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Long-term exposure to ambient ozone and respiratory health: Ozone-induced incidences of respiratory diseases

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Abstract: Ground-level ozone is a very strong oxidizing agent. Its concentration has been progressively increasing in recent decades. However, there is no information about its impact on public health in the Black Sea region of southern Russia. In order to identify ozone-induced complications in the state of the respiratory system, at the initial stage of investigation, a correlation analysis of the number of emergency medical calls due to respiratory dysfunctions and the ground-level ozone concentration (GLOC) was carried out. The data of the Unified Crimean Republican Territorial Emergency Care Center and the data on the registration of GLOC at the background environmental monitoring station of the Karadagsky State Nature Reserve for the period 2018–2022 were used. An analysis revealed a weak ($0.27 < r_s < 0.50$) but highly statistically significant ($p < 0.000$) effect of ozone on respiratory health if its average annual concentration was above $60 \mu\text{g}/\text{m}^3$, which means that possible pronounced negative effects of ozone on vulnerable groups of the population. With a lower annual average GLOC, there was no effect of ozone on the frequency of emergencies. The study of short-term (within a month) effects of ozone demonstrates ambiguous correlations that need other approaches to the analysis of short-term ozone-induced effects. However, the statement of the established fact of ozone-induced effects and its high average annual values indicate that such a problem is relevant in this region and serves as a sufficient basis for the development of regional research and the creation of an effective system for preventive risk management of negative ozone exposure in the context of climate change.

Keywords: ground-level ozone; respiratory diseases; emergency conditions

1. Introduction

Ground-level ozone (GLO) is one of the most dangerous atmospheric pollutants. Its concentration increases by 1%–2% annually in all countries [1]. It is believed that there are currently significant global health risks associated with ozone [2–5]. Particular attention is paid to the effect of increasing concentrations of GLO on respiratory health due to its high oxidative properties [6] and its direct effect on respiratory organs [7]. However, despite the rapid progress in this field, many unclear

questions remain, the answers to which are not clear at the current level of knowledge [8]. Thus, on the one hand, there is ample evidence of the negative effects of ozone on the respiratory system of adults, especially those with chronic respiratory diseases [3,4]. On the other hand, its damaging effect is not always detected, more often with short-term exposure [9,10]. To a certain extent, the reason for the inconsistency of the data may also be the peculiarities of the territories, since the formation of ozone as a secondary pollutant and the final effect of its influence depend on climatic and anthropogenic factors [11]. It is particularly important to assess the impact of GLO on health in the southern territories, where it is formed in higher concentrations, especially in pulmonological resorts, which include the southern coast of Black Sea territories of Russia. One of the most convincing criteria for the negative impact of ground-level ozone on public health is the number of registered emergencies in the form of exacerbations of chronic diseases or the initiation of new ones [12]. The purpose of this study was to establish the relevance of this problem in the specified area through analysis of the data on the number of registered emergency medical calls (EMC) due to an urgent condition of the respiratory system in relation to changes in the concentration of GLO on the southern coast of Crimea for 2018–2022.

2. Materials and methods

A retrospective analysis of statistical data from the State budgetary healthcare institution of the Republic of Crimea, the Crimean Republican Center for Disaster Medicine and Emergency Medical Care, for the period from July 2018 (the launch of the EMC automated call registration system) through December 2022, inclusive, and GLO registration data from January 2018 to December 2022. From the totality of EMC calls, calls were selected for each day, the cause of which was an emergency condition of the respiratory system for various reasons. Their number during the study period was 19,909. Thus, the general totalities of the studied medical statistics were analyzed.

The GLO databases were formed as a result of registration, which was carried out in the Karadag'sky State Nature Reserve of the Russian Academy of Science (KSNR RAS), a branch of the Institute of Biology of the Southern Seas of RAS (FIC InBUM) at the background environmental monitoring station (BEMS) (44° 9400 N, 35°2368 E, 180 m above sea level). GLO measurements were carried out using the optical method by the APOA 370 gas analyzer (HORIBA), which takes samples automatically using fluoroplastic tubes at a height of 2 m from the earth's surface [13]. The gas analyzer was calibrated once every two weeks using an ARMS-370 generator; the device underwent annual verification at the Mendeleev Metrology Institute (VNIIM) in St. Petersburg. The monitoring station is also located on the coasts of the Black Sea at a distance of 110 km. In this case, if there are some differences in the absolute values of the GLOC, then the dynamics of its change are of the same type, which should not distort the identified dependencies. Based on the data of permanent ozone registration, average concentrations were calculated over an hourly observation interval with information stored in the registrar-I/O-EXPANDER (HORIBA). Thus, the database included 24 hourly GLOC averages for each day. The hourly average GLO value was used to calculate the average GLO value for the day. Based on the latter, monthly and annual averages were calculated. In addition, episodes of extreme

increases and decreases in ozone concentration for one hour per day were noted. Considering a sharp change in GLO can be a trigger for the respiratory system’s response, the amplitude of GLO fluctuations was also calculated as the difference between max and min per day by the value of GLO. To describe the daily maximum concentrations and amplitude of GLO fluctuations, the arithmetic mean (M) and standard deviation (SD) were used.

The recorded data from Excel tables was combined in a single database in the software package Statistica-12.

The GLO levels were assessed by comparing them with the standards adopted in Russia: for the average annual GLO—30 µg/m³; for the maximum single concentration per hour—160 µg/m³, for the daily for 8 h—100 µg/m³.¹

In the same software package, the relationship between the number of EMC due to urgent conditions of the respiratory system in residents of the city of Yalta and the above-mentioned characteristics of the GLO was analyzed using Spearman correlation analysis, which is usually used in this kind of research.

Due to the small number of calls and in accordance with the main objective of the study, to establish the dependence of the number of calls on the GLO, data processing was carried out without differentiating them by gender, age and other characteristics for the entire population as a whole. The correlation coefficients (*r_s*) were considered statistically significant at a significance level of *p* < 0.05. In addition, taking into account the epidemiological rather than experimental nature of the study, correlations were taken into account at a significance level of 0.05 < *p* < 0.10, considering them as a tendency to dependence.

3. Results

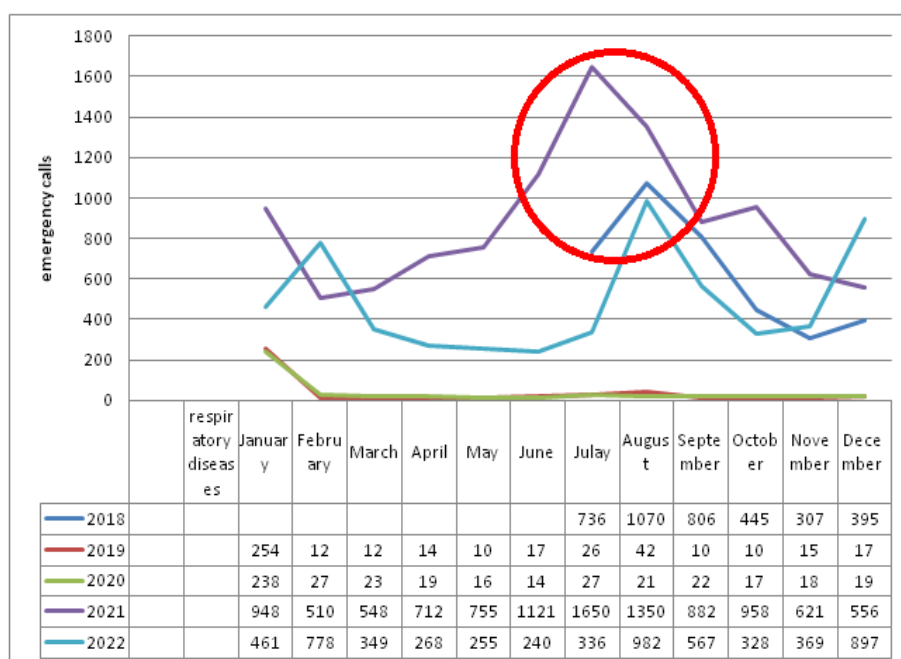


Figure 1. The absolute number of emergency calls per month in different years.

Note: The sharp decrease in the number of emergency calls due to respiratory issues in 2019–2020 is due to isolation during the COVID-19 pandemic; red line—spring and summer rise.

The total number of calls due to respiratory emergencies increased from 3410 in the second half of 2018 to 9856 in 2021 and 5743 in 2022, totaling 19,909 in 4.5 years. In 2019 and 2020, there was a sharp decrease in the number of such calls, most likely related to isolation measures for the cause of the COVID-19 pandemic.

The monthly dynamics of calls due to respiratory diseases were distributed in such a way that the largest number of them occurred in the spring-summer period in 2021 and 2022, in 2021 also in January, and in 2022 in December and February (Figure 1).

3.1. Concentration of GLO

The dynamics of GLO in these years were typical: it increased in the warm season and decreased in the cold; however, in general, the highest level of GLO was observed in 2021 and the lowest in 2022 (Figure 2). Nevertheless, over the entire observation period, there was an excess of the average annual level of GLO, which, as a rule, was at least twice as high as the standard.

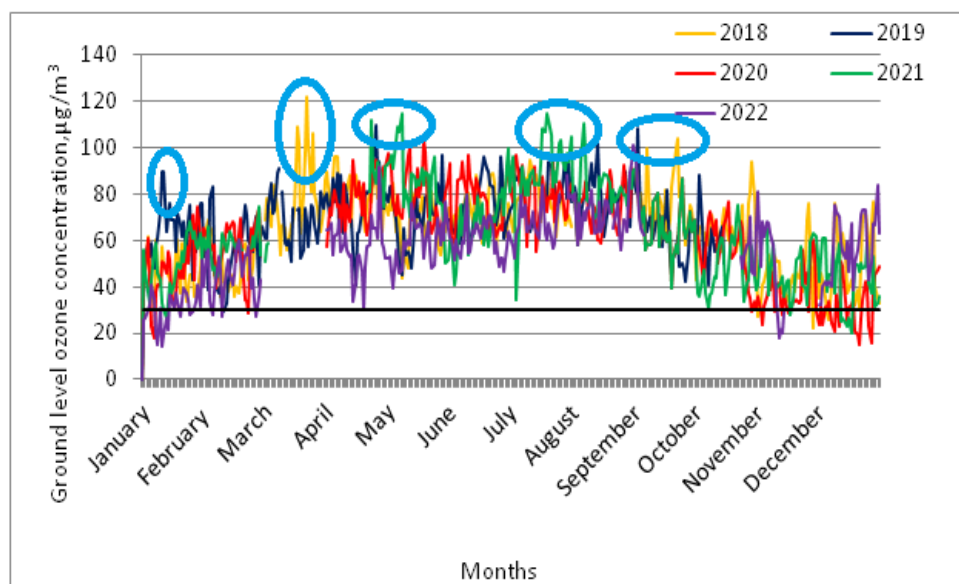


Figure 2. Average daily fluctuations of ground-level ozone concentration in 2018–2022.

Note: Black line—average annual permissible ozone concentration in Russia; blue circles—extremes of ozone concentration.

3.2. Correlation analysis

To establish the fact of the possible influence of ground-level ozone on complications in the state of the respiratory system, a correlation analysis of changes in GLOC and the number of calls for different observation periods was performed, primarily by month and for the year as a whole. All years were analyzed, but, taking into account the special situation in 2019–2020 (COVID restrictions) when there was a sharp decrease in the number of such calls, most likely due to isolation measures [14], it is hardly possible to consider the data obtained as objective. In this case the concentration of indoor air ozone is only to a certain extent determined by the concentration of ozone outside; the main part is formed by other components [15].

Therefore, they were excluded from further analysis of the ozone effects on respiratory health. Correlation analysis showed a statistically significant relationship between the number of calls to the emergency medical services (EMS) and the GLOC (**Table 1**). Its density was mostly weak, but for some groups of the population, such an influence can be sufficient to cause negative consequences. Its character was different during the observation periods if they were relatively short (months). In 2022, the analysis of monthly data revealed no such links.

Table 1. Statistically significant correlation coefficients between ground-level ozone concentration and number of emergency medical calls due to respiratory diseases.

Year	Month	With an average concentration per day	With the amplitude of concentration fluctuations per day	With maximum concentration per day	With minimum concentration per day
2018	September		0.31*		
	October			-0.32*	-0.30*
	November		0.33*		-0.28
2019	February	-0.42**			
	June		-0.34*	-0.43***	
	July		-0.34*		0.34*
	August			-0.25	
	September		0.39***		
2020	January			-0.29	
	February	-0.31*	-0.32*		
	August	0.36**	0.33*	0.38**	
	December			0.37***	
2021	January	-0.52****	-0.45***	-0.54****	
	February		0.32*		
	June		-0.35*		
	July	0.45****	0.43***		
	August		-0.30*		

Note: *, **, ***, ****—the significance level at $p < 0.1, 0.05, 0.01, 0.001$, respectively; empty cells mean the coefficient is not statistically significant.

At the same time, a correlation analysis of GLOC and the number of calls to the EMS due to respiratory dysfunctions for the entire year showed a weak ($r_s = 0.27, p < 0.000$) in 2021 and an average ($r_s = 0.53; p < 0.000$) in the second half of 2018, but with a very high probability ($p < 0.000$) direct relationship (**Figures 3 and 4**). It may be significant for a particularly vulnerable part of the population.

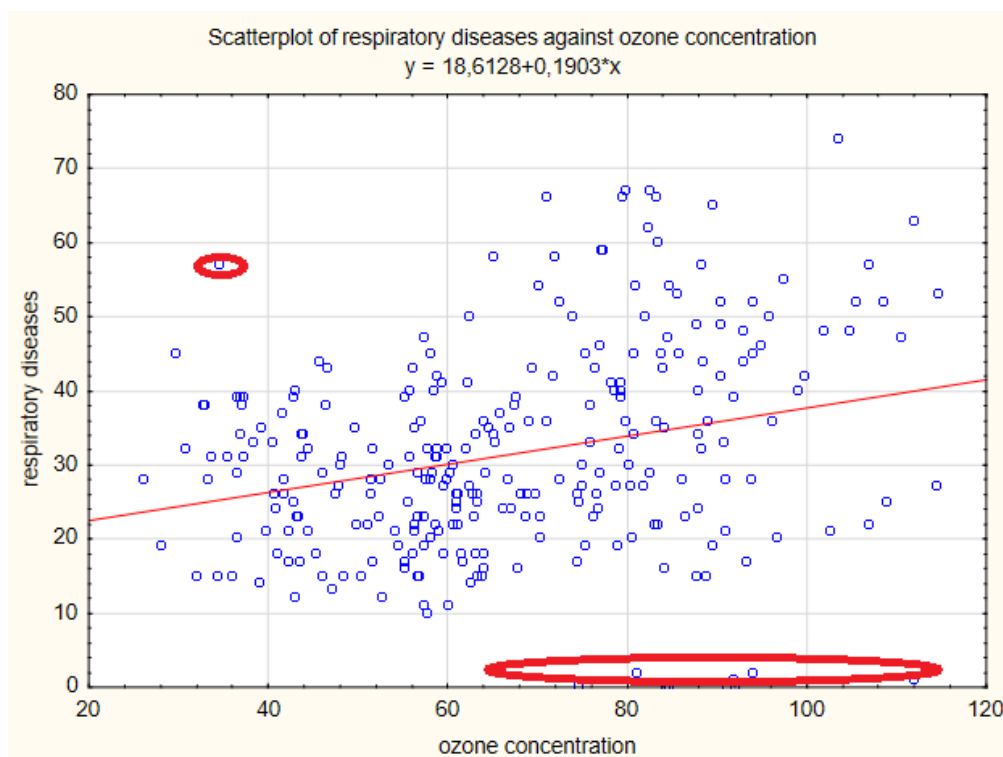


Figure 3. The aggregated number of daily average calls due to respiratory diseases at different levels of ground-level ozone concentration ($\mu\text{g}/\text{m}^3$) in 2021.

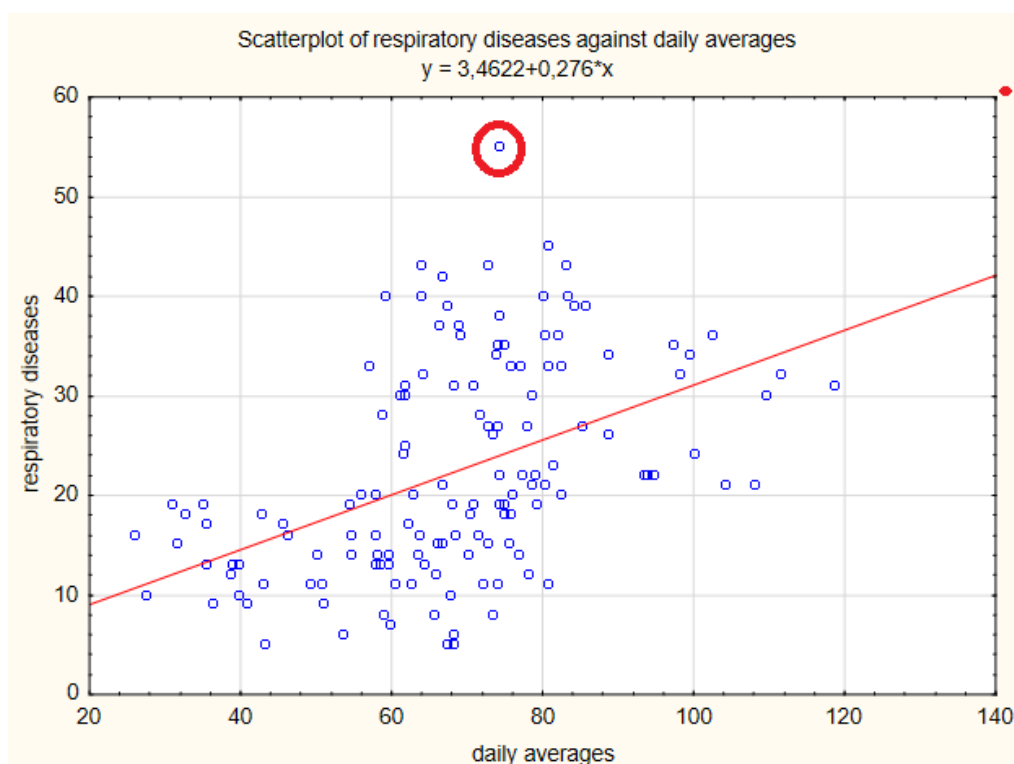


Figure 4. The aggregated number of daily average calls due to respiratory diseases at different levels of ground-level ozone concentration ($\mu\text{g}/\text{m}^3$) in 2018.

At the same time, in 2022, when the lowest annual average level of GLO was recorded, there was no statistically significant relationship between the number of emergencies and GLO (**Figure 5**).

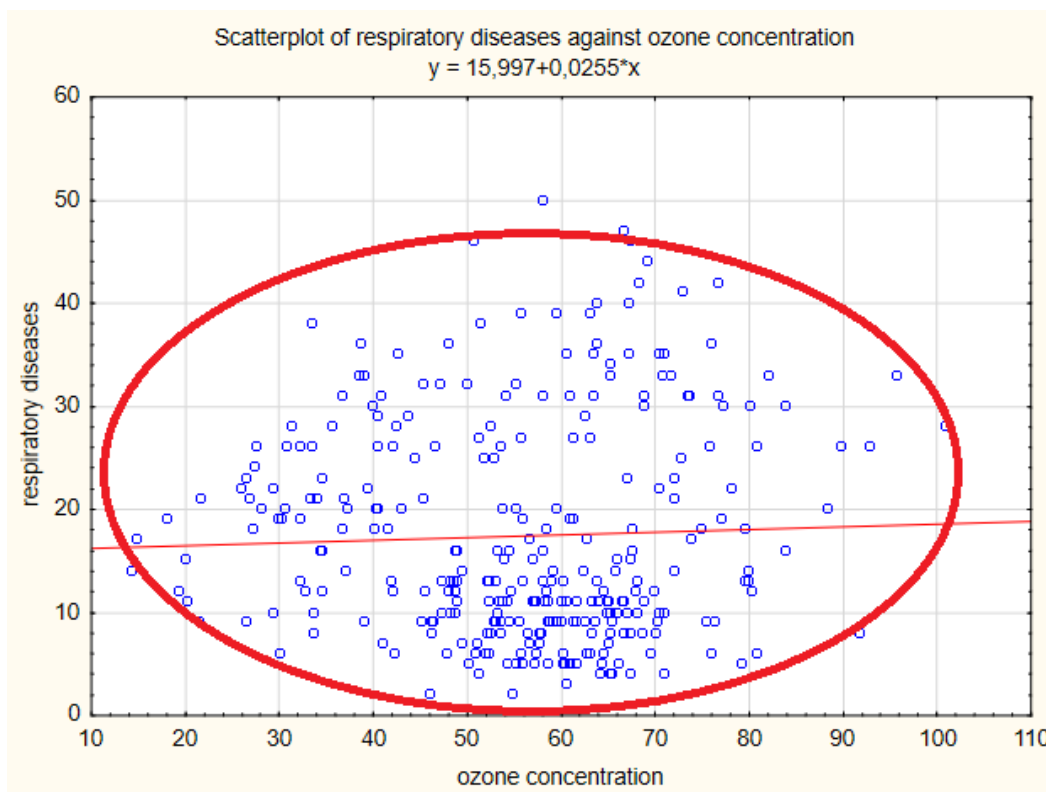


Figure 5. The aggregated number of daily average calls due to respiratory diseases at different levels of ground-level ozone concentration ($\mu\text{g}/\text{m}^3$) in 2022.

At the same time, the average annual value of GLO in 2022 was $56 \mu\text{g}/\text{m}^3$, and in 2018 and 2021— $64.4 \mu\text{g}/\text{m}^3$ and $64.5 \mu\text{g}/\text{m}^3$, respectively. It needs noted that the average annual GLO value at the Karadag station of background environmental monitoring is $63\text{--}69 \mu\text{g}/\text{m}^3$ [16], while this standard in Russia is $30 \mu\text{g}/\text{m}^3$.

4. Discussion

Retrospective analysis of the relationship between the data on the number of calls to the EMS due to urgent conditions of the respiratory system and GLOC revealed a certain relationship, which was more definite if a long-term (one year) period of exposure to ground-level ozone was analyzed. Despite the fact that there is an opinion that it is justified to study this kind of dependence only for those periods when there is an increased risk for exposure to GLOC [17], this seems to be true when considering the short-term effects of ozone. At the same time, it is believed that important information can be obtained by analyzing long-term trends in GLOC and medical data [18], which is confirmed by our results. Relatively weak character of correlation is expected because it is impossible to assume that only one, albeit a strong pollutant, will have a decisive effect on the state of the respiratory system. To increase the reliability of the results and quantify the contribution of ozone in the summary effect

of pollutants and the air quality on the state of the respiratory system, multiple regression analysis will be used at the next stage of the study.

As for the analysis of short-term follow-up periods in this study, when both direct and inverse relationships were identified without any reference to the season of the year, there are both theoretical grounds and confirmation from epidemiological observations to explain this. It is noted that most of the research on air pollution and respiratory diseases is often based on aggregated or delayed outcome indicators of acute respiratory diseases, such as emergency department visits or hospitalizations, which may not have temporal and spatial resolution [19]. As a result, the negative nature of the correlation with GLOC may rather indicate a delay in the effect [20,21], as well as the nonlinear nature of the dependence [22,23]. So, based on other extensive data on 109,927 patients with respiratory diseases from 98 hospitals, Spearman correlation analysis and a nonlinear distributed lag model were used to evaluate the short-term correlation between air pollutants and hospitalizations. It has been established that the maximum relative risk (RR) as a result of the action of most pollutants, including ozone, is achieved with a delay of five days. With such a 5-day lag, a 10% increase in the average annual GLOC increased the risk of hospitalization of pulmonological patients by 0.22% [24]. In order to identify the lag period in the conditions of this region, it needs additional research, since the present study at this stage allows us to talk only about establishing the fact of short-term influence.

In addition to the above, it should be noted that the presence of dependencies in seasons when the formation of ground-level ozone is reduced compared to the warm season can also be understood if we take into account that the final effect of its influence can be mediated by other climatic (humidity, air temperature, ultraviolet radiation level) and anthropogenic (other air pollutants) factors [25]. In this case, multiple regression analysis which permits assessing the contribution of ozone to the summary effect on respiratory health taking into account concomitant factors; the accumulation of the effect over long period allows to get more consistent results [22,23,26,27].

Due to the fact that air pollution can be a significant modifiable risk factor for exacerbation of respiratory diseases, non-admission of this plays an important role in primary prevention [28]. For example, implementation AQWS system gradually decreased the incidence of asthma by 20.5%; cardiovascular disease and stroke incidence also significantly decreased (by 34.3% and 43.0%, respectively), in Korea [29]). Such preventive measures may include both measures to reduce emissions and measures to reduce exposure time when ozone concentrations exceed acceptable values. Therefore, new perspective approaches to epidemiological research are proposed to explore potential cause-effect relationships and inform public health about strategies for the treatment of respiratory diseases [30]; that will be the next consistent stage of our investigation.

5. Conclusion

An analysis of retrospective data on EMC related to diseases of the respiratory system and the concentration of GLO in the atmospheric air in the Black Sea region of Russia from 2018 to 2022 revealed a weak ($0.27 < r_s < 0.50$) but highly statistically

significant ($p < 0.000$) effect of ozone on respiratory health, which means that there are possible pronounced negative effects of ozone on vulnerable groups of the population. Significant effects were observed if its average annual concentration exceeded $60 \mu\text{g}/\text{m}^3$; with a lower average annual GLOC value, no statistically significant effects were detected. The study of short-term (day, month) ozone exposure demonstrates ambiguous correlations and, in combination with the available literature data, indicates the need to use more sensitive approaches and methods of mathematical statistics to analyze the short-term epidemiological consequences caused by ozone exposure. The results obtained may indicate a situation with an uncomplicatedly manageable risk and provide an opportunity to consider the validity of the introduction of regional average annual standards for the Crimean territory. However, it requires further, more detailed research, analysis of long-term observations data, and the use of more advanced methods to obtain reliable results. In any case, the statement of the established fact indicates that such a problem is relevant in this region and serves as a sufficient basis for the development of regional research and the creation of an effective system for preventive risk management of the negative effects of GLO in the context of climate change.

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Conflict of interest: The authors declare no conflict of interest.

Notes

- ¹ Resolution 28.01.2021 N2 of sanitary rules Sanitary and Epidemiological requirements 01.2.3685-21.

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