Drug and alcohol use has been associated with increases in risky sexual behavior (RSB), which increase the risk of contracting human immunodeficiency virus (HIV) and other sexually transmitted infections. Drug use is often hypothesized as a causal influence of RSB but there are limited scientific findings. This study examines the genetic and environmental etiology of the association between the use of drugs and alcohol during sexual decision-making (impaired sex) and number of lifetime sexual partners (partialed for age), a highly reliable measure of RSB. Participants included over 800 twin pairs from the University of Colorado Center on Antisocial Drug Dependence. Measures included a composite index of impaired sex (e.g., items assessing the frequency that drugs or alcohol affected sexual decision making), a quasi-continuous measure of lifetime sex partners, and a general measure of substance use. Results of a bivariate twin model indicated that there is some genetic confounding (e.g., genetic factors that influence both impaired sex and number of lifetime partners), which suggest that the association is not entirely causal. However, it is possible that individuals who use drugs and alcohol generally are more likely to both 1) have impaired sex, and 2) have higher numbers of sexual partners. When controlling for general substance use in a trivariate model, sex differences emerged. For females, genetic influences on general substance use were the same influences that explain the overlap between impaired sex and number of partners. For males, genetic influences on general substance use also predicted number of partners but did not significantly correlate with impaired sex. Shared environmental influences that increase impaired sex and higher numbers of partners in males also influences drug use, more generally. In conclusion, while using drugs and alcohol during sex does predict our measure of risky sexual behavior, our results suggest correlated genetic and shared environmental mechanisms that predict both behaviors.