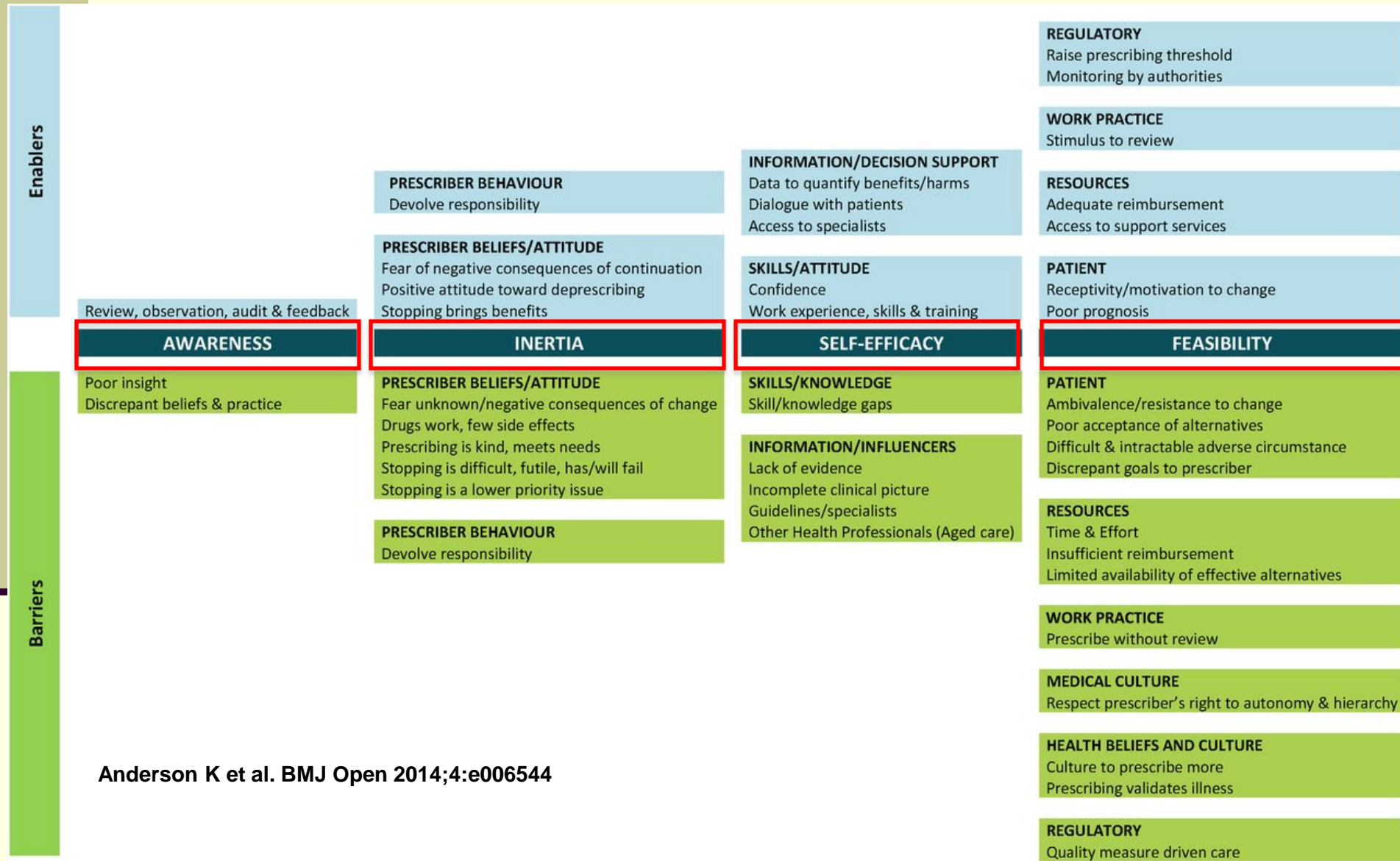
National Prescription Drug Utilization Information System Database, Canadian Institute for Health Information.



Why not Deprescribe? Factors Associated with Polypharmacy

- Factors related to the system
 - Increased life expectancy
 - Development of new therapy & technology
 - Increased use of prevention strategies
- Factors related to patients
 - Age, gender, socioeconomic, ethnicity, behavior, clinical conditions, medical therapy
- Factors related to physicians
 - Guidelines, habits, behavior, premises
- Interaction between patient and physician

Schematic representation of barriers and enablers associated with each analytical and descriptive theme.



Anderson K et al. BMJ Open 2014;4:e006544

Treatment Outcomes

- Significant to Doctor
 - Disease specific measures; HgA1C, BP, glucose, lipids, morbidity, mortality
- Significant to Patient
 - Life extension vs. quality, preservation of social and physical function, relief of symptoms
 - Fried et al; JAGS 2008

Deprescribing Barriers

■ Physicians

- Ethical dilemma between standard of practice (colleagues, clinical practice guidelines, disease specific outcomes) and clinical situation
- Lack of evidence-based approach/RCT for deprescribing
- Resistance to change
- Work load issue, lack of resources
- Fear of liability

■ Patient/family

- Fear of abandonment, reality check, situation as futile
- Medication dependence
- Resistance to change (Bain et al, JAGS 2008)



MD Attitudes to Deprescribing

- Symptomatic meds less difficult to stop than Preventative meds as poor risk/benefit info
- Beliefs about patients:
 - They have no problem with polypharmacy
 - Stopping prevention meds means “giving up”
 - Discussion of life expectancy vs quality of life difficult
- Compelled to prescribe by “The Guidelines”
- The System- collaboration with specialist colleagues

Patient Attitudes to Deprescribing

- Feeling of abandonment
- Medications represent hope
- Prescribed by a another physician (specialist; trusted GP)
- No evidence to guide discontinuation
- Fear of causing/ hastening death
- “Ageism”
- Some self- deprescribe due to poor compliance or intolerance to side effect

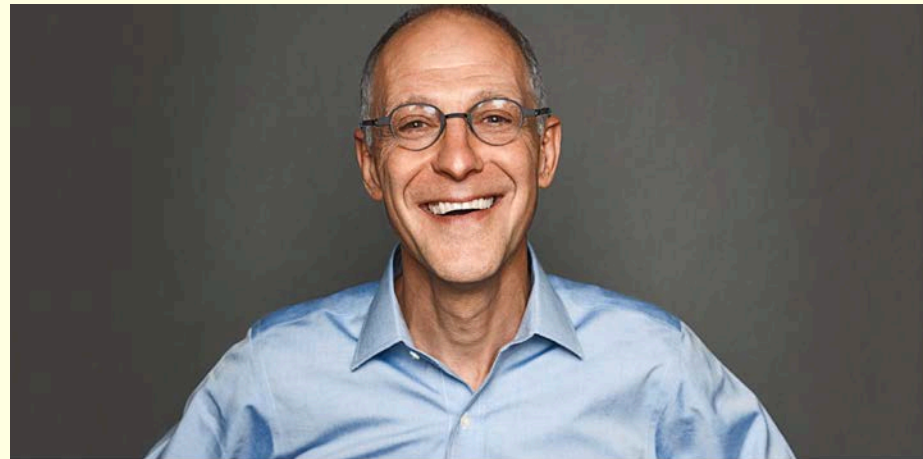


Who is a Candidate?

- Multimorbidity
- Nearer to End of Life
- Frailty
- Goals of care change
- Vulnerable brain
- Adverse reactions suspected/ identified
- Interactions suspected/ identified
- New conditions develop

Who is a Candidate?

- Adherence issues
- Patient request
- Age?



Why I Hope to Die at 75

An argument that society and families—and you—will be better off if nature takes its course swiftly and promptly


By Ezekiel J. Emanuel

Photos by Jake Chessum

OCTOBER 2014

Medication Reduction

- Prescribing is a form of decision analysis
- It's not possible to be dogmatic
- Prescribing is based on probability, and only in retrospect can benefits be partially judged
- Most of our therapies are assoc with small chance of benefit, and withdrawal off polypharmacy has improved outcomes



Reducing meds without tension to the Guidelines

- Has the medical indication expired?
- Are any of the drugs redundant?
- Is a drug treating a S/E of another drug?
- Elicit patient preferences/ priorities.
 - Expressing absolute benefit gives a more favorable impression, but absolute risk is preferable in deciding intervention
- “Mini Polypharmacy” – lower doses but not necessarily numbers of drugs

Algorithm for Prescribing at Various Points in the Lifecycle

516

Sergi et al.

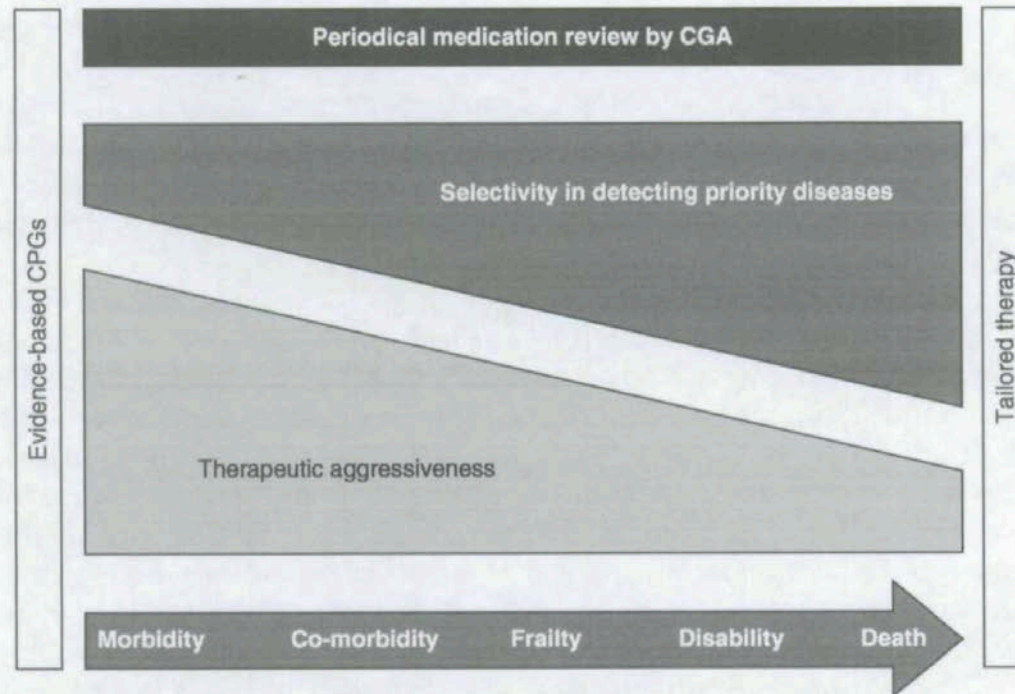
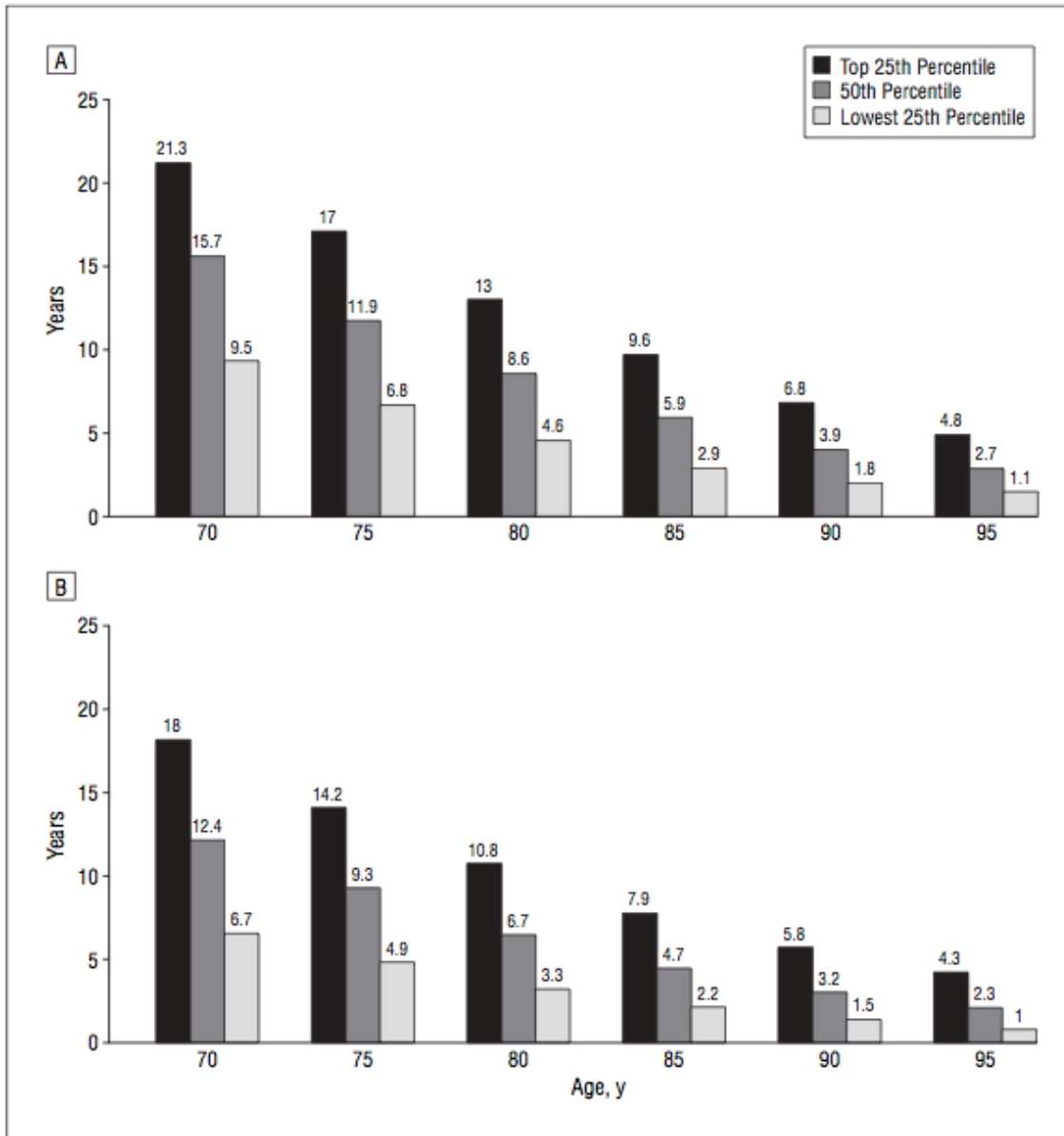


Fig. 2. Appropriate prescription model for elderly patients proceeding along the path from morbidity to co-morbidity, frailty, disability and death. **CGA**=comprehensive geriatric assessment; **CPGs**=clinical practice guidelines.



Life expectancy and general health

Figure 2. Upper, middle, and lower quartiles for life expectancies for women (A) and men (B) on the basis of the US life tables. The 3 numbers provided for each 5-year age cohort reflect remaining life expectancy for the top 25th, middle 50th, and lowest 25th percentile. For example, 75%, 50%, and 25% of 75-year-old women will live fewer than 17, 11.9, and 6.8 years, respectively. Although the median life expectancy for 75-year-old women is 11.9 years, women with advanced comorbidities and functional impairments may live fewer than 6.8 years. Reprinted with permission from *JAMA*.⁷

Tool for identifying and discontinuing potentially inappropriate drugs.

1. Accurately ascertain all current drug use

- 'brown paper bag' medication reconciliation

2. Identify patients at risk of, or suffering, ADR

- at risk: ≥ 8 medications
advanced age (>75 years)
high-risk medications
- assess for current, past or highly likely future toxicity

.....➤ All three at-risk criteria – aim for ≤ 5 drugs
Discontinue drugs for which there is unequivocal evidence of past, current or future toxicity (eg triple whammy of NSAID, diuretic, ACE inhibitor)

3. Estimate life expectancy

- clinical prognostication tools or lifespan calculators

4. Define overall care goals

- consider current functional status and quality of life with reference to estimated life expectancy

.....➤ If life expectancy less than 2 years, preservation of function and quality of life predominate over prolonging life and avoiding future complications as goals of care

5. Verify current indications for ongoing treatments

- perform diagnosis-medication reconciliation
- confirm diagnostic labels against formal diagnostic criteria
- ascertain, for each confirmed diagnosis, drug appropriateness

.....➤ Discontinue drugs for which the diagnosis is wrong or totally unsubstantiated or where, for a confirmed diagnosis, the drug is ineffective

6. Determine need for disease-specific preventive medications

- estimate clinical impact and time to future treatment benefit
- compare this estimate with expected lifespan

.....➤ Discontinue preventive drugs whose time until benefit exceeds expected lifespan

7. Determine absolute benefit-harm thresholds of medications

- reconcile estimates of absolute benefit and harm using prediction tools (see <http://www.mdcalc.com>)

.....➤ Discontinue drugs whose absolute level of harm exceeds absolute level of benefit; in 'line-ball' cases elicit patient preferences

8. Review the relative utility of individual drugs

- rank drugs according to the relative utility from high to low based on predicted benefit, harm, administration and monitoring burden

.....➤ Discontinue drugs of low utility

9. Identify drugs to be discontinued and seek patient consent

- reconcile drugs for discontinuation with patient preferences

.....➤ Discontinue drugs patients are not in favour of taking

10. Devise and implement drug discontinuation plan with close monitoring

The ARMOR Tool

Table 4
The ARMOR tool

A	Assess	<ul style="list-style-type: none"> c Beers criteria c b-blockers c Pain medications c Antidepressants c Antipsychotics c Other psychotropics c Vitamins and supplements
R	Review	<ul style="list-style-type: none"> c Drug-disease interactions c Drug-drug interactions c Adverse drug reactions
M	Minimize	c Number of medications according to functional status rather than evidence-based medicine
O	Optimize	c For renal/hepatic clearance, PT/PTT, b-blockers, pacemaker function, anticonvulsants, pain medications, and hypoglycemics; gradual dose reduction for antidepressants
R	Reassess	<ul style="list-style-type: none"> c Functional/cognitive status in 1 week and as needed c Clinical status and medication compliance

From Haque R. ARMOR: a tool to evaluate polypharmacy in elderly persons. *Annals of Long-Term Care* 2009;17(6):26–30; with permission. Available at: <http://www.annalsoflongtermcare.com/content/armor-a-tool-evaluate-polypharmacy-elderly-persons>. Accessed January 28, 2012.



Principles- Partnership

- Input from and consent of patient/ agent
- Explanation of rationale
- Agreement
- Good communication of duration, expected effects

Principles- Review and Support

- Regular review to monitor, support and feedback
- Benefits such as feeling better, spending less, better compliance should be sought and reinforced
- Review for relapse such as failure to adhere; or return of condition

Drugs Requiring More Caution in Weaning

Table 2 Medications commonly associated with discontinuation syndromes which require slow weaning

Medication	Type of discontinuation syndrome	Clinical manifestations
α -Blockers	W, R	Agitation, headache, hypertension and palpitations
ACE-inhibitors	D	Heart failure and hypertension
Antianginal agents	D	Angina
Anticonvulsants	W, D	Anxiety, depression and seizures
Antidepressants	W, D	Akathisia, anxiety, chills, coryza, gastrointestinal distress, headache, insomnia, irritability, malaise, myalgia and depression
Antiparkinsonian agents	W, D, R	Hypotension, psychosis, pulmonary embolism, rigidity and tremor
Antipsychotic	W	Dyskinesias, insomnia, nausea and restlessness
Anticholinergics	W	Anxiety, nausea, vomiting, headache and dizziness
Baclofen	W, R	Agitation, anxiety, confusion, depression, hallucinations, hypertonia, insomnia, mania, nightmares, paranoia and seizures
Benzodiazepines	W	Agitation, anxiety, confusion, delirium, insomnia and seizures
β -Blockers	W, D	Angina, anxiety, hypertension, acute coronary syndrome and tachycardia
Corticosteroid	W, R, D	Anorexia, hypotension, nausea, weakness, hypothalamic–pituitary–adrenal axis suppression and inflammatory states
Digoxin	D	Heart failure and palpitations
Diuretic	D	Heart failure and hypertension
Narcotic analgesia	W	Abdominal cramping, anger, anxiety, chills, diaphoresis, diarrhoea, insomnia and restlessness
NSAIDs	D	Recurrence of gout and arthritis

D, disease recrudescence; NSAID, non-steroidal anti-inflammatory drug; R, rebound; W, withdrawal.



Approach to Deprescribing

- 1. Prepare- discuss reduction at start of tx
- 2. Recognize- Polypharmacy, ADRs, lack of efficacy, change in goals of treatment
- 3. Prioritize- one at a time with suspect for ADR of use risk assessment tools
- 4. Wean- CNS drugs (BZD, opiates), steroids, beta blockers, levodopa over wks to months; ?25% per month for example
- 5. Monitor- withdrawal syndrome, discontinuation syndrome, rebound, recurrence of illness, cognition, falls, QOL

ANTICHOLINERGIC BURDEN





Anticholinergic Burden

- Acetylcholine is a neurotransmitter in the central and peripheral nervous system
 - CNS- activates arousal, modulates plasticity
 - PNS- activates smooth and inhibits cardiac muscle
- Cholinergic neurons present in brain, heart, GI tract, bladder, muscles
- Ach is a key chemical that allows neurons to “talk” to each other
- “Burden” refers to the total effect of all meds that block acetylcholine

Ach Burden and Mobility

- 3070 patients > 75 yr.- free of dementia in Gingko evaluation of memory study
- ACB calculated as 0,1,2 based on scores
- Movement assessed compared to ACB 0 –
 - ACB 1- like 3.2 yr OLDER
 - ACB 2 -like 7.3 yr OLDER
- Exposure to ANY level ACB assoc. with slower gait speed comparable to **FOUR YEARS OF AGING**



Other Ach Burden Effects

Any Ach drug use in hospital increases length of stay and development of delirium for demented and non-demented elderly

UK study of patients age > 65 with ACB score of 4+ points:

- 20% risk of death in 2 years vs.
- 7% risk of death in 2 years if ZERO points

Ach Burden and Falls

- Use of Ach drugs are associated with lower muscle strength and poorer reaction times in older adults
 - ?relates to central effects on psychomotor slowing +/- peripheral side effects
- ACB associated with falls in older adult psych inpatients – mean ACB for fallers 3.7 vs. 2.1 for non-fallers ($p < 0.05$)

Landi, F et al 2007

ACB Score 1 (mild)	ACB Score 2 (moderate)	ACB Score 3 (severe)
Alimemazine	Amantadine	Amitriptyline
Alprazolam	Belladonna alkaloids	Amoxapine
Alverine	Carbamazepine	Atropine
Atenolol	Cyclobenzaprine	Benztropine
Beclometasone dipropionate	Cyproheptadine	Chlorpheniramine
Bupropion hydrochloride	Loxapine	Chlorpromazine
Captopril	Meperidine	Clemastine
Chlorthalidone	Methotrimeprazine	Clomipramine
Cimetidine hydrochloride	Molindone	Clozapine
Clorazepate	Oxcarbazepine	Darifenacin
Codeine	Pethidine hydrochloride	Desipramine
Colchicine	Pimozide	Dicyclomine
Dextropropoxyphene		Diphenhydramine
Diazepam		Doxepin
Digoxin		Flavoxate
Dipyridamole		Hydroxyzine
Disopyramide phosphate		Hyoscyamine
Fentanyl		Imipramine
Fluvoxamine		Meclizine
Furosemide		Nortriptyline
Haloperidol		Orphenadrine
Hydralazine		Oxybutynin
Hydrocortisone		Paroxetine
Isosorbide preparations		Perphenazine
Loperamide		Procyclidine
Metoprolol		Promazine
Morphine		Promethazine
Nifedipine		Propentheline
Prednisone/Prednisolone		Pyrilamine
Quinidine		Scopolamine
Ranitidine		Thioridazine (withdrawn)
Theophylline		Tolterodine
Timolol maleate		Trifluoperazine
Trazodone		Trihexyphenidyl
Triamterene		Trimipramine
Warfarin		

Anticholinergics - Alternatives

The following represents a list of alternative medications developed by an interdisciplinary group of specialists within the Aging Brain Program at Indiana University. These suggestions do not supersede clinical judgment, and are intended to assist clinicians in practicing in acute health care settings who provide care for patients with cognitive impairment such as dementia, mild cognitive impairment or delirium.

Recommended alternatives to medications with Definite Anticholinergic Properties		
Class	ACB Drugs	Alternatives
First-Generation Antihistamines	Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Diphenhydramine Dimenhydrinate Hydroxyzine	Allergies or itching: Loratadine or Cetirizine orally Insomnia: Trazadone orally
Antidepressants	Amitriptyline Amoxapine Clomipramine Desipramine Doxepin Imipramine Nortriptyline Paroxetine Trimipramine	<i>(Clinical judgment to consider if taper warranted)</i> Depression: Sertraline or Citalopram orally Neuropathic pain: Gabapentin orally Insomnia: Trazadone orally
Antipsychotics	Chlorpromazine Clozapine Olanzapine Perphenazine Quetiapine Thioridazine Trifluoperazine	<i>(Recommendation does not apply to chronic use for psychiatric diagnosis)</i> Acute care environment: Haloperidol orally or IM for 72 hours only
Central Anticholinergics	Amantadine Benztropine Trihexyphenidyl Orphenadrine	Movement disorders: Dopamine agonists or levodopa

The following represents a list of alternative medications developed by an interdisciplinary group of specialists within the Aging Brain Program at Indiana University. These suggestions do not supersede clinical judgment, and are intended to assist clinicians in practicing in acute health care settings who provide care for patients with cognitive impairment such as dementia, mild cognitive impairment or delirium.

Recommended alternatives to medications with Definite Anticholinergic Properties		
Class	ACB Drugs	Alternatives
Bladder Antispasmodics	Darifenacin Flavoxate Oxybutynin Propantheline Tolterodine	Hold during acute care stay – consider scheduling toileting
GI Antispasmodics	Atropine Dicyclomine Hyoscyamine Propantheline	Reflux disorders: Esomeprazole orally Painful abdominal cramps: Morphine orally or IV
Antiemetics	Hydroxyzine Meclizine Promethazine Scopolamine	Consider ondansetron IV or PO, or Metoclopramide PO
Skeletal Muscle Relaxants	Cyclobenzaprine Methocarbamol	Acetaminophen or oxycodone/acetaminophen
Analgesics	Meperidine	Morphine sulfate orally or IV
Antiepileptics	Carbamazepine Oxcarbazepine	Seizures: Consult neurology for alternative Neuropathic pain: Gabapentin or levetiracetam orally Mood disorders: Consult psychiatry for alternative

For more information or permission to duplicate, please contact:
Noll Campbell, PharmD or Malaz A. Boustani, MD, MPH
Regenstrief Institute, Inc.
410 West 10th Street, Suite 2000
Indianapolis, IN 46202-3012
Phone: (317) 423-5633 Fax: (317) 423-5695
Email: rmanns@regenstrief.org

Do not reproduce without permission – contact rmanns@regenstrief.org

www.indydiscoverynetwork.com

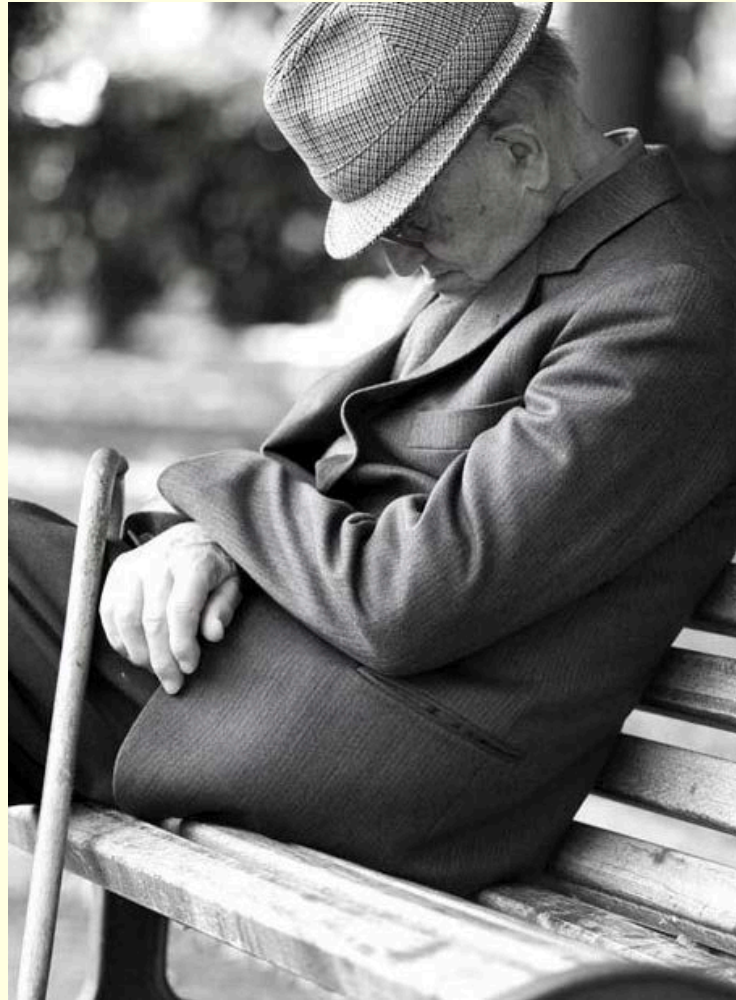


ACB Take Home Messages

- Elderly (or otherwise vulnerable) patient with frailty; gait problems; falls; cognitive issues
- Minimize the anticholinergic burden or chose those medications that have the least anticholinergic effect



The Elderly and Sleep



Seniors and Insomnia

- Age is associated with sleep disturbance
- Prevalence of approx 34% (16% severe)
- Factors- environment, illness, meds, circadian disruption (NB bedrest ^), depression, pain
- Comorbidity severity is strongest predictor
- Vision & hearing impaired sleep worse in community, protects in hospital
- Incontinence protective (? diapers/ catheters)
 - Isaia: Arch of Gerontology 52 (2011) 133-137

Prevalence -Inpatients

- 1. Prevalence of hypnotic use:
 - General medical wards: 31-41% have Rx
 - Surgical wards: 83-96% have Rx
 - ...and 33-88% receive them
- 2. Secondary disorders and sleep:
 - Delirium 22% on admit; 33% develop it; missed by MD/RN 32-66%- ? Why delirium
 - Depression-50% have sleep disturbance
 - Others – OSAS or Hypoventilation

Prevalence -Community

- Canada over 65 – 14% +
- UK study random 1000 seniors - 18%
- 80% using HS sed'n also consume alcohol
- 24% who regularly consume alcohol take HS sedation
- Commonest use– Severely obese (?OSAS), men, underweight women

Sleeping Pills- Some Evidence

- NNT 13 -for 25 minutes extra sleep +/- 1 less wakeup
- NNH 6 -falls, hip fractures, confusion
- Z drugs compared to Benzos:
 - Worse than lorazepam/ alprazolam
 - Same as valium
 - Worse than placebo -total wake time reduction
- Melatonin- mixed results
- Benadryl/ Gravol – BEERS
- Trazodone- minimal data
- Quetiapine- Anticholinergic, low BP, Black Box!

shots


HEALTH NEWS FROM NPR


[your health](#)[treatment & tests](#)[health inc.](#)[policy-ish](#)[public health](#)[health inc.](#)

Wake-Up Call: FDA Pushes Drugmakers To Weaken Sleeping Pills

by [ROB STEIN](#)

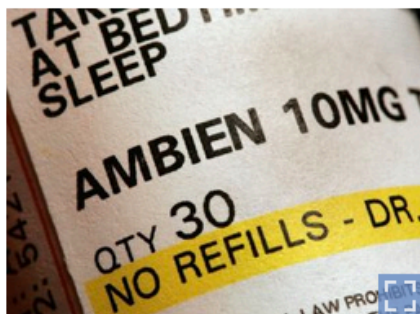
January 10, 2013 12:26 PM



[Listen to the Story](#) 

All Things Considered 3 min 25 sec

- [+ Playlist](#)
- [+ Download](#)
- [≡ Transcript](#)



Tim Boyle/Getty Images

The Food and Drug Administration announced Thursday that it was requiring companies that make Ambien and similar sleeping pills to sharply cut the doses of the drugs.

The agency [says](#) it is taking the step for the brands Ambien, Ambien CR, Edluar and Zolpimist, as well as generic versions of Ambien, because tests showed the active ingredient in the medications, [zolpidem](#), stays in the body longer than had been thought. That raises the possibility that people

taking the drugs will remain drowsy the next day, making activities such as driving and operating heavy machinery dangerous.

[Share](#)[67 Comments](#)

Hypnotics and death/ cancer

Downloaded from bmjopen.bmj.com on February 28, 2012 - Published by group.bmj.com

Open Access

Research

BMJ
open

Hypnotics' association with mortality or cancer: a matched cohort study

Daniel F Kripke,¹ Robert D Langer,² Lawrence E Kline¹



To cite: Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. *BMJ Open* 2012;2:e000850. doi:10.1136/bmjopen-2012-000850

Prepublication history and additional materials for this paper are available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2012-000850>).

DFK and RDL contributed equally to the research. Author responsibility: all authors had access to all the data and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Received 9 January 2012
Accepted 20 January 2012

This final article is available for use under the terms of the Creative Commons Attribution Non-Commercial 2.0 Licence; see <http://bmjopen.bmj.com>

¹Scripps Clinic Veterbi Family Sleep Center, La Jolla, California, USA
²Jackson Hole Center for Preventive Medicine, Jackson, Wyoming, USA

Correspondence to Dr Daniel F Kripke; kripke.daniel@scrippshealth.org

Kripke DF, Langer RD, Kline LE. *BMJ Open* 2012;2:e000850. doi:10.1136/bmjopen-2012-000850

ABSTRACT

Objectives: An estimated 6%–10% of US adults took a hypnotic drug for poor sleep in 2010. This study extends previous reports associating hypnotics with excess mortality.

Setting: A large integrated health system in the USA.
Design: Longitudinal electronic medical records were extracted for a one-to-two matched cohort survival analysis.

Subjects: Subjects (mean age 54 years) were 10 529 patients who received hypnotic prescriptions and 23 676 matched controls with no hypnotic prescriptions, followed for an average of 2.5 years between January 2002 and January 2007.

Main outcome measures: Data were adjusted for age, gender, smoking, body mass index, ethnicity, marital status, alcohol use and prior cancer. Hazard ratios (HRs) for death were computed from Cox proportional hazards models controlled for risk factors and using up to 116 strata, which exactly matched cases and controls by 12 classes of comorbidity.

Results: As predicted, patients prescribed any hypnotic had substantially elevated hazards of dying compared to those prescribed no hypnotics. For groups prescribed 0.4–18, 18–132 and >132 doses/year, HRs (95% CIs) were 3.60 (2.92 to 4.44), 4.43 (3.67 to 5.36) and 5.32 (4.50 to 6.30), respectively, demonstrating a dose–response association. HRs were elevated in separate analyses for several common hypnotics, including zolpidem, temazepam, eszopiclone, zaleplon, other benzodiazepines, barbiturates and sedative antihistamines. Hypnotic use in the upper third was associated with a significant elevation of incident cancer; HR=1.35 (95% CI 1.18 to 1.55). Results were robust within groups suffering each comorbidity, indicating that the death and cancer hazards associated with hypnotic drugs were not attributable to pre-existing disease.

Conclusions: Receiving hypnotic prescriptions was associated with greater than threshold increased hazards of death even when prescribed <18 pills/year. This association held in separate analyses for several commonly used hypnotics and for newer shorter-acting drugs. Control of selective prescription of hypnotics for patients in poor health did not explain the observed excess mortality.

ARTICLE SUMMARY

Article focus

- Estimate the mortality risks associated with specific currently popular hypnotics in a matched cohort design using proportional hazards regression models.
- Estimate the cancer risks associated with specific currently popular hypnotics.
- Explore what risk associated with hypnotics can be attributed to confounders and comorbidity.

Key messages

- Patients receiving prescriptions for zolpidem, temazepam and other hypnotics suffered over four times the mortality as the matched hypnotic-free control patients.
- Even patients prescribed fewer than 18 hypnotic doses per year experienced increased mortality, with greater mortality associated with greater dosage prescribed.
- Among patients prescribed hypnotics, cancer incidence was increased for several specific types of cancer, with an overall cancer increase of 35% among those prescribed high doses.

Strengths and limitations of this study

- Design strengths included matching patient and control cohorts by age, gender and smoking. Through stratified statistical analyses, patients with hypnotics were matched with controls diagnosed with the exactly the same combination of 12 categories of comorbidity in up to 116 strata.
- The major limitation was that residual confounding could not be fully excluded, due to possible biases affecting which patients were prescribed hypnotics and due to possible imbalances in surveillance.
- Cohort studies demonstrating association do not necessarily imply causality, but the preferable randomised controlled trial method for assessing hypnotic risks may be impractical due to ethical and funding limitations.

INTRODUCTION

Hypnotic drugs are among the most widely used treatments in adult medicine. We estimate that approximately 6%–10% of US adults used these drugs in 2010, and the percentages may be higher in parts of Europe.^{1–3} By 1979, the Cancer Prevention

- 10500 take HS sedn
- 23600 controls none
- Risk of death-
- 0.4-18 tabs: 3.6 HR
- 18-132 : 4.4 HR
- >132 : 5.3 HR (+1.35 HR - cancer)
- Dose dependent risk

Seniors and Atrial Fibrillation

- AFIB gives 6% CVA risk PER YEAR untreated
 - ASA - 21% Relative Risk reduction
 - Warfarin - 68% Relative Risk reduction
- PRIOR CVA, relative risk of subsequent CVA is 3.1 times the pre-stroke rate



Seniors and Atrial Fibrillation

- Pt on warfarin must FALL > 295 x per year for warfarin NOT to be optimal therapy
- Falls DON'T contraindicate! More important is ETOH use; COMPLIANCE with INR testing; NSAID use; history of GI bleeding
 - M Man-Son-Hing JAMA IM 1999; 159 (7)



Vitamin B12

- B12 deficiency should be screened for
- Usually subclinical
- Require acid, terminal ileum
 - Metformin association
 - PPI association
- Prevalence of B12 deficiency (also folate)
 - >5% age 65-75; >10% age >75
- Treatment
 - 1 mg. IM weekly x 8, then monthly
 - 1 mg. PO daily usually as good as IM
 - Once started, treat for life



VERY Elderly & Hypertension

- Age >80 HTN may indicate BETTER health and lower systolic numbers trouble ahead
 - J Goodwin Arch of Int Med

Elderly and Hypertension

- Risks of Treatment of Hypertension
 - Falls
 - Orthostasis
 - Electrolyte disturbance
 - Polypharmacy to treat to CPG goal
 - ?Frailty
 - ?Increased mortality

Elderly and Hypertension

- Benefit to treating to SBP lower than 160 in elderly and very elderly- less mortality but no reduction in stroke NNT 46 (HYVET)
- No evidence for recommended target of 140 made by Cdn HTN Education Program; no increase in benefit if lowered less than 160

Elderly and Hypertension

- Met analysis 2010 showed treating HTN in very elderly resulted in less CVA and CHF with NO effect on total mortality
- Review also suggests increased mortality with more intensive treatment
- Suggestion for low-maximal intensity of therapy in over 80 group
 - Thiazide as first line therapy
 - Maximum therapy of two drugs in low doses
 - Bejan-Angoulant T, et al. J HTN 2010; 28:1366-72

Elderly and Hypertension

- It's not the age that counts but the physiology, functional status and frailty
- Consider treating a “YOUNG” OLD person more aggressively than you would an “OLD” OLD person

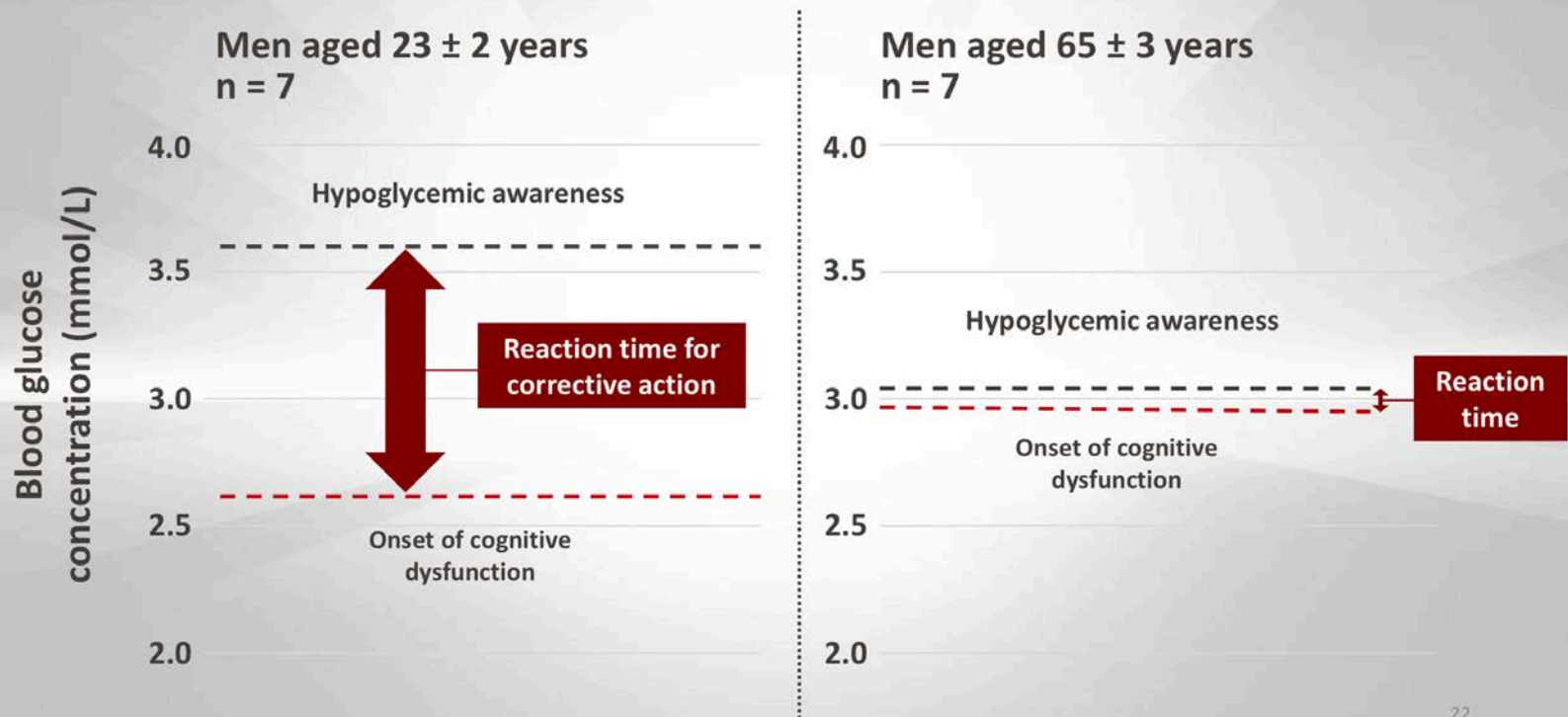


Diabetes Therapy

- In seniors, more important to **AVOID HYPOGLYCEMIA** than concern about moderate hyperglycemia

Diabetes- Hypoglycemia Awareness in the Elderly

THRESHOLDS FOR HYPOGLYCEMIC SYMPTOMS VARY WITH AGE



ORIGINAL ARTICLE

Long-Term Effects of Intensive Glucose Lowering on Cardiovascular Outcomes

The ACCORD Study Group*

ACCORD

10,251 patients age 40 -79

Intensive (HbA1c 6.4%) vs. Standard (HbA1c 7.5%)

22% excess mortality – stopped after 3.5 years

Follow up - HbA1c 7.4% vs. 7.8% - equal mortality

Gerstein HC, et al.; N Engl J Med 2008;358:2545-2559

LESS POLYPHARMACY PLEASE

ORIGINAL ARTICLE

Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes

The ADVANCE Collaborative Group*

ADVANCE

11,140 Type 2 Diabetes over age 55

Intensive (HbA1c 6.5%) vs. Standard (HbA1c 7.3%)

5 years – No difference in major CV events, CV deaths, or overall deaths

Patel A, et al. N Engl J Med 2008;358:2560-2572

LESS POLYPHARMACY PLEASE

Frequent Hypoglycemia Among Elderly Patients With Poor Glycemic Control

Medha N. Munshi, MD; Alissa R. Segal, PharmD; Emmy Suhl, RD; Elizabeth Staum, RD; Laura Desrochers, BS; Adrienne Sternthal, BS; Judy Giusti, RD; Richard McCartney, BA; Yishan Lee, MS; Patricia Bonsignore, MS; Katie Weinger, EdD

Continuous glucose monitoring was done for 36 hours on 40 adults 69 years or older with a HbA1c of 8% or greater. Fingertip glucose testing was done QID, and symptoms of hypoglycemia recorded.

26 of the 40 (65%) had at least one episode of hypoglycemia less than 3.9 mmol/L, and 12 of 40 a level below 2.8 mmol/L.

93% (95/102) of hypoglycemic episodes were not recognized by symptoms or on QID fingertip glucose testing.

“Our findings raise caution for relying on HbA1c as the sole measure of “good diabetes management” in elderly patients with diabetes, and we recommend careful and in-depth assessment for hypoglycemia by both patients and providers.”

TABLE 1 – Blood Glucose Level Guidelines for elderly residents in long term care

Less than 4.0 mmol/L	Refer to the treatment of hypoglycemia (Standard 2) in a conscious/unconscious resident
4.0 - 6.9 mmol/L	Assess symptoms (review chart for trends, history, resident status), notify physician, pharmacist or nurse practitioner
7.0 - 9.9 mmol/L	This range may be acceptable. There is a risk for hypoglycemia. If it occurs more than once a month notify physician non-urgently and consult with IDT.
10.0 - 20.0 mmol/L	This range is acceptable. However, if symptomatic notify the IDT to assess treatment.
Greater than 20 mmol/L	Refer to hyperglycemic management (Standard 3) Communicate with physician non-urgently to assess treatment if symptomatic and consult with IDT.
Greater than 33 mmol/L / “HI” reading	Notify physician immediately

Cholesterol and Statins

- Adverse effects are common:
 - Myalgia, myopathy, abnormal liver function, memory loss
- As Frailty increases:
 - Risks increase and benefits decrease
- Lowering cholesterol over age 65 may have unintended adverse effects:
 - INVERSE effect on all-cause mortality, non-**CVS** and cancer mortality. Effect became stronger with advancing age
 - Minimal association with **CVS** mortality, in the oldest old there is an inverse effect
 - Newson RS et al, J Am Ger Soc 2011;59:1779-85

Cholesterol and Statins

- Secondary Prevention and Statins:
 - Reduces coronary artery mortality and all-cause mortality in RCTs and metanalysis
- Primary Prevention and Statins:
 - Provided NO benefit in all-cause mortality in a high-risk population treated 3.7 years
 - Meta-analysis of 65229 pts in 11 RCTs
 - Ray KK et al, Arch Int Med 2010; 170:1025-31



Dementia and antipsychotic use

- Antipsychotics widely used to treat psychosis, agitation and aggression but evidence of benefit lacking and concerns re safety
- In N Am facilities, 25-63% of residents get antipsychotics for > 1 yr.
- Trial Ballard et al; most with AD had little or no neg (some had +ve) effect on function/ cognition after withdrawal.
- Randomize, DB, placebo control studies of withdrawal in severe AD- behavior no worse
- Withdraw at 6 mo., only 10% needed restart

Dementia and Anticholinesterase Inhibitors

- Anticholinesterase Inhibitors
- Study in LTC; dementia patients on AChIs;
 - 11% had mild dementia
 - 36.2% moderate dementia
 - 52.8% severe dementia
- Reduction happened only when close to death
- Consensus panel- ACIs NEVER appropriate in advanced dementia when comfort is GOC

Dementia and Medications

- Benzodiazepines increase risk of dementia
- Billotti de Gage- 1063 men and women mean age 78.2 yrs- free of dementia and no BZD until yr 3 of F/U. 253 cases of dementia over 15 yrs. New use of BZD assoc with 50% increase risk of dementia (controlled for depression, a marker of early dementia)

Depression and medications

- Depression is associated with polypharmacy
- Hosia-Randall et al found patients on ≥ 9 medications more likely to have current dx of depression
- Chiang et al found dx of depression on chart review associated with higher numbers of routine and total meds



Proton Pump Inhibitors

- Often the initial indication has resolved
- RISKS of ongoing treatment:
 - Clostridium Difficile- strongest association
 - B12 deficiency
 - Aspiration pneumonia
 - Clopidogrel interaction
 - Bone fractures- achlorhydria causing malabsorption of calcium and Vitamin D

Bone Health

- Calcium tablet supplements may increase risk of M.I. if history of cardiac disease. This is NOT the case for dietary Calcium.
- Calcium with Vitamin D reduces fractures
 - NNT 63 for 3.5 yrs.
- Calcium alone – NO benefit
- Bisphosphonates- after 5 years can be stopped and risk of fracture is unchanged

Vitamin Supplementation

- Vitamins A and E
 - INCREASE mortality- DISCONTINUE
- Vitamin D
 - it's a steroid; dose > 800 IU
 - reduces non-vertebral #, NNT 93
 - reduces hip #, NNT 168
 - REDUCES FALLS risk 19%, NNT 11 for >2mo. (why?)





Acetaminophen Dosing in Seniors

- Manufacturers recommending MAX total dose 3000 mg in 24 hrs. Why? Commonest non-intentional drug OD- can result in acute liver failure.
- Dose > 2600 mg increases GI dyspepsia S/E similar to NSAID. Why? It is a selective COX-2 inhibitor as well
- MAX total dose 2000 mg recommended if ETOH > 3 drinks/ day or if on Warfarin therapy



Case 84 yr old male

- Geriatric assessment & pharmacist review
- Sleep- Wean Zopiclone to 3.75 mg and then to off due to falls
- BPH- Stopped Proscar, no increase symptom
- Cardiac- D/C ASA, Lipitor (no evidence)
- BP- off Bisoprolol (rate), Norvasc (edema) and continue HCTZ at 12.5 mg.
- OTC- off Brain Boost, Ca, Vit E

- !50/80, HR 65, MOCA 22/30, no gait aide

Case- Medication resolution

- Proscar 5 mg OD
- Flomax 0.4 mg OD
- Norvasc 5 mg OD
- Bisoprolol 2.5 mg OD
- Zopiclone 7.5 mg HS
- Lipitor 10 mg OD
- HCTZ 25 mg. AM
- Ca++, Vit D and E
- Flomax 0.4 mg OD
- HCTZ 12.5 mg AM
- Vit D 1000 mcg OD
- Zopiclone 3.75 PRN
- Considering Aricept 5 mg OD

Take Home Messages

- There are multiple reasons why CPGs extrapolate poorly in a frail elderly population
- Medications can be safely withdrawn, often with significant benefit
- Complex decision making must include thought regarding life expectancy, time until drug benefit, goals of care and aggressiveness of disease targets

Take Home Messages

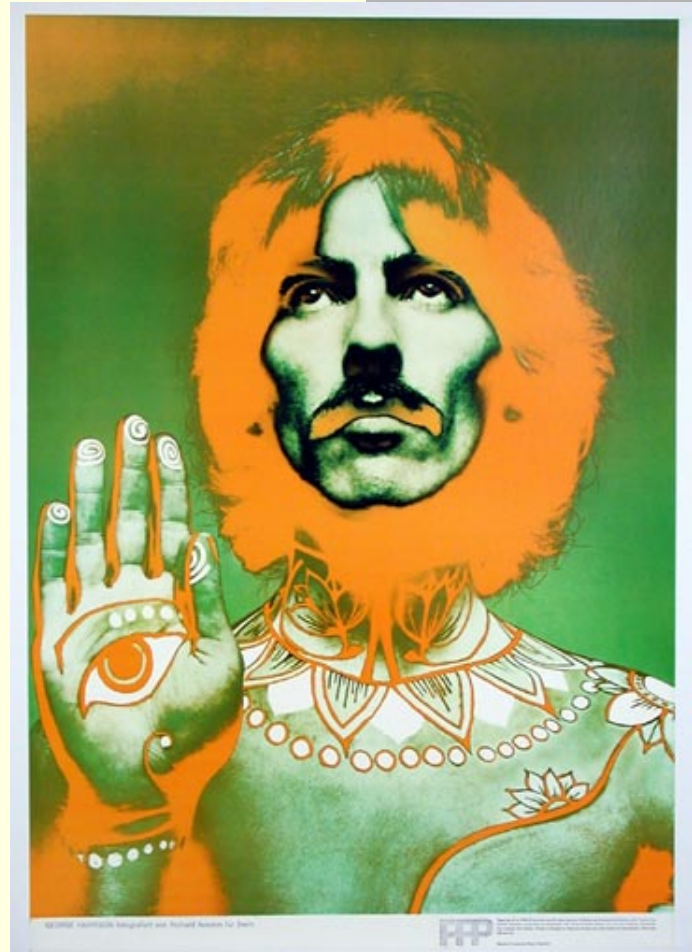
- First- do you have an accurate drug profile?
- Consider any new symptom as a possible ADR or drug interaction
- Drug Adherence issues? Simplify all drugs to OD or BID
- Could there be a “Prescribing Cascade”

Take Home Messages

- Be the one to initiate the conversation
- Progress slowly
- Remember “Mini-polypharmacy”
- Use medications with the lowest anticholinergic effect
- Overcome “Prescribing Inertia”

Be open to new evidence & studies

- “THE FURTHER ONE TRAVELS, THE LESS ONE REALLY KNOWS”
 - George Harrison
 - From ‘The Inner Light’



Number to Treat (NNT)

- ECASA high risk (1 yr) -100
- ECASA ave risk (1 yr) -1176
- HTN meds prevent CVS probs (1 yr) -100
- Lower Na⁺ after MI/ CVA prevent CVS -42
- D/C smoking after MI/ CVA prev death/ MI -8
- HRT prevent colorectal CA or back/hip # 588
- Steroid MDI for asthma -1
- Celebrex to prevent serious GI bleed -infinite
- Vioxx to cause MI, CVA, CHF -59

Medication Reduction

- What is 'appropriate' and what is 'ethical' in medication use and deprescribing?
- Guided by 4 ethical principles of beneficence, nonmaleficence, patient autonomy, justice
- Conflicts occur between physician and patient/ family
- Dilemma of balancing patient welfare, values and beliefs with desire for promising but often minimally beneficial/ possibly harmful meds

De-prescribing: step by step

- Indications for deprescribing
- Prioritize medications targeted for de-prescribing
- Communicate, coordinate
 - Patient, caregiver, team members
- Approaches:
 - Taper (psychotropics, BZD)
 - Withdraw (immediate harm, bleeding)
 - Substitute: safer alternatives
 - Re-introduce if appropriate
- Monitor for benefits or harms
- Safety of de-prescribing: successful in >80%
 - 88% report global improvement in health, incl. mobility and cognition
 - Garfinkel et al, Arch Intern Med 2010



Seniors and Medications - ADRs

- Seniors and Adverse Drug Reactions:
 - Occur in up to 35% of outpatients and 44% of hospitalized
 - Account for 10% of seniors ER visits and 12% of seniors admissions
 - 4th most common cause of death in US hospitals
 - Diuretics, cardiac drugs, anticoagulants, NSAIDs, antibiotics, narcotics, hypoglycemics

Challenges to Deprescribing

- Aiming for optimal quality of life requires shared decision making
- Exploring patient preferences regarding tx goals
- Life expectancy vs time to benefit for preventative meds
- Informing re potential benefits vs harms

Topical vs. Oral NSAIDS

- Oral NSAIDs linked to 30% drug-related hospitalizations
- 3+ MI/ CVA per yr. per 1000 patients
- 20-40 stomach bleeds /yr. per 1000 patients
- Evaluate risks: CVS, renal, GI, drug/drug
- Not all are equal: Naproxen best for CV risk; Ibuprofen < 1200 mg daily
- LOW DOSE if used at all

Topical NSAIDs

- Clinically effective for acute joint pain up to 4 weeks duration of therapy
- As effective as oral NSAIDs, with much improved safety profile
- Best for localized pain; hands and knees
- NNT 4.5
- Not as effective for headache, back pain, neuropathy

Insomnia - Extrinsic Causes

- 1. Environment
- 2. Patient Care
- 3. Meds, vitals, lab
- 4. Temperature- less subcut fat
- 5. Light
- 6. Noise- most NB irritant in study
- 7. Technology
- 8. Other patients

Insomnia - Intrinsic Causes

- 1. Changes in sleep pattern, ^ with age
- 2. Underlying medical illness, eg. Delirium, dyspnea from COPD, CHF, GERD, pain...
- 3. Medication effects- steroids, L-dopa, bronchodilators, antidepressants (bupropion, SSRIs, venlafexine)
- 4. Medication withdrawal- esp BZD, SSRIs
- 5. Alcohol withdrawal

Intrinsic causes -Drugs

- Laxatives
- Diuretics- nocturia
- Bblocker- mood alter, impair melatonin
- SSRI-decrease REM sleep
- ETOH- less REM, total sleep time (even hrs later)
- Codeine- anticholinergic; untreated pain?
- Decongestants- anticholinergic components
- Nicotine/ patch- total sleep time; dreams

Intrinsic causes -Drugs

- Caffeine- decrease sleep propensity
- Ventolin- stimulant (undertreated dyspnea)
- Steroids- anticholinergic; increase alertness
- L-Dopa- daytime sleepiness, dose related
- Dilantin- drowsiness; less REM
- Cholinesterase Inhibitors- bothersome and vivid dreams