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Opioid Use in Life Insurance Applicants

White Paper – November 2025

Optimum Re Life Research and Development – Biometric Risk

Executive summary

This study examines the prevalence of opioid and cotinine use among over 1.5 million life insurance applicants aged 20 to 80 and assesses associations with demographic factors and mortality risk. With support from ExamOne® and Brian Lanzrath, Director, Information and Analytics, ExamOne®, drug screening data were obtained and analyzed for codeine, morphine, methadone, and cotinine results, alongside age, sex, and survival information. Positive test results for codeine, morphine, and methadone were low but varied significantly by age and sex, with males more likely to test positive for cotinine and methadone, and females exhibiting higher odds of codeine presence.

Smoking status was strongly associated with greater odds of opioid presence. Cox proportional hazards models showed elevated mortality risks for codeine (HR = 3.61), morphine (HR = 5.97), and methadone (HR = 6.15). The multivariable model combining all drug types revealed attenuated risks for each individual drug but reinforced the need to look at the whole risk picture to understand the overlap in mortality among polysubstance users. These findings underscore the complexity of evaluating opioid-related mortality in a insured population and highlight the importance of comprehensive drug screening, especially for smokers given their higher opioid risk.

Layout

Introduction

Opioids are a class of drug that reduces the intensity of pain, which can be prescribed by doctors. Drugs such as codeine, morphine, and methadone are commonly used for therapeutic purposes (1), but they are also associated with potential misuse that can lead to substance use disorder. Opioid use disorder is defined in DSM-5 as a problematic pattern of opioid use within 12 months leading to significant impairment (2). In 2023, 2.2% of people aged 26 and older had an opioid use disorder (3,4). Opioid use disorder has been linked to increased risk of overdose and premature death (5). These risks are relevant not only in the general population but also in life insurance populations, where undetected opioid use can lead to underestimation of an applicant's risk, or worse, a premature benefit payout.

Existing literature focuses on opioid use among clinical populations yet less is known about the implication in non-patient populations. Life insurance applicants typically undergo medical examinations, including laboratory screening for drugs, as part of the underwriting process. Drug screening data from life insurance applicants offers an opportunity to study patterns of opioid use outside traditional clinical settings.

In the ExamOne® data, participants were tested for codeine, morphine, and methadone, which differ in their clinical uses and strength. Codeine is usually prescribed for mild pain or cough and is considered less potent. Morphine is stronger and often used to treat severe pain, especially in hospitals, but it has a higher risk of dependence. Methadone is a long-acting opioid used for chronic pain and to treat opioid addiction, though misuse can lead to overdose. These differences help set expectations for how common each drug may be and how their related health risks might compare in the insurance population.

The objective of this article is to describe the prevalence of codeine, morphine, and methadone testing results in insurance applicant population, describe the effects of age, sex, and smoking behavior related to opioid use; and to measure the mortality risk associated with opioid use.

Methods

Data was from ExamOne®, a Quest Diagnostics® company, which includes data collected from life insurance applicants at the time of underwriting. Variables include age, sex, and laboratory tests which include cotinine, codeine, morphine, and methadone. These tests were ordered based exclusively on the applicants' age and policy size, and not as a result of reflex testing. The testing period was from January 2001 to January 2019. Vital status is determined through the Social Security Death Master file, on matches by social security number and date of birth.

The initial sample included life insurance applicants of all ages. However, only 0.76% were below 20 years old, and 0.01% were above 80. Consequently, due to the lack of credible data, we restricted the analysis to participants aged 20 to 80.

Individuals with unknown sex or indeterminate laboratory test results were excluded from the analysis. A substantial proportion (24%) of the methadone results were missing due to the way the drug test was ordered by the insurance company. To address this, two separate datasets for analysis were created: one excluding and one including the methadone test. The initial data comprised 1,602,984 participants. After removing the missing data and applying the exclusion criteria, the first dataset (without methadone test) contained 1,576,262 participants, while the second dataset (with methadone test) consisted of 1,212,952 participants. Differences between participants with missing versus complete observations were assessed through t-tests or chi-square tests.

To analyze the effects of age and sex, we utilized binomial linear modeling with test results (positive or negative) as the dependent variable, and age and sex as the independent variables. Models were fitted using both continuous age and age grouped into categories (5-yr age interval). Since we have data on cotinine, we also examined the relationship between smoking behavior and test results for codeine, morphine, and methadone.

Survival analysis was conducted using the Cox proportional hazard regression. Separate models were estimated for each test, with test results as the primary exposure and age and sex included as covariates. Additionally, we constructed a combined model to evaluate the association between mortality risk and all four test results simultaneously.

All analyses were done in R version 4.5.0, with packages such as dplyr, tidyverse, ggplot2, survival, and survminer.

Results

Table 1 shows the descriptive statistics of the first dataset (without methadone) and second dataset (with methadone). For a detailed descriptive statistic of test results based on sex and age group, see Appendix Table 1.

Table 1: Basic Characteristics of the Study Population

	Female n=521,724	**Male** n=697,232	P-value*
Age (years), mean (SD)	36.0 (7.8)	37.5 (7.9)	<0.001
Deaths (n)	1,583	4,181	
Cotinine (%)			
Positive	5.36%	10.29%	<0.001
Codeine (%)			
Positive	0.12%	0.09%	<0.001
Morphine (%)			
Positive	0.08%	0.08%	0.853
Methadone (%)			
Positive	0.03%	0.06%	<0.001

*P comparing values from males and females, through chi-square or t-test.

As seen in Table 1, in this insurance population, positive test results for codeine, morphine, and methadone were low, whereas cotinine positivity was much higher.

Figure 1: Cotinine Prevalence Relative to Total Sample, by Age Group and Sex

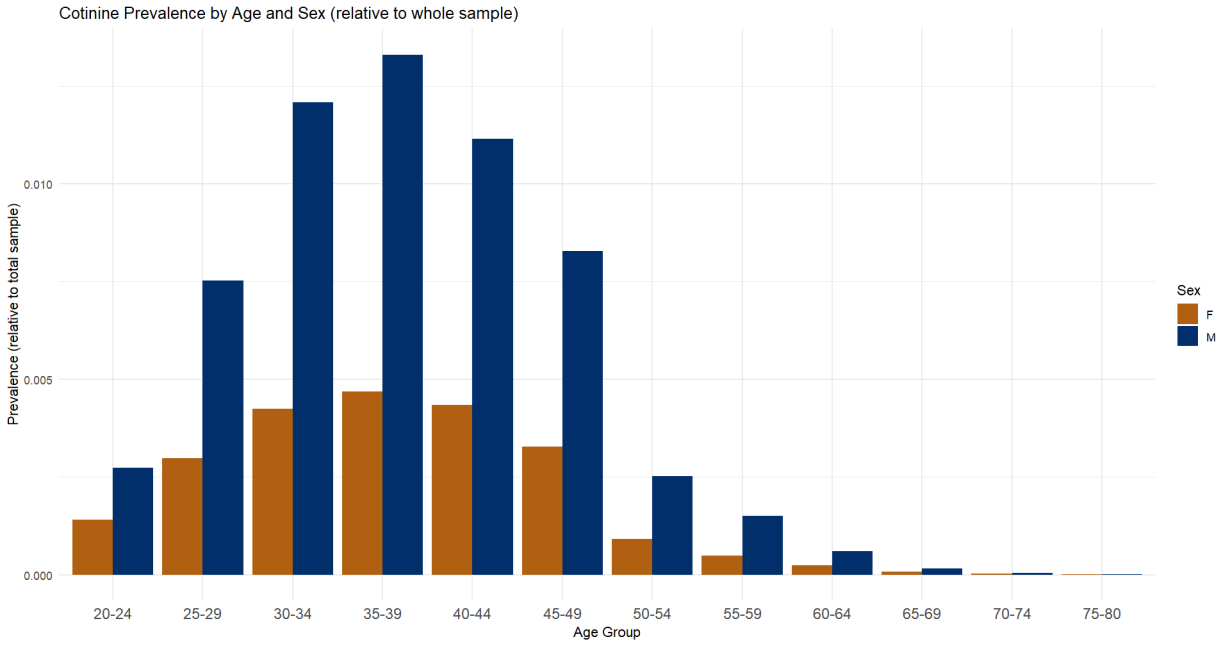
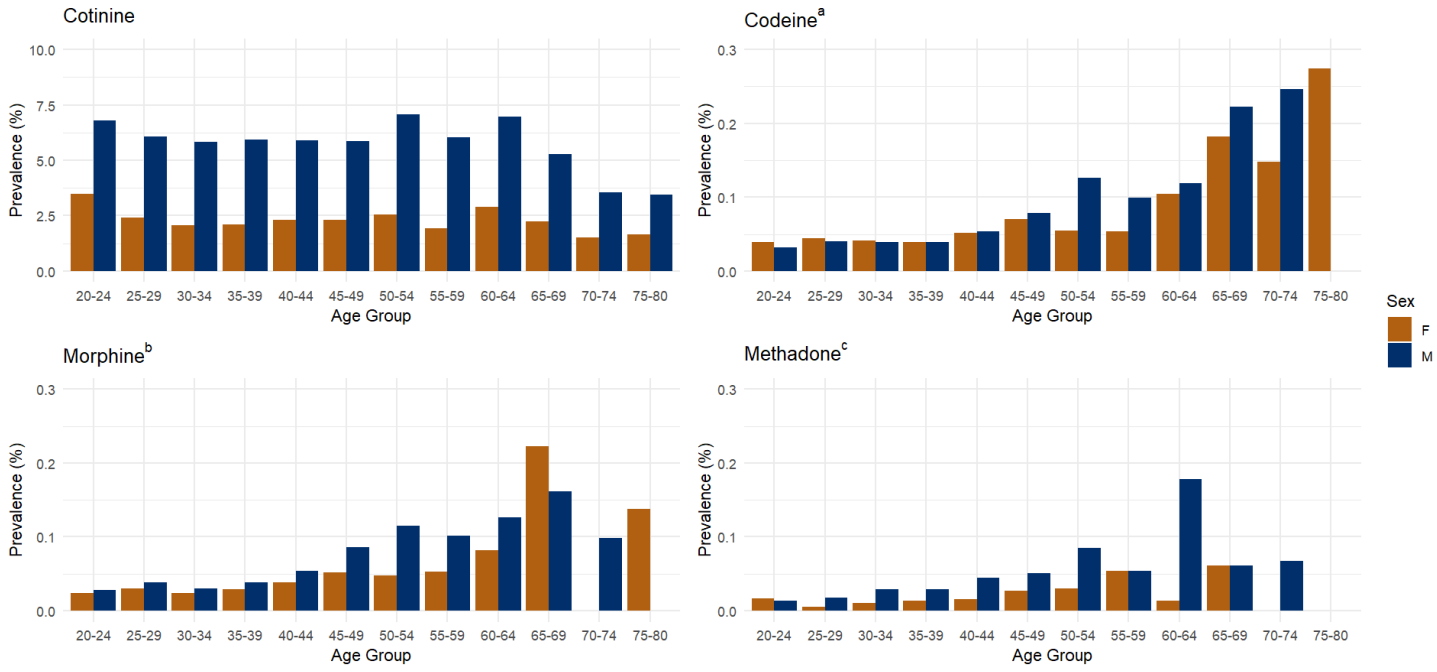


Figure 1 shows the prevalence of positive cotinine results by age group and sex, relative to total sample. In Figure 2, cotinine prevalence is quite constant by age group, only starting to decline for ages over 70. Males consistently show higher prevalence than females.

Figure 2: Prevalence of Positive Test Results, by Age Group and Sex



a) There were no males aged 75–80 who had a positive codeine test.

b) There were no females aged 70–74 who had a positive morphine test, and no males aged 75–80 who had a positive morphine test.

c) There were no females aged 70+ who had a positive methadone test, and no one aged 75+ had a positive methadone test.

Figure 2 also shows the prevalence of positive test results relative to age group and sex. In contrast with cotinine, codeine, morphine, and methadone prevalence increases with age. Because the number of positives is very small, some sex–age combinations had no cases, as noted in the footnotes.

Statistical analyses using t-tests and chi-square tests confirmed that positive drug test results are significantly associated with age and sex ($P < 0.001$), except for the association between sex and morphine, which was not significant.

Using generalized linear models, these relationships were further analyzed (Appendix, Table 2-4). Males have significantly higher odds for cotinine with a hazard ratio (HR) = 1.89 ($P<0.001$) and methadone (HR = 1.65, $P<0.001$) presence, but lower odds for codeine (HR = 0.68, $p<0.001$), compared to females. For morphine, males also showed lower odds, although this association was not statistically significant (HR = 0.90, P = 0.07).

Adding cotinine as a covariate shows that those with cotinine presence have higher odds of positive codeine (HR = 2.38, $P<0.001$), morphine (HR = 4.5,$P<0.001$), and methadone (HR = 10.6, $P<0.001$).

Younger age groups are more likely to have cotinine presence, but this is not the case for opioid presence. Middle to older age groups tend to have higher odds of opioid presence (Appendix, Table 2-5). However, estimates for older age groups, specifically age 65 and up, are unstable due to sparse data.

Cox proportional hazards models with age and sex as covariates were used to examine the association between positive drug test results and survival. In separate models for each drug (see Table 2), the mortality ratios (MR) indicated significantly increased risks.

Table 2: Survival analysis results

Results	Individual models				Combined models			
	n	deaths	MR[a]	P*	n	deaths	MR[a]	P*
Cotinine	1,576,262	10,986	2.81	<0.001	1,206,825	5,764	2.54	<0.001
Codeine	1,576,262	10,986	3.61	<0.001			1.45	0.162
Morphine	1,576,262	10,986	5.97	<0.001			4.11	<0.001
Methadone	1,212,952	5,771	6.15	<0.001			3.95	<0.001

[a]MR is the mortality ratio when the test is positive, adjusted for sex and age.

*P-value from Cox-proportional hazard models.

When combined into a single multivariable model including all drugs simultaneously, the HRs were attenuated but remained elevated for cotinine, morphine, and methadone, with statistically significant associations. This reduction does not imply that using multiple opioids is protective. It reflects the overlap in mortality risk among individuals testing positive for more than one substance. Part of the elevated risk observed in the individual models is shared among people who test positive for multiple drugs.

After accounting for this overlap, codeine's MR decreased to 1.45 in the combined model and was no longer statistically significant. These results suggest that while all positive drug tests are individually associated with increased hazard, when adjusted for each other, cotinine, morphine, and methadone remain independent predictors of hazard, whereas codeine does not. The combined model provides a more accurate estimate of the independent contribution of each substance, separating shared effects from those uniquely attributable to each drug.

Discussion

In this study, we analyzed two datasets to investigate opioid and cotinine presence and their associations with demographic factors and survival outcomes. Further analysis using generalized linear models revealed nuanced associations for both gender and age group.

As expected, positive rates for all three opioids were low. However, codeine showed a slightly higher prevalence, likely reflecting its more common therapeutic use.

Males had higher odds of cotinine and methadone detection, but lower odds of codeine presence compared to females. Prior research has shown gender differences in substance use patterns (6,7), with men generally more likely than women to use illicit drugs and tobacco/nicotine products. However, studies also note distinct patterns in prescription opioid use, where females may have higher exposure or prescription rates (8). This could explain the lower odds of codeine presence among males in our sample.

Younger age groups were more likely to test positive for cotinine, which aligns with prior research utilizing the National Survey on Drug Use and Health (2002-2018), which shows that tobacco use often begins in adolescence and peaks in young adulthood before declining in later life (9).

In contrast, opioid presence was more common in middle to older age groups. This aligns with literature as opioid use in this population may be more closely tied to medical or prescription-related factors rather than recreational use (10). However, our estimates for adults aged 65 years and older were less stable due to limited sample size and should be interpreted with caution. Further study is needed to verify patterns in that demographic.

Including cotinine as a covariate revealed strong positive associations with opioid presence, indicating a link between tobacco exposure and opioid use in this population. This aligns with prior research showing that smoking elevates the risk of opioid misuse, as nicotine use is often described as a "gateway" to illicit drug use (11,12).

Survival analysis using Cox proportional hazards models, adjusting for age and sex, demonstrated that positive drug test results were associated with mortality risk of more than 200%. When analyzed individually, each drug showed significant associations with increased hazard ratios, which is consistent with literature. However, our mortality risk is notably higher than prior studies.

This discrepancy may be explained by important differences in study populations and design. Most prior studies focus on patients with chronic noncancer pain receiving long-term opioid treatment, whereas our sample reflects an insurance population with potentially different exposure patterns and risk profiles. For example, a study looked at the all-cause mortality for patients with chronic noncancer pain who were prescribed opioids or alternative medication, found the HR for total mortality was 1.64 (13). Another study in South Korea found that long-term opioid use for chronic pain was associated with 1.21 times increase in all-cause mortality (14).

In a combined multivariable Cox model including all drugs simultaneously, the hazard ratios attenuated. This reduction does not suggest a protective effect of polysubstance use, as it reflects the overlap in mortality risk among individuals who test positive for multiple substances. The decrease of hazard ratios in the multivariable model not only validates the significance of polysubstance use but also points to the limitations of considering drugs in isolation when evaluating mortality risk.

The lower hazard ratio for codeine in the multivariable model is unsurprising, given its lower potency and wider use compared to morphine and methadone. More noteworthy is the fact that morphine and methadone have similar hazard ratios, despite morphine's association with severe pain management and methadone's use primarily in maintenance therapy or chronic pain. This similarity may indicate shared underlying vulnerabilities among users of these drugs, such as co-occurring substance use.

From an insurance perspective, these findings highlight the importance of polysubstance detection during the underwriting process. Testing that captures a broad panel of substances will allow underwriters to identify applicants with elevated risk profiles more precisely. Furthermore, our results suggest that smokers are at higher risk of opioid use, which may prompt insurance companies to update their guidelines for drug screening among smokers.

The limitation of this study includes the small sample size of those age 65 and up as well as the exclusion of those age 20 and below. In addition, our models can be further improved by incorporating more covariates such as sociodemographic variables which have been proven to be highly associated with drug use. Accounting for these social determinants of health could improve model accuracy, enable a better understanding of underlying risk factors, and improve predictive performance for subpopulations within the insurance population.

Another important limitation is that commonly used opioids, such as oxycodone and fentanyl, were not assessed. Although not routinely detected in life insurance testing, these opioids remain present, with risks increasing over time. Future studies should consider incorporating broader population-level data on these opioids.

Conclusion

This analysis reveals significant demographic patterns in drug test positivity within the insurance population and their strong implications for survival outcomes. It emphasizes the critical importance of comprehensive drug screening encompassing multiple substances during the underwriting process. Moreover, our findings suggest that insurance companies may want to review their drug screening protocol to account for the increased risk of opioid use among smokers.

Acknowledgement

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Appendix

Table 1: Basic Characteristics of the Study Population, by sex and age group

	Female					Male				
	20-34y	35-44y	45-54y	55-64y	65-80y	20-34y	35-44y	45-54y	55-64y	65-80y
Data 1: without methadone, n = 1,576,262										
Age (years), mean (SD)	36.0 (7.8)					37.5 (7.9)				
Count (%)	272,192 (42.8%)	254,272 (39.9%)	92,280 (14.5%)	14,503 (2.3%)	2,756 (0.4%)	312,646 (33.3%)	397,674 (42.3%)	186,576 (19.8%)	38,424 (4.1%)	4,939 (0.5%)
Deaths (n)	495	864	857	396	120	1,088	2,581	2,709	1,586	290
Cotinine (%)										
Positive	5.00%	5.60%	7.16%	7.91%	5.59%	11.26%	9.69%	9.13%	8.63%	7.25%
Codeine (%)										
Positive	0.10%	0.11%	0.20%	0.24%	0.51%	0.07%	0.08%	0.13%	0.14%	0.32%
Morphine (%)										
Positive	0.05%	0.09%	0.15%	0.22%	0.44%	0.06%	0.07%	0.14%	0.15%	0.20%
Data 2: with methadone, n = 1,212,952										
Age (years), mean (SD)	36.0 (7.8)					37.5 (7.9)				
Count (%)	234,838 (45.4%)	208,070 (40.2%)	66,371 (12.8%)	6,665 (1.3%)	1,835 (0.4%)	312,646 (33.3%)	397,674 (42.3%)	186,576 (19.8%)	38,424 (4.1%)	4,939 (0.5%)
Deaths (n)	370	594	457	129	35	776	1,691	1,244	368	107
Methadone (%)										
Positive	0.02%	0.04%	0.08%	0.11%	0.11%	0.05%	0.06%	0.08%	0.16%	0.09%

Table 2: Generalized linear model results for cotinine, adjusted for age group and sex.

Covariates	Risk of having positive cotinine	P-value
Age group		
20-24 years	Reference	
25-29 years	**0.79**	<0.001
30-34 years	**0.71**	<0.001
35-39 years	**0.71**	<0.001
40-44 years	**0.71**	<0.001
45-49 years	**0.70**	<0.001
50-54 years	**0.80**	<0.001
55-59 years	**0.64**	<0.001
60-64 years	**0.85**	<0.001
65-59 years	**0.64**	<0.001
70-74 years	**0.42**	<0.001
75-80 years	**0.44**	<0.001
Sex		
Female	Reference	
Male	**1.89**	<0.001

Table 3: Generalized linear model results for codeine, adjusted for age group and sex.

Covariates	Risk of having positive codeine	P-value
Age group		
20-24 years	Reference	
25-29 years	**1.20**	<0.001
30-34 years	1.17	0.27
35-39 years	1.16	0.32
40-44 years	1.57	0.37
45-49 years	**2.25**	<0.005
50-54 years	**2.80**	<0.001
55-59 years	**2.38**	<0.001
60-64 years	**3.39**	<0.001
65-59 years	**6.11**	<0.001
70-74 years	**5.96**	<0.001
75-80 years	3.99	0.056
Sex		
Female	Reference	
Male	**0.69**	<0.001

Table 4: Generalized linear model results for morphine, adjusted for age group and sex.

Covariates	Risk of having positive morphine	P-value
Age group		
20-24 years	Reference	
25-29 years	**1.32**	<0.001
30-34 years	1.04	0.16
35-39 years	1.29	0.82
40-44 years	1.79	0.17
45-49 years	**2.70**	<0.005
50-54 years	**3.22**	<0.001
55-59 years	**3.05**	<0.001
60-64 years	**1.09**	<0.001
65-59 years	**7.55**	<0.001
70-74 years	1.93	0.37
75-80 years	2.66	0.34
Sex		
Female	Reference	
Male	**0.90**	0.068

Table 5: Generalized linear model results for methadone, adjusted for age group and sex.

Covariates	Risk of having positive methadone	P-value
Age group		
20-24 years	Reference	
25-29 years	0.72	0.28
30-34 years	1.29	0.35
35-39 years	1.35	0.26
40-44 years	1.85	0.02
45-49 years	**2.39**	<0.005
50-54 years	**3.54**	<0.005
55-59 years	**3.29**	<0.005
60-64 years	**5.97**	<0.001
65-59 years	3.73	0.02
70-74 years	2.05	0.49
75-80 years	0.00	0.94
Sex		
Female	Reference	
Male	**1.64**	<0.001

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OPTIMUM RE INSURANCE COMPANY

1345 River Bend Drive, Suite 100
Dallas, TX 75247, U.S.A.
+1 214 528-2020
+1 214 528-2777

www.optimumre.com
www.optimumre.com/linkedin