

# Association between Ambient Temperature, Particulate Air Pollution and Emergency Room Visits for Conjunctivitis

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## Research article

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# Abstract

**Background** Numerous studies have confirmed that ambient temperature and air pollution are associated with higher risk of morbidities to different systems of the human body, yet few have addressed their effect on the ocular system. The purpose of this study is to determine the association between temperature, air pollution and emergency room visits for non-specific conjunctivitis.

**Methods** In this retrospective cohort study, the records of all emergency room visits to Soroka University Medical Center (SUMC) from 2009 to 2014 were reviewed for patients with conjunctivitis. Exposure to fine and coarse particulate matter and temperature were assessed by a hybrid model that incorporated daily satellite remote sensing.

**Results** The records of the 6001 patients who visited the SUMC emergency room with conjunctivitis, together with the meteorological data, revealed a positive association between temperature increment and incidence of conjunctivitis. The strongest effect was found during summer and autumn: the incidence increased 8.1% for each 1oC rise in temperature between 24oC and 28oC in the summer, and 7.2% for each 1oC rise in temperature between 13oC and 23oC in autumn. The association between fine and coarse particulate matter and incidence of conjunctivitis was not statistically significant.

**Conclusion** High ambient temperature is significantly associated with an increased risk of nonspecific conjunctivitis in summer and autumn and not in spring and winter. Conjunctivitis is not associated with air pollution. The findings can assist community clinics and hospital emergency rooms prepare for the upticks in the condition during certain seasons and acute rises in temperatures, lowering the financial costs to both the individual and the public.

# Background

Conjunctivitis is an inflammation of the conjunctiva characterized by swelling, redness, discharge and discomfort. It is a common diagnosis in the general population (Azari and Barney, 2013), and the most common ocular condition diagnosed in US emergency rooms, accounting for almost one-third of all eye-related encounters (Channa, 2016). It may be infectious (generally caused by adenovirus) or noninfectious. Although usually not sight-threatening, outbreaks can cause significant morbidity, high health care costs and loss of workdays, which eventually result in financial burdens on both individuals and the public (Azari and Barney, 2013; Channa, 2016).

Ambient temperature and air pollution are known to be associated with a variety of health problems and disorders that affect multiple body systems and in some cases mortality (Jhun, et al., 2015; Liliieveld, et al., 2015; Aditi, et al., 2016; Jun, et al., 2016). Several studies demonstrated their effect on respiratory, cardiovascular, neurological and other body systems (Eccles, 2002; Alina et al., 2015; Aditi et al., 2016). The effects of meteorological changes on the ocular system have been addressed in several studies (Bourcier et al., 2003; Hu et al., 2007; Stein et al., 2011; Christoph et al., 2016; Matthew et al., 2016; Setten et al., 2016; Augera et al., 2017), but few have studied their impact on conjunctivitis (Andre et al., 2011; Chia-Jan et al., 2012; Chiang et al., 2012; Hong et al., 2016; Szyszkowicz et al., 2016) , and those that did report inconclusive results. Moreover, those studies evaluated the incidence of conjunctivitis by seasons rather than the direct effect of temperature on the day of the incident.

The present study was undertaken to evaluate the association between air pollution, ambient temperature and emergency room visits for nonspecific conjunctivitis in the Negev Desert of southern Israel. This 13,000 km<sup>2</sup> semi-arid region lies between the Saharan and Arabian deserts and the three together constitute the world's largest dust belt. In light of climate change and desertification, the Negev can be considered a predictor of future climate change in many regions of Europe.

## Methods

### 2.1. Study Population

The study included all visits to Soroka University Medical Center (SUMC) emergency room diagnosed with conjunctivitis during the years 2009-2014. SUMC is a tertiary 1000-bed hospital in the southern Negev Desert of Israel, and the only medical center in the region for a population of 700,000 inhabitants. The Center is owned by the largest health maintenance organization HMO in Israel, the Clalit Health Services. Only residents of the southern Negev were enrolled. All patients seen in the emergency room and diagnosed with eye diseases, not only those with conjunctivitis were included in the study for purposes of comparison. Demographic and clinical features were obtained from the electronic database of Clalit Health Services. Demographic data included date of birth, gender, age and place of residence; clinical data included eye diseases and comorbidities.

### 2.2 Air pollution and meteorology data measurement

We used a hybrid method for assessing spatiotemporal resolved PM<sub>2.5</sub> and PM<sub>10</sub> exposures (Nordio, 2013; Kloog, 2014; Kloog, 2015; Shtein, 2018), and a satellite-based method for monitoring temperature in the Negev recently installed by the Israel Meteorological Service.

#### 2.2.1 Air pollution

Daily average concentrations of PM<sub>10</sub> (particulate matter 10 micrometers or less in diameter) and PM<sub>2.5</sub> (particulate matter 2.5 micrometers or less in diameter) were estimated using a hybrid satellite-based model that provides daily satellite remote sensing data at 1 × 1 km spatial resolution (; Kloog, 2015). Briefly, using an algorithm developed by NASA - MAIAC (Multi-Angle Implementation to Atmospheric Correction) (Lyapustin and others 2011) that provides aerosol optical depth (AOD) data in high resolution, we applied mixed models to regress daily PM<sub>10</sub> and PM<sub>2.5</sub>: AOD, traditional land use regression, and temporal and spatial predictors. When AOD was not available, we fitted a generalized additive model with a thin plate spline term of latitude and longitude to interpolate PM estimates. Good model performance was achieved, with out-of-sample cross validation R<sup>2</sup> values of 0.92 and 0.87 for PM<sub>10</sub> and PM<sub>2.5</sub>, respectively. Model predictions had little bias, with cross-validated slopes (predicted vs. observed) of close to 1 for both models. Exposure estimates were assigned for each patient based on his/her geocoded home address.

## 2.2.1 Meteorological Data

Daily data on air temperature, relative humidity, O<sub>3</sub>, NO<sub>2</sub>, NOX and SO<sub>2</sub> were obtained from the Ministry of Environmental Protection Meteorological Monitoring Station located in Beer-Sheva, the largest city in southern Israel.

## Statistical Analysis

The association between air pollution, ambient temperature and emergency room visits for nonspecific conjunctivitis was examined by a case-crossover design (Maclure, 1991), in which we sampled only cases and compared the mean ambient temperature on the day of the emergency room visit to the mean temperature in other time periods. Because each case serves as its own control, all measured or unmeasured characteristics that do not vary over time, such as gender, ethnicity and chronic diseases, cannot confound the association. Confounding by seasonal patterns was avoided by using the Navidi bidirectional approach, matching control days of the same day of the week, month and year (Navidi, 1998). Zero-to-seven days lag exposure were tested for mean temperature (for example, lag 3- being the parameter levels at 3 days before the admission event).

A regression analysis based on conditional logistic regression was performed to obtain odds ratios (OR) and 95% confidence intervals (CI). The impact of changes in ambient temperature everyday over the 7 days before the emergency room visit for conjunctivitis was examined.

For all analyses, estimates were calculated for the entire year and separately for seasons.

Possible non-linear association with temperature variable was tested using penalized splines with 5 degrees of freedom. Statistical analysis was performed with the IBM SPSS Statistics software package (version 23.0, IBM, Armonk, NY) and R statistical software.

The study was conducted according to the Declaration of Helsinki and approved by the Medical Helsinki Committee of the Soroka University Medical Center, Ben-Gurion University of the Negev.

## Results

### 4.1. Population

Of the 19,246 visits to the ophthalmology SUMC emergency room between 2009 and 2014, 6001 (31.1%) were diagnosed with conjunctivitis (Table 1 in the Appendix). People who did not reside in southern Israel were excluded from the analysis. Mean age of patients was 34.6 years, range 0.5-96 years, the majority, 4063 patients (67.7%), were between 16 and 65 years of age, and 54.4% were males (Table 1).

### 4.2 Pollution and Meteorology

The average daily levels of meteorological variables by seasons are presented in Table 2. The interquartile range (IQR) of PM<sub>2.5</sub> ranged between 17.2 and 24.82 µg/m<sup>3</sup>, reaching a maximum value of 53 µg/m<sup>3</sup>, with no significant differences between seasons. The IQR of PM<sub>10</sub> ranged between 38.44 and 56.66.3 µg/m<sup>3</sup>, reaching a maximum value of 193 mg/m<sup>3</sup>, slightly higher during the winter. The climate in the study region is relatively hot and dry, with average daily IQR temperatures of 11.86 °C -15.65°C in winter, 18.64 °C -20.95°C in spring, 25.06°C -27.32°C in summer, and 17.02 °C -23.39°C in autumn. The overall IQR relative humidity range was 57.00-75.00%, with no difference between seasons.

#### **4.3. Effect of anthropogenic and non-anthropogenic air pollution on the incidence of conjunctivitis**

Odds ratios and 95% confidence intervals were estimated from conditional logistic regression analysis of association between PM<sub>2.5</sub>, PM<sub>10</sub> (separately), temperature and emergency room visits due to conjunctivitis where models were adjusted for humidity. There was no statistically significant correlation between levels of PM<sub>2.5</sub>, PM<sub>10</sub> and the incidence of conjunctivitis (Table 2 in the Appendix). Levels of specific gases (O<sub>3</sub>, NO<sub>2</sub>, NOX and SO<sub>2</sub>), examined separately, were very low and had no significant effect on conjunctivitis.

#### **4.4. Effect of temperature on the incidence of conjunctivitis**

A subgroup analysis by season was conducted to assess the seasonal relationship between temperature and conjunctivitis. The number of emergency room visits for conjunctivitis were more frequent in summer (36.4%, p<0.001) than in other seasons (Figure 1) (Table 1 in the Appendix), followed by winter (26%, p<0.001), autumn (22.1%, P=0.773) and spring (15.4%, p=0.135), with July and August having the highest rate. When the incidence of conjunctivitis was compared with other ophthalmological disorders by seasons (Table 1 Appendix), the incidence of conjunctivitis was significantly higher in summer (36.4% and 32.8%, respectively, P<0.001), and significantly lower in winter (26% and 28.6%, respectively, p<0.001).

The same results were obtained when the data were stratified by age, with summer leading in each age group (P<0.001), followed by winter, autumn and spring. When was analyzed by months, July and August had the highest incidence for each age group (Fig. 1 and Table 3 in the Appendix).

There was a positive association between temperature increment and incidence of conjunctivitis in summer (Fig. 2), when the incidence increased 8.1% for each rise of 1 degree Celsius at temperatures between 24°C and 28°C. There was also a positive association between temperature and incidence of conjunctivitis in autumn (Fig. 2), when it increased 7.2% for each rise of 1 degree Celsius at temperatures between 13°C and 23°C. This association remained after taking into account a 6-day lag between exposures and developing conjunctivitis for both autumn and summer. There was no association between temperature and conjunctivitis during spring and winter (Fig. 2).

## **Discussion**

Meteorological changes and air pollution effects on humans have been a public health concern for the last several decades due to accelerated global warming and desertification. Contemporary studies document the effect of temperature and air pollution on human morbidities, especially cardiovascular, respiratory and neurological systems, as well as on human mortality, even within the normal range of temperatures. The meta-analysis of epidemiological evidence concerning the effect of temperature on overall mortality and morbidities performed by Aditi et al. (2016), covering some 4 million participants for mortality and 12 million for morbidities, reported that every rise of 1°C temperature increased cardiovascular mortality by 3.44% (95% CI 3.10–3.78), respiratory mortality by 3.60% (3.18–4.02), and cerebrovascular mortality by 1.40% (0.06–2.75). A 1°C reduction in temperature increased respiratory (2.90%, 1.84–3.97) and cardiovascular (1.66%, 1.19–2.14) mortality. A 1°C rise in temperature increased cardiovascular, respiratory and genitourinary morbidities, and the incidence of diabetes mellitus, infectious disease and heat-related morbidity.

Studies on the effect of meteorological changes on ocular disease yielded positive results. Augera et al. (2017) reported an association between elevated outdoor temperatures and an increased risk of traction retinal detachment. Hu et al. (2007) found that primary angle closure glaucoma admission rates were significantly higher with increased relative humidity, but with no correlation with temperature. Matthew et al. (2016) ascribed a higher frequency of infectious keratitis during the summer to higher temperatures and higher humidity levels. Christoph et al. (2016) showed a statistically significant correlation between the overall patient volume admission to the ophthalmology emergency room and higher weekly average temperature.

To the best of our knowledge very few studies have investigated the effect of meteorological changes on conjunctivitis, and the few that did examine the relationship between conjunctivitis and seasons (Chiang et al., 2012; Hong et al., 2016; Szyszkowicz et al., 2016) paid no attention to the isolated and direct effect of temperature on the incidence of the condition.

In our large-scale case study, there was no association between air pollution (PM<sub>2.5</sub>, PM<sub>10</sub>) and the incidence of nonspecific conjunctivitis (Table 2 in the Appendix). Our finding that southern Israel, the Negev Desert, has a very low level of anthropogenic (chemical) pollution points to the sole effect of non-anthropogenic air pollution on conjunctivitis.

Our findings of seasonal differences in the incidence of conjunctivitis are in agreement with Hong et al.'s and co-workers' (2016) findings that higher levels of ambient NO<sub>2</sub>, O<sub>3</sub>, temperature and lower humidity lead to increased outpatient visits for allergic conjunctivitis, which the authors attribute to temperature's effect on pollen concentrations in hot climates. It must be pointed out however that while our study investigated the meteorological effect on nonspecific conjunctivitis, theirs investigated the effect on a specific type of conjunctivitis, allergic conjunctivitis. In addition, our study examined the effect of temperature directly as opposed to by seasons. Chiang et al. (2012) found a peak incidence of chronic conjunctivitis in summer, mainly in rural areas and less prominent in urban areas, a difference the study attributed to other factors such as socioeconomic status, income and occupation. Szyszkowicz et al.

(2016) also showed that the number of visits to the emergency room due to nonspecific conjunctivitis was higher in warm seasons (58%) compared to cold seasons (42%), in line with our findings of a marked difference in the incidence between summer 36.4% ( $P < 0.001$ ) and winter 26% ( $P < 0.001$ ). Szyszkowicz et al. (2016) also studied the effect by season and not, as we did, by the direct effect of temperature.

The positive associations we found between temperature increment and incidence of conjunctivitis in summer and in autumn are further evidence of the isolated positive effect of temperature on conjunctivitis. The statistically significant higher incidence in summer and lower incidence in winter compared to other ophthalmological disorders imply a positive effect of higher temperature on conjunctivitis and a protective effect of lower temperatures. But, there was no association between temperature and conjunctivitis in spring, which represents the moderate range of temperatures, and a weak protective effect of temperature in winter, which represents the lower range of temperatures. It seems that there are still other factors that influence the ocular surface besides those examined in this study. Further studies are needed to address these factors to better understand the effect of temperature on the ocular surface.

## Conclusion

Temperature is significantly associated with nonspecific conjunctivitis in summer and autumn, but not in spring and winter. Incidence of conjunctivitis is significantly higher than other eye disorders in summer and lower in winter. There is no association between air pollution and conjunctivitis. These findings can assist community clinics and hospital emergency rooms prepare for the upticks in conjunctivitis during certain seasons and acute rises in temperatures.

## Abbreviations

AOD – aerosol optic depth

PM – particulate matter

IQR – interquartile range

O<sub>3</sub> – trioxygen

NO<sub>2</sub> – nitrogen dioxide

NOX – nitric oxide

SO<sub>2</sub> – sulfur-dioxide

## Declarations

**Ethics approval and consent to participate:** permission was obtained to access data The study was conducted according to the Declaration of Helsinki and approved by the Medical Helsinki Committee of the Soroka University Medical Center, Ben-Gurion University of the Negev.

Permission to access data was obtained by the Medical Helsinki Committee of the Soroka University Medical Center, Ben-Gurion University of the Negev.

**Consent to publish:** Not applicable

**Availability of data and materials:** All data generated or analysed during this study are included in this published article

**Competing interests:** The authors declare that they have no competing interests

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#### **Authors' Contributions:**

- Soltan Khalaila: Conception or design of the work; data collection; data analysis and interpretation; drafting the article.
- Tara Coreanu: Data collection.
- Alina Vodonos: Critical revision of the article.
- Itai Kloog: Data analysis and interpretation.
- Alexandra Shtein: Data analysis and interpretation.
- Victor Novack: Critical revision of the article.
- Erez Tsumi: Conception or design of the work; Critical revision of the article.

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## Tables

Table 1: Demographic characteristics of the 6001 patients with conjunctivitis.

<b>Demographic Characteristic</b>	<b>Conjunctivitis N=6001</b>
Age (Mean±SD) years	34.62±21.8
0-18 years n (%)	1,346 (22.4%)
19-65 years n (%)	4,064 (67.7%)
=>66 years n (%)	590 (9.8%)
Male n (%)	3,263 (54.4%)

Table 2. Air pollution and meteorology values between the years 2009 and 2014.

		Winter	Spring	Summer	Autumn
		Dec 7–Mar* 30	Mar 31–May* 30	*May 31–Sep 22	*Sep 23–Dec 6
<b>PM<sub>2.5</sub></b>  μg/m <sup>3</sup>	IQR	17.52-24.82	17.38-23.14	18.11-22.05	17.21-22.91
	Mean±SD	22.62±8.30	21.34±6.42	20.46±3.74	20.60±5.21
	Minimum	5.28	8.33	9.69	5.28
	Maximum	53	53	53	53
<b>PM<sub>10</sub></b>  μg/m <sup>3</sup>	IQR	39.10-56.66	40.13-51.62	40.39-47.04	38.44-52.68
	Mean±SD	56.18±34.35	49.51±20.94	44.40±8.92	47.96±17.95
	Minimum	11.53	21.08	40.39	11.53
	Maximum	193	193	193	193
<b>Temperature</b>  °C	IQR	11.86-15.65	18.64-20.95	25.06-27.32	17.02-23.39
	Mean±SD	13.94±3.42	20.90±3.33	26.14±1.81	20.16±4.40
	Minimum	3.55	7.34	16.55	4.15
	Maximum	28.11	30.87	33.62	29.80
<b>Relative humidity (%)</b>	IQR	57.00-75.00	52.00-71.50	63.00-71.54	57.00-71.40
	Mean±SD	65.43±13.83	59.66±13.68	66.46±8.20	62.70±13.40
	Minimum	15.53	13.00	17.00	13.00
	Maximum	92.45	81.77	81.77	93.14

\* Season's definition (Alpert et al., 2004)

## Figures

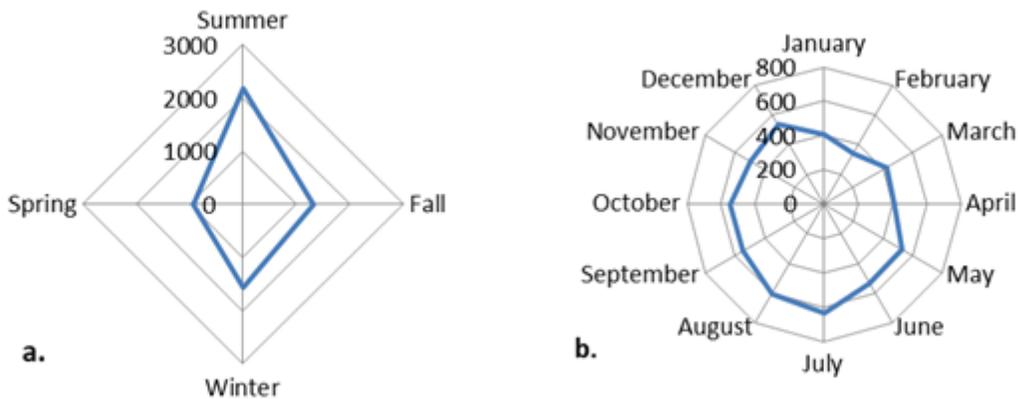


Figure 1

Rate of conjunctivitis by a. season and b. month

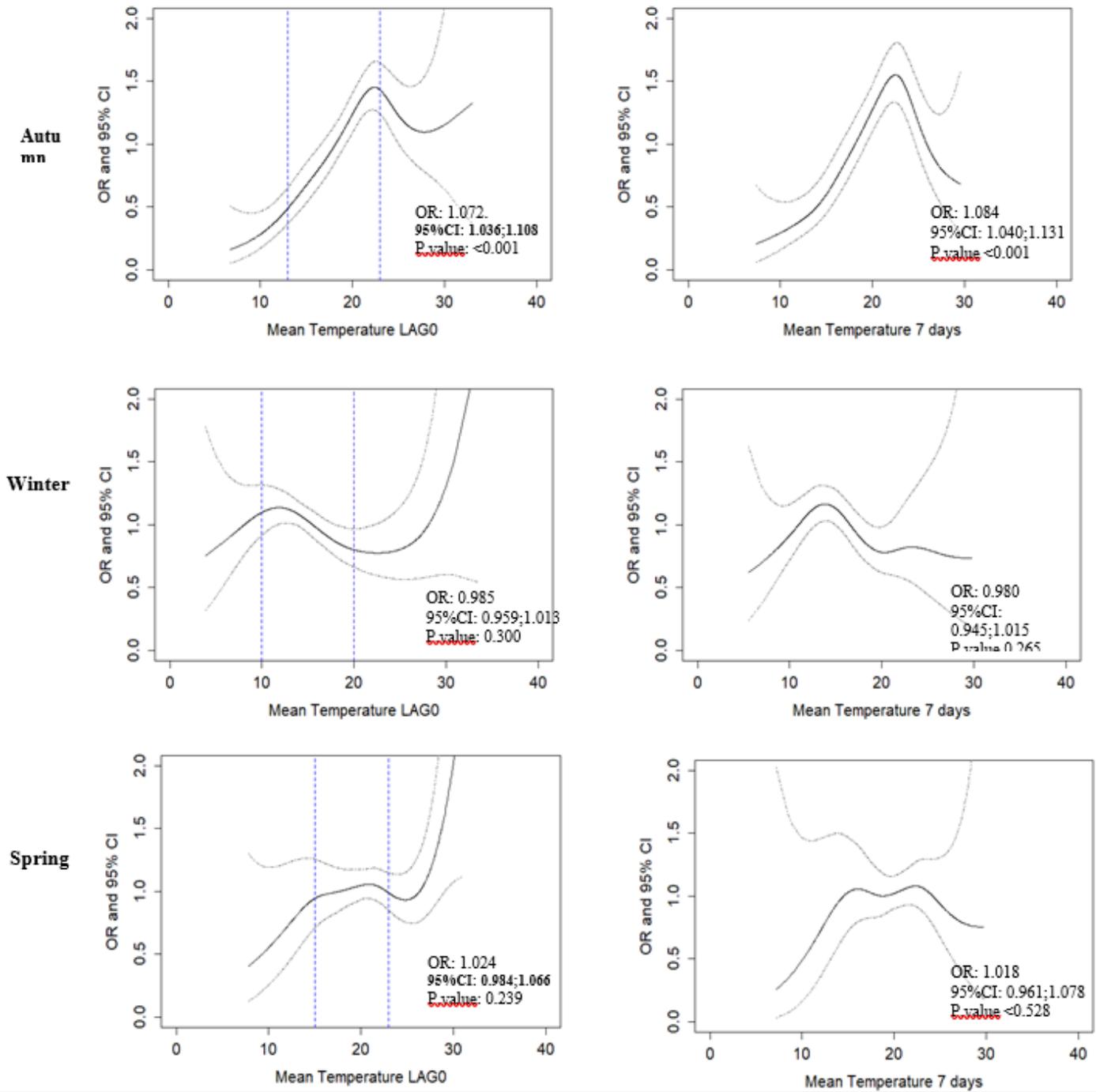


Figure 2

Association between increase in temperature and visits to the emergency room for conjunctivitis, by season. The solid lines are the odds ratios (ORs) and the dotted lines are 95% confidence intervals. Models were adjusted for humidity and PM10.

## Supplementary Files

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