SUPPLEMENT – EFFECTIVENESS OF POLICIES FOR CONTROLLING THE U.S. OPIOID EPIDEMIC: A MODEL-BASED ANALYSIS

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Figure S1A. Projections for base case model 1 in the absence of additional intervention

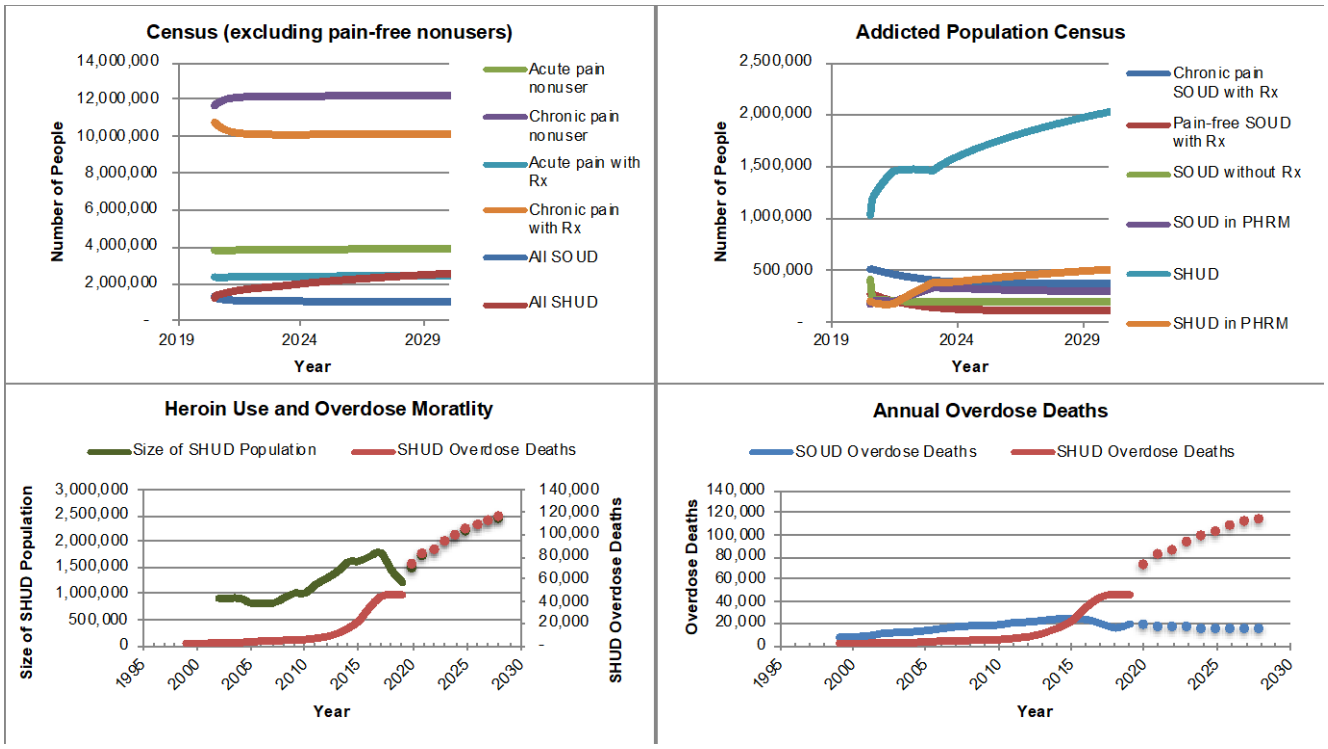


Figure S1B. Projections for base case model 2 in the absence of additional intervention

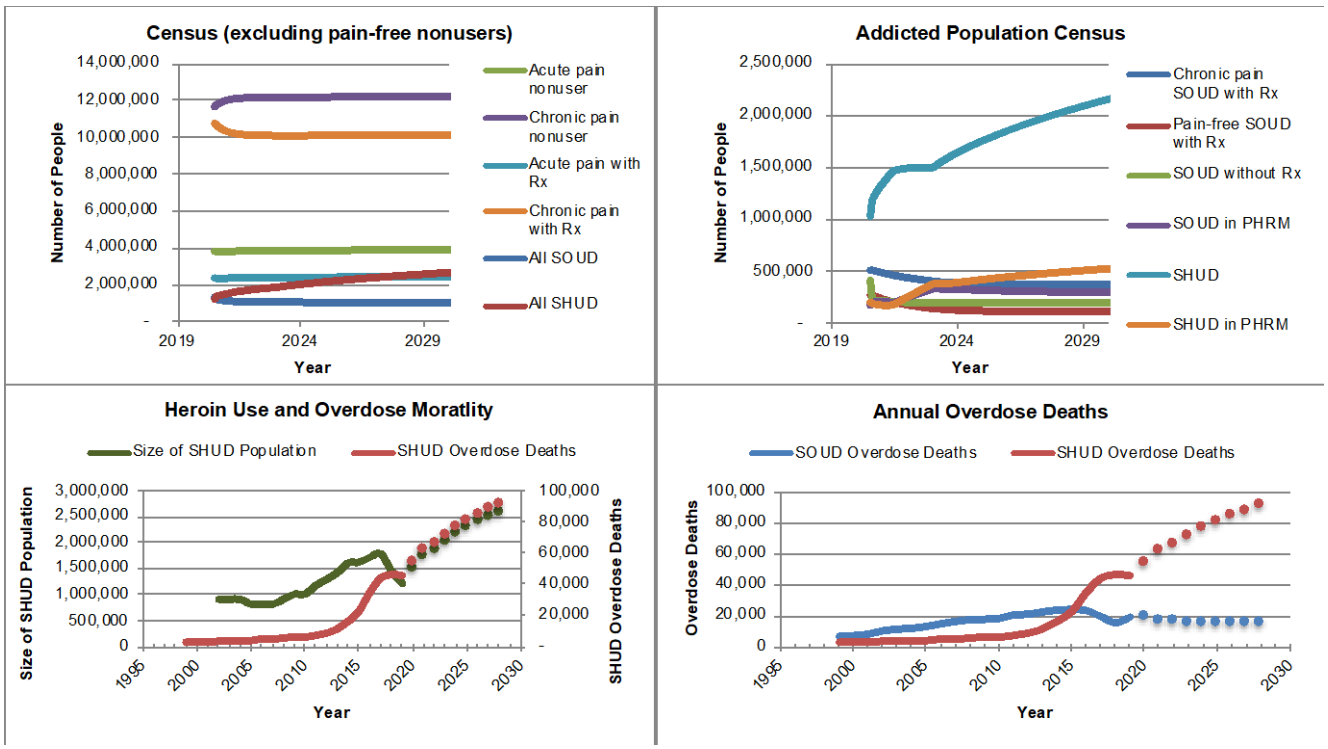


Figure S1C. Projections for base case model 3 in the absence of additional intervention

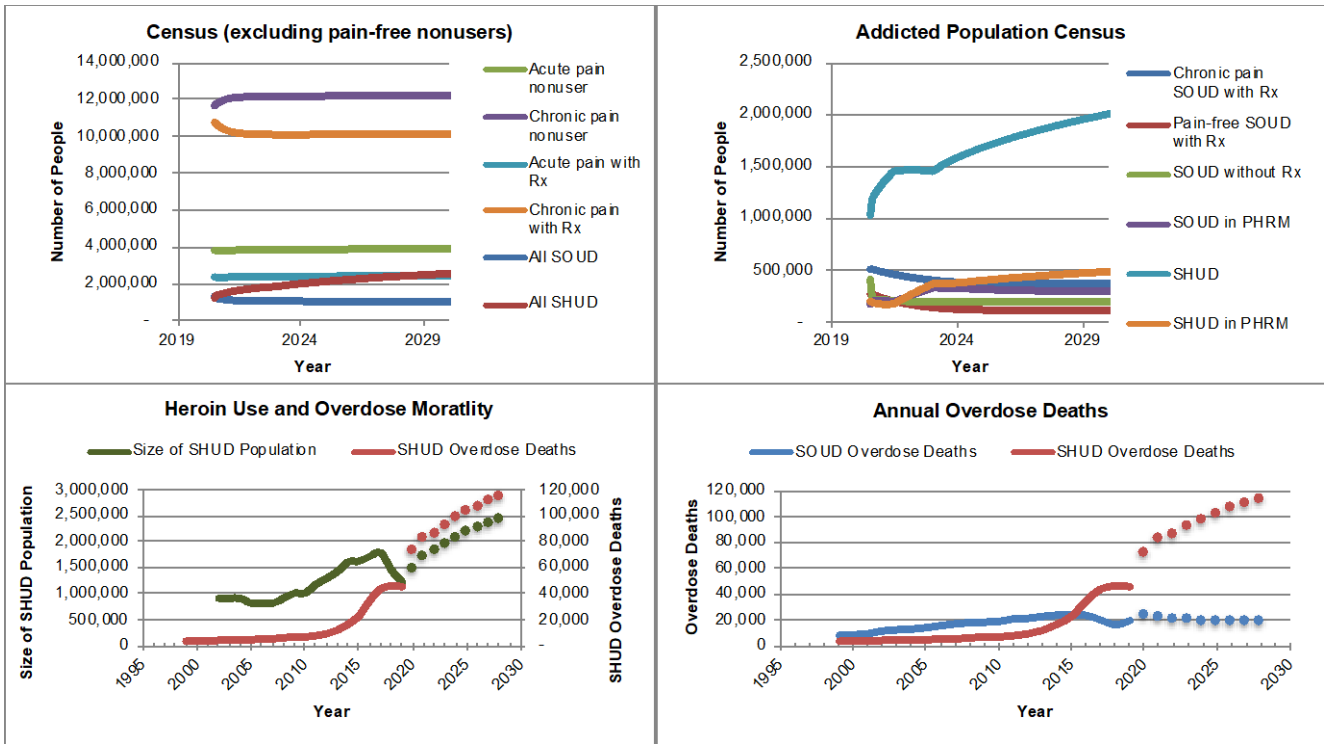


Figure S1D. Projections for base case model 4 in the absence of additional intervention

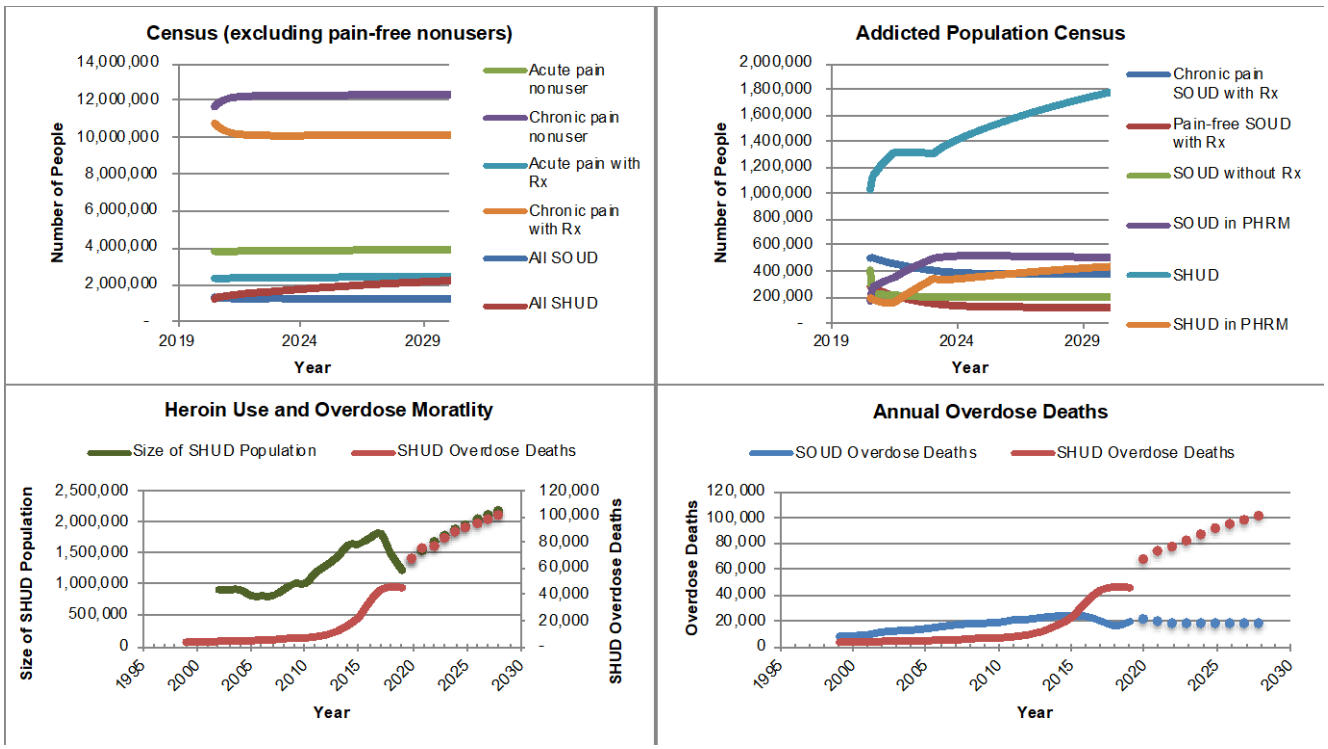


Figure S1E. Projections for base case model 5 in the absence of additional intervention

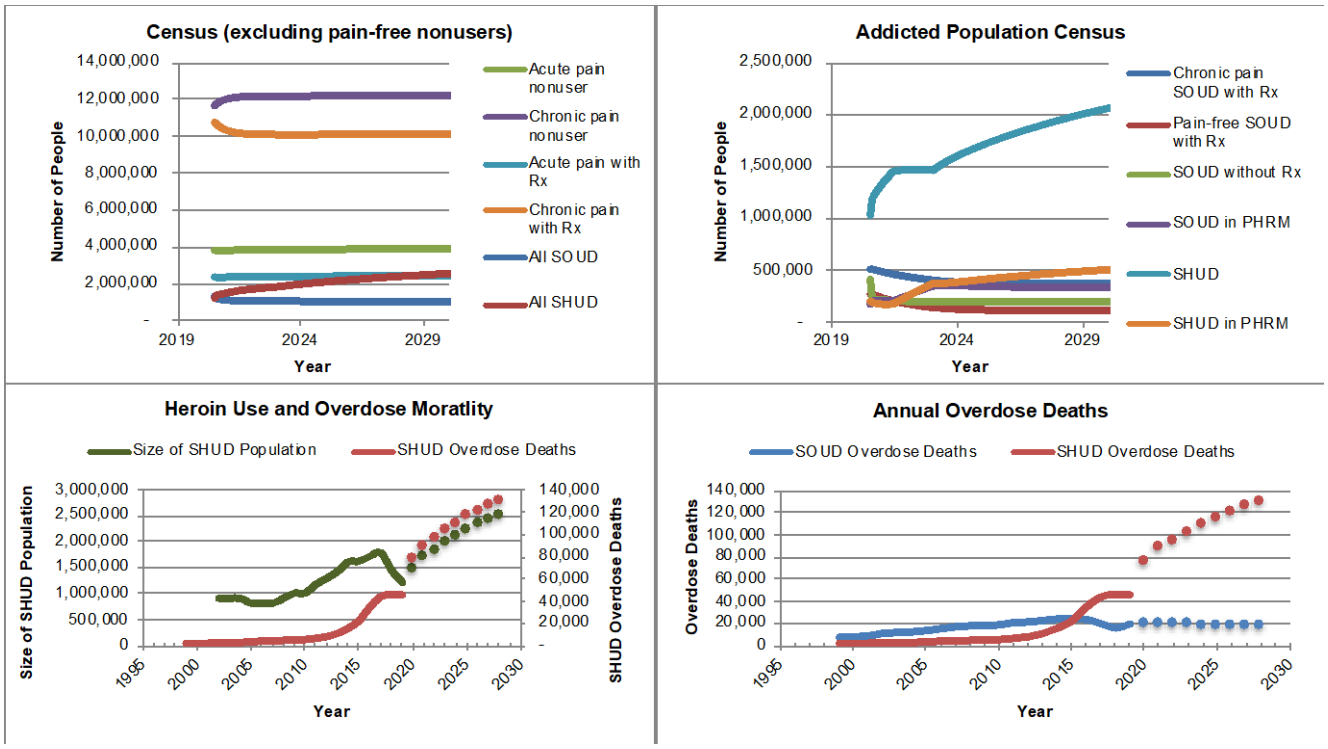


Figure S1F. Projections for base case model 6 in the absence of additional intervention

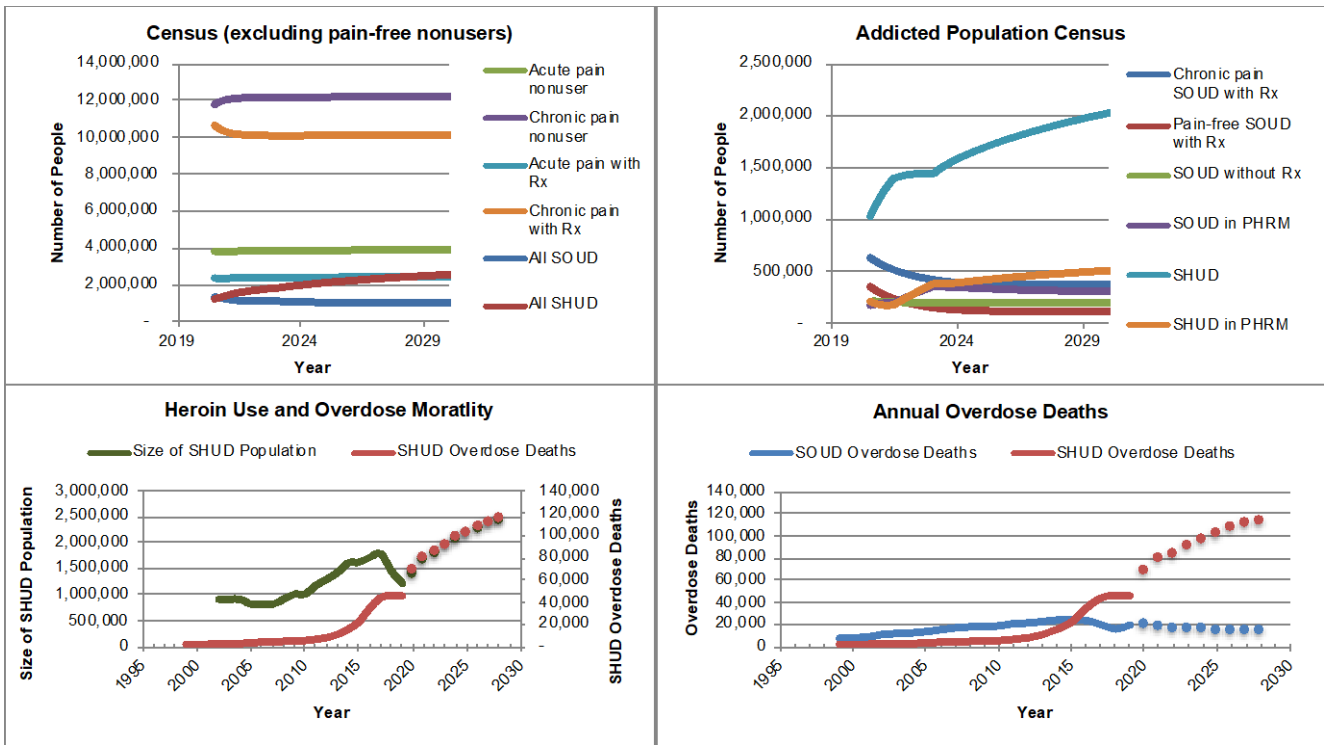


Figure S1G. Projections for base case model 7 in the absence of additional intervention

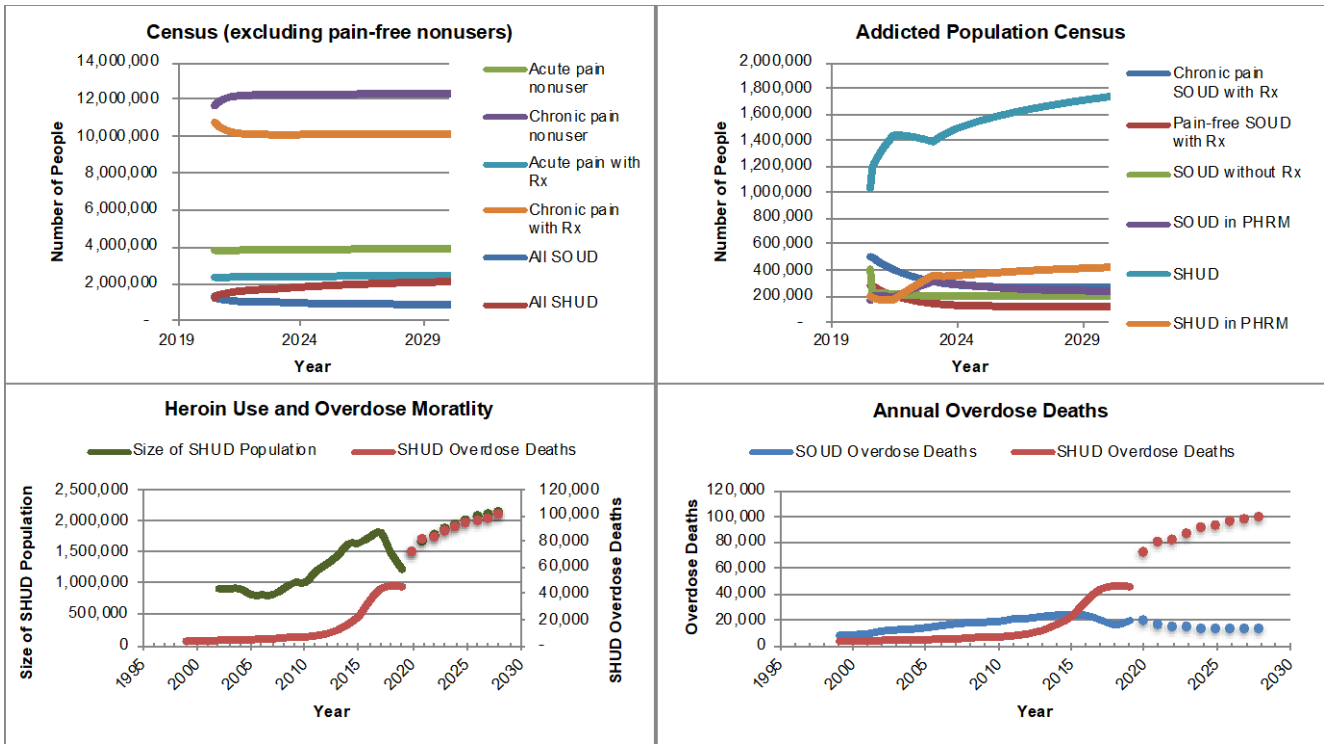


Figure S1H. Projections for base case model 8 in the absence of additional intervention

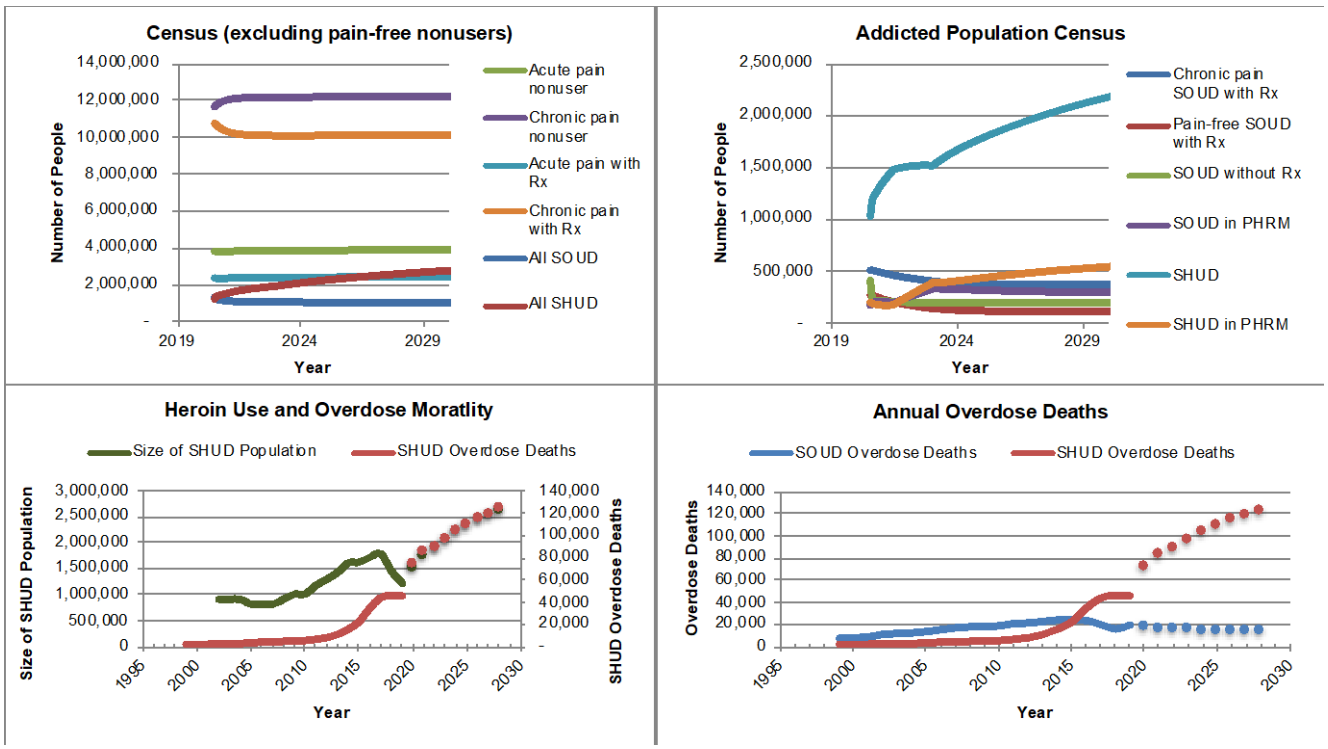


Figure S1I. Projections for base case model 9 in the absence of additional intervention

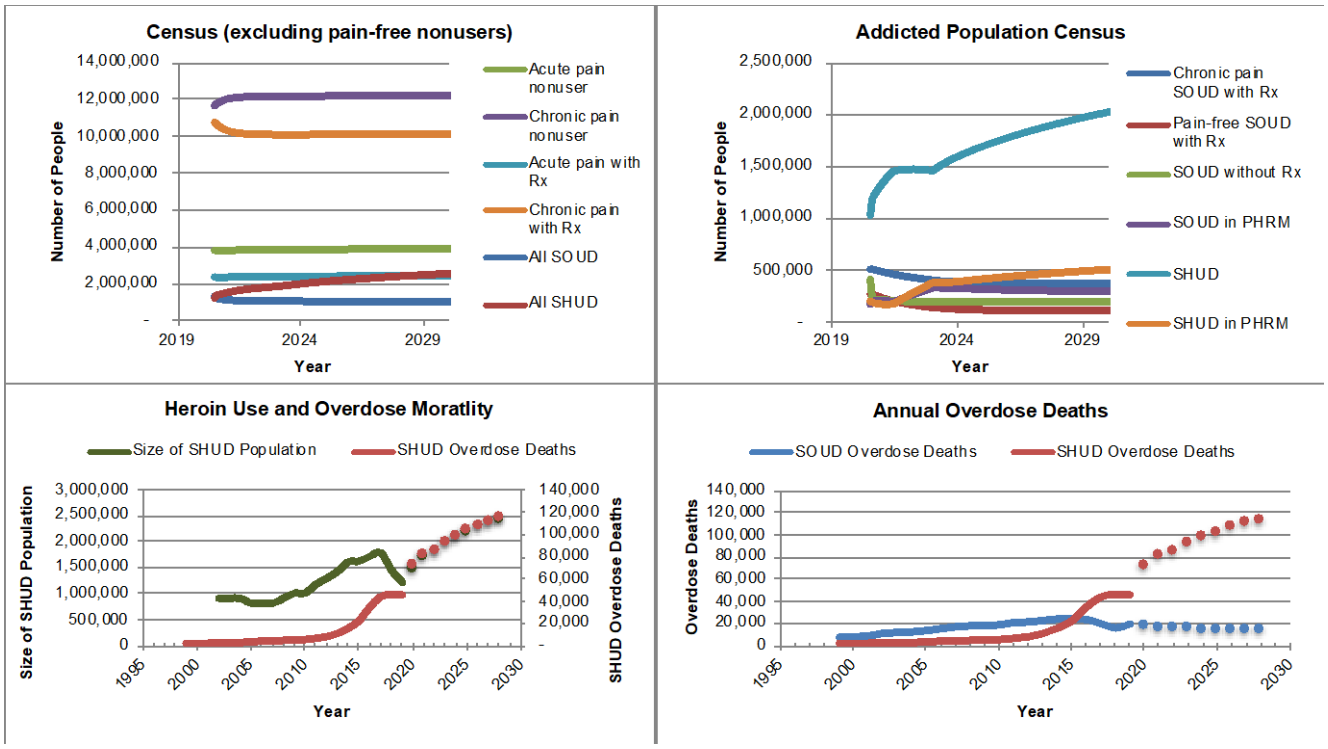
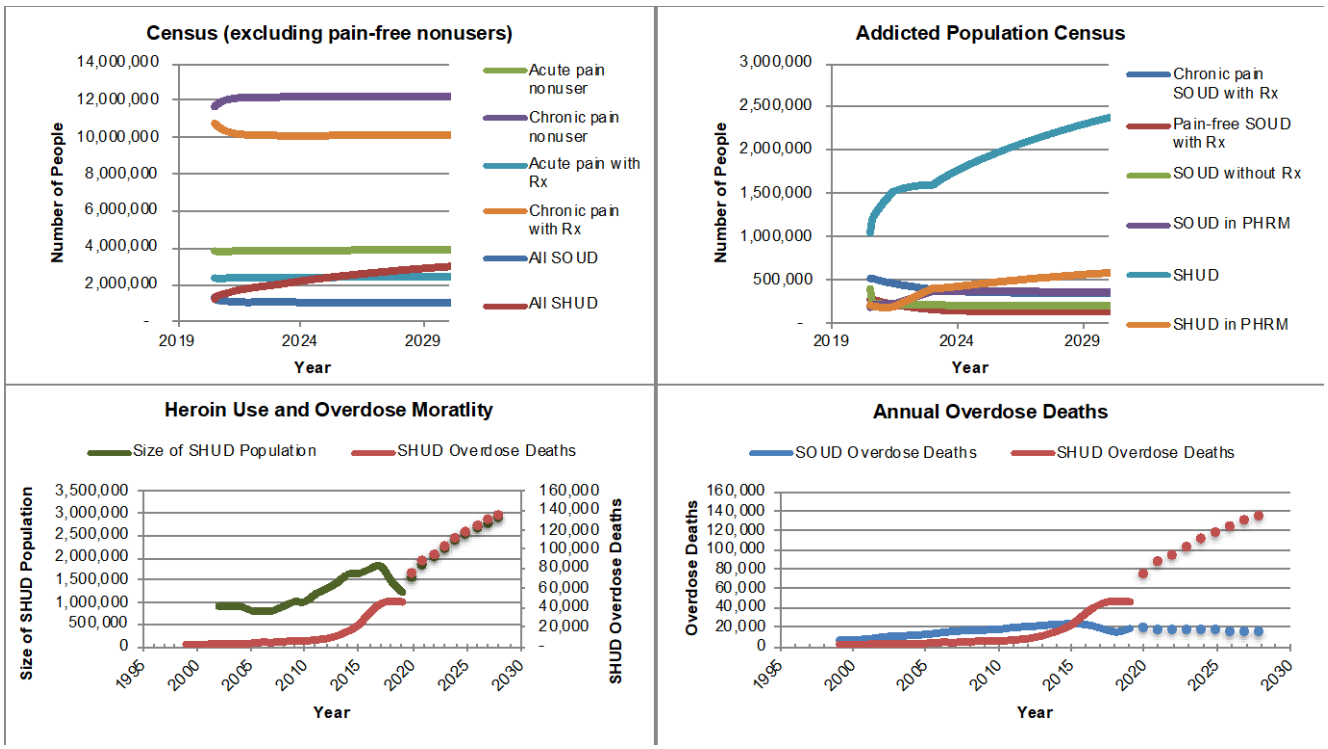


Figure S1J. Projections for base case model 10 in the absence of additional intervention



Abbreviations: SOUD = severe opioid use disorder; SHUD = severe heroin use disorder; PHRM = pharmacotherapy

Table S1. Parameter values and sources

Parameter	Value	Source
DEMOGRAPHIC DATA		
Total population size, age 12+	276,077,200	[1]
Chronic pain prevalence (moderate to severe)	8.6%	Calculated[2-5]
Acute pain prevalence (moderate to severe)	2.5%	Calculated[6-11]
Severe opioid use disorder prevalence	0.49%	Calculated[12]
Severe heroin use disorder prevalence	0.36%	Calculated[12-15]
Rate of maturation into the population, people/month	234,167	Assumed[16,17]
PAIN NATURAL HISTORY		
Acute pain incidence for pain-free nonusers, %/month	2.5%	Calculated[6,7,9,10,18,19]
Chronic pain incidence for pain-free nonusers, %/month	0.30%	Assumed
Chronic pain subsidence, %/month	8%	Assumed[20]
Probability that acute pain persists without opioid prescription	15.0%	Assumed[21]
Probability that acute pain persists with opioid prescription	14.7%	Assumed
Percent of 12+ population with chronic pain of any severity	43%	Calculated[3-5]
Percent of chronic pain population with moderate to severe pain	20%	Assumed[2]
Percent of 12+ population getting surgery or ED trauma visit	4%	Calculated[9,10,18,19]
Percent of surgeries resulting in moderate to severe pain	61%	[6]
Percent of prescription-holding SOUD population who suffer from chronic pain	65%	[22]
Percent of SOUD without Rx and SHUD populations who have with chronic pain	45%	Assumed[23]
Risk ratio for chronic pain developing during acute pain treatment with vs. without opioids	0.98	Assumed
PRESCRIBING BEHAVIOR		
Percent of acute pain patients prescribed opioids	38%	Calculated[24-28]
Probability of continued use of opioids for pain that persists from acute	50%	Assumed[24]
Percent of total population prescribed opioids for chronic pain	4%	Calculated[29]
Probability of chronic pain sufferer being prescribed opioids, %/month	7.6%	Assumed
Probability of SOUD individual being prescribed opioids, %/month	7.6%	Assumed
Probability of opioid prescription renewal for chronic pain patients without SOUD, %/month	97%	Assumed
Probability of opioid prescription renewal for individuals with SOUD, %/month	94%	Assumed[30]
Estimated annual decline in opioid prescriptions from 2018-2019	8.9%	[31]
Probability of individuals with iatrogenic SOUD continuing use of opioids after acute pain treatment	50%	Assumed

Parameter	Value	Source
Probability that chronic pain opioid user without SOUD wants to get prescription renewed, %/month	99%	Assumed
Probability that an opioid user is able to get renewal for chronic pain prescription if they choose, %/month	98%	Assumed
USE DISORDER		
Probability of developing SHUD for non-opioid users with no pain	0.002%	Assumed
Probability of iatrogenic SOUD with opioid prescription, %/month	0.20%	Calculated[32,33]
Probability of a non-medical user developing SOUD from diverted pills, %/month	7%	Calculated[34]
Baseline* rate of escalation to SHUD from SOUD without Rx, %/month	4%	Assumed
Probability of escalation to SHUD if there are not diverted pills for SOUD without Rx	75%-60%	Expert opinion
SOUD prevalence among population with opioid prescription for chronic pain	7%	Assumed[27,28,35]
Percent of SHUD population who escalated from SOUD	80%	[13,14]
Number of pain-free nonusers a prescription holder diverts opioids to, #/month	0.01	Assumed
Proportionality factory relating SOUD without Rx population able to be sustained by diverted pills to lagged number of prescription holders	0.02	Calculated
TREATMENT AND DESISTANCE		
Percent of SOUD population enrolled in pharmacotherapy	13%-26%	Asssumed[28]
Percent of SHUD population enrolled in pharmacotherapy	16%-32%	Assumed[36,37]
Rate of SOUD with Rx enrollment in pharmacotherapy, %/month	0.05%-1%	Assumed
Rate of SOUD without Rx enrollment in pharmacotherapy, %/month	2%-4%	Assumed
Rate of SHUD enrollment in pharmacotherapy, %/month	2%-4%	Assumed[38]
Rate of drop out from pharmacotherapy for SOUD, %/month	5%	Assumed
Rate of drop out from pharmacotherapy for SHUD, %/month	14%	Calculated[39]
Rate of desistance from SOUD in pharmacotherapy, %/month	1.0%	Assumed[23]
Baseline rate of desistance from SOUD without pharmacotherapy, %/month	0.5%	Calculated[23,40]
Rate of desistance from SHUD in pharmacotherapy, %/month	0.5%	Assumed
Rate of desistance from SHUD not in pharmacotherapy, %/month	0.25%	Assumed
Probability of enrollment in pharmacotherapy if there are not diverted pills for SOUD without Rx	15%-30%	Expert opinion
Probability of desistance if there are not diverted pills for SOUD without Rx	10%	Expert opinion

Parameter	Value	Source
MORTALITY		
Mortality rate for the general population, %/month	0.07%	[17]
Mortality rate for SOUD not in pharmacotherapy %/month	0.23%	Calculated[12,17,40-42]
Mortality rate for SHUD not in pharmacotherapy %/month	0.54%	Calculated[12,15,17,41-43]
Mortality rate for SOUD in pharmacotherapy %/month	0.15%	Calculated[40]
Mortality rate for SHUD in pharmacotherapy %/month	0.30%	Calculated[40]
Overdose mortality for person with SHUD, not in pharmacotherapy, %/month	0.43%	Calculated[12,15,17,41,42]
Overdose mortality for person with SOUD, not in pharmacotherapy, %/month	0.15%	Calculated[12,17,40-42]
Infection-related mortality for person with SHUD, not in pharmacotherapy, %/month	0.03%	Calculated[43]
1-month relative risk of use disorder-related mortality in vs. out of pharmacotherapy for person with severe use disorder	0.50	[40]
UTILITY VALUES		
Pain-free nonuser	1	Assumed
Chronic pain nonuser	0.85	Assumed
Acute pain nonuser	0.88	Calculated[6,44]
Acute pain with Rx	0.94	Calculated[6,44]
Chronic pain with Rx	0.85	Assumed
SOUD not in pharmacotherapy	0.83	Assumed
SOUD in pharmacotherapy	0.92	Assumed
SHUD not in pharmacotherapy	0.8	[45-47]
SHUD in pharmacotherapy	0.9	[45-47]
Dead	0	Assumed

Abbreviations: Rx = prescription; SHUD = severe heroin use disorder; SOUD = severe opioid use disorder

Table S2. Results of base-case analyses with no additional intervention

Table S2a. Results over 5 years

Set	Parameter Set Brief Description	Discounted Net Present LYs (Thousands)	Discounted Net Present QALYs (Thousands)	Total Opioid Use Disorder Deaths	Pill Deaths	Heroin Deaths
1	Reference case	6,323,398	6,224,610	551,410	86,165	465,245
2	Decreased chance of heroin death	6,327,809	6,228,243	444,130	86,166	357,964
3	Increased chance of prescription opioid death	6,322,344	6,223,704	571,413	107,318	464,094
4	Reduced probability of turning to heroin if there are not enough pills to divert	6,325,973	6,227,398	510,306	93,437	416,869
5	Reduced pharmacotherapy effectiveness	6,319,769	6,221,158	613,237	101,048	512,189
6	Increased chance of individuals with SOUD having a prescription (initial)	6,323,584	6,224,797	544,933	90,067	454,866
7	Decreased chance of iatrogenic use disorder	6,326,165	6,227,859	521,638	77,852	443,786
8	Increased chance of starting heroin from no pain non-use disorder state	6,321,941	6,222,912	569,065	86,160	482,905
9	Decreased chance of escalating from SOUD to SHUD regardless of pill supply	6,323,398	6,224,610	551,410	86,165	465,245
10	Increased likelihood of diverting opioid prescription to pain-free nonuser	6,320,089	6,220,763	591,530	87,342	504,188
Mean		6,323,447	6,224,605	546,907	90,172	456,735

Table S2b. Results over 10 years

Set	Parameter Set Brief Description	Discounted Net Present LYs (Thousands)	Discounted Net Present QALYs (Thousands)	Total Opioid Use Disorder Deaths	Pill Deaths	Heroin Deaths
1	Reference case	6,759,006	6,652,032	1,226,112	164,261	1,061,851
2	Decreased chance of heroin death	6,765,194	6,657,196	996,437	164,267	832,170
3	Increased chance of prescription opioid death	6,757,822	6,651,002	1,261,789	204,434	1,057,355
4	Reduced probability of turning to heroin if there are not enough pills to divert	6,762,881	6,656,282	1,121,251	180,671	940,580
5	Reduced pharmacotherapy effectiveness	6,753,518	6,646,673	1,383,189	196,359	1,186,830
6	Increased chance of individuals with SOUD having a prescription (initial)	6,759,171	6,652,204	1,218,802	168,333	1,050,470
7	Decreased chance of iatrogenic use disorder	6,764,316	6,658,235	1,112,636	144,093	968,542
8	Increased chance of starting heroin from no pain non-use disorder state	6,756,342	6,648,949	1,287,111	164,224	1,122,887
9	Decreased chance of escalating from SOUD to SHUD regardless of pill supply	6,759,006	6,652,032	1,226,112	164,261	1,061,851
10	Increased likelihood of diverting opioid prescription to pain-free nonuser	6,752,959	6,645,049	1,363,568	167,645	1,195,922
Mean		6,759,021	6,651,966	1,219,701	171,855	1,047,846

Abbreviations: LY = life year; QALY = quality-adjusted life year; SHUD = severe heroin use disorder; SOUD = severe opioid use disorder.

Table S3. Results of interventions: difference from the status quo (mean, minimum, and maximum)

Table S3a. Results of interventions over five years

	Mean Change *[Min, Max]*				
Policy	**Discounted Net Present LYs (Thousands)**	**Discounted Net Present QALYs (Thousands)**	**Pill Deaths**	**Heroin Deaths**	**Total Opioid-Related Deaths**
Acute Pain Prescribing	244 *[171, 323]*	-80 *[-166, 14]*	-1,110 *[-1,346, -932]*	-1,267 *[-2,189, -662]*	-2,376 *[-3,298, -1,593]*
Prescribing for Transitioning Pain	53 *[36, 72]*	71 *[51, 95]*	-555 *[-690, -421]*	217 *[25, 291]*	-339 *[-537, -203]*
Chronic Pain Prescribing	255 *[138, 360]*	360 *[227, 487]*	-3,496 *[-4,293, -3,119]*	2,327 *[1,183, 3,212]*	-1,169 *[-2,223, 93]*
Drug Rescheduling	1,000 *[345, 1,665]*	1,783 *[989, 2,600]*	-38,300 *[-46,921, -32,958]*	49,197 *[30,670, 58,905]*	10,897 *[-3,947, 18,714]*
Drug Reformulation	192 *[125, 262]*	250 *[172, 333]*	-1,628 *[-1,992, -1,415]*	57 *[-752, 614]*	-1,570 *[-2,378, -800]*
Pharmacotherapy	625 *[161, 749]*	732 *[297, 860]*	373 *[-1, 1,644]*	-10,576 *[-12,477, -4,338]*	-10,203 *[-12,228, -2,694]*
Excess Opioid Disposal 10%	211 *[156, 490]*	313 *[252, 641]*	-3,078 *[-3,758, -2,616]*	1,977 *[-1,246, 2,891]*	-1,102 *[-4,377, -309]*
Excess Opioid Disposal 15%	317 *[233, 734]*	469 *[377, 961]*	-4,618 *[-5,637, -3,924]*	2,967 *[-1,865, 4,338]*	-1,650 *[-6,563, -462]*
Naloxone 5%	970 *[881, 1,055]*	808 *[734, 878]*	-4,441 *[-5,274, -3,840]*	-19,012 *[-21,071, -15,278]*	-23,454 *[-26,032, -19,527]*
Naloxone 15%	3,026 *[2,751, 3,292]*	2,519 *[2,289, 2,738]*	-13,345 *[-15,850, -11,535]*	-57,658 *[-63,972, -46,223]*	-71,003 *[-78,884, -58,988]*
Naloxone 30%	6,436 *[5,858, 7,010]*	5,352 *[4,868, 5,823]*	-26,753 *[-31,787, -23,120]*	-117,212 *[-130,269, -93,630]*	-143,965 *[-160,180, -119,217]*
Syringe Exchange	107 *[95, 119]*	88 *[78, 98]*	0 *[0,0]*	-2,809 *[-3,116, -2,259]*	-2,809 *[-3,116, -2,259]*
PMP	515 *[342, 695]*	90 *[-114, 304]*	-3,633 *[-4,440, -3,122]*	-667 *[-2,661, 681]*	-4,300 *[-6,293, -2,441]*
Psychosocial Treatment	342 *[291, 380]*	391 *[335, 427]*	-370 *[-433, -309]*	-3,583 *[-4,033, -2,866]*	-3,953 *[-4,446, -3,213]*
Drug Rescheduling + Naloxone 5%	1,907 *[1,186, 2,639]*	2,537 *[1,689, 3,409]*	-40,870 *[-49,912, -35,186]*	28,106 *[12,003, 37,506]*	-12,764 *[-25,520, -4,835]*
Drug Rescheduling + Naloxone 15%	3,837 *[2,978, 4,711]*	4,140 *[3,176, 5,129]*	-46,016 *[-55,902, -39,646]*	-14,757 *[-26,145, -5,986]*	-60,773 *[-71,540, -51,118]*
Drug Rescheduling + Naloxone 30%	7,057 *[5,973, 8,174]*	6,809 *[5,656, 7,997]*	-53,755 *[-64,911, -46,350]*	-80,785 *[-97,600, -63,775]*	-134,540 *[-150,355, -115,965]*

	Mean Change *[Min, Max]*				
Policy	**Discounted Net Present LYs (Thousands)**	**Discounted Net Present QALYs (Thousands)**	**Pill Deaths**	**Heroin Deaths**	**Total Opioid-Related Deaths**
Drug Rescheduling + SEP	1,113 *[451, 1,789]*	1,877 *[1,078, 2,702]*	-38,300 *[-46,921, -32,958]*	46,091 *[27,926, 55,753]*	7,790 *[-6,691, 15,561]*
Drug Rescheduling + Pharmacotherapy	1,580 *[963, 2,353]*	2,454 *[1,687, 3,379]*	-37,606 *[-46,155, -32,346]*	38,285 *[21,032, 53,180]*	679 *[-13,189, 15,400]*
Drug Rescheduling + Psychosocial Treatment	1,300 *[636, 1,984]*	2,124 *[1,320, 2,962]*	-38,393 *[-47,022, -33,031]*	45,631 *[27,751, 55,197]*	7,239 *[-7,009, 14,919]*
PMP + Naloxone 5%	1,467 *[1,210, 1,727]*	883 *[609, 1,163]*	-7,895 *[-9,496, -6,807]*	-19,653 *[-23,570, -15,660]*	-27,548 *[-31,331, -23,297]*
PMP + Naloxone 15%	3,485 *[3,053, 3,916]*	2,562 *[2,142, 2,982]*	-16,439 *[-19,634, -14,194]*	-58,244 *[-66,062, -46,574]*	-74,684 *[-82,669, -62,374]*
PMP + Naloxone 30%	6,834 *[6,118, 7,556]*	5,343 *[4,685, 6,002]*	-29,306 *[-34,910, -25,314]*	-117,714 *[-131,518, -93,932]*	-147,020 *[-163,320, -122,023]*
PMP + SEP	621 *[441, 813]*	177 *[-32, 401]*	-3,633 *[-4,440, -3,122]*	-3,472 *[-5,747, -2,045]*	-7,105 *[-9,380, -5,166]*
PMP + Pharmacotherapy	1,125 *[706, 1,424]*	804 *[412, 1,141]*	-3,275 *[-4,136, -2,265]*	-11,072 *[-14,921, -4,735]*	-14,347 *[-18,313, -7,000]*
PMP + Psychosocial Treatment	851 *[663, 1,053]*	473 *[253, 714]*	-3,989 *[-4,854, -3,419]*	-4,214 *[-6,475, -2,844]*	-8,203 *[-10,442, -6,263]*
All Prescribing (Acute, Transitioning, Chronic)	553 *[348, 758]*	352 *[114, 596]*	-5,099 *[-6,252, -4,418]*	1,171 *[-1,002, 2,667]*	-3,927 *[-6,101, -1,751]*
All Prescribing + Naloxone 5%	1,502 *[1,215, 1,786]*	1,142 *[835, 1,451]*	-9,288 *[-11,218, -8,040]*	-17,894 *[-21,982, -14,198]*	-27,182 *[-31,138, -23,218]*
All Prescribing + Naloxone 15%	3,515 *[3,055, 3,968]*	2,816 *[2,365, 3,265]*	-17,688 *[-21,178, -15,299]*	-56,646 *[-64,619, -45,248]*	-74,334 *[-82,054, -62,289]*
All Prescribing + Naloxone 30%	6,856 *[6,115, 7,598]*	5,591 *[4,904, 6,276]*	-30,337 *[-36,186, -26,226]*	-116,361 *[-130,296, -92,814]*	-146,698 *[-162,772, -121,928]*
All Prescribing + SEP	659 *[448, 876]*	439 *[196, 693]*	-5,099 *[-6,252, -4,418]*	-1,645 *[-4,098, -71]*	-6,743 *[-9,198, -4,489]*
All Prescribing + Pharmacotherapy	1,161 *[733, 1,484]*	1,063 *[661, 1,430]*	-4,736 *[-5,939, -3,769]*	-9,231 *[-13,257, -2,536]*	-13,967 *[-18,111, -6,305]*
All Prescribing + Psychosocial Treatment	887 *[668, 1,113]*	733 *[479, 1,003]*	-5,447 *[-6,657, -4,709]*	-2,371 *[-4,810, -853]*	-7,818 *[-10,236, -5,563]*
All Prescribing + Drug Reformulation + Pharmacotherapy + SEP + Naloxone 5% + Psychosocial Treatment	2,689 *[2,357, 3,183]*	2,519 *[2,143, 3,057]*	-10,666 *[-13,005, -9,230]*	-33,887 *[-40,973, -27,622]*	-44,554 *[-51,593, -38,081]*

Abbreviations: LY = life year; PMP = prescription monitoring program; SEP = syringe exchange program; QALY = quality-adjusted life year.

Table S3b. Results of interventions over ten years

	Mean Change *[Min, Max]*				
Policy	**Discounted Net Present LYs (Thousands)**	**Discounted Net Present QALYs (Thousands)**	**Pill Deaths**	**Heroin Deaths**	**Total Opioid-Related Deaths**
Acute Pain Prescribing	492 *[356, 645]*	184 *[24, 363]*	-2,960 *[-3,550, -2,473]*	-6,971 *[-10,428, -4,545]*	-9,932 *[-13,365, -7,018]*
Prescribing for Transitioning Pain	120 *[87, 161]*	152 *[111, 200]*	-1,456 *[-1,787, -1,108]*	-651 *[-1,511, -353]*	-2,106 *[-2,971, -1,461]*
Chronic Pain Prescribing	615 *[395, 838]*	791 *[537, 1,052]*	-8,910 *[-10,824, -7,839]*	-1,183 *[-5,979, 2,443]*	-10,093 *[-14,812, -5,396]*
Drug Rescheduling	3,220 *[1,978, 4,626]*	4,428 *[2,933, 6,089]*	-80,415 *[-98,066, -66,948]*	43,148 *[13,352, 55,268]*	-37,267 *[-66,479, -12,009]*
Drug Reformulation	397 *[276, 532]*	492 *[351, 648]*	-3,887 *[-4,704, -3,334]*	-3,696 *[-6,733, -1,599]*	-7,583 *[-10,588, -4,933]*
Pharmacotherapy	972 *[240, 1,188]*	1,132 *[424, 1,361]*	1,215 *[286, 4,636]*	-29,228 *[-35,110, -12,098]*	-28,013 *[-34,256, -7,462]*
Excess Opioid Disposal 10%	477 *[377, 998]*	630 *[521, 1,236]*	-7,374 *[-8,919, -6,399]*	-681 *[-12,242, 1,434]*	-8,055 *[-19,738, -5,873]*
Excess Opioid Disposal 15%	716 *[565, 1,496]*	945 *[782, 1,853]*	-11,061 *[-13,379, -9,598]*	-1,010 *[-18,346, 2,161]*	-12,072 *[-29,589, -8,800]*
Naloxone 5%	1,300 *[1,140, 1,457]*	1,096 *[962, 1,226]*	-8,434 *[-10,009, -7,087]*	-39,881 *[-45,739, -33,139]*	-48,315 *[-53,982, -41,215]*
Naloxone 15%	4,056 *[3,559, 4,548]*	3,414 *[2,998, 3,825]*	-25,351 *[-30,094, -21,298]*	-121,950 *[-139,797, -100,916]*	-147,302 *[-164,569, -125,187]*
Naloxone 30%	8,628 *[7,575, 9,686]*	7,253 *[6,372, 8,133]*	-50,851 *[-60,385, -42,706]*	-251,057 *[-287,593, -206,446]*	-301,908 *[-337,268, -255,116]*
Syringe Exchange	150 *[133, 173]*	126 *[111, 145]*	0 *[0,0]*	-5,934 *[-6,791, -4,933]*	-5,934 *[-6,791, -4,933]*
PMP	1,096 *[768, 1,454]*	736 *[351, 1,153]*	-9,468 *[-11,441, -8,057]*	-11,378 *[-19,320, -5,810]*	-20,846 *[-28,717, -13,867]*
Psychosocial Treatment	661 *[561, 744]*	758 *[646, 837]*	-819 *[-1,020, -652]*	-13,626 *[-15,567, -11,118]*	-14,446 *[-16,533, -11,880]*
Drug Rescheduling + Naloxone 5%	4,396 *[3,035, 5,922]*	5,418 *[3,824, 7,179]*	-84,933 *[-103,322, -70,770]*	1,560 *[-32,882, 16,148]*	-83,373 *[-117,062, -54,621]*
Drug Rescheduling + Naloxone 15%	6,896 *[5,281, 8,676]*	7,519 *[5,713, 9,493]*	-93,988 *[-113,853, -78,424]*	-83,996 *[-127,956, -63,720]*	-177,984 *[-220,847, -142,144]*
Drug Rescheduling + Naloxone 30%	11,060 *[9,028, 13,273]*	11,011 *[8,858, 13,345]*	-107,611 *[-129,698, -89,933]*	-218,526 *[-277,349, -177,489]*	-326,136 *[-383,338, -279,408]*

	Mean Change *[Min, Max]*				
Policy	**Discounted Net Present LYs (Thousands)**	**Discounted Net Present QALYs (Thousands)**	**Pill Deaths**	**Heroin Deaths**	**Total Opioid-Related Deaths**
Drug Rescheduling + SEP	3,371 *[2,115, 4,794]*	4,554 *[3,048, 6,230]*	-80,415 *[-98,066, -66,948]*	37,011 *[6,538, 49,218]*	-43,404 *[-73,293, -17,730]*
Drug Rescheduling + Pharmacotherapy	4,076 *[2,865, 5,658]*	5,415 *[3,934, 7,258]*	-78,578 *[-96,051, -65,346]*	15,383 *[-19,553, 41,045]*	-63,194 *[-97,768, -39,404]*
Drug Rescheduling + Psychosocial Treatment	3,775 *[2,499, 5,227]*	5,061 *[3,526, 6,773]*	-80,598 *[-98,262, -67,087]*	30,780 *[-15, 43,030]*	-49,818 *[-80,003, -24,057]*
PMP + Naloxone 5%	2,362 *[1,884, 2,867]*	1,802 *[1,292, 2,343]*	-17,438 *[-20,890, -14,748]*	-50,813 *[-64,293, -41,540]*	-68,251 *[-81,470, -56,964]*
PMP + Naloxone 15%	5,045 *[4,250, 5,866]*	4,060 *[3,284, 4,863]*	-33,423 *[-39,851, -28,164]*	-131,969 *[-156,782, -108,599]*	-165,391 *[-189,563, -140,705]*
PMP + Naloxone 30%	9,499 *[8,182, 10,852]*	7,798 *[6,587, 9,045]*	-57,517 *[-68,448, -48,375]*	-259,646 *[-302,133, -213,011]*	-317,163 *[-358,421, -268,152]*
PMP + SEP	1,244 *[900, 1,624]*	859 *[462, 1,295]*	-9,468 *[-11,441, -8,057]*	-17,242 *[-25,994, -11,221]*	-26,710 *[-35,390, -19,277]*
PMP + Pharmacotherapy	2,035 *[1,454, 2,600]*	1,829 *[1,270, 2,465]*	-8,311 *[-10,406, -6,055]*	-39,788 *[-53,388, -24,290]*	-48,099 *[-61,968, -30,344]*
PMP + Psychosocial Treatment	1,738 *[1,361, 2,154]*	1,471 *[1,030, 1,955]*	-10,240 *[-12,330, -8,671]*	-24,728 *[-33,912, -18,551]*	-34,968 *[-44,028, -27,222]*
All Prescribing (Acute, Transitioning, Chronic)	1,230 *[841, 1,647]*	1,129 *[674, 1,615]*	-13,157 *[-15,953, -11,272]*	-9,090 *[-18,199, -2,734]*	-22,247 *[-31,260, -14,005]*
All Prescribing + Naloxone 5%	2,491 *[1,953, 3,053]*	2,191 *[1,612, 2,799]*	-20,946 *[-25,182, -17,805]*	-48,620 *[-63,218, -39,266]*	-69,566 *[-83,881, -57,072]*
All Prescribing + Naloxone 15%	5,163 *[4,312, 6,037]*	4,439 *[3,598, 5,307]*	-36,569 *[-43,701, -30,906]*	-129,968 *[-155,804, -106,845]*	-166,537 *[-191,709, -142,046]*
All Prescribing + Naloxone 30%	9,599 *[8,233, 10,999]*	8,162 *[6,891, 9,468]*	-60,117 *[-71,631, -50,640]*	-257,943 *[-301,301, -211,529]*	-318,060 *[-360,170, -269,226]*
All Prescribing + SEP	1,378 *[973, 1,816]*	1,252 *[785, 1,757]*	-13,157 *[-15,953, -11,272]*	-14,965 *[-24,877, -8,161]*	-28,122 *[-37,938, -19,432]*
All Prescribing + Pharmacotherapy	2,164 *[1,591, 2,785]*	2,216 *[1,664, 2,918]*	-11,990 *[-14,898, -10,006]*	-37,403 *[-52,141, -21,414]*	-49,393 *[-64,369, -31,420]*
All Prescribing + Psychosocial Treatment	1,868 *[1,430, 2,342]*	1,859 *[1,348, 2,411]*	-13,906 *[-16,815, -11,867]*	-22,378 *[-32,717, -15,421]*	-36,284 *[-46,476, -27,288]*
All Prescribing + Drug Reformulation + Pharmacotherapy + SEP + Naloxone 5% + Psychosocial Treatment	4,495 *[3,813, 5,450]*	4,508 *[3,741, 5,545]*	-23,830 *[-28,962, -20,209]*	-97,086 *[-121,612, -80,974]*	-120,916 *[-145,396, -104,291]*

Abbreviations: LY = life year; PMP = prescription monitoring program; SEP = syringe exchange program; QALY = quality-adjusted life year.

Table S4. Results of sensitivity analyses: percentage reduction in opioid-related deaths, compared to no intervention

Table S4a. Results of sensitivity analysis over five years

	Base Case	Heroin mortality		Pill mortality		Probability of escalation to heroin		QALYs for chronic pain with opioid prescription		Diversion of pills to non-users		Probability of starting pharmaco-therapy for individual with SOUD and no prescription	
Policy		**+25%**	**-25%**	**+25%**	**-25%**	**-25%**	**-50%**	**+10%**	**-2.0%**	**+50%**	**-50%**	**-25%**	**-50%**
Acute Pain Prescribing	-0.4	-0.4	-0.5	-0.5	-0.4	-0.4	-0.4	-0.4	-0.4	-0.5	-0.4	-0.4	-0.4
Transitioning Pain Prescribing	-0.1	0.0	-0.1	-0.1	0.0	-0.1	-0.1	-0.1	-0.1	-0.1	0.0	-0.1	-0.1
Chronic Pain Prescribing	-0.2	-0.1	-0.4	-0.4	-0.1	-0.3	-0.4	-0.2	-0.2	-0.3	-0.1	-0.2	-0.2
Drug Rescheduling	2.0	3.2	0.1	0.3	3.8	0.6	-1.3	2.0	2.0	1.0	3.1	2.0	1.9
PMP	-0.8	-0.7	-0.9	-0.9	-0.7	-0.8	-0.9	-0.8	-0.8	-1.0	-0.6	-0.8	-0.8
Drug Reformulation	-0.3	-0.2	-0.4	-0.3	-0.2	-0.3	-0.4	-0.3	-0.3	-0.4	-0.2	-0.3	-0.3
Excess Opioid Disposal 10%	-0.2	-0.1	-0.3	-0.3	-0.1	-0.4	-0.6	-0.2	-0.2	-0.6	0.2	-0.2	-0.3
Excess Opioid Disposal 15%	-0.3	-0.2	-0.5	-0.5	-0.1	-0.6	-0.9	-0.3	-0.3	-0.9	0.3	-0.4	-0.4
Naloxone Availability 5%	-4.3	-4.2	-4.3	-4.3	-4.3	-4.3	-4.3	-4.3	-4.3	-4.3	-4.3	-4.3	-4.3
Naloxone Availability 15%	-13.0	-12.8	-13.0	-13.0	-12.9	-13.0	-13.1	-13.0	-13.0	-13.0	-13.0	-13.0	-12.9
Naloxone Availability 30%	-26.3	-26.1	-26.4	-26.4	-26.2	-26.4	-26.5	-26.3	-26.3	-26.3	-26.3	-26.3	-26.2
Pharmacotherapy	-1.9	-1.9	-1.8	-1.8	-2.0	-1.8	-1.6	-1.9	-1.9	-1.9	-1.9	-1.5	-1.0
Psychosocial Treatment	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.7	-0.8
Syringe Exchange	-0.5	-0.4	-0.7	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5

Abbreviations: PMP = prescription monitoring program; QALY = quality-adjusted life year; SOUD = severe opioid use disorder.

Table S4b. Results of sensitivity analysis over ten years

	Base Case	Heroin mortality		Pill mortality		Probability of escalation to heroin		QALYs for chronic pain with opioid prescription		Diversion of pills to non-users		Probability of starting pharmaco-therapy for individual with SOUD and no prescription	
Policy		**+25%**	**-25%**	**+25%**	**-25%**	**-25%**	**-50%**	**+10%**	**-2.0%**	**+50%**	**-50%**	**-25%**	**-50%**
Acute Pain Prescribing	-0.8	-0.8	-0.8	-0.8	-0.8	-0.8	-0.8	-0.8	-0.8	-0.9	-0.7	-0.8	-0.8
Transitioning Pain Prescribing	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.2	-0.1	-0.2	-0.2
Chronic Pain Prescribing	-0.8	-0.7	-1.0	-1.0	-0.7	-0.9	-1.0	-0.8	-0.8	-1.0	-0.6	-0.8	-0.9
Drug Rescheduling	-3.1	-2.2	-4.4	-4.4	-1.6	-3.9	-5.2	-3.1	-3.1	-4.4	-1.6	-3.2	-3.3
PMP	-1.7	-1.6	-1.8	-1.8	-1.6	-1.7	-1.8	-1.7	-1.7	-1.9	-1.4	-1.7	-1.8
Drug Reformulation	-0.6	-0.6	-0.7	-0.7	-0.6	-0.6	-0.7	-0.6	-0.6	-0.7	-0.5	-0.6	-0.6
Excess Opioid Disposal 10%	-0.7	-0.6	-0.8	-0.8	-0.5	-0.8	-1.1	-0.7	-0.7	-1.2	-0.1	-0.7	-0.8
Excess Opioid Disposal 15%	-1.0	-0.9	-1.2	-1.2	-0.8	-1.3	-1.6	-1.0	-1.0	-1.8	-0.1	-1.1	-1.1
Naloxone Availability 5%	-4.0	-3.8	-4.1	-4.0	-3.9	-4.0	-4.0	-4.0	-4.0	-4.0	-4.0	-3.9	-3.9
Naloxone Availability 15%	-12.1	-11.8	-12.3	-12.1	-12.0	-12.1	-12.2	-12.1	-12.1	-12.1	-12.1	-12.0	-12.0
Naloxone Availability 30%	-24.8	-24.3	-25.1	-24.8	-24.7	-24.8	-24.9	-24.8	-24.8	-24.8	-24.7	-24.7	-24.6
Pharmacotherapy	-2.3	-2.3	-2.2	-2.2	-2.4	-2.2	-2.0	-2.3	-2.3	-2.3	-2.3	-1.8	-1.3
Psychosocial Treatment	-1.2	-1.2	-1.2	-1.2	-1.2	-1.1	-1.1	-1.2	-1.2	-1.2	-1.2	-1.2	-1.3
Syringe Exchange	-0.5	-0.4	-0.6	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5	-0.5

Abbreviations: PMP = prescription monitoring program; QALY = quality-adjusted life year; SOUD = severe opioid use disorder.

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