# S3 Appendix. Estimating the drug-associated fraction

The procedure described in the main text for estimating the fraction of other deaths associated with drug use is equivalent to implementing the following formula:

 $A\_{-D}=1-e^{-β\_{D}^{'}\left(M\_{D}\right)}$ , (3)

where $β\_{D}^{'}=β\_{D}+β\_{Da} $(our estimated values of $β\_{D}^{'}$are given in Table 1). Thus, the coefficient in this expression, $β\_{D}^{'}$, includes the main coefficient of $M\_{D}$in Eq. 2 as well as the interactions between $M\_{D}$ and age. When $β\_{D}^{'}$ is positive, $A\_{-D}$lies between 0 and 1. Yet, at some of the oldest ages, $β\_{D}^{'}$ is negative (Table 1), which suggests a substitution effect (i.e., higher levels of drug-coded mortality are associated with lower levels of “other” drug-associated mortality). Such a substitution effect could result from interstate variation in reporting (e.g., medical examiners/physicians in some states may be more reluctant than in those in other states to ascribe a death to drugs). Since drug-coded mortality is highest in midlife, we focus most of our analysis on the age range 15-64, where $β\_{D}^{'}$is positive (in the model that includes both drugs and smoking).[[1]](#footnote-1)

Finally, the overall drug-associated fraction for deaths from all causes is a weighted average:

 $A\_{D}=\frac{D\_{D}+A\_{-D}D\_{-DL}}{D}$(4)

where $D\_{D}$, $D\_{-DL}$*,* and $D$ represent the observed number of drug-coded deaths, number of deaths from other causes of death except those coded to drug use or lung cancer, and deaths from all causes combined, respectively.

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1. In cases where $β\_{D}^{'}$was negative in the model that includes both drugs and smoking, the value of $A\_{-D}$ (representing the reduction in other deaths as a result of drug use) was between -0.02 and zero in 98.7% of cases. The only cases where $A\_{-D}$ was less than -0.05 occurred in Alaska among women aged 85+ in 1999; men aged 85+ in 2003 & 2012; and men aged 80-84 in 2008. The lowest value of $A\_{-D}$was -0.086 among Alaskan men aged 85+ in 2012. [↑](#footnote-ref-1)