Weighing the Risks and Benefits of Medications in Older Adults

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Hospice & Palliative Care
Founded as Benton Hospice Service in 1980

Mr. Harold

Medications - before

Amlodipine 2.5mg 4x/day

Aspirin 325mg daily

Gabapentin 600mg nightly

Losartan 50mg mg daily

Losartan-HCTZ 50/12.5mg daily

Lupron injections every 3 months

Meclizine 12.5mg as needed for dizziness

Methyldopa 500mg 4x/day

Rabeprazole (aciphex) 20mg daily

Diazepam (valium) ?? As needed for anxiety, dizziness

Medications - after

Aspirin 81mg nightly

Citalopram 10mg nightly

Gabapentin 300mg nightly

Losartan 25mg mg nightly

Lupron injections every 3 months

Mr Harold

Medicalization of a day

MEDICATION	7am	8am	9am	12n	1pm	4pm	5pm	6pm	8pm	9pm
Alprazolam	X									
Aquaphor		X							X	
APAP (Tylenol)	X				X			X		
Apixiban	X						X			
Biotene		X		X		X			X	
Clotrimazole troche	X			X		X			X	
Doxepin cream			X							X
Furosemide	X				X					
Levothyroxine	X									
Metformin	X									
Metoprolol	X									X
Mirtazapine										X
Polyethylene glycol	X									
Tramadol	X			X		X				X
Trazodone										X
Venlafaxine	X					X				
Vit D3	X									

What is feasible?

MEDICATIONS

Aleve 2x/day
ASA 325mg daily
Calcitonin nasal spray daily
Carbidopa-levodopa 3x/day
CoQ10 daily
Famotidine 2x/day
Iron daily
Lyrica bedtime
MVI 2x/day
Probiotic daily
Quercetin daily
Sertraline daily
Tolterodine daily
Vit D daily
3 other supplements 1-2x/day

- 17 medications
- 4 med passes daily
- 23 doses
- Med chart, pillbox organized by family
- Misses ~2 doses weekly
- Forgets calcitonin half the time
- Timing off “several times” weekly

Objectives

- Define polypharmacy and inappropriate prescribing (IP), and their consequences for individuals and society
- Describe epidemiology and causes of polypharmacy and IP
- Identify steps for deprescribing
- Recognize opioid prescribing guidelines and when misuse may be present

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Polypharmacy *and* inappropriate prescribing

- How many is too many?
- No consensus definition, though most define as 4+ meds
- “More medications than clinically indicated”
- It’s not just about the number of medications
- The more comorbidities a person has, one can expect the number of medications to increase

What is a medication for?

- Primary prevention of disease
- Disease-directed treatment
- Control of non-life threatening and/or chronic conditions
- Symptom-focused medications

Polypharmacy *and* inappropriate prescribing

- Use of too many medications per patient
- Appropriate vs inappropriate (irrational)
- Overuse, underuse or misuse of medications
- Inappropriate dosage
- Use of injectables when oral form would be appropriate
- Failure to prescribe in accordance with (or over-compliant with) clinical guidelines
- Inappropriate self-medicating

Polypharmacy

- The number of medications a person uses is by far the strongest risk factor for drug-related problems

As # of medications goes up →	• **Adverse Drug Reactions more common** • **Medication adherence worsens** • **Out-of-pocket costs rise** • **Drug-drug interactions rise** • **Drug-disease interactions rise** • **Use of potentially inappropriate and unnecessary medications increases**

Adverse outcomes

- Adverse drug events can be difficult to recognize
- Patients don’t often report
- Even when providers aware, often fail to properly interpret and act
- 25-50% of ADE preventable

Weingart Arch Int Med 2005 ; Gandhi NEJM 2003; Gurwitz JAMA 2003; Agostini J Amer Geriatr Soc 2004; Steinman J Amer Geriatr Soc 2011

Preventable adverse drug events

- 58% at prescribing stage
  - 27% wrong drug / wrong treatment choice
  - 24% wrong dose
  - 13% drug interactions
  - 18% inadequate patient info
- 61% at monitoring stage
  - 36% failure to monitor
  - 37% failure to act on lab result or symptoms

Gurwitz JH, JAMA 2003: 289: 1107-16

Adverse drug events

- 27% of ED visits for ADEs result in hospitalization
- Among adults age 65+, hospitalization rate is 44%
- Adults age 65+ comprise increasing number of ADE cases requiring ED visit (35% in 2013-14 vs 26% in 2005-06)
- Among adults age 65+, anticoagulants, diabetes agents, and opiates implicated in 60% of ED visits for ADE

Other adverse drug outcomes

- Cost for patients
- Delaying more effective treatments
- Reduced quality of life
- Time lost to medication management
- Added stress for caregivers

Adherence declines as doses go up

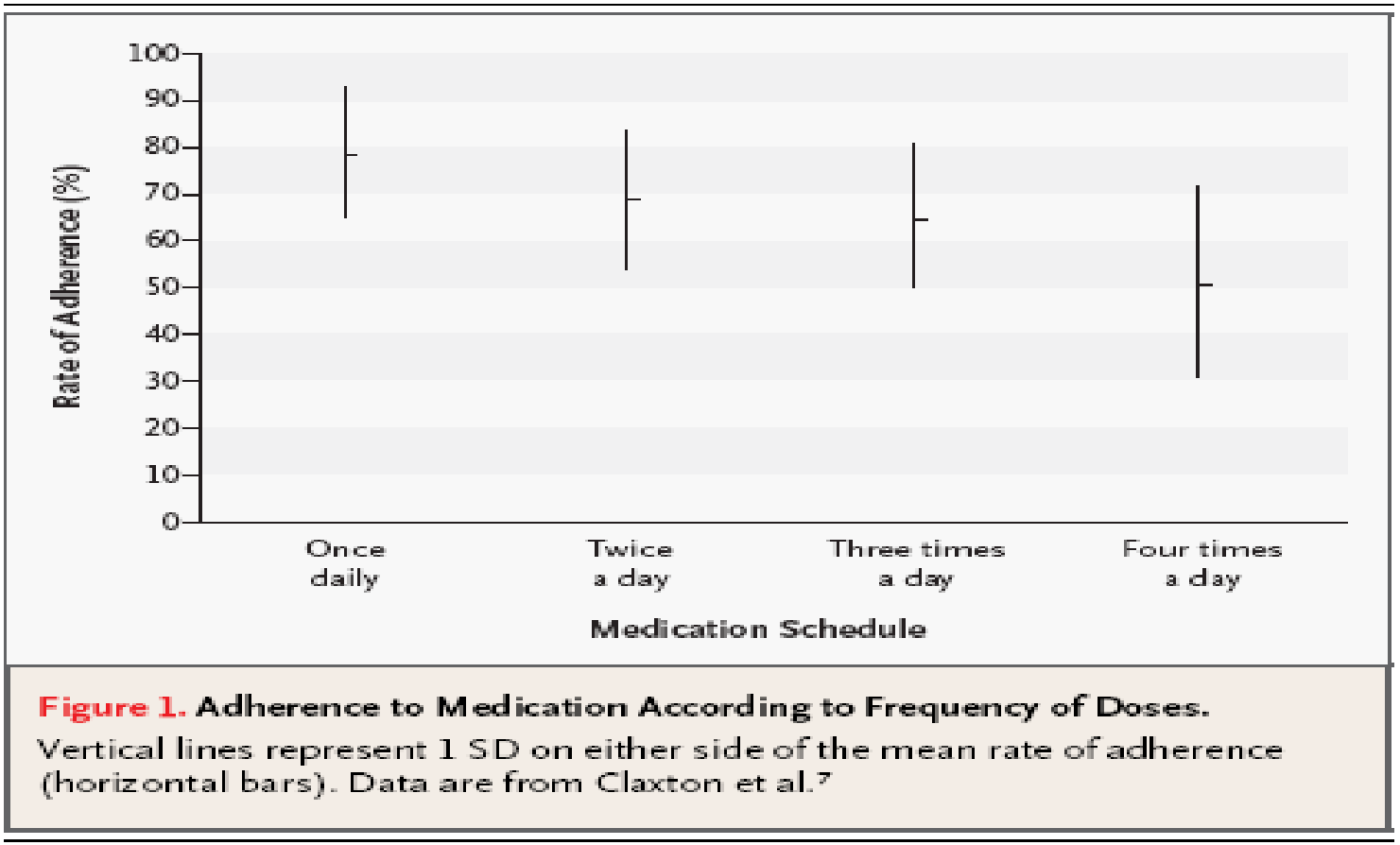

Figure 1. Adherence to Medication According to Frequency of Doses.
Vertical lines represent 1 SD on either side of the mean rate of adherence (horizontal bars). Data are from Claxton et al.[7]

Osterberg L, Blaschke T. Adherence to medication. NEJM 2005;353:487-97.

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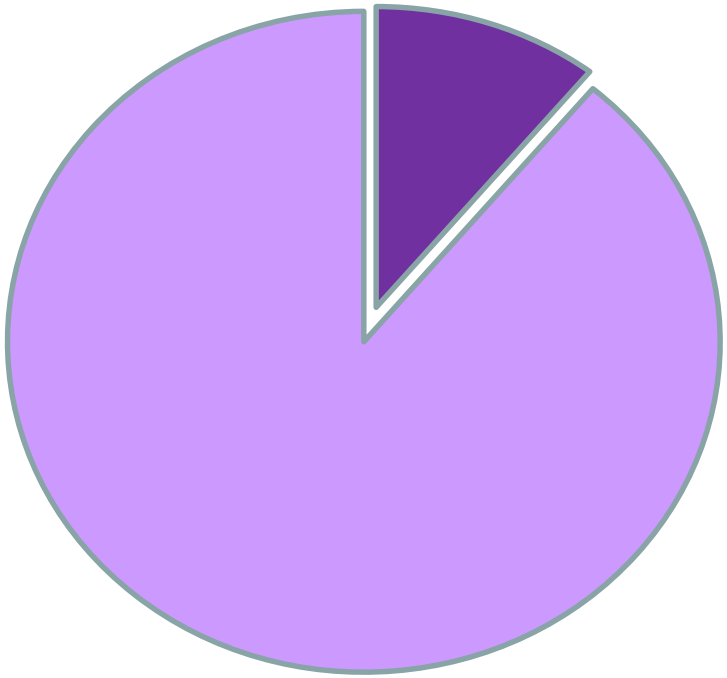
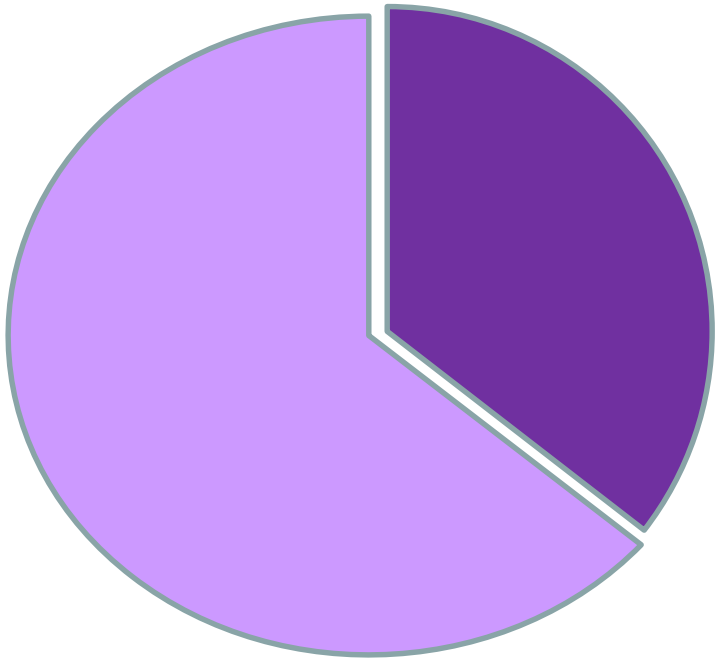
Older adult medication use



12% of US population



34% of US prescriptions

30% of OTC medications

Epidemiology

- Among all US adults, those taking 5+ prescriptions doubled from 2000 to 2012 (8 to 15%)
- Among older adults (age 62-85), >1/3 take 5+ prescriptions
- Among older adults, >2/3 take a dietary supplement
- Almost 1/3 of older adults take 4+ vit/supplements
- In long term care, 3/4 take 9+ medications

Kantor ED et al. JAMA 2015;314:1818-31
Qato DM et al. JAMA Int Med 2016;176:473-82.
Gahche JJ et al. J Nutr 2017l147(10):1968-76
Jokanovic N et al. JAMDA 2015; 16:535.e1-12

Factors leading to polypharmacy and IP

- Direct to consumer marketing; “brandname” vs generic
- Easier to start a medication than to stop it
- Failure to systematically review medications
- Self-medicating (caregivers too)
- Multiple providers
- Transitions of care
- (Not) Following guidelines
- “quick fix”

May 8, 2019 The New York Times

Drug Prices Will Soon Appear in Many TV Ads

Poly-herbacy and Poly-vitamins

- Vitamins and supplements are multi-billion $ industry
- Explosion of vitamins concurrent with processed food industry in first half of 20th century
- FDA recommendations have not been updated since 1968
- >85,000 supplement products on market

Pierre-Louis K. Popular Science, August 1, 2017.
https://www.popsci.com/what-are-vitamins-supplements

Clinical studies of dietary supplements

LACK of significant benefit compared to control groups:

- Echinacea to treat common cold
- Gingko biloba to treat dementia
- Vitamin E to prevent prostate cancer
- Cranberry juice or extract capsules to prevent UTI
- Multivitamins to prevent cancer, heart disease, dementia

Birks J, Grimley Evans J. Cochrane review 2009

Grodstein F et al. Ann Intern Med 2013;159(2):806-14

Brody JE. NYTimes, November 14, 2016.

Hypothetical 79yo woman

- Hypertension
- Diabetes
- Osteoporosis
- Osteoarthritis
- Chronic obstructive lung disease

Boyd CM et al. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA 2005;294(6):716-24.

Table 3. Treatment Regimen Based on Clinical Practice Guidelines for a Hypothetical 79-Year-Old Woman With Hypertension, Diabetes Mellitus, Osteoporosis, Osteoarthritis, and COPD*

Time	Medications†	Other
7:00 AM	Ipratropium metered dose inhaler 70 mg/wk of alendronate	Check feet Sit upright for 30 min on day when alendronate is taken Check blood sugar
	40 mg of lovastatin 250 mg of naproxen	cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
11:00 PM	Ipratropium metered dose inhaler	
As needed	Albuterol metered dose inhaler	

12 medications
$406/mo
19 doses per day
5 time points

9 drug-drug or drug-disease interactions

Boyd CM et al. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA 2005;294(6):716-24.

Prescribing cascade

- Side effects of one drug treated with another
- Geriatrics: new symptom is drug-related until proven otherwise

Patient A	Patient B
Back pain → NSAID	Heart disease → metoprolol
Elevated BP → Amlodipine	COPD → prednisone
Ankle swelling → Furosemide	Psychosis → haloperidol
Urinary frequency → Terazosin	Parkinsonism → carbi-levodopa

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Barriers to deprescribing

- Physiologic dependence
- Psychological attachment
- Patient or provider perception of abandonment
- Patient or provider discomfort with discussing life expectancy
- Multiple providers – who is responsible?

Events that should trigger med review

- Care transitions
- Annual/semi-annual medication review
- Starting a new medication
- New problem

→ Educate patients and caregivers

  - What to expect
  - Intent of the change
  - Instructions
  - Monitoring (withdrawal and exacerbation of condition)

Limits of “evidence based” care

- For treatment of older, very sick, or frail: “evidence” is mostly extrapolated
- Clinical trials of heart disease treatment: > half of trials exclude adults age 75+; 12% vs 40%
- Clinical trial of injections for knee arthritis: study participants’ average age 58 vs condition primarily of adults 70-80s

Span P. NYTimes April, 13, 2018.
Bourgeois FT et al. JAGS 2017;65(11): 2354-61

STOPP/START and Beers

- STOPP/START - UK
- Beers Criteria - US
- Expert panels weighing evidence, and applying consensus where evidence is weak
- Adults age 65+ years

STOPP/START

Psychological Intervention (eg. cognitive behavioural therapy, interpersonal therapy, behavioural activation, behavioural couple therapy), may be offered as a non-pharmacological treatment in the following conditions:

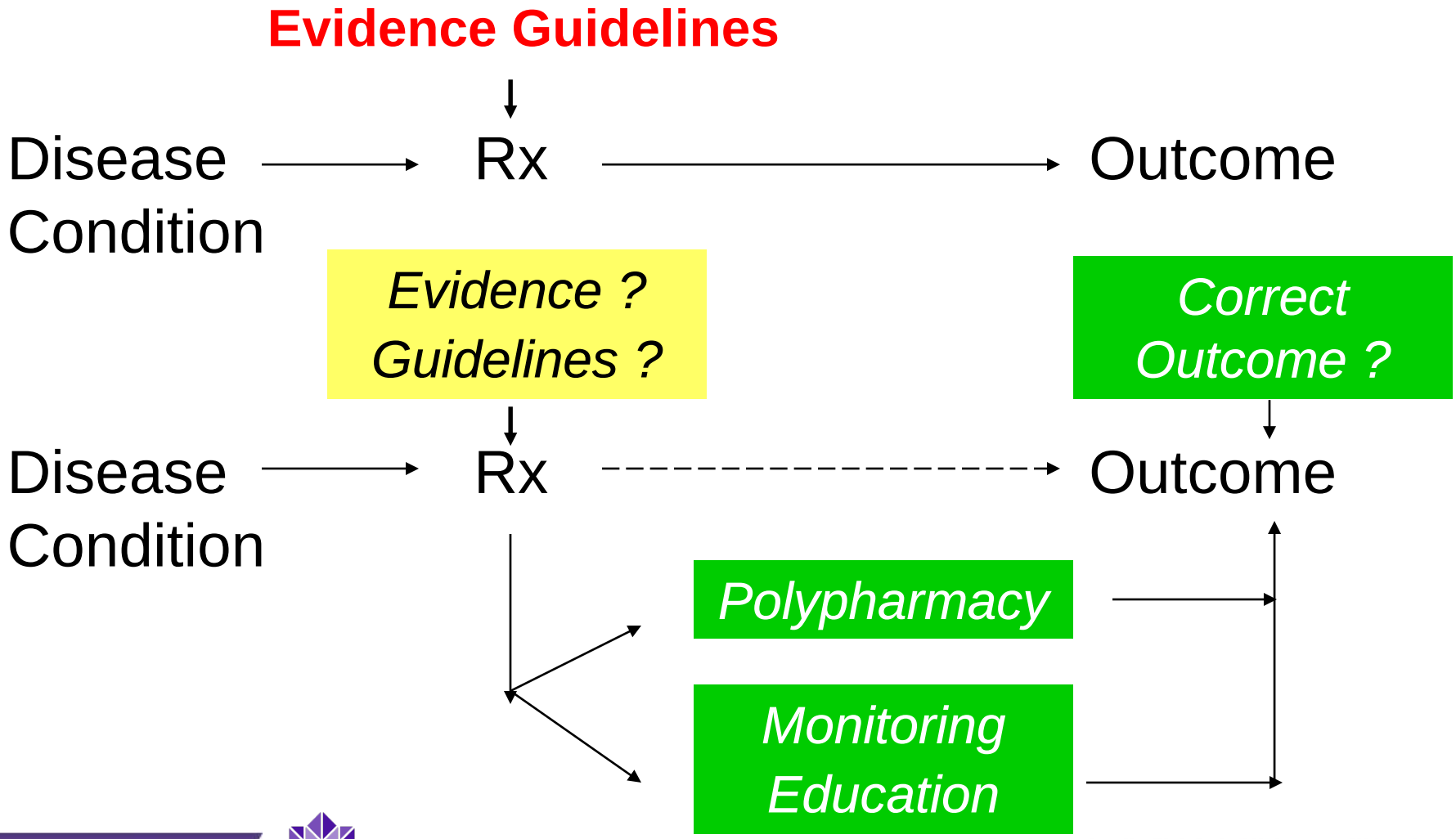
- Psychosis (or risk of) and schizophrenia in adults.
- Depression – including those thought to be at considerable risk of relapse or who have related residual symptoms. Also offer sleep hygiene advice.
- Bipolar disorder.
- Generalised anxiety disorder in adults (GAD).
- Social anxiety disorder (SAD) –specific CBT has been developed for SAD.
- Post-traumatic stress disorder (PTSD) – trauma-focused CBT for those with severe symptoms or with PTSD in the first month after the traumatic event.

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults

*By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel**

Organ System, Therapeutic Category, Drug(s)	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Central nervous system				
Antidepressants, alone or in combination Amitriptyline Amoxapine Clomipramine Desipramine Doxepin >6 mg/day Imipramine Nortriptyline Paroxetine Protriptyline Trimipramine	Highly anticholinergic, sedating, and cause orthostatic hypotension; safety profile of low-dose doxepin (≤6 mg/day) comparable to that of placebo	Avoid	High	Strong
Antipsychotics, first (conventional) and second (atypical) generation	Increased risk of cerebrovascular accident (stroke) and greater rate of cognitive decline and mortality in persons with dementia Avoid antipsychotics for behavioral problems of dementia or delirium unless nonpharmacological options (eg, behavioral interventions) have failed or are not possible *and* the older adult is threatening substantial harm to self or others	Avoid, except in schizophrenia or bipolar disorder, or for short-term use as antiemetic during chemotherapy	Moderate	Strong
Barbiturates Amobarbital Butabarbital Butalbital Mephobarbital Pentobarbital Phenobarbital Secobarbital	High rate of physical dependence, tolerance to sleep benefits, greater risk of overdose at low dosages	Avoid	High	Strong
Benzodiazepines *Short and intermediate acting:* Alprazolam Estazolam Lorazepam	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adults	Avoid	Moderate	Strong

Appropriate (rational) prescribing

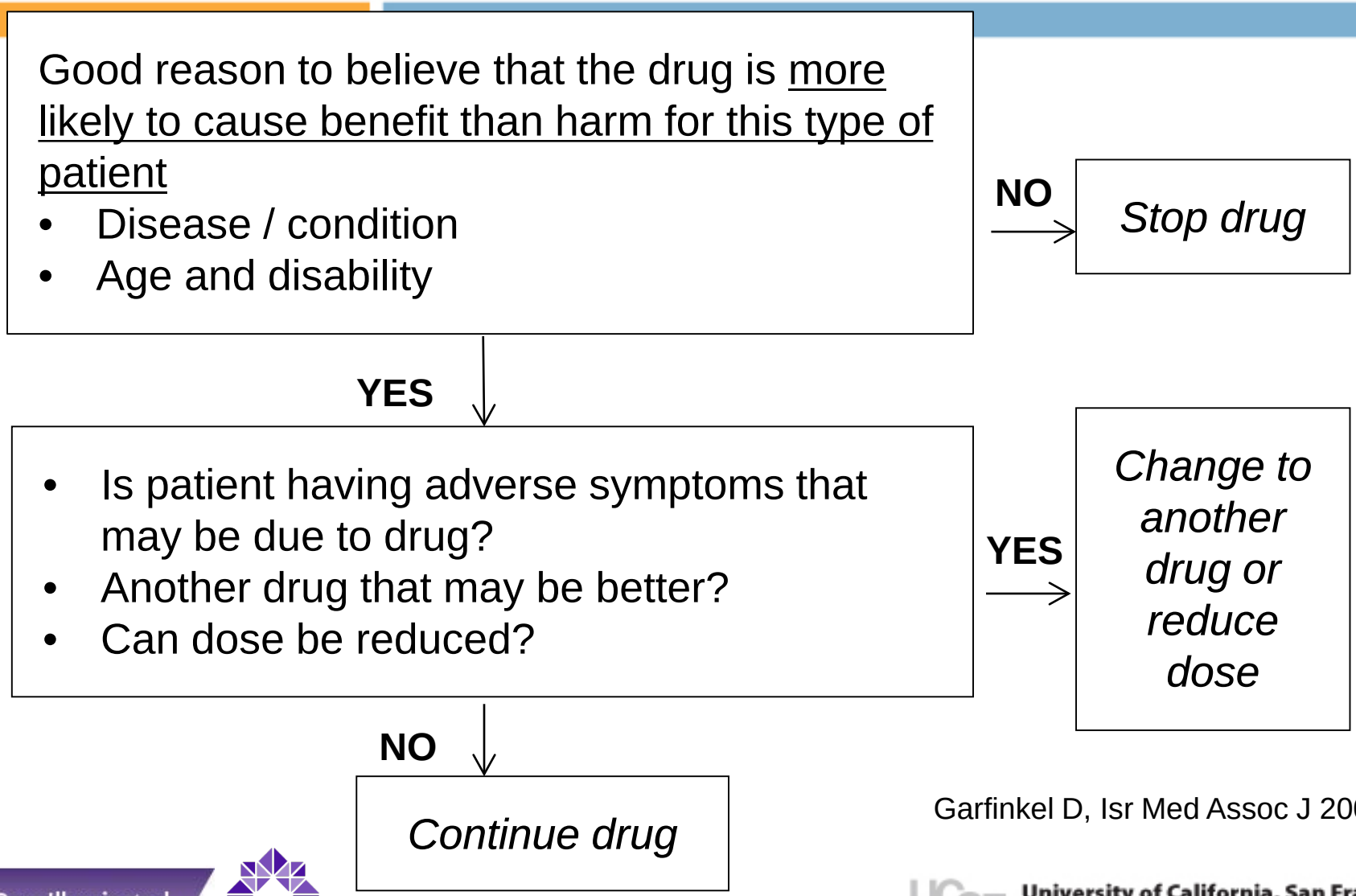


Deprescribing approach

Target medications:

- Without indication
- Have not had the intended response
- No longer needed
- Duplicate effects – benefit and harm
- Not being taken and adherence is not critical

Deprescribing



Garfinkel D, Isr Med Assoc J 2007

Considerations when starting

- Before deciding to prescribe (take) a medication
  - Is there an underlying problem that can be addressed without intensifying drug therapy?
  - Will the patient benefit from intensified med therapy?
- Once decision to prescribe is made
  - Choose drug with best balance of benefits & harms
  - Administer in safest, most effective manner
  - Maximize patient understanding and adherence

Considerations with any medication

- Assess goals
  - Delay death
  - Prevent ill health
  - Reduce symptoms
- Side effects of drugs (direct and interactions)
- Cost
- Feasibility
- Prognosis
- *Not* necessarily shared decision-making

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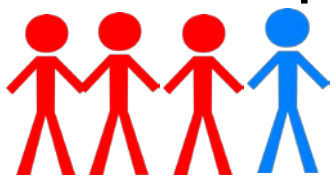
Opioid Epidemic

- Opioids killed 130 people per day (2017)
- 2.5 million people have opioid use disorder
-  who used heroin misused prescription opioids first
- of them receive treatment
- People with mental health disorder more likely to develop substance use (including opioid) disorder

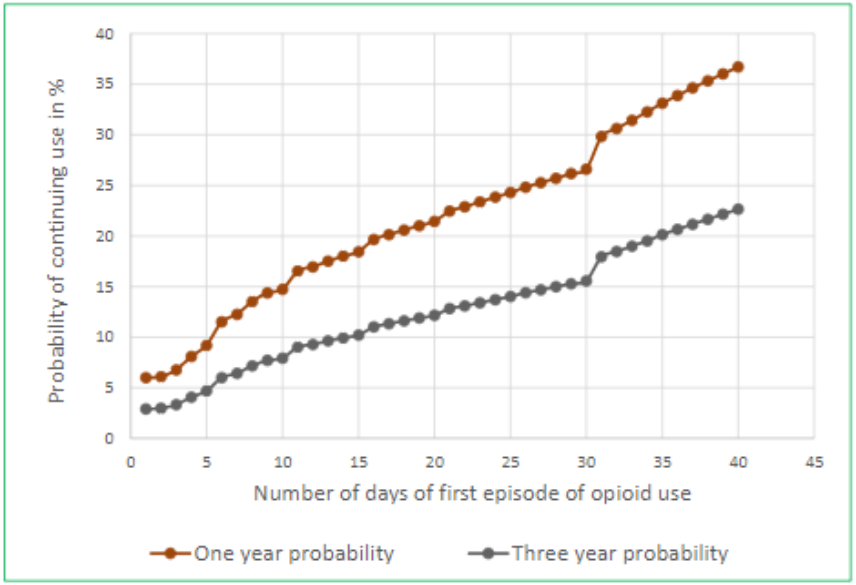
MMWR Morb Mortal Wkly Rep2017; 66:897–903

CMS Roadmap Fighting the Opioid Crisis, March 2019.

www.samhsa.gov

Probability of continued use

FIGURE 2. One- and 3-year probabilities of continued opioid use, by duration of first episode in days (base case)



Duration is expressed in terms of days (1-40) with increments of 1 day. Discontinuation is defined as 180 opioid-free days and allowable gap to assess continuous opioid use in first episode was 30 days.

Shah A et al. Characteristics of initial prescription episodes and likelihood of long-term opioid use – United States 2006-2015. MMWR, March 17, 2017; 66(10):265-269

CDC Guidelines

- Non-pharmacologic and non-opioid interventions for chronic pain
- Immediate release opioids to start
- No more than needed: 3 and 7
- Assess evidence of benefit to pain and function when considering dose increase ≥ 50mme/day
- Avoid increasing dosage to ≥ 90mme/day
- Evaluate benefits v harms at least every 3 months

CDC Guideline for prescribing opioids for chronic pain

CDC Guidelines

- Evaluate risk factors for opioid-related harms and mitigate risk (including naloxone)
- Review state Prescription Drug Monitoring Program
- Consider urine drug testing at least annually
- Avoid concurrent opioids and benzodiazepines
- Offer evidence-based treatment (usually medication-assisted treatment with buprenorphine or methadone in combination with behavioral therapies) for patients with opioid use disorder

CDC Guideline for prescribing opioids for chronic pain

Medicare Part D Policy

- 7 day limit for opioid naïve patients (none in 60 days)
- Morphine mg equivalent alert at 90mg threshold
- CMS identifies opioids and benzodiazepines as frequently abused drugs
- Case management with prescribers; patients notified of limitations in coverage for maximum 12 months (may extend additional 12 months)

A Prescriber's Guide to the New Medicare Part D Opioid Overutilization Policies for 2019

Medicare D Exceptions

- Residents of Long Term Care Facilities
- Patients in hospice care
- Patients receiving palliative or end-of-life care
- Patients being treated for active cancer-related pain

A Prescriber's Guide to the New Medicare Part D Opioid Overutilization Policies for 2019

Oregon Acute Opioid Guidelines

- Generally follow CDC Guidelines
- Do not recommend dual ranges (range of dose and range of frequency)
- Encourages system-based efforts (work flow, electronic medical record, quality improvement process etc.)

Oregon Acute Opioid Prescribing Guidelines

Oregon Chronic Opioid Guidelines

- Generally follow CDC Guidelines
- Evaluate patient within 1-4 weeks of starting opioids for chronic pain or dose escalation; then q3mo
- Document clinical justification for higher doses and
  - Have colleague evaluate patient
  - Present and discuss case to peer group or multi-disciplinary pain consultation team
  - Refer patient to pain specialist with experience tapering patients off opioids
  - Refer patient to a pain/addictions mental health specialist

Oregon misuse recommendations

- Determine if opioids can be stopped abruptly or tapered
- Medication-assisted Treatment (MAT) combines behavioral therapy and medications* to treat opioid use disorder

* methadone, naltrexone, buprenorphine (buprenorphine/naloxone)

Oregon Chronic Opioid Prescribing Guidelines

Role of behavioral therapy

- Behavioral therapy alone has limited efficacy to address opioid use disorder
- MAT is first line for OUD with behavioral therapy to:
  - Improve medication compliance
  - Address aspects of OUD not addressed by pharmacotherapy
  - Address specific weakness of pharmacotherapy
- Behavioral therapy can be used alone after stabilization to prevent relapse

Sofuoglu M et al. Pysch Res and Clin Practice 2018; https://doi.org/10.1176/appi.prcp.20180006

MAT outcomes

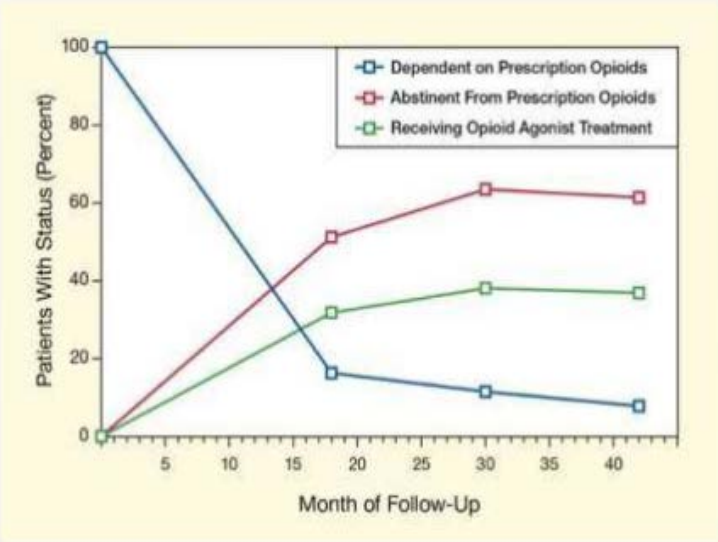


Figure. Abstinence Rate Exceeds 60 Percent in Long-Term Follow-Up of Medication-Assisted Therapy for Dependence on Opioid Pain Relievers Dependence on pain relievers dropped below 20 percent at 18 months, and below 10 percent at 42 months, after patients were stabilized on, and then tapered off, Bp/Nx. At all three follow-up points, patients who were currently engaged in opioid agonist therapy had markedly higher odds of positive outcomes.

Text Description of Graphic

% abstinent, %w/o pain relievers
At 18 mo, 51.2% and 83.7%
At 30 mo, 63.5% and 88.5%
At 42 mo, 61.4% and 92.2%

Potter JS et al. J Subst Abuse Treatment 2015; 48(1):62-69
Weiss RD et al. Drug and Alcoh Dependence 2015;150:112-19

MAT outcomes

- Reduces relapse
- Effective in reducing infectious diseases like HIV
- Effective in preventing drug overdose

130

Summary

- Polypharmacy and inappropriate prescribing are prevalent
- Reducing polypharmacy and following rational prescribing practices improves outcomes, reduces cost (and waste), and reduces care stress
- Opioid use disorder is a multifactorial problem requiring multidisciplinary approach, which includes behavioral therapy

Thank you

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