Regulatory Toxicology and Pharmacology 96 (2018) 190–196

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

journal homepage: www.elsevier.com/locate/yrtph

$PM_{2.5}$ and ozone, indicators of air quality, and acute deaths in California, 2004–2007

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ABSTRACT

Since the London Great Smog of 1952 was estimated to have killed over 4000 people, scientists have studied the relationship between air quality and acute mortality. Currently, the association between air quality and acute deaths is usually taken as evidence for causality. As air quality has markedly improved since 1952, do contemporary datasets support this view? We use a large dataset, eight air basins in California for the years 2004–2007, to examine the possible association of ozone and $PM_{2.5}$ with acute deaths after statistically removing seasonal and weather effects. Our analysis dataset is available on request. We conducted a regression-corrected, case-crossover analysis for all non-accidental deaths age 75 and older. We used stepwise regression to examine three causes of death. After seasonal and weather adjustments, there was essentially no predictive power of ozone or $PM_{2.5}$ for acute deaths. The case-crossover analysis produced odds ratio very close to 1.000 (no effect). The very narrow confidence limits indicated good statistical power. We study recent air quality in both time-stratified, symmetric, bidirectional case-crossover and time series regression and both give consistent results. There is no statistically significant association between either ozone or $PM_{2.5}$ and acute human mortality. In the absence of an association, causality is in question.

1. Introduction

A recent paper by Schwartz et al. (2016) points to many time series studies that support an association of air quality and acute mortality. In a meta-analysis of myocardial infarct triggers, 14 studies support of the claim that " … air pollution is an important trigger of myocardial infarction …" (Nawrot et al., 2011), and in another meta-analysis (Mustafic et al., 2012), another six studies are given, again making the same claim. In contrast, other studies make the case that when potential biases are taken into account, there is no association between air quality and deaths (Chay et al., 2003; Cox et al., 2013; Enstrom, 2005; Greven et al., 2011; Janes et al., 2007; Wang et al., 2015; Yang et al., 2004; Zu et al., 2016). There are studies on both sides of the question, "Is air quality causal of acute human deaths?". The weight of evidence is on the side of a positive association, but for any claim to be considered causal, it takes only one valid, negative association study to negate the causality claim.

It is becoming clear that many scientific claims are failing to replicate (Begley and Ellis, 2012; Ioannidis, 2005; Young and Karr, 2011). Failure to replicate appears to be over many different scientific areas: psychology, epidemiology, experimental biology, physics, astrophysics, etc. The replication problem is old (Mayes et al., 1988); it has recently gained prominence as people wonder about its extent and what might be done to solve it. A survey of scientists (Baker, 2016) reports that 90% of scientist think there is a crisis in reproducibility (52% a significant crisis and 38% a slight crisis). Environmental epidemiology is likely subject to the same problems of other areas of science.

One factor that exacerbates the examination of reproducibility is the general lack of access to data. Cecil and Griffin (1985) note: "As an abstract principle, the sharing of research data is a noble goal and meets with little opposition. However, when data sharing is attempted in a particular circumstance, the conflicting interests of the parties can thwart the exchange. A glance at the benefits and obstacles to data sharing … reveals the reason: few of the benefits and most of the burdens fall to the possessor of a dataset." For example, the owner of the data might consider it burdensome to defend a claim. Finally, many authors do not attempt to report negative results as editors, typically, are much less likely to accept a negative study, so publication bias is expected result.

We have three goals with this research. Our first objective is to analyze a dataset for California relating mortality to levels of ozone and PM2.5. The American Lung Association regards Ozone and PM2.5 as the

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https://doi.org/10.1016/j.yrtph.2018.05.012
Received 29 August 2017; Received in revised form 5 May 2018; Accepted 17 May 2018
Available online 18 May 2018
0273-2300/

Fig. 1. Air basins of California.

most serious air quality health risks and notes that California has 7/10 US cities with poorest air quality (http://www.lung.org/assets/documents/healthy-air/state-of-the-air/state-of-the-air-2017.pdf). We use two independent analysis approaches, a case-crossover analysis, CCO (Figueiras et al., 2005), and a standard time series regression analysis, TSR. We give odds ratios along with confidence limits and p-values, raw and adjusted, for each method. Our second objective is to present a straightforward, stepwise regression analysis of the dataset. Here, we analyze three categories of mortality, two air quality variables, with time lags of 0 or 1 day, and eight air basin subsets (defined by geographical air basins in California), Fig. 1, https://www.arb.ca.gov/ei/maps/statemap/abmap.htm, for a total of 96 separate analyses. Our third objective is to provide the analysis dataset so that others can replicate our results as well as try different analysis strategies.

2. Methods

2.1. Data

For mortality, the state of California provides access to "death public use files" for research. The cause of deaths is indicated by an ICD 10 code. We coded three mortality categories: AllCause, Cardiovascular and Respiratory (AllCause65, CV65, and Resp65 respectively). In all cases, accidental deaths were excluded. Deaths of individuals above Age 65 and older were included in the regression analysis; AllCause75 was used in the case-crossover analysis. Each type of deaths was aggregated to the day and year within each air basin. The complete mortality data can be obtained from the California Department of

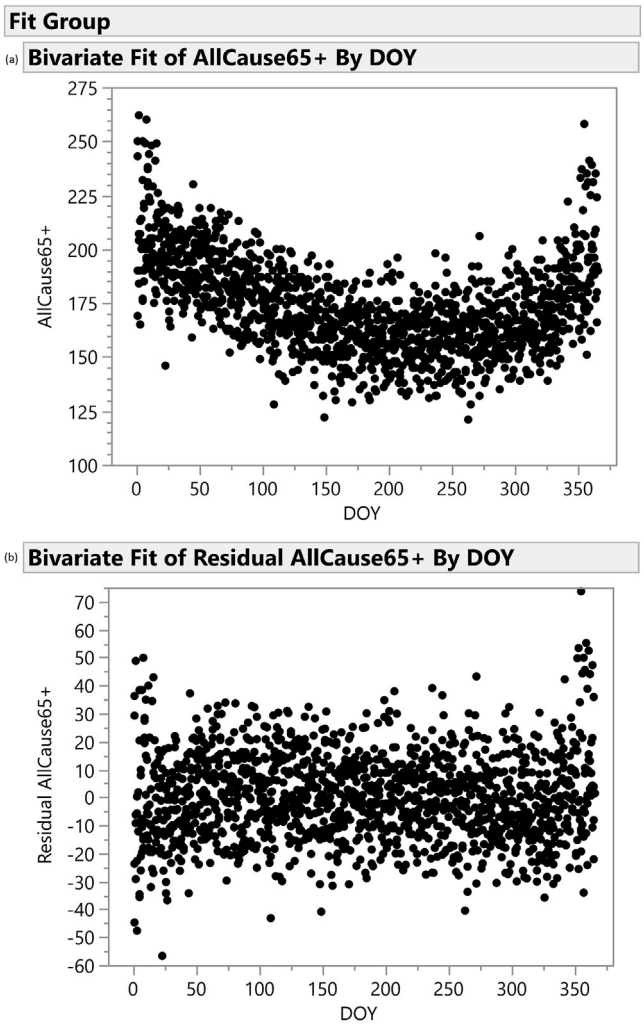

Fig. 3. South Coast Air Basin.
(a) Daily deaths versus Day of Year, DOY, for the years 2004–2007. Four years are overprinted.
(b) Deviations from Day of Year time series smoother, linear and quadratic model.

Public Health, www.cdph.ca.gov. Air quality variables, ozone and $PM_{2.5}$, were obtained from The California Environmental Protection Agency's Air Resources Board Air Quality Data (PST) Query tool at the following website https://www.arb.ca.gov/aqmis2/aqdselect.php. Daily data can be retrieved for each combination of basin, day, and year. The following statistics were retrieved on July 19, 2014: Daily Average PM $_{2.5}$ in μg m^{-3}; Daily Max 8 Hour Overlapping Average Ozone in ppb. The Carbon Dioxide Information Analysis Center (CDIAC) maintains data from the United States Historical Climatology

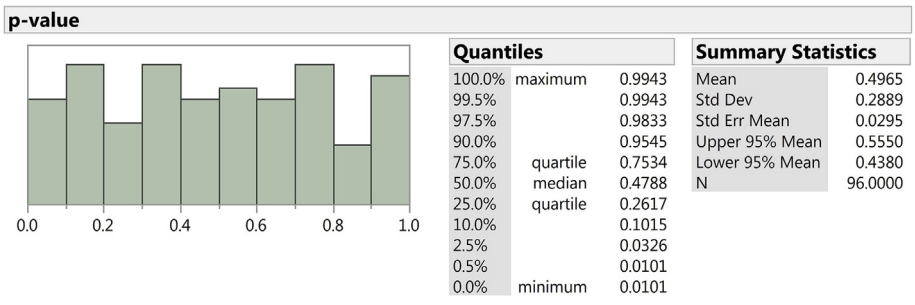

Fig. 2. Screenshot of ten observations from the South Coase Air basin.

Network. Daily temperature data was retrieved from the following website http://cdiac.ornl.gov/epubs/ndp/ushcn/ushcn.html. For each combination of basin, day, and year, the minimum and maximum temperature was obtained. The US Environmental Protection Agency maintains daily humidity data. Daily humidity data was downloaded from https://www.epa.gov/aqs. For each combination of basin, day, and year, the daily maximum relative humidity was obtained. A screenshot of ten observations in the analysis dataset is given in Fig. 2. A plot of daily deaths versus DayOfYear is given in Fig. 3 (a); the four years are overprinted. The residuals from a model including DOY and DOY2 are displayed in Fig. 3 (b).

Mortality = b0 + b1*DOY + b2* DOY2

Deviations from this model are considered “seasonally adjusted”.

The analysis dataset used in this study, years 2004–2007, eight most populous air basins, can be obtained from (Young et al., 2017). It is also deposited at http://datadryad.org/

2.2. Statistical methods

For all air basins, the daily mortality data was complete. For three of the air basins, all data was present, Sacramento Valley, San Joaquin, and South Coast. To facilitate using the using same analysis on each of the eight air basins, we imputed missing data using JMP SVD method (JMP, 2016a). Table 1 gives the number of imputations for the other air basins.

2.2.1. Case-crossover analysis

Case-crossover is a standard way to evaluate health-related effects of air quality when the data is in the form of a time series (Figueiras et al., 2005; Bateson and Schwartz, 1999). For each time point, time stratified symmetric bidirectional case-crossover is proposed as a new way of selecting “control” periods, with a multiple day control period being chosen a week, two weeks, and up to four weeks before and after the event day of interest. We use a total of eight days as controls in total. As the comparison is within a narrow time window, other factors such as age distribution, gender distribution, etc. are also controlled by the nature of the design. In our case, the outcomes are daily mortality, and the predictors are air quality measures ($PM_{2.5}$ and ozone), and weather variables. We use a Cox Proportional Hazard model:

logit(p) = b0 + b1 * tmin.0 + b2 * tmax.0 + b3 * MAXRH.0 + b4 * ($PM_{2.5}$ or ozone)

The regression coefficients, b1, b2, b3 and b4, measure the odds, p/(1-p), for each of the factors in the model. An odds ratio of 1.0 indicates the factor has no effect. Either $PM_{2.5}$ or ozone is the last variable to be fit into the model so that any effect they have after removing the weather effects is tested. The R software package “survival” was used for the computations (R survival, 2016). This model was fit for all eight air basins.

2.2.2. Time series regression

A second analysis, time series regression, was computed for each air basin. In our case, we used stepwise regression. First, to remove seasonal effects, Day of Year and Day of Year squared, DOY and DOY2, were fit into the model for each air basin. The following additional variables were available for selection: Air quality variables (ozone and $PM_{2.5}$); weather variables (tmin, tmax, relative humidity) for the day at issue and for the previous day; mortality variable for the day previous to the current day; day before current day for air quality and weather variables. A screenshot of a stepwise regression dialog is given in Fig. 4 with DOY and DOY2 fixed in the model.

For each air basin (8) and cause of deaths (3), we recorded four marker p-values (4): $PM_{2.5}$, Ozone, $PM_{2.5}$–1, and Ozone-1, considering that a change in the same day's air quality or the previous day's air quality might increase mortality. A total of 96 p-values were computed. All the predictor p-values for an air basin were examined. Terms were inserted or taken out of the analysis if they were ($p < 0.01$) or not (> 0.01) significant and affected the four marker p-values.

We examined the 96 resulting p-values in four ways. First, we looked for a consistent effect, either for one of the marker p-values, air basins or mortality types. Second, we provided a histogram of the p-values. Third, we provided summary statistics of the p-values. Finally, the 96 p-values were examined using a p-value plot: p-values plotted against their expectations under the assumption of a uniform distribution using JMP Add-In (JMP, 2016b). If p-values fall on a 45-degree line in a p-value plot, then they are consistent with there being no effect.

Both case-crossover and time series regression are standard methods for evaluating time series air quality/health effect associations (Nawrot et al., 2011). In the case-crossover analysis, we chose to look at the same day's values only and not to include the previous day's values. Lags are often introduced into the modeling process, but this approach using a large dataset does not support lags for heart attacks or stroke (Milojevic et al., 2014). We did use 0 and 1-day lags in the stepwise regression analysis.

Table 1
Numbers of data values imputed in the analysis dataset. PM25davg is the daily average PM2.5 level. Tmin and tmax are the minimum and maximum temperature. MAXRH is the maximum relative humidity.

Air Basin	Mountain	Salton Sea	San Diego	San Francisco	South Central
PM25davg	26	3	4	0	1
tmin	0	93	20	0	0
tmax	0	94	18	0	0
MAXRH	325	3	0	267	0

3. Results

3.1. Case-crossover analysis

The results of the case-crossover analysis odds ratios are given in Table 2 for $PM_{2.5}$ and ozone. There are 16 odds ratios. They range in value from 0.998 to 1.001. All these odds are very close to one, the no-effect value, for each air basin and air quality measure. The average odds ratio for the eight air basins is 1.00040 for $PM_{2.5}$ and 0.99977 for ozone. For each odds ratio, we give lower and upper confidence limits: CLL and CLH. That these confidence limits are very narrow indicates there is high statistical power. We give two p-values for each combination of air basin and air quality measure, the unadjusted p-value, p-val, and the false discovery rate p-value, FDR (Benjamini and Hochberg, 1995). The unadjusted p-value treats each combination without regard to the other statistical tests. The FDR adjusts the p-values to reflect the fact that multiple questions are at issue. With multiple tests, one expects occasional nominal statistical significance. Here, the smallest unadjusted p-value is 0.008 for ozone/San Francisco. The adjusted p-value, FDR, indicates that we would expect a p-value as small as 0.008, in about 12.8% of experiments where there are 16 statistical tests, and thus such a finding is not unexpected.

3.2. Time series regression

For each mode of deaths, air basin, and air quality measure, we undertook a stepwise regression analysis where we first put DOY and DOY2 into the model to correct for seasonal effects. Fig. 3 (a) displayed daily deaths versus DOY, overlaying all four years in the same figure. A seasonal effect is apparent. Once DOY and DOY^2 are used to detrend the time series, we see that most of the seasonal effects are removed, Fig. 3 (b). We give the four, marker p-values for each type of deaths and air basin in Table 3. There are four p-values < 0.05, but there is no consistent pattern of small p-values. The p-values are uniformly distributed

Stepwise Fit for AllCause65+

SSE	DFE	RMSE	RSquare	RSquare Adj	Cp	p	AICc	BIC
342621.67	1457	15.334783	0.4720	0.4713	21.286259	3	12120.29	12141.4

Current Estimates

Lock	Entered	Parameter	Estimate	nDF	SS	"F Ratio"	"Prob>F"
☑	☑	Intercept	171.799719	1	0	0.000	1
☐	☑	DOY	-0.0693781	2	306308.9	651.290	8e-203
☐	☑	(DOY-183.25)*(DOY-183.25)	0.00125923	1	228289	970.800	9e-164
☐	☐	PM25	0	1	97.00085	0.412	0.52089
☐	☐	PM2.5-1(0,1)	0	1	492.2427	2.095	0.14801
☐	☐	Ozone	0	1	437.1057	1.860	0.17285
☐	☐	Ozone-1	0	1	0.285911	0.001	0.9722
☐	☐	tmin	0	1	499.1733	2.124	0.14519
☐	☐	tmin-1	0	1	66.66012	0.283	0.59461
☐	☐	tmax	0	1	2008.103	8.584	0.00344
☐	☐	tmax-1	0	1	477.8137	2.033	0.1541
☐	☐	MAXRH	0	1	172.1398	0.732	0.39241
☐	☐	MAXRH-1(0,1)	0	1	1387.96	5.922	0.01507

Fig. 4. Stepwise regression dialog from SAS JMP Pro. Day Of Year, DOY, and DOY^2 were forced into the model, South Coast Air Basin.

Table 2
Results of case-crossover analysis: odds ratio(OR), for eight air basins, confidence limits, p-values (raw and adjusted for 16 test); $PM_{2.5}$ and ozone. There are 16 statistical tests of hypothesis.

Air Basin	OR	CLL	CLH	p-val	FDR
$PM_{2.5}$					
mountain-counties	0.99947	0.99780	1.00100	0.536	0.673
sacramento-valley	1.00100	0.99990	1.00200	0.092	0.288
salton-sea	1.00000	0.99800	1.00200	0.956	0.989
san-diego	1.00056	0.99940	1.00200	0.341	0.673
san-francisco	1.00098	1.00010	1.00200	0.024	0.192
san-joaquin	1.00067	1.00000	1.00100	0.044	0.235
south-central-coast	1.00052	0.99900	1.00200	0.501	0.673
south-coast	1.00000	0.99990	1.00060	0.223	0.510
Average	1.00040				
Air Basin Ozone	OR	CLL	CLH	p-val	FDR
mountain-counties	1.00017	0.99720	1.00300	0.911	0.989
sacramento-valley	1.00000	0.99930	1.00200	0.437	0.673
salton-sea	0.99795	0.99570	1.00000	0.080	0.288
san-diego	1.00048	0.99930	1.00200	0.407	0.673
san-francisco	1.00111	1.00030	1.00200	0.008	0.128
san-joaquin	1.00000	0.99890	1.00100	0.989	0.989
south-central-coast	0.99855	0.99680	1.00000	0.108	0.288
south-coast	0.99990	0.99940	1.00030	0.547	0.673
Average	0.99977				

Table 3
P-values testing health effects versus air quality. AllCause deaths; CV: cardiovascular deaths; respiratory deaths for 8 air basins. There are 96 tests of hypothesis.

Mortality	Air Basin	PM2.5	Ozone	PM2.5-1	Ozone-1
AllCause	Mountain	0.6195	0.7955	0.2183	0.6973
AllCause	Sacramento	0.2602	0.9916	0.3532	0.8088
AllCause	Salton Sea	0.4203	0.9666	0.0504	0.2702
AllCause	San Diego	0.5767	0.1055	0.4064	0.3587
AllCause	San Francisco	0.7555	0.0101	0.9943	0.9598
AllCause	San Joaquin	0.1465	0.2895	0.0457	0.2283
AllCause	South Central	0.3723	0.6815	0.4472	0.9577
AllCause	South Coast	0.5209	0.1728	0.1480	0.9722
CV	Mountain	0.2661	0.7684	0.3831	0.5008
CV	Sacramento	0.1650	0.8144	0.7806	0.3712
CV	Salton Sea	0.8177	0.1488	0.2897	0.6428
CV	San Diego	0.3004	0.4052	0.0313	0.9563
CV	San Francisco	0.5823	0.5642	0.7499	0.3862
CV	San Joaquin	0.1535	0.4022	0.8076	0.3879
CV	South Central	0.7077	0.1666	0.3564	0.3569
CV	South Coast	0.7189	0.1142	0.7544	0.3380
Resp	Mountain	0.1804	0.9537	0.9665	0.7769
Resp	Sacramento	0.4111	0.5675	0.3990	0.7982
Resp	Salton Sea	0.9185	0.9624	0.4824	0.6192
Resp	San Diego	0.5025	0.6570	0.7591	0.6939
Resp	San Francisco	0.1539	0.6546	0.0344	0.1809
Resp	San Joaquin	0.6757	0.0538	0.5801	0.0716
Resp	South Central	0.4753	0.5464	0.0710	0.7504
Resp	South Coast	0.0923	0.4710	0.5538	0.8612

over the interval 0 to 1 in the histogram of Fig. 5, indicating pure randomness. The mean and median p-values are 0.4965 and 0.4788, respectively; they indicate no effect of the same day's or the previous day's air quality on acute mortality. The p-value plot for these data is consistent with pure randomness, Fig. 6.

4. Discussion

Neither the case-crossover or stepwise regression analyses support a $PM_{2.5}$ or ozone association with acute deaths in the eight California air basins over the period 2004–2007. A common assumption today is that "air pollution," no matter what level or what component is under consideration, may be detrimental to health. During the Great Smog of London, there was a dramatic increase in statistical deaths. It is fair to say the air was polluted as there was demonstrable harm. Air quality has improved dramatically since 1952 (Schwartz and Hayward, 2007). The current paradigm, based on many epidemiological studies, is that air quality is causal of acute deaths. However, an association does not imply causation. If there is real causation, then well-conducted association studies using large datasets should almost always find an association. Multiple studies going back to at least 2000 (Krewski et al., 2000), indicate air quality geographic heterogeneity. If there is real causality, and one size fits all, there should be effects everywhere. In addition to geographic heterogeneity, a number of studies find no association between air quality and acute deaths, for example, (Cox et al., 2013; Wang et al., 2015; Yang et al., 2004). Meta-analysis studies suggest health effects of air quality (Nawrot et al., 2011; Mustafic et al., 2012; Shah et al., 2015). The primary/base studies for these meta-analysis studies are only observational. These types of studies are not free of bias as none of them correct for multiple testing or multiple modeling. Careful counting of many of these studies shows that the analysis search space, the number of possible claims at issue, is large for each paper, for example, (Young, 2017), so their reliability is questionable, and verification is needed.

In epidemiology, quasi-experiments/natural experiments are considered more reliable. In a natural experiment, there is some event that

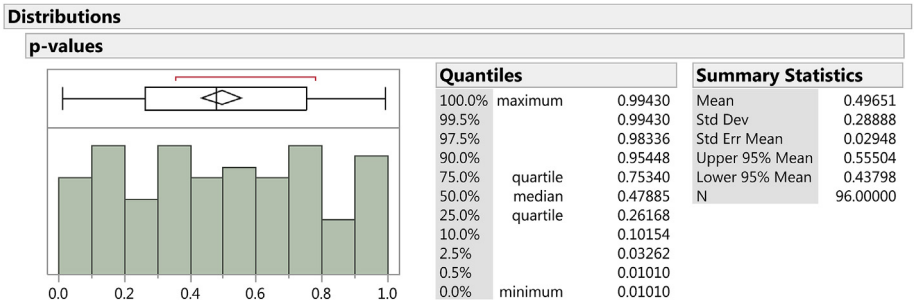

Fig. 5. Histogram of p-values. If the effects are random, we should see a uniform distribution.

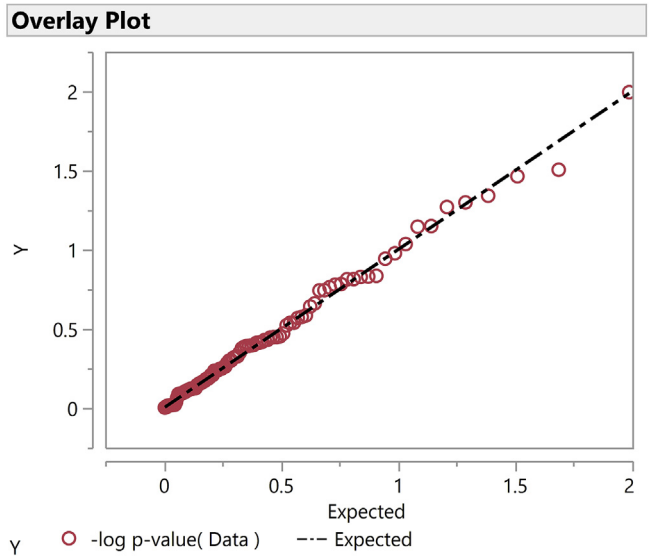

Fig. 6. P-value plot of 96 tests of hypothesis, -Log10 of p-values versus the expectation of p-values coming from a uniform distribution. If the points fall on a 45-degree line, then the results are consistent with randomness.

is largely independent of the outcome, and there are other covariates that can be used to examine the relationship between outcomes and predictors, human mortality and air quality. The process looks like a real experiment. For example, some counties in the US were designated as out of compliance with respect to air quality and special efforts were made to improve air quality in those counties (Chay et al., 2003). Air quality did improve, but elderly mortality did not. There was no experimental verification that improving air quality improved mortality. A re-analysis of the dataset in (Chay et al., 2003) reached the same conclusion (Obenchain and Young, 2017). In another study, an increase in $PM_{2.5}$ happened in New York City and Boston, due to forest fires in Canada (Zu et al., 2016). They found that $PM_{2.5}$ increased, but the mortality did not. These studies carefully controlled for confounding variables.

It is worth pointing to early evidence on etiology and atmospheric chemistry. Nemery et al. (Nemery and Hoet, 2001) examined the technical report of the Meuse Valley event of 1930. A thick fog formed, and 60 people died, of whom ten were necropsied. The necropsies showed no cardiovascular involvement, which supports Milojevic et al. (2014), discussed later. The lung effects were consistent with acid injuries. They proposed sulfuric acid carried deep into the lungs adsorbed onto small particles. Wang et al. (2016) present evidence on the atmospheric chemistry of sulfur compounds. To get to sulfuric acid you need a combination of conditions, "The sulfate formation was greatly facilitated by high RH (relative humidity), low temperature, and the presence of large fog droplets (45), yielding elevated sulfuric acid levels that persisted throughout the event." These conditions held for the London Smog and the Muse Valley fog. This combination of conditions rarely occurs in Los Angeles air basin. It appears that a complex interaction is needed for acute deaths. Over time, sulfur compounds are dramatically reduced, so this complex interaction is much less likely in the California or indeed the US.

The level of precision exhibited in our case-crossover analysis is very high; the confidence limits are very narrow. Confidence limits reflect the statistical precision of an analysis process, but do not necessarily correct for bias. In this case, any small bias could lead to what looks like a significant effect. The fact that we see no effect suggests that there is little or no bias in this dataset and analysis. The few nominally statistically significant results could be due to small biases or be due to chance.

We define acute death in this study as death due to some immediate change of weather or air quality. The hypothesis is that something happened with these variables on the same day or previous day that is associated with mortality. If one concedes that air quality is not causal of acute deaths, then there still might be a chronic causal effect. No chronic effect of fine particles in California was found using a large cohort database (Enstrom, 2005). Since then Enstrom has accumulated other estimates of the chronic effect of $PM_{2.5}$ on AllCause deaths for California. Results of relative risk, computed from several studies by (Enstrom, 2017), are given in Table 4. The average over the 20 given results is 1.010 with a standard error of the mean of 0.010. There is no apparent difference between the observed value and 1.000, the no-effect value.

Positive association studies on air quality and human mortality often point to cardiovascular effects as a possible etiology. Heart attacks and stroke were studied in a large UK dataset and the time of the event,

Table 4
AllCause risk ratios from cohort studies for $PM_{2.5}$ deaths in California. See Enstrom (2017) for details.

Reference	Years	RR	CI
McDonnell et al., 2000	1976–1992	1.03	0.95–1.12
Krewski, 2000	1982–1989	0.872	0.805–0.944
Enstrom, 2005	1973–1982	1.039	1.010–1.069
Enstrom, 2005	1983–2002	0.997	0.978–1.016
Jerrett et al., 2005	1982–2000	1.11	0.99–1.25
Enstrom, 2006	1973–1982	1.061	1.017–1.106
Enstrom, 2006	1983–2002	0.995	0.968–1.024
Zeger et al., 2008	2000–2005	0.989	0.970–1.008
Jerrett, 2010	1982–2000	0.994	0.965–1.025
Krewski, 2010	1982–2000	0.96	0.920–1.002
Krewski, 2010	1982–2000	0.968	0.916–1.022
Jerrett, 2011	1982–2000	0.994	0.965–1.024
Jerrett, 2011	1982–2000	1.002	0.992–1.012
Lipsett et al., 2011	2000–2005	1.01	0.95–1.09
Ostro et al., 2010	2002–2007	1.06	0.96–1.16
Jerrett et al., 2013	1982–2000	1.06	1.003–1.120
Jerrett et al., 2013	1982–2000	1.028	0.957–1.104
Ostro et al., 2015	2001–2007	1.01	0.98–1.05
Thurston et al., 2016	2000–2009	1.02	0.99–1.04
Enstrom, 2016 (unpub)	2000–2009	1.001	0.949–1.055

heart attack or stroke, determined down to the hour (Milojevic et al., 2014). They found no lag effects for CO, NO2, Ozone, PM10, $PM_{2.5}$, or SO2. Tellingly, they found no association between ozone and $PM_{2.5}$ and heart attacks or stroke. The association of hospital heart attack admissions for CO, NO, NO2, Ozone or $PM_{2.5}$ was investigated; no associations were found (Wang et al., 2015). The reliability of cause of death on death certificate is poor (Ravakhah, 2006), so it makes sense that attention should focus on AllCause deaths as the primary endpoint of analysis. We present an analysis of three death endpoints so that our results can be matched against the literature. We find no association between $PM_{2.5}$ and ozone and acute deaths in California.

5. Conclusions

In the absence an association of air quality, as measured by ozone or $PM_{2.5}$, with acute mortality (AllCause, Cardiovascular or Respiratory), there is no evidence supporting current air quality being causal of acute deaths in California.

Grant information

The work of S. Stanley Young was partially funded by the American Petroleum Institute. The work of Cheng You and Dennis K. J. Lin was unfunded.

Potential financial conflict of interest

Cheng You and Dennis K. J. Lin have no funding for this research and no potential competing.

Conflicts of interest

S. Stanley Young was partially funded by American Petroleum Institute.

However, API had no influence on how the research was conducted or reported. S. Stanley Young has no competing financial conflict of interest.

Contributorship statement

Cheng You performed the case crossover analysis and wrote the corresponding paragraphs. S. Stanley Young performed the stepwise regression and wrote the corresponding paragraphs. He is the corresponding author. Dennis K.J. Lin examined both analyses and provided many valuable comments. We all substantially contributed to designing the study and conducting the literature review and statistical analysis.

Data sharing statement

We share our analysis data set on request.

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.yrtph.2018.05.012.

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