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PM_{2.5} and mortality in 207 US cities: Modification by temperature and city characteristics

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Abstract

Background—The reported estimated effects between long-term PM_{2.5} exposures and mortality vary spatially. We assessed whether community-level variables, including socioeconomic status (SES) indicators and temperature, modify this association.

Methods—We used data from >35 million Medicare enrollees from 207 U.S. cities (2000–2010). For each city, we calculated annual PM_{2.5} averages, measured at ambient central monitoring sites. We used a variation of a causal modeling approach and fitted city-specific Cox models, which we then pooled using a random effects meta-regression. In this second stage, we assessed whether temperature and city-level variables, including smoking and obesity rates, poverty, education and greenness, modify the long-term PM_{2.5}–mortality association.

Results—We found an association between long-term PM_{2.5} and survival (HR = 1.2; 95%CI: 1.1–1.3 per 10 µg/m³ increase in the annual PM_{2.5} average concentrations). We observed elevated estimates in the Southeastern, South and Northwestern U.S. (HR = 1.9; 95%CI: 1.7–2.2, 1.4; 95%CI: 1.2–1.7 and 1.4; 95%CI: 1.1–1.9 respectively). We observed a higher association between long-term PM_{2.5} exposure and mortality in warmer cities. Furthermore, we observed increasing estimates with increasing obesity rates, %residents and families in poverty, %black residents and %population without a high school degree, and lower effects with increasing median household income and %white residents.

Conclusions—To our knowledge, this is the first study to assess modification by temperature and community-level characteristics on the long-term PM_{2.5}–survival association. Our findings suggest that living in cities with high temperatures and low SES is associated with higher effect estimates.

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Introduction

The association between long-term PM_{2.5} (particles with aerodynamic diameter $\leq 2.5 \mu\text{m}$) and mortality has been consistently reported in the literature.¹ The magnitude of the reported effects, however, differs by location, with heterogeneous effects having been reported both across Europe,² and across the U.S.³

Studies of both short- and long-term effects have shown that particle composition modifies the PM_{2.5}–mortality association.^{4,5} Only a few studies have examined other factors that could modify this relationship, all of which focused on acute effects.⁶ Bell et al.,⁷ for instance, reported that higher prevalence of air conditioning use was associated with lower PM_{2.5} effect estimates on health outcomes. Bell et al.,⁸ in a review examining factors potentially modifying the association between short-term PM_{2.5} exposures and adverse health, found suggestive evidence that those with lower education, income or employment status, and stronger evidence for the elderly and women, are in higher risk of death. Temperature has also been found to modify the short-term PM_{2.5}–mortality association.^{9,10}

It has not yet been examined, however, whether population characteristics, temperature, greenness, and urbanicity also modify the association between long-term PM_{2.5} exposures and mortality, explaining some of the observed effect heterogeneity in the health effects across locations and studies. For this study, we used the Medicare cohort for the period 2000–2010, consisting of more than 35 million Medicare enrollees from 207 cities, the largest study using Medicare data to date to examine the long-term PM_{2.5}–mortality association, and investigated factors that could potentially modify it. We assessed the association between long-term PM_{2.5} exposures and mortality focusing on year-to-year fluctuations of PM_{2.5} concentrations within cities.

Methods

Data collection

Study Population—We obtained data from more than 35 million Medicare enrollees (65 years old) from 207 cities across the United States (2000–2010). Medicare is an open cohort; enrollees entered in our cohort in 2000, or upon their enrollment after 2000. After enrollment, each subject was followed annually until the year of their death or the end of our study period (31 December 2010). This study was conducted under a protocol approved by the Harvard T.H. Chan School of Public Health Human Subjects Committee.

Medicare records are updated annually and they contain information on age, race, zip-code and state of residence of each enrollee. Furthermore, although cause of death is not available, information on each hospitalization of the enrollees during the study period, including dates and admission diagnoses, is also available. We used codes from the *International Classification of Diseases*, 9th Revision (ICD-9; Center for Disease Control and Prevention 2008), to obtain admission records for congestive heart failure (CHF; code 428), myocardial infarction (MI; code 410), chronic obstructive pulmonary disease (COPD; codes 490–492, 494–496) and diabetes (code 250), as well severity of each admission, expressed by the number of days spent in the coronary or intensive care units.

Although the Medicare data have limited information on individual characteristics that could potentially be confounders, it has been shown that use of these data yields similar effect estimates with previously published studies that had included individual-level variables in their analyses.^{3,11} Furthermore, because we estimate the health effects by relying on year to year variations in air pollution within each city and given our choice of analysis, potential confounding by factors varying across cities and long-term trends are eliminated.⁵

Air pollution and temperature data—We obtained PM_{2.5} concentration data from the U.S. Environmental Protection Agency's (EPA) Air Quality System (AQS) database (<http://www.epa.gov/ttn/airs/airsaqs/detaildata/downloadaqsddata.htm>). We calculated city-specific annual and 2-year PM_{2.5} averages using data from all available monitors in each city.

In addition, we calculated the average annual, summer and winter temperatures for each city, using data from the National Climatic Data Center (www.ncdc.noaa.gov).

City-level Characteristics—We obtained data on population characteristics from the 2000 U.S. Census Bureau (Census 2000, <http://www.census.gov>). In our analyses, we included data on proportion of the city population over 65 years old, city median household income, proportion in poverty, proportion of city families in poverty, proportion of white, black and Asian residents, proportion of residents with and without high-school degrees and with a college degree. Census data were obtained at the county level and we created population-weighted city averages to use in our analyses.

We also obtained city-specific smoking (2000–2010) and obesity (2004–2010) rates from the Behavioral Risk Factor Surveillance System (BRFSS, <http://www.cdc.gov/brfss/>). For each city, we created an overall average across the available years of these two variables.

Greenness—The quantity of green, natural vegetation was assessed using a satellite-image based vegetation index. Chlorophyll in plants strongly absorbs visible light (0.4–0.7 μm) for use in photosynthesis, while leaves strongly reflect near-infrared light (0.7–1.1 μm). The normalized difference vegetation index (NDVI; hereafter called vegetation index) calculates the ratio of the difference between the near-infrared region and red reflectance to the sum of these two measures. The vegetation index ranges between –1.0 and 1.0, with larger values indicating higher levels of vegetative density.¹² For this study, we used data from the Moderate-resolution Imaging Spectroradiometer (MODIS) from NASA's Terra satellite. MODIS provides images every 16 days at a 250 m resolution.¹³

We used geographic information systems (GIS) software from ArcMap (ESRI, Redlands, CA) to estimate the mean vegetation index value in each county for a representative month in each season (January, April, July, and October) over the study period. Two vegetation index metrics were calculated for our analyses as averages over 2000–2010: annual average vegetation index and summer average vegetation index.

Urbanicity—To assess urbanicity we used the 2000 urban sprawl index that was developed by Smart Growth America,¹⁴ which has previously used in health analyses.¹⁵ Because the 2000 urban sprawl index was not available for five cities in our study, we used the 2010

urban sprawl index¹⁶ to predict the 2000 sprawl index for these cities. Higher values of the sprawl index indicate more compact, denser cities. As a second indicator for urbanicity we also used population density per square mile, obtained from the 2000 Census.

Data analysis

Health Models—We used a previously described two-stage approach,^{5,17} i.e. a modification of the difference in differences approach to causal modeling.¹⁸ Specifically,

let: $Y_{ikt}^{A=E_{ikt}} = \beta_0^k + \beta_1^k E_{ikt} + \beta_2^k Z_{ik} + \beta_3^k W_{ikt} + \varepsilon$, where $Y_{ikt}^{A=E_{ikt}}$ is the potential outcome for subject i in city k and year t , under exposure $A=E_{ikt}$, E_{ikt} is the exposure, Z_{ik} the slowly varying potential confounders (e.g. SES) and W_{ikt} the confounders that vary across subjects, city and time. Then the difference in outcomes between time periods will be:

$Y_{ikt}^{A=E_{ikt}} - Y_{ikt(t-1)}^{A=E_{ik(t-1)}} = \beta_1^k (E_{ikt} - E_{ik(t-1)}) + \beta_3^k (W_{ikt} - W_{ik(t-1)})$ and Z_{ik} and β_0^k have disappeared. In addition, suppose we assign the same city level exposure to all subjects i in city k and year t . Then variations in W across subjects cannot act as confounders. Hence, all slowly varying confounders, measured or not, have been controlled by this approach.

Suppose, further, we assume that W_{ikt} varies essentially linearly over time during the study period, which is not unreasonable given the short follow-up (11 years). Then $W_{ikt} - W_{ik(t-1)}$ can be replaced by the slope of that line, and is a constant. If we, thus, regressed changes in Y against changes in E we would recover a causal estimate of β_1^k . We can weaken this assumption further. Suppose we remove a linear time trend from the outcome during the study period. Then, as long as the residuals of E_{ikt} from its long term trend are uncorrelated with the residuals of W_{ikt} from its long term trend, we have a causal estimate of β_1^k , and again W does not have to be observed for this to be true. This is not a strong assumption. For example, suppose that cities with more air pollution had worse diets, confounding the traditional cross-sectional cohort analysis. There is little reason to believe that the residuals of air pollution from their time trend in a given city, which are driven by EPA regulations and yearly variations in meteorology, would be correlated with the residuals of diet from its trend in the same city. And if we do this analysis separately for each city, there cannot be any confounding by mean contrasts in W across cities.

We used an extension of this approach and assessed whether year-to-year fluctuations in PM_{2.5} concentrations, around their long-term trends, are associated with year-to-year survival variations within cities. City-specific analyses eliminated confounding by factors that do not vary across time but vary across cities.

First, we fit separate Cox's proportional hazards models in each city, stratifying by age (5-year categories), gender, race (white, black, other) and follow-up time, with follow-up beginning on January 1st after entry in the cohort. We used annual and 2-year total PM_{2.5} mass concentrations, separately, as time-varying exposures; we used the counting process extension of the proportional hazards model by Andersen and Gill,¹⁹ and created multiple observations for each subject, with each observation representing a person-year of follow-up. In addition, we adjusted linearly for calendar year, controlling, hence, for long-term trends and focusing the analysis on variations in exposure around its time trend. We also

adjusted for any previous admission for CHF, COPD, MI or diabetes and number of days spent in the intensive and coronary care units, as these have been shown to be strongly associated with mortality,²⁰ to increase precision of our health effect estimates. Since MI-, COPD-, CHF- or diabetes-related admissions could also be intermediates in the PM_{2.5}–mortality, we repeated analyses without including these in our models. Finally, we adjusted for zip-code level median income, as a proxy for socio-economic status.

In the second stage, we combined the city-specific health effect estimates using a random effects meta-analysis.²¹ We also estimated the effect of PM_{2.5} on mortality by estimating region-specific effects. To do so, we added dummy variables for each region in the second-stage meta-regression and thus obtained the estimated deviation from the overall effect of PM_{2.5} in each region, assessing whether the effect estimate in a specific region was different from the pooled effect estimate. As regions we used the NOAA-defined climate regions, i.e. Southeast, Northeast, Central, South, East and West North Central, Southwest, West and Northwest. We combined the East and West North Central Regions, as only two cities were in the West North Central (Omaha, NE, and Fargo, ND).

Effect Modification—First, we assessed whether annual temperature levels at each city modify the association between year-to-year variations in PM_{2.5} and mortality. We included city annual temperature levels in the second stage (averaged over our study period); doing so, we assessed whether the effect estimate of PM_{2.5} on mortality (log(HR)) varies across temperature levels. Since the relationship between the PM_{2.5}–mortality estimates and temperatures has been shown to be non-linear,⁴ we also considered non-linear terms for temperature in the second stage, i.e. quadratic and cubic curves, as well as cubic splines with 1, 2 and 3 knots. We selected the best-fitting model using Akaike’s Information Criterion (AIC). We also conducted sensitivity analyses including temperatures averaged over only the summer or winter months.

We also assessed effect modification by population and city characteristics, to assess whether PM_{2.5} effects vary by levels of these characteristics, by including each of the above-mentioned Census, BRFSS, greenness and urbanicity variables separately in the second stage. We assessed effect modification as described above, i.e. by including these variables in the second-stage meta-regression and examining whether they are associated with the effect estimates of the long-term PM_{2.5}–mortality association.

There is considerable overlap between region, temperature levels, greenness, poverty, racial composition, etc., making it difficult to interpret results for any one set of modifiers. To further understand if and how these variables combined impact the PM_{2.5}–mortality association, we conducted a factor analysis allowing for a non-orthogonal solution. We determined the number of factors so that the identified factors explained at least 80% of the common variance of the variables.

All results are presented per 10 µg/m³ of PM_{2.5} to retain comparability with most previous air pollution cohort studies. For our statistical analyses we used SAS software, version 9.3 (SAS Institute Inc., Cary, NC, U.S.A), and R Statistical Software, version 2.14.1 (Foundation for Statistical Computing, Vienna, Austria).

Results

Our cohort consisted of 35,295,005 subjects and we observed 11,411,282 deaths (32%) before the end of follow-up. The number of subjects and deaths by city are presented in eTable 1. On average, the participants were 75 years old (SD=7.5), 57% were female and 86% white. Across the 207 cities, the average annual PM_{2.5} concentration was 12 (SD 1.6) µg/m³.

Overall, we observed strong, positive associations between long-term exposure to PM_{2.5} and mortality, with hazard ratios (HR) of 1.19 (95%CI: 1.11–1.28) per 10 µg/m³ increase in the annual PM_{2.5} concentrations and 1.17 (95%CI: 1.05–1.31) for 2-year PM_{2.5} average.

When we did not include the variable for prior admissions in the health models the results remained the same for annual PM_{2.5} concentrations (HR=1.19; 95%CI: 1.11–1.28), but the effect estimate for the 2-year PM_{2.5} average was only slightly attenuated (HR=1.15; 95%CI: 1.03–1.29).

Effect Modification

By Region—We observed varying associations between long-term PM_{2.5} and mortality across regions (Figure 1), with highest estimates in the Southeast and Northwest (HR = 1.9; 95%CI: 1.7–2.2 and 1.4; 95%CI: 1.1–1.9 per 10 µg/m³ increase in the annual PM_{2.5} concentrations, respectively). Increases were also observed in the South (HR = 1.4; 95%CI: 1.2–1.7) and in Central U.S. (HR = 1.2; 95%CI: 0.99–1.3). Conversely, we observed a negative association in the Southwest (HR = 0.75; 95%CI: 0.58–0.97).

Temperature—The distribution of average annual temperatures is presented in Table 1 and of summer and winter temperatures in eTable 2. We found effect modification by temperature. The models with the linear term for temperature provided the best fit for all annual, summer and winter temperatures. Specifically, we observed increased associations with increasing temperatures (Figure 2). Sensitivity analyses including only summer or winter average temperatures yielded similar results (eFigure 1).

City-level characteristics—Information on the distribution of the variables we considered in our analyses can be found in eTable 3 and the correlations across these variables in eFigure 2.

We observed modification of the association between exposure to annual PM_{2.5} concentrations and mortality by several variables. Specifically, we observed increasing effects with increasing obesity rates, proportion of the city population above 65 years, percent of residents and families in poverty, percent of black residents, percent of the population without a high school degree and greenness. Conversely, we observed decreasing effects with increasing median household income, percent white residents and percent of residents with a college degree. The results are presented in Figure 3 and eTable 3.

We identified six factors satisfying our criteria (eTable 4). Factor 1 was characterized by high poverty levels, high obesity rates, and high temperatures; factor 2 by low education and

high proportion of elderly residents; factor 3 by low percentage of white and high percentage of black residents; factor 4 by high urbanicity; factor 5 by high household income levels, high percentage of Asian and low percentage of black residents; and factor 6 by high greenness, high proportion of elderly residents and high smoking rates. When we regressed the city-specific PM_{2.5} effect estimates on these six factors in the second stage meta-regression, we observed effect modification by factors 1, 2, 3 and 6, with increasing levels in each of these factors related to higher PM_{2.5} effect estimates (eTable 5).

Discussion

We conducted a nationwide, multi-year study to assess the association between long-term PM_{2.5} exposures and mortality using data from more than 35 million Medicare enrollees. We observed positive associations for both 1- and 2-year average PM_{2.5} exposures. Our findings are consistent with previously published findings from the U.S. and Europe.^{1,5}

We observed effect modification by several city-level variables, including variables related to poverty and education. These variables can be considered community-level indicators for socioeconomic status (SES). Large disparities have been observed in air pollution exposures, with higher exposures among people living in lower SES communities,²² and SES has been identified as a modifier in the association between short-term PM_{2.5} exposures and adverse health.^{23,24} For instance, Bell et al.⁸ found several SES indicators, including lower education and income, to modify the association with short-term PM_{2.5} exposures. Our findings are consistent with worse effects in cities with lower average SES; specifically, we observed higher effect estimates among cities with high percentage of black and uneducated residents, and residents and families in poverty, and lower effects among cities with higher median income and percentage of white and college-educated residents.

One potential pathway by which low community-level SES could modify the long-term PM_{2.5} mortality association is through lower quality of and limited access to health care. The association between SES and health care access has long been recognized,^{25,26} and has been found to exist even under a universal health policy.²⁷ According to a recent report by the Agency for Healthcare Research and Quality,²⁸ the lowest quality in health care was observed in the South and in Southeastern states and, according to National Center for Health Statistics,²⁹ in 2011 both the highest age-adjusted death rates per 10,000 residents and the lowest number of active physicians and physicians in primary care per 10,000 were found in states in the South and Southeast.

A different pathway is potentially through increased psychosocial stress. Specific community characteristics have been shown to increase stress levels. Low SES and living in communities with problems, such as lack of safety, have been associated with increased psychosocial distress and chronic stress.^{30,31} Although usually neglected, studying the potentially differential risk of air pollution across levels of psychosocial stress is highly important.³² Higher traffic volume, for instance, has been associated with increased perceived stress.^{30,33} Several studies have shown positive associations between air pollution and inflammation markers,³⁴ child respiratory health,³⁵ and birth outcomes,³⁶ in the presence of higher stress levels.

Our factor analysis results are consistent with varying air pollution effects across levels of psychosocial stress. In particular, we observed higher effect estimates in communities with high poverty and low education levels, with increased obesity and smoking rates and higher percentage of black residents (eTables 3 and 5). These findings can help targeted interventions in specific communities to reduce perceived psychosocial stress and increase access to primary care, and thus ameliorate air pollution-induced adverse health.

A somewhat puzzling finding was the positive modification of greenness on the $PM_{2.5}$ –mortality association, as greenness has been associated with better health end points.³⁷ In our study, however greenness was highest in the Southeast (eTable 6), where the highest effect estimates were also observed (Figure 1). Moreover, greenness was positively correlated with the proportion of black and elderly residents in a city and smoking rates (eFigure 2). These could contribute in the observed positive modification. In an analysis within regions, however, greenness was no longer a positive modifier in any region and was in fact related to lower effect estimates in the Northeast and the Southwest (eTable 7).

One of the most consistent effect modifications in our analyses was observed by temperature; we found increasing $PM_{2.5}$ estimates with increasing temperature. Even though several studies have shown effect modification of temperature on the short-term air pollution and mortality association,^{38,39} this potential effect modification has not been examined before, to our knowledge, with long-term exposures. Annual average temperatures could be considered proxies for latitude and longitude, i.e. could be acting as indicators for other potentially modifying factors that vary across the country, such as SES. In fact, temperature was highly positively correlated with high poverty, high proportions of black residents and proportion of residents without a high school degree (eFigure 2). However, within-region analyses also yielded positive effect modification by temperature in multiple regions (eTable 7), making this explanation less likely. When we examined, furthermore, average summer temperatures only, we still observed the same positive association between temperature and long-term $PM_{2.5}$ effects.

Another possible explanation for the observed effect modification by temperature could be that temperature could be an indicator for varying particle composition, as temperature plays an important role in particulate size and composition in the urban air.⁴⁰ Higher temperatures are linked to higher concentrations of non-volatile particles and will impact semi-volatile secondary particle concentrations.⁴¹ Temperature has also been found to be highly correlated with organic and elemental carbon and sulfate.⁴² Although the association between long-term exposures to non-volatile, semi-volatile and organic particles and survival has not been widely examined, Ostro et al.⁴³ found the strongest associations with long-term organic carbon and sulfate exposures and mortality in a study of long-term exposure to particle components. A recent study also found higher effect estimates in cities with high organic carbon and sulfate contributions to the total $PM_{2.5}$ mass concentrations.⁵ Similarly, the observed modification by temperature could also reflect a modification by ozone, as ozone concentrations depend on temperature⁴⁰ and both short- and long-term ozone exposures have been associated with mortality.^{44,45}

We observed effect modification of the PM_{2.5}–mortality association by region. Specifically, in the Southeast, South and Northwest, and marginally in the central U.S., we observed higher effect estimates than the pooled estimate. This variability in effect estimates could be attributed to varying particle composition,⁵ or by other factors varying across the country, such as SES (eTable 6).

We observed lower effect estimates in the Southwest than in other regions. Even though the summer, albeit not annual, average temperatures in the Southwest are higher than in some other regions, the Southwestern cities in our analyses were characterized by low PM_{2.5} concentrations, as well as low obesity rates and proportion of black and elderly residents. Furthermore, all six factors identified through factor analysis were lower in the Southwest compared to the average national levels (eTable 6). These factors could contribute to the observed effect estimates. Moreover, crustal particles (i.e., derived from the earth's crust) are the major contributors to the total PM_{2.5} mass in the Southwest; in a previous study we showed that highest effects are observed when particles from anthropogenic sources are instead the major contributors, with lowest effects observed in cities with high crustal and oceanic contributions.⁵

Our results should be interpreted in light of the study's limitations. Information on individual-level SES or stress-related variables is limited or not available among Medicare enrollees. We were, hence, unable to assess potential effect modification at the individual level. Our results should, therefore, be interpreted at the community-level, i.e. community-level SES and community-related psychosocial stress. A potential source of non-differential measurement error could be the use of PM_{2.5} concentrations measured at ambient monitors. Any such error, however, is expected to bias our results towards the null and, thus, could not explain the observed associations.⁴⁶ Different monitor numbers across cities could result in differences in the accuracy of the city-specific annual PM_{2.5} levels; this could have influenced our results if the number of monitors is associated with the potential modifiers. Also, we were only able to assess all-cause mortality, as Medicare does not provide the underlying cause of death.

This is, to our knowledge, the largest study using Medicare data to date to examine the long-term PM_{2.5}–mortality association. Our findings are consistent with previously reported findings, showing a harmful effect of long-term PM_{2.5} exposures on survival. Furthermore, our study indicates that any findings assessing separate modifications by population, weather and city characteristics should be interpreted with caution, as these factors are highly correlated, with varying correlations across regions. This is also the first study, to our knowledge, to provide evidence of effect modification by temperature, with higher effects observed at warmer climates. Moreover, we found effect modification by several community-level variables, indicating that living in lower SES communities is associated with higher risk.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.
By-region $\text{PM}_{2.5}$ -mortality effect estimates, presented as HRs (95%CI) per 10 $\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$.

Figure 2.

The impact of annual average temperature on the PM_{2.5}–mortality association. The color of the points is a function of the precision of each city-specific HR, with darker color for higher precision.

Figure 3.

Effect modification by selected variables on the PM_{2.5}-mortality association, presented as HRs (95% CI) per 10 µg/m³ at the 25th and 75th percentiles of each variable. The variables presented here significantly modify the long-term PM_{2.5}-mortality association. The results for all variables examined are presented in eTable 3.

Table 1

Average annual temperatures (°F) and PM_{2.5} (µg/m³) by US climate region, as mean (SD).

Region	States	Cities	Temperature	PM _{2.5}
Southeast	FL, AL, GA, SC, NC, VA, DC	39	66 (5.8)	12 (1.7)
Northeast	ME, NH, VT, NY, PA, MA, RI, CT, NJ, DE, MD	49	52 (2.9)	12 (1.6)
Central	MO, IL, IN, OH, KY, TN, WV	34	54 (3.4)	14 (1.7)
South	TX, KS, OK, AR, LA, MS	21	67 (5.6)	11 (1.3)
North Central	MN, WI, MI, IA, MT, ND, SD, WY, NE	23	50 (1.9)	12 (1.2)
Southwest	AZ, UT, CO, NM	13	55 (8.4)	9 (1.1)
West	CA, NV	17	63 (4.7)	13 (2.6)
Northwest	WA, OR, ID	11	52 (2.3)	9 (1.2)