CDSE Days 2021 / SUNY Buffalo

Computational Approaches to Understanding the USA Drug Overdose Epidemic

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University of Pittsburgh

31 Mar 2021

Conflict of Interest Disclosure

Although I am a full time faculty member at the University of Pittsburgh, I am also President and Co-Founder of Epistemix, Inc, a for-profit start up company the produces and distributes software of agent-based modeling of complex social dynamics. Later in this lecture I will refer to agent based modeling done at the University of Pittsburgh, but the code has been licensed to Epistemix, Inc.

Main objectives of the lecture: To show how computational approaches can lead to better understanding of the USA Drug Overdose Epidemic

1. Epidemiology of drug overdose deaths

2. Age structure of the epidemic

   Drug and demographic structure

3. Forecasting the epidemic trajectory

Another objective of this lecture:

✓ Encourage more effective visual display of epidemiological data and analyses

EDITORIAL

Forecasting the opioid epidemic

Since 2000, almost half a million Americans have died from drug overdoses. This modern plague—largely driven by opioid addiction—degrades health, saps productivity, spawns crime, and devastates families, all at enormous societal cost. How did we get here, and what do we do now?

About 20 years ago, compassionate advocacy for better treatment of chronic pain, combined with aggressive marketing of high-dose opioid formulations, led to a sharp increase in the prescribing of legal opioids by physicians in the United States. An unintended consequence of this well-meaning movement was that millions of Americans became dependent on opioids. Drug cartels seized the opportunity to sell heroin as a cheaper alternative to this ready-made consumer base. As users switched from high-quality pharmaceuticals to street drugs of unreliable composition and quality, deaths mounted. Mortality rates surged further as potent illicit synthetic drugs—such as fentanyl—were mixed in with heroin.

Law enforcement officials have realized that "we can't arrest our way out of the epidemic" and that a new, public health–oriented approach is needed. How can a new approach be designed? Better understanding of the underlying system dynamics may prove critical. Computational models are routinely used by engineers to understand the dynamics of physical systems, and models and simulations are increasingly being used in public health to understand the dynamics of contagious disease epidemics in human populations. Today, every major public health agency has access to a modeling unit that provides policy decision support for epidemics such as HIV/AIDS, influenza, Ebola, and Zika.

The opioid epidemic can be approached as a dynamical system, composed of networks of interacting individuals including nonusers, users, legal prescribers, illicit suppliers, treatment providers, supporters (family and friends), law enforcement officials, and others. Data on the frequency of opioid drug prescribing, illicit drug availability, the natural history of substance use disorder, treatment effectiveness, availability of support services, and other key factors can then be used to construct and parameterize models. Borrowing from methods used to model contagious diseases, these dynamical models can be employed to forecast the likely future trajectory of the opioid epidemic in the population (not a single path, but a range of possible paths as bounded by uncertainty) and then to evaluate—in silico—interventions designed to alter the trajectory. Policy-makers could estimate the likely effectiveness—and cost-effectiveness—of possible public health interventions such as increasing the availability of naloxone (medication used to block the effects of opioids), decreasing prescriptions, expanding treatment, and widening education, as well as concurrent deployment of two or more of these interventions. Computational modeling can also be used to explore synergies between public health and law enforcement.

"...a new, public health–oriented approach is needed."

Increased data openness will be needed. Each country will have its own data access issues. In the United States, overdose deaths are available from public death records, but these are compiled slowly, and are not readily available at detailed geographic specificity. Prescription data can be obtained from commercial vendors and from state monitoring programs, but these are either not publicly available or are available only at exorbitant cost. Illicit drug seizure data are collected, but these are not readily shared outside law enforcement. Self-reported drug use patterns are available from national surveys, but these do not provide regional or local data. Urine drug testing data are collected, but are held as proprietary. Finding creative ways to open up and analyze these and other data sources can lead to valuable insights into the dynamics of the opioid epidemic.

The opioid epidemic is a complex, dynamical process, and it should be approached as such in the development and evaluation of policy. A coordinated national opioid epidemic modeling program could help solve this difficult problem.

–Donald S. Burke

Donald S. Burke is Dean of the Graduate School of Public Health at the University of Pittsburgh, Pittsburgh, Pennsylvania. Email: donburke@pitt.edu

PHOTOS: (INSET) PHANIE/ALAMY STOCK PHOTO; (TOP RIGHT) ALAN ADAMS

10.1126/science.aal2943

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November 4, 2016

RESEARCH

September 21, 2018

RESEARCH ARTICLE

PUBLIC HEALTH

Changing dynamics of the drug overdose epidemic in the United States from 1979 through 2016

Hawre Jalal[1], Jeanine M. Buchanich[2], Mark S. Roberts[1], Lauren C. Balmert[2,4], Kun Zhang[5], Donald S. Burke[3*]

Better understanding of the dynamics of the current U.S. overdose epidemic may aid in the development of more effective prevention and control strategies. We analyzed records of 599,255 deaths from 1979 through 2016 from the National Vital Statistics System in which accidental drug poisoning was identified as the main cause of death. By examining all available data on accidental poisoning deaths back to 1979 and showing that the overall 38-year curve is exponential, we provide evidence that the current wave of opioid overdose deaths (due to prescription opioids, heroin, and fentanyl) may just be the latest manifestation of a more fundamental longer-term process. The 38+ year smooth exponential curve of total U.S. annual accidental drug poisoning deaths is a composite of multiple distinctive subepidemics of different drugs (primarily prescription opioids, heroin, methadone, synthetic opioids, cocaine, and methamphetamine), each with its own specific demographic and geographic characteristics.

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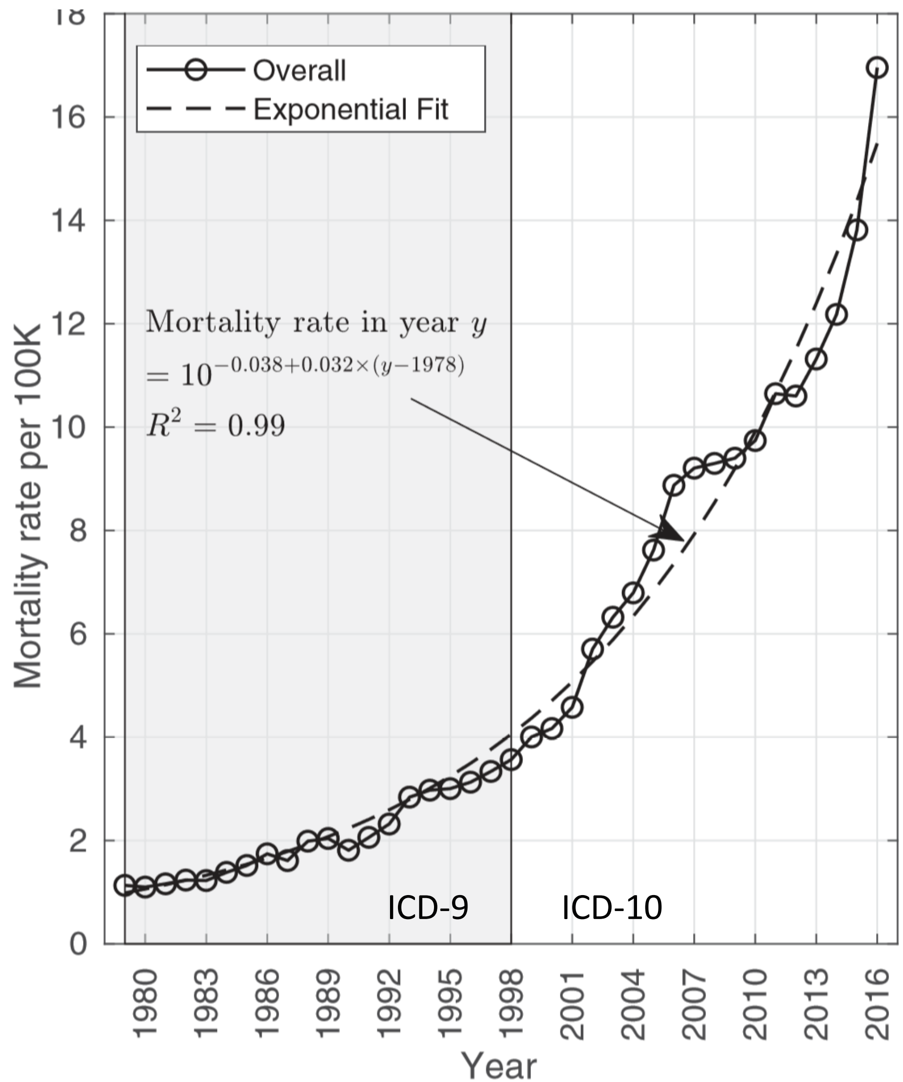
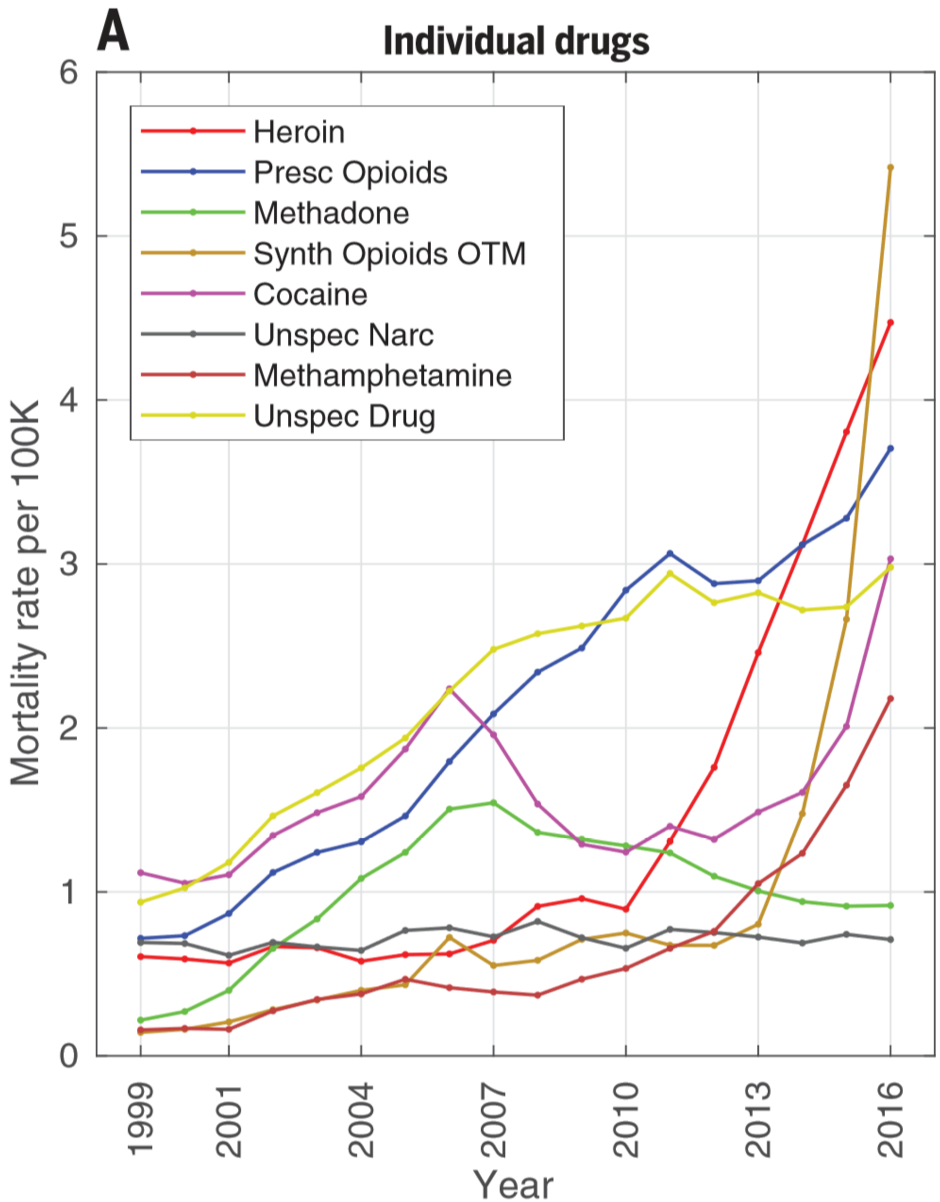
599,255 accidental drug poisoning deaths recorded by the National Vital Statistics System, 1979-2016




A
Individual drugs
Heroin
Presc Opioids
Methadone
Synth Opioids OTM
Cocaine
Unspec Narc
Methamphetamine
Unspec Drug
Mortality rate per 100K
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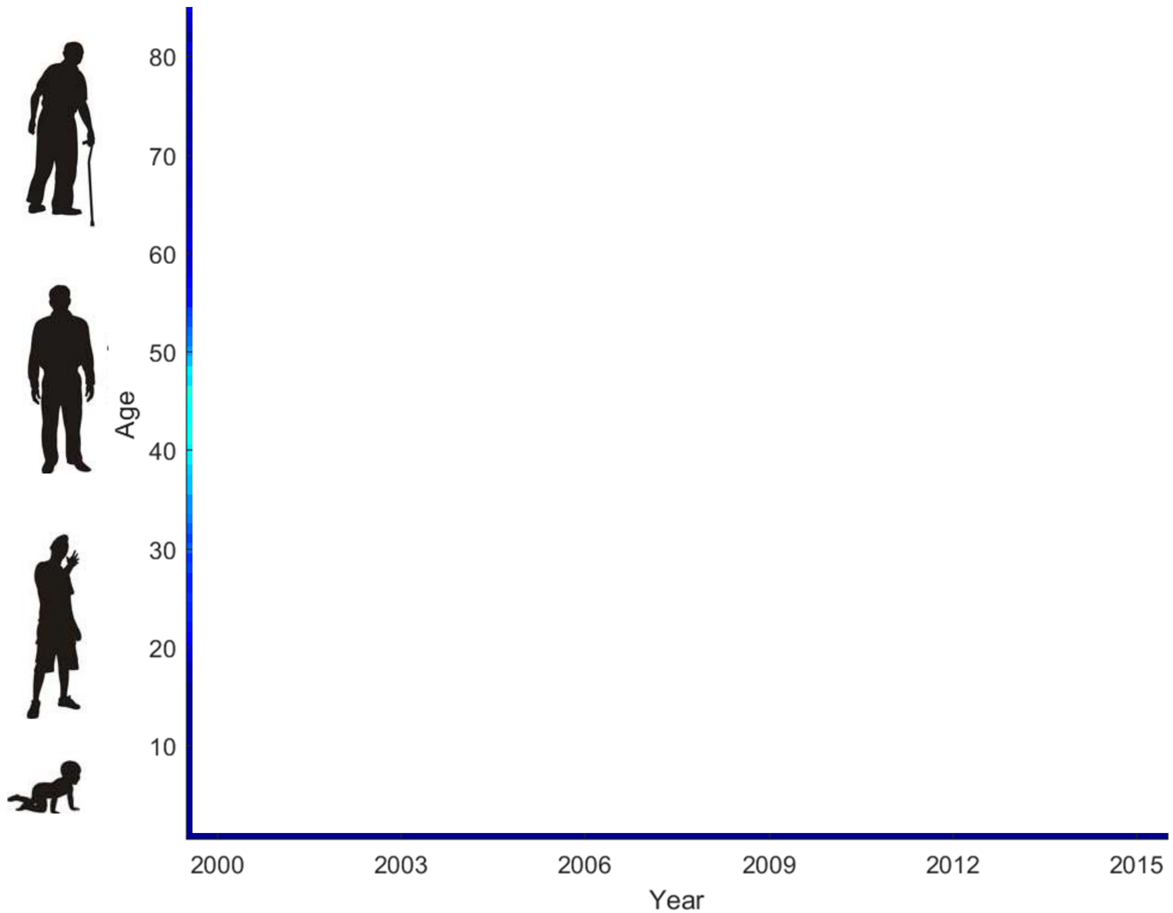
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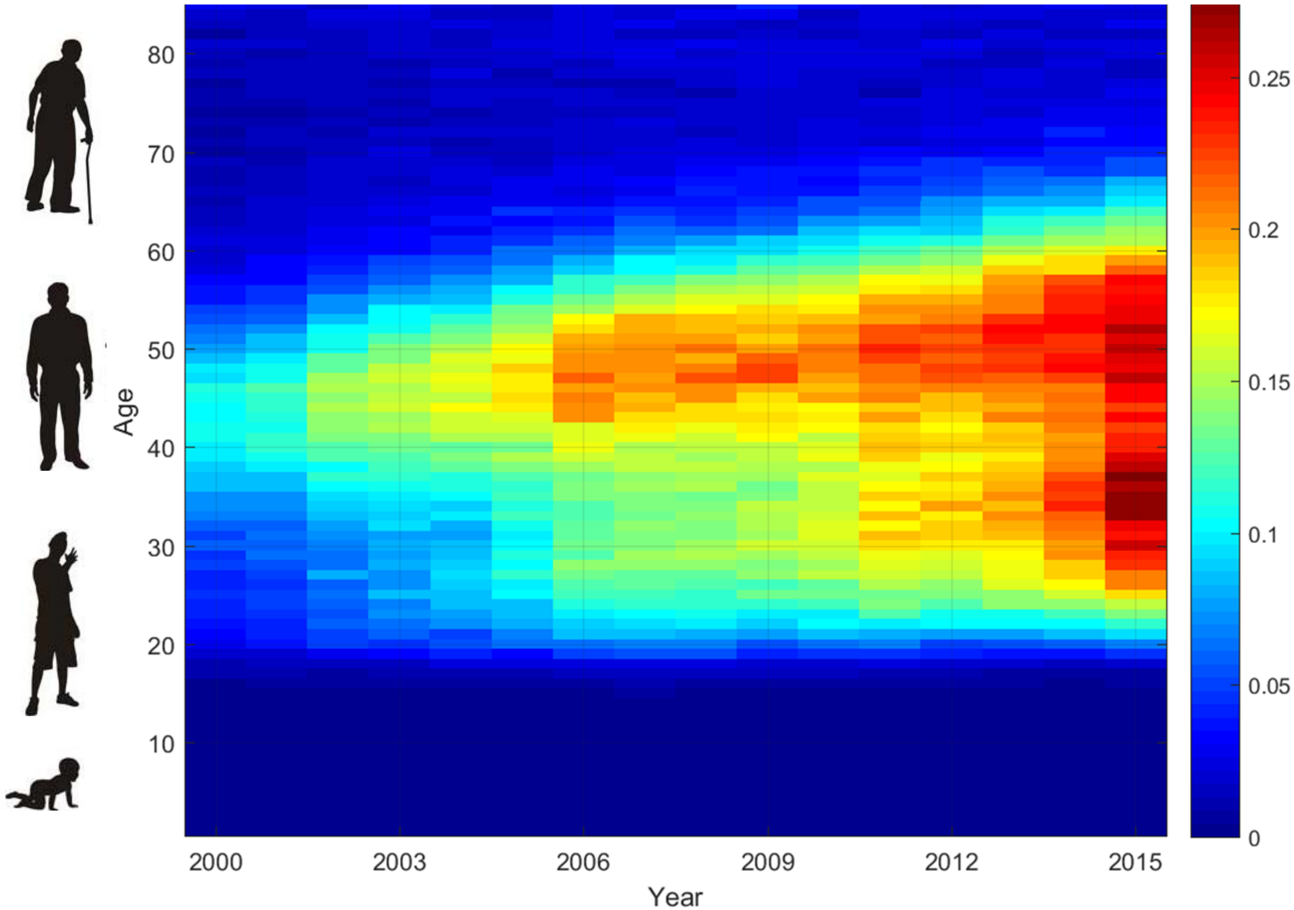

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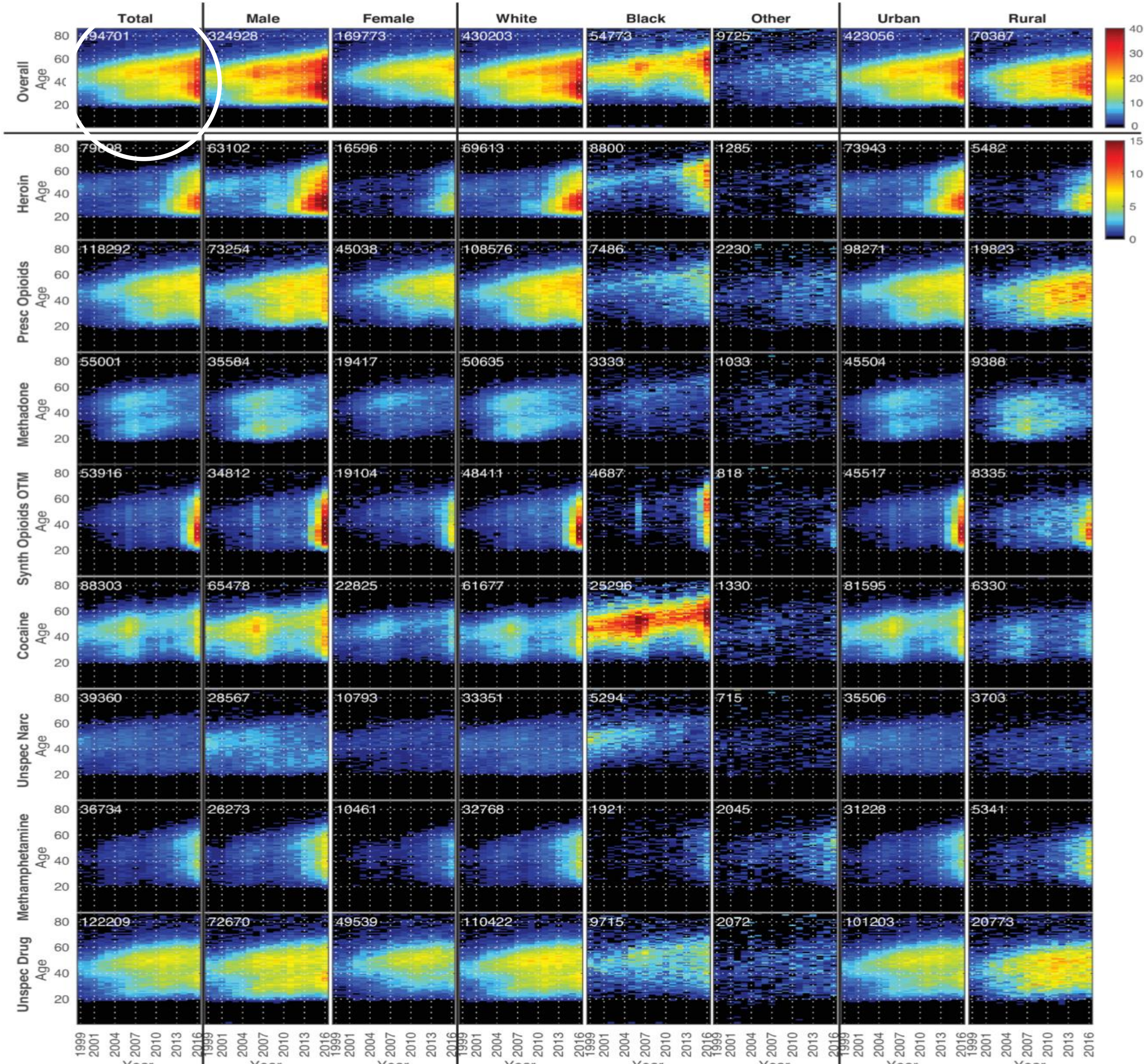

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Other
Urban
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Overall
Heroin
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Age
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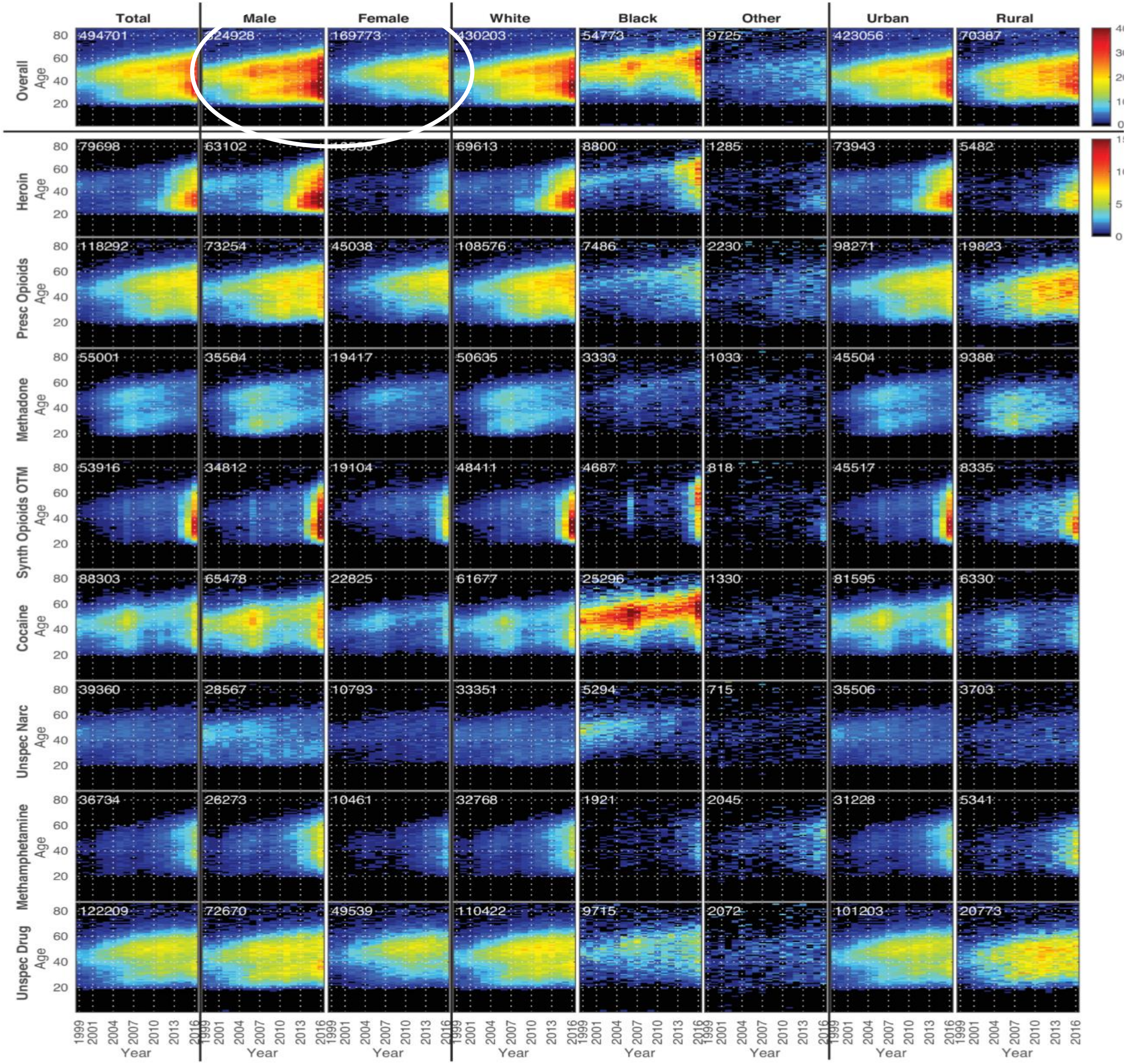

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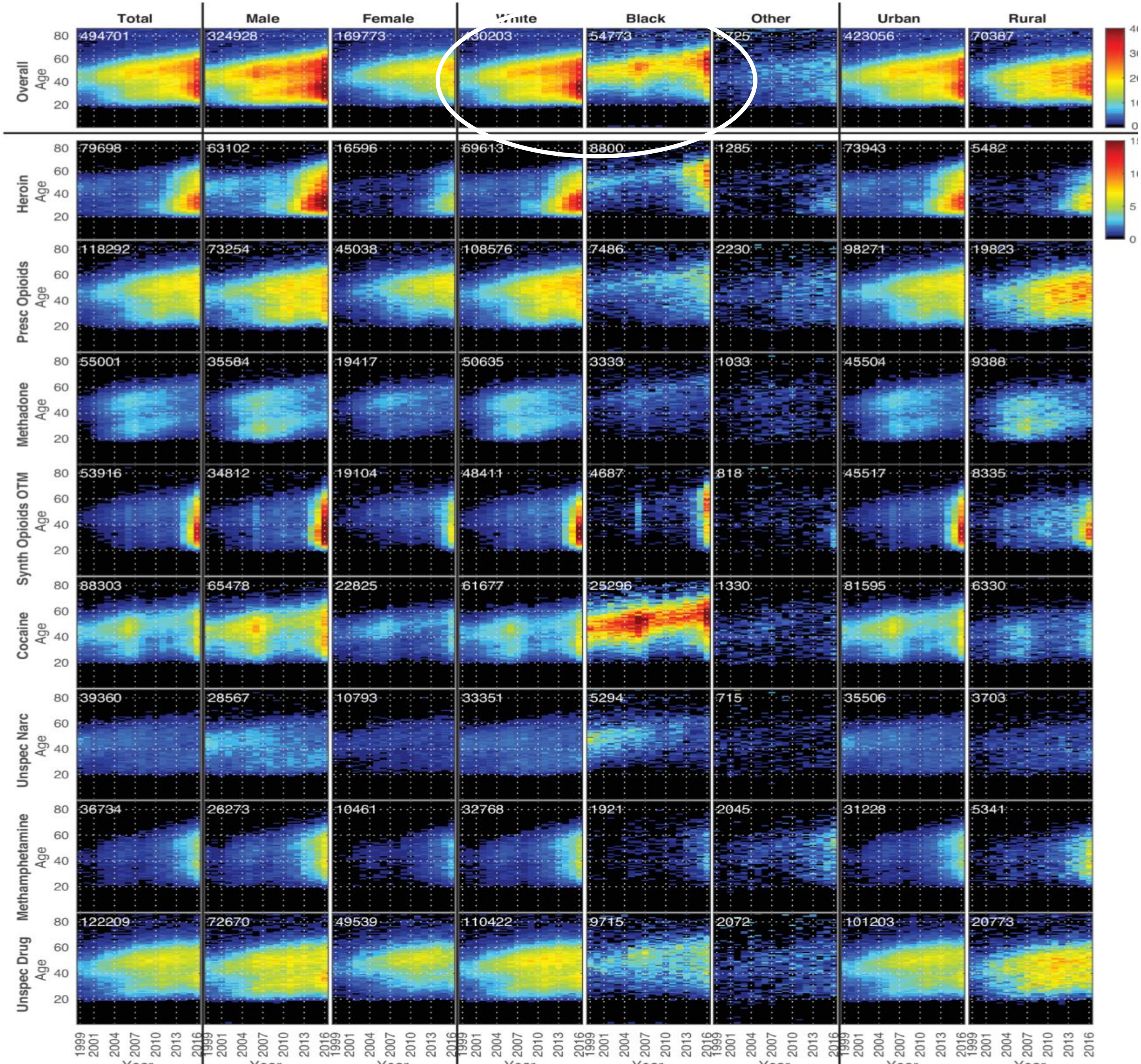

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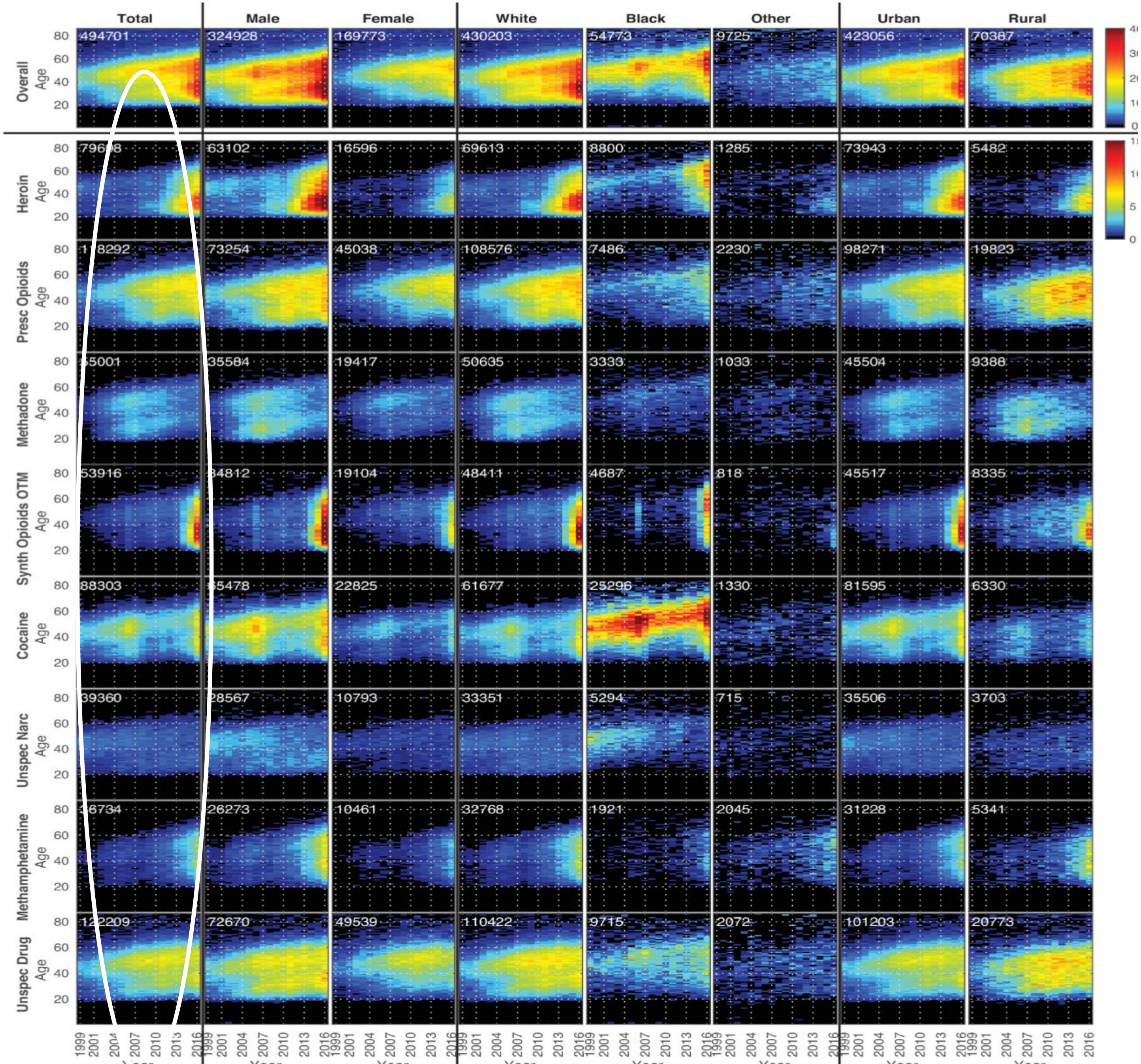

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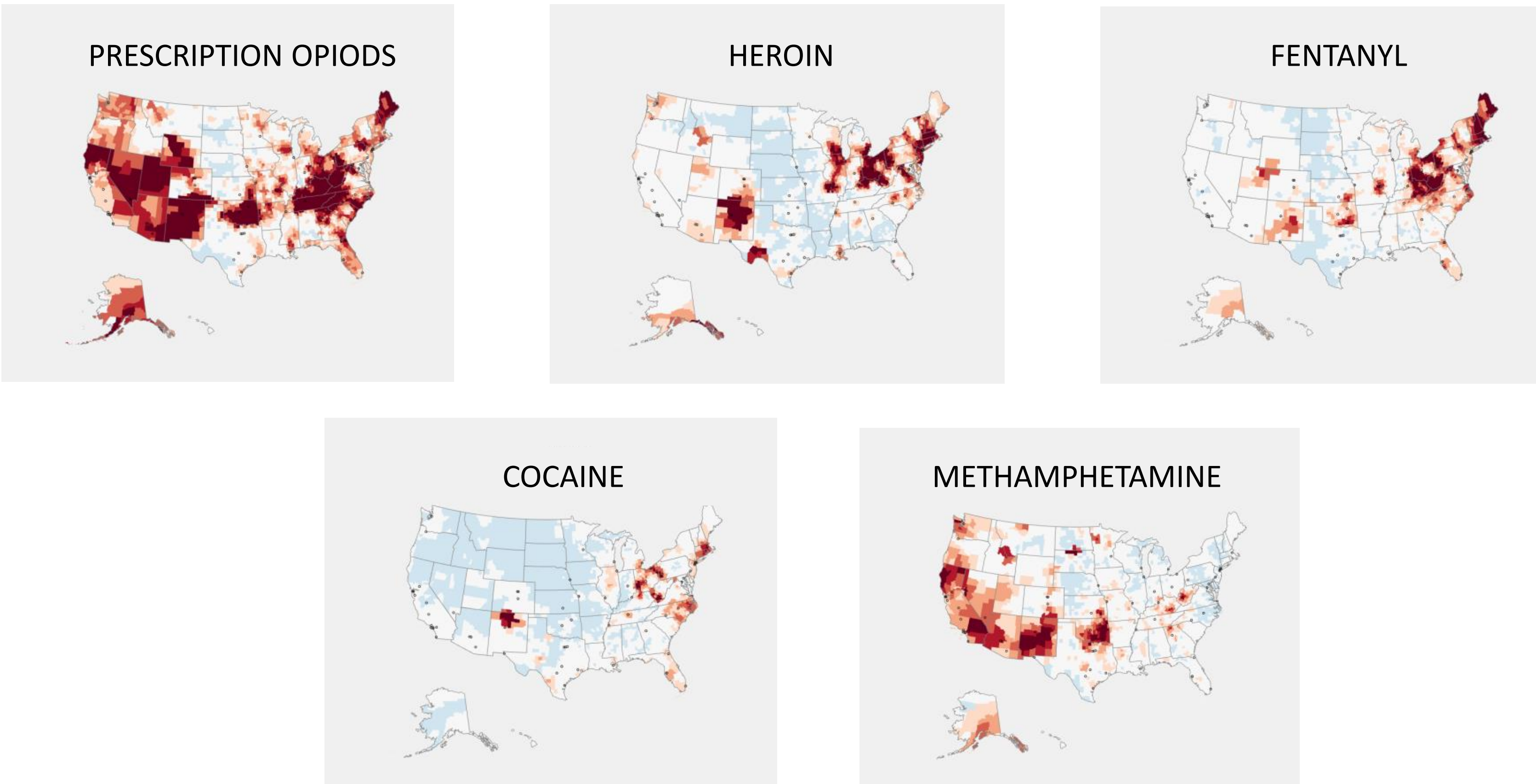
HOT SPOTS FOR OVERDOSE DEATHS, BY DRUG



Getis-Ord Gi* statistic adapted using the pooled mean and variance of the mortality rates across drugs and periods. .

Observation set #1

The overall epidemic of overdose deaths has been growing along a remarkably smooth exponential trajectory

Paradoxically, the overall epidemic is composed of multiple sub-epidemics without obvious structure

President Donald J. Trump
State of the Union Address
4 February 2020

“With unyielding commitment, we are curbing the opioid epidemic,” Trump said. “Drug overdose deaths declined for the first time in nearly 30 years …. we will not quit until we have beaten the opioid epidemic once and for all.

ADDICTION
SSA SOCIETY FOR THE STUDY OF ADDICTION
SHORT REPORT
doi:10.1111/add.15260

Carfentanil and the rise and fall of overdose deaths in the United States

Hawre Jalal[1] & **Donald S. Burke**[2]

Department of Health Policy and Management, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA[1] and Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania, USA[2]

ABSTRACT

Background and Aims It is widely believed that the 2018 decline in overdose deaths in the United States was attributable to a range of public health interventions, however, this decline also coincided with the regulation and decline in use of potent fentanyl analogs, especially carfentanil. The aim of this study was to investigate the association between overdose deaths and carfentanil availability in the United States. **Design** Secondary analysis of drug overdose deaths from the Center for Disease Control and Prevention (CDC) and carfentanil exhibit data from drug seizures submitted to drug crime labs and published by the Drug Enforcement Administration (DEA). Trends in overdose deaths were compared in states with high carfentanil exhibits with states with low or no carfentanil exhibits. **Setting** United States. **Participants** A total of 1035923 drug overdose death records in the United States from 1979 through 2019 were studied. **Measurements** The outcomes studied were number of overdose deaths and mortality rates by state. **Findings** Drug overdose deaths have been closely tracked along an exponential curve. The years 2016 and 2017 witnessed a hyper-exponential surge with increases in overdose deaths of 11228 (+21.4%) and 6605 (+10.4%), respectively. Subsequently in 2018, drug overdose deaths declined by −2870 (−4.1%). This rise and then fall coincided with a surge and then decline in carfentanil drug seizure exhibits during these same years: 0 (2015), 1292 (2016), 5857 (2017) and 804 (2018). The majority of carfentanil exhibits were localized to a few states. The 2018 decline in overdose deaths in the top five states with the greatest spike in carfentanil exhibits in 2017 (Ohio, Florida, Pennsylvania, Kentucky and Michigan) was 2848, which accounted for nearly all of the total US decline. **Conclusions** The 2016–2017 acceleration and then 2018 decline in drug overdose deaths in the United States was associated with the sudden rise and then fall of carfentanil availability. Given the regional variation, carfentanil's decreased availability may have contributed to the reduction in overdose deaths in 2018.

Keywords Carfentanil, death, drug waves, fentanyl, opioid epidemic, overdose.

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INTRODUCTION

Annual mortality rates for drug overdoses in the United States have been inexorably growing along an exponential curve for decades [1]. In 2018, for the first time since 1990, the annual number of drug overdose deaths in the United States (US) fell from 70237 in 2017 to 67367 in deaths declined for the first time in nearly 30 years.' However, in 2019, the number of overdose deaths have increased again along the historical exponential trajectory and above their 2017 level to 71148, a +5.6% increase, according to provisional data released by the Center for Disease Control (CDC) [4]. Therefore, it is not clear if the 2018 decline was the start of a long-term trend or a tran-

Altmetric – Carfentanil and the ri | The Real Reason for 2018 Drop in

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home / mental health center / mental health a-z list / reason for 2018 drop in fatal u.s. drug overdoses article

The Real Reason for 2018 Drop in Fatal U.S. Drug Overdoses

FRIDAY, Sept. 18, 2020 (HealthDay News)

A slight decline in U.S. drug overdose deaths in 2018 was due to a drop in supply of a dangerous opioid from China rather than federal government efforts, and was only temporary, a new study shows.

"The U.S. has not bent the curve on the drug overdose epidemic," said lead author Dr. Hawre Jalal, an assistant professor of health policy and management at the University of Pittsburgh.

"We are concerned that policymakers may have interpreted the one-year

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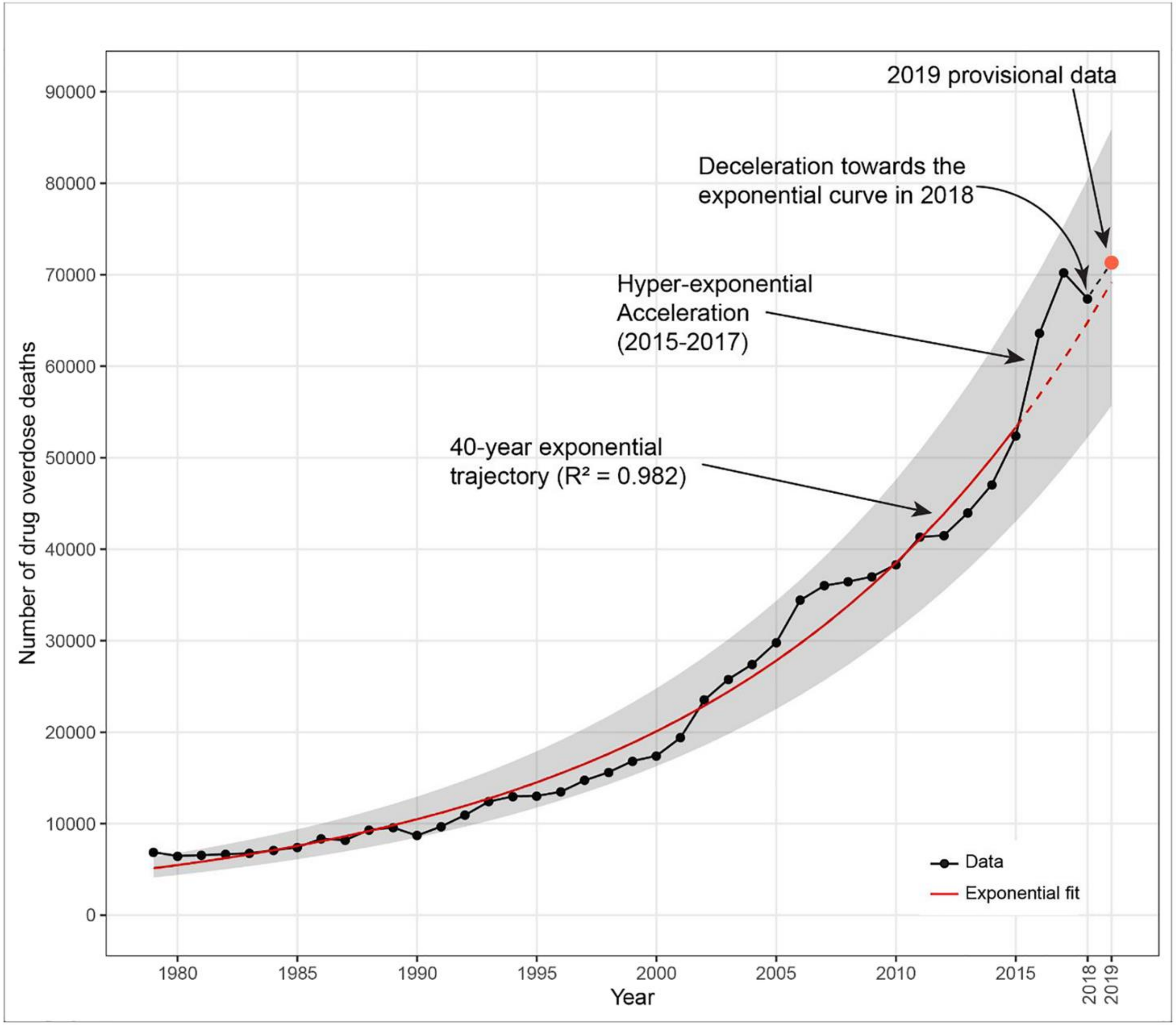
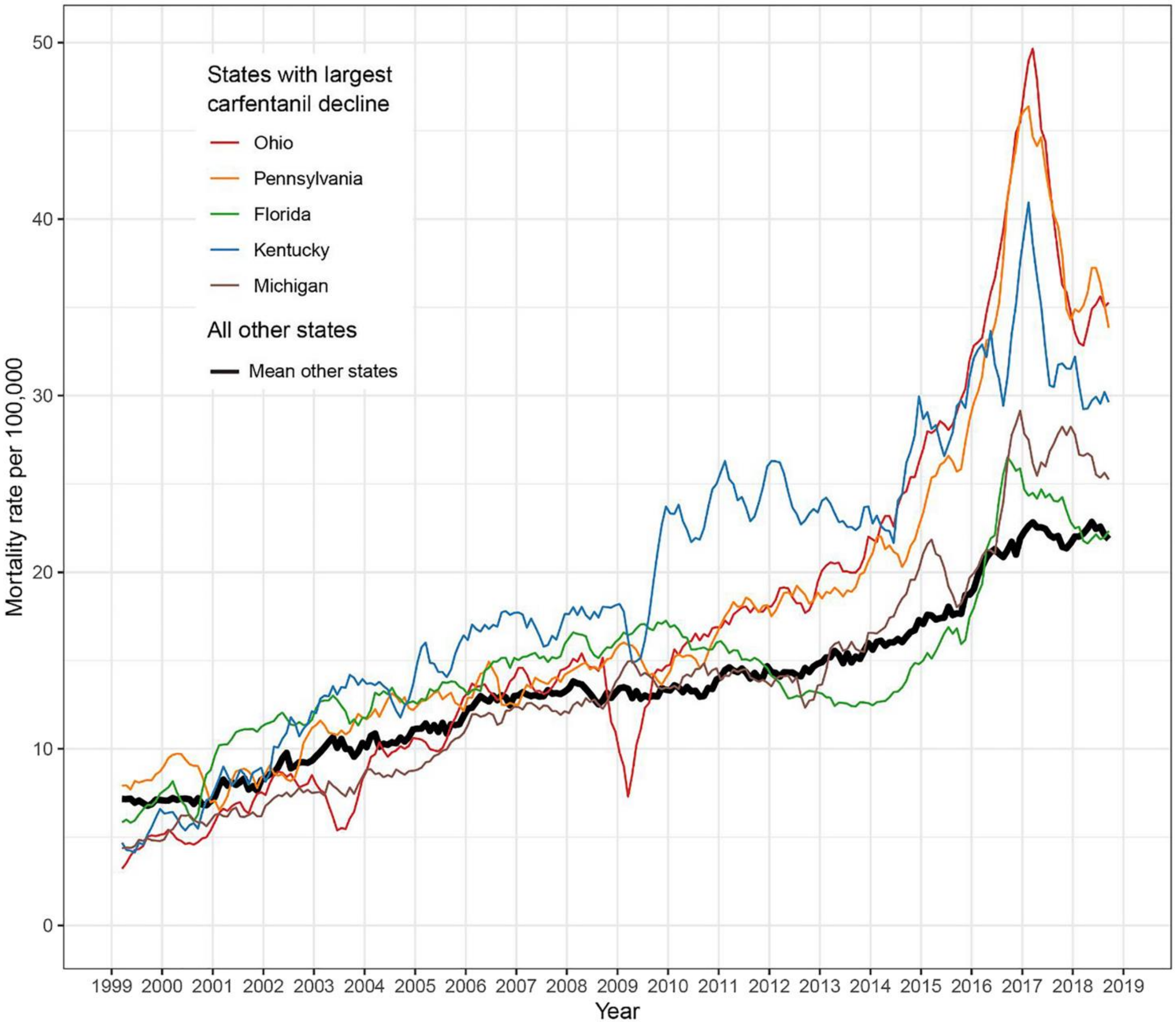

2019 provisional data
Deceleration towards the exponential curve in 2018
Hyper-exponential Acceleration (2015-2017)
40-year exponential trajectory (R² = 0.982)
Number of drug overdose deaths
Year
Data
Exponential fit

Fall in Overdose Deaths was confined to states that experienced a spike in carfentanil deaths, and the trajectory returned to its upward exponential growth pattern



Epidemic Growth Patterns

By Age and Birth-Year Cohorts (Generation)

nature medicine

LETTERS

https://doi.org/10.1038/s41591-020-0855-y

Check for updates

Age and generational patterns of overdose death risk from opioids and other drugs

Hawre Jalal[1] ✉, Jeanine M. Buchanich[2], David R. Sinclair[1,3], Mark S. Roberts[1] and Donald S. Burke[4] ✉

The ongoing substance misuse epidemic in the United States is complex and dynamic and should be approached as such in the development and evaluation of policy[1]. Drug overdose deaths (largely attributable to opioid misuse) in the United States have grown exponentially for almost four decades, but the mechanisms of this growth are poorly understood[2]. From analysis of 661,565 overdose deaths from 1999 to 2017, we show that the age-specific drug overdose mortality curve for each birth-year cohort rises and falls according to a Gaussian-shaped curve. The ascending portion of each successive birth-year cohort mortality curve is accelerated compared with that of all preceding birth-year cohorts. This acceleration can be attributed to either of two distinct processes: a stable peak age, with an increasing amplitude of mortality rate curves from one birth-year cohort to the next; or a youthward shift in the peak age of the mortality rate curves. The overdose epidemic emerged and increased in amplitude among the 1945–1964 cohort (Baby Boomers), shifted youthward among the 1965–1980 cohort (Generation X), and then resumed the pattern of increasing amplitude in the 1981–1990 Millennials. These shifting age and generational patterns are likely to be driven by socioeconomic factors and drug availability, the understanding of which is important for the development of effective overdose prevention measures.

The mortality rate for overdose deaths has been growing exponentially since at least 1979 (ref. [2]); overdose deaths are now a leading cause of premature deaths in the United States[3]. In 2017 there were 192 deaths per day due to drug overdoses. We apply the term 'epidemic' to describe this growing overall pattern. By analysis of overdose mortality patterns according to age at death (age), calendar year (period), and year of birth (cohort) of the decedents[4], and use of novel data visualization techniques, we reveal predictable patterns that describe the drug overdose epidemic from opioids and other drugs in the United States

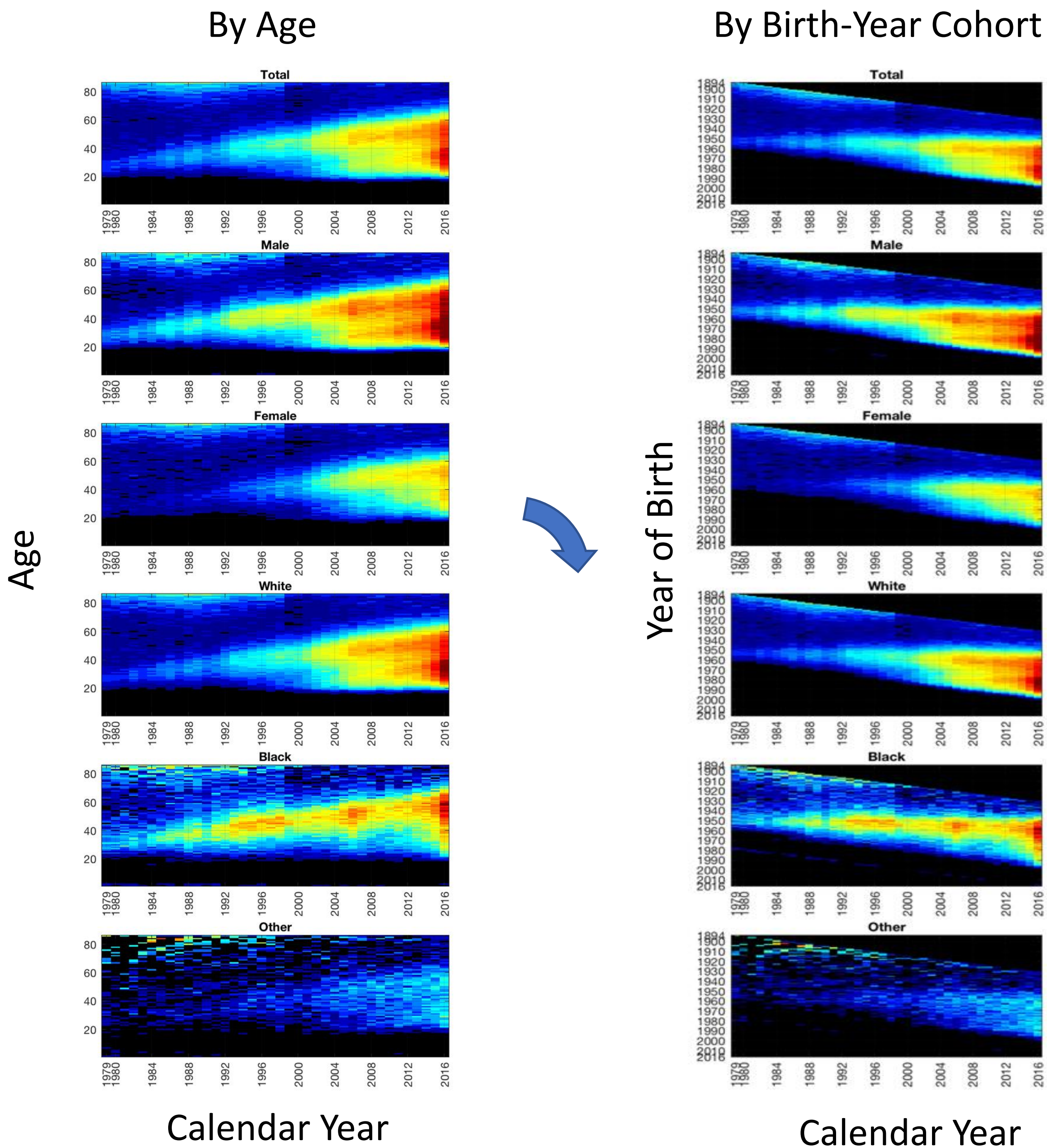
Accidental drug poisoning deaths in the United States were identified with the International Classification of Diseases codesd ICD-9 and ICD-10 and were extracted from the Mortality Multiple Cause-of-Death microdata files from 1979 to 2017 (https://www.cdc.gov/nchs/nvss/mortality_public_use_data.htm). Statistical analyses used to reveal the relationships between age, period and cohort (APC) are provided in the online Methods. We implemented our newly developed hexagonal heatmap (hexamap)[5] to a display of hexagonal datapoint pixels that are aligned by APC (Fig. 1a). Coloration of the pixels reveals patterns of overdose mortality rate by age, period, or birth year (Fig. 1b). Overall, the epidemic has a wedge-shaped pattern with an upper boundary approximately aligned along the 1945 birth-year cohort isoline, and the lower boundary aligned along the 18-year-old age isoline as shown by the dashed lines. The vast majority of overdose deaths are constrained within these boundaries.

This wedge shape of overdose mortality pattern illustrates the changing involvement of age groups and birth-year cohorts over time. The upper boundary of this wedge pattern, approximately along the post World War II 1945 birth-year cohort isoline, reveals a relatively abrupt emergence of the epidemic among the Baby Boomer generation[6]. Generations born earlier than 1945 had very low rates of overdose deaths. By tracing along any given birth-year cohort isoline upward from left to right across calendar years, it can be seen that the annual mortality rate for that birth-year cohort increases as each cohort has aged. This general pattern of increasing overdose mortality with increasing age holds true for all birth-year cohorts from 1945 to the present. Early signs of slowing in overdose mortality rates is apparent after 2015, especially among the Baby Boomers with the earliest birth years (1945–1955 cohorts), as individuals in these cohorts exceed the age of peak overdose mortality.

The lower overdose epidemic boundary runs approximately along the 18-year-old age isoline, consistent with the increase in risk-taking behaviors that occurs in adolescence. Prior to 2000, this lower epidemic boundary was closer to age 30 years, but this age boundary has since shifted to age 18 years.

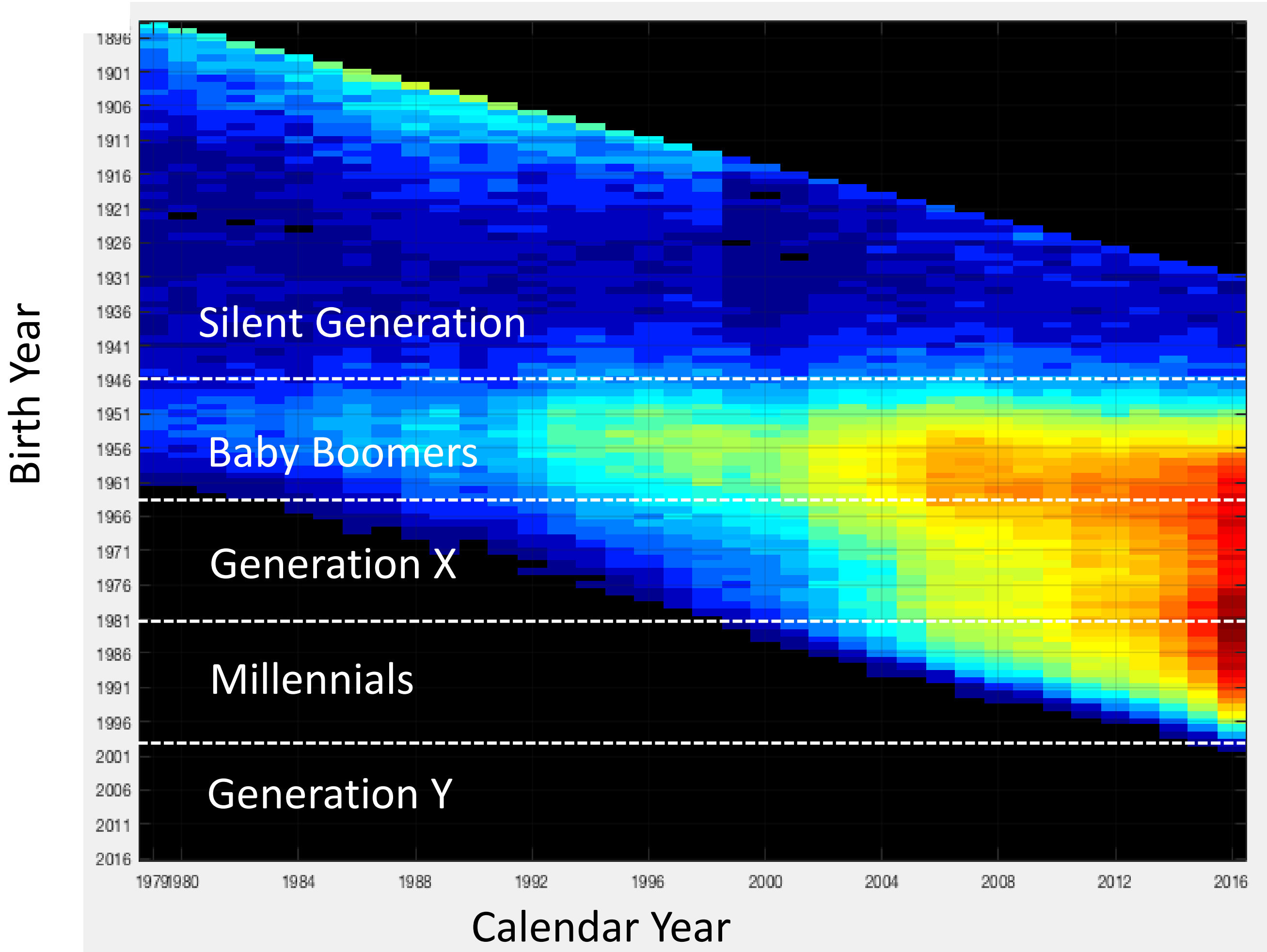
Bands of high mortality are arrayed vertically along period (year) isolines. These vertical bands of high mortality do not conform to specific birth-year cohorts or to age groups; instead they are constrained to specific time periods. One example is the strong vertical band in deaths in the most recent years 2014–2017; this recent period effect of high mortality cuts across all affected birth-year cohort and age group isolines, and coincides with the surge of fentanyl-associated deaths[7].

To examine the successive increases in mortality rates with each birth-year cohort, we graphically compared the mortality rate trajectories for all birth-year cohorts across their respective lifespans (Fig. 2). In this analysis, all birth-year cohorts are aligned on the same age axis, showing age-specific mortality rates for ages 0–85

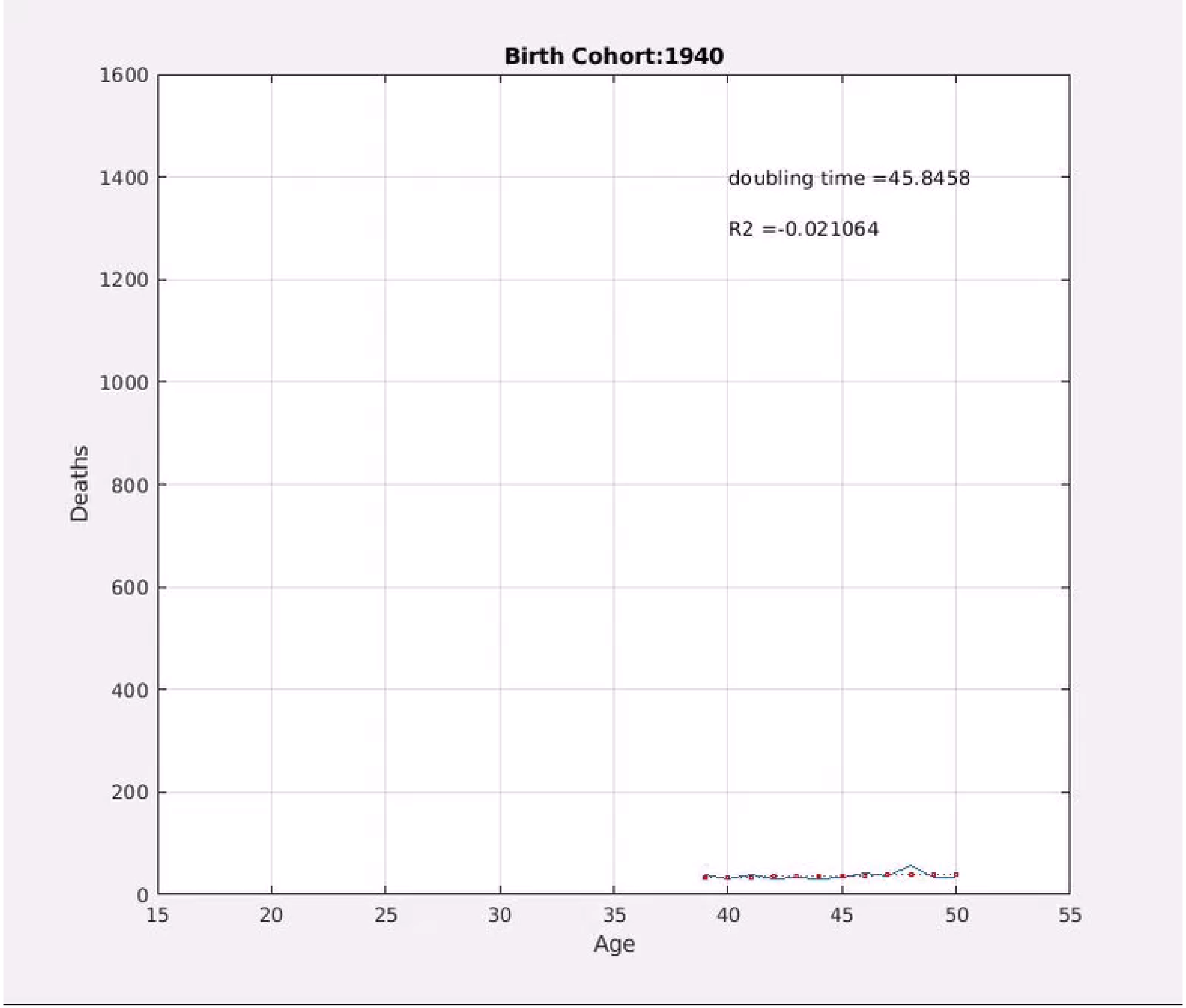


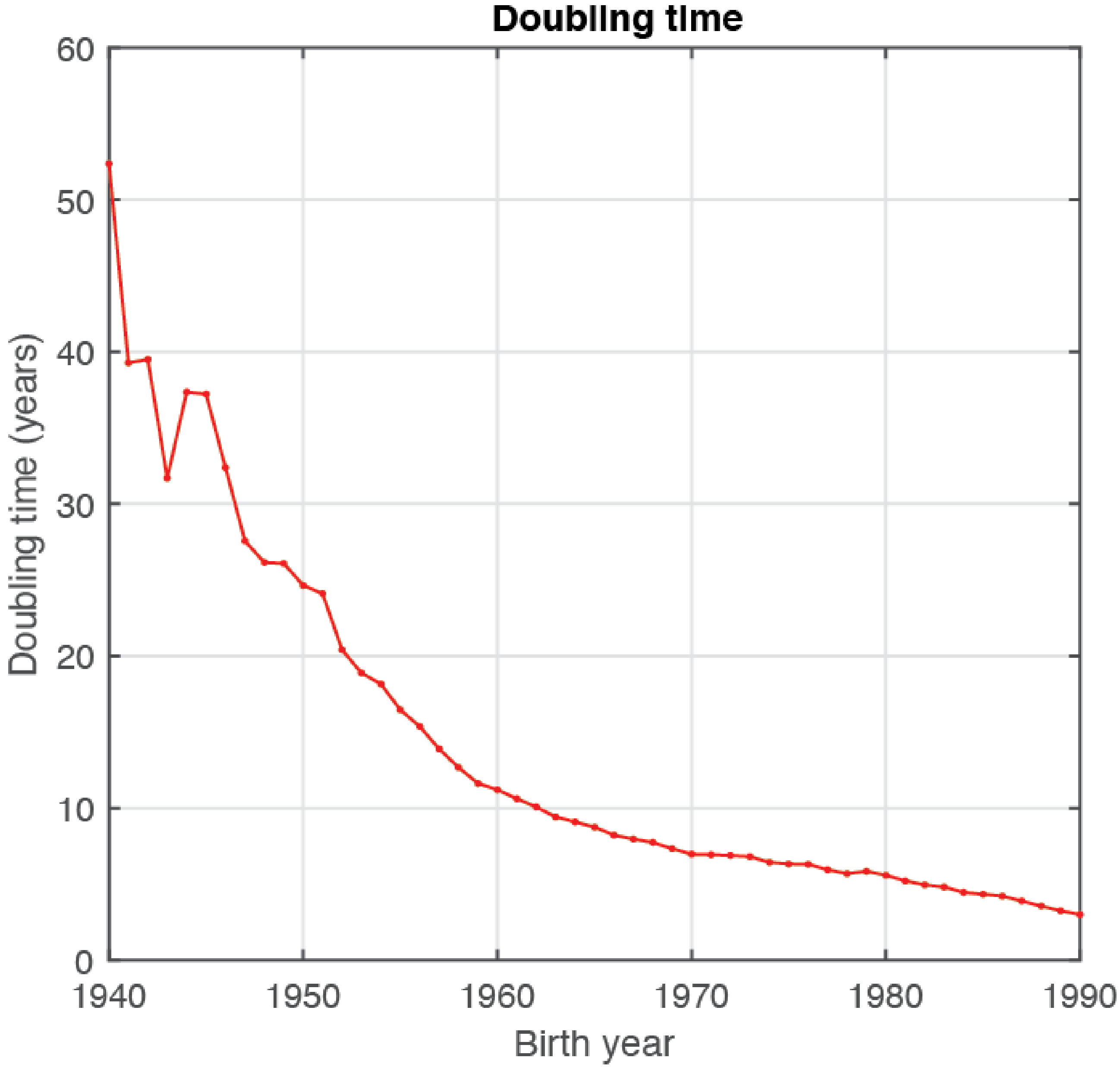
By Age
By Birth-Year Cohort
Total
Male
Female
White
Black
Other
Age
Year of Birth
Calendar Year
Calendar Year

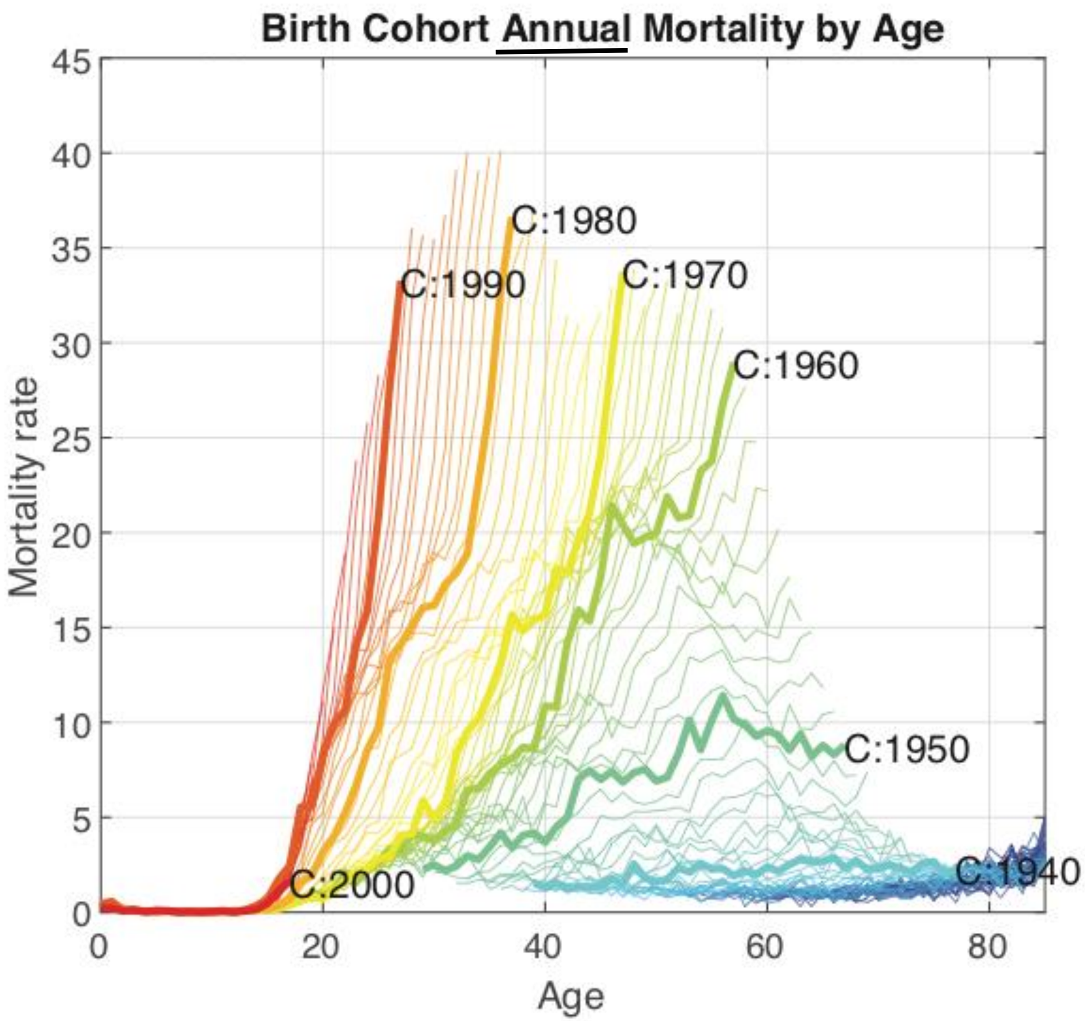
Birth Cohorts (Generations)

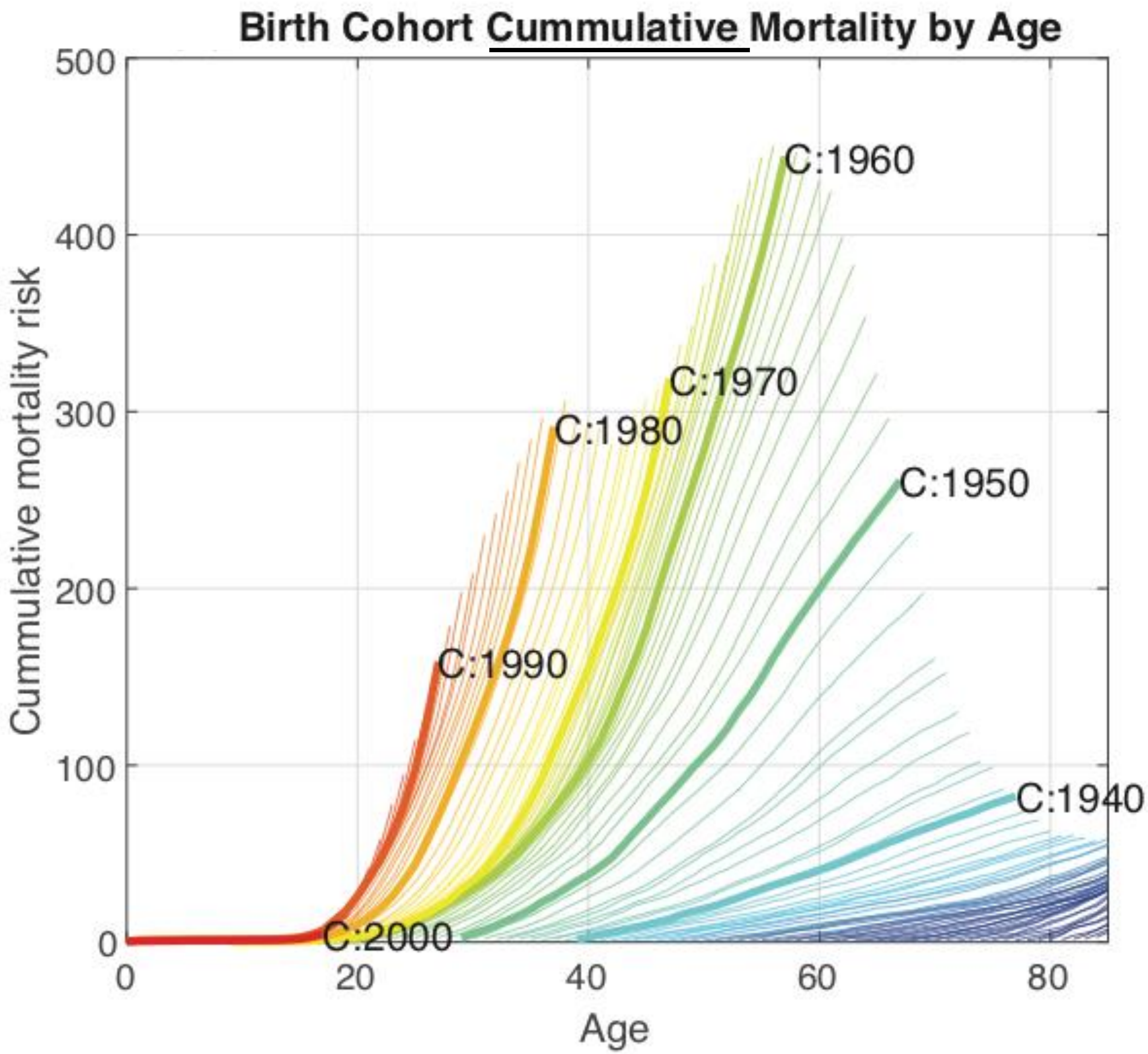


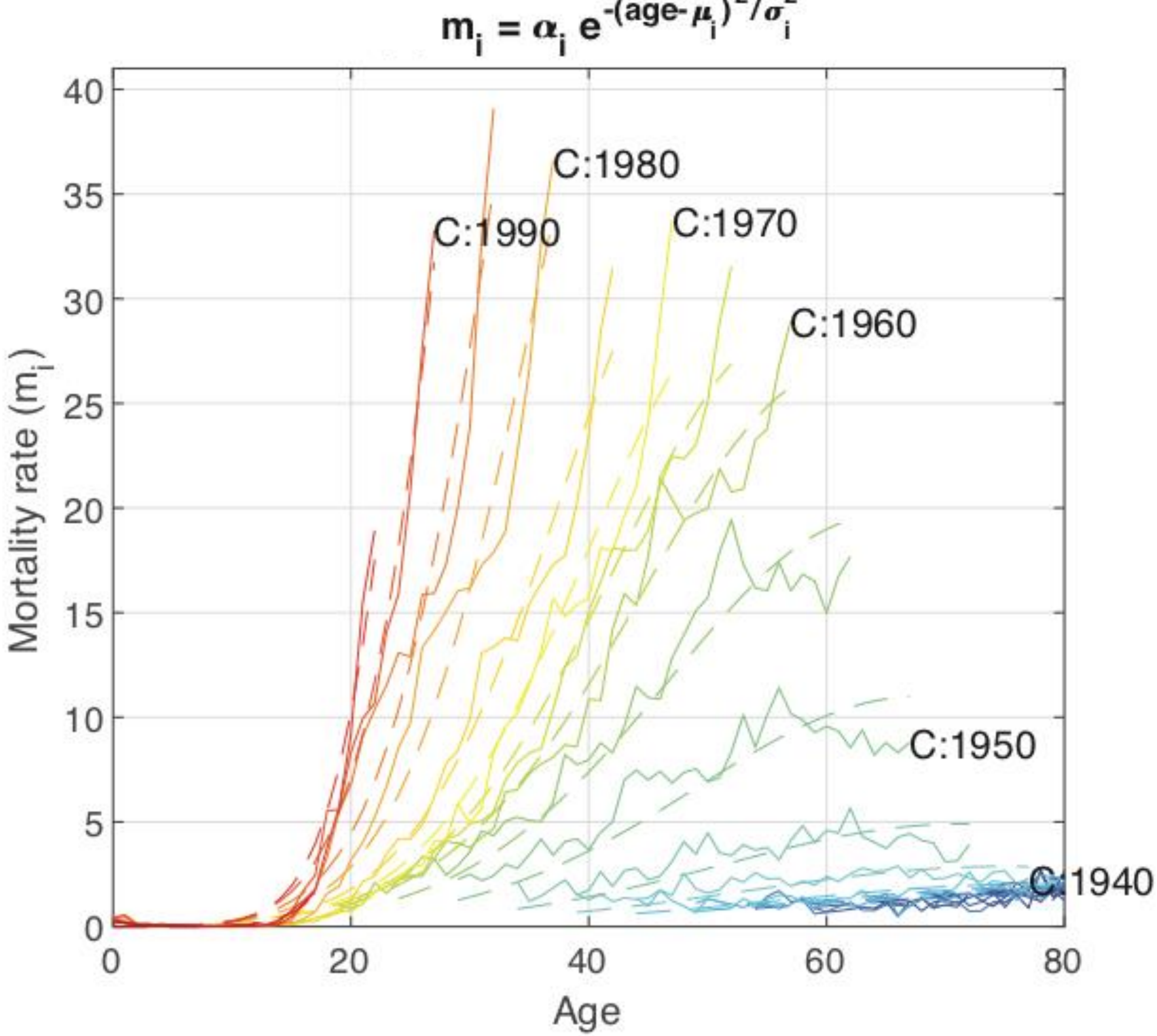
Overdose Death Doubling Times, By Birth Cohorts
(observation period from 1979 to 2016, between ages 20 and 50 y.o.)




Doubling time
Doubling time (years)
0
10
20
30
40
50
60
1940
1950
1960
1970
1980
1990
Birth year

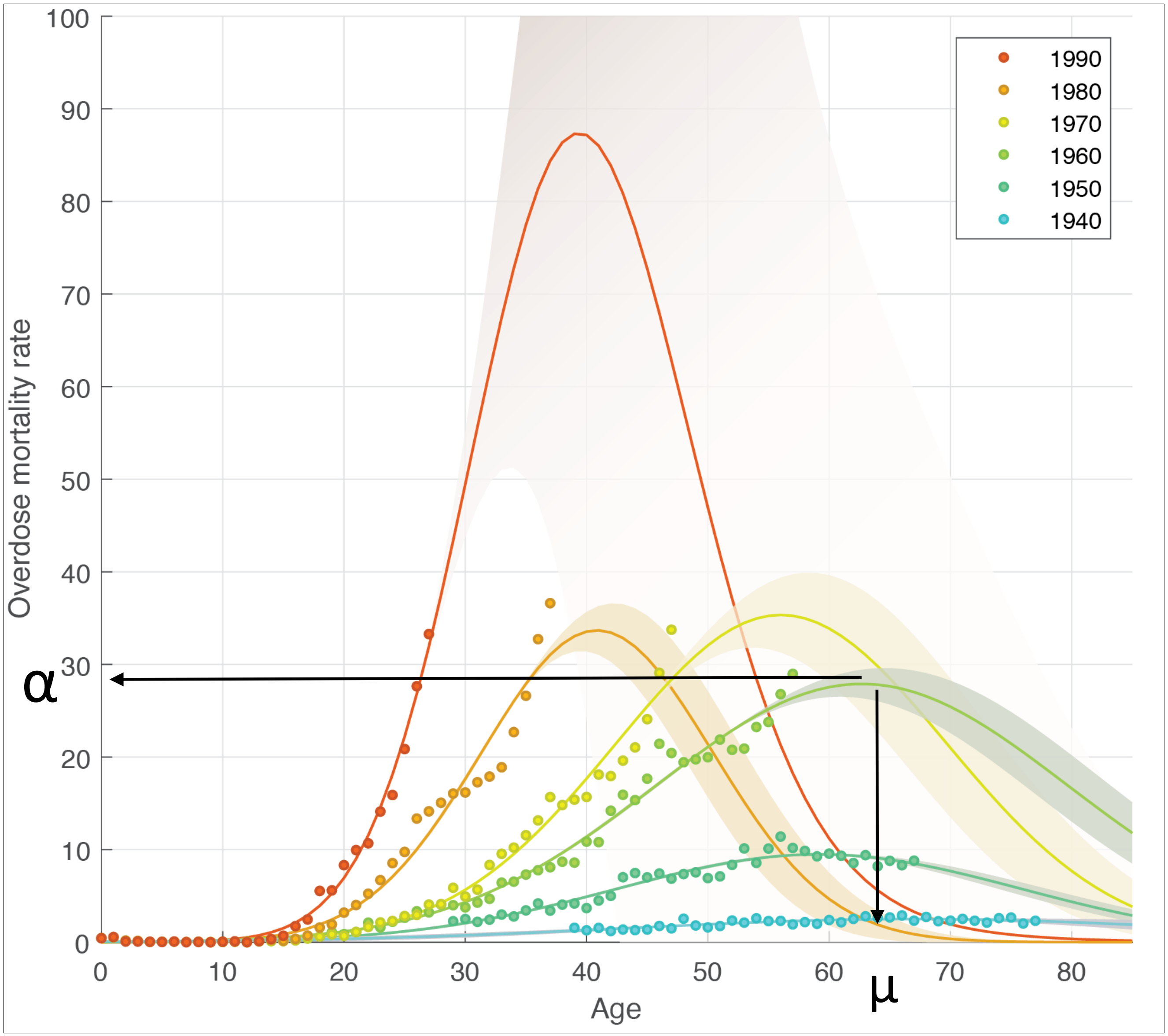

Birth Cohort Annual Mortality by Age
Mortality rate
Age
45
40
35
30
25
20
15
10
5
0
0
20
40
60
80
C:1980
C:1990
C:1970
C:1960
C:1950
C:2000
C:1940


Birth Cohort Cummulative Mortality by Age
Cummulative mortality risk
Age
0
100
200
300
400
500
0
20
40
60
80
C:1960
C:1970
C:1980
C:1950
C:1990
C:1940
C:2000

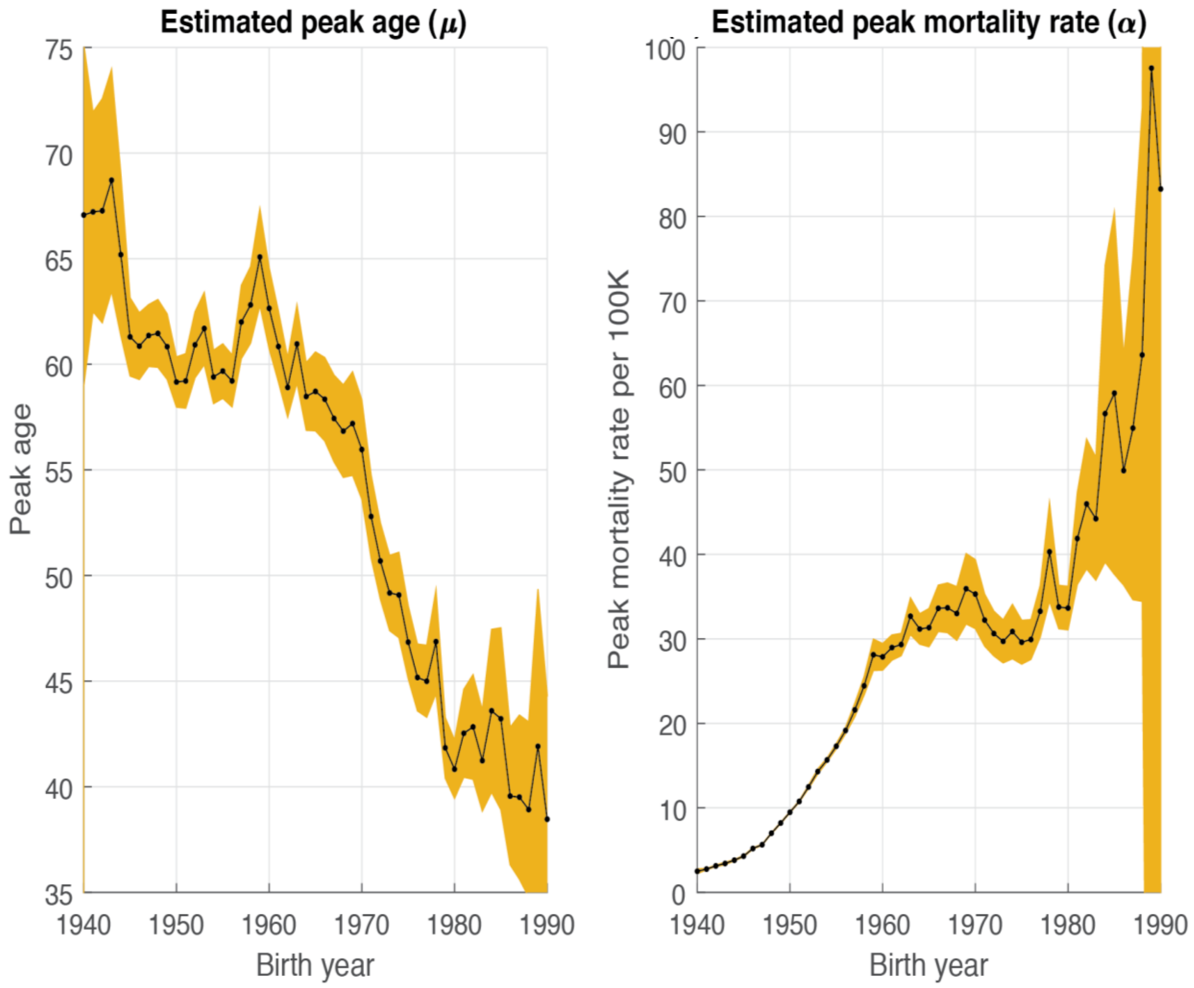


$m_i = \alpha_i \, e^{-(age-\mu_i)^2/\sigma_i^2}$
C:1980
C:1990
C:1970
C:1960
C:1950
C:1940
Mortality rate (m_i)
Age
0
20
40
60
80
0
5
10
15
20
25
30
35
40

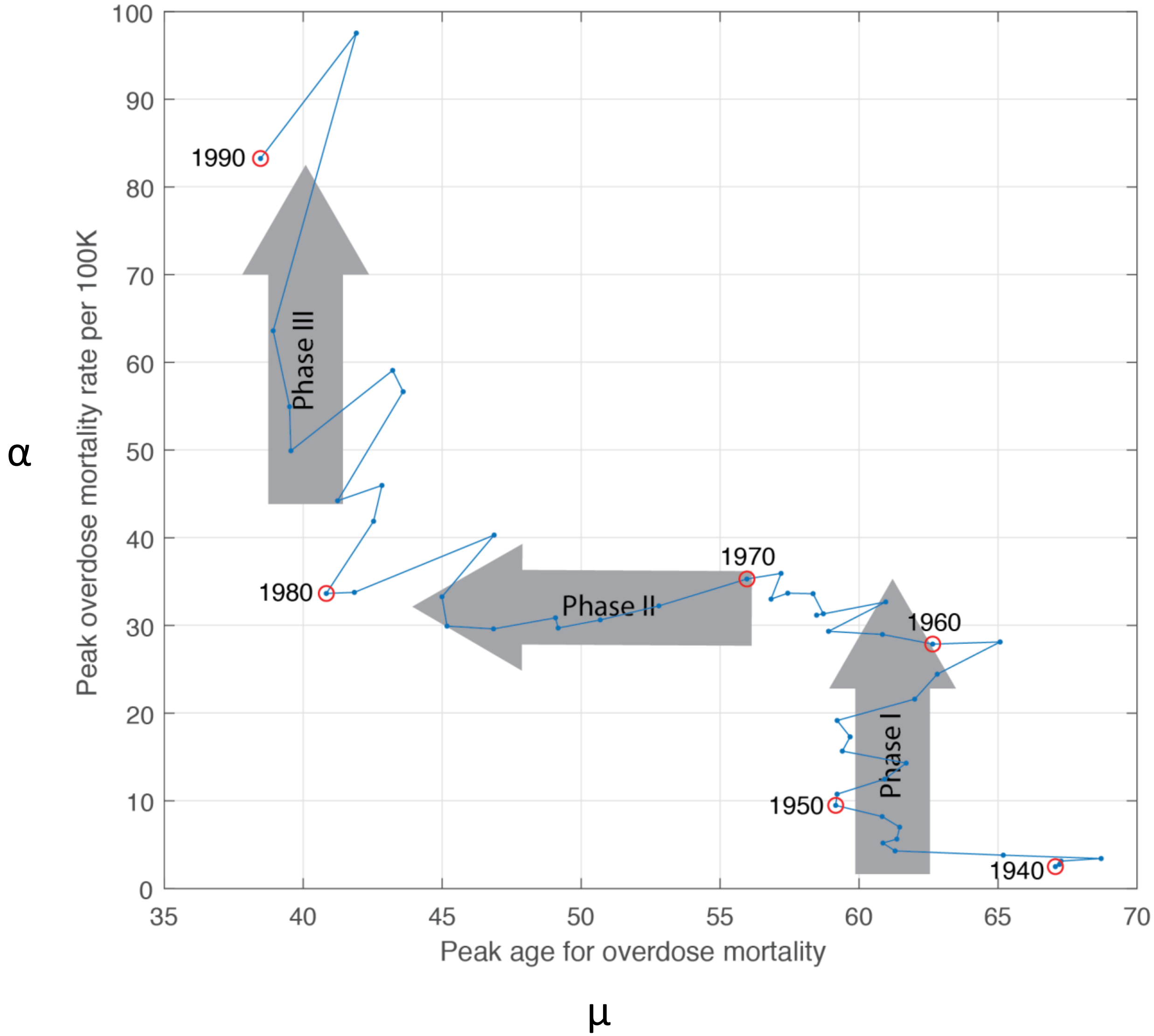
Approximation of Age-specific Overdose Mortality Trajectories, by Birth Cohort
Fitting to Gaussian Curves

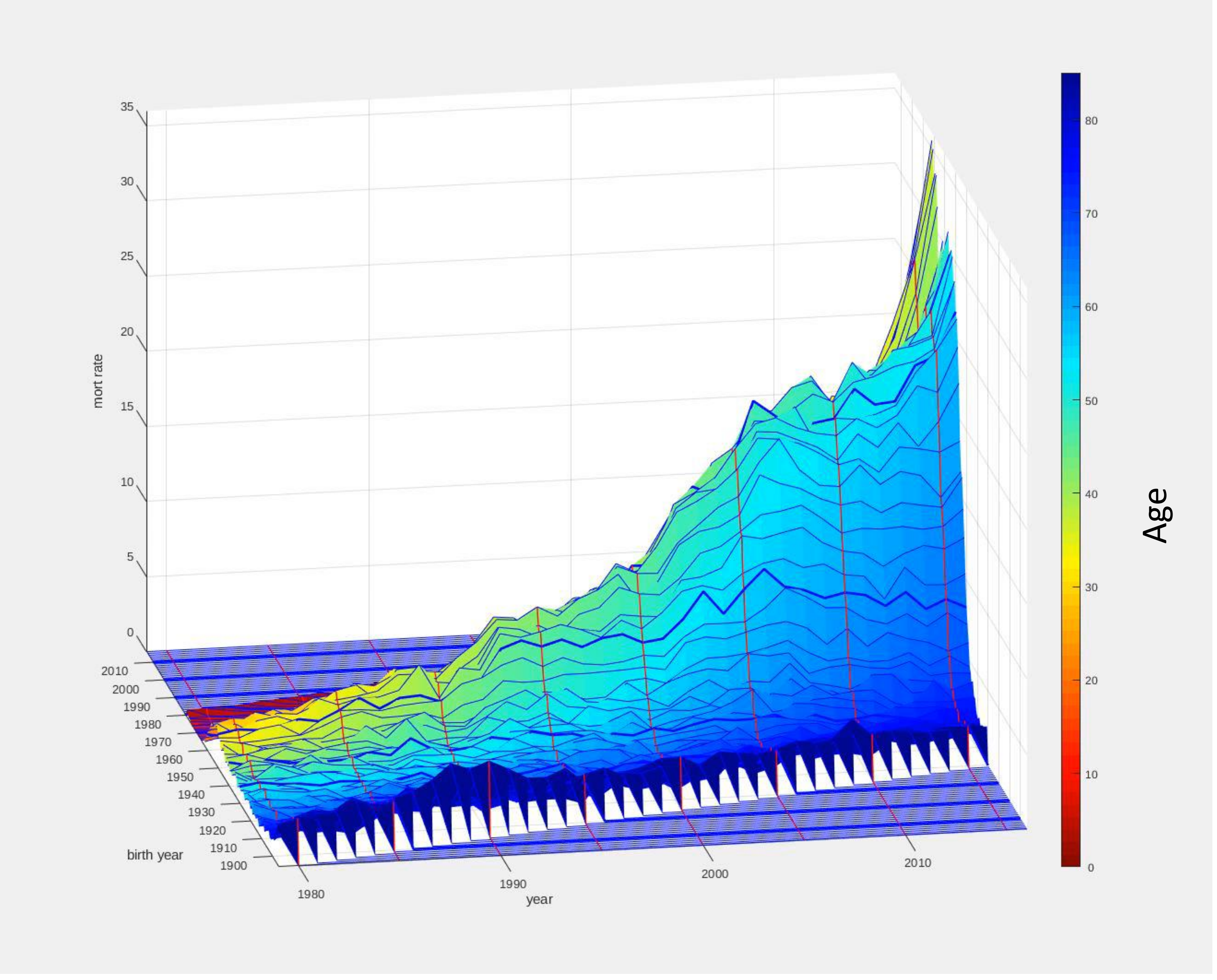


Changing epidemic curve parameters μ (peak age) and α (peak mortality rate) by birth cohort



Changing epidemic curve parameters μ (peak age) and α (peak mortality rate) by birth cohort





35
30
25
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15
10
5
0
mort rate
2010
2000
1990
1980
1970
1960
1950
1940
1930
1920
1910
1900
birth year
1980
1990
2000
2010
year
80
70
60
50
40
30
20
10
0
Age

Age, Period, and Cohort (APC) Heat Maps Using Hexagonal Coordinates

Fermat's Passage

To the Editor:

Probability and statistics are essential to epidemiology, and notoriously difficult. The rules of probability[1,2] are concisely summarized in a passage, describing a game, that Pierre de Fermat wrote to Blaise Pascal on Friday 25 September 1654.[3] Here, we explain Fermat's passage.

In the first sentence of the passage, Fermat references a prior letter where a game of "points" is described. In this game, each of k players places the same monetary stake, and chooses one side of a balanced k-sided die (for example, two people can play with a balanced coin). A player is awarded a point when a roll of the die shows their side. The first player with two points wins the pot.

The problem discussed by Fermat and Pascal is how to fairly distribute the pot, if the game of points must be stopped before anyone has won. Fermat describes the case of k=3 players, who have each contributed $9, and where in one prior round the first player won a point. The last sentence in Fermat's passage reads: "Here, in a few words, is the whole mystery, which we believe, because we both seek only reason and truth."

It is crucial to note that, because the first player with two points wins, the game *must* be finished in three more rounds or fewer. If the first player wins the next round, with a chance 1/3, then she wins the game. If the second or third player wins the next round, and the first player wins the following third round, with a chance of (2/3)(1/3)=2/9 (because independent probabilities multiply), then the first player wins the game. Finally, if the second or third player wins the next round, and the third or second player wins the subsequent round, and the first player wins the following third round, with chance 2/3(2/3)1/3 − 2/27 = 4/27 − 2/27 = 2/27, then the first player wins the game. The tricky −2/27 accounts for the two cases, 1/27 each, where the second or third player wins the next two rounds, and therefore the first player loses the game before a third round is played. The first player wins the game with probability 1/3+2/9+2/27 = 17/27 = 0.629 629… (because exclusive probabilities sum). The second and third players together win the balance of 1 − 17/27 = 10/27 = 0.370 370… (because exclusive and exhaustive probabilities sum to one), or 5/27 = 0.185 185…, each. If one argues to divide the pot of $27 according to the chances of winning, conditional on the round already played, then the first, second, and third players receive $17, $5, and $5, respectively. Arguments for other rules are possible, for example, "calling off" the bet (each player is returned $9), or "whoever is ahead wins" (first player receives all $27). But without such a rule in place, before play begins, division (of the pot) according to conditional chances seems fairest.

The three rules of probability are given parenthetically above. There, in the highly communicable form of a game, we have the rules of probability theory, which provides foundation for statistics, epidemiology, and reason, if not truths.

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REFERENCES

1. Lindley DV. *Making Decisions*. 2nd ed. New York: Wiley; 1985:30–37.
2. Greenland S. Probability logic and probabilistic induction. *Epidemiology*. 1998;9:322–332.
3. Tanneuy P, Henry C eds. Oeuvres de Fermat. Paris: Gauthier-Villars; 1894:310–313.

Hexamaps for Age–Period–Cohort Data Visualization and Implementation in R

To the Editor:

Age–period–cohort (APC) analyses often reveal important insights into patterns of disease incidence and mortality, such as cancer. A widely recognized issue in APC analyses is the identification issue caused by the inseparability of the linear effects of cohort, age, and period. While analytical solutions are an active area of research,[1] visual displays can be useful tools to reveal patterns in these data.[2] Despite their potential, to date, there is a lack of APC-specific visualization tools. For example, a commonly used display of APC data is the traditional Lexis diagram (Figure A), which consists of a simple two-dimensional heatmap with a field of colored square tiles representing a quantity of interest such as mortality rate. While it is informative, the main issue with a Lexis diagram is that the researcher has to make a choice to represent only two of the three dimensions (often age and period) on the *XY* axes, leaving cohorts to be represented on the diagonal. This setup introduces substantial visual distortion in how cohort patterns are presented relative to age and period. Specifically, relative to age and period, this setup compresses patterns between adjacent cohorts by 30% $(1-\sqrt{2}/2)$, while stretches patterns within each cohort by 41% $(\sqrt{2}-1)$. In addition to these distortions, tracing cohort patterns is further complicated because adjacent square pixels along any cohort isoline only share

The authors report no conflicts of interest.

SDC Supplemental digital content is available through direct URL citations in the HTML and PDF versions of this article (www.epidem.com).

All data used in this article are publicly available from the Center for Disease Control and Prevention (CDC). In addition, the code used to illustrate the method is available as an eAppendix; http://links.lww.com/EDE/B696.

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DOI: 10.1097/EDE.0000000000001236

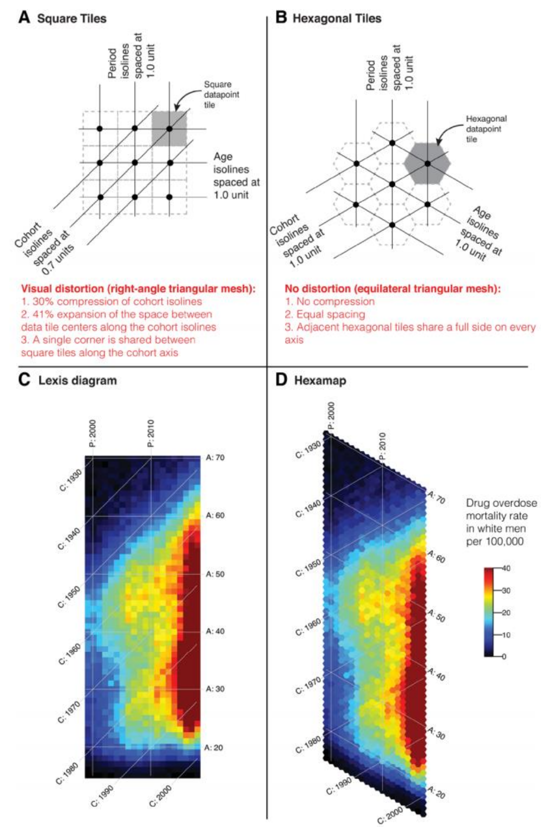


FIGURE. Hexamaps correcting the visual distortion in Lexis diagrams. A, The distortion of cohort isolines using square tiles in a Lexis diagram; (B) corrects for this visual distortion using hexagonal tiles. C and D, Comparing the patterns of accidental drug overdose deaths among white men in a traditional Lexis diagram versus a hexamap, respectively (A = age ranging from 15 to 70 years, P = period ranging from 1999 to 2018, C = cohort ranging from 1929 to 2003).

a single corner. Together, these distortions can substantially impede cohort pattern recognition in Lexis diagrams.

We developed a hexamap as a simple solution to the limitations of a traditional Lexis diagram (Figure B). A hexamap consists of a field of colored hexagonal tiles. Hexagons are the preferred shape for visualizing heatmaps because they are the most rounded shape that can be tiled evenly edge-to-edge.[3] A hexagonal grid is especially powerful for visualizing APC data because it places all three APC axes at equal 60° angles. Because of this placement, a hexamap overcomes all the visual

APC (Age, Period and Cohort) Effects

Calendar Year (Period)

Events happening at a certain <u>point in time</u> (eg “Viet Nam War”)

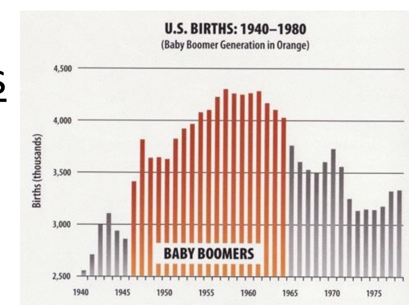
Age = Calendar Year – Birth Year

Age

Events characteristically occurring at certain human <u>life stages </u>/ ages (“teenagers’)

Birth Year (Cohort)

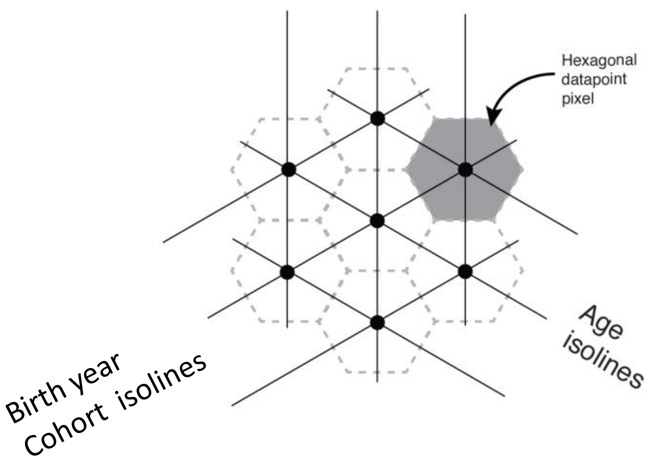
<u>Shared life experiences</u> of cohorts of persons born around the same time (“generations”)



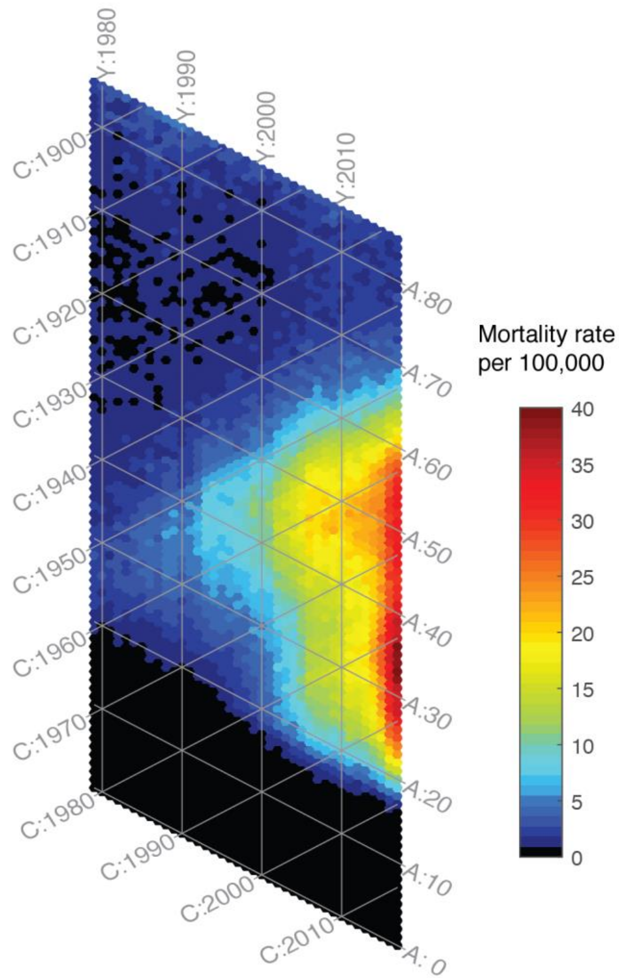
Hexamaps: Hexagonal coordinate Age / Period (Year) / Cohort heat maps

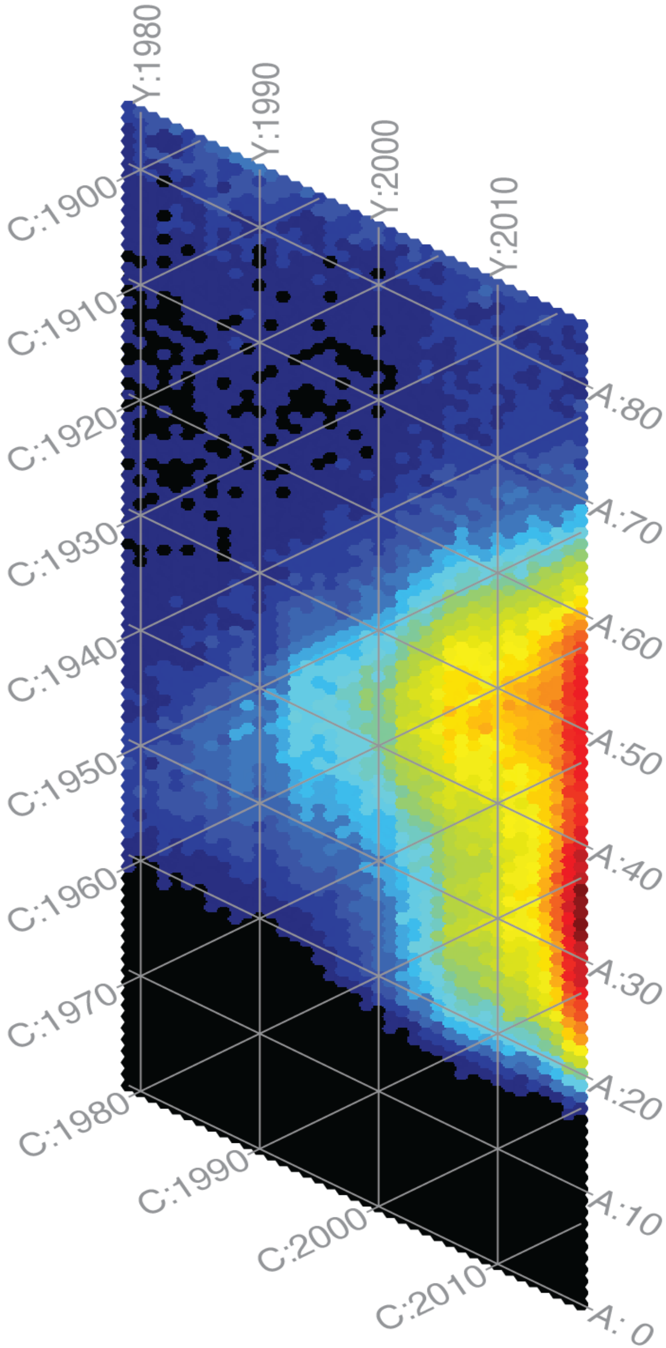
Age = Calendar Year – Birth Year

(A) Hexamap illustration

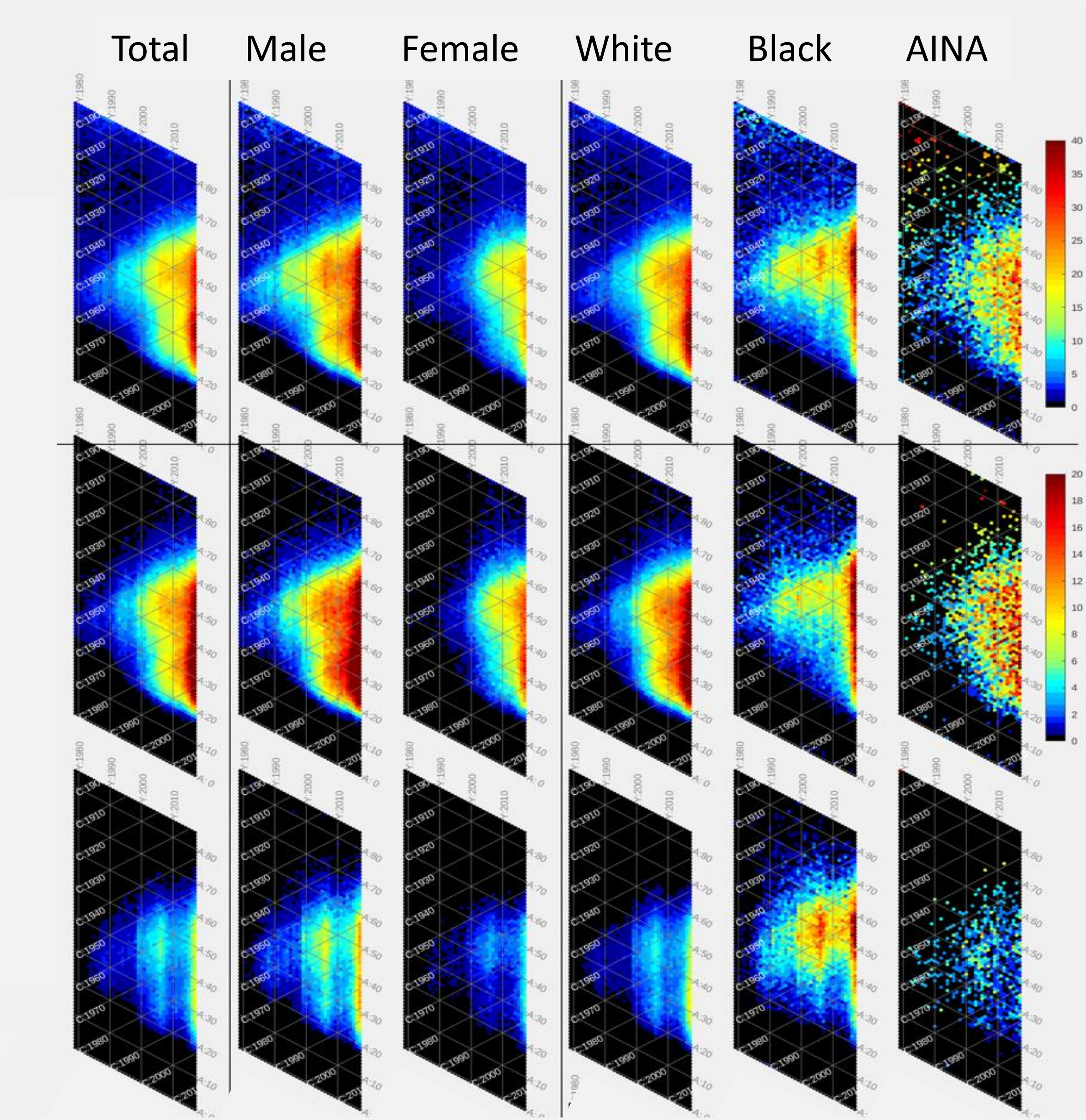


(B) Hexamap for overall overdoses





Having trouble looking at hexagonal APC heat maps? Here's how


Total
Male
Female
White
Black
AINA

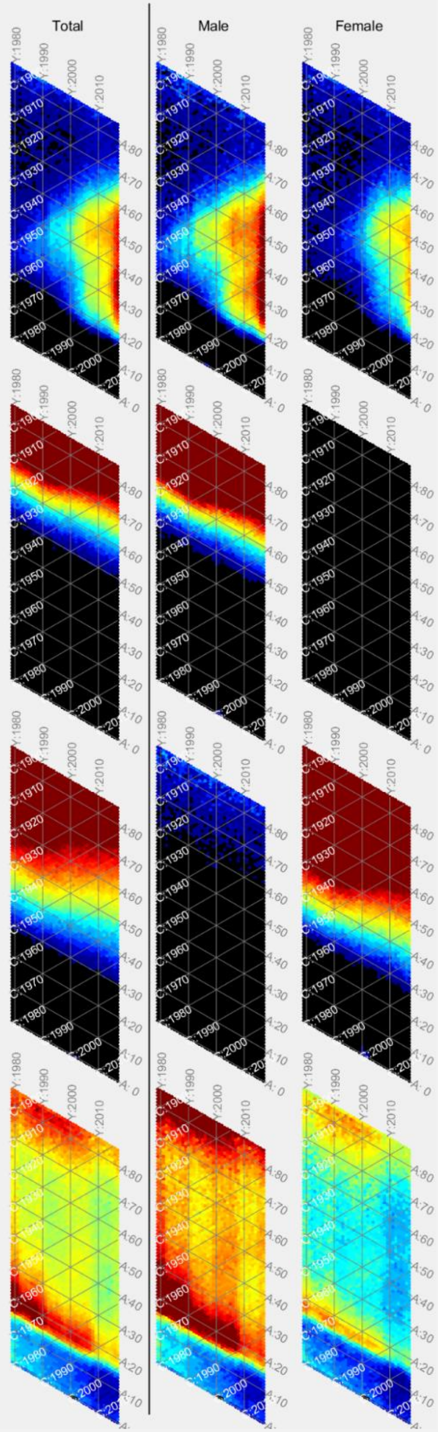
APC Hexagon Heat Maps for Other Causes of Death (Controls)

Overdoses

Prostate Cancer

Breast Cancer

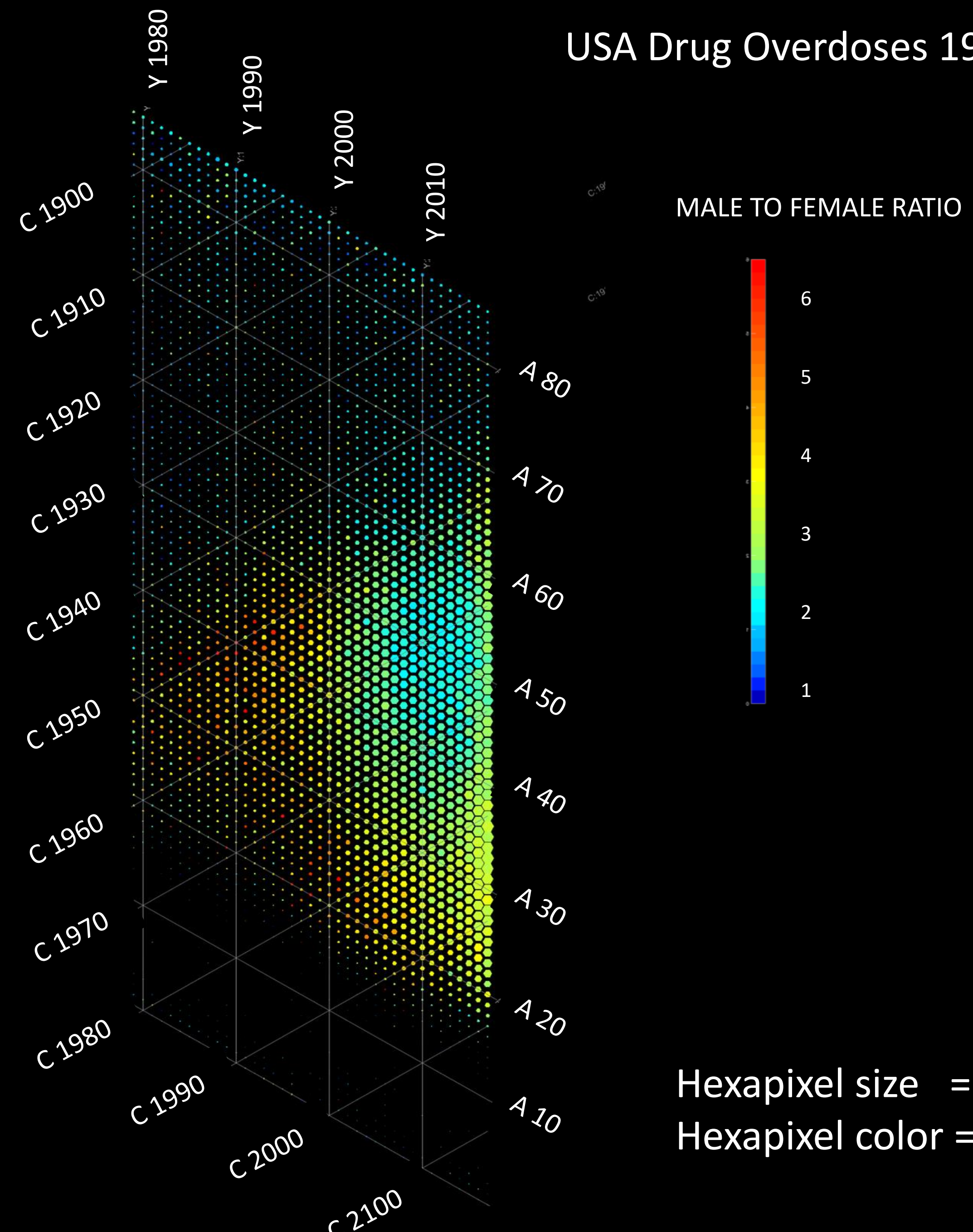
Motor Vehicle Accidents



APC - Hexagon Heat Maps / Variable Pixel Sizes

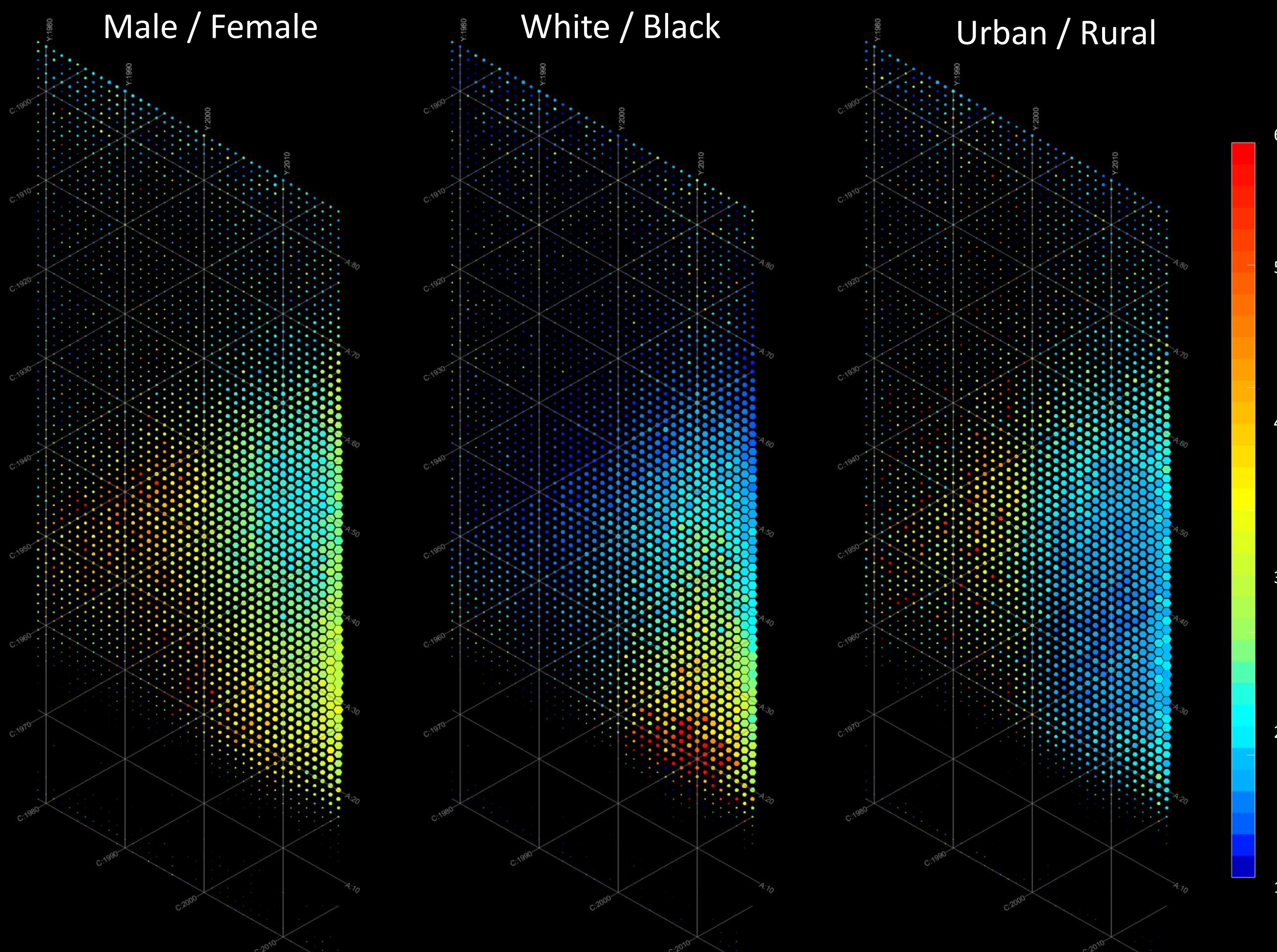
- Set hexagon pixel size proportional to mortality rate
- Use color to convey other information about that pixel eg male/female ratio
- Creates tool to examine how other variables map onto APC patterns

USA Drug Overdoses 1979 - 2017



Hexapixel size = rate
Hexapixel color = sex ratio

USA Drug Overdoses 1979 - 2017



Hexapixel size = rate   Hexapixel color = demographic ratio

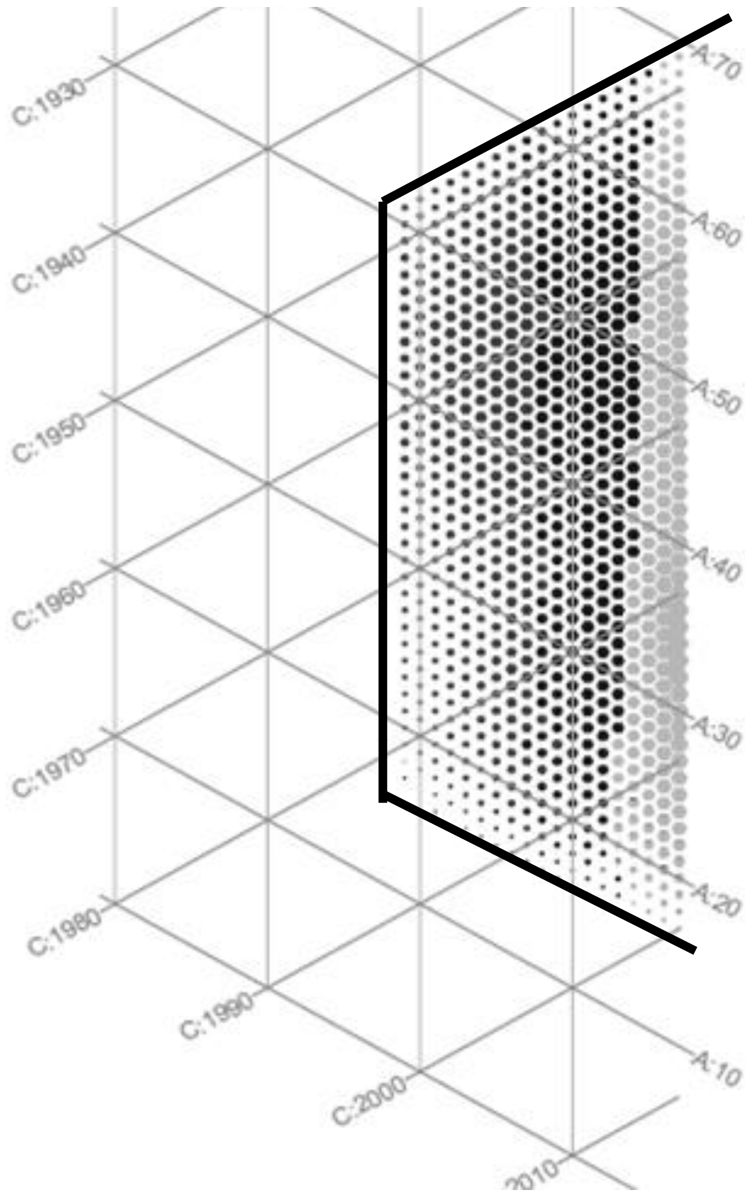
Changing Demographics of the USA Drug Overdose Epidemic 1979 - present

Male -> Female (especially older)
Black -> White (especially younger)
Urban -> Rural

Drug patterns by Age and Generation

(percentage of deaths from cocaine, prescription drugs, methadone, heroin, fentanyl, methamphetamine, unspecified drug, and unspecified narcotic)

K-means clustering of APC hexagon pixels



Analytic frame delimited by

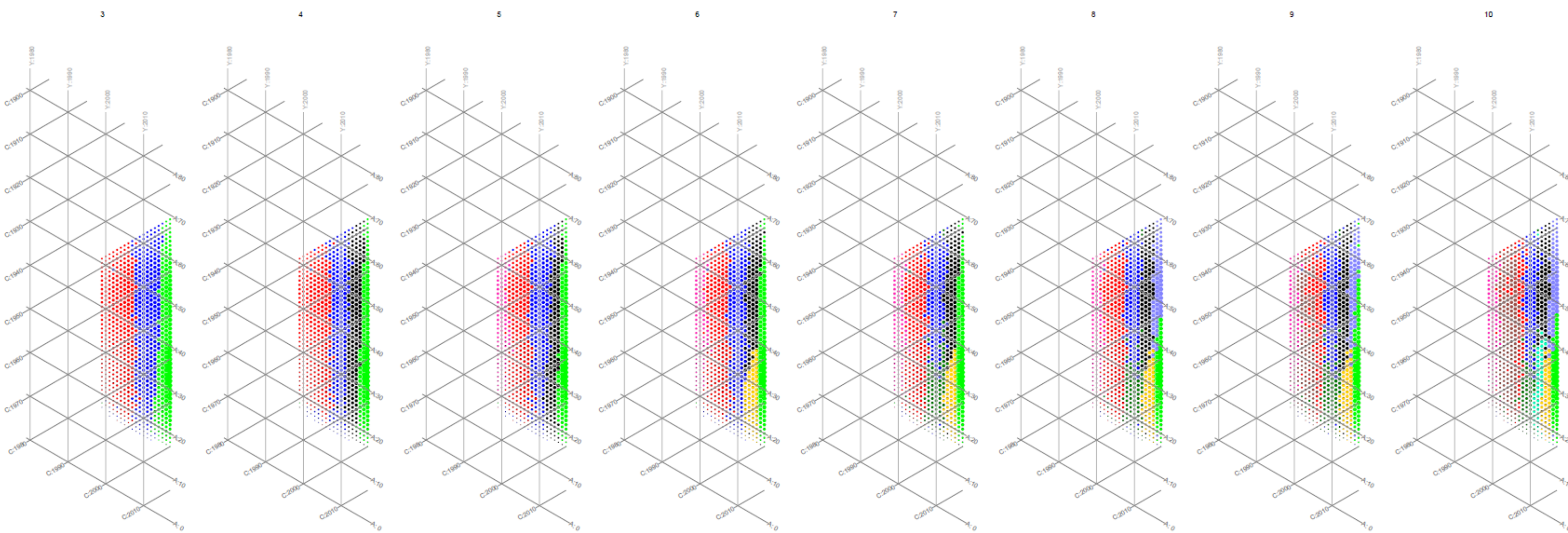
Calendar year = 1999 ->

Birth cohort = 1948 ->

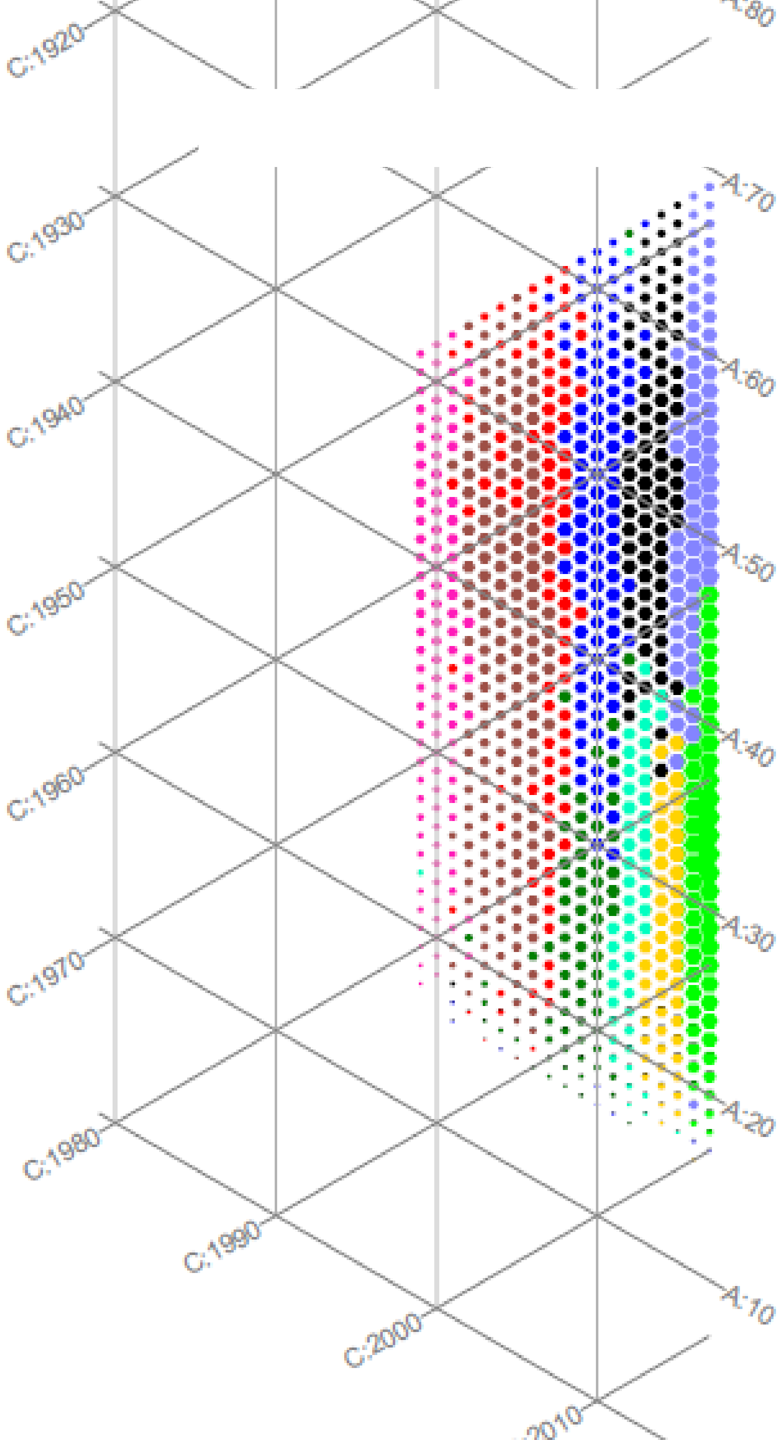
Age >15 yo

K-means clustering of APC hexagon pixels

By drug patterns (percentage of deaths from cocaine, prescription drugs, methadeon, heroin, fentanyl, methamphetamine, unspecified drug, and unspecified narcotic)



Note: Although no data on year, age, nor birth cohort were used to generate the drug cluster patterns, the derived drug use cluster patterns nonetheless track along year and birth cohort isolines


C:1920
C:1930
C:1940
C:1950
C:1960
C:1970
C:1980
C:1990
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A:80
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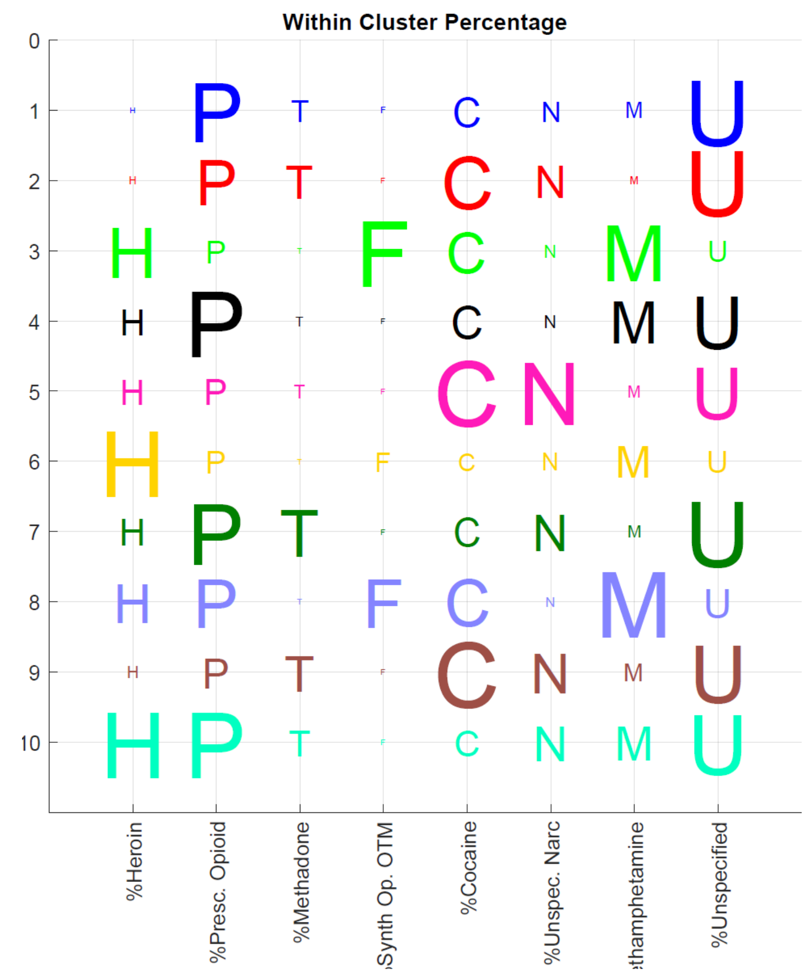
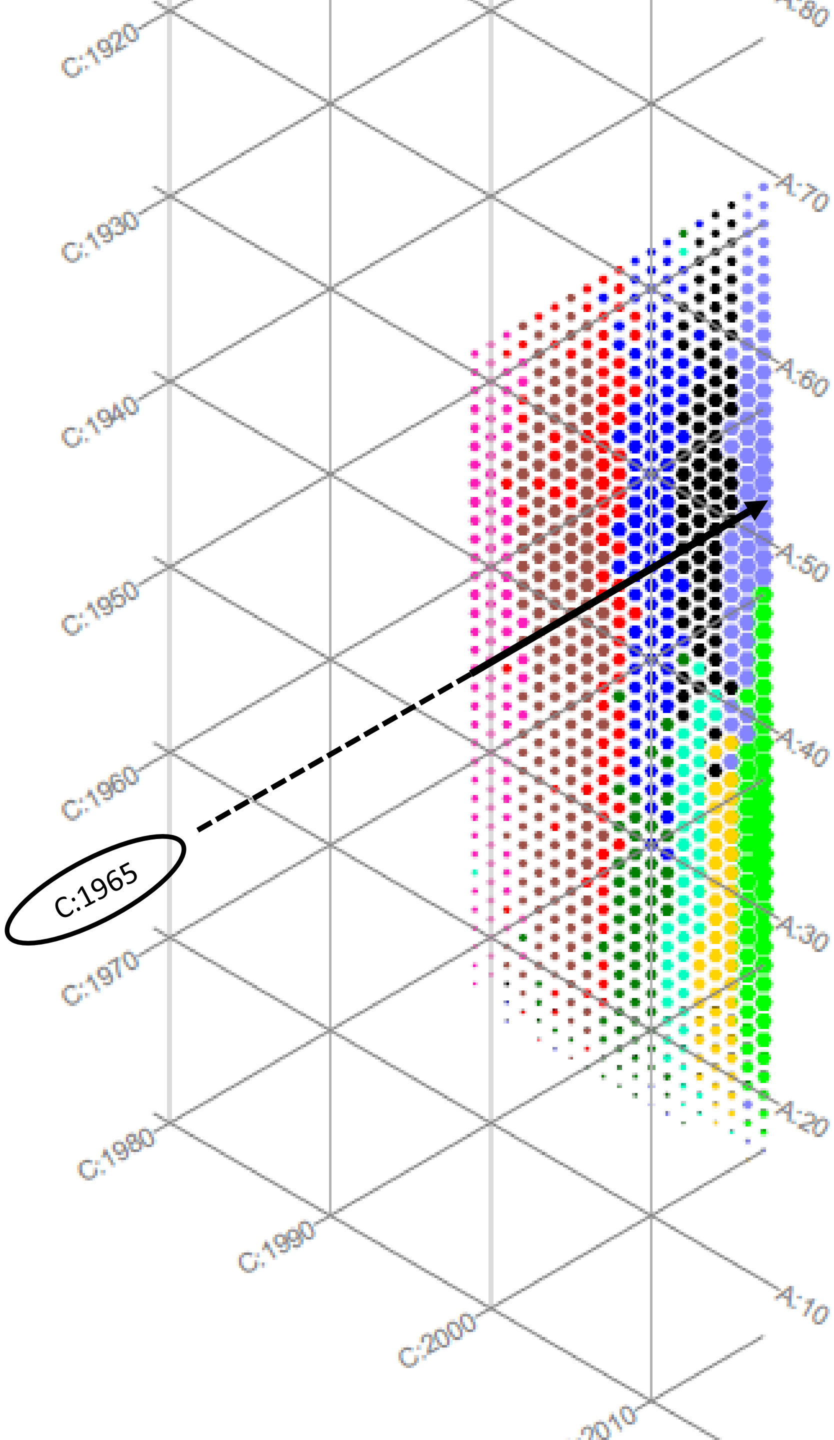
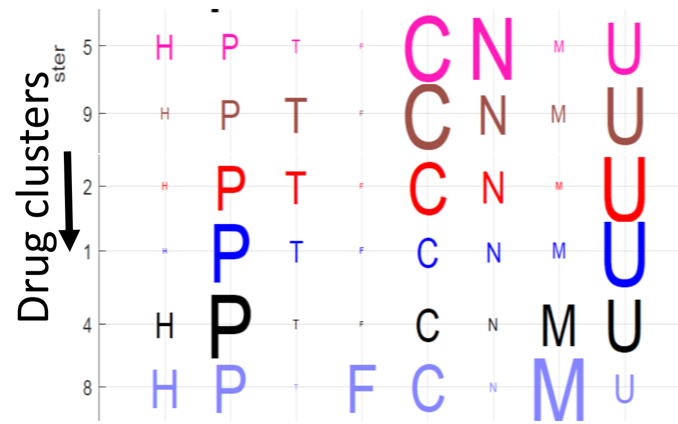
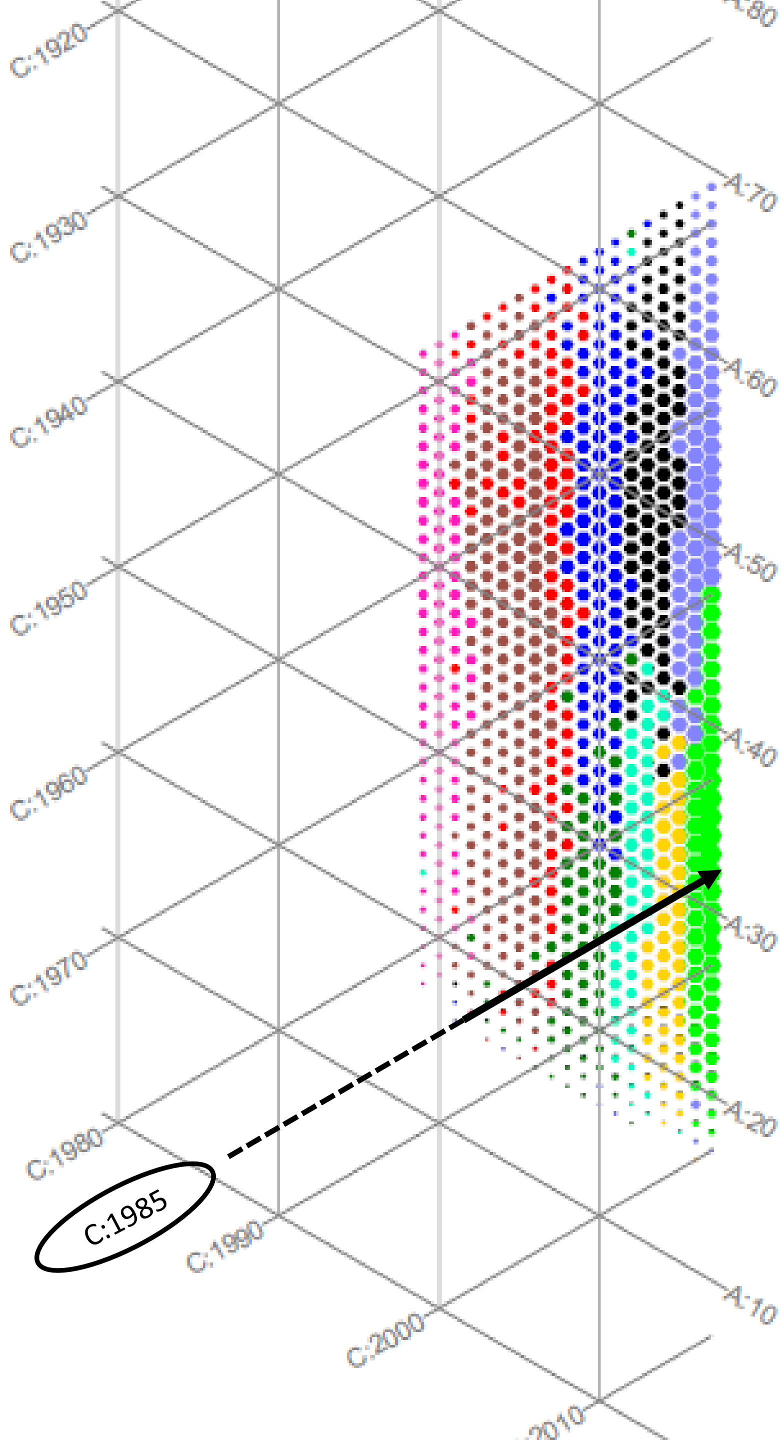

Within Cluster Percentage
0
1
2
3
4
5
6
7
8
9
10
%Heroin
%Presc. Opioid
%Methadone
Synth Op. OTM
%Cocaine
%Unspec. Narc
ethamphetamine
%Unspecified

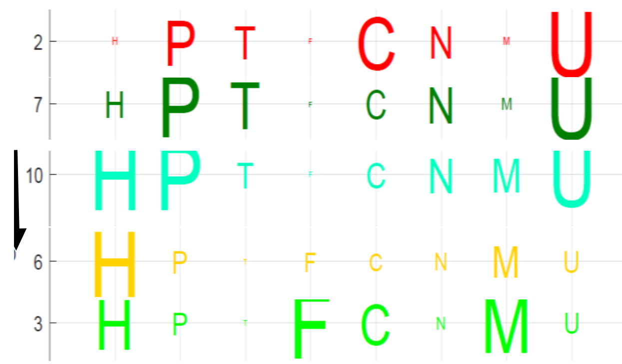


<u>1965</u> Birth Cohort / Sequential Drug Clusters
Pink->Brown->Red->Blue->Black->Purple

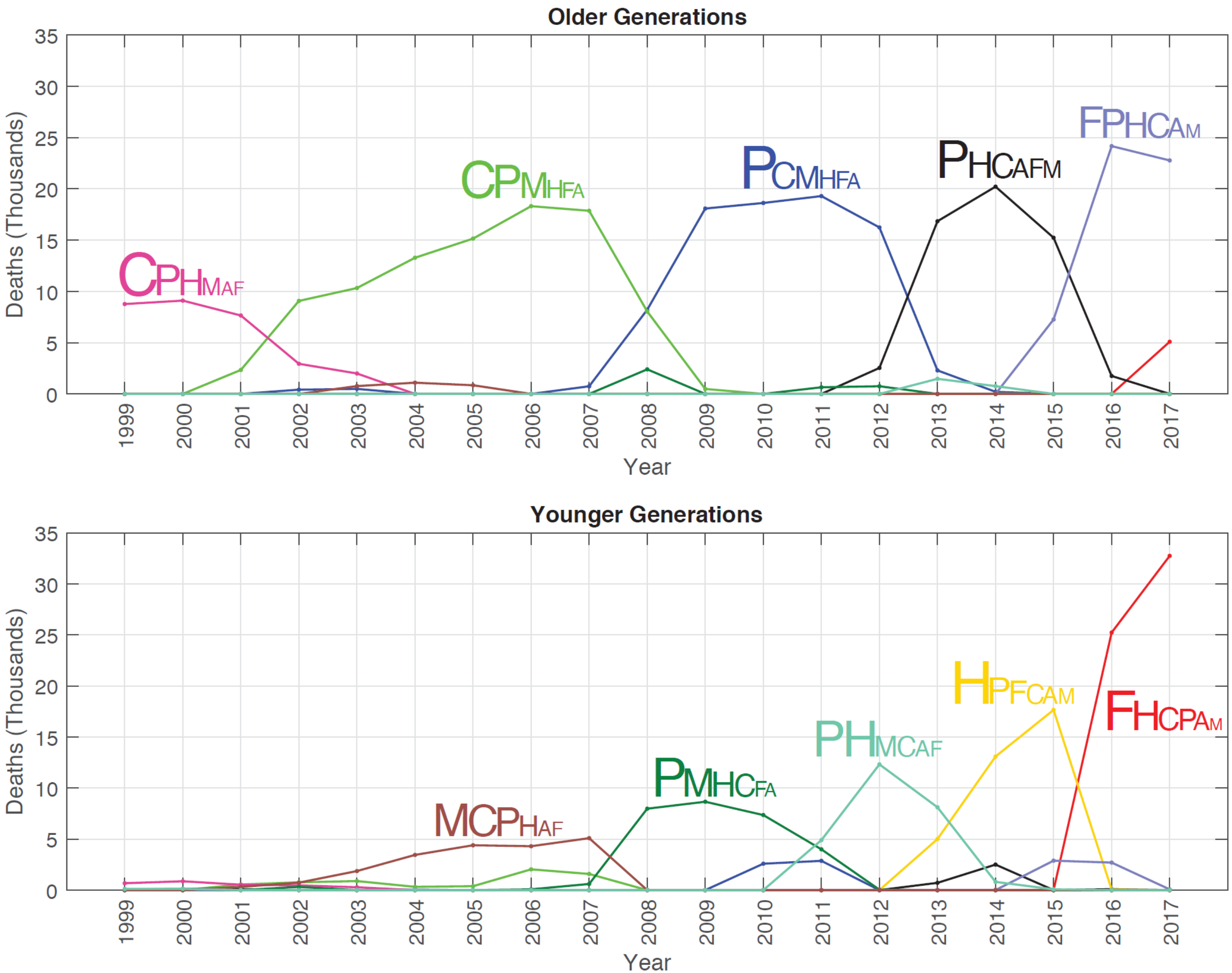




1985 Birth Cohort / Sequential Drug Clusters
Red->Olive->Turquoise->Yellow->Chartreuse



Statistically Defined Wave Structure of the Overdose Epidemic



Observation set #3

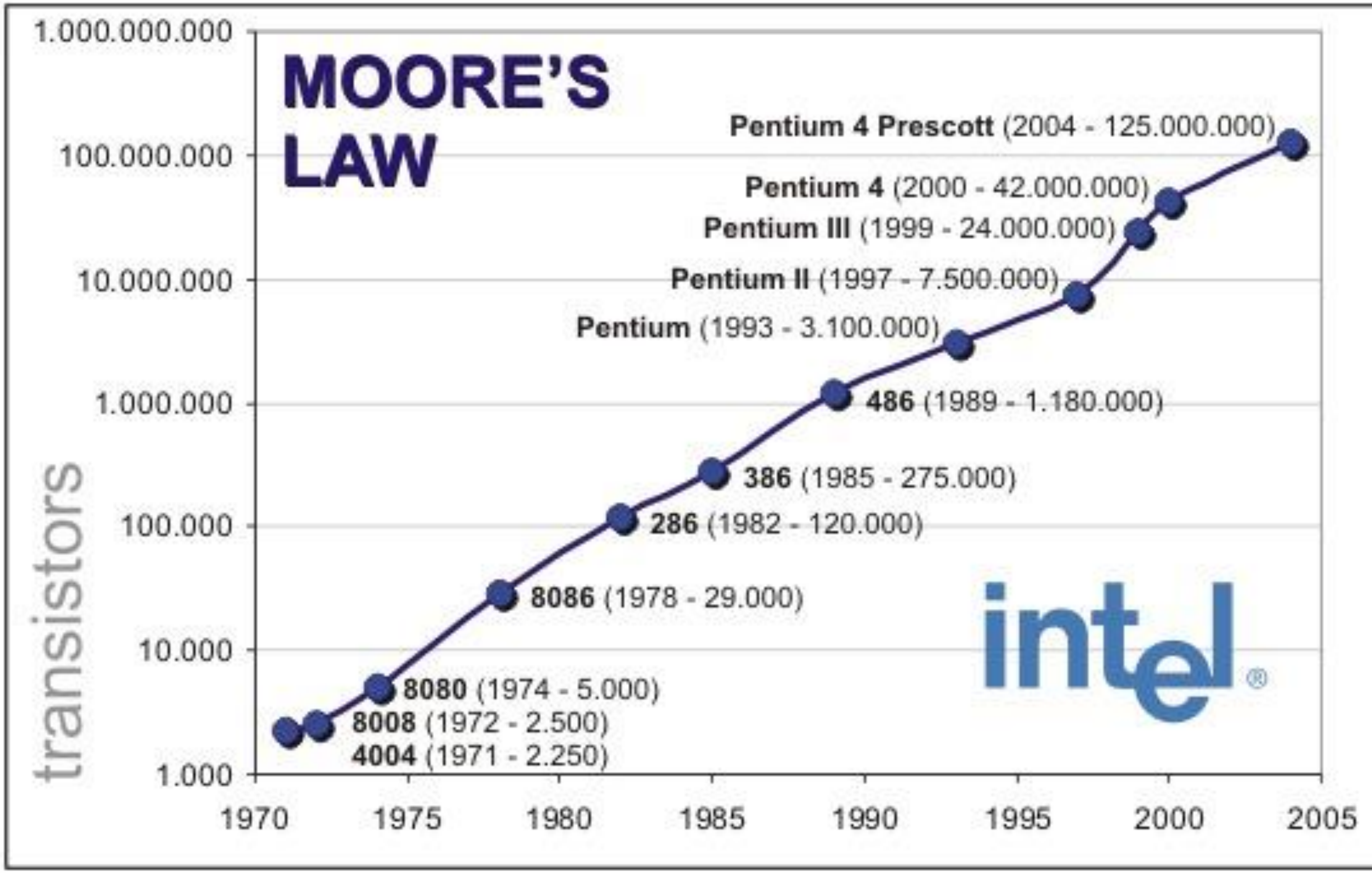
The slowing of the epidemic growth by birth year cohorts around 1975 also marked a bifurcation in the epidemic. Drug patterns in overdose deaths differ between cohorts born before and after 1975

How did the Opioid Overdose Epidemic happen?

Paradox: The overall smooth and predictable epidemic curve of drug overdose deaths is composed of heterogeneous sub-epidemic processes

What forces are holding these sub-epidemics together ?

Moore’s Law: The number of transistors in a dense integrated circuit doubles approximately every two years



http://www.2020techblog.com/2016/03/at-intel-moores-law-unstables-as-intel.html

How did the Opioid Overdose Epidemic happen?

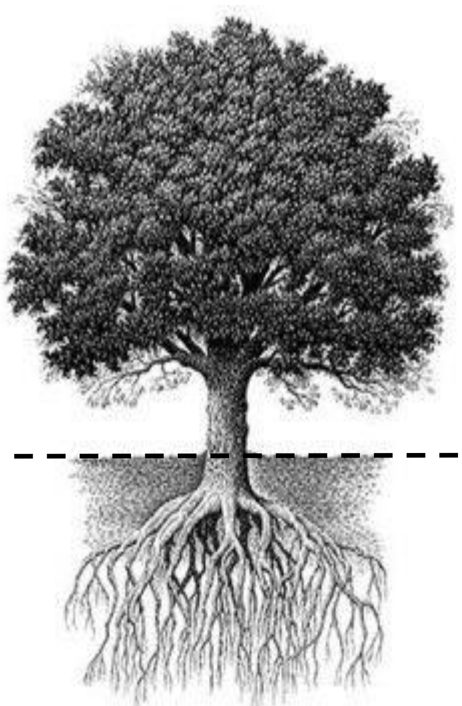
Advocacy for increased treatment of chronic pain

New higher dose drug formulations aggressively marketed

Cheap heroin supply introduced

Fentanyl replaced heroin

IMMEDIATE CAUSES



How did the Opioid Overdose Epidemic happen?

Advocacy for increased treatment of chronic pain

New higher dose drug formulations aggressively marketed

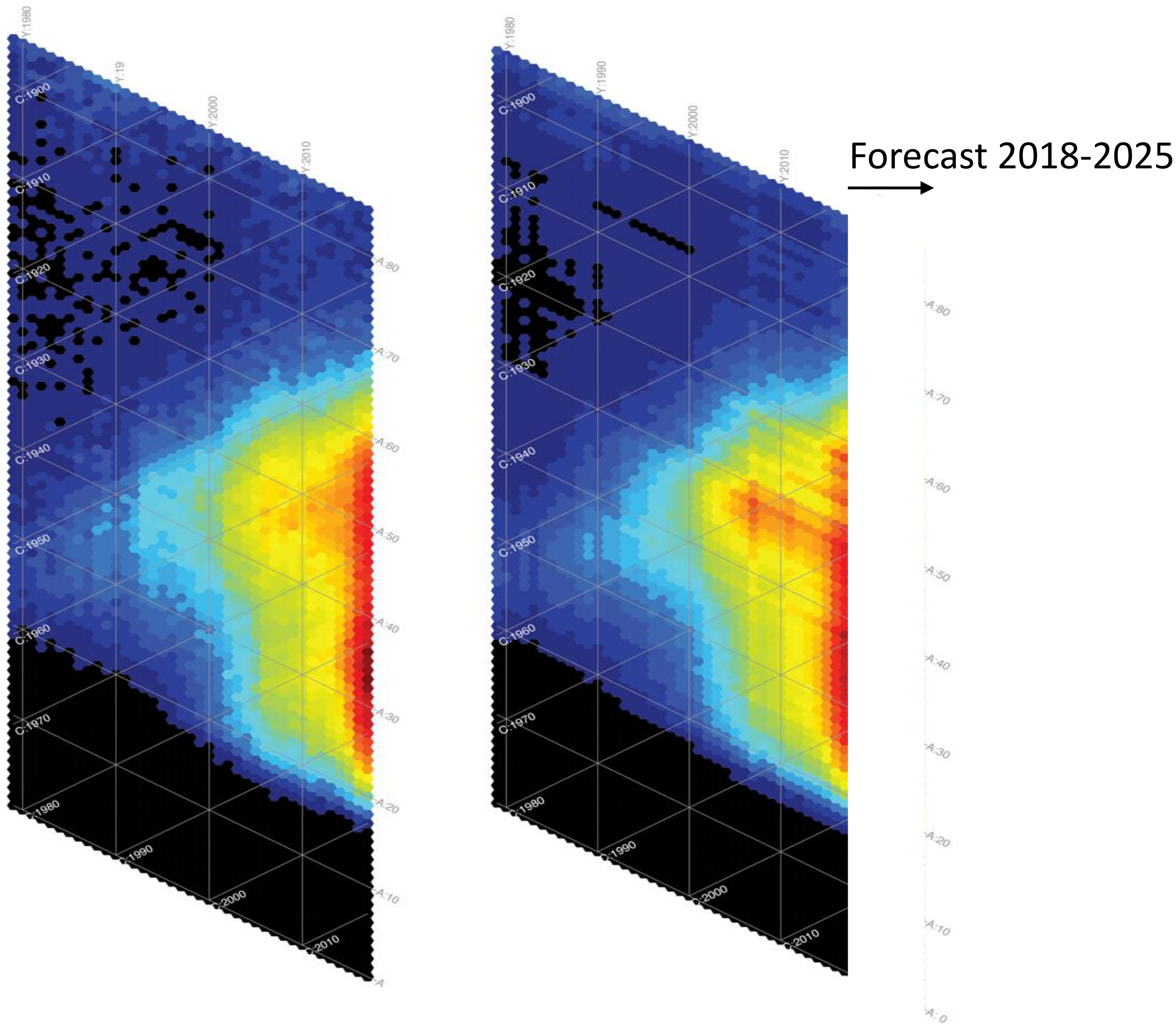
Cheap heroin supply introduced

Fentanyl replaced heroin

PUSH (Supply)	PULL (Demand)
Lower drug prices	Loss of sense of purpose

ROOT CAUSES

Forecast


Forecast 2018-2025

Agent Based Modeling

https://fred.publichealth.pitt.edu/cdc_opioids

FRED Software Simulations Publications Help Login Register

FRED Simulator for Opioid Use Disorder and Overdose

Application User Guide.

FRED (A Framework for Reconstructing Epidemiological Dynamics) is an agent-based simulation modeling system for exploring the spatial and temporal patterns of epidemics. In this application, we have incorporated a detailed representation of opioid use disorder (OUD) and overdose into FRED and have calibrated the model from multiple data sources relevant to each county represented. The disease model of OUD, representing possible disease states at an individual-level, is described in more detail here. The model currently estimates the impact of two evidence-based strategies for preventing opioid overdose deaths: 1) the provision of Naloxone, an opioid antidote that can reverse the effects of an opioid overdose, and 2) the availability of office-based buprenorphine as medication for opioid use disorder (MOUD). These two strategies are part of the HHS 5-point strategy to combat the opioid crisis.

In the current model, increasing the availability of naloxone at a county level decreases the probability that an individual will die from an overdose. Increasing the number of office-based buprenorphine prescriptions will increase the availability of MOUD, which will increase the probability that a person with OUD will enter treatment. In the model, individuals in treatment do not experience an overdose unless they relapse.

Please note that because there are multiple pathways among the disease states in the OUD model, a single intervention may impact multiple disease states. For example, increasing naloxone availability will not only decrease overdose deaths but also increase the number of agents (i.e., individuals) in the disease state of OUD and the number of agents receiving MOUD treatment.

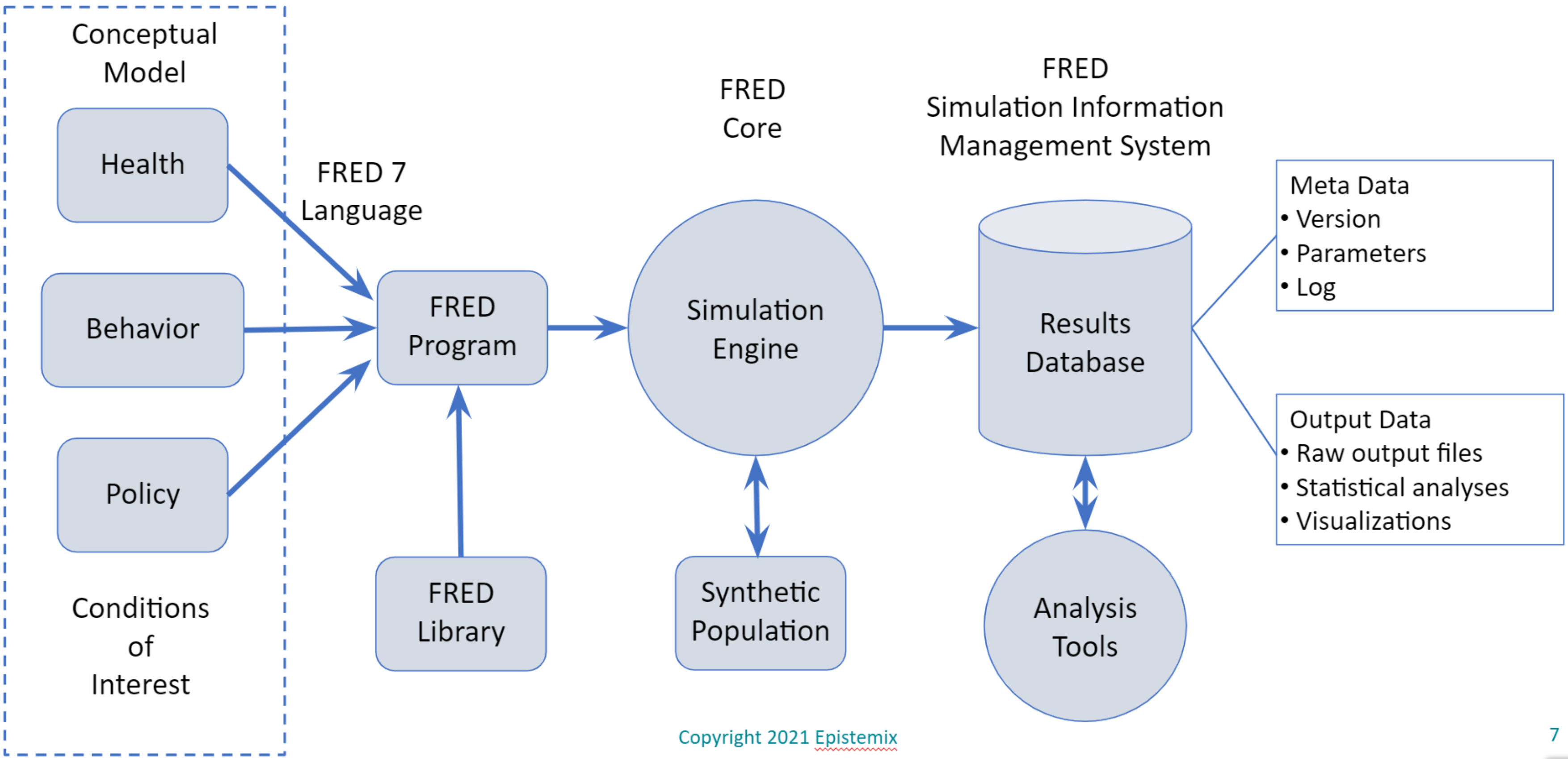
Below, you can choose a state/county to simulate the impact of the two interventions considered on OUD prevalence and opioid overdose. The policy sliders, originally set to baseline levels, can then be used to select a desired level of intervention. The accompanying maps visualize the geographic locations of individuals with opioid use disorder and overdose deaths. The map on the left predicts the expected number of opioid deaths with the county's current levels of Naloxone and MOUD available, while the map on the right estimates the expected number of opioid deaths under the combination of Naloxone and MOUD selected in the policy sliders.

Opioid Overdose and OUD Simulation Model by County

Please select a State...

Please select a county

What is FRED?



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FRED Web (pitt.edu)

Carfentanil and the rise and fall | Carfentanil and the rise and fall | hsls - Bing | Carfentanil and the rise and fall | FRED Web

https://fred.publichealth.pitt.edu/cdc_opioids

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Pennsylvania

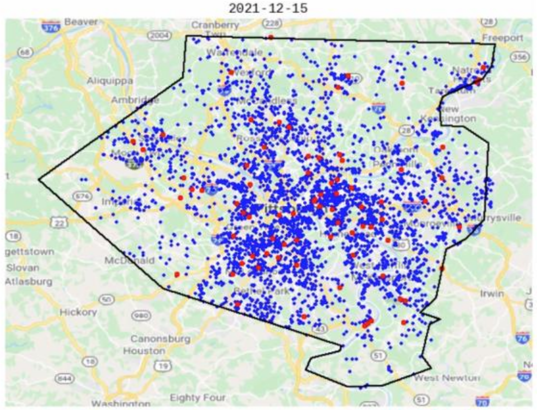
Allegheny

Total Naloxone Doses Available Annually at County Level	2,150 (baseline)	2,687 (+25%)	3,225 (+50%)	3,762 (+75%)	4,300 (+100%)
Annual Office Based Buprenorphine Prescriptions	216,610 (baseline)	270,762 (+25%)	324,915 (+50%)	379,067 (+75%)	433,220 (+100%)

Pause Simulation | Restart Simulation

Opioid Use Disorder & Opioid Overdose Death
Allegheny County, PA

2021-12-15



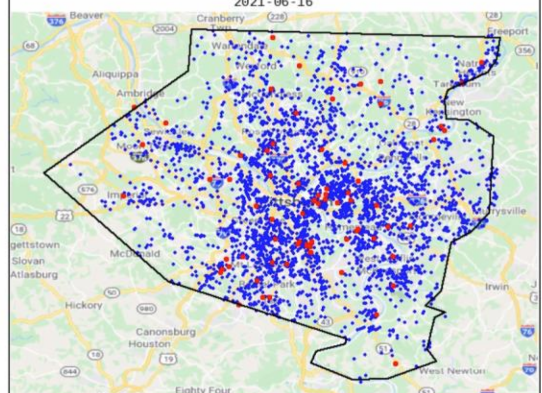
Opioid Use Disorder   Overdose Death

Over the baseline simulation period (2020 through 2024),

- 68,324 +/- 79 cases of opioid use disorder (mean +/- S.E.M.)
- 2,407 +/- 22 overdose deaths (mean +/- S.E.M)

Opioid Use Disorder & Opioid Overdose Death
Allegheny County, PA

2021-06-16



Opioid Use Disorder   Overdose Death

25% increase in naloxone and 50% increase in MOUD over the simulation period (2020 through 2024),

- 67,407 +/- 74 cases of opioid use disorder (mean +/- S.E.M.) (-1% change)

FRED Web v3.1.0, © 2019 Public Health Dynamics Laboratory, University of Pittsburgh

1:43 PM 3/30/2021

Conclusions

The drug overdose epidemic has been following a smooth and predictable exponential growth trajectory for four decades.

Paradoxically, the epidemic is composed of sub-epidemics that differ by drug, race, sex, and geography and that do not (thus far) show predictable patterns.

Age structure analysis shows that the overall epidemic can be seen as having three major components – the “boomer” start, the youthward bifurcation, and the recent fentanyl surge.

Forecasts based on historical patterns suggest continued exponential growth of the epidemic.

Some New Questions

How has the epidemic been held onto an exponential trajectory for almost four decades?

What accounts for the strong generational effects? Why did the “Boomer” generation kick of the epidemic? What gave rise to the generational pre/post 1975 birth year bifurcation in drug use and mortality patterns?

Do the socio-economic drivers and behavioral dynamics vary in parallel with drug use and demographic patterns?

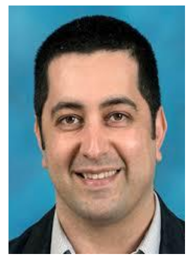
Is the national emphasis on prescription drugs addressing the younger half of the epidemic?

Through the use of computational analytics, modeling, and visualization, we can gain understanding the deeper social, economic, and behavioral drivers of the epidemic.

Increased understanding of these deeper drivers will lead to a sustainable reduction of substance use disorders and overdose deaths.

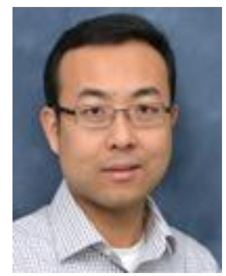
Thank you to my Colleagues / Co-authors

Hawre Jalal



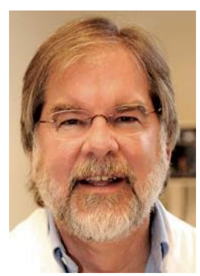
Lauren Balmert

Jeanine Buchanich



Kun Zhang (CDC)

Mark Roberts



David Sinclair


Thank you for
your attention
https://sites.google.com/site/mdpafganistan/project definition

The Boston Globe

WEDNESDAY, JUNE 28, 2017

Trying to recover, Bond decides best choice is jail

Drug treatment center won't take her after trial

By Maria Cramer

Rachelle Bond, a recovering heroin user who has already spent 22 months behind bars, had been expected to be set free, one day after her ex-boyfriend was convicted of killing her 3-year-old daughter.

But rather than face the temptations of life outside, she chose Tuesday to remain in jail after learning that a drug treatment center refused to take her, apparently because of her role in the notorious case.

"She has nowhere to go," her lawyer, Janice Bassil, told reporters.

"She does not want to be released to the streets," Bassil said. "Her goal right now is to stay clean and sober and get back on her feet."

Suffolk Superior Court Judge Janet L. Sanders postponed sentencing to July 12, in the hopes another opening at a drug treatment center would

BOND, Page A12

Deadly toll from opioids in US will only get worse, experts say

Worst-case projection is a huge jump during next decade; best case shows no decline for years

By Max Blau

STAT

Opioids could kill nearly half a million people across America over the next decade as the crisis of addiction and overdose accelerates.

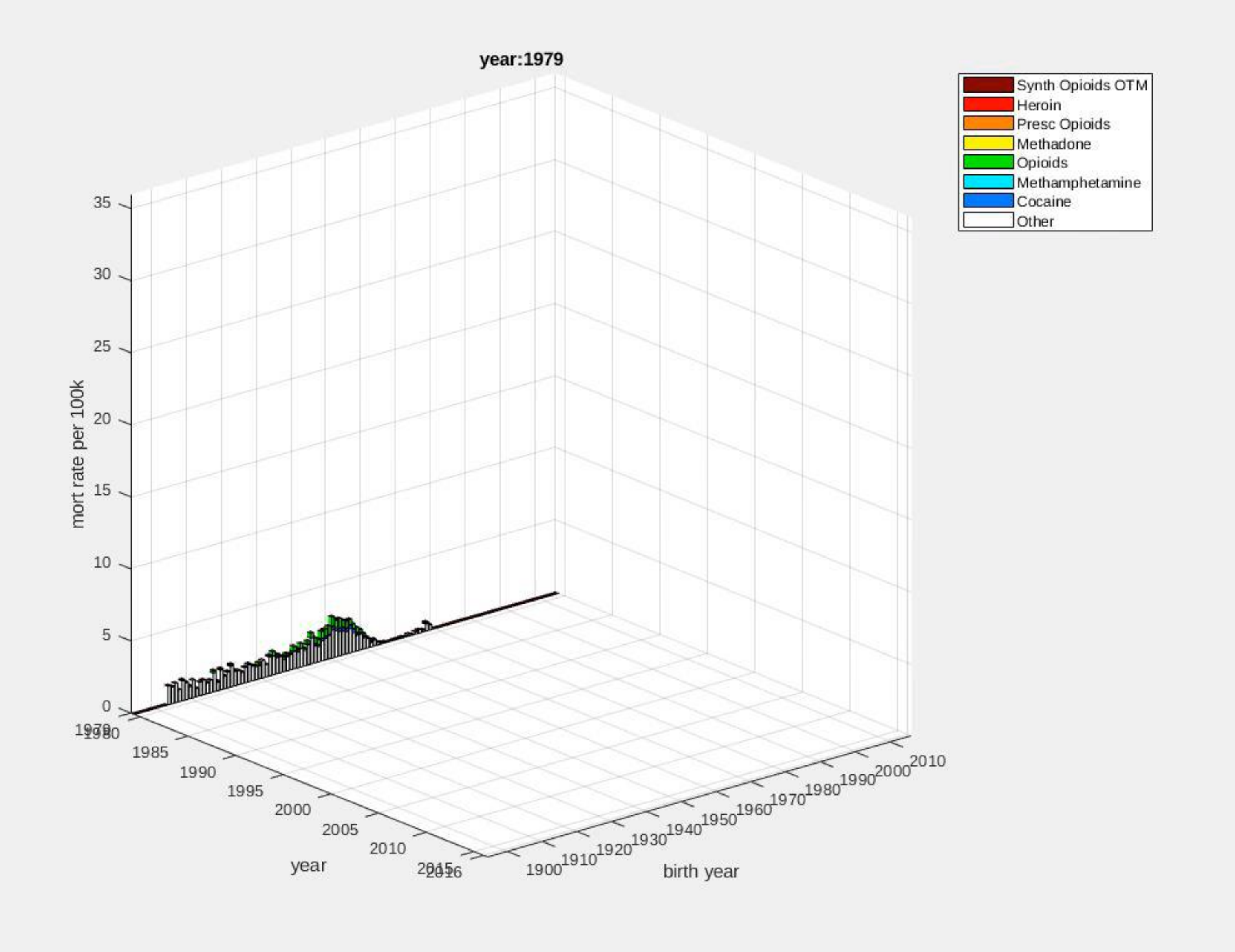
Deaths from opioids have been rising sharply for years, and drug overdoses already kill more Americans under age 50 than anything else. STAT asked leading public health experts at 10 universities to forecast the arc of the epidemic over the next decade. The consensus: It will get worse before it gets better.

There are now nearly 100 deaths a day from opioids, a swath of destruction that runs from tony New England suburbs to the farm country of California, from the beach towns of Florida to the Appalachian foothills. In the worst case scenario put forth by STAT's expert panel, that total could spike to 250 deaths a day, if potent synthetic opioids like fentanyl and carfentanil continue to spread rapidly and the waits for treatment continue to stretch weeks in hard-hit states like West Virginia and New Hampshire.

If that prediction proves accurate, the death toll over the next decade could top 650,000. The average toll across all 10 fore-

OPIOIDS, Page A6

Facing defeat, GOP pulls back



year:1979
Synth Opioids OTM
Heroin
Presc Opioids
Methadone
Opioids
Methamphetamine
Cocaine
Other
mort rate per 100k
35
30
25
20
15
10
5
0
year
1985
1990
1995
2000
2005
2010
birth year
1900
1910
1920
1930
1940
1950
1960
1970
1980
1990
2000
2010