My Patient is Admitted on Buprenorphine or Methadone—What Now?

New processes, best practices and tools for managing patients with substance use disorders in PALTC

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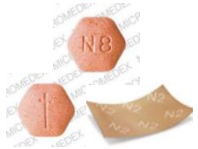
Medications for Opioid Use Disorders

What Is Medication for Opioid Use Disorders?

Methadone

Delivered by Opioid Treatment Providers (OTPs)

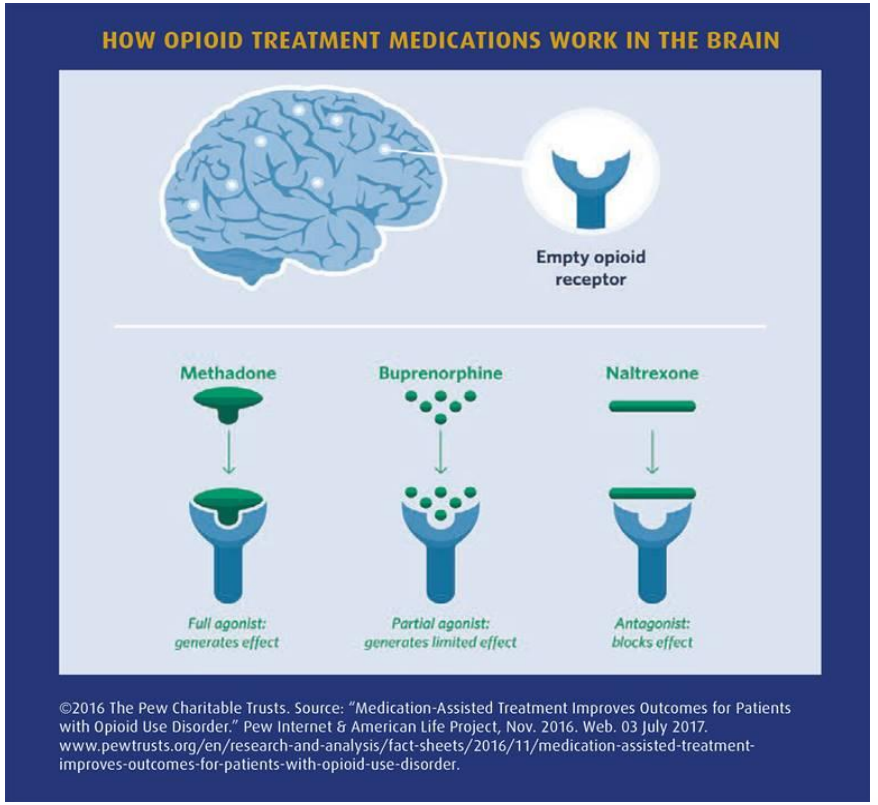


Buprenorphine

Delivered by providers in office-based practice & OTPs

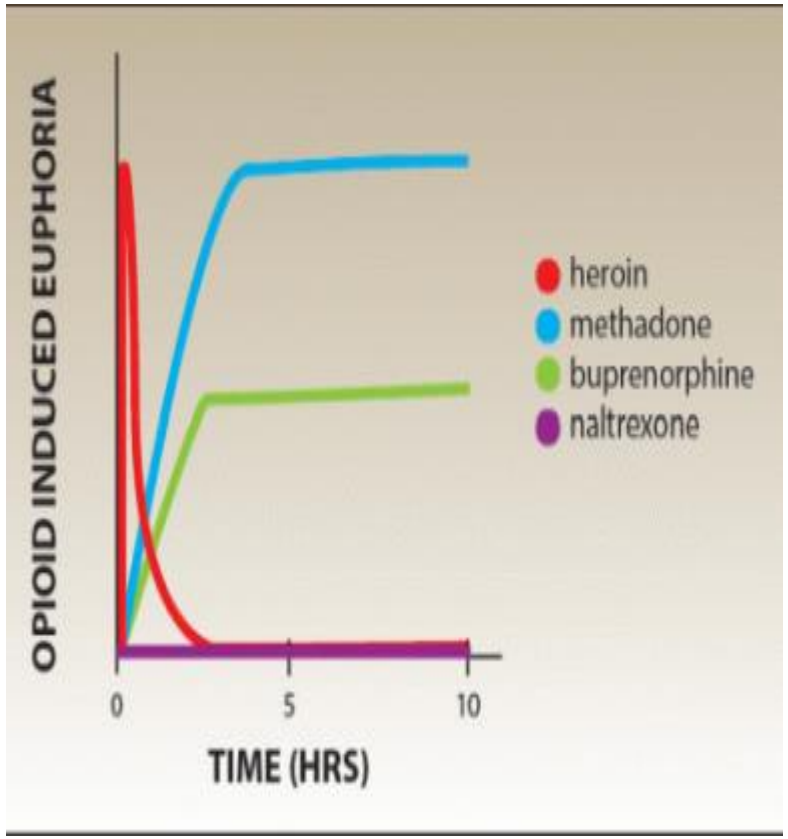
Naltrexone

Delivered by providers in office-based practice



Opioid Receptor Activity

- Heroin (red line) activates opioid receptors fully and quickly.
- Methadone (blue) is also a full agonist, but the activation is much slower and longer lasting.
- Buprenorphine (green) activates the receptors partially, with a similar time course to methadone.
- Naltrexone (purple) is an opioid receptor antagonist and therefore prevents receptor activation.



Sources: Cruciani & Knotkova, 2013; Goodman et al., 2006

Methadone

- Methadone is a full agonist
- Can only be dispensed in OTP setting for the treatment of OUD
- Reduces withdrawal and craving by attaching to the Mu receptors in brain
- Starting dose 30 mg then titrate up to gain steady state of medication over 24 hour period
- Daily medication administration required for 90 days must “earn” take-home medication through time and compliance

Abuse Potential of Methadone

- High abuse potential when taking more than recommended dose
- High overdose risk when taken by opiate naïve individual
- Potential for OD when taken with other drugs such as alcohol or benzodiazepines
- Physician reviews adequate dosage with individual
- OTPs have diversion control policy

Methadone Treatment Limitations

- Limited access to OTPs, mostly located in urban areas
- Highly regulated
- Effective for unstable patients that have difficulty maintaining compliance to medication regimen and treatment compliance
- Required counseling and drug screens
- Lack of privacy within clinic setting
- Stigma

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Buprenorphine Products

- Partial agonist, partial activator
- Most commonly used in combination w/naloxone
- Very strong receptor affinity
- Low dose regimens allow induction for people on high dose methadone or fentanyl
- Reduces craving & withdrawal; improves treatment retention
- Overdose risk is minimal
- Any sedative hypnotic, alcohol, will add to the risk of respiratory depression, overdose and death
- If injured or in pain patients may need higher doses of opioids to treat it

Abuse Potential of Buprenorphine

- Euphoria in non-opioid dependent individuals
- Abuse potential less than full agonists
- Abuse among opioid-dependent individuals is relatively low
- Combination product theoretically less likely to be abused by IV route
- Most illicit use is to prevent or treat withdrawal and cravings

Yokel MA et al. *Curr Drug Abuse Rev. 2011*

Lofwall MR, Walsh SL. *J Addict Med. 2014*

Vivitrol®(naltrexone)

- An opioid antagonist, blocker
- Given by injection every 4 weeks
- When using for opioid use disorder, wait 7-10 days (up to 14 for methadone)
- Most common side effects
  - Nasuea, vomiting, headache, dizziness, fatigue, anxiety, somnolence
- Reduces craving
- Injection effects can be overcome with high dose opioids
- Tolerance resolves quickly and return to prior doses of opioids can lead to overdose

Potential Naltrexone Candidates

- Occupational Obstacles: Healthcare providers
- Not interested/Failed agonists
- High Motivation for AA Model of Recovery
- Currently Abstinent: High risk of relapse
- Maybe younger, shorten duration of OUD
- Don’t want to be physically dependent
- Tired of regulations, stigma and pressure from others

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Medication Treatment Prevents Opioid Related Deaths

- English National Drug Treatment Database
- Followed 151,983 persons over 4 years, 2005-2009
- Compared fatal drug related poisoning across residential, MAT and psychologic support combinations
- During treatment death rate was 2.9/1000 (CI 2.7-3.1) vs. 4.5/1000 (CI 4.3-4.7) when on MAT
- Risk of death was not different between those who completed and didn't complete residential treatment (50-80%) higher

Pierce, et.al. Addiction, 2015; 111:298-308

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MAT Prevents Opioid Related Deaths

- Risk of treatment being in psychologic treatment alone doubled the risk of death
- 6x higher risk 1st 28 days after DC
- 3.5x higher 1st 28 days after MAT stopped
- THE BOTTOM LINE: MAT SAVES LIVES

Outcomes for cardiovascular disease

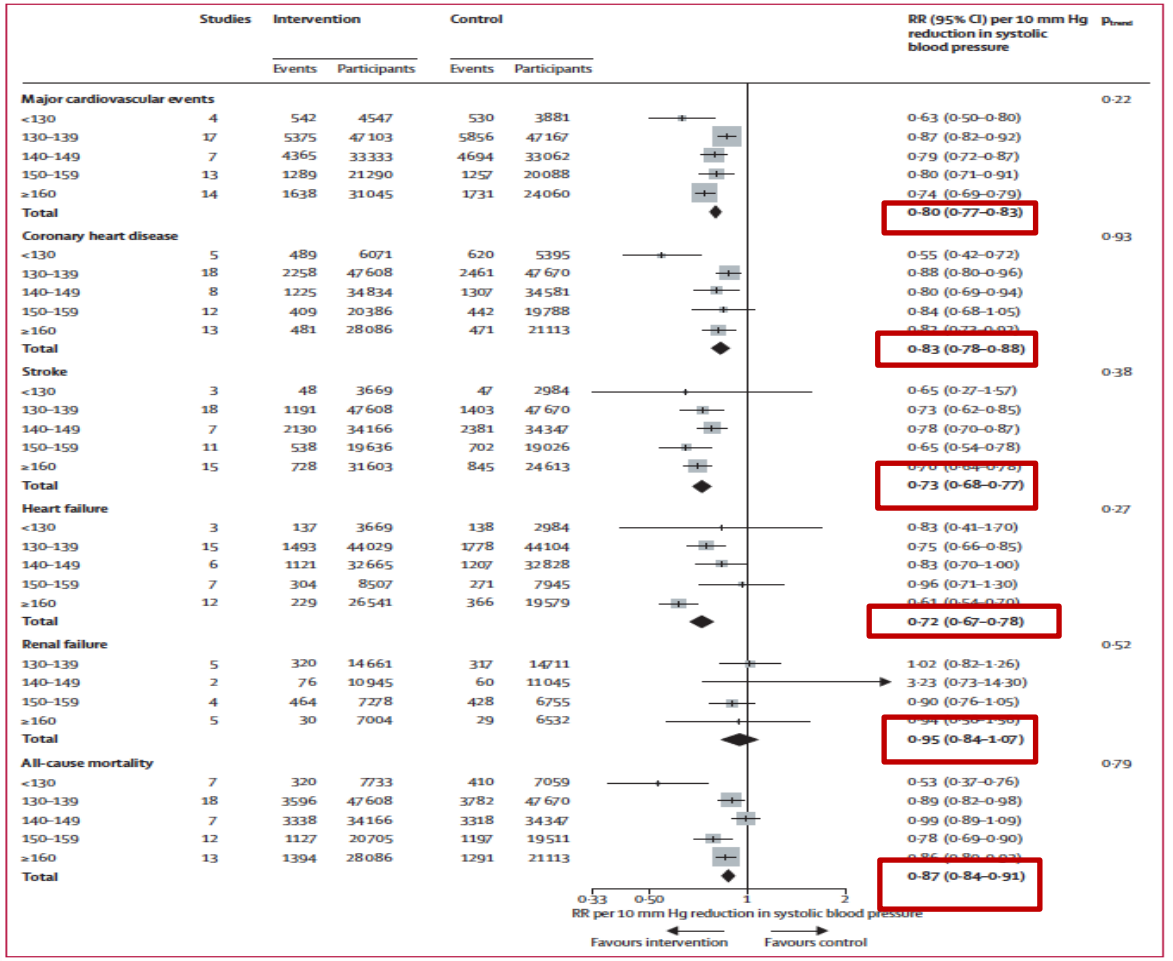


Figure 4: **Standardised effects of a 10 mm Hg reduction in systolic blood pressure stratified by blood pressure**
Blood pressure strata are baseline blood pressure values, not achieved blood pressure after treatment. RR=relative risk.

Ettehad D, et.al. Blood pressure lowering for prevention of cardiovascular disease And death: a systematic review and meta-analysis. Lancet. 2016:387: 957-967

All cause mortality with treatment for opioid use disorder

	No of deaths/ person years		All cause mortality rate/ 1000 person years (95% CI)		All cause mortality rate/ 1000 person years (95% CI)	
	In treatment	Out of treatment			In treatment	Out of treatment
Methadone						
Gearing et al 1974	110/14 474	33/1170			7.6 (6.2 to 9.2)	28.2 (19.4 to 39.6)
Cushman 1977	25/1655	14/297			15.1 (9.8 to 22.3)	47.1 (25.8 to 79.1)
Grönbladh et al 1990	16/1085	32/740			14.8 (8.4 to 23.9)	43.2 (29.6 to 61.0)
Caplehorn et al 1994	11/1975	36/2279			5.6 (2.8 to 10.0)	15.8 (11.1 to 21.9)
Fugelstad et al 1995	8/242	5/45			33.1 (14.3 to 65.1)	111.1 (36.1 to 259.3)
Fugelstad et al 1998	7/177	4/57			39.5 (15.9 to 81.4)	69.9 (19.1 to 179.0)
Scherbaum et al 2002	18/1114	14/172			16.2 (9.6 to 25.5)	81.4 (44.5 to 136.6)
Fugelstad et al 2007	77/3354	74/1311			23.0 (18.1 to 28.7)	56.5 (44.3 to 70.9)
Clausen et al 2008	90/6450	46/1303			14.0 (11.2 to 17.1)	35.3 (25.9 to 47.1)
Degenhardt et al 2009	648/111 538	1510/105 735			5.8 (5.4 to 6.3)	14.3 (13.6 to 15.0)
Cornish et al 2010	30/5129	71/4288			5.8 (4.0 to 8.3)	16.6 (12.9 to 20.9)
Peles et al 2010	42/3985	52/727			10.5 (7.6 to 14.2)	71.5 (53.4 to 93.8)
Evans et al 2015	163/25 277	848/48 122			6.4 (5.5 to 7.5)	17.6 (16.5 to 18.8)
Kimber et al 2015	636/91 792	563/45 265			6.9 (6.4 to 7.5)	12.4 (11.4 to 13.5)
Nosyk et al 2015	89/3979	206/1582			22.4 (18.0 to 27.5)	130.2 (113.0 to 149.3)
Cousins et al 2016	115/22 648	98/6247			5.1 (4.2 to 6.1)	15.7 (12.7 to 19.1)
Overall					11.3 (8.4 to 15.2)	36.1 (24.5 to 53.3)
Buprenorphine						
Cornish et al 2010	7/740	10/751			9.5 (3.8 to 19.5)	13.3 (6.4 to 24.5)
Reece 2010	3/1119	40/6911			2.7 (0.6 to 7.8)	5.8 (4.1 to 7.9)
Kimber et al 2015	87/21 936	314/31 239			4.0 (3.2 to 4.9)	10.1 (9.0 to 11.2)
Overall					4.3 (2.1 to 8.9)	9.5 (3.9 to 23.4)

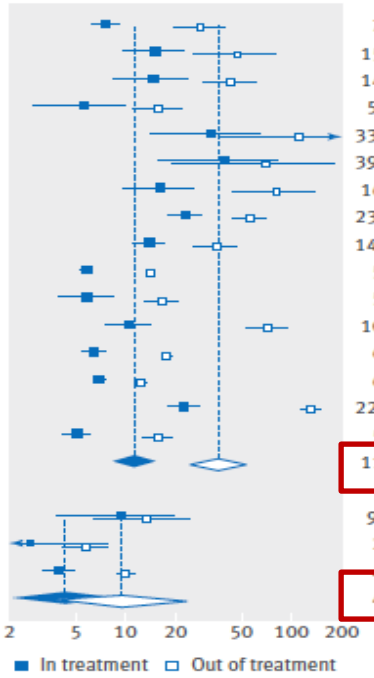
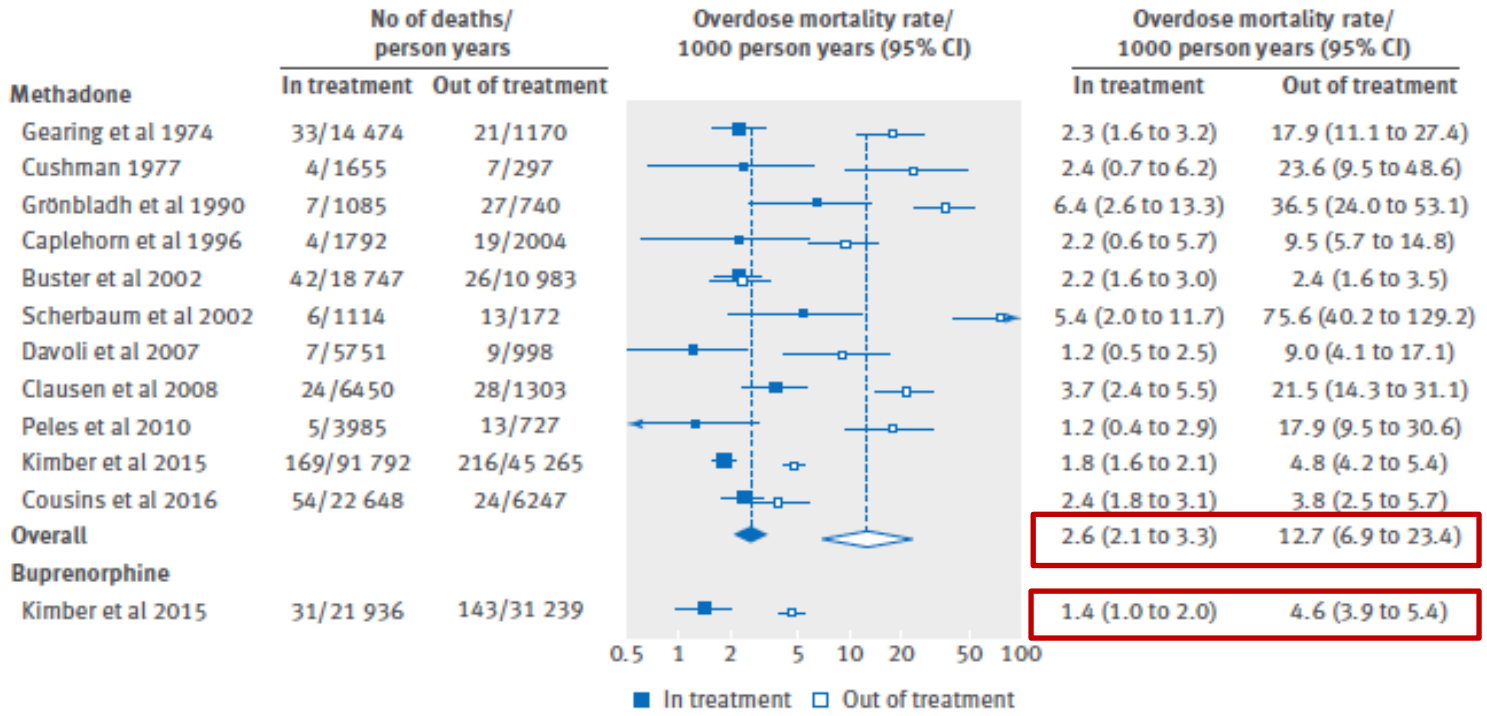


Fig 2 | All cause mortality rates in and out of opioid substitution treatment with methadone or buprenorphine and overall pooled all cause mortality rates, 1974-2016. Area of each square is proportional to study weight in meta-analysis. Horizontal lines represent exact 95% confidence intervals based on Poisson distribution. Diamonds represent pooled all cause mortality rates during periods in and out of treatment across all methadone or buprenorphine cohorts estimated from bivariate random effects meta-analysis on log transformed rates in both treatment periods

BMJ 2017;357:j1550 http://dx.doi.org/10.1136/bmj.j1550

Overdose mortality with treatment for opioid use disorder



	No of deaths/ person years		Overdose mortality rate/ 1000 person years (95% CI)	
	In treatment	Out of treatment	In treatment	Out of treatment
Methadone				
Gearing et al 1974	33/14 474	21/1170	2.3 (1.6 to 3.2)	17.9 (11.1 to 27.4)
Cushman 1977	4/1655	7/297	2.4 (0.7 to 6.2)	23.6 (9.5 to 48.6)
Grönbladh et al 1990	7/1085	27/740	6.4 (2.6 to 13.3)	36.5 (24.0 to 53.1)
Caplehorn et al 1996	4/1792	19/2004	2.2 (0.6 to 5.7)	9.5 (5.7 to 14.8)
Buster et al 2002	42/18 747	26/10 983	2.2 (1.6 to 3.0)	2.4 (1.6 to 3.5)
Scherbaum et al 2002	6/1114	13/172	5.4 (2.0 to 11.7)	75.6 (40.2 to 129.2)
Davoli et al 2007	7/5751	9/998	1.2 (0.5 to 2.5)	9.0 (4.1 to 17.1)
Clausen et al 2008	24/6450	28/1303	3.7 (2.4 to 5.5)	21.5 (14.3 to 31.1)
Peles et al 2010	5/3985	13/727	1.2 (0.4 to 2.9)	17.9 (9.5 to 30.6)
Kimber et al 2015	169/91 792	216/45 265	1.8 (1.6 to 2.1)	4.8 (4.2 to 5.4)
Cousins et al 2016	54/22 648	24/6247	2.4 (1.8 to 3.1)	3.8 (2.5 to 5.7)
Overall			2.6 (2.1 to 3.3)	12.7 (6.9 to 23.4)
Buprenorphine				
Kimber et al 2015	31/21 936	143/31 239	1.4 (1.0 to 2.0)	4.6 (3.9 to 5.4)

Fig 3 | Overdose mortality rates in and out of opioid substitution treatment with methadone or buprenorphine and overall pooled overdose mortality rates, 1974-2016. Area of each square is proportional to study weight in meta-analysis. Horizontal lines represent exact 95% confidence intervals based on Poisson distribution. Diamonds represent pooled overdose mortality rates during periods in and out of treatment across all methadone cohorts estimated from bivariate random effects meta-analysis on log transformed rates in both treatment periods

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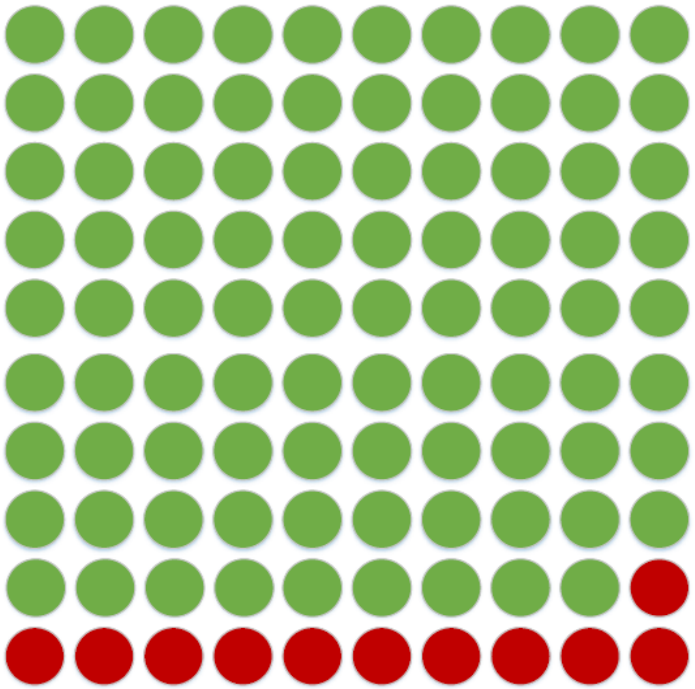
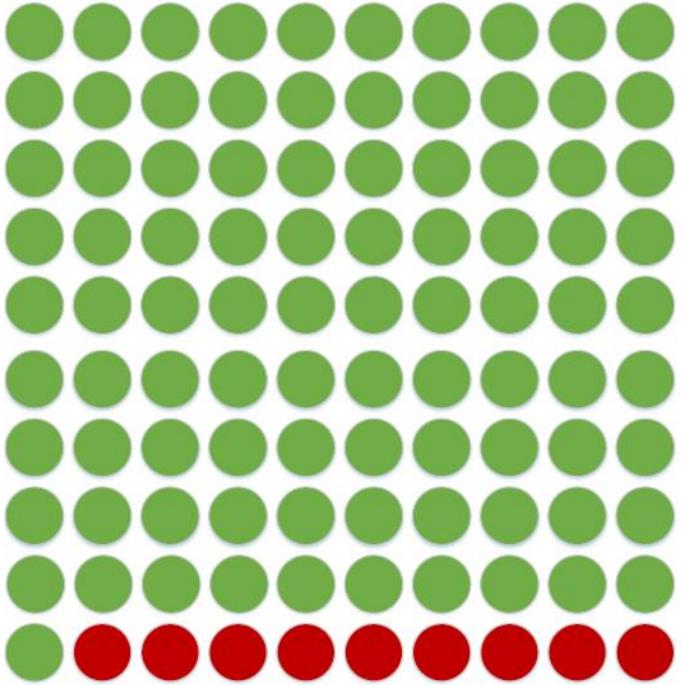
Effects of BP Treatment on Cardiac Events

No Treatment

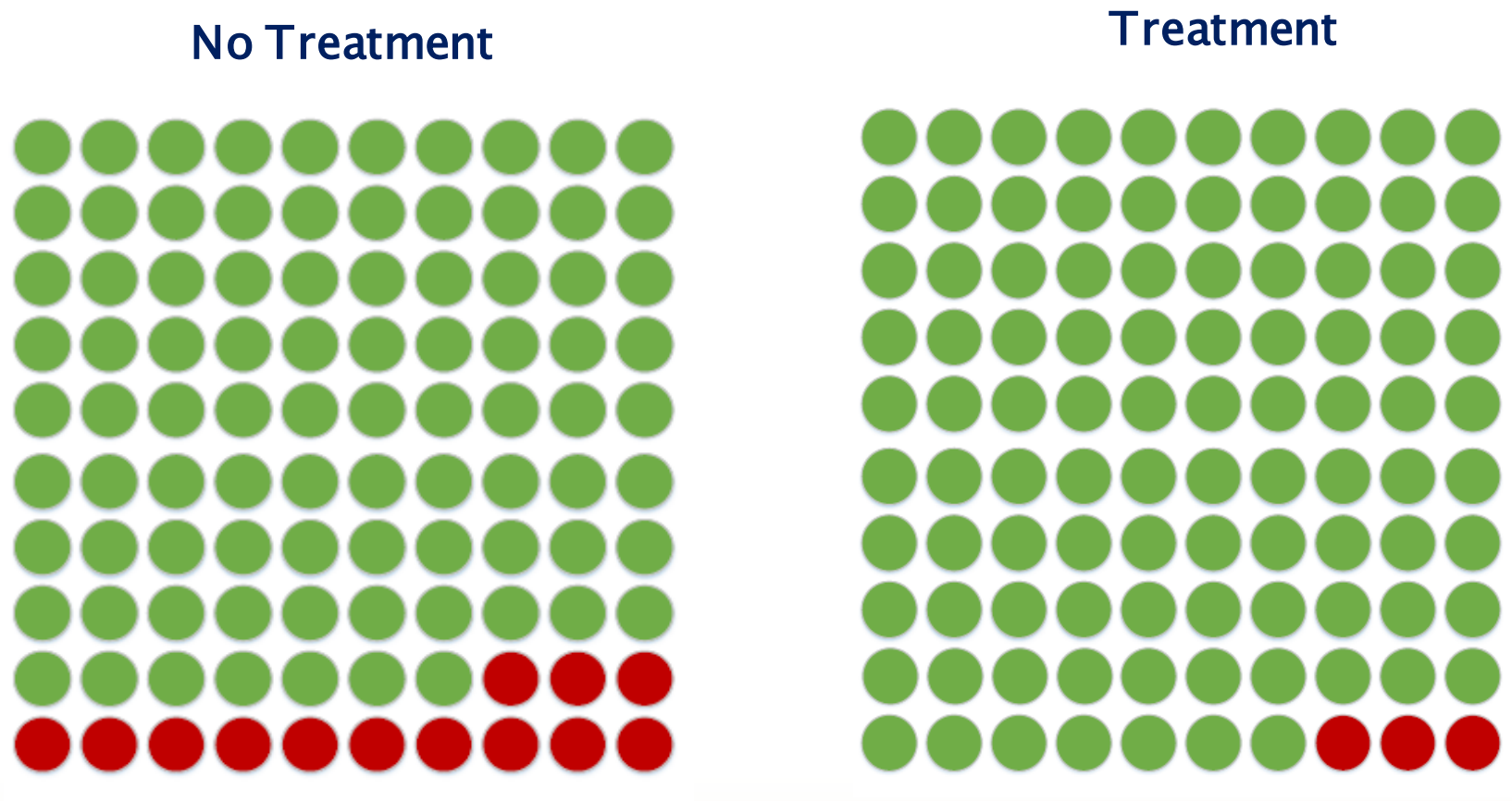


Treatment



Ettehad D, et.al. Blood pressure lowering for prevention of cardiovascular disease And death: a systematic review and meta-analysis. Lancet. 2016:387: 957-967

Effect of Methadone Treatment on Overdose Death



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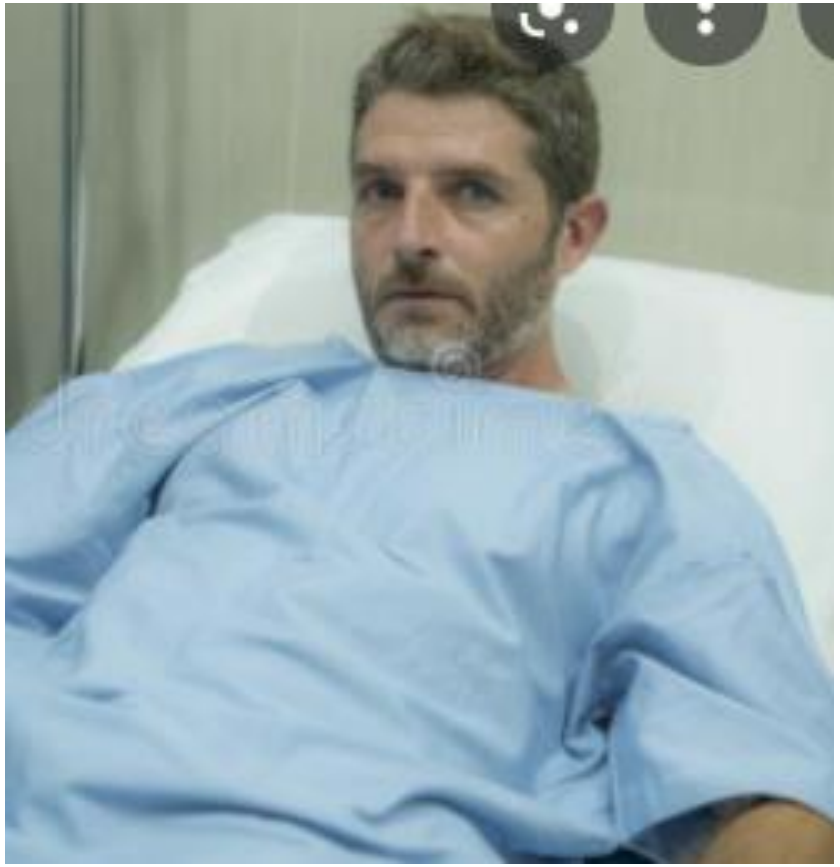
Questions ?

Kevin S.

Kevin S. is a 45 years old software engineer, married with 3 children, with a Hx of opioid use disorder. He is seen by an addiction specialist and on **buprenorphine 8mg twice a day**. The patient was involved in an MVA and is now admitted for post-acute care with pelvic fractures, external fixator and NWB for 10 weeks.

He is admitted to your post-acute service on his baseline dose of buprenorphine and oxycodone 10 – 20mg q 4 hours prn.



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