Pain, Anxiety, and Aging: Overprescribing and Polypharmacy in the Aging Population

SUBTITLE: Benzodiazepines and all of that other stuff

Donovan T. Maust, MD, MS
Department of Psychiatry, University of Michigan
Center for Clinical Management Research, VA Ann Arbor

Outline:

1. What is happening with psychotropic and opioid use for older adults?
2. Focus on benzodiazepine prescribing.
3. What exactly is being treated and what are the alternatives?
4. How to address benzodiazepine prescribing?

What is happening with psychotropic and opioid use for older adults?

Going up across the board.

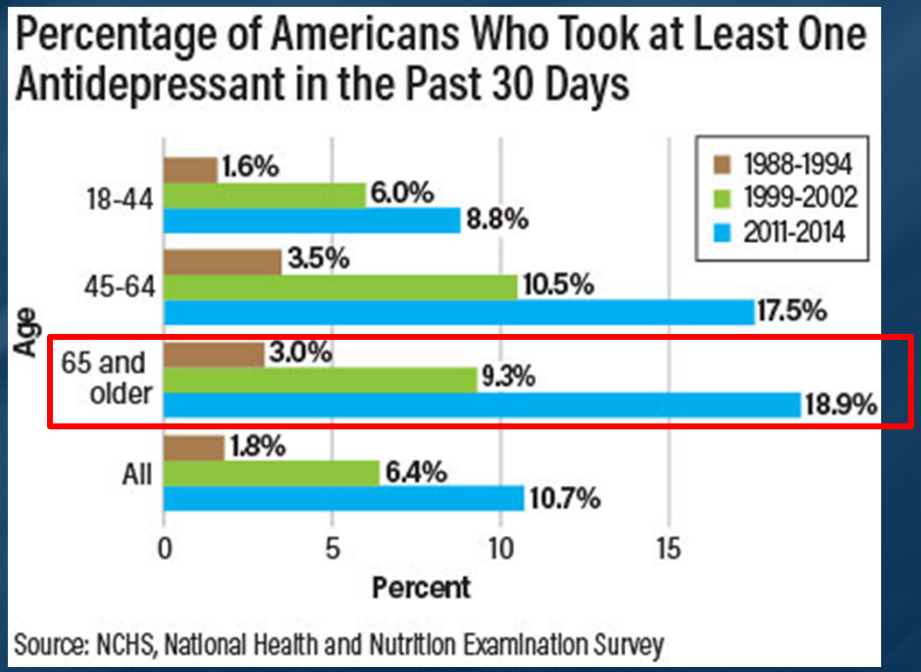
- Analysis using NAMCS (national sample of all visits to office-based physicians)
- Limited to adults ≥65 years old

	Primary Care (n = 14,282)					Psychiatry (n = 1,095)				
	2003–2005	2010–2012	Adjusted[a]			2003–2005	2010–2012	Adjusted[a]		
	%[b]	%[b]	OR	95% CI	*P*	%[b]	%[b]	OR	95% CI	*P*
Antidepressants	9.9	12.3	1.28	1.06–1.54	.01	70.1	59.8	0.62	0.40–0.96	.03
Benzodiazepines	5.6	8.7	1.62	1.30–2.02	<.001	32.1	29.5	0.83	0.57–1.22	.34
Other sedative-hypnotics	3.4	4.7	1.39	1.07–1.79	.01	8.5	11.7	1.41	0.70–2.86	.34

	%[b]	%	OR	95% CI	p
Opioids	**6.1**	**11.5**	**2.10**	**1.73-2.56**	**<0.001**

Maust et al., *J Clin Psychiatr* 2017

You could just put Prozac in the water . . .



http://psychnews.psychiatryonline.org/doi/full/10.1176/appi.pn.2017.pp9b2

Almost 1 in 5 adults ≥65 took an antidepressant in the past 30 days.

But it's depressing to get old, right?

A reminder:

- Depression is less common in older adults.

Table 1. *Thirty-day, 12-month and lifetime prevalence estimates of DSM-IV/CIDI MDE by age and sex*

	Age groups (years)					Age difference:
	All ages	18–34	35–49	50–64	⩾65	$\chi^2(3)$
I. Total						
30-day	3.1 (0.2)	3.7 (0.3)	3.7 (0.3)	3.0 (0.4)	1.0 (0.3)	46.9*
12-month	8.3 (0.3)	10.4 (0.5)	9.4 (0.5)	7.7 (0.7)	2.6 (0.4)	103.5*

Kessler et al., *Psychol Med* 2010

Part 1, conclusion:

- Use of CNS-active medication among older adults is going up across the board

DTM1

Part 2: focusing specifically on benzodiazepines

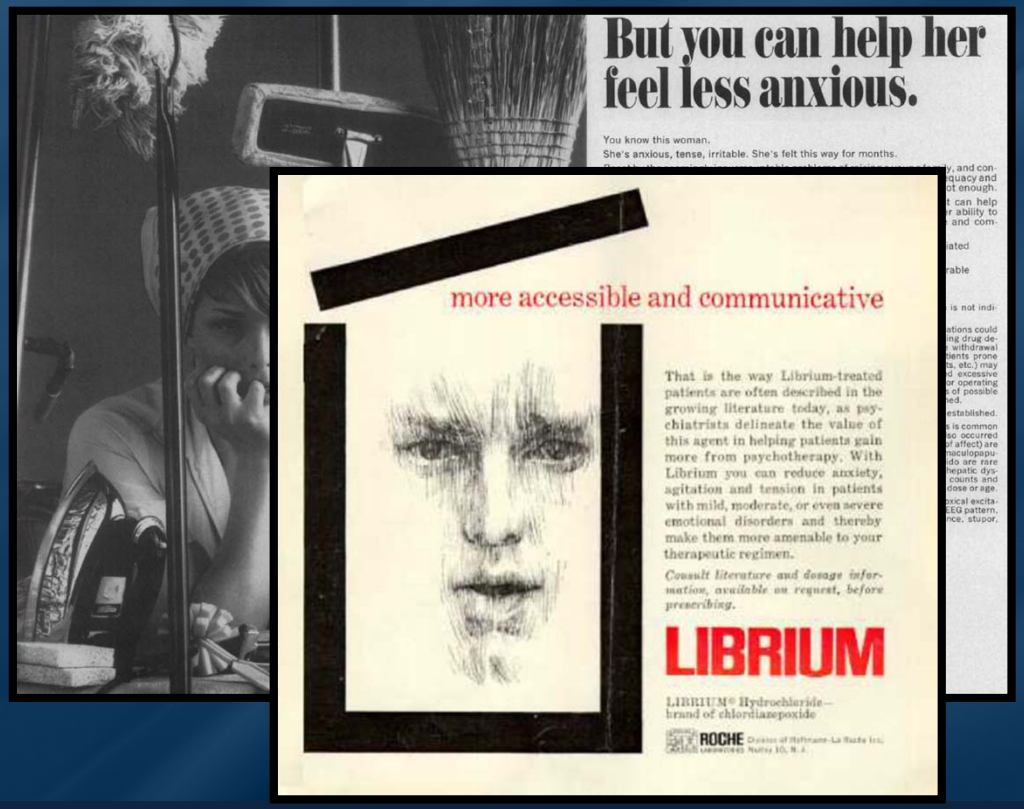
Slide 6

DTM1 Need a reference here re: efficacy
Donovan Maust, 9/18/2017

What are benzodiazepines?

- In use since the 1960s to treat anxiety and as sleep aids.
- People feel better, and they feel better quickly.
- DEA schedule IV (can be refilled up to 5x in 6 months)

➢ Ativan (lorazepam)
➢ Xanax (alprazolam)
➢ Klonopin (clonazepam)



What is the problem with BZD?

- Decades of evidence re: fall risk in older adults (e.g., *JAMA* paper in 1989)[1,2]
- Motor vehicle accidents[3]
- Overdose (OD) deaths[4]
- Impaired cognition (+/- evidence for dementia)[5]
- Reduce the efficacy of psychotherapies for insomnia, PTSD

DTM [2]1

→

In studies of short-, intermediate- and long-acting benzodiazepine drugs (n = 68 trials), these drugs consistently induced both amnestic and non-amnestic cognitive impairments, with evidence of a dose-response relationship.

1. Woolcott JC et al., *Arch Int Med* 2009. 2. Wang PS et al., *AJP* 2001. 3. Dassanayake T, *Drug Saf* 2011. 4. Jones et al., *JAMA* 2010. 5. Tannenbaum C et al., *Drugs Aging* 2012.

Slide 8

DTM [2]1 Need a reference here re: efficacy
Donovan Maust, 9/18/2017

Based on all the evidence for harms:

Multiple guidelines and professional organizations say to avoid:

1. Have been on Beers Criteria in some form since first developed in 1990s. Since 2012 version, all BZD considered potentially inappropriate except for a few specific indications.
2. Choosing Wisely (www.choosingwisely.org) recommendation against their use
3. VA/DoD Clinical Practice Guideline for PTSD = “strong against”

So it's really easy to get patients to stop?

Patients:

- "I don't mentally think I would have survived without it and that's the truth."
- "It makes me feel like I wanna go on living."
- "[My physician] wouldn't have given it to me if he thought it was gonna hurt me."
- "I'm not gonna experiment with myself, not at this age."

Cook et al., *JGIM* 2007

Doctors are taking all their patients off them?

Doctors:

- “If it works and she doesn’t abuse it, who cares?”
- “It’s literally like taking candy from a baby . . . I can’t lose patients over this.”
- “It’s just so much easier to just prescribe something and just walk away.”

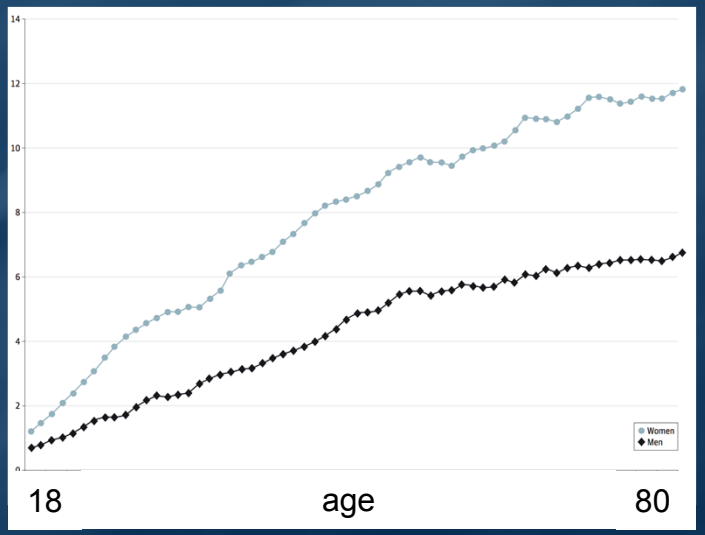
Cook et al., *JGIM* 2007

Who gets prescribed BZD?

The people most at risk (older adults) use the most

because

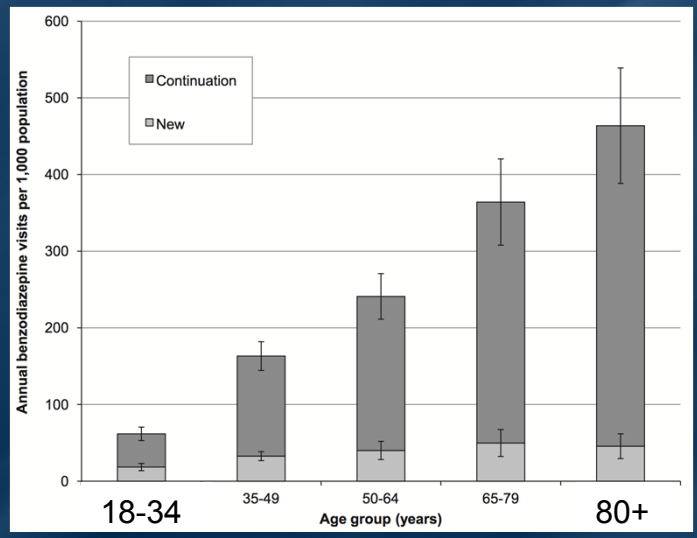
Use accumulates with age



women
12%

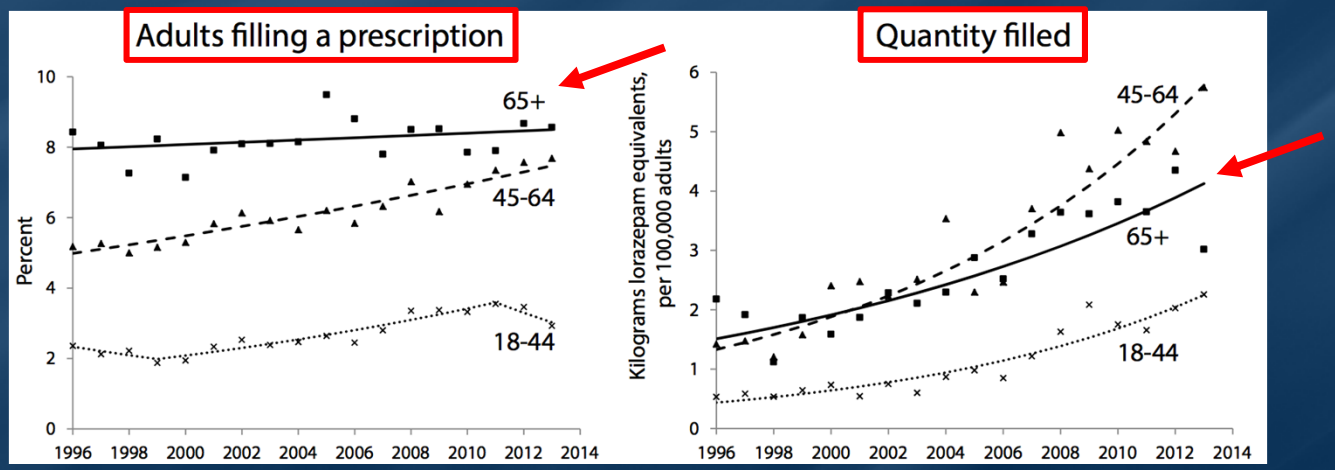
men
7%

Olfson et al., *JAMA Psychiatry* 2015



Maust et al., *JAGS* 2016

Bad News 1: use is not going down

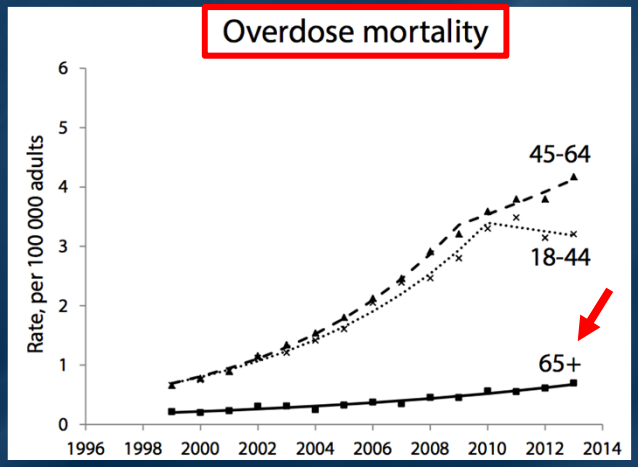


Bachhuber et al., *AJPH* 2016

Bad News 2: bad outcomes are going up

Coben et al. analysis of Nationwide Inpatient Sample from 1999-2006:

- U.S. hospitalizations for prescription drug poisoning (i.e., OD) up 65%
- Largest increase = benzodiazepines (up 39%)
- Patients less likely to live in large urban area



Bachhuber et al., *AJPH* 2016

For whom is BZD use rising?

- Men
- White
- Pain
- No diagnosis

	Primary Care (n=14,282)				
	2003-2005	2010-2012	Adjusted[a]		
	%[b]	%[b]	OR	95% CI	p
Overall[c]	**5.6**	**8.7**	**1.62**	**1.30-2.02**	**<0.001**
Demographics					
Age					
65-74 years	5.1	7.9	1.59	1.16-2.17	0.004
75-84 years	5.8	8.8	1.66	1.23-2.24	0.001
85+ years	6.8	11.5	1.60	0.96-2.66	0.07
Sex					
Male	3.8	7.1	1.88	1.30-2.71	0.001
Female	6.7	10.0	1.52	1.20-1.93	0.001
Ethnicity					
Non-Hispanic white	5.8	9.4	1.69	1.33-2.16	<0.001
Non-Hispanic black	4.4	3.9	0.72	0.30-1.75	0.48
Hispanic	4.4	7.0	1.66	0.86-3.18	0.13
Clinical Characteristics					
Diagnoses[d]					
Depression	15.8	24.2	1.72	0.87-3.43	0.12
Anxiety	44.6	48.1	1.22	0.62-2.42	0.57
Insomnia	9.5	22.1	2.19	0.62-7.78	0.22
Dementia	7.2	14.9	2.01	0.46-8.76	0.35
Pain	5.9	10.0	1.74	1.19-2.56	0.005
No mental health or pain dx	4.5	6.9	1.62	1.27-2.06	<0.001
Other psychotropic medication					
Antidepressant	15.7	19.6	1.36	0.91-2.02	0.13
Other anxiolytic/sedative-hypnotic	12.9	11.7	0.93	0.46-1.89	0.83

Maust et al., *JCP* 2017

What about BZD + other meds?

Table 3. Association of clinical and visit characteristics with benzodiazepine use among older adult patients of non-psychiatrist physicians in the U.S. from 2007-2010 (n=32,544)

				Adjusted[a]	
Clinical Characteristic	Visits with benzodiazepines (n=1,748)	Visits without benzodiazepines (n=30,796)	p	OR[b]	95% CI
Other psychotropic medication					
Antidepressant	26.9	7.8	<.001	4.1	3.6-4.8
Antipsychotic	2.6	.8	<.001	3.3	2.1-5.2
Opioid	10.0	2.9	<.001	3.6	2.5-5.0
Mean total continued medications (SEM[e])	4.6 (.1)	3.6 (.1)	<.001	1.1	1.1-1.2

Maust et al., *JAGS* 2016

What's bad about combining BZD + other med?

- New Beers Criteria measure for CNS-active polypharmacy (includes opioids, antidepressants, BZD, Z-drugs)
    - Higher burden = greater risk for falls[1] and cognitive decline[2]
- BZD + opioids = #1 pharmaceutical combo for OD deaths[3]
- August 2016 black-box warning from U.S. FDA re: increased risk of respiratory suppression and death from opioids + CNS-depressants, incl:
    - BZD
    - Antipsychotics
    - Muscle relaxants

1. Hanlon et al., *J Gerontol Series A* 2009. 2. Wright et al., *JAGS* 2009. 3. Jones et al., *JAMA* 2010.

What has happened to combo prescribing?

It has gone up.
(noticing a trend?)

	CNS polypharmacy visits per 100 visits[b]				
	2004-2006	2007-2010	2011-2013	AOR[c]	(95% CI[d])
OVERALL (n=97,910)	**0.6**	**1.0**	**1.4**	**3.12**	**(2.28-4.28)**
Demographics					
Age					
65-74 years	0.8	1.0	1.4	2.40	(1.59-3.63)
75-84 years	0.5	0.8	1.5	4.28	(2.44-7.51)
85+ years	0.4	1.1	1.5	4.15	(2.04-8.43)
Sex					
Male	0.4	0.7	1.1	3.10	(1.73-5.57)
Female	0.8	1.1	1.7	3.15	(2.25-4.40)
Ethnicity					
Non-Hispanic white	0.6	1.0	1.5	3.23	(2.33-4.46)
Non-Hispanic African-American	0.5	0.7	0.9	1.74	(0.51-5.99)
Hispanic	0.7	1.0	1.7	3.28	(0.93-11.59)
Dual-eligible					
Yes	0.8	0.5	0.7	0.46	(0.03-6.63)
No	0.6	1.0	1.5	3.21	(2.37-4.34)
Geography					
Urban	0.6	0.9	1.4	2.91	(2.03-4.17)
Rural	0.7	1.0	2.2	4.99	(2.67-9.33)

Maust DT et al., *JAMA IM* 2017.

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	2004-2006	2007-2010	2011-2013	AOR[c]	(95% CI[d])
OVERALL (n=97,910)	**0.6**	**1.0**	**1.4**	**3.12**	**(2.28-4.28)**
Clinical Characteristics[e]					
Anxiety	8.9	4.4	5.4	0.65	(0.21-1.96)
No anxiety	0.6	0.9	1.4	3.31	(2.39-4.60)
Insomnia	7.6	3.9	5.3	0.78	(0.16-3.93)
No insomnia	0.6	0.9	1.4	3.18	(2.31-4.37)
Depression	6.7	6.7	10.4	1.31	(0.66-2.60)
No depression	0.5	0.8	1.3	3.24	(2.28-4.60)
Dementia	1.2	2.2	2.4	2.14	(0.55-8.27)
No dementia	0.6	0.9	1.4	3.11	(2.26-4.29)
Substance use disorder	0.5	3.3	2.3	2.63	(0.43-16.01)
No substance use disorder	0.6	0.9	1.4	3.13	(2.28-4.30)
Pain	0.9	1.8	2.8	4.54	(2.59-7.97)
No pain	0.6	0.8	1.2	2.64	(1.82-3.83)
Any mental health or pain dx	1.5	2.3	3.6	3.34	(2.25-4.94)
No mental health or pain dx	0.4	0.6	0.9	2.65	(1.65-4.27)
Visit Characteristics					
Provider					
Family practice	0.9	0.9	2.3	3.92	(2.04-7.55)
Internal medicine	0.6	1.3	1.4	2.48	(1.31-4.72)
Psychiatry	7.7	8.9	8.2	0.92	(0.40-2.14)
Other medical specialty	0.4	0.7	1.0	3.72	(2.14-6.46)

Part 2, conclusion:

- Benzodiazepine use is growing, both alone and in combination
- Medication poisoning (OD) and mortality also appear to be growing
- Use is growing in patients with pain but also those w/o any clear mental health diagnosis
    - ????

Part 3: What exactly are all those benzodiazepines being prescribed for?

Good Question. I'm not sure.

Table 4. Association of clinical and visit characteristics with continuation versus new benzodiazepine use among older adult patients of non-psychiatrist physicians in the U.S. from 2007-2010 (n=1,748)

				Adjusted[a]	
Clinical Characteristic	Continuation benzodiazepines (n=1,559)	New benzodiazepines (n=189)	p	OR[b]	95% CI
Diagnoses/visit complaint					
Anxiety, %[c]	6.4	21.3	<.001	.2	.1-.3
Insomnia	2.3	11.6[d]	<.001	.2	.1-.4
Depression	5.0	6.4[d]	.54	.7	.3-1.7
Dementia	.6[d]	.2[d]	.11	3.0	.6-14.1
Substance use disorder	.4[d]	1.1[d]	.35	.4	.0-3.7
Any mental health diagnosis	16.0	40.3	<.001	.2	.2-.4

Maust et al., *JAGS* 2016

What do their charts say?

Study of older adults in primary care prescribed a new BZD.

- Chart review to see why the med was started

<50% is for anxiety or insomnia

	Number	Percentage of all new users
Total	200	100
Anxiety/~~depression/ situational stress~~	54	27
Insomnia	30	20
~~Back/neck pain~~	27	13.5
~~Headache or other~~ pain	49	24.5
~~No indication give~~	30	15

Simon et al., *J Clin Epi* 1996

What about BZD for anxiety or ~~insomnia?~~

Psychotherapy generally works as well or better.

Co-prescribing BZD may reduce the benefit of the therapy.

Insomnia:

McClusky et al., *AJP* 1991:

- Medication helped right away, sleep problem returned when stopped
- Behavioral treatment helped starting 2nd week, maintained improvement

Morin et al., *JAMA* 2009:

- Potential benefit from therapy + med initially (6wks)
- But during 6mo follow-up, those who had therapy + med as needed had MORE sleep problems than those with monthly therapy booster

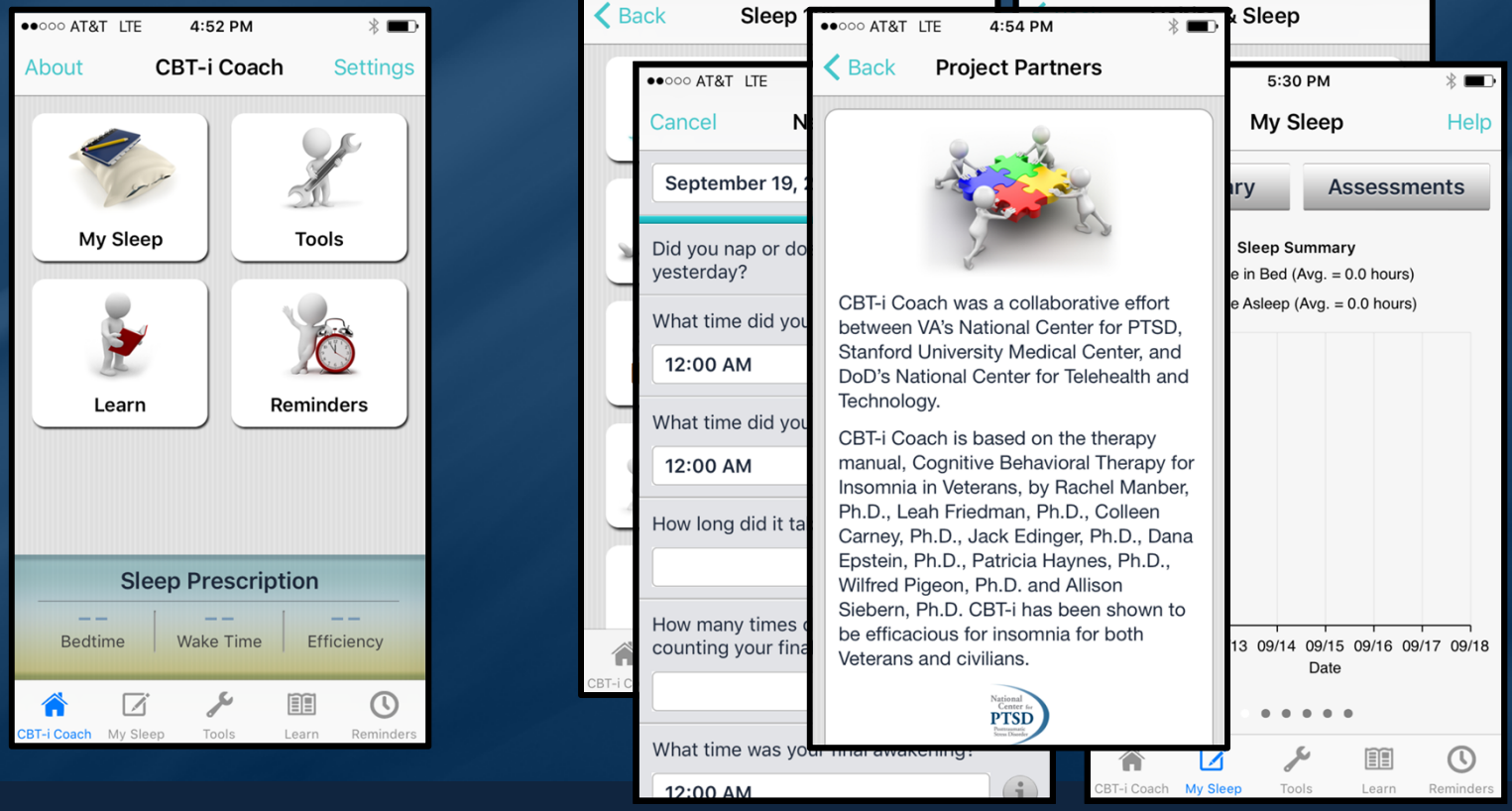
What does therapy for insomnia look like?

Table 1. Summary of CBT-I Components

CBT-I Component[a]	Treatment Goal
Behavioral	
Stimulus control	Reestablish the bed/bedroom as a stimulus for sleep
Sleep restriction	Reduce time in bed to increase homeostatic sleep drive, thereby improving sleep efficiency and consolidating sleep
Cognitive	
Cognitive therapy	Address maladaptive thoughts and dysfunctional beliefs that interfere with sleep and daytime functioning
Optional	
Sleep hygiene	Eliminate habits that are counterproductive for sleep
Relaxation training	Reduce physiologic and cognitive arousal

Wu et al., *JAMA IM* 2015

CBT-i Coach


AT&T LTE 4:52 PM
About
CBT-i Coach
Settings
My Sleep
Tools
Learn
Reminders
Sleep Prescription
Bedtime
Wake Time
Efficiency
CBT-i Coach
My Sleep
Tools
Learn
Reminders
Back
Project Partners
CBT-i Coach was a collaborative effort between VA's National Center for PTSD, Stanford University Medical Center, and DoD's National Center for Telehealth and Technology.
CBT-i Coach is based on the therapy manual, Cognitive Behavioral Therapy for Insomnia in Veterans, by Rachel Manber, Ph.D., Leah Friedman, Ph.D., Colleen Carney, Ph.D., Jack Edinger, Ph.D., Dana Epstein, Ph.D., Patricia Haynes, Ph.D., Wilfred Pigeon, Ph.D. and Allison Siebern, Ph.D. CBT-i has been shown to be efficacious for insomnia for both Veterans and civilians.
5:30 PM
My Sleep
Help
Assessments
Sleep Summary
09/14 09/15 09/16 09/17 09/18
Date
Cancel
September 19,
12:00 AM
12:00 AM

What about BZD for ~~anxiety~~ or ~~insomnia?~~

Psychotherapy generally works as well or better; alternative meds are as good or better.

Panic disorder: Gould et al, *Clin Psychol Review* 1995:

- Largest effect from therapy (CBT) alone; also best at maintaining improvement
- BZD no better than antidepressants

PTSD: Guinda et al., *J Psychiatr Practice* 2015:

- *"BZDs are associated with specific problems in patients with PTSD: worse overall severity, significantly increased risk of developing PTSD with use after recent trauma, worse psychotherapy outcomes, aggression, depression, and substance use"*

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Many different alternatives for anxiety:

Information from the VA's Academic Detailing Service

CBT
SSRIs

Management of anxiety and trauma related disorders					
	Generalized Anxiety Disorder	**Obsessive Compulsive Disorder**	**Panic Disorder**	**Social Anxiety Disorder**	**Posttraumatic Stress Disorder**
Non-drug treatments	CBT ← Exposure therapy Applied relaxation	Exposure therapy CBT ←	CBT ←	CBT ← Exposure therapy	CPT Prolonged exposure EMDR
First-line medication treatment options	SSRIs ← SNRIs Buspirone Mirtazapine Pregabalin	SSRIs ← Clomipramine	SSRIs ← Venlafaxine	SSRIs ← Venlafaxine	SSRIs ← Venlafaxine
Other non-benzodiazepine medication treatment options (limited by evidence or side effects)	Hydroxyzine Quetiapine	Mirtazapine Venlafaxine Augmentation of SSRI: - Antipsychotics - Lamotrigine - Topiramate	Mirtazapine TCA	Gabapentin Pregabalin Propranolol*	Mirtazapine TCA Nefazodone Prazosin (nightmares)

CBT = Cognitive Behavioral therapy; CPT = Cognitive Processing Therapy; EDMR = Eye Movement Desensitization and Reprocessing; SSRI=Selective Serotonin Reuptake Inhibitor; SNRI= Selective Norepinephrine Reuptake Inhibitor; TCA= Tricyclic Antidepressant; * Performance anxiety only. Benzodiazepines may be used for short-term emergency management of generalized anxiety and panic disorders and may be useful on an as needed basis for the management of social anxiety disorders.

But do patients actually need any alternative?

Curran et al., *Psychol Med* 2003:

- 104 chronic users (avg = 13.5 years)
- Gradual taper over ≥2 months
- Group that stopped had improved cognitive performance compared to continuers
- Anxiety, irritability, lack of energy WORSE in group that continued; no change in sleep

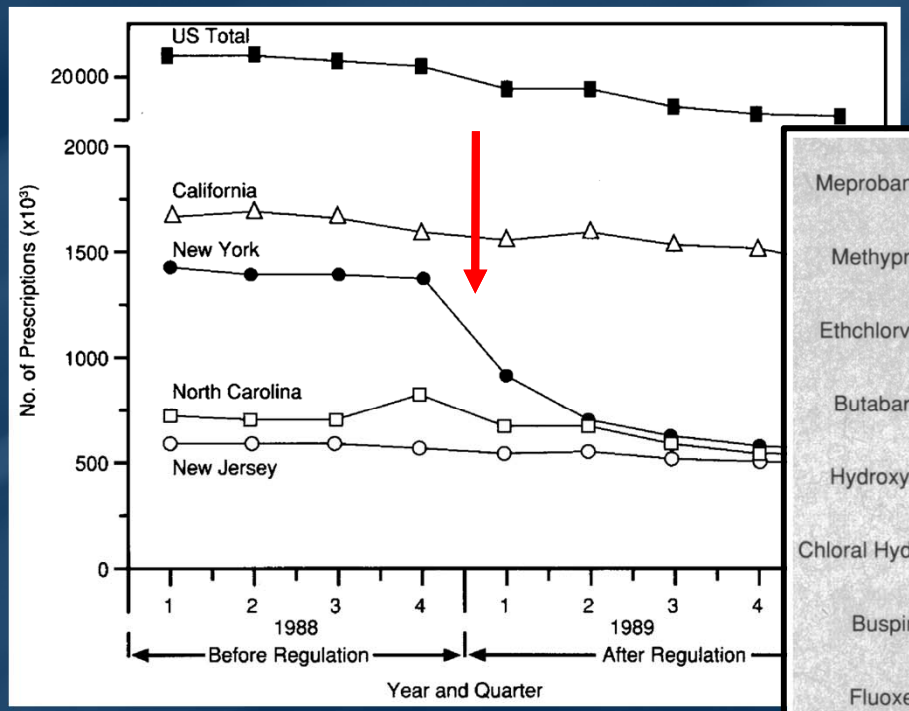
When patients have been prescribed for years or DECADES, impossible to know what has happened to the underlying symptoms.

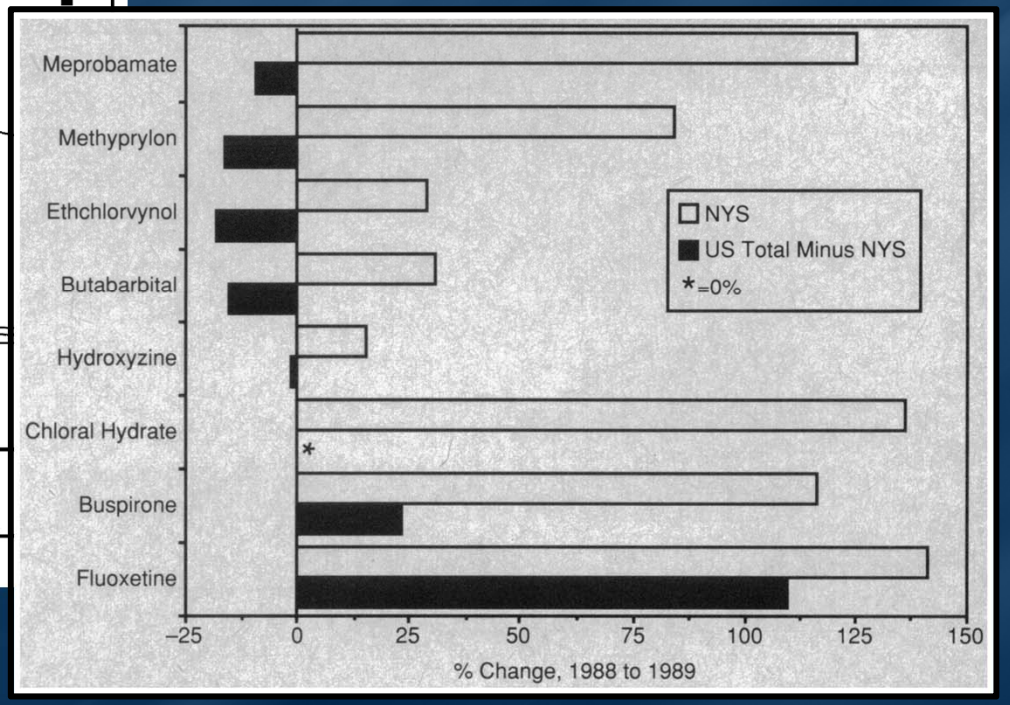
Part 4: How to address the prescribing?

Policy approach: NY state

New York state's triplicate prescribing policy

- Started in 1989; had been required for all schedule II drugs
- Special pad to registered practitioners
- Physician retains copy for 5 years
- Pharmacist keeps 1 copy, forwards 2nd to DOH
- With few exceptions, all Rx for 30-day supply only with NO refills
- This all generally still applies with e-prescribing (e.g., 30d supply, no refills)

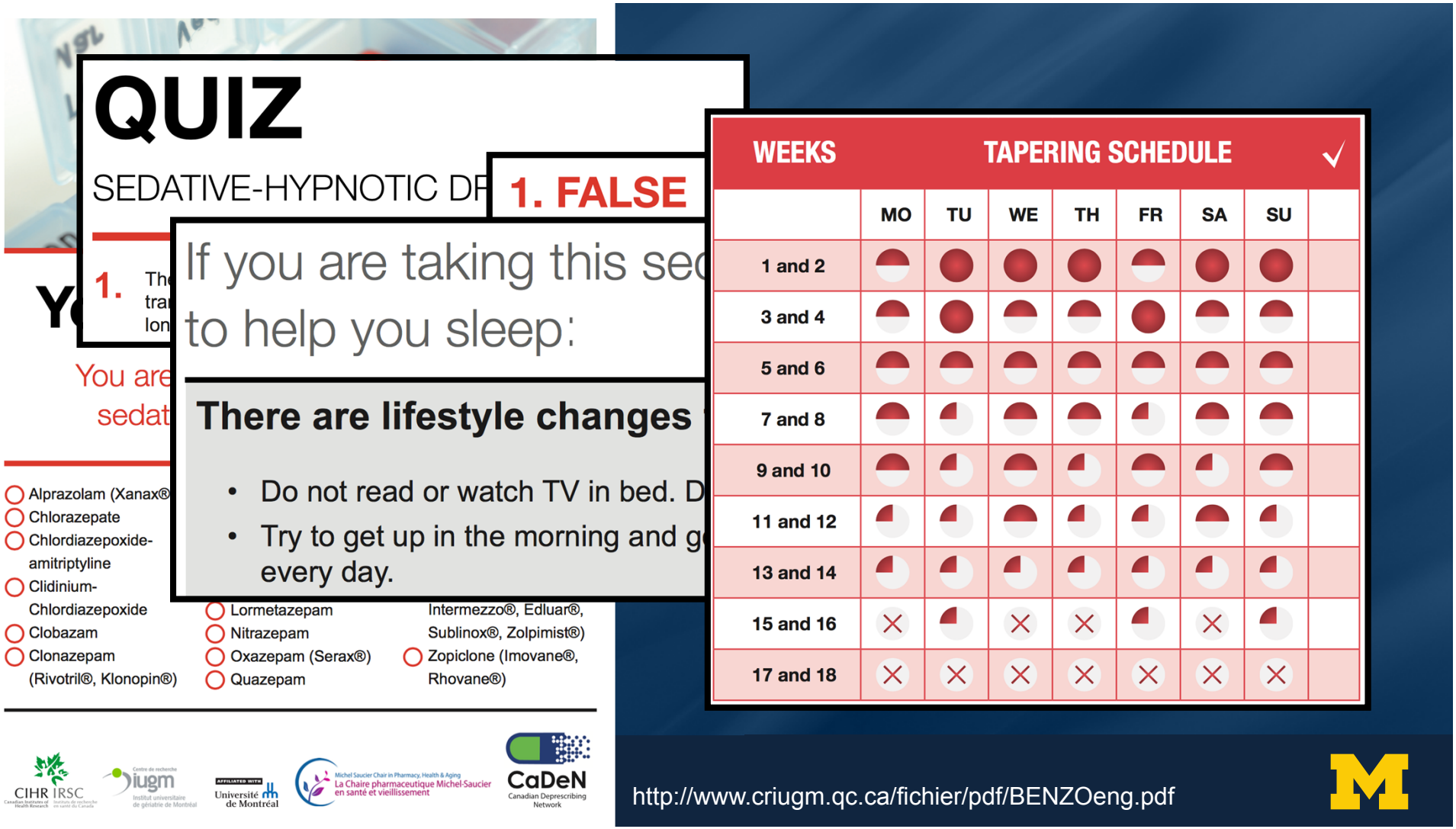




Weintraub et al., *JAMA* 1991

Educational approach (targeting pt): EMPOWER

- Tannenbaum et al., *JAMA IM* 2014.
- Randomized clinical trial in Quebec, Canada
- Adults ≥65 on long-term BZD therapy (defined as Rx for ≥3 months before the study)
    - Average patient 75y
    - Prescribed BZD for 10 years
    - 60% for insomnia; 45% anxiety
    - On total of 10 prescription medications


QUIZ
SEDATIVE-HYPNOTIC DR
1. FALSE
1. Th
tra
lon
If you are taking this sed
to help you sleep:
There are lifestyle changes
• Do not read or watch TV in bed. D
• Try to get up in the morning and g
every day.
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sedat
Alprazolam (Xanax®
Chlorazepate
Chlordiazepoxide-amitriptyline
Clidinium-Chlordiazepoxide
Clobazam
Clonazepam (Rivotril®, Klonopin®)
Lormetazepam
Nitrazepam
Oxazepam (Serax®)
Quazepam
Intermezzo®, Edluar®, Sublinox®, Zolpimist®)
Zopiclone (Imovane®, Rhovane®)
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La Chaire pharmaceutique Michel-Saucier en santé et vieillissement
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7 and 8
9 and 10
11 and 12
13 and 14
15 and 16
17 and 18
http://www.criugm.qc.ca/fichier/pdf/BENZOeng.pdf

You May Be at Risk

You are taking one of the following sedative-hypnotic medications:

- Alprazolam (Xanax®)
- Chlorazepate
- Chlordiazepoxide-amitriptyline
- Clidinium-Chlordiazepoxide
- Clobazam
- 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®, Sublinox®, Zolpimist®)
- Zopiclone (Imovane®, Rhovane®)

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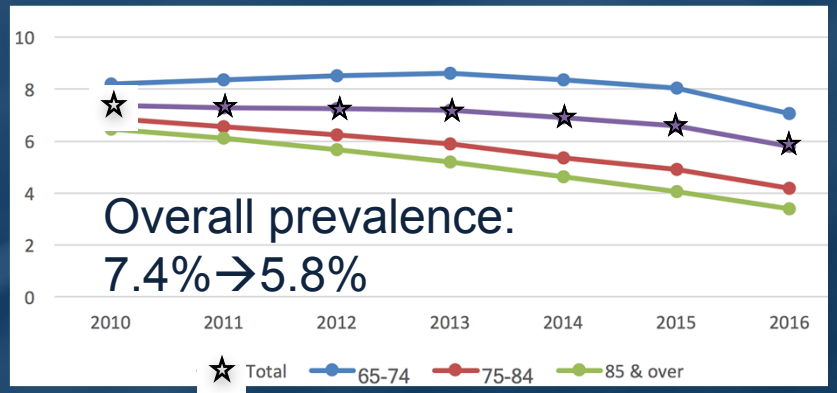
Results:

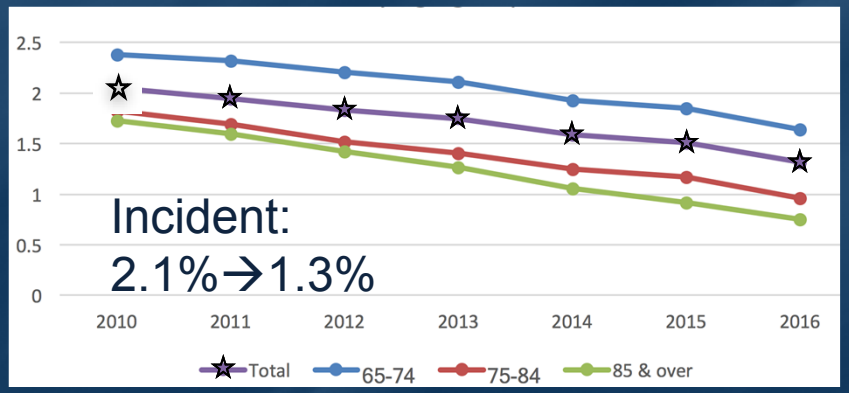
- At 6 months, 27% of patients had stopped their BZD (compared to 5% in the control group)
- Another 11% reduced their dose.

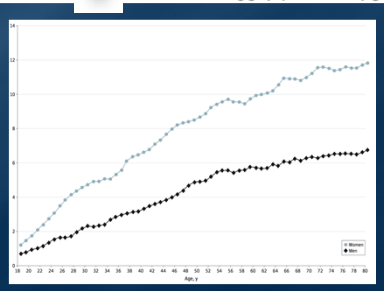
A real-world success story? The VA.

PREVALENT



INCIDENT





- Unlike general population, use in Veterans lowest among the old-old

What is going on in the VA?

- Public attention is very motivating.
- Strong, top-down emphasis on safe/appropriate prescribing:
    - Opioid Safety Initiative
    - Psychotropic Drug Safety Initiative

- What can we learn from approaches by facilities within the VA that appear to be helping reduce BZD prescribing?

Conclusions:

1. What is happening with psychotropic and opioid use for older adults?
    - It is all going up, with pronounced growth for white patients and men
2. Focus on benzodiazepine prescribing.
    - Particularly concerning growth among middle-aged adults with associated bad outcomes (OD/death)
3. What exactly is being treated and what are the alternatives?
    - Sleep, anxiety, pain, and __?__
    - Other, safer options for all of these indications
4. How to address prescribing?
    - For some patients, education may be enough
    - Careful of unintended shifts in prescribing
    - Stay tuned for lessons from the VA

Acknowledgments

U-M Funding: Beeson Career Development Award Program (NIA K08AG048321, the American Federation for Aging Research, The John A. Hartford Foundation, and The Atlantic Philanthropies)

Fred Blow, PhD
Helen C. Kales, MD
Lauren Gerlach, DO
Mark Olfson, MD, MPH

VA Funding: Office of Reporting, Analytics, Performance, Improvement and Deployment (RAPID) (10EA)

Eve Kerr, MD, MPH
Tim Hofer, MD, MS
Fred Blow, PhD
Amy Bohnert, PhD
Rose Ignacio, MS

Thank you!

maustd@umich.edu
@dtmaust