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An Examination of the Association between Altitude and Suicide Deaths, Suicide Attempts, and Suicidal Ideation among Veterans at both the Patient and Geospatial Level

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Keywords

altitude; suicide mortality; suicide ideation; suicide attempts; geospatial; veterans; firearms related suicide; adjusted variables; mental health

1. Introduction

Recent estimates from the Department of Veterans Affairs (VA) Office of Mental Health and Suicide Prevention (OMHSP) reveal that, after adjusting for age and sex, the suicide mortality rate (SMR) among Veterans is 51% higher than the rate among civilians. Numerous variables have been associated with risk for suicide and suicidal behavior (Franklin et al., 2017). One such risk factor is geography, as the Mountain West region of the U.S. has a significantly higher SMR compared to the rest of the country. Many factors have been postulated to explain this difference, including rurality, firearm ownership, race,

ethnicity, access to health care, isolation, substance abuse, and domestic violence (Betz et al., 2011, Reno et al., 2018); however, given that the increased SMR observed in the Mountain West is consistent across many demographic differences (Pepper et al., 2017), it seems implausible that these factors alone could account for the robust effects observed. Thus, there has been a growing interest in exploring the association between high altitude and risk for suicide.

Haws and colleagues were among the first to explicitly hypothesize that SMR might be higher in western states partly due to the effects of high altitude on oxygen saturation. Specifically, they and others have hypothesized that chronic hypobaric hypoxia might promote suicide and depression by altering brain bioenergetics and serotonin metabolism (Haws et al., 2009, Kioussis et al., 2018). This hypothesis is based on ecological and animal studies, short-term human studies, and studies examining the effects of hypoxic medical conditions on suicide and depression. Several ecological studies have now demonstrated a significant correlation between mean altitude and suicide rates at both the state and county level within the U.S. For example, Brenner and colleagues reported a positive correlation between mean altitude and suicide rate ($r=0.50$, $p < 0.001$) and a negative correlation between altitude and all-cause mortality ($r=-0.31$, $p < 0.001$) across 2,584 U.S. counties (Brenner et al., 2011). Moreover, this study reported that higher-altitude counties still exhibited significantly higher SMR than lower-altitude counties after accounting for the effects of age, sex, race, income, and population density.

Utilizing an ecological design, Sabic and colleagues (Sabic et al., 2019) reported that mean state altitude was associated with veteran suicide deaths ($r=0.68$, $p<0.001$). They also observed that the correlation between altitude and suicide was stronger for veterans than for non-veterans. Studies conducted at the individual level have reported varying results. For instance, Betz and colleagues (Betz et al., 2011) found that individuals who died by suicide in high-altitude areas have different characteristics than those living in low-altitude areas and concluded that these factors, rather than hypoxia or altitude itself, may explain increased SMR at high altitude. On the other hand, Riblet and colleagues (Riblet et al., 2019) recently showed that after adjusting for variables such as age, gender, race, ethnicity, and population density, suicide rates increased as altitude and other hypoxic factors increased.

Thus, while there is growing evidence that altitude could represent an important risk factor for suicide and suicidal behavior among veterans, numerous questions regarding the nature and magnitude of this association remain. Published studies to date have either failed to take into account key differences between high- and low-altitude suicide decedents (individual level), or to take into account the heterogeneity in the altitude of the geographic units (county and ZIP codes levels), or to include other suicide-related outcomes such as suicide attempt and ideation. Accordingly, the objective of the present research was to conduct a comprehensive analysis of the association between altitude and suicide deaths, suicide attempts, and suicidal ideation among U.S. veterans at both the patient and geospatial level.

2. Data and Methods

We used International Classification of Disease (ICD) codes from the VA's Corporate Data Warehouse (CDW) and data from the National Death Index (NDI) to identify veterans who have: 1) died by suicide; 2) attempted suicide; and 3) experienced suicidal ideation. The study included a cohort of 14 million veterans who have enrolled for VHA (Veterans Health Administration) care and have available electronic health record (EHR) data from two or more visits within the study period, 2000–2018 (Supplementary 1 Table 1). We collected SMR data from the NDI, which includes mortality data on veterans under VHA residing in the U.S. We calculated the suicide mortality counts by using the ICD Version 10 (ICD-10) codes X60–84, Y87.0. We collected suicide attempt data from CDW by using both ICD-9 codes (World Health Organization, 2011) E95 and ICD-10 codes T14.91. We collected suicidal ideation data from CDW by using ICD-9 codes V62.84 and ICD-10 codes R45.851.

2.1 County Level and Zip-Code Level Analyses

VHA records the Veterans' address for each outpatient visit, which we used to obtain their corresponding county FIPS codes that uniquely identify geographic areas. We summed the suicide cases for each county to obtain the results at county-level. We used aggregated data from 2000–2018 to avoid having counties with zero or few cases. To determine the altitude of each patient's residence county, we used the National Altitude Dataset (United States Geological Survey), which contains a total of 3143 county FIPS. The altitude for each county was calculated as the average of the polygons. While USGS does not have true county elevation averages, they provide a list of all populated locations, sortable by county, with elevation values of those locations. We calculated the county elevation averages based on that list. We followed a similar process for the ZIP-code level analysis using the National Altitude Dataset, which contains a total of 42631 ZIP codes.

2.1.1 Linear Regression Model—We used a linear regression model to determine the influence of each covariate on suicide-specific rates (i.e., suicide deaths, suicide attempts, suicidal ideation, or the combination of events) and adjusted the outcome results by those covariates at county and ZIP-code levels. We calculate adjusted suicide-specific rate (adjustedSSR) as follows:

$$adjustedSSR = LR \left(SSR \sim altitude + \sum_{i=1}^6 covariate_i \right)$$

where LR was the linear regression model, SSR was the outcome variable, altitude was the independent variable, and covariate_i represented the six covariates: percentage age \geq 50 years old, percentage male, percentage white, percentage non-Hispanic, median household income, and population density. We included these variables as covariates because they could potentially account for observed associations between suicide and altitude and because they were included as covariates in the literature that motivated the present work (i.e., Brenner et al., 2011, and Riblet et al., 2019). Supplementary 1 Table 2 shows the characteristics and SMR of the US veteran population. We chose the midpoint of these variables based on our study period (i.e. 2009). Age/gender/race/ethnicity data were

extracted from the CDW database, whereas median household income estimates of census tract were derived based on US Vet data via Monte Carlo simulation (Christian, et al, 2021). We then calculated median household income estimates at the county and ZIP-code levels by using the census crosswalk. The imputation of the median household income resulted in some missing data when adjusting the dataset. The population density data were generated from the 2009 census dataset.

The SMR for the different demographic variables at the county level are presented in (Supplementary 1 Table 3). There were 45,803 suicide deaths and 4,261,198 all-cause deaths for the U.S. veteran Populations. Thus, suicide mortality represented 1.07% of all US Veterans deaths.

We used SMR data for 2887 counties, suicide attempt data for 3158 counties, suicidal ideation data for 3188 counties, and a combination of suicide mortality, suicide attempt, and suicidal ideation data for 3193 counties. After adjusting for covariates, we had 2054 counties with SMR data, 2262 counties with suicide attempts data, 2289 counties with suicide ideation data, and 2294 counties with combined data. For the ZIP-code level analysis, we used SMR data for 16,077 ZIP codes, suicide attempt data for 20,667 ZIP codes, suicidal ideation data for 27,421 ZIP codes, and a combination of suicide mortality, suicide attempt, and suicidal ideation data for 29,253 ZIP codes. After adjusting for covariates, we had 13,316 ZIP codes with SMR data, 16,747 with suicide attempts data, 22,017 with suicide ideations data, and 23,314 with combined data. In order to make a fair comparison between unadjusted and adjusted results, we used the same counties and ZIP codes for the adjusted (with missing data) and unadjusted studies. However, we did an analysis using all the counties for unadjusted and adjusted cases which are different and observed similar trends as shown in sections 3.1 and 3.2.

2.1.2 Geospatial Model—Because the geographical and community-level effect also needs to be taken into account when estimating SSR, we used the Simultaneously AutoRegressive (**SAR**) model implemented in the Python-based spreg package (David, et al., 2013). It allows for a wide selection of connectivities including neighbors with no common borders. The SAR regression model follows an autoregressive approach, which is indicated by the presence of a dependence relationship among a set of observations or spatial units (Anselin, et al., 1988).

$$\text{adjusted geospatial SSR} = W_SSR\rho + X\beta + u;$$

where $X = (\text{altitude} + \sum_{i=1}^6 \text{covariate}_i)$ is a matrix of independent variables ($n \times m, m = 7$)

The outcome, adjusted geospatial SSR, is a vector of n observations on the dependent variable ($n \times 1$)

ρ is spatial autoregressive coefficient ($n \times 1$),

W_SSR is standardized spatial weights matrix ($n \times n$),

β is a vector of parameters of the model (regression coefficients) ($m \times 1$),

u is a vector of error terms assumed to have autocorrelation ($n \times 1$).

There are two types of SAR models. One is the spatial lag regression model, in which the outcome is influenced by the corresponding outcomes from neighbors. Another is the spatial error regression model which uses an error term that is calculated as the difference between the corresponding neighboring units. We used the former model in our analysis because we were primarily interested in neighbors' influences, rather than their differences. We refer to the model as SAR-lag. The package allows for different choices for neighborhood connectivities: queen and k-nearest neighbors (knn). The queen option defines neighbors as spatial units sharing a common edge whereas knn is determined by the shortest distance to a predetermined k number of neighbors using inter-centroid distances. We selected the queen option because we realized that a predetermined k may not represent well the actual spatial connectivities.

2.1.3 Logistic Regression Model—Finally, we used logistic regression to select optimal cut points for altitude levels in relation to suicide mortality rate that maximized discrimination among veterans. We calculated different metrics to describe the performance of the model: AUC (area under the curve), coefficient of the features in the decision function, accuracy, specificity (also called the true negative rate), sensitivity (also called true positive rate or recall), negative predictive value (NPV), positive predictive value (PPV), and Youden index. We selected as the optimal cut point, the altitude that optimized the most metrics.

2.2 Individual-Level Analysis

The individual-level analysis was based on a Person-Year study, which considers altitude status during each year of life a person contributed to observation, as well as an indicator for new cases of suicide-specific events as the dependent variable. We collected information on altitude from 2000–2018 for each year an eligible person contributed to the observation. We estimated the suicide-specific rate per person-years (SSR-PYR) at risk by dividing total number of recorded suicide-specific events (i.e. deaths, attempts, ideation or the combination of the three) during the 2000–2018 period by total observed person-years, calculated as the total years contributed by each person under observation during the study period. Loss to follow-up or suicide-specific events were accounted for as a one-half year contribution for the year of occurrence. We assessed the association between suicide-specific events and altitude using:

$$SSR - PYR = \frac{\# \text{ recorded suicide-specific counts in 2000-2018}}{\sum_{2000}^{2018} \left(\text{full person-years observed in year } i + \frac{1}{2} \text{ year*lost to follow in year } i + \frac{1}{2} \text{ year*suicide-specific counts in year } i \right)}$$

We divided the altitude into 4 groups:

1. high altitude: codes above 1500m,
2. medium-high altitude: codes between 1000 and 1500m,

3. medium-low: codes between 500 and 999m, and
4. low altitude: codes above sea level but below 500m.

We generated SSR-PYR based on the above 4 altitude groups.

All the code used in the analyses can be found in our github repository https://github.com/CrivelliLab/Altitude_vs_SuicideRate_in_VA.

3. Results

3.1 County-Level Analysis

Figure 1 shows the unadjusted and adjusted SMR of the U.S. veterans population based on 2054 counties as well as the SMR after adjusting and considering the geospatial effects. The figure shows SMR by 50 quantiles (x-axis) vs. mean county altitude (y-axis). The legend shows the first and last quantile values (x-axis) with their corresponding mean elevation (y-axis) for the 3 analyses: unadjusted SMR, adjusted SMR using LR, and adjusted SMR using SAR-lag. The higher-altitude counties had significantly higher suicide rates than the lower-altitude counties. The significant positive correlation between altitude and SMR at the county level was even stronger after adjusting for covariates. The correlation was 0.8842 for the LR model, 0.8298 for the SAR model and 0.2898 for the unadjusted data. Supplementary 2 Fig. 1 shows a similar plot using median instead of mean altitude. Supplementary 2 Figs. 2 and 3 show similar plots for SSR using mean and median altitude, respectively.

Notice that because we do not have firearm ownership data at county or ZIP codes levels, we did not adjust for this variable. However, we analyze this covariate below.

To investigate the firearm vs. non-firearm effect, we studied the adjusted association between county altitude and SMR for 3 cases: death by all means, death by firearm and death by non-firearm between 2000–2018. We divided the altitude into 9 intervals, by increments of 1000 feet, and we calculated the corresponding suicide beta value as the increment of the SMR of the corresponding altitude interval with respect to the reference interval (0–1000]. Figure 2 summarizes these results. We observed that increasing altitude deciles are associated with higher SMR when considering death by all means, firearm and non-firearm. SMR, and SMR by firearm are higher than by non-firearm. The adjusted associations between county altitude and SMR, firearm-related SMR, and non-firearm-related SMR are also shown in Supplementary 2 Table 1.

To further investigate the altitude-suicide association, we created 2 groups of counties based on SMR: one with the highest SMR and another with the lowest SMR. If altitude and SMR were not related, then the mean altitude between both groups would be similar. That is not the case as it can be seen in Figure 3 which shows the comparison between the 50 counties with the highest SMR and the 50 counties with the lowest SMR. The mean altitude between the 50 counties with the highest SMR compared with those with the lowest rates is significantly different (3198.86 vs. 1116.87 ft). The ratio between the average SMR of the 50 highest and lowest counties was 18.74 (104.41:5.57). Like Brenner et al. did, we

removed the counties from the Mountain Region (CDC 8) which has high SMR and repeated the analysis considering the 50 counties with the highest and lowest SMR. The results, which can be seen in Figure 3, show that the ratio between SMR remained high ($93.81:5.66 = 16.59$) and the mean altitude between the highest and lowest rates counties without the Mountain Region, was 2173.54 and 999.21ft, respectively.

As shown in Supplementary 1 Table 3, the median SMR is higher for firearms than non-firearms cases for the U.S. veterans Population ($19.37:7.58$ at county level). Because SMR involving firearms is higher, we compared the 50 counties with the highest and lowest firearm SMR. Figure 3 shows that the ratio of the suicide rates in these two groups of counties was also elevated ($85.06:3.58 = 23.75$). It also shows that the mean altitude between the 50 counties with the highest firearm SMR was significantly higher than the mean altitude of those counties with the lowest firearm SMR (3116.27 vs. 676.73 ft). The positive association between altitude and suicide for the highest and lowest SMR counties was also observed when considering suicides by non-firearms, indicating that the high SMR was not related to people owning more firearms in high-altitude places than in low-altitude places. In fact, we found a significant difference ($51.34:1.63$) in SMR between the counties with the 50 highest non-firearm suicides versus those with the lowest non-firearm suicides. We conducted a similar study for SSR at ZIP codes level and observed significant differences when comparing the top and lowest counties based on suicide ideation, suicide attempt or the combination of all suicide-specific rates.

We used logistic regression to identify an optimal cut point for levels of altitude in relation to county SMR that maximized the model performance. As can be seen in Table 1, a cut point of 800 meters or higher had the highest overall J statistic (i.e., Youden index = .52). This cut point also maximized both positive predictive value (0.63) and specificity (0.66). We also generated a logistic regression model based on suicide mortality rates at ZIP-code level (Supplementary 3 Table. 1)

3.2 Zip-Code-Level Analysis

As Brenner et al., 2011 suggested, a potential limitation of their study was the heterogeneity in altitude within counties. To address this limitation, we used ZIP codes tabulation areas (ZCTAs), which are smaller area units than counties. In most cases, the ZCTA are the same as its ZIP Codes (we refer to them as ZIP codes in this paper). Because ZCTAs are based on the most recent Census, they are more stable than ZIP codes and do not change as frequently. Using ZIP codes has two advantages: it increases the amount of data points and allows for a higher accuracy, as ZIP codes vary much less in altitude than counties.

Figure 4 shows the unadjusted and adjusted SSR using LR and SAR-lag by 50-quantiles of U.S. ZIP codes using mean altitudes. The figure shows that the adjusted SMR (suicides per 100,000) at the ZIP code-level positively correlates with altitude ($r=0.55$ for LR and $r=0.54$ for SAR-lag) although the correlation coefficients are lower than those at county level (0.88 and 0.83, respectively). Like the county-level analysis shown in Figure 1, the suicide rates curve by ZIP codes increases gradually with altitude and shows a spike at the highest SMR quantiles. The correlation between altitude and suicide attempts shows a similar trend ($r=0.40$ for LR and $r=0.37$ for SAR-lag). However, the correlation between

altitude and suicide ideation or the combination are weaker ($r=0.17$, $r=0.33$ respectively for LR and $r=0.15$, $r=0.31$ respectively for SAR-lag.) Unadjusted values show a small correlation. Supplementary 3 Fig. 1 shows a similar plot using median instead of mean altitude.

3.3 Individual-Level Analysis

We conducted a population-based cohort study to evaluate the association between altitude and suicide-specific rate per person-years or SSR-PYR based on the formula described in section 2.2. This study includes a total of 14,196,130 veterans, with 45,648 deaths by suicide, and 83,807 suicide attempts and 222,567 suicide ideations diagnosed. Table 2 shows increases in SMR and suicide attempt rates at higher altitudes but not in ideation or the combination of the three variables. Notably, we observed that the largest increase in SMR occurred between less than 500m and 500–1000m, which suggests that factors other than hypoxia may be responsible for this increase. A similar observation was made by Brenner et al., 2011 and Riblet et al., 2019. The individual-level results, which are unadjusted, are similar to the unadjusted ZIP codes results in that they do not show an increasing trend except for the suicide mortality in which a tenuous increasing trend can be observed (Figure 4 and Supplementary 3 Fig. 1).

4. Discussion

Using VA data from 2000–2018, we conducted three studies to investigate the correlation between altitude and suicide-specific events, namely suicide deaths, suicide attempts, suicidal ideation, and the combination of the three. The three studies analyzed data at county, ZIP codes, and individual levels. In all cases, controlling for potential confounding factors improved the correlation substantially. Our results show that there is a strong correlation between SMR and altitude at the county level even after adjusting by socio-demographic variables and spatial effects. The county-level analysis showed a higher correlation for suicide attempts, ideation, and combination than the ZIP-code level analysis. At the ZIP codes level, our results show a strong correlation between suicide mortality/suicide attempts and altitude and a weak correlation between altitude and ideation or the combination of suicide-specific events. The individual-level results are similar to the unadjusted ZIP codes results in that they do not show an increasing trend except for the suicide mortality in which a tenuous increasing trend can be observed. The individual-level results for SMR are similar to those shown in (Riblet et al., 2019) Our results are based on a large dataset and are consistent at the county, ZIP codes and individual levels and even after accounting for spatial effects and the effects of age, sex, race, ethnicity, income, and population density. Overall, we see a trend which is strongest for deaths, moderate for attempts, and modest for ideation and the combination of the three. We hypothesize that this could be the result of ideation being under-reported among people who live in high altitude places either because of infrequent access to mental health providers or for stigma. More work needs to be done to understand these phenotypes.

We also analyzed the 50 counties with the highest suicide rates and the 50 counties with the lowest suicide rates for the U.S. veterans Population and found that there was a 3-fold

difference in the mean altitude between these two groups of counties. When suicides were divided by firearm and non-firearm, there was a 5-fold difference in altitude between the 50 counties with the highest and lowest suicide rates by firearms and a 3-fold difference by non-firearms. When removing the counties in the Mountain Region, we found that there was a 2-fold difference in mean altitude between these two groups of counties.

We used the logistic regression model to select an optimum cut point for levels of altitude in relation to SMR that maximize performance. We showed that the model achieves the highest overall J statistic (i.e., Youden index = .52), positive predictive value (0.63) and specificity (0.66) at a cut point of 800m.

These analyses still have limitations. Suicide ideation and suicide attempts data may not be as accurate as suicide mortality data. The cases of suicide ideation and attempt are recorded only if the patients show up at a facility and they are assessed and diagnosed with these conditions. Many people may not be able to go to facilities due to circumstances like long driving hours and lack of facilities nearby or may not report their symptoms due to stigma. On the other hand, suicide deaths are measured through the NDI and they are captured even if the patient has no contact with a facility. Another limitation of the study is that it does not include telehealth visits, which should be considered in future analyses.

Gun ownership data when available, should be used for an adjusted study. Moreover, other confounding factors should be identified and included in the models. These include socioeconomic factors such as education level, isolation, substance abuse, and domestic violence, geospatial factors such as rurality (CDC scheme) and gun shops, environmental factors such as air quality and temperature, and hypoxia-related factors such as COPD and tobacco use. Nevertheless, our work suggested that geospatial factors such as altitude may be significant and should be included in suicide prediction models. Future studies should incorporate altitude and other hypoxia-related variables into the suicide prediction models in order to further investigate how altitude and associated variables are related to suicide.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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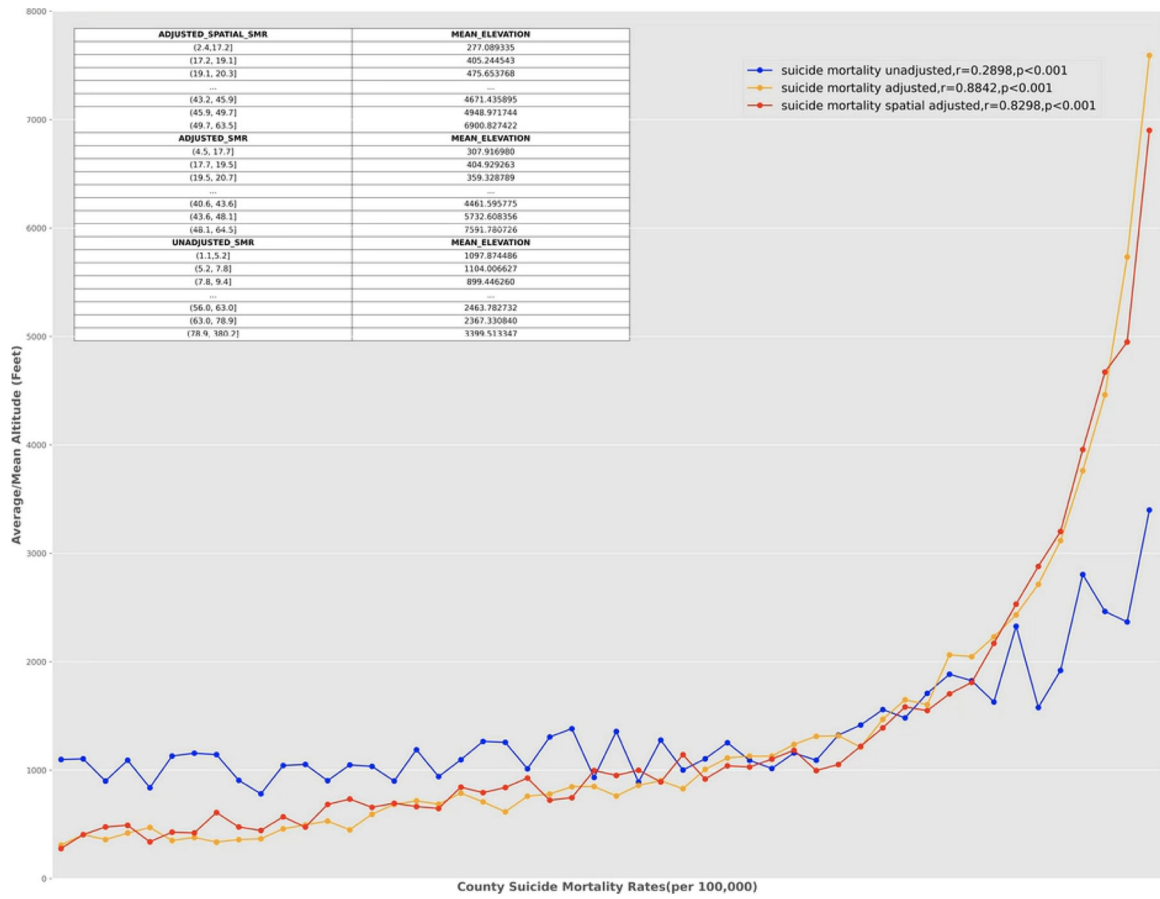


Figure 1. Adjusted and unadjusted SMR. The legend on the left shows the lowest and highest 50 quantiles (x-axis) with their corresponding mean altitude (y-axis) for each case: unadjusted SMR, adjusted for covariates via LR, and spatially adjusted via SAR-lag. 2054 counties were used.

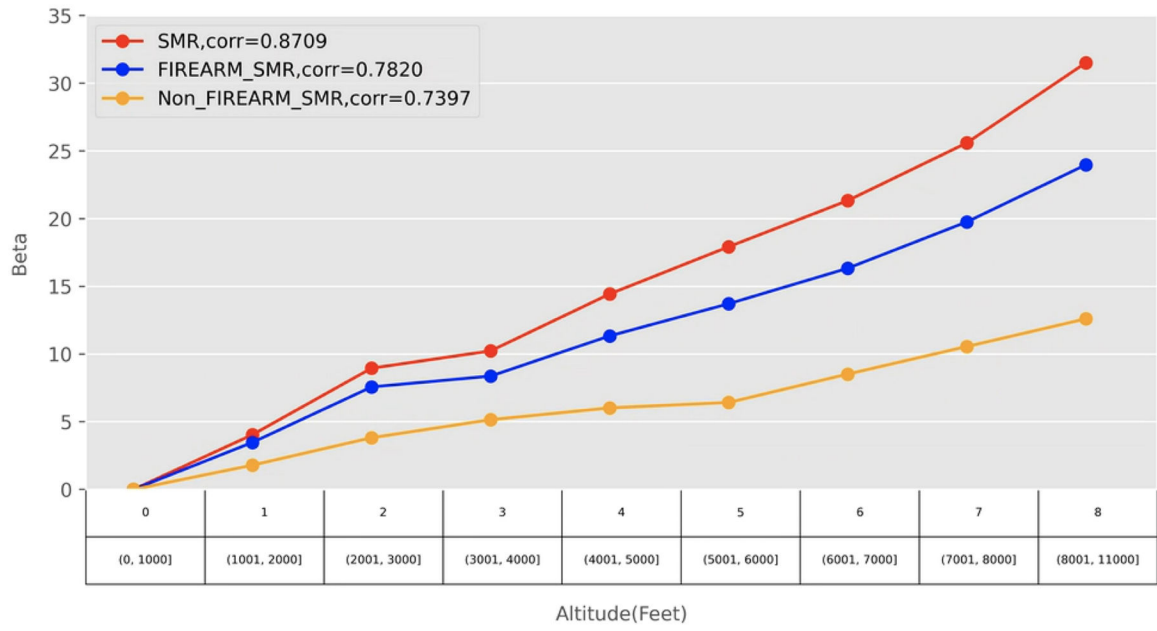


Figure 2. Adjusted association between county altitude and SMR for death by all means, by firearm and by non-firearm. The x-axis displays the altitude intervals.

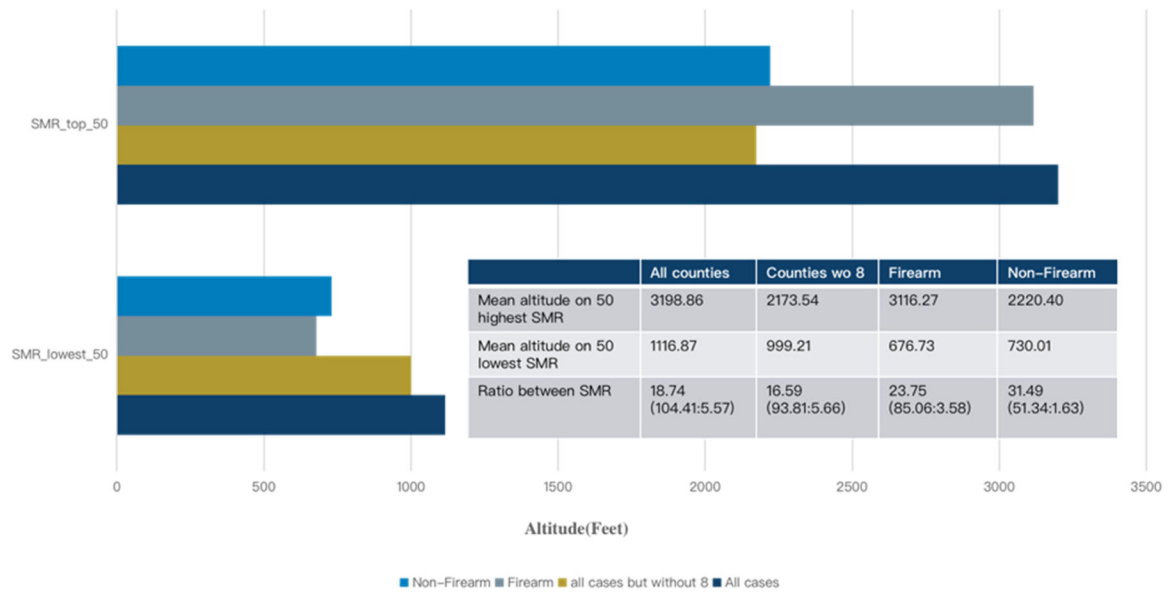


Figure 3. Mean altitude of counties with top 50 vs. lowest 50 SMR considering all counties, all counties except the Mountain Region, death by firearm and death by non-firearm.

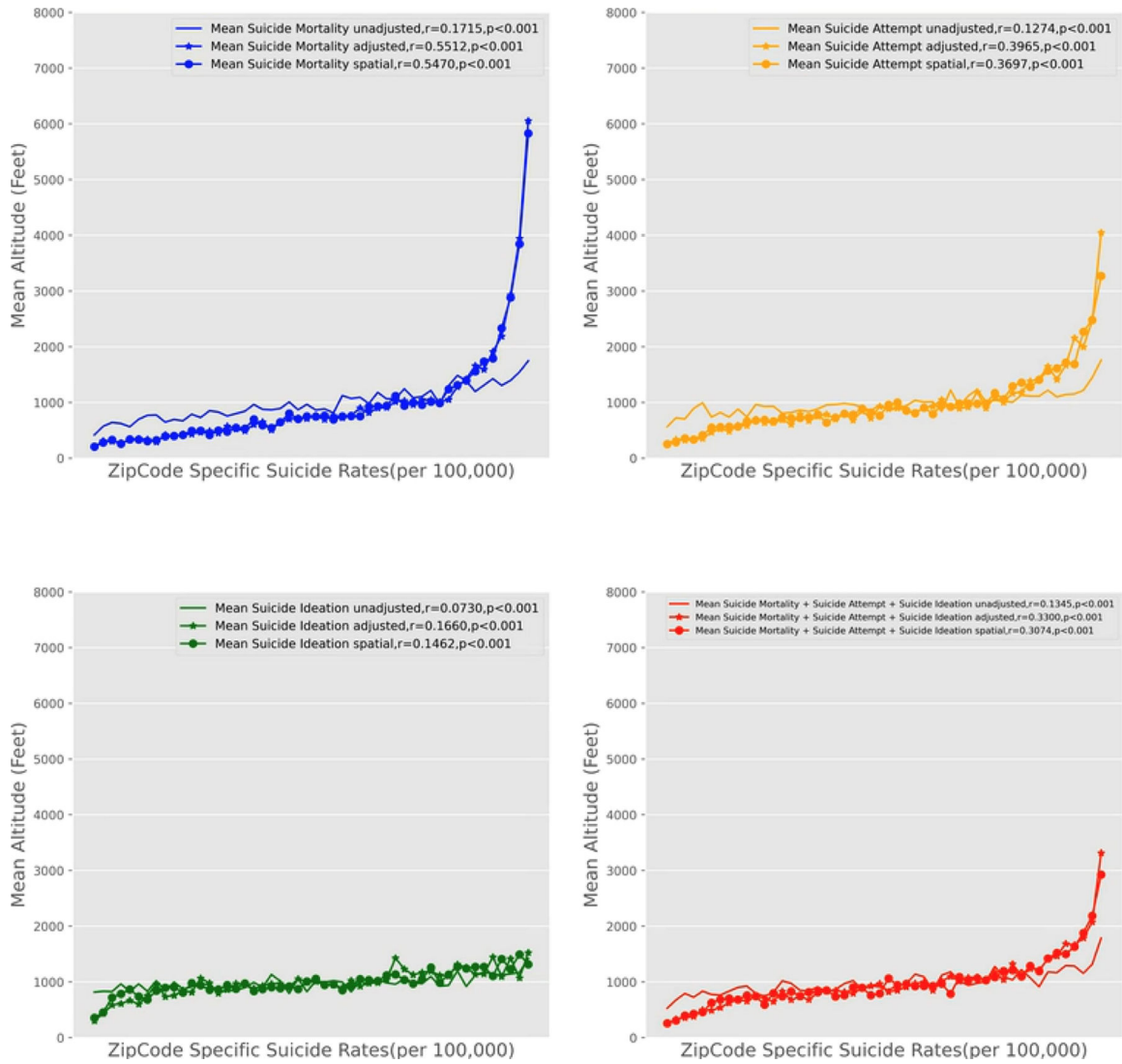


Figure 4. Adjusted spatial, adjusted nonspatial and unadjusted SSR of the U.S.Veterans Population by 50-quantiles of U.S. ZIP codes using mean altitudes. The x-axes represent to the 50 quantiles for each suicide-specific event: SMR (top left), attempt (top right), ideation (bottom left), and the combination of the three (bottom right).

Table 1.

Metrics for the Logistic Regression model using different altitude cut off values.

	AUC mean	Coef_ele	Accuracy	Specificity	Sensitivity (Recall)	NPV	PPV (Precision)	Youden
200	0.6142	0.2130	0.5661	0.5366	0.5933	0.5477	0.5824	0.4267
400	0.6220	0.5870	0.5895	0.5772	0.6007	0.5703	0.6075	0.4029
600	0.6471	0.9621	0.6012	0.6463	0.5597	0.5740	0.6329	0.4808
800	0.6441	1.0264	0.5992	0.6585	0.5448	0.5704	0.6348	0.5250
1000	0.6364	1.1096	0.5914	0.6463	0.5410	0.5638	0.6250	0.4245
1200	0.6298	1.0752	0.5798	0.6423	0.5224	0.5224	0.6140	0.4069
1400	0.6312	1.1659	0.5798	0.5528	0.6045	0.5620	0.5956	0.4192
1600	0.6307	1.0449	0.5914	0.5325	0.6455	0.5796	0.6007	0.4507
1800	0.6298	1.0617	0.5895	0.5325	0.6418	0.5771	0.5993	0.4515
2000	0.6177	0.9776	0.5856	0.5325	0.6343	0.5721	0.5965	0.4573

AUC (area under the curve), coefficient of the features in the decision function, accuracy, specificity (also called the true negative rate), sensitivity (also called true positive rate or recall), negative predictive value (NPV), positive predictive value (PPV), and Youden index.

Table 2.

Association between altitude and SMR, suicide attempts, suicidal ideation, and the combination of the three for 2000–2018.

	Altitude (m)	Suicide Counts	Person-years + ½ LF + ½ newcases	SSR-PYR (per 100,000 person-years)
Suicide Mortality	500–	35,251	109,007,245.5	32.34
	500–999	3,801	8,750,082.5	43.44
	1000–1499	2,514	5,200,640	48.34
	1500+	2,335	4,739,731	49.26
Suicide Attempts	500–	71,276	109,258,860.5	65.24
	500–999	5,754	5,206,022.5	65.64
	1000–1499	3,103	5,200,640	59.60
	1500+	3,674	4,749,494	77.36
Suicidal Ideation	500–	193,911	110,399,497.5	175.65
	500–999	12,898	8,836,305.5	145.97
	1000–1499	7,801	5,249,918	148.59
	1500+	7,957	4,792,875.5	166.02
SMR+SA+SI	500–	234,621	111,074,622.5	211.23
	500–999	16,506	8,887,670	185.72
	1000–1499	9,838	5,279,088.5	186.36
	1500+	10,291	4,824,377.5	213.31