

Estimating the Actual Death Rate Caused by Prescription Opioid Medication and Illicit Fentanyl

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Introduction

The U.S. is said to be suffering from a crisis in deaths from opioid overdoses, prompting legislative and other efforts to clamp down on physician prescribing of these drugs. This article is an effort to identify the causes of these deaths, using data from the National Institute on Drug Abuse (NIDA)¹ through 2015, and the Wonder database compiled by the Centers for Disease Control and Prevention (CDC).²

NIDA publishes actual numbers through 2015, but as of Feb 24, 2018, its data had not been updated. The CDC Wonder database was used to estimate the total number of prescription opioid deaths from 2014 to 2016.

NIDA uses the International Classification of Diseases, 10th Revision, (ICD-10 codes) to determine the extent of opioid drug use in the United States. It has made specific assumptions in order to fit entire ICD-10 codes into specific categories. The number of deaths designated by a particular ICD-10 code includes deaths due to both prescription medication and illicit drugs.

This article looks at the ICD-10 codes used by NIDA and CDC with reference to overdose deaths. The causes of death include: unintentional drug poisoning (X40-X44), suicide drug poisoning (X60-X64), homicide drug poisoning (X85), and drug poisoning of undetermined intent (Y10-Y14). ICD-10 codes for all prescription drugs include: T36-T39, T40.2-T40.4, T41-T43.5, and T43.8-T50.8. ICD-10 codes for prescription opioid pain relievers include: T40.2, T40.3, and T40.4. Table 1 presents the codes for various drugs.

Table 1. Drugs and ICD-10 Codes

Drug Category	ICD-10 Code	Drugs
Natural and semi-synthetic opioid analgesics (aka "other opioids")	T40.2	Morphine, Oxycodone, Hydrocodone, Hydromorphone
Methadone	T40.3	Methadone
Synthetic opioid analgesics, excluding methadone (aka "Other synthetic narcotics")	T40.4	Fentanyl, Meperidine
Heroin	T40.1	Heroin
Cocaine	T40.5	Cocaine
Other or unspecified narcotic	T40.6	

Methods

A Microsoft Excel data file linked to the Overdose Death Rates page, as revised September 2017, on the NIDA website¹ (click on "view/download supporting data document") was used for actual numbers of overdose deaths from 1999 to 2015.

The CDC Wonder website was used to collect the number

of deaths per year and the age-adjusted rate per 100,000 population deaths per year for the following ICD-10 codes and groups of codes: T40.2-T40.4, T40.4, and [T40.2 or T40.3 and T40.4]. The numbers used by NIDA on its website are all from the CDC Wonder data base.

Results

NIDA released an estimate of 20,000 for synthetic opioid (T40.4) deaths in 2016, a steep increase from approximately 10,000 shown on the same graph for 2015.¹ In the Excel database, T40.4 is included in the line labeled "Prescription Drugs" and also in the line labeled "Opioid Pain Relievers." We now know that the numbers in those two lines for 2014 and 2015 contained deaths due to illicit fentanyl. Using the NIDA definition of prescription opioid pain relievers (T40.2—T40.4), and the 2016 deaths from the CDC Wonder database, there was a 43.6 percent increase in just one year from 22,590 in 2015 to 32,445 in 2016.

The problem with evaluating the CDC Wonder numbers is the T40.4 code. I submitted a query to the CDC Wonder website (click on "contact us"): "Does the ICD-10 code T40.4 (synthetic opioids other than methadone) include prescription medication as well as similar illegal drugs?" The reply was, "ICD-10 code T40.4 classifies deaths due to poisoning by a class of similar synthetic opioid compounds, other than compounds classified by ICD-10 codes T40.2 (Other opioids) or T40.3 (Methadone), with no distinction on whether a compound or formula was obtained or manufactured legally or illegally."

Historically, deaths due to T40.4 have been almost exclusively due to prescription fentanyl. Since 2013, there has been a surge in illicit fentanyl. The CDC's *Morbidity and Mortality Weekly Report* of Aug 26, 2016, covered the increase in illicit fentanyl deaths.³ The graph on page 840 shows the number of fentanyl prescriptions decreasing at the same time that the deaths increased from 3,105 in 2013 to 5,544 in 2014. The increase was due to illicit fentanyl manufactured in China and Mexico, primarily mixed with heroin, and smuggled into the United States. Fentanyl and its analogues are preferred because of their efficacy and the fact that no natural source of an opiate is needed for their manufacture.

A graph of the T40.4 deaths from 2000 to 2016, from CDC Wonder, is shown in Figure 1. (All graphs in the figures below were prepared by the author from numbers in the CDC Wonder data base.) Before 2013, deaths can primarily be attributed to prescription fentanyl. Actual numbers from the CDC Wonder database were used to estimate the total number of prescription opioid deaths from 2014 to 2016. The deaths from prescription opioids from 2014 to 2016 were essentially unchanged, while

deaths from illicit fentanyl over the same time period increased 635 percent (see line 4 in Table 2).

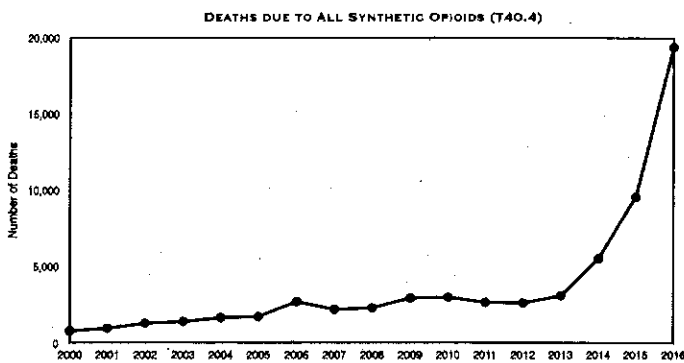


Figure 1. Deaths due to All Synthetic Opioids (T40.4)

The years 2000 to 2013 were considered to be the baseline. This graph was then projected forward to 2016 using a linear regression line (red line in Figure 2) to estimate the baseline prescription fentanyl deaths that occurred during those three years.

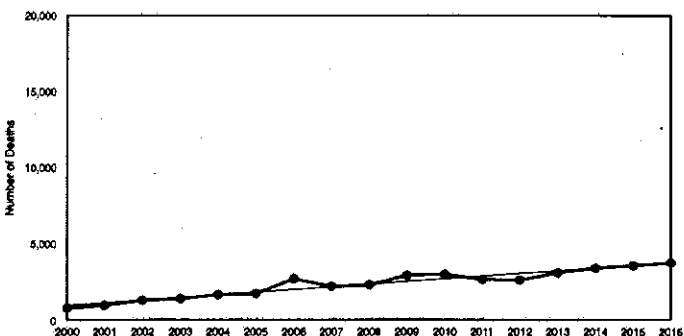


Figure 2. Baseline Deaths from Synthetic Opioids Projected through 2016

The deaths from 2014 to 2016 above the baseline are presumably due to illicit fentanyl. Figure 3 shows an area graph of the baseline prescription fentanyl deaths in blue and the illicit fentanyl deaths in red. The blue area is from Figure 2. The red area is the difference between Figure 1 and Figure 2.

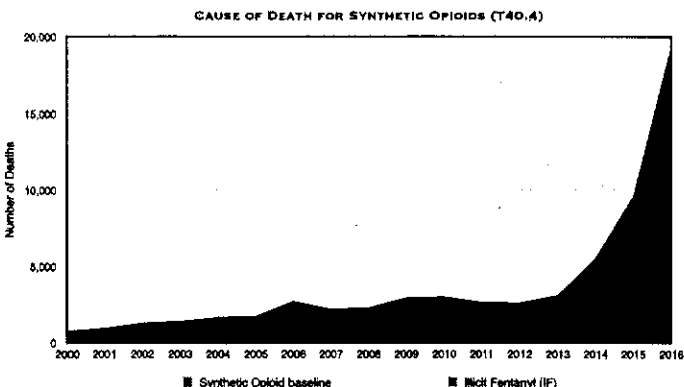


Figure 3. Synthetic Opioid Deaths Attributable to Fentanyl

Could some of those illicit fentanyl deaths also include prescription opioids? Using the CDC Wonder website, the deaths due to the other prescription opioids (T40.2 or T40.3) and T40.4 were extracted by forming a Boolean query, represented by the green line on Figure 4. The blue line is the baseline for the T40.4 deaths from 2000 to 2016. The green line is below the blue line and barely rises to the level of the blue line in 2016. Since the concurrent deaths do not rise above the baseline, they were not included in the estimations. Table 2 shows the step-by-step calculations for 2014 to 2016. Lines 1 and 2 are the numbers from the CDC Wonder database. Line 3 is the baseline calculation to estimate the number of prescription fentanyl deaths. Line 4 is the number of illicit fentanyl deaths, which is line 2 minus line 3. This is how the illicit fentanyl was separated from the prescription fentanyl in the T40.4 category. Line 5 is line 1 minus line 4, which is the total of all prescription opioid deaths.

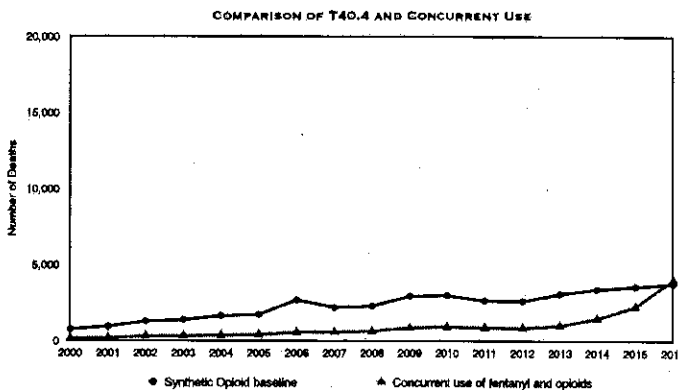


Figure 4. Comparison of Synthetic Opioid Baseline with Concurrent Use of Fentanyl and Opioids

Table 2. Calculation of Deaths Attributable to Illicit Fentanyl and All Prescription Opioids

Classification of Deaths	2014	2015	2016
1 Pain Relievers (Opioids: T40.2 – T40.4)	18,893	22,596	32,455
2 Synthetic Opioids (T40.4)	5,544	9,580	19,413
3 Baseline Synthetic Opioids (T40.4)	3,416	3,592	3,767
4 Illicit Fentanyl (2 - 3)	2,128	5,988	15,646
5 All Prescription Opioids not including illicit fentanyl (1 - 4)	16,765	16,610	16,809

Discussion

NIDA's categorization is inaccurate and misleading. In 2014 and 2015, it counted all of the T40.4 deaths as prescription opioids, but also included them as illicit opioids. It was previously noted that deaths due to prescription opioid pain relievers showed an increase of 43.6 percent in just one year from 2015 to 2016. That large an increase in one year from legal prescriptions does not make sense, particularly as these were being strongly discouraged. From 2007 to 2013 the maximum

annual increase was 6.8 percent, and the average annual increase was 2.6 percent.

Rather than legal prescription drugs, illicit fentanyl is rapidly increasing and becoming the opioid of choice for those who misuse opioids. It will probably surpass all prescription opioid deaths in one or two years. Figure 5 shows the deaths due to all prescription opioid medicine and illicit fentanyl. The area in blue representing all prescription opioid deaths has leveled out. The area in red is illicit fentanyl deaths as estimated in this paper.

As more constraints are placed on legal prescriptions, it appears that market competition is driving opioid misusers from prescription opioid medication to illicit fentanyl. Because of its high potency and the variability of dosing of illegally obtained drugs, illicit fentanyl is far more likely to result in death.

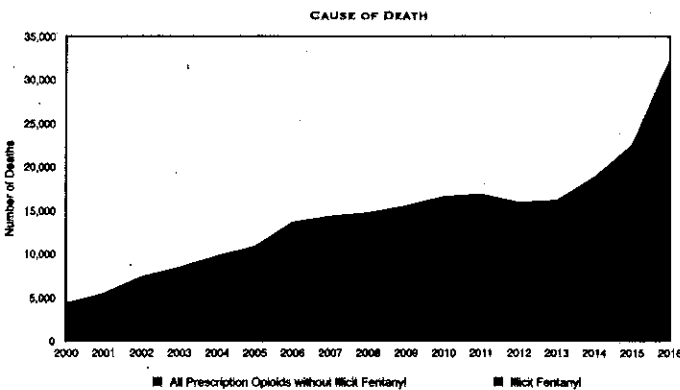


Figure 5. Opioid Overdose Deaths 2000-2016, with and without Illicit Fentanyl

Conclusion

Not all opioids are identical in abuse potential and likely lethality, yet government statistics group causes of death in a way that obscures the importance of identifying specific agents involved in deadly overdoses. Searching the CDC Wonder database reveals that the recent spike in deaths is primarily due to illicit fentanyl. Targeting legal prescriptions is thus unlikely to reduce overdose deaths, but it may increase them by driving more users to illegal sources.

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Disclaimer: Any views expressed in this paper are solely mine and do not necessarily reflect the positions of any business or organization with which I am affiliated.

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1. National Institute on Drug Abuse. Overdose Death Rates. Available at: <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates>. Accessed Feb 7, 2018.
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3. Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths—27 states, 2013–2014. *MMWR* 2016;65:837-843.
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