Antipsychotics and Sedatives

Hello!

I am Jillian Belanger

PharmD Student → 90 day chart review

Overview

- Antipsychotics
  - BPSD
- Sedatives
  - Insomnia

1 in 10

Seniors in Canada use a benzodiazepine on a regular basis to treat insomnia, agitation or delirium[1]

39%

Of seniors in LTC had at least 1 claim for an antipsychotic[2]

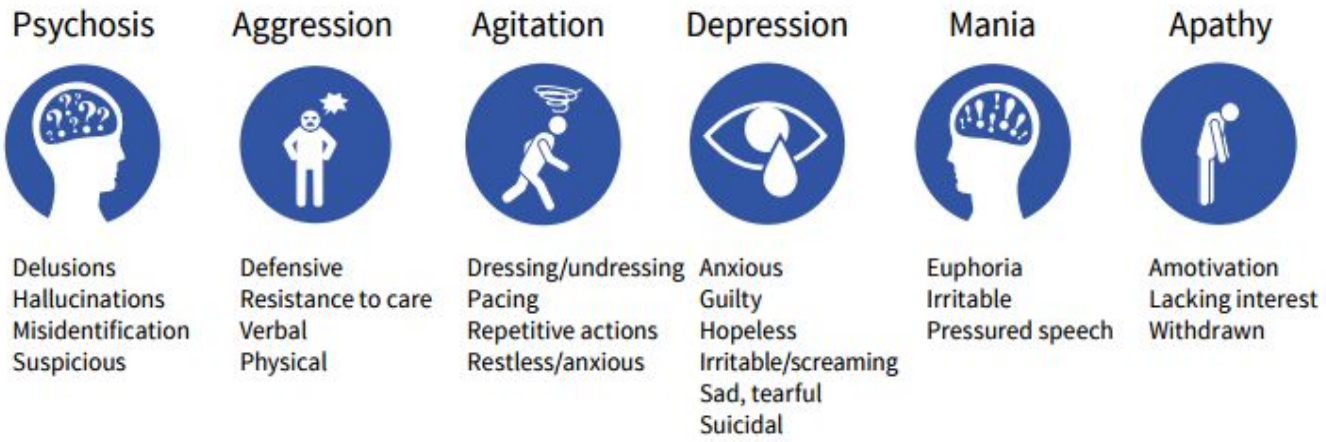
22.4%

Were considered chronic users of antipsychotics[2]

1.
Antipsychotics

Indication[3,4]

- BPSD: Behavioural and Psychological Symptoms of Dementia
  - Hyperactivity: Agitation, aggression, euphoria, disinhibition, irritability, aberrant motor activity
  - **Psychosis: Hallucinations, delusions**
  - Mood lability: Depression, anxiety
  - Instinctive: Appetite disturbance, sleep disturbance, apathy



Efficacy[4,5,6]

- When compared to placebo, antipsychotic therapy results in behaviour benefit in 1/5 people.

Symptom Likelihood to Respond to Antipsychotic Therapy

Cluster	Likely	Unlikely
Psychosis	• Delusions • Hallucinations • Misidentification • Suspicious	
Aggression	• Defensive • Physical	• Verbal • Resistance to care
Agitation	• Restless/anxious	• Dressing/undressing • Pacing • Exit seeking[17] • Repetitive actions[45-47]
Depression	• see below*,**	• see below*,**
Mania	• see below*	• Euphoria [45-48] • Irritable [45-48] • Pressured speech
Apathy[45-48,45]		• Amotivation • Lack of interest • Withdrawn
Other		• Hiding or hoarding[45] • Wandering without aggression[17,45] • Disinhibition (e.g., sexual)[45-47]

* The role of antipsychotics in those with dementia and depression is beyond the scope of this evidence review.
**In cases where depression treatment may be indicated, consider psychiatric consultation to determine appropriate pharmacotherapy options.

Safety[4]

- Bottom line: Adverse effects offset advantages in efficacy
- Side effects: Sedation, falls, postural hypotension, QT prolongation, confusion, EPS, diabetes, weight gain
- Increased risk of death (NNH:100)
  - Health Canada Advisory
- Increased risk of stroke

Considerations When Reviewing a New Order...[4]

- **Is the patient at risk for harming themself or others?**
- Have we optimized non-drug therapy?
- Is there a symptom present that is likely to respond to drug therapy?
- Have we ruled out underlying causes? (pain, constipation, delirium)

Non-Pharmacological Approaches[4,7,8,9]

- Environmental considerations
  - Decrease clutter
  - Decrease noise
  - Add signs, cues or pictures
  - Reduce reflections (mirrors, dark windows)
- Caregiver approach
  - Distraction
  - Approach slowly
  - Keep same routine
  - Individualize social and leisure activities to reduce boredom
  - Short simple words and phrases

Assessment of Underlying Causes[4,10]

- P.I.E.C.E.S. Tool
- Recent changes to environment
  - Hospital admission? 😏
- Medication review
  - Anticholinergic load
  - Medication induced hypotension
  - Orthostatic hypotension (quetiapine??)
  - Medication that may contribute to constipation and urinary retention
  - Drugs that may increase agitation (acetylcholineserase inhibitors, antiparkinson, prednisone etc)
- Physical exam
  - Pain, hydration, sensory loss, CNS change, infection, hypo-perfusion, constipation/urinary retention

Maintenance and Follow-up[4,11]

- Reassess in 1-2 weeks for improvement or ADRs
- Taper and discontinue if no improvement after 12 weeks
- Review should occur every 3-6 months
  - Consider reducing or discontinuing after 3 months of stable behaviours.

Considerations When Tapering[4]

- Deprescribing may not be indicated where symptoms are:
  - due to psychosis
  - dangerous or disruptive
- Optimize non-pharmacological measures for BPSD
- Taper gradually
  - by 25-50% every 2-4+ weeks and look for any resulting behaviour changes.
  - Once on lowest dose, may discontinue in 2-4+ weeks
- Continue to reassess for emergence of responsive behaviour

Note: **In hospitals the tapering can be more aggressive, if needed**

Tools

- Dementia observational tool
  - Nursing tool to assess behaviours
- P.I.E.C.E.S. Tool
  - Helps to identify causes
- P.I.E.C.E.S. RISKS tool
  - Helps to identify risks to resident and others.
- Deprescribing.org
- effectivepractice.org

2.

Benzodiazepines and other sedatives

Indication[12,13]

- Insomnia
- Drug therapy is last line
- Duration of therapy should be short-term if used
  - Ideally 1-2 weeks
  - No longer than 1 month

Efficacy[12]

Drug	Notes	Usual Dosage
Zopiclone	Sleep onset latency: 19 min Total Sleep time: 45 min Wake after sleep onset: 11 min	3.75-7.5mg Max: 5mg in elderly
Zolpidem	Sleep onset latency: 15 min Total Sleep time: 23 min	5-10 mg
Doxepin	3mg: total sleep time: 12 min, wake after sleep onset: 10 mins 6mg: total sleep time: 17 min, wake after sleep onset 14 mins Note: Do not take within 3 hr of food→ delayed absorption	3-6 mg T (not available in Canada, lowest 10 mg cap)
Trazodone	Limited evidence in insomnia 	25-150 mg
Benzodiazepines	Sleep onset latency 10 mins Total sleep time: 30-60 mins	Temazepam 15-30 mg
Melatonin	Sleep onset latency: 7 mins Total sleep time: 8 mins	1-3 mg

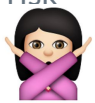
Safety[12,13]

Z-DRUGS

- Risk of physical tolerance and dependence
- Daytime drowsiness, dizziness, amnesia, nausea, headaches, falls
- Zolpidem: Less hangover

BENZOS

- Avoid in elderly due to risk of cognitive and behavioural adverse effects, falls, fractures
- Physical dependence/tolerance
- Daytime sedation and motor vehicle accidents



NHP

Melatonin

- No tolerance
- Purity concerns
- Fatigue, headache, irritability

ANTIDEPRESSANTS

Doxepin/Trazodone

- Minimal risk of physical dependence/tolerance
- Low anticholinergic activity (doxepin at low doses)
- Lower hangover effects

OTC

Antihistamines/Antinauseants

- Lack of evidence
- Psychomotor impairment
- Anticholinergic activity
- Fast tolerance

ANTIPSYCHOTICS

- Lack of evidence
- Anticholinergic and neurological toxicities
- Metabolic toxicity
- Increased risk of stroke and death

Sedatives

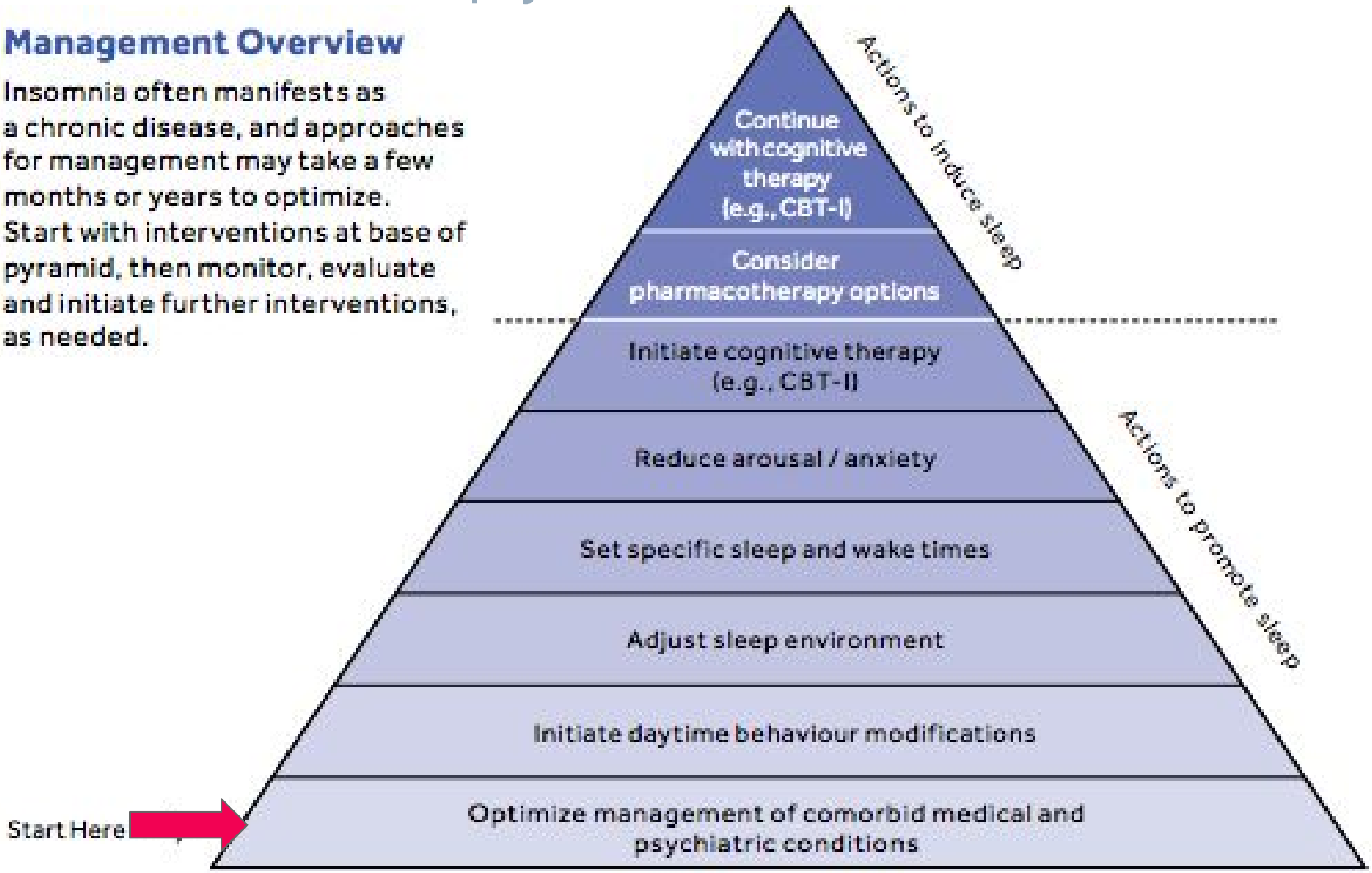
High risk, Low benefit

NNT 13, NNH 6[12,14,15]

Treatment pyramid[12]

Management Overview

Insomnia often manifests as a chronic disease, and approaches for management may take a few months or years to optimize. Start with interventions at base of pyramid, then monitor, evaluate and initiate further interventions, as needed.



Treatment pyramid[12]

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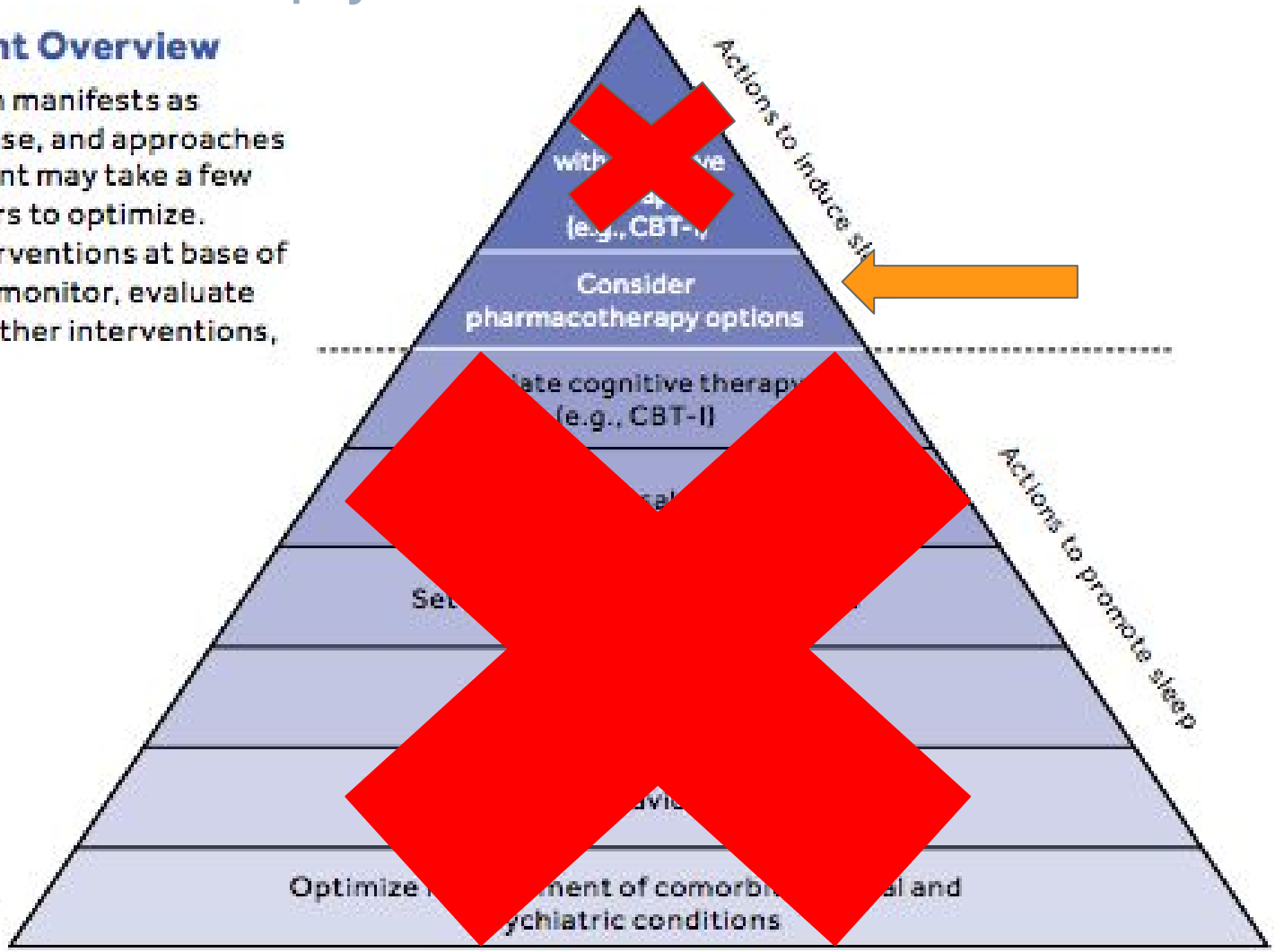


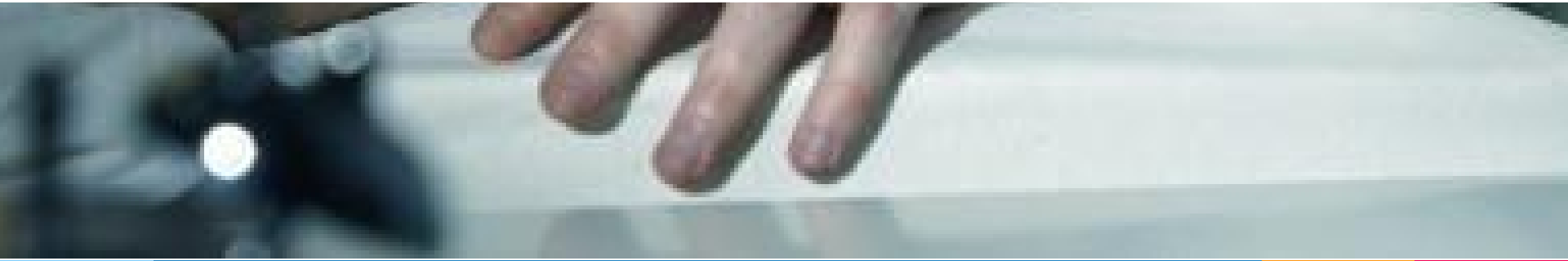
Potential Underlying Conditions[12,16]

Common comorbid medical disorders, conditions or symptoms	
Cardiovascular	Angina, CHF, dyspnea
Endocrine	Thyroid disorders, Diabetes
Genitourinary	BPH, Incontinence, UTI
Mental Health	Anxiety, depression, stress
Neurological	Stroke, dementia, Parkinson's, pain
Sleep	Sleep apnea, RLS
Environmental	**Noise, temperature, uncomfortable bed**
Other	Allergies, alcohol or other substance use/ dependence/ withdrawal

Consider Pharmacological Causes[12]

Drugs that may cause fragmented sleep, nightmares, nocturia or stimulation	
Antidepressants	Bupropion, MAOIs, **SNRIs**, **SSRIs**
Cardiovascular	Alpha-blockers, b-blockers, diuretics, statins
Decongestants	Phenylephrine, pseudoephedrine
Opioids	In combination with caffeine
Respiratory	B2-Agonists, theophylline
Stimulants	Amphetamine, caffeine, modafinil etc
Others	Acetylcholinesterase inhibitors, alcohol, antineoplastics, **corticosteroids**, **dopamine receptor antagonists**, nicotine, medroxyprogesterone, phenytoin, thyroid supplements

The Placebo Effect



Suggested Taper for Benzos and Z-drugs[12,17,18]

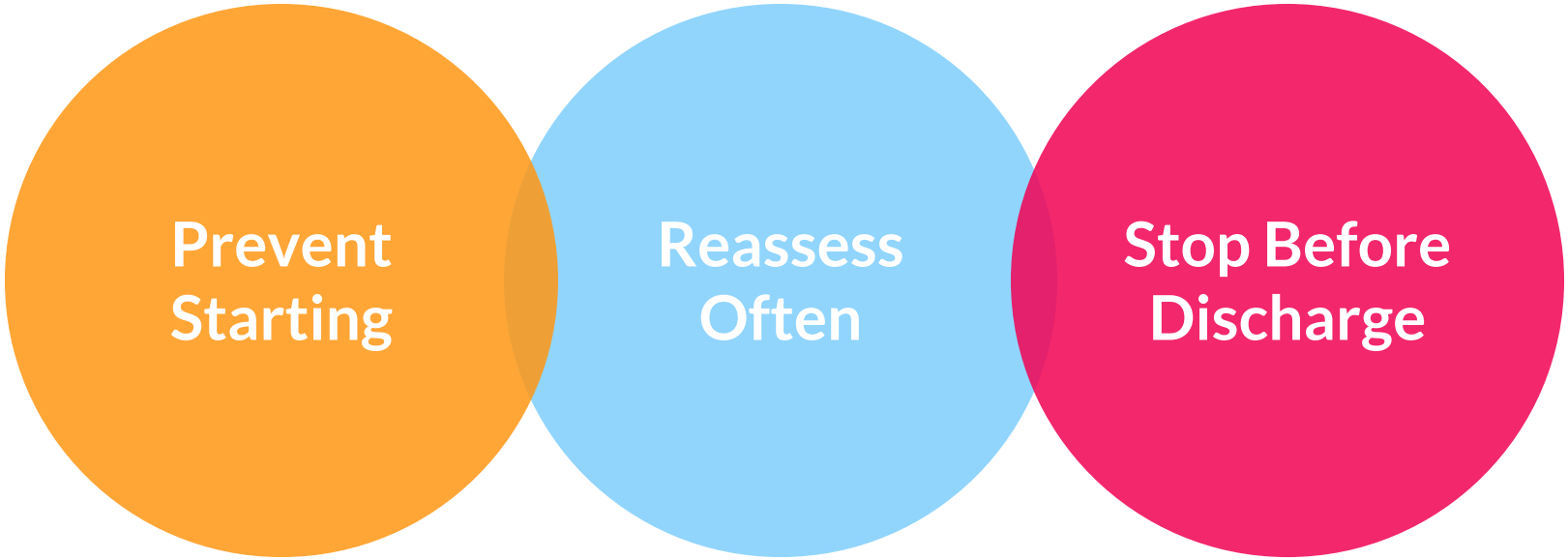
- Taper by 10 % of the dose every 1-2 weeks until the dose is at 20% of the original dose
- Then taper by 5% every 2-4 weeks
- The use of adjuvant agents during taper(ie antidepressants, melatonin) have limited evidence for success
- Longer acting agents such as diazepam or clonazepam are suggested (caution in elderly due to risk of prolonged sedation)

Some approaches to tapering benzodiazepines or Z-drugs[33]

Duration of use	Recommended taper length	Comments
< 8 weeks	Taper may not be required	• Depending on clinical judgment and patient stability/preference, consider implementing a taper, particularly if patient is using a high-dose benzodiazepine or an agent with a short-intermediate half-life (e.g., alprazolam, triazolam).
8 weeks - 6 months	Slowly over 2 to 3 weeks	• Go slower during the latter half of taper. Tapering will reduce, not eliminate, withdrawal symptoms. Patients should avoid alcohol and stimulants during benzodiazepine or Z-drug withdrawal.
6 months - 1 yr	Slowly over 4 to 8 weeks	
> 1 year	Slowly over 2 to 4 months or longer	• Reduce dose by 10% a week, until 10mg diazepam equivalent is reached. Maintain reduced dose for months before final taper. For the final taper, decrease dose by 10% every 1-2 weeks. When 20% of the dosage remains, begin a 5% dose reduction every 2-4 weeks.

Wow! That was the best sleep I've ever had!

Conclusion



Thanks!

Any questions?

After Jon’s presentation...

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