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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

DEPRESCRIBING IN PSYCHIATRY

STEPHEN THIELKE

PSYCHIATRIC AND BEHAVIORAL SCIENCES

UNIVERSITY OF WASHINGTON

UW Medicine
UW SCHOOL OF MEDICINE

Integrated Care Training Program
UW Psychiatry & Behavioral Sciences

project ECHO

"To write prescriptions is easy, but to come to an understanding with people is hard."

-Franz Kafka, *A Country Doctor*

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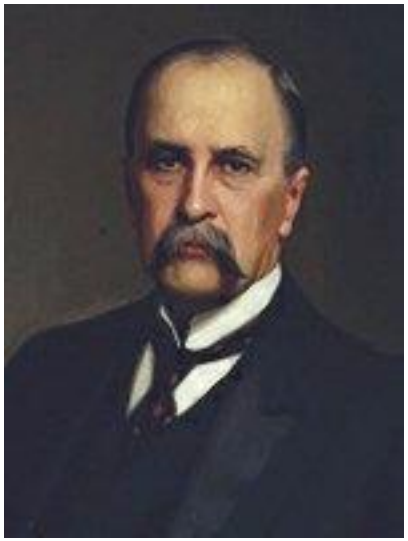
One of the first duties of the physician is to educate the masses not to take medicine.



Far too large a section of the treatment of disease is today controlled by the big manufacturing pharmacists, who have enslaved us in a plausible pseudo-science.

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Disclosures:

I have no conflicts of interest to report.

I am an employee of the University of Washington.

All opinions in this talk are my own.

Most of the issues here relate mainly to older adults.

All of the prescription recommendations in this talk are off-label.

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OBJECTIVES:

- Reflect on the assumption of risk in medical care.
- Consider specific challenges in psychopharmacology.
- Review challenges in deprescribing.
- Suggest methods to deprescribe.

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CONSENT TO SURGERY OR SPECIAL PROCEDURE

1. Your doctors have recommended the following operation or procedure: _____

   _____

   and the following type of anesthesia: _____

   Upon your authorization and consent, this operation or procedure, together with any different or further procedures which, in the opinion of the doctor(s) performing the procedure, may be indicated due to any emergency, will be performed on you. The operations or procedures will be performed by the doctor named below (or in the event the doctor is unable to perform or complete the procedure, a qualified substitute doctor), together with associates and assistants, including anesthesiologists, pathologists, and radiologists from the medical staff of *(name of hospital)* _____ _____ to whom the doctor(s) performing the procedure may assign designated responsibilities.

2. Name of the practitioner who is performing the procedure or administering the medical treatment[1]:

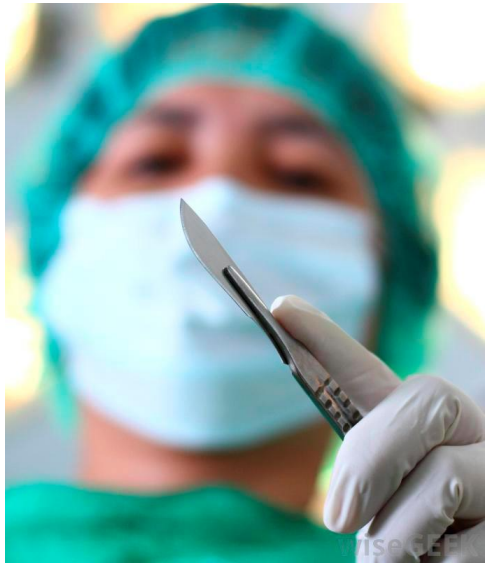
   _____

   The hospital maintains personnel and facilities to assist your doctors in their performance of various surgical operations and other special diagnostic or therapeutic procedures. However, your doctors, surgeons, and the persons in attendance for the purpose of performing specialized medical services such as anesthesia, radiology, or pathology are not employees or agents of the hospital or of doctor(s) performing the procedure. They are independent medical practitioners.

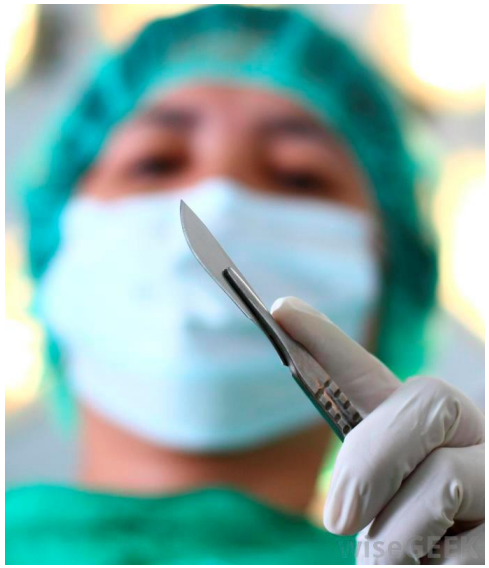
3. All operations and procedures carry the risk of unsuccessful results, complications, injury, or even death, from both known and unforeseen causes, and no warranty or guarantee is made as to result or cure. You have the right to be informed of:

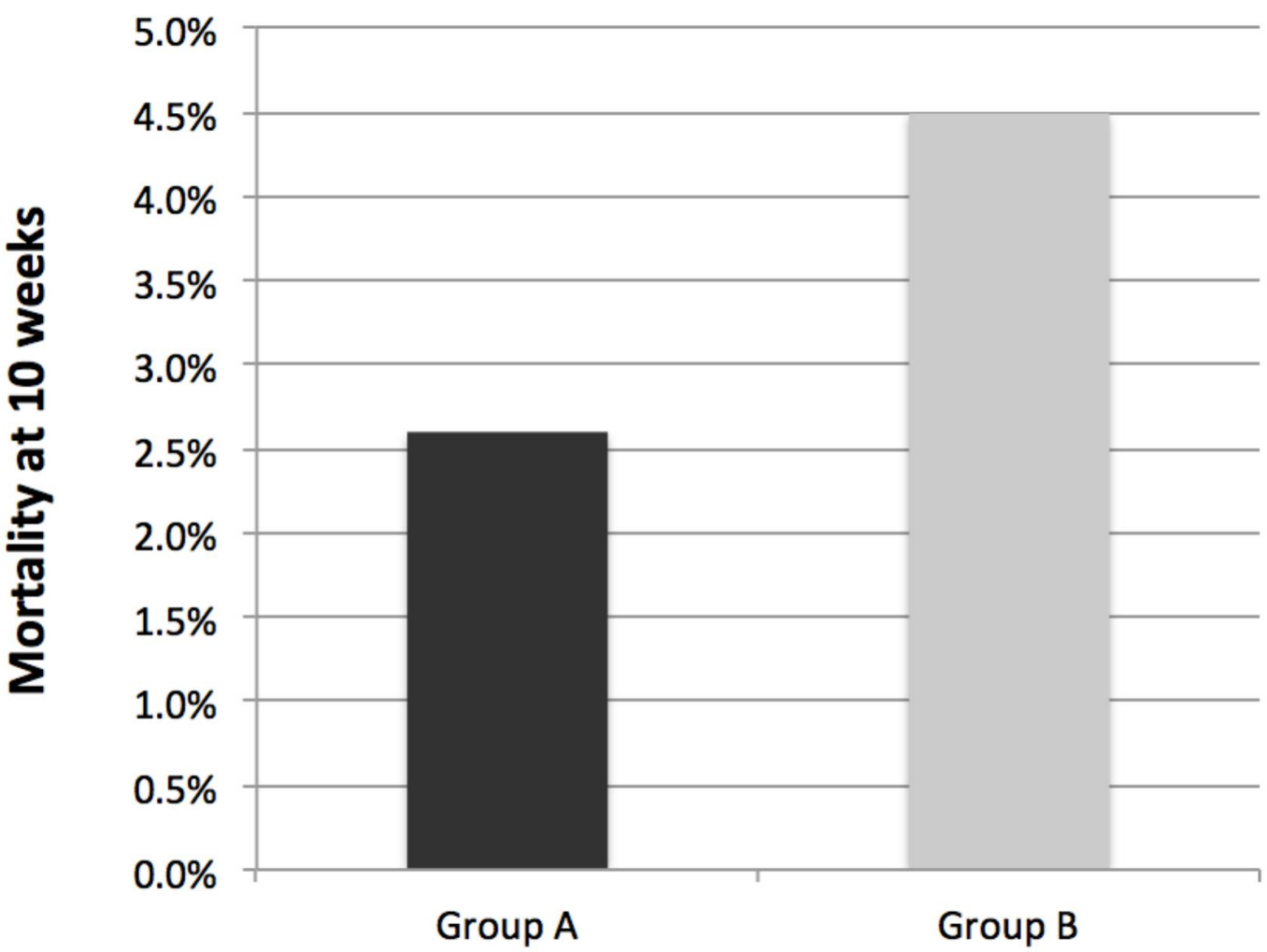
   - The nature of the operation or procedure, including other care, treatment or medications;
   - Potential benefits, risks or side effects of the operation or procedure, including potential problems that might occur with the anesthesia to be used and during recuperation;
   - The likelihood of achieving treatment goals;
   - Reasonable alternatives and the relevant risks, benefits and side effects related to such alternatives, including the possible results of not receiving care or treatment; and
   - Any independent medical research or significant economic interests your doctor may have related to the performance of the proposed operation or procedure.

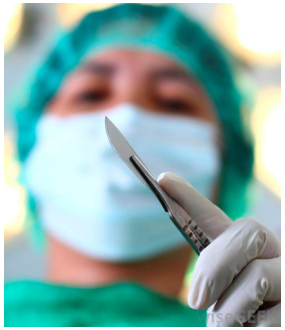
   Except in cases of emergency, operations or procedures are not performed until you have had the opportunity to receive this information and have given your consent. You have the right to give or refuse consent to any proposed operation or procedure at any time prior to its performance.



Are risks from pills different than risks from procedures?







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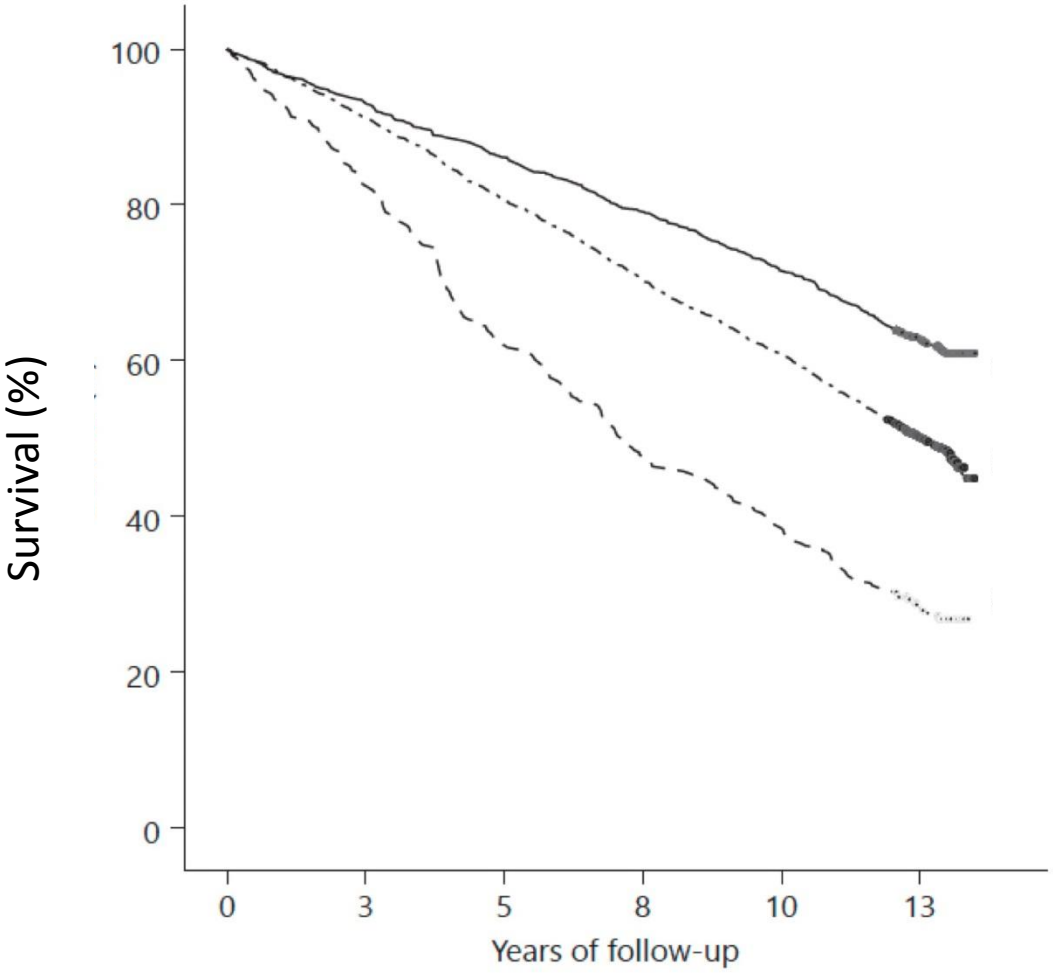

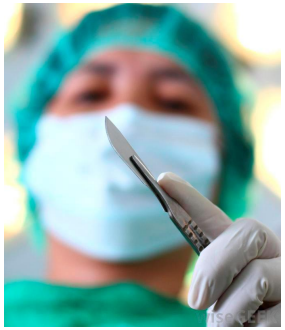

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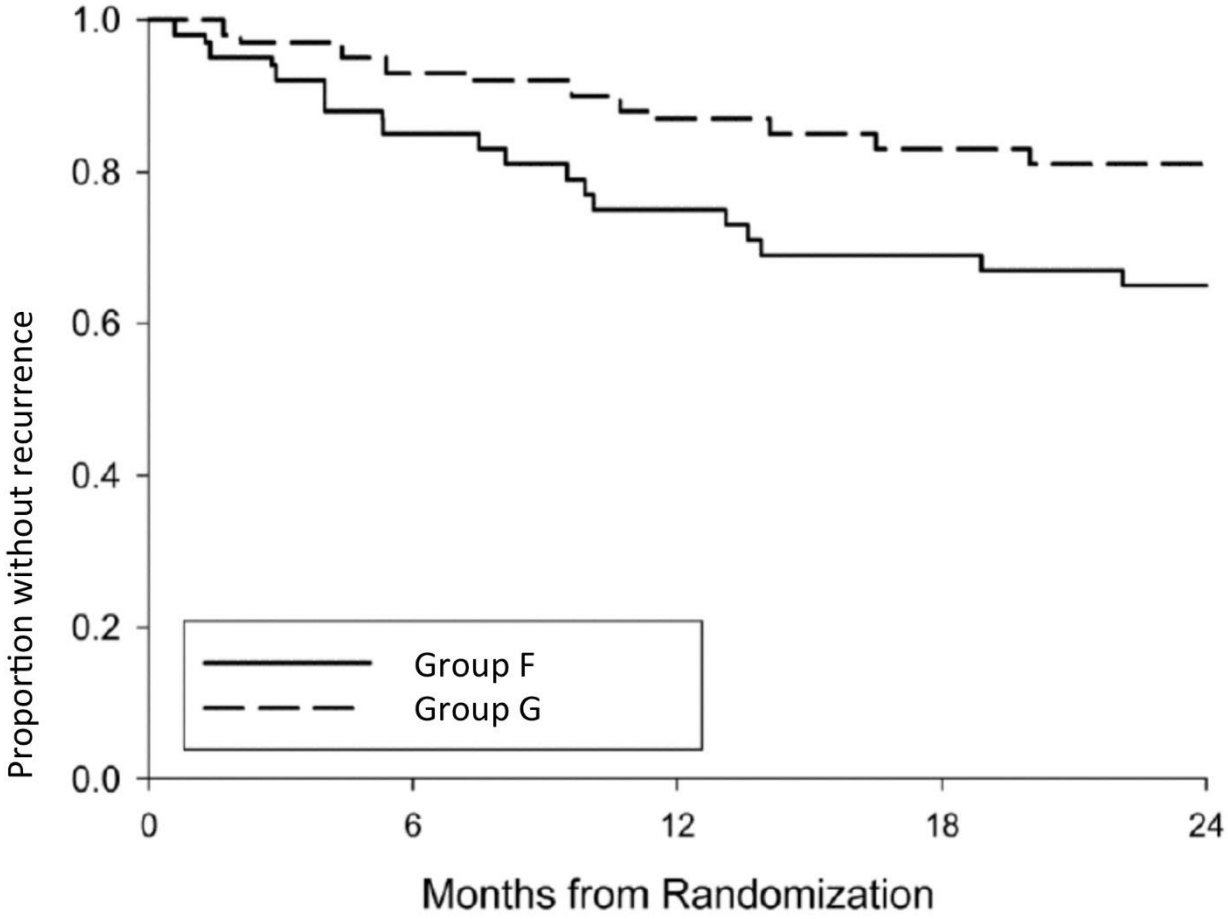

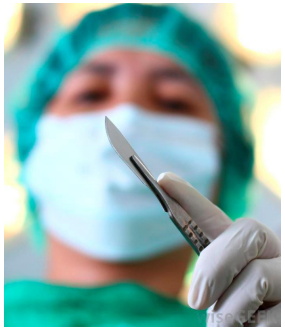

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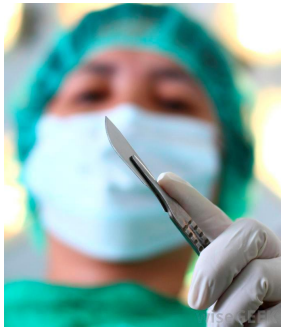

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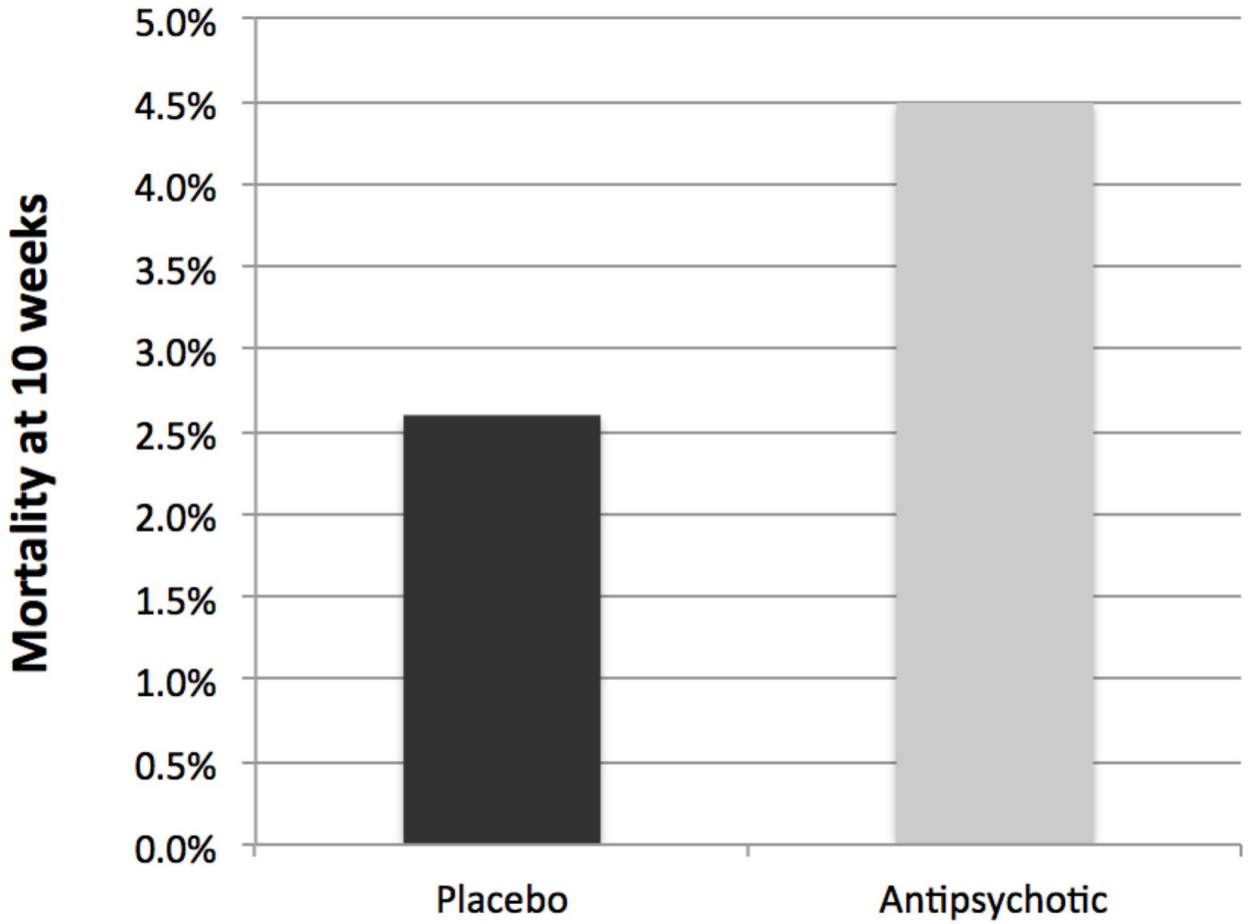
Is your estimate of risk contingent on the potential benefit of the treatment?

("This treatment is so effective that the patient does not need to know the risks.")

What risks do we ask our patients to undertake?

ANTIPSYCHOTICS IN DEMENTIA



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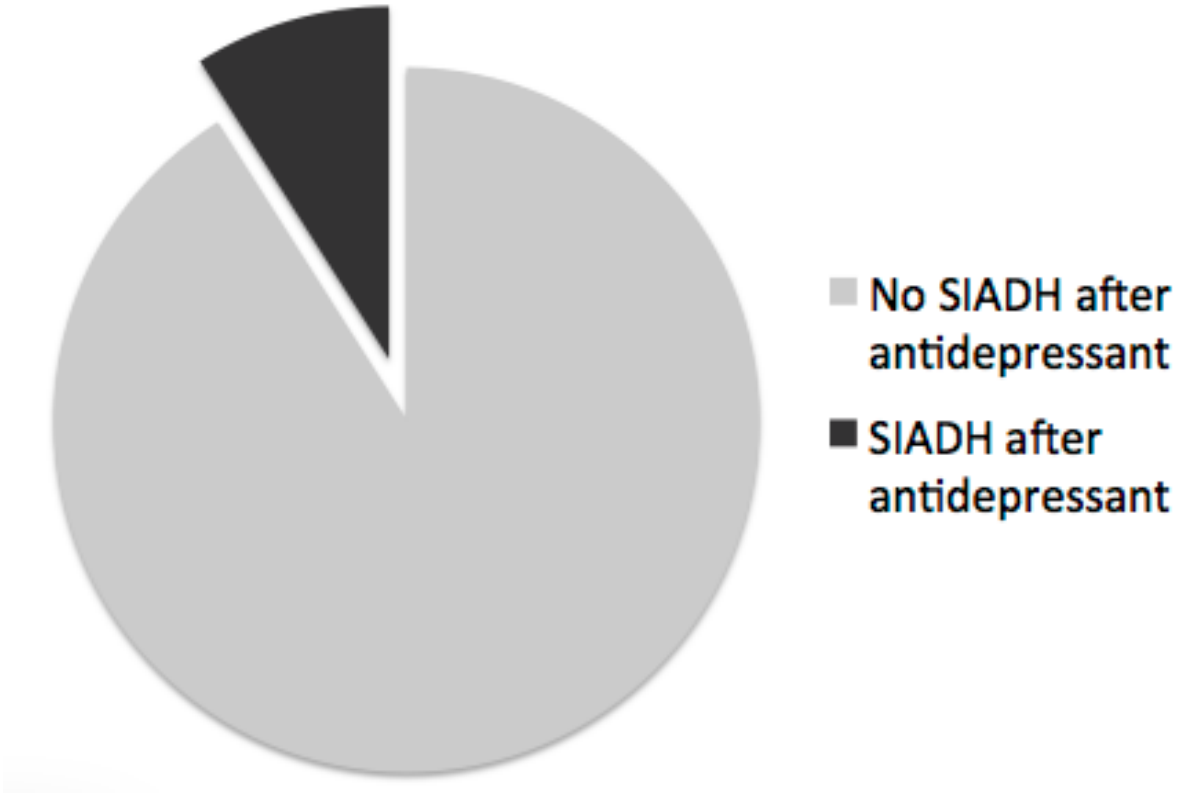
WARNING: Increased Mortality in Elderly Patients With Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration* of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a **risk of death in drug-treated patients of between 1.6 to 1.7** times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group.

Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infections (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality.

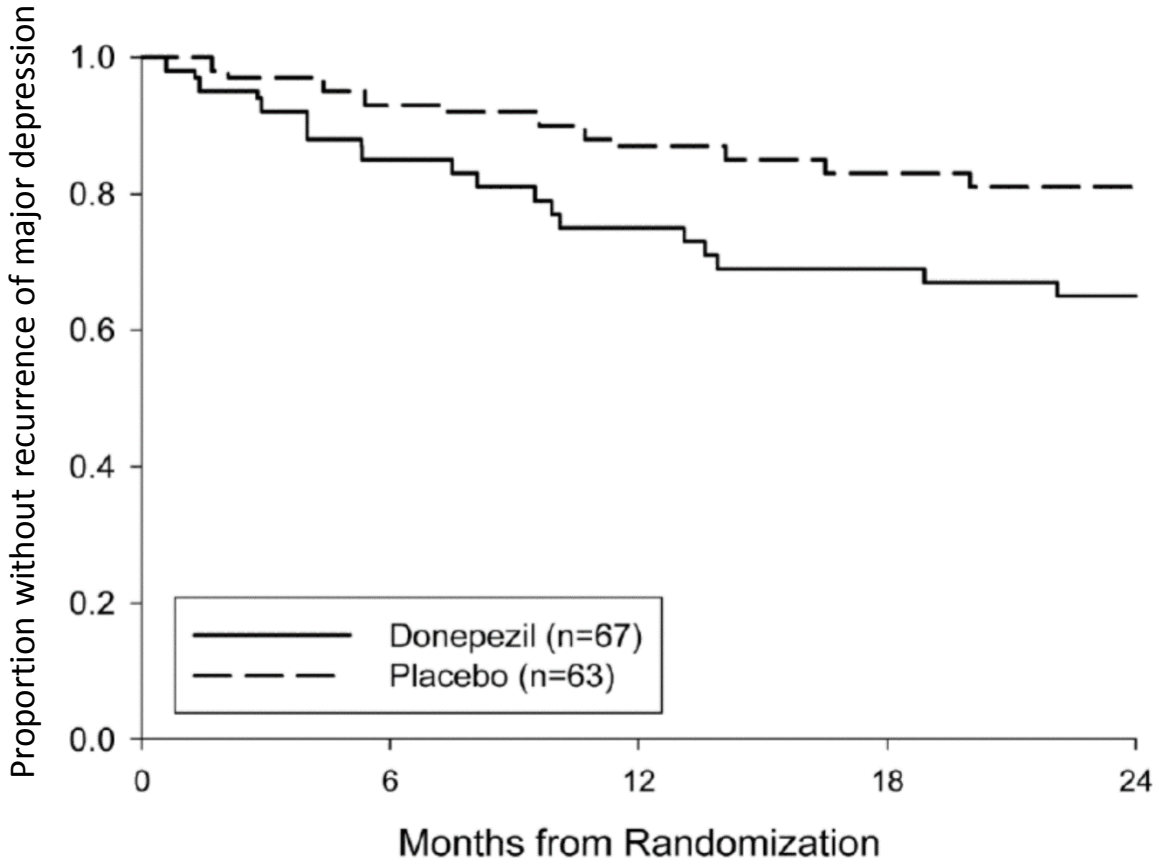
HYPONATREMIA AFTER STARTING ANTIDEPRESSANTS



Mannesse C.K., et al. Characteristics, prevalence, risk factors, and underlying mechanism of hyponatremia in elderly patients treated with antidepressants: A cross-sectional study. *Maturitas* 2013; 76: 357-363.

What are the clinical symptoms of hyponatremia?

DONEPEZIL IN DEMENTIA



Reynolds et al, *Arch Gen Psychiatry.* 2011; 68(1): 51–60.

DRUGS AND FALLS IN OLDER ADULTS

Fall-Risk-Increasing Drugs: A Systematic Review and Meta-Analysis: II. Psychotropics

Conclusions: Antipsychotics, antidepressants, and benzodiazepines are consistently associated with a higher risk of falls. It is unclear whether specific subgroups such as short-acting benzodiazepines and selective serotonin reuptake inhibitors are safer in terms of fall risk. Prescription bias could not be accounted for. Future studies need to address pharmacologic subgroups as fall risk may differ depending on specific medication properties. Precise and uniform classification of target medication (Anatomical

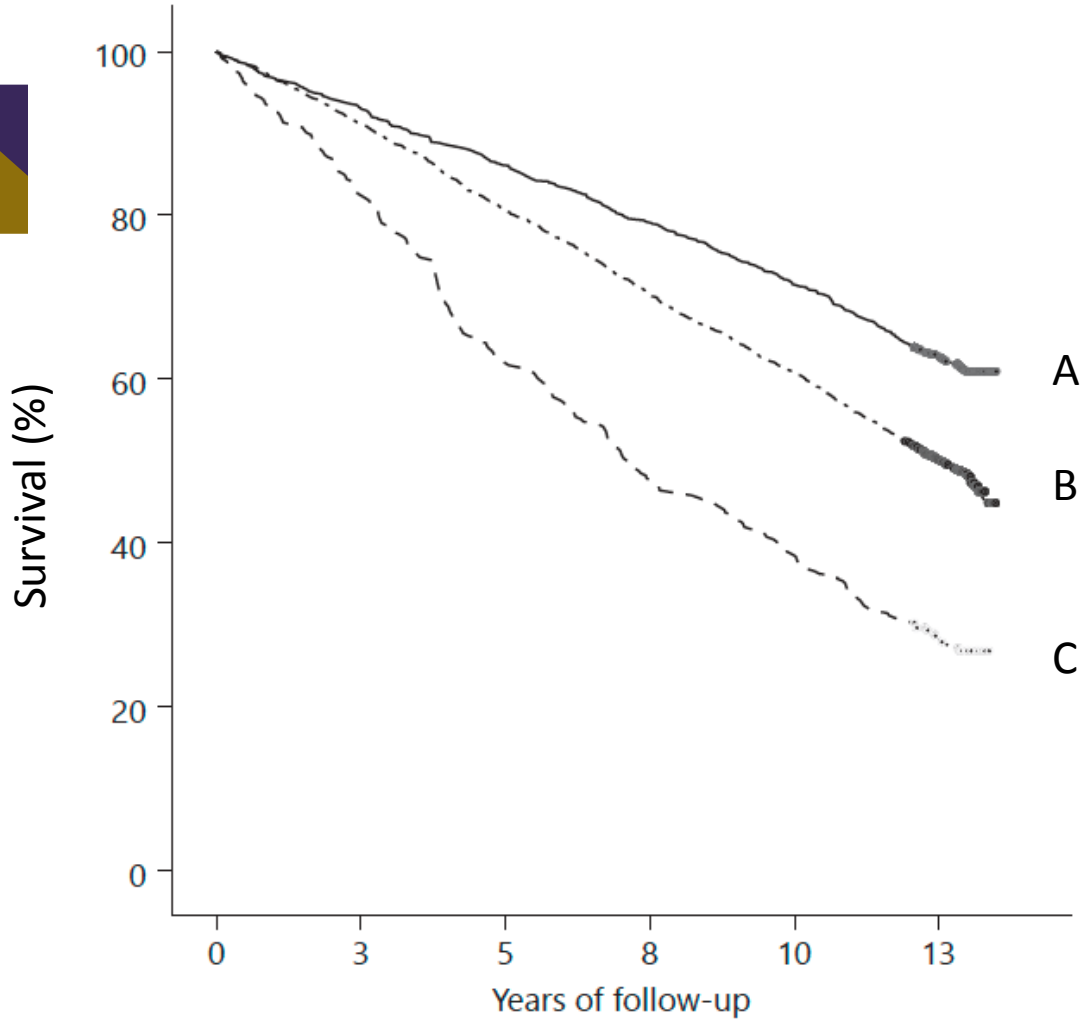
Odds ratios for falls in patients 60+ years old:

-Antipsychotics (1.54)

-Antidepressants (1.57)

-Benzodiazepines (1.42)

Seppala et al. *JAMDA* 19(2018).



Adjusted for sociodemographic factors and disease severity

Group	Hazard ratio for death
A	Reference
B	1.47
C	2.78

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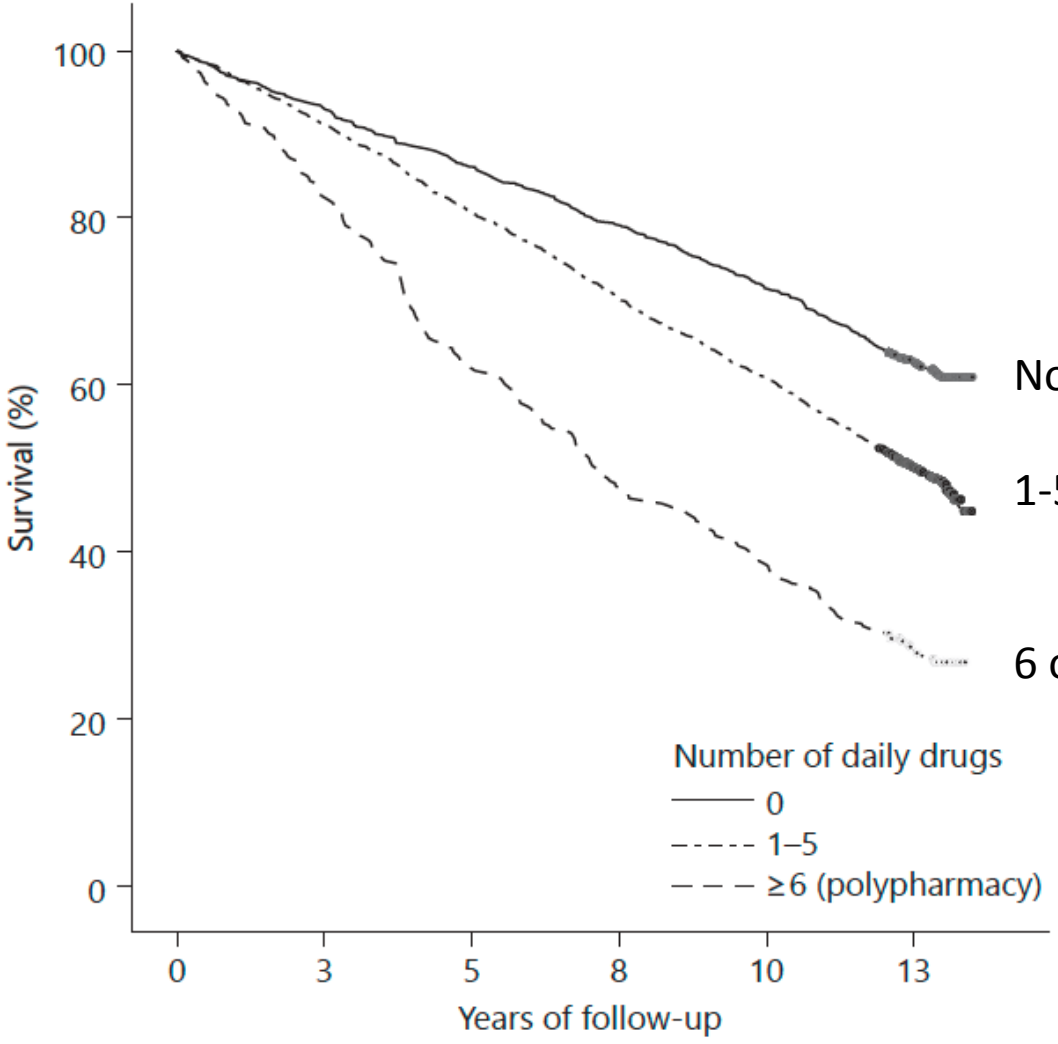
Polypharmacy and Mortality



No medications

1-5 medications

6 or more medications

Gomez et al. Polypharmacy in the Elderly: A Marker of Increased Risk of Mortality in a Population-Based Prospective Study (NEDICES). *Gerontology* 2015;61:301-309.

POLYPHARMACY AND ADVERSE DRUG EVENTS

Increased risk for adverse drug events over one year (compared to none):

2 medications	13%
5 medications	58%
>7 medications	82%

Patterson, S. M. et al. Interventions to Improve the Appropriate Use of Polypharmacy for Older People. *Cochrane Database of Systematic Reviews*(John Wiley & Sons, Ltd, 2012).

POLYPHARMACY AND ADVERSE DRUG EVENTS

About 30% of **all** hospitalizations in adults 65+ years old are due to ADEs

Rehospitalization rates are about 2-3 times higher for those on 8+ medications compared to those on 1-2

Budnitz DS et al. Emergency hospitalizations for adverse drug events in older Americans. *N. Engl. J. Med.*365,2002–2012 (2011).

Fabbietti P et al. Impact of potentially inappropriate medications and polypharmacy on 3-month readmission among older patients discharged from acute care hospital: a prospective study. *Aging Clin Exp Res* 2017.

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“I’M JUST FOLLOWING GUIDELINES.”

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MRS M'S TRIP TO THE DOCTOR

79 year-old woman

Some shortness of breath from COPD

Fasting blood sugar 147

Osteoporosis

Blood pressure 142/97

Knee pain on walking

No medications

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MRS M'S TRIP FROM THE DOCTOR

Based on published clinical practice guidelines, **how many medications** would Mrs B start?

How much would these medications **cost**?

How many **potentially harmful interactions** are recognized between them?

Boyd, CM et al. Clinical Practice Guidelines and Quality of Care for Older Patients with Multiple Comorbid Diseases. *JAMA* 2005: 294(6).

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MRS M'S TRIP FROM THE DOCTOR

Based on published clinical practice guidelines, **how many medications** would Mrs B start? **12**

How much would these medications **cost**? **$406** out of pocket

How many **potentially harmful interactions** are recognized between them? At least **12**

Boyd, CM et al. Clinical Practice Guidelines and Quality of Care for Older Patients with Multiple Comorbid Diseases. *JAMA* 2005: 294(6).

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MRS Q'S TRIP TO THE DOCTOR

81 year-old woman

Taking 15 medications; complains of dry mouth, fatigue, GI upset related to them

Started exercise program two years ago, changed diet

Very occasional shortness of breath, does not bother her

Rare knee pain after walking over two miles

Was depressed, mood is good now

Fasting blood sugar 102

Osteoporosis - stable

Blood pressure 108/78

MRS Q'S TRIP **FROM** THE DOCTOR

Based on published clinical practice guidelines, how many medications would Mrs B **stop**?

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TREATMENT GUIDELINES

Tell you when and how to start treatments.

Almost never say when to stop.

Deprescribing often requires challenging or undermining guidelines.

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PREVALENCE OF POLYPHARMACY IN OLDER ADULTS (AGE 65+)

Average number of medications: **4.6**

5 or more medications: **44%**

10 or more medications: **12%**

Increasing with advancing age

Quinn KJ. A dataset quantifying polypharmacy in the United States. *Scientific Data* 2017 4:170167.

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WHO IS RESPONSIBLE FOR POLYPHARMACY?

DO YOU COUNT THE TOTAL NUMBER OF MEDICATIONS YOUR PATIENTS RECEIVE?

WHAT IF YOU START THE 5TH / 8TH / 12TH MEDICATION?

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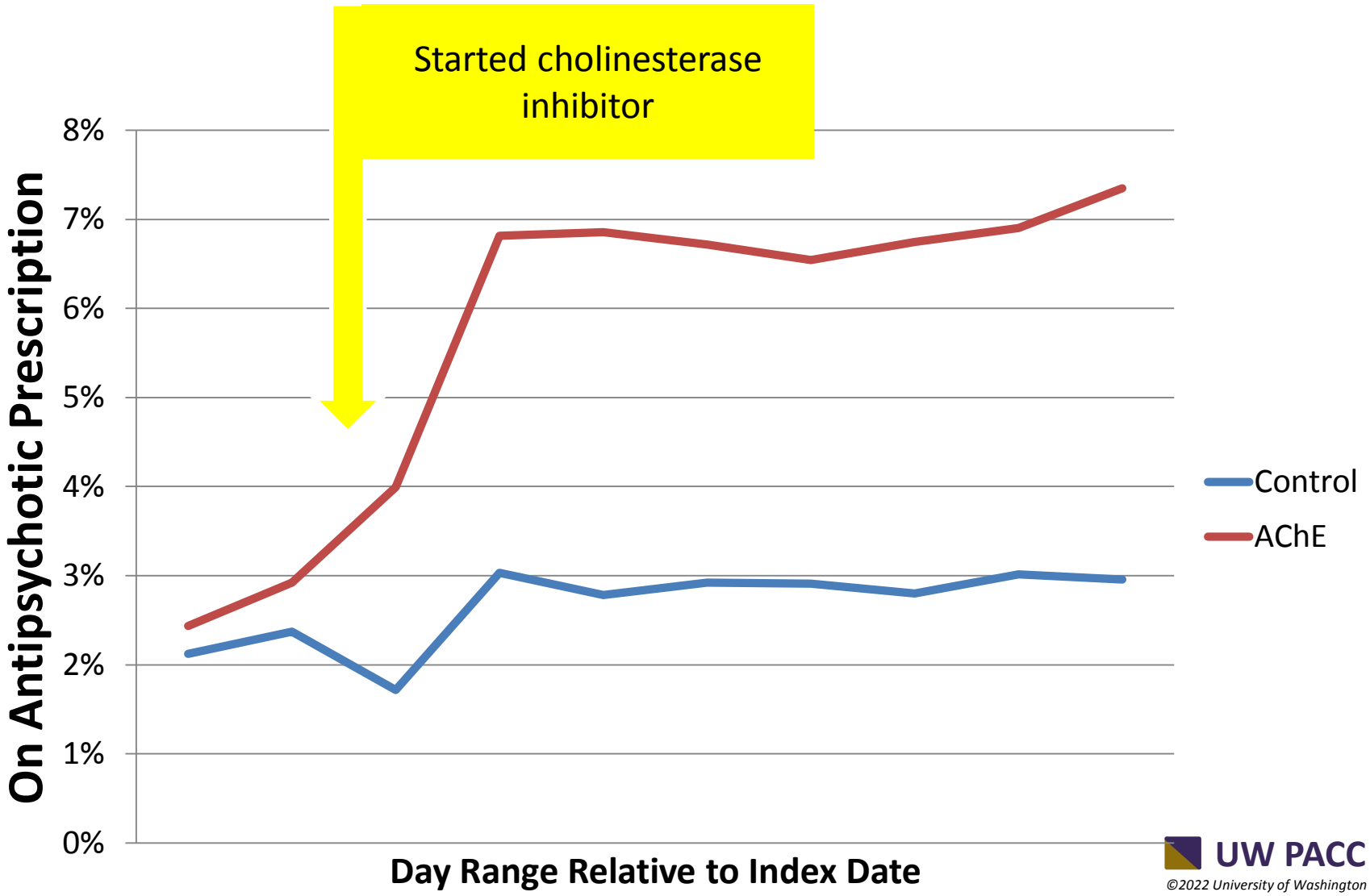
DO PILLS BEGET PILLS?



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STOPPING PILLS IS HARDER THAN STARTING THEM

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DEPRESCRIBING IS DIFFICULT FOR PROVIDERS

"I had a patient experience a side effect from starting this medication." → *I'll be more careful next time.*

"I had a patient who got worse when they stopped this medication." → *I'll never stop it again.*

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“Mrs ____ had worsening insomnia when she stopped donepezil. Stopping it is **absolutely contraindicated**.”

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DEPRESCRIBING IS DIFFICULT FOR PATIENTS AND FAMILIES

If you have a condition, you should be taking a pill for it.

Giving a pill is often a sign of caring and not giving up hope.

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“We thought about stopping the dementia medication, but decided it was best to **let nature take its course**.”

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DEPRESCRIBING IS LOGICALLY MESSY

All sorts of events happen.

We can easily attribute reasons for them.

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PRACTICAL DEPRESCRIBING

Consider the end game when starting a pill.

Figure out what the patient thinks and wants about pills.

Trial and error is the only reasonable approach, and is easy to sell.

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PROCESS STEPS IN DEPRESCRIBING

Surveillance

Permission

Measurement

Reasoning

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Can psychotropics be deprescribed?

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Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia

Evidence-based clinical practice guideline

"Antipsychotics are associated with harms and can be safely tapered."

- Antipsychotics have the potential for considerable harm, including an increased overall risk of death, cerebrovascular adverse events, extrapyramidal symptoms, gait disturbances and falls, somnolence, edema, urinary tract infections, weight gain, and diabetes; the risk of harm is higher with prolonged use and in the elderly.
- A systematic review of antipsychotic deprescribing (dose reduction or discontinuation) in patients taking them to control BPSD failed to demonstrate negative outcomes resulting from deprescribing.

Bjerre et al, Deprescribing antipsychotics for behavioral and psychological symptoms of dementia and insomnia, *Canadian Family Physician*, January 2017.

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DEPRESCRIBING ANTIPSYCHOTICS

Figure 1

Antipsychotic (AP) Deprescribing Algorithm

October 2016

Why is patient taking an antipsychotic?

- Psychosis, aggression, agitation (behavioural and psychological symptoms of dementia - BPSD) treated ≥ 3 months (symptoms controlled, or no response to therapy).
- Primary insomnia treated for any duration or secondary insomnia where underlying comorbidities are managed
- Schizophrenia
- Schizo-affective disorder
- Bipolar disorder
- Acute delirium
- Tourette's syndrome
- Tic disorders
- Autism
- Less than 3 months duration of psychosis in dementia
- Mental retardation
- Developmental delay
- Obsessive-compulsive disorder
- Alcoholism
- Cocaine abuse
- Parkinson's disease psychosis
- Adjunct for treatment of Major Depressive Disorder

Recommend Deprescribing

Strong Recommendation (from Systematic Review and GRADE approach)

Taper and stop AP (slowly in collaboration with patient and/or caregiver; e.g. 25%-50% dose reduction every 1–2 weeks)

Stop AP
Good practice recommendation

Continue AP
or consult psychiatrist if considering deprescribing

Monitor every 1–2 weeks for duration of tapering

Expected benefits:
- May improve alertness, gait, reduce falls, or extrapyramidal symptoms

Adverse drug withdrawal events (closer monitoring for those with more severe baseline symptoms):
- Psychosis, aggression, agitation, delusions, hallucinations

If BPSD relapses:

Consider:
- Non-drug approaches (e.g. music therapy, behavioural management strategies)

Restart AP drug:
- Restart AP at lowest dose possible if resurgence of BPSD with re-trial of deprescribing in 3 months
- At least 2 attempts to stop should be made

Alternate drugs:
- Consider change to risperidone, olanzapine, or aripiprazole

If insomnia relapses:

Consider
- Minimize use of substances that worsen insomnia (e.g. caffeine, alcohol)
- Non-drug behavioural approaches (see reverse)

Alternate drugs
- Other medications have been used to manage insomnia. Assessment of their safety and effectiveness is beyond the scope of this deprescribing algorithm. See AP deprescribing guideline for details.

Bjerre LM, Farrell B, Hogel M, Graham L, Lemay G, McCarthy L, et al. Deprescribing antipsychotics for behavioural and psychological symptoms of dementia and insomnia. Evidence-based clinical practice guideline. *Can Fam Physician* 2018;64:17-27 (Eng), e1-12 (Fr).

deprescribing.org · Institut de recherche Bruyère Research Institute · ontario pharmacy research collaboration

Bjerre et al, Deprescribing antipsychotics for behavioral and psychological symptoms of dementia and insomnia, *Canadian Family Physician*, January 2017

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A SAFER ALTERNATIVE TO ANTIPSYCHOTICS

Prazosin for the Treatment of Behavioral Symptoms in Patients With Alzheimer Disease With Agitation and Aggression

Lucy Y. Wang, M.D., Jane B. Shofer, M.S., Kirsten Rohde, R.N., Kim L. Hart, P.A.-C., David J. Hoff, P.A.-C., Yun H. McFall, R.Ph., Murray A. Raskind, M.D., Elaine R. Peskind, M.D.

Am J Geriatr Psychiatry 17:9, September 2009

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A Randomized Placebo-Controlled Discontinuation Study of Cholinesterase Inhibitors in Institutionalized Patients With Moderate to Severe Alzheimer Disease

Nathan Herrmann MD [a,b,c], Jordana O'Regan MSc [d], Myuri Ruthirakuhan MSc [b], Alexander Kiss PhD [b], Goran Eryavec MD [c], Evelyn Williams MD [e], Krista L. Lanctôt PhD [a,b,d,f,*]

Objectives: Cholinesterase inhibitors (ChEIs) offer modest benefits in Alzheimer disease (AD), which must be balanced against risks. Relatively few data delineate the benefits and risks of long-term ChEI administration in institutionalized patients with advanced AD. This study investigated the effects of ChEI discontinuation in institutionalized patients with AD.

Design: Institutionalized patients with moderate to severe AD (standardized Mini- Mental Status Examination ≤15) and treated with a ChEI for ≥2 years were randomized, double-blind, to ChEI continuation or placebo, with a 2-week tapering phase, for 8-weeks.

Measurements: The primary outcome of this pilot study was change on the Clinician's Global Impression of Change (CGI-C) scale. Secondary outcomes included safety, efficacy, and tolerability. Baseline (BL) predictors of clinical deterioration were also determined.

Results: Forty patients (mean ± standard deviation age = 89.3 ± 3.5 years, standardized Mini-Mental Status Examination = 8.1 ± 5.2, Neuropsychiatric Inventory–Nursing Home version total score = 21.1 ± 15.9, 80% male) were randomized to ChEI continuation (n = 21) or placebo (n = 19). There was no significant difference in clinical worsening in the ChEI continuation (28.6%) and placebo groups (36.8%) on CGI-C (odds ratio for worsening 1.58, 95% confidence interval .38–6.55, $P = .53$). The occurrence of adverse events was similar in both groups. There were no significant differences in any of the secondary outcome measures. In the placebo group, BL hallucinations predicted CGI-C worsening [$F(1,17) = 6.4$, $P = .02$], and there was a trend for BL delusions to predict CGI-C worsening [$F(1,15) = 3.5$, $P = .08$].

Conclusions: These results suggest that ChEI discontinuation is safe and well tolerated in the majority of institutionalized patients with moderate to severe AD. When discontinuing ChEI, the presence of hallucinations and delusions may predict clinical deterioration, suggesting the need for increased caution.

Discontinuing Psychiatric Medications: A Survey of Long-Term Users

Laysha Ostrow, Ph.D., M.P.P., Lauren Jessell, L.M.S.W., Manton Hurd, M.S.N., P.M.H.N.P., Sabrina M. Darrow, Ph.D., David Cohen, Ph.D., M.S.W.

Objective: Individuals undergoing long-term psychiatric treatment frequently choose to stop taking psychiatric medications. To enhance service user choice and prevent undesirable outcomes, this first U.S. survey of a large sample of longer-term users sought to increase knowledge about users' experience of medication discontinuation.

Methods: A sample of 250 U.S. adults with a diagnosis of serious mental illness and a recent goal to stop up to two prescribed psychiatric medications, which they had taken for at least nine months, completed a web-based survey about experiences, strategies, and supports during discontinuation.

Results: About half (54%) met their goal of completely discontinuing one or more medications; 46% reported another outcome (use was reduced, use increased, or use stayed the same). Concerns about medications' effects (for example, long-term effects and side effects) prompted the decision to discontinue for 74% of respondents. They used various strategies to cope with withdrawal symptoms, which 54% rated as severe. Self-education and contact with friends and with others who had discontinued or reduced medications were most frequently cited as helpful. Although more than half rated the initial medication decision with prescribers as largely collaborative, only 45% rated prescribers as helpful during discontinuation. Of respondents who completely discontinued, 82% were satisfied with their decision.

Conclusions: Discontinuing psychiatric medication appears to be a complicated and difficult process, although most respondents reported satisfaction with their decision. Future research should guide health care systems and providers to better support patient choice and self-determination regarding the use and discontinuation of psychiatric medication.

Psychiatric Services 2017; 68:1232–1238; doi: 10.1176/appi.ps.201700070

54% successfully discontinued; of these, 82% satisfied

54% experienced severe withdrawal effects → of many different types

A Prescription for "Deprescribing" in Psychiatry

Swapnil Gupta, M.B.B.S., M.D., and John Daniel Cahill, M.B.B.S., B.Med.Sci.

The term "deprescribing," initially coined in geriatric medicine, describes a process of pharmacologic regimen optimization through reduction or cessation of medications for which benefits no longer outweigh risks. Burgeoning rates of polypharmacy, growing appreciation of long-term adverse effects, and a focus on patient-centered practice present specific indications for deprescribing in psychiatry. A strong therapeutic alliance, appropriate timing, and consideration of the meaning of medication for the patient must accompany the following established elements: review of all medications, identification of medications that could be ceased or reduced, collaborative planning of the deprescribing regimen, and provision of review and support to the patient and caregivers. The authors discuss how deprescribing might be adapted for and implemented in psychiatry, identify potential barriers, and make recommendations for future directions.

Psychiatric Services 2016; 67:904–907; doi: 10.1176/appi.ps.201500359

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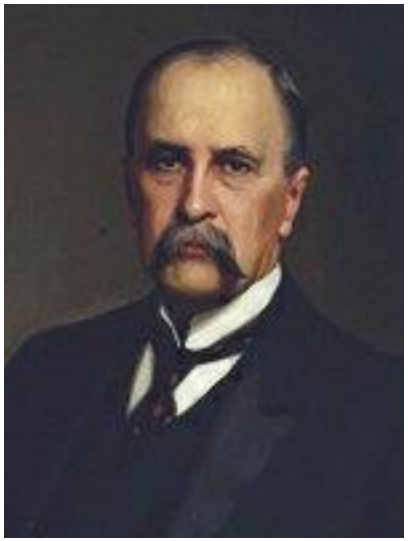
One of the first duties of the physician is to educate the masses not to take medicine.



Far too large a section of the treatment of disease is today controlled by the big manufacturing pharmacists, who have enslaved us in a plausible pseudo-science.

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