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Depot Buprenorphine: an under-utilized yet critical tool amidst the opiate epidemic

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Lifelong TRUST Clinic
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Alameda County Health Care for the Homeless

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Who we are....

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Alameda County **Health Care for the Homeless**

And who we are not…

- Addiction specialists
- Employees of an addiction center
- Paid by any addiction or pharmaceutical entities

Presentation Overview

- PEH and the opiate epidemic
- What is Buprenorphine?
- What is Depot Buprenorphine?
- Why should services for PEH consider using Depot Buprenorphine?
- An operational guide to Depot Buprenorphine use
- TRUST Clinic Depot Buprenorphine Program data presentation
- Depot Buprenorphine – the patient experience
- Successes, failures, and lingering questions
- Questions/comments

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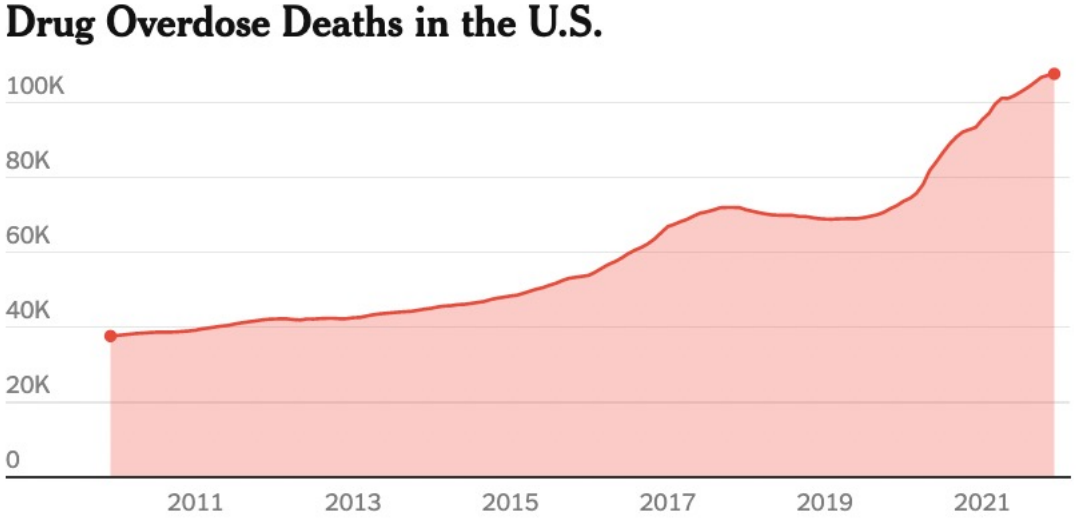
Overdose Deaths Continue Rising, With Fentanyl and Meth Key Culprits

New data show a surge in overdose deaths involving fentanyl and methamphetamine; overall, the nation saw a 15 percent increase in deaths from overdoses in 2021.

Give this article 1

Mary DiAntonio kissed a portrait of her son Angelo DiAntonio, at a memorial for overdose victims in August in Pittsburgh. Nate Guidry/Pittsburgh Post-Gazette, via AP



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Premature death in PEH: an American Tragedy

- 1 in 4 deaths in PEH secondary to drug overdose (JAMA 2022)
- “drug overdose caused one in three deaths among those under the age of 45 years, a death rate 16 to 24 times higher than in the Massachusetts general population” (BHCHC 2016)
  - Opiates implicated in 81%
- TRUST Clinic
  - 76 deaths since Jan 1 2020 (4% of clinic population)
  - 24% of deaths suspected secondary to opiate overdose

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A call to action: Overdose Prevention

- Narcan distribution
- Fentanyl test strip distribution
- Patient education programs (opiate and stimulant users)
- Street outreach
- Recovery support counselors
- Peer counselors
- Recovery groups
- Methadone linkage
- Advocacy (safe injection sites)
- ***Medication-assisted treatment***

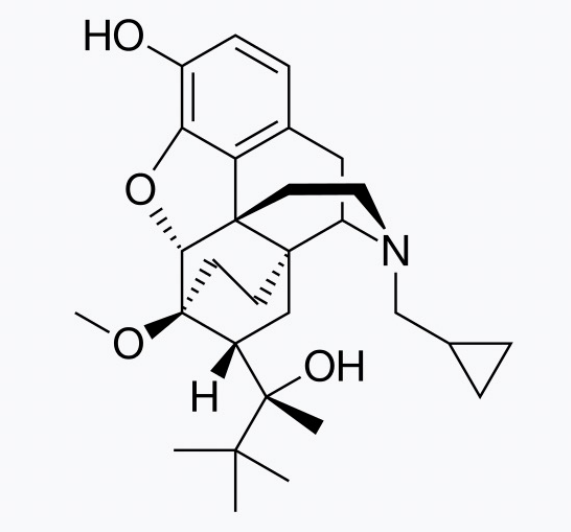
What is Buprenorphine?

1874

1966

1972

2002



First Methadone Clinic established in United States

Discovery of buprenorphine

First documentation of heroin creation

Buprenorphine receives FDA approval

What is Buprenorphine?

- Opiate (binds at mu receptor)
- Partial agonist
- 25-100 times higher affinity for receptor than morphine ("preferentially displaces")
- Low potential for overdose
- Few drug interactions
- Long half life 20-70 hours
- Tablets/Film/buccal approved for OUD and pain (patches)

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What is Buprenorphine?

- Induction requires withdrawal
- No cardiotoxicity
- Can be prescribed outpatient
- Requires X waiver (DATA 2000)
- Must take on a daily basis
- Standard of care 7-30 day scripts (typically 7-14 days)
- Diversion exists
- Available in tablets, films, patch, and now depot injection

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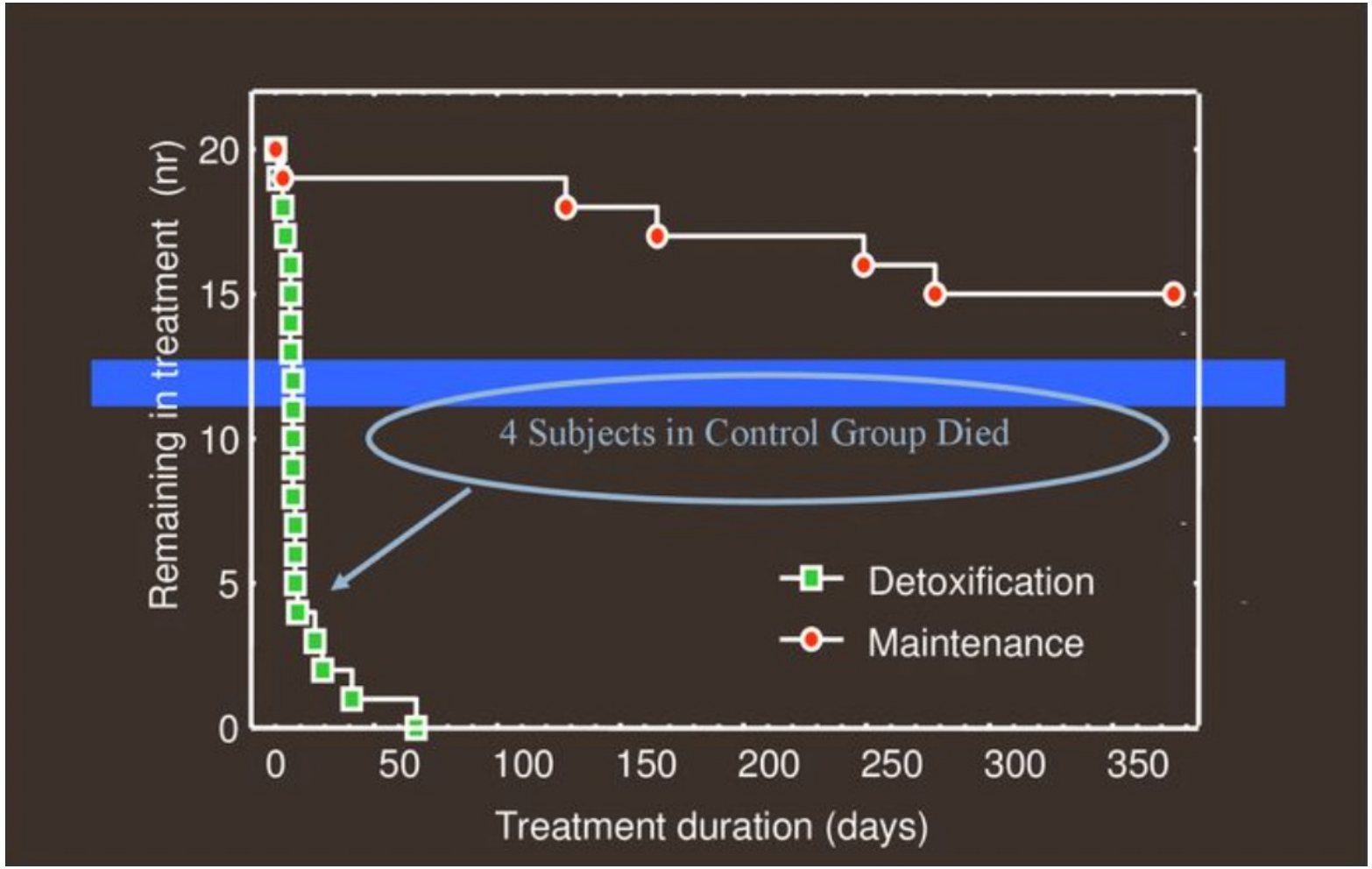
SL Buprenorphine treatment retention

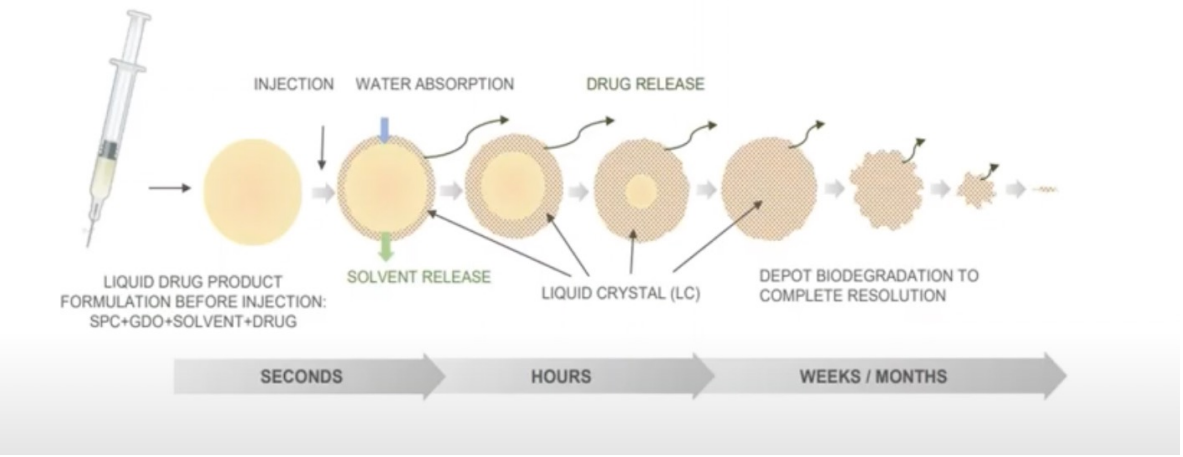


Rationale behind depot buprenorphine

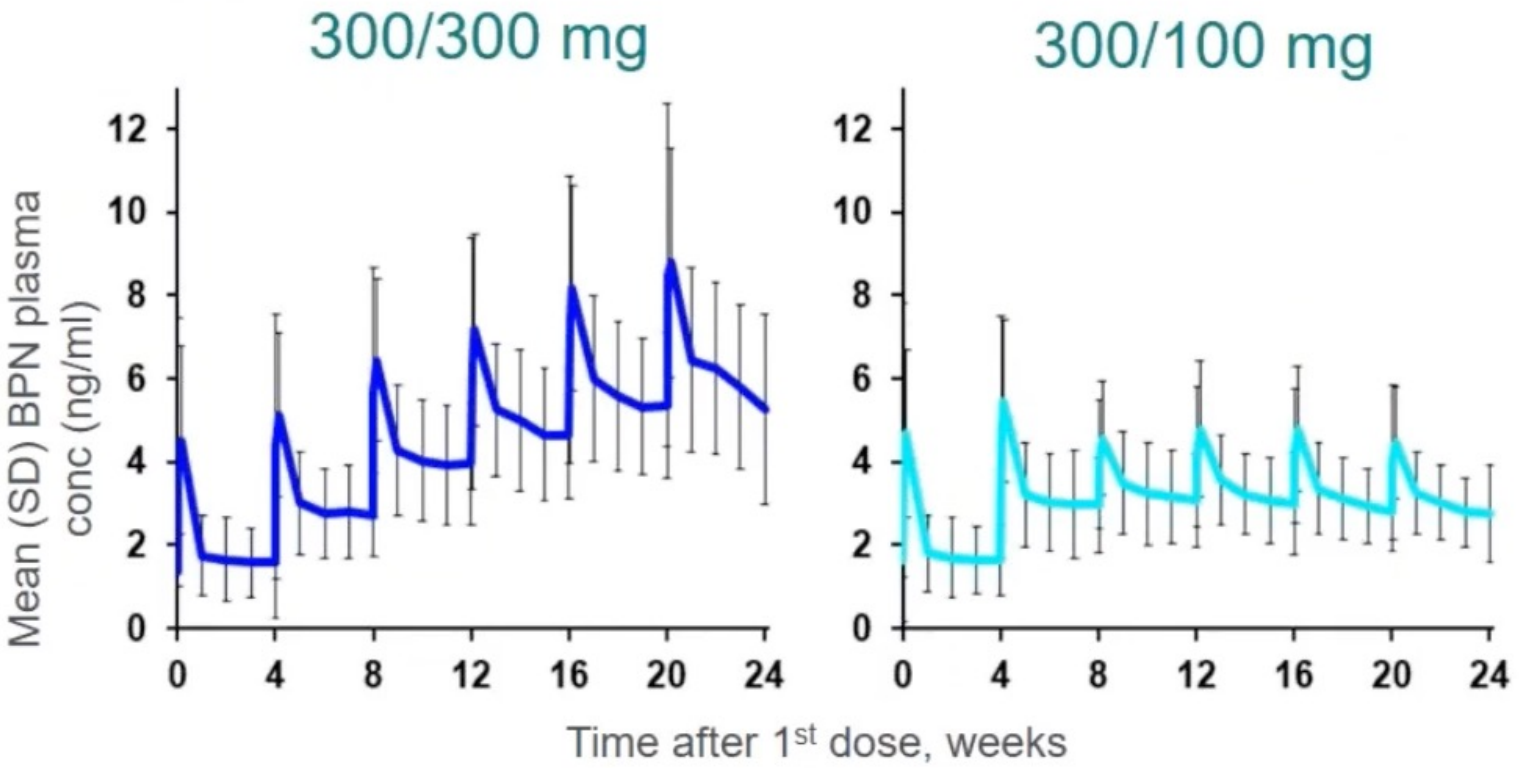
- Reduces frequency of clinic/pharmacy visits
- Increased convenience for patients and providers
- Improved adherence = improved outcomes
- Decreased diversion
- Reduces costs

What is Depot Buprenorphine?

- Subcutaneous injection
  - Weekly (Buvidal – EU and Australia)
    - Room temperature
    - Multiple injection sites
  - Monthly (Sublocade - US)
    - Cold storage (2-8 degree C)
    - Single injection site (abdomen)
    - 26-42 days
  - Ready-for-use prefilled syringes
  - Injection by health care professional (provider or RN)
- Buprenorphine implant (Probuphine)



Sublocade Pharmacokinetics



Summary of evidence supporting Depot Buprenorphine

- Blockade effects – positive feedback reducing supplemental opioid use
- Evidence of efficacy
  - retention in treatment
  - reduction in other opioid use

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Adverse Events and Safety issues

- Local injection related adverse events
  - Pain swelling and redness in 10-15%
  - Transient
- “Depots”
- Systemic
  - Comparable to SL buprenorphine
    - Nausea, constipation, headache, sedation, poor sleep
- Sedation – recommend against driving while stabilizing
- Drug-drug interactions with other sedatives
- Avoid in hepatic failure due to poor clearance

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Summary of Advantage and Disadvantages

Advantages

- Reduced need for attendance
- Convenience for patients
- Decreased diversion
- Increased adherence
- Less need for monitoring
- Less potential for conflict
- Better outcomes
- Overdose prevention

Disadvantages

- Loss of patient autonomy
- Side effects (injection pain, ”depots”)
- Reduction in intensity of patient interaction

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Cessation of Depot Buprenorphine

- Not well characterized in studies
- Case reports of no withdrawal to mild withdrawal weeks to months after last dose
- Promising profile for reduction/cessation

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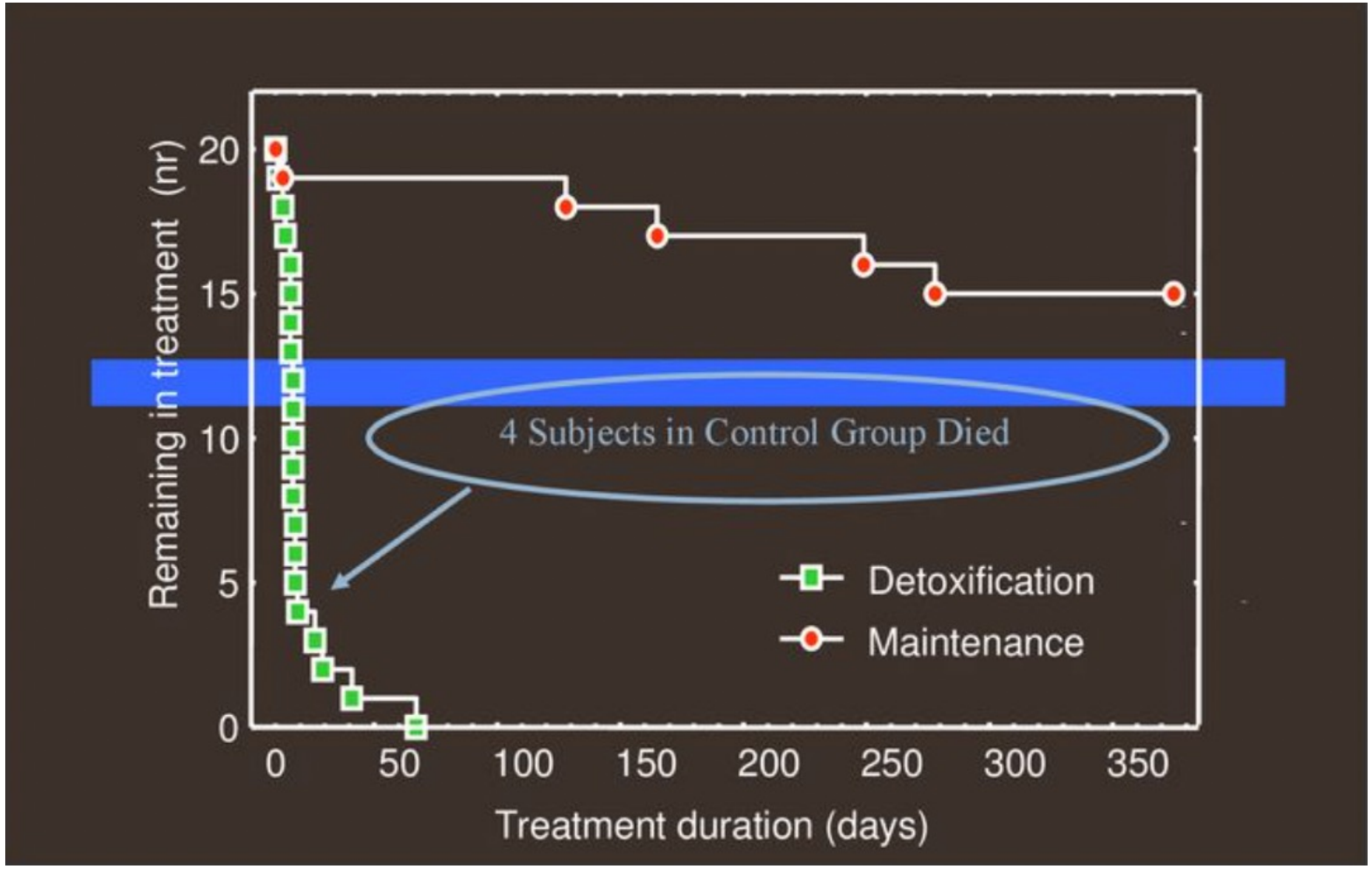

- Requires attendance, adherence, organization, stability for success

Depot Buprenorphine in PEH

- reduced need for attendance
  - Decreased need for transportation
  - Decreased cost of transportation
- Increased adherence
  - Reducing the pressure of literally living amidst the opiate epidemic
  - Reducing burden of adherence in SMI and cognitive impairment
- Decreased diversion
  - Lost or stolen medications
  - Refocusing on “therapeutic” relationship amidst diversion pressures
- Less potential for conflict
  - Relationships are everything
- Contributing towards stability
  - Increased time for support engagement
  - Removing/decreasing a cause/persistence in homelessness

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Sublocade Logistics

- Specialty Pharmacies
- Insurance Coverage
- Storage and Handling Requirements
- Licensing
- Injection Techniques
- Protocol

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Health Care for the Homeless

Specialty Pharmacies

- Finding a specialty pharmacy to work with in the community is key to program success.
- Some road blocks in the past have been pharmacy requirements for distribution of controlled substances – needing to reach patient for consent before shipment of medication (hard in our population of patients without phones or addresses).
- Other road blocks in the past with various pharmacies have been long times to ship medication or to process through insurance – delaying patient's access to MAT in the short window we have where they are engaged and interested.

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Genoa Healthcare Pharmacy

- Located in San Francisco, CA
- We work closely with Genoa for all of our Sublocade patients
- They help us to troubleshoot insurance issues
- FedEx Next Day delivery Mon-Thursday
- No prior patient consent required for delivery – patient signs at first injection appointment
- Call to “register” new patients by providing social security number or insurance information if needed – and schedule deliveries for target injection dates- seamless process

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Insurance requirements

- Covered under Medi-cal
- Private Insurance – Requires a Prior Authorization
  - Co-pay will depend on insurance plan
  - Coupons are available to offset higher co-pays
- Medicare – Requires a Prior Authorization
  - If you are on a low income plan you could have a co-pay of $4
  - Each Part D plan will vary, some co-pays may be higher than others

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Storage and Handling Requirements

- “Chain of Custody”- Sublocade must be signed for upon delivery and pharmacy must receive faxed receipt of medication received. All paperwork is saved and logged.
- Sublocade must be logged into Clinic Medication Log with Rx #, patient name and date
- Double Lock Requirements: Sublocade must be stored in a locked room in a locked refrigerator that is securely attached to the wall or floor.
- Temperature of refrigerator must be kept between 36 - 46 degrees Farenheit – with the ideal temperature being at 40 degrees Farenheit (same as vaccine fridge requirements).

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Storage and Handling Requirements

- Important to Note: We do not “store” Sublocade – we target delivery date for day of injection.
- Sublocade must be wasted within 2 weeks if not used.
- Wasting of Sublocade:
  - Contact Indivior (manufacturer) via indivior@wdsrx.com with:
  - Prescriber name
  - DEA license number
  - Quantity
  - NDC number
  - Lot number
  - Expiration date
  - RN contact number
  - They will send a shipping label to return medication. Medication will be mailed back.

Injection Tips and Techniques

- Sublocade must be removed from fridge at least 15 minutes before injection. Once removed from the fridge – it must be used within 7 days
- Should only be given subcutaneously in a rotation of one of the four abdominal quadrants in between the transpyloric and transtubercular planes
- Patient should lie flat or almost flat on table if possible to receive injection.
- Adipose tissue must be pinched and grasped firmly and needle completely inserted at 45 degree angle. Sublocade should be pushed in slowly and steadily – while skin is pinched the entire time.
- Normal for a small amount of fluid to come out after injection is finished- cover with a bandaid.
- Instruct patients not to rub injection site and inform that it will become a hard lump – which is normal. This is the depot that will slowly disperse over time.


NDC 12496-0100-1
Sublocade
(buprenorphine extended-release)
injection for subcutaneous use
100 mg
WARNING: SERIOUS HARM OR DEATH
COULD RESULT IF INJECTED INTRAVENOUSLY
FOR ABDOMINAL
SUBCUTANEOUS
INJECTION ONLY.
PLEASE READ COMPLETE
INSTRUCTIONS PRIOR TO USE.
PLEASE SEE ACCOMPANYING
FULL PRESCRIBING
INFORMATION.
Keep out of reach of children.
Remove SUBLOCADE from the refrigerator 15 minutes prior to administration.
The product requires at least 15 minutes to reach room temperature.
Attach the needle at the time of administration.
Use only the needle provided.
Store at 2°–8°C (35.6°–46.4°F).
Once outside the refrigerator, this product may be stored in its original packaging at
room temperature, 15°–30°C (59°–86°F), for up to 7 days prior to administration.
Discard SUBLOCADE if left at room temperature for longer than 7 days.
Discard after ___/___/__
For more information, visit SUBLOCADE.com
NDC 12496-0300-1
Sublocade
(buprenorphine extended-release)
injection for subcutaneous use
300 mg
WARNING: SERIOUS HARM OR DEATH
COULD RESULT IF INJECTED INTRAVENOUSLY
FOR ABDOMINAL
SUBCUTANEOUS
INJECTION ONLY.
PLEASE READ COMPLETE
INSTRUCTIONS PRIOR TO USE.
PLEASE SEE ACCOMPANYING
FULL PRESCRIBING
INFORMATION.
Keep out of reach of children.
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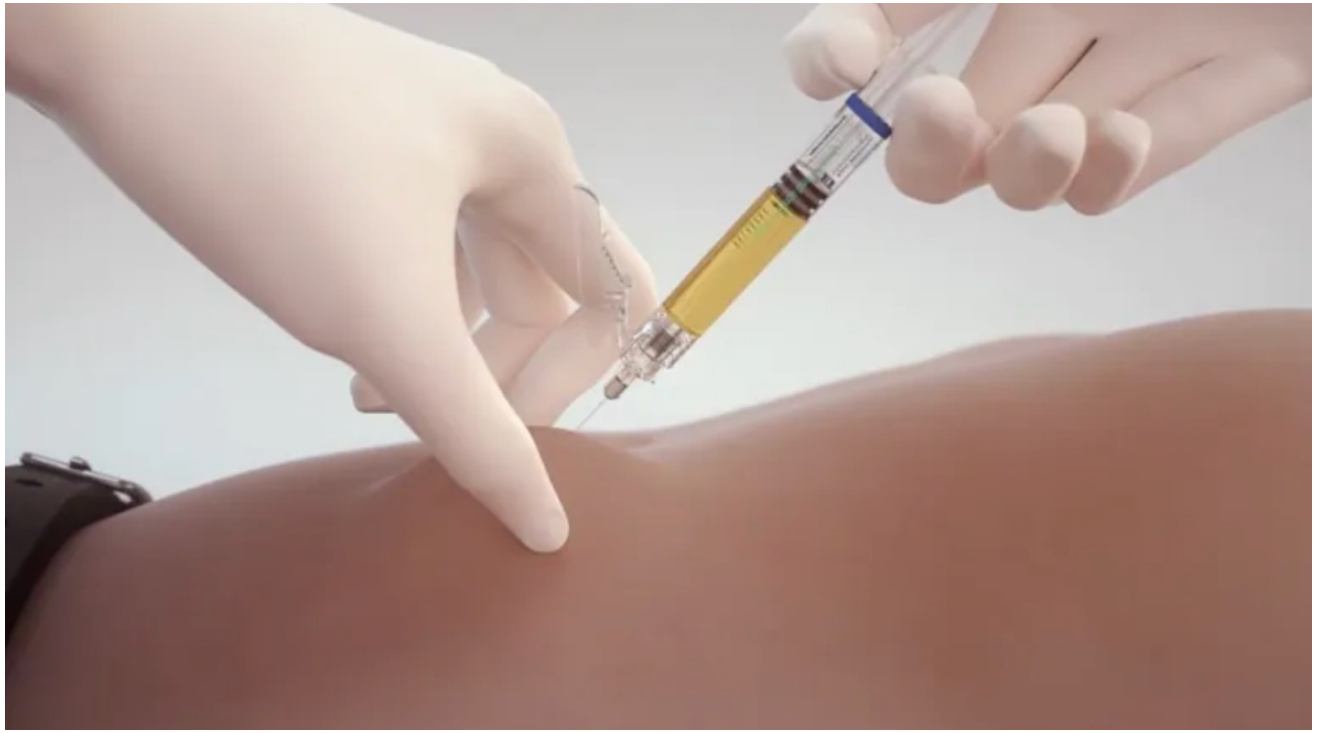

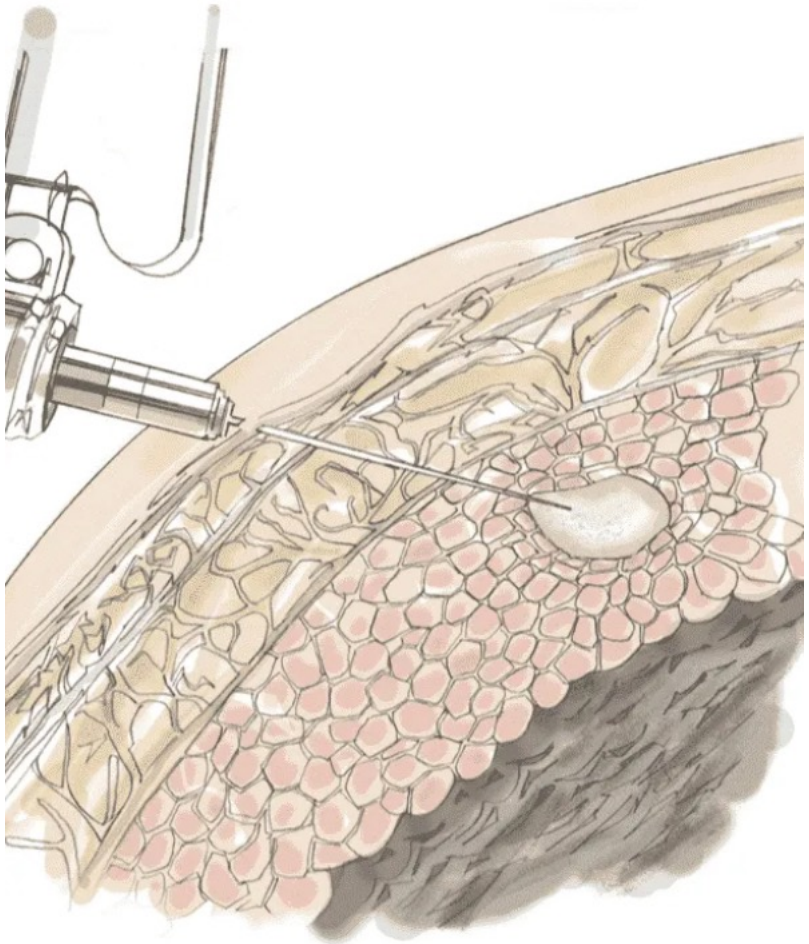

Injection Tips and Techniques

- **Important to note: Sublocade injection is very painful!**
- Give patients options to avoid painful injections and in turn give them a more positive association with receiving Sublocade.

1. Lidocaine with Epinephrine – First choice of most of our patients, most clinicians use approx. 2 mL in a small wheal surrounding predicted injection site. Positive feedback from all patients.
2. Ethyl Chloride “freezing” spray – applied immediately before injection. Mixed feedback
3. Ice Pack – applied before and after injection- rarely used

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TRUST Clinic Sublocade Protocol

TRUST RN Sublocade Protocol
Last Updated 4/12/2022

Rationale: To provide guidance to RNs regarding Sublocade as treatment for opioid use disorder (OUD). Sublocade (injectable extended release buprenorphine) is a long-acting injectable medication designed to prevent opioid withdrawal symptoms and curb cravings to reduce or stop illicit opioid use. Sublocade is used when patients prefer it over a daily medication or when patients have difficulty attending frequent appointments, continue to use opioids or experience withdrawal or cravings while receiving oral medications.

Context: Provider prescribes Sublocade for patient with OUD after tolerance to buprenorphine oral product is determined.

Consent: Patient must sign the Sublocade Agreement form prior to their first injection. Typically, this is during in-person visit, although a telehealth visit with PCP prior the first injection is acceptable.

Initial prescription: Sublocade 300mg IM, #1 refill

Pharmacy:
Genoa Pharmacy
245 11th St # P-1, San Francisco, CA 94103
(415) 871-0117

Procedure:
When provider writes first prescription, they will send an Epic message to the RN to inform them of the new Sublocade prescription for the patient.

Sublocade medication should be logged in Medication Log and stored according to protocol (temperature controlled and in separate locked fridge). RN will sign the delivery manifest and fax it back to the pharmacy upon delivery.
When Sublocade arrives, RN calls patient to schedule injection #1.

1st Injection Day: Patient will sign pharmacy consent form. A provider (priority #1 PCP, #2 POD) will have a co-visit with the RN on the day of the first injection and complete the Sublocade consent form if needed.

Appointment documentation: chief complaint should be listed as "injection". Injection should be documented in the MAR.

Patient should have a POC urine toxicology screen at every visit for Sublocade injection, including fentanyl testing. Patients should be offered harm reduction supplies at each visit.

RN will make sure patients have follow up appointments with provider (to assess cravings, withdrawal symptoms and side effects at:

- 30 days (injection #2 300mg). Provider orders Sublocade 100mg #3 refills.
- 60 days (injection #3 100mg)
- 90 days (injection #4 100mg)
- 120 days (injection #5 100mg) Provider orders Sublocade 100mg #3 refills
- Then every 90 days ongoing

Complex cases: Some patients find they have continued cravings or withdrawal symptoms at the 100mg dose, in those cases, the PCP may choose to continue the 300mg dose. Some patients find the medication lasts longer than 4 weeks, in those cases the patient will need to inform RN 1 week before they would like their next dose to allow for medication delivery.

Missed doses: RN will give the missed dose as soon as possible. Dosing delays of up to 2 weeks may not affect treatment. RN will task provider and RSC or Health Coach to inform them that patient missed their Sublocade injection appointment. The RCS or Health Coach will outreach patient to reschedule 3 times over the course of 1 week. Should a patient return to clinic unannounced >2 weeks beyond missed dose date MUST have appt with provider.

Early Doses: no sooner per dosing standards than q26 days.

Disposal
If a patient does not attend their appointment for Sublocade injection, staff will outreach the patient per above. If the outreach efforts have been exhausted, the medication must be disposed of.

Reverse Distributor Indivior (855-443-4522):
Email Indivior@wdsrx.com with:

- prescriber name
- DEA license number
- Quantity
- NDC number
- Lot number
- expiration date
- TRUST RN contact number

They will send a shipping label to return medication. Medication will be mailed back.

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TRUST Clinic Sublocade Protocol

- Mechanism for enrolling patient into sublocade program by provider
- Patient signed consent
- RN logging protocol
- Schedule for RN vs covisits (every 3 months)
- Missed visits
- Correct disposal

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TRUST Clinic

- Located in downtown Oakland, CA
- Brick and mortar clinic with 5 street medicine outreach teams
- Eligibility criteria
  - >18 y/o
  - Housing unstable or frankly homeless
  - Must agree to primary care services at clinic (not an urgent care)
- Integrated primary care clinic with 6 major service programs
  - Primary medical care
  - Behavioral health care (therapy and psychiatry)
  - Case management (light touch and intensive)
  - Recovery support
  - Housing coordination
  - Street medicine
- 1959 total active patients (seen once in last 2 years)

TRUST Clinic and Opiate Use Disorders

- 17% of patients with coded opiate use disorder (333)
- Opiate use disorders almost exclusively (98%) heroin and fentanyl use
- 75% of all opiate use disorder patients with buprenorphine product prescribed at least once (249)
- 3 RSCs who panel manage and counsel active buprenorphine patients

TRUST Clinic Sublocade Data

Opiate of choice	Number of sublocade injections	Current opiate statu	Opiate status during treatment	Dose	average interval
heroin	2	lost to follow-up		300	1
heroin	3	opiate dependent	decreased opiate use	300	1
heroin	4	current	decreased opiate use	300	1
fentanyl	4	current	decreased opiate use	300	1
heroin	4	current	opiate free	300	1
heroin	5	current	opiate free	300	1.1
heroin/fentanyl	5	lost to follow-up	decreased opiate use	100	1
heroin	7	opiate dependent	decreased opiate use	300	1.3
heroin	8	opiate free	opiate free	100	2
heroin	8	Current	decreased opiate use	300	1.8
heroin	8	opiate dependent	decreased opiate use	300	1.1
heroin	8	methadone	decreased opiate use	300	1.5
heroin	9	current	opiate free	300	1
heroin	9	lost to follow-up	opiate free	100	1
heroin	10	current	decreased opiate use	300	1.6
heroin	10	lost to follow-up	opiate free	300	1
heroin	11	opiate dependent	decreased opiate use	300	1

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TRUST Clinic Sublocade Demographics

	All patients prescribed Sublocade (50)
Average Age	48
Gender	14 female, 36 male
Diagnosis	44 heroin, 6 fentanyl
Insurance	47 medi-cal, 3 medicare

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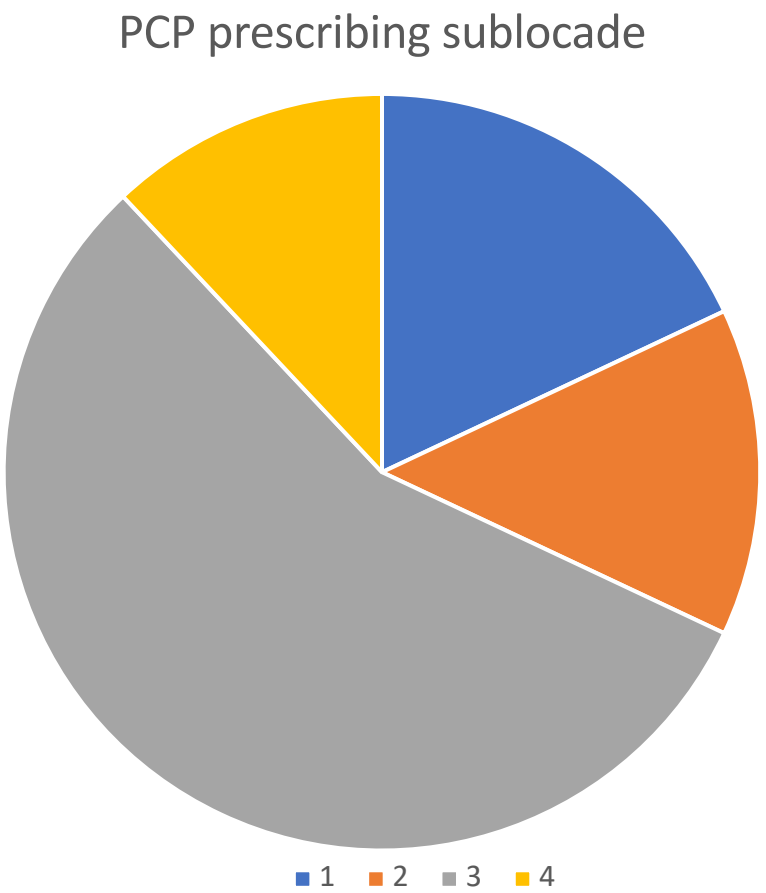
TRUST Clinic Prescribers



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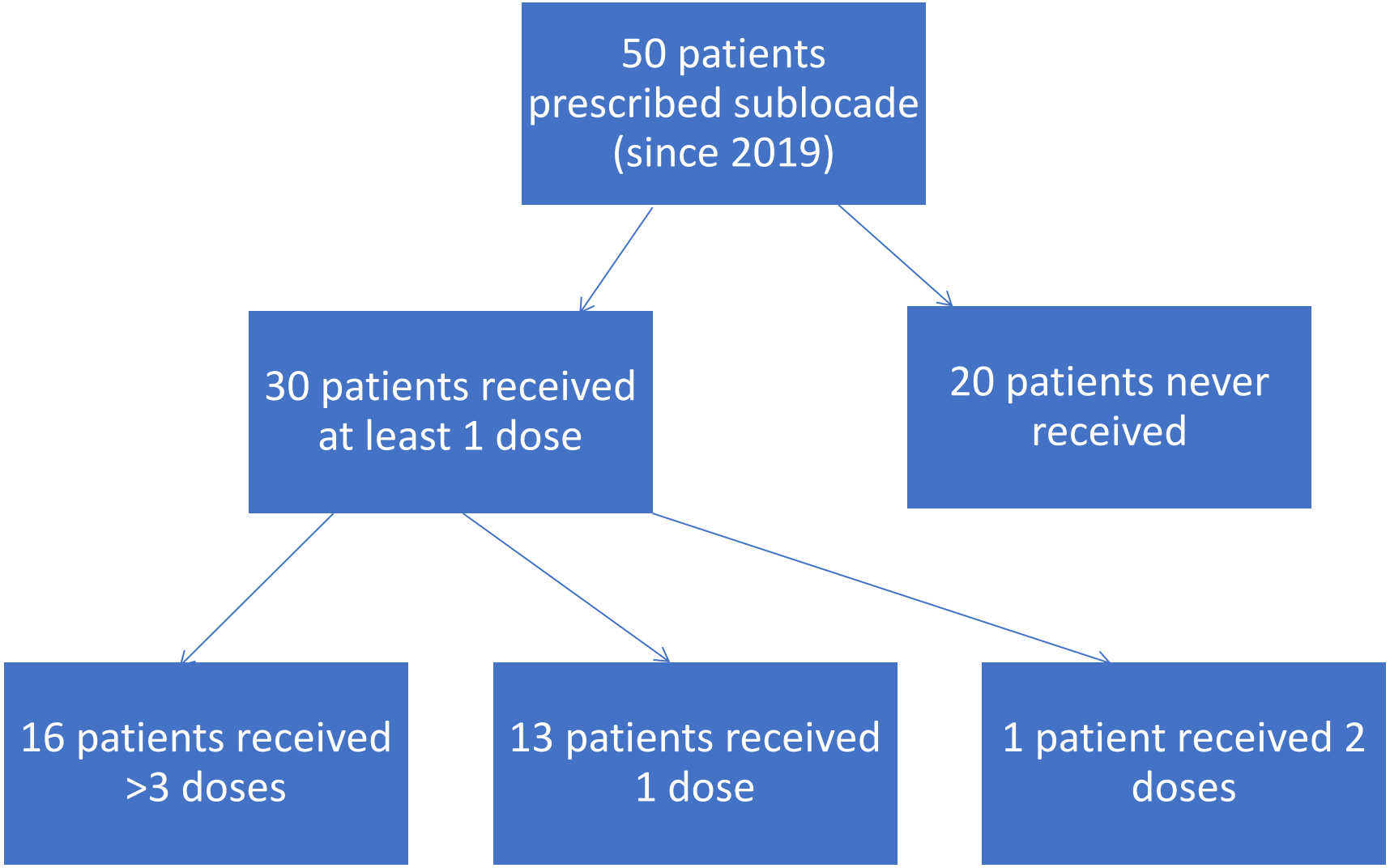
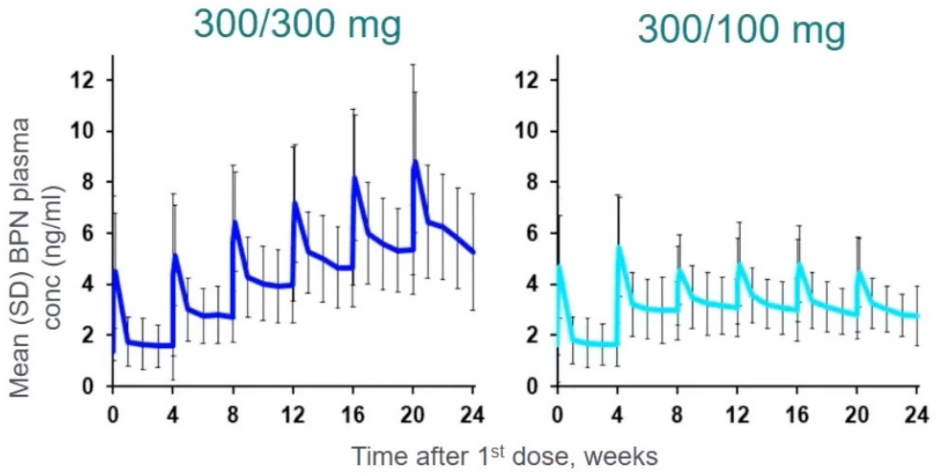

50 patients prescribed sublocade (since 2019)
30 patients received at least 1 dose
20 patients never received
16 patients received >3 doses
13 patients received 1 dose
1 patient received 2 doses

Sublocade Dose Strength

- 300mg and 100mg strengths from manufacturer
- Of 16 patients receiving more than 3 doses
  - 13 remained on 300mg
  - 3 transitioned to 100mg



Administration Intervals

- Sublocade recommends 28-42 days, no sooner than 26 days
- Average interval 1.2 months
  - 4 patients averaged 6 weeks or more

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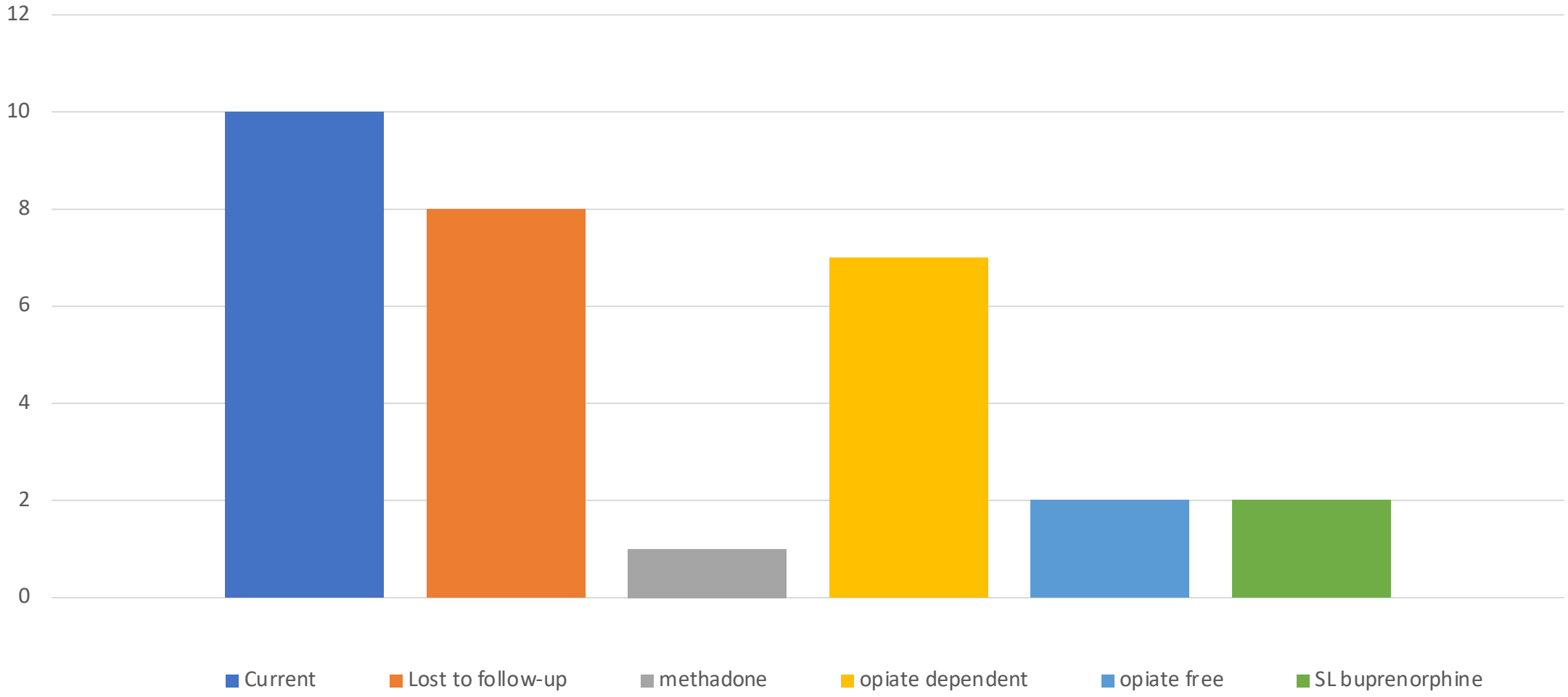
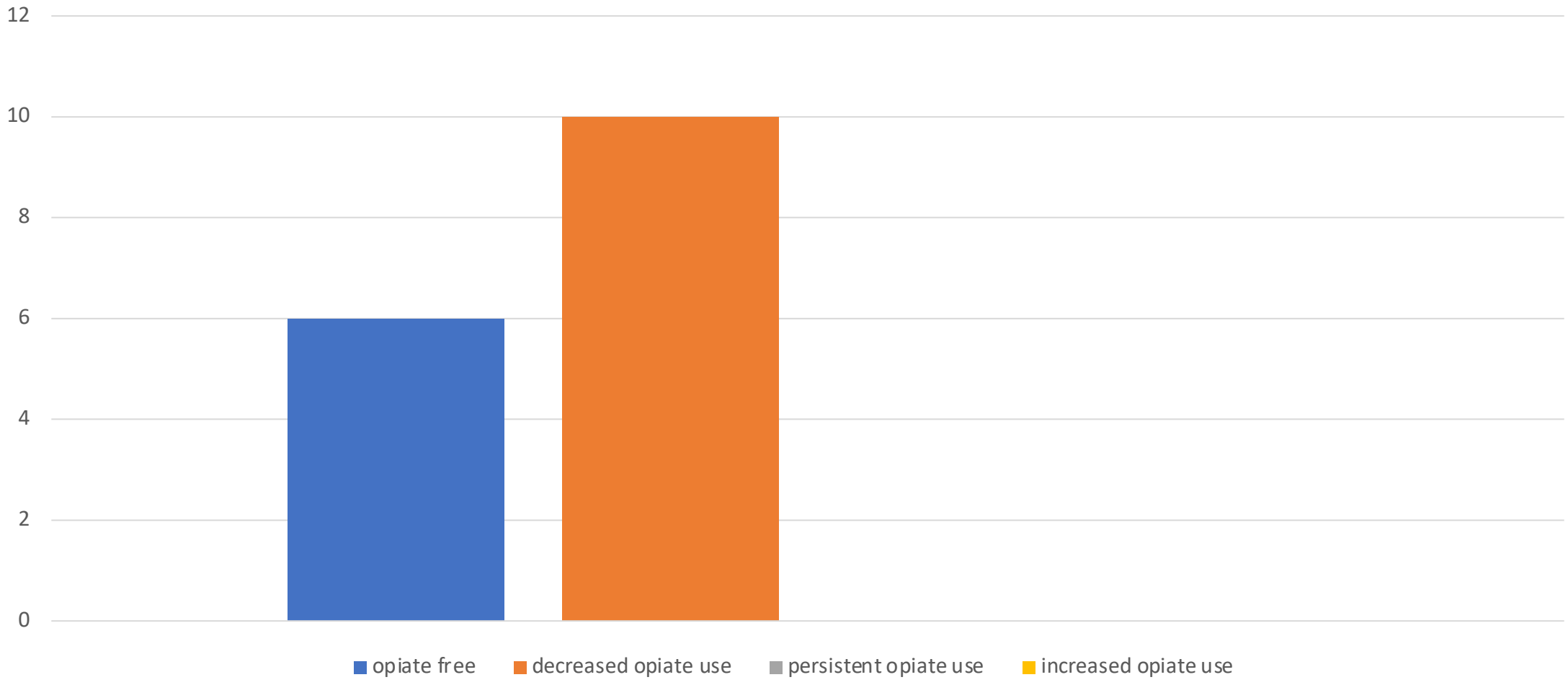
Current outcomes of patients that received at least 1 dose of Sublocade



In-treatment Sublocade patient outcomes



Consumer Perspectives

“Once I learned to trust…”

“At first I thought it wasn’t going to hold me. I even took extra strips to get through the first month. But I just had to learn to trust the medication. Its hard because in the beginning you constantly think you might be starting to get sick. But once I learned to trust the medication I realized that I was living free.”

“New time"

“Yeah - sometimes I still use. People don’t know what its like when all your friends use – there’s no escaping it. But I use SO much less than I used to and I save all sorts of money, have all sorts of new time, and don’t have to risk it everyday trying to hustle on these streets.”

"I wasn't ready."

"I hated it. I hated it because it was doing exactly what I thought it was going to do. I just wanted to get high and sublocade was in the way. I told myself it was making me sick so I stopped, but now I think I just wasn't ready. But I think I want to try again."

Lessons Learned

- Champions needed – onsite providers, RNs, pharmacy, and organizational support
  - Monthly MAT meetings
- Improving prescription to administration efficiency
  - Signed consent and agreement
  - Minimizing over-selling
- Heroin and Fentanyl users are opting for ‘high dose’ Sublocade
- Longer dosing intervals non-inferior
- In-treatment >3 administration outcomes very positive
- Supplemental SL buprenorphine can be helpful early

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Lessons Learned

- Accompaniment critical (RNs and RSCs)
- Clinic wide protocol for standardization important
- Use lidocaine!
- There is such a thing as too much buprenorphine (nausea)
- First visit introduction of Sublocade concept
- Administrations outside of clinic walls not allowed
- Dispensary stocking of sublocade (non-pharmacy procurement) preferred but difficult for FQHCs

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Questions and Struggles

- Is 25% of patients prescribed Sublocade with positive outcomes justifiable to continue?
- How do we prevent sublocade over-sell?
- Is it appropriate for sublocade to be leveraged in cases of poor SL adherence or suspected diversion?
- Would a one week depot buprenorphine product lead to better outcomes?
- Can full agonist dependent patients consent to sublocade administration (risking likely precipitated withdrawal?)
  - Can a protocol be developed for full agonist dependent patients to induce directly onto sublocade?
- Should we continue to offer lidocaine for every injection?
- Should we save pharmacy delivered sublocade for patients beyond 2

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Thank you's

- All the providers and RNs at TRUST Clinic
- Seth Gomez, PharmD
- Leslie Stavig, RN
- Our resilient patient community whose bravery in the midst of the unknown is heroic

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Questions/Comments