SUBSTANCE ABUSE
http://dx.doi.org/10.1080/08897077.2016.1261070

Routledge
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COMMENTARY

Turning the tide or riptide? The changing opioid epidemic

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ABSTRACT

The US opioid epidemic has changed profoundly in the last 3 years, in ways that require substantial recalibration of the US policy response. This report summarizes the changing nature of overdose deaths in Jefferson County (home to Birmingham, Alabama) using data updated through June 30, 2016. Heroin and fentanyl have come to dominate an escalating epidemic of lethal opioid overdose, whereas opioids commonly obtained by prescription play a minor role, accounting for no more than 15% of reported deaths in 2015. Such local data, along with similar reports from other localities, augment the insights available from the Centers for Disease Control and Prevention's current overdose summary, which lacks data from 2015–2016 and lacks information regarding fentanyl in particular. The observed changes in the opioid epidemic are particularly remarkable because they have emerged despite sustained reductions in opioid prescribing and sustained reductions in prescription opioid misuse. Among US adults, past-year prescription opioid misuse is at its lowest level since 2002. Among 12th graders it is at its lowest level in 20 years. A credible epidemiologic account of the opioid epidemic is as follows: although opioid prescribing by physicians appears to have unleashed the epidemic prior to 2012, physician prescribing no longer plays a major role in sustaining it. The accelerating pace of the opioid epidemic in 2015–2016 requires a serious reconsideration of governmental policy initiatives that continue to focus on reductions in opioid prescribing. The dominant priority should be the assurance of subsidized access to evidence-based medication-assisted treatment for opioid use disorder. Such treatment is lacking across much of the United States at this time. Further aggressive focus on prescription reduction is likely to obtain diminishing returns while creating significant risks for patients.

KEYWORDS

Opioids; opioid use disorder; overdose; pain; prescriptions; primary care; treatment access

A decade-long rise in opioid overdose[1] and opioid use disorder prevalence[2] has spurred several major initiatives. These include new federal guidelines on prescribing,[3] revised labeling for pharmaceutical opioids,[4] a personal appeal from the US Surgeon General to every US doctor (TurntheTideRx), a renewed federal commitment to prosecution of physicians,[5] a reduction in opioid production,[6] and the Comprehensive Addiction and Recovery Act, which was unfunded for most of 2016.[7] Most of these initiatives reflect a credible view that a decade-long rise in physician prescribing helped cause the current opioid epidemic.[8] What caused the epidemic and what sustains it today, however, are not the same. Neglecting this distinction invites responses that could fail to protect persons most at risk, including both patients with addiction and patients with pain. Opioid prescribing has been in decline since 2012,[9–11] and misuse of prescription pain relievers has fallen in tandem over several years.[12,13] Despite favorable trends in prescribing and painkiller misuse, opioid overdoses have risen precipitously. This perspective article's review of the changing epidemiology of overdose in Jefferson County, Alabama, will help to illustrate this change. The epidemiologic shift raises the question of whether the ongoing public campaign against opioid prescriptions fails to advance more relevant policy solutions crucial to ending an accelerating epidemic, while creating new risks to patients who receive opioids for care of pain.

Shortcomings of national data

Any effort to describe contemporaneous changes in the epidemiology of overdose based on national data from the Centers for Disease Control and Prevention (CDC) is subject to serious limitations. The CDC's most widely cited report on drug overdoses[1] lacks data from 2015–2016, and it relies primarily on the National Vital Statistics System (NVSS) multiple cause of death mortality file. The NVSS relies on International Classification of Diseases 10th revision (ICD-10) codes and thus lacks a unique code for fentanyl (a rising cause of overdose[14]), hindering efforts to explore the potential source of opioids that can be licitly prescribed or illicitly manufactured.[14] The CDC has also acknowledged that its data reflect large jurisdictional inconsistencies in testing and reporting,[15] with many local coroners not testing for fentanyl absent reason to do so.[16] Of note, Alabama was reported by federal agencies to have only low fentanyl activity in the first half of 2014,[17] and no activity in the latter half of 2014.[18]

Jefferson county coroner data: An illustration of the changing trends

Current and publicly available statistics from the Medical Examiner of Jefferson County Alabama, which contains

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Alabama's largest metropolitan area (Birmingham), can help to illustrate recent changes in the opioid epidemic. Jefferson County's Office of the Medical Examiner relies on 3 forensic pathologists. In Alabama, the Coroner or Medical Examiner is mandated to evaluate any unusual or unexpected death (including suspected overdose, accidental death, and suicide).[19] Analytic procedures entail immunoassay-based analysis of urine, bile, or blood, followed by gas chromatography/mass spectrometry (GC-MS) testing in any case where drug overdose is suspected, with a liberal policy toward ordering GC-MS since the 1990s (personal communication from Chief Deputy Coroner Bill Yates, October 12, 2016). The Medical Examiner records findings, notes from the death scene investigation, and its final forensic determinations in a single electronic database. Although most findings for 2015 have been publicly reported,[20] updated summaries are available on request. This summary of public mortality data current through June 30, 2016, was deemed not to constitute human subjects research by the institutional review board of the University of Alabama at Birmingham.

In 2015, there were 220 accidental deaths due to drugs (prescribed and illicit, not including alcohol), including opioids and other prescription medications. Although this number represented a modest decline from 2014, drug overdose deaths more than doubled since 2010 (Figure 1). Between January 1 and June 30, 2016, there were 124 such deaths (which would result in 248 for the year if the trend holds).

Figure 1 shows time trends for specific opioids identified as causal in deaths from 2010 to 2016 (the annualized frequency for 2016 was computed by doubling the figures for the first 6 months of 2016). Because more than one drug can be assigned causality in a single death, an individual death may be reflected in more than one line. Single lines are offered for heroin, for fentanyl, and for a combined category of opioids whose availability usually reflects direct receipt or diversion of a physician prescription (hydrocodone, oxycodone, morphine, tramadol, methadone, hydromorphone). Since it is not known whether decedents obtained these drugs through direct or diverted prescription (or pharmacy diversion), the latter category is titled "drugs commonly obtained through prescription."

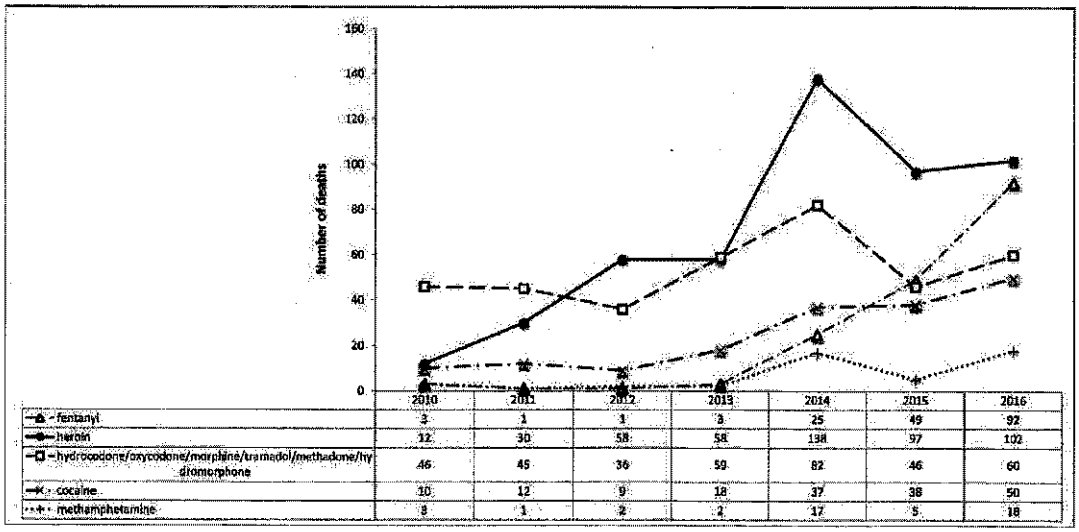
As shown in Figure 1, fentanyl has become a common cause of overdose, rising from 3 deaths in 2013 to 46 for the first half of 2016 (92 projected). Heroin deaths rose to a peak of 138 in 2014 and declined to 97 in 2015. There were 8 deaths in which both fentanyl and heroin were causal, rising to 17 for the first 6 months of 2016.

Additional information from the Medical Examiner suggests an illicit source for the fentanyl flagged in these deaths. In death scene notes, the word "syringe" appeared in 21 (46%) of 46 fentanyl deaths from 2016, whereas reference to a "patch" (the most commonly prescribed form of fentanyl) appeared once. Discussion with a member of the County Sheriff's office revealed that when undercover officers purchased product labeled "heroin," the purchased product often contained fentanyl, without any detectable heroin.

Drugs commonly obtained through prescription have declined since their peak in 2014 (Figure 1). Among 30 deaths attributed to these drugs in the first half of 2016, 11 included heroin or fentanyl, leaving just 19 of 124 drug overdose deaths (15% of the total) in which the only identified drugs are ones commonly obtained or redistributed via prescription.

In summary, overdose deaths in Jefferson County reflect an important epidemiologic shift: a rapid 3-year rise in the role of fentanyl as cause of overdose, even though Alabama was not cited by the Drug Enforcement Administration (DEA) as a fentanyl hotspot in 2015.[18] Reports from law enforcement align with a 2016 CDC report that most fentanyl deaths reflect illicit manufacture and not physician prescriptions.[14] Heroin remains a contributor to local opioid overdose deaths. The role played by opioids commonly obtained through prescription, absent concomitant fentanyl and heroin, is on a downward trajectory.

This epidemiologic shift is not unique to Jefferson County. Data from Cuyahoga County (Cleveland) show that total drug overdoses as of August 31, 2016 (n = 494), exceeded the



	2010	2011	2012	2013	2014	2015	2016
fentanyl	3	1	1	3	25	49	92
heroin	32	30	58	58	138	97	102
hydrocodone/oxycodone/morphine/tramadol/methadone/hydromorphone	46	45	36	59	82	46	60
cocaine	10	12	9	18	37	38	50
methamphetamine	3	1	2	2	17	5	18

Figure 1. Drugs assigned causal role in overdose deaths (Jefferson County, Alabama, 2010–2016, annualized) based on a record review of Medical Examiner cases in Jefferson County, Alabama, 2010–2016. More than one drug may be assigned causality in a given death, and therefore a single death may contribute information in more than one line in this graph.

yearlong total of 350 for 2015.[21] Among these, fentanyl was found in 424 (rising from 92 in 2015), heroin in 350 (rising from 184 in 2015), and commonly prescribed opioids in 82 (it was 80 in 2015). In Massachusetts, a 3-year analysis of overdose found that only 8.3% of decedents had a prescribed opioid at the time of their death, and 85% died due to either heroin or fentanyl.[22] The changing epidemiology of overdose has implications for policy.

Revising today's opioid narrative

The first implication concerns the dominant public narrative accounting for opioid misuse. The historical account of how today's opioid epidemic acquired its present vigor[8] should be distinguished from an explanation of the factors sustaining it in 2016.

The origination of today's epidemic has been attributed to the actions of prescribers and pharmaceutical companies that have been profiled as naive,[23] unscientific,[24] or venal.[25] A decade-long increase in opioid prescribing (2000–2010) coincided with a quadrupling of overdose mortality.[26] Clearly, rising opioid misuse was partly dependent on physician-mediated supply increases. The causal association is not entirely straightforward. There is poor geographic correlation between opioid prescribing and overdose prevalence,[27] and the CDC reported that de novo addiction among patients receiving chronic opioids for pain is infrequent at lower doses, affecting 0.7% of persons receiving 36 milligrams morphine equivalent (MME), rising to 6.1% among persons receiving 120 MME.[3] Similarly, most persons treated for prescription opioid use disorder do not have any chronic pain diagnosis.[28] These facts confound a dominant narrative of an inexorable, single-arrow trajectory from pain care to addiction. That narrative, relevant as it can be (especially in young adults), aligns poorly with the last 25 years of addiction science in which social environment, genetics, and age combine to determine who is at risk for developing addiction and whether addiction remits.[29,30]

The origination narrative from prescription to addiction has become less relevant for policy today. Opioid prescribing by physicians leveled off from 2010 to 2011, and has fallen since 2012.[10,17] Alabama data show that by 2015, hydrocodone prescriptions had dropped by 35%, in parallel with other opioids. The US Department of Veterans Affairs has reduced the number of veterans receiving opioids for chronic pain by 30% since 2013.[11] The pullback among prescribers would be expected to choke the market for redistributed pain medications. Confirming that expectation, the federal government reports a continuous decline in seizures of commonly prescribed opioids since 2011.[31] Similarly, federal data show that the percentage of adults with past-year misuse of prescription pain relievers in 2014 was at its lowest since 2002 (at 3.8%).[12] A federal survey of youth shows that the percentage of 12th graders with past-year nonmedical opioid use fell from 9.2% in 2009 to 5.4% in 2015, the lowest figure in the last 20 years.[13]

Despite this multiyear continuous reduction in opioid prescribing, there has been a continuous escalation in opioid mortality, a surprising pattern. Overdose reports from Jefferson County (whose embrace of fentanyl remained off the CDC's radar in a late-2015 report[18]), along with similar reports from across the country,[21,22,32] indicate that the force accelerating today's epidemic is a booming market for potent heroin and fentanyl and its analogs (e.g., carfentanil), with most fentanyl being of illicit origin.[14] To the extent that federal policy continues to prioritize reducing opioid availability for adults with chronic pain over other policy responses, it will achieve diminishing returns in terms of saving lives.

Policy implications

The first implication of this epidemiologic shift is the imperative for a revised policy response. As has been noted repeatedly, what remains lacking across much of the United States is access to evidence-based, medication-assisted treatment for opioid use disorder.[33,34] Medication-based treatments such as methadone and buprenorphine have proven effective,[35] and may save lives.[36] While physicians have pulled back from prescribing, treatment access has progressed in limited fashion. The state of Alabama has only one publicly funded program for medication-assisted treatment for opioid use disorder (OUD). Jefferson County has no maintenance therapy options for persons who cannot afford charges of $14 to $16 daily at oversubscribed clinics, or more in private offices.

Although one could hope that federal authorities such as the Surgeon General, the CDC, the Congress, and the Office of National Drug Control Policy would race to address a devastating treatment chasm with public fanfare, such efforts have been subtle at best. In Jefferson County, the leading advocates are a committee of volunteers led by a dean from a school of public health, a United States Attorney, and a county health official. Resources are scarce. The US Substance Abuse and Mental Health Services Administration (SAMHSA), which in 2016 provided $1.86 billion dollars in grants for addiction treatment (this figure has failed to keep pace with inflation since 2009), shifted its language to "encourage" states to promote medication-assisted treatment. However, its resources do not typically cover medication or prescriber costs.[37] SAMHSA's 2016 Targeted Capacity Expansion funding opportunity to support medication-assisted treatment allocated $11 million to 23 states, excluding Alabama.[38] As of this writing, Congress has passed but failed to adequately fund the Comprehensive Addiction Recovery Act, which promised $1.1 billion in additional treatment support.[7] If the goal is to prevent death, then this gap requires more serious attention.

Implications for clinical care

A final implication of this epidemiologic shift concerns the appropriate message for physicians and patients where opioid prescription is under consideration. The logic of the CDC guideline demands a calculus of risk and benefit that can be difficult in practice.[3] That calculus resembles the logic physicians apply to many other clinical management challenges in which uncertainty exists. Two patient populations currently receiving prescribed opioids are particularly vulnerable.

Some patients have a longstanding history of receiving opioids and give every indication to their care team of clinical and functional stability. The public press is replete with stories of involuntary tapering of these stable patients by doctors who

anticipate regulatory or administrative problems if they fail to do so.[39–41] Patients and their advocates report that the consequences sometimes include loss of function and suicide.[42] The CDC guideline reported that data to support such involuntary tapers is lacking, and it did not endorse them. If even a small number of involuntarily tapered but otherwise stable patients proceed to the increasingly lethal illicit market[43] or commit suicide,[44] the mortal risks could outweigh the overdose reduction benefit, since the absolute overdose risk remains very low in large retrospective studies of pain patients.[45] particularly at the dose range most common in the United States (<50 MME).[46,47] These considerations need not discourage discussion of voluntary taper in light of opioids' modest benefits, potential harms, and potential for benefit after discontinuation.[24,47] However, they remind us that causal associations are complex. The situation demands careful, individualized clinical decision-making, a stance endorsed by the CDC guideline, even when publicity for that guideline struck a contradictory note.[48]

In more cartoonish form (Figure 2), the situation faced by prescribing clinicians is as follows. A clinician cares for person A, who has received opioids at a given dose for a long time. Person A reports benefit and appears to function well. Should we trust that the involuntary taper or discontinuation of person A's opioid prescription will serve to protect person B, a young adult whose drug career began with marijuana and alcohol, proceeded to diverted oxycodone pills, and now consists predominantly of injected heroin and fentanyl? Ought person A have any say in this? Despite the CDC guideline's recommendation that decisions be individually tailored, many doctors have heard and acted upon a generalized message of discouragement in headlines driven by the CDC's press briefings,[48] in the DEA's plan to restrict opioid production by 25%,[6] and in the actions and statements of politicians and policymakers, many of whose statements presume a linear association between care of pain and the current overdose epidemic, despite the aforementioned complexities.

The above analysis of person A is not offered to defend opioids per se, but to uphold the individualized decision-making now jeopardized for many patients speaking out on their own behalf.[40,49] The risks of opioids are quantifiable,[3,45] and their durability of benefit debatable. As with every alternative treatment for chronic pain, opioids' mean benefit is low to moderate, not large.[50,51] That statistical mean, however, reflects an underlying diversity: some patients derive substantial benefit, others none, and patients need multiple options. Individualized, patient-centered decision-making should remain our watchword.[3]

The clinician's dilemma acquires a more problematic contour for patients prescribed opioids who show no convincing evidence of clinical benefit and whose clinical symptoms suggest an opioid use disorder. This population accounts for 3% to 26% of patients in primary care who receive chronic opioids.[3] Termination of the prescribed opioid and referral to evidence-based addiction treatment seems the obvious step. But what if evidence-based treatment with medication is wholly

Figure 2. Care of patients receiving opioids for pain is increasingly subject to change based on pressures unrelated to an individualized assessment of each patient's well-being. Illustration by Lissa Mathis.

inaccessible, as is the case in large sections of United States for persons of limited means? There are ten states in which Medicaid covers less than 10% of buprenorphine prescription costs, mostly in the South.[52] Discontinuation of prescribed opioids, coupled with encouragement to seek an inaccessible treatment, frees the physician from risk of prosecution or sanction. Inevitably, some patients so discharged will die from drugs they purchase on an increasingly lethal illicit market.[43] At that point, an assertion of "clean hands" (Matthew 27:24)[53] by physicians, regulatory authorities, or the federal government seems facile.

The changing epidemiology of opioid overdose in 2016 offers no easy resolution to such difficult challenges. But it suggests that a relentless focus on physician prescribing for pain has become less relevant to correcting the forces behind a wave of deaths in 2016. Federal efforts to "turn the tide" risk becoming a riptide for patients, physicians, and communities where access to evidence-based treatment remains a priority neglected for too long.

Acknowledgments

The author gratefully acknowledges summaries provided by Bill Yates, Chief Deputy Coroner of the Jefferson County Coroner/Medical Examiners' Office. He also thanks Dr. Saul Weiner for critical review of the manuscript. The author declares that he has no conflicts of interest. Views presented in this article are solely those of the author and do not represent positions or views of the US Department of Veterans Affairs, the State of Alabama, or the Jefferson County Coroner/Medical Examiners' Office. Dr. Kertesz serves on the Treatment Access Subcommittee of the collaborative group mentioned in this article (www.knowdope.org).

Funding

No external funding was received in support of this article.

Author contributions

Dr. Kertesz conceived of this work and authored it. He obtained information from public agencies (Jefferson County Coroner/Medical Examiner and the Alabama Board of Medical Examiners) but did not collect or analyze data for this article.

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