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Analysis of Indoor CO_2 Concentration Using Split Ventilation Systems as an Indicator of COVID-19 Transmission

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Abstract: We measured the indoor CO_2 concentration in occupied areas with ventilation systems that recirculate air without an external air supply. The average time required to achieve the highest probability of contagion was also measured based on the number of participants in the group. Three different experimental groups were evaluated: Group One (G1), which included 5 participants; Group Two (G2), with 10 participants; and Group Three (G3), with 15 participants. Before the measurements, the CO_2 concentration was measured to be homogeneous and its sampled value was given by the difference between the indoor and outdoor CO_2 measurements (>5000 ppm or 0.5% CO_2 in air) averaged over an 8-h work day Time-Weighted Average (TWA.). G1 and G3 group participants performed low-intensity daily office activities, such as reading and talking. In contrast, Group Two (G2) was asked to perform moderate intensity activities, such as frequently lifting 10 kg items and walking quickly. The CO_2 concentration was measured with two instruments to compare the outdoor and indoor measurements. Both devices were configured to take one reading every second for 30 min. A mathematical model was developed from the CO_2 concentrations measured, the group size, and the retention factor of the mask being worn to determine the probability of inhaled air contaminated with an aerosol of SARS-CoV-2. We concluded that the likelihood of contagion in enclosed areas such as study areas, offices, and meeting rooms, among others, which use ventilation without a circulation of fresh air, is high. Despite proper distancing and masking, there is a 99% chance of contagion in one of the modeled extreme case scenarios in less than 10 min of exposure. The study took place in Albrook, Republic of Panama, which is a tropical developing coastal geographic location where split air conditioning units are widely used and, like many other countries in Latin America, where indoor air quality has only recently started being discussed publicly and enforced.

Keywords: Air Quality Monitoring, CO_2 Concentration, Instrument Accuracy, Pathogens, Environmental Monitoring, Ventilation, Mathematical Model, COVID-19

Introduction

The COVID-19 pandemic has emphasized the importance of air quality and its impact on viral prevalence in the environment and human health (Wardhani and Susan 2021) SARS-CoV-2 virus transmission through respiratory aerosols has been established, by now, as one of the main contagion routes during the pandemic (Watson *et al*., 2022) Space occupancy, duration of exposure, mask use, aerosol

generating actions (e.g., cough, sneeze, vocalization, laughter, breathing), ventilation (or lack thereof) and other factors can all affect the likelihood of indoor transmission by modulating the amount of infectious "doses" generated by infected individuals in a space, that can then infect other susceptible individuals (Morawska and Cao, 2020; Morawska *et al*., 2009) Public buy-in to comply with interventions focusing on these variables is a big hurdle in the third year of the pandemic, partly due to lower mortality rates and many severe cases attributed to vaccinations and the beforementioned indoor transmission-limiting interventions (Watson *et al*., 2022). Thus, studies that can help visualize the air quality in terms of the probability of COVID-19 transmission could greatly inform the population and help maintain low infection rates even during routine indoor activities.

For decades, carbon dioxide measurements have been used to quantify airflow and zonal mixing in buildings and inform the design of HVAC systems (Fisk, 2000; Seppänen *et al*., 1999). Since O_2 sensors are affordable, they have been used as a natural data source for indoor air quality, considering that CO_2 levels in indoor environments have been linked to harmful health in general (Satish *et al*., 2012). This includes using CO_2 levels as a biomarker for the probability of indoor airborne viral contagion (Rudnick and Milton, 2003). CO_2 levels in offices (Milton *et al*., 2000; Seppänen *et al*., 1999) can be directly proportional to illness-related absenteeism. Direct relationships between CO_2 levels and airborne bacteria concentrations have also been discovered (Li *et al*., 2007). A link between outdoor air exchange rates and dorm respiratory illnesses has also been reported (Sun *et al*., 2011). Despite the overwhelming evidence of such correlations and numerous economic analyses highlighting the negative societal consequences of bad air quality (Fisk, 2000; Milton *et al*., 2000) the use of CO_2 monitors to make quantitative assessments of the risk of indoor disease transmission is a relatively new concept (Li *et al*., 2007), especially in developing countries.

The United States (U.S.) Environmental Protection Agency (EPA) specifies that the concentration of CO_2 in enclosed spaces can be 10-100 times greater than in outdoor or open spaces (OSHA, 2001). This becomes relevant because the urban population, representing more than 85% of the total population in a country like the U.S., invests between 80 and 90% of their time in enclosed environments (Parker *et al*., 2018). Hence, the analysis of indoor CO_2 concentrations as an air quality indicator seems considerably relevant in these pandemic times. Therefore, modeling CO_2 as an indicator for SARS-CoV-2 virus transmission and other respiratory diseases (Peng and Jimenez, 2021) is of great interest to the general public. Particular attention should be given to retirement homes, libraries, meeting rooms, classrooms, offices, and other places where high levels of CO_2 are generated and require good air quality (Salud, 2020). Air conditioning, heating, and ventilation systems can become hotspots for SARS-CoV-2 transmission, depending on how (or if) these systems exchange, sterilize or recirculate air in the room where they are installed (ASHRAE, 2019). A comparative study was recently published between aerosols containing SARS-CoV-2 and SARS-CoV-1 and their surface stability (Schöne-Seifert and Van Aken 2020). It determined decay rates on different surfaces or environments. Among the evaluated spaces (e.g., aerosols, stainless steel, plastic, copper, and cardboard), more excellent stability of SARS-CoV-2 was detected on plastic and stainless steel. The virus remained viable even 72 h after being deposited on the surface. In the case of aerosols, the study showed that the SARS-CoV-2 virus could be infectious up to 3 h later, with a high probability of causing health effects. Thus, the presence of SARS-CoV-2 in aerosols leads to the most significant risk of spreading the virus to multiple people, with poorly ventilated indoor spaces presenting the highest risk compared to well-ventilated indoor areas or outdoors. Proper ventilation of indoor spaces largely depends on the design of the building and the type of ventilation used: Natural ventilation or forced ventilation employing ventilation/air conditioning systems (Atkinson, 2009; Shahzad *et al*., 2021; Bocharov *et al*., 2018; Peter *et al*., 2021; Ivorra *et al*., 2020; Pinto Neto *et al*., 2021; Ali *et al*., 2021; Adak *et al*., 2021). Most countries in Latin America, in general, and Panama does not strictly enforce indoor air quality guidelines and regulations, and only in the last 5-0 years has the topic received more attention (Moreno-Rangel *et al*., 2021).

This study proposes a distribution model for the probability of contagion by COVID-19 based on the type of mask, number of people, growth rate of indoor CO_2 and time. The study occurred in Panama City, Republic of Panama, a tropical developing coastal country with mostly lowlands (89%). During the day, the average temperature is 30° degrees with an average relative humidity of 80% (Corella *et al*., 2021).

Materials and Methods

The CO_2 concentration was measured in spaces occupied by three different groups. All participants were of legal age, exercising their routine office functions. Group One (G1) had five people, Group Two (G2) had 10 people, and group three (G3) had 15 people. The groups worked in offices of 24.8 (4×3.1×2 m), 49.2 (4×6.2×2 m), and 75.92 m^3 (5.2×7.3×2 m), respectively. The density of people per square meter was the same. G1 and G3 participants were asked to perform low-intensity daily office activities like reading and talking. In contrast, G2 participants were asked to perform high-intensity activities, such as frequently lifting 10 kg and walking quickly for 5 min.

All offices had a split air conditioning unit that recirculated air and did not have access to a fresh air source (i.e., no central ventilation). The study collected CO_2 measurements during a 30 min window, with a sampling rate of 2 min and independently repeated every two days for two months. The measurements started being collected 10 min after the rooms were occupied by the designated number of participants and repeated for each group under the same conditions.

Two instruments were used to measure CO_2 concentrations: A HOBO data logger MX1102 and an L21I-D04508, each with an accuracy of +/-50 ppm.

Theory

The categorization of indoor air quality, according to the Department of environmental health of Spain (Salud, 2020) is given by the following Eq. (1):

$$[CO_2]_{in} - [CO_2]_{ext} < 500\,ppm \quad (1)$$

where, $[CO_2]$ is the concentration of CO_2 in parts per million inside an enclosure and $[CO_2]_{ext}$ the outdoor CO_2 concentration in parts per million. A risk model for airborne contagion was used based on the Wells-Ridley model, as shown in Eq. (2):

$$p = 1 - exp\left[\frac{(-Itqfn)}{R}\right] \quad (2)$$

where, p is the probability that the virus will infect a person in an hour, I is the number of infectious sources in the enclosure, t is the time of exposure to the pathogen in hours, q is the infectious dose, f is the fraction of indoor air that is exhaled or expelled, n is the number of people exposed and R is the fraction of particles in the air that do not venture into the airways. The distribution of the infectious and contagious particles in the air is assumed to have a Poisson distribution, with f being the fraction of the air exhaled, which is defined by Eq. (3):

$$f = \frac{[CO_2]_{in} - [CO_2]_{ext}}{[CO_2]_{exh}} \quad (3)$$

$[CO_2]_{exh}$ is the fraction of the exhaled air. Note that all parameters in (Eqs. 2-3) are measurable. The equation focuses on the transportation of viral load and the likelihood of it being inhaled regardless of whether it may or may not infect the person. The level of immunization of the population affects the rate of infection. Peng and Jimenez (2021) consider the level of immunity of the people, the average concentration of the virus in real-time, the average breathing of a susceptible adult, and the virus's loss rate, variables considered negligible at the time of this research (Peng and Jimenez 2021).

Equation (2) also considers particle retention capacity in masks. Asadi *et al*. (2020) analyzed the retention capacity of particles 0.3-0.5 µm in diameter while breathing, speaking, and coughing. For KN95 masks, a retention factor of approximately 79.5% was presented; however, this value is affected if the leakage phenomenon in the mask seal is considered, which is between 5 and 20% Patel *et al*., (2016). In the case of our study, we considered an average leak of 12.5%, where smaller particles can enter the airways. Thus, in (Eq. 2), the R parameter using the above considerations was estimated to be R = 79.5%-12.5% = 67%, representing an intermediate risk. For a low risk, R = 79.5-5 = 74.5 and for a high risk, R = 79.5%-20% = 59.5%.

Results

Data corresponding to the infectious dose (q) were considered from the contributions made by other studies, including that the contagious amount tends to be distributed randomly in the air in confined spaces and each room within the enclosure would have the same probability of containing the pathogen; thus, the infectious dose is constant in the enclosure (Lai and Cheng, 2007). There is currently no way to determine the infectious amount of SARS-CoV-2 as the causative agent of COVID-19. Still, studies indicate that the form of transmission will be comparable to other coronaviruses (Doremalen *et al*., 2020). Table 1 presents data from other studies that were used for our calculations.

The other parameters necessary for the calculations in the mathematical model were obtained through field evaluations, using instruments for measuring the CO_2 concentration both indoors and outdoors. The averaged results of the measurements given by the measurement instruments were recorded for each test time for 30 min, as shown in Table 2. The CO_2 measurements for the three groups evaluated were carried out under the same ambient temperature conditions. Humidity and ventilation conditions. The number of participants per group increased proportionally to the size of the room to maintain the same density of people per square meter.

From our analysis, the CO_2 concentration obtained through a randomized block design (sample group) depends on the test time (treatment), resulting in the model:

$$Y_{ij} = \mu + \tau_i + \beta_j + \varepsilon_{ij} \quad (4)$$

where, y_{ij} represents the $[CO_2]$ in ppm; μ is the global average of the $[CO_2]$ in ppm; τ_i is the sampling time in minutes; β_j refers to the size of the groups (i.e., j = 5, 10-15); and ε_{ij} corresponds to the experimental error in group j of

time *i*. Table 3 shows the analysis of variance for the CO_2 concentration in different groups: For this case, 3 degrees of freedom were considered for the model and 47 degrees of freedom for the error. On the other hand, in the analysis of the other, they indicate that the proposed model is statistically significant.

Table 1: Summary of previously established parameters considered in this study

		Input parameters value			Sensitivity of analysis values		
Parameters	Description	Low-risk (L.R.)	Intermediate (H.R.)	High-risk (H.R)	Low limit (-75%)	High limit (+75)	Source
[CO_2] exhaled	Exhaled CO_2 fraction in ppm	37,500	37,500	37,500	-	-	Rudnick and Milton (2003)
[CO_2] exhaled	The outdoor CO_2 level in ppm	400	400	400	-	-	ASHRAE (2019)
q	Infectious dose due to coronavirus	11.4	28.94	295.5	7.23	50.65	Park *et al*. (2023)

Table 2: CO_2 concentration data according to occupied space

Sampling time (min)	G1. CO_2 (ppm)	G2. CO_2 (ppm)	G3. CO_2 (ppm)
0	500	594	857
2	589	659	957
4	646	728	1050
6	708	773	1117
8	762	829	1193
10	822	878	1262
12	878	921	1321
14	943	950	1406
16	996	986	1463
18	1035	1020	1533
20	1087	1077	1587
22	1148	1117	1627
24	1192	1193	1626
26	1238	1230	1695
28	1312	1346	1783
30	1314	1355	1799

*Data was taken every second. Table 2 displays only measurements recorded every 2 min

Table 3: Analysis of variance of CO_2 concentration for groups

Source	DoF	Sum of squares	Average squares	F	Pr > F
Model	3	5193310,833	1731103,611	1240,201	<0,0001
Error	47	65603,756	1395,825	-	-
Total corrected	50	5258914,588	-	-	-

Table 4: Model parameters for CO_2 concentration using Eq. 5

Source	Value	Standard error	t	Pr > |t|	Lower limit (95%)	Upper limit (95%)
Intercept	982,096	12,443	78,926	<0,0001	957,063	1007,129
Time	27,369	0,580	47,196	<0,0001	26,203	28,536
Group-G1	-412,000	12,815	-32,151	<0,0001	-437,780	-386,220
Group-G2	-443,882	12,815	-34,639	<0,0001	-469,662	-418,103
Group-G3	0,000	0,000	-	-	-	-

Table 5: Comparison of CO_2 averages

Category	L.S. average	Standard error	Lower limit (95%)	Upper limit (95%)
G1	940,706	9,061	922,477	958,935
G2	972,588	9,061	954,359	990,817
G3	1384,588f	9,061	1366,359	1402,817

At a significance level of 5%, the results suggest that the model is appropriate to explain the CO_2 concentration in the three sample groups and that the model would generally be given by:

$$CO_2 = 982.096 + 27.37.\tau - 412G_1 - 443.882G_2 \quad (5)$$

Table 4 shows the parameters of the generalized model according to Eq. 5: For example, the value obtained for the intercept is approximately 982.096, for a standard error of 12.443 and the value of Pr is less than 0.0001, which indicates that the intercept is highly significant, just like time. In the case of Group-G1 and Group-G2, the estimated values for the coefficients were -412.0 and -437.78 respectively with very similar standard errors and both presented a negative impact on the concentration of carbon dioxide; for Group-G3 the estimated value was zero, which means that it does not have a statistically significant effect on the CO_2 concentration.

The R^2 = 0,988 coefficient of determination indicates that 98.8% of CO_2 variability is explained by the time and sample groups in the proposed model. As can be seen, all groups are essential in the model and the sampling time. Table 5 shows a comparison of the means of CO_2 concentration for different groups (G1, G2, and G3). The results show that there are significant differences in the measurements of CO_2 concentration between the groups studied. Note that the confidence intervals provide a range in which the true mean of the CO_2 concentration measured by the instruments is likely to lie. Group 3 has the highest CO_2 concentration, while Group 2 has the lowest concentration; all groups are statistically different.

According to (Eqs. 2-3), the probability of virus contagion was estimated for each group's low, intermediate, and high-risk scenario. The parameter values considered I = 1 since the analysis was only pondered for the COVID-19 virus, assuming this was the only infectious source. For q and [CO_2] exhaled, we used the values cited in Table 1 and the data for t between 0-30 min from Table 2, and the results are shown in Table 6.

When we calculated the risk of contagion with the proposed mathematical model, we found that the risk of contagion with COVID-19 increases with time, as well as with group size, following a logarithmic curve, in most cases (Fig. 1A-C). The behavior of the curve also depended on the risk scenario used to calculate *R* (i.e., low, intermediate, or high), which we defined as the fraction of particles in the air that do not venture into the airways and that correlate with mask use. The slope of the curves in their linear region and how fast they approached the exponential saturation region around the maximum probability value (i.e., p = 1), were directly related to the size of the group and the fraction of particles trapped by masks, *R*.

Table 6: The probability of COVID-19 virus affectation was assessed for low, intermediate, and high risk for the different sample groups

Time	Probabilities for a low-risk			Probabilities for an intermediate risk			Probabilities for a high risk		
(min)	G1	G2	G3	G1	G2	G3	G1	G2	G3
1	0.00569646	0.00711550	0.04281994	0.01599645	0.01995542	0.11620923	0.16923787	0.20686728	0.75837940
2	0.01411333	0.01872888	0.09366016	0.03932821	0.05196952	0.24239537	0.36955044	0.45861502	0.95889934
3	0.02428548	0.03191973	0.15051030	0.06704509	0.08750379	0.36899933	0.54974121	0.65106651	0.99497921
4	0.03710699	0.05192249	0.20913728	0.10123821	0.13972846	0.48434042	0.70690231	0.82280595	0.99950706
5	0.05053520	0.07491555	0.26813637	0.13617041	0.19732840	0.58569722	0.81419420	0.92012872	0.99996019
6	0.06377615	0.09992560	0.32494135	0.16974491	0.25708595	0.67018477	0.88221062	0.96718514	0.99999711
7	0.08102937	0.12562826	0.38246123	0.21221261	0.31542401	0.74349624	0.93559403	0.98718548	0.99999984
8	0.09796465	0.15612452	0.44343154	0.25250807	0.38070019	0.80872505	0.96478351	0.99595138	0.99999999
9	0.11386494	0.18738294	0.49863798	0.28910663	0.44329012	0.85757142	0.98022715	0.99881074	1.00000000
10	0.13544396	0.22352691	0.55194785	0.33689585	0.51038764	0.89629934	0.99111673	0.99972838	1.00000000
11	0.15555042	0.25583975	0.60243839	0.37951015	0.56574559	0.92600340	0.99586102	0.99993163	1.00000000
12	0.17485264	0.29481420	0.64500099	0.41871669	0.62692497	0.94624787	0.99804581	0.99998807	1.00000000
13	0.19261621	0.33179285	0.69403171	0.45335109	0.67954669	0.96466672	0.99903570	0.99999792	1.00000000
14	0.21182199	0.37462122	0.73542829	0.48926639	0.73419727	0.97655911	0.99955857	0.99999976	1.00000000
15	0.23726578	0.41406730	0.77264325	0.53444933	0.77884942	0.98471957	0.99984783	0.99999997	1.00000000
16	0.25294941	0.44795525	0.80063704	0.56096767	0.81308105	0.98945470	0.99992247	1.00000000	1.00000000
17	0.27738503	0.48561716	0.82739908	0.60030649	0.84688111	0.99297979	0.99997365	1.00000000	1.00000000
18	0.29452638	0.51136243	0.85668978	0.62649500	0.86754080	0.99584696	0.99998791	1.00000000	1.00000000
19	0.32003418	0.55292188	0.87978972	0.66337223	0.89693443	0.99747135	0.99999634	1.00000000	1.00000000
20	0.34715537	0.57955180	0.89656155	0.69991023	0.91333819	0.99834546	0.99999902	1.00000000	1.00000000
21	0.37133771	0.61646105	0.90824601	0.73023900	0.93313624	0.99882041	0.99999971	1.00000000	1.00000000
22	0.39285137	0.64807789	0.92463620	0.75549251	0.94755260	0.99932315	0.99999991	1.00000000	1.00000000
23	0.42249388	0.66960214	0.93091693	0.78770995	0.95611119	0.99947056	0.99999998	1.00000000	1.00000000
24	0.45467198	0.70213156	0.94027585	0.81942976	0.96724382	0.99964896	1.00000000	1.00000000	1.00000000
25	0.47768554	0.72949699	0.95042632	0.84012238	0.97504522	0.99979251	1.00000000	1.00000000	1.00000000
26	0.49822865	0.75176201	0.96067386	0.85724294	0.98041815	0.99989208	1.00000000	1.00000000	1.00000000
27	0.52724906	0.77976565	0.96794168	0.87934013	0.98603255	0.99993938	1.00000000	1.00000000	1.00000000
28	0.54756916	0.80107044	0.97364682	0.89341309	0.98951928	0.99996514	1.00000000	1.00000000	1.00000000
29	0.57428636	0.81769241	0.97772942	0.91023955	0.99180737	0.99997832	1.00000000	1.00000000	1.00000000
30	0.60276271	0.82843481	0.98261197	0.92617367	0.99309806	0.99998922	1.00000000	1.00000000	1.00000000

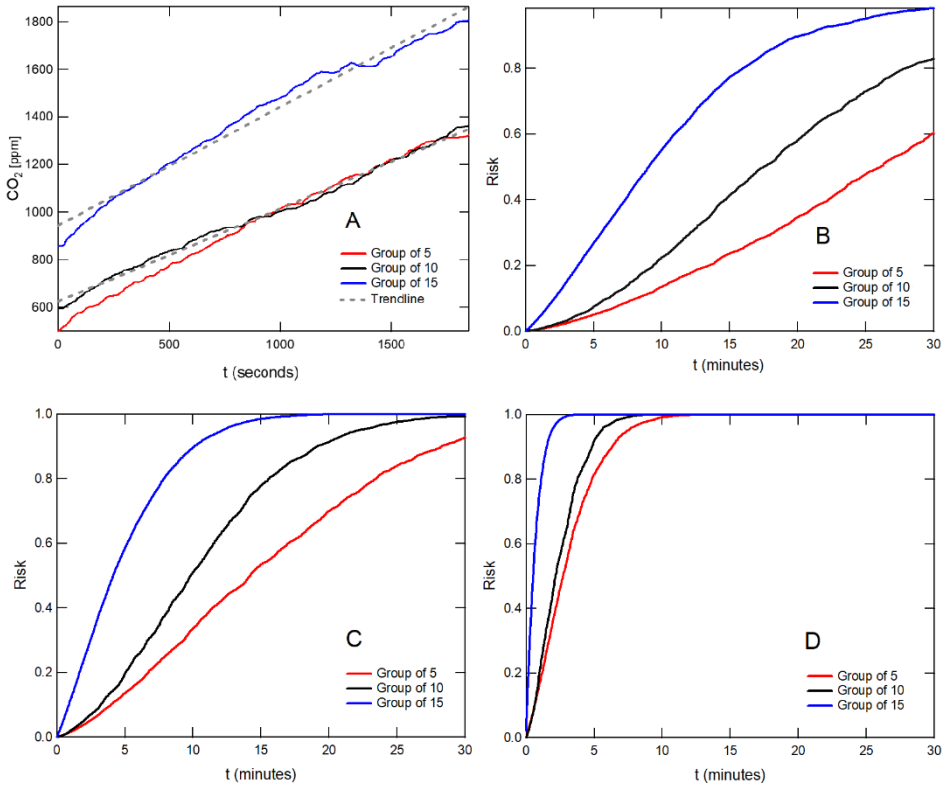

Fig. 1: (A) CO_2 concentration (ppm) against time for the different groups. Probability curves were plotted against different risk scenarios; (B) Low; (C) Intermediate and; (D) High

For instance, in the case of a COVID-19 infectious individual among the participants, the risk of contagion in low-risk conditions resulted in 60% for G1, 80% for G2, and 99% for G3 at the end of the 30 min of evaluation (Fig. 1B). In the case of an intermediate-risk scenario, the probability assessment yielded 98 (at 30 min), 99 (at 30 min) and 100% (at 20 min) for groups G1, G2 and G3, respectively (Fig. 1C). For a high-risk scenario, all groups achieved a 100% probability in 24, 16 and 9 min for groups G1, G2 and G3, respectively (Fig. 1D).

Discussion

COVID-19, caused by the novel coronavirus SARS-CoV-2, primarily infects respiratory epithelial cells through the binding of the viral spike protein to the ACE2 receptor (Zhou *et al*., 2020). Following entry, the virus replicates and spreads, leading to local inflammation and damage to the respiratory tract (Zeng *et al*., 2020). This triggers an immune response characterized by the release of pro-inflammatory cytokines, causing a cytokine storm that further contributes to tissue damage and systemic inflammation (Mehta *et al*., 2020). Additionally, SARS-CoV-2 can induce endothelial dysfunction, leading to microvascular thrombosis and organ damage (Varga *et al*., 2020). The pathogenesis of COVID-19 involves complex interactions between viral replication, immune response dysregulation, and endothelial dysfunction, contributing to the diverse clinical manifestations observed in infected individuals (Chen *et al*., 2020).

Our results showed that the CO_2 concentration increases directly proportional to the elapsed time. The CO_2 concentration did not show a directly proportional relationship with the size of the group of participants or the intensity of the activities carried out. Instead, in terms of group size, there seemed to be a threshold above 10 participants that needed to be crossed to see an increase in CO_2 concentration levels. Regarding the level of physical activity in the room, the result seemed contradictory: The higher intensity of physical activity exerted by the participants in G2 did not significantly affect the CO_2 levels due to exhalation and resulted in a lower average CO_2 concentration (Wiryasaputra *et al*., 2023; Rowe *et al*., 2022).

It is important to consider that the study took into account the following variables: Number of people, occupied space, time, and type of ventilation, among others. The size of the groups had an effect on the experimental results since the equations included coefficients for each group, which implies that each group

tended to contribute differently to the concentration of carbon dioxide, time was a variable that allowed to visualize the variation of the CO_2 concentration and its relationship with the exposure time.

Table 6 shows the results of the probability calculation considering (Eq. 2) for low, medium, and high risk: It is observed that despite the fact that CO_2 concentrations tended to increase in groups G1 and G2, the risk of contagion showed a direct relationship with the size of the group, with G1 having the lowest contagion probability and G3 exhibiting the exponentially higher contagion probability. The risk scenario, which was correlated with the use and effectiveness of the mask, also had a great impact on the probability of contagion. One of the assumptions of our study is that all participants are susceptible to the virus and that the concentration of the virus is distributed homogeneously in the environment. We must also assume that the environmental conditions during the measurement, such as ambient temperature, relative humidity, and air speed, make it possible to become infected with the virus.

The CO_2 production rate is higher when larger groups share the same closed-ventilated room with a split unit, without air exchange. Intuitively, since the measurements were made 10 min after the room was occupied, the initial CO_2 concentration was higher for the larger groups. The results suggest that indoor spaces with a density of approximately 0.2 people per square meter and a recirculating forced ventilation system, as typically found in offices and classrooms throughout Latin America, achieve CO_2 concentrations above 500 ppm (that is, that is, exterior-interior difference) in less than 20 min, even with the recommended distancing and masking interventions. It is imperative to consider the entry of outside or fresh air in closed spaces to minimize the risk of contagion.

Conclusion

Finally, our results suggest the importance of minimizing people's length of stay in poorly ventilated indoor spaces. If occupants carry out activities that increase their breathing frequency, this could lead to higher exhaled gas concentrations and, thus, higher CO_2 concentrations; however, our study could not find differences in groups with ten or fewer participants, regardless of their level of physical activity (i.e., low vs moderate) during 30 min of recorded measurements.

The increase in CO_2 concentration indicates the probability of contagion with pathogens capable of traveling through aerosols. It is vitally important to communicate and make visible the connection between the length of stay, space, and activity carried out by people in confined indoor spaces. The COVID-19 pandemic has made clear that to achieve proper public health, enclosed indoor spaces such as study areas, offices and meeting rooms, among others, require ventilation designs that allow good air quality since contagion may occur through aerosols containing microorganisms generated by the exhalation of infected people.

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Author's Contributions

Manuel Batista: Conceptualization, methodology, research, formal analysis, resources, project administration, funding acquisition, written original drafted, reviewed and edited.

Oscar Bulgim: Methodology, research, formal analysis, resources, funded acquisition, project administration, written of original drafted, reviewed and edited.

Ericka Matus: Formal analysis, reviewed, validation and reviewed, edited of the original drafted.

Jaime Estrella: Written of initial drafted, reviewed and edited of the manuscript.

Jay Molino and Rolando Gittens: Methodology, research, formal analysis, validation, data curation, resources, funding acquisition, written original drafted, reviewed, edited and correspondence.

Ethics

Ethics approval was not required for our study in accordance with national guidelines and local legislation. All participants agreed to a written informed consent to participate in this research. None of the participants had COVID-19 at the time of the study.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

Adak, D., Majumder, A., & Bairagi, N. (2021). Mathematical perspective of COVID-19 pandemic: Disease extinction criteria in deterministic and stochastic models. *Chaos, Solitons & Fractals*, *142*, 110381. https://doi.org/10.1016/j.chaos.2020.110381

Ali, Z., Rabiei, F., Shah, K., & Khodadadi, T. (2021). Qualitative analysis of fractal-fractional order COVID-19 mathematical model with case study of Wuhan. *Alexandria Engineering Journal*, *60*(1), 477-489. https://doi.org/10.1016/j.aej.2020.09.02

Asadi, S., Cappa, C. D., Barreda, S., Wexler, A. S., Bouvier, N. M., & Ristenpart, W. D. (2020). Efficacy of masks and face coverings in controlling outward aerosol particle emission from expiratory activities. *Scientific Reports*, *10*(1), 1-13. https://doi.org/10.25338/B87C9V

ASHRAE. (2019). Handbook HVAC Applications. SI Edition. https://www.ashrae.org/technical-resources/ashrae-handbook

Atkinson, J. (2009). Natural Ventilation for Infection Control in Health-Care Settings, Geneva: *World Health Organization*. https://www.ncbi.nlm.nih.gov/books/NBK143284/

Bocharov, G., Volpert, V., Ludewig, B., & Meyerhans, A. (2018). Mathematical immunology of virus infections (Vol. 245). Cham, Switzerland: Springer International Publishing. https://doi.org/10.1007/978-3-319-72317-4

Chen, G., Wu, D. I., Guo, W., Cao, Y., Huang, D., Wang, H., ... & Ning, Q. (2020). Clinical and immunological features of severe and moderate coronavirus disease 2019. *The Journal of Clinical Investigation*, *130*(5), 2620-2629. https://doi.org/10.1172/JCI137244DS

Corella, F., Díaz, A., García, A. L., Valles, N., Vaña, M., Martínez, L., ... & Molino, J. (2021). Growth of pigeon pea (*Canajus Cajan*) using auxin irrigation in a home garden in Panamá. http://repositorio2.udelas.ac.pa/handle/123456789/1024

Doremalen, N. V., Bushmaker, T., Morris, D. H., Holbrook, M. G., Gamble, A., Williamson, B. N., Tamin, A., Harcourt, J. L., Thornburg, N. J., Gerber, S. I., Lloyd-Smith, J. O., Wit, E. D., & Munster, V. J. (2020). Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *New England Journal of Medicine*. *382*(16):1564-1567. https://doi.org/10.1056/NEJMc2004973

Fisk, W. J. (2000). Health and productivity gains from better indoor environments and their relationship with building energy efficiency. *Annual Review of Energy and the Environment*, *25*(1), 537-566.

Ivorra, B., Ferrández, M. R., Vela-Pérez, M., & Ramos, A. M. (2020). Mathematical modeling of the spread of the coronavirus disease 2019 (COVID-19) taking into account the undetected infections. The case of China. *Communications in Nonlinear Science and Numerical Simulation*, *88*, 105303. https://doi.org/10.1016/j.cnsns.2020.105303

Lai, A. C., & Cheng, Y. C. (2007). Study of expiratory droplet dispersion and transport using a new Eulerian modeling approach. *Atmospheric Environment*, (35), 7473-7484. https://doi.org/10.1016/j.atmosenv.2007.05.04

Li, Y., Leung, G. M., Tang, J. W., Yang, X., Chao, C. Y., Lin, J. Z., ... & Yuen, P. L. (2007). Role of ventilation in airborne transmission of infectious agents in the built environment-a multidisciplinary systematic review. *Indoor Air*, *17*(1), 2-18. https://doi.org/10.1111/j.1600-0668.2006.00445.x

Mehta, P., McAuley, D. F., Brown, M., Sanchez, E., Tattersall, R. S., & Manson, J. J. (2020). COVID-19: consider cytokine storm syndromes and immunosuppression. *The Lancet*, *395*(10229), 1033-1034. https://doi.org/10.1016/S0140-6736(20)30628-0

Morawska, L. J. G. R., Johnson, G. R., Ristovski, Z. D., Hargreaves, M., Mengersen, K., Corbett, S., ... & Katoshevski, D. (2009). Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *Journal of Aerosol Science*, *40*(3), 256-269. https://doi.org/10.1016/j.jaerosci.2008.11.002

Morawska, L., & Cao, J. (2020). Airborne transmission of SARS-CoV-2: The world should face the reality. *Environment International*, *139*, 105730. https://doi.org/10.1016/j.envint.2020.105730

Milton, D. K., Glencross, P. M., & Walters, M. D. (2000). Risk of sick leave associated with outdoor air supply rate, humidification and occupant complaints.

Moreno-Rangel, A., Musau, F., Sharpe, T., & McGill, G. (2021). Indoor air quality assessment of Latin America's first Passivhaus home. *Atmosphere*, *12*(11), 1477. https://doi.org/10.3390/atmos12111477

OSHA, O. (2001). Department of Labor: Occupational Safety and Health Administration. *Occupational exposure to bloodborne pathogens: Final Rule*, *29*, 64003-64182. https://www.osha.gov/

Parker, K., Horowitz, J., Brown, A., Fry, R., Cohn, D. V., & Igielnik, R. (2018). What unites and divides urban, suburban and rural communities. https://apo.org.au/node/173886

Park, S., Song, D. (2023). CO_2 concentration as an indicator of indoor ventilation performance to control airborne transmission of SARS-CoV-2. *Journal of Infection and Public Health*, 16(7), 1037-1044. https://doi.org/10.1016/j.jiph.2023.05.011

Patel, R. B., Skaria, S. D., Mansour, M. M., & Smaldone, G. C. (2016). Respiratory source control using a surgical mask: An in vitro study. *Journal of Occupational and Environmental Hygiene*, *13*(7), 569-576. https://doi.org/10.1080/15459624.2015.1043050

Peng, Z., & Jimenez, J. L. (2021). Exhaled CO_2 as a COVID-19 infection risk proxy for different indoor environments and activities. *Environmental Science & Technology Letters*, *8*(5), 392-397. https://doi.org/10.1021/acs.estlett.1c00183

Peter, O. J., Qureshi, S., Yusuf, A., Al-Shomrani, M., & Idowu, A. A. (2021). A new mathematical model of COVID-19 using real data from Pakistan. *Results in Physics*, *24*, 104098. https://doi.org/10.1016/j.rinp.2021.104098

Pinto Neto, O., Kennedy, D. M., Reis, J. C., Wang, Y., Brizzi, A. C. B., Zambrano, G. J., ... & Zângaro, R. A. (2021). Mathematical model of COVID-19 intervention scenarios for São Paulo-Brazil. *Nature Communications*, *12*(1), 418. https://doi.org/10.5281/zenodo.4263126

Rowe, B. R., Canosa, A., Meslem, A., & Rowe, F. (2022). Increased airborne transmission of COVID-19 with new variants, implications for health policies. *Building and Environment*, *219*, 109132. https://doi.org/10.1016/j.buildenv.2022.109132

Rudnick, S. N., & Milton, D. K. (2003). Risk of indoor airborne infection transmission estimated from carbon dioxide concentration. *Indoor Air*, *13*(3), 237-245. https://doi.org/10.1034/j.1600-0668.2003.00189.x

Salud, G. M. (2020). Medición de la concentración de CO_2 como indicador de una ventilación adecuada de edificios y locales. COVID19. *Madrid Salud*, InfSAM 33. pp: 6.

Satish, U., Mendell, M. J., Shekhar, K., Hotchi, T., Sullivan, D., Streufert, S., & Fisk, W. J. (2012). Is CO_2 an indoor pollutant? Direct effects of low-to-moderate CO_2 concentrations on human decision-making performance. *Environmental Health Perspectives*, *120*(12), 1671-1677. https://doi.org/10.1289/ehp.1104789

Schöne-Seifert, B., & Van Aken, H. K. (2020). COVID-19 pandemic: Urgent need for action in care homes and senior citizens' homes from a medical-ethics perspective. *Current Opinion in Anaesthesiology*, *33*(4), 481. https://doi.org/10.1097/ACO.0000000000000896

Seppänen, O. A., Fisk, W. J., & Mendell, M. J. (1999). Association of ventilation rates and CO_2 concentrations with health andother responses in commercial and institutional buildings. *Indoor Air*, *9*(4), 226-252. https://doi.org/10.1111/j.1600-0668.1999.00003.x

Shahzad, M., Abdel-Aty, A. H., Attia, R. A., Khoshnaw, S. H., Aldila, D., Ali, M., & Sultan, F. (2021). Dynamics models for identifying the key transmission parameters of the COVID-19 disease. *Alexandria Engineering Journal*, 60(1), 757-765. https://doi.org/10.1016/j.aej.2020.10.006

Sun, Y., Wang, Z., Zhang, Y., & Sundell, J. (2011). In China, students in crowded dormitories with a low ventilation rate have more common colds: Evidence for airborne transmission. *PloS One*, *6*(11), e27140. https://doi.org/10.1371/journal.pone.0027140

Varga, Z., Flammer, A. J., Steiger, P., Haberecker, M. andermatt, R., Zinkernagel, A. S., ... & Moch, H. (2020). Endothelial cell infection and endotheliitis in COVID-19. *The Lancet*, *395*(10234), 1417-1418. https://doi.org/10.1016/S0140-6736(20)30937-5

Wardhani, D. K., & Susan, S. (2021). The Adaptation of Indoor Health and Comfort Criteria to Mitigate Covid-19 Transmission in the Workplace. *Humaniora*, *12*(1), 29-38. https://doi.org/10.21512/humaniora.v12i1.6767

Watson, O. J., Barnsley, G., Toor, J., Hogan, A. B., Winskill, P., & Ghani, A. C. (2022). Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *The Lancet Infectious Diseases*, *22*(9), 1293-1302. https://doi.org/10.1016/S1473-3099(22)00320-6

Wiryasaputra, R., Huang, C. Y., Kristiani, E., Liu, P. Y., Yeh, T. K., & Yang, C. T. (2023). Review of an intelligent indoor environment monitoring and management system for COVID-19 risk mitigation. *Frontiers in Public Health*, *10*, 1022055. https://doi.org/10.3389/fpubh.2022.1022055

Zeng, Z., Xu, L., Xie, X. Y., Yan, H. L., Xie, B. J., Xu, W. Z., ... & Yuan, J. P. (2020). Pulmonary pathology of early-phase COVID-19 pneumonia in a patient with a benign lung lesion. *Histopathology*, *77*(5), 823-831. https://doi.org/10.1111/his.14138

Zhou, P., Yang, X. L., Wang, X. G., Hu, B., Zhang, L., Zhang, W., ... & Shi, Z. L. (2020). A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*, *579*(7798), 270-273. https://doi.org/10.1038/s41586-020-2012-7