

SARS-CoV-2 and Exposure to Pollution of the Population Near an Industrial Area in the Metropolitan Region in São Paulo State, Brazil

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Abstract

Industrial installations close to residential areas could cause health risks. Our objectives are to evaluate the interaction between pre-existing conditions (i.e., rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases (OPDs), conjunctivitis, dermatitis and primary hypothyroidism (PH)) and a higher risk of complications when infected with SARS-CoV-2 in residents exposed to long-term air pollutants. With a focus on the area affected by the Capuava Petrochemical Complex (CPC) (Region 1) and combining the AERMOD dispersion model with the Weather Research Forecast (WRF) (2016), we evaluated the Greater ABC region, Brazil. The concentrations of the nitrogen dioxide (NO₂), carbon monoxide (CO), particulate matter (PM₁₀), sulfur dioxide (SO₂) and volatile organic compounds (VOCs) were analyzed in 2017 and these data were correlated with data obtained in a survey of 2004 residents 8–72 years of age of both sexes; 1002 (Region 1), and 1002 of them reside within the areas surrounding various industrial areas (Region 2). SARS-CoV-2 cases were collected from the Greater ABC region. Region 1 showed higher average concentrations of all pollutants analyzed. Among the 2004 total residents, there were significant differences between Region 1 and Region 2 in the incidence of cases of rhinitis, sinusitis, pharyngitis, OPDs, conjunctivitis, dermatitis and PH demonstrating that there is a higher incidence of the evaluated diseases in residents who live closer to the CPC. Compared with residents with these diseases, the residents of Region 1 had a higher relative risk of complications when infected with SARS-CoV-2 than did the residents of Region 2.

Introduction

Industrial installations close to residential areas, together with unfavorable topographic conditions for the dispersion of pollutants, could cause health risks (Ribeiro and Assunção 2001). The health risks associated with residing near petrochemical industrial complexes represent a critical concern due to potential air pollution emissions. Metropolitan regions are important for public health because of the large number of people living in them, and the air pollution levels in metropolitan regions are usually higher than those in other areas. Industrial plants can increase the concentrations of hazardous substances in surrounding areas and cause respiratory symptoms among residents (Zhang et al. 2010). Exposure to air pollution has been associated with compromised pulmonary immune defense mechanisms in both animals and humans (Billionnet et al. 2012; Stieb et al. 2012).

In the last decade, associations between exposure to air pollution and acute health outcomes have been demonstrated in a number of studies (Burnett et al. 1998; Lin et al. 2005; Stieb et al. 2008, 2009; Turner et al. 2011; Villeneuve et al. 2013), and air pollution also increases morbidity, especially in individuals with asthma and/or chronic obstructive pulmonary disease (COPD) (Burnett et al. 1998; Lin et al. 2005; Stieb et al. 2009). A study conducted in Spain used the International Study on Asthma and Allergies in Children's questionnaire to survey the population. They observed a higher prevalence of nocturnal cough among children (aged 6–7 years) and adolescents (aged 13–14 years) who lived within a petrochemical industrial complex in Tarragona than among children and adolescents who lived in areas of the country in which no petrochemical complexes were located (Rovira et al. 2014).

Since coronavirus disease 2019 (COVID-19) emerged in Wuhan, China in December 2019 (Li et al. 2020), the epidemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes clusters of severe respiratory illness (Huang et al. 2020), has rapidly developed into a pandemic. A rapid and robust response by the global scientific community has described many essential aspects of SARS-CoV-2 transmission and its natural history (Backer et al. 2020; Bi et al. 2020; Chan et al. 2020; Chen et al. 2020; Lauer et al. 2020), but critical questions remain (Bi et al. 2020).

The World Health Organization (WHO) has defined this new syndrome using the acronym COVID-19 for Coronavirus Disease 2019 (WHO 2020). At the beginning of April 2020, marked differences in the rate of transmission and in the mortality associated with outbreaks of COVID-19 in different countries were noted. Early studies concluded that the risk factors associated with the development of the disease are older age (Wu et al. 2020 a), history of smoking (Liu et al. 2020), and heart disease (Shi et al. 2020).

Subsequently, the number of infected people increased rapidly, and a month later, the outbreak had developed into a national crisis, with infected individuals diagnosed all over the country (Chan et al. 2020).

As of June 16, 2020, there were 7,941,791 confirmed cases of COVID-19 and 434,796 deaths worldwide and 867,624 confirmed cases of COVID-19 and 43,332 deaths in Brazil (Johns Hopkins University 2020; World Health Organization Coronavirus Disease (COVID-19) 2020).

COVID-19 has been associated with high rates of infection and lethality, especially in patients with comorbidities (Kakodkar et al. 2020). It is characterized by fever, cough, fatigue, shortness of breath, pneumonia, and other respiratory tract symptoms (Chen et al. 2020; Wang et al. 2020 a) and, in many cases, progresses to death.

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality in high- and low-income countries and represents a significant public health burden worldwide (Liu et al. 2016). In the United States, COPD affects over 6.5% of adults, is the third leading cause of death, and incurs 700,000 inpatient stays, 1.5 million emergency room visits, and USD 32 billion in cost annually (Ford et al. 2015).

In the 1960s, the prevalence of asthma and allergic diseases began to increase worldwide. Currently, more than 300 million people are affected by these diseases (Litonjua and Weiss 2007).

The association between air pollution and respiratory infections has been a matter of public health concern in recent years (Su et al. 2019); however, both public and scientific interest has heightened since the outbreak of the coronavirus disease 2019 (COVID-19) pandemic (Lewis 2020).

Petroleum processing can emit various organic compounds that can threaten human health (Godoi et al. 2013). Petrochemical industrial complexes (PICs) generate various air pollutants such as volatile organic compounds (VOCs), sulfur dioxide (SO₂), particulate matter (PM), and nitrogen oxides (NO_x) (Rodríguez

et al. 2004; Wichmann et al. 2009; Tanyanont and Vichit-Vadakan 2012; Hsu et al. 2018; Omidvarborna et al. 2018).

VOCs are organic compounds containing one or more carbon atoms; they have very high vapor pressure and readily evaporate into the atmosphere at room temperature. Some examples include acetone, benzene, ethylene glycol, formaldehyde, methylene chloride, perchloroethylene, toluene, xylene, and 1,3-butadiene (Minnesota Department of Health 2010).

High NO₂ concentrations are significantly associated with respiratory mortality (Chen et al. 2007; Hoek et al. 2013) and also generate harmful secondary pollutants such as nitric acid (HNO₃) and ozone (O₃) (Khoder 2002).

The question of whether COVID-19 can be spread by airborne transmission has been asked both in the scientific community and by the general public since the arrival of the virus. Similar to fine particulate matter (PM_{2.5}), viruses are among the inhalable biological particles that may be airborne. Recent studies have shown that viruses become airborne through sneezing and coughing and that they may be dispersed further as they commingle with PM_{2.5} (Frontera et al. 2020).

Coarse particulate matter (PM_{10-2.5}) consists of aerodynamically inhalable particles between 10 µm and 2.5 µm in size. Such particles are generally found near roadways and dust-generating industries. They are considered to be of regulatory interest because they may penetrate up to the level of the lower respiratory tract and the portion of the lung in which gas exchange occurs (Frontera et al. 2020).

There are few epidemiologic studies that relate air pollution and chemical industries to rhinitis, sinusitis, pharyngitis and obstructive pulmonary diseases (OPDs) such as asthma and COPD. Studies in South America have identified associations between residential proximity to a petrochemical plant and asthma, rhinitis, cough and wheezing (Wichmann et al. 2009; Moraes et al. 2010).

Previous studies have found that air pollution is a risk factor for respiratory infection because it carries microorganisms and affects the body's immunity (Zhu et al. 2020). Furthermore, recent studies suggest that the cause of death of many COVID-19 patients is related to cytokine storm syndrome (Guo et al. 2020; Mehta et al. 2020). In this syndrome, which is also known as hypercytokinemia, uncontrolled release of proinflammatory cytokines occurs (Tisoncik et al. 2012). It is a severe reaction of the immune system that leads to a chain of destructive processes in the body that can end in death.

São Paulo State (SP), the most populous and industrialized state in Brazil, has approximately 45 million inhabitants and 7,012 industries (IBGE 2016 a). Our previous studies (Zaccarelli-Marino 2012; Zaccarelli-Marino et al. 2016, 2019) involved subjects living in a densely populated area of SP surrounding the Capuava Petrochemical Complex (CPC). We reported primary hypothyroidism (PH) (Zaccarelli-Marino et al. 2016, 2019) and an increase in the incidence of chronic autoimmune thyroiditis (CAT) over the years (Zaccarelli-Marino 2012) and showed evidence that iodine should not be considered the agent responsible for autoimmune thyropathies in Santo André (Marino et al. 2009). Some of the results of the

current study have been previously reported in the form of an abstract and poster presented at the ABC University Medical Congress (Zacarelli-Marino et al. 2016a, b, 2017a, b, 2018a, b).

Objective

The objective of this study was to evaluate the interaction between pre-existing conditions (i.e., rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases such as asthma and chronic obstructive pulmonary disease, conjunctivitis, dermatitis and primary hypothyroidism) and a higher risk of complications when infected with SARS-CoV-2 in residents exposed to long-term air pollutants.

Methods

Study Population and Data Collection

This is a cohort study. We evaluated residents living in the area close to the Capuava Petrochemical Complex (CPC) (Fig. 1) in the Greater ABC region from July 2003 through June 2005.

The residents were divided into two groups (A and B) based on their proximity to the industrial areas; those who were considered nonexposed (not including a consideration of ambient air pollution) lived in the surroundings of a different industrial area, mainly steel industries in which no petroleum byproducts are manufactured.

The research population was defined after the purpose of this study had been explained to the participants. Prior to data collection, written informed consent was obtained (where appropriate, from the father or mother of the participant or from another responsible person), and authorization for this realization was obtained from the residents.

The data collection consisted of obtaining information on the residents, and a home-based questionnaire was administered to participating residents 8–72 years of age of both sexes who had lived in the area since 2004. The survey was developed and applied by the authors of this study.

Group A comprised 1002 residents, males and females, living in the surroundings of the CPC. This industrial area was named Region 1 and is occupied by 14 industries that produce polyethylene and polypropylene from naphtha distillation as well as various intermediary substances that are used as raw materials in the manufacture of other products. The area is located on the boundaries of Santo André, Mauá and São Paulo (located 0.5 km, 1.0 km, and 2.0 km from the CPC, respectively) in the State of São Paulo (SP), Brazil.

Group B comprised 1002 residents, males and females, living in the surroundings of various industrial areas; these industrial areas harbor mainly steel industries that generate no petroleum byproducts. The area occupied by Group B is located on the boundaries of Santo André, São Bernardo do Campo, and São Caetano do Sul (7.5 km, 8.0 km, and 8.5 km from Region 1, respectively) in SP, Brazil. This industrial area was named Region 2, and the residents of this region were treated as the control group.

Information on the city's population density was obtained from the Brazilian Institute of Geography and Statistics (IBGE) (IBGE 2016 b). Regions 1 and 2 were each divided into five cities; 334 residents were evaluated according to their distance from the CPC.

Each resident had lived in the same home in either Region 1 or Region 2 for more than 10 years, and the controls were matched to the participants with respect to their social and economic situations. The socioeconomic conditions of the participants were evaluated through the questionnaire. The residents were selected based on their personal reporting of similar salaries and social habits (these residents do not have the economic means to move far from the polluted areas).

The residents were considered adults if they were at least 18 years of age, and children and adolescents were under the age of 18. When the residents were children or adolescents, the questions were presented to their parents or to the person(s) responsible for the children.

The visits occurred once in each house; to guarantee maximal participation, we included weekends as a time for visits.

During the study period (2003–2005), there was no preselection of residents from Regions 1 or 2, and only spontaneous answers were considered.

The inclusion criteria were age between 8 and 72 years and having lived in the same house in either Region 1 or Region 2 for more than 10 years. Residents who worked at the CPC were excluded.

Written questionnaires (WQs) have been widely used in epidemiologic studies. The International Study of Asthma and Allergies in Childhood (ISAAC) WQ has been previously validated by a comprehensive study (Vanna et al. 2001).

The ISAAC was an important milestone among epidemiological studies on the prevalence of asthma and allergic illnesses in children and adolescents. The ISAAC was designed to evaluate the prevalence of asthma and allergic problems in children in different parts of the world using the standard method (self-administered written questionnaire and/or video questionnaire (Asher et al. 1995; ISAAC 1998)).

The written questionnaire (WQ) self-application of ISAAC was the more utilized instrument due to its ease of understanding, low cost, and independence of a trained interviewer (Asher et al. 1995; ISAAC 1998).

The questionnaire "The International Study of Asthma and Allergies in Childhood (ISAAC)" is an important epidemiological survey instrument established in 1991 to investigate asthma, rhinitis, and eczema in adolescents. ISAAC for nasal symptoms was chosen for the epidemiological diagnosis of rhinitis in children and adolescents; it included questions about sneezing, coryza, watery eyes, and itchy eyes (Vanna et al. 2001).

The European Community Respiratory Health Survey II (ECRHS II) was chosen for the epidemiological diagnosis of asthma; it includes questions about the prevalence of wheezing, coughing, panting, previous

diagnoses, and use of medication for the treatment of asthma. It is also used to determine the incidence of allergic diseases, asthma, and reduced pulmonary function and how ambient factors may be associated with allergic diseases and low pulmonary function (Jarvis and Burney 2002).

The survey respondents were asked their names (initials), age (years), sex (male, female), address and time at local residency, profession and education (adults), education (children and adolescents), and questions about their social and economic situation (adults) and medical history. Rhinitis was investigated through questions based on the same questionnaire: symptoms of sneezing, coryza, watery eyes, itchy eyes, nasal itching, rhinorrhea, blocked nose, cough, sputum production, shortness of breath and rhinitis. All of the symptoms were evaluated in children, adolescents, and adults. Sinusitis was investigated through questions about frontal headache or pain in the jaw region, posterior secretion, watery eyes, itchy eyes and sinusitis; pharyngitis was investigated through questions regarding oropharyngeal pain, scratchiness in the throat, and difficulty swallowing, and OPDs such as asthma and COPD were investigated through questions based on the questionnaire. OPD was based on personal reporting of symptoms such as cough, sputum production and shortness of breath, chest wheezing, and asthma or COPD.

Responses regarding rhinitis, sinusitis, pharyngitis, and OPDs such as asthma and COPD were only considered positive when the patient had been diagnosed and treated by a doctor and had been prescribed medication to treat these pathologies.

We selected only residents who presented with OPD with asthma and COPD and took medications for these pulmonary pathologies. Individuals who were taking medication that could interfere with this study, including those undergoing treatment for other otorhinolaryngological and pulmonary pathologies, were excluded. Individuals with a history of smoking or who suffered from other otorhinolaryngological pathologies, emphysema, bronchiectasis, lung surgery, or other lung diseases were also excluded.

Conjunctivitis was based on personal reports of signs and symptoms such as pink or red color in the white part of the eye, watery eyes, itchiness, a gritty feeling in the eye, irritation and/or burning sensation in the eye, pain in the eye, and photophobia.

The response for conjunctivitis was only considered positive when its diagnosis and treatment had been performed by a physician. We selected only residents presenting with conjunctivitis who were taking medications for this pathology.

Individuals who were taking medication to treat other eye diseases or who had a history of smoking, eye surgery, viral conjunctivitis, or bacterial infection of the eye were excluded.

Dermatitis was based on personal reports of symptoms such as redness, swelling, intense itching, and skin lesions such as red bumps, blisters, and pustules. The response to dermatitis was only considered positive when the residents' information about their diagnosis and treatment was based on a diagnosis

made by a physician. We selected only residents presenting with dermatitis who were taking medications for this skin pathology.

PH was evaluated through a questionnaire; we selected only residents presenting with PH and using thyroid hormone.

SARS-CoV-2 Database

The number of SARS-CoV-2 cases was collected from each city in the Greater ABC region, a traditionally industrial region of São Paulo State, Brazil, that is part of the São Paulo Metropolitan Region. Five cities were chosen: Santo André, Mauá, the Eastern Region of São Paulo City, São Bernardo do Campo and São Caetano do Sul. All information about SARS-CoV-2 cases was obtained from the five ABC Paulista prefectures, the São Paulo State Health Secretariat, and the Brazilian Ministry of Health (Brazil Ministry of Health 2020; Johns Hopkins University 2020).

Atmospheric Pollutants

The concentrations of atmospheric pollutants were analyzed in 2017 by numerical simulation with the AERMOD model using meteorological data for the period 2005 to 2009, data on the physical characteristics of the environment (topography and type of land use), and data on pollutant sources (information on the physical characteristics of the sources and their emissions), and these data were correlated with the results of research for the period 2003 to 2005.

AERMOD is a dispersion model developed by the American Meteorological Society (AMS) and the U.S. Environmental Protection Agency (EPA 2008) and made available for public use. The area influenced by atmospheric emissions from the CPC was evaluated using a combination of the AERMOD dispersion model with the Weather Research Forecast (WRF) meteorological model (Kumar et al. 2016).

According to recommendations made by the U.S. Environmental Protection Agency (EPA 2008), the dispersion model should only be applied when 5 years of meteorological data are available. This was accomplished by the fields provided by the WRF model; based on a combination of the meteorological fields with the pollutant emissions data, the concentration isopleths for the regulated pollutants were calculated for the receptor grid (Kumar et al. 2016).

The map of the concentrations of each pollutant was used to identify the hot spots in which the population was more exposed. The only documentation on the building downwash algorithm in AERMOD (American Meteorological Society/U.S. Environmental Protection Agency Regulatory Model), referred to as PRIME (Plume Rise Model Enhancements), refers to the fact that recent field and wind tunnel studies have shown that AERMOD can overpredict concentrations by factors of 2–8 for certain building configurations. While a wind tunnel equivalent building dimension study (EBD) can be conducted to approximately correct the overprediction bias, previous field and wind tunnel studies indicate that there are notable flaws in the PRIME building downwash theory. Although AERMOD/PRIME may provide accurate and unbiased estimates (within a factor of 2) for some building configurations, a major review and update are needed so that accurate estimates can be obtained for other building configurations for

which significant overpredictions or underpredictions are common due to downwash effects (Petersen et al. 2017).

Two categories of pollutants were analyzed: 1) volatile organic compounds (VOCs), the main source of which is evaporation and leakage from storage tanks; and 2) NO₂, CO, PM10, and SO₂, which are emitted from chimneys after processing and controlled by São Paulo State legislation (Fig. 1). Although Brazilian legislation does not regulate VOC concentrations, the dispersion curves of VOCs were also analyzed due to the impact of these compounds on health.

Ethical Statement

This research was approved by the Committee of Ethics in Research of the ABC School of Medicine, SP, Brazil and registered under number 087/2002.

Statistical Analysis

The likelihood of an individual's developing rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases such as asthma and chronic obstructive pulmonary disease, conjunctivitis, dermatitis, and primary hypothyroidism in each city were computed for each combination and compared through Wald tests with Bonferroni correction for multiple comparisons.

The association between both regions (Region 1 and Region 2) and diseases (rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases such as asthma and chronic obstructive pulmonary disease, conjunctivitis, dermatitis, and primary hypothyroidism) was compared by the chi-square test.

The different incidences and relative complication risks of SARS-CoV-2 in association with diseases such as rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases, conjunctivitis, dermatitis and primary hypothyroidism were compared using the chi-square test.

A polynomial regression that employed the logarithm of the odds of diseases as response and pollutant concentration up to the third degree, along with their interactions, was fitted to the pollutant, which exhibited a consistent trend of increase in concentration with increasing distance from the Capuava Petrochemical Complex (CPC).

Results

Demographic Characteristics and Determination of Risk Factors for SARS-CoV-2

Among the total residents (2004), there were significant differences in the distributions of individuals with rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases, conjunctivitis, dermatitis and primary hypothyroidism in Region 1 and Region 2, demonstrating that there is a higher incidence of the evaluated diseases in areas closer to the CPC (Tables 1 and 2).

Table 2 indicates the population density, the distances of the regions from the CPC, and the number of SARS-CoV-2 deaths per 10,000 cases.

Table 3 displays the number of confirmed cases and deaths due to coronavirus 2 (SARS-CoV-02) in Region 1 and Region 2 according to ABC Paulista prefectures, the São Paulo State Health Secretariat, and the Brazilian Ministry of Health.

Table 1

Incidence of rhinitis (RH), sinusitis (SI), pharyngitis (P), obstructive pulmonary diseases (OPDs), conjunctivitis (CO), dermatitis (DER) and primary hypothyroidism (PH) among individuals in Regions 1 and 2 (number of residents in each group = 1,002)

Disease/Relation	RH	SI	P	OPD	CO	DER	PH	TOTAL
Region 1	395	214	143	156	284	95	324	703
Region 2	253	150	76	55	121	58	65	244
Region 3	648	364	219	211	405	153	389	947
Ratio Region 1/ Region 3	1.56	1.43	1.88	2.84	2.35	1.64	4.98	2.88

Table 2

Population densities, distances of regions from the Capuava Petrochemical Complex (CPC), and SARS-CoV-2 deaths per 10,000 cases.

Regions and industrial area distance	Region 1	Region 2
Population density (1,000 hab/km ²)	5.90	5.40
Industrial area distance (km)	1.20	8.00
SARS-CoV-2 deaths ratio (average/10,000 cases)	9.7	5.5
Brazilian Institute of Geography and Statistics (IBGE). Coronavirus 2 (SARS-CoV-02) data for five prefectures of ABC Paulista, the São Paulo State Health Secretariat and the Brazilian Ministry of Health		

Compared with other residents who reported having had one or more of the evaluated diseases, the residents in Region 1 had a higher relative risk of complications from SARS-CoV-2 than the residents in Region 2 associated with each disease between the regions (Fig. 2).

Table 3

Number of confirmed cases and deaths relative to coronavirus 2 (SARS-CoV-02) in the cities of Santo André (North), Mauá and eastern São Paulo (Region 1) and Santo André (South), São Bernardo do Campo and São Caetano do Sul (Region 2).

Region	Region 1			Region 2		
	Santo André (north)	Mauá	São Paulo* (east)	Santo André (south)	São Bernardo	São Caetano
Cities	Santo André (north)	Mauá	São Paulo* (east)	Santo André (south)	São Bernardo	São Caetano
Confirmed	2,348	560	2,181	2,348	3,482	1,592
Deaths	101.5	106	121	105.5	274	69
Deaths ratio/10,000	4.5	18.9	5.6	4.5	7.8	4.3
*São Rafael (São Mateus). Consulted on June 16, 2020, from Coronavirus 2 (SARS-CoV-02) data. Five prefectures of ABC Paulista, the State Health Secretariat of São Paulo and the Brazilian Ministry of Health						

Based on the dispersion model, it was possible to estimate the average concentrations of NO₂, CO, PM10, SO₂ and VOCs for Region 1 and Region 2; these are presented in Table 4.

Table 4
Average concentrations of NO₂, CO, PM10, SO₂ and VOCs obtained via the simulated plume along with the distance from the CPC.

Location	Distance (km)	NO ₂	CO	PM10	SO ₂	COVs
		(µg/m ³)				
Region 1	0.5	13.16	3.95	0.93	1.36	477.4
	1	10.21	2.84	1.49	3.54	313.0
	2	4.32	1.21	0.83	2.03	69.3
Region 2	7.5	2.15	0.69	0.19	0.34	10.5
	8	1.82	0.59	0.16	0.33	9.2
	8.5	1.84	0.59	0.16	0.31	10.3

Region 1, which is closer to the CPC than Region 2, showed higher average concentrations of all pollutants, and we also found differences in the incidence of rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases, conjunctivitis, dermatitis, and primary hypothyroidism in these two regions (Table 1).

Discussion

According to our results, the average concentrations of NO₂, CO, PM₁₀, SO₂, and VOCs obtained from the simulated plumes in the cities studied are more significant in areas closer to the CPC (Table 4); this suggests that people living in those areas are more exposed to atmospheric pollutants than people who live far from the petrochemical industries and is consistent with many other studies (Kalabokas et al. 2001; Ragothaman and Anderson 2017; Zaccarelli-Marino et al. 2019).

Our epidemiological surveys were conducted through questionnaires completed from July 2003 to June 2005 by residents living close to the CPC, and our findings showed different incidences of rhinitis, sinusitis, pharyngitis, OPD, conjunctivitis, dermatitis, and PH among a total of 2,004 residents from two different regions (Region 1, which is close to the CPC, and Region 2, which is further away; the respondents included 1,002 residents from each region) (Table 1) and differences in the risk of developing complications from SARS-CoV-2 for the residents of the two regions (Fig. 2).

The concentrations of atmospheric pollutants were analyzed in 2017 using numerical simulations with the AERMOD model using meteorological data for the period from 2005 to 2009, correlating these data with the research done in 2003 to 2005.

Researchers have shown that short-term (hours, days) and long-term (months, years) exposure to PM_{2.5} is associated with aggravation of asthma and respiratory symptoms and with increased hospital admissions. The adverse health effects of acute (hours to days) and chronic (months to years) exposure to air pollution range from minor irritation of the upper respiratory system to an impact on morbidity in the form of chronic respiratory diseases (asthma, chronic obstructive pulmonary disease (COPD), heart disease, diabetes, hypertension, lung cancer, and death (Burnett et al. 1998; Andersen et al. 2012; Hoffmann et al. 2012; Ko and Hui 2012; Lavigne et al. 2012; Wellenius et al. 2012). More specifically, both acute and chronic exposure to fine particulate matter (PM_{2.5}) has been shown to induce a systemic inflammatory response that can increase the risk of cardiorespiratory morbidity (Stieb et al. 2002; Fink et al. 2012; Nachman and Parker 2012).

PM_{2.5} consists of particles with median aerodynamic diameter of 2.5 μm or less; particles of this size are small enough to invade even the smallest airways, and PM_{2.5} is associated with adverse health impacts. It generally results from activities that burn fossil fuels, such as operating fuel-powered automotive engines, smelting, and metal processing. The World Health Organization estimated that PM_{2.5} accounted for 3.1 million deaths and approximately 3.1% of the global disability-adjusted life years (DALYs) in 2010 (WHO 2013).

Because the petroleum refining and petrochemical industries produce emissions at many stages of their operations, releasing pollutants such as volatile organic compounds, greenhouse gases, and particulate matter (Ragothaman and Anderson 2017), we believe that our findings are related to CPC emissions and that these emissions can significantly decrease the air quality and cause short-term and long-term health impacts for people living near the sites and in the same regions as these industries.

It is important to know the atmospheric lifetime of VOCs to gain an understanding of the distances they might travel in air. A higher atmospheric lifetime indicates that VOCs can travel a greater distance in the atmosphere, possibly leading to impacts much farther from the emission source (Ragothaman and Anderson 2017).

A wide variety of hazardous chemicals may originate from industrial facilities and other activities to the environment, and these chemicals are harmful to human health and to the environment (Ragothaman and Anderson 2017).

Exposure to air pollution is a known risk factor for asthma and COPD. Individuals with asthma–chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS) have a more rapid decline in lung function, more frequent exacerbations, and poorer quality of life than those with asthma or COPD alone (To et al. 2016).

Air pollution has indirect systemic effects linked to pro-inflammation and oxidation mechanisms of the lungs, and alterations in immunological processes increase the population's vulnerability to COVID-19 (Contini and Costabile 2020). This is consistent with studies that linked prolonged exposure to air pollution to acute respiratory inflammation, asthma attacks, and death from cardiorespiratory disease (Bates et al. 1990; Schwartz and Dockery 1992; Schwartz et al. 1993; Dockery and Pope 1994), and the possibility of a detrimental effect of air pollution on the prognosis of patients affected by COVID-19 is plausible.

In this study, the relative SARS-CoV-2 risk was higher for residents with rhinitis, sinusitis, pharyngitis, OPD, conjunctivitis, dermatitis, and PH who live closer to the CPC than the risk for residents who do not have these diseases, and these residents displayed increased vulnerability to COVID-19.

Chemical composition influences ecotoxicity, cytotoxicity, and genotoxicity in different ways so that different biological outcomes are expected even in cases of similar number and mass concentrations (Lionetto et al. 2019).

According to the World Health Organization, 41 million people died from noncommunicable diseases (NCDs) worldwide in 2016; this represents 71% of global deaths (WHO 2018b).

An important cause of these NCDs is industrial air pollution. However, its quantity and composition vary considerably with location. As an example, living in proximity to industrial facilities appears to be an adverse condition. Environmental air pollution contributes to this huge burden through the initiation and promotion of respiratory diseases that are leading causes of death (WHO 2010).

The respiratory tract is one of the parts of the body that is most involved in susceptibility to air pollution. In particular, asthma and COPD had a major impact on the overall worldwide mortality of 4.2 million caused by respiratory diseases in 2008 (WHO 2010). In addition to mortality, the chronic nature of asthma and COPD causes considerable morbidity. In 2012, 6.62 million disability-adjusted life years

(DALYs) for COPD alone worldwide (WHO 2016) indicated an immense socioeconomic impact of noncommunicable respiratory diseases.

It is well established that individuals with both asthma and COPD and those with asthma - COPD overlap syndrome (ACOS) have more frequent exacerbations, a more rapid decline in lung function, and worse quality of life than individuals with asthma or COPD alone (Kauppi et al. 2011; Miravitlles et al. 2013; Menezes et al. 2014; Papaiwannou et al. 2014).

It is recognized that these conditions or their expression may be influenced by both host and environmental factors (Papaiwannou et al. 2014), including exposure to air pollution.

Research has shown that short-term exposure to O₃ is associated with decreased lung function (Rice et al. 2013) and increased hospitalizations for COPD (Medina-Ramón et al. 2006; Ko et al. 2007; Halonen et al. 2010), whereas long-term exposure to O₃ is associated with increased respiratory mortality (Jerrett et al. 2009).

Similarly, ground-level ozone (O₃) or ambient O₃ pollution is another major source of air pollution that is also associated with adverse health impacts. The World Health Organization has estimated that 0.1% of the global DALYs in 2010 can be attributed to O₃ exposure (WHO 2011).

Concentrations of NO₂, CO, PM₁₀, SO₂, and VOCs that are above the levels specified in the São Paulo air quality standards are present inside the CPC area (Region 1); this can be related to the main signs and symptoms associated with exposure to VOCs, including conjunctival irritation, nose and throat discomfort, allergic skin reactions and dyspnea (EPA 2017). The health effects of VOCs may include eye, nose, and throat irritation, which are also the initial symptoms of COVID-19.

It is essential to know the atmospheric lifetime of VOCs to understand the distances they might travel in the air. A higher atmospheric lifetime indicates that VOCs can travel a greater distance in the atmosphere, possibly impacting areas much farther away from the emission source (Ragothaman and Anderson 2017).

This supports our findings, which showed that the highest levels of VOCs were localized in proximity to the CPC; the levels in the limited area of the CPC were higher than those allowed in the standard for air quality, and increased incidences of rhinitis, sinusitis, pharyngitis, OPD, conjunctivitis, dermatitis, and PH were found in this area.

According to our results, 143 residents of the region closer to the CPC had pharyngitis, affected by air pollution. In the case of COVID-19, one of the initial symptoms is sore throat. Hence, while sore throat may be the symptom described by the patient, the examination might also reveal nasopharyngitis (Renner et al. 2012), and residents near the CPC should be alert to the risk of COVID-19.

Brazil is currently among the group of countries with the highest prevalence of allergic rhinitis in the world (Solé et al. 2006). Rhinosinusitis (RS) is characterized by inflammation of the mucosae of the nose and paranasal sinuses, and it is one of the most prevalent disorders of the upper airways.

According to our results, 395 of the residents in the region closer to the CPC had rhinitis, and 214 of them had sinusitis. Due to their high degree of contact with the environment and their limited defense mechanisms, the nasal cavity is one of the organic systems that is most vulnerable to environmental pollutants (Shusterman 1997); that could tend to increase the vulnerability of this population to COVID-19.

Riediker et al. (2001) found that rhinoconjunctival tissue is sensitive to irritant stimuli during ongoing allergic inflammation; thus, symptoms of allergic rhinoconjunctivitis might be exacerbated in areas with increased levels of air pollutants.

Conjunctivitis is most associated with O₃ and NO₂ exposure, although PM₁₀ and SO₂ exposure are also correlated (Chang et al. 2012).

Our findings showed that levels of NO₂, SO₂, and MP₁₀ that exceeded the levels indicated in the São Paulo air quality standard were localized in proximity to the CPC, where we found more cases of conjunctivitis.

According to our results, 284 of the residents in Region 1 had conjunctivitis. The dense innervation of the ocular surface is extremely sensitive to chemical substances present in the environment. Additionally, human eyes are protected only by a thin layer of tear film, causing them to be very susceptible to the harmful effects of air pollution (Chang et al. 2012; Hong et al. 2016; Fu et al. 2017); if these residents are affected by COVID-19, they could be at higher risk of dangerous eye complications such as retinopathies.

Air pollution is associated with COPD risk (Schikowski et al. 2014). It may also be a factor in transforming asthma into COPD (To et al. 2016).

In this study, 156 residents of the region closer to the CPC had OPD, a condition that is also affected by air pollution. It causes breathlessness in most patients with severe chronic respiratory disease, and in cases of COVID-19, one of the initial symptoms is shortness of breath.

Elevated exposure to NO₂ has been associated with hypertension (Shin et al. 2020), heart and cardiovascular diseases (Mann et al. 2002; Pope et al. 2004; Gan et al. 2012), increased rates of hospitalization (Mann et al. 2002), COPD (Euler et al. 1988; Abbey et al. 1993), significant deficits in the development of lung function in children (Gauderman et al. 2000; Avol et al. 2001), reduced lung function or lung injury in adults (Rubinfeld et al. 2005; Bowatte et al. 2017) and diabetes (Shin et al. 2020).

Aging has been associated with a decline in immune defenses and respiratory function that can result in a higher predisposition to respiratory infections. Moreover, among the chronic diseases that affect the elderly population, COPD and asthma can accelerate pulmonary function decline and increase mortality risk (Bentayeb et al. 2012).

This study shows that the closer participants lived to Region 1, the higher was their risk of death from SARS-CoV-2. This finding should direct the attention of authorities to these populations.

Our findings showed that higher values of NO₂ were localized in regions that are in proximity to the CPC. NO₂ is a common tracer of air pollution/industrial activity associated with morbidity and mortality (He et al. 2020a, b).

Interdisciplinary research in air pollution and biomedical science can explain how exposure to air pollutants may affect respiratory viral infections, especially in populations already at risk of increased morbidity and mortality rates after infection with respiratory viruses such as SARS-CoV-2.

Exposure to ambient air pollution has recently been implicated in the occurrence and development of autoimmune diseases (Zhao et al. 2019). Autoimmune diseases represent a broad spectrum of disorders characterized by direction of the body's immune responses against its own tissues, resulting in prolonged inflammation and subsequent tissue damage (Zhao et al. 2019).

According to our results, 324 residents of Region 1 had PH. In iodine-sufficient regions, the primary cause of PH is CAT (Dayan and Daniels 1996) and sufficiency of iodine (Marino et al. 2009; de Freitas et al. 2010), and an increase in CAT incidence over the years (Zaccarelli-Marino 2012) was demonstrated in a previous study in Region 1. This finding could draw attention to a risk factor for complications of SARS-CoV-2.

Region 1 is unique because its residents live near petrochemical industries, and environmental factors could affect the cases of rhinitis, sinusitis, pharyngitis, OPD, conjunctivitis, and PH. This chronic exposure could be an important contributor to disease and to the higher risk of complications of SARS-CoV-2 in individuals with long-term exposure to air pollutants.

China, where the COVID-19 epidemic started, is severely affected by air pollution (He et al. 2020a, b). An association between short-term exposure to air pollution and COVID-19 infection has also been described for the recent outbreak in China (Zhu et al. 2020).

In recent decades, environmental pollution has increased and air quality has deteriorated in China, mainly due to the country's rapid industrialization (Zhang et al. 2012).

The spatial analysis performed in our study was conducted on a regional scale and combined with the number of deaths that occurred in 66 administrative regions in Italy, Spain, France, and Germany (Ogen 2020). The results showed that of the 4,443 fatality cases, 3,487 (78%) occurred in five regions located in northern Italy and central Spain. Additionally, the same five regions show the highest NO₂ concentrations and downwards airflow, a factor that prevents efficient dispersion of air pollution. These results indicate that long-term exposure to NO₂ may be one of the most critical contributors to fatalities caused by the SARS-CoV-2 virus in these regions and perhaps across the whole world (Ogen 2020).

Since the presence of comorbidities appeared to be a determinant of the etiology and severity of COVID-19 symptoms (Chen et al. 2020; Wang et al. 2020b; Wu et al. 2020b), a role of atmospheric pollution in contributing to the high levels of SARS-CoV-2 lethality in northern Italy has been hypothesized (Conticini et al. 2020). In this study, we also show that higher values of NO₂ localized in regions in proximity to CPC could increase the risk of complications in cases of SARS-CoV-2. Air pollution has been termed the "silent killer" by the World Health Organization (WHO 2018a) because its effects often go unnoticed or are not easily measured.

In the present case of SARS-CoV-2, air pollution may facilitate the upsurge of more severe symptoms of the disease of the eye (Chang et al. 2012; Hong et al. 2016; Fu et al. 2017), nose (Shusterman 1997), and throat (Renner et al. 2012), since the virus may travel through the cranial nerves, producing anosmia, ageusia (lack of taste) and possibly retinopathy.

To date, only a limited number of epidemiological studies have actually identified and/or quantified the risk of rhinitis, sinusitis, pharyngitis, OPD, conjunctivitis, dermatitis, and PH. Our study adds evidence that chronic exposure to air pollution may contribute to significant morbidity and that it may contribute to SARS-CoV-2 risk in individuals with preexisting diseases. Better knowledge of the risks posed by exposure to environmental pollutants and SARS-CoV-2 may help us understand and develop preventive strategies to modify the progressive deterioration of lung function that leads to death.

The results of this survey may help to identify susceptible populations that are vulnerable to air pollution and to target preventive strategies.

In addition to the increasing frequency of health service use, we can put forth the hypothesis that individuals living near the CPC, a petrochemical industrial complex, have more symptoms that affect their daily lives and have lower health-related quality of life.

This is a pioneering study related to inflammatory diseases, such as diseases of the upper and lower airways, conjunctivitis, thyroid diseases, and air pollution, and of the impact of these diseases on SARS-CoV-2 pandemic infection in a population living in the area surrounding a petrochemical complex in Brazil.

We recommend that patients affected by SARS-CoV-2 be followed up for a long period of time after medical discharge as they may experience consequences of COVID-19 such as vascular complications and pulmonary fibrosis.

Given the magnitude of the problem of air pollution and the major global health problems generated by SARS-CoV-2 and COVID-19, it is essential that any link between air pollution and respiratory, immunological and hormonal diseases be firmly established.

This study has several strengths, including its use of large-scale population-based data covering a 15-year period and its use of well-defined geographic regions in residents living in the CPC influence area in

the Greater ABC region.

The data used in this study were also linked to data on provincial air pollution and to population survey data gathered over a period of multiple years to permit a broader evaluation of the impact of risk factors for SARS-CoV-2 and the development of COVID-19 in the population. The study is also strengthened by its adjustment for important health risk factors, including rhinitis, sinusitis, pharyngitis, OPD, conjunctivitis, dermatitis, and PH, in the analysis of the relationship between air pollution and SARS-CoV-2. Future research in this area should be conducted.

Conclusion

This study found that residents with rhinitis, sinusitis, pharyngitis, obstructive pulmonary diseases, conjunctivitis, dermatitis, and primary hypothyroidism who were exposed to higher levels of NO₂, CO, PM₁₀, SO₂, and VOCs had an increased risk of complications from SARS-CoV-2 infection.

Given the asymptomatic characteristic of coronavirus disease in its initial development and the risks posed by its complications, we suggest that SARS-CoV-2 be continuously evaluated in chemical plant employees and in residents living near industrial areas.

Declarations

Ethics approval and consent to participate

This research was approved by the Committee of Ethics in Research of the ABC School of Medicine, SP, Brazil, and registered under number 087/2002.

Consent for publication

The authors declare that they have no competing interests.

Availability of data and materials

The data generated and used in the analysis of the present study are included in published articles.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Maria Angela Zaccarelli-Marino participated in the design of the study, the acquisition of the data, the interpretation of the results, and the drafting of the manuscript and critically revised the manuscript.

Thalles Zaccarelli Balderi participated in the design of the study, the acquisition of the data, the interpretation of the results, the statistical analysis and the critical revision of the manuscript.

Felipe Mingorance Crepaldi participated in the design of the study, the acquisition of the data, the interpretation of the results and the literature revision.

Rudá Alessi participated in the design of the study and the acquisition of the data and critically revised the manuscript.

Marco Antonio Garcia Martins participated in the design of the study and the interpretation of the results. He also critically revised the manuscript and supervised the study.

All authors have read and approved the final manuscript.

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Figures

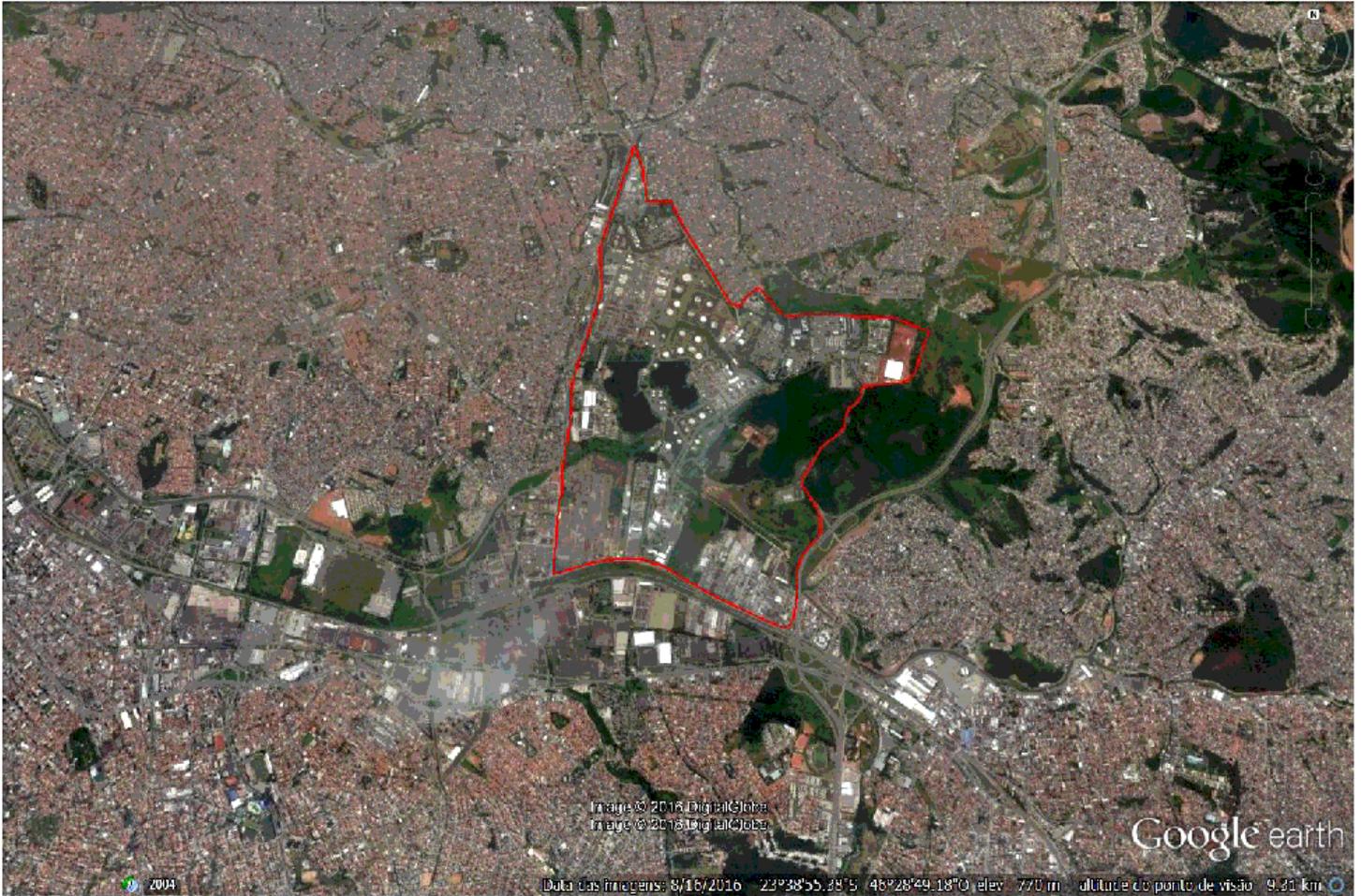


Figure 1

Satellite image showing the Capuava Petrochemical Complex (CPC) area (outlined in red)

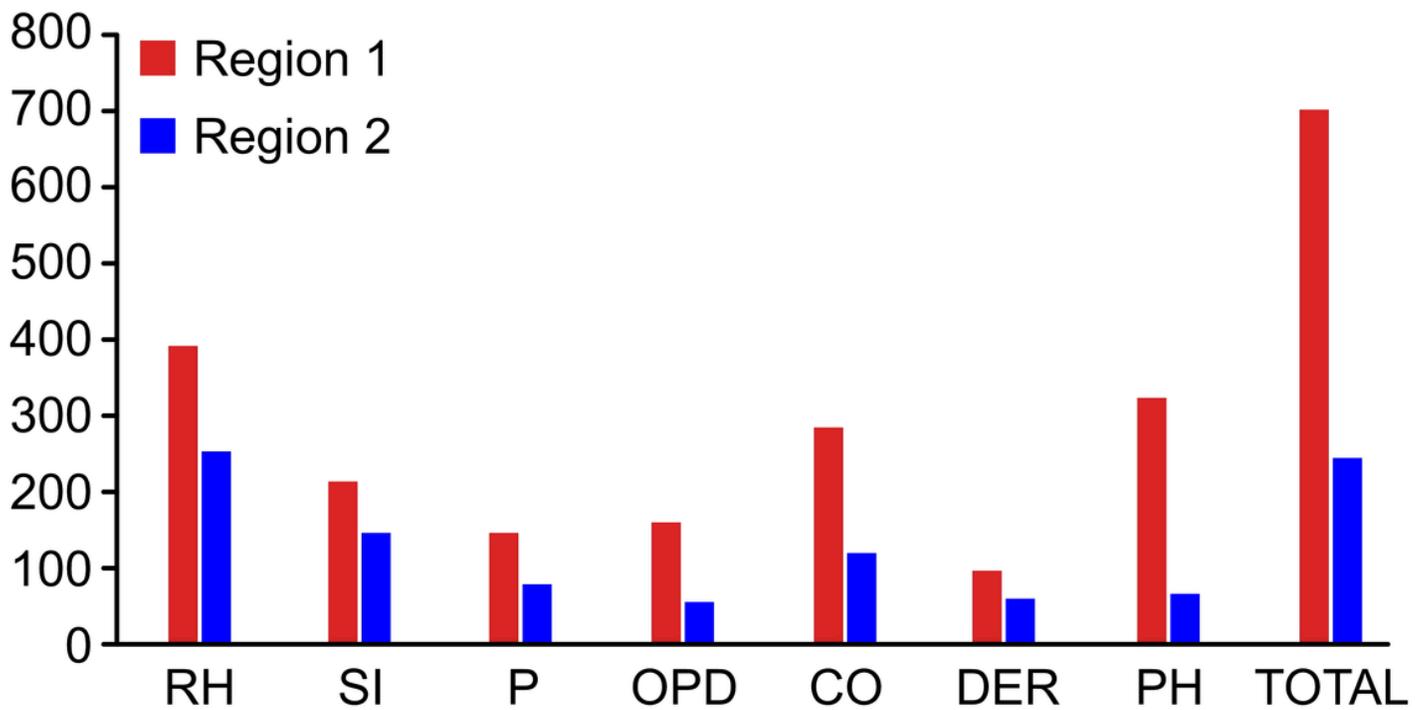


Figure 2

Difference in relative SARS-CoV-2-related complication risk associated with rhinitis (RH), sinusitis (SI), pharyngitis (P), obstructive pulmonary diseases (OPDs), conjunctivitis (CO), dermatitis (DER) and primary hypothyroidism (PH)

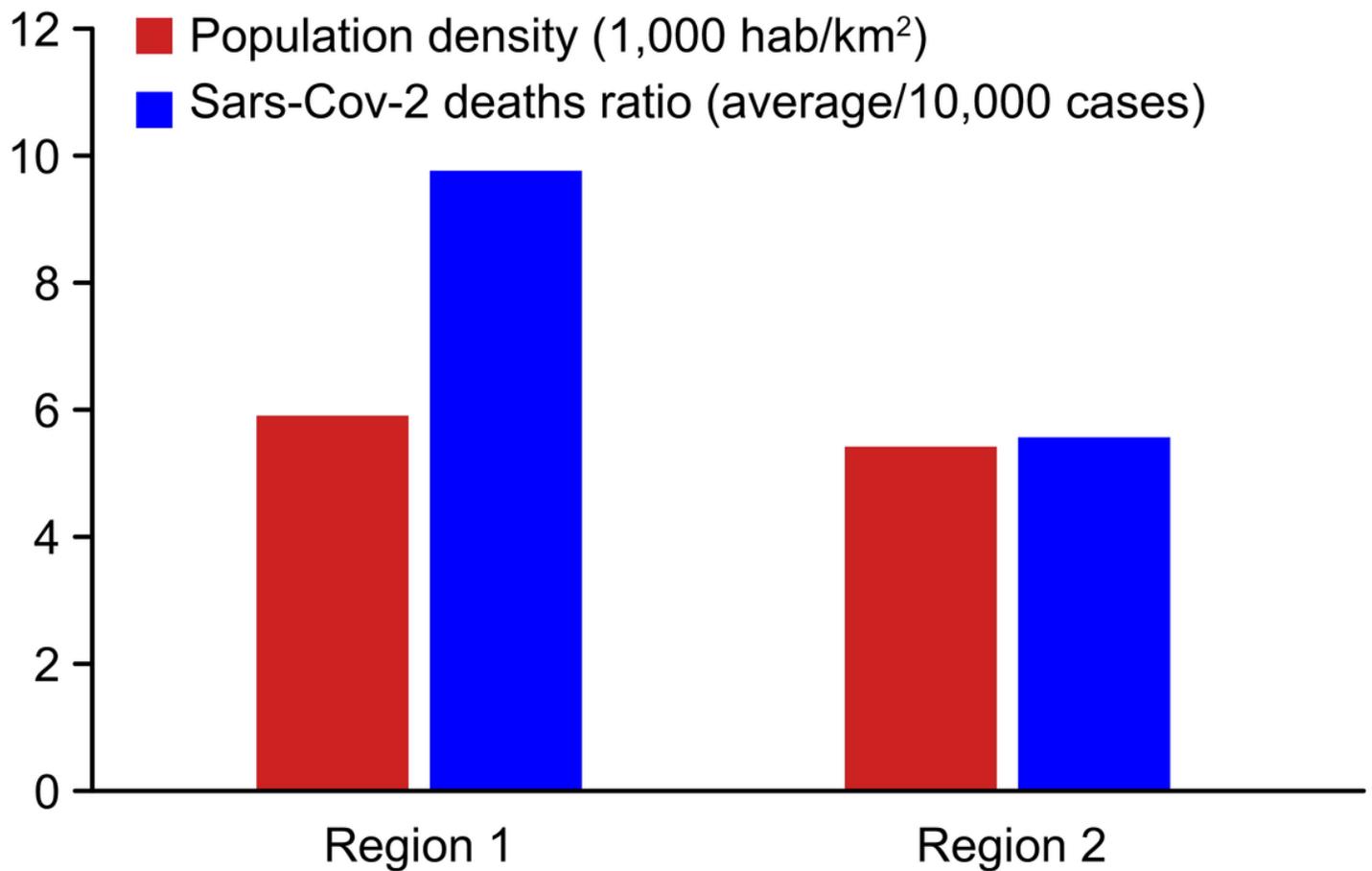


Figure 3

Absolute relation between SARS-CoV-2 deaths and the proximity of each region to the CPC. The regions have similar population densities