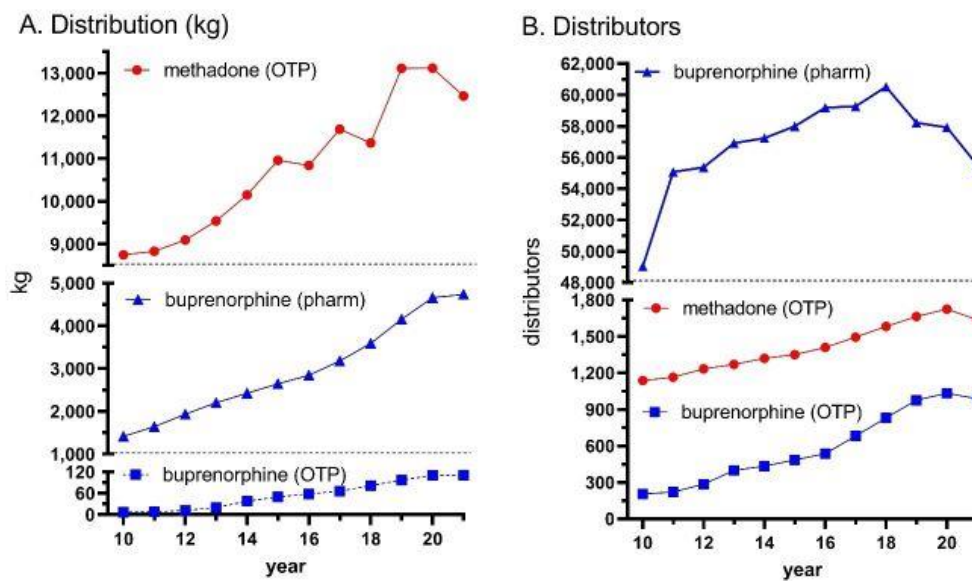
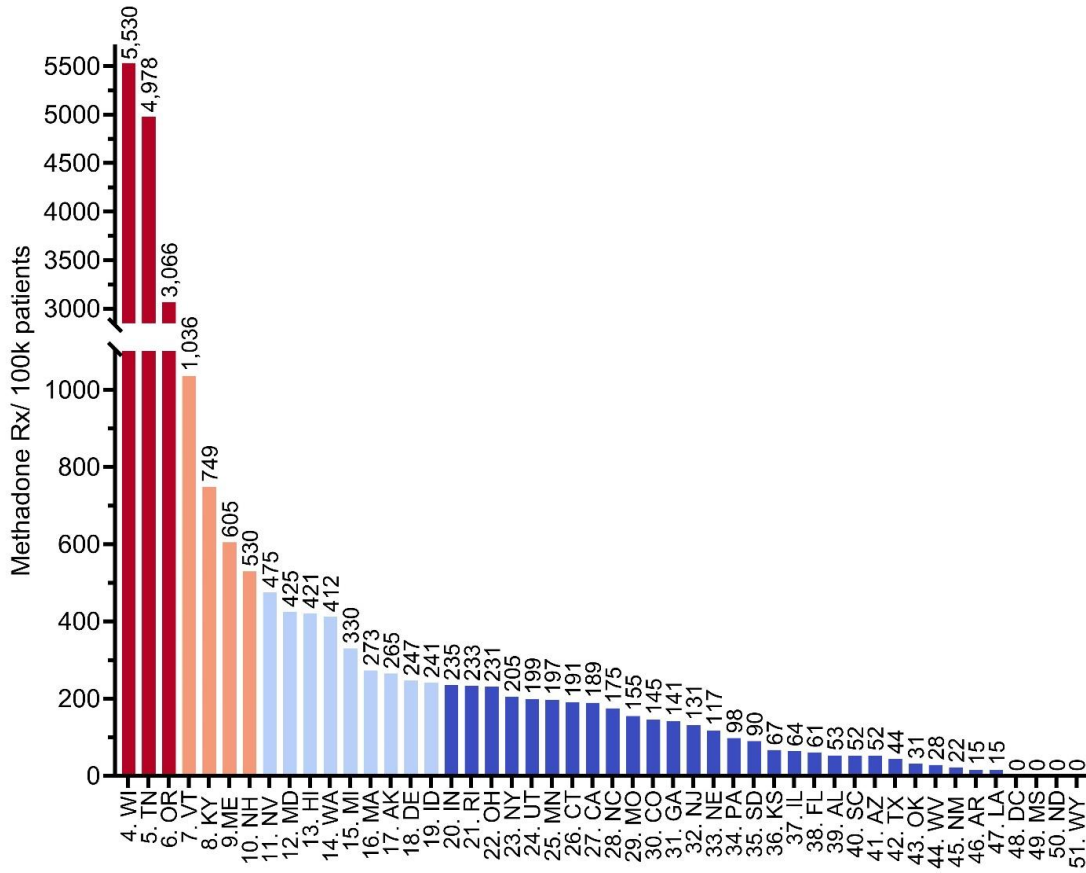


**Supplemental Figure 1.** Number of patients receiving methadone for opioid use disorder in the United States per year as reported by Substance Abuse and Mental Health Services Administration's National Survey of Substance Abuse Treatment Services data. The years 2014 and 2018 were not available and were omitted.



**Supplemental Figure 2.** Distribution in kg (A) and number of buyers and registrants (B) in Opioid Treatment Programs (OTP) and pharmacies (pharm, buprenorphine only) for methadone and buprenorphine as reported to the United States Drug Enforcement Administration's Automated Reports and Consolidated Orders system for the fifty states, Washington DC, and the US Territories. Methadone in 2021 (12.4 metric tons) was 5.69% lower than 2019 (13.1 metric tons) and 5.71% below 2020 (13.1 metric tons). Methadone by weight was 2.49-fold greater than buprenorphine from pharmacies and OTPs in 2021. The number of pharmacies distributing buprenorphine was 33.3 to 47.3-fold greater than the number of OTPs distributing methadone from 2010 to 2021.



**Supplemental Figure 3.** Methadone prescriptions, per 100K Medicaid patients, for 48 US states, and Washington DC.

**Supplemental Table 1.** Comparison of the pharmacological and therapeutic properties of methadone and buprenorphine.

	<b>Methadone</b>	<b>Buprenorphine</b>
Year developed	1937	1969
Opioid receptor activity	mu full-agonist	mu partial agonist
Other mechanism(s)	NMDA antagonist	non-selective for other opioid receptors
Potency (x morphine)	8 – 12	10
Metabolism	CYP2D6, CYP3A4	CYP3A4
Active metabolite(s)	none	norbuprenorphine
Half-life	8 – 59 hours for oral	24 – 48 hours for buccal
Formulation	mono	mono or combination with naloxone
Present in breast milk	yes, < 3% maternal dose	yes, < 1% maternal dose
Availability (US)	narcotic treatment programs	providers with an X-waiver
Schedule (US)	II	III
Crowdsourc (price/mg)	\$0.96	\$2.13
Black box warnings	addiction, abuse, misuse, QT prolongation	addiction, abuse, misuse <sup>1</sup> , child exposure can result in overdose
Opioid rank	#1	#4
2021 Distribution (US)	12.4 metric tons <sup>3</sup>	5.2 metric tons <sup>4</sup>
WHO Essential Medication <sup>2</sup>	Yes	yes

<sup>1</sup>buccal formulation; <sup>2</sup>complimentary; <sup>3</sup>Opioid Treatment Programs (OTP); <sup>4</sup>total of pharmacies, hospitals, and OTP.

**Supplementary Table 2.** Medicaid's State Drug Utilization Data reported National Drug Codes (NDC) for methadone prescribed for opioid use disorder.

<b>NDC</b>
54039168
54039268
54355344
54355563
54421825
54421925
54453825
54457025
54457125
54855324
54855424
406052710
406054034
406254001
406575501
406575523
406575562
406577101
406577123
406577162
406872510
904653061
13107000000
17478000000
31722000000

42806000000

60687000000

63739000000

66689000000

67457000000

67877000000

68084000000

68462000000

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**Supplemental Table 3.** Opioid treatment programs as reported to the Drug Enforcement Administration's Automated Reports and Consolidated Orders System per one million persons.

State	2010	2015	2020	2021
1. Rhode Island	16.1	16.1	21.0	24.6
2. Delaware	6.7	10.6	14.1	17.9
3. Maryland	9.9	11.4	14.4	14.3
4. Connecticut	10.1	10.3	11.9	14.1
5. Massachusetts	7.9	9.1	12.1	13.7
6. Vermont	11.2	14.4	12.4	12.4
7. New Mexico	4.8	6.7	11.3	9.5
8. Arizona	5.0	5.7	9.2	9.3
9. DC	8.3	5.9	7.3	9.0
10. Alaska	2.8	5.4	5.5	8.2
11. Maine	6.8	9.0	7.3	7.3
12. Illinois	5.1	5.6	7.2	7.2
13. Pennsylvania	5.4	5.8	6.9	7.0
14. Georgia	4.7	6.3	7.0	6.7
15. Kentucky	3.0	3.4	6.2	6.4
16. North Carolina	3.8	5.1	7.9	6.4
17. Iowa	1.3	2.2	5.6	6.0
18. New York	5.7	5.3	6.0	5.8
19. New Hampshire	4.6	6.0	7.3	5.8
20. Ohio	1.5	1.8	4.8	5.5
21. Oregon	3.4	3.7	5.2	5.4
22. Nevada	4.4	4.5	5.2	5.4
23. Utah	3.6	4.4	5.5	5.1
24. West Virginia	4.9	4.9	5.0	5.0
25. Oklahoma	3.7	3.6	5.3	5.0
26. Colorado	2.2	2.6	4.9	5.0
27. Michigan	3.3	4.3	4.5	4.8
28. New Jersey	0.11	3.7	4.7	4.7
29. Virginia	2.1	3.6	4.5	4.7
30. South Carolina	1.9	3.7	4.7	4.6
31. California	3.8	3.8	4.0	4.2
32. North Dakota	0.0	0.0	3.8	3.9
33. Wisconsin	2.3	3.0	3.7	3.7
34. Montana	2.0	2.9	3.7	3.6
35. Indiana	2.2	2.1	3.4	3.5
36. Washington	3.0	3.0	3.9	3.5
37. Alabama	2.9	4.5	4.6	3.2
38. Texas	3.3	3.2	3.3	3.1
39. Kansas	2.5	3.1	3.1	3.1
40. Minnesota	1.5	3.3	2.8	3.0
41. Missouri	1.7	2.5	2.6	2.9

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42. Tennessee	1.9	1.8	2.3	2.9
43. Louisiana	1.8	2.1	2.2	2.8
44. Hawaii	2.9	2.8	2.8	2.8
45. Florida	1.3	2.6	2.9	2.5
46. Idaho	1.9	1.8	2.2	2.1
47. Arkansas	1.0	2.0	2.0	2.0
48. South Dakota	0.0	1.2	1.1	1.1
49. Nebraska	1.6	1.6	1.5	1.0
50. Mississippi	0.3	0.3	1.7	1.0
51. Wyoming	0.0	0.0	0.0	0.0
<b>Mean</b>	<b>3.8</b>	<b>4.6</b>	<b>5.7</b>	<b>5.9</b>
<b>SEM</b>	<b>0.4</b>	<b>0.5</b>	<b>0.6</b>	<b>0.6</b>

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