Buprenorphine Treatment in the Primary Care Setting: Cases and Clinical Issues

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Disclosures

- None

Buprenorphine History

- Synthesized in 1969—derived from thebaine
- First marketed for pain in the early 1970s
- Marketed for addiction first in France 1995; in the US in 2003 (DATA 2000)
- Available in a variety of strengths and dosage forms; with and without naloxone

Buprenorphine History

- Also available in transdermal patch (Butrans) and buccal (Belbuca)--not approved for addiction
- In 2010, of 23,000 doctors with waiver only about half had ever written a prescription.
- 20% treat fewer than 3 patients and < 10% treat more than 75

A side note on pain

Journal of
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Commentary

The clinical analgesic efficacy of buprenorphine

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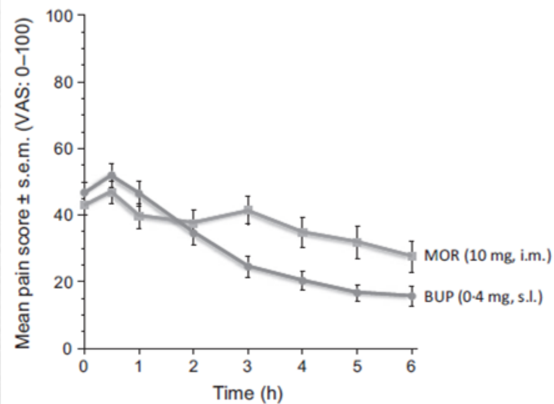
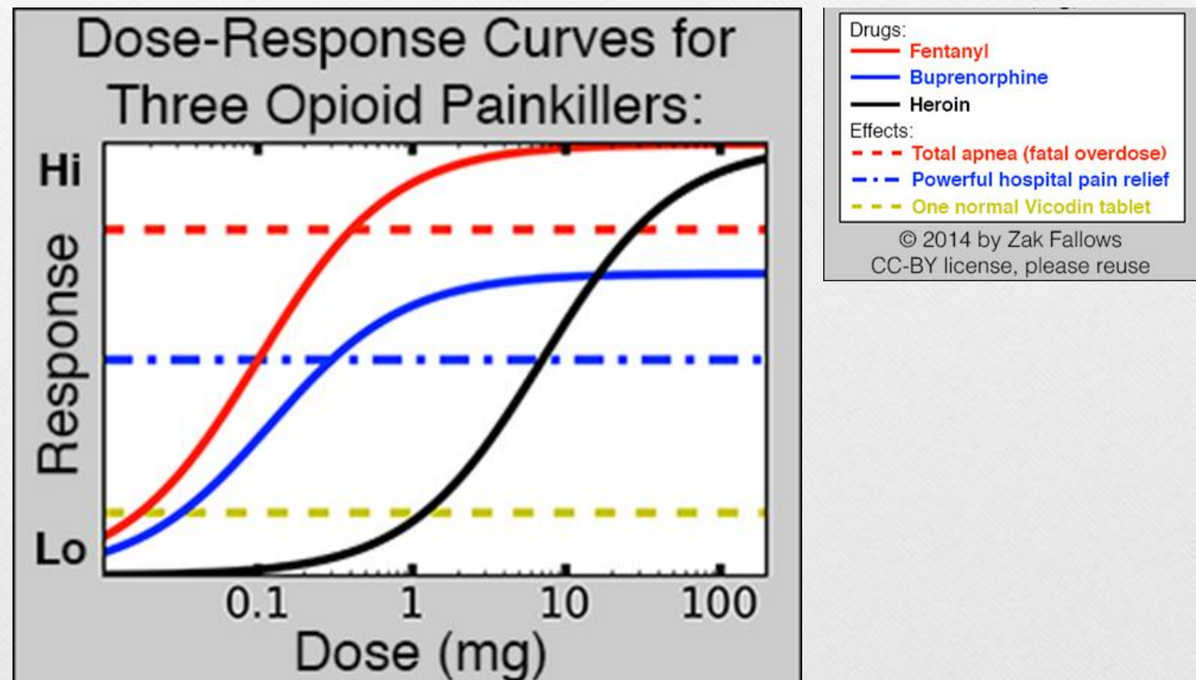


Fig. 2. The analgesic efficacy of s.l. buprenorphine (0·4 mg) was compared with that of i.m. morphine (10 mg) in a randomized, double-blind study of post-op pain of 101 patients (mean age: 40–45 years). Pain was measured using a 10-cm pain scale (0 = none, 10 = as much as imaginable). Buprenorphine produced the same pain relief as did morphine during the first 2 h and modestly greater pain relief from 2 to 6 h. Redrawn from Edge *et al.*[22]

But isn’t buprenorphine a partial agonist?



Take-home point about pain

There is no compelling evidence that there is a ceiling effect for **analgesia**, though there is lots of clinical lore

There *is* a ceiling effect for respiratory depression

Kappa antagonism may help with opioid induced hyperalgesia

Back to Opioid Use Disorder

You've all heard about the twin epidemics of opioid addiction and overdose.

Back to Opioid Use Disorder

Opioid use disorder is *endemic* in Baltimore: it persists and is transmitted across generations and sociodemographic groups.

Maryland localities outside of Baltimore are struggling as well

Table 6. Number of Opioid-Related Intoxication Deaths[1,2] by Place of Occurrence, Maryland, 2007-2016 and YTD 2017 Through September.[3]

Jurisdiction	Opioid Intoxication Deaths										
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017 YTD
Maryland Total	628	523	570	504	529	648	729	888	1,089	1,856	1,501
Allegany	12	7	6	11	8	10	11	11	20	55	29
Anne Arundel	54	57	45	44	53	68	67	85	89	169	145
Baltimore City	256	154	199	139	142	189	212	275	354	628	523
Baltimore County	95	92	83	95	93	104	125	146	195	305	238
Calvert	12	6	11	4	10	11	5	16	19	25	15
Caroline	0	2	1	2	8	4	2	7	3	9	7
Carroll	12	15	16	12	7	27	21	29	34	44	39
Cecil	23	9	21	21	24	22	22	25	26	28	43
Charles	8	9	10	9	10	12	9	16	17	36	24
Dorchester	2	3	1	6	2	5	5	0	1	5	8
Frederick	12	7	18	12	28	23	33	34	37	80	46
Garrett	0	2	3	1	1	0	4	2	4	0	3
Harford	24	31	28	38	28	32	34	38	45	76	72
Howard	14	13	11	9	18	17	26	18	25	40	35
Kent	2	4	2	3	1	0	4	3	3	4	4
Montgomery	35	29	31	25	28	36	40	53	59	84	60
Prince George's	27	33	38	27	24	30	38	48	45	106	93
Queen Anne's	4	2	3	4	4	2	7	9	4	6	5
Somerset	5	3	2	1	3	2	4	2	4	6	3
St. Mary's	3	9	7	10	6	9	10	8	12	13	28
Talbot	3	3	2	2	1	3	6	4	5	10	8
Washington	11	21	14	13	16	20	26	34	57	63	36
Wicomico	6	7	10	10	10	17	14	15	17	44	23
Worcester	8	5	8	6	4	5	4	10	14	20	12
Unknown	0	0	0	0	0	0	0	0	0	0	2

[1]Includes deaths that were the result of recent ingestion or exposure to prescription and illicit opioids.

[2]Includes only deaths for which the manner of death was classified as accidental or undetermined.

[3]Counts for 2017 are not complete.

Figure 2. Number of Opioid-Related Deaths Occurring in Maryland from January through September of Each Year.*

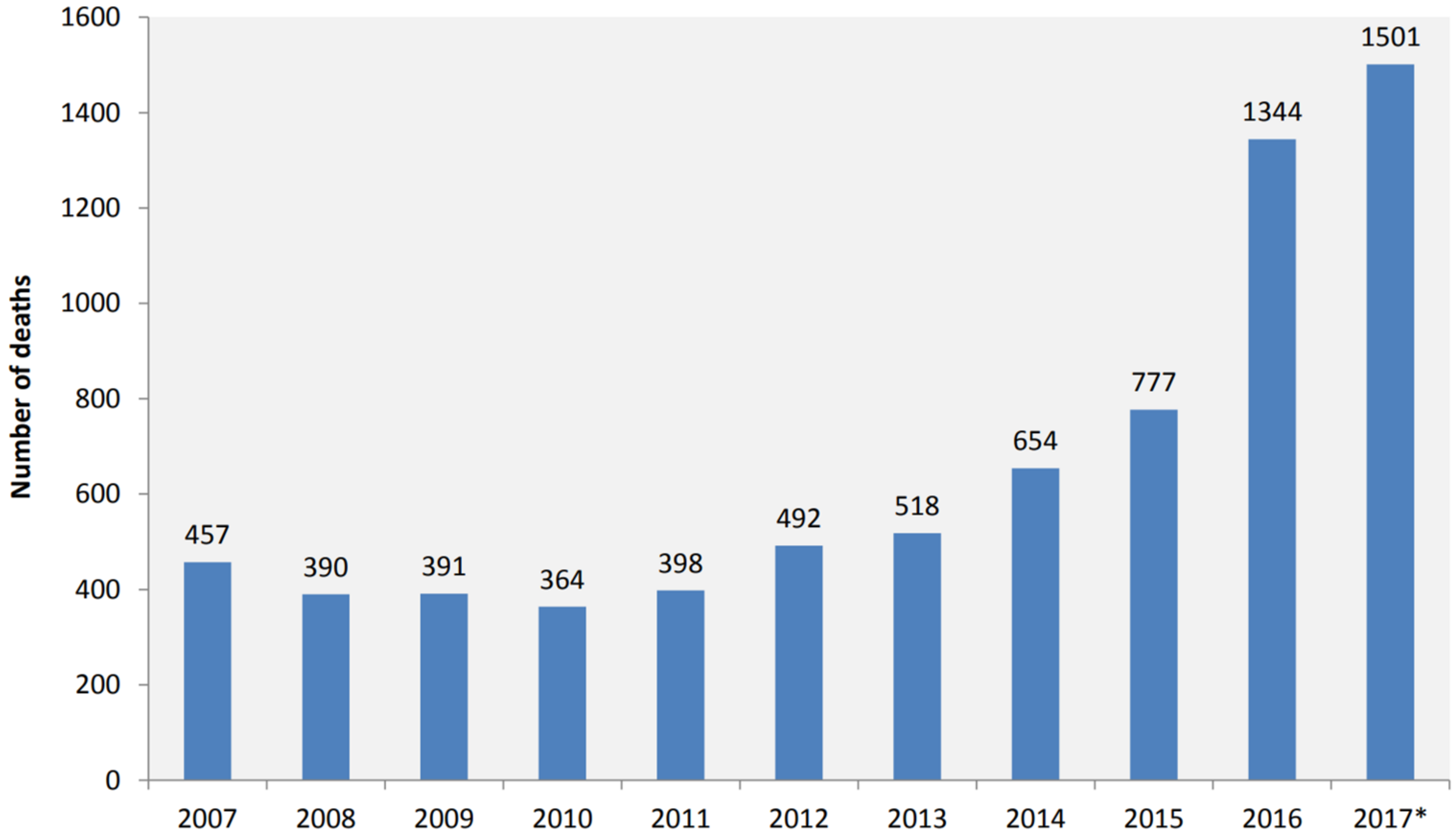


Table 8. Number of Fentanyl-Related Intoxication Deaths[1,2] by Place of Occurrence, Maryland, 2007-2016 and YTD 2017 Through September.[3]

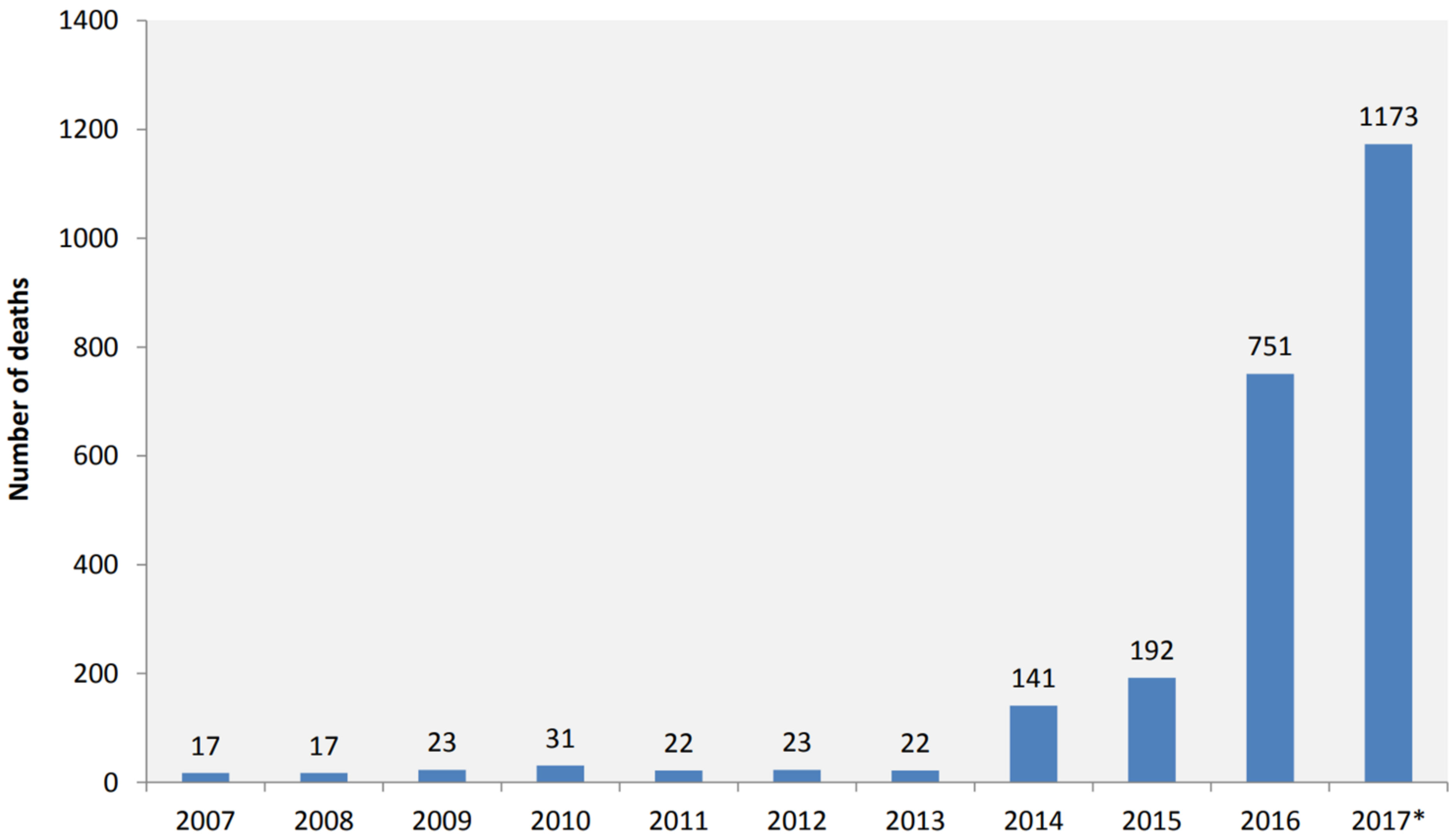
Jurisdiction	Fentanyl Intoxication Deaths										
	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017 YTD
Maryland Total	26	25	27	39	26	29	58	186	340	1,119	1,173
Allegany	3	0	1	2	1	1	1	1	5	29	22
Anne Arundel	3	5	3	5	2	3	6	23	29	98	108
Baltimore City	3	2	4	4	2	4	12	72	120	419	427
Baltimore County	6	9	9	6	4	5	11	36	65	182	185
Calvert	0	1	1	0	1	0	0	5	2	11	11
Caroline	0	0	0	1	4	0	0	0	1	3	6
Carroll	0	2	0	2	0	1	2	4	11	20	30
Cecil	2	1	0	2	2	0	0	1	7	9	32
Charles	0	0	0	0	1	1	3	1	4	17	17
Dorchester	0	0	0	2	0	0	2	0	1	3	5
Frederick	0	0	0	2	3	1	2	6	11	49	33
Garrett	0	1	0	0	1	0	0	0	2	0	1
Harford	1	1	0	3	2	1	1	2	16	46	55
Howard	1	0	0	0	0	2	3	5	7	27	25
Kent	0	0	0	0	0	0	0	1	0	3	3
Montgomery	2	0	1	1	0	2	0	8	17	43	46
Prince George's	1	0	2	2	0	1	6	7	15	58	77
Queen Anne's	1	0	0	0	0	0	1	1	0	4	4
Somerset	1	1	0	1	0	0	2	0	1	6	3
St. Mary's	0	0	1	1	1	0	1	3	3	4	23
Talbot	1	1	0	1	0	1	0	2	2	7	3
Washington	0	0	0	2	1	1	4	1	14	31	27
Wicomico	1	1	3	1	1	4	1	7	1	34	19
Worcester	0	0	2	1	0	1	0	0	6	16	9
Unknown	0	0	0	0	0	0	0	0	0	0	2

[1]Includes deaths that were the result of recent ingestion or exposure to prescription or illicit fentanyl.

[2]Includes only deaths for which the manner of death was classified as accidental or undetermined.

[3]Counts for 2017 are not complete.

Figure 4. Number of Fentanyl-Related Deaths Occurring in Maryland from January through September of Each Year.*



Diagnosis of OUD (DSM5)

Opioid Use Disorder
Diagnostic Criteria

A problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.

Diagnosis of OUD (DSM5)

7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of opioids to achieve intoxication or desired effect.
    b. A markedly diminished effect with continued use of the same amount of an opioid.

    Note: This criterion is not considered to be met for those taking opioids solely under appropriate medical supervision.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic opioid withdrawal syndrome (refer to Criteria A and B of the criteria set for opioid withdrawal).
    b. Opioids (or a closely related substance) are taken to relieve or avoid withdrawal symptoms.

Diagnosis of OUD (B-more)

- "I'm Tired"

Levels of Care

- White-knuckling/cold turkey
- Self-help/12-step
- Pharmacotherapy--OBOT vs OTPs
- Outpatient and Intensive Outpatient
- Day Hospitalization
- Residential Treatment
- Supportive housing (often coupled with OP, IOP, or day hospitalization)

Special Rules on Confidentiality

- 42 CFR Part 2 supersedes HIPAA
- Need written release to disclose participation in drug/alcohol treatment
- A program is covered by “Part 2” if there are “medical personnel or other staff...whose primary function is the provision of alcohol or drug abuse diagnosis, treatment or referral for treatment and who are identified as such providers.” (42 CFR § 2.11 (b), (c))

How to treat OUD with buprenorphine/naloxone

- Start
- Stabilize
  - Regular visits and monitoring
  - Appropriate level of care
- Continue
  - Regular visits and monitoring
  - Appropriate level of care

Cases

Case 1: Mike

48 year old M, HIV & HCV Ab positive. On HAART.

CC: "I'm tired."

HPI: Intranasal heroin for 20 years. Past tx--two month-long stays in residential treatment (Gaudenzia and Tuerk House). On methadone for three weeks in 2010--didn't like having to go every day. Using 2-3 pills/day. Also smokes one blunt daily and ½ PPD Newports. Denies alcohol and other illicit drug use.

Case 1: Mike

Rapid urine toxicology: +fentanyl, +buprenorphine, +benzodiazepines, +THC

CMP: AST 75, ALT 85 (lab ULN 40)

No objective signs of withdrawal

Thoughts?

Case 1: Mike

"Oh yeah, I took like a tiny piece of a bute on Wednesday"

"I'm starting to feel sluggish."

"Benzos? I don't take pills. It must be in the scramble!"

Case 1: Mike

How to start?

MACS

1-855-337-6227 (MACS)

Maryland Addictions Consultation Service *Components:*

- Phone Consultation Service via telephone "Warm Line"
  - Clinical questions, resources, and general referral information
- Continuing Education
  - Training opportunities related to Opioid Use Disorders
- Resource & Referral Networking
  - Assistance identifying addiction and behavioral health resources that meet the needs of your patients

What type of questions are appropriate?

- ✓ Initiation and maintenance of buprenorphine
- ✓ Diagnostic questions
- ✓ Screening tools
- ✓ Psychopharmacology
- ✓ Alternative medication treatments
- ✓ Comorbid diagnoses
- ✓ Community resources and referrals

Case 1: Mike

"Oh yeah, I took like a tiny piece of a bute on Wednesday"

"I'm starting to feel sluggish."

"Benzos? I don't take pills. It must be in the scramble!"

Case 1: Mike

How to start?

Before doing the buprenorphine/naloxone part:

- a clinic-specific treatment agreement
- appropriate level of psychosocial care (per clinic policy and clinical assessment--cf. ASAM Criteria)
- establish expectations regarding other drugs of abuse, including alcohol
- Check the PDMP

Case 1: Mike

How to start?

Insurance note: Maryland MA will pay for 2 films/tablets per day of any dosage strength

Case 1: Mike

Home induction:

Most important instruction: WAIT UNTIL YOU ARE REALLY FEELING A LOT OF WITHDRAWAL

Then take 2 to 4mg (or equiv.) of the medication under your tongue.

Wait an hour. If you are still feeling sick, you may take another dose.

Case 1: Mike

Home induction:

Consensus is that a patient may take up to 8 to 12 mg of buprenorphine the first day, in divided doses.

Remember that medications take 4-5 half-lives to reach steady state. Buprenorphine has a >24hr half-life.

This means that even on the same daily dose, the patient will feel better and better over the first few days.

Case 1: Mike

Home induction:

Some patients do well on lower doses. I have many patients who are stable on doses between 2 and 12 mg per day. It is not usually appropriate (or necessary) to prescribe 16mg daily starting on day 1.

Case 1: Mike

Home induction:

Have a follow up visit one week after initial visit

Case 1: Mike

Home induction:

Possible wrinkle: Mike calls 4 days after his initial visit and says "I've been taking 3 strips a day and I'm all out of medication.

Case 1: Mike

Home induction:

How long an rx at a time?

Case 1: Mike

Home induction:

How long an rx at a time?

Frequency of urine monitoring?

Case 1: Mike

Home induction:

How long an rx at a time?

Frequency of urine monitoring?

Type of urine monitoring?

Case 2: Lili

Lili is a 31 year old F who presented for treatment of opioid use disorder, specifically addiction to prescription oxycodone, which she was initially prescribed for her "exploded disc."

Case 2: Lili

After 2 months, Lili is able to remain abstinent from oxycodone on 16mg/day of buprenorphine/naloxone. At treatment initiation she agreed to attend weekly appointments with her addiction counselor.

However, she is persistently positive for THC and cocaine on her urine toxicology.

Case 2: Lili

When you point this out, Lili says “so you’re going to detox me?”

Case 2: Lili

- Assess patient goals--the collaborative spirit of MI
- Review level of care
- Remember contingency management (esp. as reflected in frequency of visits)
- Check the PDMP

Case 3: Rhonda

Rhonda (age 60) came in to start buprenorphine for her heroin addiction. She is stabilized at 12mg/day for the first three months, and she sees her addiction counselor weekly.

Initial urine toxicology was similar to Mike's, and then was positive for buprenorphine only.

Recently, Rhonda's urine has been positive for benzodiazepines the last two checks. She has been consistently negative for opioids.

Case 3: Rhonda

Next steps?

Case 3: Rhonda

Next steps?

- PDMP
- Frequency of monitoring
- Call-backs
- Level of care
- CDC letter

MACS

1-855-337-6227 (MACS)

Conclusions

Buprenorphine is safe.

It is very satisfying to be able to treat a deadly condition quickly and effectively.

MACS can help you when you get stuck.

Thank you

Email: agreenbl@som.umaryland.edu

Please fill out evaluation emailed to you!