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Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

SORTING THROUGH POLYPHARMACY: MY PATIENT IS ON 6 DIFFERENT PSYCHIATRIC MEDICATIONS. HOW DO I SIMPLIFY THAT?

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GENERAL DISCLOSURES

The University of Washington School of Medicine also gratefully acknowledges receipt of educational grant support for this activity from the Washington State Legislature through the Safety-Net Hospital Assessment, working to expand access to psychiatric services throughout Washington State.

GENERAL DISCLOSURES

UW PACC is also supported by Coordinated Care of Washington

SPEAKER DISCLOSURES

- ✓ No conflicts of interest

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OBJECTIVES

1. Recognize potentially harmful or inappropriate medication combinations
2. Apply a standard approach to assessing polypharmacy
3. List the five steps of an evidence-based, patient-centered deprescribing process

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UW PACC REGISTRATION

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CASE: 70 YO MAN PRESENTING FOR FOLLOW-UP

- HPI:
  - History of MDD, in remission. Last episode of MDD occurred in 1990.
  - No acute concerns. Wife is present and denies concerns.
- PPH:
  - Two past inpatient stays (both 10+ years ago). One suicide attempt. No other med trials.
  - Three pasts TBIs (1951, 1965, 2005)
- Medical history:
  - COPD, CHF, HTN, PVD, OSA, T2D with recent toe amputation
  - Poor sleep (untreated OSA)
- Medications:
  - Carbamazepine 200 mg TID “for mood”
  - Nortriptyline 25 mg QHS ”for mood” (did not tolerate attempted taper in 2014)
  - Fluoxetine 20 mg daily
  - Bupropion SA 200 mg daily
- Labs/Studies
  - Carbamazepine level therapeutic Dec 2018
  - CBC, Na normal in 2018
  - EKG- QTc 440-460 per chart; repeat 458 today

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WHAT WOULD YOU PRIORITIZE?

a) Taper/discontinue carbamazepine
b) Taper/discontinue nortriptyline
c) Taper/discontinue fluoxetine
d) Taper/discontinue bupropion
e) Other

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POLYPHARMACY INTRO

- Polypharmacy- the use of two or more medications in the same patient for a psychiatric indication
- Reasons for polypharmacy (Kukreja et al., 2013; Preskorn & Lacey, 2007)
  - Single medication is ineffective in adequately treating symptoms
  - Target specific symptoms
  - Treat two distinct but co-morbid illnesses in one patient
  - Treat side effects produced by a primary drug
  - Provide acute symptom relief while awaiting the delayed effect of another medication
  - Treat intervening phases of an illness

POLYPHARMACY IS INCREASING

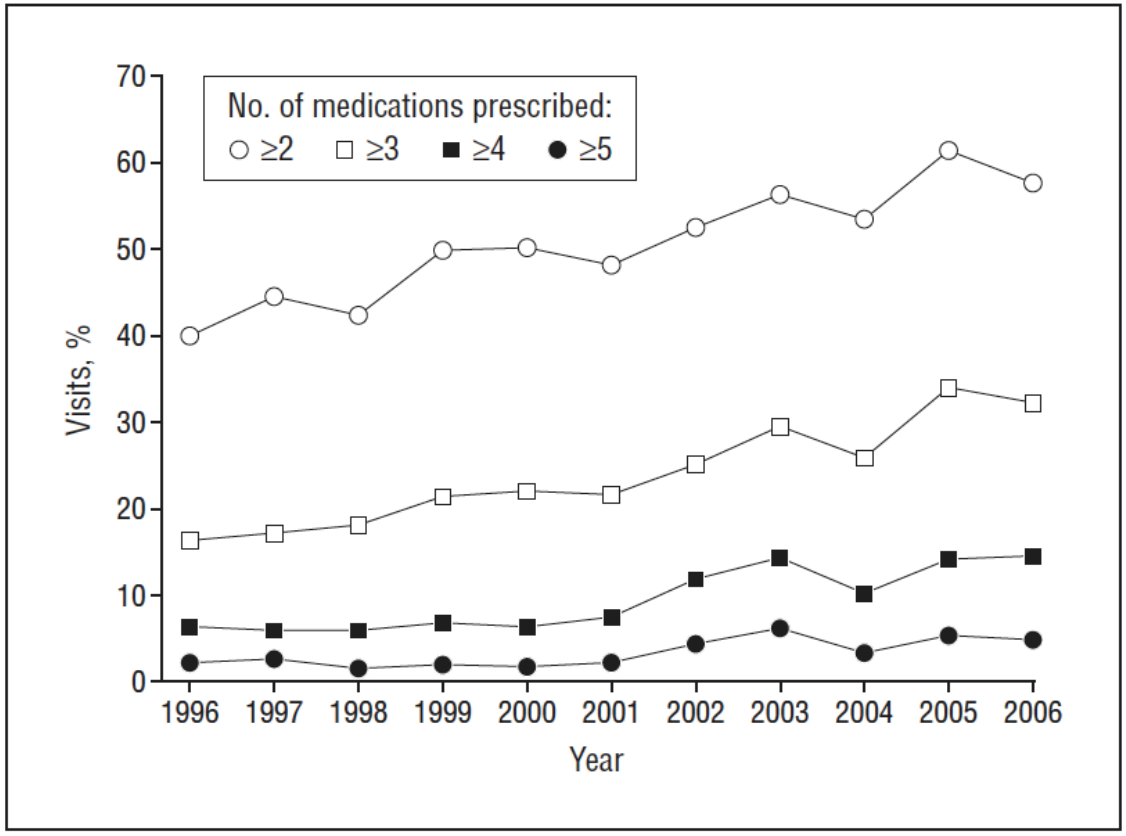

Figure. Trends in psychotropic polypharmacy in visits to office-based psychiatrists between 1996 and 2006. (Mojtabai & Olfson, 2010)

NOT ALL POLYPHARMACY IS BAD

- Rational polypharmacy- intentional, evidence-based, taking into consideration principles of neurobiology and pharmacology

- Irrational polypharmacy- using combinations of medications that are redundant, antagonistic, pointless or even harmful (Zigman & Blier, 2012).
  - Increases drug costs, the complexity of treatment regimens and risks, and side effect burden without the likelihood of additional beneficial effects

A STANDARD APPROACH TO SORTING THROUGH POLYPHARMACY

- Consider the appropriateness of each individual medication
- Consider the appropriateness of the medication combination

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MEDICATION APPROPRIATENESS

Medication Appropriateness Index (Hanlon et al., 1992; Hanlon & Schmader, 2013)

1) Is there an indication for the drug?
2) Is the medication effective for the condition?
3) Is the dosage correct?
4) Are the directions correct?
5) Are the directions practical?
6) Are there clinically significant drug-drug interactions?
7) Are there clinically significant drug-disease/condition interactions?
8) Is there unnecessary duplication with other drugs?
9) Is the duration of therapy acceptable?
10) Is this drug the least expensive alternative compared to others of equal utility?

MEDICATION APPROPRIATENESS IN PRACTICE

Chart/records

- Charted indication for drug, clinical response, side effects, duration of use
- Past taper attempts and response
- Past medical history- kidney and liver disease, cognitive status, cardiac status

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MEDICATION APPROPRIATENESS IN PRACTICE

History

- What is your understanding of why are you taking this drug?
- Did you find this medication helpful when you started it? Are you finding it helpful currently, and if for what?
- Do you have any side effects from this drug? (Also ask about common side effects)
- Did you find increasing the dosage helpful?
- How are you taking this medication? Do you take it regularly/as prescribed?
- Did your provider talk with you about how long you'd be on this medication?
- What is your understanding of how long this drug is typically used?

- Past medical history
- Past Psychiatric History: severity of illness, other past trials (dose, duration, adherence), past trials of medication taper and response

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MEDICATION APPROPRIATENESS IN PRACTICE

Other considerations

- Evidence base for use of the drug in the condition/diagnosis, (and evidence base for combination)
- Usual dosage range for the drug, lowest therapeutic dose, maximum dose
- Need for daily use versus PRN, use with food, timing of dose and duration of drug effect
- Drug-drug interactions
- Drug-disease interactions
  - Does this drug have an impact on another medical condition in this patient?
  - Does a medical condition in this patient influence drug impact?
- Typical duration of treatment

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RECOGNIZING IRRATIONAL POLYPHARMACY: PHARMACODYNAMIC REDUNDANCY (ZIGMAN & BLIER, 2012)

Table 1. Common causes and examples of irrational polypharmacy in psychiatry.

Causes of irrational polypharmacy	Explanation	Examples
Pharmacodynamic redundancy	• Two or more medications have the same or overlapping mechanism of action	• Two benzodiazepines • Two anticholinergics • Two antipsychotics (except clozapine) • SSRI + SNRI • Mirtazapine + quetiapine • Buspirone + aripiprazole, quetiapine, ziprasidone, clozapine, asenapine or vilazodone

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RECOGNIZING IRRATIONAL POLYPHARMACY: PHARMACODYNAMIC INTERACTION (ZIGMAN & BLIER, 2012)

Causes of irrational polypharmacy	Explanation	Examples
Phamacodynamic interaction	• One medication inhibits the action of another	• Acetylcholinesterase inhibitor + low potency FGA, TCA, olanzapine, clozapine or oxybutinin • Stimulant + haloperidol or aripiprazole

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RECOGNIZING IRRATIONAL POLYPHARMACY: PHARMACOKINETIC INTERACTION (ZIGMAN & BLIER, 2012)

Causes of irrational polypharmacy	Explanation	Examples
Pharmacokinetic interaction	• One medication increases the metabolism of another, rendering the second ineffective	• Carbamazepine, oxcarbazepine, modafinil, barbiturates, St John's wort + CYP3A4 substrates • Lamotrigine + quetiapine (may require quetiapine dose increase)

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RECOGNIZING IRRATIONAL POLYPHARMACY: INADEQUATE DOSING (ZIGMAN & BLIER, 2012)

Causes of irrational polypharmacy	Explanation	Examples
Inadequate dosing	• One medication in a combination is under-dosed, the combination becomes no better than monotherapy	*Medications often under-dosed:* • Mirtazapine, TCAs, duloxetine and venlafaxine (to recruit SNRI effects), lithium, anticonvulsants

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RECOGNIZING IRRATIONAL POLYPHARMACY: REGULARLY REASSESS & REDUCE (ZIGMAN & BLIER, 2012)

Causes of irrational polypharmacy	Explanation	Examples
Clinical assessment and judgment issues	• A medication is initiated to manage side effects and is continued unnecessarily • A medication is started to manage deterioration of illness and is continued unnecessarily • A neuropsychiatric side effect is attributed to a psychiatric disorder and an additional medication is added to treat the 'residual symptom'	• An anticholinergic was started when a patient was taking a FGA, no attempt is made to taper it after the patient switches to a SGA • A hypnotic was started during a relapse of depression and no attempt is made to taper it after the patient recovers • A patient taking a SSRI complains of feeling 'numb' and apathetic without other depressive symptoms and combinations are tried rather than a dose reduction or switch

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RETURN TO OUR CASE

- 70 YO man with MDD in remission, TBI history presenting for follow-up, without acute concerns.
- Medication regimen
  - Carbamazepine 200 mg TID “for mood”
  - Nortriptyline 25 mg QHS ”for mood”
  - Fluoxetine 20 mg daily
  - Bupropion SA 200 mg daily
- Do any of these individual medications seem potentially inappropriate?
- Do you see any signs of irrational polypharmacy?

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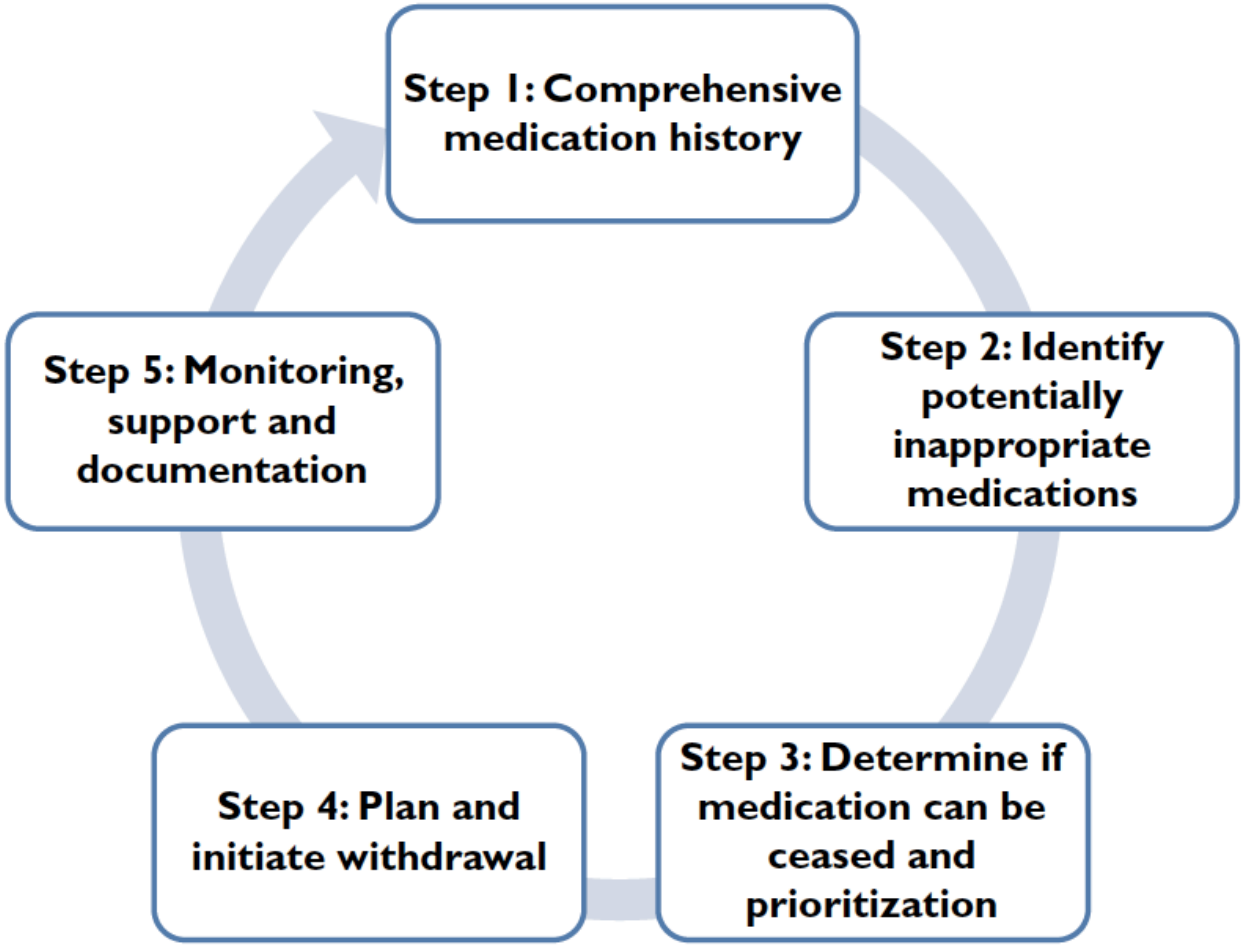
SO I'VE IDENTIFIED IRRATIONAL POLYPHARMACY- NOW WHAT? (REEVE ET AL., 2013)

- A patient centered approach to deprescribing is key
  - Majority of patients want to be involved in the decision-making process
  - Patient as key source of information on history and goals
  - Patient mediated interventions among the most effective
- Patient engagement throughout process
- The trust that the patient has in the PCP influences patient willingness to cease medications

THE FIVE-STEP PATIENT-CENTERED DEPRESCRIBING PROCESS (REEVE ET AL., 2013)



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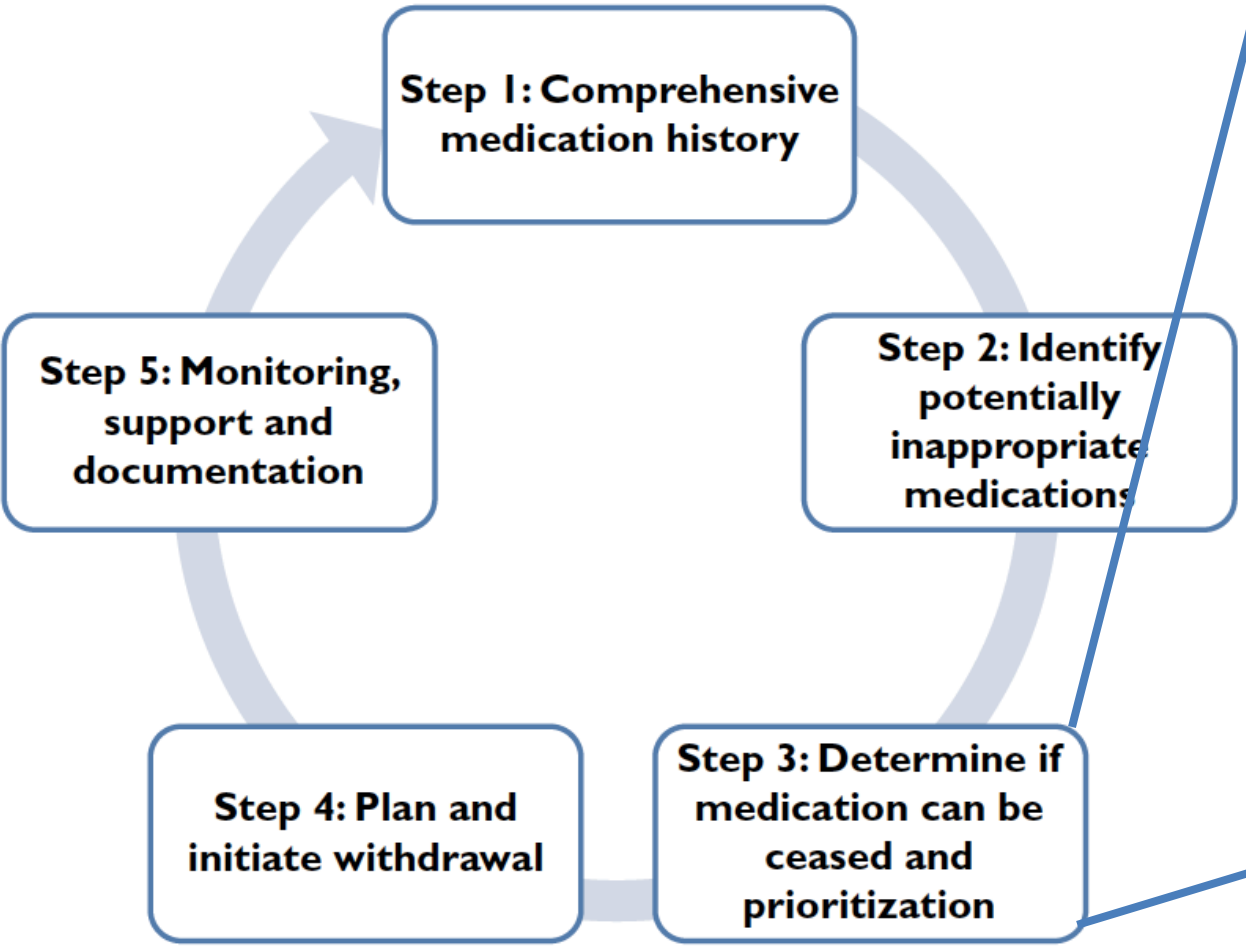

Optimizing patient willingness:

- Introduce deprescribing in a way that does not evoke fear or stress
- Recommendations are being made to achieve therapeutic goals
- Discuss the lack of benefits/necessity of the medication and the potential risks
- Discuss the steps that will be taken to minimize the risks, and confirmation that deprescribing is a "trial"

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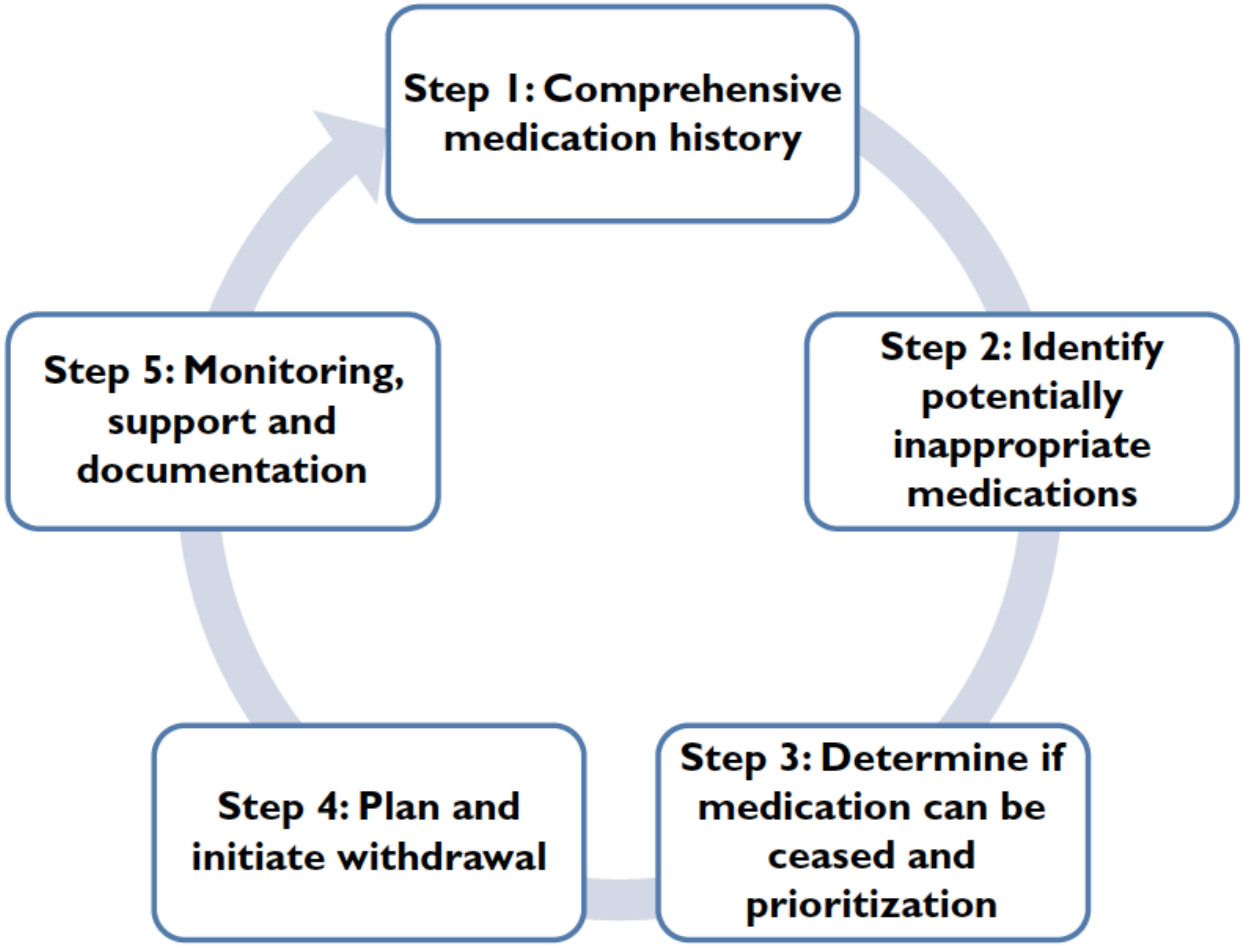

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APPLICATION TO CASE

- Step 1: comprehensive history obtained
- Step 2: identified potentially inappropriate medications
- Step 3:
  - Patient and wife's preference were to continue all medications.
  - Discussed risks (arrythmia with nortriptyline), sedation
  - Timing considerations: patient is stable, but this was our first meeting and unable to follow-up with me specifically
  - Would have offer one at a time changes, considering patient priorities
- In this case, plan for close follow-up with incoming fellow to allow for time to build rapport and more longitudinal relationship and follow-up

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PITFALLS

- DON'T focus only on medication- remember psychosocial interventions, psychotherapy
- DON'T pick the wrong time (crisis, active phase of illness, not enough rapport/treatment alliance) (Gupta & Cahill, 2016)
- DON'T approach this in an authoritarian manner
  - Remember importance of patient-centered approach!

SUMMARY RESOURCES

(FROM REEVE, THOMPSON, & FARRELL, 2017)

Box 1

Importance of consumer involvement in deprescribing.

- The consumer/caregiver is ultimately in control of the medication that they/their care recipient takes (continue to fill repeats/seek out an alternative GP) [70]
- It is a right, and in accordance with the ethical principle of autonomy (principlism) [64]
  - A majority of patients want to be involved with the decision-making process [63]
- Patient-centred care has been associated with improved outcomes [71–74]
  - Increased patient satisfaction
  - Increased medication adherence
  - Increased quality of life and well-being
  - Improved health outcomes
- They are a source of knowledge which is required to determine if it is suitable to withdraw the medication [20,62,75,76]
  - About medications (what prescription and non-prescription medications they are taking) and medical conditions (what the indications are)
  - About their values, preference and beliefs and establishing care goals
- Required to preserve the doctor-patient relationship [77]
- Patient-mediated interventions are among the most effective approaches to cessation of prescribing [69]

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SUMMARY RESOURCES

(FROM REEVE, THOMPSON, & FARRELL, 2017)

Box 2
Elements of a deprescribing process [40,45].

- Collect a complete and comprehensive medication history
  - Regular, intermittent and 'as required' prescription and non-prescription medications (including vitamins, supplements, "herbals")
  - Include dose, frequency, duration of use, indication and effectiveness
  - Identify possible adverse drug reactions
  - Assess adherence
- Assess overall risk of harm and benefit and individual patient factors which may affect deprescribing
  - Discuss patients'/caregivers' values, preferences, beliefs and goals of care surrounding continued medication use versus deprescribing
  - Drug related factors: polypharmacy, pill burden (medication regimen complexity), drug-drug interactions, use of 'high risk' drugs
  - Patient related factors: life expectancy, cognitive and functional impairments, falls risk, co-morbidities multiple prescribers, palliative care
  - Ask "which medications are most important for you to keep taking? Why?"
- Identify potentially inappropriate medications
  - Consider medications without an indication (condition resolved, unconfirmed, questionable efficacy, altered risk, non-pharmacological alternative), part of a prescribing cascade, causing an adverse drug reaction, potential for future harm
  - Use tools such as explicit lists of medications which are inappropriate in older adults, e.g. Beers list, STOPP criteria [93,94]
  - Use algorithms to determine drug appropriateness, e.g. Medication Appropriateness Index, Good Palliative-Geriatric Practice algorithm [4,32]
- Decide on medication withdrawal (shared-decision making)
  - If more than one medication identified for withdrawal prioritize order of drugs for discontinuation (e.g. based on potential for harm, patient preference)
- Plan tapering or withdrawal process and monitoring with documentation and communication to all persons relevant to care
  - Appropriate timing of withdrawal (e.g. consider patient's use of dosage administration aids)
  - Tapering plan - Identify if the medication is commonly associated with an adverse drug withdrawal event (see Bain et al. [95] and online resource medstopper.com). Slow dose reduction prior to discontinuation may also identify lowest effective dose, minimize the impact of return of symptoms if they do occur and increase patient comfort with the process.
  - Patient management plan (symptoms to look out for, symptom action plan, monitoring required by a health care professional, person to contact)
- Conduct monitoring and support
  - Monitor for adverse drug withdrawal reactions, return of condition, reversal of drug-drug and drug-disease interactions
  - Monitor for benefits (resolution of adverse drug reactions)
  - Use non-pharmacological approaches to reduce reliance on medication where possible
- Documentation
  - Document reasons for, process and outcome (e.g. medication ceased, dose reduced or withdrawal attempted with reasons for failure) of deprescribing
  - Share documentation with all relevant health care professionals

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OTHER RESOURCES

(FROM REEVE, THOMPSON, & FARRELL, 2017)

Box 3
Resources available to support health care providers in deprescribing activities.

Websites containing information, resources and tools to aid deprescribing

- http://deprescribing.org/
  - Information about deprescribing for researchers, health care professionals and consumers
  - Evidence-based decision-support algorithms for deprescribing proton pump inhibitors, benzodiazepines, antipsychotics and antihyperglycemics
  - Information about Canadian Deprescribing Network (CaDeN) and research occurring on deprescribing in Canada and internationally
  - Links to additional resources
- http://medstopper.com/
  - Enter medications to see information about benefits and risks
  - Suggested tapering approach for medications
  - Links to additional resources
- http://rxisk.org/
  - Information about drug side effects for consumers
  - Drugs to avoid lists
  - Additional information on antidepressants, antipsychotics, dopamine agonists and others
  - Links to additional resources
- http://sydney.edu.au/medicine/cdpc/documents/about/outcome-statement-national-stakeholders-meeting.pdf
  - Outcome statement of the 2015 National Stakeholders' meeting on quality use of medicines to optimise ageing in older Australians, convened by the NHMRC Cognitive Decline Partnership Centre and NPS MedicineWise involving the Australian Deprescribing Network (ADeN).
- http://www.primaryhealthtas.com.au/resources/deprescribing
  - Guides on deprescribing several medication classes
- http://pathclinic.ca/resources/
  - Resources for prescribing and deprescribing in frail older adults and palliative care
- http://www.polypharmacy.scot.nhs.uk/
  - Information and resources for assessing medication appropriateness
- http://www.bpac.org.nz/BPJ/2010/April/stopguide.aspx
  - A practical guide to stopping medicines in older people

Tools for consumer engagement

- 5 questions to ask about your medications - https://www.ismp-canada.org/medrec/5questions.htm
- Steps for conducting deprescribing through shared-decision making [68]
- Consumer deprescribing information pamphlets - http://deprescribing.org/resources/deprescribing-information-pamphlets/
- Questionnaire to capture how older adults and caregivers feel about deprescribing – revised Patients' Attitudes Towards Deprescribing (rPATD) questionnaire [111]

Further reading

- Deprescribing clinical vignettes – see case reports on polypharmacy management section http://deprescribing.org/resources/publications/
- List of medications commonly associated with adverse drug withdrawal reactions [95]
- Other key references - [40,91]

Please note: The resources and tools listed above have been developed using a variety of methods including unstructured and structured literature reviews, expert consensus and external peer-review. The robustness of development and validity of the content have not been formally assessed by the authors of this article.

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CASE 2: 55 YO WOMAN PRESENTING WITH LOW ENERGY AND DEPRESSION

- HPI:
  - Low energy and depression greatest concerns. Worse since partner died about 1.5 years ago.
  - ?mania- periods of irritable mood with paranoia; vague description
  - Past trauma history
- PPH:
  - Two past suicide attempts and IP stays. PCP has been managing medications. Diagnosis of ADHD, anorexia in teen years, questionable OCD. Many past trials.
- Medical history:
  - Postmenopausal on HRT
- Medications:
  - Adderall XR 15 mg daily
  - Adderall IR 10 mg daily
  - Venlafaxine 300 mg daily
  - Fluoxetine 20 mg daily
  - Wellbutrin XL 300 mg daily
  - Alprazolam 0.5 mg PRN insomnia
- Labs/Studies:
  - CBC, CMP within normal limits