

Polysubstance Use and Overdose Visualized via Maps: Opioids

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Abstract

Polysubstance (combinations of substances) abuse and overdose deaths now surpass mono-substance abuse and overdose deaths. Several international and governmental organizations such as the WHO (World Health Organization), CDC (Centers for Disease Control and Prevention), several of the Institutes of the NIH (National Institutes of Health), Regulators, and Enforcement Agencies, among others, track and provide a valuable source of statistical information about drug (prescription and illicit) (mis)use and overdose. The information is disseminated free to stakeholders and the general public for use. Although the numeric presentations of the data are helpful and adequate for professionals, the non-expert and the visual learner often find visual representation more clear and more compelling. With this in mind, the aim of this study was to present polysubstance use and overdose using visual maps of the available data. This article considers the opioids.

Keywords

Polysubstance, Use Disorder, Overdose, Maps, Opioids

1. Introduction

There is an increasing trend that drug-overdose deaths involve more than one drug (*i.e.*, polysubstance use and overdose) [1] [2]. Indeed, recent estimates suggest that more than half of drug overdose deaths now result from polysubstance use and/or abuse [3]. The particular danger of polysubstance versus mono-substance use derives from the potential additive, or even greater-than-additive (synergistic), interaction between the pharmacologic/toxicologic effects of the

individual drugs [4]. For example, well-known deleterious interactions are known to occur with combinations of opioids and benzodiazepines [4] [5] [6], methamphetamine [7], cocaine [8], alcohol [9], muscle relaxants [10] [11], and others.

Ritchie & Roser (2018) have provided a series of open-access illustrative and instructive graphs that provide a visual guide to both the extent and the temporal progression of substance use/abuse and overdose deaths [12]. Since the majority of polysubstance overdose deaths involve the opioids, intentionally or unknowingly, we first consider them. All maps herein are reproduced with permission.

2. Opioids

2.1. Molecular Pharmacology

The opioids produce their analgesic (pain-relieving), antidiarrheal, and other beneficial therapeutic effects by binding to (affinity) and activating (intrinsic activity, efficacy) a family of 7-transmembrane G protein-coupled opioid receptor types and subtypes [13]. Signals are transduced by several 2nd-messenger pathways [14], sometimes preferentially in response to “biased” ligands (and drugs) that activate subsets of the transducing biochemical paths [15]. The parent drug, as well as its major metabolite(s), contribute to the overall clinical profile of each opioid.

2.2. Respiratory Depression

The precipitating cause of opioid overdose death is an excess opioid receptor occupation (overstimulation), resulting in opioid-induced respiratory depression [16]. Although more than one mechanism is involved, a primary action is at the pre-Bötzinger and other nuclei located in the brainstem [17]. Due to variations in pharmacokinetic (*i.e.*, absorption, distribution, metabolism, and elimination) and/or pharmacodynamic profiles, each opioid has its unique relative safety. High potency (e.g., fentanyl and analogs) is one factor that decreases the safety margin when opioids (or other drugs) are used/abused.

3. Geographic Opioid Overdose Death Rates

Despite a multiplicity of criteria used to define an opioid-induced or opioid-related overdose, and a multiplicity of measuring tools, some better than others [18], there seems to be no question that death rates due to opioid overdose have risen worldwide, but particularly in the United States. **Figure 1** shows the increase in worldwide death rates from opioid overdoses over the past ≥ 30 years. Opioid overdose death rates have gone down over this time in some countries (**Figure 2**), or at least the reporting has, but the trend is upward, contributed to by the stress and other factors related to the COVID-19 pandemic [19].

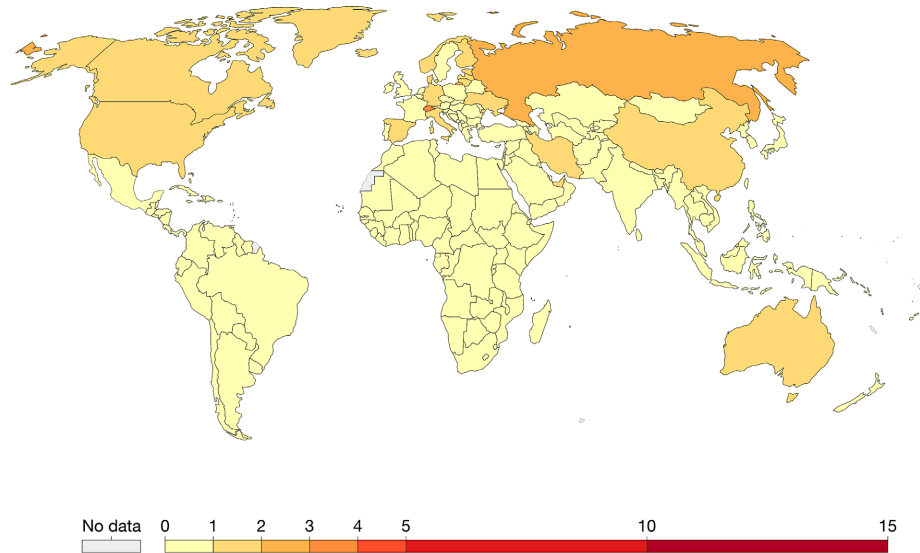
4. Opioid Overdose Death Rates in North America

Over the period 1990 to 2019, the death rates attributed to opioid use in North

America (computed as the number of deaths per 100,000 of the population) rose in relation to Europe and the rest of the world. The largest rate in North America over this time period consistently was for the United States: 1.53/100,000 in 1990 to 13.69/100,000 in 2019 (Figure 3). The rate for Canada also rose sharply during the same period, from 1.13 to 4.67 per 100,000 (Figure 2).

Death rate from opioid overdoses, 1990

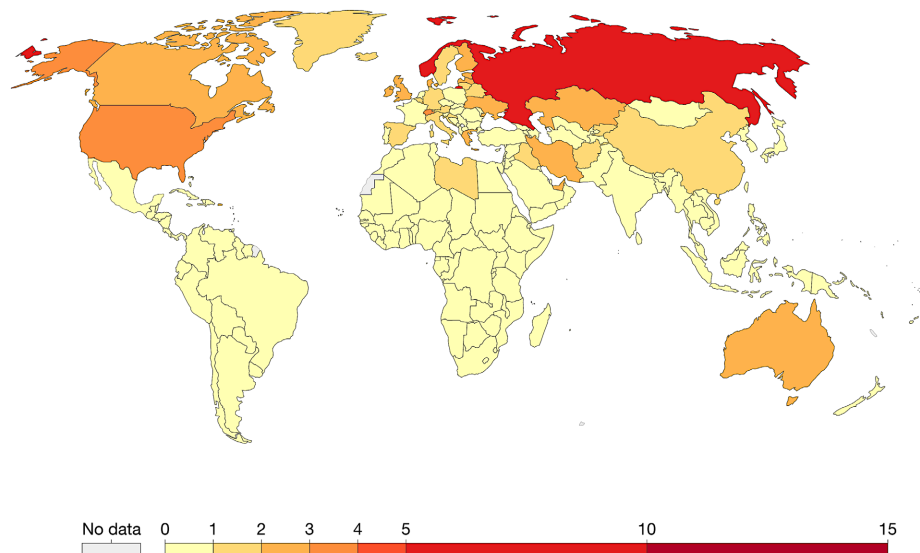
Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Death rate from opioid overdoses, 2000

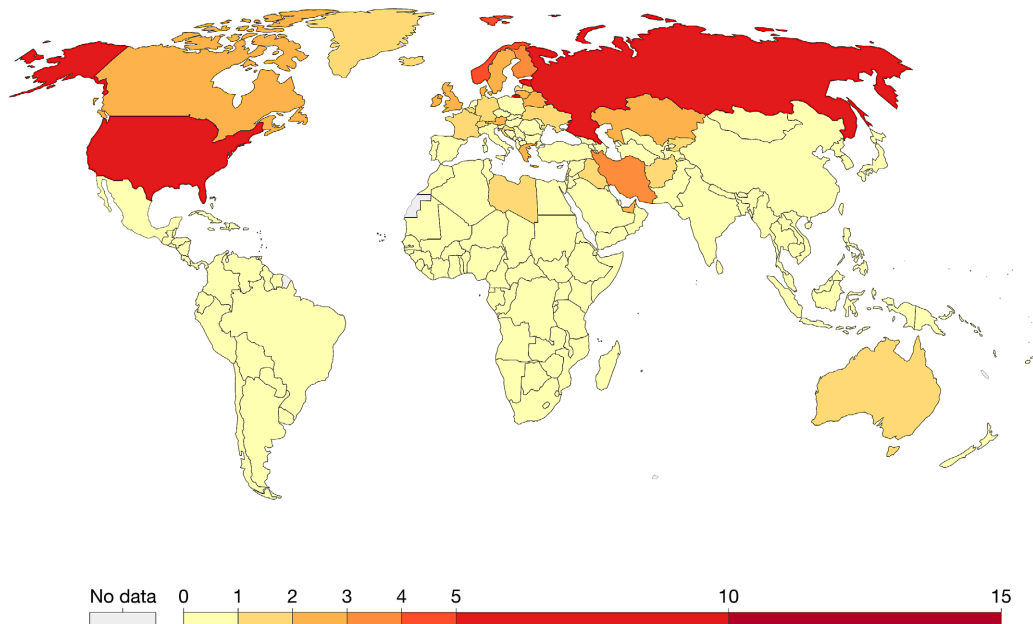
Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Death rate from opioid overdoses, 2010

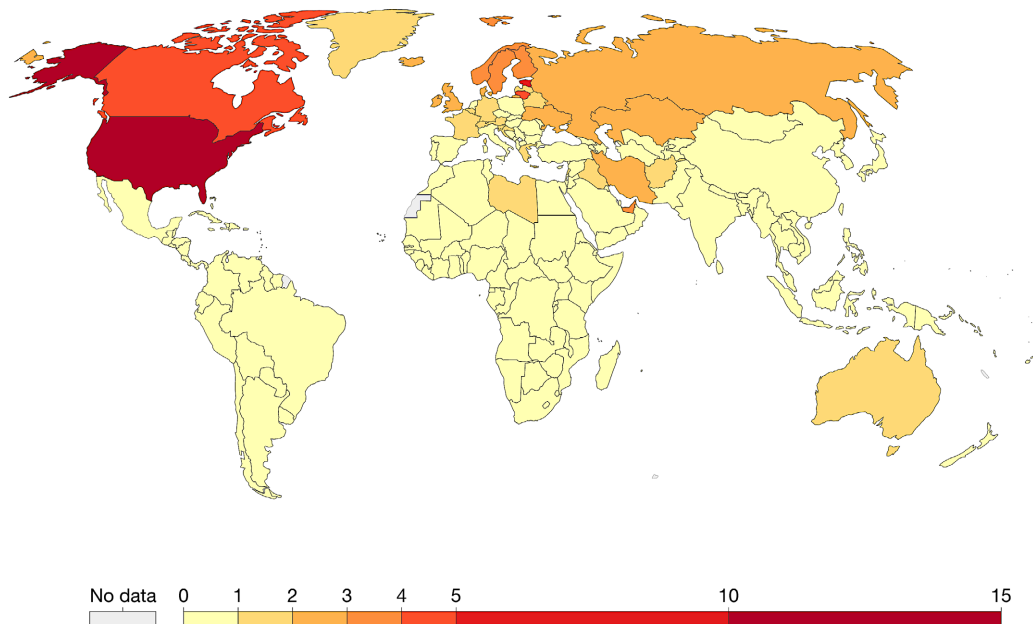
Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Death rate from opioid overdoses, 2019

Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



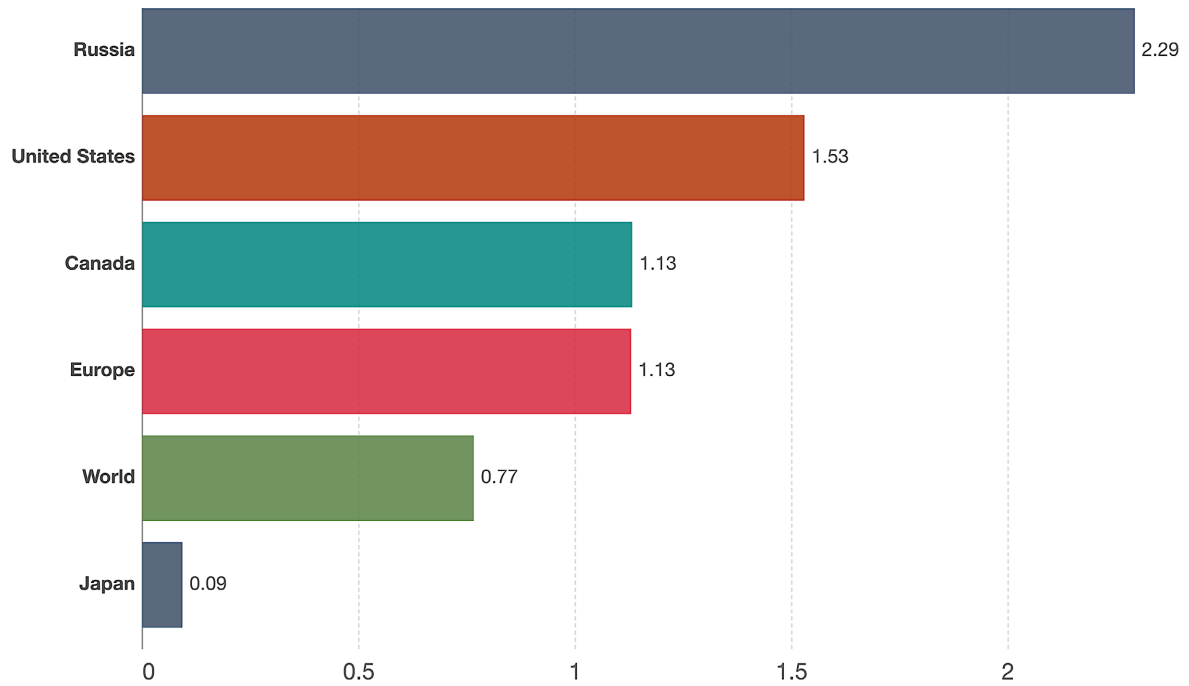
Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Figure 1. Death rates worldwide from opioid overdoses 1990 to 2019.

Death rate from opioid overdoses, 1990

Our World in Data

Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.

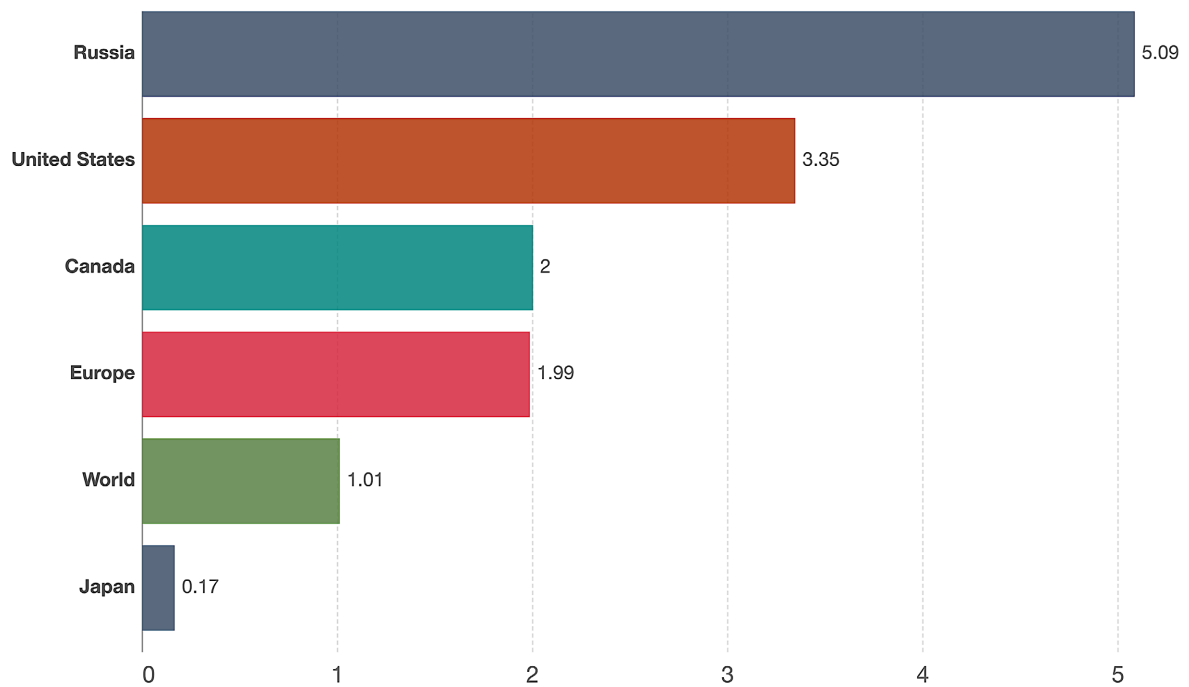


Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Death rate from opioid overdoses, 2000

Our World in Data

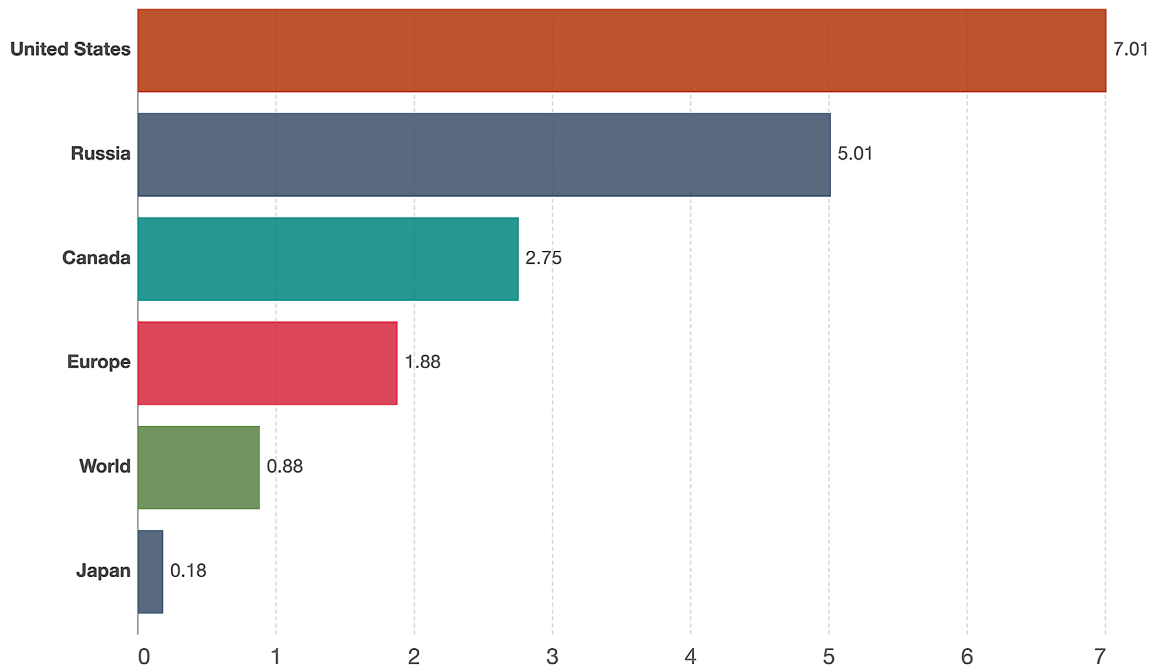
Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Death rate from opioid overdoses, 2010

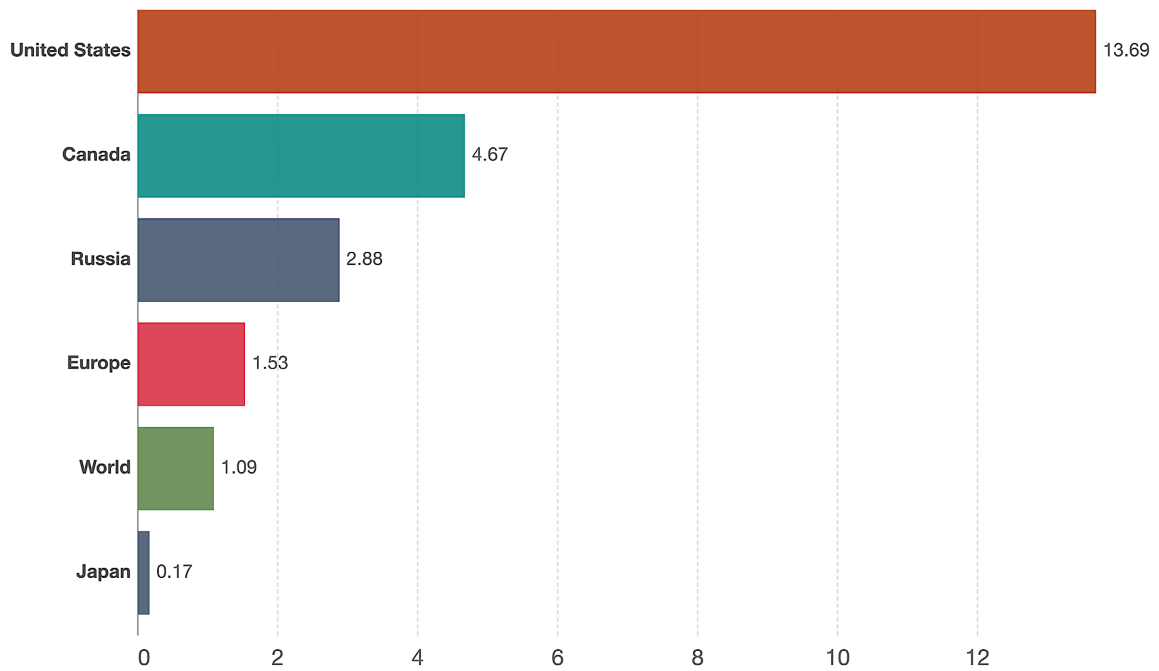
Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Death rate from opioid overdoses, 2019

Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.

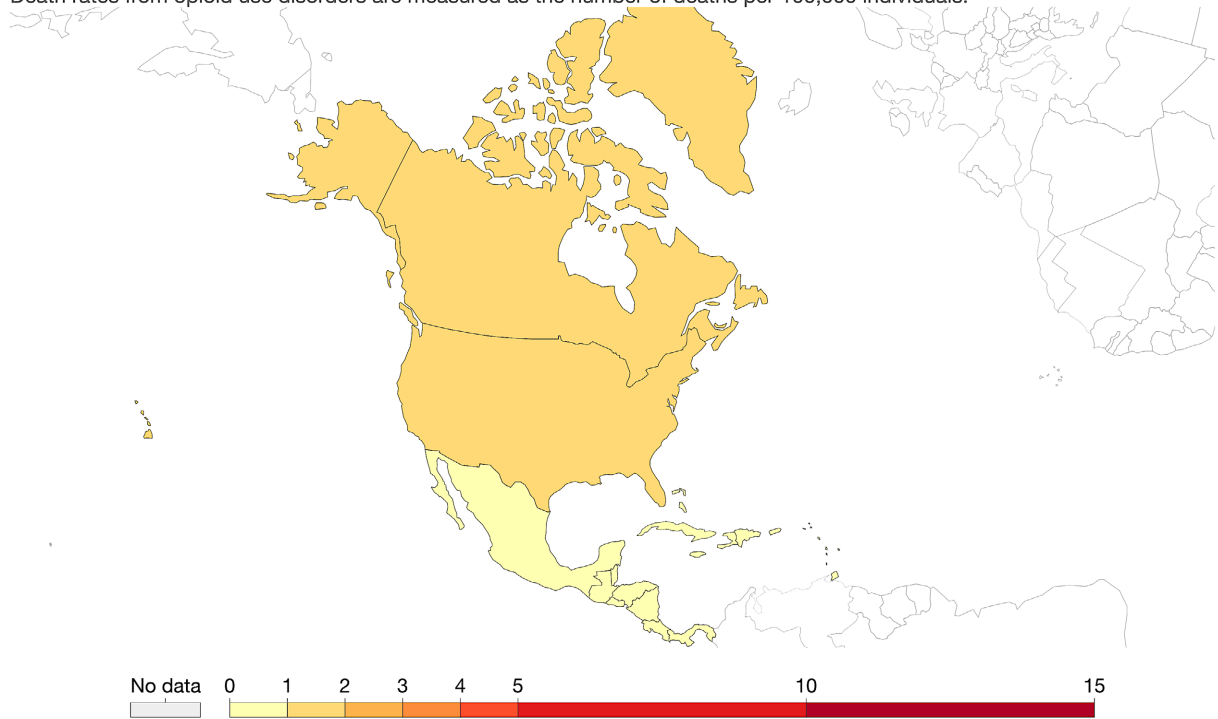


Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

Figure 2. Opioid overdose death rate country comparisons: 1990 to 2019.

Death rate from opioid overdoses, 1990

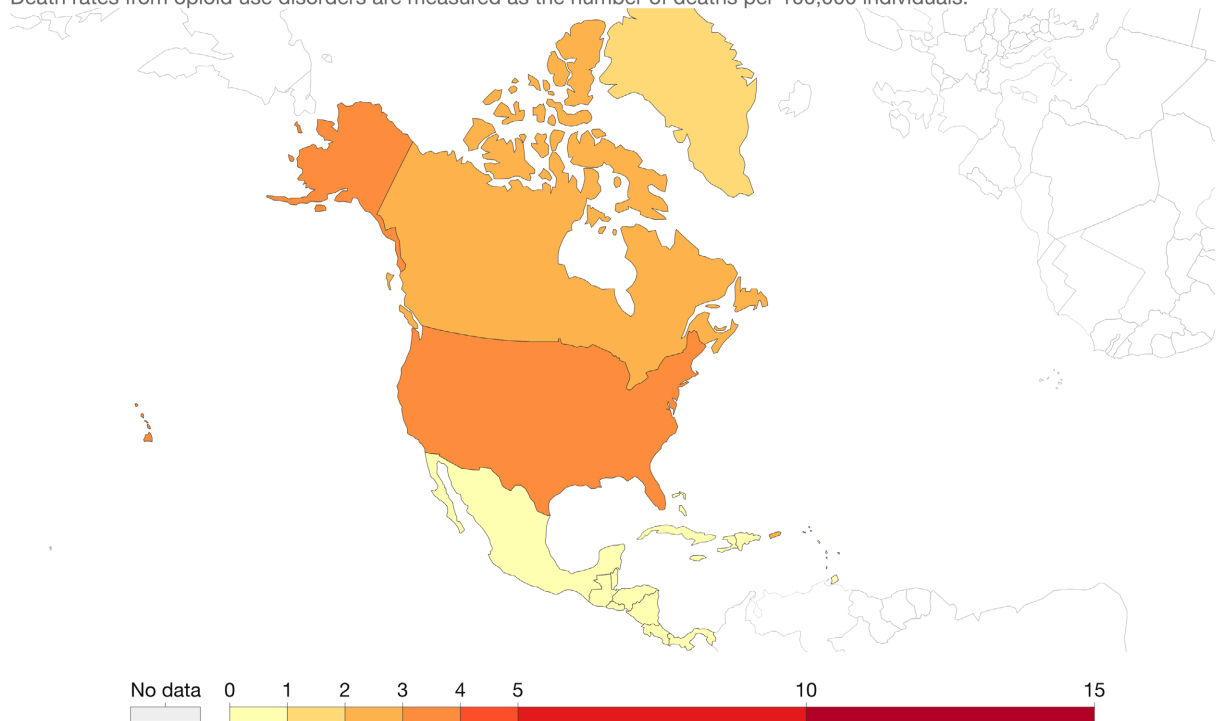
Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Source: IHME, Global Burden of Disease (GBD) to allow comparisons between countries and over time this metric is age-standardized./ • CC BY

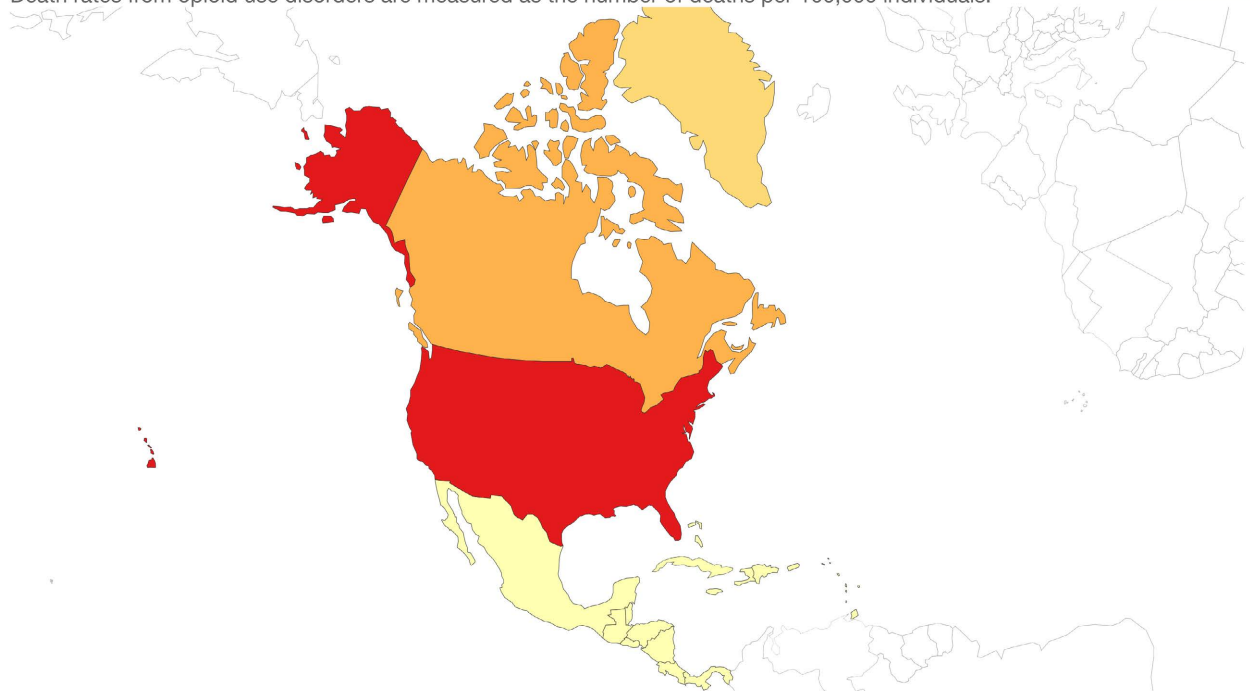
Death rate from opioid overdoses, 2000

Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Death rate from opioid overdoses, 2010

Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.



Death rate from opioid overdoses, 2019

Death rates from opioid use disorders are measured as the number of deaths per 100,000 individuals.

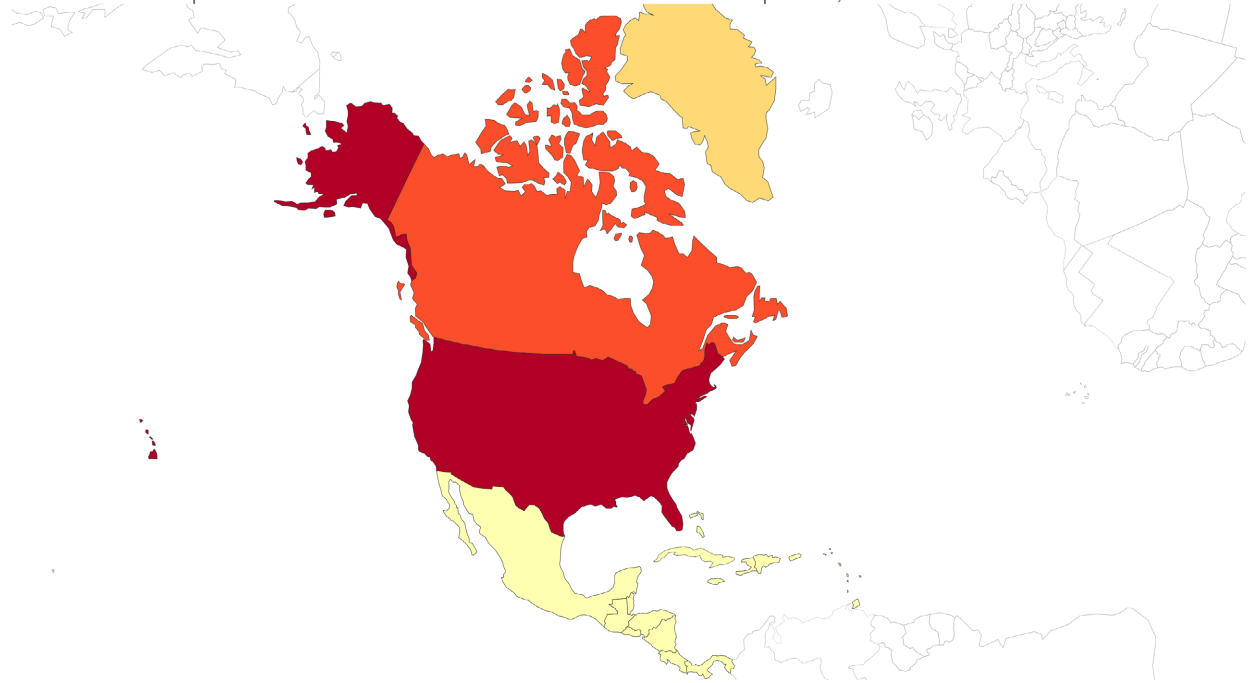


Figure 3. Opioid overdose death rate: North America 1990 to 2019.

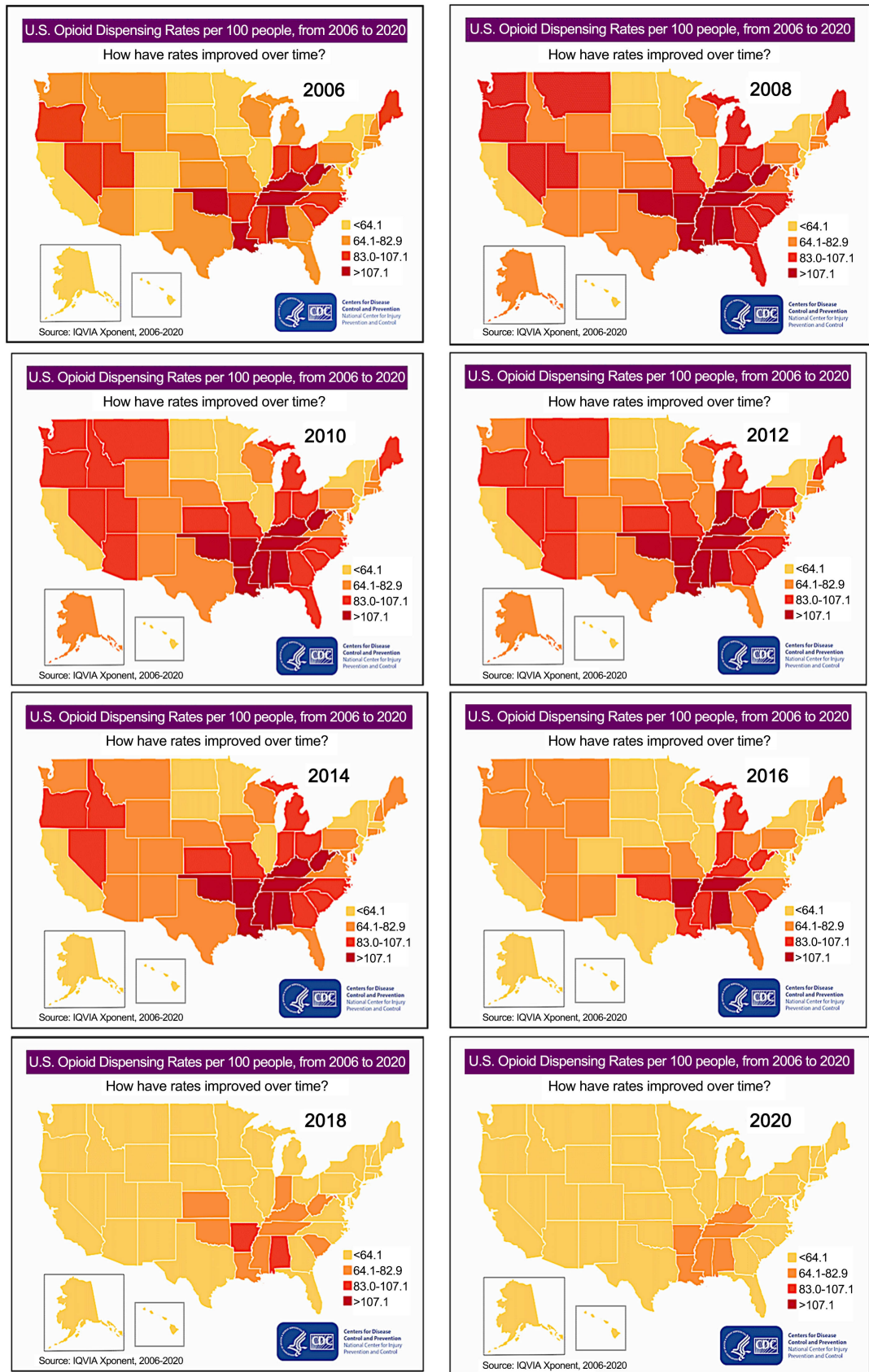


Figure 4. Opioid dispensing rate: United States 2006 to 2020.

5. Possible Explanations

A variety of possible explanations for the increased rate over this time period have been proposed: psychosocial, economic, financial, over-promotion of opioids for pain, the pandemic, and others. One possible explanation can be tested and visualized by reference to the maps: What if prescribing of opioids increased proportionally, or at least increased together with, the increase in opioid overdose deaths. The maps shown in **Figure 4** do not support this conjecture. In fact, dispensing rates in the United States over this period peaked during the period about 2008 to 2012, then actually substantially declined through 2020. This is not the perception or headlines of the news media or litigators [20], but suggests that overzealous sales practices or good-intentioned, but misguided, overprescribing are not the only possible explanations.

Further insight is obtained by reference to the death rates in the United States from cocaine and amphetamine over the same period. Notably, death rates for both classes of drugs increased dramatically over the period [12], suggesting that the opioid-related overdose deaths are not necessarily attributable to something unique about the opioids per se (such as their psychopharmacology or dispensing), but instead something more nuanced, perhaps a response to one or more (or a combination of) other factors (psychosocial, economic, ...?). A popular suggestion has referred to “deaths of despair” [21]. Modern psychology theories are more comprehensive, in which the used drug is just one factor among many [22].

6. Conclusion

The multiplicity of sources providing information about drug overdose deaths can be perplexing, rather than elucidating. Reference to the “maps” supplied in Ritchie & Roser [12] provides an opportunity to visualize at a glance the extent, distribution, and temporal relationship of the problem, and to support, or discount, notions of causality or trends.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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