Web Material

Who is More Affected by Ozone Pollution? A Systematic Review and Meta-Analysis

Web Appendix - Search strategy and criteria

Search of MEDLINE through PubMed for studies indexed by 21June2013.

Search A: (“modified” or “modification” or “modify” or “modifying” or modifier or modifiers) AND (effect or effects) AND (“air pollution” or “air pollutant” or “air pollutants”) AND (“time series” or “case crossover” or “short term”)

Search B: (“modified” or “modification” or “modify” or “modifying” or modifier or modifiers) AND (effect or effects) AND (“ozone” or “O3” or “O(3)”)

Search C: (“emergency department” or “emergency visit” or “emergency visits” or “emergency room” or “hospital” or “hospitals” or “hospitalizations” or “hospitalisation” or “hospitalisations” or “mortality”) AND (“ozone” or “O3” or “O(3)”) AND (“time series” or “case crossover” or “short term”)

Search D: (“air pollution” or “air pollutant” or “air pollutants” or “ozone” or “O3” or “O(3)”) AND (“susceptible” or “susceptibility”) AND (“emergency department” or “emergency visit” or “emergency visits” or “emergency room” or “hospital” or “hospitals” or “hospitalizations” or “hospitalisation” or “hospitalisations” or “mortality”)

Search E: ("ozone" OR "O3" OR "O(3)") AND (age OR sex OR gender OR SES OR income) AND ("emergency department" OR "emergency visit" OR "emergency visits" OR "emergency room" OR "hospital" OR "hospitals" OR "hospitalizations" OR "hospitalisation" OR "hospitalisations" OR "mortality")

Exclusion criteria:
1. Published 1988 or later
2. Published in a language other than English
3. Non-research article including review, workshop report, commentary, etc.
4. Not a population-based (epidemiology) study, such as human exposure studies, toxicology, or ecology
5. Did not address human health outcomes of mortality, hospital admissions, or emergency room visits
6. Study population other than adults. Studies comparing risks in children versus adults, with no other analysis of modification were excluded
7. Did not report results for modification of ozone estimates of associations, such as studies that did not consider ozone, considered ozone main associations but not modification, or considered ozone as a confounder only
8. Did not examine short-term ozone exposure

Web Table 1. Summary of studies of modification for associations between ozone and mortality

Note: The results presented show (+) when a higher level of the modifier is associated with a higher health risk estimate and a (-) when a higher level of the modifier is associated with a lower health risk estimate. Only statistically significant associations are reported in the table. Reference numbers refer to the reference list for the Web Material, which differs from the reference list for the main text.

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Anderson et al. (2001)[1]	West Midlands conurbation, U.K. (10/94-12/96). Average (avg) 61 total, 28 CVD, and 10 respiratory (resp) deaths/day.	Daily maximum 8-hour average. Based on 2 monitoring sites. *Lag:* 0, 1, 2, 3, 02, 03. Results presented for lag 01 based on previous studies.	Total, CVD, resp	**Individual:** age (0-14, 15-64, ≥65 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar).	Generalized additive model. Stratification for modification by age; interaction terms for season.	Season: higher in warm for total mortality
Atkinson et al. (2012)[2]	10 conurbations (5 urban, 5 rural), U.K. (1993-2006). median of 11-155/day per area	Daily 8-hr max. Lag 01.	Total	**Temporal:** season (Spring: Apr.-June, summer: July-Sep., Fall: Oct.-Dec.; Winter: Jan.-Mar.)	City-specific Poisson regression. Meta-analysis to combine city-specific associations. Stratification for modification.	Season: higher for spring than summer in urban areas.
Bell et al. (2004)[3]	95 communities, U.S. (1/87-12/00)	Daily O_3. Lag 0, 1, 2, 3, 06	Non-accidental	**Individual:** age (<65, 65-74, >75 yr) **Temporal:** season (warm: Apr.-Oct., all year)	City-specific Poisson regression. Bayesian hierarchical modeling to generate overall estimates. Stratification for modification.	n/a
Bell et al. (2005)[4]	144 estimates from 39 previously conducted studies. Not all estimates in all analyses. (studies published 1999 to 21Jun04)	O_3 metrics in original studies converted to 24-hr avg. Multiple short-term lags.	Total, CVD, resp	**Community:** region (US, non-US), age (elderly, all ages), season (warm season, all year)	Meta-analysis of results from previously conducted studies. 2-stage Bayesian hierarchical modeling. Stratification for modification.	n/a
Bell and Dominici (2008)[5]	98 communities, U.S. (1/87-12/00)	Daily O_3. Lag 06	Non-accidental	**Temporal:** season (warm: Apr.-Oct., all year) **Community:** prevalence of central air conditioning (AC), unemployment, use of public transportation, long-term temperature	City-specific Poisson regression. Bayesian hierarchical modeling with community-level characteristics for modification.	Unemployment (+): higher with higher unemployment Race: higher with higher % African-Americans Transportation (+): higher with higher use of public transportation AC (-): higher with lower central AC Temperature (-): higher with lower long-term temperature

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Berglind et al. (2009)[6]	5 cities (Augsburg, Barcelona, Helsinki, Rome, Stockholm), Europe (recruited 1992-2002, followed 6-12 yr), 25,006 myocardial survivors (>35 yr)	Daily 8-hr max, Apr.-Sep. Lag 01, 05, 0-14.	For survivors of myocardial infarction: CVD, total	**Individual:** age (35-64, 65-74, >75 yr, all ages), time after MI (<1 yr, >1 yr after first MI)	City-specific Poisson regression of cohort data. Meta-analytic pooling to generate overall estimates.	Age (-): higher for youngest age group.
Borja-Aburto et al. (1998)[7]	Mexico City, Mexico (1/93-7/95), avg 32 deaths/day	24-hr avg. Lags up to 5 previous days.	Non-accidental	Individual: age (>65, all)	Poisson regression. Stratification for modification.	n/a
Bremner et al. (1999)[8]	London, U.K. (1992-1994). avg 169 deaths/day	24-hr avg. Lag 0, 1, 2, 3, 01, 02, 03.	All cause, resp, CVD	**Individual:** age (0-64, >65, 65-74, >75) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Interaction terms for modification by season.	Season: higher in warm season (CVD and resp for >75 yr), higher in cool season (all cause for >65 yr)
Cakmak et al. (2007)[9]	7 urban centers in Santiago, Chile (1/97-12/03). avg 69.69 non-accidental deaths/day.	Daily 1-hr max. Population-weighted.	Non-accidental, CVD, resp	**Individual:** age (<64, 65-74, 75-85, >85 yr) **Temporal:** season (warm: Oct.-Mar., cool: Apr.-Sep.)	Center-specific Poisson regression. Restricted maximum-likelihood methods used to pool center-specific estimates. Results for modification presented across all centers.	Age (+): higher for older persons
Cakmak et al. (2011)[10]	7 urban centers, Chile (1/97-12/07). avg 7.29-15.8 days/day per center	Daily 8-hr max. Lag 06.	Non-accidental	**Individual:** age (<64, 65-74, 75-84, >85 yr), sex, education (<primary school, primary school, high school, some college, university), employment (unemployed, blue collar, white collar) **Community:** income at census tract level (quartiles)	City-specific Poisson regression. Random effects model to estimate overall associations. Stratification for modification. Results for modification presented across all cities.	Age (+): higher for >85 than <64 yr Education (-): higher <primary school than university Employment (-): higher for unemployed than white collar
Cheng and Kan (2012)[11]	Shanghai, China (1/01-12/04)	8-hr avg (10 am-6 pm). Lag 0	Non-accidental, CVD, resp	**Temporal:** temperature (low, medium, high, using 5 sets of cutoffs)	Generalized additive model. Stratification for modification.	Temperature (-): higher during cool days (total non-accidental, CVD, resp)
Chock et al. (2000)[12]	Pittsburgh, PA, US (1989-1991). 25,609 deaths.	1-hr max from noon-8 pm. Lag 0	Total	**Individual:** age (<75, >75 yr, all year and by season) **Temporal:** season (spring, summer, winter, autumn)	Poisson regression. Stratification for modification by age; interaction terms for modification by season.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
de Almeida et al. (2011)[13]	Oporto, Portugal (2000-04). avg 38.5 deaths/day.	Daily 8-hr max. Lag 0, 1, 2, 3, 01, 03.	Non-accidental, CVD, resp	**Individual:** age (all ages, >65 yr) **Temporal:** season (all year, summer: Apr.-Sep., winter: Oct.-Mar., total non-accidental)	Generalized additive models. Stratification for modification	n/a
de Leon et al. (2003)[14]	New York, NY (1/85-12/94). avg. 179.42 admissions/day	24-hr avg. Lag 01	Circulatory, cancer	**Individual:** age (<75 yr, >75 yr), co-morbidities (with and without contributing resp causes)	Poisson regression. Stratification for modification.	n/a
de Oliveira et al. (2011)[15]	Rio de Janeiro State, Brazil (1/02-12/06) 1,058 deaths	24-hr avg.. Lag 0, 1, 2, 3, 4, 5, 6, 7, 8, 9	Resp	**Individual:** sex (by age: all ages, >65 yr), age (all ages, >65 yr, by sex)	Time-series model. Stratification for modification.	n/a
Faustini et al. (2012)[16]	Rome, Italy (1/05-11/09). 15,884 deaths of COPD patients. 145,681 COPD patients.	Daily 8-hr max. Apr.-Sep. Lag 0, 01, 2-5, 0-5.	Non-accidental, CVD, cerebrovascular, resp (>35 yr)	**Individual:** co-morbidity (COPD patient, general population without COPD)	Poisson regression and case crossover. Stratification for modification.	n/a
Fischer et al. (2003)[17]	The Netherlands (1986-1994). ~330 deaths/day	Daily 8-hr max. Lag 1	CVD, COPD, pneumonia	**Individual:** age (<45, 45-64, 65-74, >75 yr)	Poisson regression. Stratification for modification.	Age (+): higher in oldest 2 groups than <45 for COPD, than 45-64 for pneumonia
Garrett and Casimiro (2011)[18]	Lisbon, Portugal (1/04-12/06). 1,042 deaths	24-hr average, Lag 0, 1, 2, 3, 4, moving averages Lag 1 to 4.	Non-accidental all cause, CVD	**Individual:** age (>65 yr, all ages)	Generalized additive modeling. Stratification for modification.	n/a
Goldberg et al. (2001)[19]	Montreal, Canada (1984-1993). 133,904 deaths	24-hr avg. Lag 0, 1, 02.	Non-accidental, neoplasm, lung cancer, CVD, coronary artery disease resp (all ages, >65, season), nonmalignant digestive diseases, injuries and poisonings, other non-accidental causes, diabetes mellitus, renal diseases (warm, all year)	**Individual:** age (<65 yr, >65 yr, all) **Temporal**: season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Stratification for modification.	Age (+): higher for older group (non-accidental). Season: Higher in warm season (non-accidental, neoplasm, resp)
Goldberg et al. 2006)[20]	Montreal, Canada (1984-1993). 3,653 diabetes deaths	24-hr avg. Lag 0, 1, 02.	Underlying cause of diabetes, diabetes within <1 yr of death and comorbidity (CVD, cancer, airway disease, chronic coronary artery disease, congestive failure, atherosclerosis) (>65 yr)	**Individual:** sex, co-morbidities **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Stratification for modification	n/a
Gouveia and Fletcher (2000)[21]	Sâo Paulo, Brazil (1991-3). 151,756 deaths	Daily 1-hr max. Lag 0, 1, 2	All cause, resp	**Individual:** age (all cause: all, >65; resp: <5, >65)	Poisson regression. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Gryparis et al. (2004)[22]	23 European cities (1990-7, years differed by city). avg 6-347 deaths/day per city	Daily 1-hr and 8-hr max. Lag 01.	Total, resp, CVD	**Temporal:** season (warm: Apr.-Sep, cool: Oct.-Mar.)	City-specific Poisson regression. Fixed effects pooled regression and random effects modeling to estimate overall associations.	Season: higher in summer for all-cause, resp, CVD
Hoek et al. (1997)[23]	Rotterdam, The Netherlands (1983-91). Median 18 deaths/day	24-hr avg. Lag 0, 1, 2	Total	**Individual:** age (<78 yr, >78 yr) **Temporal:** season (warm: May-Oct., cool: Nov.-Apr.)	Poisson regression. Stratification for modification.	n/a for season (full associations not provided for associations by age)
Hoek et al. (2000)[24]	The Netherlands (1986-1994). Separate analyses for 4 major cities, The Netherlands without the 4 cities, entire country. avg 328 deaths/day. 3287 deaths.	8-hr avg (noon-8 pm). Lag 0, 1, 2, 06.	Non-accidental (>1 month)	**Temporal:** season (summer: May-Sep., winter: Nov.-Mar., all year) **Community:** urbanicity (4 major cities, remaining areas)	Poisson regression. Stratification for modification.	Season: higher in summer
Ito et al. (2005)[25] [Two studies from this paper]	43 previously conducted studies (published 1990-2003)	24-hr avg.	Total	**Temporal:** season (winter, summer, all year) **Community:** long-term pollution levels (O_3, PM_{10}, NO_2), temperature	Meta-analysis of results from previously conducted studies. Stratification for modification.	Season: higher associations in warm season
Ito et al. (2005)[25] [Two studies from this paper]	6 cities, U.S. (1985-94)	24-h. Lag 01.	Non-accidental	**Temporal:** season (warm: Apr.-Sep, cool: Oct.-Mar.)	Poisson regression. Stratification for modification. City-specific results combined to estimate overall associations. Modification results by season provided by city and overall.	n/a
Kan et al. (2008)[26]	Shanghai, China (1/01-12/04). 173,911 deaths. avg 119.0 deaths/day	Daily 8-hr max. Lag 01.	Non-accidental, CVD, resp	**Individual:** sex (all cause), age (5-44, 45-64, >65 yr) (all cause), education (illiterate or primary school, middle school of above) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Time-series model. Stratification for modification.	Season: higher effect in cool season for total mortality.
Kim et al. (2004)[27]	Seoul, Republic of Korea (1/95-12/99). Avg 90.08 deaths/day	Daily 1-hr max. Lag 1	Non-accidental	**Temporal:** season (summer: June-Aug., all year)	Poisson regression. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Kwon et al. (2001)[28]	Seoul, Republic of Korea (1994-8). 1,807 CHF patients. avg 1/0 deaths/day for CHF patients, 90.4 deaths/day for all causes	Daily 1-hr max. Lag 0.	Non-accidental deaths for persons with CHF (admitted with CHF 1994-6, died 1994-8)	**Individual:** pre-existing conditions (CHF patients, general population). For CHF patients: sex, age (<75, >75 yr), time from CHF admission to death (<4, >4wk)	Case crossover and Poisson regression. Stratification for modification.	Time from CHF admissions (+): higher effect for >4 weeks from admission to death
Levy et al. (2005)[29]	Meta-analysis of 48 estimates from 28 existing studies	Short-term exposure.	Total (as defined by original study) for all ages	**Temporal:** season (summer, winter, as defined by the original study) **Community:** region (N. America, Europe); AC prevalence, long-term O_3, cooling degree days based on monthly mean temperature (<median, >median)	Meta-regression to generate with hierarchical linear model to generate overall effect and investigate modification.	O_3 level (-): higher with low ozone levels. AC (-): higher for cities with cities with lower AC prevalence Season: higher in summer
Liang et al. (2009)[30]	Central Taiwan (1997-9)	8-hr avg (9 am-5 pm). Lag 0, 1, 2, 3, 4, 5, cumulative lags up to 5 days	Non-accidental, resp, CVD	**Individual:** age (>65 yr, all ages) **Temporal:** season (summer: June-Aug., winter: Dec.-Feb.)	Time-series analysis. Stratification for modification.	n/a
Lin and Liao (2009)[31]	Kaohsiung, Taiwan (1995-9). 33,818 deaths. avg. 3.18 deaths/day	24-hr avg. Lag 0, 1, 2, 3-5.	Non-accidental, CVD	**Individual:** age (>65 yr, all ages) **Temporal:** temperature (days with mean temperature 19.7, 24.8, 27.6^{o}C)	Poisson regression. Stratification for modification.	n/a
Lipfert et al. (1995)[32]	Philadelphia, PA, U.S. (1991-5). avg 120.2 deaths/day	Daily 1-hr max. Lag 01.	Non-accidental	**Individual:** age (<65 yr, >65 yr)	Regression model. Stratification for modification.	n/a (Central estimates presented only)

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Medina-Ramon and Schwartz (2008)[33]	48 cities, U.S. (May-Sep. 1989-2000). 2,729,640 deaths.	Daily 8-hr max. Lag 02.	Non-accidental	**Individual:** sex (all ages, <60 yr, >60 yr), race (black, other), education (≤high school, other), co-morbidities as secondary cause (asthma, COPD, atherosclerosis, atherosclerotic CVD, atherosclerotic heart disease, CHF, atrial fibrillation, stroke, diabetes, inflammatory) **Community:** mean O_3 level, central AC prevalence, population density, mean temperature (for populations >65 yr, women >60 yr, blacks, those with atrial fibrillation)	City-specific case only model. Interaction terms for individual-level effect modifiers. Random effects meta-regression to generate overall effect and investigate modification of community characteristics.	Age (+): higher for older persons Sex: higher for women (>60 yr) Co-morbidity: higher for those with atrial fibrillation Ozone (-): higher with lower long-term O_3 levels (for the elderly or black populations) AC (+): higher with higher AC prevalence (those with atrial fibrillation)
Moolgavkar (2000)[34]	3 counties (Cook Co., IL; Los Angeles, CA; Maricopa, CA), U.S. avg 40-116 deaths/day per county	24-hr avg. Lag 0, 1, 2, 3, 4, 5	Non-accidental	**Temporal:** season (warm: Apr.-Sep., all year)	Poisson regression. Stratification for modification. Modification analyzed separately for each county.	n/a
Ng et al. (2013)[35]	20 cities, Japan (1/02-12/07). 791,507 deaths. avg 0.5-133.9 per city.	Daily 8-hr max. Lag 02.	Non-accidental, CVD, resp (>65 yr)	**Temporal:** season (warm: June-Aug., cool: Dec.-Feb., moderate: Mar.-May and Sep.-Nov.)	City-specific generalized linear regression. Inverse-variance meta-analysis to generate overall association. Stratification for modification	Season: higher for moderate than cool or warm seasons (all cause), higher for moderate than cool (CVD), higher for cool than warm (resp)
O'Neill et al. (2004)[36]	Mexico City, Mexico (1996-8). 206,510 deaths	24-hr avg. Lag 01.	Non-accidental	**Individual:** age (>65 yr, all ages) Community: % homes with electricity, % with piped water, % with drainage (3 strata); % literacy (4 strata); % indigenous language speakers (5 strata); SES index (3 strata) (by age)	Poisson regression. Stratification for modification.	SES index: higher for high than medium SES (all ages, ≥65 yr) Literacy (+): higher for most literate than 2nd least literate (of 4 strata) (>65 yr) Indigenous speakers (-): higher for medium (of 5 strata) than 2nd most indigenous speakers (of 5 strata) (all ages, >65 yr)

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Ou et al. (2008)[37]	Hong Kong (1998) 24,357 deaths	Daily 8-hr max. Lag 0, 1, 2, 3	Non-accidental (>30 yr)	**Individual:** age (>30, >65 yr), education (none, primary, secondary or higher); employment (never employed, white-collar, blue-collar); housing (private permanent, public rental) for all ages and >65 yr	Poisson regression model. Stratification for modification by age; interaction terms for SES indicators (occupation)	Occupation (+/-): higher for blue-collar than never-employed or white-collar (all ages, or >65 yr)
Ou et al. (2012)[38]	Hong Kong (1998) 23,484 deaths	24-hr avg. Lag 02.	Non-accidental (>30 yr)	**Individual:** diet (fish, meat, vegetables, fruits, soy, dairy products) (regular consumption: >1/week, <1 week)	Case crossover. Interaction terms for modification.	Fruit intake (-): higher with less fruit consumption
Parodi et al. (2005)[39]	Genoa, Italy (8/93-12/96). 27,228 deaths. avg 21.8 deaths/day	24-h, daily 8-hr max, 8-hr (10 am-6 pm). Lag 0, 1, 02	Non-accidental, CVD	**Individual:** age (>75 yr, all ages) **Temporal:** season (warm: May-Oct., all year, by age); temperature (>26, <26°C)	Poisson regression. Interaction terms for modification by temperature; stratification for modification by season and age.	Temperature (+): higher on hotter days (CVD)
Pattenden et al. (2010)[40]	15 conurbations, U.K. (May-Sep., 1993-2003). 592,320 deaths. avg 5-154 deaths/day per conurbation.	Daily 8-hr max. Lag 01. Other lags in sensitivity analysis.	Non-accidental, CVD, resp	**Individual:** age (0-64, 65-74, 75-84, >85 yr, all-cause) **Temporal:** temperature (hot: 2-day average >95th percentile, cool: <95th percentile)	Community-specific Poisson regression. Random effects meta-analysis to generate overall effect. Interaction terms for modification by temperature; stratification for modification by age. Modification results for temperature presented for each conurbation and overall.	Temperature (+): higher on hot days (London and Cardiff: all-cause; overall, all cause: 65-74 yr)

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Peng et al. (2013)[41]	86 U.S. cities, 23 European cities, 12 Canadian cities (1987-97, years varied by city). 85 cities with year-round data.	Daily 1-hr max. Lag 1, 01, 02.	Non-accidental	**Individual:** age (<75, $\geq$75 yr) **Temporal:** season (warm: Apr.-Sep., all year) **Community:** NO_2 coefficient of variation (CV), SO_2, O_3 CV, NO_2/PM_{10}, temperature, age (% >75 yr), age standardized mortality, unemployment	City-specific Poisson regression. Hierarchical modeling to generate region-specific estimates (U.S., Europe, Canada). Stratification for modification by age and season; hierarchical regression for modification by community-level characteristics.	Higher associations with lower NO_2 CV (-) (U.S.); higher SO_2 (+) (Canada, U.S.), higher O_3 CV (+) (U.S.), lower O_3 CV (-) (Europe), higher NO_2/PM_{10} (+) (U.S.) Temperature (-): higher with lower temperature (U.S.) Age (+): higher for older communities (Canada) Unemployment (+): higher with more unemployment (U.S.)
Penttinen et al. (2004)[42]	Helsinki, Finland (1988-1996). 3,288 deaths, median 17 deaths/day.	Daily 8-hr and 1-hr max. Lag 0, 1, 03	Non-accidental, resp	**Individual:** age (15-64, 65-74, >75 yr) **Temporal:** season (summer: Apr.-July, non-summer: Aug.-Mar.)	Poisson regression. Stratification for modification.	Season: higher in summer (all cause, resp)
Prescott et al. (1998)[43]	Edinburgh, Scotland (10/92-6/95). avg 14.5 deaths/day.	24-h. Lag 0, 1, 02.	Non-accidental	**Individual:** age (<65 yr, >65 yr)	Poisson regression. Stratification for modification.	n/a
Qian et al. (2007)[44]	Wuhan, China (7/00-6/04). 89,131 deaths	8-hr avg (10 am-6 pm). Lag 0, 1, 2, 3, 03.	Non-accidental, CVD, stroke, cardiac, resp, cardiopulmonary	**Individual:** age (<65 yr, >65 yr)	Poisson regression. Stratification for modification.	Age (+): higher for older group (stroke)
Qian et al. (2010)[45]	Wuhan, China (7/00-6/04). 89,131 deaths. avg 61.0 deaths/day.	8-hr avg (10 am-6 pm). Lag 0, 1, 2, 3, 4, 01, 03	Non-accidental, CVD, stroke, cardiac, resp, cardiopulmonary, non-cardiopulmonary	**Individual:** age (<65 yr, >65 yr), sex **Temporal:** temperature (lowest 5% of days, avg 2.2 ^oC, highest 5% of days: avg 33.1 ^oC, normal: avg 18.0 ^oC,)	Generalized additive models. Stratification for modification.	Temperature (+): higher on high temperature days (non-accidental)

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Rainham et al. (2005)[46]	Toronto, Canada (1981-1999). avg. 46.7 deaths/day	24-hr avg. Lag 0, 1, 2.	Non-accidental, cardio-resp, non-cardio-resp, other causes	**Temporal:** air mass type by synoptic weather category (dry moderate, dry polar, moist moderate, moist polar, moist tropical, transition); season (warm: June-Aug., cool: Dec.-Feb., by air mass type)	Generalized linear models. Stratification for modification.	Season: higher for summer season (all-cause; all-cause, cardio-resp, or other causes in dry moderate; cardio-resp in moist moderate; all-cause and other causes in moist tropical; other causes in transition) Air mass: higher for some air mass types than others, varying by season and cause: lower for moist tropical, dry moderate, transition, dry polar, moist moderate, moist polar, moist tropical
Ren et al. (2008)[47]	60 cities, eastern US.. (1987-2000)	24-hr avg. Lag 02.	Non-accidental	**Temporal:** maximum temperature (non-linear continuous; categories: low, medium, high)	City-specific Poisson regression. Two-stage hierarchical model to estimate overall associations. Non-linear interaction terms and stratification for modification. Modification results presented for each city and overall.	Temperature (+): higher on higher temperature days (overall across 60 cities)
Ren et al. (2009)[48]	95 cities, U.S. (May-Oct., 1987-2000)	24-hr avg. Lag 0, 1, 2, 03.	CVD	**Temporal:** maximum temperature (non-linear continuous; categories: low, medium, high)	City-specific Poisson regression. Bayesian meta-analysis to generate overall effect. Non-linear interaction terms and stratification for modification.	Temperature (+): higher on high temperature days for some regions (Northeast, industrial Midwest, Northwest)
Ren et al. (2010)[49]	3 counties in eastern Massachusetts, U.S. (May-Sep., 1995-2002). 60,302 deaths	Daily 8-hr max, Lag 03, and other lags.	Non-accidental, CVD, resp disorders, diabetes (>35 yr)	**Individual:** age (35-64, 65-74, 75-84, >85 yr); race (white and non-Hispanic black, American Indian, Hispanic, Asian or Pacific, other); gender; education (>8, 9-12, 13-16, >17 yr), marital status (never, married or separated, widowed, divorced) **Community:** population density, household income, poverty (quartiles)	Case crossover. Interaction terms for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Revich and Shaposhnikov (2010)[50]	Moscow, Russia (2003-2005). avg 331.2 all cause, 114.5 ischemic heart disease, 68.8 cerebrovascular disease deaths/day	24-hr avg. Lag 0, 1, 01.	Non-accidental, ischemic heart disease, cerebrovascular	**Individual:** age (all ages, >75 yr)	Time-series model. Stratification for modification.	n/a
Renya et al (2012)[51]	Mexicali, Mexico (2003-2007). avg 9 deaths/day.	Daily 8-hr max, 1-hr max Lag 0, 1, 2, 3, 4, 5, 6, 7	Non-accidental	**Temporal:** season (winter, summer)	Poisson regression. Interaction models for modification.	n/a
Romieu et al. (2012)[52]	6 cities, Latin America (Brazil, Chile, Mexico) (1997-2005). avg 12.0-165.44 deaths/day per city.	Daily 8-hr max. Lag 0, 1, 2, 3, 03.	Non-accidental, cardiopulmonary, resp, CVD, cerebrovascular-stroke, COPD, lower resp infection. Not all outcomes and cities used in all analyses.	**Individual:** age (>65 yr, all ages, all outcomes but lower resp infection); <1 and 1-4 yr (resp), <1, 1-14 yr (lower resp infection) for 3 cities. (by season and SES) **Temporal:** season (warm: Oct.-Mar., cool: Apr.-Sep for Brazil and Chile; warm: May-Sep., cool: Oct.-Apr. for Mexico) **Community**: SES index based on education, income, housing conditions (areas within 4 cities)	City-specific Poisson regression. Meta-regression and meta-analyses to generate overall effect. Stratification for medication. Modification results presented for each city and overall (age)	Age (+/-): higher for some ages others, varying by season and cause: higher for all ages, >65 yr, children (<1 or 1-4 yr), infants (<1 yr) Season: higher for some season than others, varying by age and cause: higher for warm or cool season SES (+/-): higher for some SES levels, varying by cause and city: higher for high or low SES
Sacks et al. (2012)[53]	Philadelphia, PA, U.S. (May 12, 1992- Sep. 30, 2005). 17,968 deaths.	Daily 8-hr max. Lag 01.	CVD	**Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Time series model. Indicator variable for modification.	n/a
Schwartz (2005)[54]	14 counties, U.S. (1986-93). 847.406 deaths	Daily 1-hr max. Lag 0.	Non-accidental	**Temporal:** season (warm: May-Sep., cool: Oct.-Apr.)	City-specific case crossover. Random effects model to generate overall associations. Stratification for modification.	Season: higher in warm season
Simpson et al. (1997)[55]	Brisbane, Australia (1/97-10/93). 2,496 deaths	8-hr avg (10 am-6 pm), daily 1-hr max. Lag 0, 1, 2, 3, 4, 5, 04, 05, 06	Non-accidental, CVD, resp	**Individual:** age (<65 yr, >65 yr) **Temporal:** season (summer: Oct.-Mar., winter: Apr.-Sep., yearly)	Poisson regression. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Simpson et al. (2000)[56]	Melbourne, Australia (Jan.-Aug., 1/91-8/96). avg 55.3 deaths/day	24-h, daily 1-hr and 4-hr max. Lag 0, 1, 2, 02, 04.	Non-accidental, CVD, resp	**Individual:** age (all ages, >65 yr, by season) **Temporal:** season (warm: Nov.-Mar., cool: Apr.-Oct.)	Poisson regression. Stratification for modification by age; interaction terms for modification by season.	n/a
Smith et al. (2009)[57]	98 cities, U.S. (1987-2000).	24-hr avg, daily 1-hr and 8-hr max Lag 0, 1, 2, 01	Non-accidental	**Temporal:** season (summer: Apr.-Oct, all year) **Community:** central or window AC prevalence; 77 variables, primarily related to population distribution, housing, education, race, income; long-term summer O_3, PM_{10}, $PM_{2.5}$, SO_2, temperature (> or < median)	City-specific Poisson regression. Random effects model to generate overall effect and investigation community-level modification. Stratification for modification by age or season.	Temperature (+): higher on higher temperature days (summer), higher in communities with lower temperature SO (+)$_2$: higher on high SO_2 days (year round analysis), higher in communities with higher long-term SO_2 PM_{10} (+): higher on high PM_{10} days (year round analysis, summer) AC (+/-): higher for cities with higher window AC prevalence, lower for cities with higher central AC prevalence Residential mobility (-): lower for cities with higher mobility (different house in 1995; proportion >65 yr, renters >65 yr, home owners >65 yr moved since 1995) Transportation: higher with more use of public transportation, or less proportion driving to work Latitude (+): higher with higher latitudes
Son et al. (2012)[58]	Seoul, Republic of Korea (1/00-12/07). 261,952 deaths.	Daily 8-hr max. Lag 0, 1, 2, 01, 1-2, 02	Total, CVD, resp	**Individual:** sex (by sex and education), age (35-64, 75-74, >75 yr, education (none, <12, >12 yr, unknown), marital status, occupation (professional; manual; technical service, mechanic, or physical labor; unemployed; unknown) **Temporal:** season (warm: May-Sep., all year) (total)	Case crossover. Interaction terms for modification by individual-level variables; stratification for modification by season.	Employment (-): higher for unemployed than professional (total) Education: higher for unknown than none (CVD: all, women), higher for none than unknown (total, resp) Age (-): higher for 35-65 than >75 yr (CVD: women)

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Stafoggia et al. (2010)[59]	10 cities, Italy (Apr.-Sep., 2001-2005). 127,860 deaths	Daily 8-hr max. Lag 0, 1, 2, 3, 4, 5, 01, 2-5, 05.	Non-accidental (>35 yr)	**Individual:** sex, age (35-64, 65-74, 75-84, >85 yr, by sex) **Community:** census-block income (low, medium, high, 4 cities), location of death (out of hospital, out of hospital with last discharge 2-28d death, in hospital, nursing home), co-morbidities (diabetes, hypertension, MI, cardiac ischemic disease, pulmonary circulation, conduction disorders, dysrhythmias, heart failure, cerebrovascular, chronic pulmonary disease, number of chronic conditions (0, 1, 2, >3)). Out of hospital admissions analyzed separately by age, sex, income, and co-morbidities.	City-specific case crossover. Random effects meta-analysis to generate overall effect. Stratification for effect medication.	Sex: higher for women. Age (+): higher for >85 yr than 75-84 yr (women), higher for >85 yr than all other age groups and all ages
Sunyer et al. (1996)[60]	Barcelona, Spain (1985-91). 2,557 deaths.	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5, 03.	Total, CVD, resp	**Individual:** age (>70 yr, all ages, all cause) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Interaction terms for modification.	Season: higher in warm season (CVD)

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Sunyer et al. (2002)[61]	Barcelona, Spain (1985-95) 1,080 deaths	Daily 1-hr max. Lag 02.	Total for persons with emergency department visits for asthma 1985-95 (≥14 yr)	**Individual:** co-morbidity (1 previous asthma admissions, >1 asthma admissions, >1 asthma/COPD admission), severity of previous emergency department visit (released within 24h, hospital referral), # emergency department visits within 1000days (<2.26, ≥2.26), sex, age (≥65 yr, >65 yr), season (Apr.-Sep., Oct.-Mar.) (by admission status)	Case-crossover within a cohort study. Stratification for modification by previous admission; interaction terms for other effect modifiers.	Age (-): higher for younger group (1 previous asthma admissions)
Verhoeff et al. (1996)[62]	Amsterdam, The Netherlands (1986-92). avg 19 deaths/day	Daily 1-hr max. Lag 0, 1, 2	Total	**Temporal:** season: (warm: May-Oct., all year)	Poisson regression. Stratification for modification.	n/a
Vichit-Vadakan et al. (2010)[63]	Bangkok, Thailand (6/97-5/03) avg 95 deaths/day.	Daily 8-hr max. Lag 0, 1, 2, 3, 4, 5, 01, 02, 03, 04, 05	Non-accidental	**Individual:** sex, age (0-4, 5-44, 18-50, 45-64, >50, >65, >75 yr)	Poisson regression. Stratification for modification.	Age (+): higher for >75 yr than 18-50 yr
Villeneuve et al. (2003)[64]	Vancouver, Canada (1/86-12/98). 93,612 deaths.	24-hr avg. Lag 0, 1, 2. 02	All cause, resp, CVD (>65 yr)	**Community:** family income (quintiles)	Time series model. Stratification for modification.	n/a
Wong et al. (2007)[65]	Hong Kong (1/08-12/08). 24,053 deaths	24-h. Lag 0, 1, 2, 3	Non-accidental, cardio-resp (>30 yr)	**Individual:** age (>30, >65 yr, by exercise status), exercise status (never: <1, ever: >1/month; never: <1/month, low: >1/month and <1/week, moderate: 1-3/week, high: >4/week; by age)	Poisson regression. Stratification and interaction terms for modification by exercise status. Stratification for modification by age.	Exercise status (+/-): higher for never than ever exercisers; higher for never or low than moderate or high exercisers, higher for high than moderate exercisers (all cause, >30 yr); higher for never exercisers than other groups; higher for low than moderate or high exercisers; higher for high than moderate exercisers (all cause, >65 yr); higher for never or low than moderate exercisers; higher for high than moderate exercisers (cardio-resp, >30 yr); higher for never or low than moderate exercisers, higher for low than high exercisers (cardio-resp, >65 yr)
Wong et al. (2008)[66]	Hong Kong (1/96-12/02). 215,240 deaths. avg 19 deaths/day.	Daily 8-hr max (1 am-6 pm) Lag 0, 1, 2, 3, 4	Mortality: non-accidental, CVD, resp	**Community:** social deprivation index (low, med, high)	Poisson regression and case only model. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Wong et al. (2009)[67]	Hong Kong (1996-2002). avg 16.2 resp, 5.8 COPD, and 23.8 CVD deaths/day.	Daily 8-hr max. Lag 01	Mortality: resp, COPD, CVD	**Community:** influenza	Poisson regression. Interaction terms for modification.	Influenza intensity (+): higher at higher influenza intensity (resp, COPD)
Wong et al. (2010)[68]	Hong Kong (mortality: 1/92-12/02). avg 84.2 deaths/day	Daily 8-hr max. Lag 0, 1, 2, 3, 4, 01, 04.	Non-accidental, CVD, resp	**Individual:** age (>65 yr, all ages) **Community:** social deprivation index (low, medium, high)	Poisson regression and case only model. Stratification for modification.	n/a
Wong et al. (2012)[69]	Hong Kong (1/85-6/95). avg 72 deaths/day	8-hr avg (10 am-6 pm). Lag 01	Non-accidental, CVD, resp	**Individual:** age (>65 yr, all) **Temporal:** pre- and post-intervention to lower fuel S content	Poisson regression. Stratification for modification.	Age (+): Higher in older persons (CVD) Intervention (+): higher after intervention (all cause, resp)
Yang et al. (2012)[70]	Jiangsu Province, China (1/06-12/08). avg 33.6 deaths/day	24-hr avg, daily 1-hr and 8-hr max. Lag 0, 1, 2, 3, 4, 5, 6, 01, 04, 06.	Non-accidental.	**Individual:** age (0-4, 5-44, 45-64, >65 yr), sex, education (low: illiterate or primary school, high: middle school or above). **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Stratification for modification.	Age (+): higher for >65 than 5-44 yr Season: higher in cool season
Zanobetti and Schwartz (2008)[71]	48 cities, U.S (1989-2000). 1,614,124 deaths	Daily 8-hr max. Summer: June-Aug. Lag 0, long-term lags up to 20 days	All cause, CVD, resp, stroke	**Community:** income (% households >65 yr with income >$50,000), % population >65 yr poverty, % population with central CA, summer apparent temperature, variance of summer apparent temperature, population density	City-specific Poisson regression. Meta-regression to estimate overall associations. Meta-regression for modification.	n/a
Zanobetti and Schwartz (2008)[72]	48 cities, U.S. (1989-2000). 6,951,395 deaths.	Daily 8-hr max. Lag 0.	All cause	**Individual:** age (0-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, >80 yr) **Temporal**: season (winter: Dec.-Feb., spring: Mar.-May, summer: June-Aug., autumn, Sep.-Nov.)	City-specific case crossover. Meta-regression to generate overall effect. Interaction terms for modification.	Season: higher for spring or summer than winter or autumn.

Study	Location and Time Frame	Exposure and Lag Structure	Mortality Outcome	Potential Modifiers	Statistical Models	Statistically Significant Results
Zhang et al. (2006)[73]	Shanghai, China (1/01-12/04). avg 119.0 deaths/day	8-hr (10 am-6 pm) avg. Lag 01, 04.	Total non-accidental, CVD, stroke, heart disease, resp, COPD, acute resp infection	**Individual:** age (0-4, 5-44, 45-64, >65 yr) (non-accidental), sex (non-accidental) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Generalized additive model. Stratification for modification.	Season: higher for cold season (non-accidental)

Web Table 2. Studies of modification for associations between ozone and hospital admissions or emergency room visits

Note: The results presented show (+) when a higher level of the effect modifier is associated with a higher health risk estimate and a (-) when a higher level of the effect modifier is associated with a lower health risk estimate. Only statistically significant associations are reported in the table. Reference numbers refer to the reference list for the Web Material, which differs from the reference list for the main text.

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Anderson et al. (1997)[74]	6 European cities (Amsterdam, Barcelona, London, Milan, Paris, Rotterdam). (1977-91, varied by city). avg 1-20 admissions/day per city.	8-hr avg (9 am-5 pm), daily max 1-hr. Lag 0, 1, 2, 3, 4, 5.	*Hospital admissions:* COPD	**Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar)	City-specific Poisson regression. City-specific associations pooled. Stratification for modification (overall across cities).	Season: higher in warm season
Anderson et al. (1998)[75]	London, U.K. (4/87-2/92). avg 35.1 admissions/day.	8-hr avg (9 am-5 pm) and daily max 1-hr. Lag 0, 1, 2, cumulative lags up to 3 days.	*Emergency hospital admissions*: asthma	**Individual**: age (0-14, 15-64, ≥65 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar)	Poisson regression. Stratification for modification.	Season: higher in warm season (all ages, 0-14 yr).
Anderson et al. (2001)[1]	West Midlands conurbation, U.K. (10/94-12/96). avg 71 CVD and 66 respiratory admissions/day.	Daily 8-hr max. Lag 0, 1, 2, 3, 0-2, 0-3.	*Hospital admissions*: respiratory, CVD, cardiac, ischemic heart disease (IHD) (65+), stroke (65+), asthma (15-64), COPD (65+)	**Individual**: age (0-14,15-64,≥65 yr) (resp) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar).	Generalized additive model. Stratification for modification by age; interaction terms for season.	n/a
Arbex et al. (2009)[76]	São Paulo, Brazil (2/01-12/03). 1,769 ED visits, avg 1.66 visits/day	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5, 6, cumulative effect of 2, 3, and 6 days.	*Emergency department visits:* COPD (≥40 yr)	**Individual**: sex, age (40-64, ≥64 yr)	Poisson regression. Stratification for modification.	n/a
Atkinson et al. (1999)[77]	London, U.K. (1/92-12/94). Average 150.6 resp and 172.5 lower resp disease/day.	Daily 8-hr and 1-hr maxes. Lag 0, 1, 2, 3, 01, 02, 03.	*Emergency hospital admissions*: resp, asthma, COPD+asthma (≥65 yr), lower resp (≥65 yr), CVD, IHD	**Individual:** age (0-14,15-64, ≥65y for resp, asthma; 0-64, ≥65y for CVD) **Temporal:** temperature and humidity (tertiles) for resp and CVD, season (warm: Apr.-Sep, cool: Oct.-Mar.)	Poisson regression. Stratification for modification by age, interaction terms for season.	Age (+): higher for older persons for CVD.
Atkinson et al. (1999)[78]	London, U.K. (1/92-12/94). 121,610 admissions.	Daily 8-hr and 1-hr max. Lag 0,1,2,3, 03, 01, 02	*Hospital admissions*: all resp complaints, asthma, other resp complaints	**Individual:** age (0-14, 15-64, ≥65y for other and all resp complaints; 0-14, 15-64, all ages) (for asthma) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar)	Poisson regression. Stratification for modification by age, interaction terms for season.	Age (+): higher for older persons.

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Ballester et al. (2001)[79]	Valencia, Spain (1994-6). avg 7.0 CVD admissions/day.	Daily 8-hr and 1-hr max. Lag 0, 1, 2, 3, 4, 5.	*Emergency hospital admissions*: CVD, heart, cerebrovascular, digestive disease	**Temporal**: season (warm: May-Oct., cool: Nov.-Apr.)	Poisson regression. Stratification for modification.	n/a.
Bhaskaran et al. (2011)[80]	15 conurbations, England and Wales (2003-2006). 79,288 MIs.	Sub-daily metrics of 1-6, 7-12, 13-18, 19-24, 25-72h	*Hospital admissions*: MI, other acute coronary syndromes	**Individual:** age (<60, 60-69, 70-79, ≥80 yr), prior coronary heart disease, smoking (current, former, never) **Temporal:** season (summer: July-Aug., other).	Case-crossover. Interaction terms for modification.	n/a
Buadong et al. (2009)[81]	Bangkok, Thailand (4/02-12/06). 33, 458 hospital visits, avg 19 cases/day.	Daily 1-hr max. Lag 0, 1, 01, 02.	*Hospital visits:* CVD	**Individual:** age (<15, 15-64, ≥65 yr)	Poisson regression. Stratification for modification.	Age (+): higher for older persons.
Burnett et al. (1995)[82]	Ontario, Canada (1/83-12/88). avg 14.4 CVD and 16.0 resp admissions/day.	Daily 1-hr max. Lag 1	*Hospital admissions*: CVD, resp	**Temporal**: season (warm: Apr.-Sep., cool: Oct.-Mar. for CVD, warm: May-Aug., cool: Sep.-Apr. for resp)	Time series model. Stratification for modification.	n/a
Cakmak et al. (2006)[83]	10 cities, Canada (4/93-3/00). 316,234 hospitalizations. avg 1.9-48 admissions/day per city.	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5	*Emergency hospital admissions*: cardiac	**Individual:** sex **Community:** family education (quartiles), family income (quartiles)	City-specific time series model. Random effects model to estimate overall associations. Stratification for modification. Results for modification presented across all cities.	n/a
Cakmak et al. (2006)[84]	10 cities, Canada (4/93-3/00). 215,544 hospitalizations. avg 1.9-28.2 admissions/day per city	24-hr avg. Lag 0, 1, 2, 3, 4, 5.	*Hospital admissions:* resp	**Individual:** sex **Community:** income (quartiles), education (<grade 9, 9-13, some trade school or university, university)	City-specific Poisson regression. Random effects model to estimate overall associations. Stratification for modification. Results for modification presented across all cities.	n/a
Cakmak et al. (1998)[85]	Toronto, Canada (4/81-12/91)	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5.	*Hospital admissions:* resp	**Temporal:** season (summer: June-Aug., all year)	Multiple regression approaches. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Canova et al. (2012)[86]	London, U.K. (5/08-7/10). 209 subjects age ≥18y	Daily 8-hr max. Lag 0, 1, 2, 3, 01, 03.	*Hospital admissions:* asthma or COPD	**Individual:** sex; age (18-54, 55-74, ≥75 yr); previous diagnosis of asthma, COPD, or asthma+COPD; smoking (yes/no); uric acid, Vitamin A, Vitamin C, Vitamin E, Vitamin A or E corrected for cholesterol (high, low); 12 gene polymorphisms **Temporal:** season (warm: Apr.-Sep., all year)	Case-crossover. Stratification for modification.	Vitamin E (-): higher for lower Vitamin E during warm season. Genetic variant (NQO1 (rs1800566)): higher for CC than CC, TT for all year data.
Carlsen et al. (2013)[87]	Reykajavik, Iceland (1/03-12/09). 24,430 visits, avg 9.6 visits/day	Daily 8-hr max. Lag 0, 02, 05.	*Emergency room visit, summed with admissions for stroke or cardio-resp* (≥18 yr)	**Individual:** sex, age (<70, >70 yr) **Temporal:** season (warm: Apr. 16- Oct. 15, cool: remaining days)	Poisson regression. Stratification for modification.	n/a
Cassino et al. (1999)[88]	New York, U.S. (1/89-12/93). 3,020 visits	24-hr and daily 1-hr max. Lag 0, 1, 2, 3	*Emergency department visits*: asthma	**Individual**: age (continuous), sex, race (African-American, Hispanic, other), smoking (never, <13 pack-yr, ≥13 pack-yr).	Poisson regression. Stratification for modification for smoking. For other modifiers, used logistic regression to compare risk of one group (e.g., males) to another (e.g., females) after high O_3 days.	Smoking (+): higher for ≥13 pack-yr than <13 pack-yr or never smokers; ≥31 pack-yr more likely to have ED visit after high O_3 day than never smoker. Sex: women more likely to have ED visit after high O_3 day than men.
`Castellsague et al. (1995)[89]	Barcelona, Spain (1986-9). avg. 1.7 visits/day in summer	Daily 1-hr max. Lag 0, 1, 2, 3, 4, and cumulative lags.	*Emergency room visits*: asthma (15-64 yr)	**Temporal**: season (warm: July-Sep., cool: Jan.-Mar.)	Poisson regression. Stratification for modification.	n/a
Chang et al. (2005)[90]	Taipei, Taiwan (1997-2001). avg 40.80 admissions/day	24-hr avg. Lag 02	*Hospital admissions*: CVD	**Temporal**: temperature (warm: ≥20°C, cool: <20°C)	Case crossover. Stratification for modification.	Temperature (+): higher for warmer days
Cheng et al. (2007)[91]	Kaohsiung, Taiwan (1996-2004). 82,587 admissions. avg. 25 admissions/day	24-hr avg. Lag 02	*Hospital admissions:* pneumonia	**Temporal:** temperature (warm: ≥23°C, cool: <23°C)	Case crossover. Stratification for modification.	n/a
Cheng et al. (2009)[92]	Kaohsiung, Taiwan (1996-2002) 9,349 admissions. avg 2.33 admissions/day.	24-hr avg. Lag 02	*Hospital admissions*: MI	**Temporal:** temperature (warm: >25°C, cool: <25°C)	Case crossover. Stratification for modification.	Temperature (+): higher on warm days after adjustment by PM_{10}

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
`Cheng et al. (2009)[93]	Kaohsiung, Taiwan (1996-2006) 110,013 admissions	24-hr avg. Lag 02.	*Hospital admissions:* pneumonia	**Individual:** co-morbidity of secondary diagnosis (hypertension, diabetes, dysrhythmia, COPD, upper resp infections, asthma, cerebrovascular disease, congestive heart failure (CHF), ischemic heart failure) (on cool and warm days) **Temporal:** temperature (warm: >25^{o}C, cool: <25^{o}C)	Case crossover. Stratification for modification.	n/a
Chiu et al. (2009)[94]	Taipei, Taiwan (1996-2004). 152,594 admissions. avg 46 admissions/day.	24-hr avg. Lag 02	*Hospital admissions:* pneumonia.	**Temporal:** temperature (warm: ≥23^{o}C, cool: <23^{o}C)	Case crossover. Stratification for modification.	Temperature (+): higher on warm days
Chiu et al. (2009)[95]	Taipei, Taiwan (2000-6). 21,581 ER visits. avg 8.44 visits/day	24-h. Lag 0.	*Hospital admissions:* arrhythmia	**Individual**: secondary diagnosis (hypertension, diabetes, CHF) **Temporal:** temperature (warm: >23^{o}C, cool: <23^{o}C)	Case crossover. Stratification for modification.	Co-morbidity: higher for those with CHF on warm days, higher for those with hypertension on cool days
Corea et al. (2012)[96]	Mantua, Italy (1/06-12/08). 781 admissions.	Daily 8-hr max. Lag 0.	*Hospital admissions:* ischemic stroke, cerebrovascular	**Individual:** sex	Case crossover. Stratification for modification.	n/a
Dales et al. (2009)[97]	7 urban centers, Santiago Province, Chile (2001-5). avg 2.5 admissions/day	24-hr avg. Lag 0, 1, 2, 3, 4, 5.	*Hospital admissions:* migraine, headache with specified cause, headache not otherwise specified	Individual: age (≤64, >64 yr), sex **Temporal**: season (warm: Oct.-Mar., cool: Apr.-Sep.)	Center-specific Poisson regression. Random effects modeling to generate overall estimate. Stratification for modification. Results for modification presented across all centers.	n/a
Dales et al. (2010)[98]	7 municipalities, Santiago, Chile (2001-2005). avg 1.549 venous thrombosis and 0.754 pulmonary embolism admissions/day.	Daily 1-hr max. distributed lags 0-14 days.	*Hospital admissions:* venous thrombosis, pulmonary embolism	**Individual:** sex, age (≤64, >64 yr) **Temporal:** season (warm: Oct.-Mar.), cool: Apr.-Sep.)	Municipality-specific time-series model. Random effects model to generate overall associations. Stratification for modification.	Age: higher for younger (venous thrombosis, pulmonary embolism) Season: higher in warm season (pulmonary embolism)
Dales et al. (2012)[99]	Santiago, Chile (1/01-12/08). avg 1.79 admissions/day	24-h. Lag 0, 1, 2, 3, 4, 5	*Hospital admissions:* principal diagnosis of diabetes	**Individual:** age (≤64, 65-74, 75-84, ≥85 yr), sex **Temporal**: season (warm: Oct.-Mar., cool: Apr.-Sep.)	Generalized linear model. Stratification for modification.	Sex: higher for women

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Díaz et al (2001)[100]	Madrid, Spain (2/91-9/96). avg 59.9 admissions/day	24-hr avg. Multiple single day lags explored.	*Hospital admissions:* unscheduled admissions excluding traumas and births, circulatory, resp	**Temporal:** season (summer: June-Sep., winter: Dec.-Mar., all year)	Univariate AutoRegressive Integrated Moving Average (ARIMA) modeling. Stratification for modification by season.	n/a (Central estimates presented only)
Freitas et al. (2010)[101]	Lisbon, Portugal (1999-2004). avg 17 resp and 31 circulatory admissions/day	Daily 1-hr max. Lag 0.	*Hospital admissions:* resp, COPD, circulatory, asthma, cardiac, IHD	**Individual:** age (<15, 15-64, >64 yr, all)	F and t tests, Pearson correlations, linear trend analysis. Stratification for modification.	n/a
Glad et al. (2012)[102]	Allegheny County, PA, U.S. (1/02-12/05). 6,979 visits	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5, 05	*Emergency room visits:* asthma as primary diagnosis	**Individual:** age (<18, 18-64, >64, all), sex, race (Caucasian American, African American, all)	Case crossover. Stratification for modification.	n/a
Gwynn and Thurston (2001)[103]	New York, NY, U.S. (1988-90). 1,096 admissions	24-hr avg. Lag 1.	*Hospital admissions:* unscheduled resp	**Individual:** race (white, non-white), insurance (privately insured or Medicare, Medicaid or uninsured)	Negative binomial regression. Stratification for modifications.	Race: higher for non-whites
Halonen et al. (2010)[104]	Helsinki (1998-2004). 36,313 CVD admissions (median 33 admissions/day), 18,465 resp admissions (median 45 admissions/day)	Daily 8-hr max during warm season (May-Sep.). Lag 0, 1, 2, 3, 4, 5, 04.	*Hospital admissions*: coronary heart disease, stroke, arrhythmia, pneumonia, asthma-COPD, CVD, resp (≥15 yr)	**Individual:** age (15-64, ≥65 yr)	Poisson regression. Stratification for modification.	n/a
Hsieh et al. (2010)[105]	Taipei, Taiwan (1996-2006). 23,420 MI admissions, avg 5.83 admissions/day	24-hr avg. Lag 02.	*Hospital admissions:* MI	**Temporal:** temperature (warm: >23^{o}C, cool: <23^{o}C)	Case crossover. Stratification for modification.	Temperature: higher on cool days (when adjusted by CO)
Jalaludin et al. (2006)[106]	Sydney, Australia (1/97-12/01). avg 55.2 CVD visits/day	24-hr avg. Lag 0, 1, 2, 3, 0-1	*Emergency department visits* (≥65 yr): CVD, cardiac disease, IHD, stroke	**Temporal:** season (warm: Nov.-Apr., cool: May-Oct.)	Time series model. Stratification for modification.	n/a
Jones et al. (1995)[107]	Baton Rouge, LA, U.S. (6.90-8/90). 1,265 visits	24-hr avg. Lag 0, 0-2.	*Emergency department visits*	**Individual:** age (0-17, 18-60, ≥61 yr)	Times series model. Stratification for modification.	Age (+/-): higher for adults than older or younger populations.
Kaplan et al. (2009)[108]	Calgary, Canada (4/99-12/06). 5,191 patients.	Daily 1-hr max. Lag 0, 1, 3, 04, 06.	*Hospital admissions:* appendicitis ≥18y	**Individual:** age (18-34, 35-64, ≥65 yr), sex **Temporally:** season (Spring: Mar.-May, Summer: June-Aug., Autumn: Sep.-Nov., winter: Dec.-Feb.)	Case crossover. Stratification for modification	Season: Higher in Autumn than Spring (some lag)
Kim et al. (2007)[109]	Seoul, Republic of Korea (2002). 92,535 visits	Daily 1-hr max, summer only. Lag 2.	*Emergency out-patient hospital visits:* asthma	**Individual:** insurance premiums (quintiles). **Community:** insurance premium by district	Case crossover. Interaction terms and stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Ko et al. (2007)[110]	Hong Kong (1/00-12/05). 61,176 hospitalizations. avg 31.9 admissions/day	Daytime avg (9 am-5 pm). Lag 0, 1, 2, 3, 4, 5, 01, 02, 05	*Emergency hospital admissions:* asthma	**Individual:** age (0-14, 15-65, >65 yr) **Temporal:** season (warm: Apr.-Nov., cool: Dec.-Mar.)	Poison regression. Stratification for modification by age; interaction terms for modification by season.	Age (-): higher for younger (15-65) than older (>65 yr)
Larrieu et al. (2007)[111]	8 cities, France (1998-2003, years varied by city). 11,105,389 admissions	24-hr avg. Lag 01	*Hospital admissions:* CVD, cardiac, IHD, stroke (all excluding outpatient units)	**Individual:** age ($\geq$65 yr, all ages)	City-specific Poisson regression. Random effects model to generate overall estimates. Stratification for modification.	n/a
Lee et al. (2007)[112]	Kaohsiung, Taiwan (1996-2003). 25,108 admissions, avg 8.6 admissions/day.	24-hr avg. ag L02	*Hospital admissions*: COPD	**Temporal:** temperature ($\geq$25°C, <25°C)	Case crossover. Stratification for modification.	n/a
Lee et al. (2007)[113]	Kaohsiung, Taiwan (1996-2004). 13,475 admissions, avg. 4.1 admissions/day	24-hr avg. Lag 02. For days >20°C	*Hospital admissions*: CHF	**Temporal:** temperature (warm: $\geq$25°C, cool: <25°C)	Case crossover. Stratification for modification.	n/a
Lee et al. (2008)[114]	Taipei, Taiwan (1996-2005). 28,070 admissions, avg 7.68 admissions/day.	24-hr avg. Lag 02.	*Hospital admissions:* primary diagnosis CHF	**Individual:** co-morbidities (with and without secondary diagnosis) (warm days only)	Case crossover. Stratification for modification.	n/a
Lee et al. (2003)[115]	Republic of Korea (12/97-12/99). avg 12.4 admissions/day	Daily 1-hr max. Lag 1, 2, 3	*Hospital admissions:* IHD ($\geq$64 yr)	**Individual:** age ($\geq$64 yr, all ages) **Temporal:** season (summer: June-Aug., all year)	Time-series model. Stratification for modification.	Age (+): higher for older populations than all ages (year-round results).
Linn et al. (2000)[116]	Los Angeles, CA, U.S. (1992-Dec. 21, 1995). Avg 406-450 CVD, 172-241 pulmonary, 72-77 cerebrovascular admissions/day per season	Daily 1-hr max. Lag 0, 1.	*Hospital admissions:* CVD, pulmonary, cerebrovascular, abdominal ($\geq$30 yr)	**Temporal**: season (winter: Jan.-Mar., spring: Apr.-June, summer: July-Sep., autumn: Oct.-Dec.)	Poisson regression. Stratification for modification.	Season: higher in summer than winter (abdominal); higher in spring than summer than winter (CVD)
Luginaah et al. (2005)[117]	Windsor, Ontario, Canada (4/95-12/00). 4,214 admissions	24-h. Lag 0, 01, 02	*Hospital admissions*: resp diseases	**Individual:** sex (by age), age (0-14, 15-64, $\geq$65 yr)	Time-series. Case crossover. Stratification for modification.	n/a
Mann et al. (2012)[118]	Southern California Air Basin, U.S. (1988-95). 54,863 admissions.	Daily 8-hr max (Apr.-Oct.). Lag 0, 1, 2, 01, 02, 03	*Hospital admissions:* IHD (Southern California Kaiser Permanente members)	**Individual**: co-morbidities (with or without secondary diagnosis of CHF or arrhythmia) **Temporal:** season (warm season: Apr.-Oct., all year)	Poisson regression. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Medina-Ramon et al. (2006)[119]	36 cities, U.S. (1986-99). 578,006 COPD admissions, 1,384,813 pneumonia admissions.	Daily 8-hr max. Lag 0, 1, 2	*Hospital admission:* emergency or urgent admissions COPD, pneumonia ($\geq$65 yr)	**Temporal:** season (warm, cool) (16 cities) **Community:** mean summer (June-Aug.) apparent temperature, variance of summer apparent temperature, % of those $\geq$65y in poverty, prevalence of central AC, annual mortality rate for emphysema for those $\geq$65y as smoking indicator (all for warm season only)	Case crossover. Random effects model to generate overall effect and investigate modification.	Season: higher in warm season (COPD, pneumonia) Temperature variance (-): higher with lower variance of summer apparent temperature (COPD) AC: higher with lower AC prevalence (pneumonia)
Middleton et al. (2008)[120]	Nicosia, Cyprus (1/95-12/04). 178,091 admissions	24-hr avg, daily 8-hr max. Lag 0, 1, 2	*Hospital admission:* total, CVD, resp, CVD+resp	**Individual:** sex, age (<15, $\geq$15 yr, for total admissions, resp) **Temporal:** season (warm: Apr.-Sep., cool: Nov.-Mar.) (total, CVD, resp)	Poisson regression. Stratification for modification by age; interaction terms for modification by season.	Sex: higher in women (resp) Season: higher in warm season for persons $\geq$15
Moolgavkar (2000)[121]	Los Angeles Co., CA; Maricopa Co., AZ, Cook County, IL (1987-95). Median 33-172 CVD and 13-63 resp admissions/day	24-hr avg. Lag 0, 1, 2, 3, 4, 5	*Hospital admissions:* CVD, cerebrovascular ($\geq$65 yr)	**Temporal**: season (warm: Apr.-Sep., all year)	County-specific Poisson regression. Stratification for modification. Modification results for each city.	n/a
Morgan et al. (1998)[122]	Sydney, Australia (1/91-12/94). avg 47.2 heart disease admissions/day, 15.5 (1-14 yr) and 9.0 (15-64 yr) asthma admissions/day	Daily 1-hr max. Lag 0, 1, 2, cumulative lags.	*Hospital admissions*: asthma, heart disease	**Individual:** age (1-14, 15-64y for asthma; 0-64, $\geq$65 yr, all ages for heart disease)	Poisson regression. Stratification for modification.	n/a
Namdeo et al. (2011)[123]	Lees, West Yorkshire, UK (4/02-12/05). 20,961 admissions	Daily 8-hr max. Lag 1, 2, 3	*Hospital admissions:* resp	**Individual:** age (<60, 60-69, 70-74, 75-79, $\geq$80 yr)	Poisson regression. Stratification for modification.	Age (+/-): higher for 70-74 than $\geq$80 or <60y for lag 0, higher for $\geq$80 than <60y for lag 2
Nauenberg and Basu (1999)[124]	Los Angeles, CA, U.S. (1991-4). 11,240 asthma admissions. 34,564 control admissions	24-hr avg. Lag 0, 07.	*Emergency and urgent hospital admissions*: asthma, non-resp (control group)	**Individual::** insurance (total asthma; asthma with Medical, CA's Medicare program; insurance other than Medical; uninsured)	Poisson regression. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Oudin et al. (2010)[125]	Scania, Sweden (1/01-12/05). 11,267 ischemic stroke admissions, 1,681 hemorrhagic stroke admissions	24-hr avg. Lag 0, 1, 2	*Hospital admissions:* ischemic stroke, hemorrhagic stroke	**Individual:** sex, age at diagnosis (<78, >78 yr), smoking (≥1 cigarette/day 3 months prior to stroke, <1 cigarette/day), residence in major city (yes, no) **Temporal:** season (warm: May-Sep., cool: Oct.-May)	Poisson regression. Case crossover. Stratification and interaction terms for modification.	n/a
Paulu and Smith (2003)[126]	Maine, U.S. (2000-2). 8,020 visits	Daily 8-hr max. Lag 0, 1, 2, 3, 4, 03.	*Hospital emergency department visits:* asthma (≥2 yr)	**Individual:** age (2-14, 15-34, 35-64, ≥65 yr), sex (by age) **Temporal:** season (warm: 28-day period starting May 22 or 23 and ending Sep. 10 or 11, cool: remaining days)	Case crossover. Stratification for modification.	n/a
Peel et al. (2007)[127]	Atlanta, GA, U.S. (1/93-8/00). 156,283 visits	Daily 8-hr max (warm season). Imputed values for days missing data. Lag 02	*Emergency department visits:* IHD, dysrhythmia, peripheral and cerebrovascular disease, CHF	**Individual:** co-morbidity of secondary diagnosis (hypertension, diabetes, COPD, CHF, dysrhythmia)	Case crossover. Stratification for modification.	Co-morbidity: higher for those with COPD (peripheral and cerebrovascular disease)
Pereira Filho et al. (2008)[128]	Sao Paulo, Brazil (1/01-7/03). avg 17.4 visits/day	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5, 6, cumulative lags from lag 01 to 06.	*Emergency room visits:* CVD (≥18 yr)	**Individual:** comorbidity (with and without diabetes)	Times series. Stratification for modification.	n/a
Petroeschevsky et al. (2001)[129]	Brisbane, Australia (1/97-12/94). avg 30.1 admissions/day	Daily 1-hr max, 8-hr avg (10 am-6 pm). Lag 0, 1, 2, 3, 02, 04.	*Emergency hospital admissions:* resp, asthma, CVD	**Individual:** age (resp: 0-4, 5-14, 15-64, ≥65y; asthma: 0-14, 15-64; CVD: 15-64, ≥65 yr)	Poisson regression. Interaction terms for modification by season; stratification for modification by age.	Age (+): higher for ≥65 than 0-4y (resp) Season: higher for winter (resp 15-64 yr), lower in autumn (resp ≥65 and all ages), lower in winter (asthma 0-14 yr), higher in summer (CVD all ages), lower in spring (CVD, all ages)
Poloniecki et al. (1997)[130]	London, U.K. (4/87-3/94). avg 26.7 admissions/day	8-hr avg (9 am-5 pm). Lag 1	*Hospital admissions*: acute MI	**Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Stratification for modification.	n/a
Ponce de Leon et al. (1996)[131]	London, U.K. (4/87-2/92). avg 125.7 admissions/day	Daily 1-hr max, 8-hr avg (9 am-5 pm). Lag 0, 1, 2, 01, 02	*Hospital admission:* resp	**Individual:** age (0-14, 15-64, ≥65 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Stratification for modification.	Age (+): higher for ≥65 than 0-4y Season: higher in warm season (all ages, 15-64, ≥65 yr)

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Prescott et al. (1998)[43]	Edinburgh, Scotland (10/92-6/95). avg 12.1 CVD and 6.9 resp admissions/day	24-hr avg. Lag 0, 1, 02.	*Hospital admissions*: CVD, resp	**Individual:** age (<65, >65 yr), co-morbidities: previous CVD/resp admissions (all, >1, >2, >4)	Poisson regression. Stratification for modification.	n/a
Qiu et al. (2012)[132]	Hong Kong (1/98-12/07). 3,652 admissions	8-hr avg (10 am-6 pm). Lag 0, 1, 2, 3, 01, 02, 03.	*Emergency hospital admissions:* IHD	**Temporal:** season (warm: May-Oct., cool: Nov.-Apr.), relative humidity (<80%, >80%), season and humidity (warm/dry, warm/humid, cool/dry, cool/humid)	Poisson regression. Interaction terms for modification.	Season: higher for cool season Humidity (-): higher for low humidity days Season/humidity: lower for warm/humid than warm/dry or cool/dry
Sarnat et al. (2013)[133]	Atlanta, GA (1/99-12/02). 270,816 visits	24-hr avg. Lag 02	*Emergency department visits*: asthma and wheeze	**Community:** low or high air exchange rate (AER) (above or below median, tertiles), % in poverty (low, high).	Poisson regression for each of 186 zip codes. Interaction terms for modification by AER, stratification for modification by both poverty and AER.	n/a
Santus et al. (2012)[134]	Milan, Italy (1/07-12/08). 45,770 admissions.	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5, 02, 3-5.	*Emergency room admissions:* upper resp tract infection, asthma, pneumonia, COPD exacerbation	**Individual:** sex, age (COPD exacerbation: >65 yr, all ages; other causes: >16, >65 yr, all ages), race (Caucasian, other) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Case crossover. Stratification for modification.	Sex: higher for women (COPD exacerbation) Race: lower for Caucasian (asthma, pneumonia), higher for Caucasian (COPD exacerbation) Season: higher for warm season (upper resp tract infection, asthma)
Schouten et al. (1996)[135]	Amsterdam and Rotterdam, The Netherlands (1977-89). avg 6.70 (Amsterdam) and 4.79 (Rotterdam) resp admissions/day	24-hr avg, daily 8-hr max. Lag 0, 1, 2, 01, 02, 03, 04, 05.	*Hospital admissions:* resp, COPD, asthma (Amsterdam only)	**Individual:** age (15-64, >65 yr, resp) (age for Rotterdam modeled separately for 1977-81, 1982-4, 1985-9) **Temporal**: season (summer: May-Oct., winter: Nov.-Apr. , by age)	Poisson regression. Interaction terms for modification. Method to generate overall effect not specified. Modification results presented for each city. Modification for both cities combined for resp all ages.	Age (+): higher for older group (resp, Rotterdam, 1977-81) Season: higher in summer (resp, all ages, overall)
Schwartz (1994)[136]	Birmingham, AL, U.S. (Mar.-Nov., 1/86-12/89). avg 5.9 pneumonia and 2.2 COPD admissions/day	24-hr avg, daily 1-hr max. Lag 0, 1, 2	*Hospital admissions:*	**Temporal:** season (warm: Apr.-Aug., all year, for pneumonia); temperature (excluding extreme temperature, all days)	Poisson regression. Stratification for modification.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Schwartz (1996)[137]	Spokane, WA, U.S. (Apr.-Oct., 1/88-12/90). 4,241 admissions. avg. 2.9 admissions/day.	24-h, daily 1-hr max. Lag 0, 1, 2	*Hospital admissions*: resp (≥65 yr)	**Temporal:** temperature (all days, exclude extreme temperature: <16.4^{o}F or >76.6^{o}F) (resp)	Poisson regression. Stratification for effect medication.	n/a
Silverman and Ito (2010)[138]	New York, NY, U.S. (Apr.-Aug., 1999-2006). 6,008 ICU admissions, median 5 admissions/day. 69,375 non-ICU admissions, median 54 admissions/day.	Daily 8-hr max. Lag 01, 04	*Hospital admissions:* ICU asthma, non-ICU asthma	**Individual:** age (<6, 6-18, 19-49, ≥50 yr)	Poisson regression. χ^2 test for heterogeneity of effect estimates by age groups.	Age (+/-): higher for 6-18 than other age groups (non-ICU asthma admissions)
Son et al. (2013)[139]	8 cities, Republic of South Korea (1/03-12/08). avg 5.7-36.3 admissions/day per city	Daily 8-hr max. Lag 0, 1, 2, 3, 01, 02, 03.	*Hospital admissions:* allergic disease, asthma, selected resp disease, CVD	**Individual:** sex, age (0-14, 15-64, 65-74, ≥75 yr) (overall) **Temporal:** weekday (weekdays, all days), season (spring, summer, fall, winter)	City-specific Poisson regression. Bayesian hierarchical modeling to generate overall effect. Stratification for modification. Modification results for weekday and season presented for each city and overall.	Season: higher for fall than spring (Ulsan: allergic disease, asthma), higher in winter than other seasons (overall: resp), higher for winter than summer or fall (Seoul: resp), higher for summer than fall (Busan: CVD), higher for summer than spring (Ulsan: CVD)
Spix et al. (1998)[140]	4 European cities (London, Amsterdam, Rotterdam, Paris) (1977-92, years differed by city)	Daily 8-hr max from 9 am-5 pm, daily 1-hr max	*Hospital admissions:* emergency and non-emergency admissions for Paris, emergency admissions for other cities.	**Individual:** age (15-64, ≥65 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	City-specific Poisson regression. Random effects and fixed effects modeling to generate overall estimates. Analysis for season by age.	n/a
Stieb et al. (2000)[141]	Saint John, Canada (7/92-6/94). 19,821 visits. avg 14.4 visits/day.	24-hr avg, daily 1-hr max. Single day lags up to lag 10, multi-day lags up to previous 5 days.	*Emergency department visits:*	**Temporal:** season (May-Sep., all year)	Generalized additive models. Stratification for modification.	n/a
Sunyer et al. (1997)[142]	4 cities (Barcelona, Helsinki, Paris, London), Europe (1986-92, years differed by city). avg 0.7-13.1 adult admissions/day	Daily 8-hr max. Lag 0, 1, 2, 3, 01, 02, 03, 04.	*Emergency room visits and admissions*:	**Individual:** age (<15, 15-64 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	City-specific Poisson regression. Fixed effects and random effects models to generate overall effect. Stratification for modification.	n/a
Szyszkowicz (2008)[143]	Edmonton, Canada (4/92-3/02). 10,881 visits	24-h, daily 1-hr max. Lag 02.	*Emergency department visits:* acute ischemic stroke	**Individual:** age (20-64, 65-100 yr), sex **Temporal:** season (warm: Apr.-Sep, cool: Oct.-Mar., all)	Generalized linear mixed models. Clusters by time (year, month, day of week). Stratification for modification.	n/a (Central estimates presented only)

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Szyszkowicz et al. (2008)[144]	Edmonton, Canada (4/92-3/02). 62,563 visits	24-hr avg. Lag 0, 1, 2	*Emergency department visits:* asthma	**Individual:** sex (by age), age (<10, ≥10 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar., by age and sex)	Poisson regression using cluster analysis. Stratification for modification.	Age (-): higher for younger group (women in warm season)
Szyszkowicz et al. (2010)[145]	Edmonton, Canada (4/92-3/02). 69,547 visits	24-hr avg. Lag 0, 1, 2, 3, 4	*Emergency department visits:* cellulitis	**Individual:** sex, age men: 0-2, 12-14, 15-34, 35-65, ≥66y; women: 3-11, 15-34, 35-64, ≥66 yr) **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Case crossover. Stratification for modification.	Sex: higher for men (all year, cool season), higher for women (warm season) Age (+/-): higher for 0-2 than 15-34 (men), higher for 35-65 than 15-43 (women) Season: higher for warm season (all, women)
Szyszkowicz et al. (2010)[146]	Vancouver, Canada (1/99-2/03). avg 1.1 visits/day. 1,605 visits.	24-hr avg. Lag 0, 1, 2	*Emergency department visits:* suicide attempt or ideation	**Individual:** sex **Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression to clustered counts. Case crossover. Stratification for modification.	n/a (Central estimates presented only)
Szyszkowicz and Rowe (2010)[147]	Edmonton, Canada (3/92-3/02) 68,714 chest pain visits, 66,092 weakness visits	24-h. Lag 0, 1, 2	*Emergency department visits:* chest pain, weakness	**Individual:** sex **Temporal:** season (warm, cool, designations not specified)	Poisson regression to clustered counts. Stratification for modification.	n/a (Central estimates presented only)
Ténias et al. (1998)[148]	Valencia, Spain (1994-5). avg 1 visit/day	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5	*Hospital emergency visits:* asthma (≥14 yr)	**Temporal:** season (warm: May-Oct., cool: Nov.-Apr.)	Poisson regression. Stratification and interaction terms for modification.	n/a
Tenías et al. (2002)[149]	Valencia, Spain (1/94-12/95). 1,298 admissions	Daily 1-hr max. Lag 0, 1, 2, 3, 4, 5	*Hospital admissions:* COPD (≥14 yr)	**Temporal:** season (warm: May-Oct., cool: Nov.-Apr.)	Poisson regression. Interaction terms for modification.	n/a
Tsai et al. (2003)[150]	Kaohsiung, Taiwan (1997-2000). 23,179 admissions. avg 3.55 primary intracerebral hemorrhage, 8.73 ischemic stroke admissions/day	24-hr avg, Lag 02	*Hospital admissions*: stroke (primary intracerebral hemorrhage, ischemic stroke)	**Temporal:** temperature (<20°C, ≥20°C)	Case crossover. Stratification for modification	n/a
Tsai et al. (2006)[151]	Kaohsiung, Taiwan (1996-2003). 17,682 admissions. avg 6.05 admissions/day	24-hr avg. Lag 02	*Hospital admissions*: asthma	**Temporal:** temperature (warm: ≥25°C, cool: <25°C)	Case crossover. Stratification for modification.	Temperature (+): higher on warm days (adjusted for NO_2 or PM_{10})
Tsai et al. (2009)[152]	Taipei, Taiwan (2000-6). 21,581 visits. avg 8.44 visits/day	24-hr avg. Lag 0	*Emergency room visits*: cardiac arrhythmia	**Temporal:** temperature (<23°C, ≥23°C)	Case crossover. Stratification for modification.	n/a

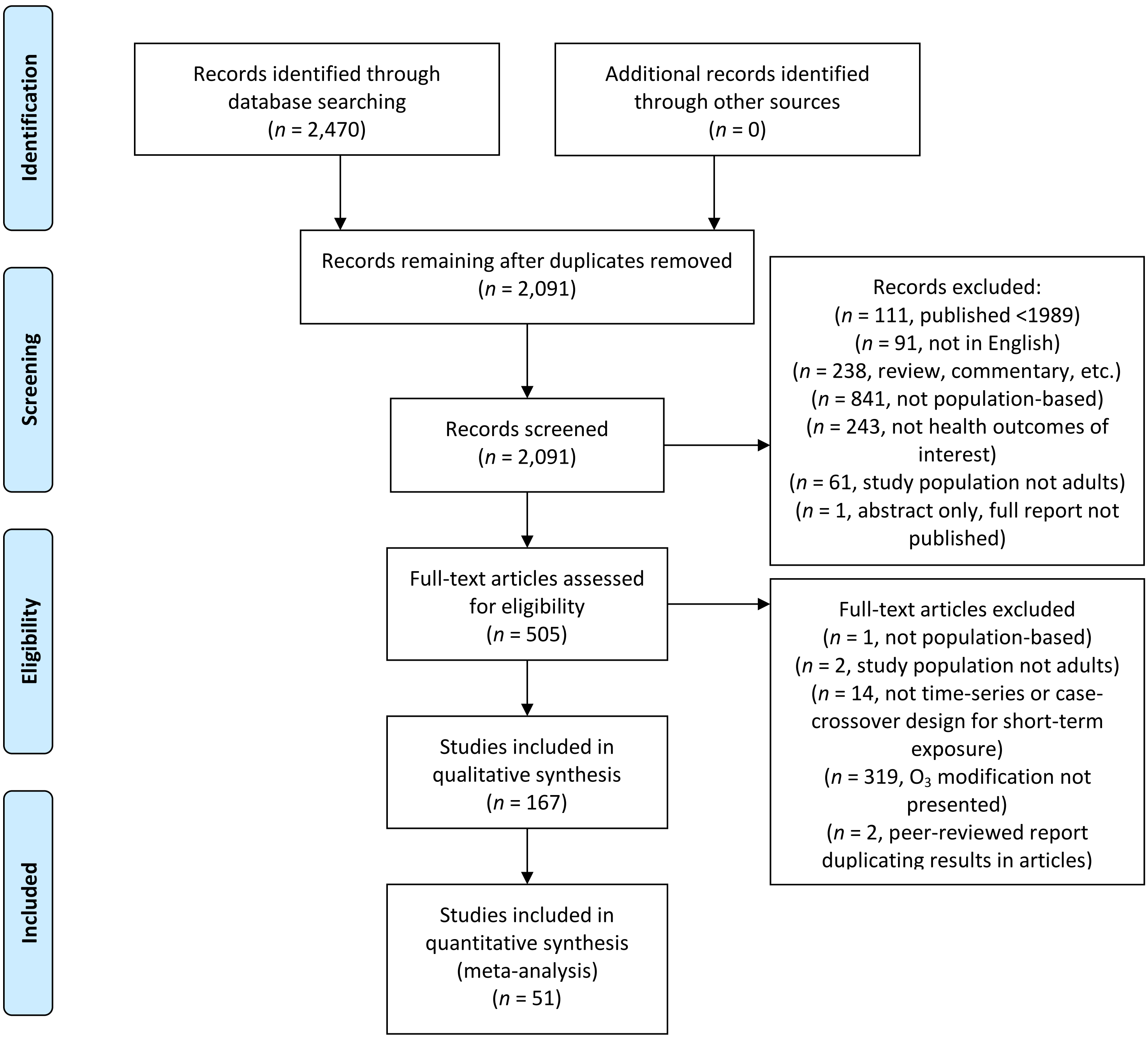
Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Tsai et al. (2012)[153]	Taipei, Taiwan (1999-2009). avg 6.86 admissions/day	Lag 02.	*Hospital admission:* primary diagnosis of MI	**Individual:** Secondary diagnosis of hypertension, diabetes, dysrhythmia, CHF, COPD, pneumonia, upper resp infections, asthma **Temporal:** temperature (warm: >23°C, cool: <23°C)	Case crossover. Stratification for modification by both temperature and comorbidity.	n/a
Villeneuve et al. (2006)[154]	Edmonton, Alberta, Canada (4/92-3/02). 12,422 visits	Daily 1-hr max. Lag 0, 12, 02	*Emergency department visits:* acute ischemic stroke, hemorrhagic stroke, transient cerebral ischemic (≥65 yr)	**Individual**: sex (by season) **Temporal**: season (warm: Apr.-Sep., cool: Oct.-Mar.)	Case crossover. Stratification for modification.	Season: higher in warm season for transient cerebral ischemic
Villeneuve et al. (2007)[155]	Edmonton, Alberta, Canada (4/92-3/02). 58,888 visits.	Daily 1-hr max. Lag 0, 1, 02, 04	*Emergency department visits:* asthma	**Individual:** age (2-4, 5-14, 15-44, 45-64, 65-74, ≥75 yr) **Temporal**: season (warm: Apr.-Sep., cool: Oct.-Mar.)	Case crossover. Stratification for modification.	Age (-): higher 2-4 than 65-74y (cool season) Season: higher for cool than warm (5-14 yr)
Villeneuve et al (2012)[156]	Edmonton, Alberta, Canada (2003-2009). 5,927 visits	Daily 1-hr max. Lag 0, 01, 02	*Hospital visits*: all strokes, ischemic stroke, hemorrhagic stroke, transient ischemic attack	**Temporal**: season (warm: Apr.-Sep., cool: Oct.-Mar.)	Case crossover. Stratification for modification.	Season: higher in warm season (ischemic stroke, hemorrhagic stroke), higher in cool season (transient ischemic stroke)
Wilson et al. (2005)[157]	Portland, Maine, US (Apr.-Sep., 1998-2000) and Manchester, New Hampshire, US (Apr.-Sep., 1996-2000). avg 2.6-7.4 asthma, 16.6-49.0 resp admissions/day per city	Daily 8-hr max. Lag 1, 01, 04, and other unspecified lags.	*Emergency room visits:* resp, asthma	**Individual:** age (0-14, 15-64, ≥65 yr) **Community:** season (summer: June-Aug., Apr.-Sep.)	Poisson regression. Stratification for modification. Associations presented separately for each city.	n/a

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Winquist et al. (2012)[158]	St. Louis, U.S. (1/01-6/07). 5,709,926 emergency department visits, 1,999,708 hospital admissions	Daily 8-hr max. Lag 04.	*Emergency department visits, hospital admissions, hospital admissions through emergency department, non-elective hospital admissions*: resp, asthma/wheeze, pneumonia, CVD, dysrhythmia, CHF	**Individual:** age (0-1, 2-18, 19-64, $\geq$65 yr, not all age categories for all outcomes) **Community:** zip-code level poverty area (yes, no)	Poisson regression. Stratification for modification.	Age (+/-): lower for $\geq$65 than 0-1 or 2-18y (emergency department visits: resp); lower for $\geq$65 than 2-18 y (hospital admissions through ED: resp); lower for 19-64 than 2-18y (emergency department: asthma/wheeze); higher for 0-1 than 2-18 or 19-64y (hospital admissions: pneumonia); higher for 0-1y than other age groups (non-elective hospital admissions, hospital admission through ED: pneumonia); higher for $\geq$65 than 19-64y (hospital admissions through ED: CVD) Poverty (+): higher for poverty areas (emergency department visits: CVD, dysrhythmia)
Wong et al. (1999)[159]	Hong Kong (1994-5). avg 131 resp, 101 CVD admissions/day	24-hr avg. Lag 0, 1, 2, 3, 4, 5, cumulative lags up to 5 days	*Emergency hospital admissions*: resp, CVD	**Individual:** age (0-4, 5-64, $\geq$65 yr) **Temporal:** season (cool: Dec.-Mar., all year)	Poisson regression. Interaction terms for modification by season; stratification for modification by age.	Age (+): higher for eldest than 5-64 than 0-4y (resp)
Wong et al. (2002)[160]	Hong Kong (1995-7), London, U.K. (1992-4)	Daily 8-hr max. Lag 0, 1, 2, 3, 01.	*Emergency hospital admissions:* asthma (15-64 yr), resp ($\geq$65 yr), cardiac (all ages), IHD (all ages)	**Temporal**: season (warm: Apr.-Sep., cool: Oct.-Mar.)	Poisson regression. Interaction terms for modification. Modification results presented for each city.	Season: higher in cool season (cardiac, all ages, Hong Kong.), higher in warm season (although protective) in warm season (asthma, 15-64 yr, London)
`Xu et al. (2013)[161]	Allegheny Co., PA, U.S. (9/94-12/00). 26,210 stroke admissions	24-hr avg. Lag 0, 1, 2, 3	*Hospital admission:* stroke, ischemic stroke $\geq$65y	**Individual:** age (65-79, $\geq$80 yr), sex	Case crossover. Stratification for modification.	n/a
Yang et al. (2003)[162]	Vancouver, CA, U.S. (1986-98). avg 9.4 admissions/day ($\geq$65 yr)	24-hr avg, daily 1-hr max. Lag 1, 2, 3, 4, 5	*Hospital admissions:* resp (<3, $\geq$65 yr)	**Community:** family income (quintiles)	Case crossover. Stratification for modification.	n/a
Yang et al. (2004)[163]	Kaohsiung, Taiwan (1997-2000). 29,661 admissions. avg. 20 admissions/day.	24-hr avg. Lag 02.	*Hospital admissions:* CVD	**Temporal:** temperature (warm: $\geq$25°C, cool: <25°C)	Case crossover. Stratification for modification.	Temperature (+): higher effect for warmer days.
Yang et al. (2006)[164]	Taipei, Taiwan (1996-2004). 24,240 admissions. avg. 7.37 admissions/day.	24-hr avg.	*Hospital admissions:* CHF	**Temporal:** temperature (warm: $\geq$20°C, cool: <20°C)	Case crossover. Stratification for modification	Temperature (+): higher effect for warmer days.

Study	Location and Time Frame	Exposure and Lag Structure	Health Outcome	Potential Effect Modifiers	Statistical Models	Statistically Significant Results
Yang et al. (2007)[165]	Taipei, Taiwan (1996-2003). 25,602 admissions, avg 8.76 admissions/day	24-hr avg. Lag 02.	*Hospital admissions:* asthma	**Temporal:** temperature (warm: $\geq$25°C, cool: <25°C)	Case crossover. Stratification for modification.	Temperature (-): higher for cooler days
Yang et al. (2007)[166]	Taipei, Taiwan (1996-2003). 46,491 admissions. avg 15.91 admissions/day	24-hr avg. Lag 02.	*Hospital admissions:* COPD	**Temporal:** temperature (warm: $\geq$20°C, cool: <20°C)	Case crossover. Stratification for modification.	Temperature (+): higher for warmer days
Zanobetti and Schwartz (2006)[167]	Boston, MA (1995-9). 15,578 MI admissions, 24,857 pneumonia admissions.	24-hr avg. Lag 0, 01.	*Emergency hospital admissions:* MI, pneumonia	**Temporal:** season (warm: Apr.-Sep., cool: Oct.-Mar.)	Case crossover. Interaction terms for modification.	n/a

Web Figure 1 – PRISMA flow diagram showing number of studies identified, included, or excluded from analysis

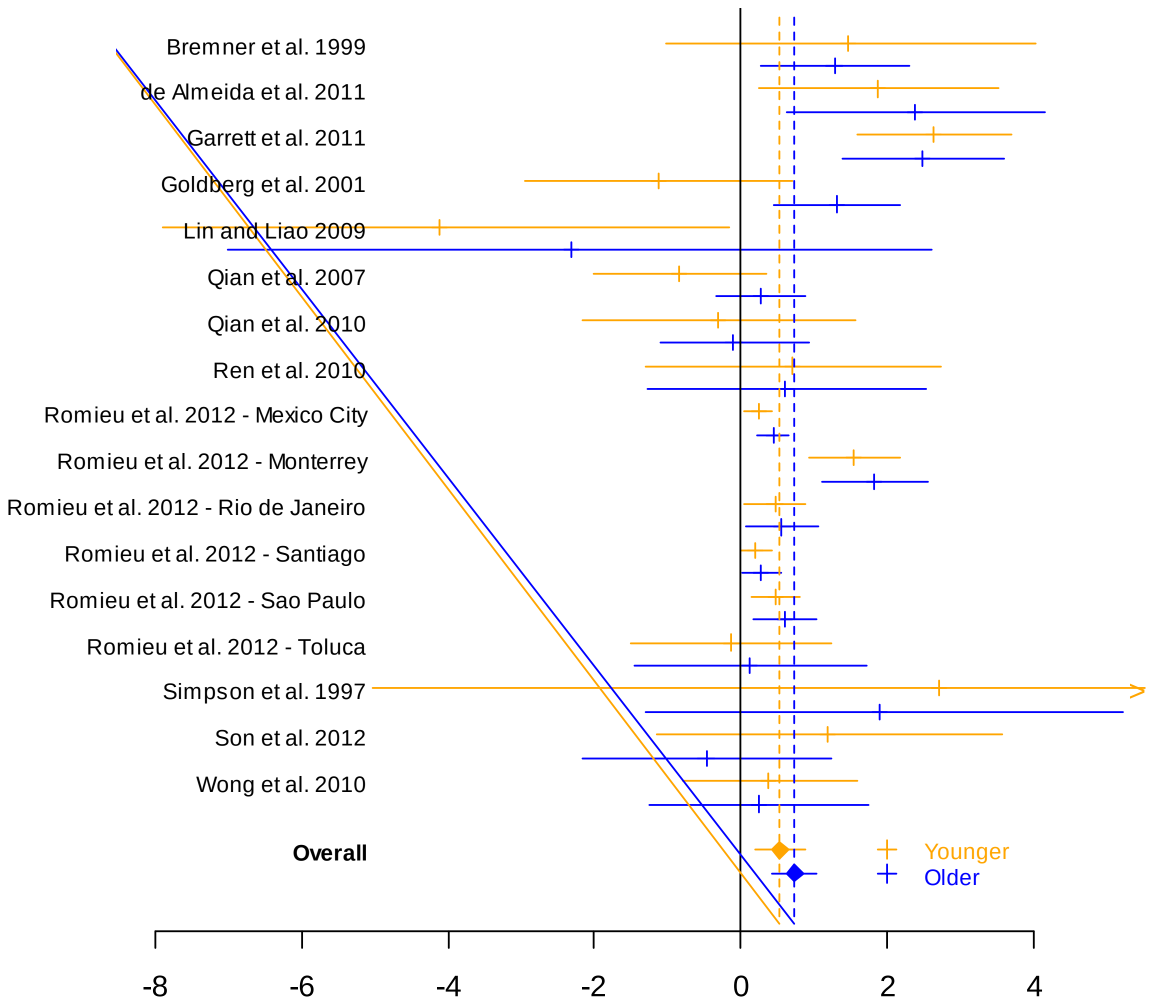
Note: Format from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med.* 2009;6(6): e1000097. (doi:10.1371/journal.pmed1000097).
For more information, visit www.prisma-statement.org.



Web Figure 2. Summary of study characteristics across 167 studies of ozone and mortality or hospital admissions

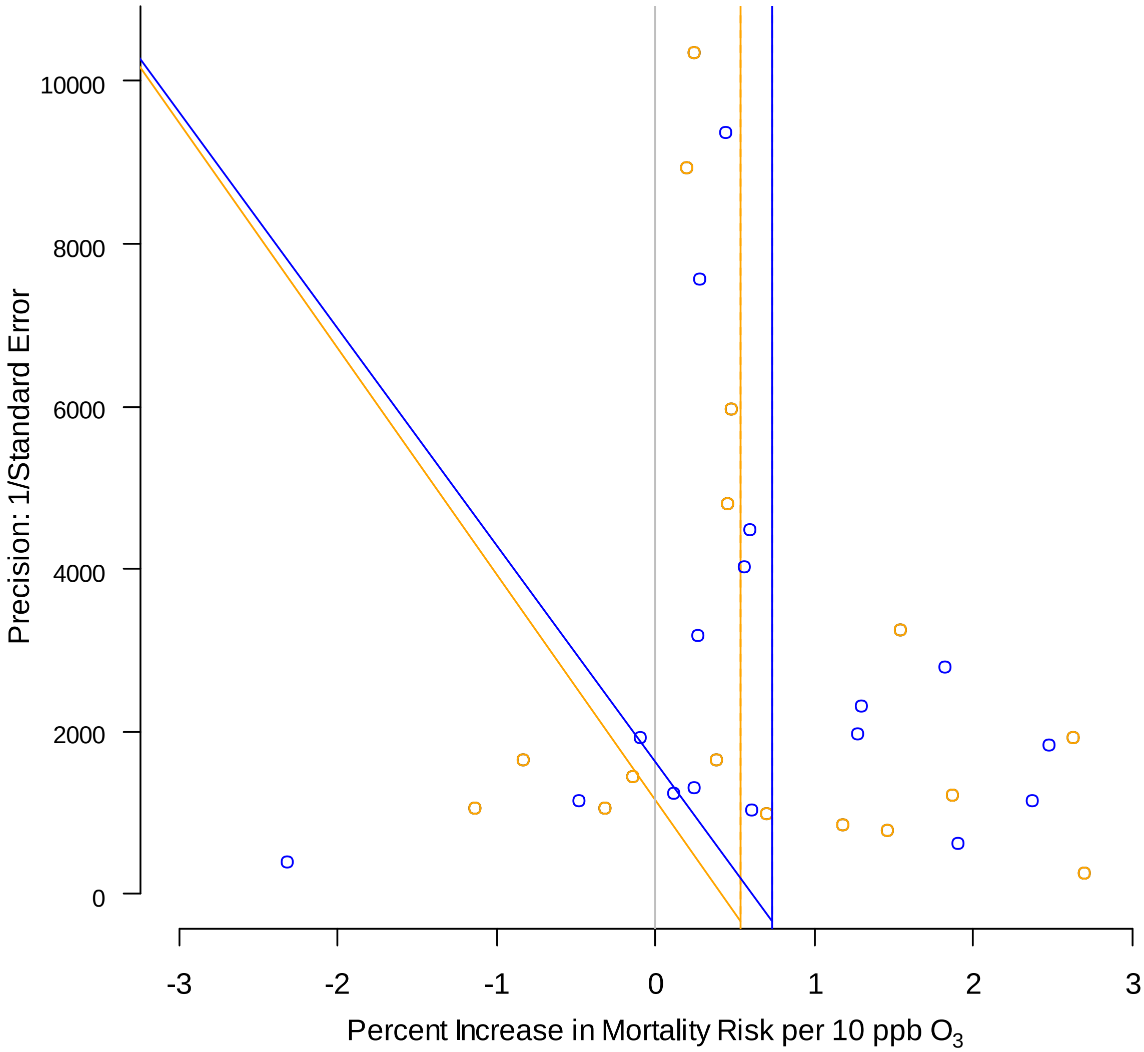
Web Figure 3. Percent increase in risk of cardiovascular mortality for 10-ppb increase in 8-hr ozone for studies included in meta-analysis, by age

Note: Horizontal lines represent 95% intervals. The overall results reflect meta-analysis findings.



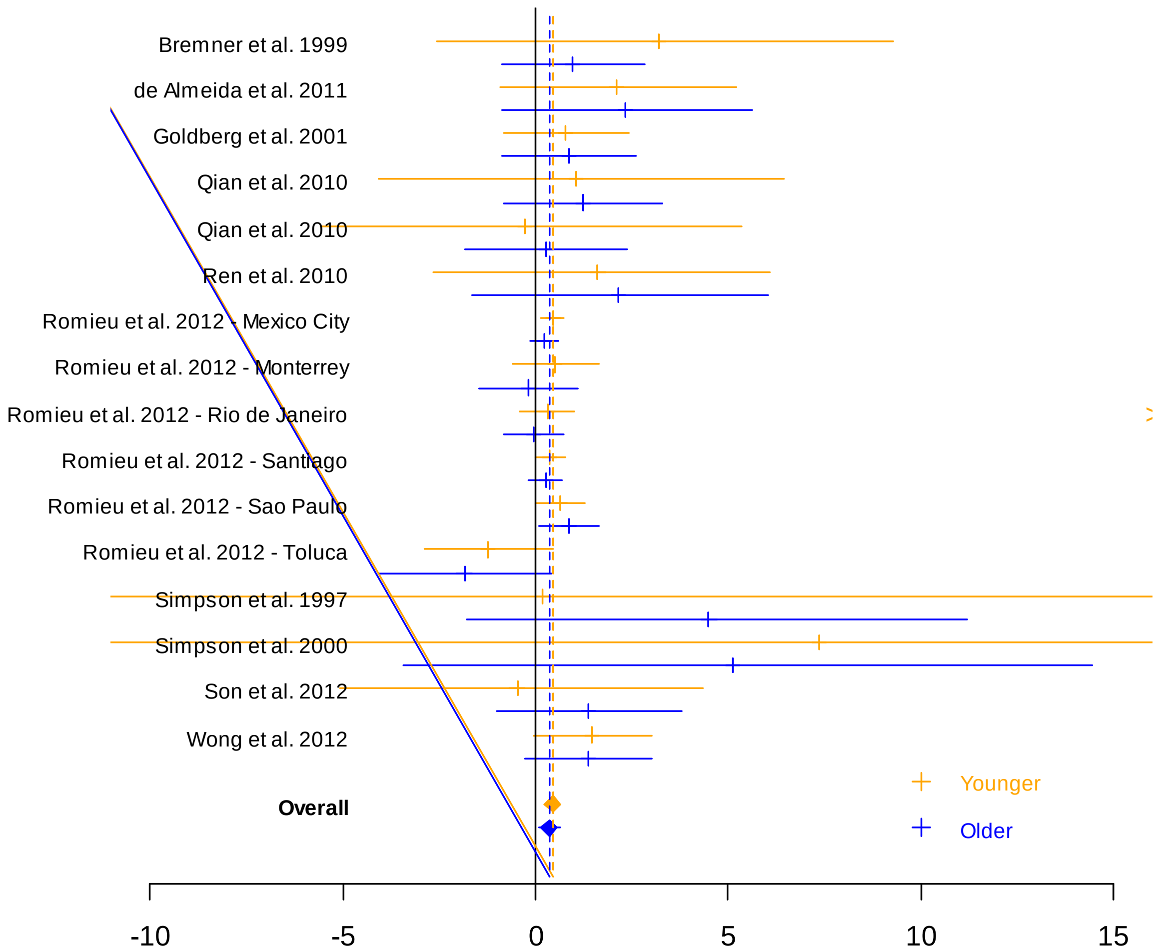
Web Figure 4. Funnel plot for estimates of association between ozone and cardiovascular mortality for studies included in meta-analysis, by age

Note: Effect estimates show the percentage increase in risk per 10-ppb increase in 8-hr ozone. Open circles represent study estimates. Solid vertical lines represent overall estimates based on study results. Orange and blue represent estimates for younger and older populations, respectively.



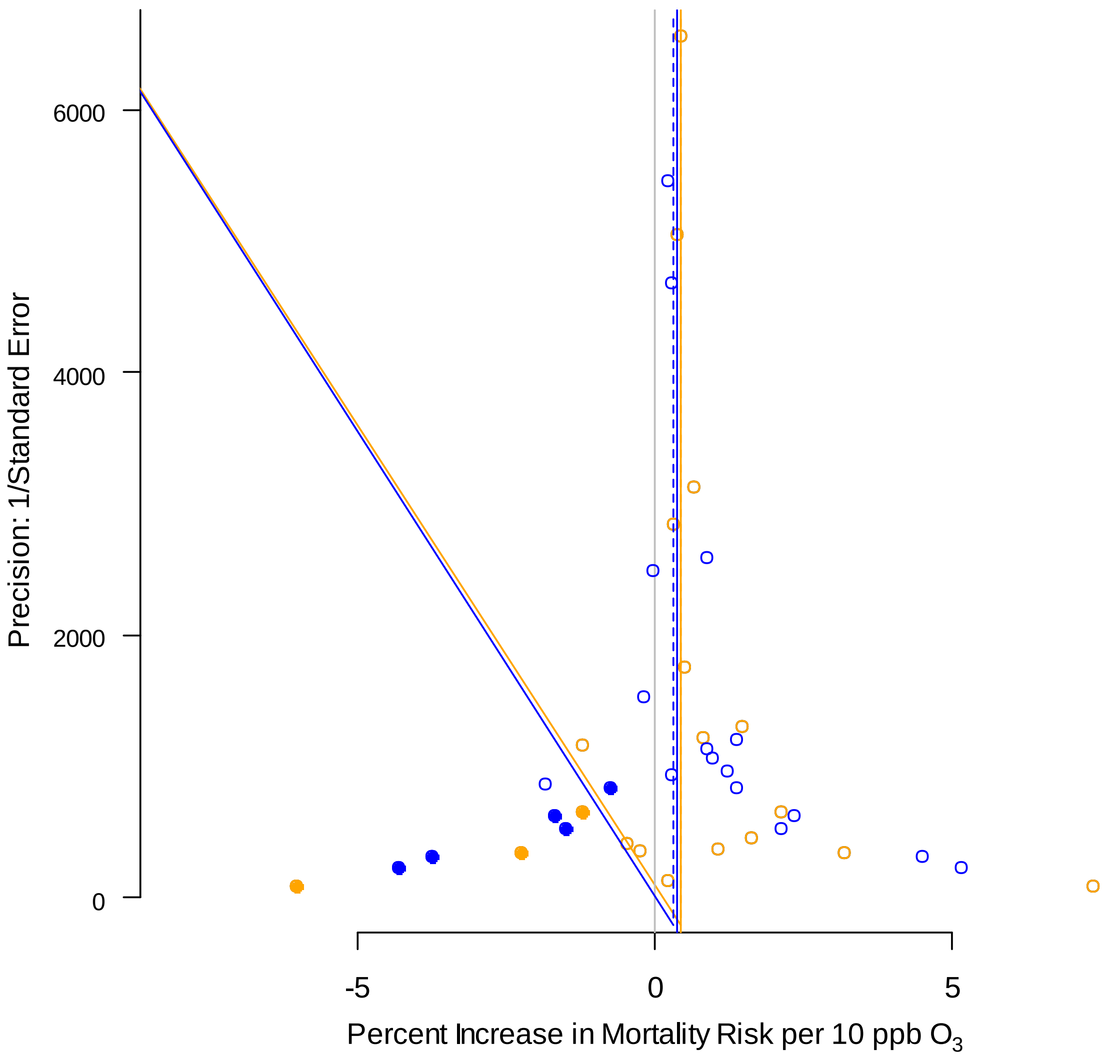
Web Figure 5. Percent increase in risk of respiratory mortality for 10-ppb increase in 8-hr ozone for studies included in meta-analysis, by age

Note: Horizontal lines represent 95% intervals. The overall results reflect meta-analysis findings.



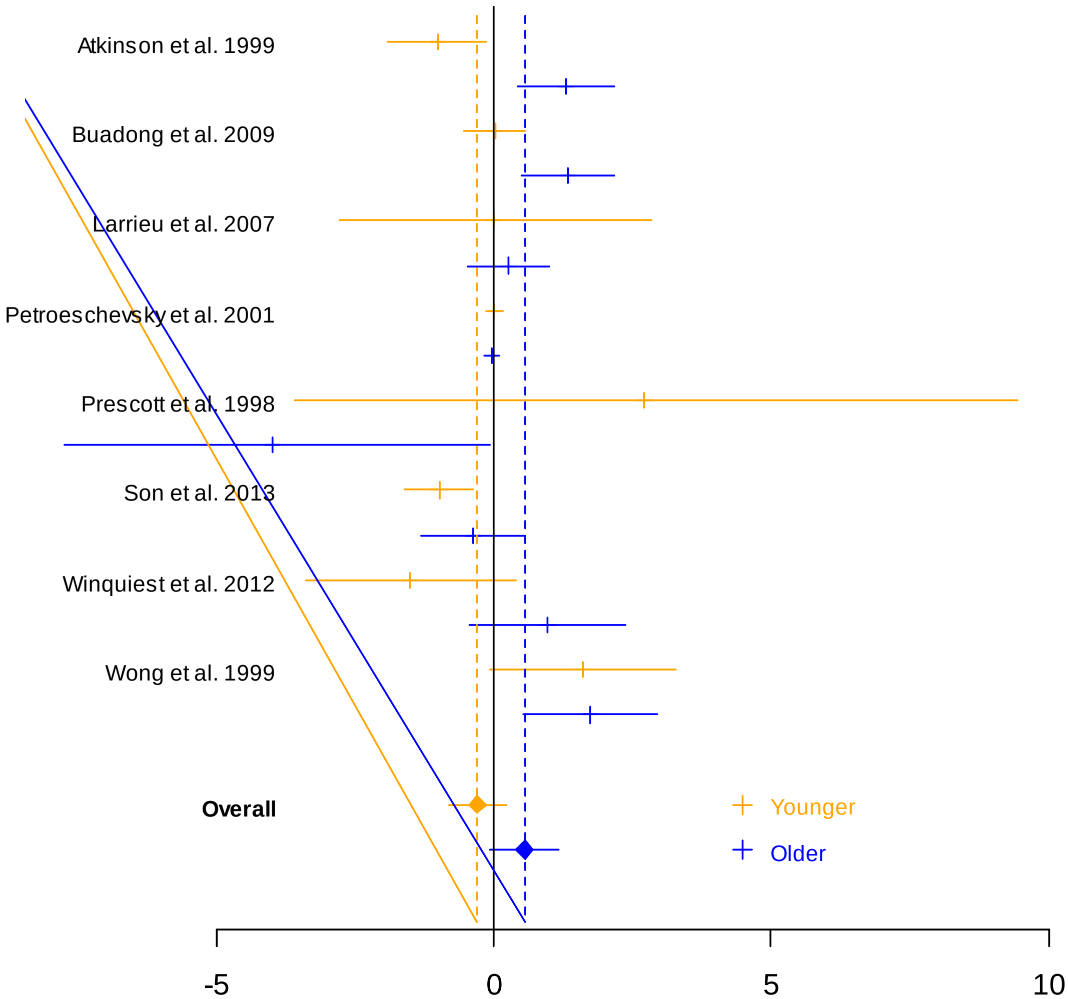
Web Figure 6. Funnel plot for estimates of association between ozone and respiratory mortality for studies included in meta-analysis, by age

Note: Effect estimates show the percentage increase in risk per 10-ppb increase in 8-hr ozone. Open circles represent study estimates; closed circles represent "missing studies" from the trim-and-fill method to adjust for publication bias. Solid vertical lines represent overall estimates based on study results; dashed lines represent overall estimates adjusted for publication bias. Orange and blue represent estimates for younger and older populations, respectively.



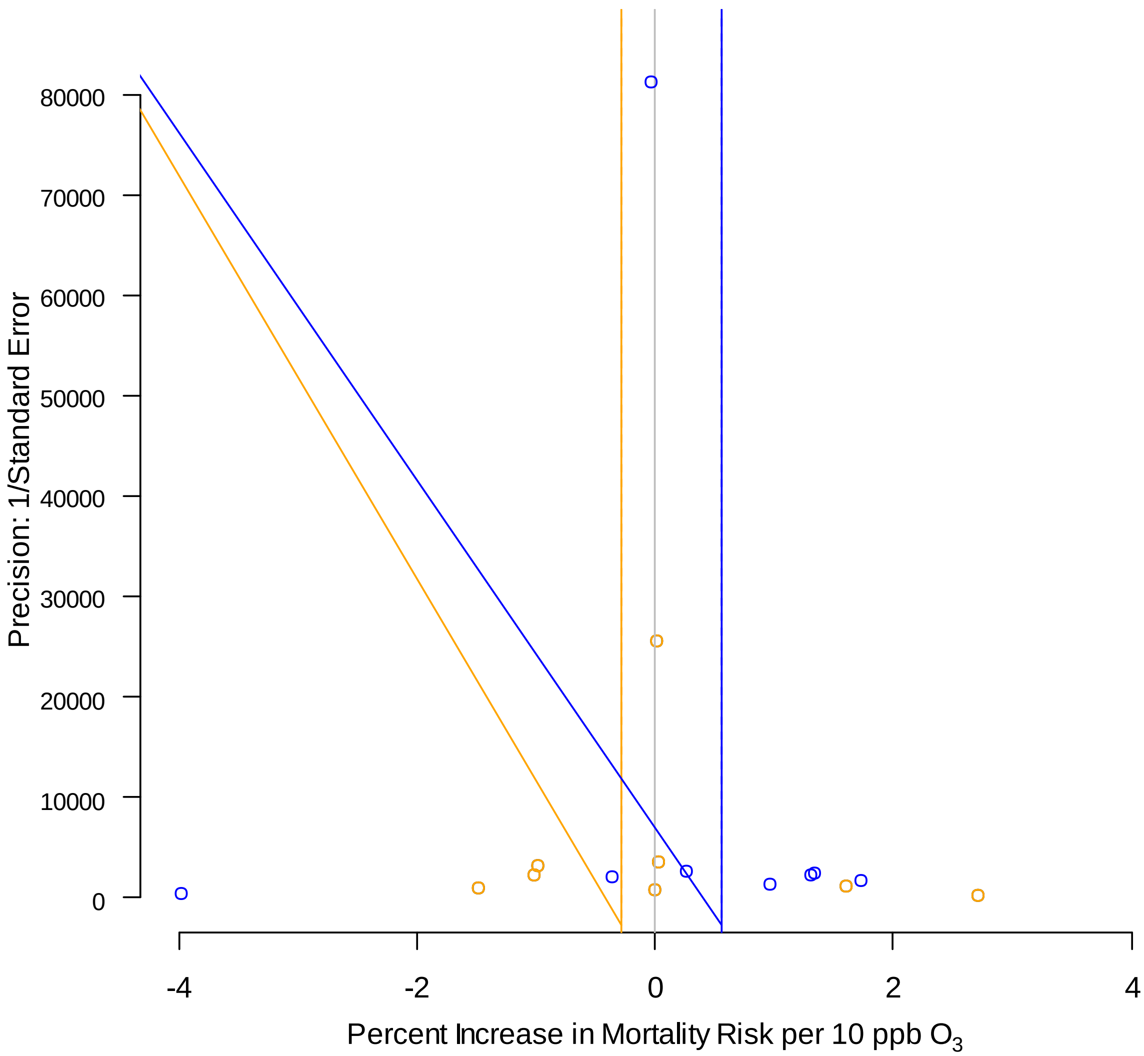
Web Figure 7. Percent increase in risk of cardiovascular hospital admissions for 10-ppb increase in 8-hr ozone for studies included in meta-analysis, by age

Note: Horizontal lines represent 95% intervals. The overall results reflect meta-analysis findings.



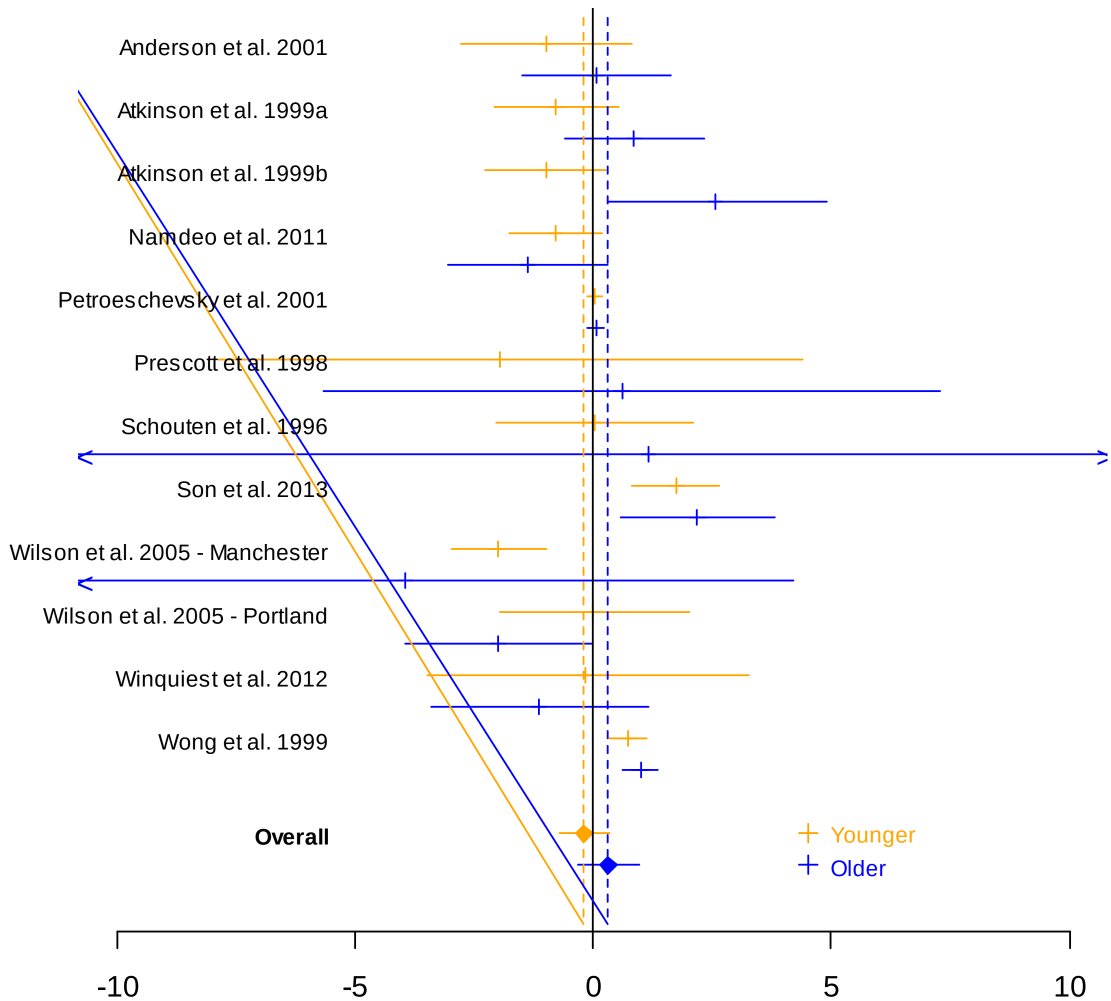
Web Figure 8. Funnel plot for estimates of association between ozone and cardiovascular hospital admissions for studies included in meta-analysis, by age

Note: Effect estimates show the percentage increase in risk per 10-ppb increase in 8-hr ozone. Open circles represent study estimates. Solid vertical lines represent overall estimates based on study results. Orange and blue represent estimates for younger and older populations, respectively.



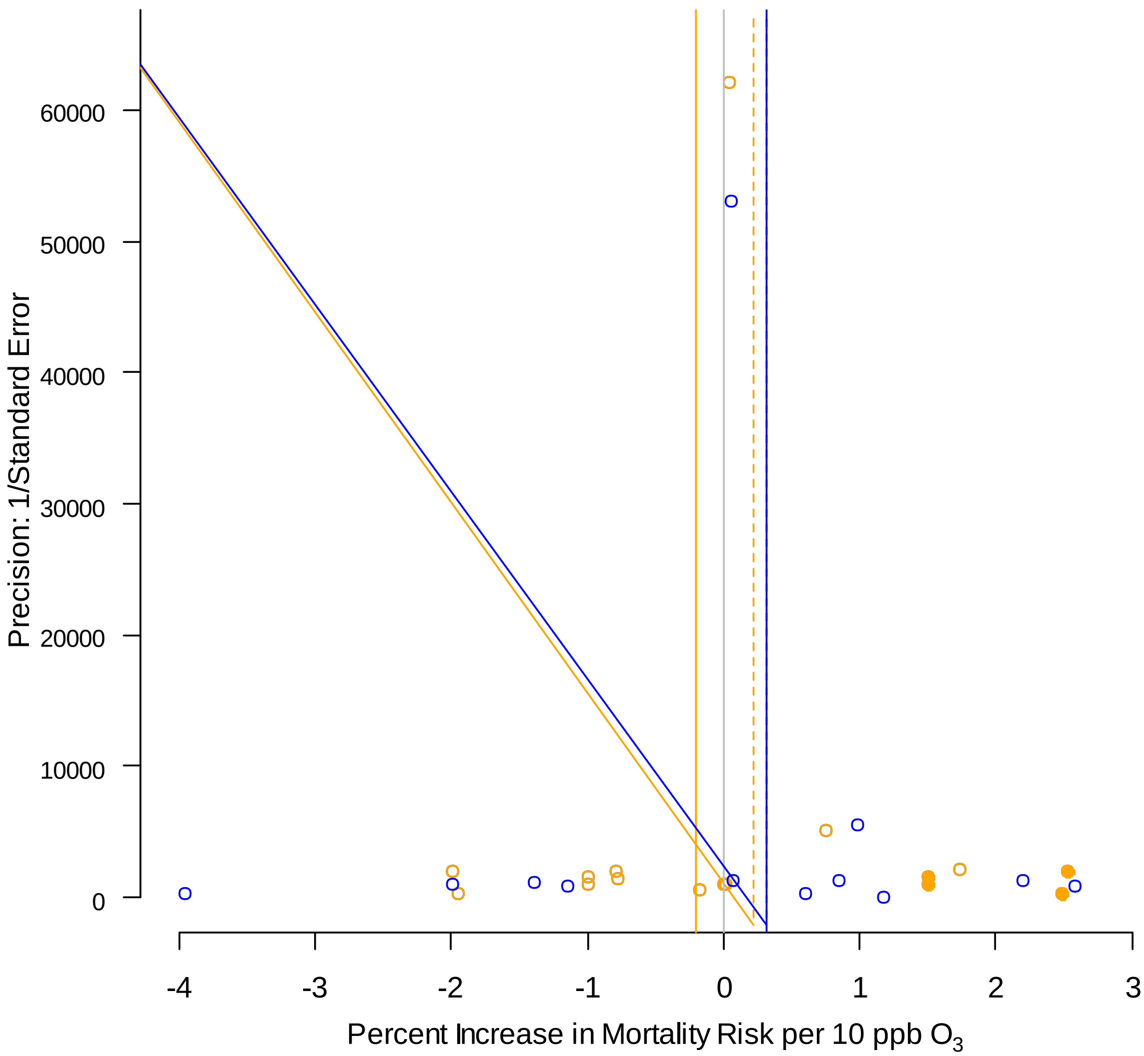
Web Figure 9. Percent increase in risk of respiraotry hospital admissions for 10-ppb increase in 8-hr ozone for studies included in meta-analysis, by age

Note: Horizontal lines represent 95% intervals. The overall results reflect meta-analysis findings.



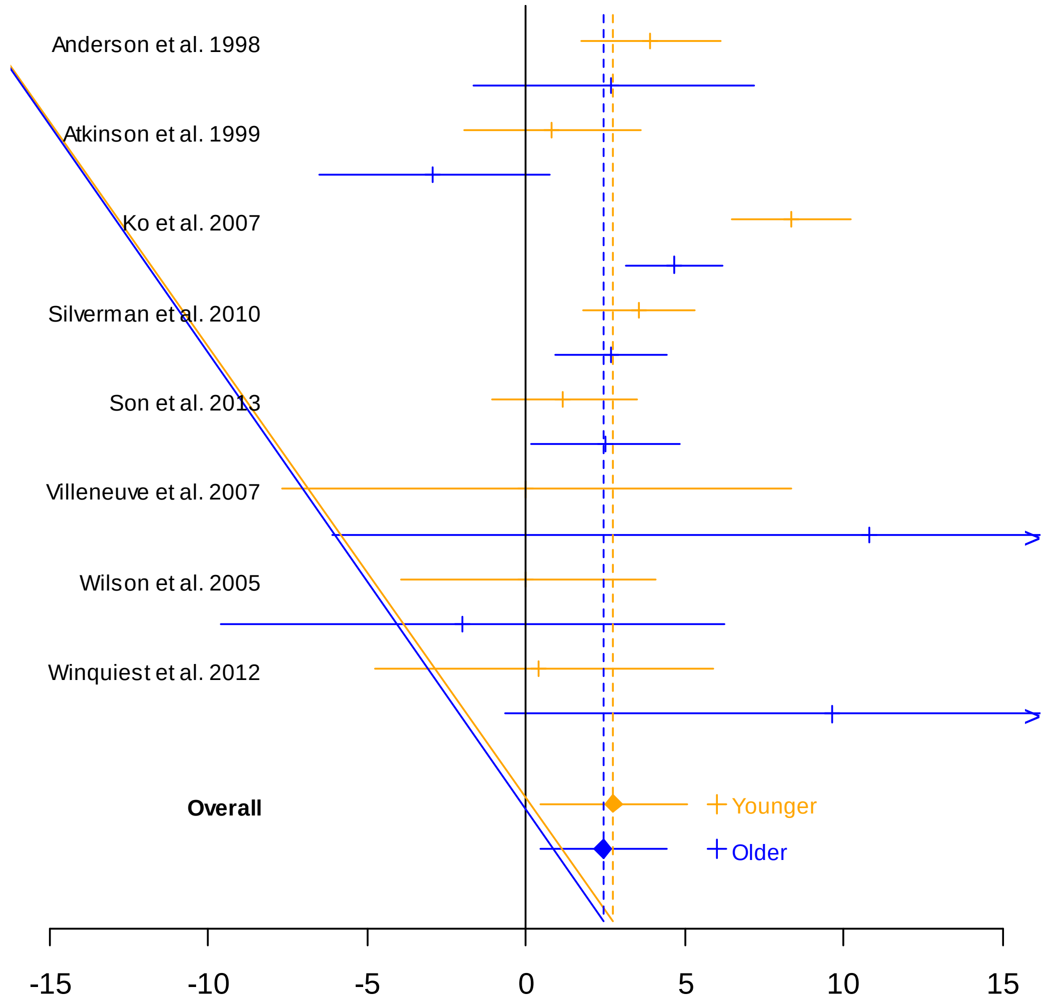
Web Figure 10. Funnel plot for estimates of association between ozone and respiratory hospital admissions for studies included in meta-analysis, by age

Note: Effect estimates show the percentage increase in risk per 10-ppb increase in 8-hr ozone. Open circles represent study estimates; closed circles represent "missing studies" from the trim-and-fill method to adjust for publication bias. Solid vertical lines represent overall estimates based on study results; dashed lines represent overall estimates adjusted for publication bias. Orange and blue represent estimates for younger and older populations, respectively.



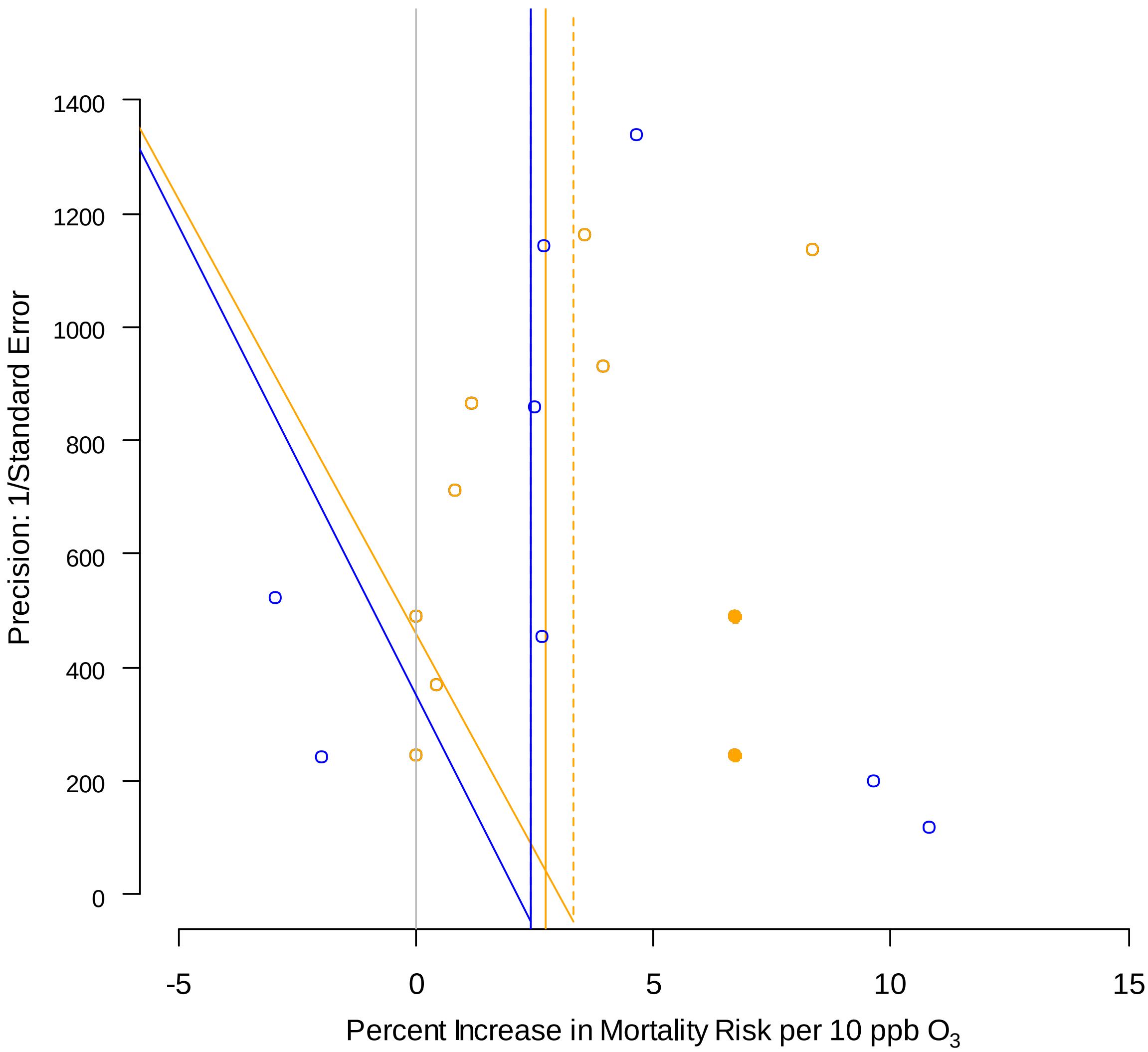
Web Figure 11. Percent increase in risk of asthma hospital admissions for 10-ppb increase in 8-hr ozone for studies included in meta-analysis, by age

Note: Horizontal lines represent 95% intervals. The overall results reflect meta-analysis findings.



Web Figure 12. Funnel plot for estimates of association between ozone and asthma hospital admissions for studies included in meta-analysis, by age

Note: Effect estimates show the percentage increase in risk per 10-ppb increase in 8-hr ozone. Open circles represent study estimates; closed circles represent "missing studies" from the trim-and-fill method to adjust for publication bias. Solid vertical lines represent overall estimates based on study results; dashed lines represent overall estimates adjusted for publication bias. Orange and blue represent estimates for younger and older populations, respectively.



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