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Drought and All-Cause Mortality Rates among Adults in the United States: 1968-2014

By

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Environmental Health and Epidemiology

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Drought and All-Cause Mortality Rates among Adults in the United States: 1968-2014

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ABSTRACT

Drought and All-Cause Mortality Rates among Adults In the United States: 1968-2014 By Katie Lynch

Introduction: Drought can cause widespread and complex regional impacts and numerous pathways have been hypothesized connecting drought to health effects. One area of drought research that is lacking is the effects of drought on all-cause mortality, especially in higher income countries such as the United States. This study aims to evaluate the associations between droughts and same-year all-cause mortality in adults in the United States from 1968-2014 in order to better understand the health impacts of drought.

Methods: Drought exposure was classified using an annual drought severity score for each county derived from a dataset of 1-month, county-level Standardized Precipitation and Evapotranspiration Index (SPEI). An analogous score for abnormally wet years was also derived. All-cause mortality data came from a dataset from the United States Centers for Disease Control and Prevention's (CDC) mortality counts, censored on counts 1-9 across narrow demographic strata. We modeled county-stratum-year mortality using interval-censored [1,9] negative binomial regression with random intercepts by each combined age-race-sex stratum with and without further stratification by National Oceanographic and Atmospheric Association climate regions, and with and without inclusion of years classified as abnormally wet. False discovery-rate adjusted-p values were obtained to correct for multiple testing. Random effects meta-regressions were completed to test the associations between the predictors with the drought-mortality regression coefficient. Meta-analyses were then completed to obtain a pooled IRR and I² as a measure of between-study heterogeneity.

Results: Most of the results were null for the association of drought severity and mortality, across categories of race, age, sex and region for all analyses. A small number of IRRs were significant after accounting for the multiple testing for certain subgroups, but without clear patterns by age, race, sex or region. The meta-analyses resulted in a pooled IRR of 0.999 (0.999, 1.000) from the analyses that stratified by NOAA region, with and without wet county-years included. The I² of approximately 50% for both analyses suggests that about half of the total variation across stratified groups is due to heterogeneity.

Discussion: These results suggest that, for the majority of demographic subgroups and across climate regions, there is no significant effect of drought intensity on mortality rates within the same year in the contiguous United States over 1968-2014. The handful of significant results that remained after accounting for multiple testing suggest a possible health effect for certain subgroups, but this heterogeneity was not consistent across broad patterns of age, race, sex or region. The findings could indicate contextual heterogeneity in the effects of drought on mortality, and either true null associations for most subgroups, or limitations in study design for observing the effects.

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INTRODUCTION

The Intergovernmental Panel on Climate Change reported in 2012 that medium confidence exists that droughts have increased in duration and intensity in some areas since the 1950s, particularly semi-arid and sub-humid regions (i.e. South Europe, West Africa), while decreasing in others (i.e. North America, Northwestern Australia), and that droughts will continue to intensify in certain regions of the world including southern and central Europe, the Mediterranean, North and Central America and southern Africa [1]. Within the United States, specific areas including California and the Midwest are projected to experience the strongest increase in drought intensity [2].

Drought is generally considered a water deficit for a given area, but the actual classification of drought, and therefore definition, differs depending on the measures considered, such as precipitation or and evapotranspiration [3]. Droughts are commonly divided into four major types based on their environmental and human impacts. These include meteorological drought (i.e., abnormally low precipitation), hydrological drought (i.e., precipitation shortages that impact the surface and groundwater levels), agricultural drought (i.e., decreased soil moisture that impacts crops), and socioeconomic drought (i.e., weather-related decreased water supply that affects people and supply of goods) [4]. Further, droughts can be characterized by additional factors such as duration, intensity, spatial distribution, frequency, and rate of onset [3].

Droughts can cause widespread and complex regional impacts. Recent droughts in Kenya, the Mediterranean and California have led to crises in food insecurity, political instability, and economic damage, respectively [5]. Droughts can also coincide with, and increase the risk of heat waves, wildfires, and dust-storms [5]. With the extensive effects and potential for future increased impact of droughts, it is important to understand the possible health consequences of this natural disaster.

Numerous pathways have been hypothesized connecting drought to health effects. Theoretically, in extreme cases, some of these health effects could lead to increased mortality, especially among vulnerable populations. One mechanism could be through decreased freshwater availability and water quality, which can increase the risk of contamination with, and concentration of, pathogens, chemicals (i.e. organophosphates, sulfates and nitrates), and harmful algae blooms in surface and groundwater [6, 7]. Contact with or ingestion of microbially contaminated water could result in infection (i.e. ear, eye, wound or gastrointestinal) [5, 8]. If water restrictions lead to decreased hand hygiene, this could promote the spread of infections. Cyanobacteria toxin exposure can occur through dermal contact, ingestion, or inhalation, and can cause skin rash, injury or even death [9]. Although decreased water availability and other drought conditions could affect agricultural production, and contribute to food insecurity, this is less likely to be a problem in higher income countries such as the United States. High income countries generally have food sources from more geographically diverse areas and greater food security at baseline, although food prices could increase and disproportionately affect individuals of lower socioeconomic status [10, 11]. Heat waves that may coincide with drought could also impact health, resulting in increased heat-related mortality [12, 13]. Heat and droughts are linked because increased temperature is a factor in drought development and severity through evapotranspiration, and because drought may create conditions that promote increased temperatures and heat waves [14]. Droughts could also affect air quality, thereby impacting heath. This can occur through a variety of complex

processes related to natural emissions, chemistry, and deposition [15]. A recent study found a correlation between decreased air quality, including increased concentrations of PM_{2.5} and ozone and drought severity in the United States from 1990-2014 [15]. Drought can increase the risk of wildfires, which, in addition to immediate harms such as burn injuries or death, produce emissions that contain air pollutants including CO, $PM_{2.5}$, and PM_{10} [15, 16]. Additionally, drought conditions may lead to processes other than wildfires that increase airborne particulate matter and distribution, including dust storms [5, 17]. Decreased precipitation, which helps wash out air pollutants, could further compromise air quality [18]. PM_{2.5} is associated with respiratory morbidity and mortality, including exacerbation of asthma and COPD and an increased risk of respiratory infections [19-21]. It has also been linked to and cardiovascular morbidity and mortality including ischemic heart disease and stroke [22, 23]. Wildfire emissions, specifically, have been linked to cardiovascular and respiratory morbidity, all-cause mortality, and low-birth weight [16, 22, 24, 25] Dust can also transport pathogens, which could result in spread of diseases such as coccidioidomycosis (Valley Fever) [26]. Studies have shown relationships between Valley Fever disease incidence and drought intensity or rain after periods of drought [27, 28]. Drought might also affect human health through changes in vector-borne disease transmission that could occur, especially among mosquito-borne diseases, due to stagnant water or changes in host-vector disease dynamics [18, 29, 30]. West Nile Virus and other mosquito-borne diseases have been found associated with drought or decreased precipitation [30-32]. Finally, drought can lead to economic hardship, population displacement, and other major psychological stressors with health relevance [33, 34].

A recent systematic review of evidence for the health effects of droughts showed that high-quality, quantitative studies on the association of drought and mortality are limited [10]. Cross sectional studies made up the majority of those identified [10]. While they may have shown high prevalence of mortality at the time of droughts, they could not prove causality [10]. Additionally, the studies mostly focused on lower income countries which often experienced famines during drought. In general, because higher income countries are probably less vulnerable to drought in terms of food and water scarcity, and may have increased capacity to adapt, the potential causal pathways from drought to mortality in the United States might differ. One of the few quantitative studies that exist on drought and mortality includes a meta-analysis of death rates among children underage-five in Ethiopia from aggregated mortality surveys. The authors did not find death rates above the Sub-Saharan Africa emergency and baseline threshold and concluded there was no likely association between drought and the under-age-five death rate, but did find the under-age-five death rate increased as prevalence of acute malnutrition increased [35]. For the reasons mentioned, this study is probably not generalizable to the United States.

A few studies in Australia have looked at suicide as a specific cause of mortality during droughts[10]. One study found the relative risk of suicide between 1970 and 2007 among rural males, age 30-49 in New South Wales, Australia increased 15% when drought index rose from the 1st to the 3rd quartile, after controlling for season, region and long-term trends [36]. They also found that the risk of suicide in rural females >30 years of age decreased as drought became more severe [36]. Another study from New South Wales found an increased risk of suicide with decreased precipitation, but did not

specifically classify periods of drought based on an index [37]. A third study did not find any increase in farming suicides during a prolonged drought in Australia [38].

Only one other study that we are aware of has directly analyzed the association between droughts and all-cause mortality in the United States [29]. This retrospective study focused on individuals 65 years and older from counties in the western U.S. between 2000 and 2013 [29]. They compared drought to non-drought period days using the U.S. Drought Monitor to identify droughts based on full drought, non-drought and worsening drought periods, stratifying by severity [29]. They found a 1.55% (Posterior Interval: 0.17, 2.95) increased risk of all-cause mortality during high-severity worsening drought periods [29]. They also found increased mortality during worsening drought compared to non-drought periods in counties where drought occurred less frequently [29].

Because of the lack of studies on the association between drought and mortality, the importance of understanding the health impacts of drought, and the potential specificity of drought health effects for specific subpopulations, we aimed in this study to evaluate the associations between droughts and same-year all-cause mortality in adults in United States from 1968-2014.

METHODS

Data

Standardized Precipitation and Evapotranspiration Index

We derived an annual drought severity score for each county from a dataset of 1month, county-level Standardized Precipitation and Evapotranspiration Index (SPEI) data for years 1968-2014 for the contiguous United States and District of Columbia. The Standardized Precipitation and Evapotranspiration Index (SPEI) is a climatic drought index based on precipitation and temperature data [39]. Drought indices are quantitative measures derived from the integration of relevant drought indicators (i.e. precipitation) into a single numerical value for drought characterization [3]. Different indices use different variables as indicators, and therefore may reflect different characteristics of drought (i.e. meteorological vs. hydrological). The SPEI is similar to the Standardized Precipitation Index (SPI), but also accounts for the effects of temperature variability on drought assessments through potential evapotranspiration [39].

The SPEI can be calculated for timescales ranging from 1 to 48 months [39]. The calculation of the SPEI includes the difference between precipitation and potential evapotranspiration (PET), known as the climatic water balance [39]. It uses meteorological data, and usually includes numerous parameters such surface temperature, air humidity, water vapor pressure [39]. SPEI calculation involves summation of deficits and surpluses across time [39] For an SPEI of a given timescale, k months, a time series is constructed by summing the PET values from the proceeding k-1 months then fitted to a probability density function of a log-logistic function to standardize the values (mean 0, SD 1) making it comparable across time, space, and time scales [40].

The SPEI ranges from -3 to 3. Values above 0 indicate relatively wet conditions, and values below 0 indicate relatively dry conditions, with numbers further from zero in either direction representing more extreme conditions [39].

Drought Severity Score

The drought severity score we derived represents a continuous measure of drought severity based on the duration and intensity of abnormal dryness across the 12-month period for each county. We defined drought as when contiguous months have each sustained at least a "moderately dry" SPEI= -1, with the drought accruing a cumulative SPEI \leq -5. The indicator for a month being part of a drought was multiplied by the SPEI of that month to calculate a monthly drought score for each county. The annual drought severity score was then calculated by summing the monthly drought scores within each year, for each county. The code for calculating this score is provided in **Appendix I.**

We also created an analogous severity score for annual wetness. A wet period was defined as when contiguous months have sustained at least a "moderately wet" SPEI=1, with the wet period accruing cumulative SPEI \geq 5. We multiplied the wet period indicator by SPEI (positive during wet period) to obtain a wetness severity score.

All-Cause Mortality

The all-cause mortality data came from a United States Centers for Disease Control and Prevention's (CDC) National Vital Statistics System dataset, managed through the University of Pittsburg Project Tycho. The dataset included mortality counts, by county-year, for counties and county-equivalents within the contiguous United States over 1968-2014, among narrow demographic strata (i.e., age group, race and sex joint categories). The dataset included 13 categories of age, 3 categories of race (black, white, other) and 2 categories of sex. Our analysis included data from adults ages 25 and older with age categories 25-34, 35-44, 45-54, 55-64, 65-74, 75-84, and 85 and older. If the number of deaths was 0 or \geq 10 the exact number was reported, but if the number fell between 1 and 9, the number was censored and only reported as being in that interval. The dataset also included population count data by county-year for each demographic stratum.

Climate Region

The National Oceanic and Atmospheric Association (NOAA) Climate Regions (**Table 1**) for the United States were used to explore geographic heterogeneity in the association between droughts and mortality. The regions were determined by climatological analyses which considered distributions of precipitation and temperature in the contiguous United States [41]. The District of Columbia is geographically located between the Northeast and Southeast regions [42]. We chose to include it with the Northeast region for analysis.

Study Sample

This was a complete case analysis that included a total of 5,099,479 observations from 42 demographic strata in 3004 counties and county-equivalents with complete data on stratum-year mortality counts, stratum-year population, and county-year drought scores.

In the CDC mortality dataset, county-year-stratum population size was recorded as 0 for 1,013,237 observations of the 6,137,544 (16.5%); we regarded these as indicating missing data for the actual population size in that county-demographic stratum-year, although it is possible that in some instances a demographic stratum was not represented within a county within a year. These records were therefore excluded from the complete case analysis.

Nine counties were missing SPEI data for all years (0.17%) and were thus excluded entirely from our study. The remaining counties included in the analysis had no missing data on SPEI from 1968-2014. There were 16,380 observations without mortality count data (0.27%). This missingness usually occurred over a consecutive span of several years. For example, La Paz County, Arizona was missing 26 county-years (1092 observations) from 1968-1993, but had complete data from the remaining years, 1994-2014. La Paz County, Arizona did not form officially until 1983 after separating from Yuma County [43]. This highlights the fact that some of the missing data may be related to changing Federal Information Processing System (FIPS) Codes for the given spatial location, and counties that formed officially after 1968. FIPS codes are unique numerical identifiers for each county or county-equivalent, but the geographic boundaries of counties can change over time, and new counties can form or merge with other counties [43]. As a result, changes to the size and location of a given county in our dataset could occur across time. For example, Yuma County would have decreased in size with the formation of La Paz County.

Statistical Analysis

We modeled county-stratum-year mortality using an interval censored [1,9] negative binomial regression model with random intercepts. The interval censoring accounts for the censored deaths, while the random intercepts allow different countylevel baseline mortality rates and account for correlations due to repeated observations of the same county. Our negative binomial regression model assumed a linear predictor for the mean number of deaths of the following form:

$$\ln(\mu_{ij}) = (\beta_0 + b_{0i}) + \beta_1 x_{ij} + \sum_{t=2}^k \beta_t z_{ijt} + f_i ,$$

where x_{ij} is the drought score for county i in year j, z_t variables are confounders (e.g., year) and (b_{0i}) the random intercept. The offset, f_i , is the log(population) for each countystratum-year. When the number of deaths (y_{ij}) is 0 or ≥ 10 and not censored, the likelihood contribution for county *i* in year *j*, conditional on the random intercept, is given by

$$\Pr(\mathbf{Y}_{ij} = \mathbf{y}_{ij} \mid \mathbf{X}_{ij} = \mathbf{x}_{ij}, \mathbf{Z}_{ij} = \mathbf{z}_{ij}) = \frac{\Gamma(\alpha^{-1} + \mathbf{y}_{ij})}{\Gamma(\alpha^{-1}) \mathbf{y}_{ij}!} \left(\frac{\alpha \mu_{ij}}{1 + \alpha \mu_{ij}}\right)^{\mathbf{y}_{ij}} \left(\frac{1}{1 + \alpha \mu_{ij}}\right)^{1/\alpha}$$

where α is the negative binomial dispersion parameter. When the number of deaths is censored over the interval [1, 9], the conditional likelihood contribution becomes

$$\Pr(1 \le Y_{ij} \le 9 | X_{ij} = x_{ij}, \mathbf{Z}_{ij} = \mathbf{z}_{ij})$$
,

based on the negative binomial model.

We implemented maximum likelihood (ML) estimation for this model using the general likelihood facility available in the SAS NLMIXED procedure using SAS 9.3 software (SAS, Cary, NC), which permits user specification of the log-likelihood conditional on the random effects. We specified the contributions for censored observations by taking advantage of recursive properties of the gamma function.

We ran models separately for each of the 42 age-race-sex joint strata. We also further stratified by the nine NOAA climate regions in a second analysis, for a total of 378 strata, to account for potential geographic heterogeneity in the association of drought score with mortality. We repeated the analysis after excluding abnormally wet county-years from analysis (wetness severity score >0) to assess a counterfactual of "drought" vs. "normal" years, rather than "drought" vs. "non-drought" years.

We accounted for multiple testing using the SAS PROC MULTTEST procedure using SAS 9.3 (SAS, Cary, NC) using the FDR option, which estimates false discovery rate (FDR) -adjusted p values. We adjusted p values separately for each of the four sets of analyses: with and without stratification by NOAA regions, and with and without inclusion of abnormally wet years. We used the estimates from the models that successfully converged. Because we had four sets of analyses, we used a Bonferronicorrected threshold of adjusted p < 0.0125 (alpha=0.05/4) for a stratum-specific association (e.g., association of drought with mortality among white men aged 25-34 in the South) to be considered statistically significant. Only models that converged were included in the multiple testing correction.

We completed random effects meta-regressions using *metareg* in Stata/SE 14.2 to assess whether a linear relationship exists between the regression coefficients from the main analysis (i.e., differences in log-rates of mortality given drought, within each stratum, adjusted for year and conditional on random effects), and potential modifiers of the drought-to-mortality association: age, race, sex, and region[44]. Significance of the association of each predictor, adjusted for the others, with the drought-mortality regression coefficient was assessed by Wald test.

After finding that there was no evident heterogeneity in the association of drought severity with same-year mortality by these predictors, we pooled the estimates in a meta-

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analysis using the Stata/SE 14.2 *metan* procedure. We report the pooled effect estimate along with the I^2 as a measure of the percentage of residual variation attributable to the between-study heterogeneity[45].

RESULTS

Most models in the analyses successfully converged, but there were some estimation problems, where models failed to converge without errors. This issue occurred among "other race" female subgroup for age categories (years) "24-34", "35-44" and "45-55" in age, race and sex (but not region) stratified analyses. When stratified by a fourth variable, NOAA climate region, 36 of the 378 models failed to converge without error in the analysis including abnormally wet county-years. We excluded two additional models which converged, but had unstable or unrealistic estimates, for example an IRR, 95% CI of 0.119 (5.001E-8, 283832.31). Additionally, for the analysis stratified by NOAA region which excluded abnormally wet county-years, 31 of 378 models failed to converge without error. We excluded one additional model that resulted in unrealistic IRR, 95% CI of 0.119 (4.797E-8, 297567.77). The majority of the models that failed to converge were in the "other race" strata.

Overall, most results were null across categories of race, region, age and sex, with IRRs for all-cause mortality close to 1. When further stratified by NOAA region, the majority of results stayed null. Exclusion of wet county-years resulted in little to no change in the effect estimates.

A small number of IRRs were significant after accounting for the multiple testing (adjusted p values <0.0125). For IRRs by demographic age, race and sex subgroups,

ignoring region, with and without wet county-years, there were 4 significant results after adjustment. These were for white males, 25 to 34, 35 to 44, 75 to 84 and 85 plus years of age. All suggested a slight protective effect of increasing drought severity on all-cause mortality with IRRs less than 1. When further stratified by NOAA region, there were 10 significant IRRs with inclusion of abnormally wet county-years in the analysis, and 11 with exclusion of abnormally wet county-years in the analysis. Most of these significant estimates were seen in the white, male subgroups, across a range of ages and NOAA regions, most frequently the South region. Most of the significant IRRs for white males were from the South region. For this subgroup, the estimates suggested a slightly protective effect of drought severity on mortality, with IRRs below 1. One significant IRR was greater than 1, with an IRR, 95% Cl of 1.015 (1.008, 1.022), in both the analyses with and without abnormally wet county-years. This was among the 75 to 84year-old black males in the Northeast region, suggesting a possible increase in all-cause mortality with increasing drought severity for this subgroup. When wet county-years were excluded, the IRR for 65 to 75-year-old "other race" males in the West-North-Central region was also significant with an IRR, 95% CI of 1.066 (1.033, 1.099). This model did not converge in the analysis that included the wet county-years. In general, the results for the black and "other race" subgroups usually had wider confidence intervals than the white subgroup due to smaller sample sizes in some climate regions.

All of the tests for the significance of associations of each predictor, age, race, sex and region, with the drought-mortality regression coefficient from the meta-regression were null. This suggests that no linear relationship exists between the regression coefficients from the main analysis and any of these mutually-adjusted demographic and geographic predictors. In other words, there are no consistent differences in the relationship of drought intensity with mortality across these broad population characteristics.

The meta-analyses resulted in a pooled IRR of 0.999 (0.999, 1.000) from the analyses that stratified by NOAA region, with and without wet county-years included. The I² of 49.9% for the analysis that included the wet county-years, and 49.5% for the analysis that excluded them, suggests that about half of the total variation across stratified groups is due to heterogeneity.

DISCUSSION

Overall, these results suggest that, for the majority of demographic subgroups and across climate regions, there is no significant effect of drought intensity on mortality rates within the same year in the contiguous United States over 1968-2014. Nonetheless, after accounting for multiple hypothesis testing, we found significant associations for some of the stratified analyses, suggesting a possible health effect for certain subgroups, but this heterogeneity was not consistent across broad patterns of age, race, sex or region. This finding might suggest the effects of drought are contextual, based on specific characteristics of the drought and the vulnerability of the populations they impact.

Differences in exposure and vulnerability to climate-related events, the key determinants of disaster risk and impacts, exist that often leave marginalized groups disproportionately impacted [11]. This can often be attributed to intersecting social processes such as discrimination based on class, gender, or ethnicity, and not a single cause[11]. Stratifying the analysis by age, race, sex and region may be an oversimplification of this intersectionality. Differences in risk may be better considered at a local level to account for population and drought heterogeneity on a smaller spatial scale. Additionally, other variables not considered in the analysis, such as socioeconomic status or rural vs. urban residence, may be important modifiers.

Although we did not detect an association of drought intensity with same-year mortality for most subgroups, it is possible that drought conditions could increase some cause-specific mortality rates, while decreasing others cause-specific mortality rates, resulting in an overall null result. This analysis only considered all-cause mortality, and specific types of mortality, such as respiratory or cardiovascular mortality could still have increased rates due to drought. If there are cause-specific mortalities that increase due to drought, it is important to understand the causes for targeted interventions.

There were numerous strengths in this study, including the creation of the novel drought severity score. This was designed to capture drought intensity and duration over the year with a continuous scale from the available one-month SPEI data. This scale allowed us to look for effects related to drought severity, and not simply classify exposure as drought vs. non-drought in the analysis. Since drought severity is a factor in human and societal impacts such degree of water shortages or fire risk, we would expect it to cause differences in the effect on mortality [1]. Additionally, the analysis stratified by joint categories of age, race, sex and NOAA climate region to account for possible interactions of these variables with drought severity on mortality, allowing for potentially higher-order interactions between these dimensions of vulnerability. We found evidence for higher-order interactions, in that the pairwise interactions (i.e., meta-regression)

coefficients) were not significant, while the effects of drought were distinct by joint strata of these variables.

This study also has some limitations, including the censoring of the number of deaths on the interval [1,9] in the dataset. We used interval censored negative binomial regression to handle the missing data, but this reduced our estimation precision compared to what it would have been if these counts had not been censored. Additionally, there was missing data on population, mortality, and SPEI, which decreased the sample size, and could lead to bias if the missing observations differed in terms of drought exposure or mortality from those included. Small strata resulted in non-convergence and wide confidence intervals for some models. This especially affected the "other race" category, which had the greatest number of non-converging models. If the more frequently excluded demographic groups due to smaller N are more vulnerable than the included groups, and if they also differ in terms of inclusion based on drought exposure status, selection bias could result for the overall effect estimate, and we may be oblivious to identifying particularly vulnerable groups.

Also, despite the strengths of the SPEI, we only used one index for creating the annual drought severity score, whereas another index might have resulted in different classification of drought periods and severity [3]. On a related note, our analysis did not specifically account for differences in the types of droughts, such as agricultural vs. meteorological, which could theoretically affect health outcomes differently since they focus on different issues (i.e. effects on crops for agricultural drought) [4]. Additionally, we did not account for the effect of previous years of drought, except when classifying drought vs. non-drought months for the derivation of the drought severity score. Duration

and frequency of drought might impact a community's adaptive capacity, and also result in different exposure durations to potentially harmful or preventative drought-related conditions [11]. We also did not account for potential interactions between abnormally wet periods following drought, or drought following abnormally wet periods. Hypothetically, differences could exist from increased rainfall after a drought due to mudslides, flooding, or indirect factors such as changes in disease transmission and water quality, as noted with the increased incidence of Valley Fever after a period of rain following drought [10, 28]. Increased plant growth from a wet period followed by drought might lead to further fuel for wildfires in the form of vegetation, which is related to fire risk and spread [46]. These may be useful avenues for further investigation. While we also did not include a variable for temperature in the analysis, SPEI accounts for temperature when calculating evapotranspiration [39]. Temperature has a complex relationship with drought. Since heat can cause heat-related all-cause mortality and influence drought severity through evapotranspiration, it could be considered a confounder [2, 12, 14, 40]. Multiple variables are considered in the calculation of evapotranspiration, and two droughts of the same SPEI could have different extreme or average high temperatures, and therefore differences in heat-related deaths [39]. Still, because heat is a factor of drought it may be impractical to separate the two [12, 39]. Heat could also be a mediator on the causal pathway between drought and mortality, since drought conditions can increase temperature, which can in turn increase heat related mortality [14]. Interactions could also possibly occur between the effects of heat and drought on all-cause mortality.

CONCLUSION:

In conclusion, the lack of significant associations between drought severity and all-cause mortality overall, and for many, but not all, subgroups after adjusting for multiple testing, could suggest a true null association except for a few subgroups, contextual heterogeneity in the effects of drought, an observed null effect of subgroups due to cancellation of the protective and harmful effects, limitations in the methods of our analysis, or some combination of these factors.

The next phase of analysis should try to address possible limitations and explore additional factors. For example, the analysis could include variables for lagged drought and abnormally wet years, and the interactions between combinations of these variables (i.e. lagged drought and current abnormally wet years, current drought, and lagged drought, etc.). It could also account for socioeconomic status and rural and urban residence to further develop the understanding of how drought impacts might play out across different segments of the United States population. In addition, the analysis could be repeated using a drought severity score derived from a drought index other than SPEI which might result in a different classification of droughts, or by focusing on droughts that meet the criteria for specific categories (i.e. hydrological vs. agricultural).

As a result of the possible contextual differences noted by the differences in subgroups, but not broad categories of region, age, race or sex, future investigations may be better tailored to local settings with smaller spatial scales than our analyses. Future research could also consider the association between droughts and cause specific mortality, such as respiratory or cardiovascular mortality, because of the proposed mechanisms for harm. Understanding the effects of drought on human health, and who is most at risk, is necessary for prevention and adaptation strategies, and is especially critical due to the projected increase in intensity and frequency of droughts for certain areas of the world.

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TABLES

| regions and states for the United States | | | | |
|--|--|--|--|--|
| Region | States | | | |
| Central | IL, IN, KY, MO, OH, TN, WV | | | |
| East-North-Central | IA, MI, MN, WI | | | |
| North-East | CT, DE, ME, MD, MA, NH, NJ, NY, PA, RI, VT, DC | | | |
| North-West | ID, OR, WA | | | |
| South | AR, KS, LA, MS, OK, TX | | | |
| South-East | AL, FL, GA, NC, SC, VA | | | |
| South-West | AZ, CO, NM, UT | | | |
| West | CA, NV | | | |
| West-North-Central | MT, NE, ND, SD, WY | | | |

 Table 1. National Oceanic and Atmospheric Administration climate

| ADHOLI | lany wel y | ears melu | ueu ili allaly | / 515. | | | | |
|--------|------------|-----------|----------------|--------|-------|--------|------------|--|
| Age | Race | Sex | IRR | LCL | UCL | Raw P | Adjusted P | |
| 25-34 | White | Male | 0.991 | 0.987 | 0.995 | <.0001 | <.0001 | |
| 35-44 | White | Male | 0.994 | 0.991 | 0.997 | <.0001 | 0.0008 | |
| 75-84 | White | Male | 0.998 | 0.997 | 0.999 | 0.0001 | 0.0017 | |
| 85 + | White | Male | 0.998 | 0.997 | 0.999 | 0.0004 | 0.0043 | |

Table 2. Incidence Rate Ratio (IRR) of all-cause mortality per increasing drought intensity by demographic subgroup, with 95% confidence intervals (LCL, UCL), raw p-values and false discovery rate adjusted p values for IRRs with adjusted p values <0.0125. Abnormally wet years included in analysis.

| Table 3. Incidence Rate Ratio (IRR) of all-cause mortality per increasing drought intensity by |
|--|
| demographic and climate region subgroup, with 95% confidence intervals (LCL, UCL), raw p- |
| values and false discovery rate adjusted p values for IRRs with adjusted p values <0.0125. |
| Abnormally wet years included in analysis. |

| Age | Race | Sex | Region | IRR | LCL | UCL | Raw P | Adjusted P |
|-------|-------|--------|-----------|-------|-------|-------|--------|------------|
| 25-34 | White | Male | South | 0.987 | 0.980 | 0.993 | <.0001 | 0.0045 |
| 35-44 | White | Male | South | 0.990 | 0.985 | 0.995 | 0.0001 | 0.0055 |
| 55-64 | White | Male | Northeast | 0.991 | 0.987 | 0.996 | 0.0002 | 0.0057 |
| 55-64 | White | Male | Southeast | 0.992 | 0.988 | 0.996 | 0.0002 | 0.0057 |
| 65-74 | White | Male | South | 0.996 | 0.994 | 0.998 | 0.0001 | 0.0055 |
| 65-74 | White | Female | West | 0.991 | 0.988 | 0.995 | <.0001 | 0.0022 |
| 75-84 | White | Male | South | 0.996 | 0.994 | 0.998 | <.0001 | 0.0042 |
| 75-84 | White | Female | West | 0.995 | 0.992 | 0.997 | <.0001 | 0.0053 |
| 75-84 | Black | Male | Northeast | 1.015 | 1.008 | 1.022 | <.0001 | 0.0045 |
| 85+ | White | Male | South | 0.995 | 0.993 | 0.997 | <.0001 | 0.0021 |

| intensity by demographic subgroup, with 95% confidence intervals (LCL, UCL), raw p-values and false discovery rate adjusted p values for IRRs with adjusted p values <0.0125. Abnormally wet years excluded from analysis. | | | | | | | |
|--|-------|------|-------|-------|-------|--------|------------|
| Age | Race | Sex | IRR | LCL | UCL | Raw P | Adjusted P |
| 25-34 | White | Male | 0.991 | 0.987 | 0.995 | <.0001 | <.0001 |
| 35-44 | White | Male | 0.994 | 0.991 | 0.997 | <.0001 | 0.0007 |
| 75-84 | White | Male | 0.998 | 0.997 | 0.999 | 0.0002 | 0.0020 |
| 85 + | White | Male | 0.998 | 0.997 | 0.999 | 0.0004 | 0.0043 |

Table 4. Incidence Rate Ratio (IRR) of all-cause mortality per increasing drought

| excluded from analysis. | | | | | | | | |
|-------------------------|-------|--------|--------------------|-------|-------|-------|--------|------------|
| Age | Race | Sex | Region | IRR | LCL | UCL | Raw P | Adjusted P |
| 25-34 | White | Male | South | 0.987 | 0.981 | 0.993 | <.0001 | 0.0050 |
| 35-44 | White | Male | South | 0.990 | 0.985 | 0.995 | 0.0002 | 0.0061 |
| 55-64 | White | Male | Northeast | 0.991 | 0.987 | 0.996 | 0.0002 | 0.0068 |
| 55-64 | White | Male | Southeast | 0.992 | 0.988 | 0.996 | 0.0002 | 0.0069 |
| 65-74 | White | Male | South | 0.996 | 0.994 | 0.998 | 0.0001 | 0.0054 |
| 65-74 | White | Female | West | 0.991 | 0.988 | 0.995 | <.0001 | 0.0025 |
| 65-74 | Other | Male | West North Central | 1.066 | 1.033 | 1.099 | <.0001 | 0.0050 |
| 75-84 | White | Male | South | 0.996 | 0.995 | 0.998 | <.0001 | 0.0050 |
| 75-84 | White | Female | West | 0.995 | 0.992 | 0.997 | 0.0001 | 0.0054 |
| 75-84 | Black | Male | Northeast | 1.015 | 1.008 | 1.022 | <.0001 | 0.005 |

Table 5. Incidence Rate Ratio (IRR) of all-cause mortality per increasing drought intensity by demographic and climate region subgroup, with 95% confidence intervals (LCL, UCL), raw p-values and false discovery rate adjusted for IRRs with adjusted p values <0.0125. Abnormally wet years excluded from analysis.

| Table 6. Metaregression p values by covariate, with and without abnormally wet years included in analysis | | | | |
|---|---------|--|--|--|
| Covariate P value | | | | |
| Wet Years In | ncluded | | | |
| Race | 0.996 | | | |
| Sex | 1.000 | | | |
| Age | 1.000 | | | |
| Region | 1.000 | | | |
| Wet Years E | xcluded | | | |
| Race | 0.996 | | | |
| Sex | 0.995 | | | |
| Age | 1.000 | | | |
| Region | 1.000 | | | |

Table 7. Pooled IRRs of mortality per increasing drought intensity, with 95% confidence intervals (LCL, UCL), I² statistic from tests for heterogeneity. These were calculated from meta-analyses across demographic and climate region subgroups, with and without abnormally wet years included in analysis.

| Wet Years | IRR | LCL | UCL | \mathbf{I}^2 |
|-----------|-------|-------|-------|----------------|
| Included | 0.999 | 0.999 | 1.000 | 49.9% |
| Excluded | 0.999 | 0.999 | 1.000 | 49.5% |

APPENDIX I. Drought Severity Score Stata Code

*Create month lag for SPEI, by county

```
by fips: gen spei_lag1 = spei[_n-1]
by fips: gen spei_lag2 = spei[_n-2]
by fips: gen spei_lag3 = spei[_n-3]
by fips: gen spei_lag4 = spei[_n-4]
by fips: gen spei_lead1 = spei[_n+1]
by fips: gen spei_lead2 = spei[_n+2]
by fips: gen spei_lead3 = spei[_n+3]
by fips: gen spei_lead4 = spei[_n+4]
```

*The default condition for drought severity is 'not a drought'.

gen is_drought = 0

*Drop the missing SPEI values from the five counties

drop if spei<-90

*Berman et al, 2017 [29] defined "is a drought" if 5 continuous months of moderate drought.

replace is_drought = 1 if ((spei_lag4 <= -1 & spei_lag4 !=.) & (spei_lag3 <= -1 & spei_lag3 !=.) &
(spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag3 <= -1 & spei_lag3 !=.) & (spei_lag1 <= -1 & spei_lag2 !=.) &
(spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei_lag2 !=.) & (spei_led1 <= -1 & spei_led1 !=.))
replace is_drought = 1 if ((spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_led1 !=.))
replace is_drought = 1 if ((spei_lag2 <= -1 & spei_led1 !=.) & (spei_led2 <= -1 & spei_led2 !=.) &
(spei_<= -1 & spei_!=.) & (spei_led1 <= -1 & spei_led1 !=.) & (spei_led2 <= -1 & spei_led2 !=.) &
(spei_lead1 <= -1 & spei_led1 !=.) & (spei_led2 <= -1 & spei_led2 !=.) &
(spei_lead3 <= -1 & spei_led3 !=.))
replace is_drought = 1 if ((spei_<= -1 & spei_led2 <= -1 & spei_led2 !=.) & (spei_lead3 <= -1 & spei_lead3 !=.))
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_led2 <= -1 & spei_lead2 !=.) & (spei_lead3 <= -1 & spei_lead3 <= -1 & spei_lead3 !=.))
replace is_drought = 1 if ((spei_<= -1 & spei_lead2 <= -1 & spei_lead1 <= -1 & spei_lead3 <= -1 & spei_lead3 !=.))
replace is_drought = 1 if ((spei_<= -1 & spei_!=.) & (spei_lead1 <= -1 & spei_lead3 <= -1 & spei_lead3 !=.))
replace is_drought = 1 if ((spei_<= -1 & spei_!=.) & (spei_lead1 <= -1 & spei_lead4 <= -1 & spei_lead4 !=.))</pre>

```
*At least one of 4 months has an SPEI <=-2
```

replace is_drought = 1 if ((spei_lag3 <= -2 & spei_lag3 !=.) & (spei_lag2 <= -1 & spei_lag2 !=.) &
(spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag3 <= -1 & spei_lag3 !=.) & (spei_lag2 <= -2 & spei_lag2 !=.) &
(spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag3 <= -1 & spei_lag3 !=.) & (spei_lag2 <= -1 & spei_lag2 !=.) &
(spei_lag1 <= -2 & spei_lag1 !=.) & (spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag3 <= -1 & spei_lag3 !=.) & (spei_lag2 <= -1 & spei_lag2 !=.) &
(spei_lag1 <= -2 & spei_lag1 !=.) & (spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag3 <= -1 & spei_lag3 !=.) & (spei_lag2 <= -1 & spei_lag2 !=.) &
(spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -2 & spei!=.))</pre>

```
replace is_drought = 1 if ((spei_lag2 <= -2 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -1 & spei!=.) & (spei_lead1 <= -1 & spei_lead1 !=.))
replace is_drought = 1 if ((spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -2 & spei_lag1 !=.) &
(spei <= -1 & spei!=.) & (spei_lead1 <= -1 & spei_lead1 !=.))
replace is_drought = 1 if ((spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -2 & spei!=.) & (spei_lead1 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -2 & spei!=.) & (spei_lead1 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -2 & spei!=.) & (spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -1 & spei!=.) & (spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -1 & spei!=.) & (spei_lag1 <= -2 & spei_lag1 !=.))</pre>
```

```
replace is_drought = 1 if ((spei_lag1 <= -2 & spei_lag1 !=.) & (spei <= -1 & spei !=.) &
(spei_lead1 <= -1 & spei_lead1 !=.) & (spei_lead2 <= -1 & spei_lead2 !=.))
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -2 & spei !=.) &
(spei_lead1 <= -1 & spei_lead1 !=.) & (spei_lead2 <= -1 & spei_lead2 !=.))
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei !=.) &
(spei_lead1 <= -2 & spei_lead1 !=.) & (spei_lead2 <= -1 & spei_lead2 !=.))
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei !=.) &
(spei_lead1 <= -2 & spei_lead1 !=.) & (spei_lead2 <= -1 & spei_lead2 !=.))
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei !=.) &
(spei_lead1 <= -1 & spei_lead1 !=.) & (spei_lead2 <= -2 & spei_lead2 !=.))</pre>
```

```
replace is_drought = 1 if ((spei <= -2 & spei !=.) & (spei_lead1 <= -1 & spei_lead1 !=.) &
(spei_lead2 <= -1 & spei_lead2 !=.) & (spei_lead3 <= -1 & spei_lead3 !=.))
replace is_drought = 1 if ((spei <= -1 & spei !=.) & (spei_lead1 <= -2 & spei_lead1 !=.) &</pre>
(spei_lead2 <= -1 & spei_lead2 !=.) & (spei_lead3 <= -1 & spei_lead3 !=.))</pre>
replace is_drought = 1 if ((spei <= -1 & spei !=.) & (spei_lead1 <= -1 & spei_lead1 !=.) &</pre>
(spei_lead2 <= -2 & spei_lead2 !=.) & (spei_lead3 <= -1 & spei_lead3 !=.))</pre>
replace is_drought = 1 if ((spei <= -1 & spei !=.) & (spei_lead1 <= -1 & spei_lead1 !=.) &
(spei_lead2 <= -1 & spei_lead2 !=.) & (spei_lead3 <= -2 & spei_lead3 !=.))</pre>
*At least one of 3 months has an SPEI of <=-3
replace is drought = 1 if ((spei_lag2 <= -3 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -3 & spei_lag1 !=.) &</pre>
(spei <= -1 & spei!=.))
replace is_drought = 1 if ((spei_lag2 <= -1 & spei_lag2 !=.) & (spei_lag1 <= -1 & spei_lag1 !=.) &
(spei <= -3 & spei!=.))
replace is_drought = 1 if ((spei_lag1 <= -3 & spei_lag1 !=.) & (spei <= -1 & spei!=.) &</pre>
(spei_lead1 <= -1 & spei_lead1 !=.))</pre>
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -3 & spei!=.) &</pre>
(spei lead1 <= -1 & spei lead1 !=.))</pre>
replace is_drought = 1 if ((spei_lag1 <= -1 & spei_lag1 !=.) & (spei <= -1 & spei!=.) &</pre>
(spei_lead1 <= -3 & spei_lead1 !=.))</pre>
replace is_drought = 1 if ((spei <= -3 & spei !=.) & (spei_lead1 <= -1 & spei_lead1 !=.) &
(spei_lead2 <= -1 & spei_lead2 !=.))</pre>
replace is_drought = 1 if ((spei <= -1 & spei !=.) & (spei_lead1 <= -3 & spei_lead1 !=.) &</pre>
(spei lead2 <= -1 & spei lead2 !=.))</pre>
replace is_drought = 1 if ((spei <= -1 & spei !=.) & (spei_lead1 <= -1 & spei_lead1 !=.) &
(spei_lead2 <= -3 & spei_lead2 !=.))</pre>
* Two adjacent months have SPEIs <=-2 and <=-3
replace is_drought = 1 if ((spei_lag1 <= -3 & spei_lag1 !=.) & (spei <= -2 & spei!=.))
replace is_drought = 1 if ((spei_lag1 <= -2 & spei_lag1 !=.) & (spei <= -3 & spei!=.))
replace is_drought = 1 if ((spei <= -3 & spei!=.) & (spei_lead1 <= -2 & spei_lead1 !=.))</pre>
replace is drought = 1 if ((spei <= -2 & spei!=.) & (spei lead1 <= -3 & spei lead1 !=.))</pre>
* Generate monthly score and sum for each county-year to calculate drought score
gen month_score = is_drought*spei
bysort fips year: egen drought_score = total(month_score)
replace drought_score=. if spei<-90</pre>
gen drought_index = drought_score * -1
```

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APPENDIX II. Missing Data Tables

| Table A1. FIPS code and frequency of observations missing drought score data, among subgroups 25 and older before removal of observations where population equals 0. | | | | |
|---|--------|---------|--|--|
| FIPS | Freq. | Percent | | |
| 12009 | 1,974 | 19.26 | | |
| 13999 | 168 | 1.64 | | |
| 30113 | 882 | 8.61 | | |
| 51515 | 1,344 | 13.11 | | |
| 51560 | 924 | 9.02 | | |
| 51595 | 1,512 | 14.75 | | |
| 51610 | 1,512 | 14.75 | | |
| 51620 | 1,512 | 14.75 | | |
| 51780 | 420 | 4.1 | | |
| Total | 10,248 | 100 | | |

Table A2. FIPS code and frequency
of observations missing drought
score data among subgroups of ages25 and older, after removal of
observations where population
equals 0.

| FIPS | Freq. | Percent |
|-------|-------|---------|
| 12009 | 1,974 | 23.37 |
| 30113 | 230 | 2.72 |
| 51515 | 1,130 | 13.38 |
| 51560 | 702 | 8.31 |
| 51595 | 1,307 | 15.47 |
| 51610 | 1,445 | 17.1 |
| 51620 | 1,294 | 15.32 |
| 51780 | 366 | 4.33 |
| Total | 8,448 | 100 |

| FIPS | County- Years Missing | Number Observations Missing | Percent Missing |
|-------|-----------------------------|-----------------------------------|-----------------|
| 4012 | 26 | 1092 | 6.67 |
| 8014 | 35 | 1470 | 8.97 |
| 35006 | 21 | 882 | 5.38 |
| 51520 | 11 | 462 | 2.82 |
| 51530 | 11 | 462 | 2.82 |
| 51540 | 11 | 462 | 2.82 |
| 51570 | 11 | 462 | 2.82 |
| 51580 | 11 | 462 | 2.82 |
| 51590 | 11 | 462 | 2.82 |
| 51600 | 11 | 462 | 2.82 |
| 51630 | 11 | 462 | 2.82 |
| 51640 | 11 | 462 | 2.82 |
| 51660 | 11 | 462 | 2.82 |
| 51670 | 11 | 462 | 2.82 |
| 51678 | 11 | 462 | 2.82 |
| 51680 | 11 | 462 | 2.82 |
| 51683 | 11 | 462 | 2.82 |
| 51685 | 11 | 462 | 2.82 |
| 51690 | 11 | 462 | 2.82 |
| 51720 | 11 | 462 | 2.82 |
| 51730 | 11 | 462 | 2.82 |
| 51735 | 11 | 462 | 2.82 |
| 51740 | 11 | 462 | 2.82 |
| 51750 | 11 | 462 | 2.82 |
| 51760 | 11 | 462 | 2.82 |
| 51770 | 11 | 462 | 2.82 |
| 51775 | 11 | 462 | 2.82 |
| 51790 | 11 | 462 | 2.82 |
| 51820 | 11 | 462 | 2.82 |
| 51830 | 11 | 462 | 2.82 |
| 51840 | 11 | 462 | 2.82 |
| Total | 390 | 16,380 | 100 |

 Table A3. FIPS code and frequency of county-years and observations missing mortality data among subgroups of ages 25 and older.

APPENDIX III. Forest Plots















