

**Supplementary Table S1.** Generic names of opioid agents.

Opioid agents	
Buprenorphine	Methadone
Codeine	Morphine
Fentanyl	Oxycodone
Hydrocodone	Oxymorphone
Hydromorphone	Tapentadol
Meperidine	Tramadol

Listed agents may be present in medications alone or in combination with other opioid or non-opioid agents.

**Supplementary Table S2.** Population prevalence of self-reported prescription opioid use, cannabis use, and co-use within the past 30 days.

	Opioid use	Cannabis use	Co-use
<b>Overall (2009–2018)</b>	5.59 ± 0.43	17.75 ± 0.72	1.03 ± 0.19
<i>By survey cycle:</i>			
<b>2009–2010</b>	6.32 ± 0.98	15.64 ± 1.46	1.18 ± 0.43
<b>2011–2012</b>	6.57 ± 1.05	15.63 ± 1.54	1.01 ± 0.43
<b>2013–2014</b>	5.89 ± 0.96	17.16 ± 1.54	1.15 ± 0.43
<b>2015–2016</b>	4.16 ± 0.85	19.70 ± 1.69	0.90 ± 0.40
<b>2017–2018</b>	5.06 ± 0.97	20.41 ± 1.78	0.92 ± 0.42

Values are presented as proportion (%) ± standard error.

All proportions displayed are weighted to represent the non-institutionalized population in the continental United States. Survey weights are adjusted by the number of years of data included in analysis.

**Supplementary Table S3.** Primary multivariable logistic regression model for recent cannabis use, with recent prescription opioid use as primary exposure.

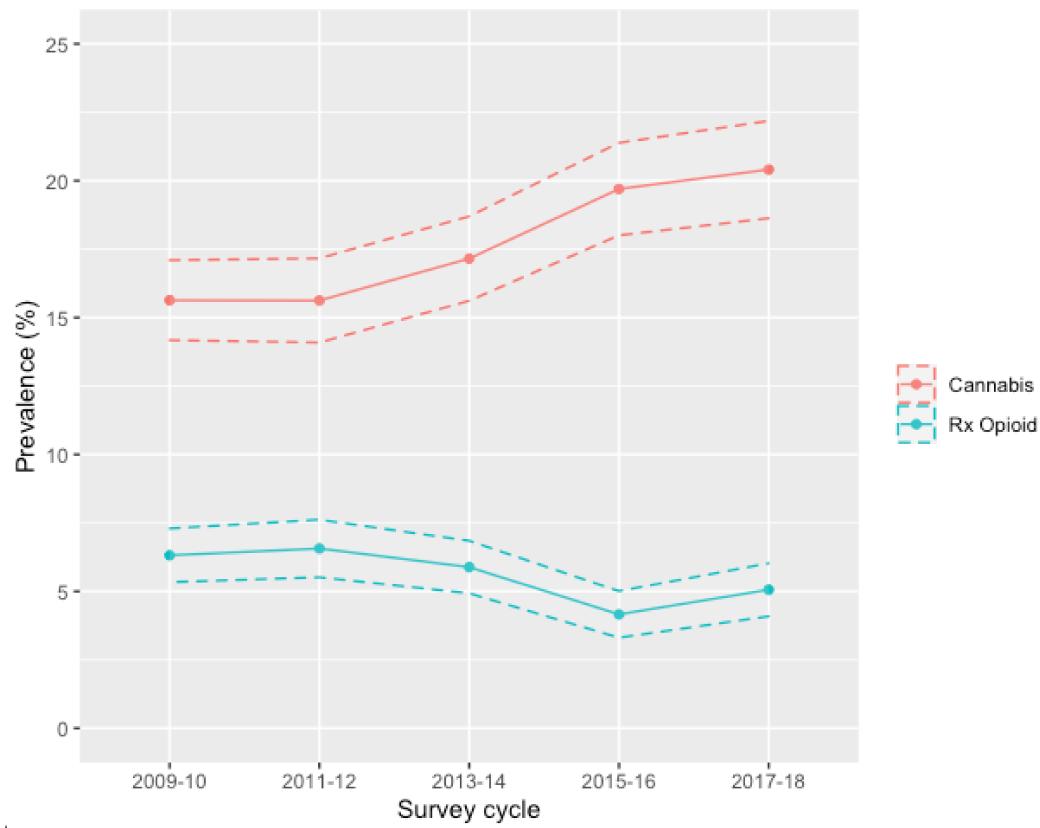
	Recent cannabis use				
	beta	OR	95% CI		p-value
			Lower	Upper	
(Intercept)	-1.340	0.26	0.17	0.39	<0.001
<b>Recent prescription opioid use</b>	-0.352	<b>0.70</b>	0.51	0.97	<b>0.032</b>
<b>Age (years)</b>					
18–25	--	1 (ref)	--	--	
26–40	-0.731	<b>0.48</b>	0.40	0.58	<0.001
41–59	-1.299	<b>0.27</b>	0.21	0.35	<0.001
<b>Sex</b>					
Male	--	1 (ref)	--	--	
Female	-0.338	<b>0.71</b>	0.62	0.81	<0.001
<b>Ethnicity</b>					
Hispanic	--	1 (ref)	--	--	
White	0.436	<b>1.55</b>	1.25	1.91	<0.001
Black	1.116	<b>3.05</b>	2.47	3.76	<0.001
Other	0.357	<b>1.43</b>	1.10	1.86	<b>0.008</b>
<b>Education beyond high school</b>	-0.028	0.97	0.83	1.14	0.735
<b>Family income-to-poverty ratio</b>					
≤1	--	1 (ref)	--	--	
1–3	-0.141	0.87	0.74	1.02	0.094
>3	-0.360	<b>0.70</b>	0.57	0.85	<0.001
<b>Health insurance</b>	-0.298	<b>0.74</b>	0.61	0.90	<b>0.003</b>
<b>Self-rated health status</b>					
Poor or fair	--	1 (ref)	--	--	
Good, very good, or excellent	-0.042	0.96	0.77	1.19	0.710
<b>Hypertension</b>	0.070	1.07	0.90	1.28	0.430
<b>Diabetes</b>	-0.193	0.82	0.57	1.18	0.295
<b>BMI (kg/m<sup>2</sup>)</b>					
<25	--	1 (ref)	--	--	
25–30	-0.285	<b>0.75</b>	0.65	0.87	<0.001
≥30	-0.441	<b>0.64</b>	0.55	0.76	<0.001
<b>Coronary artery disease</b>	0.041	1.04	0.37	2.91	0.938
<b>Heart failure</b>	-0.583	0.56	0.25	1.22	0.146

	Recent cannabis use				
	beta	OR	95% CI		p-value
			Lower	Upper	
<b>Stroke</b>	-0.407	0.67	0.31	1.44	0.301
<b>Asthma</b>	0.001	1.00	0.86	1.17	0.988
<b>COPD</b>	0.281	1.32	0.95	1.85	0.100
<b>Cancer</b>	0.349	<b>1.42</b>	1.00	2.01	<b>0.050</b>
<b>Arthritis</b>	0.139	1.15	0.94	1.40	0.165
<b>Depression</b>	0.457	<b>1.58</b>	1.23	2.02	<b>&lt;0.001</b>
<b>Smoker</b>	0.816	<b>2.26</b>	1.94	2.63	<b>&lt;0.001</b>
<b>Heavy alcohol use</b>	0.329	<b>1.39</b>	1.17	1.65	<b>&lt;0.001</b>
<b>Any illicit substance use</b>	1.305	<b>3.69</b>	3.10	4.40	<b>&lt;0.001</b>
<b>Survey cycle</b>					
2009–10	--	1 (ref)	--	--	
2011–12	-0.006	0.99	0.78	1.27	0.962
2013–14	0.131	1.14	0.93	1.40	0.214
2015–16	0.432	<b>1.54</b>	1.10	2.16	<b>0.012</b>
2017–18	0.527	<b>1.69</b>	1.28	2.24	<b>&lt;0.001</b>

**Supplementary Table S4.** Multivariable logistic regression model for recent cannabis use with interaction terms between recent prescription opioid use (exposure) and year of survey administration.

	Recent cannabis use				
	beta	OR	95% CI		p-value
			Lower	Upper	
(Intercept)	-1.364	<b>0.26</b>	0.17	0.39	<b>&lt;0.001</b>
<b>Recent prescription opioid use</b>	0.021	1.02	0.63	1.65	0.932
<b>Survey cycle</b>					
2009–10	--	1 (ref)	--	--	
2011–12	0.035	1.04	0.80	1.35	0.795
2013–14	0.151	1.16	0.93	1.45	0.181
2015–16	0.454	<b>1.57</b>	1.13	2.20	<b>0.008</b>
2017–18	0.563	<b>1.76</b>	1.30	2.38	<b>&lt;0.001</b>
<b>(Interaction terms)</b>					
Opioid * 2009–10	--	1 (ref)	--	--	
Opioid * 2011–12	-0.614	0.54	0.24	1.20	0.132
Opioid * 2013–14	-0.303	0.74	0.32	1.70	0.475
Opioid * 2015–16	-0.305	0.74	0.27	2.02	0.553
Opioid * 2017–18	-0.632	0.53	0.23	1.24	0.142
<b>Age (years)</b>					
18–25	--	1 (ref)	--	--	
26–40	-0.729	<b>0.48</b>	0.40	0.58	<b>&lt;0.001</b>
41–59	-1.299	<b>0.27</b>	0.21	0.35	<b>&lt;0.001</b>
<b>Sex</b>					
Male	--	1 (ref)	--	--	
Female	-0.340	<b>0.71</b>	0.62	0.81	<b>&lt;0.001</b>
<b>Ethnicity</b>					
Hispanic	--	1 (ref)	--	--	
White	0.437	<b>1.55</b>	1.25	1.91	<b>&lt;0.001</b>
Black	1.116	<b>3.05</b>	2.48	3.77	<b>&lt;0.001</b>
Other	0.357	<b>1.43</b>	1.10	1.86	<b>0.008</b>
<b>Education beyond high school</b>	-0.028	0.97	0.83	1.14	0.736
<b>Family income-to-poverty ratio</b>					
≤1	--	1 (ref)	--	--	
1–3	-0.142	0.87	0.74	1.02	0.093
>3	-0.359	<b>0.70</b>	0.57	0.85	<b>&lt;0.001</b>

<b>Recent cannabis use</b>					
	<b>beta</b>	<b>OR</b>	<b>95% CI</b>		<b>p-value</b>
			Lower	Upper	
<b>Health insurance</b>	-0.297	<b>0.74</b>	0.61	0.90	<b>0.003</b>
<b>Self-rated health status</b>					
Poor or fair	--	1 (ref)	--	--	
Good, very good, or excellent	-0.044	0.96	0.77	1.19	0.693
<b>Hypertension</b>	0.069	1.07	0.90	1.27	0.433
<b>Diabetes</b>	-0.193	0.82	0.57	1.18	0.294
<b>BMI (kg/m<sup>2</sup>)</b>					
<25	--	1 (ref)	--	--	
25–30	-0.285	<b>0.75</b>	0.65	0.87	<b>&lt;0.001</b>
≥30	-0.444	<b>0.64</b>	0.54	0.76	<b>&lt;0.001</b>
<b>Coronary artery disease</b>	0.043	1.04	0.37	2.93	0.935
<b>Heart failure</b>	-0.604	0.55	0.24	1.23	0.144
<b>Stroke</b>	-0.404	0.67	0.31	1.45	0.307
<b>Asthma</b>	0.005	1.00	0.86	1.17	0.953
<b>COPD</b>	0.283	1.33	0.95	1.85	0.097
<b>Cancer</b>	0.346	1.41	1.00	2.00	0.053
<b>Arthritis</b>	0.139	1.15	0.95	1.40	0.162
<b>Depression</b>	0.457	<b>1.58</b>	1.23	2.02	<b>&lt;0.001</b>
<b>Smoker</b>	0.818	<b>2.26</b>	1.95	2.64	<b>&lt;0.001</b>
<b>Heavy alcohol use</b>	0.329	<b>1.39</b>	1.17	1.65	<b>&lt;0.001</b>
<b>Any illicit substance use</b>	1.307	<b>3.70</b>	3.09	4.41	<b>&lt;0.001</b>



**Supplementary Figure S1.** Weighted prevalence of self-reported prescription opioid use and self-reported cannabis use in the past 30 days from participants of the National Health and Nutrition Examination Survey, 2009–2018. Values have been adjusted using survey sample weights to represent the non-institutionalized population of the continental United States.

