RGA

An increase in opioid misuse has contributed to a rise in overdose mortality, gaining the attention of the media, Hollywood, and legislators. RGA has analyzed the effects this growing epidemic has had on the United States. Using the Centers for Disease Control and Prevention's Multiple Cause of Death mortality data (MCOD), we have analyzed U.S. overdose mortality, aggregating experience data by several demographic characteristics to better understand the potential impact of opioid abuse on the insurance industry.

We have found:

- Opioid-related overdose mortality rates have steadily increased for all levels of education since 2005.
- Opioid-related overdose mortality rates are higher for men than women. However, rates for university-educated males decrease with age, while rates for university-educated females peak in middle age.
- Abuse of prescription opioids has been the main driver of opioid-related overdose mortality historically, but the increased use of heroin, fentanyl and other synthetic opioids caused a surge in opioid-related overdose mortality in the period from 2012 to 2017.
- While preliminary estimates of 2018 synthetic opioid overdose deaths are projected to rise, overdose mortality from heroin and prescription opioids are projected to fall, resulting in the first overall drop in opioid-related overdose mortality in over a decade.
- Opioid-related overdose mortality risk is heightened with the simultaneous use of benzodiazepines.

We have further explored the impact of opioids on all-cause mortality risk in the U.S. using a prescription history database that includes information on 12 million opioid prescriptions for 3.2 million individuals to better understand the relationship between the duration of the prescription and drug potency on all-cause mortality risk. This analysis excluded people who would likely not qualify for life insurance.
The prescription drug analysis showed:

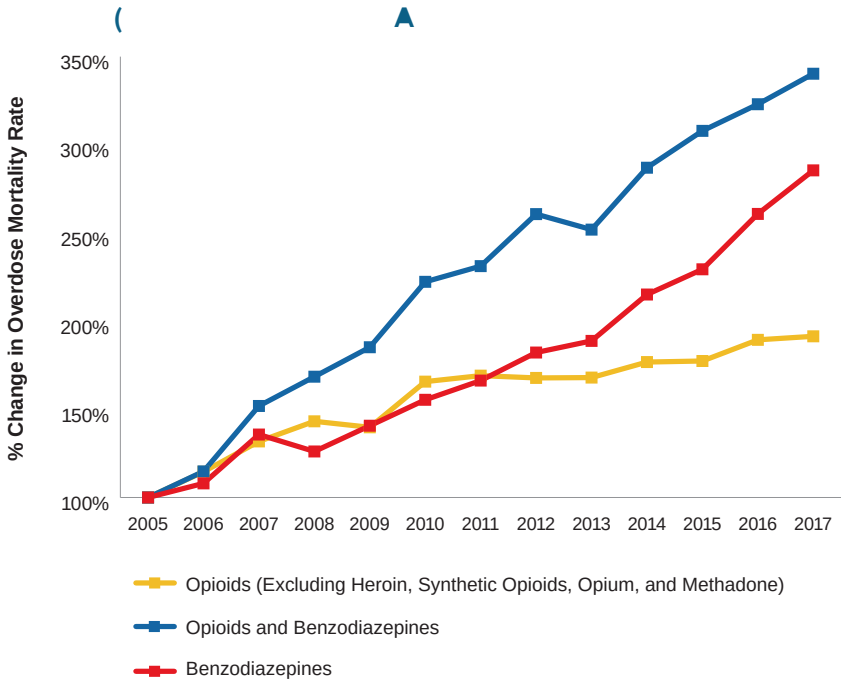
- Individuals who were prescribed opioids for more than 120 days over a two-year period and who had an average daily morphine milligram equivalent (MME) intake at or above the 90th percentile relative to others who were prescribed opioids for more than 120 days experienced 4.4 times higher all-cause mortality than the entire opioid-taking population.
- Regardless of prescription potency, an increase in the duration of the prescription is associated with an increase in all-cause mortality risk.
- All-cause mortality risk varies substantially by the type of opioid prescribed.
- All-cause mortality experience is worse for those who are prescribed benzodiazepines and opioids. Long-term, high-dose prescriptions of opioids alongside long-term use of benzodiazepines are associated with over 6 times worse all-cause mortality experience compared to those who use neither drug.

Rates of opioid-related overdose mortality are substantially higher among less educated Americans. While the insured population is likely less a□ected by opioid-related overdose mortality, the rise in opioid misuse and overdose mortality is impacting population mortality improvement trends and

Figure 3 shows that opioid-related overdose mortality rates vary by sex and age group in the university-educated population.

surrounding prescription drug misuse. Figure 5 shows how overdose mortality rates have changed between 2005 and 2017 for the university-educated population that is 25 years old or older by the presence of opioids, benzodiazepines, or both.

Figure 5



Source: RGA analysis of mortality data from the MCOD and population data from the U.S. Census Bureau.

**Population consists of United States civilian non-institutionalized population with bachelor's, master's, professional, and doctorate degrees. Excludes associate, vocational, and occupational degrees.*

In 2017, nearly half of opioid-related overdose deaths also featured a non-opioid narcotic as a contributing cause of death, and almost a quarter included multiple classes of opioids. [2] In particular, the sedative response from combining opioids and benzodiazepines has been linked to staggering overdose mortality; a study of individuals prescribed benzodiazepines and opioids simultaneously demonstrated overdose mortality rates 10 times greater than for those prescribed opioids alone. [10] Analysis of the MCOD shows that benzodiazepines were involved in about one-third of prescription opioid-related overdose deaths in 2017, with the proportion increasing from 21% in 2005. These statistics reveal an alarming link between the concurrent use of benzodiazepines and opioids and an elevated risk of overdose death.

Prescription opioids, which include drugs like OxyContin (oxycodone), Percocet (oxycodone and acetaminophen), Vicodin (hydrocodone and acetaminophen), and codeine, have historically been the leading contributing cause of opioid-related overdose deaths in America. Prescription opioids are a common treatment for pain in the U.S. and are generally prescribed for pain attributed to surgery recovery, childbirth, cancer, and chronic conditions. While prescription opioids are an approved and e□ective treatment for pain, they are highly addictive, particularly when taken for longer durations and in higher dosages.

There is a great deal of evidence that America's opioid problems were caused, at least in part, by the prescription and subsequent abuse and misuse of legal opioids. [4] Misuse of prescription opioids has been linked to abuse of heroin, fentanyl, and other synthetic opioids; according to a study published in the Journal of the American Medical Association, 75% of post-2000 heroin users initially used prescription opioids before moving to heroin. [11] Analyzing prescription drug history could provide insurers the opportunity to better understand the relationship between prescription opioid use and all-cause mortality experience.

To better understand the risks opioids pose to the life insurance industry, RGA analyzed the relationship between opioid prescriptions and all-cause mortality, using prescription history data. It is important to understand that this

The comparison of dosages across di erent opioids requires a standardized metric of opioid strength due to the di erent potencies of each specific opioid. For example, one milligram of morphine is equivalent in strength to 1.5 milligrams of oxycodone, one of the most popular prescription opioids. Throughout this analysis, the opioid dosage is converted to morphine milligram equivalent (MME), a commonly used standardized measure of opioid dosage using conversion factors released by the Centers for Medicare & Medicaid Services. [12]

The average MME consumed per day is calculated by comparing the total MME consumed by an individual in the two-year period to the total days' supply of opioids the individual received in the two-year period.

$$\textit{Average Daily MME} = \frac{\textit{Total MME in Two-Year Period}}{\textit{Total Days' Supply of Opioids in Two-Year Period}}$$

Previous research by the Centers for Disease Control and Prevention (CDC) indicates that daily MME consumption is strongly linked to increased risk of overdose death. [13]

This study classifies users into one of three groups based on the total days' supply of opioids prescribed in the two-year period. The majority of individuals had a short-term opioid prescription history, defined as a total days' supply of 30 days or less. This is likely the result of a single prescription fill. The other days' supply groups are comprised of individuals who were prescribed opioids more regularly and are designed to distinguish between moderate and long-term use. It is important to note that since we are not looking at an individual's entire prescription history, it is possible for opioid prescription experience to be misclassified if the opioid prescription history was significantly atypical during our two-year observation period. Figure 6 shows the percentage of total opioid users by total days' supply prescribed over the two-year observation period.

The analysis shows higher all-cause mortality experience for long-term opioid prescriptions, especially those with the highest strength prescriptions.

Figure 6

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1-30 days	81.2%
31-120 days	10.3%
121+ days	8.5%

81-90 PCTL

Average daily MME strength varies by the days’ supply group. Those with the highest number of days’ supplied also have higher-strength prescriptions. Interestingly, individuals with an opioid prescription duration between 31

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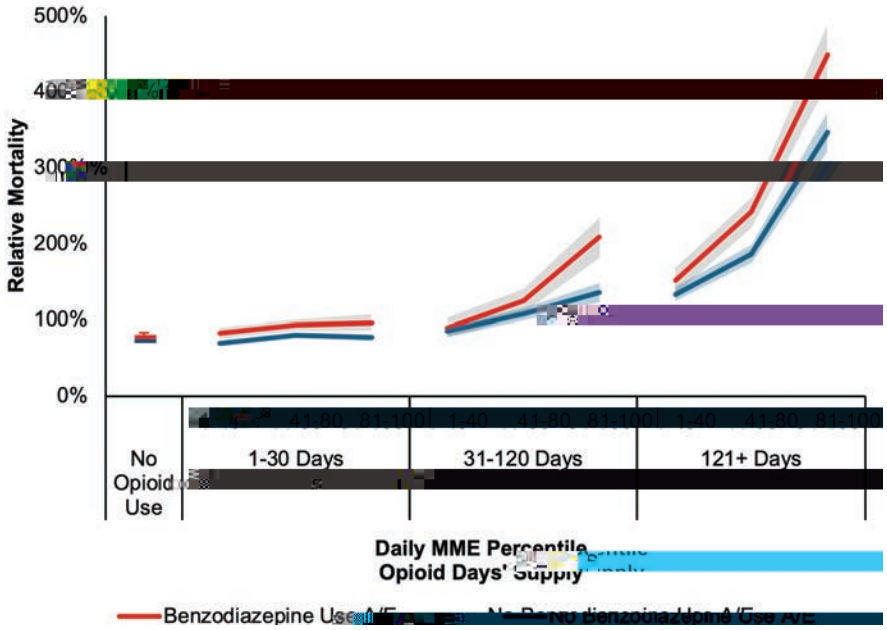
Although the potency of opioids can be standardized by converting to MME, there

Figure 10



All-cause mortality experience worsens with increasing prescriptions of both opioids and benzodiazepines. The prescription of 121+ days' supply of high-strength opioids alongside benzodiazepines is associated with nearly 6.2 times the all-cause mortality experience of individuals taking neither opioids nor benzodiazepines; people without a prescription of either drug type have a relative all-cause mortality risk 28% lower than those prescribed opioids. The concurrent use of opioids and benzodiazepines, especially at high levels of both drugs, is an important consideration for underwriters assessing an insurance applicant's risk.

Although the future scope and duration of the opioid epidemic are difficult to anticipate, there is reason for optimism: Preliminary 2018 reports from the CDC show a slight drop in opioid-related overdose mortality, ending a troubling decade-long rise. [15] That said, opioid-related overdose mortality rates remain near historically high levels, and a continued rise of synthetic opioid overdose mortality demonstrates that opioid misuse could continue to be a standard component of all-cause mortality experience in the future.

This rise of opioid-related overdose mortality in America is undoubtedly a challenge that threatens Americans of all socioeconomic statuses and age groups, albeit to different degrees. While there are certainly limitations with using age and education level aien473 (x)-71.3 (s)7 ((t)10.8 (t)3.8 ((r)-4 ar)11 -9.2 (t)-128.7 (r)-12 (a)-9.2 ()-16.3 (t)-5.3 (e)

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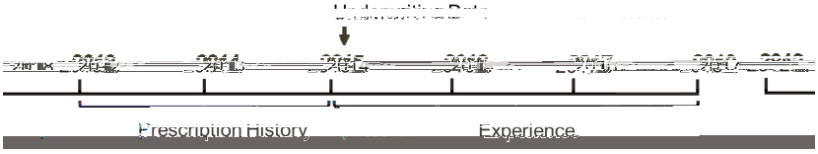
The study includes prescription history for 3.2 million people aged 30-69, totaling 12 million opioid prescription fills over a two-year period from January 1, 2013, to December 31, 2014. The analysis compares actual deaths of 15,571 people to expected deaths over the next three years (January 1, 2015, to December 31, 2017), where expected deaths account for age, gender, and calendar year. All experience is then standardized by the RGA Rx Severity Score.

In order to produce results that will be applicable to the insurance industry, our research was designed to replicate the time frame of an underwriting decision. Assuming an underwriting date of January 1, 2015, we looked back over two years of prescription history and analyzed the all-cause mortality experience over the next three years. Figure 11 provides a visual representation of this methodology.

Figure 11



Defining the Study Population

For the purposes of this analysis, an opioid user is anyone who had been prescribed any type of opioid between

1. National Institute on Drug Abuse. (2019, January). Overdose Death Rates. Retrieved December 11, 2019, from Trends and Statistics: https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates
2. National Center for Health Statistics. (2019). Retrieved from https://www.cdc.gov/nchs/index.htm
3. Felter, C. (2019, September 17). The U.S. Opioid Epidemic. Retrieved December 11, 2019, from Council on Foreign Relations: https://www.cfr.org/backgrounder/us-opioid-epidemic