

MORTALITY ASSOCIATED WITH POSITIVE COCAINE TEST RESULTS



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Introduction

There is ongoing debate regarding the mortality risk associated with cocaine use because there has been no follow-up data available for populations similar to life insurance applicants. The currently available data is limited to populations treated for cocaine abuse, and populations identified in emergency rooms or by medical examiners at autopsy who tested positive for cocaine and/or its metabolites.¹⁻⁴ Risk associated with cocaine use in those without a history of substance abuse treatment or illness cannot be estimated from this data.

The most common complaints of cocaine users who come to emergency rooms are psychiatric (altered mental status, suicide attempts), cardiac (chest pains, palpitations or syncope) and neurologic (seizures).¹ Cocaine is the most common cause of chest pain in young adults presenting to emergency departments, and in the U.S. is the cause of 25% of myocardial infarction in people under 45 years of age.⁵ Cocaine also has been associated with hypotension, cardiac arrhythmias, sudden death, thrombotic stroke, hyperthermia, hallucinations and psychosis, as well as mortality associated with accidents.

In response to the perceived risk, life insurance applicants found to have cocaine metabolites in their urine samples may be declined or have their applications postponed for a period followed by retesting. When the retest is negative, these applicants may then be offered a policy with a temporary flat extra premium. Whether or not these approaches match the risk is unknown. To resolve this dilemma, the authors conducted a long-term follow-up mortality study of life insurance applicants who tested positive for cocaine.

Executive Summary *Current approaches to underwriting positive cocaine tests include decline or postponement followed by retesting and (if the retest is negative) assignment of a temporary flat extra premium. This study of over 4,500,000 insurance applicants followed for a mean of 11 years shows that the excess risk from cocaine use is moderately elevated and stable for many years, and is dependent on age, sex and smoking status; this calls into question these approaches. Those under age 60 have the highest prevalence and mortality ratios.*

How the Study Was Done

This study was performed on 4,574,562 insurance applicants ages 20 and over who had urine samples tested for cocaine at Clinical Reference Laboratory (CRL) between 1991 and 2000. In our analysis, a positive cocaine result was determined by the presence of cocaine's primary metabolite, benzoylecgonine. Cocaine itself has a very short half-life in the blood—about 1 hour.¹ Benzoylecgonine has a half-life of approximately 6 hours, and the window for detection in urine is about 1 to 2 days for the enzyme-linked immunoassay test that CRL uses to screen samples. The cutoff concentration for a positive urine test is 150 ng/mL. All positive tests are confirmed with gas chromatography with mass spectroscopy (GC/MS).

Mortality follow-up of applicants was done in 2008, utilizing the Social Security Administration Death Master File—we found 140,496 deaths within our study population after a mean of 10.93 years (range 0 to 17) of follow-up. Because prevalence and excess risk associated with cocaine use varied by age, sex and cotinine status, we split analysis of the study population by those factors. We compared mortality results within the different sex and age groups by urine coti-

nine result, with a positive cotinine considered to be 200 ng/ml (0.2 ug/ml) or higher. Cotinine indicates current nicotine use, which is most often associated with tobacco use. Male nonsmokers provided the largest demographic group in our study, allowing analysis by 10-year age groups. The other age-sex groups had fewer deaths, so analysis was limited to two age bands (20 to 49 years, 50+ years).

We calculated mortality rates for male nonsmokers based on the number of people who died (numerator) and the total number of people in that subgroup (denominator). From these rates we calculated mortality ratios (MRs) and their 95% confidence intervals.⁶ Our MRs compared the mortality rate of a subgroup positive for cocaine divided by the rate of the reference group: those who were negative for cocaine. No outside reference group was needed because the study population itself provided sufficiently large numbers of cases to provide stable and representative benchmarks for comparison.

For the other age-sex groups, Cox regression was used to calculate the MRs and their 95% confidence intervals. Age was included as a covariate so that the broader age bands necessary because of fewer deaths did not skew the mortality results based on the uneven distribution of cocaine use between younger and older ages. The software used was PASW for Windows release 17.0.2.

What the Study Found

The MRs and excess death rates for positive cocaine status by 10-year age groups for male nonsmokers are listed in Table 1. MRs by age group (20 to 49 years, 50+ years) and cotinine status are shown in Table 2 for females and Table 3 for males. Figures 1 and 2 show the prevalence and MRs for positive cocaine tests by 10-year age group for male nonsmokers. Using life table methods, Figure 3 shows cumulative survival for male nonsmokers by cocaine status for ages 20 to 29 and 40 to 49 to illustrate the survival trends seen in all of the 10-year age groups.

Our results demonstrate that positive cocaine status in individual life insurance applicants carries an increased mortality risk relative to those negative for cocaine, with the highest relative risk at the youngest ages. The prevalence of positive cocaine use among life insurance applicants also decreases with age. In comparison with the general population, the prevalence of positive cocaine detected among young males who apply for life insurance (.30% for ages 20 to 29, .30% for ages 30 to 39) is about half of the reported

current use of cocaine among the general U.S. population ages 26 and up (.7%).⁷

When cocaine status is examined by tobacco use (as indicated by urine cotinine), the relative risk of mortality is lower in cocaine-positive smokers than cocaine-positive nonsmokers, while the prevalence of cocaine use is higher among smokers than nonsmokers.

The level of mortality risk for positive cocaine tests over time is shown by the survival results for male nonsmokers in Figure 3. For each age group, the mortality ratio for cocaine users relative to nonusers is consistent as time goes on. There is little change in the pattern of survival between early and later years after the detection of cocaine, up to 16 years after detection was made.

What Do the Study Results Contribute to Risk Assessment?

This is the first publication that looks at the actual long-term mortality risk from cocaine use in an insurance applicant population (or in any general population). The relative mortality ranges from about 500% for male nonsmokers ages 20 to 29 to a nonsignificant difference for female smokers ages 50 and up. When combined with the prevalence data, it is apparent that testing for cocaine below age 60 has by far the greatest impact in reducing exposure to excess mortality risk.

Among male nonsmokers, the risk associated with cocaine use as measured by relative mortality (MRs) decreases with age, but the excess deaths increase with age up to age 70. Both approaches require banding by age to accurately express the risk. It is also clear from the life table survival analysis of the male nonsmokers (similar to other groups, data not shown) that the additional mortality risk is relatively stable for 16 years when expressed as a mortality ratio, although the number of deaths are limited after 10 years of follow-up in our study.

The reduction in relative mortality risk for cocaine use for smokers when compared to nonsmokers may be an indication of mortality attributable to a "lifestyle" risk that is common to both cocaine users and smokers. Despite this overlap, excess mortality was still found among cocaine-positive smokers, indicating additional risk associated with cocaine use.

A commonly used approach for life insurance applicants with a positive cocaine result is postponement

for a period of time, followed by retesting. When the retest is negative, the applicant may be accepted with a temporary flat extra premium that is identical for all applicants. Other typical actions include immediate declination of the risk at the time of the initial positive cocaine result. Our study found that the excess risk in the first year is similar to that in all subsequent years as measured by mortality ratios. Whether this reflects continued cocaine use or other associated lifestyle and substance use issues is uncertain from our data.

However, our findings call into question current underwriting approaches, and suggest the increased risk may be better approximated by an age-, sex- and cotinine-specific table rating or flat extra applied at the time of the initial application and maintained for at least 10 years. The extent of the risk shown in this study may be mitigated through underwriting review

taking into account other history, but the pattern of risk by age, sex, cotinine status and duration would be expected to be similar to what we have found.

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About the Authors

Vera F. Dolan, MSPH, FALU, Research Associate at Clinical Reference Laboratory, is a consultant specializing in underwriting research and product development. At CRL Vera assists with the analysis and publication of CRL's mortality study data. In her consulting practice, Vera develops risk assessment tools for underwriters, including underwriting manuals, as automated risk assessment systems and underwriter training. Vera provides litigation support for misrepresentation and other underwriting issues, as well as life expectancy calculations for use during litigation.

Vera has a BA in Public Health from the Johns Hopkins University, and a master's in Public Health in Epidemiology from the University of North Carolina at Chapel Hill. Vera was employed as an underwriting researcher at Lincoln Re and Transamerica Occidental Life before starting her consultancy in 1989. Vera is an Associate Editor of *ON THE RISK*, and regularly speaks to actuaries and underwriters on risk assessment topics.

Robert L. Stout, PhD, is President and Director of the Clinical Reference Laboratory based in Lenexa, Kansas. He completed undergraduate studies at California State University (Fullerton) and obtained a PhD in Biological Chemistry from UCLA School of Medicine. Since 1978 he has been directly responsible for introducing many of the new tests and procedures used in risk assessment such as urine and saliva HIV. Dr. Stout has produced nine patents over the last decade.

Dr. Stout has published numerous articles in the *Journal of Insurance Medicine* and *ON THE RISK*. He has made presentations to the Institute of Home Office Underwriters, the ACLI Medical Section, AAIM, the Home Office Life Underwriter's Association, the Canadian Institute of Underwriters, the International Underwriting Congress, ICLAM, the Impaired Risk Group and numerous regional underwriters associations. Dr. Bob is grandfather of three and an avid golfer, fisherman and gardener.

Michael Fulks, MD, Consulting Medical Director, analyzes, interprets and writes up CRL's mortality study results. Dr. Fulks is a graduate of the University of California at Davis, completing his residency at the University of Wisconsin and practicing for eight years before joining Allmerica in 1987. He became VP & Medical Director of Phoenix Life in 1989, working with its direct and reinsurance areas, group health and disability. Moving to Merrill Lynch in 1997, he developed an underwriting approach for its older age clientele. In 2001, he joined MassMutual creating its first electronic underwriting manual and updating its requirements, preferred programs and ratings. He moved home to northern California in 2005 and now mixes ranch work with consulting, including ongoing research work for CRL.

Mike has contributed to articles in the *Journal of Insurance Medicine* and *ON THE RISK* on laboratory testing. He regularly speaks to medical directors and underwriters on various topics including predictive value of testing and patterns of mortality in general and in relation to specific impairments ranging from coronary disease to hepatitis. Mike is board-certified in Insurance and Internal Medicine.

Table 1. Cocaine Mortality Rates and Ratios by Age Group, Male Nonsmokers*

Age Group (years)	Cocaine Status	Deaths	Total Applicants	Mortality Rate	Mortality Ratio (%)	95% CI** (%)	Excess Deaths per 1,000/year†
20 to 29	Negative (reference)	1,476	221,163	.00667	100		
	Positive	22	656	.03354	503	330-766	2.5
30 to 39	Negative (reference)	5,960	750,756	.00794	100		
	Positive	57	2,234	.02551	321	248-417	1.6
40 to 49	Negative (reference)	11,586	727,709	.01592	100		
	Positive	56	1,553	.03606	226	174-294	1.8
50 to 59	Negative (reference)	16,169	438,392	.03688	100		
	Positive	28	349	.08023	218	150-315	4.0
60 to 69	Negative (reference)	19,205	177,648	.10811	100		
	Positive	14	66	.21212	196	116-331	9.5
70+	Negative (reference)	15,065	53,885	.27958	100		
	Positive	5	14	.35714	128	53-307	7.1

* Urine cotinine <200 ng/mL

** See Reference 6

† Difference between positive and negative mortality rates multiplied by 1,000, divided by 10.93 years mean follow-up

Table 2. Cocaine Prevalence, Mortality Rates and Ratios by Age Group and Cotinine Status, Females

Cotinine Status	Cocaine Status	Deaths	Total Applicants	Cocaine Prevalence (%)	Mortality Ratio† (%)	95% CI† (%)
Females, 20 to 49						
<i>Negative*</i>	Negative (reference)	8,416	1,108,304		100	
	Positive	18	1,005	.09	233	147-370
<i>Positive**</i>	Negative (reference)	2,876	142,347		100	
	Positive	45	1,269	.88	202	151-272
Females, 50+						
<i>Negative*</i>	Negative (reference)	23,924	344,172		100	
	Positive	6	65	.02	269	121-598
<i>Positive**</i>	Negative (reference)	5,999	41,883		100	
	Positive	5	62	.15	91	38-220

* Urine cotinine <200 ng/mL

** Urine cotinine =>200 ng/mL

† Calculated with Cox regression including age as a covariate

Table 3. Cocaine Prevalence, Mortality Rates and Ratios by Age Group and Cotinine Status, Males

<i>Cotinine Status</i>	<i>Cocaine Status</i>	<i>Deaths</i>	<i>Total Applicants</i>	<i>Cocaine Prevalence (%)</i>	<i>Mortality Ratio† (%)</i>	<i>95% CI† (%)</i>
Males, 20 to 49						
<i>Negative*</i>	Negative (reference)	19,022	1,699,628		100	
	Positive	135	4,443	.26	279	235-330
<i>Positive**</i>	Negative (reference)	9,881	350,529		100	
	Positive	203	4,329	1.22	185	161-213
Males, 50+						
<i>Negative*</i>	Negative (reference)	50,439	669,925		100	
	Positive	47	429	.06	201	151-268
<i>Positive**</i>	Negative (reference)	15,736	110,596		100	
	Positive	56	361	.33	140	108-182

* Urine cotinine <200 ng/mL

** Urine cotinine =>200 ng/mL

† Calculated with Cox regression including age as a covariate

Figure 1. Prevalence of Positive Cocaine Results by Age Group for Male Nonsmokers

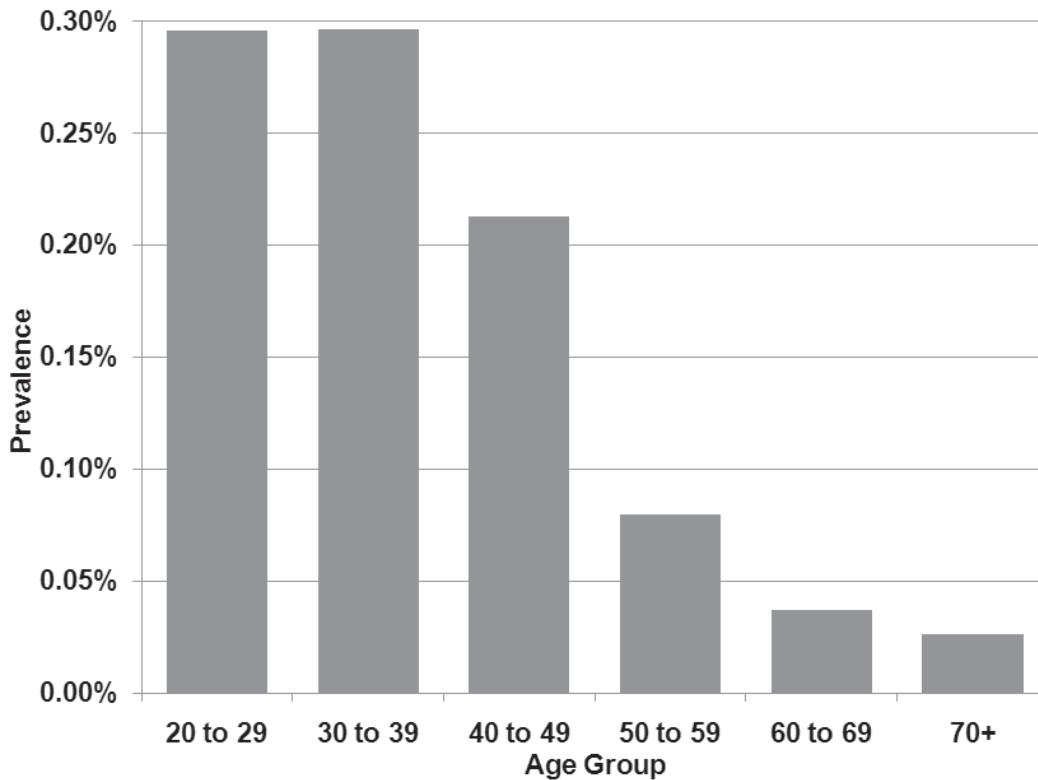


Figure 2. Mortality Ratios for Positive Cocaine Results by Age Group, Male Nonsmokers

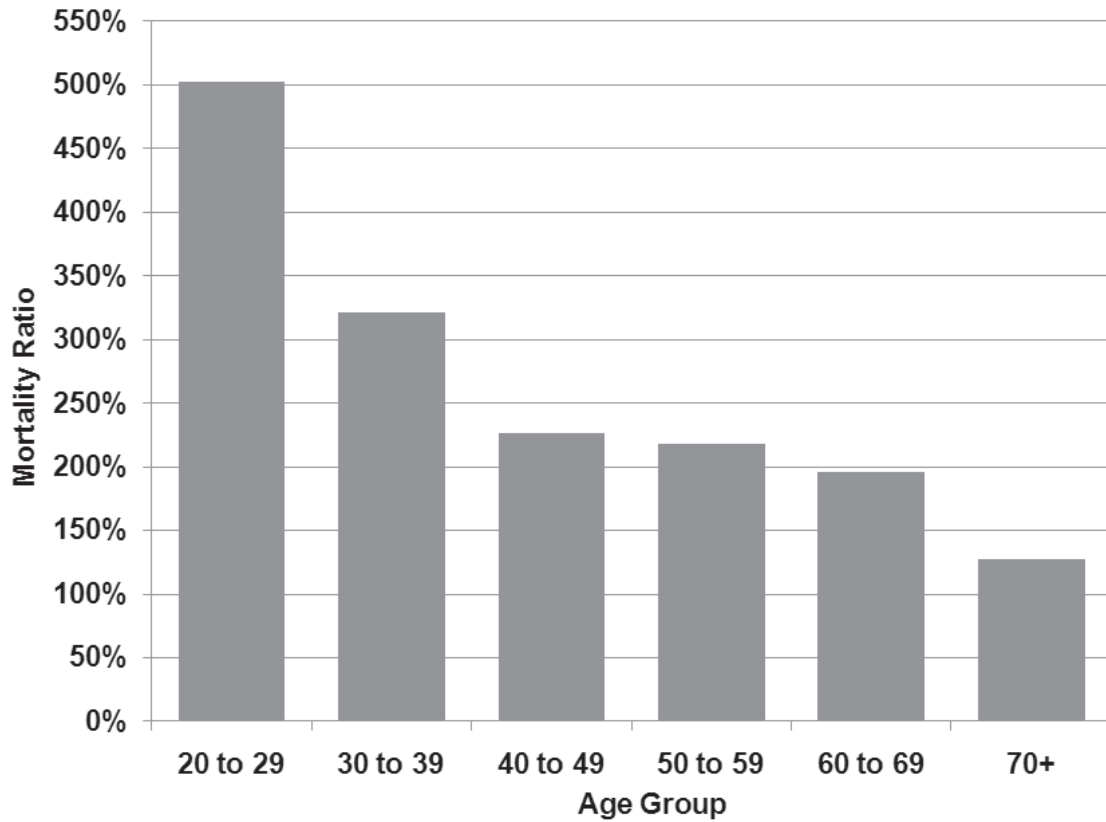


Figure 3. Cumulative Survival by Cocaine Status for Ages 20 to 29 and Ages 40 to 49 Years for Male Nonsmokers

