

Clinical Case Discussion

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An 85-year-old woman living in a skilled nursing facility for the last 6 years is admitted with delirium, dehydration and a UTI.

PMH:

CAD with MI 12 years ago with a stent placed at that time.

Type 2 DM. Last HgbA1C 7.8%

HTN

OA

Over the last year, her appetite has been poor and she has lost about 15 lbs. She is nonambulatory due to osteoarthritis of both knees. She has also had chronic constipation.

85-yr-old woman with delirium, dehydration and a UTI: medication list

- Aspirin 81 mg po daily
- Lisinopril 10 mg po daily
- Plavix 75 mg po daily
- Calcium carbonate 500 mg po bid
- Vitamin D 400 IU po daily
- Simvastatin 40 mg po daily
- Percocet 5/325 po q 6hrs prn pain
- Vesicare 10 mg po daily
- Fosamax 70 mg po weekly
- Prilosec 20 mg po daily
- Glipizide 5 mg po bid
- Cardizem CD 120 mg po daily
- HCTZ 25 mg po daily
- Benadryl 25 mg po qhs

85-yr-old woman with delirium, dehydration and a UTI:

On exam: Thin frail appearing elderly woman

Vitals: bp 100/60 p 60 RR 20 temp 99.5F O2 sat 93%
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Poor skin turgor

Cardiac: r/r/r

Lungs: clear

Abdomen: scaphoid with a palpable tender bladder

Extremities: chronic venous stasis changes.

Neuro: nonfocal

Skin: Stage 1 sacral decubitus ulcer

A 90-year-old woman is seen in the office for worsening confusion. Her family is concerned about her living alone. She has fallen three times in the last two months.

PMH:

CVA age 81

HTN

Hyperlipidemia

CKD

Recurrent UTIs

Hip fracture repair at age 78

A 90-year-old woman with hx confusion and falls: medication list

- ASA 325 mg po daily
- Vesicare 10 mg po daily
- HCTZ 25 mg po daily
- Metoprolol 25 mg po bid
- Xanax 0.25 mg po tid prn anxiety
- Digoxin 0.125 mg po every other day
- Pepcid 20 mg po bid
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- Simvastatin 20 mg po daily
- Ibuprofen 200 mg po tid prn pain

On exam, she is a frail appearing elderly woman

Vitals: bp 110/60 p 62 RR 20 afebr

HEENT: dry mucous membranes

Cardiac: neck veins flat; r/r/r without murmur; no edema; dp pulse trace bilaterally

Abd: soft, scaphoid with a palpable bladder

Neuro: cranial nerves: EOMI; face symmetric.

Motor: mild L hemiparesis

Delirium . . .

DSM-V Criteria for Delirium

Frances J and Young G UptoDate 2023

- Disturbance in attention (reduced ability to direct, focus, sustain, and shift attention) and awareness.
- The disturbance develops over a short period of time (usually hours to days), represents a change from baseline, and tends to fluctuate during the course of the day.
- An additional disturbance in cognition (memory deficit, disorientation, language, visuospatial ability, or perception).

DSM-V Criteria for Delirium

Frances J and Young G UptoDate 2023

- The disturbances are not better explained by another preexisting, evolving, or established neurocognitive disorder, and do not occur in the context of a severely reduced level of arousal, such as coma.
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by a medical condition, substance intoxication or withdrawal, or medication side effect.

Delirium: Bedside Assessment

- Vital signs/ABCs/IV access
- Blood glucose
- O2 sat
- Medications: especially recently administered
 - Opiates
 - Benzodiazepines
 - Other sedating or psychoactive meds

Delirium: Bedside Assessment

- PMH:
 - CVA/TIA
 - Cardiovascular disease
 - Chronic liver disease
 - Chronic kidney disease
 - Alcohol/substance abuse
 - Psychiatric history
 - Dementia

Causes of Delirium

- Hypoglycemia
- Hyperglycemia
- Medications: Review ALL
 - Sedatives
 - Opiates
 - Cholinergics
 - Abrupt cessation of chronic opiates, benzodiazepines or others

Causes of Delirium

- Hypoxemia
- Hypercarbia
- Anemia

Causes of Delirium

- Cerebral ischemia
- Dehydration
- Renal failure

Causes of Delirium

- Electrolyte imbalances
 - Sodium
 - Potassium
 - Calcium
 - Magnesium

Causes of Delirium

- Thyroid abnormalities
- Alcohol withdrawal
- Wernicke-Korsakoff Syndrome

Causes of Delirium

- Liver failure/hepatic encephalopathy
- Heart failure
- Sepsis/CNS infections

What is polypharmacy?

Polypharmacy management

- Stop all nonessential medications!
- Taper medications associated with physical dependence or withdrawal symptoms
 - Opiates
 - Benzodiazepines
 - SSRIs
 - Miscellaneous (ex: baclofen)

Polypharmacy

(Rochon P, UptoDate 2023)

- The use of multiple medications by a patient
- Generally 5 to 10 medications or more
- An estimated 50% of Medicare patients take 5 or more medications

The Risks of Polypharmacy

- Drugs are generally studied in middle aged patients; sometimes elderly patients are excluded in clinical trials.
- Elderly patients have decreased rates of drug clearance due to altered metabolism.

The Risks of Polypharmacy

- A drug side effect can result in a new symptom in an elderly patient which prompts the addition of another drug = **prescribing cascade**. Examples
 - Statin causes constipation; lactulose given for constipation; lactulose causes diarrhea; diarrhea causes dehydration.
 - Lasix causes incontinence; oxybutinin is given for incontinence; oxybutinin causes delirium

The Risks of Polypharmacy

- Prescribing cascades can rapidly lengthen drug lists and in turn, side effects.

Considerations for a better approach to prescribing drugs in the elderly

- Level of function or disability
- Estimated life expectancy
- Goals of care
 - Active medical treatment
 - Palliative care
 - Hospice care

“ The War gainst polypharmacy: A new Cost- Effective Geriatric-Palliative Approach for Improving Drug Therapy in Disabled Elderly People” (Garfinkel et al. IMAJ 2007;9: 430-434.)

- Residents of a geriatric medical center in Israel
- Study groups:
 - Intervention group : 119 disabled nursing home patients
 - Control group: 71 patients in the same facility
- Intervention
 - Discontinue as many medications as possible without adverse consequences per study algorithm

An Approach to Stopping Meds in the Elderly

Evidence-based consensus exists for using the drug for the indication given in its current dosing rate in *this patient's age group and disability level*, and the *benefit outweighs all possible Known adverse effects?*

↓ No/Not sure

Indication seems valid and relevant in this Patient's age group and disability level?

→ No

Stop drug

↓ Yes

Do the known possible adverse reactions of the drug outweigh possible benefits in old, disabled patients?

→ Yes

Stop drug

↓ No

Any adverse symptoms or signs that May be related the drug?

→ Yes

Shift to another drug

↓ No

Is there another drug that may be superior to the one in question?

→ Yes

Shift to another drug

↓ No

Can the dosing be reduced with no significant risk?

→ No

Continue same dose

→ Yes

Reduce dose

Yes



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Drug Discontinuation

Drug	Criteria for Discontinuation	Discontinuation Failure/ Criteria for Restarting Drug
Nitrates	No chest pain for prior 3 months	Return of symptoms or EKG changes
H2 blockers	No proven peptic ulcer disease, GI bleeding or dyspepsia for prior 1 year	Return of upper GI symptoms

Drug Discontinuation

Drug	Criteria for Discontinuation	Discontinuation Failure/ Criteria for Restarting Drug
Potassium Supplements	K above 4.0 meQ/L	K below 3.5 mEq/L
Iron Supplements	Serum iron more than 80 micrograms/dl.	Serum iron below 50 micrograms/dl.

Drug Discontinuation

Drug	Criteria for Discontinuation	Discontinuation Failure/ Criteria for Restarting Drug
One or more antihypertensives	One drug discontinued and others continued at current doses	Systolic bp > 140 or Diastolic bp > 90 mm Hg

Main Outcomes

- Rate of successful drug discontinuation 12 months after intervention
- Annual incidence of deaths in intervention and control groups
- Annual incidence of referrals to hospitals in intervention and control groups.

Discontinuation of Drugs in Nursing Home Residents: General Results

- Drugs were discontinued in 63% of patients
- Average number of medications taken: 7
- About 3 drugs per patient were discontinued

Discontinuation of Drugs in Nursing Home Residents: General Results

- Overall failure rate of drug discontinuation (ie. Drugs had to be restarted)
 - 18% of all patients
 - 10% of all drugs

Which drugs were stopped?

One year success rate of drug discontinuation

Drug	% of patients in whom drug was discontinued	% successful discontinuation at one year
nitrates	18%	100%
H2 blockers	29%	94%
Antihypertensives	43%	82%
Furosemide	23%	85%
Pentoxifylline	13%	100%

One year success rate of drug discontinuation

Drug	% of patients in whom drug was discontinued	% successful discontinuation at one year
Potassium supplement	17%	100%
Iron supplement	16%	95%
Sedatives and Tranquilizers	13%	88%
Antidepressants	16%	74%
Antipsychotics	11%	69%

Other drugs discontinued without detectable adverse consequences

- NSAIDs
- Analgesics
- Statins
- Oral hypoglycemics
- Amantadine
- Carbamazepine
- Digoxin

Small numbers of patients did not allow

Statistical analysis



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Number of drugs stopped vs. failure rate (ie. Drugs had to be restarted)

Number of drugs discontinued	Number of patients	Failure rate: % of patients Needing drug readministration	Failure rate: % of drugs Needing readministration
7	2	100%	21%
6	4	50%	21%
5	13	38%	20%
4	15	33%	8%

Number of drugs stopped vs. failure rate (ie. Drugs had to be restarted)

Number of drugs discontinued	Number of patients	Failure rate: % of patients Needing drug readministration	Failure rate: % of drugs Needing readministration
3	29	14%	6%
2	26	4%	2%
1	30	7%	7%
Overall	119	18%	10%

Mortality and Hospitalizations

Outcome	Study Group (ie. reduced medications)	Control Group	P value
One-year mortality	21%	45%	< 0.001
One-year hospitalization rate	11.8%	30%	< 0.002

What about community-dwelling elderly patients with polypharmacy?

“ Feasibility Study of a Systematic Approach for Discontinuation of Multiple Medications in Older Adults: Addressing Polypharmacy” (Garfinkel et al. Arch Int Med. 2010;170(18): 1648-1654.

- Prospective cohort study
- Patients referred for comprehensive geriatric assessment in Israel
- Exclusion criteria:
 - Estimated life expectancy < 3 months
 - Follow up availability < 4 months

Discontinuing Drugs in Community-Dwelling Elderly

- Drugs discontinued according to same protocol used in first study of nursing home patients.

Drug Discontinuation

Drug	Criteria for Discontinuation	Discontinuation Failure/ Criteria for Restarting Drug
Nitrates	No chest pain for prior 6 months	Return of symptoms or EKG changes
H2 blockers or Proton pump inhibitors	No proven peptic ulcer disease, GI bleeding or dyspepsia for prior 1 year	Return of upper GI symptoms

Drug Discontinuation

Drug	Criteria for Discontinuation	Discontinuation Failure/ Criteria for Restarting Drug
One or more antihyper-tensives	One drug discontinued at a time and others continued at current doses	Systolic bp > 150 or systolic > 160 with no target organ damage OR Diastolic bp > 90 mm Hg

Drug Discontinuation

Drug	Criteria for Discontinuation	Discontinuation Failure/ Criteria for Restarting Drug
Benzodiazepines	Essentially all gradually tapered to off	Return of symptoms
NSAIDS	Essentially all gradually tapered to off	Return of symptoms

Drug Discontinuation

Drug	Discontinuation Failure/ Criteria for Restarting Drug
Oral hypoglycemics	Hgb A1C > 8%
Furosemide	Recurrent CHF

Drug Discontinuation

Drug	Discontinuation Failure/ Criteria for Restarting Drug
Levodopa	Return of Parkinsonism
Iron supplements	Return of anemia

Drug Discontinuation

Drug	Discontinuation Failure/ Criteria for Restarting Drug
Potassium supplements	Return of hypokalemia

Other drugs considered for discontinuation

- Antidepressants
- Antipsychotics
- Digoxin
- Anticoagulants
- Aspirin
- Dipyridamole
- Pentoxifylline

Stopping Meds in Community-Dwelling Elderly: Results

Discontinuation of Drugs in Community-Dwelling Elderly Patients General Results

- Drug discontinuation recommended per algorithm in 91% of patients
- Consent obtained to discontinue 83% of drugs recommended per algorithm.
- Average number of medications taken: 8
- About 4 drugs per patient were discontinued

Discontinuation of Drugs Community-Dwelling Elderly Patients: General Results

- Combining nonconsent to discontinue drugs and failure of discontinuation (ie. Drugs had to be restarted), over 81% of drugs recommended per algorithm were successfully discontinued
- Mean follow-up about 1.5 years

Which drugs were stopped?

One year success rate of drug discontinuation

Drug	Number of patients taking drug	% of patients in whom drug was discontinued	% successful discontinuation at one year
nitrates	5	100%	100%
H2 blockers	8	75%	75%
Antihyper-tensives	95	53%	84%

One year success rate of drug discontinuation

Drug	Number of patients taking Drug	% of patients in whom drug was discontinued	% successful discontinuation at one year
Furosemide	18	72%	79%
Aspirin	24	8%	100%
Statins	26	54%	72%

One year success rate of drug discontinuation

Drug	Number of patients taking Drug	% of patients in whom drug was discontinued	% successful discontinuation at one year
Sulfonylurea	6	83%	100%
Omeprazole	18	50%	90%
Benzodiazepines	36	97%	97%

One year success rate of drug discontinuation

Drug	Number of patients taking Drug	% of patients in whom drug was discontinued	% successful discontinuation at one year
SSRIs	33	33%	77%
Other antidepressants	12	75%	90%
Antipsychotics	12	37%	100%
Levodopa-carbidopa	10	50%	71%

One year success rate of drug discontinuation

- Other than return of symptoms, there were no adverse adverse events

Drug Discontinuation and Cognitive Function

- Three patients had significant increases in Mini mental status exam scores within the first few months after discontinuation of 6 or 7 drugs.

Mortality after Drug Discontinuation

- No deaths related to original indication for discontinued drugs
- Of 10 patients who died, 7 had reported improved quality of life in their last months of life.

Classes of Medications to Avoid in the Elderly when possible: Anticholinergic Medications. Clinical Effects

Anticholinergic Effects	Clinical Manifestations
“Mad as a hatter”	Memory impairment Confusion Hallucinations
“Blind as a bat”	Blurred vision
“Red as a beet”	Impaired sweating
“Dry as a bone”	Dry mouth



Medications with High Anticholinergic Activity: examples

- First generation antihistamines:
diphenhydramine
- Antimuscarinic for muscle spasms:
hyoscyamine
- Antiparkinson:
benztropine
- Antiemetics:
**hydroxyzine,
promethazine,
meclizine**
- Antimuscarinic for overactive bladder:
oxybutinin

Medications with High Anticholinergic Activity: examples

- Muscle relaxants:
tizanidine
- First generation antipsychotics:
thioridazine
- Tricyclic antidepressants:
amitriptyline

Back to our patients . . .

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Any adverse symptoms or signs that May be related the drug?

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Is there another drug that may be superior to the one in question?

↓ No

Can the dosing be reduced with no significant risk?

No

Yes

Continue same dose

Reduce dose

Nonambulatory
Dehydration
UTI
Borderline low bp

No → Stop drug

Yes → Stop drug

Yes → Shift to another drug

Yes → Shift to another drug

ASA
Lisinopril
Plavix
Calcium
Vit D
Simvastatin
Percocet
Vesicare
Fosamax
Prilosec
Glipizide
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85-yr-old woman with dehydration and a UTI: new medication list

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Confusion
Hx Falls
Hx CVA
Normotensive
Low HR

Stop drug

Stop drug

Shift to another drug

Shift to another drug

ASA
Vesicare
HCTZ
Metoprolol
Xanax
Digoxin
Pepcid
Coenzyme Q10
Simvastatin
Ibuprofen



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Hx Falls
Hx CVA
Normotensive
Low HR

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Stop drug

Shift to another drug

Shift to another drug

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Metoprolol
Xanax
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A 90-year-old woman with hx confusion and falls:
new medication list

- ASA
- Metoprolol decreased from 25 mg to 12.5 mg po bid
- Simvastatin

Summary and Conclusions

- Drug prescribing in the elderly has unique challenges
- Elderly patients have decreased drug clearance
- Many drugs are not studied adequately in elderly patients.

Summary and Conclusions

- Drug side effects in the elderly can cause new symptoms which lead to a **prescribing cascades**
- Elderly patients are likely to have **polypharmacy** (at least 5 to 10 chronic drugs)
- Polypharmacy can lead to **increased morbidity and mortality** in elderly patients

Summary and Conclusions

- There is evidence for a **stepwise approach to drug discontinuation** among elderly patients in long term care facilities and dwelling in the community which takes into account
 - Level of function and disability
 - Estimated life expectancy
 - Goals of care

Summary and Conclusions

- There is evidence that stepwise discontinuation of drugs in the elderly can lead to improved quality of life and decreased mortality
- Larger, randomized prospective trials are needed

Delirium, Dementia or both?

- Dementia definition: “Gradual onset of short term memory and functional impairments in more than one domain.”
 - Executive functions
 - Basic activities of daily living

Delirium, Dementia or both?

- Rule of thumb: delirious patients generally look sick; demented patients generally look well.
- Can demented patients become delirious? **ABSOLUTELY**

Management of Delirium: Nonpharmacologic

- Maintain hydration
- Avoid restraints if possible
- Reduce ambient noise

Management of Delirium: Nonpharmacologic

- Orienting stimuli: family members, clocks, calendars
- Reassurance
- Bedside sitters

Pharmacologic Management

Medication	Dose	Route and Frequency	Comments
Haloperidol	Start 0.5 to 1 mg; up to 5 to 10 mg	po or IV; may repeat IV doses q 10 minutes to q 30 minutes prn agitation. IV dosing requires continuous cardiac monitoring	Onset of action about 30 minutes when given IV; risk of extrapyramidal side effects (rigidity; tremor). Risk of QT prolongation and increased risk of cardiac death among elderly patients with dementia

Pharmacologic management

Medication	Dose	Route and frequency	Comments
Lorazepam	0.5 mg to 1 mg	po or IV; may repeat IV doses q 5 minutes prn agitation	Onset of action about 5 minutes when given IV; greater risk of respiratory depression; tends to be overprescribed.

Pharmacologic management

Medication	Dose	Route and frequency	Comments
Quetiapine	12.5 to 50 mg	po q 6 hrs	Generally well-tolerated; preferred for treatment of psychosis in the setting of Parkinson's disease

Prevention of Delirium

- Adequate sleep
- Attention to medications-- acute and chronic
- Substance abuse history
- Psychiatric history, including dementia

Think of “the list of 16”

- Hypoglycemia
- Hyperglycemia
- Medications
- Hypoxemia
- Hypercarbia
- Anemia
- Cerebral ischemia
- Dehydration
- Renal failure
- Electrolyte imbalances
- Thyroid abnormalities
- Alcohol withdrawal
- Wernicke-Korsakoff Syndrome
- Liver failure/hepatic encephalopathy
- Heart failure
- Sepsis/CNS infections

Summary and Conclusions

- Search for and treat the underlying cause!

Summary and Conclusions

- Nonpharmacologic management
- Pharmacologic management
- Consider psychiatric consultation

Questions?

Thank you!