Benzodiazepine Deprescribing in the Elderly
A Community Family Medicine Approach

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CONFLICT AND DISCLOSURE INFORMATION

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Program: NYGH, North York Family Health Team, University of Toronto Department of Family and Community Medicine

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Objectives

1. Describe the risks and side effects of benzodiazepine (BZD) use in elderly patients

2. Explore techniques for deprescribing that can be used effectively in a busy family practice setting

3. Explore various treatment modalities as alternatives to BZD use in elderly patients
Outline

1. Case
2. Rationale
   • BZD harms and indications
3. De-prescribing
   • EMPOWER Study
4. Pharmacologic
   • Tapering schedules
5. Quality Improvement Project
   • Practical implementation
6. Behavioural strategies
   • Motivational Interviewing
   • Cognitive Behavioural Therapy for Insomnia (CBTi)
7. Summary and resources
True or False?

Using Z-drugs (Zopiclone, Zolpidem) is a safer alternative for the treatment of insomnia compared to BZD

FALSE
True or False?

In Denmark seniors on long-acting sleeping pills (half-life >10 hr) are not allowed to renew their driving license

TRUE

After a single dose of BZD with a half-life < 10 hr it is recommended not to drive the next day

TRUE

Eriksen and Bjerrum, 2015
MS. ES: 78 yo female, multiple medical issues:

- Migraines
- Chronic Kidney Disease
- Diabetes
- COPD, asthma (~ 60 pack year smoker)
- Osteoporosis
- GERD
- Spinal stenosis, DDD, Degenerative disease, L shoulder
- Hypertension
- Codeine addiction in past
- Essential tremor
- Hyperlipidemia
- Insomnia
- Depression
Meds:

- Cafergot 1 tab OD
- *Diazepam 10 mg TID prn* (prescribed years earlier for “facial migraines”)
- Dimenhydrinate 2 caps OD prn for migraines
- Fluticasone propionate/Salmeterol 200 mcg 1 puff BID
- Fluoxetine 20 mg OD
- Hydrochlorothiazide 25 mg OD
- Pravastatin 40 mg OD
- Rabeprazole 20 mg OD
- Topiramate 100 mg qhs

*In reality: using Diazepam 30 mg and Dimenhydrinate 5 tabs daily for sleep*
Choosing Wisely Canada Recommendation:

“Don’t use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation or delirium”
Rationale

- Increased risk of:
  - Daytime sedation (3.8x)
  - Balance issues causing falls and hip fractures (2.6x)
  - Cognitive impairment (5x)
  - MVC’s (2x)

**Total cost in 2013: $135 million**

Glass, et al., 2005, BMJ
Long-term use of BZD changes the brain chemistry, posing substantial risk when abruptly stopping

TRUE
Rationale

• Physiologic dependence within 2 weeks
• Ineffective for sleep: 23-25 minutes improvement

Glass, et al., 2005, BMJ
Rationale

**POLYPHARMACY!!!**
- ↑ rates of hospitalization and ED visits
- Delirium
- Drug interactions
- Reduced overall function
- Cognitive Impairment

- Culprit drugs
  - Hypnotics, anti-depressants, neuroleptics, anticonvulsants, opiates and alcohol

Farrell et al., 2014
Maher Jr, et al., 2014
Rationale: Cognitive Impairment

Benzodiazepines are known to cause amnesia (e.g., Midazolam) impairing short-term memory, acquisition of new information, concentration and attention.

A lifetime use of more than 90 doses of benzodiazepines (translation: 2x/wk x 1 year) = 50% higher risk of Alzheimer’s disease and double the risk of overall death.

Tannenbaum, 2015
Bottom Line

NNT: 13
NNH: 6

RISK >> BENEFIT

Glass, et al., 2005, BMJ
True or False?

It is safe to slowly taper BZD in patients with severe anxiety

FALSE
Appropriate indications

- Seizures
- Alcohol withdrawal
- Refractory anxiety
- Restless leg syndrome
- Acute agitation in psychosis

Appropriate use

- Short-term (<2 weeks)
• Multiple hospital admissions for low back pain and COPD exacerbations – all at same hospital
  • Diazepam was inconsistently listed amongst admission medications

• **August 2012**: admission for 8 month hx of unsteady gait, slurred speech and blurred vision
  • Diazepam was not listed amongst her admission meds at this visit
  • Discharge Dx: Topiramate intoxication secondary to acute renal disease
Ms E.S. Admissions

- **June 2015:**
  - lightheadedness, poor balance, and stumbling
  - Admission meds included Diazepam 10 mg TID 5 days/wk
  - Dx: vasovagal episodes

- **October 2016:**
  - COPD exacerbation
  - Diazepam is listed on home meds list at 10 mg bid prn
  - Discharge meds include:
    - Diazepam (continue as previous)
    - Zopiclone 3.75 mg (new)
    - Tylenol #3 for headaches (new)
Ms. ES

1. What is wrong with this picture?
2. Could anything have been done differently?
De-prescribing

What percentage of Canadian seniors are willing to stop a medication if their doctor says it’s possible?

71%
Approach to De-prescribing

Simple Strategies and gradual dose-tapering
You May Be at Risk
You are taking one of the following sedative-hypnotic medications:

- Alprazolam (Xanax®)
- Clonazepam
- Chloralhydrate
- Clomipramine
- Clobazam
- Chlorpromazine
- Clonazepam
- (Rivotril®, Klonopin®)
- Diazepam (Valium®)
- Estazolam
- Flurazepam
- Loprazolam
- Lorazepam (Ativan®)
- Lormetazepam
- Nitrazepam
- Oxazepam (Serax®)
- Quazepam
- Temazepam (Restoril®)
- Triazolam (Halcion®)
- Eszopiclone (Lunesta®)
- zaleplon (Sonata®)
- Zolpidem (Ambien®, Intermezzo®, Edluar®, Sublimaze®, Zolpidem®)
- Zopiclone (Imovane®, Rovers®)

EMPOWER Tool

TEST YOUR KNOWLEDGE ABOUT A SEDATIVE-HYPNOTIC DRUG

1. The medication I am taking is a mild tranquilizer that is safe when taken for long periods of time.  
   - [ ] TRUE  [ ] FALSE

2. The dose that I am taking causes no side effects.  
   - [ ] TRUE  [ ] FALSE

3. Without this medication I will be unable to sleep or will experience unwanted anxiety.  
   - [ ] TRUE  [ ] FALSE

4. This medication is the best available option to treat my symptoms.  
   - [ ] TRUE  [ ] FALSE

---

1. FALSE
   It is no longer recommended to take a sedative-hypnotic drug to treat insomnia or anxiety. People who take it are putting themselves at a:
   - 50% increased risk of Alzheimer’s disease
   - 5-fold higher risk of memory and concentration problems
   - 4-fold increased risk of daytime fatigue
   - 2-fold increased risk of falls and fractures (hip, wrist)
   - 2-fold increased risk of having a motor vehicle accident while driving
   - Problems with urine loss

2. FALSE
   Even if you think that you have no side effects, and even if you take only a small dose, a sedative-hypnotic drug worsens your brain performance and slows your reflexes.

3. TRUE
   Your body has probably developed a physical addiction to this medication. If you stop it abruptly, you may have trouble sleeping and feel greater anxiety. Millions of people have succeeded in slowly cutting this drug out of their lives and finding alternatives to help their problem.

4. FALSE
   Although it is effective over the short term, studies show that sedative-hypnotic drugs are not the best long-term treatment for your anxiety or insomnia. Sedative-hypnotic medication covers up the symptoms without actually solving the problem. Please keep on reading to learn more about developing healthier sleep patterns and diminishing stress.

EMPOWER Tool

ALTERNATIVES

If you are taking this sedative-hypnotic drug to help you sleep:

There are lifestyle changes that can help.

- Do not read or watch TV in bed. Do so in a chair or on your couch.
- Try to get up in the morning and go to bed at night at the same time every day.
- Before going to bed, practice deep breathing or relaxation exercises.
- Get exercise during the day, but not during the last three hours before you go to bed.
- Avoid consuming nicotine, caffeine and alcohol as they are stimulants and might keep you awake.
- Ask your doctor for the use of a sleep diary, which can help you understand disruptive sleep patterns.

If you are taking this sedative-hypnotic drug to help reduce your anxiety:

There are other solutions to deal with your stress and anxiety.

- Talking to a therapist is a good way to help you work out stressful situations and talk about what makes you anxious.
- Support groups help to relieve your stress and make you feel you are not alone.
- Try relaxation techniques like stretching, yoga, massage, meditation or tai chi that can help relieve you of everyday stress and help you work through your anxiety.
- Talk to your doctor about other anti-anxiety medications that have less serious side effects.

# EMPOWER Tool

<table>
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<tr>
<th>WEEKS</th>
<th>TAPERING SCHEDULE</th>
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<tr>
<td>17 and 18</td>
<td>❌</td>
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**EXPLANATIONS**
- 🟢 Full dose
- 🟧 Half dose
- 🟦 Quarter of a dose
- ❌ No dose

# BZD Equivalence

<table>
<thead>
<tr>
<th>Benzodiazepine</th>
<th>Oral Formulation</th>
<th>Approximate Equivalent to 5 mg diazepam (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-Acting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triazolam (Halcion®)</td>
<td>Tabs (small, oval)</td>
<td>0.25</td>
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<tr>
<td><strong>Intermediate-Acting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alprazolam (Xanax®)</td>
<td>Tabs (small, oval)</td>
<td>0.5</td>
</tr>
<tr>
<td>Lorazepam (Ativan®)</td>
<td>Tabs (small)</td>
<td>0.5 - 1</td>
</tr>
<tr>
<td>Oxazepam (Serax®)</td>
<td>Tabs</td>
<td>15</td>
</tr>
<tr>
<td>Temazepam (Restoril®)</td>
<td>Caps</td>
<td>10 – 15</td>
</tr>
<tr>
<td><strong>Long-Acting</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clonazepam (Rivotril®)</td>
<td>Tabs</td>
<td>0.5 – 1</td>
</tr>
<tr>
<td>Diazepam (Valium®)</td>
<td>Tabs</td>
<td>5</td>
</tr>
</tbody>
</table>

Slide courtesy of E. Lui, 2017
Ashton CH, 2002
Alternate Approach

Taper is most difficult during last 1/4
Stay on same dose but skip pill q2-3 days

↓10% q1-2 wks until at 20% original

↓5/% taper q2-4 wks

Slide courtesy of E. Lui, 2017

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Appendix B-6: Benzodiazepine Tapering
http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b06.html#table_b_app_06_01
Long vs. Short Acting

• May taper with either; insufficient evidence to support either
• Factors to consider:
  – Daytime drowsiness?
  – Withdrawal symptoms?
  – Ease of dose reduction?

• Use your community pharmacist!

Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain. Appendix B-6: Benzodiazepine Tapering: http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b06.html#table_b_app_06_01
Tapering

• Expected benefits:
  – Improved alertness, cognition, daytime sedation
  – Reduced falls

• Withdrawal symptoms:
  – Insomnia
  – Anxiety
  – Irritability
  – Sweating
  – GI symptoms (IBS)

**Use of EMPOWER brochure can cut down frequency of visits**

**Warning of withdrawal ahead of time can increase success**

Trouble Shooting

Difficulty tapering:
- Slow down pace
- Avoid “up-dosing”
- Do not introduce a new sleeping pill
- Consider behavioral strategies
# Alternative Medications

<table>
<thead>
<tr>
<th>Sedating Meds</th>
<th>Examples</th>
<th>Other Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants</td>
<td>Amitriptyline (Elavil®), Trazodone (Desyrel®), Mirtazapine (Remeron®)</td>
<td>Dry mouth, Dry eyes, Constipation, Difficulty urinating</td>
</tr>
<tr>
<td>Antihistamines (over-the-counter)</td>
<td>Diphenhydramine (Benadryl®, Sleep-Eze®, Unisom®), Dimenhydrinate (Gravol®)</td>
<td>Dry mouth, Dry eyes, Constipation, Difficulty urinating</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Quetiapine (Seroquel®)</td>
<td>↑ blood sugars &amp; lipids, Involuntary Movements and death from CVD/CAD</td>
</tr>
<tr>
<td>Anti-Seizure Meds</td>
<td>Gabapentin (Neurontin®)</td>
<td>Stomach upset, Swelling</td>
</tr>
<tr>
<td>Orexin Receptor Antagonists</td>
<td>Suvorexant (Belsomra®) – Not approved in Canada</td>
<td>Headache, abnormal dreams, abnormal cognition, anxiety, behavioral changes, hallucination, sleep paralysis, sleep driving, suicidal ideation, ↑ chol, diarrhea, dry mouth, cough</td>
</tr>
</tbody>
</table>
### Herbal Supplements

<table>
<thead>
<tr>
<th>Herbal Products</th>
<th>Effectiveness</th>
<th>Potential Side Effects / Drug Interactions</th>
</tr>
</thead>
</table>
| **Melatonin**                                        | - More for jet lag  
- ↓ time to fall asleep by 10 min  
- ↑ sleep duration by 15 min | Daytime sleepiness, confusion, depression, ↑ risk bleeding with Aspirin or other anticoagulants            |
| *Ramelteon (Rozerem®) works on the same melatonin receptors. Not approved in Canada.* |                                                                               |                                                                                                           |
| **L-Tryptophan** / 5-Hydroxytryptophan (5-HTP)       | - Conflicting results  
- Anecdotal                                                                 | Dizziness, nausea, diarrhea, interacts with St. John’s Wort & many antidepressants                         |
| **Valerian / Valerian root**                         |                                                                               | Headaches, dizziness                                                                                        |
| **Kava**                                             |                                                                               | Liver toxicity, tremor                                                                                      |
| **Skullcap**                                         |                                                                               | Liver toxicity, confusion                                                                                   |
| **Passionflower**                                    |                                                                               | Rarely may ↑ heart rate                                                                                     |
| **Chamomile**                                        |                                                                               | Allergic reactions                                                                                          |

Slide courtesy of E. Lui, 2017
Alternative Medications

Bottom Line

- Lower risk for physical dependency in general
- Have other side effects and may still affect:
  - Memory
  - Concentration
  - ↑ daytime fatigue
  - ↑ risk of falls
- **Short-term** use only
- Monitor for drug-interactions, even with herbals

Slide courtesy of E. Lui, 2017
Quality Improvement Project

Aim:

*To reduce the benzodiazepine dose in 10% of patients aged 65 and older, over 6 months, from 4 community family physician’s offices by utilizing patient education empowerment and a multi-disciplinary team*

Outcome Measures:

- Patients > 65 with Rx BZD in CPP
- % patients that d/c BZD
- % patients that reduced dose
Quality Improvement Project

deprescribing.org | Benzodiazepine & Z-Drug (BZRA) Deprescribing Algorithm

**Why is patient taking a BZRA?**
If unsure, find out if history of anxiety, past psychiatrist consult, whether may have been started in hospital for sleep, or for grief reaction.

* Insomnia on its own OR insomnia where underlying comorbidities managed
  - For those ≥ 65 years of age: taking BZRA regardless of duration (avoid as first line therapy in older people)
  - For those 18-64 years of age: taking BZRA ≥ 4 weeks

**Engage patients** (discuss potential risks, benefits, withdrawal plan, symptoms and duration)

**Recommend Deprescribing**

**Taper and then stop BZRA**
(taper slowly in collaboration with patient, for example ~25% every two weeks, and if possible, 12.5% reductions near end and/or planned drug-free days)

* For those ≥ 65 years of age
  (strong recommendation from systematic review and GRADE approach)
* For those 18-64 years of age
  (weak recommendation from systematic review and GRADE approach)
* Offer behavioural sleeping advice; consider CBT if available (see reverse)

**Monitor every 1-2 weeks for duration of tapering**

**Use non-drug approaches to manage insomnia**
Use behavioral approaches and/or CBT (see reverse)

**If symptoms relapse:**
Consider
* Maintaining current BZRA dose for 1-2 weeks, then continue to taper at slow rate

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

How to target patients:

- Renewal request
- Medication review
- Opportunistic clinic visit
- Office posters
Quality Improvement Project

PDSA’s:

- Provider Education
- Initial Contact
- EMPOWER Tool
- Pharmacy Led Taper
- CBTi
Quality Improvement Project

Results

93 pts > 65 with benzo in med profile

21 pts eligible after chart review
15 engaged in deprescribing
2 same dose
8 tapered partially

13 reduced dose
6 pre-contemplative

72 excluded

5 tapered off completely

62% of patients either reduced or completely stopped their BZD
Quality Improvement Project

You May Be at Risk
You are taking one of the following sedative-hypnotic medications:

- Aprazolam (Xanax®)
- Chlorazepate
- Chlordiazepoxide-amitriptyline
- Clonazepam
- Chlordiazepoxide
- Clorazapam
- Clonazepam (Rivotril®, Klonopin®)
- Clorazepate
- Temazepam (Restoril®)
- Triazolam (Halcion®)
- Etizolam (Lunesta®)
- Zaleplon (Sonata®)
- Zolpidem (Ambien®, Intermezzo®, Edluran®, Silmion®, Zolpidem®)
- Zopiclone (Imovane®, Rhovane®)

VS

CBTi

Alternative Supports

Social Worker

Pharmacist
Motivational Interviewing

- Empathy
- Avoid argumentation
- Relate discrepancies
- Self-Efficacy
- Roll with resistance
Motivational Interviewing

Goal: increase patient awareness of problem behaviour and consequences, to develop intrinsic motivation for change

My Approach:

1. **Frame** – Med review, sleep counselling
2. **Connect** – Personal or family health consequence
3. **Introduce** – “Deprescribing”, evidence
4. **Ascertain** – Stage of change
5. **Engage** – Change talk, readiness
6. **Educate** – EMPOWER Brochure
7. **Plan** – Patient-centered, follow up
Create “Inner Turmoil”

THIS PILL IS NOT ADDICTIVE! I SHOULD KNOW, I HAVE TAKEN IT EVERY NIGHT FOR TWENTY YEARS NOW.
True or False?

Sleep hygiene is the most effective behavioural strategy to improve sleep

FALSE
Sleep Hygiene

GENERAL TIPS FOR HAVING HEALTHY SLEEP HYGIENE

- Go to bed and wake up at the same time every day (even on the weekends!)
- Avoid caffeine consumption (e.g., coffee, soft drinks, chocolate) starting in the late afternoon
- Expose yourself to bright light in the morning – sunlight helps the biological clock to reset itself each day
- Make sure your bedroom is conducive to sleep – it should be dark, quiet, comfortable, and cool
- Sleep on a comfortable mattress and pillow
- Don’t go to bed feeling hungry, but also don’t eat a heavy meal right before bed
- Develop a relaxing routine before bedtime – ideas include bathing, music, and reading
- Reserve your bedroom for sleeping only – keep cell phones, computers, televisions and video games out of your bedroom
- Exercise regularly during the day
- Don’t have pets in your bedroom
Cognitive Behavioural Therapy for Insomnia

Goal
• Restrict time in bed to improve quality of sleep first, then increase quantity

Evidence
• American College of Physicians recommends CBTi as proven to be more effective than sedative-hypnotics to improve sleep

Access
• Social work/trained psychotherapists
• Sleep clinics
• Online resources/books/apps
• Pamphlets (see additional resources)

ACP, Qaseem et al., 2016
Stimulus control
- Reduce “bed = awake” association
- Increase “bed = sleep” association

Sleep restriction
- Sleep diary
- Sleep prescription
  - Bed when sleepy
  - Out of bed if unable to sleep
  - Consistent bed time and rise

Geiger-Brown et al., 2014
### Example of Sleep Diary

<table>
<thead>
<tr>
<th>Sample</th>
<th>Consensus Sleep Diary-Core</th>
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<tbody>
<tr>
<td>Today's date</td>
<td>4/5/08</td>
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<table>
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<tr>
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<tbody>
<tr>
<td>10:15 p.m.</td>
<td>11:10</td>
<td>11:00</td>
<td>11:30</td>
<td>11:15</td>
<td>11:00</td>
<td>11:15</td>
<td>11:30</td>
</tr>
<tr>
<td>11:30 p.m.</td>
<td>12:00</td>
<td>11:30</td>
<td>12:30</td>
<td>12:00</td>
<td>11:30</td>
<td>12:00</td>
<td>12:00</td>
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</tbody>
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<table>
<thead>
<tr>
<th>2. What time did you try to go to sleep?</th>
<th>4/5/08</th>
<th>4/6/08</th>
<th>4/7/08</th>
<th>4/8/08</th>
<th>4/9/08</th>
<th>4/10/08</th>
<th>4/11/08</th>
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<tbody>
<tr>
<td>55 min.</td>
<td>20 mins</td>
<td>10 mins</td>
<td>15 mins</td>
<td>20 mins</td>
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<td>3</td>
<td>Once</td>
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<tbody>
<tr>
<td>1 hour, 10 min.</td>
<td>4 hrs, 20 min</td>
<td>1 hr.</td>
<td>20 min</td>
<td>15-20 min</td>
<td>10 min</td>
<td>1 hr, 30 min</td>
<td>1 hr, 30 min</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>5. In total, how long did these awakenings last?</th>
<th>4/5/08</th>
<th>4/6/08</th>
<th>4/7/08</th>
<th>4/8/08</th>
<th>4/9/08</th>
<th>4/10/08</th>
<th>4/11/08</th>
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<td>7:20 a.m.</td>
<td>9</td>
<td>8:30</td>
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<tr>
<td>8</td>
<td>5 mg</td>
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</thead>
<tbody>
<tr>
<td>9. Comments (if applicable)</td>
<td>I have a cold</td>
<td>5 mg</td>
<td>5 mg</td>
<td>5 mg</td>
<td>5 mg</td>
<td>5 mg</td>
<td>5 mg</td>
</tr>
</tbody>
</table>
Sleep Efficiency Ratio

- Calculate total time asleep – deduct night awakenings
- Calculate total time in bed

\[
\frac{\text{Total sleep time}}{\text{Total time spent in bed}} \times 100
\]

What is the target sleep efficiency ratio?

85%
Online tools

Sleepwell NS

http://sleepwellns.ca/get-your-sleep-back

EMPOWER Tool Brochure

http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf

Sleep Brochure

http://www.criugm.qc.ca/fichier/pdf/Sleep_brochure.pdf
Take-home points

- **Educating** on BZD harms and utilizing deprescribing regimen streamlines de-prescribing

- **Deprescribe** tailored to patient’s needs

- Consider **stage of change**

- **EMPOWER tool** is valuable
  - Motivated patients are able to deprescribe on their own with instructions on how to taper
Take-home points

• De-prescribing is an **iterative** process
  • Revisiting of deprescribing may move the patient to a different stage of change

• Set **realistic goals**
  • Goal is not always zero
  • Some patients may never reduce – goal is *harm reduction*
  • Recognize when not clinically appropriate
How can we help Ms. ES?
Ms. E.S.

- **February 2017**
  - Ms. ES was participant in QIP
  - over the course of several months, slowly convinced to try the tapering schedule

- **June 2017**
  - off Fluoxetine, on Duloxetine 30 mg OD and Diazepam 10 mg OD (reduced from 10 mg TID)
  - Nabilone 0.5mg bid was added for pain control
  - Admitted to “feeling better than she had in years” with improved energy and appetite

- **July 2017**
  - maintained on Diazepam 5 mg qhs
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References


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Thank you