Cardiovascular and Cerebrovascular Emergency Department Visits Associated With Wildfire Smoke Exposure in California in 2015

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Background—Wildfire smoke is known to exacerbate respiratory conditions; however, evidence for cardiovascular and cerebrovascular events has been inconsistent, despite biological plausibility.

Methods and Results—A population-based epidemiologic analysis was conducted for daily cardiovascular and cerebrovascular emergency department (ED) visits and wildfire smoke exposure in 2015 among adults in 8 California air basins. A quasi-Poisson regression model was used for zip code–level counts of ED visits, adjusting for heat index, day of week, seasonality, and population. Satellite-imaged smoke plumes were classified as light, medium, or dense based on model-estimated concentrations of fine particulate matter. Relative risk was determined for smoky days for lag days 0 to 4. Rates of ED visits by age- and sex-stratified groups were also examined. Rates of all-cause cardiovascular ED visits were elevated across all lags, with the greatest increase on dense smoke days and among those aged ≥65 years at lag 0 (relative risk 1.15, 95% confidence interval [1.09, 1.22]). All-cause cerebrovascular visits were associated with smoke, especially among those 65 years and older, (1.22 [1.00, 1.49], dense smoke, lag 1). Respiratory conditions were also increased, as anticipated (1.18 [1.08, 1.28], adults >65 years, dense smoke, lag 1). No association was found for the control condition, acute appendicitis. Elevated risks for individual diagnoses included myocardial infarction, ischemic heart disease, heart failure, dysrhythmia, pulmonary embolism, ischemic stroke, and transient ischemic attack.

Conclusions—Analysis of an extensive wildfire season found smoke exposure to be associated with cardiovascular and cerebrovascular ED visits for all adults, particularly for those over aged 65 years. (*J Am Heart Assoc*. 2018;7:e007492. DOI: 10.1161/JAHA.117.007492.)

Key Words: heart failure • ischemic heart disease • particulate matter • stroke • wildfire

Wildfire season in North America has increased in intensity and duration, resulting in a greater population at high risk of wildfire smoke exposure.[1–3] Exposure to wildfire smoke is already contributing to substantial clinical, public health, and economic societal burdens, and yet, large-scale wildfire events are projected to increase through the end of the century in many regions, including in California.[2,4,5]

Wildfire smoke contains numerous air pollutants, including particulate matter, ozone, carbon monoxide, polycyclic aromatic compounds, and nitrogen dioxide, all of which have previously been associated with respiratory and cardiovascular outcomes in health studies of air pollution.[6–10] Fine particulate matter (<2.5 μm in diameter [$PM_{2.5}$]) is a known respiratory irritant and causally related to cardiovascular morbidity.[11–13] $PM_{2.5}$ passes deep into the lung and has been shown to increase systemic inflammation, oxidative stress, and coagulation through $PM_{2.5}$-mediated changes in the autonomic nervous system.[11,14] This has been linked to cardiovascular health impacts such as ischemic heart disease and cerebrovascular events such as ischemic stroke in the ambient air pollutant $PM_{2.5}$ literature.[11,15–18] Other air pollutants in wildfire smoke have also been linked to cardiovascular and respiratory outcomes in urban and ambient air pollution studies, including nitrogen oxides, carbon monoxide, and ozone.[7–10]

ORIGINAL RESEARCH

Clinical Perspective

What Is New?

- Wildfire smoke exposure was associated with increased rates of emergency department visits for numerous cardiovascular disease outcomes, including ischemic heart disease, dysrhythmia, heart failure, pulmonary embolism, and stroke.
- The observed risk was greatest among adults aged>65 years.
- This analysis used data from nearly the entire wildfire season across a large area of California, which is one of the most extensive studies of wildfire health impacts in California to date.

What Are the Clinical Implications?

- Individuals with underlying cardiovascular disease risk factors may be at risk for an acute cardiovascular or cerebrovascular event during a period of wildfire smoke exposure.
- Further studies should explore individual-level behavioral interventions that may help reduce exposure to smoke during wildfires.
- Hospital administrators and public health planners may want to use these results to inform surge planning of emergency departments, particularly among stroke centers and hospitals with cardiac catheterization facilities.

Among the pollutants during wildfire smoke episodes, fine particulate matter is the primary pollutant of concern to human health because of its abundance.[19] It is therefore surprising that the literature is less consistent about the cardiovascular and cerebrovascular effects associated with wildfire smoke exposure.[11–13] In contrast to respiratory impacts, fewer studies have examined cardiovascular and cerebrovascular outcomes and fewer yet reported positive associations with respect to exposure to wildfire smoke, potentially as a result of underpowered studies or limited population exposed, as these studies generally were conducted during solitary wildfire events.[11,12,20]

This study investigates a particularly widespread wildfire season in 2015 in California, during which a series of fire complexes encompassing over 800 000 acres burned in northern and central parts of the state. We examined the relative risk of combined and specific cardiovascular-, cerebrovascular-, and respiratory-related emergency department (ED) visits on light, medium, and dense plumes relative to days without wildfire smoke exposure. Data were used from the entirety of this intense fire season across a vast region of California to elucidate the cardiovascular and cerebrovascular health impacts previously inconclusive in the literature.

Methods

The data, analytic methods, and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure. The analytic methods and the statistical program code can be made available but access to the data requires institutional review board approval from the Committee for the Protection of Human Subjects (CPHS) under the California Health and Human Services Agency.

Study Setting

All ED visits between May 1 and September 30 were included within 8 of the 15 California air basins in the northern and central regions of the state that were most exposed to smoke during the 2015 wildfire season: Great Basin Valleys, Lake County, Lake Tahoe, Mountain Counties, North Coast, Northeast Plateau, Sacramento Valley, and San Joaquin Valley. The largest and longest fires during this study occurred in the North Coast, Lake County, Sacramento Valley, and San Joaquin Valley air basins but smoke plumes were present in all 8 air basins during the study period. During this period, precipitation was low and present mainly at higher elevations.

Exposure Data

Exposure data were from the publicly available National Oceanic and Atmospheric Administration (NOAA) Hazard Mapping System (HMS) Fire and Smoke product. The HMS provides geospatial boundaries of smoke plumes as seen by visible band satellite imagery. The HMS incorporates data from 7 NOAA and National Aeronautics and Space Administration environmental satellites, recording multiple plumes throughout each day. Each smoke plume in HMS is accompanied by estimated concentrations of $PM_{2.5}$ attributed to wildfire smoke, generated using atmospheric models, and grouped into light ($PM_{2.5}$ range 0–10 µg/m^3), medium (10.5–21.5 µg/m^3), and dense smoke categories (range 22+ µg/m^3).[21,22] Daily maximum density of smoke at each zip code was used to characterize exposure. All HMS smoke plume densities are published daily as shapefiles on the NOAA website and are used to communicate smoke plume locations to researchers and the public.

Healthcare Utilization Data

Daily counts of ED visits for each zip code in the study area and period came from the California Office of Statewide Health Planning and Development (OSHPD). The OSHPD Emergency Department Dataset (EDD) and Patient Discharge

Dataset (PDD) contain records of over 14 million annual ED visits from hospitals across California. Diagnoses were included for all adults aged ≥19 years. *International Classification of Disease, Ninth Edition (ICD-9)* codes were used for diagnoses of interest, using all 25 discharge diagnosis code positions in the OSHPD data set.[13,23–26] Cardiovascular end points were hypertension (*ICD-9* codes 401–405), myocardial infarction (410), ischemic heart disease (410–411, 413), pulmonary embolism (415), dysrhythmia and conduction disorder (426–427), heart failure (428), peripheral arterial disease (444), and all-cause cardiovascular (401–405, 410–411, 413, 415, 426–428, 444). Cerebrovascular end points included non-traumatic subarachnoid hemorrhage (430), intracerebral hemorrhage (431), non-traumatic intracranial hemorrhage (432), precerebral vascular occlusion (433), ischemic stroke (434), transient ischemic attack (TIA) (435), lateral medullary syndrome (436), and all-cause cerebrovascular events (430–436). Ischemic stroke and TIA were analyzed individually, while the other outcomes were included only in the all-cause cerebrovascular category given their rarity. Respiratory end points were included for external validity: asthma (493), COPD (491–492, 496), pneumonia (480–486), other non-cardiac chest pain or respiratory syndrome (786), and all-cause respiratory (480–486, 491–493, 496, 786). Control end points were acute appendicitis (540–542) and long-bone fracture (812–813, 820–821, 823) given their independent pathophysiology from $PM_{2.5}$-related inflammation and coagulation, as has been done elsewhere.[26] The category of all visits was used to approximate overall ED volume, which included discrete ED visits for any diagnosis code.

Covariate Data

US Census American Communities Survey 2015 population estimates were used for zip code population estimates. Daily mean temperature and relative humidity were obtained for 50 California airports from Weather Underground Data and History Archive. The daily heat index, a combined metric of temperature and relative humidity, was calculated for each zip code based on the mean temperature and relative humidity for the nearest airport to the zip code centroid.[27]

Statistical Analysis

A population-based epidemiological analysis was conducted to examine zip code–level associations between daily maximum smoke density (low, medium, and dense) and ED visits using a quasi-Poisson regression model. A quasi-Poisson regression analysis was used to allow for under- and over-dispersion of the data. Each health outcome was analyzed separately and associations were examined for exposure lagged between 0 and 4 days, with each lag analyzed independently. Estimated relative risk (RR) of each health outcome is reported for all adults, as well as for sex- and age-stratified adults. Relative risk is expressed as rate of outcome-specific ED visits on smoke days relative to the days with no smoke. The statistical model included indicator variables of smoke plume density (light, medium, dense), day of week, and smoothing splines for heat index (3 degrees of freedom) and for temporal trend (3 degrees of freedom), as done elsewhere[25,26] Logged zip code–population size was used as an offset to adjust for differences in baseline rate of visits by location. The sensitivity of the results was examined for different degrees of freedom for the smoothing splines of the covariates, and Bayesian Information Criteria (BIC) was used to choose the best fitting model.[28] No adjustment was made for multiplicity of comparisons.

Statistical analyses were conducted using the R Project for Statistical Computing Version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria) and emergency department data cleaning and management was conducted with SAS® software, Version 9.4, of the SAS System for Windows (SAS Institute Inc, Cary, NC).

Ethics

The study was approved by the Committee for the Protection of Human Subjects (CPHS) under the California Health and Human Services Agency and the subject informed consent requirement was waived.

Results

Descriptive Statistics

This analysis included 1 196 233 emergency department outcomes that occurred in the study region and time-period: 361 087 cardiovascular, 15 505 cerebrovascular, and 230 029 respiratory diagnoses, in addition to 2520 acute appendicitis and 13 473 long-bone fracture diagnoses for the controls. Age- and sex-stratified counts of ED visits delineated by diagnosis categories are shown in Table 1.

Medium- and dense-smoke days were most frequent in August, followed by September (Table 2). Three air basins shared the largest burden of smoke days, including the North Coast, Sacramento Valley, and San Joaquin Valley air basins (Figure 1). These were also the air basins with the largest population centers in the study region.

Cardiovascular Outcomes

ED visits for all-cause cardiovascular diagnoses and for individual cardiovascular diagnoses were associated with

Table 1. Counts of Cardiovascular, Cerebrovascular, Respiratory, and Control Emergency Department Visits; by Age and Sex; 8 California Air Basins, May 1 to September 30, 2015

	ICD-9 Code	19 to 44 y	45 to 64 y	≥65 y	Female	Male	Total
All-cause cardiovascular	401 to 405, 410 to 411, 413, 415, 426 to 428, 444	48 330	136 644	176 113	193 559	167 528	361 087
Hypertension	401 to 405	41 368	122 267	153 270	172 865	144 040	316 905
Ischemic heart disease	410 to 411, 413	808	5707	11 188	7732	9971	17 703
Myocardial infarction	410	436	3064	5155	3630	5025	8655
Pulmonary embolism	415	462	1095	1485	1529	1513	3042
Dysrhythmia and conduction disorder	426 to 427	6522	18 823	54 467	39 012	40 800	79 812
Heart failure	428	3226	16 719	36 741	27 963	28 723	56 686
Peripheral arterial disease	444	54	242	367	286	377	663
All-cause cerebrovascular	430 to 436	725	4276	10 504	7890	7615	15 505
Subarachnoid hemorrhage (non-traumatic)	430	72	174	192	268	170	438
Intracerebral/intraventricular hemorrhage	431	95	337	690	516	606	1122
Epidural/subdural hemorrhage (non-traumatic)	432	81	217	586	358	526	884
Precerebral vascular occlusion	433	63	858	3783	2339	2365	4704
Ischemic stroke	434	281	1990	3976	3117	3130	6247
Transient ischemic attack	435	174	992	2222	1873	1515	3388
Lateral medullary/Wallenberg syndrome	436	8	23	57	49	39	88
All-cause respiratory	480 to 486, 491 to 493, 496, 786	72 816	80 573	76 640	134 426	95 603	230 029
Asthma	493	35 483	26 133	17 712	53 728	25 600	79 328
COPD	491 to 492, 496	1937	20 825	32 732	28 911	26 583	55 494
Pneumonia	480 to 486	4240	7587	13 526	12 708	12 645	25 353
Other chest/respiratory syndrome	786	35 587	35 989	25 293	54 514	42 355	96 869
Control diagnoses							
Acute appendicitis	540 to 542	1478	707	335	1198	1322	2520
Long bone fracture	812 to 813, 820 to 821, 823	3110	3994	6369	8374	5099	13 473
All visits	Includes all discrete ED visits	568 448	361 696	266 089	680 874	515 359	1 196 233

All visits includes all discrete ED visits for any diagnosis in the study region during the same period. COPD indicates chronic obstructive pulmonary disease; ED, emergency department; *ICD-9*, *International Classification of Disease, Ninth Edition*.

wildfire smoke density for all adults (Table 3, Figure 2) and were more pronounced among adults aged ≥65 years (Tables 4 and 5). Risk increased for all-cause and individual cardiovascular diagnoses across multiple lags (Figure 3). The greatest change in risk was observed for myocardial infarction (RR [95% confidence interval (CI)]) (1.42 [1.09, 1.84]) and ischemic heart disease (1.22 [1.01, 1.47]) with dense smoke at lag 1, among adults aged ≥65 years. Risk of dysrhythmia was greatest among adults aged ≥65 years on days with dense smoke exposure but was elevated across most lags and

smoke densities for all adults and those over aged >65 years. Heart failure was associated most strongly with dense smoke at lag 3 among adults aged ≥65 years (1.22 [1.10, 1.35]) and elevated across all lags. Risk of heart failure was not increased in other age groups (Tables 3 and 4). Associations with all levels of smoke density were observed with hypertension in adults aged ≥65 years, at lags 0 through 4. Increased risk of pulmonary embolism was observed only at lags 2 and 3 with medium and dense smoke, among adults aged ≥65 years (1.71 [1.12, 2.62]).

Table 2. Proportion of Days Corresponding to Wildfire Smoke Plume Density (Based on PM$_{2.5}$ Concentration Estimates) and Descriptive Summary of Heat Index, by Month; 8 California Air Basins, May 1 to September 30, 2015

Smoke Density Estimate	May	June	July	August	Sept.
None (%)	91.6	87.2	88.4	54.1	72.7
Light (%)	7.6	11.4	8.9	25.5	17.8
Medium (%)	0.8	1.3	2.4	13.3	7.5
Dense (%)	0.0	0.2	0.3	7.2	2.0
Heat index, mean (°F)	61.1	73.3	75.1	74.3	70.1
Heat index, maximum (°F)	83	95	93	91	89

Cerebrovascular Outcomes

Risk of all-cause cerebrovascular ED visits on smoky days was most pronounced among adults aged ≥65 years and persisted at lag days 0 through 4 (Tables 3 through 5, Figure 2). Increased risk was observed with all 3 levels of smoke density, although not consistently statistically significant, possibly because of the fewer number of cerebrovascular events. Among adults aged >65 years, the highest relative risk was observed at dense smoke levels on lag day 0 (1.22 [1.00, 1.48]) and lag day 1 (1.22 [1.00, 1.49]). However, elevated risks were also seen for all adults and light smoke (1.09 [1.03, 1.15]) and medium smoke at lag days 1 and 3 (1.17 [1.06, 1.28], 1.14 [1.04, 1.26])]) (Table 3). In contrast, ischemic stroke diagnoses were increased only at longer lags and driven by the ≥65 age group. Among adults aged ≥65, ischemic stroke was statistically significant at lag 3 for light (1.16 [1.04, 1.29]) and medium smoke (1.25 [1.04, 1.50]), and was also increased for all adults at lag 3 days (1.16 [1.00, 1.34]) and adults 19 to 44 years at lag 4 (1.90 [1.26, 2.85]) (Table S1). Associations with transient ischemic attack were
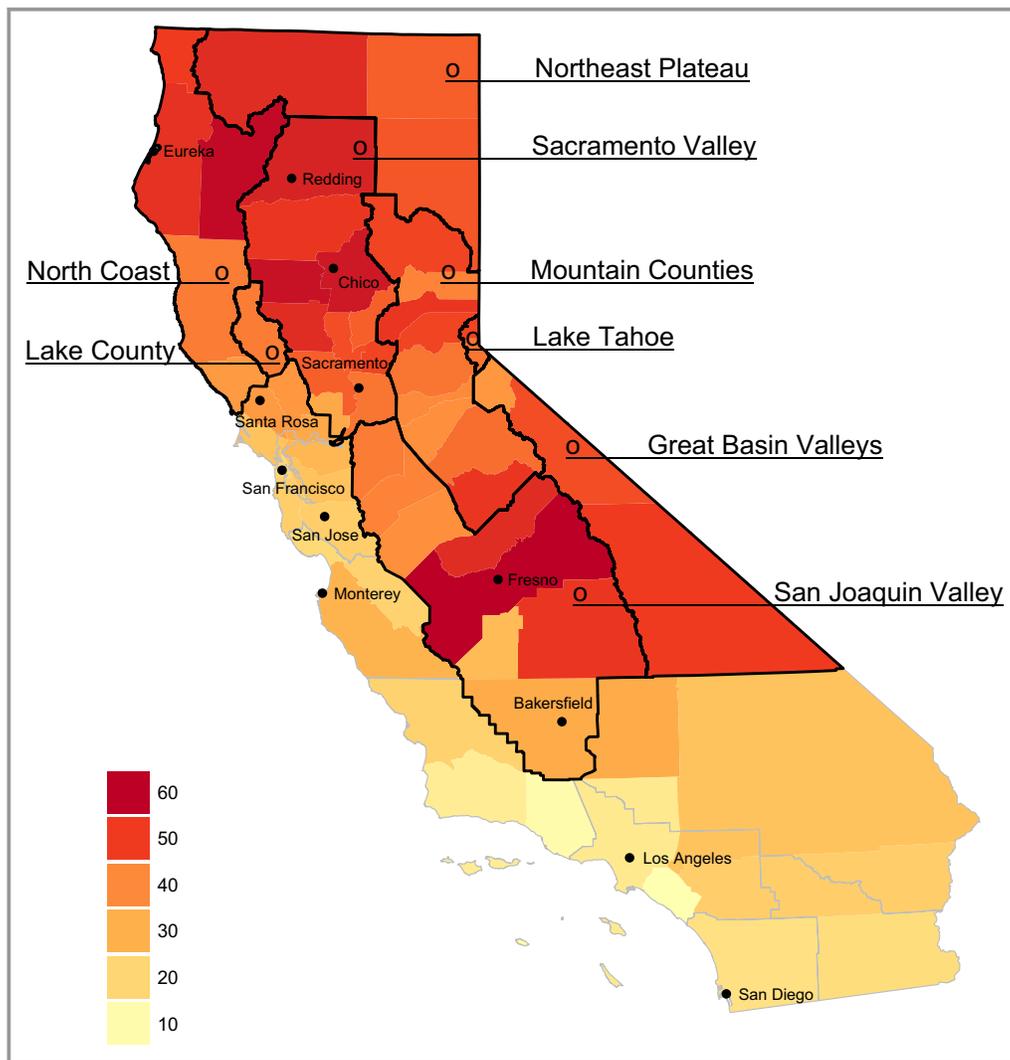

Figure 1. Total number of days with any smoke plumes by county from May 1 through September 30, 2015. California air basins in the study region are labeled and outlined in black, those excluded in gray.

Table 3. Relative Risk of Selected Emergency Department Visits on Wildfire-Smoke Days Relative to Days Without Smoke Across Lags 0 Through 4 Days for Adults Aged 19 Years and Older, 8 California Air Basins (May 1–September 30, 2015)

	Lag d	0		1		2		3		4	
Outcome	Smoke Density	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
All-cause cardiovascular	Light	1.02	1.00, 1.03	1.04*	1.03, 1.05*	1.03*	1.02, 1.05*	1.02	1.00, 1.03	1.01	1.00, 1.03
	Medium	1.05*	1.03, 1.08*	1.05*	1.03, 1.08*	1.04*	1.01, 1.07*	1.06*	1.04, 1.09*	1.06*	1.03, 1.08*
	Dense	1.08*	1.03, 1.12*	1.04	1.00, 1.09	1.07*	1.03, 1.12*	1.04	1.00, 1.09	1.02	0.98, 1.06
Hypertension	Light	1.01	1.00, 1.03	1.03*	1.02, 1.05*	1.03*	1.02, 1.05*	1.02	1.00, 1.03	1.01	1.00, 1.03
	Medium	1.05*	1.02, 1.07*	1.05*	1.02, 1.07*	1.04*	1.01, 1.07*	1.06*	1.04, 1.09*	1.06*	1.03, 1.08*
	Dense	1.08*	1.03, 1.12*	1.03	0.98, 1.08	1.05	1.00, 1.10	1.03	0.99, 1.08	1.01	0.97, 1.06
Ischemic heart disease	Light	1.02	0.97, 1.08	1.02	0.97, 1.08	1.06	1.00, 1.11	1.01	0.96, 1.06	1.02	0.97, 1.08
	Medium	1.01	0.92, 1.11	1.03	0.94, 1.13	1.00	0.91, 1.09	1.07	0.98, 1.17	0.95	0.87, 1.05
	Dense	1.01	0.86, 1.19	1.14	0.97, 1.33	1.16	1.00, 1.35	1.11	0.96, 1.29	0.94	0.80, 1.11
Myocardial infarction	Light	1.02	0.94, 1.10	0.98	0.91, 1.06	1.03	0.95, 1.11	1.00	0.93, 1.08	1.01	0.94, 1.09
	Medium	1.03	0.91, 1.18	1.07	0.94, 1.22	1.05	0.92, 1.20	1.04	0.91, 1.18	0.97	0.84, 1.11
	Dense	1.05	0.83, 1.32	1.30*	1.06, 1.61*	1.35*	1.10, 1.65*	1.22	0.98, 1.51	1.08	0.86, 1.35
Dysrhythmia	Light	1.06*	1.04, 1.09*	1.08*	1.05, 1.11*	1.05*	1.02, 1.08*	1.04*	1.01, 1.07*	1.04*	1.02, 1.07*
	Medium	1.10*	1.05, 1.15*	1.10*	1.06, 1.16*	1.05*	1.01, 1.10*	1.09*	1.05, 1.15*	1.06*	1.01, 1.11*
	Dense	1.16*	1.08, 1.25*	1.04	0.96, 1.13	1.18*	1.09, 1.27*	1.10*	1.02, 1.19*	1.04	0.97, 1.13
Heart failure	Light	1.01	0.98, 1.04	1.03	1.00, 1.06	1.04*	1.01, 1.08*	1.06*	1.03, 1.09*	1.03	1.00, 1.06
	Medium	1.06*	1.01, 1.12*	1.06*	1.01, 1.12*	1.01	0.96, 1.06	1.05	1.00, 1.10	1.08*	1.02, 1.13*
	Dense	1.09	1.00, 1.19	1.09	0.99, 1.19	1.10*	1.01, 1.20*	1.13*	1.04, 1.24*	1.08	0.99, 1.18
Pulmonary embolism	Light	1.04	0.91, 1.19	1.11	0.98, 1.27	1.13	0.99, 1.29	1.09	0.95, 1.24	1.00	0.87, 1.14
	Medium	0.98	0.77, 1.24	1.06	0.84, 1.35	1.06	0.83, 1.34	1.21	0.97, 1.51	1.07	0.85, 1.34
	Dense	1.11	0.74, 1.65	0.93	0.60, 1.45	1.43	1.00, 2.05	1.33	0.93, 1.92	1.02	0.68, 1.52
All-cause cerebrovascular	Light	1.05	1.00, 1.11	1.09*	1.03, 1.15*	1.05	0.99, 1.11	1.05	1.00, 1.11	1.06	1.00, 1.12
	Medium	1.07	0.97, 1.18	1.17*	1.06, 1.28*	1.08	0.98, 1.19	1.14*	1.04, 1.26*	1.10	1.00, 1.21
	Dense	1.12	0.95, 1.32	1.07	0.90, 1.27	1.06	0.90, 1.26	0.97	0.82, 1.16	0.96	0.81, 1.14
Ischemic stroke	Light	1.04	0.96, 1.14	1.08	0.99, 1.18	1.06	0.97, 1.16	1.08	0.99, 1.18	1.08	0.99, 1.17
	Medium	1.03	0.88, 1.20	1.10	0.94, 1.28	1.05	0.90, 1.23	1.16	1.00, 1.34	1.09	0.94, 1.27
	Dense	1.11	0.86, 1.45	1.03	0.78, 1.36	0.96	0.72, 1.27	0.94	0.71, 1.25	0.96	0.73, 1.27
Transient ischemic attack	Light	1.00	0.89, 1.13	1.01	0.89, 1.14	1.01	0.89, 1.14	1.05	0.93, 1.18	1.03	0.91, 1.16
	Medium	1.14	0.94, 1.40	1.14	0.93, 1.40	1.01	0.82, 1.25	1.22	1.00, 1.49	1.08	0.88, 1.33
	Dense	1.23	0.87, 1.73	0.92	0.62, 1.37	1.07	0.74, 1.54	0.98	0.67, 1.43	0.90	0.61, 1.33
All-cause respiratory	Light	1.02	1.00, 1.04	1.04*	1.02, 1.06*	1.03*	1.01, 1.05*	1.02	1.00, 1.03	1.00	0.98, 1.02
	Medium	1.09*	1.05, 1.12*	1.08*	1.05, 1.11*	1.05*	1.02, 1.08*	1.08*	1.05, 1.12*	1.07*	1.04, 1.10*
	Dense	1.09*	1.03, 1.15*	1.10*	1.04, 1.16*	1.09*	1.04, 1.15*	1.10*	1.05, 1.16*	1.04	0.99, 1.10
Acute appendicitis	Light	1.07	0.92, 1.26	0.99	0.84, 1.17	1.11	0.95, 1.31	1.00	0.84, 1.17	0.95	0.81, 1.12
	Medium	0.79	0.57, 1.08	1.12	0.85, 1.47	0.83	0.60, 1.14	0.84	0.62, 1.15	0.96	0.72, 1.28
	Dense	0.83	0.48, 1.43	0.92	0.54, 1.56	1.28	0.81, 2.02	1.00	0.60, 1.67	1.01	0.61, 1.68
Long bone fractures	Light	1.09*	1.02, 1.16*	1.10*	1.03, 1.17*	1.04	0.97, 1.11	1.04	0.97, 1.11	1.02	0.95, 1.09
	Medium	1.12	1.00, 1.26	1.09	0.97, 1.22	1.05	0.94, 1.18	1.01	0.90, 1.13	1.04	0.92, 1.16
	Dense	1.31*	1.09, 1.56*	1.30*	1.09, 1.56*	1.22*	1.01, 1.47*	0.96	0.78, 1.18	1.12	0.92, 1.36

Models adjusted for heat index, day of week, time trend, and log-population offset. CI indicates confidence interval; RR, relative risk.
*Statistically significant relative risks.
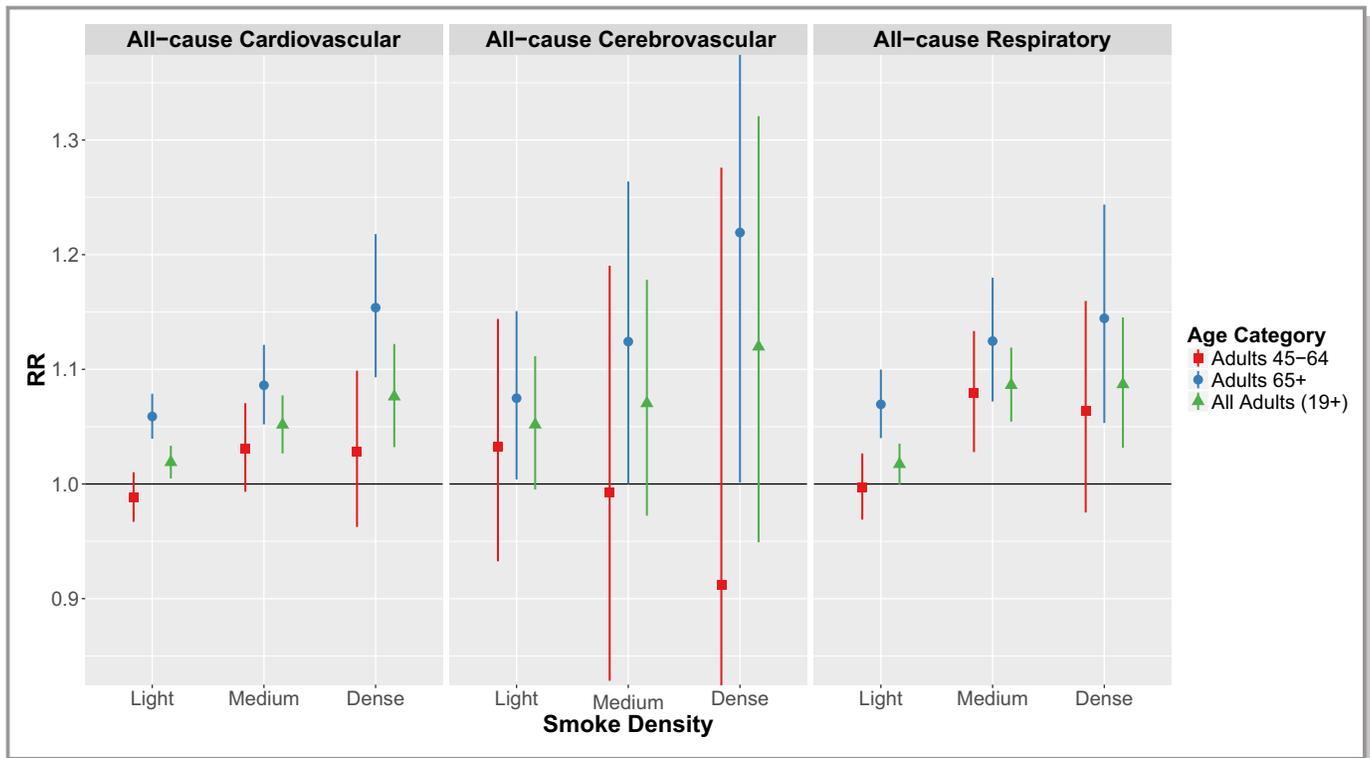
Figure 2. Relative risk and 95% confidence intervals for select cardiovascular, cerebrovascular, and respiratory outcomes relative to smoke-free days, at lag 0 days, stratified by age; 8 California air basins (May 1–September 30, 2015). Models adjusted for heat index, day of week, time trend, and log-population offset. RR indicates relative risk.

significant only among adults 45 to 64 and medium smoke at lag day 3 (1.39 [1.01, 1.92]) and consistently increased but with wider CIs for older populations at multiple lags (Tables 4 and 5).

Respiratory and Control Outcomes

All-cause respiratory outcomes were increased with medium and dense smoke exposure (Table 3), but most pronounced in adults aged ≥65 years (Figure 2). The risk of asthma related ED visits among younger adults on medium and dense smoke plume days was the highest but was elevated in other age groups as well (Table S1). Risk for COPD and pneumonia were increased across multiple lags and highest on dense smoke days for adults aged ≥65 years (Table S1). Statistically significant differences were not found among sex-stratified results for these respiratory diagnoses (Table S2).

No association was found between wildfire smoke density and acute appendicitis diagnoses. Long-bone fractures, however, were observed to have a significant association with $PM_{2.5}$ among all adults at lags 0 through 2 and dense smoke (1.31 [1.09, 1.56]), primarily adults 65 years and older (1.47 [1.12, 1.92]). When stratified by sex, the association was significant among women (1.37 [1.09, 1.70]) but not among men (1.22 [0.90, 1.65]) (Table S2).

Sensitivity Analysis

Additional sensitivity analysis was conducted by assessing zip code-specific associations between wildfire smoke density and health outcomes and summarizing results using random-effects meta-analysis to account for possible geographic heterogeneity of outcomes (Table S3). Sparsely populated zip codes had too low a count of diagnoses to perform the analysis so a population cutoff of 13 250 per zip code was used. The results are generally consistent with those presented here, with smaller standard errors, since the data were subset to larger zip code populations. Additional sensitivity analysis was conducting using the zip code-specific proportion of the population below the poverty level and the results were also consistent with those of the original analysis.

Additional age- and sex-stratified results, and those of rarer outcomes, can be found in Tables S1 and S2.

Discussion

In this investigation, a positive association was found between wildfire smoke density and ED visits attributable to cardiovascular, cerebrovascular, and respiratory disease in northern and central California in the summer of 2015. The impacts

Table 4. Relative Risk of Selected Emergency Department Visits on Wildfire-Smoke Days Relative to Days Without Smoke Across Lags 0 Through 4 Days for Adults Aged 45 to 64 Years, 8 California Air Basins (May 1–September 30, 2015)

Outcome	Smoke Density	Lag (Days) 0		1		2		3		4	
		RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
All-cause cardiovascular	Light	0.99	0.97, 1.01	1.02	1.00, 1.04	1.01	0.99, 1.03	1.00	0.98, 1.02	1.00	0.98, 1.02
	Medium	1.03	0.99, 1.07	1.01	0.97, 1.05	1.00	0.96, 1.04	1.05*	1.01, 1.09*	1.04	1.00, 1.08
	Dense	1.03	0.96, 1.10	0.98	0.92, 1.05	1.04	0.97, 1.11	1.01	0.95, 1.08	0.96	0.90, 1.03
Hypertension	Light	0.99	0.96, 1.01	1.02	1.00, 1.04	1.01	0.99, 1.03	1.00	0.98, 1.02	1.00	0.97, 1.02
	Medium	1.03	0.99, 1.07	1.01	0.97, 1.05	1.00	0.96, 1.04	1.05*	1.01, 1.10*	1.05*	1.01, 1.09*
	Dense	1.03	0.96, 1.10	0.97	0.90, 1.04	1.03	0.96, 1.10	1.01	0.94, 1.08	0.96	0.89, 1.03
Ischemic heart disease	Light	0.97	0.88, 1.08	0.95	0.86, 1.05	1.03	0.93, 1.13	0.99	0.90, 1.09	1.09	0.99, 1.20
	Medium	0.94	0.79, 1.12	0.98	0.82, 1.16	0.96	0.80, 1.14	0.96	0.81, 1.14	0.94	0.79, 1.12
	Dense	0.85	0.62, 1.18	0.95	0.70, 1.29	1.21	0.93, 1.59	1.22	0.94, 1.59	1.06	0.80, 1.41
Myocardial infarction	Light	1.01	0.89, 1.15	0.92	0.80, 1.05	1.04	0.91, 1.19	1.04	0.91, 1.18	1.05	0.92, 1.20
	Medium	0.93	0.74, 1.18	1.00	0.79, 1.25	1.02	0.81, 1.28	0.89	0.70, 1.14	0.94	0.74, 1.19
	Dense	0.96	0.63, 1.44	1.13	0.78, 1.65	1.33	0.94, 1.89	1.28	0.89, 1.82	1.13	0.78, 1.66
Dysrhythmia	Light	1.02	0.97, 1.08	1.05	0.99, 1.10	1.02	0.97, 1.07	1.02	0.97, 1.07	1.06*	1.01, 1.11*
	Medium	1.09	1.00, 1.19	1.06	0.97, 1.16	0.98	0.89, 1.08	1.08	0.99, 1.18	0.95	0.87, 1.04
	Dense	1.05	0.90, 1.23	1.03	0.88, 1.21	1.16	1.00, 1.34	1.03	0.88, 1.20	1.02	0.88, 1.20
Heart failure	Light	0.99	0.94, 1.04	1.02	0.97, 1.08	1.00	0.95, 1.05	1.03	0.98, 1.09	1.01	0.96, 1.07
	Medium	1.01	0.92, 1.11	1.02	0.93, 1.12	0.97	0.88, 1.06	1.02	0.93, 1.11	1.02	0.93, 1.12
	Dense	0.91	0.76, 1.08	1.02	0.86, 1.20	1.06	0.91, 1.25	1.02	0.87, 1.20	0.98	0.83, 1.16
Pulmonary embolism	Light	0.84	0.65, 1.11	1.05	0.82, 1.35	1.00	0.78, 1.30	1.09	0.85, 1.40	0.96	0.74, 1.24
	Medium	1.00	0.65, 1.54	0.80	0.49, 1.32	1.01	0.65, 1.58	1.07	0.69, 1.64	1.23	0.83, 1.83
	Dense	1.22	0.60, 2.45	0.94	0.42, 2.09	1.19	0.59, 2.40	1.27	0.65, 2.50	0.77	0.33, 1.77
All-cause cerebrovascular	Light	1.03	0.93, 1.14	1.10	1.00, 1.22	1.01	0.91, 1.12	0.97	0.87, 1.07	0.99	0.89, 1.10
	Medium	0.99	0.83, 1.19	1.12	0.94, 1.33	1.02	0.85, 1.23	1.12	0.94, 1.33	1.01	0.85, 1.21
	Dense	0.91	0.65, 1.28	0.66	0.44, 0.99	1.10	0.80, 1.49	1.01	0.74, 1.38	0.83	0.59, 1.17
Ischemic stroke	Light	1.01	0.87, 1.18	1.05	0.91, 1.22	0.94	0.80, 1.10	0.93	0.80, 1.09	1.01	0.86, 1.17
	Medium	0.91	0.69, 1.20	0.99	0.76, 1.30	1.00	0.77, 1.31	0.99	0.76, 1.29	1.05	0.81, 1.36
	Dense	0.84	0.50, 1.42	0.57	0.30, 1.08	0.90	0.55, 1.48	0.70	0.40, 1.20	0.64	0.36, 1.13
Transient ischemic attack	Light	1.13	0.92, 1.38	1.20	0.99, 1.46	1.07	0.88, 1.31	1.04	0.84, 1.27	0.94	0.77, 1.16
	Medium	1.13	0.80, 1.60	1.12	0.79, 1.60	1.05	0.73, 1.50	1.39*	1.01, 1.92*	0.93	0.65, 1.34
	Dense	1.23	0.68, 2.22	0.63	0.28, 1.45	1.17	0.63, 2.15	1.12	0.60, 2.06	0.88	0.45, 1.70
All-cause respiratory	Light	1.00	0.97, 1.03	1.03	1.00, 1.06	1.02	0.99, 1.05	1.01	0.98, 1.04	1.00	0.97, 1.03
	Medium	1.08*	1.03, 1.13*	1.09*	1.03, 1.14*	1.04	0.99, 1.09	1.10*	1.05, 1.15*	1.07*	1.02, 1.12*
	Dense	1.06	0.98, 1.16	1.07	0.98, 1.16	1.09	1.00, 1.18	1.07	0.98, 1.16	1.04	0.96, 1.14
Acute appendicitis	Light	1.20	0.85, 1.70	1.17	0.82, 1.66	1.14	0.80, 1.63	1.05	0.74, 1.51	1.07	0.74, 1.53
	Medium	1.11	0.59, 2.08	1.29	0.71, 2.33	0.84	0.42, 1.71	0.69	0.32, 1.48	1.36	0.76, 2.44
	Dense	1.48	0.57, 3.82	1.53	0.59, 3.97	1.59	0.63, 4.01	1.55	0.61, 3.90	1.21	0.42, 3.45
Long bone fracture	Light	1.06	0.95, 1.19	1.14*	1.02, 1.27*	1.08	0.97, 1.21	1.13*	1.01, 1.26*	1.02	0.91, 1.14
	Medium	1.16	0.97, 1.39	1.10	0.91, 1.32	1.06	0.88, 1.28	1.04	0.85, 1.26	0.97	0.80, 1.18
	Dense	1.12	0.82, 1.54	1.14	0.83, 1.56	1.46*	1.10, 1.95*	0.85	0.59, 1.23	0.92	0.64, 1.31

Models adjusted for heat index, day of week, time trend, and log-population offset. CI indicates confidence interval; RR, relative risk.
*Statistically significant relative risks.

Table 5. Relative Risk of Selected Emergency Department Visits on Wildfire-Smoke Days Relative to Days Without Smoke Across Lags 0 Through 4 Days for Adults Aged 65 Years and Older, 8 California Air Basins (May 1–September 30, 2015)

	Lag (Days)	0		1		2		3		4	
Outcome	Smoke Density	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
All-cause cardiovascular	Light	1.06*	1.04, 1.08*	1.07*	1.05, 1.09*	1.06*	1.04, 1.08*	1.03*	1.02, 1.05*	1.03*	1.01, 1.05*
	Medium	1.09*	1.05, 1.12*	1.10*	1.06, 1.13*	1.08*	1.05, 1.12*	1.08*	1.04, 1.11*	1.07*	1.04, 1.11*
	Dense	1.15*	1.09, 1.22*	1.12*	1.06, 1.18*	1.13*	1.07, 1.20*	1.10*	1.05, 1.17*	1.05	1.00, 1.11
Hypertension	Light	1.05*	1.03, 1.07*	1.06*	1.04, 1.08*	1.06*	1.04, 1.08*	1.04*	1.02, 1.06*	1.03*	1.01, 1.05*
	Medium	1.08*	1.04, 1.11*	1.09*	1.05, 1.12*	1.08*	1.05, 1.12*	1.07*	1.03, 1.10*	1.07*	1.04, 1.11*
	Dense	1.15*	1.09, 1.21*	1.10*	1.04, 1.17*	1.10*	1.04, 1.16*	1.08*	1.03, 1.15*	1.04	0.98, 1.10
Ischemic heart disease	Light	1.04	0.98, 1.11	1.07	1.00, 1.14	1.06	1.00, 1.13	1.02	0.95, 1.09	1.00	0.93, 1.06
	Medium	1.01	0.90, 1.14	1.06	0.94, 1.18	1.00	0.89, 1.13	1.12	1.00, 1.25	0.96	0.85, 1.08
	Dense	1.10	0.90, 1.33	1.22*	1.01, 1.47*	1.15	0.95, 1.39	1.07	0.89, 1.30	0.89	0.72, 1.09
Myocardial infarction	Light	1.02	0.93, 1.13	1.02	0.92, 1.12	1.01	0.91, 1.11	0.98	0.88, 1.08	0.99	0.90, 1.09
	Medium	1.05	0.89, 1.25	1.08	0.91, 1.28	1.05	0.89, 1.25	1.13	0.96, 1.34	0.96	0.81, 1.15
	Dense	1.10	0.82, 1.48	1.42*	1.09, 1.84*	1.37*	1.05, 1.78*	1.20	0.91, 1.59	1.09	0.82, 1.46
Dysrhythmia	Light	1.08*	1.04, 1.11*	1.10*	1.06, 1.13*	1.07*	1.03, 1.10*	1.05*	1.02, 1.09*	1.04*	1.01, 1.08*
	Medium	1.12*	1.06, 1.18*	1.13*	1.07, 1.19*	1.09*	1.03, 1.15*	1.09*	1.03, 1.16*	1.09*	1.03, 1.15*
	Dense	1.24*	1.13, 1.36*	1.07	0.96, 1.18	1.19*	1.09, 1.31*	1.15*	1.05, 1.26*	1.04	0.95, 1.15
Heart failure	Light	1.04	1.00, 1.07	1.05*	1.01, 1.09*	1.07*	1.04, 1.11*	1.06*	1.03, 1.10*	1.05*	1.01, 1.09*
	Medium	1.10*	1.03, 1.17*	1.10*	1.03, 1.17*	1.03	0.97, 1.10	1.07	1.00, 1.14	1.11*	1.04, 1.18*
	Dense	1.20*	1.08, 1.33*	1.16*	1.04, 1.30*	1.15*	1.03, 1.28*	1.22*	1.10, 1.35*	1.11	1.00, 1.24
Pulmonary embolism	Light	1.12	0.95, 1.32	1.15	0.97, 1.35	1.21*	1.03, 1.42*	1.08	0.92, 1.28	0.97	0.82, 1.15
	Medium	0.82	0.59, 1.13	1.26	0.95, 1.66	1.14	0.85, 1.53	1.39*	1.06, 1.81*	1.00	0.74, 1.34
	Dense	1.03	0.61, 1.72	1.00	0.58, 1.74	1.71*	1.12, 2.62*	1.55*	1.01, 2.37*	1.20	0.75, 1.93
All-cause cerebrovascular	Light	1.07	1.00, 1.15	1.09*	1.01, 1.16*	1.05	0.98, 1.13	1.08*	1.01, 1.16*	1.08*	1.01, 1.16*
	Medium	1.12	1.00, 1.26	1.21*	1.08, 1.35*	1.12	0.99, 1.26	1.16*	1.04, 1.30*	1.12	1.00, 1.26
	Dense	1.22	1.00, 1.48	1.22	1.00, 1.49	1.08	0.88, 1.33	0.98	0.79, 1.21	1.03	0.84, 1.27
Ischemic stroke	Light	1.07	0.96, 1.20	1.08	0.96, 1.21	1.12	1.00, 1.25	1.16*	1.04, 1.29*	1.11	1.00, 1.24
	Medium	1.12	0.93, 1.36	1.16	0.96, 1.41	1.07	0.88, 1.31	1.25*	1.04, 1.50*	1.07	0.88, 1.30
	Dense	1.25	0.91, 1.71	1.26	0.92, 1.73	0.95	0.66, 1.35	1.08	0.77, 1.52	1.08	0.78, 1.51
Transient ischemic attack	Light	0.96	0.82, 1.13	0.96	0.82, 1.13	0.96	0.82, 1.13	1.06	0.91, 1.24	1.04	0.89, 1.22
	Medium	1.18	0.91, 1.53	1.16	0.89, 1.51	1.04	0.79, 1.37	1.19	0.91, 1.54	1.17	0.90, 1.52
	Dense	1.30	0.85, 2.01	1.09	0.68, 1.75	1.12	0.71, 1.79	0.93	0.57, 1.54	0.94	0.57, 1.53
All-cause respiratory	Light	1.07*	1.04, 1.10*	1.08*	1.05, 1.11*	1.06*	1.04, 1.09*	1.03	1.00, 1.06	1.02	0.99, 1.05
	Medium	1.12*	1.07, 1.18*	1.11*	1.06, 1.17*	1.08*	1.03, 1.14*	1.09*	1.04, 1.14*	1.08*	1.03, 1.13*
	Dense	1.14*	1.05, 1.24*	1.18*	1.08, 1.28*	1.15*	1.06, 1.25*	1.19*	1.10, 1.29*	1.07	0.99, 1.17
Acute appendicitis	Light	1.10	0.69, 1.75	1.07	0.67, 1.69	1.46	0.95, 2.24	1.02	0.65, 1.61	0.90	0.56, 1.44
	Medium	0.99	0.42, 2.34	0.89	0.37, 2.15	0.86	0.34, 2.20	0.73	0.29, 1.83	0.72	0.29, 1.78
	Dense	1.27	0.35, 4.65	0.52	0.07, 3.83	0.79	0.15, 4.16	0.42	0.06, 3.04	0.85	0.21, 3.48
Long bone fracture	Light	1.12*	1.02, 1.24*	1.11	1.00, 1.22	1.06	0.96, 1.17	1.03	0.93, 1.14	1.11	1.00, 1.22
	Medium	1.09	0.92, 1.30	1.06	0.89, 1.27	1.00	0.84, 1.20	1.04	0.87, 1.23	1.10	0.93, 1.31
	Dense	1.46*	1.12, 1.90*	1.47*	1.12, 1.92*	1.05	0.77, 1.43	1.15	0.86, 1.54	1.24	0.94, 1.64

Models adjusted for heat index, day of week, time trend, and log-population offset. CI indicates confidence interval; RR, relative risk ratio.
*Statistically significant relative risks.
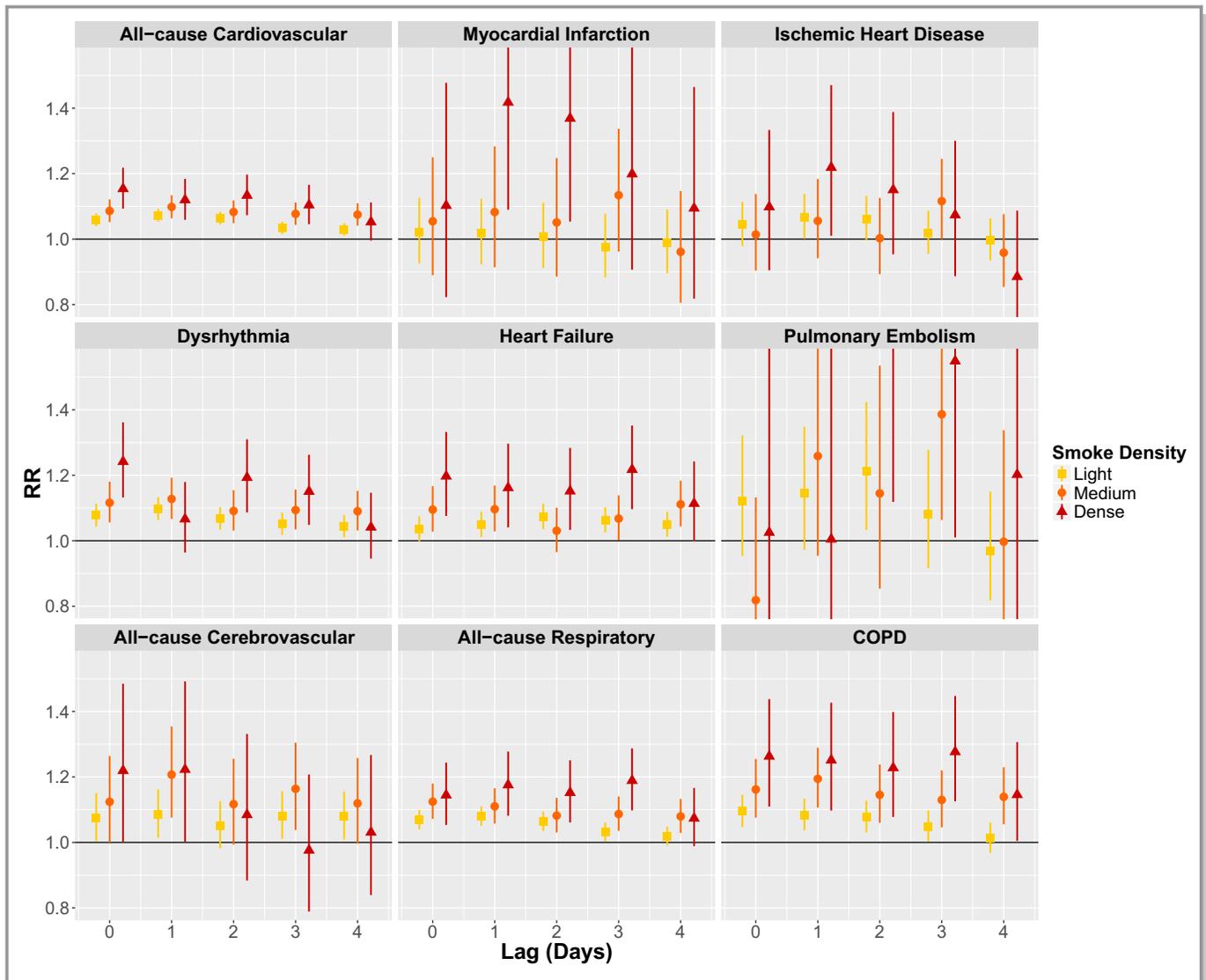
Figure 3. Relative risk and 95% confidence intervals for select cardiovascular, cerebrovascular, respiratory, and control outcomes relative to smoke-free days, across lags 0 to 4 days, adults aged ≥65 years, 8 California air basins (May 1–September 30, 2015). Models adjusted for heat index, day of week, time trend, and log-population offset. RR indicates relative risk.

were greatest on medium and dense smoke days and among adults aged ≥65 years, although also observed among younger age groups for some clinical conditions. In addition to the all-cause cardiovascular and cerebrovascular categories, relative risk was elevated for specific outcomes including myocardial infarction, ischemic heart disease, dysrhythmia, heart failure, pulmonary embolism, ischemic stroke, and transient ischemic attack. All-cause respiratory outcomes were statistically significant as well and surprisingly, so were long-bone fractures. No association was found with the control condition of acute appendicitis.

The evidence for particulate matter-mediated mechanisms for cardiovascular disease has been discussed elsewhere.[18] Recent reviews on the topic have identified 3 main pathophysiologic mechanisms: modulation of autonomic balance and neural input to the heart, release of pro-inflammatory mediators by lung tissue with attendant systemic effects, and penetration of particulate matter into the systemic circulation.[18,29–34] These 3 pathways can lead to an increase in systemic oxidative stress, endothelial dysfunction, and other inflammatory responses, in addition to platelet activation, hypercoagulability, and vasoconstriction.[18,29,30] Acute $PM_{2.5}$ exposure and the resulting autonomic stimulation, procoagulability, and inflammation all favor the underlying pathophysiology of the cardiovascular disease outcomes observed in this investigation, including cardiac dysrhythmia, ischemic heart disease, heart failure exacerbation, pulmonary embolism, and cerebrovascular events.

These pathophysiologic mechanisms are consistent with the apparent triggering of cardiovascular and cerebrovascular

clinical events based on the temporal relationships observed between short-term exposures to wildfire smoke and the clinical outcomes.[35] Dysrhythmia, likely precipitated by immediate changes in the balance of the autonomic nervous system, first appeared at lag 0.[36] Myocardial infarction and ischemic heart disease appeared second at lag 1. Epidemiologic studies indicate that ambient particulate matter exposure is more strongly associated with ST-elevation myocardial infarction than non–ST-elevation myocardial infarction, suggesting that the mechanism is dependent upon erosion of a rupture-prone plaque and changes in the balance of pro-thrombotic and anti-thrombotic processes promoting more extensive thrombosis.[37] ED visits for heart failure appeared first at lag 0 and increased with time, with the highest RR at lag 3. In contrast to the mechanisms accounting for the triggering of myocardial infarction, hospitalizations for heart failure are most likely secondary to exacerbations of pre-existing heart failure worsened by PM-induced increases in systemic blood pressure, and systemic and pulmonary vasoconstriction.[38–41] All these outcomes were most strongly associated with the aged. Cerebrovascular responses primarily manifested among older people and appeared within the first day and continued through lag 4, consistent with endothelial dysfunction and vasoconstriction, as well as thromboembolic phenomena.

Studies of wildfire-related cardiovascular outcomes have reported inconsistent findings. One recent review found that most studies with combined cardiovascular outcomes have found no significant associations, although some specific outcomes have been shown to be increased in the context of wildfire smoke, such as out-of-hospital cardiac arrest, heart failure, and ischemic heart disease.[11] Another review found that 6 of 14 studies revealed statistically significant associations of wildfires and cardiovascular outcomes.[12] Since the publication of that review, however, at least 4 subsequent investigations have identified elevated risk of cardiovascular events associated with wildfire smoke exposure, which may reflect recent use of more sophisticated methods or utilization of more specific outcomes.[15,20,26,42]

With respect to specific cardiovascular diagnoses, previous research has shown mixed results on ischemic heart disease. No association was found with wildfire smoke and ischemic heart disease hospitalizations in California, while another study found an increase in clinic-based ischemic heart disease visits among Native Americans of the Hoopa tribe of northern California.[43,44] An Australian study mentioned earlier found increased rates of hospital admissions and ED visits for ischemic heart disease among women and adults aged >65 years at lag day 2.[15]

Similarly, heart failure was found to be associated with wildfire smoke in this study. Elsewhere, heart failure–related ED visits were elevated in the context of peat bog fires in North Carolina in 2008, but the association was not significant when repeated for fires in 2011 and only suggestive among wildfires in 1 study from California.[15,16,26,43,45] Other cardiovascular outcomes, such as cardiac dysrhythmia, or pulmonary embolism, have not been found to have a clear association with wildfire-$PM_{2.5}$, although some suggestive effects have been found for dysrhythmia.[26,43,46] This investigation contributes to those significant findings of dysrhythmia and pulmonary embolism, but no association was found with peripheral arterial disease, potentially because of a small number of related ED visits.

Hypertension is another cardiovascular outcome that some have found to have a significant association with wildfire-$PM_{2.5}$ and may play an important role in the pathogenesis of more significant cardiovascular outcomes, such as ischemic heart disease and non-traumatic intracranial hemorrhage.[25,26] In this study, significant associations were also found between wildfire smoke and hypertension diagnoses in the ED.

In contrast to the evidence from the ambient $PM_{2.5}$ literature, few studies discussed cerebrovascular impacts associated with wildfire-$PM_{2.5}$, and mostly in the context of all cardiovascular disease outcomes combined.[8,18] This study is one of the few to explicitly investigate cerebrovascular outcomes and to find significant associations with smoke density defined by wildfire-$PM_{2.5}$. Of 3 studies that described this association, only 1 found elevated impacts.[43,46,47] Another study of 1 wildfire season in New Mexico found statistically significant elevated rates among adults aged 20 to 64 years (1.69 [1.03–2.77]) during the fire period.[20]

While the aim of this study was to explore cardiovascular and cerebrovascular health impacts attributable to wildfire smoke, respiratory outcomes were included for external validity, given the strong associations between wildfire-$PM_{2.5}$ and respiratory disease that have been documented elsewhere, including asthma, COPD, and some respiratory infections such as pneumonia.[11,12] As with other studies, positive associations were found between wildfire smoke and asthma, COPD, pneumonia, and respiratory-related chest pain symptoms. In 1 study of long-term wildfire-$PM_{2.5}$ exposure and asthma, adult women were found to be at greatest risk of asthma-related ED visits. Differential impacts of wildfire- and urban-$PM_{2.5}$ are still being explored; 1 study found increased pulmonary toxicity of wildfire-$PM_{2.5}$ compared with background urban sources in an animal model.[48] In addition to differences in component particles in $PM_{2.5}$ between urban and wildfire sources, urban exposures can be an order of magnitude lower but more persistent over time, while wildfire particulate exposure can vary significantly, peaking at much higher levels.[49,50]

We also used acute appendicitis and long-bone fractures as control conditions that were not expected to be associated

with wildfire-$PM_{2.5}$ given their inflammation- and coagulation-independent pathophysiology. No association was found with acute appendicitis but acute appendicitis events were rare and the resulting CIs were wide. Interestingly, an association was found with long-bone fractures and wildfire smoke among older adults at lag 0. Another study has used bone fractures as a control condition and while their results were not statistically significant, risk of bone fractures among all adults exposed to wildfire smoke was increased (RR 1.06, 95% CI: 0.97−1.15).[26] This could be because of trauma or falls, particularly among older adults, in the context of the wildfire response or evacuation. Motor vehicle accidents, for example, may precipitate long-bone fractures and may be more common during wildfire smoke events and evacuations, during which "superfog"—a combination of smoke and precipitation—may form at the ground level and can drastically reduce visibility on roadways.[51] Additionally, cardiac and cerebrovascular events can also precipitate falls and, given the associations found with cardiac dysrhythmias and other cardiac outcomes in this study, may offer another explanation for the surprising association with long-bone fractures. Based on the number of appendicitis-related visits and the possible connection between cardiovascular outcomes and bone fractures among older adults, we interpret the results for these conditions with these considerations in mind.

A major strength of this study was using data from the entirety of the 2015 wildfire season across a large area of California, during which a substantial population was exposed to a particularly intense season. This may have increased the statistical power of detecting rare health events, such as the cardiovascular and cerebrovascular effects observed in this study. The HMS data set provided estimates of smoke density on a smaller spatial resolution compared with the ground-based monitoring data, particularly in rural areas of California, where wildfires were more prevalent and monitors less so. In some instances, an individual county may have only 1 ground-based air monitor for $PM_{2.5}$. In addition, the OSHPD healthcare utilization data provided comprehensive state-wide data of ED visits based on discharge diagnoses, whereas some other studies have relied upon syndromic surveillance.[16,26,52] One study evaluated syndromic surveillance for cardiovascular disease in New York City and found high specificity for many of the disease entities, but often a low sensitivity and positive-predictive value, which may underestimate the impact of wildfire smoke on cardiovascular disease.[53]

This analysis is not without limitations. In the current analysis, because we focused on age-stratified and specific cardiovascular outcomes, we were not able to further refine daily counts of ED visits by other factors. For example, we did not examine the effect of personal traits or characteristics such as socioeconomic status, past medical history, race, sex

and other factors that may modify the association between daily variation in smoke exposure and ED visits. The modifying effect of these factors has previously been observed and discussed in the literature.[11,25,54] However, we did examine the sensitivity of these results to the confounding by socioeconomic status, such as poverty, and did not find evidence of confounding between poverty, smoke exposure, and health outcomes (Table S3).

The HMS data set provides smoke plume density based on estimated $PM_{2.5}$ concentrations and is characterized as light, medium, and dense smoke, where cutoff points are chosen with some degree of subjectivity.[21] These categorical exposure estimates made it difficult to complete a more nuanced assessment of incremental changes in $PM_{2.5}$ or other air pollutants on outcomes. Additionally, the number of smoky days was not evenly distributed between the different smoke levels, leading to wider CIs among dense smoke results and making the evaluation of a dose-dependent response more challenging.

The HMS data, however, are convenient, publicly available, and obtained via remote sensors providing more complete, timely data compared with other publicly available ground-based sources in California. Additionally, HMS data provide a classification of categorical smoke density which is a convenient representation for the purposes of making timely public health announcements. The results of the current analysis suggest that development of rapid ground-level air pollutant concentration validation methods based on satellite data could potentially be beneficial to public health risk messaging.

While $PM_{2.5}$ is a primary pollutant of concern from the perspective of population wide exposures, smoke plumes contain other pollutants that have known impacts on respiratory outcomes, such as ozone, nitrogen dioxide, carbon monoxide, coarse particulate matter ($PM_{10-2.5}$), and ultrafine particulate matter (0.1 μm or less). These pollutants may play an interactive role with $PM_{2.5}$ on health outcomes. However, other air pollutants are measured to a lesser extent with poor geographic and spatial coverage. Additionally, a recent study demonstrated that $PM_{2.5}$ estimates alone significantly underestimated the particulate matter emissions of wildfire smoke plumes in the western United States by a factor of 2 to 3.[19] Therefore, examining health effects based on plume density as visible by satellites may have its own advantages as the plume may represent multiple air pollutants emitted from the fire. Future research would benefit from an inclusion of co-pollutant exposure in the analysis when such data are available.

These results may be useful for public health practitioners in decision-making surrounding risk mitigation during wildfire smoke events. Hospital administrators may find this information helpful for hospital and emergency department surge planning for increased volume, including staffing, bed

utilization, and discharge challenges during ongoing wildfires. Similarly, stroke centers and hospitals with cardiac catheterization capabilities may find these results applicable to surge preparation.

On the level of the individual patient, the Center for Medicaid and Medicare Services and the Centers for Disease Control and Prevention, as part of the *Million Hearts® 2022* framework (https://millionhearts.hhs.gov/files/MH-Framework.pdf), have identified counseling of patients and family on the risks of airborne particulate matter, along with nutrition, physical activity, tobacco use, and referral to community-based physical activity programs and cardiac rehabilitation, as healthcare strategies to optimize care. Healthcare professionals may benefit from utilizing these results for patient risk stratification and subsequent education on risk mitigation for optimizing health care in the context of wildfire smoke exposure. Interventions for higher-risk individuals range from the well-established, such as evacuation from the affected area or transport to a clean air shelter, and reduction of outdoor activity, to other methods under study, such as indoor air filtration of fine particulates or use of N-95 respirators.[55,56] Further study is needed to define patient populations at increased risk for specific events, but these results suggest that patients with vascular and cardiac risk factors would be among the most susceptible, including patients with underlying coronary artery disease, heart failure, peripheral vascular disease, atrial fibrillation, cerebrovascular disease, hypertension, and diabetes mellitus.[18]

Conclusions

Time-series analysis was conducted of wildfire smoke and emergency department visits for the 2015 wildfire season in northern and central California. Despite the inconsistent findings discussed elsewhere, in this study wildfire smoke exposure was found to be positively associated with many cardiovascular and cerebrovascular health events, including ischemic heart disease, dysrhythmia, heart failure, and pulmonary embolism. Impacts were greatest among adults ≥65 years. This epidemiologic evidence helps strengthen the association between wildfire smoke exposure and cardiovascular disease outcomes and highlights the increased risk to the older population. These findings, along with others, support the need for clinical research to assess the clinical and public health value of interventions to decrease exposure to particulate matter, and particularly to wildfire smoke, among those at highest risk.[11,12,55,57–59] As wildfire season intensity and duration is projected to increase in California, understanding adverse health impacts of wildfire smoke and identifying the most susceptible populations is relevant to a broad group of stakeholders, including state and local officials responsible for land and air quality management, environmental scientists, policy makers, public health officials, and frontline public health and healthcare practitioners.

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SUPPLEMENTAL MATERIAL

Table S1. Age-Stratified Relative Risk of Emergency Department Visits on Wildfire-Smoke Days Relative to Days Without Smoke Across Lags 0 through 4 Days, 8 California Air Basins (May 1 - September 30, 2015). Statistically Significant Relative Risks are Shown in Bold.

Models adjusted for heat index, day of week, time trend, and log-population offset. RR indicates relative risk; CI, confidence interval.
NA - Not applicable - counts were too insufficient for analysis

Outcome	Lag	Exposure	All Adults RR	All Adults 95% CI	Adults 19-44 RR	Adults 19-44 95% CI	Adults 45-64 RR	Adults 45-64 95% CI	Adults 65+ RR	Adults 65+ 95% CI
All-cause cardiovascular	0	Light	1.02	(1.00, 1.03)	0.97	(0.94, 1.00)	0.99	(0.97, 1.01)	**1.06**	**(1.04, 1.08)**
		Medium	**1.05**	**(1.03, 1.08)**	0.99	(0.94, 1.04)	1.03	(0.99, 1.07)	**1.09**	**(1.05, 1.12)**
		Dense	**1.08**	**(1.03, 1.12)**	0.94	(0.85, 1.03)	1.03	(0.96, 1.10)	**1.15**	**(1.09, 1.22)**
	1	Light	**1.04**	**(1.03, 1.05)**	0.98	(0.95, 1.01)	1.02	(1.00, 1.04)	**1.07**	**(1.05, 1.09)**
		Medium	**1.05**	**(1.03, 1.08)**	1.01	(0.96, 1.07)	1.01	(0.97, 1.05)	**1.10**	**(1.06, 1.13)**
		Dense	1.04	(1.00, 1.09)	0.94	(0.85, 1.04)	0.98	(0.92, 1.05)	**1.12**	**(1.06, 1.18)**
	2	Light	**1.03**	**(1.02, 1.05)**	0.99	(0.96, 1.02)	1.01	(0.99, 1.03)	**1.06**	**(1.04, 1.08)**
		Medium	**1.04**	**(1.01, 1.07)**	1.00	(0.95, 1.06)	1.00	(0.96, 1.04)	**1.08**	**(1.05, 1.12)**
		Dense	**1.07**	**(1.03, 1.12)**	0.96	(0.88, 1.06)	1.04	(0.97, 1.11)	**1.13**	**(1.07, 1.20)**
	3	Light	1.02	(1.00, 1.03)	1.01	(0.98, 1.04)	1.00	(0.98, 1.02)	**1.03**	**(1.02, 1.05)**
		Medium	**1.06**	**(1.04, 1.09)**	**1.06**	**(1.01, 1.12)**	**1.05**	**(1.01, 1.09)**	**1.08**	**(1.04, 1.11)**
		Dense	1.04	(1.00, 1.09)	0.92	(0.84, 1.02)	1.01	(0.95, 1.08)	**1.10**	**(1.05, 1.17)**
	4	Light	1.01	(1.00, 1.03)	0.98	(0.95, 1.01)	1.00	(0.98, 1.02)	**1.03**	**(1.01, 1.05)**
		Medium	**1.06**	**(1.03, 1.08)**	1.04	(0.99, 1.10)	1.04	(1.00, 1.08)	**1.07**	**(1.04, 1.11)**
		Dense	1.02	(0.98, 1.06)	1.05	(0.96, 1.15)	0.96	(0.90, 1.03)	1.05	(1.00, 1.11)
Hypertension	0	Light	1.01	(1.00, 1.03)	0.95	(0.92, 0.98)	0.99	(0.96, 1.01)	**1.05**	**(1.03, 1.07)**
		Medium	**1.05**	**(1.02, 1.07)**	0.99	(0.94, 1.05)	1.03	(0.99, 1.07)	**1.08**	**(1.04, 1.11)**
		Dense	**1.08**	**(1.03, 1.12)**	0.95	(0.86, 1.05)	1.03	(0.96, 1.10)	**1.15**	**(1.09, 1.21)**
	1	Light	**1.03**	**(1.02, 1.05)**	0.98	(0.95, 1.01)	1.02	(1.00, 1.04)	**1.06**	**(1.04, 1.08)**
		Medium	**1.05**	**(1.02, 1.07)**	1.02	(0.96, 1.07)	1.01	(0.97, 1.05)	**1.09**	**(1.05, 1.12)**
		Dense	1.03	(0.98, 1.08)	0.95	(0.86, 1.05)	0.97	(0.90, 1.04)	**1.10**	**(1.04, 1.17)**
	2	Light	**1.03**	**(1.02, 1.05)**	0.99	(0.96, 1.03)	1.01	(0.99, 1.03)	**1.06**	**(1.04, 1.08)**
		Medium	**1.04**	**(1.01, 1.07)**	1.01	(0.96, 1.07)	1.00	(0.96, 1.04)	**1.08**	**(1.05, 1.12)**
		Dense	1.05	(1.00, 1.10)	0.94	(0.85, 1.03)	1.03	(0.96, 1.10)	**1.10**	**(1.04, 1.16)**
	3	Light	1.02	(1.00, 1.03)	1.02	(0.99, 1.05)	1.00	(0.98, 1.02)	**1.04**	**(1.02, 1.06)**
		Medium	**1.06**	**(1.04, 1.09)**	1.06	(1.00, 1.11)	**1.05**	**(1.01, 1.10)**	**1.07**	**(1.03, 1.10)**
		Dense	1.03	(0.99, 1.08)	0.93	(0.84, 1.03)	1.01	(0.94, 1.08)	**1.08**	**(1.03, 1.15)**

	4	Light	1.01	(1.00, 1.03)	0.99	(0.96, 1.02)	1.00	(0.97, 1.02)	**1.03**	**(1.01, 1.05)**
		Medium	**1.06**	**(1.03, 1.08)**	1.02	(0.97, 1.08)	**1.05**	**(1.01, 1.09)**	**1.07**	**(1.04, 1.11)**
		Dense	1.01	(0.97, 1.06)	1.05	(0.95, 1.16)	0.96	(0.89, 1.03)	1.04	(0.98, 1.10)
Ischemic heart disease	0	Light	1.02	(0.97, 1.08)	1.06	(0.88, 1.28)	0.97	(0.88, 1.08)	1.04	(0.98, 1.11)
		Medium	1.01	(0.92, 1.11)	**1.44**	**(1.07, 1.94)**	0.94	(0.79, 1.12)	1.01	(0.90, 1.14)
		Dense	1.01	(0.86, 1.19)	1.08	(0.59, 1.95)	0.85	(0.62, 1.18)	1.10	(0.90, 1.33)
	1	Light	1.02	(0.97, 1.08)	0.97	(0.80, 1.18)	0.95	(0.86, 1.05)	1.07	(1.00, 1.14)
		Medium	1.03	(0.94, 1.13)	1.06	(0.76, 1.49)	0.98	(0.82, 1.16)	1.06	(0.94, 1.18)
		Dense	1.14	(0.97, 1.33)	1.50	(0.90, 2.48)	0.95	(0.70, 1.29)	**1.22**	**(1.01, 1.47)**
	2	Light	1.06	(1.00, 1.11)	1.21	(1.00, 1.45)	1.03	(0.93, 1.13)	1.06	(1.00, 1.13)
		Medium	1.00	(0.91, 1.09)	1.19	(0.86, 1.66)	0.96	(0.80, 1.14)	1.00	(0.89, 1.13)
		Dense	1.16	(1.00, 1.35)	0.83	(0.41, 1.66)	1.21	(0.93, 1.59)	1.15	(0.95, 1.39)
	3	Light	1.01	(0.96, 1.06)	1.03	(0.85, 1.24)	0.99	(0.90, 1.09)	1.02	(0.95, 1.09)
		Medium	1.07	(0.98, 1.17)	1.20	(0.88, 1.64)	0.96	(0.81, 1.14)	1.12	(1.00, 1.25)
		Dense	1.11	(0.96, 1.29)	0.75	(0.38, 1.47)	1.22	(0.94, 1.59)	1.07	(0.89, 1.30)
	4	Light	1.02	(0.97, 1.08)	0.97	(0.80, 1.18)	1.09	(0.99, 1.20)	1.00	(0.93, 1.06)
		Medium	0.95	(0.87, 1.05)	1.02	(0.72, 1.43)	0.94	(0.79, 1.12)	0.96	(0.85, 1.08)
		Dense	0.94	(0.80, 1.11)	0.83	(0.44, 1.59)	1.06	(0.80, 1.41)	0.89	(0.72, 1.09)
Myocardial infarction	0	Light	1.02	(0.94, 1.10)	1.06	(0.80, 1.41)	1.01	(0.89, 1.15)	1.02	(0.93, 1.13)
		Medium	1.03	(0.91, 1.18)	**1.59**	**(1.03, 2.45)**	0.93	(0.74, 1.18)	1.05	(0.89, 1.25)
		Dense	1.05	(0.83, 1.32)	1.13	(0.46, 2.75)	0.96	(0.63, 1.44)	1.10	(0.82, 1.48)
	1	Light	0.98	(0.91, 1.06)	0.94	(0.69, 1.27)	0.92	(0.80, 1.05)	1.02	(0.92, 1.12)
		Medium	1.07	(0.94, 1.22)	1.49	(0.94, 2.34)	1.00	(0.79, 1.25)	1.08	(0.91, 1.28)
		Dense	**1.30**	**(1.06, 1.61)**	1.28	(0.55, 2.97)	1.13	(0.78, 1.65)	**1.42**	**(1.09, 1.84)**
	2	Light	1.03	(0.95, 1.11)	1.18	(0.90, 1.56)	1.04	(0.91, 1.19)	1.01	(0.91, 1.11)
		Medium	1.05	(0.92, 1.20)	1.24	(0.77, 2.01)	1.02	(0.81, 1.28)	1.05	(0.89, 1.25)
		Dense	**1.35**	**(1.10, 1.65)**	1.13	(0.46, 2.77)	1.33	(0.94, 1.89)	**1.37**	**(1.05, 1.78)**
	3	Light	1.00	(0.93, 1.08)	1.07	(0.80, 1.43)	1.04	(0.91, 1.18)	0.98	(0.88, 1.08)
		Medium	1.04	(0.91, 1.18)	0.93	(0.54, 1.59)	0.89	(0.70, 1.14)	1.13	(0.96, 1.34)
		Dense	1.22	(0.98, 1.51)	1.01	(0.41, 2.53)	1.28	(0.89, 1.82)	1.20	(0.91, 1.59)
	4	Light	1.01	(0.94, 1.09)	1.00	(0.71, 1.39)	1.05	(0.92, 1.20)	0.99	(0.90, 1.09)
		Medium	0.97	(0.84, 1.11)	1.25	(0.73, 2.16)	0.94	(0.74, 1.19)	0.96	(0.81, 1.15)
		Dense	1.08	(0.86, 1.35)	0.41	(0.08, 2.11)	1.13	(0.78, 1.66)	1.09	(0.82, 1.46)
Dysrhythmia	0	Light	**1.06**	**(1.04, 1.09)**	1.06	(0.98, 1.14)	1.02	(0.97, 1.08)	**1.08**	**(1.04, 1.11)**
		Medium	**1.10**	**(1.05, 1.15)**	1.01	(0.88, 1.15)	1.09	(1.00, 1.19)	**1.12**	**(1.06, 1.18)**

		Dense	**1.16**	**(1.08, 1.25)**	0.82	(0.63, 1.07)	1.05	(0.90, 1.23)	**1.24**	**(1.13, 1.36)**
	1	Light	**1.08**	**(1.05, 1.11)**	1.02	(0.94, 1.10)	1.05	(0.99, 1.10)	**1.10**	**(1.06, 1.13)**
		Medium	**1.10**	**(1.06, 1.16)**	1.04	(0.91, 1.19)	1.06	(0.97, 1.16)	**1.13**	**(1.07, 1.19)**
		Dense	1.04	(0.96, 1.13)	0.87	(0.68, 1.12)	1.03	(0.88, 1.21)	1.07	(0.96, 1.18)
	2	Light	**1.05**	**(1.02, 1.08)**	1.01	(0.94, 1.09)	1.02	(0.97, 1.07)	**1.07**	**(1.03, 1.10)**
		Medium	**1.05**	**(1.01, 1.10)**	0.97	(0.85, 1.11)	0.98	(0.89, 1.08)	**1.09**	**(1.03, 1.15)**
		Dense	**1.18**	**(1.09, 1.27)**	1.15	(0.93, 1.43)	1.16	(1.00, 1.34)	**1.19**	**(1.09, 1.31)**
	3	Light	**1.04**	**(1.01, 1.07)**	0.99	(0.92, 1.07)	1.02	(0.97, 1.07)	**1.05**	**(1.02, 1.09)**
		Medium	**1.09**	**(1.05, 1.15)**	**1.15**	**(1.01, 1.30)**	1.08	(0.99, 1.18)	**1.09**	**(1.03, 1.16)**
		Dense	**1.10**	**(1.02, 1.19)**	0.89	(0.70, 1.14)	1.03	(0.88, 1.20)	**1.15**	**(1.05, 1.26)**
	4	Light	**1.04**	**(1.02, 1.07)**	0.99	(0.92, 1.07)	**1.06**	**(1.01, 1.11)**	**1.04**	**(1.01, 1.08)**
		Medium	**1.06**	**(1.01, 1.11)**	1.14	(1.00, 1.29)	0.95	(0.87, 1.04)	**1.09**	**(1.03, 1.15)**
		Dense	1.04	(0.97, 1.13)	1.13	(0.91, 1.42)	1.02	(0.88, 1.20)	1.04	(0.95, 1.15)
Heart failure	0	Light	1.01	(0.98, 1.04)	0.87	(0.76, 1.00)	0.99	(0.94, 1.04)	1.04	(1.00, 1.07)
		Medium	**1.06**	**(1.01, 1.12)**	0.98	(0.78, 1.23)	1.01	(0.92, 1.11)	**1.10**	**(1.03, 1.17)**
		Dense	1.09	(1.00, 1.19)	0.83	(0.53, 1.30)	0.91	(0.76, 1.08)	**1.20**	**(1.08, 1.33)**
	1	Light	1.03	(1.00, 1.06)	0.91	(0.80, 1.04)	1.02	(0.97, 1.08)	**1.05**	**(1.01, 1.09)**
		Medium	**1.06**	**(1.01, 1.12)**	0.92	(0.73, 1.16)	1.02	(0.93, 1.12)	**1.10**	**(1.03, 1.17)**
		Dense	1.09	(0.99, 1.19)	0.65	(0.40, 1.06)	1.02	(0.86, 1.20)	**1.16**	**(1.04, 1.30)**
	2	Light	**1.04**	**(1.01, 1.08)**	0.96	(0.84, 1.09)	1.00	(0.95, 1.05)	**1.07**	**(1.04, 1.11)**
		Medium	1.01	(0.96, 1.06)	0.99	(0.79, 1.25)	0.97	(0.88, 1.06)	1.03	(0.97, 1.10)
		Dense	**1.10**	**(1.01, 1.20)**	0.75	(0.48, 1.19)	1.06	(0.91, 1.25)	**1.15**	**(1.03, 1.28)**
	3	Light	**1.06**	**(1.03, 1.09)**	1.09	(0.96, 1.24)	1.03	(0.98, 1.09)	**1.06**	**(1.03, 1.10)**
		Medium	1.05	(1.00, 1.10)	1.02	(0.80, 1.28)	1.02	(0.93, 1.11)	1.07	(1.00, 1.14)
		Dense	**1.13**	**(1.04, 1.24)**	0.80	(0.50, 1.27)	1.02	(0.87, 1.20)	**1.22**	**(1.10, 1.35)**
	4	Light	1.03	(1.00, 1.06)	0.96	(0.84, 1.10)	1.01	(0.96, 1.07)	**1.05**	**(1.01, 1.09)**
		Medium	**1.08**	**(1.02, 1.13)**	0.98	(0.77, 1.23)	1.02	(0.93, 1.12)	**1.11**	**(1.04, 1.18)**
		Dense	1.08	(0.99, 1.18)	1.22	(0.83, 1.78)	0.98	(0.83, 1.16)	1.11	(1.00, 1.24)
Peripheral arterial disease	0	Light	0.98	(0.67, 1.43)	0.73	(0.23, 2.25)	0.87	(0.51, 1.49)	1.09	(0.62, 1.92)
		Medium	0.97	(0.50, 1.87)	0.79	(0.12, 5.12)	1.10	(0.47, 2.59)	0.91	(0.32, 2.59)
		Dense	1.08	(0.36, 3.26)	3.09	(0.47, 20.52)	1.41	(0.36, 5.53)	0.62	(0.07, 5.43)
	1	Light	0.98	(0.67, 1.44)	0.77	(0.24, 2.48)	1.01	(0.60, 1.69)	1.00	(0.56, 1.79)
		Medium	1.26	(0.69, 2.31)	1.40	(0.28, 7.14)	1.08	(0.44, 2.64)	1.36	(0.56, 3.32)
		Dense	1.25	(0.42, 3.79)	1.79	(0.12, 26.69)	1.23	(0.25, 5.92)	1.21	(0.22, 6.54)
	2	Light	1.02	(0.70, 1.49)	0.89	(0.31, 2.50)	1.06	(0.64, 1.78)	1.01	(0.57, 1.80)

		Medium	1.08	(0.56, 2.08)	1.46	(0.31, 6.84)	1.18	(0.48, 2.89)	0.96	(0.34, 2.73)
		Dense	1.00	(0.31, 3.23)	*NA*	*NA*	1.06	(0.22, 5.18)	1.10	(0.20, 5.99)
	3	Light	1.27	(0.89, 1.81)	1.20	(0.45, 3.17)	1.16	(0.70, 1.92)	1.35	(0.80, 2.29)
		Medium	1.61	(0.91, 2.84)	1.48	(0.30, 7.17)	1.65	(0.76, 3.60)	1.61	(0.68, 3.80)
		Dense	1.22	(0.41, 3.65)	*NA*	*NA*	1.53	(0.38, 6.12)	1.20	(0.23, 6.32)
	4	Light	1.00	(0.68, 1.48)	0.90	(0.31, 2.63)	1.15	(0.69, 1.91)	0.93	(0.50, 1.71)
		Medium	1.57	(0.90, 2.74)	1.31	(0.27, 6.33)	1.56	(0.72, 3.39)	1.62	(0.70, 3.78)
		Dense	1.94	(0.81, 4.64)	*NA*	*NA*	1.14	(0.24, 5.50)	2.71	(0.87, 8.48)
Pulmonary embolism	0	Light	1.04	(0.91, 1.19)	1.26	(0.93, 1.71)	0.84	(0.65, 1.11)	1.12	(0.95, 1.32)
		Medium	0.98	(0.77, 1.24)	1.42	(0.87, 2.31)	1.00	(0.65, 1.54)	0.82	(0.59, 1.13)
		Dense	1.11	(0.74, 1.65)	1.10	(0.42, 2.88)	1.22	(0.60, 2.45)	1.03	(0.61, 1.72)
	1	Light	1.11	(0.98, 1.27)	1.15	(0.85, 1.57)	1.05	(0.82, 1.35)	1.15	(0.97, 1.35)
		Medium	1.06	(0.84, 1.35)	1.12	(0.65, 1.91)	0.80	(0.49, 1.32)	1.26	(0.95, 1.66)
		Dense	0.93	(0.60, 1.45)	0.69	(0.21, 2.24)	0.94	(0.42, 2.09)	1.00	(0.58, 1.74)
	2	Light	1.13	(0.99, 1.29)	1.18	(0.86, 1.61)	1.00	(0.78, 1.30)	**1.21**	**(1.03, 1.42)**
		Medium	1.06	(0.83, 1.34)	0.90	(0.49, 1.66)	1.01	(0.65, 1.58)	1.14	(0.85, 1.53)
		Dense	**1.43**	**(1.00, 2.05)**	1.23	(0.49, 3.12)	1.19	(0.59, 2.40)	**1.71**	**(1.12, 2.62)**
	3	Light	1.09	(0.95, 1.24)	1.11	(0.81, 1.51)	1.09	(0.85, 1.40)	1.08	(0.92, 1.28)
		Medium	1.21	(0.97, 1.51)	1.06	(0.61, 1.83)	1.07	(0.69, 1.64)	**1.39**	**(1.06, 1.81)**
		Dense	1.33	(0.93, 1.92)	0.85	(0.29, 2.45)	1.27	(0.65, 2.50)	**1.55**	**(1.01, 2.37)**
	4	Light	1.00	(0.87, 1.14)	1.19	(0.87, 1.62)	0.96	(0.74, 1.24)	0.97	(0.82, 1.15)
		Medium	1.07	(0.85, 1.34)	0.87	(0.48, 1.59)	1.23	(0.83, 1.83)	1.00	(0.74, 1.34)
		Dense	1.02	(0.68, 1.52)	1.07	(0.43, 2.68)	0.77	(0.33, 1.77)	1.20	(0.75, 1.93)
All-cause cerebrovascular	0	Light	1.05	(1.00, 1.11)	0.84	(0.69, 1.03)	1.03	(0.93, 1.14)	1.07	(1.00, 1.15)
		Medium	1.07	(0.97, 1.18)	0.77	(0.53, 1.11)	0.99	(0.83, 1.19)	1.12	(1.00, 1.26)
		Dense	1.12	(0.95, 1.32)	0.91	(0.50, 1.67)	0.91	(0.65, 1.28)	1.22	(1.00, 1.48)
	1	Light	**1.09**	**(1.03, 1.15)**	1.00	(0.83, 1.20)	1.10	(1.00, 1.22)	**1.09**	**(1.01, 1.16)**
		Medium	**1.17**	**(1.06, 1.28)**	0.93	(0.66, 1.31)	1.12	(0.94, 1.33)	**1.21**	**(1.08, 1.35)**
		Dense	1.07	(0.90, 1.27)	1.14	(0.64, 2.02)	0.66	(0.44, 0.99)	1.22	(1.00, 1.49)
	2	Light	1.05	(0.99, 1.11)	1.25	(1.05, 1.48)	1.01	(0.91, 1.12)	1.05	(0.98, 1.13)
		Medium	1.08	(0.98, 1.19)	0.87	(0.60, 1.25)	1.02	(0.85, 1.23)	1.12	(0.99, 1.26)
		Dense	1.06	(0.90, 1.26)	0.51	(0.22, 1.19)	1.10	(0.80, 1.49)	1.08	(0.88, 1.33)
	3	Light	1.05	(1.00, 1.11)	1.15	(0.96, 1.37)	0.97	(0.87, 1.07)	**1.08**	**(1.01, 1.16)**
		Medium	**1.14**	**(1.04, 1.26)**	0.97	(0.69, 1.38)	1.12	(0.94, 1.33)	**1.16**	**(1.04, 1.30)**
		Dense	0.97	(0.82, 1.16)	0.64	(0.30, 1.37)	1.01	(0.74, 1.38)	0.98	(0.79, 1.21)

			Est	CI	Est	CI	Est	CI	Est	CI
	4	Light	1.06	(1.00, 1.12)	1.10	(0.91, 1.32)	0.99	(0.89, 1.10)	**1.08**	**(1.01, 1.16)**
		Medium	1.10	(1.00, 1.21)	**1.38**	**(1.02, 1.86)**	1.01	(0.85, 1.21)	1.12	(1.00, 1.26)
		Dense	0.96	(0.81, 1.14)	0.68	(0.32, 1.45)	0.83	(0.59, 1.17)	1.03	(0.84, 1.27)
Ischemic stroke	0	Light	1.04	(0.96, 1.14)	0.83	(0.62, 1.12)	1.01	(0.87, 1.18)	1.07	(0.96, 1.20)
		Medium	1.03	(0.88, 1.20)	0.51	(0.26, 1.00)	0.91	(0.69, 1.20)	1.12	(0.93, 1.36)
		Dense	1.11	(0.86, 1.45)	1.10	(0.46, 2.62)	0.84	(0.50, 1.42)	1.25	(0.91, 1.71)
	1	Light	1.08	(0.99, 1.18)	1.37	(1.06, 1.77)	1.05	(0.91, 1.22)	1.08	(0.96, 1.21)
		Medium	1.10	(0.94, 1.28)	0.83	(0.46, 1.50)	0.99	(0.76, 1.30)	1.16	(0.96, 1.41)
		Dense	1.03	(0.78, 1.36)	0.81	(0.28, 2.35)	0.57	(0.30, 1.08)	1.26	(0.92, 1.73)
	2	Light	1.06	(0.97, 1.16)	1.17	(0.89, 1.53)	0.94	(0.80, 1.10)	1.12	(1.00, 1.25)
		Medium	1.05	(0.90, 1.23)	1.06	(0.63, 1.78)	1.00	(0.77, 1.31)	1.07	(0.88, 1.31)
		Dense	0.96	(0.72, 1.27)	1.68	(0.78, 3.59)	0.90	(0.55, 1.48)	0.95	(0.66, 1.35)
	3	Light	1.08	(0.99, 1.18)	1.19	(0.91, 1.55)	0.93	(0.80, 1.09)	**1.16**	**(1.04, 1.29)**
		Medium	1.16	(1.00, 1.34)	1.03	(0.61, 1.74)	0.99	(0.76, 1.29)	**1.25**	**(1.04, 1.50)**
		Dense	0.94	(0.71, 1.25)	0.77	(0.27, 2.23)	0.70	(0.40, 1.20)	1.08	(0.77, 1.52)
	4	Light	1.08	(0.99, 1.17)	1.01	(0.76, 1.35)	1.01	(0.86, 1.17)	1.11	(1.00, 1.24)
		Medium	1.09	(0.94, 1.27)	**1.90**	**(1.26, 2.85)**	1.05	(0.81, 1.36)	1.07	(0.88, 1.30)
		Dense	0.96	(0.73, 1.27)	1.67	(0.78, 3.58)	0.64	(0.36, 1.13)	1.08	(0.78, 1.51)
Transient ischemic attack	0	Light	1.00	(0.89, 1.13)	0.86	(0.57, 1.30)	1.13	(0.92, 1.38)	0.96	(0.82, 1.13)
		Medium	1.14	(0.94, 1.40)	0.80	(0.39, 1.66)	1.13	(0.80, 1.60)	1.18	(0.91, 1.53)
		Dense	1.23	(0.87, 1.73)	0.40	(0.06, 2.52)	1.23	(0.68, 2.22)	1.30	(0.85, 2.01)
	1	Light	1.01	(0.89, 1.14)	0.59	(0.37, 0.95)	1.20	(0.99, 1.46)	0.96	(0.82, 1.13)
		Medium	1.14	(0.93, 1.40)	0.99	(0.52, 1.88)	1.12	(0.79, 1.60)	1.16	(0.89, 1.51)
		Dense	0.92	(0.62, 1.37)	0.41	(0.07, 2.57)	0.63	(0.28, 1.45)	1.09	(0.68, 1.75)
	2	Light	1.01	(0.89, 1.14)	1.19	(0.82, 1.71)	1.07	(0.88, 1.31)	0.96	(0.82, 1.13)
		Medium	1.01	(0.82, 1.25)	0.51	(0.20, 1.28)	1.05	(0.73, 1.50)	1.04	(0.79, 1.37)
		Dense	1.07	(0.74, 1.54)	NA	NA	1.17	(0.63, 2.15)	1.12	(0.71, 1.79)
	3	Light	1.05	(0.93, 1.18)	1.01	(0.68, 1.50)	1.04	(0.84, 1.27)	1.06	(0.91, 1.24)
		Medium	1.22	(1.00, 1.49)	0.77	(0.36, 1.66)	**1.39**	**(1.01, 1.92)**	1.19	(0.91, 1.54)
		Dense	0.98	(0.67, 1.43)	0.90	(0.25, 3.26)	1.12	(0.60, 2.06)	0.93	(0.57, 1.54)
	4	Light	1.03	(0.91, 1.16)	1.41	(0.99, 2.02)	0.94	(0.77, 1.16)	1.04	(0.89, 1.22)
		Medium	1.08	(0.88, 1.33)	0.84	(0.39, 1.80)	0.93	(0.65, 1.34)	1.17	(0.90, 1.52)
		Dense	0.90	(0.61, 1.33)	0.54	(0.09, 3.27)	0.88	(0.45, 1.70)	0.94	(0.57, 1.53)
All-cause respiratory	0	Light	1.02	(1.00, 1.04)	0.99	(0.96, 1.01)	1.00	(0.97, 1.03)	**1.07**	**(1.04, 1.10)**
		Medium	**1.09**	**(1.05, 1.12)**	**1.05**	**(1.01, 1.10)**	**1.08**	**(1.03, 1.13)**	**1.12**	**(1.07, 1.18)**

		Dense	**1.09**	**(1.03, 1.15)**	1.05	(0.97, 1.14)	1.06	(0.98, 1.16)	**1.14**	**(1.05, 1.24)**
	1	Light	**1.04**	**(1.02, 1.06)**	1.02	(1.00, 1.05)	1.03	(1.00, 1.06)	**1.08**	**(1.05, 1.11)**
		Medium	**1.08**	**(1.05, 1.11)**	1.05	(1.00, 1.09)	**1.09**	**(1.03, 1.14)**	**1.11**	**(1.06, 1.17)**
		Dense	**1.10**	**(1.04, 1.16)**	1.06	(0.98, 1.14)	1.07	(0.98, 1.16)	**1.18**	**(1.08, 1.28)**
	2	Light	**1.03**	**(1.01, 1.05)**	1.02	(0.99, 1.04)	1.02	(0.99, 1.05)	**1.06**	**(1.04, 1.09)**
		Medium	**1.05**	**(1.02, 1.08)**	1.04	(0.99, 1.09)	1.04	(0.99, 1.09)	**1.08**	**(1.03, 1.14)**
		Dense	**1.09**	**(1.04, 1.15)**	1.03	(0.96, 1.12)	1.09	(1.00, 1.18)	**1.15**	**(1.06, 1.25)**
	3	Light	1.02	(1.00, 1.03)	1.00	(0.98, 1.03)	1.01	(0.98, 1.04)	1.03	(1.00, 1.06)
		Medium	**1.08**	**(1.05, 1.12)**	**1.06**	**(1.02, 1.11)**	**1.10**	**(1.05, 1.15)**	**1.09**	**(1.04, 1.14)**
		Dense	**1.10**	**(1.05, 1.16)**	1.06	(0.98, 1.14)	1.07	(0.98, 1.16)	**1.19**	**(1.10, 1.29)**
	4	Light	1.00	(0.98, 1.02)	0.99	(0.96, 1.01)	1.00	(0.97, 1.03)	1.02	(0.99, 1.05)
		Medium	**1.07**	**(1.04, 1.10)**	**1.07**	**(1.03, 1.12)**	**1.07**	**(1.02, 1.12)**	**1.08**	**(1.03, 1.13)**
		Dense	1.04	(0.99, 1.10)	1.01	(0.93, 1.09)	1.04	(0.96, 1.14)	1.07	(0.99, 1.17)
Asthma	0	Light	1.02	(0.99, 1.05)	1.02	(0.98, 1.06)	0.99	(0.95, 1.04)	1.05	(1.00, 1.11)
		Medium	**1.07**	**(1.02, 1.12)**	**1.09**	**(1.03, 1.17)**	1.01	(0.93, 1.10)	1.09	(1.00, 1.19)
		Dense	1.05	(0.97, 1.14)	1.10	(0.98, 1.23)	1.01	(0.87, 1.17)	1.02	(0.87, 1.19)
	1	Light	**1.04**	**(1.02, 1.07)**	1.04	(1.00, 1.08)	1.03	(0.99, 1.08)	**1.08**	**(1.03, 1.13)**
		Medium	**1.07**	**(1.02, 1.12)**	**1.11**	**(1.04, 1.18)**	1.04	(0.95, 1.13)	1.04	(0.96, 1.14)
		Dense	1.06	(0.98, 1.16)	1.10	(0.98, 1.23)	1.04	(0.89, 1.20)	1.03	(0.88, 1.21)
	2	Light	1.03	(1.00, 1.06)	1.03	(0.99, 1.07)	1.02	(0.97, 1.07)	**1.07**	**(1.02, 1.12)**
		Medium	1.03	(0.98, 1.08)	1.05	(0.98, 1.12)	1.01	(0.93, 1.10)	1.02	(0.93, 1.11)
		Dense	**1.09**	**(1.01, 1.19)**	**1.22**	**(1.09, 1.35)**	1.03	(0.89, 1.19)	0.95	(0.81, 1.11)
	3	Light	1.01	(0.98, 1.03)	1.00	(0.96, 1.03)	1.02	(0.97, 1.07)	1.02	(0.97, 1.07)
		Medium	**1.06**	**(1.01, 1.11)**	1.07	(1.00, 1.14)	1.05	(0.97, 1.15)	1.02	(0.94, 1.12)
		Dense	1.06	(0.97, 1.15)	1.07	(0.96, 1.20)	1.02	(0.88, 1.18)	1.08	(0.94, 1.25)
	4	Light	0.98	(0.95, 1.01)	0.97	(0.94, 1.01)	0.97	(0.93, 1.02)	1.00	(0.95, 1.05)
		Medium	1.02	(0.98, 1.07)	1.07	(1.00, 1.14)	1.00	(0.91, 1.08)	0.97	(0.89, 1.06)
		Dense	1.03	(0.95, 1.11)	0.97	(0.86, 1.09)	1.11	(0.97, 1.27)	1.02	(0.88, 1.18)
COPD	0	Light	**1.07**	**(1.03, 1.11)**	1.09	(0.95, 1.25)	1.03	(0.97, 1.10)	**1.09**	**(1.05, 1.15)**
		Medium	**1.19**	**(1.12, 1.26)**	**1.33**	**(1.07, 1.65)**	**1.22**	**(1.11, 1.34)**	**1.16**	**(1.08, 1.25)**
		Dense	**1.30**	**(1.17, 1.43)**	**1.58**	**(1.11, 2.24)**	**1.32**	**(1.12, 1.55)**	**1.26**	**(1.11, 1.44)**
	1	Light	**1.07**	**(1.04, 1.11)**	1.04	(0.91, 1.19)	1.06	(1.00, 1.12)	**1.08**	**(1.04, 1.13)**
		Medium	**1.20**	**(1.13, 1.27)**	1.18	(0.94, 1.48)	**1.21**	**(1.09, 1.33)**	**1.19**	**(1.11, 1.29)**
		Dense	**1.26**	**(1.13, 1.40)**	1.38	(0.95, 2.01)	**1.26**	**(1.06, 1.49)**	**1.25**	**(1.10, 1.43)**
	2	Light	**1.07**	**(1.03, 1.10)**	0.97	(0.84, 1.11)	1.06	(1.00, 1.12)	**1.08**	**(1.03, 1.13)**

		Medium	**1.15**	**(1.09, 1.23)**	1.18	(0.95, 1.47)	**1.16**	**(1.05, 1.28)**	**1.15**	**(1.06, 1.24)**
		Dense	**1.25**	**(1.12, 1.38)**	1.17	(0.80, 1.71)	**1.28**	**(1.09, 1.51)**	**1.23**	**(1.08, 1.40)**
	3	Light	**1.04**	**(1.01, 1.08)**	0.97	(0.85, 1.12)	1.04	(0.98, 1.10)	1.05	(1.00, 1.10)
		Medium	**1.18**	**(1.11, 1.25)**	**1.29**	**(1.04, 1.59)**	**1.24**	**(1.13, 1.36)**	**1.13**	**(1.05, 1.22)**
		Dense	**1.29**	**(1.16, 1.42)**	1.42	(1.00, 2.02)	**1.29**	**(1.09, 1.51)**	**1.28**	**(1.13, 1.45)**
	4	Light	1.03	(0.99, 1.07)	1.01	(0.88, 1.16)	1.06	(1.00, 1.12)	1.01	(0.97, 1.06)
		Medium	**1.17**	**(1.10, 1.24)**	**1.44**	**(1.17, 1.77)**	**1.18**	**(1.07, 1.30)**	**1.14**	**(1.06, 1.23)**
		Dense	**1.23**	**(1.11, 1.36)**	**1.87**	**(1.37, 2.56)**	**1.30**	**(1.11, 1.53)**	1.15	(1.00, 1.31)
Pneumonia	0	Light	1.04	(0.99, 1.09)	0.91	(0.82, 1.01)	0.97	(0.89, 1.07)	**1.12**	**(1.05, 1.19)**
		Medium	1.09	(1.00, 1.18)	1.02	(0.85, 1.22)	1.06	(0.90, 1.24)	1.13	(1.00, 1.26)
		Dense	**1.23**	**(1.07, 1.42)**	1.07	(0.77, 1.47)	**1.32**	**(1.02, 1.71)**	**1.23**	**(1.02, 1.50)**
	1	Light	1.05	(1.00, 1.10)	1.01	(0.91, 1.11)	0.97	(0.89, 1.07)	**1.12**	**(1.05, 1.19)**
		Medium	1.08	(1.00, 1.18)	1.03	(0.85, 1.23)	1.09	(0.93, 1.28)	1.10	(0.98, 1.23)
		Dense	**1.20**	**(1.04, 1.38)**	1.07	(0.78, 1.48)	1.18	(0.90, 1.55)	**1.25**	**(1.03, 1.52)**
	2	Light	1.05	(1.00, 1.10)	1.08	(0.98, 1.20)	1.00	(0.91, 1.10)	1.07	(1.00, 1.14)
		Medium	1.04	(0.95, 1.13)	1.05	(0.88, 1.27)	0.97	(0.82, 1.14)	1.08	(0.96, 1.21)
		Dense	**1.17**	**(1.01, 1.35)**	0.94	(0.66, 1.32)	1.29	(1.00, 1.67)	1.17	(0.96, 1.42)
	3	Light	**1.07**	**(1.03, 1.13)**	1.07	(0.96, 1.18)	1.05	(0.96, 1.15)	**1.09**	**(1.02, 1.16)**
		Medium	**1.14**	**(1.05, 1.24)**	**1.24**	**(1.05, 1.48)**	1.05	(0.89, 1.24)	**1.16**	**(1.03, 1.30)**
		Dense	**1.26**	**(1.10, 1.45)**	1.16	(0.84, 1.59)	1.31	(1.00, 1.70)	**1.27**	**(1.06, 1.54)**
	4	Light	1.04	(0.99, 1.09)	1.01	(0.91, 1.12)	1.05	(0.96, 1.15)	1.04	(0.97, 1.11)
		Medium	**1.20**	**(1.10, 1.30)**	1.18	(0.99, 1.41)	1.05	(0.90, 1.24)	**1.29**	**(1.15, 1.43)**
		Dense	**1.21**	**(1.05, 1.40)**	1.34	(0.99, 1.80)	**1.31**	**(1.01, 1.69)**	1.13	(0.92, 1.37)
Other chest/respiratory symptom	0	Light	0.99	(0.97, 1.01)	0.95	(0.92, 0.99)	0.98	(0.94, 1.02)	1.05	(1.00, 1.10)
		Medium	**1.06**	**(1.02, 1.10)**	1.01	(0.95, 1.07)	1.07	(1.00, 1.15)	**1.12**	**(1.04, 1.21)**
		Dense	1.00	(0.93, 1.07)	0.98	(0.88, 1.09)	0.96	(0.85, 1.09)	1.07	(0.93, 1.22)
	1	Light	1.03	(1.00, 1.05)	1.01	(0.97, 1.04)	1.01	(0.97, 1.05)	**1.08**	**(1.03, 1.13)**
		Medium	1.04	(1.00, 1.08)	0.99	(0.93, 1.05)	1.07	(1.00, 1.15)	1.07	(0.98, 1.15)
		Dense	1.06	(0.99, 1.14)	1.03	(0.93, 1.14)	1.03	(0.91, 1.16)	1.15	(1.00, 1.31)
	2	Light	1.02	(0.99, 1.04)	1.00	(0.97, 1.04)	1.00	(0.97, 1.04)	**1.06**	**(1.01, 1.11)**
		Medium	1.03	(0.99, 1.07)	1.03	(0.97, 1.09)	1.02	(0.95, 1.09)	1.04	(0.96, 1.12)
		Dense	1.02	(0.95, 1.10)	0.88	(0.79, 0.99)	1.03	(0.91, 1.16)	**1.21**	**(1.06, 1.37)**
	3	Light	1.00	(0.98, 1.03)	1.00	(0.97, 1.04)	1.00	(0.96, 1.04)	1.00	(0.96, 1.05)
		Medium	1.05	(1.00, 1.09)	1.03	(0.97, 1.10)	1.06	(0.99, 1.14)	1.04	(0.96, 1.13)
		Dense	1.07	(1.00, 1.14)	1.06	(0.96, 1.18)	1.01	(0.90, 1.14)	**1.16**	**(1.02, 1.32)**

	4	Light	1.00	(0.98, 1.03)	1.00	(0.97, 1.03)	1.00	(0.96, 1.04)	1.02	(0.97, 1.06)
		Medium	**1.06**	**(1.01, 1.10)**	1.05	(0.99, 1.11)	**1.09**	**(1.02, 1.16)**	1.02	(0.94, 1.11)
		Dense	0.97	(0.91, 1.05)	0.99	(0.89, 1.10)	0.90	(0.80, 1.02)	1.05	(0.92, 1.20)
Acute appendicitis	0	Light	1.07	(0.92, 1.26)	1.01	(0.85, 1.21)	1.20	(0.85, 1.70)	1.10	(0.69, 1.75)
		Medium	0.79	(0.57, 1.08)	0.62	(0.42, 0.90)	1.11	(0.59, 2.08)	0.99	(0.42, 2.34)
		Dense	0.83	(0.48, 1.43)	0.46	(0.21, 1.02)	1.48	(0.57, 3.82)	1.27	(0.35, 4.65)
	1	Light	0.99	(0.84, 1.17)	0.89	(0.74, 1.08)	1.17	(0.82, 1.66)	1.07	(0.67, 1.69)
		Medium	1.12	(0.85, 1.47)	1.08	(0.80, 1.47)	1.29	(0.71, 2.33)	0.89	(0.37, 2.15)
		Dense	0.92	(0.54, 1.56)	0.75	(0.39, 1.43)	1.53	(0.59, 3.97)	0.52	(0.07, 3.83)
	2	Light	1.11	(0.95, 1.31)	1.03	(0.86, 1.25)	1.14	(0.80, 1.63)	1.46	(0.95, 2.24)
		Medium	0.83	(0.60, 1.14)	0.81	(0.57, 1.17)	0.84	(0.42, 1.71)	0.86	(0.34, 2.20)
		Dense	1.28	(0.81, 2.02)	1.23	(0.73, 2.07)	1.59	(0.63, 4.01)	0.79	(0.15, 4.16)
	3	Light	1.00	(0.84, 1.17)	0.96	(0.80, 1.16)	1.05	(0.74, 1.51)	1.02	(0.65, 1.61)
		Medium	0.84	(0.62, 1.15)	0.93	(0.67, 1.30)	0.69	(0.32, 1.48)	0.73	(0.29, 1.83)
		Dense	1.00	(0.60, 1.67)	0.90	(0.49, 1.64)	1.55	(0.61, 3.90)	0.42	(0.06, 3.04)
	4	Light	0.95	(0.81, 1.12)	0.91	(0.75, 1.10)	1.07	(0.74, 1.53)	0.90	(0.56, 1.44)
		Medium	0.96	(0.72, 1.28)	0.84	(0.60, 1.19)	1.36	(0.76, 2.44)	0.72	(0.29, 1.78)
		Dense	1.01	(0.61, 1.68)	0.97	(0.54, 1.74)	1.21	(0.42, 3.45)	0.85	(0.21, 3.48)
Long bone fracture	0	Light	**1.09**	**(1.02, 1.16)**	1.04	(0.90, 1.19)	1.06	(0.95, 1.19)	**1.12**	**(1.02, 1.24)**
		Medium	1.12	(1.00, 1.26)	1.13	(0.89, 1.42)	1.16	(0.97, 1.39)	1.09	(0.92, 1.30)
		Dense	**1.31**	**(1.09, 1.56)**	1.27	(0.87, 1.85)	1.12	(0.82, 1.54)	**1.46**	**(1.12, 1.90)**
	1	Light	**1.10**	**(1.03, 1.17)**	1.02	(0.89, 1.17)	**1.14**	**(1.02, 1.27)**	1.11	(1.00, 1.22)
		Medium	1.09	(0.97, 1.22)	1.12	(0.89, 1.40)	1.10	(0.91, 1.32)	1.06	(0.89, 1.27)
		Dense	**1.30**	**(1.09, 1.56)**	1.21	(0.84, 1.76)	1.14	(0.83, 1.56)	**1.47**	**(1.12, 1.92)**
	2	Light	1.04	(0.97, 1.11)	0.95	(0.83, 1.09)	1.08	(0.97, 1.21)	1.06	(0.96, 1.17)
		Medium	1.05	(0.94, 1.18)	1.13	(0.90, 1.41)	1.06	(0.88, 1.28)	1.00	(0.84, 1.20)
		Dense	**1.22**	**(1.01, 1.47)**	1.24	(0.85, 1.80)	**1.46**	**(1.10, 1.95)**	1.05	(0.77, 1.43)
	3	Light	1.04	(0.97, 1.11)	0.93	(0.81, 1.07)	**1.13**	**(1.01, 1.26)**	1.03	(0.93, 1.14)
		Medium	1.01	(0.90, 1.13)	0.93	(0.73, 1.18)	1.04	(0.85, 1.26)	1.04	(0.87, 1.23)
		Dense	0.96	(0.78, 1.18)	0.69	(0.42, 1.14)	0.85	(0.59, 1.23)	1.15	(0.86, 1.54)
	4	Light	1.02	(0.95, 1.09)	0.86	(0.74, 0.99)	1.02	(0.91, 1.14)	1.11	(1.00, 1.22)
		Medium	1.04	(0.92, 1.16)	0.99	(0.78, 1.26)	0.97	(0.80, 1.18)	1.10	(0.93, 1.31)
		Dense	1.12	(0.92, 1.36)	1.15	(0.77, 1.72)	0.92	(0.64, 1.31)	1.24	(0.94, 1.64)
All visits	0	Light	**1.02**	**(1.01, 1.03)**	0.99	(0.98, 1.01)	1.01	(0.99, 1.03)	**1.07**	**(1.06, 1.09)**
		Medium	**1.04**	**(1.02, 1.06)**	1.01	(0.99, 1.04)	**1.05**	**(1.02, 1.08)**	**1.10**	**(1.07, 1.13)**

		Dense	**1.06**	**(1.03, 1.10)**	1.01	(0.98, 1.05)	**1.05**	**(1.01, 1.11)**	**1.19**	**(1.13, 1.25)**
	1	Light	**1.02**	**(1.01, 1.03)**	0.99	(0.98, 1.01)	**1.02**	**(1.01, 1.04)**	**1.07**	**(1.05, 1.09)**
		Medium	**1.05**	**(1.03, 1.07)**	1.02	(1.00, 1.05)	**1.05**	**(1.02, 1.08)**	**1.11**	**(1.07, 1.14)**
		Dense	**1.04**	**(1.01, 1.07)**	0.98	(0.95, 1.02)	1.03	(0.98, 1.08)	**1.17**	**(1.12, 1.23)**
	2	Light	1.01	(1.00, 1.02)	1.00	(0.98, 1.01)	1.01	(1.00, 1.03)	**1.06**	**(1.04, 1.07)**
		Medium	**1.04**	**(1.02, 1.06)**	1.02	(1.00, 1.04)	1.03	(1.00, 1.06)	**1.09**	**(1.06, 1.12)**
		Dense	**1.04**	**(1.01, 1.07)**	0.98	(0.94, 1.02)	**1.06**	**(1.01, 1.11)**	**1.15**	**(1.10, 1.21)**
	3	Light	1.01	(1.00, 1.02)	1.00	(0.99, 1.02)	1.01	(1.00, 1.03)	**1.03**	**(1.01, 1.04)**
		Medium	**1.04**	**(1.02, 1.06)**	1.03	(1.00, 1.05)	**1.04**	**(1.02, 1.07)**	**1.07**	**(1.04, 1.10)**
		Dense	1.04	(1.00, 1.07)	0.99	(0.96, 1.03)	1.05	(1.00, 1.10)	**1.11**	**(1.06, 1.16)**
	4	Light	1.00	(0.99, 1.01)	0.99	(0.98, 1.00)	1.01	(0.99, 1.02)	**1.03**	**(1.01, 1.05)**
		Medium	**1.03**	**(1.01, 1.05)**	1.02	(0.99, 1.04)	**1.04**	**(1.01, 1.07)**	**1.06**	**(1.03, 1.09)**
		Dense	1.01	(0.98, 1.04)	0.99	(0.95, 1.02)	1.02	(0.97, 1.07)	**1.06**	**(1.01, 1.11)**

Table S2. Sex-Stratified Relative Risk of Emergency Department Visits on Wildfire-Smoke Days Relative to Days Without Smoke Across Lags 0 through 4 Days, 8 California Air Basins (May 1 - September 30, 2015). Statistically Significant Relative Risks are Shown in Bold.

Models adjusted for heat index, day of week, time trend, and log-population offset. RR indicates relative risk; CI, confidence interval.

Outcome	Lag	Exposure	All Adults		Female Adults		Male Adults	
			RR	95% CI	RR	95% CI	RR	95% CI
All-cause cardiovascular	0	Light	1.02	(1.00, 1.03)	1.01	(0.99, 1.03)	**1.03**	**(1.01, 1.05)**
		Medium	**1.05**	**(1.03, 1.08)**	1.03	(1.00, 1.06)	**1.08**	**(1.04, 1.12)**
		Dense	**1.08**	**(1.03, 1.12)**	**1.08**	**(1.02, 1.13)**	**1.08**	**(1.01, 1.14)**
	1	Light	**1.04**	**(1.03, 1.05)**	**1.03**	**(1.02, 1.05)**	**1.05**	**(1.03, 1.07)**
		Medium	**1.05**	**(1.03, 1.08)**	1.03	(1.00, 1.06)	**1.08**	**(1.04, 1.12)**
		Dense	1.04	(1.00, 1.09)	1.01	(0.96, 1.06)	**1.08**	**(1.02, 1.15)**
	2	Light	**1.03**	**(1.02, 1.05)**	**1.04**	**(1.02, 1.06)**	**1.03**	**(1.01, 1.05)**
		Medium	**1.04**	**(1.01, 1.07)**	1.03	(1.00, 1.06)	**1.05**	**(1.01, 1.08)**
		Dense	**1.07**	**(1.03, 1.12)**	**1.07**	**(1.01, 1.12)**	**1.08**	**(1.02, 1.15)**
	3	Light	1.02	(1.00, 1.03)	1.02	(1.00, 1.04)	1.02	(1.00, 1.04)
		Medium	**1.06**	**(1.04, 1.09)**	**1.07**	**(1.04, 1.11)**	**1.05**	**(1.02, 1.09)**
		Dense	1.04	(1.00, 1.09)	1.03	(0.98, 1.09)	1.06	(0.99, 1.12)
	4	Light	1.01	(1.00, 1.03)	1.01	(1.00, 1.03)	1.01	(0.99, 1.03)
		Medium	**1.06**	**(1.03, 1.08)**	**1.05**	**(1.02, 1.08)**	**1.07**	**(1.03, 1.10)**
		Dense	1.02	(0.98, 1.06)	1.03	(0.98, 1.08)	1.01	(0.95, 1.07)
Hypertension	0	Light	1.01	(1.00, 1.03)	1.01	(0.99, 1.03)	1.02	(1.00, 1.04)
		Medium	**1.05**	**(1.02, 1.07)**	1.03	(1.00, 1.06)	**1.07**	**(1.03, 1.11)**
		Dense	**1.08**	**(1.03, 1.12)**	**1.08**	**(1.02, 1.13)**	**1.08**	**(1.01, 1.15)**
	1	Light	**1.03**	**(1.02, 1.05)**	**1.03**	**(1.01, 1.05)**	**1.04**	**(1.02, 1.06)**
		Medium	**1.05**	**(1.02, 1.07)**	1.03	(1.00, 1.06)	**1.07**	**(1.03, 1.11)**
		Dense	1.03	(0.98, 1.08)	0.99	(0.94, 1.05)	**1.08**	**(1.01, 1.15)**
	2	Light	**1.03**	**(1.02, 1.05)**	**1.04**	**(1.02, 1.06)**	1.02	(1.00, 1.05)
		Medium	**1.04**	**(1.01, 1.07)**	1.03	(1.00, 1.07)	**1.05**	**(1.01, 1.08)**
		Dense	1.05	(1.00, 1.10)	1.05	(1.00, 1.11)	1.04	(0.98, 1.11)
	3	Light	1.02	(1.00, 1.03)	1.02	(1.00, 1.04)	1.02	(1.00, 1.04)
		Medium	**1.06**	**(1.04, 1.09)**	**1.07**	**(1.04, 1.11)**	**1.05**	**(1.01, 1.09)**
		Dense	1.03	(0.99, 1.08)	1.03	(0.98, 1.09)	1.04	(0.97, 1.10)

	4	Light	1.01	(1.00, 1.03)	1.01	(1.00, 1.03)	1.01	(0.99, 1.03)
		Medium	**1.06**	**(1.03, 1.08)**	**1.04**	**(1.01, 1.08)**	**1.07**	**(1.04, 1.11)**
		Dense	1.01	(0.97, 1.06)	1.02	(0.97, 1.08)	1.00	(0.93, 1.06)
Ischemic heart disease	0	Light	1.02	(0.97, 1.08)	1.00	(0.92, 1.08)	1.04	(0.97, 1.11)
		Medium	1.01	(0.92, 1.11)	1.01	(0.88, 1.17)	1.00	(0.89, 1.13)
		Dense	1.01	(0.86, 1.19)	1.02	(0.80, 1.30)	1.01	(0.81, 1.25)
	1	Light	1.02	(0.97, 1.08)	1.04	(0.96, 1.12)	1.01	(0.94, 1.09)
		Medium	1.03	(0.94, 1.13)	1.06	(0.93, 1.22)	1.00	(0.89, 1.14)
		Dense	1.14	(0.97, 1.33)	1.07	(0.83, 1.36)	1.19	(0.98, 1.45)
	2	Light	1.06	(1.00, 1.11)	1.08	(1.00, 1.17)	1.04	(0.97, 1.11)
		Medium	1.00	(0.91, 1.09)	0.97	(0.84, 1.12)	1.01	(0.90, 1.15)
		Dense	1.16	(1.00, 1.35)	1.08	(0.85, 1.36)	**1.23**	**(1.01, 1.49)**
	3	Light	1.01	(0.96, 1.06)	1.01	(0.93, 1.09)	1.01	(0.94, 1.08)
		Medium	1.07	(0.98, 1.17)	1.07	(0.94, 1.23)	1.06	(0.94, 1.20)
		Dense	1.11	(0.96, 1.29)	1.19	(0.95, 1.49)	1.05	(0.86, 1.29)
	4	Light	1.02	(0.97, 1.08)	1.03	(0.96, 1.12)	1.02	(0.95, 1.09)
		Medium	0.95	(0.87, 1.05)	0.97	(0.84, 1.11)	0.95	(0.84, 1.07)
		Dense	0.94	(0.80, 1.11)	1.01	(0.80, 1.28)	0.88	(0.71, 1.10)
Myocardial infarction	0	Light	1.02	(0.94, 1.10)	1.03	(0.92, 1.14)	1.01	(0.91, 1.13)
		Medium	1.03	(0.91, 1.18)	0.97	(0.80, 1.18)	1.08	(0.90, 1.29)
		Dense	1.05	(0.83, 1.32)	1.10	(0.80, 1.52)	1.02	(0.73, 1.41)
	1	Light	0.98	(0.91, 1.06)	1.00	(0.90, 1.12)	0.96	(0.86, 1.07)
		Medium	1.07	(0.94, 1.22)	1.09	(0.91, 1.31)	1.05	(0.88, 1.26)
		Dense	**1.30**	**(1.06, 1.61)**	1.35	(1.00, 1.81)	1.28	(0.95, 1.71)
	2	Light	1.03	(0.95, 1.11)	1.02	(0.92, 1.14)	1.03	(0.93, 1.15)
		Medium	1.05	(0.92, 1.20)	1.02	(0.84, 1.23)	1.07	(0.89, 1.29)
		Dense	**1.35**	**(1.10, 1.65)**	1.32	(0.98, 1.76)	**1.37**	**(1.03, 1.82)**
	3	Light	1.00	(0.93, 1.08)	1.05	(0.94, 1.17)	0.97	(0.87, 1.08)
		Medium	1.04	(0.91, 1.18)	1.10	(0.92, 1.32)	0.99	(0.82, 1.19)
		Dense	1.22	(0.98, 1.51)	1.21	(0.89, 1.65)	1.22	(0.91, 1.64)
	4	Light	1.01	(0.94, 1.09)	1.00	(0.90, 1.11)	1.02	(0.92, 1.13)
		Medium	0.97	(0.84, 1.11)	0.92	(0.76, 1.12)	1.00	(0.83, 1.21)
		Dense	1.08	(0.86, 1.35)	1.21	(0.89, 1.64)	0.98	(0.71, 1.37)
Dysrhythmia	0	Light	**1.06**	**(1.04, 1.09)**	**1.05**	**(1.02, 1.09)**	**1.07**	**(1.03, 1.11)**
		Medium	**1.10**	**(1.05, 1.15)**	**1.10**	**(1.03, 1.16)**	**1.11**	**(1.04, 1.18)**

		Dense	**1.16**	**(1.08, 1.25)**	**1.17**	**(1.06, 1.29)**	**1.16**	**(1.03, 1.29)**
	1	Light	**1.08**	**(1.05, 1.11)**	**1.08**	**(1.04, 1.12)**	**1.08**	**(1.04, 1.12)**
		Medium	**1.10**	**(1.06, 1.16)**	**1.09**	**(1.03, 1.16)**	**1.12**	**(1.05, 1.19)**
		Dense	1.04	(0.96, 1.13)	1.00	(0.90, 1.12)	1.08	(0.96, 1.21)
	2	Light	**1.05**	**(1.02, 1.08)**	**1.07**	**(1.03, 1.11)**	1.04	(1.00, 1.08)
		Medium	**1.05**	**(1.01, 1.10)**	**1.07**	**(1.01, 1.14)**	1.04	(0.97, 1.11)
		Dense	**1.18**	**(1.09, 1.27)**	**1.16**	**(1.05, 1.28)**	**1.20**	**(1.08, 1.34)**
	3	Light	**1.04**	**(1.01, 1.07)**	**1.05**	**(1.02, 1.09)**	1.02	(0.99, 1.06)
		Medium	**1.09**	**(1.05, 1.15)**	**1.10**	**(1.03, 1.17)**	**1.09**	**(1.02, 1.16)**
		Dense	**1.10**	**(1.02, 1.19)**	1.07	(0.97, 1.19)	**1.13**	**(1.01, 1.26)**
	4	Light	**1.04**	**(1.02, 1.07)**	**1.05**	**(1.01, 1.09)**	1.04	(1.00, 1.08)
		Medium	**1.06**	**(1.01, 1.11)**	1.05	(0.99, 1.12)	1.07	(1.00, 1.14)
		Dense	1.04	(0.97, 1.13)	1.05	(0.95, 1.17)	1.04	(0.93, 1.16)
Heart failure	0	Light	1.01	(0.98, 1.04)	0.99	(0.95, 1.03)	1.03	(0.99, 1.08)
		Medium	**1.06**	**(1.01, 1.12)**	1.04	(0.97, 1.12)	**1.08**	**(1.01, 1.17)**
		Dense	1.09	(1.00, 1.19)	**1.17**	**(1.04, 1.31)**	1.01	(0.88, 1.16)
	1	Light	1.03	(1.00, 1.06)	1.04	(1.00, 1.08)	1.03	(0.98, 1.07)
		Medium	**1.06**	**(1.01, 1.12)**	1.05	(0.98, 1.12)	1.07	(1.00, 1.16)
		Dense	1.09	(0.99, 1.19)	1.05	(0.92, 1.18)	1.13	(0.99, 1.28)
	2	Light	**1.04**	**(1.01, 1.08)**	**1.04**	**(1.01, 1.09)**	1.04	(1.00, 1.09)
		Medium	1.01	(0.96, 1.06)	0.99	(0.92, 1.06)	1.03	(0.95, 1.11)
		Dense	**1.10**	**(1.01, 1.20)**	1.12	(1.00, 1.26)	1.08	(0.95, 1.23)
	3	Light	**1.06**	**(1.03, 1.09)**	**1.07**	**(1.03, 1.11)**	1.04	(1.00, 1.09)
		Medium	1.05	(1.00, 1.10)	1.07	(1.00, 1.15)	1.02	(0.95, 1.11)
		Dense	**1.13**	**(1.04, 1.24)**	1.12	(0.99, 1.26)	**1.15**	**(1.01, 1.30)**
	4	Light	1.03	(1.00, 1.06)	1.04	(1.00, 1.09)	1.02	(0.98, 1.07)
		Medium	**1.08**	**(1.02, 1.13)**	1.06	(0.99, 1.13)	**1.09**	**(1.01, 1.18)**
		Dense	1.08	(0.99, 1.18)	1.07	(0.95, 1.20)	1.09	(0.96, 1.24)
Peripheral arterial disease	0	Light	0.98	(0.67, 1.43)	1.27	(0.82, 1.96)	0.77	(0.42, 1.40)
		Medium	0.97	(0.50, 1.87)	0.94	(0.40, 2.20)	0.99	(0.39, 2.54)
		Dense	1.08	(0.36, 3.26)	0.28	(0.02, 4.05)	1.70	(0.46, 6.25)
	1	Light	0.98	(0.67, 1.44)	0.93	(0.58, 1.51)	1.02	(0.59, 1.77)
		Medium	1.26	(0.69, 2.31)	1.25	(0.60, 2.62)	1.27	(0.52, 3.11)
		Dense	1.25	(0.42, 3.79)	1.14	(0.29, 4.42)	1.36	(0.27, 6.92)
	2	Light	1.02	(0.70, 1.49)	1.15	(0.73, 1.80)	0.92	(0.52, 1.63)

		Medium	1.08	(0.56, 2.08)	0.98	(0.42, 2.30)	1.15	(0.45, 2.96)
		Dense	1.00	(0.31, 3.23)	0.89	(0.18, 4.25)	1.08	(0.21, 5.51)
	3	Light	1.27	(0.89, 1.81)	1.17	(0.75, 1.82)	1.35	(0.81, 2.26)
		Medium	1.61	(0.91, 2.84)	1.40	(0.68, 2.87)	1.79	(0.79, 4.05)
		Dense	1.22	(0.41, 3.65)	1.45	(0.44, 4.81)	1.01	(0.17, 6.23)
	4	Light	1.00	(0.68, 1.48)	0.93	(0.56, 1.55)	1.06	(0.61, 1.84)
		Medium	1.57	(0.90, 2.74)	1.71	(0.87, 3.39)	1.46	(0.63, 3.38)
		Dense	1.94	(0.81, 4.64)	**2.71**	**(1.04, 7.07)**	1.36	(0.30, 6.08)
Pulmonary embolism	0	Light	1.04	(0.91, 1.19)	0.95	(0.80, 1.13)	1.14	(0.93, 1.39)
		Medium	0.98	(0.77, 1.24)	0.91	(0.66, 1.24)	1.05	(0.74, 1.49)
		Dense	1.11	(0.74, 1.65)	1.31	(0.82, 2.09)	0.91	(0.47, 1.76)
	1	Light	1.11	(0.98, 1.27)	1.15	(0.97, 1.35)	1.08	(0.88, 1.32)
		Medium	1.06	(0.84, 1.35)	0.92	(0.67, 1.27)	1.20	(0.86, 1.68)
		Dense	0.93	(0.60, 1.45)	1.30	(0.80, 2.10)	0.56	(0.24, 1.32)
	2	Light	1.13	(0.99, 1.29)	1.11	(0.94, 1.31)	1.15	(0.95, 1.40)
		Medium	1.06	(0.83, 1.34)	0.97	(0.71, 1.33)	1.14	(0.81, 1.61)
		Dense	**1.43**	**(1.00, 2.05)**	**1.58**	**(1.02, 2.45)**	1.29	(0.73, 2.26)
	3	Light	1.09	(0.95, 1.24)	1.08	(0.91, 1.28)	1.09	(0.90, 1.34)
		Medium	1.21	(0.97, 1.51)	**1.36**	**(1.04, 1.79)**	1.07	(0.75, 1.52)
		Dense	1.33	(0.93, 1.92)	**1.74**	**(1.15, 2.62)**	0.96	(0.51, 1.80)
	4	Light	1.00	(0.87, 1.14)	0.95	(0.79, 1.13)	1.05	(0.86, 1.29)
		Medium	1.07	(0.85, 1.34)	0.95	(0.70, 1.28)	1.19	(0.86, 1.66)
		Dense	1.02	(0.68, 1.52)	1.03	(0.62, 1.70)	1.00	(0.54, 1.85)
All-cause cerebrovascular	0	Light	1.05	(1.00, 1.11)	1.02	(0.95, 1.10)	1.08	(1.00, 1.17)
		Medium	1.07	(0.97, 1.18)	1.05	(0.92, 1.20)	1.09	(0.95, 1.25)
		Dense	1.12	(0.95, 1.32)	1.17	(0.94, 1.46)	1.06	(0.83, 1.36)
	1	Light	**1.09**	**(1.03, 1.15)**	1.05	(0.97, 1.13)	**1.13**	**(1.04, 1.22)**
		Medium	**1.17**	**(1.06, 1.28)**	**1.17**	**(1.03, 1.33)**	**1.16**	**(1.01, 1.33)**
		Dense	1.07	(0.90, 1.27)	1.01	(0.80, 1.29)	1.12	(0.88, 1.43)
	2	Light	1.05	(0.99, 1.11)	1.01	(0.94, 1.09)	1.09	(1.00, 1.18)
		Medium	1.08	(0.98, 1.19)	1.08	(0.95, 1.23)	1.08	(0.94, 1.24)
		Dense	1.06	(0.90, 1.26)	1.09	(0.87, 1.36)	1.04	(0.81, 1.33)
	3	Light	1.05	(1.00, 1.11)	0.99	(0.91, 1.07)	**1.12**	**(1.04, 1.21)**
		Medium	**1.14**	**(1.04, 1.26)**	**1.16**	**(1.03, 1.32)**	1.12	(0.98, 1.29)
		Dense	0.97	(0.82, 1.16)	1.06	(0.85, 1.33)	0.88	(0.67, 1.14)

	4	Light	1.06	(1.00, 1.12)	1.04	(0.96, 1.12)	1.08	(0.99, 1.17)
		Medium	1.10	(1.00, 1.21)	1.02	(0.89, 1.16)	**1.19**	**(1.04, 1.36)**
		Dense	0.96	(0.81, 1.14)	1.08	(0.87, 1.35)	0.83	(0.64, 1.09)
Ischemic stroke	0	Light	1.04	(0.96, 1.14)	1.00	(0.89, 1.12)	1.09	(0.96, 1.24)
		Medium	1.03	(0.88, 1.20)	1.07	(0.88, 1.31)	0.99	(0.78, 1.24)
		Dense	1.11	(0.86, 1.45)	1.16	(0.82, 1.64)	1.07	(0.72, 1.59)
	1	Light	1.08	(0.99, 1.18)	1.05	(0.93, 1.18)	1.12	(0.99, 1.27)
		Medium	1.10	(0.94, 1.28)	1.01	(0.81, 1.24)	1.19	(0.96, 1.48)
		Dense	1.03	(0.78, 1.36)	1.14	(0.80, 1.62)	0.92	(0.60, 1.41)
	2	Light	1.06	(0.97, 1.16)	1.02	(0.90, 1.14)	1.11	(0.97, 1.26)
		Medium	1.05	(0.90, 1.23)	1.14	(0.94, 1.39)	0.96	(0.76, 1.22)
		Dense	0.96	(0.72, 1.27)	0.96	(0.66, 1.39)	0.95	(0.63, 1.44)
	3	Light	1.08	(0.99, 1.18)	1.02	(0.90, 1.14)	**1.15**	**(1.02, 1.31)**
		Medium	1.16	(1.00, 1.34)	1.18	(0.97, 1.44)	1.13	(0.91, 1.41)
		Dense	0.94	(0.71, 1.25)	1.01	(0.71, 1.45)	0.87	(0.56, 1.34)
	4	Light	1.08	(0.99, 1.17)	1.11	(0.99, 1.25)	1.04	(0.91, 1.18)
		Medium	1.09	(0.94, 1.27)	1.03	(0.84, 1.27)	1.14	(0.92, 1.42)
		Dense	0.96	(0.73, 1.27)	1.10	(0.78, 1.56)	0.81	(0.52, 1.27)
Transient ischemic attack	0	Light	1.00	(0.89, 1.13)	0.98	(0.83, 1.17)	1.03	(0.86, 1.22)
		Medium	1.14	(0.94, 1.40)	1.16	(0.88, 1.53)	1.12	(0.84, 1.50)
		Dense	1.23	(0.87, 1.73)	1.34	(0.84, 2.13)	1.08	(0.64, 1.80)
	1	Light	1.01	(0.89, 1.14)	0.97	(0.81, 1.15)	1.06	(0.90, 1.25)
		Medium	1.14	(0.93, 1.40)	1.18	(0.90, 1.56)	1.08	(0.80, 1.45)
		Dense	0.92	(0.62, 1.37)	0.71	(0.38, 1.32)	1.21	(0.74, 2.00)
	2	Light	1.01	(0.89, 1.14)	1.01	(0.86, 1.20)	1.00	(0.84, 1.19)
		Medium	1.01	(0.82, 1.25)	0.95	(0.70, 1.29)	1.09	(0.81, 1.46)
		Dense	1.07	(0.74, 1.54)	1.06	(0.63, 1.77)	1.08	(0.64, 1.82)
	3	Light	1.05	(0.93, 1.18)	1.02	(0.86, 1.20)	1.09	(0.92, 1.29)
		Medium	1.22	(1.00, 1.49)	1.23	(0.94, 1.62)	1.21	(0.91, 1.60)
		Dense	0.98	(0.67, 1.43)	1.02	(0.60, 1.71)	0.94	(0.55, 1.61)
	4	Light	1.03	(0.91, 1.16)	0.99	(0.83, 1.17)	1.08	(0.92, 1.28)
		Medium	1.08	(0.88, 1.33)	0.98	(0.73, 1.32)	1.22	(0.92, 1.61)
		Dense	0.90	(0.61, 1.33)	1.05	(0.63, 1.73)	0.71	(0.39, 1.32)
All-cause respiratory	0	Light	1.02	(1.00, 1.04)	1.01	(0.99, 1.03)	1.03	(1.00, 1.06)
		Medium	**1.09**	**(1.05, 1.12)**	**1.08**	**(1.04, 1.12)**	**1.10**	**(1.05, 1.15)**

		Dense	**1.09**	**(1.03, 1.15)**	1.06	(0.99, 1.13)	**1.13**	**(1.05, 1.22)**
	1	Light	**1.04**	**(1.02, 1.06)**	**1.04**	**(1.02, 1.06)**	**1.04**	**(1.02, 1.07)**
		Medium	**1.08**	**(1.05, 1.11)**	**1.08**	**(1.04, 1.12)**	**1.09**	**(1.04, 1.13)**
		Dense	**1.10**	**(1.04, 1.16)**	1.07	(1.00, 1.14)	**1.14**	**(1.06, 1.23)**
	2	Light	**1.03**	**(1.01, 1.05)**	**1.04**	**(1.02, 1.06)**	1.02	(0.99, 1.05)
		Medium	**1.05**	**(1.02, 1.08)**	**1.05**	**(1.01, 1.09)**	**1.06**	**(1.01, 1.11)**
		Dense	**1.09**	**(1.04, 1.15)**	**1.09**	**(1.02, 1.16)**	**1.10**	**(1.02, 1.19)**
	3	Light	1.02	(1.00, 1.03)	1.01	(0.99, 1.04)	1.02	(0.99, 1.05)
		Medium	**1.08**	**(1.05, 1.12)**	**1.09**	**(1.05, 1.13)**	**1.08**	**(1.03, 1.13)**
		Dense	**1.10**	**(1.05, 1.16)**	**1.10**	**(1.04, 1.17)**	**1.11**	**(1.03, 1.20)**
	4	Light	1.00	(0.98, 1.02)	0.99	(0.97, 1.01)	1.01	(0.99, 1.04)
		Medium	**1.07**	**(1.04, 1.10)**	**1.06**	**(1.03, 1.10)**	**1.08**	**(1.04, 1.13)**
		Dense	1.04	(0.99, 1.10)	1.03	(0.97, 1.10)	1.06	(0.98, 1.14)
Asthma	0	Light	1.02	(0.99, 1.05)	1.01	(0.98, 1.04)	1.03	(0.99, 1.08)
		Medium	**1.07**	**(1.02, 1.12)**	**1.07**	**(1.02, 1.13)**	1.05	(0.97, 1.14)
		Dense	1.05	(0.97, 1.14)	1.02	(0.93, 1.13)	1.11	(0.97, 1.27)
	1	Light	**1.04**	**(1.02, 1.07)**	1.03	(1.00, 1.07)	**1.06**	**(1.02, 1.11)**
		Medium	**1.07**	**(1.02, 1.12)**	**1.07**	**(1.02, 1.13)**	1.07	(0.98, 1.16)
		Dense	1.06	(0.98, 1.16)	1.04	(0.95, 1.15)	1.10	(0.96, 1.27)
	2	Light	1.03	(1.00, 1.06)	1.04	(1.00, 1.07)	1.03	(0.98, 1.07)
		Medium	1.03	(0.98, 1.08)	1.02	(0.97, 1.08)	1.05	(0.97, 1.14)
		Dense	**1.09**	**(1.01, 1.19)**	1.09	(1.00, 1.20)	1.10	(0.96, 1.26)
	3	Light	1.01	(0.98, 1.03)	1.00	(0.97, 1.03)	1.02	(0.98, 1.07)
		Medium	**1.06**	**(1.01, 1.11)**	1.05	(0.99, 1.10)	1.07	(0.99, 1.16)
		Dense	1.06	(0.97, 1.15)	1.05	(0.96, 1.15)	1.07	(0.94, 1.23)
	4	Light	0.98	(0.95, 1.01)	0.97	(0.94, 1.00)	1.00	(0.95, 1.05)
		Medium	1.02	(0.98, 1.07)	1.02	(0.97, 1.08)	1.03	(0.95, 1.12)
		Dense	1.03	(0.95, 1.11)	1.02	(0.93, 1.12)	1.04	(0.91, 1.20)
COPD	0	Light	**1.07**	**(1.03, 1.11)**	**1.06**	**(1.01, 1.11)**	**1.09**	**(1.03, 1.14)**
		Medium	**1.19**	**(1.12, 1.26)**	**1.16**	**(1.07, 1.25)**	**1.22**	**(1.12, 1.33)**
		Dense	**1.30**	**(1.17, 1.43)**	**1.37**	**(1.20, 1.55)**	**1.22**	**(1.05, 1.42)**
	1	Light	**1.07**	**(1.04, 1.11)**	**1.08**	**(1.03, 1.13)**	**1.06**	**(1.01, 1.12)**
		Medium	**1.20**	**(1.13, 1.27)**	**1.21**	**(1.12, 1.30)**	**1.19**	**(1.09, 1.30)**
		Dense	**1.26**	**(1.13, 1.40)**	**1.19**	**(1.04, 1.37)**	**1.33**	**(1.15, 1.54)**
	2	Light	**1.07**	**(1.03, 1.10)**	**1.09**	**(1.04, 1.14)**	1.04	(0.98, 1.09)

		Medium	1.15	(1.09, 1.23)	1.19	(1.10, 1.29)	1.11	(1.02, 1.22)
		Dense	1.25	(1.12, 1.38)	1.28	(1.12, 1.46)	1.21	(1.04, 1.41)
	3	Light	1.04	(1.01, 1.08)	1.07	(1.02, 1.12)	1.02	(0.97, 1.07)
		Medium	1.18	(1.11, 1.25)	1.20	(1.11, 1.30)	1.15	(1.06, 1.26)
		Dense	1.29	(1.16, 1.42)	1.31	(1.15, 1.49)	1.26	(1.09, 1.46)
	4	Light	1.03	(0.99, 1.07)	1.03	(0.99, 1.08)	1.03	(0.97, 1.08)
		Medium	1.17	(1.10, 1.24)	1.18	(1.10, 1.28)	1.15	(1.05, 1.25)
		Dense	1.23	(1.11, 1.36)	1.21	(1.06, 1.38)	1.25	(1.08, 1.45)
Pneumonia	0	Light	1.04	(0.99, 1.09)	1.04	(0.98, 1.11)	1.04	(0.97, 1.11)
		Medium	1.09	(1.00, 1.18)	1.06	(0.94, 1.19)	1.12	(0.99, 1.26)
		Dense	1.23	(1.07, 1.42)	1.25	(1.02, 1.51)	1.22	(1.00, 1.49)
	1	Light	1.05	(1.00, 1.10)	1.03	(0.97, 1.10)	1.07	(1.00, 1.15)
		Medium	1.08	(1.00, 1.18)	1.12	(1.00, 1.26)	1.05	(0.92, 1.18)
		Dense	1.20	(1.04, 1.38)	1.30	(1.07, 1.58)	1.10	(0.89, 1.35)
	2	Light	1.05	(1.00, 1.10)	1.05	(0.99, 1.12)	1.05	(0.98, 1.12)
		Medium	1.04	(0.95, 1.13)	0.98	(0.87, 1.11)	1.10	(0.98, 1.24)
		Dense	1.17	(1.01, 1.35)	1.12	(0.91, 1.37)	1.22	(1.00, 1.49)
	3	Light	1.07	(1.03, 1.13)	1.06	(0.99, 1.13)	1.09	(1.02, 1.16)
		Medium	1.14	(1.05, 1.24)	1.15	(1.02, 1.28)	1.13	(1.01, 1.28)
		Dense	1.26	(1.10, 1.45)	1.22	(1.01, 1.48)	1.31	(1.08, 1.59)
	4	Light	1.04	(0.99, 1.09)	1.01	(0.95, 1.08)	1.06	(0.99, 1.13)
		Medium	1.20	(1.10, 1.30)	1.18	(1.06, 1.32)	1.21	(1.08, 1.36)
		Dense	1.21	(1.05, 1.40)	1.23	(1.01, 1.49)	1.20	(0.98, 1.47)
Other chest/respiratory symptom	0	Light	0.99	(0.97, 1.01)	0.98	(0.95, 1.00)	1.00	(0.97, 1.04)
		Medium	1.06	(1.02, 1.10)	1.06	(1.01, 1.12)	1.06	(1.00, 1.13)
		Dense	1.00	(0.93, 1.07)	0.91	(0.82, 1.00)	1.12	(1.01, 1.24)
	1	Light	1.03	(1.00, 1.05)	1.03	(1.00, 1.06)	1.02	(0.99, 1.06)
		Medium	1.04	(1.00, 1.08)	1.02	(0.97, 1.07)	1.07	(1.00, 1.13)
		Dense	1.06	(0.99, 1.14)	1.02	(0.93, 1.12)	1.11	(1.00, 1.24)
	2	Light	1.02	(0.99, 1.04)	1.02	(0.99, 1.05)	1.01	(0.98, 1.05)
		Medium	1.03	(0.99, 1.07)	1.03	(0.98, 1.08)	1.02	(0.96, 1.09)
		Dense	1.02	(0.95, 1.10)	1.01	(0.92, 1.11)	1.04	(0.93, 1.15)
	3	Light	1.00	(0.98, 1.03)	1.00	(0.97, 1.03)	1.01	(0.98, 1.05)
		Medium	1.05	(1.00, 1.09)	1.05	(1.00, 1.10)	1.04	(0.98, 1.10)
		Dense	1.07	(1.00, 1.14)	1.07	(0.99, 1.17)	1.06	(0.96, 1.18)

	4	Light	1.00	(0.98, 1.03)	1.00	(0.97, 1.03)	1.02	(0.98, 1.05)
		Medium	**1.06**	**(1.01, 1.10)**	1.05	(1.00, 1.10)	1.06	(1.00, 1.13)
		Dense	0.97	(0.91, 1.05)	0.97	(0.88, 1.06)	0.98	(0.88, 1.10)
Acute appendicitis	0	Light	1.07	(0.92, 1.26)	1.19	(0.94, 1.51)	0.97	(0.79, 1.20)
		Medium	0.79	(0.57, 1.08)	0.76	(0.46, 1.25)	0.82	(0.55, 1.22)
		Dense	0.83	(0.48, 1.43)	1.08	(0.51, 2.29)	0.61	(0.27, 1.38)
	1	Light	0.99	(0.84, 1.17)	1.07	(0.83, 1.37)	0.92	(0.74, 1.15)
		Medium	1.12	(0.85, 1.47)	1.15	(0.76, 1.74)	1.09	(0.76, 1.57)
		Dense	0.92	(0.54, 1.56)	0.80	(0.34, 1.89)	1.04	(0.54, 2.01)
	2	Light	1.11	(0.95, 1.31)	1.17	(0.92, 1.49)	1.07	(0.86, 1.32)
		Medium	0.83	(0.60, 1.14)	0.75	(0.45, 1.25)	0.91	(0.61, 1.36)
		Dense	1.28	(0.81, 2.02)	1.14	(0.55, 2.36)	1.42	(0.80, 2.50)
	3	Light	1.00	(0.84, 1.17)	0.87	(0.67, 1.13)	1.13	(0.92, 1.39)
		Medium	0.84	(0.62, 1.15)	0.66	(0.40, 1.11)	1.03	(0.71, 1.50)
		Dense	1.00	(0.60, 1.67)	0.95	(0.44, 2.05)	1.06	(0.55, 2.03)
	4	Light	0.95	(0.81, 1.12)	0.82	(0.63, 1.07)	1.08	(0.88, 1.33)
		Medium	0.96	(0.72, 1.28)	0.84	(0.53, 1.34)	1.08	(0.75, 1.56)
		Dense	1.01	(0.61, 1.68)	0.97	(0.45, 2.09)	1.06	(0.55, 2.03)
Long bone fracture	0	Light	**1.09**	**(1.02, 1.16)**	**1.10**	**(1.02, 1.20)**	1.06	(0.95, 1.18)
		Medium	1.12	(1.00, 1.26)	**1.16**	**(1.01, 1.33)**	1.06	(0.88, 1.28)
		Dense	**1.31**	**(1.09, 1.56)**	**1.37**	**(1.09, 1.70)**	1.22	(0.90, 1.65)
	1	Light	**1.10**	**(1.03, 1.17)**	**1.11**	**(1.02, 1.20)**	1.07	(0.96, 1.19)
		Medium	1.09	(0.97, 1.22)	1.10	(0.95, 1.26)	1.07	(0.88, 1.29)
		Dense	**1.30**	**(1.09, 1.56)**	**1.32**	**(1.06, 1.66)**	1.27	(0.94, 1.71)
	2	Light	1.04	(0.97, 1.11)	1.04	(0.96, 1.13)	1.04	(0.94, 1.16)
		Medium	1.05	(0.94, 1.18)	1.02	(0.88, 1.18)	1.10	(0.92, 1.33)
		Dense	**1.22**	**(1.01, 1.47)**	**1.31**	**(1.05, 1.64)**	1.07	(0.77, 1.49)
	3	Light	1.04	(0.97, 1.11)	1.05	(0.97, 1.14)	1.01	(0.91, 1.13)
		Medium	1.01	(0.90, 1.13)	1.03	(0.89, 1.19)	0.97	(0.80, 1.18)
		Dense	0.96	(0.78, 1.18)	1.09	(0.85, 1.39)	0.75	(0.51, 1.09)
	4	Light	1.02	(0.95, 1.09)	1.05	(0.97, 1.14)	0.97	(0.86, 1.08)
		Medium	1.04	(0.92, 1.16)	1.08	(0.93, 1.24)	0.98	(0.80, 1.18)
		Dense	1.12	(0.92, 1.36)	1.17	(0.92, 1.49)	1.04	(0.75, 1.44)
All visits	0	Light	**1.02**	**(1.01, 1.03)**	1.01	(1.00, 1.02)	**1.03**	**(1.01, 1.04)**
		Medium	**1.04**	**(1.02, 1.06)**	**1.03**	**(1.01, 1.05)**	**1.06**	**(1.03, 1.08)**

		Dense	**1.06**	**(1.03, 1.10)**	**1.04**	**(1.01, 1.08)**	**1.09**	**(1.05, 1.14)**
	1	Light	**1.02**	**(1.01, 1.03)**	1.02	(1.00, 1.03)	**1.02**	**(1.01, 1.04)**
		Medium	**1.05**	**(1.03, 1.07)**	**1.04**	**(1.02, 1.06)**	**1.06**	**(1.04, 1.09)**
		Dense	**1.04**	**(1.01, 1.07)**	1.01	(0.98, 1.05)	**1.07**	**(1.03, 1.12)**
	2	Light	1.01	(1.00, 1.02)	1.01	(1.00, 1.02)	1.02	(1.00, 1.03)
		Medium	**1.04**	**(1.02, 1.06)**	**1.03**	**(1.01, 1.05)**	**1.04**	**(1.02, 1.07)**
		Dense	**1.04**	**(1.01, 1.07)**	1.02	(0.99, 1.06)	**1.07**	**(1.02, 1.11)**
	3	Light	1.01	(1.00, 1.02)	1.01	(1.00, 1.02)	1.01	(1.00, 1.03)
		Medium	**1.04**	**(1.02, 1.06)**	**1.04**	**(1.02, 1.06)**	**1.04**	**(1.02, 1.06)**
		Dense	1.04	(1.00, 1.07)	1.02	(0.98, 1.05)	**1.06**	**(1.02, 1.11)**
	4	Light	1.00	(0.99, 1.01)	1.00	(0.99, 1.01)	1.01	(0.99, 1.02)
		Medium	**1.03**	**(1.01, 1.05)**	**1.03**	**(1.01, 1.05)**	**1.04**	**(1.02, 1.07)**
		Dense	1.01	(0.98, 1.04)	1.01	(0.98, 1.04)	1.02	(0.98, 1.06)

Table S3. Sensitivity Analysis - Risk of Select Outcomes Associated with Wildfire Smoke Exposure Among All Adults (19+) on Lag 0 Days, Calculated Using ZIP code Meta-Analysis, Poverty-Adjusted Analysis, and Compared to Manuscript Methods without ZIP code Stratification; 8 California Air Basins (Modeled, May 1 - September 30, 2015). Statistically Significant Relative Risks are Shown in Bold.

Models adjusted for heat index, day of week, time trend, and log-population offset. RR indicates relative risk; CI, confidence interval.
Meta-analysis excluded ZIP codes with populations less than 13,250 for model convergence.
Poverty-Adjusted analysis did not include 9 of 738 ZIP codes for which ZIP code-specific poverty data were not available.

Outcome	Density	Meta-Analysis		Poverty-Adjusted		Manuscript	
		RR	CI	RR	CI	RR	CI
All-cause Cardiovascular	Light	0.99	(0.98, 1.00)	**1.03**	**(1.01, 1.04)**	1.02	(1.00, 1.03)
	Medium	1.01	(0.99, 1.03)	**1.06**	**(1.03, 1.08)**	**1.05**	**(1.03, 1.08)**
	Dense	**1.05**	**(1.01, 1.09)**	**1.09**	**(1.04, 1.13)**	**1.08**	**(1.03, 1.12)**
Hypertension	Light	0.99	(0.98, 1.00)	**1.02**	**(1.01, 1.04)**	1.01	(1.00, 1.03)
	Medium	1.01	(0.99, 1.03)	**1.05**	**(1.03, 1.08)**	**1.05**	**(1.02, 1.07)**
	Dense	**1.07**	**(1.03, 1.11)**	**1.09**	**(1.04, 1.13)**	**1.08**	**(1.03, 1.12)**
Ischemic heart disease	Light	0.97	(0.92, 1.03)	1.01	(0.96, 1.07)	1.02	(0.97, 1.08)
	Medium	**1.17**	**(1.07, 1.26)**	1.01	(0.92, 1.10)	1.01	(0.92, 1.11)
	Dense	**1.58**	**(1.40, 1.75)**	1.01	(0.86, 1.18)	1.01	(0.86, 1.19)
Dysrhythmia	Light	0.99	(0.97, 1.01)	**1.05**	**(1.03, 1.08)**	**1.06**	**(1.04, 1.09)**
	Medium	**1.06**	**(1.02, 1.10)**	**1.10**	**(1.05, 1.15)**	**1.10**	**(1.05, 1.15)**
	Dense	**1.14**	**(1.06, 1.21)**	**1.15**	**(1.06, 1.24)**	**1.16**	**(1.08, 1.25)**
Heart failure	Light	0.99	(0.96, 1.02)	1.02	(0.99, 1.05)	1.01	(0.98, 1.04)
	Medium	**1.08**	**(1.03, 1.13)**	**1.07**	**(1.02, 1.12)**	**1.06**	**(1.01, 1.12)**
	Dense	**1.23**	**(1.14, 1.32)**	**1.10**	**(1.01, 1.20)**	1.09	(1.00, 1.19)
All-cause Cerebrovascular	Light	1.03	(0.98, 1.09)	1.05	(0.99, 1.11)	1.05	(1.00, 1.11)
	Medium	**1.27**	**(1.17, 1.36)**	1.07	(0.97, 1.18)	1.07	(0.97, 1.18)
	Dense	**1.71**	**(1.53, 1.89)**	1.11	(0.95, 1.31)	1.12	(0.95, 1.32)
All-cause Respiratory	Light	0.98	(0.97, 1.00)	**1.03**	**(1.01, 1.05)**	1.02	(1.00, 1.04)
	Medium	**1.05**	**(1.02, 1.07)**	**1.09**	**(1.06, 1.12)**	**1.09**	**(1.05, 1.12)**
	Dense	**1.05**	**(1.01, 1.10)**	**1.10**	**(1.05, 1.16)**	**1.09**	**(1.03, 1.15)**
Long bone fractures	Light	1.06	(1.00, 1.12)	**1.09**	**(1.02, 1.16)**	**1.09**	**(1.02, 1.16)**
	Medium	**1.29**	**(1.18, 1.40)**	**1.12**	**(1.01, 1.25)**	1.12	(1.00, 1.26)
	Dense	**2.32**	**(2.13, 2.51)**	**1.30**	**(1.09, 1.55)**	**1.31**	**(1.09, 1.56)**