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Indoor air pollution affects the early COVID-19 fatality: A multiple linear regression analysis

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Abstract

In this study, early COVID-19 mortality and reproduction rates were settled as dependent variables and they were investigated to understand the most effective factors on these parameters. For this, various urban-related and host factor-related variables such as household type, GDP rates, etc., were collected for 56 countries from different sources, and stepwise multi-linear regression analyses were conducted to get regression equations to explain these dependent variables. Based on the results, indoor air pollution death rates were the most effective independent variable with the biggest partial contribution to the fatality of the COVID-19 regression equation. Moreover, due to the clusters of countries that show the highest and lowest indoor air pollution death rates, which may represent a global organization of the human population, it may be concluded that microbial circulations of the biologically evolving ecosystem also may be connected to the human factors, especially based on supply chains of these countries among agriculture, energy, and technology. The results suggest that the air quality within buildings, which are crucial elements of urban systems, could be the primary global factor influencing both the fatality and spread of COVID-19. This implies that both the building structures and the population compositions of cities may have a more significant impact on the trajectory of microbial diseases than previously acknowledged.

Keywords

COVID-19, Fatality, Indoor Air Pollution, Regression, Toxicity

Introduction

Toxic is a substance that is poisonous to other substances or organisms, and toxicity is the quality of being toxic(Mückter, 2003). Although the term toxic usually refers to a poison that affects a particular organism in a particular way, the term has changed over time. Modern toxicology - the science of toxics - does not treat toxics simply as a poison. The one-dimensional term toxic has evolved into a multidimensional perspective: toxics are not seen as a substance with only one effect; they act differently in several domains and can even be influenced by the actions of organisms(Krebs & McKeague, 2020; Libralato et al., 2010; Maeder et al., 2004; Mückter, 2003). So, toxicity therefore implies a broad relationship between the toxic substance and the organism. Ecotoxicology is the branch of toxicology that deals with the study of toxic effects caused by natural and synthetic pollutants on ecosystem components, animals (including humans), plants, and microbial in an integrated context (Anderson et al., 1994; Clements & Rohr, 2009). There are various classes of toxins known for different organisms, such as metalloids, pesticides, hydrocarbon compounds, etc. All of them have different effects on environmental elements, and they are also pollution-related (Gautam & Anbumani, 2020; Kishor et al., 2021; Menéndez-Pedriza & Jaumot, 2020; Palmer & Herat, 2021). Toxic substances can differ from each other based on molecular size, concentration, effects on different organisms, and so on. In terms of indoor air pollution, the networks of ecotoxicology become important since, with human factors and in human ecosystems, the toxic compounds are mainly created by both human population structure and human actions collectively (C. Lu et al., 2022; Rabha et al., 2018; Shi et al., 2022; Sriprapat et al., 2014).

Toxic substances are taken up by organisms through different mechanisms such as dermis, grids, pores, etc. The ingested substances accumulate in the cells of the organism (bioaccumulation: the net result of uptake, biotransformation, and elimination), and within the foot chain, toxic substances cumulatively accumulate in the bodies of different organisms (biomagnification) (Gobas et al., 2016; C.

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Lu et al., 2022; Sriprapat et al., 2014). Once in the organism's body, the toxic substance can be transformed into another form by different mechanisms (biotransformation) (Gray, 2002; Soffers et al., 2001). In addition, once in the body, the contaminant may disappear (elimination), such as through excretion or excretion (de Sousa et al., 2018). Moreover, a toxic substance can affect different organisms in different ways. Sometimes a substance may be toxic to some populations - groups of organisms of the same species - or sometimes it may be toxic only to some individuals in a population. Also, sometimes a substance can be toxic to a community - groups of different populations living in the same area - or only affect some populations in the same community(Cho et al., 2012; Mironenko et al., 2000a; Yang et al., 2014; Zhdanova et al., 2000). In addition, different organisms can react to the same toxic substance in different ways(Mironenko et al., 2000a). Through biotransformation, they can carry out elimination, detoxification, activation, redistribution, and sequestration processes for the toxic substance in the body. As a result of these processes, the effect of the toxic substance is changed by the organism and the environment due to the modifying process performed by the organism on the toxic substance(de Sousa et al., 2018; Messaoudi et al., 2019). Organisms can also react with the toxic substance genetically (Anderson et al., 1994). If somehow the toxic substance changes the genetic material in such a way that the organism can adapt the material so that it is no longer harmful to the organism, the material can no longer be considered toxic(Mironenko et al., 2000a; Yang et al., 2014).

The toxicity, pollution, and microbial evolution are interconnected and all these dimensions have impacts on the human population (Koechler et al., 2015a; Parsek et al., 1995; van der Meer, 2003). Evolution is mainly time-dependent because the evolution of a population requires the number of generations to come to an end (HO et al., 2011). So, depending on the size of the organisms - and of course depending on the size of the population, generation times, the size of the genomes, etc. - the generation time of populations, and also their response to environmental changes such as climate change, varies (Orive, 1993; Sheridan & Bickford, 2011). For instance, some bacterial populations can evolve from one species to another within days, but the transition from mammoths to the current elephants takes a much longer time, thousands of years (Krause et al., 2006; Ochman & Wilson, 1987; Ziebuhr et al., 1999). Moreover, in terms of microbial evolution and microbial circulations among organisms, feedback mechanisms become important to understand the relations between the organisms and their ecosystems (Biedermann & Rohlfs, 2017; Moreno-Fenoll et al., 2017). There are two types of feedback mechanisms (Baer & Blair, 2008; Crespi, 2004; Lashof et al., 1997). In a given homeostatic system, a negative feedback mechanism operates. A negative feedback system is a loop system that ensures that conditions are maintained within set limits. Within these limits, changes can be reversed. For instance, arterial blood pH is normally maintained at 7.40 within the range of 7.35 and 7.45. If there are some fluctuations within this range, the internal influence of external influences can be reversed back to the normal position(Breen, 2001). The process of reversal of normal conditions is called a negative feedback mechanism because the effects are controlled by the opposite reaction, which is the opposite of the effect. In the positive feedback mechanism, homeostatic protection is disrupted through new states, and a range of normal conditions are irreversible changes. The effect of positive feedback, despite negative feedback, cannot be reversed by another opposite reaction, rather the effect itself makes the change. The effect grows by feeding on itself until it reaches another homeostatic range of conditions. For instance, Atlantic cod stocks were severely overexploited in the 1970s and 1980s, leading to their sudden collapse in 1992 (Collie et al., 2013). Overexploitation is irreversible, and the effect of overexploitation - the extinction of fish - is self-perpetuating, with more extinctions occurring after a threshold level is crossed.

Although negative feedback works in a way that stabilizes traits rather than creating chaotic conditions on organisms -in the case of a positive feedback mechanism-, it can gradually change the threshold levels for migration and reproduction rates of organisms with negative feedback mechanisms (Procacci et al., 1975). For instance, two different genes for the same trait may have the same fitness values -this means that natural selection will not work on these different traits because of the same fitness, and character types can evolve in equally varying directions. Thus, with gradual change with negative feedback, it is conceivable that the population could evolve into another population with more stabilized genes(Zamorano et al., 2023). Moreover, the feedback interval may also change due to the separation of traits, as some members migrate or there are some barriers between individuals of the same population. This means that the separated individuals will evolve in different ways, resulting in different species (Bader et al., 2015). This kind of change can take decades or billions of years, depending on the size of the organisms and the speed of changing conditions. In general, small-sized organisms, such as bacteria or phytoplankton, evolve faster and further than large-sized organisms, such as humans or birds (Krause et al., 2006; Ochman & Wilson, 1987). This condition is also applicable to human ecosystems, in the case of COVID-19, the viral evolution is much stronger and has a higher rate compared to the host -the human- (Decaro & Lorusso, 2020) and the circulation of the virus in human environments may represent both the human population structure and organization in terms of connecting the microbial environment with human ecosystems (Dowd et al., 2020; Madrazo Cabo et al., 2020).

If there are some major impacts, the positive feedback mechanism may work. This means that if the species survive during and after the positive feedback, the new homeostatic range, which is different from the initial conditions, will be established. For instance, a mutation in some individuals in a colony of bacteria exposed to UV radiation helps the bacteria to survive. In this case, the mutation will be maintained and this process will result in the creation of a new homeostatic plateau for the new colony (Alcantara-Diaz, 2004). This kind of change is difficult to see in a large-sized organism. Due to the complexity of large organisms, such as humans, an effect that causes a positive feedback mechanism will usually kill the organisms (Benton & Twitchett, 2003). But in small-sized organisms, especially single-celled organisms such as fungi or bacteria - and viruses such as SARS-CoV-2 - such changes have large effects, and survival and reproduction rates are higher than in large sizes (Alcantara-Diaz, 2004; Decaro & Lorusso, 2020; Lashof et al., 1997; Pereson et al., 2021; Petrosillo et al., 2020).

Response to toxic compounds varies among organisms in a population, and the human population structure that is based on their responses to various toxic compounds is also predictable by combining the data of various cell lines (Eduati et al., 2015; Möller et al., 2001). Since all living things are the result of evolution, these organisms have somehow acquired resistance to existing toxics in the past (Baquero et al., 2009; Koechler et al., 2015b) such as in Chernobyl, after the well-known nuclear power plant explosion, some fungi were able to use radioactive decay to survive (Mironenko et al., 2000b). The accumulation of antibiotics in nature due to human activities such as poultry or drug treatments causes microorganisms to become resistant to these substances (Baquero et al., 2009). In addition, due to the accumulation of plastics, there are plastic-eating bacteria that have evolved(Yang et al., 2014). Since organisms are part of the environment and affect the environment, interactions between toxins and organisms also affect the environment. For instance, after the evolution of photosynthetic plants, the earth's atmosphere changed irreversibly, contributing to higher oxygen levels (Scoffoni et al., 2016). Moreover, COVID-19 is related to human factors, pollution, microbial evolution, and toxicity(Bloem & Salemi, 2021; Madrazo Cabo et al., 2020; Petrosillo et al., 2020). Microbial evolution, fatality, and reproduction of SARS-CoV-2 are also related to several human population-related factors such as disease rates, household types, etc. which may represent human population organization with its connection to the environment(Connolly et al., 2020; Dowd et al., 2020; Lulbadda et al., 2021).

When the words come to the human population, the connection between humans and the environment includes various aspects such as trade relationships between humans, such as war conditions, educational or cultural organizations of humans, etc (Gilmour et al., 2007; Landrigan et al., 1999). Human actions are diverse and create lots of toxic compounds that affect environmental conditions and promote the evolution of biological organisms (Mironenko et al., 2000b; Yang et al., 2014; Zhdanova et al., 2000). Supply chains, such as agriculture, technology, and energy, are global networks that have huge impacts on the environment and also connect the human microenvironments by providing coordination of releases of materials and resources (de Kok & Fransoo, 2003; Todeva & Rakhmatullin, 2016). All these processes also have impacts on the environment, such as, the outputs of these processes may be toxic compounds, or the result in population structure based on these actions may create stratification among the human population and these may create outputs of human-environment relations (Wang et al., 2022). In this case, global supply chains are highly related via air pollution hotspots (Moran & Kanemoto, 2016; Song et al., 2020). To represent these complex interactions between the human population and the environment, there are need for indicators to simplify and model the relationships of complex interaction networks (Spangenberg, 2002). Indicators are data types that help to reduce a larger and more complex event or structure and evaluate it in terms of a single or a few parameters, and there are needs for indicators such as the sustainability of cities and ecological validity (Kogan et al., 1977; Munier, 2011). In this study, we argue that indoor air pollution mortality rates can be an indicator that is the representative parameter of the organizational and spatial structure of the human population, both because it is economically and collectively relevant to the global human population structure (Moran & Kanemoto, 2016)and because it is a variable that predicts COVID-19-related mortality according to literature (Azuma et al., 2020; Domínguez-Amarillo et al., 2020) and our results of this study. Since the data from COVID-19 is incredibly diverse (Chen et al., 2021; Hasell et al., 2020; Tsai et al., 2021; Zawbaa et al., 2022)-such as time of viral spread, variant data of each mutant, country and city-dependent factors of the disease, treatment responses, etc-, it may provide an insight of understanding microbial circulations among human population via considering human population structure that represent the host interactions of SARS-CoV-2(Kuchipudi et al., 2023). Determining the structure of human populations is particularly important in disciplines such as urban ecology and human ecosystem studies, but it is also important for today's challenges and problems of climate change, microbial evolution, and urbanization. For this purpose, human population modeling requires the identification of parameters that can represent both the micro-world - such as microbial circulations among hosts (Kuchipudi et al., 2023). Therefore this study focuses on using results of data analysis in a theoretical framework to represent human population structure in theory with its connection to SARS-CoV-2 fatality and reproduction; and argues that indoor air pollution death rates as an indicator is suitable for both of these purposes, with a case study from COVID-19 and human population related data.

Method

Data for 44 host-dependent parameters were collected for 56 countries (Supplementary Material:DATA.docx). The countries were Aruba, Australia, Austria, Bangladesh, Belgium, Brazil, Bulgaria, Canada, Chile, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Ghana, Greece, Hungary, Iceland, India, Indonesia, Ireland, Israel, Italy, Japan, Kenya, Latvia, Lithuania, Luxembourg, Malawi, Mexico, Netherlands, New Zealand, Nigeria, North Macedonia, Norway, Poland, Portugal, Qatar, Romania, Russia, Singapore, Slovakia, Slovenia, South Africa, South Korea, Spain, Sweden, Switzerland, Turkey, Uganda, Uk, USA, Zimbabwe. The parameters for all the countries were Gross Domestic Product (GDP), Gini index, Conflict rates, Tax rates, Household size, Body-mass index (BMI), Vegetable oil consumption, Animal fat consumption, Sugar consumption, Undernourishment levels, Antibiotic resistance levels, Cancer rates, Lung cancer rates, Asthma rates, Chronic obstructive pulmonary disease (COPD) rates, Pneumonia rates, Noncommunicable diseases (NDC) rates, Diabet rates, Diarrheal diseases rates, Colorectal cancer rates, Dyspepsia rates, Constipation rates, Irritable bowel syndrome (IBS) rates, Anemia rates, Vitamin A deficiency levels, Zinc deficiency levels, Vitamin D levels, Iodine uptake levels, Sunlight exposure levels, Temperature levels, Rainfall levels, Air toxicity levels, General toxicity levels, Forest area, Population size, Population growth type, Urbanization percent, COVID-19 mortality rates, Indoor air pollution death rates, Outdoor air pollution death rates, Carbon dioxide (CO2) emission rates, Food insecurity rates, COVID-19 fatality rates and COVID-19 reproduction rates. COVID-19 fatality rates and COVID-19 reproduction rates were used as dependent variables and the others were used as independent variables (Supplementary Material: Variables.docx). For each dependent variable (COVID-19 fatality rates and COVID-19 reproduction rates) stepwise regression was performed via IBM SPSS Statistics version 26. For parameters with missing data, the missing value analysis was conducted. For those whose significant value in the missing value analysis was greater than 0.05, the mean of the series was used, and new parameter sets were subsequently created by transferring missing values. It was verified that the blank answers were distributed at random. The values with significance values of the EM mean values greater than 0.05 were thought to be randomly distributed based on the analysis findings, and the null values that resulted from this assumption were assigned using SPSS's replace missing value assignment feature using the series mean method. For the analyses, the values obtained served as SMEAN values. All variables were subsequently standardized. For this, new standardized variables (Zvariable) were created, and the Z-scores for these variables—which serve as a representation of deviations—were obtained by using the standardization method in SPSS's Descriptive option. Additional analyses used these standardized values. All independent parameters were included in the stepwise regression analysis to reach the most reasonable equation. The stepwise approach is one way to get the regression equation's maximum value. The regression equation is constructed using the largest partial correlation, not the largest correlation between the independent and dependent variables, and attempts to incrementally increase the regression result by adding each independent variable to the previous equation using a separate equation (Wilkinson, 1979). Therefore, it has been investigated which of these 42 independent parameters contributed more to the regression equation to explain the dependent variables. All the details about data and variable information can be found in Supplementary Materials. As the model equation, the classical multiple linear regression approach was used (Y = a + b1X1 + b2X2...).

Results

Multiple linear regression was calculated to predict COVID-19 fatality based on all parameters. A regression equation was found (F(3,36)=26.556, p<.000), with an adjusted R2 of 0.663 (Table 1, Table 2). The predictor variables were Indoor air pollution death rates, Conflict rates, and Anemia rates of the countries (Table 1). There were three regression equations created to predict the outcome variable based on the stepwise method (Table 2). Indoor air pollution death rates had the highest partial contribution to the regression equations as (F(1,38)=33.649, p<.000) (Table 3), with an adjusted R2 of 0.456 (Table 2). Conflict situations and Anemia rates have also emerged in the equation as one of the determinants of fatality, albeit with more minor effects compared to indoor air pollution death rates (Table 1, Table 2).

Table 1. Entered Independent Variables to Multiple Linear Regression Equation to Predict COVID-19 Fatality*

Model	**Variables Entered**	**Method**
1	indoordeath	Stepwise (Criteria: Probability-of-F-to-enter <= ,050, Probability-of-F-to-remove >= ,100).
2	conflict	Stepwise (Criteria: Probability-of-F-to-enter <= ,050, Probability-of-F-to-remove >= ,100).
3	anemi	Stepwise (Criteria: Probability-of-F-to-enter <= ,050, Probability-of-F-to-remove >= ,100).

*Dependent Variable: Zscore(cov19fatality)

Table 2. Model Summary of Stepwise Regression Results For COVID-19 Fatality.

Model	**R**	**R Square**	**Adjusted R Square**	**Std. Error of the Estimate**
1	,685 (a)	,470	,456	,78236625
2	,779 (b)	,607	,586	,68267517
3	,830 (c)	,689	,663	,61575519

a. Predictors: (Constant), Zscore(indoordeath)
b. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(conflict)
c. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(conflict), Zscore(anemi)

Table 3. ANOVA (a) Results Table For COVID-19 Fatality

Model		**Sum of Squares**	**df**	**Mean Square**	**F**	**Sig.**
1	Regression	20,597	1	20,597	33,649	,000(b)
	Residual	23,260	38	,612	-	-
	Total	43,856	39	-	-	-
2	Regression	26,613	2	13,306	28,552	,000(c)
	Residual	17,244	37	,466	-	-
	Total	43,856	39	-	-	-
3	Regression	30,207	3	10,069	26,556	,000 (d)
	Residual	13,650	36	,379	-	-
	Total	43,856	39	-	-	-

a. Dependent Variable: Zscore(cov19fatality)
b. Predictors: (Constant), Zscore(indoordeath)
c. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(conflict)
d. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(conflict), Zscore(anemi)

Another multiple linear regression was calculated to predict COVID-19 reproduction based on all parameters. The predictor variables were Indoor air pollution death rates, Air toxicity levels, and Vegetable oil consumption (Table 4). A regression equation was found (F(3,36)=7.485, p<.001), with an adjusted R2 of 0.333 (Table 5, Table 6). The predictor variables were Indoor air pollution death rates, Air toxicity levels, and Vegetable oil consumption rates of the countries. There were 3 regression equations created to predict the outcome variable based on the stepwise method. All three predictor variables nearly had equal contributions to the equation; there were no significant differences between the partial contributions of the entered variables for the creation of the multiple linear equations compared to the COVID-19 (as dependent variable) results.

Table 4. Entered Independent Variables to Multiple Linear Regression Equation to Predict COVID-19 Reproduction*

Model	**Variables Entered**	**Method**
1	indoordeath	Stepwise (Criteria: Probability-of-F-to-enter <= ,050, Probability-of-F-to-remove >= ,100).
2	airtoxicty	Stepwise (Criteria: Probability-of-F-to-enter <= ,050, Probability-of-F-to-remove >= ,100).
3	vegetableoil	Stepwise (Criteria: Probability-of-F-to-enter <= ,050, Probability-of-F-to-remove >= ,100).

**Dependent Variable: Zscore(cov19reproduction)*

Table 5. Model Summary of Stepwise Regression Results For COVID-19 Fatality

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	,352 (a)	,124	,101	,87381789
2	,559 (b)	,312	,275	,78463951
3	,620 (c)	,384	,333	,75260701

a. Predictors: (Constant), Zscore(indoordeath)
b. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(airtox)
c. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(airtox), Zscore: SMEAN(vegoil)

Table 6. ANOVA (a) Results Table For COVID-19 Reproduction

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	4,095	1	4,095	5,363	,026(b)
	Residual	29,015	38	,764	-	-
	Total	33,110	39	-	-	-
2	Regression	10,331	2	5,165	8,390	,001(c)
	Residual	22,779	37	,616	-	-
	Total	33,110	39	-	-	-
3	Regression	12,719	3	4,240	7,485	,001(d)
	Residual	20,391	36	,566	-	-
	Total	33,110	39	-	-	-

a. Dependent Variable: Zscore(cov19reprodcution)
b. Predictors: (Constant), Zscore(indoordeath)
c. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(airtox)
d. Predictors: (Constant), Zscore(indoordeath), Zscore: SMEAN(airtox), Zscore: SMEAN(vegoil)

Conclusion

This study aimed to identify the most influential factors in the early lethality and spread of COVID-19. For this purpose, data on the virulence and spread of COVID-19 were analyzed using multiple linear regression with various data collected from countries in different geographical regions of the world. Stepwise regression was used to understand which of the variables selected as independent variables would have a larger partial contribution in a significant regression equation and to eliminate insignificant independent variables. As a result, the indoor air pollution rates of the countries were found to be the most influential factor in COVID-19 mortality compared to other factors. Indoor air pollution rates were also found to be effective in the spread of COVID-19.

Discussion

Indoor air pollution is directly related to the use of coal in home heating systems, resulting in CO, sulfur oxides, nitrate oxides, aldehydes, and possible other chemicals that cause lung-related diseases as well as impaired immune response (Bruce et al., 2006) and the majority of human exposure to pollutants occurs indoors (Ferreira & Barros, 2022). People spend much more time indoors than in outdoor environments, nearly 80 percent of the individual’s time is spent in indoor areas (Wadden & Scheff, 1983; Zhang et al., 1994). Moreover, for several toxic chemicals, compared to indoor exposures, the outdoor exposures were insignificant in terms of influencing the host. Although exposure to toxins indoors may in some cases depend on seasonal conditions, there are still differences between indoor and outdoor exposures (Kornartit et al., 2010). Indoor human activities such as cleaning also influence the toxic chemical composition of indoor environments (Q.-O. Lu et al., 2023). Essentially, an accurate risk assessment depends on the exposure pathways and bioaccessibility of the contaminants (He et al., 2016). Indoor air Technology is needed to eliminate indoor air pollution. Therefore, this is an item that perpetuates the supply chain loop between countries (Dionova et al., 2020; Yue et al., 2021).

It is an obvious fact that indoor air pollution is related to poverty (Bruce et al., 2006). Some of the countries with the highest levels of indoor air pollution deaths in the data set used in this study are Bangladesh, Zimbabwe, Malawi, India, Ghana, Kenya, Uganda, Indonesia, Nigeria, North Macedonia, Mexico, Bulgaria, and Hungary (Supplementary Data). A few key features of the clustering of these countries are more prominent in terms of urban structure and organization of human populations of these countries, including their wide range of political systems, rapid urbanization, the relatively high rate at which their natural environment is being destroyed due to urbanization, and the fact that agriculture is the major GDP provider in these countries (Abdullah et al., 2022; Arriola, 2009; David &

Ardiansyah, 2017; Diao et al., 2010; Dionova et al., 2020; Güneralp et al., 2017; Middlebrook, 1981; Mondal, 1970; Ochoa-Noriega et al., 2020; Rana, 2011; Rodriguez Lopez et al., 2017; Yue et al., 2021). Some of the countries with the lowest levels of indoor air pollution deaths in the data set used in this study are Israel, Finland, France, Luxembourg, New Zealand, Australia, Denmark, Netherlands, USA, Canada, Singapore, South Korea, Iceland and Russia. A few key features of commonalities of these countries are more prominent in terms of urban structure and organization of human populations of these countries, including their political stability, food safety, security qualifications, democratic governance, and the fact that their primary production is not agriculture, but that they sustain their economic existence with varying degrees of contribution from various sectors (Abu-Saad et al., 2000; Borch & Kjærnes, 2016; ERSSON & LANE, 1983; Haas, 2022; Ottelin et al., 2019; Rashid et al., 2017; White et al., 2017). While the countries that belong to the developing countries are working to increase their building stock to develop, they are also increasing their energy demand. However, since they do not have enough resources and their only markets are agriculture and raw materials, trade with other countries in other clusters creates a kind of loop (Kumar et al., 2016). Therefore, since the continuity of the global supply chain between countries depends on the technological and economic differences between these countries, by selecting a parameter such as indoor air pollution, a representation of the global organization of the human population can be obtained, in other words, indoor air pollution can be an indicator data for the human population structure. When this parameter is selected as an indicator, the basic human organization provider here may be concretized by looking at the network of organizations formed by microenvironments -which is the indoors that humans spend time-, rather than focusing on the global networks such as countries or cities. Since the human microenvironment is embodied by the creation of closed spaces, especially in urban ecosystems (Schweizer et al., 2007a), within these structures, basic human activities such as trade, nutrition, shelter, reproduction, population maintenance, and generation activities are carried out. The need for humans, who have similarities in social structure with other great apes in the hominid group, especially in terms of population continuity, to stabilize their position in contrast to their relative great apes, may also be seen as an evolutionary output to ensure the continuity of the human population (Mogielnicki & Pearl, 2020), hence the idea that the human microenvironment is also the basic cells that make up a global human population structure.

There are studies in the literature that close contact with the human microenvironment increases and influences the spread of the virus (Nielsen & Xu, 2022). Closer proximity in enclosed spaces, where the human microenvironment requires close contact with each other, increases the spread of viral variants. According to our study, from a global perspective, both external air pollution and internal pollution may be important determinants of spread. In addition, the fact that indoor air pollution deaths also explain COVID-19 deaths may give a clue that air pollution may be more important than other factors in both spread and deaths. The link between air pollution and the disease such as COVID-19, which spreads through air circulation, may be related both to the fact that there is more micro-material in the air for viral particles to attach to, and to the increased impact of SARS-CoV-2 due to the microbial damage caused by existing and continuous air pollution on the human body (Ott et al., 1992). Since human exposures are dependent on human activities, structures such as enclosures can be a representation of human actions (Figure 1). Therefore, incorporating human activities globally can also be done by focusing on human microenvironments. In contrast to differences between cities, more than 90% of the variation in indoor time-microenvironment-activity patterns originated within and between subjects (Schweizer et al., 2007b). Therefore, in future studies, human microenvironments may be used to address the global organization of human populations.

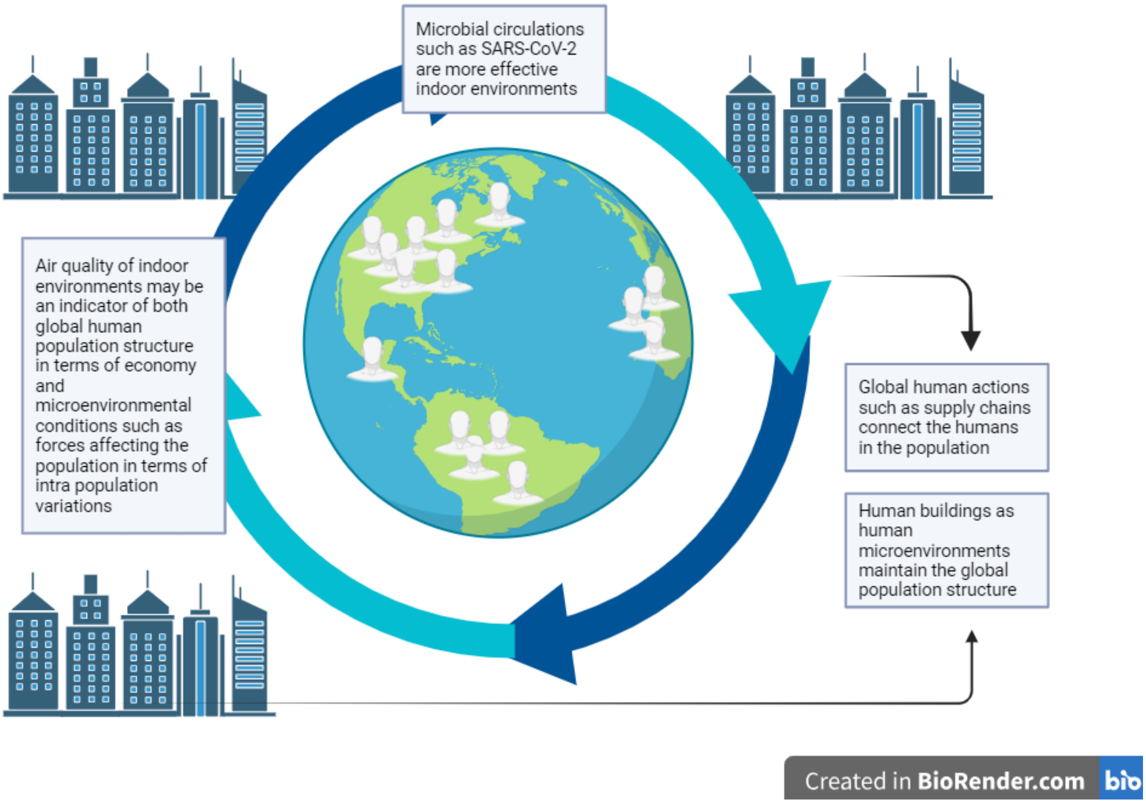

Figure 1. Indoor Air Toxicity May Be an Indicator of Human Population Structure, which is Composed of Activities and Relations of Humans.

The human population, looking closely at the hominid group, has fought against external factors by bonding together as a population (Mogielnicki & Pearl, 2020). For instance, the size gap between the male and female of the human population has been reduced relative to other great apes by the development of sexual selection in the human population on cultural and property-based grounds (Mogielnicki & Pearl, 2020). Examples of this include the clustering behavior around a leader, the establishment of patriarchy and the cooperation between men and women in the maintenance of property for the care of offspring, despite the fact that women's reproductive abilities do not coincide with the establishment of patriarchy(Fletcher et al., 2015; Mogielnicki & Pearl, 2020; Rantala, 2007; Stringer, 2016). From this point of view, the economic organization of the human population must also have a place in the structure of the population (STEUDELNUMBERS et al., 2007). The functions of protection and nutrition, which are the most basic components of population cooperation, not only have a sustaining effect on the care of offspring by human women and men, but also, as we suggest, ensure the continuity of a population structure through what we call the global supply chain (Mogielnicki & Pearl, 2020; STEUDELNUMBERS et al., 2007). Within this structure, small groups of people clustered in small microenvironments - in this case buildings - maintain the continuity of exchange between them, and in fact maintain the stratification of the population. Indoor air pollution rates can be an important parameter for this stratification to both represent global chains and to identify the impact of local and smaller microenvironments. Because this variable could be an indicator that relates both globally to the homo sapiens population and micro and locally to the microenvironment of homo sapiens groups.

In this study, Stepwise regression was used to analyse more than 40 variables that are related to urban systems and human population organisation to understand the fatality and spread of COVID-19 disease. Although many elements of the organisational structure of urban systems have already been used in the literature to describe the impacts of microbial diseases such as COVID-19, the possibility that a factor such as indoor air pollution could be the main element affecting both the spread and fatalities of COVID-19 has not yet been comprehensively addressed in this way (Table 1, Table 4). Indoor air pollution is a parameter that is representative of the smallest elements of urban systems: homes and the building structures in which all people live. Within cities, people spend their time, interact and communicate in builded structures. Therefore, the possibility that the pollution of the air inside the buildings -which are one of the main elements of the architecture of the city- is one of the main elements that are effective in both the spread and the fatalities of a microbe such as COVID-19, which has affected the whole world, brings to the fore the importance of biological impacts of the environment, especially toxicity, in the design and architecture of city systems. Biological systems' movement, particularly microbiological circulations within buildings, constitutes one of the key aspects of urban life. It is influenced by the city's structure, as well as the shape and characteristics of buildings, thereby impacting the design and architecture aimed at human populations' resistance against toxic compounds and microbial diseases. The architecture of indoor spaces may therefore play a more important role in health than we realise.

The datasets used in this study were acquired to find a global pattern, but the results point to the importance of the human microenvironment, especially when considered in the context of COVID-19 mortality. The most important point here is that when considering global supply chains or other global parameters and relationships between countries, these grand relationships have a significant angle that determines - or at least influences - the human microenvironment. Given that this virus is spread by human contact and spreads through microenvironments, and considering that one of the main parameters on which these deaths depend may be indoor air pollution, it can be argued that the large intercontinental human population of people on the planet in total becomes a suppressive external factor - perhaps an evolutionary selection factor - that determines microbial relationships in smaller structures such as houses or buildings. Thus, global microbial cycles may be propagated within the population by selection factors that are the result of the materialization of an intrapopulation selection force. Of course, this proposition requires more data than the scope of this study, but more future work should be done in this direction. Since every living organism is intimately dependent on its environment to live, survive, and reproduce, changes in environments will have major impacts on living things in the future, as they have in the past. Increasing knowledge about environments and the relationships between human populations and environmental factors will provide important information for understanding and predicting the evolution of organisms.

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