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Measurement-based assessment of health burdens from long-term ozone exposure in the United States, Europe, and China

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Abstract
Long-term ozone (O₃) exposure estimates from chemical transport models are frequently paired with exposure-response relationships from epidemiological studies to estimate associated health burdens. Impact estimates using such methods can include biases from model-derived exposure estimates. We use data solely from dense ground-based monitoring networks in the United States, Europe, and China for 2015 to estimate long-term O₃ exposure and calculate premature respiratory mortality using exposure-response relationships derived from two separate analyses of the American Cancer Society Cancer Prevention Study-II (ACS CPS-II) cohort. Using results from the larger, extended ACS CPS-II study, 34 000 (95% CI: 24, 44 thousand), 32 000 (95% CI: 22, 41 thousand), and 200 000 (95% CI: 140, 253 thousand) premature respiratory mortalities are attributable to long-term O₃ exposure in the USA, Europe and China, respectively, in 2015. Results are approximately 32%–50% lower when using an older analysis of the ACS CPS-II cohort. Both sets of results are lower (~20%–60%) on a region-by-region basis than analogous prior studies based solely on modeled O₃, due in large part to the fact that the latter tends to be high biased in estimating exposure. This study highlights the utility of dense observation networks in estimating exposure to long-term O₃ exposure and provides an observational constraint on subsequent health burdens for three regions of the world. In addition, these results demonstrate how small biases in modeled results of long-term O₃ exposure can amplify estimated health impacts due to nonlinear exposure-response curves.

Introduction

There is strong epidemiological and toxicological evidence linking exposure to ambient ozone (O₃) with adverse health impacts (US EPA 2013). While historical research has largely focused on impacts attributable to short-term O₃ exposure, there is a growing body of literature suggesting a significant association between long-term ambient O₃ exposure and increased premature mortality, in particular from respiratory diseases (Jerrett et al 2009, Lipset al 2011, Zanobetti and Schwartz 2011, REVIHAAP 2013, Turner et al 2016). Consequently, exposure-response relationships, specifically derived from an analysis of the American Cancer Society Cancer Prevention Study-II (ACS CPS-II) cohort (Jerrett et al 2009), have been used to estimate the global health burden from long-term O₃ exposure (e.g. Anenberg et al 2010, Lelieveld et al 2013, Brauer et al 2015).

Due to spatial and temporal limitations of ground-based monitors, as well as difficulty in relating the vertical column density of O₃ observed by satellites to surface values (Duncan et al 2014), global estimates of long-term O₃ exposure are generally estimated using output from state-of-the-art chemical transport models (CTMs); (e.g. Anenberg et al 2010, Silva et al 2013, Brauer et al 2015, Lelieveld et al 2015, Malley et al 2017, Shindell et al 2018). Using results from a CTM, the global burden of disease (GBD) project estimated that approximately 254 000 global premature...
mortalities from chronic obstructive pulmonary disease (COPD) were attributable to long-term ambient O₃ exposure in 2015 (Cohen et al 2017). Results from other impact studies can vary substantially due to different CTMs being employed to estimate exposure, updates to exposure-response curves, changing theoretical minimum risk exposure levels, varying baseline mortality rates, and different reference years, making inter-study comparisons of long-term O₃ exposure health burdens challenging. In addition, there is evidence suggesting that long-term O₃ exposure is not only associated with COPD, but a more comprehensive set of respiratory diseases (Jerrett et al 2009, US EPA 2013, Turner et al 2016). Some studies even report significant associations with increased premature cardiovascular mortality (Lipsett et al 2011, Jerrett et al 2013, Crouse et al 2015, Cakmak et al 2016, Turner et al 2016, Day et al 2017). When incorporating these epidemiological updates, the estimated health burden attributable to long-term O₃ exposure increases (Malley et al 2017, Shindell et al 2018), indicating that efforts to reduce long-term O₃ exposure could be more effective in reducing total air pollution-attributable premature mortalities than previously identified (Schwartz 2016).

Many regions of the world, such as the United States, Europe, and China, now have dense ground-based monitoring networks to assess compliance with air quality standards. Application of these networks to estimate long-term O₃ exposure for health impact assessments, rather than CTMs, has a number of advantages. First, this would provide a consistent framework in relation to many of the underlying epidemiological studies, which often incorporate these networks to estimate exposure of the study population (e.g. Jerrett et al 2009, Turner et al 2016). Second, the use of compliance monitoring networks to assess health burdens adds consistency between health burden quantification and regulatory air quality standard monitoring. Third, while the CTMs used to model ozone are extensively evaluated and capable of reproducing significant features of atmospheric chemistry, many of the health-based O₃ exposure metrics are high biased in model predictions (Schnell et al 2015, Seltzer et al 2017). Lastly, seasonal and spatial trends of observationally derived exposure metrics can be used in model evaluations to help diagnose drivers of bias or provide a reference for bias correction.

In this study, we estimate long-term O₃ exposure in the United States, Europe, and China for 2015 through the exclusive use of ground-based observation measurements. We then combine these results with exposure-response relationships to estimate premature mortalities attributable to long-term O₃ exposure in each region. We compare health impact estimates using multiple exposure-response curves and averaging metrics, as well as estimates from previously reported O₃ health burdens, discuss the implications of different averaging metrics, and provide seasonal population-weighted exposure concentrations that can be used for model evaluations.

Methods

To estimate premature mortalities attributable to long-term O₃ exposure, the exposure-response relationships and averaging metrics reported by Jerrett et al (2009) and Turner et al (2016) were utilized. Jerrett et al (2009) used data from the ACS CPS-II cohort and air pollution data to estimate changes in various cause-specific deaths attributable to incremental changes in the April–September average of the daily 1 h maximum O₃ concentration (6mMDA1). Their cohort spanned 18 years of follow-up and included 448 850 subjects with 118 777 deaths. Turner et al (2016) estimated changes in cause-specific deaths attributable to incremental changes in the annual average of the maximum daily 8 h average O₃ concentration (MDA8) using updated values from the ACS CPS-II cohort. The Turner et al (2016) cohort spanned 22 years of follow-up and included 669 046 subjects with 237 201 deaths. It is noted that the use of these results globally assumes homogeneity in the long-term O₃ exposure-response relationship for cause-specific mortality. While there is evidence from other cohort studies in North America showing a significant relationship between long-term O₃ exposure and premature mortality (Crouse et al 2015, Di et al 2017), none of the cohort studies conducted in Europe (no studies are available for Asia) have reported a significant relationship with respiratory mortality (Carey et al 2013, Bentayeb et al 2015). This may be due to differences in study design, such as exposure estimation methods, length of follow-up, and number of events (Jerrett et al 2013). Additional cohort studies are required to evaluate the validity of globally extrapolating these exposure-response relationships.

Ground based measurements in the United States were retrieved from the air quality system (AQS) and the Clean Air Status and Trends Network (CASTNET), in Europe from the European Union air quality e-reporting data repository, and in China from the Beijing Municipal Environmental Monitoring Center and the China National Environmental Monitoring Center. This compilation has a significant overlap with the Tropospheric Ozone Assessment Report dataset (Schultz et al 2017) in the USA and Europe, but vastly expands the extent of observations in China. All results referring to Europe include the 28 European Union Member States, plus Norway and Switzerland. Gridded surface maps were generated using an objective-mapping algorithm that combines a modified form of inverse distance weighting with a declustering scheme and trapezoidal integration (Schnell et al 2014). This algorithm has previously been used to evaluate O₃ predictions by a suite of CTMs over North America and Europe (Schnell et al 2015).
Daily gridded maps of maximum 1 and 8 h concentrations were generated and appropriately averaged to calculate each metric (e.g. annual average for the Turner et al 2016 metric). Details regarding the calculation of the population-weighted exposure concentrations, as well as the implementation and evaluation of the exposure algorithm, can be found in the supporting information (available online at stacks.iop.org/ERL/13/104018/mmedia). Both long-term O₃ exposure metrics were calculated at 0.25° × 0.25°, 0.5° × 0.5°, and 1° × 1° grid resolutions. Since changes in the mean bias and average root mean square error of the predicted site values were generally insensitive to grid resolution (see tables S1 and S2), all results presented here utilize 0.5° × 0.5° resolution.

Premature mortality attributable to long-term O₃ exposure was calculated using previously established methods (Anenberg et al 2010, Silva et al 2016, Malley et al 2017) and is summarized below.

$$ \Delta X = \begin{cases} 0 & \text{if } [O₃] \leq \text{TMREL} \\ [O₃] - \text{TMREL} & \text{if } [O₃] > \text{TMREL} \end{cases} $$

$$ HR = \exp^{\beta \Delta Y} $$

$$ AF = 1 - \exp^{-\beta \Delta X} $$

$$ \Delta \text{Mort} = y_0 \times AF \times \text{Population}, $$

where TMREL is the theoretical minimum risk exposure level (i.e. the ‘counterfactual’), ΔX is the O₃ exposure in a particular grid box above the TMREL, β is the exposure-response factor (i.e. the slope of the log-linear relationship between the change in exposure and mortality), HR is the hazard ratio reported in the epidemiological study, which links incremental changes in long-term O₃ exposure, ΔY (10 ppb in both studies, albeit a 10 ppb in a different long-term exposure metric), to changes in cause-specific mortality rates, AF is the attributable fraction of the disease burden attributable to long-term O₃ exposure, y₀ is the cause-specific baseline mortality rate, Population is the population count in a particular grid box, and ΔMort is the estimated number of premature, cause-specific mortalities. Further details regarding the population and baseline mortality rates can be found in the supporting information.

Changes in cause-specific risk varied based on the underlying epidemiological study. For respiratory diseases, a hazard ratio of 1.040 (95% CI: 1.013, 1.067) and 1.12 (95% CI: 1.08, 1.16) was used, corresponding to the Jerrett et al (2009) and Turner et al (2016) results, respectively. In addition, while there is more limited evidence for effects of long-term O₃ exposure on cardiovascular mortality, the hazard ratio of 1.03 (95% CI: 1.01, 1.05) from the Turner et al (2016) study was applied. The TMREL’s used were 33.3 ppb when using the Jerrett et al (2009) averaging metric and 26.7 ppb when using the Turner et al (2016) averaging metric. These values correspond to the minimum O₃ exposure reported in each of the respective epidemiological studies. Since many studies generate results without the use of a TMREL (e.g. Anenberg et al 2010, Fang et al 2013, Silva et al 2013), a sensitivity analysis was carried out to estimate the mortality burdens without the use of a threshold. This test assumes that the standard TMREL values are limited by low concentration observations rather than true thresholds below which no impacts occur and is illustratively included to provide an upper bound on health impacts.

**Results**

Observationally derived estimates of the Jerrett et al (2009) averaging metric featured distinct patterns in each of the three regions considered here (figure 1). In the USA, there is a peak exceeding 60 ppb over inland southern California. Due to seasonally operating monitors, some parts of the upper northwest did not pass the internal quality assurance test and provide results. Nonetheless, 99% of the population was captured in grid boxes that did generate results, with a population-weighted O₃ concentration of 49.0 ppb (table 1).
Europe featured a decreasing gradient in 6mMDA1 concentrations from south to north, with a peak of approximately 60 ppb in the Po valley region of Italy, consistent with previous analyses (EEA 2017). Ireland and Italy had the lowest and highest population-weighted 6mMDA1 O3 concentrations, respectively (21.3 ppb and 56.7 ppb; see table S3). Overall, the population-weighted 6mMDA1 O3 concentration in Europe was 46.7 ppb (table 1). Across China, there was an increasing gradient in 6mMDA1 concentrations from south to north, peaking near 90 ppb in the North China Plain. Large areas of western China were without monitoring data and exposure estimates were not generated. However, more than 99% of the population resides in the grid cells for which results were generated and the population-weighted 6mMDA1 O3 concentration was 67.9 ppb (table 1).

Observationally derived estimates of the Turner et al (2016) averaging metric featured qualitatively similar spatial patterns (figure 2) when compared to the 6mMDA1 concentrations, but were quantitatively smoother. Over the USA, the difference between the 5th and 95th concentration percentiles was 16.2 ppb and 11.2 ppb for the 6mMDA1 and MDA8 concentrations, respectively. The MDA8 concentrations were not calculated for a larger number of grid cells due to some monitors going off-line during winter months. Nonetheless, with 96% of the USA population still captured by the reporting grid cells, the population-weighted MDA8 concentration was 38.1 ppb. Substantial seasonal variations occur throughout the year, influencing the spatial distribution of the annual MDA8 metric (see figures S1–S6). Peak population-weighted seasonal MDA8 concentrations occurred during the summer, with a drop of 14 ppb during the winter (table 1).

In Europe, the difference between the 5th and 95th concentration percentiles for the 6mMDA1 and MDA8 concentrations was 21.9 ppb and 13.2 ppb, respectively. A peak of seasonal MDA8 concentrations did occur over the Po valley during the summer (figures S4) but was the location of low concentrations during the winter (figure S6). Ireland featured the lowest population-weighted MDA8 concentration of 19.3 ppb, but it was anomalous when compared to the rest of the continent. While Italy still featured some of the highest population-weighted concentrations (38.8 ppb), exposure was comparable in many other European nations (table S3).

In China, the differences between the 5th and 95th concentration percentiles were 43.7 ppb and 34.5 ppb for the 6mMDA1 and MDA8 concentrations, respectively. A peak of seasonal MDA8 concentrations did occur over the Po valley during the summer (figures S4) but was the location of low concentrations during the winter (figure S6). Ireland featured the lowest population-weighted MDA8 concentration of 19.3 ppb, but it was anomalous when compared to the rest of the continent. While Italy still featured some of the highest population-weighted concentrations (38.8 ppb), exposure was comparable in many other European nations (table S3).

In Europe, the differences between the 5th and 95th concentration percentiles for the 6mMDA1 and MDA8 concentrations was 21.9 ppb and 13.2 ppb, respectively. A peak of seasonal MDA8 concentrations did occur over the Po valley during the summer (figures S4) but was the location of low concentrations during the winter (figure S6). Ireland featured the lowest population-weighted MDA8 concentration of 19.3 ppb, but it was anomalous when compared to the rest of the continent. While Italy still featured some of the highest population-weighted concentrations (38.8 ppb), exposure was comparable in many other European nations (table S3).

In China, the differences between the 5th and 95th concentration percentiles were 43.7 ppb and 34.5 ppb for the 6mMDA1 and MDA8 concentrations, respectively. With 99% of the population captured in grid cells for which exposure estimates were generated, the population-weighted MDA8 concentration was 45.3 ppb. Large seasonal variations, driven mainly by low winter concentrations in the North China Plain, led to a 31.4 ppb difference in the population-weighted seasonal

### Table 1. Population-weighted concentrations (ppb) of the Jerrett et al (2009) averaging metric and the Turner et al (2016) averaging metric for 2015.

| Region | Jerrett et al (2009) metric | Turner et al (2016) metric |
|--------|-----------------------------|---------------------------|
|        | April–September | AMJ | JAS | Annual | MAM | JJA | SON | DJF |
| USA    | 49.0          | 48.9 | 49.0 | 38.1  | 43.0 | 43.7 | 35.9 | 29.7 |
| Europe | 46.7          | 46.6 | 46.8 | 33.9  | 38.9 | 45.5 | 27.1 | 24.0 |
| China  | 67.9          | 67.0 | 68.7 | 45.3  | 51.2 | 59.4 | 42.7 | 28.0 |

Note: AMJ = April, May, June; JAS = July, August, September; MAM = March, April, May; JJA = June, July, August; SON = September, October, November; DJF = December, January, February.

![Figure 2. The annual average of the maximum daily 8 h average (Turner et al 2016 averaging metric) for 2015. Concentration is reported in ppb. Note: color bar has non-uniform intervals.](image-url)
Table 2. Regional estimates of premature respiratory and cardiovascular mortalities attributable to long-term O₃ exposure using the Jerrett et al (2009) and Turner et al (2016) averaging metrics and exposure-response functions for 2015.

| Region | Respiratory | Cardiovascular |
|--------|-------------|----------------|
|        | w/ thres.  | w/o thres.     | w/ thres.  | w/o thres. |
| USA    | 17 (6–27)  | 48 (17–75)     | 34 (24–44) | 95 (69–117) |
| Europe | 20 (7–33)  | 69 (24–107)    | 32 (22–41) | 132 (95–164) |
| China  | 135 (46–210) | 246 (89–374)   | 200 (140–253) | 423 (310–515) |

Note: All results reported as thousands and rounded to the nearest thousand. 95% CI of each estimate included in parenthesis.

Table 3. Regional estimates of premature respiratory and cardiovascular mortalities per 100 000 people attributable to long-term O₃ exposure using the Jerrett et al (2009) and Turner et al (2016) averaging metrics and exposure-response functions for 2015.

| Region | Respiratory | Cardiovascular |
|--------|-------------|----------------|
|        | w/ thres.  | w/o thres.     | w/ thres.  | w/o thres. |
| USA    | 5.2 (1.8–8.4) | 10.6 (7.4–13.6) | 5.4 (2.7–8.0) |  |
| Europe | 3.8 (1.3–6.1) | 5.9 (4.1–7.7) | 4.5 (2.3–6.7) |  |
| China  | 9.6 (3.3–15.1) | 14.3 (10.1–18.1) | 9.2 (4.7–13.6) |  |

Note: 95% CI of each estimate included in parenthesis.

MDA8 concentrations between the summer and winter months.

The estimated average number of premature respiratory mortalities attributable to long-term O₃ exposure for 2015 using the Turner et al (2016) exposure-response relationship was 34 000 (95% CI: 24, 44 thousand), 32 000 (95% CI: 22, 41 thousand), and 200 000 (95% CI: 140, 253 thousand) for the USA, Europe, and China, respectively. When using the Jerrett et al (2009) exposure-response relationship, the premature respiratory mortality impacts were lower: 17 000 (95% CI: 6, 27 thousand), 20 000 (95% CI: 7, 33 thousand), and 135 000 (95% CI: 46, 210 thousand) in the USA, Europe, and China, respectively (table 2 and table S4 for European country-level estimates). While population-weighted O₃ concentrations of both averaging metrics are higher in the USA than Europe, estimates of premature respiratory mortalities attributable to long-term O₃ exposure are similar in the two regions. This is largely due to differences in population density and age-related demographics, with some contributions from differences in baseline mortality rates (figure S7). In addition, while exposure concentrations are consistently higher for the 6mMDA1 metric than the MDA8 metric, health impacts are consistently higher when using the Turner et al (2016) exposure-response relationship due to its larger hazard ratio and lower TMREL.

Normalized results, with impacts reported as premature mortalities attributable to long-term O₃ exposure per 100 000 people, show health burdens higher in the USA than Europe (table 3). This reflects the influence of higher population-weighted O₃ concentrations found in the USA. Respiratory mortality rates attributable to long-term O₃ exposure are quite variable between European countries (table S5), reflecting heterogeneity in population-weighted exposure concentrations (table S3), age demographics, and baseline mortality rates. For all countries considered in this analysis, baseline respiratory mortality rates are highest among the oldest age bin of the population (i.e. 80+). As a result, age demographics strongly influence the health impacts calculated here (table S6), with more than 75% of the respiratory premature mortalities attributable to long-term O₃ exposure consistently occurring among the population aged 70 and above.

When a TMREL is not used, average estimates increase in all three regions (table 2). In addition, the estimated average number of premature cardiovascular mortalities attributable to long-term O₃ exposure was 17 000 (95% CI: 9, 26 thousand), 24 000 (95% CI: 12, 36 thousand), and 129 000 (95% CI: 65, 190 thousand) for the USA, Europe, and China, respectively, in 2015. While the hazard ratio of long-term O₃ exposure is larger for respiratory disease than cardiovascular disease (averages of 1.12 versus 1.03), the larger mortality rate of cardiovascular disease drove the substantial estimated impacts.

To compare directly with the GBD project, COPD related premature mortalities attributable to long-term O₃ exposure were also estimated. Consistent with the Jerrett et al (2009) study, these calculations utilized the maximum daily 1 h average O₃ concentration spanning June–August and a hazard ratio of 1.029 (95% CI: 1.010, 1.048). Health burdens for the USA, Europe, and China in 2015 were 7000 (95% CI: 3, 12 thousand), 11 000 (95% CI: 4, 17 thousand), and 88 000 (95% CI: 32, 139 thousand), respectively. In comparison, the GBD project estimated that there were 11 600, 13 330, and 71 850 premature COPD related mortalities in the three regions attributable to long-term O₃ exposure in 2015 (HEI: Health Effects Institute 2017). The high biases in the USA and Europe and low bias in China suggests that the exposure estimates did not adequately capture the ~40% increase in population-weighted concentrations over China...
Table 4. Comparison of long-term O₃ exposure results for respiratory-related mortalities with prior studies. All results rounded to the nearest thousand.

| Metric                  | USA/NA (Count) | Europe (Count) | China/East Asia/Asia (Count) | Exposure method        | Year    | References                  |
|-------------------------|----------------|----------------|-----------------------------|------------------------|---------|----------------------------|
| J2009 USA               | (17 000)       | (20 000)       | China (135 000)             | Obs. derived w/ TMREL  | 2015    | This study                  |
| J2009 NA                | (25 000)       | (23 000)       | Asia (370 000)              | CTM-PI comparison     | 2000    | Anenberg et al (2010)      |
| J2009 NA                | (34 000)       | (33 000)       | East Asia (203 000)         | CTM-PI comparison     | 2000    | Silva et al (2013)         |
| J2009 NA                | (26 000)       | (31 000)       | East Asia (183 000)         | CTM-PI comparison     | 2000    | Fang et al (2013)          |
| J2009 NA                | (38 000)       | (73 000)       | China (273 000)             | CTM-PI comparison     | 2005    | Lieveleid et al (2013)     |
| J2009 NA                | (37 000)       | (33 000)       | East Asia (175 000)         | CTM-PI comparison     | 2005    | Silva et al (2016)         |
| J2009 USA               | (30 000)       | (39 000)       | China (154 000)             | CTM w/ TMREL          | 2010    | Malley et al (2017)        |
| J2016 USA               | (34 000)       | (32 000)       | China (200 000)             | Obs. derived w/ TMREL | 2015    | This study                  |
| J2016 USA               | (64 000)       | (79 000)       | China (316 000)             | CTM w/ TMREL          | 2010    | Malley et al (2017)        |
| J2016 USA               | (23 000)       | (33 000)       | China (181 000)             | Bias-adjusted CTM w/ TMREL | 2015    | Shindell et al (2018)      |

Note: J2009 = Jerrett et al (2009); T2016 = Turner et al (2016); NA = North America; CTM-PI comparison = chemical transport model calculated difference in present day concentrations and preindustrial concentrations, without the use of a TMREL.

Discussion

Consistent with two recent studies utilizing CTM derived exposure (Malley et al 2017, Shindell et al 2018), the observationally derived results presented here show that respiratory health impacts attributable to long-term O₃ exposure are higher when using the Turner et al (2016) averaging metric and exposure-response relationship than the Jerrett et al (2009) methodology. These findings have important implications for policy makers and the public for a number of reasons. First, health impacts attributable to long-term O₃ exposure are indeed likely higher when using the newest ACS CPS-II cohort analysis and expanded further if the association between long-term O₃ exposure and cardiovascular mortality is shown to be causal and included in the total health burden estimates. Second, the Turner et al (2016) averaging metric considers annual O₃ exposure, rather than 6 months. This is particularly relevant for the three regions included in this analysis, where the seasonal cycle and regional distributions of O₃ have shifted over the last few decades (Parrish et al 2012, Clifton et al 2014, Simon et al 2015, Lefohn et al 2017, Seltzer et al 2017). Finally, this also highlights the importance of chemistry transport models accurately capturing O₃ seasonal cycles in generating exposure estimates for health impact assessments. Overall, the results presented here are generally lower than what has been reported in recent model-based studies (table 4). However, as previously noted, each study may use different TMRELs, baseline mortality rates, and reference years. Only one study, Shindell et al (2018), which utilized a bias-adjustment, generated results comparable to what is reported here.

An additional reason for the differences between the results presented here and those in prior studies relates to biased exposure estimates and the interaction between these exposure estimates and nonlinear exposure-response curves. For this study, a log-linear exposure-response function (figure S8) was selected since it is most commonly applied in health impact assessments (e.g. Anenberg et al 2010, Silva et al 2013, Silva et al 2016, Malley et al 2017, Shindell et al 2018). However, other forms of exposure-response functions can be used. For example, Di et al (2017) reported a linear connection between long-term O₃ exposure and mortality and the World Health Organization suggests linear exposure-response relationships for short-term O₃ exposure studies (REVIHAAP 2013). The shape of exposure-response curves have been previously discussed in health impact studies focused on exposure to ambient fine particulate matter (Pope et al 2009, Smith and Peel 2010, Apte et al 2015). While prior studies have indeed noted that high biased O₃ predictions are consistent in models that are typically used to estimate long-term O₃ exposure (e.g. Schnell et al 2015, Yan et al 2016, Travis et al 2016, Seltzer et al 2017), an effort to translate how this bias might influence health impacts has yet to be undertaken.

To test this interaction, the observationally derived exposure metrics were artificially scaled and the resulting health impacts were subsequently calculated. The new health impact estimates were then compared to the reference impact estimates (figure 3). Since the impact estimates are normalized to a reference case,
variations are exclusively due to changes in exposure (i.e. differences in population demographics do not influence these normalized results). When using the Jerrett et al (2009) averaging metric and exposure-response relationship, a 10% increase in exposure (i.e. a 10% high bias in the population-weighted exposure concentration) yields a 29%, 35%, and 18% increase in the estimated health impacts in the USA, Europe, and China, respectively. When using the Turner et al (2016) methodology, a 10% increase in exposure yields a 29%, 44%, and 21% increase in the estimated health impacts in the USA, Europe, and China, respectively.

In the prior example, normalized impacts for Europe were consistently most sensitive to changes in the exposure metrics, followed by the USA and then China. Population-weighted concentrations of each metric follow the same order (table 1). This relationship illustrates how a larger normalized change in health impacts occurs at the lower exposure end of each curve. For example, when using the Turner et al (2016) averaging metric, the USA and China feature average exposures of 38.1 ppb and 45.3 ppb, respectively (table 1). The exposure-response curve using the Turner et al (2016) hazard ratio (figure S8) is steeper at 38.1 ppb than 45.3 ppb, which leads to the stronger marginal response in impacts (figure 3). This relationship is important from a health impacts perspective and should also be noted when considering how bias in exposure estimates influence health calculations in various regions.

Some uncertainties in the results presented here include a small bias in the gridding method (see figures S9 and S10). Though, the mean bias of estimated concentrations at each monitor from the complete population of observations is nearly zero for the three regions. Second, inherent in the mapping algorithm is the assumption that non-observed locations can be estimated using nearby observations. The exposure results show that the final gridded surface maps (figures 1 and 2) have coherent spatial gradients, providing confidence in these assumptions. Third, it is assumed that the gridded surface maps generated here are of sufficient resolution to capture exposure estimates. While all results presented here are at $0.5° \times 0.5°$ resolution, additional gridded surface maps of both metrics were calculated at horizontal resolutions of $0.25° \times 0.25°$ and $1.0° \times 1.0°$. Health impact estimates at each of these resolutions show little difference (tables S1 and S2). Fourth, the Jerrett et al (2009) averaging metric used here was calculated using the April–September average of the 1 h daily maximum O₃ concentration rather than a grid-by-grid calculation to account for changes in regional O₃ seasons. This was performed to provide consistent population-weighted exposure concentrations that can subsequently be used for model and exposure evaluations. To test the influence of this assumption, population-weighted concentrations for all possible 6 month averaging periods in 2015 were calculated. The April–September average yielded the highest exposure estimates for the USA, China, and a majority of the European countries.

**Conclusions**

Gridded surface maps of long-term O₃ exposure for 2015 in the USA, Europe, and China were estimated through the exclusive use of ground-based monitoring networks and an objective-mapping algorithm (Schnell et al 2014). This estimation of exposure differs from the widely used method of chemical transport modeling, which can incorporate model biases. Seasonal population-weighted concentrations of two exposure metrics were presented and can be used by the modeling community for model evaluation, to elucidate drivers of model bias, and possibly as correction factors to reduce persistent bias. Using the Jerrett et al (2009) averaging metric and exposure-response
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