

Opioid Crisis: No Easy Fix to Its Social and Economic Determinants

The accepted wisdom about the US overdose crisis singles out prescribing as the causative vector. Although drug supply is a key factor, we posit that the crisis is fundamentally fueled by economic and social upheaval, its etiology closely linked to the role of opioids as a refuge from physical and psychological trauma, concentrated disadvantage, isolation, and hopelessness.

Overreliance on opioid medications is emblematic of a health care system that incentivizes quick, simplistic answers to complex physical and mental health needs. In an analogous way, simplistic measures to cut access to opioids offer illusory solutions to this multidimensional societal challenge.

We trace the crisis' trajectory through the intertwined use of opioid analgesics, heroin, and fentanyl analogs, and we urge engaging the structural determinants lens to address this formidable public health emergency. A broad focus on suffering should guide both patient- and community-level interventions. (*Am J Public Health*. Published online ahead of print December 21, 2017: e1–e5. doi:10.2105/AJPH.2017.304187)

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The accepted wisdom about the US opioid crisis singles out opioid analgesics as causative agents of harm, with physicians as unwitting conduits and pharmaceutical companies as selfish promoters.¹ Although invaluable for infection control, this vector model² of drug-related harm ignores root causes. Eroding economic opportunity, evolving approaches to pain treatment,^{1,3} and limited drug treatment have fueled spikes in problematic substance use, of which opioid overdose is the most visible manifestation. By ignoring the underlying drivers of drug consumption, current interventions are aggravating its trajectory. The structural and social determinants of health framework is widely understood to be critical in responding to public health challenges. Until we adopt this framework, we will continue to fail in our efforts to turn the tide of the opioid crisis.

THREE PHASES OF AN INTERTWINED EPIDEMIC

The roots of the opioid crisis are deeper than popular narrative suggests.^{4,5} In 1980, acute pain was so frequently treated with opioids that propoxyphene was the second-most dispensed drug in the United States.⁶ The Carter White House stated, "Diversion, misuse, and abuse of legal drugs may be involved in as many as seven out of ten reports of drug-related injury or

death."^{7(p301)} A decade later, US medicine was shaken by revelations of undertreated chronic pain, motivating normative practice and policy shifts.⁸ Previously, chronic pain was managed largely with cognitive behavioral therapy, even hypnosis.

An Institute of Medicine report⁹ attributed the rise in chronic pain prevalence during the 1990s to the following:

1. greater patient expectations for pain relief,
2. musculoskeletal disorders of an aging population,
3. obesity,
4. increased survivorship after injury and cancer, and
5. increasing frequency and complexity of surgery.

As insurers limited coverage of behavioral pain therapy, biopharmaceutical manufacturers sensed an opportunity. Pharmaceutical innovation propagated extended-release formulations, transdermal patches, nasal sprays, and oral dissolving strips. Medical device manufacturers drove a proliferation of novel pain-modulating implants. By 2000,

chronic pain was big business. Withdrawals from the market of popular nonopioid analgesics because of cardiovascular risk and acetaminophen toxicity raised concerns about nonopioid alternatives.¹⁰ Short lived but indelible, some pharmaceutical marketing improperly minimized addiction potential (OxyContin)¹¹ and promoted off-label use (Actiq),¹² later giving rise to physician kickback schemes (Subsys),¹³ lucrative speaking fees,¹⁴ and lobbying.¹⁵ In addition, a small proportion of physicians were unscrupulous, doling out opioids without adequate regard for medical need.^{16,17} These factors are widely believed to have caused the steady rise in opioid analgesic consumption over the past three decades, while rates of overdose and addiction increased in tandem.

Around 2010, the second phase started, marked by concern over intertwining opioid analgesic and heroin use.¹⁸ After remaining relatively stable for years, heroin overdose deaths spiked, tripling between 2010 and 2015.¹⁹ The vector model attributes this transformation to

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an expanded pool of susceptible individuals: with rising dependency and tolerance, some people who used prescription opioids transitioned to a more potent and cheaper alternative.²⁰ This phase is contemporaneous with the reformulation of OxyContin that made it difficult to crush, although this reformulation's contribution to the increase in heroin use is contested.²¹ More broadly during this time, clinicians and policymakers widely reassessed the effectiveness and safety of outpatient use of opioid analgesics.²²

The third phase began in late 2013 and continues today.²³ Increasingly efficient global supply chains and a sharp intensification in interdiction efforts created the conditions for the emergence of potent and less bulky products, for example, illicitly manufactured fentanyl and its analogs,²⁴ which are increasingly present in counterfeit pills and heroin.²⁵ Between 2013 and 2016, deaths attributed to fentanyl analogs spiked by a shocking 540% nationally,²⁶ with pronounced regional increases.^{19,25} The rapid acceleration of the crisis has led to its designation as a national public health emergency. Contradicting the singular blame on health care as the gateway to addiction, individuals entering drug treatment are now more likely to report having started opioid use with heroin, not prescription analgesics.²⁷

In the vector model, the blame for this trajectory of opioid analgesic to heroin to synthetic opioid use rests with the drugs themselves and those who make them available. Although increased availability of prescription opioids fueled the overdose crisis, we have not adequately explored the source of the demand for these medicines.

ROOT CAUSES

The vector argument must grapple with contradictory data. Prescription opioid overdose death rates have not yet dropped following declining opioid prescribing: the number of outpatient opioid analgesic prescriptions dropped 13% nationally between 2012 and 2015²⁸ (with sharper regional declines). Yet, the national overdose death rate surged 38% during those years.²⁹ Overdose deaths attributable to prescription opioids have not decreased proportionally to dispensing. Although there is a strong historic linear association between dispensed volume and overdose nationally,² these associations are less pronounced at the county level.³⁰ Alternative explanations include misclassification of synthetic opioid deaths,³¹ evolving autopsy protocols, time lag effects,³² and unused medication.

There are intuitive causal connections between poor health and structural factors such as poverty, lack of opportunity, and substandard living and working conditions. A comprehensive discussion of structural determinants of pain, addiction, and overdose is beyond the scope of this commentary. What is pertinent is that, although expansion of opioid availability may have catalyzed overdose rates,³³ an exclusive focus on opioid supply hampers effective responses.²⁷

One powerful line of structural analysis focuses on “diseases of despair,” referring to the interconnected trends in fatal drug overdose, alcohol-related disease, and suicide.³⁴ Since 1999, age-specific mortality attributed to these conditions has seen an extraordinary rise.^{34,35} The trend is especially pronounced among middle-aged Whites without a college degree,

who are now dying earlier on average than did their parents—which is anomalous outside of wartime. In an analysis focused on the Midwest, Appalachia, and New England (where the heroin, fentanyl, and both comingled epidemics are most pronounced), combined mortality rates for diseases of despair increased as county economic distress worsened.³⁶

An alternate hypothesis suggests that an environment that increasingly promotes obesity coupled with widespread opioid use may be the underlying drivers of increasing White middle-class mortality.³⁷ Complex interconnections between obesity, disability, chronic pain, depression, and substance use have not been adequately explored. Additionally, suicides may be undercounted among overdose deaths.³⁸ Under both frameworks, social distress is a likely upstream explanatory factor.

The “reversal of fortunes”^{37,39} in life expectancy saw rapid diffusion, going from largely limited to Appalachia and the Southwest in 2000 to nationwide by 2015.³⁴ The unprecedented 20-year difference in life expectancy between the healthiest and least healthy counties is largely explained by socioeconomic factors correlated with race/ethnicity, behavioral and metabolic risk, and health care access.⁴⁰ These indicators are the most recent evidence of a long-term process of decline: a multidecade rise in income inequality and economic shocks stemming from deindustrialization and social safety net cuts. The 2008 financial crisis along with austerity measures and other neoliberal policies have further eroded physical and mental well-being.⁴¹

Poverty and substance use problems operate synergistically, at the extreme reinforced by

psychiatric disorders and unstable housing. The most lucrative employment in poorer communities is dominated by manufacturing and service jobs with elevated physical hazards, including military service. When sustained over years, on-the-job injuries can give rise to chronically painful conditions, potentially resulting in a downward spiral of disability and poverty. Although opioid analgesics may allow those with otherwise debilitating injuries to maintain employment, individuals in manual labor occupations appear to be at increased risk for non-medical use.⁴² In much of the country, the counties with the lowest levels of social capital have the highest overdose rates.⁴³ The interplay between social and genetic factors, too, is being elucidated. Individuals living in low socioeconomic neighborhoods were more likely to develop chronic pain after car crashes, a process mediated by stress response genes.⁴⁴ Interactions between environment and genetic polymorphisms may in part explain substance use early in life.⁴⁵

The interpretation of the vector model has justified mass incarceration for minor drug charges, creating further tears in the social fabric of communities already reeling from a lack of opportunity.⁴⁶ Perversely, incarceration of people with opioid dependence leads to interrupted opioid tolerance and a drastic elevation in overdose risk.⁴⁷ Having a public record because of a drug conviction limits one's ability to obtain meaningful employment, reinforcing the penury that drove problematic drug use in the first place. Although those who see the crisis through the vector lens do not necessarily advocate punishment, the rhetorical dominance of this model has crowded out

investment in evidence-driven demand reduction and harm reduction approaches.²⁴

In recasting pain as a broader condition that includes economic and social disadvantage, we urge an alternative explanation for the rising demand for opioids. It has been observed that people somaticize social disasters into physical pain. Subjective economic hardship was associated with new onset low back pain following the Great East Japan Earthquake.⁴⁸ Intensifying substance use may be a normal societal response to mass traumatic events, especially when experienced by people in lower socioeconomic strata. Increased alcohol use and binge drinking were noted after Hurricanes Katrina and Rita, with the greatest compensatory drinking among those with lower lifetime income trajectories.⁴⁹ Women experiencing work stressors after September 11, 2001, were more likely to have increased alcohol use.⁵⁰ Longitudinal housing relocation studies suggest that drug use improves when people move to neighborhoods with less economic disadvantage.⁵¹ Adverse childhood experiences have been strongly linked to subsequent substance use; likewise, childhood trauma, is associated with increased opioid use years later.⁵² People who use heroin in a deindustrialized steel production area of Pennsylvania cited economic hardship, social isolation, and hopelessness as reasons for drug use, explicitly calling for jobs and community reinvestment to stem overdoses.⁵³ Yet, some communities' protective family⁵⁴ and social structures generate resilience that mitigates negative impacts from the collision of economic hardship, substance use, and depression.⁵⁵

Collectively, these observations challenge us to expand our

conceptualizations of the opioid crisis beyond the vector model. A seminal National Academy of Sciences report provides this summary:

overprescribing was not the sole cause of the problem. While increased opioid prescribing for chronic pain has been a vector of the opioid epidemic, researchers agree that such structural factors as lack of economic opportunity, poor working conditions, and eroded social capital in depressed communities, accompanied by hopelessness and despair, are root causes of the misuse of opioids and other substances.^{56(p1-9)}

TO TURN THE TIDE, FOCUS ON SUFFERING

The observation that Canada and the United States have the highest per capita opioid analgesic consumption is central to the belief that these medicines are overprescribed, leading to the unrealistic expectation that curtailment of dispensing will automatically reduce overdose. In practice, overprescribing is an amalgamation of prescribing behaviors encompassing starting dose, number of units in a prescription, dosing schedules, potency, and other factors. A rational approach would treat these as parallel but distinct issues. Yet, the legislative and clinical reaction has included efforts to bring dosage below arbitrary targets or abandon patients who do not conform to clinically arbitrary expectations.³⁰

The emphasis on prescribing volume may be a manifestation of subconscious racial bias that frames the famously White opioid crisis as inadvertently induced by physicians; this stands in direct contrast with previous drug panics perceived to afflict minorities, whose drug use was considered a moral failing.^{57,58}

This framing, along with the medicalized view of addiction, leaves intact the dignity of people seeking drug treatment—no doubt a positive rhetorical change if applied to all people. Yet, we have spent decades pathologizing members of minority communities for turning to drugs to cope with social stressors and structural inequities. That these phenomena may also afflict White, rural, and suburban communities is emerging as a new realization in public discourse. However, overdose is not isolated to these areas: approximately 41% of drug overdose deaths occur in urban counties, 26% in the suburbs, 18% in small metropolitan areas, and 15% in rural communities.⁵⁹ Native Americans are disproportionately affected by overdose deaths as are African Americans in Illinois, Wisconsin, Missouri, Minnesota, West Virginia, and Washington, DC, among other places.^{60a, 60b}

This is not merely a story about disadvantage (in income, race, place, etc.). On the basis of epidemiological studies, structural advantages in health care access may have contributed to increased opioid prescribing⁶¹ and availability⁶² among White patients. However, reverse associations were observed in controlled clinic-based experiments in which Black patients ended up receiving more opioids, possibly mediated through interactions with patient assertiveness,⁶³ physician gender, and cognitive load.⁶⁴ Regardless, the experience of many seeking health care to manage long-term pain and substance use disorders is tinged with racial undertones. Diez Roux warns:

We should guard against the unintended consequence that the focus on the increase in death rates in some Whites (significant as they are) detract attention from the persistent health inequities by

race and social class, which are so large that they dwarf the size of what is a very troublesome increase in some Whites.^{65(p1566)}

Alas, the US health care system is unprepared to meet the demands elucidated by a structural factors analysis. Even at the patient level, the intersection of social disadvantage, isolation, and pain requires meaningful clinical attention that is difficult to deliver in high-throughput primary care. Some providers struggle with addressing complex, chronic medical conditions requiring regular follow-up, especially with limited recourse to nonpharmacological alternatives and the predominantly urban concentration of specialty services. Patient contracts, urine drug tests, and prescription monitoring can generate mutual distrust in the provider-patient relationship when applied inconsistently, giving rise to uneven care delivery and inducing perceptions of intentional mistreatment.⁶⁶ In Wisconsin, the prescription drug monitoring program includes patients' convictions and suspected drug violations, straying into ethically hazy realms of social control. Patients suspected of drug-seeking behavior are "fired" instead of receiving enhanced care, as compassion would dictate.⁶⁷ Institutional, legal, and insurance architecture have robbed clinicians of time and incentives to continue care for these patients.

Access to evidence-based treatment for opioid use disorder, such as methadone and buprenorphine, must be rapidly improved. The hardest hit states, such as West Virginia and Kentucky, prohibit Medicaid coverage of methadone maintenance, and insurance preauthorization prevents low threshold

access among privately insured patients. The Appalachian Regional Commission recommended economic development strategies in addition to increased access to treatment services, prevention, and overdose medications.⁶⁸ Yet, proposed federal health care reforms threaten to further exacerbate existing service gaps.⁶⁹ Although national policy emphasizes medically assisted treatment, the social stigma of these treatments is widespread, carrying unrealistic expectations for quick fixes and a pervasive belief in “detox,” as exemplified by television shows popularizing coercive interventions.

“Suffering” may be a better focus for physicians than “pain.”⁷⁰ Others have argued for “compassion.”⁶⁷ Health care providers have a role in reducing suffering historically and ethically. We have lost the commonsense imperative to engage those who use opioids in comprehensive care, especially during periods when access to opioids may be fluctuating. These tenets also may justify limited regimes to treat acute pain for veritable patient need.

The social determinants lens lays bare the urgency of integrating clinical care with efforts to improve patients’ structural environment.⁷¹ Training health care providers in “structural competency” is promising,⁷² as we scale up partnerships that begin to address upstream structural factors such as economic opportunity, social cohesion, racial disadvantage, and life satisfaction. These do not typically figure into the mandate of health care but are fundamental to public health.

As with previous drug crises and the HIV epidemic, root causes are social and structural and are intertwined with

genetic, behavioral, and individual factors. It is our duty to lend credence to these root causes and to advocate social change. **AJPH**

CONTRIBUTORS

N. Dasgupta and L. Beletsky contributed equally to this commentary. All authors participated in conceptualization, research, drafting, and editing of the commentary.

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REFERENCES

- Madras BK. The surge of opioid use, addiction, and overdoses: responsibility and response of the US health care system. *JAMA Psychiatry*. 2017; 74(5):441–442.
- Dasgupta N, Kramer ED, Zalman MA, et al. Association between non-medical and prescriptive usage of opioids. *Drug Alcohol Depend*. 2006;82(2):135–142.
- Meldrum ML. The ongoing opioid prescription epidemic: historical context. *Am J Public Health*. 2016;106(8):1365–1366.
- Jenkins P. *Synthetic Panics: The Symbolic Politics of Designer Drugs*. New York, NY: New York University Press; 1999.
- Herzberg D, Guarino H, Mateu-Gelabert P, Bennett AS. Recurring epidemics of pharmaceutical drug abuse in America: time for an all-drug strategy. *Am J Public Health*. 2016;106(3):408–410.
- Schnoll S, Pain. In: Cohen S, Katz D, Buchwalk C, Solomon J, eds. *Frequently Prescribed and Abused Drugs, Their Indications, Efficacy and Rational Prescribing*. Rockville, MD: National Institute on Drug Abuse; 1982:41–55.
- US Government. Summary and recommendations of the 1980 White House conference on prescription drug misuse, abuse and diversion. In: Wilford BB, ed. *Balancing the Response to Prescription Drug Abuse*. Chicago, IL: American Medical Association; 1990:301–307.
- Wailoo K. *Pain: A Political History*. Baltimore, MD: Johns Hopkins University Press; 2014.
- Institute of Medicine. *Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research*.

Washington, DC: National Academies Press; 2011.

10. Conaghan PG. A turbulent decade for NSAIDs: update on current concepts of classification, epidemiology, comparative efficacy, and toxicity. *Rheumatol Int*. 2012; 32(6):1491–1502.

11. Griffin H, Miller B. OxyContin and a regulation deficiency of the pharmaceutical industry: rethinking state-corporate crime. *Crit Criminol*. 2011; 19(3):213–226.

12. US Department of Justice. Biopharmaceutical company, Cephalon, to pay \$425 million & enter plea to resolve allegations of off-label marketing. Available at: <https://www.justice.gov/archive/opa/pr/2008/September/08-civ-860.html>. Accessed August 11, 2017.

13. US Attorney’s Office District of Massachusetts. Pharmaceutical executives charged in racketeering scheme. Available at: <https://www.justice.gov/usao-ma/pr/pharmaceutical-executives-charged-racketeering-scheme>. Accessed August 11, 2017.

14. Hadland SE, Krieger MS, Marshall BDL. Industry payments to physicians for opioid products, 2013–2015. *Am J Public Health*. 2017;107(9):1493–1495.

15. Becker WC, Fiellin DA. Abuse-deterrent opioid formulations—putting the potential benefits into perspective. *N Engl J Med*. 2017;376(22):2103–2105.

16. Wesson D. Prescription drug abuse, fault-finding, and responsibility. In: Wilford B, ed. *Balancing the Response to Prescription Drug Abuse*. Chicago, IL: American Medical Association; 1990.

17. Davis CS, Carr DH. Self-regulating profession? Administrative discipline of “pill mill” physicians in Florida. *Subst Abuse*. 2017;38(3):265–268.

18. Unick GJ, Rosenblum D, Mars S, Ciccarone D. Intertwined epidemics: national demographic trends in hospitalizations for heroin- and opioid-related overdoses, 1993–2009. *PLoS One*. 2013; 8(2):e54496.

19. Centers for Disease Control and Prevention. Increases in heroin overdose deaths—28 states, 2010 to 2012. *MMWR Morb Mortal Wkly Rep*. 2014;63(39):849–854.

20. Mars SG, Bourgeois P, Karandinos G, Montero F, Ciccarone D. “Every ‘never’ I ever said came true”: transitions from opioid pills to heroin injecting. *Int J Drug Policy*. 2014;25(2):257–266.

21. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med*. 2016;374(2):154–163.

22. Knight KR, Kushel M, Chang JS, et al. Opioid pharmacovigilance: a clinical-social history of the changes in opioid prescribing for patients with co-occurring

chronic non-cancer pain and substance use. *Soc Sci Med*. 2017;186:87–95.

23. Ciccarone D. Fentanyl in the US heroin supply: a rapidly changing risk environment. *Int J Drug Policy*. 2017;46:107–111.

24. Beletsky L, Davis CS. Today’s fentanyl crisis: prohibition’s iron law, revisited. *Int J Drug Policy*. 2017;46:156–159.

25. Prekuc MP, Mansky PA, Baumann MH. Misuse of novel synthetic opioids: a deadly new trend. *J Addict Med*. 2017; 11(4):256–265.

26. Katz J. The first count of fentanyl deaths in 2016: up 540% in three years. Available at: <https://www.nytimes.com/interactive/2017/09/02/upshot/fentanyl-drug-overdose-deaths.html>. Accessed October 9, 2017.

27. Cicero TJ, Ellis MS, Kasper ZA. Increased use of heroin as an initiating opioid of abuse. *Addict Behav*. 2017;74:63–66.

28. US Food and Drug Administration. Utilization patterns of opioid analgesics in the pediatric population, background package addendum. Available at: <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/UCM519724.pdf>. Accessed May 25, 2017.

29. Centers for Disease Control and Prevention. About multiple cause of death 1999–2015. Available at: <https://wonder.cdc.gov/mcd-icd10.html>. Accessed May 1, 2017.

30. Kertesz SG. Turning the tide or rip-tide? The changing opioid epidemic. *Subst Abuse*. 2017;38(1):3–8.

31. Dasgupta N, Proescholdbell S, Sanford C, et al. Defining controlled substances overdose: should deaths from substance use disorders and pharmaceutical adverse events be included? *J Clin Toxicol*. 2013; 3(3):1–8.

32. Alexandridis AA, McCort A, Ringwalt CL, et al. A statewide evaluation of seven strategies to reduce opioid overdose in North Carolina. *Inj Prev*. 2017; Epub ahead of print.

33. McCaig L. *Historical Estimates From the Drug Abuse Warning Network, 1978–94. Estimates of Drug-Related Emergency Department Episodes*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 1996.

34. Case A, Deaton A. Mortality and morbidity in the 21st century. Available at: https://www.brookings.edu/wp-content/uploads/2017/03/6_casedeaton.pdf. Accessed May 25, 2017.

35. Stein EM, Gennuso KP, Ugboaja DC, Remington PL. The epidemic of despair among White Americans: trends in the leading causes of premature death, 1999–2015. *Am J Public Health*. 2017;107(10):1541–1547.

36. Monnat SM. Deaths of despair and support for Trump in the 2016 presidential election. Available at: <http://aese.psu.edu/directory/smm67/Election16.pdf>. Accessed May 31, 2017.
37. Masters RK, Tilstra AM, Simon DH. Mortality from suicide, chronic liver disease, and drug poisonings among middle-aged US White men and women, 1980–2013. *Biodemography Soc Biol*. 2017; 63(1):31–37.
38. Rockett IR, Smith GS, Caine ED, et al. Confronting death from drug self-intoxication (DDSI): prevention through a better definition. *Am J Public Health*. 2014;104(12):e49–e55.
39. Ezzati M, Friedman AB, Kulkarni SC, Murray CJ. The reversal of fortunes: trends in county mortality and cross-county mortality disparities in the United States. *PLoS Med*. 2008;5(4):e66. [Erratum in *PLoS Med*. 2008;5(5):e66]
40. Dwyer-Lindgren L, Bertozzi-Villa A, Stubbs RW, et al. US county-level trends in mortality rates for major causes of death, 1980–2014. *JAMA*. 2016;316(22):2385–2401.
41. Ruckert A, Labonté R. Health inequities in the age of austerity: the need for social protection policies. *Soc Sci Med*. 2017;187:306–311.
42. Rigg KK, Monnat SM. Urban vs. rural differences in prescription opioid misuse among adults in the United States: informing region specific drug policies and interventions. *Int J Drug Policy*. 2015; 26(5):484–491.
43. Zoorob MJ, Salemi JL. Bowling alone, dying together: the role of social capital in mitigating the drug overdose epidemic in the United States. *Drug Alcohol Depend*. 2017;173:1–9.
44. Ulirsch JC, Weaver MA, Bortsov AV, et al. No man is an island: living in a disadvantaged neighborhood influences chronic pain development after motor vehicle collision. *Pain*. 2014;155(10):2116–2123.
45. Windle M, Kogan SM, Lee S, et al. Neighborhood × serotonin transporter linked polymorphic region (5-HTTLPR) interactions for substance use from ages 10 to 24 years using a harmonized data set of African American children. *Dev Psychopathol*. 2016;28(2):415–431.
46. Dumont DM, Allen SA, Brockmann BW, Alexander NE, Rich JD. Incarceration, community health, and racial disparities. *J Health Care Poor Underserved*. 2013;24(1):78–88.
47. Beletsky L, LaSalle L, Newman M, Paré JM, Tam JS, Tochka A. Fatal re-entry: legal and programmatic opportunities to curb opioid overdose among individuals newly released from incarceration. *Northeast Univ Law J*. 2015; 7(1):155–215.
48. Yabe Y, Hagiwara Y, Sekiguchi T, et al. Influence of living environment and subjective economic hardship on new-onset of low back pain for survivors of the Great East Japan Earthquake. *J Orthop Sci*. 2017;22(1):43–49.
49. Cerdá M, Tracy M, Galea S. A prospective population based study of changes in alcohol use and binge drinking after a mass traumatic event. *Drug Alcohol Depend*. 2011;115(1–2):1–8.
50. Richman JA, Wislar JS, Flaherty JA, Fendrich M, Rospenda KM. Effects on alcohol use and anxiety of the September 11, 2001, attacks and chronic work stressors: a longitudinal cohort study. *Am J Public Health*. 2004;94(11):2010–2015.
51. Linton SL, Haley DF, Hunter-Jones J, Ross Z, Cooper HLF. Social causation and neighborhood selection underlie associations of neighborhood factors with illicit drug-using social networks and illicit drug use among adults relocated from public housing. *Soc Sci Med*. 2017;185:81–90.
52. Quinn K, Boone L, Scheidell JD, et al. The relationships of childhood trauma and adulthood prescription pain reliever misuse and injection drug use. *Drug Alcohol Depend*. 2016;169:190–198.
53. McLean K. “There’s nothing here”: deindustrialization as risk environment for overdose. *Int J Drug Policy*. 2016;29:19–26.
54. Caetano R, Vaeth PA, Canino G. Family cohesion and pride, drinking and alcohol use disorder in Puerto Rico. *Am J Drug Alcohol Abuse*. 2017;43(1):87–94.
55. Caetano R, Vaeth PA, Mills B, Canino G. Employment status, depression, drinking, and alcohol use disorder in Puerto Rico. *Alcohol Clin Exp Res*. 2016; 40(4):806–815.
56. National Academies of Sciences, Engineering, and Medicine. *Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use*. Washington, DC: National Academies Press; 2017.
57. Lassiter MD. Impossible criminals: the suburban imperatives of America’s war on drugs. *J Am Hist*. 2015;102(1):126–140.
58. Netherland J, Hansen H. White opioids: pharmaceutical race and the war on drugs that wasn’t. *Biosocieties*. 2017; 12(2):217–238.
59. Kneebone E, Allard SW. A nation in overdose peril: pinpointing the most impacted communities and the local gaps in care. Available at: <https://www.brookings.edu/research/pinpointing-opioid-in-most-impacted-communities>. Accessed September 28, 2017.
- 60a. Murphy T, Pokhrel P, Worthington A, Billie H, Sewell M, Bill N. Unintentional injury mortality among American Indians and Alaska Natives in the United States, 1990–2009. *Am J Public Health*. 2014;104(suppl 3):S470–S480.
- 60b. Bechteler SS, Kane-Willis K. White-washed: the African American opioid epidemic. Available at: https://www.thechicagourbanleague.org/cms/lib/IL07000264/Centricity/Domain/1/Whitewashed%20AA%20Opioid%20Crisis%2011-15-17_EMBARGOED_%20FINAL.pdf. Accessed December 14, 2017.
61. Anderson KO, Green CR, Payne R. Racial and ethnic disparities in pain: causes and consequences of unequal care. *J Pain*. 2009;10(12):1187–1204.
62. Green CR, Ndao-Brumblay SK, West B, Washington T. Differences in prescription opioid analgesic availability: comparing minority and white pharmacies across Michigan. *J Pain*. 2005;6(10):689–699.
63. Burgess DJ, Crowley-Matoka M, Phelan S, et al. Patient race and physicians’ decisions to prescribe opioids for chronic low back pain. *Soc Sci Med*. 2008;67(11):1852–1860.
64. Burgess DJ, Phelan S, Workman M, et al. The effect of cognitive load and patient race on physicians’ decisions to prescribe opioids for chronic low back pain: a randomized trial. *Pain Med*. 2014; 15(6):965–974.
65. Diez Roux AV. Despair as a cause of death: more complex than it first appears. *Am J Public Health*. 2017;107(10):1566–1567.
66. Merrill JO, Rhodes LA, Deyo RA, Marlatt GA, Bradley KA. Mutual mistrust in the medical care of drug users: the keys to the “narc” cabinet. *J Gen Intern Med*. 2002;17(5):327–333.
67. Rothstein MA. The opioid crisis and the need for compassion in pain management. *Am J Public Health*. 2017;107(8):1253–1254.
68. Meit M, Heffernan M, Tanenbaum E, Hoffmann T. Appalachian diseases of despair. Available at: https://www.arc.gov/assets/research_reports/AppalachianDiseasesofDespairAugust2017.pdf. Accessed September 1, 2017.
69. Young K, Zur J. Medicaid and the opioid epidemic: enrollment, spending, and the implications of proposed policy changes. Available at: <https://www.kff.org/report-section/medicaid-and-the-opioid-epidemic-enrollment-spending-and-the-implications-of-proposed-policy-changes-issue-brief>. Accessed October 9, 2017.
70. Cassel EJ. The nature of suffering and the goals of medicine. *N Engl J Med*. 1982; 306(11):639–645.
71. Scutchfield FD, Keck CW. Deaths of despair: why? What to do? *Am J Public Health*. 2017;107(10):1564–1565.
72. Neff J, Knight KR, Satterwhite S, Nelson N, Matthews J, Holmes SM. Teaching structure: a qualitative evaluation of a structural competency training for resident physicians. *J Gen Intern Med*. 2017;32(4):430–433.