SUPPLEMENTAL MATERIAL

Supplemental Methods

Population Estimates.

As described in the *Methods* section, we used two approaches to estimate the control population (i.e., the population who lived through the observation period or died from causes other than suicide and homicide). One was simply to use the 1990 census to estimate the population at risk during the 1990-2004 period. However, to allowed use of use period (year of death or census) as a covariate or stratification variable, we needed an estimate of the population for every year for which death certificate data was analyzed. This "time-averaged" sample was assembled by combining the 1990 and 2000 U.S. census samples with the 2004 American Community Survey sample. Prior to combing these three data sets, data for individuals that matched on all other covariates were aggregated into a single data row (record) and assigned a weight that corresponded to the number of people represented by that row. For example, all White women born in Alabama in 1953 who also matched on education and emigration status were represented as a single data row, with a weight variable used to reflect the number of people represented by that record. Records from the three single-year data sets were merged, and blank columns were created that corresponded to intercensal years, namely 1991-1999 and 2001-2003. Weights for those years were then imputed based on the assumption that population changes within each record were linear between each pair of years for which explicit population data was available.

Analytical Approach

Our analytical method is an extension of a classical "differences in differences" approach. In the classical approach, two groups are compared at two different points in time. One of the groups underwent an environmental change or treatment, while the other serves as a control to account for the effects of group and time, enabling an estimate of the treatment effect (Ashenfelter and Card, 1985; Snow, 1855). The logistic regression approach we use extends this method to multiple groups at multiple time points. In our case, the groups correspond to states, and time points correspond to birth years because state and birth year determine the MLDA policy to which a person was exposed. Therefore, state and year of birth are included in all models as fixed-effect categorical covariates (Equation 1 in *Results)*. State effects account for all time-invariant characteristics of each state, and birth year effects account for all state-invariant characteristics of each birth-year. Hence, as with the classical approach, this analysis compares states that underwent a policy change to states that did not undergo policy change. Measurements from both kinds of states from throughout the period of change contribute to estimates of the parameters of interest (Angrist and Pischke, 2008).

Supplemental Results.

We are interested in determining the degree to which the risk factor (exposure to MLDA<21) is correctly predicted using an individual's state of birth (S_{birth}) as a proxy for the state in which they were residing between ages 18 through 20 (S_{exp}). We also are interested in whether observed patterns in emigration from birth state resemble those that would be expected if migration were random with regard to policy of the destination state. As described in the body of the manuscript, this approximation can be evaluated using U.S. census data for people between the ages of 18 and 20 during the years 1970 and 1980. These subjects' ability to legally purchase alcohol was contingent on the state in which they were living. As described in the manuscript, MLDA exposures are correctly classified for 88.0% of subjects when it is assumed that $S_{exp} = S_{birth}$. But we are also interested in determining whether misclassifications are randomly distributed with respect to false positive and false negative exposure classifications. A "false positive" for example, is an observation for which the person was born in an MLDA < 21 state, and therefore classified as exposed to MLDA< 21 using birth-state as a proxy, but resided in an MLDA=21 state from ages 18 through 20. Misclassification occurs only in cases of migration – non-random or selective migration to states with respect to MLDA policy could bias effect size estimates in either direction.

The probability of exposure to the risk factor (MLDA<21) is defined as "$P_{x.}$" For the majority of subjects who reside in their state of birth when they responded to the census, risk factor assignment is always correct. For those who move, their risk factor exposure has a probability of being misclassified under the $S_{exp} = S_{birth}$ assumption, depending on whether they moved into a state where the laws differ from their native state.

The probability of moving from state of birth is defined as "P_{move}". The probability of moving may correlate with birth state MLDA for reasons unrelated to selective migration. For example, California is a large state with an above average rate of domestic in-migration and maintained an MLDA of 21 throughout the post-prohibition era. New York, on the other hand, is a large state with a low domestic in-migration rate during this period, and had more permissive MLDA laws. As we show below, low MLDA states had more movers than high MLDA states. Hence, using census data, we calculated P_{move} separately for each type of state, conditional on MLDA: $P_{move|x=0}$ and $P_{move|x=1}$. If we assume that the *direction* of the exposure change is random, we can then calculate *expected* prevalence of each exposure classification outcome – true positive, true negative, false positive and false negatvive – under conditions of random migration. These can then be compared with the observed classification prevalences.

To calculate the expected prevalence of true-positive exposure classification, we sum the number of individuals born in states with MLDA=21 who did not move, and those born in states with MLDA=21 who moved to other states with MLDA=21. This expected value, TP_{exp}, is the sum of the probability being a non-mover, given x=1, multiplied by the probability of being exposed to the risk factor, plus the probability of being a mover, multiplied by the probability that exposure would have occurred in both the out-migration and in-migration states.

$$TP_{exp} = P_x\left(1 - P_{move|x=1}\right) + P_{move|x=1}P_x^2 \qquad \text{[Equation A1]}$$

Similarly, the expected prevalence of true negative classification is the sum of the probability of being born in an MLDA<21 state and the probability of moving from one MLDA<21 state to another:

$$TN_{exp} = \left(1 - P_x\right)\left(1 - P_{move|x=0}\right) + P_{move|x=0}\left(1 - P_x^2\right) \qquad \text{[Equation A2]}$$

False positive and false negative classifications, on the other hand, occur only among movers. The relevant move probability is multiplied by the probabilities that exposure occurred in one state but did not occur in the other:

$$FP_{exp} = P_{move|x=1}\, P_x\left(1 - P_x\right) \qquad \text{[Equation A3]}$$

$$FN_{exp} = P_{move|x=0}\, P_x\left(1 - P_x\right) \qquad \text{[Equation A4]}$$

Hence, the observed parameters P_x, $P_{move|x=0}$ and $P_{move|x=1}$ for 1970 and 1980 were tabulated, and used to calculate expected values for each of the four classification possibilities. These were then compared with the observed census values for the four each classification. Results are tabulated in Supplemental Table 3.

Supplemental Table 3 shows that the observed classification rates are very close to those expected under the assumption of non-selective migration, but there are some differences that we will address below. First, we consider how misclassification in the absence of selective migration would impact our observed odds ratios. Because we are studying outcomes of low prevalence, we will assume that odds ratios (OR) are identical to relative risk ratios (RR). False positives were not actually exposed to the risk factor, but were classified as being exposed, and false negatives were exposed to the risk factor, but were classified as unexposed. On average, false-negatives are expected to resemble true positives in terms of risk, and vice-versa. Hence, the observed prevalences among those classified as unexposed and exposed, respectively can be expressed as:

$$P_0^{obs} = f_{TN} P_0 + f_{FN} P_1 \quad \text{and} \quad P_1^{obs} = f_{TP} P_1 + f_{FP} P_0 \qquad \text{[Equation A5]}$$

Where P_0 and P_1 are the true prevalances among the unexposed and exposed, and f_{FN} , f_{FP} represent the misclassification rate in the negative and positive exposure categories, respectively; e.g., f_{FP}= FP/(TP+FP). The fractions f_{TP} and f_{TN} are equal to (1-f_{FP}) and (1-f_{FN}), respectively. For simplicity, Equation A5 assumes all prevalence values have been adjusted for covariates. The observed risk ratio is

$$RR^{obs} = \frac{P_1^{obs}}{P_0^{obs}} = \frac{f_{TP} RR^{true} + f_{FP}}{f_{TN} + f_{FN} RR^{true}} \qquad \text{[Equation A6]}$$

where $\mathrm{RR}^{\mathrm{true}}$ represents the “true” risk ratio we would expect to observe in the absence of misclassification ($\mathrm{P}_1/\mathrm{P}_0$), which converges to $\mathrm{RR}^{\mathrm{obs}}$ when the misclassification rates approach zero, and as $\mathrm{RR}^{\mathrm{true}}$ approaches 1. Examination of this expression shows the effect of migration, which is a relative increase in f_{FP} and f_{FN}, is to make the numerator and denominator closer to each other in magnitude, bringing the observed relative risk ratio closer to one than the true relative risk ratio. In other words, true risk (or protective effect) is always larger than that observed when birth state is used as a proxy as exposure state. If we were to correct the odds ratio listed in Table 2 describing the associations between MLDA and suicide and homicide, respectively for women, the resulting point estimates would be 1.16 and 1.21, respectively, *versus* 1.12 and 1.15.

The above analysis assumes random migration, that is, there is no relationship between a person's tendency to move to a state with a particular MLDA policy and their risk of death by suicide or homicide, after adjusting for MLDA exposure and other covariates. The parameters in Supplemental Table 3 demonstrate migration patterns expected under the hypothesis of unselective migration are very close, but not identical to those actually observed. Hence, we must consider the effects on the observed risk ratio if subjects who migrated from their state of birth differed substantially in their risk for suicide or homicide than those who did not. Specifically, we want to know whether a statistically significant relative risk might be observed solely as a result of selective migration.

As a heuristic to consider this situation, Equation A6 can be re-written to express the bias introduced by portions of the migrating population in the exposed and unexposed groups who differ in their risk from their non-migrating counterparts:

$$RR^{obs} = \frac{f_{TP} RR^{true} + f_{FP}(\gamma_1 + \gamma_2 RR_1^{Bias})}{f_{TN} + f_{FN}(\gamma_3 RR^{true} + \gamma_4 RR_0^{Bias})} \qquad \text{[Equation A7]}$$

where γ_1 and γ_3 represent the proportions of misclasssified movers who experience similar risk differentials to their non-moving counterparts – presumably the majority – and γ_2 and γ_4

represent the proportions who are at significantly different risk ($\gamma_1+\gamma_2=1, \gamma_3+\gamma_4=1$). The RR^{Bias} terms constitute the risks for these subjects, relative to the unexposed non-movers. While it is impossible to simulate all possible scenarios, the situations most likely to lead to false positive observed risk would arise when those who migrate from MLDA=21 states to MLDA<21 states (false positives) exhibit very high risk, independently of actual MLDA effects, while those who migrate from MLDA<21 states to MLDA=21 states (false negatives) exhibit very low risk. Accordingly, we set $RR_1^{Bias} = 2$ and $RR_0^{Bias} = 0.5$ FigureS1 plots observed relative risks as a function of true relative risk under three scenarios; one in which there is no selective migration ($\gamma_1=\gamma_3=0$), one in which 10% of misclassified observations arise from selective migration ($\gamma_1=\gamma_3=0.1$), and one in which 25% arise from selective migration ($\gamma_1=\gamma_3=0.25$). The figure illustrates that if migration is completely random (solid line), the risk estimate is always biased toward the null hypothesis; that is, the true risk ratio is further from 1 than the observed risk ratio. Under 10% selective migration, the true risk ratio is still higher than the observed risk ratio for $RR^{obs} > 1.08$. Only under very high selective migration (25%), do we see possible bias towards false rejection of the null hypothesis (i.e., $RR^{obs} > RR^{true}$ for $R^{obs} > 1$), and only under conditions chosen to maximally bias the observed estimate (large RR^{Bias} parameters in opposite directions for each class of movers).

From the analyses and calculations presented in this Appendix, we conclude that (1.) The accuracy of our risk-factor assignment, when using the state-of-birth as a proxy for state-of-residence at ages 18-20, is quite high. (2.) Move patterns are very close to those based on what would be expected for random, or unselective migration. (3.) The largest source of bias in the observed odds ratio (or risk ratio) estimates is due to misclassification, and this would bias the effect size toward the null hypothesis. (4.) Only under very rare circumstances of high rates of selective migration, and associated high risks, would introduced bias be sufficient to incorrectly reject the null hypothesis.

Supplemental References

Angrist J, Pischke J-S (2008) *Mostly Harmless Econometrics: An Empiricist's Companion.* Princeton University Press.

Ashenfelter O, Card D (1985) Using the Longitudinal Structure of Earnings to Estimate the Effect of Training Programs. The Review of Economics and Statistics 67(4):648-660.

Snow J (1855) *On the Mode of Communication of Cholera.* Churchill, London.

Supplemental Table 1: Fixed Effects Logistic Regression – Suicide and Homicide Predicted from MLDA exposure among likely non-movers. State and year of birth included in all models.

	Suicide		Homicide	
Additional Covariates:	**Odds Ratio (95% CI)**	P	**Odds Ratio (95% CI)**	P
Sex, Race/Ethnicity	0.99 (0.96, 1.01)	0.27	1.02 (0.94, 1.11)	0.60
Sex, Race/Ethnicity, Sex x MLDA Interaction:				
MLDA: Women	1.12 (1.03, 1.21)	0.006	1.21 (1.08, 1.35)	0.0007
MLDA: Men	0.96 (0.93, 0.99)	0.007	0.97 (0.90, 1.04)	0.41
Interaction (Men vs. Women)	0.86 (0.78, 0.94)	0.001	1.25 (1.11, 1.41)	0.00024

Supplemental Table 2: Fixed Effects Logistic Regression – Suicide and Homicide Predicted from MLDA exposure imputed based on state of residence. State and year of birth included in all models.

Additional Covariates:	Suicide **Odds Ratio (95% CI)**	Suicide P	Homicide **Odds Ratio (95% CI)**	Homicide P
Sex, Race/Ethnicity	0.99 (0.97, 1.01)	0.24	1.02 (0.95, 1.10)	0.52
Sex, Race/Ethnicity, Sex x MLDA Interaction:				
MLDA: Women	1.08 (1.02, 1.16)	0.014	1.17 (1.05, 1.30)	0.003
MLDA: Men	0.96 (0.93, 0.98)	0.002	0.97 (0.90, 1.04)	0.43
Interaction (Men vs. Women)	0.89 (0.82, 0.96)	0.003	0.83 (0.75, 0.92)	0.0006

Supplemental Table 3: Observed and expected classification frequencies based on risk factor exposure and move probabilities[a]

	Observed	Expected	Difference
P_x	56.5%	----	----
P_{move}	27.2%	----	----
$P_{move\|x=1}$	26.4%	----	----
$P_{move\|x=0}$	28.3%	----	----
TP	51.2%	51.4%	-0.2%
TN	36.8%	35.3%	+1.5%
FP	5.3%	6.4%	-1.1%
FN	6.7%	6.9%	-0.2%

[a] Note: Derived from Equations A1-A4 and observed parameters in first four rows of Table

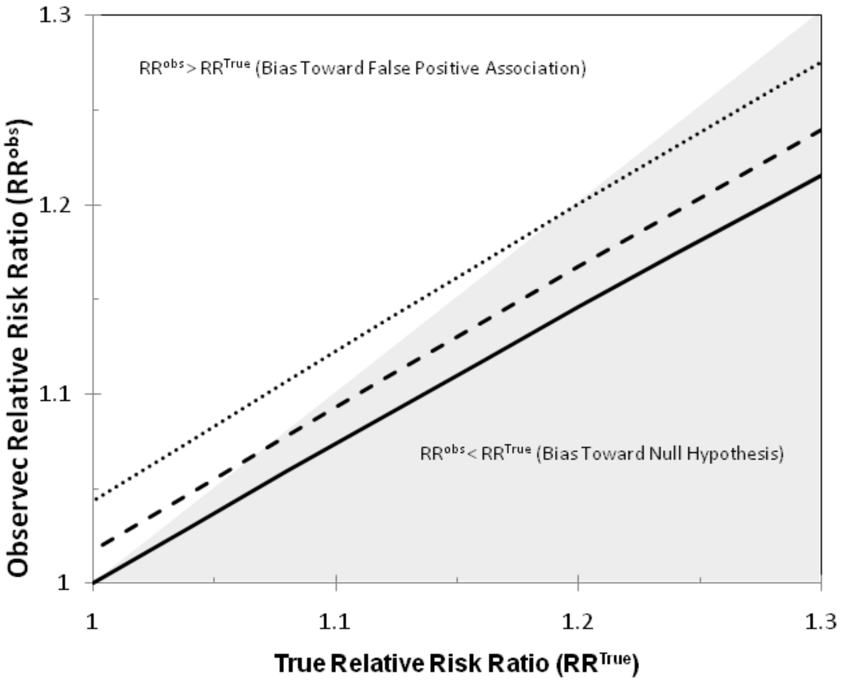

Figure S1: Observed relative risk ratio when state-of-birth is used as a proxy for state of exposure *versus* true risk ratio when exposure status can be inferred. Solid black line: RR^{obs} under assumption of non-selective migration, using parameters derived from the 1970 and 1980 censuses, and listed in Table S3. Dashed and dotted lines: RR^{obs} under two different selective migration scenarios, described in Technical Appendix. Gray shaded area indicates $RR^{obs} < RR^{true}$, or bias toward the null hypothesis; non-shaded area indicates $RR^{obs} > RR^{true}$, or bias toward false rejection of the null hypothesis.

Supplemental Figure Legend

Figure S1: Observed relative risk ratio when state-of-birth is used as a proxy for state of exposure *versus* true risk ratio when exposure status can be inferred. Solid black line: RR^{obs} under assumption of non-selective migration, using parameters derived from the 1970 and 1980 censuses, and listed in Table S3. Dashed and dotted lines: RR^{obs} under two different selective migration scenarios, described in Technical Appendix. Gray shaded area indicates $RR^{obs} <$ RR^{true}, or bias toward the null hypothesis; non-shaded area indicates $RR^{obs} > RR^{true}$, or bias toward false rejection of the null hypothesis.