Supplemental Material

Appendix 1

Opioid Topic Area	Epidemiology/Surveillance
Author(s):	Hedegaard H, Miniño AM, Warner M.
Paper Title:	Drug Overdose Deaths in the United States, 1999-2017
Reference:	NCHS Data Brief. 2018; (329): 1-8. https://www.cdc.gov/nchs/data/databriefs/db329-h.pdf
Aim/Objective:	To examine trends in drug overdose deaths in the United States from 1999 to 2017 by demographic and geographic characteristics and to identify shifts in the types of drugs involved.
Country:	United States
Health Outcome:	Drug overdose mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	All ages, including trends for 15-24, 25-34, 35-44, 45-54, 55-64, and 65+ years Male, Female N/A (didn't classify) N/A (didn't classify) The entire United States consisting of all 50 states and the District of Columbia
Factors of interest:	Age-specific and gender-specific trends, state-specific pattern
Methods:	**Sample Size:** All drug overdose deaths in the United States between 1999 and 2017. **Database:** National Vital Statistics System, Mortality Database. **Analysis:** The direct method was used to calculate age-adjusted death rates, which were adjusted to the 2000 US standard population. The two-sided significance tests at the 0.01 level were used to calculate the difference between national and state estimates with the national rate fixed as a parameter. The Joinpoint Regression Program using weighted least-squares models was used to calculate trends in death rates and most, if not all, comparisons were considered statistically significant at the 0.05 level of significance. Drug overdose death codes were extracted from the International Classification of Diseases, Tenth Revision.
Study Period:	1999-2017
Results/Findings:	From 1999 to 2017, the age-adjusted rate of drug overdose deaths in the United States more than tripled (from 6.1 per 100,000 population to 21.7). During the same time period, males had much higher mortality rates than females (rates increasing from 8.2 to 29.1 for males and 3.9 to 14.4 for females). Adults aged 25-34, 35-44, and 45-54 years had the highest drug overdose death rates (38.4, 39.0, and 37.7 per 100,000 population, respectively). Adults aged 55-64 had the largest percentage increase in drug overdose death rates, a 6-fold increase between 1999 and 2017. West Virginia, Ohio, Pennsylvania, and the District of Columbia had the highest age-adjusted drug overdose death rates, while Texas, North Dakota, South Dakota, and Nebraska had the lowest drug overdose death rates. During 1999-2017, the age-adjusted rates of drug-overdose mortality involving natural and semisynthetic opioids increased more than 4-fold, those involving synthetic opioids other than methadone increased 30-fold, and those involving heroin increased 7-fold.
Conclusions	The data brief mostly included facts and figures regarding drug overdose death rates for all ages and for adults aged ≥15 years. It did not identify any epidemiologic, socioeconomic, or health care factors responsible for the observed mortality trends.

Opioid Topic Area	Epidemiology/Pain Management/Treatment/Policy
Author(s):	Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC.
Paper Title:	The Prescription Opioid and Heroin Crisis: A Public Health Approach to an Epidemic of Addiction
Reference:	Annual Review of Public Health. 2015; 36:559-574
Aim/Objective:	To investigate the causes underlying the overprescription of opioid pain relievers and offer primary, secondary, and tertiary opioid addiction prevention strategies.
Country:	United States
Health Outcome:	Drug overdose mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adolescents and Young Adults, Working Age, Elderly Male, Female White, Black/African American, American Indian/Alaska Native, Asian/Pacific Islander, Hispanic/Latino Education, income, poverty Rural-Urban, State, Region, Counties
Factors of interest:	Prescription drug abuse, drug overdose, drug over-prescription, prevention strategies, heroin, addiction
Methods:	**Sample Size:** N/A **Database:** Facts and figures generally acquired from other papers and government sources such as the Centers for Disease Control and Prevention (CDC), National Survey on Drug Use and Health (NSDUH), Substance Abuse and Mental Health Services Administration (SAMHSA), and Food and Drug Administration (FDA). **Analysis:** Review paper that compiled the history leading to the opioid crisis and other facts and figures from private and public sources and then offered specific primary, secondary, and tertiary opioid addiction prevention strategies. 15-24, 25-34, 35-44, 45-54, 55-64, and 65+.
Study Period:	1840-2015 (includes history of opioid use)
Results/Findings:	Opioid-related morbidity and mortality is not limited to nonmedical users. The paper noted that opioid pain reliever (OPR) deaths occur most frequently in adults ages 45-54 and the greatest increase in overdose mortality in the past decade has been in the 55-64 age group. Papers with low-quality evidence, sponsorships by Purdue Pharma to the American Pain Society and related groups, and campaigns encouraging the long-term use of opioid pain relievers (OPRS) have likely significantly contributed to the recent opioid crisis. In particular, the 1995 "Pain is the Fifth Vital Sign" campaign increased the use of opioids for chronic non-cancer pain by health care professionals.
Conclusions	The paper suggests primary, secondary, and tertiary prevention strategies to decrease the incidence of addiction, screen for addiction after onset but before serious addiction occurs, and treat and rehabilitate serious addiction, respectively. Primary strategies include providing accurate information related to opioid addiction risks to providers, secondary strategies include increase use of prescription drug monitoring programs designed to identify opioid-addicted individuals, and tertiary strategies include specific treatments such as pharmacotherapeutic drug naltrexone.

Opioid Topic Area	Epidemiology/Treatment/Health Policy
Author(s):	US Department of Health and Human Services, Office of the Surgeon General.
Paper Title:	Facing Addiction in America: Surgeon General's Report on Alcohol, Drugs, and Health
Reference:	Washington, DC: US Department of Health and Human Services; 2016.
Aim/Objective:	To examine neurobiological causes and social factors leading to opioid addiction and propose prevention, intervention, and treatment plans to mitigate the crisis.
Country:	United States
Health Outcome:	Drug addiction
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Children, Adolescents and Young Adults, Youth, Adults, Working Age, Elderly Male, Female White, Black/African American, American Indian/Alaska Native, Asian/Pacific Islander, Hispanic/Latino Education, income, employment status, housing tenure, poverty National
Factors of interest:	Drug overdose, neurobiological and socioeconomic factors/causes, social stigmas, prevention/intervention/treatment strategies
Methods:	**Sample Size:** N/A **Database:** Facts generally acquired from journal articles and government sources including the National Institute on Drug Abuse; Center for Behavioral Health Statistics and Quality, SAMHSA; National Drug Intelligence Center, Department of Justice; CDC Wonder; and National Cancer Institute's SEER Program. **Analysis:** Report that summarized current research on opioid addiction, its neurobiological causes, and effective prevention, intervention, and treatment plans.
Study Period:	2015-2016
Results/Findings:	The report highlights that addiction is a health condition, not a moral failure or character flaw. Moreover, evidence-based prevention and treatment work. In short, people can and do recover. Therefore, society should work to rehabilitate drug addicts through coordination of the healthcare system, community leaders, researchers, and other public, private, and voluntary entities part of the public health system. It should be noted, however, that this report was written in 2016, as many changes have since been made to the health care system.
Conclusions	The summary report concludes with five general messages: (1) Substance misuse and substance use disorders severely hurt individuals and their communities, (2) Existing community-based prevention programs and policies should be more widely adopted, (3) Services for substance use disorders should be fully integrated with the rest of healthcare, (4) Health reform and parity laws should seek to increase access to services for people with substance use disorders, and (5) Current research points to biological and psychological causes of substance use and misuse as opposed to the individual's personal failings and supports the use of prevention, treatment, and recovery support services.

Opioid Topic Area	Epidemiology
Author(s):	Gomes T, Tadrous M, Mamdani MM, Paterson JM, Juurlink DN.
Paper Title:	The Burden of Opioid-Related Mortality in the United States
Reference:	JAMA Network Open. 2018; 1(2): e180217. doi: 10.1001/jamanetworkopen. 2018.0217
Aim/Objective:	To examine the distribution of opioid-related mortality in the United States from 2001 to 2016.
Country:	United States
Health Outcome:	Opioid-related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	0-14, 15-24, 25-34, 35-44, 45-54, 55-64, ≥65 years Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Opioid-related deaths, age and gender burdens
Methods:	**Sample Size:** 9,489 deaths in 2001; 42,245 deaths in 2016 **Database:** Centers for Disease Control and Prevention (CDC) WONDER Multiple Cause of Death Online Database to acquire data on age and gender burdens of opioid-related deaths from 2001 to 2016. **Analysis:** Used CDC Wonder to derive number of opioid-related deaths in the US from 2001 to 2016. WONDER database contains US mortality data classified by age and sex and cause of death data from death certificates of US residents. CDC defined, opioid-related deaths are those underlying cause of death pertaining to poisoning and multiple cause of death code pertaining to an opioid.
Study Period:	2001-2016
Results/Findings:	From 2001 to 2016, the number of opioid deaths in the U.S. increased from 9,489 to 42,245 (33.3 to 130.7 deaths per million population). In 2016, men comprised 67.5% of all opioid-related deaths. Percent of opioid-related deaths increased from 0.4% in 2001 to 1.5% in 2016. The highest burden among adults was the 24-35 age group in which 20.0% of deaths were opioid-related. From 2001 to 2016, the largest absolute increase was the 25-34 age group (4.2% to 20.0%). The largest relative increases, however, were the 55-64 and 65+ age groups (0.2 to 1.6% and 0.01 to 0.07%). Opioid-related deaths resulted in 1,681,359 YLL in the U.S. in 2016 with the highest burden in the 25-34 and 35-44 age groups (12.9 YLL and 9.9 YLL per 1000 population, respectively).
Conclusions	Opioid-related deaths represent a significant public health concern in the U.S. The recent increase in opioid-related deaths among adolescents and young adults, especially men, is very concerning. Moreover, given that the burden of opioid overdose among the 55-64 age group is quickly growing, the issue regarding the aging population of people with opioid use disorder should be addressed.

Opioid Topic Area	Epidemiology/Surveillance/Treatment
Author(s):	Madras BK.
Paper Title:	The President's Commission on Combating Drug Addiction and the Opioid Crisis: Origins and Recommendations
Reference:	Clinical Pharmacology and Therapeutics. 2018; 103(6):943-945
Aim/Objective:	To examine the events leading to the opioid crisis and the government's response to combat drug addiction and the opioid crisis.
Country:	United States
Health Outcome:	Misuse, Addiction, Overdose Deaths
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Children, Adolescents and Young Adults, Youth, Adults, Working Age, Elderly Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Causes, Treatment, Research
Methods:	**Sample Size:** N/A **Database:** Facts acquired from the following: The Lancet, Centers for Disease Control, JAMA, JAMA Psychiatry, and the President's Commission on Combating Drug Addiction and the Opioid Crisis as found on the White House page. **Analysis:** Review paper that summarized President Trump's Commission on Combating Drug Addiction and the Opioid Crisis while examining the root causes of the crisis, the possibility of reverse engineering the root causes and obstacles, treatment, recovery, and rescue, research and development, and lessons learned.
Study Period:	2017 (when commission was published)
Results/Findings:	1: Root Causes of the Crisis – a prime driver is the healthcare system. Specific causes included inadequate FDA evaluation of opioid abuse liability, disconnected information flow between physicians and pharmacies regarding a history of patient opioid prescriptions, and health insurers' quick approval of opioid analgesics; 2: Reverse Engineering of Root Causes and Obstacles – strategies to prevent initiation of use, screening for substance use and mental health disorders, and referrals to quality treatment services; 3: Treatment, Recovery, Rescue – For prisoners, expanding Federal drug courts to offer rehabilitation; 4: Research and Development – The development of analgesics with limited or no abuse liability, antagonists to reverse high-potency opioid agonists and reduce withdrawal symptoms, and pharmacotherapies to treat opioid addiction; 5: Lessons Learned – The paper succinctly summarizes the Commission's tracking of the opioid crisis as "a myriad of imprudent policies and decisions, aggressive advocacy, misinformation, and heavily financed marketing."
Conclusions	Despite strict federal regulations on production quotas, transportation, chain-of-custody, DEA Licensing and dispensing of Schedule II and III prescription opioids, an aggressive, financially-driven campaign to promote opioids managed to cause a nation-wide crisis. Therefore, all stakeholders (including sectors within the public and private domain) must carefully examine the current literature and collaborate to find an effective solution.

Opioid Topic Area	Epidemiology
Author(s):	Seth P, Scholl L, Rudd RA, Bacon S.
Paper Title:	Overdose Deaths Involving Opioids, Cocaine, and Psychostimulants – United States, 2015-2016
Reference:	Morbidity and Mortality Weekly Report (MMWR). 2018: 67(12):349-358.
Aim/Objective:	To examine trends and patterns in opioid-involved overdose mortality in the United States by age, sex, race/ethnicity, and state of residence from 2015 through 2016.
Country:	United States
Health Outcome:	Opioid-involved overdose mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	0-14, 15-24, 25-34, 35-44, 45-54, 55-64, ≥65 years Male, Female Non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic AIAN, non-Hispanic API Generally encompasses all socioeconomic statuses Large central, fringe, medium, and small metro; non-metro, micropolitan, non-metro noncore
Factors of interest:	Drug overdose, Racial inequality, Socioeconomic Status, Increases in Rates
Methods:	**Sample Size:** N/A. **Database:** Drug overdose deaths were identified in the National Vital Statistics System multiple cause-of-death mortality files through ICD-10. **Analysis:** Age-adjusted overdose death rates were calculated for 2015 and 2016 for all opioids, opioid subcategories (prescription opioids [such as natural/semisynthetic opioids and methadone], heroin, and synthetic opioids), cocaine, and psychostimulants in the U.S. and by age, sex, racial/ethnic group, urbanization level, and state. Only states that met the following criteria were examined: 1) ≥80% of drug overdose death certificates pointed to at least one specific drug in 2015 and 2016, 2) change from 2015 to 2016 in the percentage of death certificates naming at least one specific drug was <10 percentage points, and 3) ≥20 deaths in 2015 and 2016 occurred in at least two drug categories.
Study Period:	2015-2016
Results/Findings:	From 2015 to 2016, the age-adjusted rate of overdose deaths increased 21.5% from 16.3 to 19.8 per 100,000 population in the US. In 2016, 66.4% of drug overdose deaths comprised opioids, a 27.9% rate increase from 2015. Synthetic opioids represented the largest increase of opioid-related deaths. During the 2015-2016 time period, opioid-related deaths increased in males and females, people aged ≥15 years, whites, blacks, Hispanics, and Asian/Pacific Islanders, from which the largest relative rate change were among blacks and the largest absolute rate increases were among males aged 25-44 years and people aged 25-34 years. Lastly, state-specific increases from 2015 to 2016 were not considered statistically significant although thirteen states and DC had significant increases in heroin-involved death rates, whereas New Hampshire had a significant decrease. States including New Hampshire, Ohio, and West Virginia had the highest overdose death rates for several drug categories.
Conclusions	Three major waves of opioid overdose deaths: 1) in the 1990s included prescription opioid deaths, 2) In 2010, heroin death rates significantly increased, and 3) In 2013, increases in synthetic opioid-related deaths significantly increased (i.e. IMF and fentanyl analogs). There have been some efforts to resolve the crisis such as CDC's Enhanced State Opioid Overdose Surveillance program, which funds 32 states and DC to compile more timely and comprehensive nonfatal and fatal overdose data, specifically for improved comprehensive toxicologic testing to identify emerging drug threats in opioid-involved fatal overdoses.

Opioid Topic Area	Epidemiology
Author(s):	Chen X, Wang Y, Yu X, Schoenfeld E, Saltz M, Saltz J, Wang F.
Paper Title:	Large-scale Analysis of Opioid Poisoning Related Hospital Visits in New York State
Reference:	American Medical Informatics Association Symposium Proceedings. 2017; 2017:545-554.
Aim/Objective:	To analyze opioid poisoning related hospital visits in New York state based on demographics, temporal trends, co-occurrence patterns, and spatial distribution.
Country:	United States
Health Outcome:	Opioid Poisoning Related Hospital Visits
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	5-year age groups from 0-100 Male, Female White, African American, Asian, Hispanic or Latino Generally encompasses all socioeconomic statuses New York State
Factors of interest:	Demographics, Temporal Trends, Comorbidities, Spatial Distribution
Methods:	**Sample Size:** N/A **Database:** New York State Statewide Planning and Research Cooperative System (SPARCS). **Analysis:** Records of opioid poisoning hospital visits were extracted based on ICD-9 codes for poisonings by opiates, opium, heroin, methadone, and other related narcotics. Frequent co-occurrence patterns were determined by an Apriori-like algorithm (a common data mining technique that efficiently compared supports with a designated minimum support threshold). Spatial analysis was conducted based on patients' residential ZIP codes, while spatial clustering incorporated Moran's I.
Study Period:	2003-2014
Results/Findings:	Demographic-based **Analysis:** While 51.5% of the state's population is female, only 40.0% of patients with opioid poisoning are, implying that females are less likely to visit the hospital for opioid poisoning. Opioid poisoning patients disproportionately comprised whites and Asians, which had significantly higher and lower representation, respectively. Opioid poisoning was most common in the 21-25 age category; Temporal Trends: While both inpatient stays and outpatient EDs for drug poisoning increased from 2005 to 2014, outpatient EDs increased at a rising rate; Frequent Co-Occurrence Patterns: The top co-morbidities associated with opioid poisoning hospital visits are tobacco use disorder, unspecific essential hypertension, and depressive disorder (in that order); Spatial **Analysis:** Most areas of NYC had lower opioid poisoning hospital visits than those outside of NYC.
Conclusions	The analysis provides guidelines for stakeholders to improve prevention, intervention, and recovery of opioid poisoning and advocates for the government's sponsorship of increased accessibility of health data.

Opioid Topic Area	Epidemiology/Health Policy
Author(s):	Ford JA, Hinojosa MS, Nicholson HL.
Paper Title:	Disability Status and Prescription Drug Misuse Among U.S. Adults
Reference:	Addictive Behaviors. 2018; 85: 64-69
Aim/Objective:	To investigate the relationship between disability status and prescription drug misuse.
Country:	United States
Health Outcome:	Prescription drug misuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	18-25, 26-34, 35-49, 50-64, ≥65 Male, Female White, Non-White Generally encompasses all socioeconomic statuses Generally encompasses all geographies
Factors of interest:	Disability status, physical and mental health, social engagement/isolation
Methods:	**Sample Size:** 68,073 **Database:** 2015 National Survey on Drug Use and Health **Analysis:** Multinomial logistic regression model for 1) baseline model for demographic characteristics, heavy drinking, marijuana use, and other illicit drugs, 2) health-related measures added to baseline model, and 3) social engagement/isolation measures added to baseline. Two measures of disability were examined: 1) People with disabilities to activities of daily living (ADL) and 2) disability related to instrumental activities of daily living (IADL).
Study Period:	2015
Results/Findings:	ADL respondents had an increased risk for opioid misuse, while IADL respondents had increased risks for benzodiazepine misuse and both opioids and benzodiazepines misuse. After adding health measures to the baseline model, the relationships between ADL disability status and opioid misuse and IADL disability status and benzodiazepine misuse were no longer significant. Only the increased risk for opioids and benzodiazepines misuse for IADL disability respondents remained significant. Social engagement/isolation measures did not seem to have a significant impact on the relationship between disability status and prescription drug misuse.
Conclusions	That the disabled population has lower rates of substance use compared to the general population should not entail that research on substance use in the disabled should be neglected as it has been in the past. Findings suggest that efforts to decrease prescription drug misuse among the disabled should 1) educate disabled people on more effective methods to manage pain and daily limitations, 2) provide better access to professional support to complete difficult tasks, 3) advocate for more social support from family, and 4) provide aid from counselors and support groups.

Opioid Topic Area	Epidemiology
Author(s):	Nicholson HL, Ford JA.
Paper Title:	Correlates of prescription opioid misuse among Black Adults: Findings from the 2015 National Survey on Drug Use and Health
Reference:	Drug and Alcohol Dependence. 2018; 186: 264-267
Aim/Objective:	To investigate the factors contributing to prescription opioid misuse among black adults.
Country:	United States
Health Outcome:	Prescription opioid misuse (POM)
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	18-25, 26-34, 35-49, 50+ Male, Female Black, White Marital status, educational attainment, employment status Large metro, small metro, non-metro
Factors of interest:	Racial Inequality, Socioeconomic Status, Educational Attainment
Methods:	**Sample Size:** 68,073 **Database:** 2015 National Survey on Drug Use and Health. **Analysis:** Multivariate logistic regression model that examined number of covariates including demographic characteristics (age, gender, socioeconomic status, marital status, educational attainment, and employment status), current geographic residence, past year church attendance, major depressive episode, general health, past year emergency department visits, access to health insurance, and government assistance. Prescription drug misuse was defined as using prescription drugs in any way a doctor did not direct respondents to use them.
Study Period:	2015
Results/Findings:	The overall prevalence of POM is similar for whites and blacks (4.84% and 4.28%, respectively). These factors are only significant among black respondents: gender (males more likely for POM), socioeconomic status (some government assistance more likely), educational attainment (did not graduate high school more likely). These factors were only significant among white respondents: employment status (unemployed more likely), church attendance (didn't regularly attend more likely), health insurance (uninsured more likely), being arrested in the past year, heroin use, and measure of risk taking (more risky more likely). The following factors were significant among white and black respondents: major depressive episode, general health, and being approached by someone who wanted to sell drugs.
Conclusions	These findings point towards proposed areas of focus for prevention and treatment programs. For example, given that the gender gap in substance use is wider among blacks than other racial/ethnic groups, such programs should especially target black men. Programs should address structural disadvantage for blacks and seek to resolve disparities in government assistance, educational attainment, and residence.

Opioid Topic Area	Epidemiology/Surveillance
Author(s):	Curtin SC, Tejada-Vera B, Warner M.
Paper Title:	Drug Overdose Deaths Among Adolescents Aged 15-19 in the United States: 1999-2015
Reference:	NCHS Data Brief. 2017; 282:1-8.
Aim/Objective:	To examine specific trends underlying drug overdose deaths among adolescents aged 15-19 in the United States from 1999–2015.
Country:	United States
Health Outcome:	Drug Overdose Deaths
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	15-19 Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses entire United States
Factors of interest:	Adolescents, Drug Overdose Deaths
Methods:	**Sample Size:** N/A **Database:** National Center for Health Statistics' 1999-2015 mortality data. **Analysis:** Trends evaluated through the Joinpoint Regression Program, and *z*-Test statistic was applied at the end of 2-3-year periods. Drug overdose death codes were based on the International Classification of Diseases, Tenth Revision and those specifically associated with heroin, natural and semisynthetic opioids excluding heroin, methadone, and synthetic opioids excluding methadone, cocaine, benzodiazepines, and psychostimulants with abuse potential.
Study Period:	1999-2015
Results/Findings:	During the 1999-2015 time period, the following drug overdose mortality trends occurred among adolescents aged 15-19: 1) more than doubled from 1999 to 2007 (1.6 per 100,000 to 4.2), 2) declined by 26% from 2007 to 2014 (3.1), and 3) increased in 2015 (3.7). From 1999 to mid-2000, both males and females experienced an increase in drug overdose death rate, but then the rate for males declined from 2007 to 2014. While most drug overdose deaths in 2015 were unintentional (80.4% in 2015), female deaths were more than twice as likely to be suicides as male deaths. Overdose death rates for adolescents were highest for opioid drugs including heroin. Opioid overdose death rates more than tripled from 1999 to 2007 (0.8 per 100,000 to 2.7), stabilized from 2007 to 2011, declined from 2012 to 2014 (2.0), and finally increased from 2014 to 2015 (2.4).
Conclusions	The data brief mostly comprised facts and figures regarding drug overdose death rates for adolescents. It did not include any summarizing conclusions or calls to action based on its findings.

Opioid Topic Area	Epidemiology/Pain Management/Treatment/Health Policy
Author(s):	US Department of Health and Human Services, Office on Women's Health.
Paper Title:	White Paper: Opioid Use, Misuse, and Overdose in Women
Reference:	Washington, DC: US Department of Health and Human Services; December 2016
Aim/Objective:	To provide all stakeholders with the same level of understanding on the effect of the opioid epidemic on women across age, race, geography, and income levels.
Country:	United States
Health Outcome:	Use, Misuse, and Overdose
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	12-17 (adolescents), 17-65 (adults), 65+ (older adults) Female White Non-Hispanic, Hispanic, Black Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Gender Inequality, Racial Inequality, Socioeconomic Status, Trend
Methods:	**Sample Size:** N/A **Database:** Generally acquired from other papers in digests and journals such as Morbidity and Mortality Weekly Report and the American Journal of Drug and Alcohol Abuse and government sources including the CDC National Center for Injury Prevention and Control, CDC Wonder Multiple Cause of Death Database. **Analysis:** Review paper that compiled research on opioid epidemic related to women and investigated reasons for the gender differences based on biological pathways, social pathways, and social determinants and demographics. Proposed areas of further research.
Study Period:	1999-2016
Results/Findings:	From 1999 to 2010, overdose deaths from prescription pain killers increased by more than 400% for women and 237% for men. From 2002 to 2013, heroin use increased 100% for women and 50% for men. Research has shown that women are more likely to experience chronic pain and use prescription opioid pain medications for longer periods and in higher doses than men, and women who use opioids become dependent more quickly and experience more cravings than men. On March 26, 2015, HHS Secretary announced the HHS Opioid Initiative, which incorporates three priority areas: 1) opioid prescribing practices, 2) use of naloxone, and 3) use of Medication-assisted Treatment (MAT). Evidence has shown that naloxone and MAT are effective in reducing opioid use disorder (OUD).
Conclusions	The paper underscores that there remains significant gaps in knowledge in research on the opioid crisis for women. It offers the following for further investigation: 1) biological and environmental differences related to physical dependence and risk of prescription opioids death among women, 2) research on differences in motivations for treatment utilization and barriers to seeking treatments for substance use disorders, 3) research on access and health insurance coverage for pharmacologic treatment of opioid use among women, 4) research on external factors and social determinants as barriers to treatment programs for women, and 5) approaches to best train providers to prevent and treat OUD.

Opioid Topic Area	Epidemiology/Health Policy
Author(s):	Ghertner R, Groves L.
Paper Title:	The Opioid Crisis and Economic Opportunity: Geographic and Economic Trends
Reference:	ASPE Research Brief. Office of the Assistant Secretary for Planning and Evaluation; 2018
Aim/Objective:	To examine the relationship between indicators of economic opportunity and rates of prescription opioids and substance use in the US.
Country:	United States
Health Outcome:	Overdose deaths, Substance use
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	All ages Male/Female N/A (didn't further classify) – generally encompasses all races/ethnicities Poverty, unemployment rates, employment-to-population ratio Appalachia, West, Midwest, New England, South
Factors of interest:	Economic opportunity, geographic distribution
Methods:	**Sample Size:** N/A. **Database:** Retail Prescription Opioid Sales from Drug Enforcement Administration's (DEA) Automation of Reports and Consolidated Orders System (ARCOS), Opioid-Related Hospitalizations from State Inpatient Databases (SID) and State Emergency Department Databases (SEDD), Medicare Part D Opioid Prescriptions from CMS Patient Drug Event (PDE) File, Poverty and Unemployment Rates from US Census Bureau's Small Area Income and Poverty Estimates (SAIPE). **Analysis:** Moran's I, a measure of spatial dependency, to determine geographic clustering of variables: poverty and unemployment rate, and opioid-related hospitalization rate. Statistical relationship between these indicators was determined through population-weighted linear regression models.
Study Period:	2006-2016
Results/Findings:	1) Certain geographic areas, especially rural such as those in Appalachia, parts of West and Midwest, and New England, are experiencing an increasing number of overdose deaths and opioid prescriptions; 2) Poverty, unemployment rates, and employment-to-population ratio are highly correlated with prevalence of prescription opioids and with substance use measures. From 2006 to 2016, an increase of 1% in county's poverty rate resulted in 1.4% increase in per capital retail opioid sales, 3.3% increase in Medicare Part D opioid prescription rate, and 1.7% increase in overdose death rate. From 2011 to 2014, a 1% increase in county's poverty rate yielded a 2.7% increase in rate of opioid-related hospitalizations. A 1% increase in a county's unemployment rate resulted in a 5.1% increase in opioid-related hospitalization rate; 3) The opioid epidemic did not affect some high-poverty regions of the country. These regions were more likely in the South. Some counties in New England, the Mid-Atlantic, and the West had higher rates of drug measures but low poverty and unemployment rates.
Conclusions	Federal, state, and local decision-makers should target low-income areas and work to mitigate these disparities, perhaps by providing more primary care providers, substance use and mental health treatment, and other support services. Efforts have been made by the 2018 Consolidated Appropriates Act, which provided $1 billion for State Targeted Response to the Opioid Crisis Grants through the Substance Abuse and Mental Health Services Administration and $400 million for the Health Resources and Services Administration to improve access to addiction treatment in rural and underserved areas.

Opioid Topic Area	Epidemiology/Health Policy
Author(s):	Zoorob MJ, Salemi JL.
Paper Title:	Bowling Alone, Dying Together: The Role of Social Capital in Mitigating the Drug Overdose Epidemic in the United States
Reference:	Drug and Alcohol Dependence. 2017; 173: 1-9.
Aim/Objective:	To determine the relationship between social capital and drug overdose death rates in communities.
Country:	United States
Health Outcome:	Drug overdose mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	All ages Male, Female Non-Hispanic Whites, Non-Hispanic Blacks, Hispanic Median household income, % living in poverty, percent <high school education, rural-urban County-level
Factors of interest:	Relationship between drug overdose mortality and social capital
Methods:	**Sample Size:** County-level estimates of overdose deaths from 1999-2014 and county-level measurements of social capital for 1997, 2005, and 2009. **Database:** Estimate of overdose deaths from CDC's National Vital Statistics System and Health Indicators Warehouse; measurements of social capital from Rupasingha et al. 2006 paper "The production of social capital in US counties". **Analysis:** This ecological temporal trends study produced an analytic dataset comprising (1) age-adjusted drug overdose mortality, (2) social capital, (3) availability of drug abuse treatment centers, (4) prescription drug claim prescribed by health care providers, (5) population demographics, (6) urbanicity, and (7) socioeconomic status. Stable estimates of county-level age-adjusted death rates for each year were calculated with small-area estimation techniques. The social capital index at the county level used the following four factors: (1) density of civic associations and non-profit organizations in the county, (2) percentage of county adults who voted in presidential elections, (3) county's response rate to census, and (4) number of tax-exempt non-profit organizations in the county. Statistical analysis included descriptive statistics and multinomial logistic regression to estimate adjusted odds ratios and 95% confidence intervals.
Study Period:	1999-2014
Results/Findings:	The authors observed a strong and statistically significant inverse association between county-level social capital and age-adjusted drug overdose mortality ($p<0.01$). Compared to the lowest quintile of social capital, counties at the highest quintile were 83% less likely to fall in the "high-overdose" category and 75% less likely to fall in the "moderate-overdose" category. Counties that had low rates of overdose mortality tended to be rural (<2500 population), to have ≥25% of their population who were non-white and <5% who were Hispanic, to have ≥20% with<high school education, to have populations with median household income <$35,000 but lower proportion of residents who live in poverty, and to have a lower percent of all Medicare Part D prescription claims that were for opiate analgesics.
Conclusions	This study finds large-sample evidence that social capital protects communities against drug overdose, which could help policymakers target where overdose epidemics are likely to occur and how to resolve them. In particular, social capital may prevent the initial onset of drug-taking, help in the recovery of drug users and abusers, and reduce the case-fatality rate of drug overdose.

Opioid Topic Area	Epidemiology/Pain Management/Treatment/Health Policy
Author(s):	Dasgupta N, Beletsky L, Ciccarone D.
Paper Title:	Opioid Crisis: No Easy Fix to Its Social and Economic Determinants
Reference:	American Journal of Public Health. 2018; 108(2): 182-186
Aim/Objective:	To investigate the roots of the opioid crisis and entreat physicians and policymakers to view the opioids crisis through a structural-determinants lens.
Country:	United States
Health Outcome:	Opioid overdose and misuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A N/A Focuses especially on White Americans N/A N/A
Factors of interest:	Social and economic determinants of opioid crisis
Methods:	**Sample Size:** N/A **Database:** N/A **Analysis:** This paper is a commentary.
Study Period:	1990s – now
Results/Findings:	The opioid crisis could be sectioned into three different phases. In the first phase from the 1990s to 2010, as insurers limited coverage of behavior pain therapy, pharmaceutical companies heavily marketed opioids while minimizing addiction potential (OxyContin) and even utilized physician kickback schemes, lucrative speaking fees, and lobbying. In the second phase around 2010, some people who used prescription opioids resorted to more potent and cheaper alternatives. The third phase, which began in 2013 and continues today, consists of increasingly efficient global supply chains, which has led to more potent opioids. Yet, while opioid prescription has contributed to the opioid epidemic, there are many other significant, contributing factors including lack of economic opportunity, poor working conditions, and meager social capital in depressed communities.
Conclusions	The authors advocate for training health care providers in "structural competency" and encourage policymakers to focus on upstream structural factors including economic opportunity, social cohesion, racial disadvantage, and life satisfaction. More importantly, the authors entreat physicians to focus on overall patient "suffering" as opposed to "pain", thereby avoiding the unrealistic expectation that simply reducing opioid prescribing will resolve the opioid crisis.

Opioid Topic Area	Epidemiology
Author(s):	Bohnert ASB, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC.
Paper Title:	Association Between Opioid Prescribing Patterns and Opioid Overdose-Related Deaths
Reference:	Journal of the American Medical Association (JAMA). 2011; 305:(13):1315-1321.
Aim/Objective:	To examine the relationship between opioid prescribing patterns and risk of unintentional overdose death.
Country:	United States
Health Outcome:	Opioid-related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	18-29, 30-39, 40-49, 50-59, 60-69, ≥70 years Male Black, White, Other/missing; Hispanic Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Veterans Health Administration (VHA) patients with cancer, chronic pain, acute pain and substance use disorders
Methods:	**Sample Size:** N=750 (unintentional prescription opioid overdose deaths before 2008) out of 155,434-case cohort (individuals receiving opioid therapy for pain) **Databases:** VHA National Patient Care Database (FY2004 and FY2005), VHA Pharmacy Benefits Management Services, National Death Index. **Analysis:** Study only included those treated with opioids and excluded those with palliative or hospice care. Study assumed that patients took medication as prescribed (maximum dose on the recommended schedule). The sample was stratified by age, race/ethnicity, and pain-related diagnosis.
Study Period:	2004-2008
Results/Findings:	Overall rate of opioid-related overdose death in this population for this period was 0.04% or 40 per 100,000 population. Opioid overdose decedents were statistically significantly more likely to be middle-aged and white; more likely to have chronic or acute pain, substance use disorders, and other psychiatric diagnoses; and less likely to have cancer. While the overall rate of overdose was lower among cancer patients compared to other patients, there was a statistically significant association of prescribing patterns with overdose risk among cancer patients receiving opioid therapy. Cancer patients also had increased risk of overdose when prescribed as-needed opioids alone compared with being prescribed opioids on a regular schedule. The study does not take into account opioids received from non-VHA medical settings (doctor shopping) or from non-medical contacts. This may be a factor in increasing risk for patients with substance use disorders.
Conclusions	Findings indicate a dose-response relationship between maximum prescribed daily dose of opioids and risk of opioid overdose in a large, national cohort of individuals with a variety of medical conditions.

Opioid Topic Area	Epidemiology
Author(s):	King NB, Fraser V, Boikos C, Richardson R, Harper S.
Paper Title:	Determinants of Increased Opioid-Related Mortality in the US and Canada, 1990-2013: A Systematic Review
Reference:	American Journal of Public Health. 2014; 104(8):e32-e42.
Aim/Objective:	To perform a systematic review of determinants contributing to increased opioid-related mortality.
Country:	United States and Canada
Health Outcome:	Opioid-related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify)
Factors of interest:	Determinants of opioid-related mortality and mortality increase
Methods:	**Sample Size:** n=47 articles **Database:** Ovid MEDLINE and MEDLINE In-process and Other Non-Indexed Citations, EMBASE, ProQuest ABI/INFORM Complete. **Analysis:** Literature review of 47 articles for qualitative synthesis. Initial search yielded 3142 titles for abstract review, after which 144 articles remained for full text review. After this review, 47 articles remained.
Study Period:	1990-2013
Results/Findings:	Authors identified 17 determinants of increased opioid-related mortality. Determinants fall into 3 categories: prescriber behavior (prescribing more opioids, higher doses, oxycodone, methadone, and high volumes); user behavior (diversion, doctor/pharmacy shopping, polydrug use, or drug substitution) and characteristics (sociodemographic categories and substance use history); and environmental and systemic determinants (guideline, policies, and consensus statements; area urbanization or SES; geography; intervention; prescription drug monitoring programs; and media coverage). Determinants are independent but may interact with and influence each other. There are more studies for some determinants than for others; however, this does not imply stronger evidence. Generalizing from a single study is inadvisable. Determinants vary in effect over time, space (geography), and population. Only 5 of 47 studies used quantitative evidence to associate a particular determinant with an increase in opioid-related mortality.
Conclusions	Current efforts to reduce mortality act on a single determinant. However, the authors argue that interventions will need to address multiple determinants and be tailored to specific locations and populations.

Author(s):	Jones CM, Mack KA, Paulozzi LJ.
Paper Title:	Pharmaceutical Overdose Deaths, United States, 2010
Reference:	Journal of the American Medical Association (JAMA). 2013; 309(7):657-658.
Aim/Objective:	To show the impact of opioid overdose deaths on drug overdose deaths.
Country:	United States
Health Outcome:	Mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify)
Factors of interest:	Overdose deaths by specific type of drug
Methods:	**Sample Size:** 38,329 drug overdose deaths of which 22,134 involved pharmaceuticals **Database:** National Vital Statistics System multiple cause-of-death file, 2010. **Analysis:** ICD-10 codes used for underlying cause of death
Study Period:	2010
Results/Findings:	Opioid analgesics accounted for 16,651 (75.2%) of all pharmaceutical overdose deaths. More than half of those involved other pharmaceuticals: benzodiazepines (30.1%), antidepressants (13.4%), antiepileptic and antiparkinsonism drugs (6.8%), and antipsychotics and neuroleptics (4.7%). These other drugs are typically prescribed for mental health conditions, meaning that those with mental health disorders are also at risk for opioid-related overdose. Numbers reported are likely an undercount due to the limitations of death certificate data.
Conclusions	Drug overdose deaths increase for the 11th consecutive year in 2010. Opioid analgesics, taken alone or in combination with other drugs, are driving this increase. Prescription drug monitoring programs and electronic health records can help clinicians identify risky medication use and inform treatment decisions.

Opioid Topic Area	Epidemiology
Author(s):	Cerdá M, Gaidus A, Keyes KM, Ponicki W, Martins S, Galea S, Gruenewald P.
Paper Title:	Prescription Opioid Poisoning Across Urban and Rural Areas: Identifying Vulnerable Groups and Geographic Areas
Reference:	Addiction. 2016; 112:103-112.
Aim/Objective:	To determine whether prescription-related opioid poisoning differs across rural and urban areas and to identify features of the local environment that contribute to the growth in PO-related hospital discharges.
Country:	United States
Health Outcome:	Prescription opioid (PO) poisoning, hospital discharges
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) All zip codes in California
Factors of interest:	Findings suggest lower income may contribute to PO poisoning risk in exurban and rural areas.
Methods:	**Sample Size:** N=18,517 postal codes **Database:** California Office of Statewide Health Planning and Development **Analysis:** Hierarchical Bayesian Poisson space-time analysis to relate annual discharges from community hospitals to postal code characteristics over 10 years. Three community-level factors may drive prescription opioid poisoning: 1 – PO availability (increase is strongly correlated with PO poisoning); 2 – medical need for POs (due to high concentration of patients with need for pain relief from workplace-related injuries, cancer, or arthritis), which leads to increased supply; 3 – economic stressors (unemployment, low median income, poverty produces risk of using opioids to manage chronic stress, and mood/anxiety disorders).
Study Period:	2001-2011
Results/Findings:	Rates of PO-related hospital discharges per capita increased from 2.4 cases per 10,000 in 2001 to 4.5 cases per 10,000 people in 2011. Three major findings: (1) Poisoning spreads from rural and suburban/exurban hot spots to urban areas; (2) Zip codes with a higher concentration of arthritis-related discharges, greater pharmacy density, and more manual labor industries had a greater rate of PO-related discharges; (3) The effects of community-level factors were heterogeneous across urban and rural areas. Limitation: Use of hospital discharge data prevents inferences about PO poisoning cases that do not result in hospitalization or death.
Conclusions	Findings suggest that policies to address work-related needs for pain management and investment in screening and treatment programs may be a promising approach in communities with a high prevalence of manual labor occupations.

Opioid Topic Area	Epidemiology
Author(s):	Keyes KM, PhD, Cerdá M, Brady JE, Havens JR and Galea S.
Paper Title:	Understanding the Rural-Urban differences in nonmedical prescription opioid use and abuse in the US
Reference:	American Journal of Public Health. 2014; 104(2): e52-e59
Aim/Objective:	To propose 4 hypotheses as to why opioid use and abuse are more prevalent in rural areas.
Country:	United States
Health Outcome:	Opioid use and abuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	18-24 vs 65+ N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) Rural vs urban
Factors of interest:	Four factors that explain increases in nonmedical prescription opioid misuse in rural more than urban areas
Methods:	**Sample Size:** N/A **Database:** N/A **Analysis:** Authors take a 3-step approach: 1) Explain the risk factors for illicit drug use in general; 2) Consider which of these are risk factors for non-medical prescription opioid use specifically; 3) Link THESE risk factors to a rural context, hypothesizing how they lead to the excess burden of prescription opioid misuse in rural areas compared to urban areas.
Study Period:	N/A
Results/Findings:	Rural areas are heterogeneous and non-binary, existing on a continuum of population density with urban areas. Authors developed hypothesis regarding four factors: 1) Increased sales of opioids in rural areas (compared to urban areas) leads to greater supply for nonmedical use through diversion; 2) Out-migration of upwardly mobile young adults from rural areas increases economic deprivation and creates an aggregation of young adults at high risk for drug use; 3) Kinship and social networks are tighter in rural areas, which allows faster diffusion of nonmedical prescription opioids among those at risk; 4) Increasing economic deprivation and unemployment create a stressful environment that places individuals at risk.
Conclusions	Hypotheses do not explain all observed patterns of nonmedical prescription opioid use and overdose. The intersection of demographic factors and abuse of other prescription drugs (some of which are also increasing) remains to be explained. More data are needed to test these hypotheses and identify points of intervention and prevention.

Opioid Topic Area	Epidemiology
Author(s):	Dart RC, Surratt HL, Cicero TJ, Parrino MW, Severtson SG, Bucher-Bartelson B, Green JL.
Paper Title:	Trends in Opioid Analgesic Abuse and Mortality in the U.S.
Reference:	New England Journal of Medicine. 2015; 372(3): 241-248.
Aim/Objective:	To show trends in diversion and abuse of prescription opioid painkillers.
Country:	United States
Health Outcome:	Prescription opioid diversion and abuse, and heroin use
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify) N/A (didn't further classify)
Factors of interest:	As prescription opioid diversion and abuse goes down, heroin use goes up. The same pattern exists for mortality.
Methods:	**Sample Size:** n=656,509 cases involving opioid analgesics **Databases:** Five programs from the Researched Abuse, Diversion, and Addiction-Related Surveillance (RADARS) System used to describe trends in the diversion and abuse of all products and formulations of 6 prescription opioid analgesics (oxycodone, hydrocodone, hydromorphone, fentanyl, morphine, and tramadol), from 2002 to 2013. In addition to prescription opioids, data on heroin use is available from three of the RADARS sources, the National Poison Data System, and the National Survey of Drug Use and Heath (NSDUH). **Analysis:** Quarterly case rates per 100,000 were computed, adjusted for population changes over time. Poisson regression model with linear and quadratic terms for time was used.
Study Period:	2002-2013
Results/Findings:	Prescriptions for opioid analgesics increased substantially from 2002 to 2010, then decreased slightly from 2011-2013. Rates of opioid diversion and abuse also increased from 2002-2010, then flattened and decreased from 2011-2013. The rate of deaths followed a similar pattern. Nonmedical use did not change significantly. Heroin use generally increased over time, even while rates of oxycodone abuse decreased after the release of an abuse-deterrent reformulation in 2010. NSDUH found that 79.5% of new heroin initiates originally had an opioid prescription and reported use of heroin by patients in substance abuse programs doubled after the introduction of abuse-deterrent oxycodone.
Conclusions	The findings suggest that the US may be making progress in controlling the abuse of prescription opioids. However, the increased use of heroin suggests users are switching to it from prescription opioids.

Opioid Topic Area	Epidemiology
Author(s):	Brady K, McCauley J, Back S.
Paper Title:	Prescription Opioid Misuse, Abuse, and Treatment in the United States: An Update
Reference:	American Journal of Psychiatry. 2016, 173(1):18-26.
Aim/Objective:	To review the scope of abuse and overdose, prescription practices, and the assessment, treatment and prevention of prescription opioid misuse and dependence.
Country:	United States
Health Outcome:	Opioid-related misuse and abuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A (did not classify) – can include all at risk age groups Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Opioid-related treatment and prevention initiatives
Methods:	**Sample Size:** N/A review of literature from 2006-2015 **Database:** Reviewed of various studies. **Analysis:** Reviewed prescription practices and education of providers and patients as well as government strategies to prevent misuse and abuse. Review of effectiveness of treatments showed methadone maintenance therapy from 20% to 70%, however, effectiveness was directly correlated with dosage of maintenance therapy. For long-term therapy substitution therapy with buprenorphine or Suboxone can promote sustained abstinence; however, overdose deaths associated with oral naltrexone are 3-7 times higher than those associated with methadone maintenance therapy. Analysis of the Prescription Opioid Addiction Treatment Study examined counseling and buprenorphine-naloxone treatment for patients with DSM-IV dependence on opioid analgesics and was a multisite randomized controlled trial.
Study Period:	2006-2015
Results/Findings:	Phase 1 consisted of a 2-week medication stabilization, 2-week medication taper, and 8-week post medication follow-up which showed a 7% success rate. Phase 2 was initiated for patients who relapsed during phase 1. Phase 2; 12-week medical stabilization, 4-week medication taper, and an 8-week follow-up. Success rates for phase 2 were 49%. Follow-up at 18 months and 42 months showed 31.7% of treatment completers were still abstinent and discontinued medication therapy, 29.4% continued to receive medication therapy but did not meet criteria for opioid use disorder.
Conclusions	The prevalence of prescription opioid abuse and misuse has increased at a high rate. Although replacement therapies and psychosocial treatments are adequate options, access and utilization are limited. Research is needed to develop and evaluate treatments specific to prescription opioid use disorders and comorbidities.

Opioid Topic Area	Epidemiology/Health Policy
Author(s):	Volkow ND, McLellan TA.
Paper Title:	Curtailing Diversion and Abuse of Opioid Analgesics Without Jeopardizing Pain Treatment
Reference:	JAMA. 2011; 305(13):1346-1347.
Aim/Objective:	To provide recommendations and best practices in pain management and prevention of drug diversion.
Country:	United States
Health Outcome:	Reduction of opioid diversion and subsequent opioid related overdose.
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adolescents and young adults Male, Female N/A N/A Nationwide
Factors of interest:	Opioid-related prescribing practices, pain management
Methods:	**Sample Size:** 121,091 **Database:** Treatment Episode Dataset, Drug and Alcohol Services Information System. Substance Abuse and Mental Health Services Administration (SAMHSA). **Analysis:** Since 2002, there has been an increase of high school seniors reporting past-tear non-medical use of opioids from 8% to 10% for hydrocodone and from 4% to 5% for oxycodone. After excluding alcohol and tobacco, prevalence of hydrocodone abuse is second only to marijuana. Also, a 5-fold increase in admissions for drug treatment related to pharmaceutical opioid use between the 10-year period from 1998-2008; from 19,941 in 1998 to 121,091 in 2008. Also, an increase in the number of emergency department visits related to pharmaceutical opioids increasing from 144,644 in 2004, to 305,885 in 2008. There has been a sharp increase in unintentional opioid-related deaths shown from 3,000 deaths in 1999 to 12,000 in 2007.
Study Period:	1998-2008
Results/Findings:	It is possible the increased abuse of opioids represents the belief that prescribed medications are safer than illicit drugs. It is also likely the increase in abuse patterns is due to greater access and availability. More aggressive tactics in pain management had been precipitated in part by the mandate from the Joint Commission to screen and manage pain, but also by concerns over the safety of non-opioid analgesics, particularly those that are classified as nonsteroidal anti-inflammatory drugs. Some patients may misrepresent pain in order to obtain, misuse, and divert medications.
Conclusions	Clinical teaching and training practices for all healthcare providers in the areas of pain management, opioid pharmacology, and abuse/addiction should be considered. Due to newer medication formulations and types of pain medications available, a more comprehensive approach to training is warranted. In addition to the training for healthcare providers, educational campaigns for the general public are necessary to build awareness of responsible practices for storage and disposal.

Opioid Topic Area	Epidemiology/Pain Management
Author(s):	Pletcher M, Kertesz S, Kohn M, Gonzales R.
Paper Title:	Trends in Opioid Prescribing by Race/Ethnicity for Patients Seeking Care in US Emergency Departments
Reference:	JAMA. 2008; 299(1):70-78.
Aim/Objective:	To determine whether opioid prescribing has increased and if non-Hispanic whites are more likely to receive an opioid prescription compared to other racial/ethnic groups.
Country:	United States
Health Outcome:	Opioid-related prescribing practices
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	<12, 12-17, 18-25, 26-64, and ≥65 years Male, Female White, Black, Hispanic, Asian/others Patient insurance type addressed: Private Insurance, Medicare, Medicaid, Worker's Compensation, self/no-charge/other/unknown Northeast, Midwest, South, West. Also included rural/urban setting
Factors of interest:	Opioid-related prescribing practices, age, and racial/ethnic disparities
Methods:	**Sample Size:** 374,891 **Database:** The National Hospital Ambulatory Care Survey (NHAMCS) from 1993-2005. **Analysis:** Using a four stage probability sample design the NHAMCS collected samples of all visits to emergency departments which excluded federal, military, and Veterans Administration hospitals. A random 4 week reporting was assigned for each year from 1993-2005. Visits were categorized as long bone fracture, nephrolithiasis, migraine, abdominal pain, and back pain. Up to six medications (eight from 2003-2005) prescribed at discharge were recorded for each visit.
Study Period:	1993-2005
Results/Findings:	From 1993-2005, a pain related diagnosis code was recorded for 42% (N=156,729) of emergency department visits. Non-Hispanic whites accounted for 66% of all visits, blacks 20%, Hispanics 11%, and Asians/others 2%. Prescribing of opioid analgesics increased from 23% in 1993 to 37% in 2005. Non-Hispanic whites were prescribed medication at a rate of 31%, blacks at 23%, Hispanics at 24%, and Asians/others at 28%. Difference in prescribing in non-Hispanic whites compared to other groups were disparate as pain increased 45% vs. 36% for back-pain, 35% vs. 24% for headache, and 32% vs. 22% for abdominal pain. Non-opioid analgesia alone was prescribed more frequently for non-whites, compared to non-Hispanic whites (32% vs. 26%).
Conclusions	Overall prescription rates have increased for patients presenting to the emergency department with complaints of pain, especially since the implementation of initiatives to improve pain-related care. Increases in opioid prescribing in emergency departments is consistent with national data that has shown an overall increase since the mid-1990s. The differences in opioid prescribing among race/ethnicity show that there are disparities in pain management among those seeking treatment in emergency departments.

Opioid Topic Area	Epidemiology/Pain Management
Author(s):	Singhal A, Tien YY, Hisa RY.
Paper Title:	Racial-Ethnic Disparities in Opioid Prescriptions at Emergency Department Visits for Conditions Commonly Associated with Prescription Drug Abuse
Reference:	PLoS One. 2016; 11(8): e0159224. doi: 10.1371/journal.pone. 0159224.
Aim/Objective:	To examine racial-ethnic disparities present among opioid prescriptions for conditions that are associated with non-medical use, but not for objective pain related medical conditions.
Country:	United States
Health Outcome:	Opioid-related treatment for pain
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Ages 18-35, 36-45, 46-65 years Male, Female Non-Hispanic White, Non-Hispanic Black, Hispanic, Non-Hispanic Other Stratified by insurance type: Private Insurance, Medicare, Medicaid, Uninsured, Other/Unknown Stratified by non-metropolitan area and metropolitan area
Factors of interest:	Opioid-related treatment, health disparities, racial/ethnic disease burden
Methods:	**Sample Size:** All Emergency Department (ED) visits in the United states by adults aged 18-65 during 2007-2011 (N=63.2 million) for the following five conditions: Toothache, back pain, abdominal pain, long-bone fractures, and kidney stones. **Database:** Analyzed the National Hospital Ambulatory Medical Care Survey (NHAMCS) data from 2007-2011 available through the Centers for Disease Control and Prevention. **Analysis:** The weights, strata and primary sampling units provided to the NHAMCS were applied to all of the analyses. Descriptive analyses were done to examine the sample distribution across all covariates. Rates of opioid administration in the ED and prescription at discharge were also reviewed. Multivariate logistic regressions were used to assess the racial-ethnic disparities in both modes of opioid administration. The first model assessed racial-ethnic differences in the odds of opioid administration and prescription after adjustment for pain severity. The second, was controlled for covariates that were described in the first. Multivariate regressions were conducted separately for opioid administration and prescription for the five conditions.
Study Period:	2007-2011
Results/Findings:	Most of the ED visits for all conditions included in the study led to patients receiving opioid or non-opioid analgesics ranging from 61% for abdominal pain to 92% for kidney stones given in the ED or at discharge. Non-Hispanic blacks had lower odds (0.51 to 0.67) of receiving opioids during ED visits for back and abdominal pain compared to Non-Hispanic whites. No racial-ethnic differences were found in opioid prescription administration for ED visits for toothache, long-bone fracture, and kidney stones.
Conclusions	There are significant racial-ethnic disparities that exist in opioid prescription at ED visits for conditions that include back and abdominal pain, but not for other conditions such as toothache, kidney stones, and long-bone fracture. A differential prescription of opioids by race-ethnicity could contribute to the widening disparities in health and possibly correlate with increased burden of the epidemic among non-Hispanic whites.

Opioid Topic Area	Epidemiology/Health Policy
Author(s):	Manchikanti L, Helm S 2nd, Fellows B, Janata JW, Pampati V, Grider JS, Boswell MV.
Paper Title:	Opioid Epidemic in the United States
Reference:	Pain Physician. 2012; 15(Supplement 3): ES9-ES38
Aim/Objective:	To describe various aspects of the crisis of opioid use in the United States.
Country:	United States
Health Outcome:	Opioid-abuse and related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Various. Source dependent. Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Opioid-related deaths, increases in inappropriate prescribing
Methods:	**Sample Size:** N/A. – Various. Source dependent **Database:** Substance Abuse and Mental Health Services Administration (SAMHSA). *Results from the 2010 National Survey on Drug Use and Health: Summary of National Findings*; SAMHSA, Office of Applied Studies, National Survey on Drug Use and Health, 1998-2010; IMS Health, National Prescription Audit, Dec. 2011 (175); www.deadiversion.usdoj.gov/arcos/retail_drug_summary/index.html, 2007 data - www.justice.gov/ndic/pubs33/33775/dlinks.htm; SDI, Vector One®: National; IMS Health, LifeLink, Dec 2011; International Narcotics Control Board, United Nations data; Centers for Disease Control and Prevention (CDC), Unintentional Drug Poisoning in the United States, July 2010; CDC, Vital signs: Overdoses of prescription opioid pain relievers – United States, 1999-2008. MMWR. 60, 1487-1492 (2011); CDC grand rounds: Prescription drug overdoses – a U.S. epidemic. MMWR. 61, 10-13 (2012). **Analysis:** Not specified. Detailed observational review of multiple data sources
Study Period:	1998-2010
Results/Findings:	The increased supply of opioids, high medical users, doctor shoppers, and patients with multiple comorbid factors contribute to the majority of fatalities. In 2008, one or more prescription drugs were involved in 20,044 of the 27,153 deaths with a specified drug. Opioid pain relievers were involved in 14,800 drug overdose deaths, compared to 11,500 of 27,500 fatal unintended drug overdose deaths in 2007 – an increase of 3,300 in just one year.
Conclusions	Over the past 20 years, there has been an escalation of the therapeutic use of opioids and other psychotherapeutics as well as their abuse and nonmedical use. As a consequence, hydrocodone has become the number one prescribed medication in America, it is not difficult to see the significant impact that this has had on the overall patterns of abuse and nonmedical use, particularly since the illicit use of prescribed psychotherapeutics (including opioids, which are currently at the top of that list) now overshadows the use of nonprescription illicit drugs. Drug dealers are no longer the primary source of illicit drugs.

Opioid Topic Area	Epidemiology/Health Policy
Author(s):	Fischer B, Rehm J.
Paper Title:	Revisiting the 'Paradigm Shift' in Opioid Use: Developments and Implications 10 Years Later
Reference:	Drug and Alcohol Review. 37(Supplement 1):S199-S202.
Aim/Objective:	To provide commentary/update on previous paper and the importance of identifying barriers to reducing the determinants of prescription opioid (PO) misuse
Country:	United States and Canada.
Health Outcome:	Reduction in PO misuse and opioid-related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Generally encompasses all ages Not gender specific Non-Hispanic whites referenced. Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses entire United States and Canada
Factors of interest:	Prescription opioids, heroin, burden of disease
Methods:	**Sample Size:** N/A **Database:** Canadian Institute for Health Information and Canadian Centre on Substance Abuse. Hospitalizations and Emergency Department Visits Due to Opioid Poisoning in Canada. Ottawa, ON: CIHI, 2016; National Institute of Drug Abuse (NIDA). Overdose Death Rates 2015; European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). European Drug Report 2016: Trends and Developments; International Narcotics Control Board (INCB). Availability of Internationally Controlled Drugs: Ensuring Adequate Access for Medical and Scientific Purposes; Substance Abuse and Mental Health Services Administration (SAMHSA). Treatment Episode Data Set (TEDS) 2004–2014; Centers for Disease Control and Prevention (CDC). Number and Age-Adjusted Rates of Drug-Poisoning Deaths Involving Opioid Analgesics and Heroin. **Analysis:** Not specified. Detailed observational review of multiple data sources
Study Period:	2007-2016
Results/Findings:	By about 2010, as many as 1 in 20 general population adults reported non-medical PO use; By 2014, there were almost 19 000 PO-related overdose deaths in the US; PO related overdose deaths have killed an estimated 150 000–200 000 people in the US and Canada; PO-related deaths has contributed to a measurable decline of life expectancy among middle-aged non-Hispanic whites since 2000, and to an overall stagnation of life expectancy in the US population; Consumption levels of POs are far higher in North America than in any other global region; The number of heroin users in the USA has increased by 145% in the period 2007–2014 and heroin-related deaths and demand for treatment have increased similarly.
Conclusions	The PO crisis, as it unfolded primarily in North America, began as a 'home-made' drug problem, created by a combination of prescribing excesses in the medical system and aggressive promotion efforts by the pharmaceutical industry, with ample warning signs. It has evolved—without much effective policy action—into an epidemic public health problem.

Opioid Topic Area	Epidemiology/Pain Management/Health Policy
Author(s):	Fischer B, Keates A, Bühringer G, Reimer J, Rehm J.
Paper Title:	Non-Medical Use of Prescription Opioids and Prescription Opioid-Related Harms: Why So Markedly Higher in North America Compared to the Rest of the World?
Reference:	Addiction. 2014; 109(2):177-81.
Aim/Objective:	To identify possible system-level factors contributing to the marked differences in the levels of non-medical prescription opioid use (NMPOU) and prescription opioid (PO)-related harms in North America (i.e. the United States and Canada) compared to other global regions.
Country:	United States and Canada
Health Outcome:	Opioid-related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Generally encompasses all ages Not gender specific Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses entire United States and Canada
Factors of interest:	Opioid misuse, policy, prescription, and-related deaths.
Methods:	**Sample Size:** Various. Source dependent. **Database:** United Nations Office on Drugs and Crime. World Drug Report 2011; European Monitoring Center on Drugs and Drug Abuse. Annual Report 2011; Substance Abuse and Mental Health Services Administration (SAMHSA). State Estimates of Substance Use and Mental Disorders from the 2008–2009 National Surveys on Drug Use and Health; International Narcotics Control Board. Narcotic Drugs Technical Report: Estimated World Requirements for 2012—Statistics for 2010; **Analysis:** Scientific literature and information related to relevant areas of health systems, policy and practice were reviewed and integrated.
Study Period:	2008-2012
Results/Findings:	1. North American health-care systems consume substantially more POs than any other global region, with dispensing levels associated strongly with levels of NMPOU and PO-related harms. North American health-care systems, compared to other systems, appear to have lesser regulatory access restrictions for, and rely more upon, community based dispensing mechanisms of POs, facilitating higher dissemination level and availability (e.g. through diversion) of POs implicated in NMPOU and harms. 2. Generally high levels of psychotropic drug use, dynamics of medical–professional culture (including patient expectations for 'effective treatment'), as well as the more pronounced 'for-profit' orientation of key elements of health care, may have boosted the PO-related problems observed in North America.
Conclusions	Differences in the organization of health systems, prescription practices, dispensing and medical cultures and patient expectations appear to contribute to the observed inter-regional differences in non-medical prescription opioid use and prescription opioid-related harms, although consistent evidence and causal analyses are limited. Further comparative examination of these and other potential drivers is needed, and also for evidence-based intervention and policy development.

Opioid Topic Area	Epidemiology/Mortality
Author(s):	Martins SS, Sampson L, Cerdá M, Galea S.
Paper Title:	Worldwide Prevalence and Trends in Unintentional Drug Overdose: A Systematic Review of the Literature
Reference:	American Journal of Public Health. 2015; 105(11), e29–e49.
Aim/Objective:	To conduct a scientific review of peer-reviewed literature of the worldwide epidemiological profile of unintentional drug overdoses and prevalence, time trends, mortality rates, and correlates of drug overdoses.
Country:	United States, Canada, United Kingdom, Europe, Russia & Australia
Health Outcome:	Opioid-related mortality and unintentional drug overdoses
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Youth, Adults Male and female Non-Hispanic Whites; Non-Hispanic Blacks; Hispanics; American Indians/Alaska Natives Low-income and rural communities Rural and urban areas, cities
Factors of interest:	Opioid-related overdoses and deaths among low-income and rural groups. Certain subgroups; homeless individuals, HIV-positive individuals, and recently released prisoners. Overdose associated with psychiatric disorders, suicidal ideation, and attempted suicide.
Methods:	**Sample Size:** 169 relevant articles; **Database:** A review of publications available in the US National Library of Medicine's PubMed electronic database using different combinations of Medical Subject Headings (MeSH) search terms. Researchers limited the search to English-language articles published between 1980 and July 2013 on unintentional overdose. **Analysis:** The review of article abstracts concentrated on reported population-based prevalence measures, percentage of changes over time in trends of overdose, mortality rates and correlates of overdose as the key constructs.
Study Period:	1980 until July 2013
Results/Findings:	Studies reported increased rates of worldwide deaths from opioids, heroine, and cocaine use and decreased deaths from illicit drug use. In the US, there was a 467.7% increase in Methadone deaths between 1999 and 2005, and a 129.2% increase in prescription opioids deaths between 1999 and 2002. The highest rates were among high-poverty communities and rural areas, no longer relegating the issue to only urban environments. In the United States, much of the increase in drug overdose is credited in large part to high increases in rates of nonmedical prescription drug use and overdose. Between 1974 and 1992 in England and Wales, there was an 1186% increase in fatal self-poisonings solely due to heroine. Conversely, Australia experienced a 60% decrease in opioid deaths between 1990 and 2001. Globally, there is sparse data on the magnitude of unintentional drug overdose and to what extent environment plays a role.
Conclusions	Race/ethnicity and social environment are significant factors when examining overdose rates. In New York City, prescription opioid death rates are higher among non-Hispanic Whites, and 15.2% of injection drug users in Los Angeles, California are either homeless or residing in temporary housing. Experts endorse capitalizing on examples used in Canada where resources are directed toward prevention and intervention strategies that focus on harm reduction strategies while also offering treatment options.

Opioid Topic Area	Epidemiology/Pain Management/Treatment
Author:	Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN.
Paper Title:	Opioid Dose and Drug-Related Mortality in Patients with Nonmalignant Pain.
Reference:	Archives of Internal Medicine. 2011; 171(7):686-691.
Aim/Objective:	To illustrate the relationship between opioid dose and opioid-related mortality.
Country:	Canada
Health Outcome:	Opioid dose and mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	15-64 years Male, Female White Unemployment, disability Ontario, Canada (Rural and Urban)
Factors of interest:	Opioid dose and opioid-related mortality
Methods:	**Sample Size:** N=1,463 **Database:** Ontario Public Drug Benefit Program and computerized database of Ontario residents with cancer, and the Canadian Institute for Health Information's Discharge Abstract Database. Researchers performed a review using a 2 population-based nested case-control for patients who were prescribed opioids for nonmalignant pain. Researchers identified 498 eligible patients **Analysis:** Researchers use descriptive statistics to calculate baseline characteristics and standardized differences were tested for differences between groups. Standardized difference was determined at greater than 0.10 and deemed as a meaningful difference. The study used conditional logistic regression to estimate the odds ratio (OR) for the association between average daily opioid dose and opioid-related mortality. Breakdown of the study revealed that patients were classified based on average daily opioid dose: less than 20 mg, 20 to 49 mg, 50 to 99 mg, 100 to 199 mg, and 200 mg or more of morphine equivalents.
Study Period:	August 1, 1997 through December 31, 2006
Results/Findings:	After multivariable adjustment, an average daily dose of 200 mg or more of morphine (or equivalent), was associated with a nearly 3-fold increase in the risk of opioid-related mortality relative to low daily doses (20 mg of morphine, or equivalent). Investigators found significant but diminished increases in opioid-related mortality with intermediate doses of opioids (50-99 mg/d of morphine: OR, 1.92; 95% CI, 1.30-2.85; 100 199 mg/d of morphine: OR, 2.04; 95% CI, 1.28-3.24).
Conclusions	Researchers determined a significant association between prescribed average daily dose of opioids and opioid-related mortality in adults with nonmalignant pain. Moreover, the risk was highest for patients who were prescribed 200 mg or more of morphine (or equivalent), on average per day. Researchers conclude that most opioid-related deaths are avoidable and prevalent among young people; therefore, efforts should be directed to educate doctors on the relevance and consequences of prescribing high doses of opioids and understand better long-term opioids use to treat chronic, non-cancer-related pain.

Opioid Topic Area	Pain Management/Health Policy
Author(s):	Hagemeier NE.
Paper Title:	Introduction to the Opioid Epidemic: The Economic Burden on the Healthcare System and Impact on Quality of Life
Reference:	American Journal of Managed Care. 2018; 24:S200-S206
Aim/Objective:	To investigate the economic burden of the opioid epidemic on the healthcare system and the impact on quality of life.
Country:	United States
Health Outcome:	Opioid long-term use, addiction, and overdose deaths
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adults Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Economic Burden, Trend, Prescription Opioids
Methods:	**Sample Size:** N/A **Database:** Facts generally acquired from other papers in journals such as the Journal of Pain, JAMA Internal Medicine, and the Journal of Pain Research as well as government sources including the National Institutes of Health (NIH), Substance Abuse and Mental Health Services Administration, and CDC National Center for Injury Prevention and Control **Analysis:** Review paper that compiled the history of patient treatment leading to the opioid epidemic and highlighted key research regarding the economic burden of the epidemic on the healthcare system and impact on quality of life. The paper discussed recent legislation on addiction and possible avenues to resolve the growing crisis.
Study Period:	1990-2017 (including history)
Results/Findings:	In 2016, more than 60 million patients had at least 1 prescription for opioid analgesics filled or refilled to treat acute and chronic pain. In the US healthcare system, chronic pain is often treated as a disease due to major events such as the American Pain Society's 1996 phrase "pain as the 5th vital sign", the Joint Commission's 2001 standards for inpatient and outpatient pain management that underscored the patient's right to pain relief, the FDA's 1995 oxycodone formulation (OxyContin). This has led to an explosion in opioid prescriptions and the US Department of Health and Human Services declaration of the opioid crisis as a public health emergency. Research has shown significant correlations between amounts of prescribed opioids in 2008 and greater population size, lower education level, higher percentage of non-Hispanic whites and African-Americans, higher poverty, higher percentage without insurance and <65 years, higher physicians per capita, and higher percentages of all surgeons, psychiatrists, and pediatricians.
Conclusions	The opioid epidemic has negatively impacted individuals and their families in the US as well as society as a whole. Some work has been done to resolve the issue such as the CDC's work to promote awareness to reduce opioid prescribing practices and the passing of the Comprehensive Addiction and Recovery Act in 2016. To resolve this crisis that developed largely as a result of the healthcare system and treatment of pain by providers, drastic action needs to be taken by public and private organizations.

Opioid Topic Area	Pain management/Health Policy
Author(s):	Burgess DJ, van Ryn M, Crowley-Matoka M, Malat J.
Paper Title:	Understanding the Provider Contribution to Race/Ethnicity Disparities in Pain Treatment: Insights from Dual Process Models of Stereotyping
Reference:	Pain Medicine. 2006; 7(2):119-134.
Aim/Objective:	To illustrate unintentional provider bias in decisions about pain treatment.
Country:	United States
Health Outcome:	The effect of unconscious bias on prescribing practices related to pain
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A Male, Female Non-Hispanic white, African American N/A Nationwide
Factors of interest:	Opioid-related prescribing practices, pain management
Methods:	**Sample Sizes:** 111 and 2,872 (respectively) **Vignette studies:** Primary care and national sample of emergency physicians. **Analysis:** First vignette, primary care physicians (n=111) were asked to treat three hypothetical patients with pain (kidney stones and back pain) or with a control condition. Patient aspects were constant except race and gender. Male physicians provided more pain relief to non-Hispanic whites and female physicians provided more pain relief to African-Americans. In the second, a national sample of emergency physicians (n=2,872) were given three different conditions: non-traumatic back pain, ankle fracture, and migraine headache. They were randomly assigned to read different vignettes that differed in patient race/ethnicity and in cues of social desirability (SD) (i.e. having a high prestige occupation and a strong relationship with a primary care provider). Race/ethnicity was not shown as a factor in deciding to prescribe opioids, but patients with more SD characteristics who presented with uncertain etiology of back pain or migraine were more likely to be prescribe opiates.
Study Period:	N/A
Results/Findings:	Although it may appear that racial/ethnic disparities in pain treatment decisions may be apparent due to a belief on the part of the provider that non-Hispanic white patients may appear to have more socially desirable characteristics when compared to patients who are from a racial/ethnic minority group. However interpreting these results does not provide clear cut evidence of this.
Conclusions	Automatic stereotyping may impact treatment disparities in which a negative aspects of racial/ethnic stereotypes influences a provider's interaction and the treatment of patients. This process is unconscious on the part of the provider. This unconscious bias is most likely to manifest itself when providers have limited cognitive resources and they are unable to incorporate individual information. Due to the small sample size, it would be beneficial to further study this topic area to see if race/ethnicity does serve as an influencing factor in prescribing practices of healthcare providers.

Opioid Topic Area	Pain Management/Treatment/Health Policy
Author:	Gellad WF, Good CB, Shulkin DJ.
Paper Title:	Addressing the Opioid Epidemic in the United States: Lessons from the Department of Veterans Affairs
Reference:	JAMA Internal Medicine. 2017; 177(5):611-612.
Aim/Objective:	To present the lessons learned and strategies the Veterans Administration (VA) system used to address the opioid epidemic.
Country:	United States
Health Outcome:	Fewer patient/veterans prescribed opioids, fewer patients/veterans receiving 100 morphine-milligram equivalent dosages, and decrease in number of patient/veteran overdoses.
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adults ≥18, Working Age, Elderly Male, Female Generally encompasses all races/ethnicities Veterans United States
Factors of interest:	Drug Prescriptions, Management, Alternative Meds, Trends
Methods:	**Sample Size:** 900,000 In 2013, the VA launched the Opioid Safety Initiative to address opioid overuse. The VA employed 4 strategies; 1) education (i.e., dashboards with real-time prescriber data to engage clinicians in adopting best practices and other education); 2) pain management (i.e., expanding complementary and integrative medicine and access to topical gels or acupuncture, pain therapy); 3) risk mitigation (i.e., clinician, facility, and system-level measurement of opioid safety percent of veterans dispensed opioids including with/without other drugs and dosage amount; and 4) addiction treatment to include inpatient and outpatient.
Study Period:	FY2003-FY2016
Results/Findings:	By mid-2016 compared with mid-2012, the number of veterans dispensed an opioid each quarter had decreased by 172,000, or about 25%. There were 57,000 (47%) fewer patients receiving concomitant opioids and benzodiazepines and 22,000 (36%) fewer patients receiving daily opioid dosages of more than 100 morphine-milligram equivalents, both measures of potentially unsafe opioid use. Between 2010 and 2015 the rate of opioid overdose among veterans dispensed a prescription opioid, decreased from 0.16% to 0.08%.
Conclusions	The prescription opioid epidemic has required the VA to find better ways to manage pain in veterans while limiting the risks of opioids. In 2017, fewer veterans were receiving high doses of opioids or concomitant interacting medicines like benzodiazepines, and more veterans were receiving non-opioid pain therapies, naloxone, and treatment for substance use disorders. The VA provides an example of how technology, data and organizational leadership can make a difference in improving opioid prescribing.

Opioid Topic Area	Pain Management/Treatment/Policy
Author:	Dowell DD, Haegerich TM, Haegerich, Chou R.
Paper Title:	Centers for Disease Control Guideline for Prescribing Opioids for Chronic Pain - United States, 2016
Reference:	The Journal of the American Medical Association (JAMA). 2016; 315(15): 1624-1645.
Aim/Objective:	To provide recommendations about opioid prescribing for primary care clinicians treating adult patients with chronic pain outside of active cancer treatment, palliative care, and end-of-life-care.
Country:	United States
Health Outcome:	Improve physician-patient dialogue regarding long-term opioid related therapy.
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adults aged ≥18 years Male/Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Prescriptions, Non-opioid Therapy
Methods:	CDC updated a 2014 systematic review on effectiveness and risks of opioids and conducted a supplemental review on benefits and harms, values and preferences, and costs. CDC used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework to assess evidence type and determine the recommendation category. Evidence consisted of observational studies or randomized clinical trials with notable limitations, characterized as low quality using GRADE methodology. Meta-analysis was not attempted due to the limited number of studies, variability in study designs and clinical heterogeneity, and methodological shortcomings of studies. No study evaluated long-term (longer than 1 year) benefit of opioids for chronic pain.
Study Period:	2016 update of 1999-2014 review
Results/Findings:	There are 12 recommendations. Of primary importance, non-opioid therapy is preferred for treatment of chronic pain. Opioids should be used only when benefits for pain and function are expected to outweigh risks. Clinicians should establish treatment goals with patients and consider how opioids will be discontinued. When used, clinicians should prescribe the lowest effective dosage, carefully reassess benefits and risks when considering increasing dosage to 50 morphine mg equivalents or more per day, and avoid concurrent opioids and benzodiazepines. Clinicians should evaluate benefits and harms of continued opioid therapy with patients every 3 months or more frequently. For patients with opioid use disorder, clinicians should offer or arrange evidence-based treatment.
Conclusions	The guideline is intended to improve communication between clinicians and patients about the risks and benefits of opioid therapy for chronic pain, improve the safety and effectiveness of pain treatment, and reduce the risks associated with long-term opioid therapy, including opioid use disorder, overdose, and death.

Opioid Topic Area	Pain Management/Treatment/Policy
Author:	Katzman JG, Fore C, Bhatt S, Greenberg N, Salvador JG, George CC, et al.
Paper Title:	Evaluation of American Indian Health Service Training in Pain Management and Opioid Substance Use Disorder
Reference:	American Journal of Public Health. 2016; 106(8):1427-1429.
Aim/Objective:	To examine the benefits of collaboration between IHS and an academic medical center to mandate training in pain and opioid substance use disorder for all prescribing clinicians.
Country:	United States
Health Outcome:	Effective provider education in pain management and opioid abuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adults, Working Age ≥18 years Male, Female All, American Indian/Alaska Native (AIAN) Generally encompasses all socioeconomic statuses 28 States relevant to IHS (heavily skewed to states with large, rural areas in the West, Southwest, and Midwest regions)
Factors of interest:	Prescriber education, Indian Health Service, New Mexico
Methods:	The Indian Health Service (IHS) mandated prescribing clinicians be trained in pain and opioid substance use disorder in 2015. A CEU course was designed to educate clinicians who received 5 hours of no-cost CEUs. Didactics included: "Overview of Public Health Crises of Pain and Drug Overdose Deaths," "Safe Opioid Prescribing," "Use of Non-Opioid Medications in Pain Management," "Pediatric/Adolescent Pain Management," "Opioid Substance Use Disorder/ Screening," "Federal Regulations Pertaining to Opioid Pre-scribing," and 2 case vignettes "Controlled Substance Agreement" and Comorbid Pain/Psychiatric Condition.
Study Period:	January-June 2015
Results/Findings:	Survey comparing pre and post course scores (of a sample size of 1079 clinicians) demonstrated a positive change in knowledge, self-efficacy and 12-item attitude surveys. The knowledge questions included questions on screening for opioid substance use disorder, naloxone as a harm reduction measure for opioid overdose, and the use of non-opioid medications.
Conclusions	Pre-licensure pain education across many disciplines does not instill the optimal skills for many practicing clinicians, who sometimes lack the knowledge and confidence to care for patients with pain, opioid substance use disorder and co-occurring mental health conditions. Because the AIAN population is at increased risk for nonmedical use of opioid analgesics and an increased risks for substance use disorder in general, clinician education is of paramount importance for reducing drug overdose deaths. Only 5 states (Kentucky, Massachusetts, New Mexico, Vermont, and West Virginia) require pain management and opioid education for their prescribing clinicians.

Opioid Topic Area	Pain Management/Treatment/Policy
Author:	Hansen H, Kline N, Netherland J.
Paper Title:	Is the Prescription Opioid Epidemic a White Problem?
Reference:	American Journal of Public Health December. 2016; 106(12): 2127-2129.
Aim/Objective:	To prove that narcotics policies need to be scrutinized for racial targeting/reinforcing inequalities in health and law enforcement.
Country:	United States
Health Outcome:	Death
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Adults, Working adults aged ≥18 All Caucasian/White, Hispanic, Black Generally encompasses all socioeconomic statuses United States
Factors of interest:	Life expectancy, incarceration, criminal justice, racial inequality
Methods:	Review of previous literature
Study Period:	2016
Results/Findings:	The life expectancy of US whites has declined, largely as a result of drug overdose/increased opioid analgesic use. Access to prescription opioids illustrate how racially disparate drug polices and health care practices ultimately hurt white patients. The decrease in white life expectancy began after the US Food and Drug Administration approved OxyContin as a minimally addictive painkiller. Deaths from opioid abuse reached an all-time high of 18,893, a 3.4 fold increase from 2001. At the same time, addiction neuroscience, biotechnology, federal regulation and drug marketing contributed the representation of the opioid overdose epidemic as a White problem subject to interventions district from those of the US War on Drugs. The resulting racialized differences between heroin and prescription opioid control resembled those created by the law distinguishing crack from powder cocaine that led the US to the highest incarceration in the world with Black and Hispanic men six and three times respectively as likely as White men. Insurance coverage and access to physicians is racially stratified increasing access to opioids. White communities, rather than arresting consumers, regulators mandated physicians to use Prescription Drug Monitoring Programs. Prescription opioid use exceeded heroin use but arrest rate for sale or possession is 4 times less.
Conclusions	There is an opportunity to reorient US drug policy to make proven harm reduction strategies widely available, such as naloxone for overdose reversal, treatment facilities and medication assisted treatments, psycho social treatments, behavior therapy and relapse prevention must be accessible. Must increase accessibility and decriminalize personal possession of drugs and expunging arrest records of thousands of mostly young men of color.

Opioid Topic Area	Pain Management/Treatment
Author(s):	Compton WM, Boyle M, Wargo E.
Paper Title:	Prescription Opioid Abuse: Problems and Responses
Reference:	Preventive Medicine. 2015; 80:5-9.
Aim/Objective:	This commentary considers the factors that have led to over-prescription of opioids by clinicians, discusses recent evidence casting doubt on the efficacy of opioids for treating chronic pain, and describes the ongoing efforts by federal and community stakeholders to address this epidemic.
Country:	United States
Health Outcome:	Reduce over-prescription of opioids; address interventions for misuse and abuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Generally encompasses adults Generally classified adults and young adults Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Opioid over-prescription for pain, interventions for misuse/abuse, prescription opioid abuse, addiction, overdose
Methods:	**Analysis:** Commentary/Literature Review. Prescription opioid abuse and addiction, along with consequences such as overdose death and increasing transition to heroin use, constitute a devastating public health problem in the United States. Increasingly it is clear that over-prescription of these medications over the past two decades has been a major upstream driver of the opioid abuse epidemic. This commentary considers the factors that have led to over-prescription of opioids by clinicians, discusses recent evidence casting doubt on the efficacy of opioids for treating chronic pain, and describes the ongoing efforts by federal and community stakeholders to address this epidemic.
Study Period:	1999-2015
Results/Findings:	Although opioids have a legitimate role in pain management and are indicated in some cases, it is clear that they are sometimes overprescribed and that their misuse can have devastating effects. While abuse-deterrent formulations reduce these consequences to an extent, their effectiveness is limited (Cicero and Ellis, 2015).
Conclusions	The United States is by far the biggest consumer of opioids in the world (International Narcotics Control Board, 2009). While new pain treatment approaches await discovery, strategies to reduce the availability of opioids have been implemented and proven effective.

Opioid Topic Area	Pain Management/Treatment
Author(s):	Becker WC, Starrels JL, Heo M, Li X, Weiner MG, Turner BJ.
Paper Title:	Racial Differences in Primary Care Opioid Risk Reduction Strategies
Reference:	Annals of Family Medicine. 2011; 9(3):219-225.
Aim/Objective:	To discuss why racial disparities in treating pain with opioids are widely reported, while differences in use of recommended strategies to reduce the risk of opioid misuse by race/ethnicity have not been evaluated.
Country:	United States
Health Outcome:	Reduce risk of opioid misuse
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	N/A (didn't further classify) – 18 years and older Male, Female African American, White Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Race/ethnicity, opioid analgesics, safety monitoring, disparities, drug testing, practice-based research, primary care
Methods:	In a retrospective cohort of black and white patients with chronic non-cancer pain prescribed opioid analgesics for at least 3 months, the study assessed physicians' use of 3 opioid risk reduction strategies: (1) urine drug testing, (2) regular office visits (at least 1 visit per 6 months on opioids and within 30 days of an opioid change), and (3) restricted early opioid refills (receipt of a refill >1 week early less than twice). Nonlinear mixed effect regression models accounted for clustering within physician and adjusted additively for demographics, substance abuse, mental health and medical comorbidities, health care factors, and practice site.
Study Period:	2004-2008
Results/Findings:	Of the 1,612 patients studied, 62.1% were black. Black patients were more likely than white patients to receive urine drug testing (10.4% vs 4.1%), regular office visits (56.4% vs 39.0%), and restricted early refills (79.4% vs 72.0%). In fully adjusted models, black patients had significantly higher odds than their white counterparts of receiving regular office visits (odds ratio=1.51; 95% confidence interval, 1.06-2.14) and restricted early refills (odds ratio=1.55; 95% confidence interval, 1.03-2.32), but not urine drug testing (odds ratio=1.41; 95% confidence interval, 0.78-2.54). Findings suggest a "reverse disparity" in use of opioid monitoring raising concerns about a "lax in monitoring" of prescription abuse/misuse among whites.
Conclusions	In this cohort of primary care patients receiving opioid analgesics on a long-term basis, use of risk reduction strategies was very limited overall; however, black patients were more likely than white patients to receive 2 of 3 guideline-recommended strategies. These data raise questions about lax monitoring, especially for white patients taking opioids long term.

Opioid Topic Area	Pain Management/Treatment
Author(s):	Green CR, Anderson KO, Baker TA, Campbell LC, Decker S, Fillingim RB, et al.
Paper Title:	The Unequal Burden of Pain: Confronting Racial and Ethnic Disparities in Pain
Reference:	Pain Medicine. 2003; 4(3): 277-294.
Aim/Objective:	To provide health care providers, researchers, health care policy analysts, government officials, patients, and the general public with pertinent evidence regarding differences in pain perception, assessment, and treatment for racial and ethnic minorities.
Country:	United States
Health Outcome:	Improve underrated pain management and perception by providers among racial and ethnic minorities
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	Generally encompasses adults Generally classified adults and young adults Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Generally encompasses the entire United States
Factors of interest:	Racial/Ethnic Disparities, Pain, Treatment, Provider/Pain Assessment and Perception
Methods:	Literature review. A selective literature review was performed by experts in pain.
Study Period:	1984-2003
Results/Findings:	The pain experts developed abstracts with relevant citations on racial and ethnic disparities within their specific areas of expertise. Scientific evidence was given precedence over anecdotal experience. The abstracts were compiled for this manuscript. The draft manuscript was made available to the experts for comment and review prior to submission for publication.
Conclusions	Consistent with the Institute of Medicine's report on health care disparities, racial and ethnic disparities in pain perception, assessment, and treatment were found in all settings (i.e., post-operative, emergency room) and across all types of pain (i.e., acute, cancer, chronic nonmalignant, and experimental). The literature suggests that the sources of pain disparities among racial and ethnic minorities are complex, involving patient (e.g., patient/health care provider communication, attitudes), health care provider (e.g., decision making), and health care system (e.g., access to pain medication) factors. There is a need for improved training for health care providers and educational interventions for patients. A comprehensive pain research agenda is necessary to address pain disparities among racial and ethnic minorities.

Opioid Topic Area	Treatment/Health Policy
Author(s):	Faul M, Dailey MW, Sugarman DE, Sasser SM, Levy B, Paulozzi LJ.
Paper Title:	Disparity in Naloxone Administration by Emergency Medical Service Providers and the Burden of Drug Overdose in US Rural Communities
Reference:	American Journal of Public Health. 2015; 105 (Supplement 3):e26-e32. doi: 10.2105/AJPH.2014.302520.
Aim/Objective:	To determine the factors that affect naloxone (Narcan) administration in drug overdoses, including the certification level of emergency medical technicians (EMTs).
Country:	United States
Health Outcome:	Opioid-related mortality
Age Category: **Gender:** **Race/Ethnicity:** **Socioeconomic Status:** **Geography:**	0-19, 20-29, 30-39, 40-49, 50-59, 60-99 Male, Female Generally encompasses all races/ethnicities Generally encompasses all socioeconomic statuses Classified "urbanicity" into 4 different groups (urban, suburban, rural, and wilderness)
Factors of interest:	Opioid-related deaths, probability of emergency treatment delivery by age and gender
Methods:	**Sample Size:** 262,676 suspected drug overdose events in 2012. **Database:** National Emergency Medical Services Information System to acquire demographic data, basic 911 call information, details about the scene of injury or illness, medications administered, and other variables recorded by EMS in 2012. The data set is a convenience sample that is not weighted to reflect national estimates. **Analysis:** Used logistic regression model to measure the association between naloxone administration and emergency medical services certification level, age, gender, geographic location (urban, suburban, rural, and wilderness), and patient primary symptom. Logistic regression results are presented as adjusted odds ratios (AORs) with 95% confidence intervals (CIs) and P values.
Study Period:	2012
Results/Findings:	The odds of naloxone administration were much higher among EMT-intermediates than among EMT-basics (adjusted odds ratio [AOR] = 5.4; 95% CI=4.5, 6.5). Naloxone use was higher in suburban areas than in urban areas (AOR=1.41; 95% CI=1.3, 1.5), followed by rural areas (AOR=1.23; 95% CI=1.1, 1.3). Although the odds of naloxone administration were 23% higher in rural areas than in urban areas, the opioid drug overdose rate is 45% higher in rural communities.
Conclusions	Naloxone is less often administered by EMT-basics, who are more common in rural areas. In most states, the scope-of-practice model prohibits naloxone administration by basic EMTs. Reducing this barrier could help prevent drug overdose death.