Ventilation strategies to minimise the airborne virus transmission in indoor environments

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ABSTRACT

A key challenge to fight the Covid-19 pandemic is to minimise the airborne transmission of the SARS-CoV-2 virus. Highly crowded indoor environments, such as schools, become possible hotspots for virus spreading because the basic non-pharmaceutical mitigation measures applied until now are not effective in reducing the virus airborne transmission mode, which is the principal one in indoor environments and requires improved ventilation. In the present study, a mass balance equation was applied to typical school scenarios to evaluate (i) required air exchange rates for mechanically-ventilated classrooms and (ii) adequate airing procedures for naturally ventilated classrooms. In the case of naturally ventilated classrooms, a feedback control strategy was evaluated using the measurements of indoor CO_2. Our results show how these procedures can be applied in real life to support continued in-person instruction during a pandemic.

INTRODUCTION

This worldwide uncontrolled spread of the SARS-CoV-2 virus has put indoor environments in the spotlight for their significant contribution to the virus transmission (Blocken et al., 2020; Miller et al., 2020; Morawska et al., 2020). In most cases, indoor environments present poor ventilation, also in the case of highly crowded environments such as schools. This condition does not allow a proper dilution of the possible virus-laden respiratory droplets emitted by an infected subject, leading to high percentages of secondary infections amongst subjects present in the same confined space (Buonanno, Morawska, & Stabile, 2020; Buonanno, Stabile, & Morawska, 2020; Li et al., 2007; Miller et al., 2020). For this reason, governments worldwide have imposed temporary shutdowns of most of the indoor environments, including schools (Farsalinos et al., 2021; Klimek-Tulwin & Tulwin, 2020; Petretto, Masala, & Masala, 2020; Viner et al., 2020), being in the uncomfortable role of deciding whether to prioritize socio-economic development and the right to education or health. After the first pandemic wave, guidelines for reopening schools focused their attention mainly on personal behaviours and basic non-pharmaceutical mitigation measures, such as social distancing, hand washing hand, and wearing masks. These essential rules are most effective at mitigating close contact transmission (Chen, Zhang, Wei, Yen, & Li, 2020), which is (if a social distance is guaranteed) a minor route of transmission in indoor environments (Z. Ai, Hashimoto, & Melikov, 2019; Z. T. Ai & Melikov, 2018). After the first reopening, schools were closed again during fall and winter in many countries worldwide (Edmunds, 2020; Ziauddeen, Woods-Townsend, Saxena, Gilbert, & Alwan, 2020), highlighting the limited effect of such measures in the indoor environments. In light of this, it becomes mandatory to consider the airborne transmission route of the virus to open schools safely because it is potentially the dominant mode of transmission of numerous respiratory infections, including SARS-CoV-2 (Leung et al., 2020; Morawska et al., 2020; Tang et al., 2020; Tellier, 2009). Hence, while waiting for a massive vaccination campaign, a possible solution to limit the virus transmission potential in schools is providing ad-hoc ventilation rates able to lower the virus concentration indoors (Buonanno, Stabile, et al., 2020; de Man et al., 2020; Li et al., 2007; Rudnick & Milton, 2003). Nonetheless, it is not an easy solution to provide a proper ventilation rate because most schools worldwide rely upon natural ventilation and manual airing (e.g. 86% of the European school buildings (Baloch et al., 2020)). For these schools, a good solution could be using a proxy to provide real-time information on the virus concentration in the indoor environment and, consequently, suggest applying manual procedures to control and minimise the virus spread in indoor environments.

Some studies propose the occupant's exhaled CO_2 as a possible proxy for virus spreading in an indoor environment. (Pavilonis, Ierardi, Levine, Mirer, & Kelvin, 2021; Zhu et al., 2020). Still, this approach could be considered an extremely oversimplified way to against the problem of the virus spread in indoor environments. In fact, whereas the exhaled CO_2 could be a good proxy for indoor-generated gaseous pollutants (as VOCs) (Stabile, Buonanno, Frattolillo, & Dell'Isola, 2019), it can be hardly adopted to forecast behaviours and dynamics of virus-laden droplets that instead are affected by phenomena typical of airborne particles as deposition, filtration and virus inactivation (in the case of the virus). Thanks to the decay dynamics of the CO_2 concentration, the exhaled CO_2 can be used to estimate the air exchange rate of indoor environments (Bakó-Birób, Clements-Croomea, Kochhara, Awbia, & Williamsc, 2011; Mahyuddin & Awbi, 2012).

Moreover, if droplet deposition rate and virus inactivation rate are known, the indoor virus concentration is just affected by the air exchange rate; thus, the exhaled CO_2 could somehow predict and limit the virus spreading in confined-closed environments (Mendell et al., 2013; Pavilonis et al., 2021; Zemouri et al., 2020). At the time of the COVID-19 pandemic, the question is not just demonstrating the qualitative association between ventilation and the transmission of infectious diseases (Bhagat, Davies Wykes, Dalziel, & Linden, 2020; Blocken et al., 2020; Buonanno, Stabile, et al., 2020; Li et al., 2007; Rudnick & Milton, 2003; Zhu et al., 2020), but quantifying and guaranteeing adequate ventilation in highly crowded environments (e.g. schools) to reduce the virus transmission via airborne route whether mechanical ventilation systems are installed or not. For this reason, the present paper aims to evaluate the required air exchange rates for mechanically-ventilated schools and adequate airing procedures for naturally ventilated schools. Such results were estimated to reduce respiratory disease transmission due to the virus's airborne route in classrooms. Moreover, in this study, different mitigations (reducing vocal modulation, wearing face masks or reducing the lesson time) were taken into account to limit the virus's spread in classrooms. To this end, simulations based on the virus and exhaled CO_2 mass balance equations considering typical school scenarios were carried out.

METHODS

Using the virus and CO_2 mass balance equations and under the simplified hypothesis that the concentrations of both (CO_2 and airborne virus) are instantaneously and evenly distributed in the indoor environment under investigation (box-model), the required air exchange rates and the adequate airing procedures to guarantee an acceptable virus transmission were calculated. In this study, the deposition and the virus inactivation phenomena were taken into account, and dynamic scenarios were simulated within a 5-hour school day. In this study, the authors have taken into account two different viruses (SARS-CoV-2 and seasonal influenza), characterised by extremely different emission rates (i.e. different viral loads and infectious doses) (A. Mikszewski). The study involves infected people breathing and/or speaking and does not apply to severely symptomatic persons frequently coughing or sneezing. The simulations were performed under the hypothesis that the students are adequately spaced, such that virus transmission is only due to the airborne route.

Estimation of the virus transmission

The virus transmission due to the airborne route was evaluated in terms of event reproduction number (R_{event}), adopting the proposed approach in our previous paper (Buonanno, Morawska, et al., 2020; Buonanno, Stabile, et al., 2020; Moreno et al., 2021). By means of this approach, it will be possible to evaluate (i) the quanta emission rate, (ii) the exposure to quanta concentration in the microenvironment, (iii) the dose of quanta received by exposed susceptible subjects, (iv) the probability of infection based on a dose-response model, (v) the individual risk of the exposed person, and, finally, (vi) the event reproduction number defined as the expected number of new infections arising from a single infectious individual at an event. Through an ad-hoc model described in previous papers we evaluated the quanta emission rate (ERq, quanta h-1) taking into account: viral load, infectious dose, respiratory activity, activity level, and droplet volume concentration expelled by the contagious person (A. Mikszewski; Buonanno, Morawska, et al., 2020; Buonanno, Stabile, et al., 2020). Such a model, here not reported for the sake of brevity, provides a distribution of quanta emission rates, i.e. the probability density function of ERq. This approach represents a step forward to simulate and predict infection risk in different indoor environments. Until now had been used estimates based on retrospective assessments of infectious outbreaks. (Rudnick & Milton, 2003; Wagner, Coburn, & Blower, 2009). The indoor quanta concentration over time, n(t,ERq), is evaluated, for each possible ERq value, adopting the above-mentioned simplified mass balance equation:

$$n(t, ER_q) = n_0 \cdot e^{-(AER+k+\lambda)\cdot t} + \frac{ER_q \cdot I}{(AER+k+\lambda)\cdot V} \cdot \left(1 - e^{-(AER+k+\lambda)\cdot t}\right) \quad \text{(quanta m}^{-3}\text{)} \qquad (1)$$

where AER (h^{-1}) is the air exchange rate, k (h^{-1}) is the deposition rate on surfaces, λ (h^{-1}) is the viral inactivation rate, I is the number of infectious subjects, and V is the volume of the indoor environment.

The dose of quanta (Dq) received by a susceptible subject exposed to a certain quanta concentration for a certain time interval, T, can be evaluated by integrating the quanta concentration over time as:

$$D_q(ER_q) = IR \int_0^T n(t, ER_q)dt \quad \text{(quanta)} \qquad (2)$$

where IR is the inhalation rate of the exposed subject which is a function of the subject's activity level and age (Adams et al., 1993; ICRP, 1994).

The probability of infection (PI, %) of exposed persons (for a certain ERq), is evaluated on the basis of simple

Poisson dose-response model (Sze To & Chao, 2010; Watanabe, Bartrand, Weir, Omura, & Haas, 2010) as:

$$P_I(ER_q) = 1 - e^{-D_q(ER_q)} \quad (\%) \quad (3)$$

The individual risk of infection (R) of an exposed person for a given exposure scenario is then calculated integrating, over for all the possible ERq values, the product between the conditional probability of the infection for each ERq (PI(ERq)) and the probability of occurrence of each ERq value (P_{ERq}):

$$R = \int_{ER_q} \left(P_I(ER_q) \cdot P_{ERq}\right) dER_q \quad (\%) \quad (4)$$

Such an individual risk, R, for a given exposure scenario, basically represents the ratio between the number of new infections (number of cases, C) and the number of exposed susceptible individuals (S); thus, the R_{event} (expected number of new infections, C, arising from a single infectious individual, I, at a specific event) can be obtained as the product of R and S:

$$R_{event} = C/I = R \cdot S \quad \text{(infections)} \quad (5)$$

Therefore, the maximum number of susceptibles that can stay simultaneously in the confined space under investigation for an acceptable $R_{event} < 1$ (hereinafter referred as maximum room occupancy, MRO) is:

$$\text{MRO} < 1/R \quad \text{(susceptibles)} \quad (6)$$

Evaluation of the CO_2 indoor levels

To estimate the trend of indoor (exhaled) CO_2 concentration over time (CO_2-in), a mass balance equation was applied considering the initial indoor CO_2 concentration (at t=0) equals to the outdoor one (CO_2-out), the mass balance equation can be simplified as (Mahyuddin & Awbi, 2012):

$$CO_{2-in}(t) = CO_{2-out} + \frac{ER}{V \cdot AER} \cdot \left(1 - e^{-AER \cdot t}\right) \quad \text{(ppm)} \quad (7)$$

ER represents the overall exhaled CO_2 emission rate in the indoor environment under investigation. The emission rate per-capita is available in the scientific literature (typically expressed in L s-1 person-1) as a function of the activity level age, and gender (Persily & de Jonge, 2017). As mentioned above, for a known and steady-state emission rate and outdoor CO_2 concentration, the indoor concentration is just affected by the air exchange rate of the room, and the AER can be back-calculated from the eq. 7 based on continuous monitoring of the indoor CO_2 concentration ($CO_{2\text{-in}}$): this AER estimation method is known as "constant injection rate method" (Mahyuddin & Awbi, 2012; Nazaroff, 2021).

Simulate scenarios

The R_{event} and the individual risk of infection related to the virus's airborne transmission route were evaluated considering a high-school classroom with a floor area of 50 m^2 and a ceiling height of 3 m. A crowding index equal to 2 m^2 person^{-1} was adopted, leading to a total number of occupants (including the teacher) equal to 25 persons (15251, 2008). For the simulation we considered an exposure time of 5 hours. All the simulations have been performed considering only one infected subject (I=1) (the teacher or one of the students) and 24 exposed susceptibles (S=24), hypothesising that none of them is already immune. In light of this, to obtain a $R_{event} < 1$, the individual risk of infection (R) of the exposed susceptible over the 5-hour school time should be less than 4.2%. The simulations were conducted for different scenarios, considering two different emitting subjects: the teacher and the student. In particular, simulations were performed considering (a) the infected teacher giving lesson (i.e. speaking or loudly speaking) for one hour; in particular, the first hour of the lesson was considered as it is the worst exposure scenario for susceptible students attending the lesson, or (b) the infected student attending lessons (just breathing). For the susceptibles we assumed an IR = 0.54 m^3 h-1 characteristic of people performing activities in a sitting position (Adams et al., 1993; ICRP, 1994). The quanta emission rate for SARS-CoV-2 and seasonal influenza viruses, as a function of respiratory activity, virus inactivation rate and droplet deposition rate, are summarised in Table 1 (Buonanno, Stabile, et al., 2020). Additional model input parammeters are summarised in Table 2. For both viruses, the ERq increases for more severe respiratory activities; besides, due to its higher infectious dose, for similar activity levels and respiratory activities, the SARS-CoV-2 ERq values were much higher than the seasonal influenza ones (A. Mikszewski; Alford, Kasel, Gerone, & Knight, 1966; Bueno de Mesquita, Noakes, & Milton, 2020; Buonanno, Stabile, et al., 2020; Gale, 2020) (e.g. more than 10-fold). To reduce vocal modulation we assumed using a microphone reduced the ERq for loudly speaking to that of speaking (scenario T-60-S). Whereas concerning wearing masks we assumed an overall 40% reduction of the dose of quanta received by the susceptible (Eikenberry et al., 2020) (scenario T-60-LS-M). In the simulations of the CO_2 concentrations we adopted an outdoor CO_2 equal to 500 ppm. Instead, for indoor (exhaled) CO_2 we used a per-capita emission rate equal to 0.0044 L s^{-1} person^{-1} as an average value between males and female teenager students (e.g. aged 17-18) with a level of physical activity of 1.3 met (Persily & de Jonge, 2017), which is the suggested level for reading, writing, and typing in sitting position at school.

Table 1. Quanta emission rate (ERq, quanta h^{-1}) expressed as 75th percentiles for SARS-CoV-2 and Seasonal Influenza viruses as a function of respiratory activity. Virus inactivation rate, λ (h^{-1}), and droplet deposition rate, k (h^{-1}) are also reported.

	SARS-CoV-2	**Seasonal Influenza**
Oral breathing	3.710	0.147
Speaking	16.57	0.626
Loudly speaking	102.2	4.271
Virus inactivation rate, λ (h^{-1})	0.63	0.80

Droplet deposition rate, k (h^{-1})	0.24

Air exchange rates and airing procedures

Following the methodology described in the previous sections, especially the eq. 1-5, it is possible to calculate the required air exchange rate to guarantee a R_{event}<1. In fact, after defining (i) the quanta emission rate related to the activity of the emission subject (Table 1), (ii) the geometry of the classroom, (iii) the virus inactivation rate (λ) for SARS-CoV-2 (0.63 h^{-1}) (van Doremalen et al., 2020) and seasonal influenza (0.80 h^{-1}) (Yang & Marr, 2011) as well as (iv) the droplet deposition rate (k=0.24 h^{-1}) (Chatoutsidou & Lazaridis, 2019); the individual risk of infection (R) and, consequently, the event reproduction number, depends solely on the air exchange rate and the airing procedure of the classroom.

For mechanically ventilated classrooms, the required air exchange rate is guaranteed by default when it is within the limits of the designed outdoor air flow rate. However, the majority of the schools are not equipped with a mechanical ventilation system. For this reason, to guarantee a R_{event} < 1 in naturally-ventilated classrooms, ad-hoc manual airing procedures based on manual airing cycles (L. Stabile et al., 2019; Stabile, Dell'Isola, Russi, Massimo, & Buonanno, 2017) are needed. Indeed, unlike mechanical ventilation systems, which can provide a constant air exchange rate AER, the manual airing cycles will alternate periods at low AER (with the window closed) and periods at higher AER (with the window open). One of the most critical points is represented by the fact that such air exchange rates are not known *a priori*. Due to this, in naturally-ventilated schools, the required air exchange rate cannot be defined and adopted as a design parameter. The air exchange rate of the manual airing procedure can just be calculated *a-posteriori* as school-day average resulting from the airing cycles:

$$AER = \frac{(AER_{NV} \cdot t_{NV} + AER_{MA} \cdot t_{MA})}{(t_{NV} + t_{MA})} \quad (8)$$

AER_{NV} and AER_{MA} represent the air exchange rates with the window closed (natural ventilation, NV) and window open (manual airing, MA), and t_{NV} and t_{MA} are the time during which the window was kept closed and open. Since the air exchange rate is not constant all over the school day, the time at which the airing is adopted can affect the quanta concentration trends significantly. In fact, when windows are closed and a high quanta emission occurs, the susceptibles are exposed to higher quanta concentrations then leading to a dose of quanta larger than expected for a constant air exchange rate causing a higher infection risk. For this reason, in the case of manual airing, it is necessary to provide a higher AER to guarantee a R_{event} < 1 as compared to classrooms equipped with mechanical ventilation systems, especially when the virus emission is high. In this study, the manual airing cycles were applied at the end of each school hour, only to reduce the number of scenarios to be simulated.

Nonetheless, this adoption does not undermine the findings and the procedures we described. Moreover, as mentioned above, not knowing the exact AER can lead to exceeding the R_{event}<1 condition. To avoid this situation, a proper feedback control strategy based on CO_2 monitoring to correct the airing procedure was proposed and applied.

RESULTS AND DISCUSSION

Trends of quanta concentration, individual risk, Maximum Room Occupancy (MRO) for R_{event}<1, and indoor CO_2 concentration are reported for the scenarios T-60-LS (teacher giving lesson loudly speaking for the first 60 min of the school day) and T-60-S (i.e. speaking using a microphone instead of loudly speaking) are reported in Figure 1 in the case of SARS-CoV-2 virus when required AERs (to guarantee a R_{event} < 1). Such examples are representative of the school provided a mechanical ventilation system hypothesizing a perfect (homogeneous) air distribution in the room. In particular, for the scenario T-60-LS, as summarized in Table 3, the required AER is 9.5 h^{-1} (i.e. > 15 L s^{-1} $person^{-1}$). As shown from Figure 1, the quanta concentration trend increases in the first 60 min (the time in which the infected subject is still in the classroom), then quickly exponentially decays as soon as the teacher leaves the room and goes to zero at about 90 min. The individual risk increases reaching the maximum permitted value (4.2%) already at 90 min, then remaining constant up to the end of the school day (300 min), under the condition that no infectious people enter the classroom.

The MRO decreases to the needed value of 24 persons at the end of the school day. The CO_2 concentration in the classroom, due to the high (and constant) AER of 9.5 h^{-1}, reaches the (very low) equilibrium concentration (about 750 ppm) in about half an hour. In the case of scenario T-60-S, a much lower AER (0.8 h^{-1}; equal to 1.3 L s^{-1} $person^{-1}$) is required to guarantee a R_{event} < 1, indeed, the CO_2 indoor concentration does not even reach an equilibrium level and continuously increases up to more than 3000 ppm by the end of the school-day, and such a value is well above the concentrations suggested by the indoor air quality standards (15251, 2008). The necessary AERs in order to guarantee a R_{event} < 1 for all the investigated scenarios are reported in Table 3 for SARS-CoV-2 (for mechanically-ventilated classrooms). The required AER for R_{event} < 1 for seasonal influenza-infected subjects is not reported since it is < 0.1 h^{-1} for all the scenarios under investigation.

For this reason, all the ventilation techniques can protect against the spreading of the seasonal influenza virus in the classroom through the airborne route. Instead, for SARS-CoV-2-infected subjects, the AERs to guarantee a R_{event}<1 can be quite high: as mentioned above, for a teacher giving a lesson for one hour, the required AER is 9.5 h^{-1}. It is possible to reduce such AERs keeping the voice down while speaking using microphones, and this adoption could reduce the required AERs down to 0.8 h^{-1}. In the case of the infected subject being a student, and he does not speak for the entire school day, the required AER to guarantee a $R_{event}<1$ is equal to 0.8 h^{-1}.

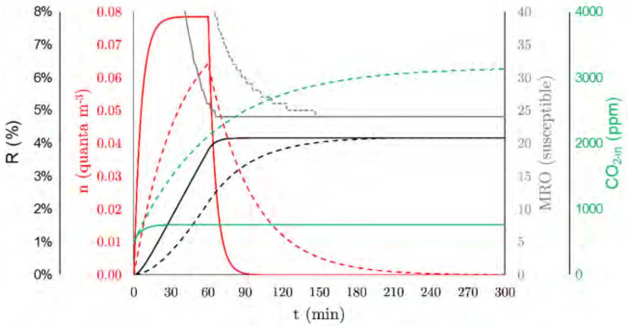

Figure 1 Trends of quanta concentration (n), individual risk (R), Maximum Room Occupancy (MRO), and indoor CO_2 concentration ($CO_{2\text{-}in}$) resulting from the simulation of the base scenarios T-60-LS (infected teacher giving lesson loudly speaking for the first 60 min of the school day, solid lines) and T-60-S (infected teacher giving lesson speaking for the first 60 min of the school day; dotted lines) in the case of SARS-CoV-2 virus having adopted the required constant AERs to guarantee a Revent < 1 (9.5 h^{-1} and 0.8 h^{-1} for T-60-LS and T-60-S, respectively) through a mechanical ventilation system.

Table 3 Required constant AER (h^{-1}) to guarantee a R_{event} < 1 for all the scenarios investigated for SARS-CoV-2 for mechanically-ventilated classrooms.

Scenarios		**AER** (h^{-1})
Base scenarios	T-60-LS	9.5
	S-0-S	0.8
Voice modulation effect	T-60-S	0.8
Mask effect	T-60-LS-M	5.8
Voice modulation & mask effect	T-60-S-M	0.2

For different scenarios in the case of the SARS-CoV-2-infected teacher (giving lesson for 60 min) as a function of the AER in a classroom equipped with a mechanical ventilation system, the individual risk R is showed in Figure 2 for the base scenario T-60-LS (teacher loudly speaking) and the mitigation solutions T-60-S and T-60-LS-M (voice modulation and use of mask). The individual risk decreases for higher AERs and, as shown in Table 3, very high AERs are required when the teacher is loudly speaking. Such high AERs are likely unachievable in schools without mechanical ventilation systems, and are potentially beyond the design capacity of standard mechanical systems. In Figure 2, the expected CO_2 peak concentrations at the end of the school day as a function of the AERs are also reported. The graph shows that the CO_2 level could be misleading when not interpreted with a critical eye; in fact, even if acceptable CO_2 levels are guaranteed (e.g. 1000 ppm), an unacceptable individual risk can occur. In light of this, for high-emitting activities (i.e. loudly speaking), the mitigation solutions (e.g. using a microphone) are more effective than the classroom ventilation itself.

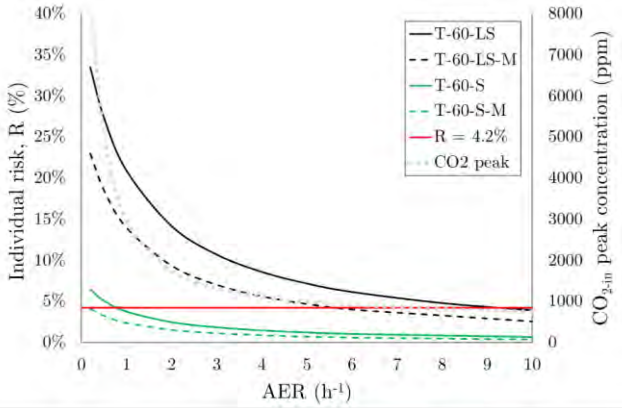

Figure 2 Individual risk R (%), for different exposure scenarios in the case of a SARS-CoV-2 infected teacher giving lesson for 60 min as a function of the air exchange rate in mechanically-ventilated classrooms: loudly speaking (T-60-LS), speaking (T-60-S), loudly speaking and wearing a mask (T-60-LS-M). In addition, Expected CO_2 peak concentrations (i.e. at the end of the school day) as a function of the AERs are also reported.

As previously mentioned in the methodology section, in mechanically-ventilated classrooms, the R_{event} < 1 condition is easily and automatically guaranteed if the required AERs obtained for the selected scenarios are adopted and are within the capacity limits of the system. In that case, a simple constant air volume flow system is enough to supply the necessary AER, and no complex control algorithms are needed. Once we defined the scenario, applying the methodology previously described, we know the required AER to guarantee the $R_{event}<1$. At this point, it is necessary just to set the needed airflow rate of the mechanical ventilation system.

In the case of naturally-ventilated schools, to guarantee a R_{event} < 1 could be challenging, especially for scenarios characterised by high emitting infected subjects for two main reasons: i) keeping the windows opened could be not enough to guarantee very high fresh air flow rates, ii) keeping the windows opened for long periods could be detrimental for thermal comfort and energy conservation (Heebøll, Wargocki, & Toftum, 2018; Stabile, Dell'Isola, Frattolillo, Massimo, & Russi, 2016; Luca Stabile et al., 2019). Nonetheless, the adoption of manual airing cycles represents a practical solution to operate schools during a pandemic. Still, it should be kept in mind that (i) the scheduling of window opening and closing period can affect the infection risk of the exposed susceptibles and (ii) the required AER cannot be determined *a-priori*. For example, if AER_{NV} and AER_{MA} were equal (and constant) to 0.2 and 4.0 h^{-1}, respectively, for the scenario T-60-S, a R_{event} < 1 could be achievable by opening the windows for about 10 min each hour. The resulting school day average AER would be equal to 0.8 h^{-1}, which is similar to that needed in the case of mechanical ventilation systems. But for lower AERs,

AER_{NV}=0.15 and AER_{MA}=0.2 h^{-1}, the required opening period for each hour is 36 min then resulting in a school-day average AER of 1.3 h^{-1} that is significantly higher than that required in the case of the mechanical ventilation system (0.8 h^{-1}). From this example, the airing strategies are strongly affected by the AER values; therefore, AER_{NV} and AER_{MA} need to be continuously monitored and corrected. As a result, the naturally-ventilated school's procedure is more complex and difficult to implement. In this study, we will use as feedback information the indoor CO_2 concentration continuously measured and, based on the number of persons and their activity levels and of the initial indoor CO_2 concentration, we will back-calculate the actual AERs during both the period with windows close (AER_{NV}) and open (AER_{MA}) using the CO_2 mass balance equation (Eq. 7). Based on the actual AERs, the corrected t_{MA} and t_{NV} periods will be calculated and scheduled to obtain a R_{event} < 1. Because the AER_{NV} and AER_{MA} values are not known *a-priori*, during the first hour/cycle, it is possible to use tentative opening and closing periods (for example, 50 min with windows closed and 10 min with windows open). Then, the evaluation of the actual AERs will allow scheduling the equally-spaced opening periods of the remaining four hours to obtain a R_{event} < 1 including the entire school day (i.e. 300 minutes) in the calculation. At the end of the second cycle, AER_{NV} and AER_{MA} will be back-calculated again, and in case, the opening and closing periods will be modified again. This procedures is illustrated in Figure 3, showing a step by step schematic of the entire procedure to be applied to maintain R_{event} < 1.

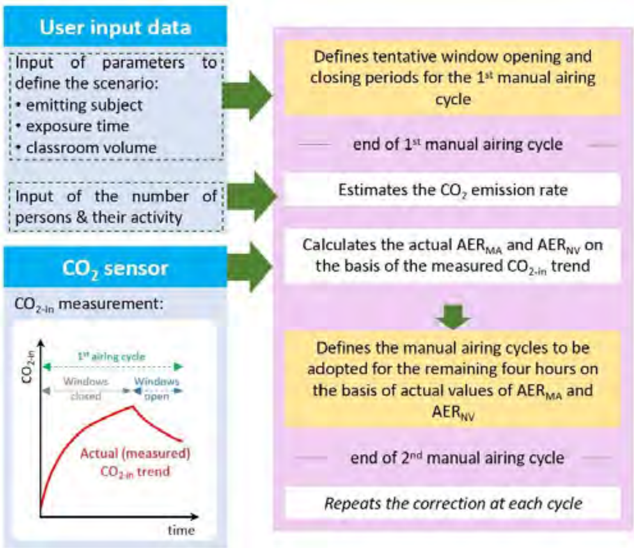

Figure 3 Scheme, step by step, of the suggested procedure to be applied in schools without mechanical ventilation to maintain R_{event} < 1.

Figure 4 shows an example of the application of the correction procedure in scenario T-60-S, and the indoor CO_2 concentration, SARS-CoV-2 quanta concentration, and individual risk trend are reported.

In the first hour, a tentative airing cycle of 50 min with windows closed and 10 min with windows open was adopted. From the CO_2 trend (related to the first cycle), the actual AER_{NV} and AER_{MA} values were back-calculated and (in this illustrative example) resulted in values of 0.15 (AER_{NV}) and 2.0 (AER_{MA}) h^{-1}. Based on the actual AERs (back-calculated), to guarantee a R_{event} < 1, we calculate a new equally spaced value of t_{MA} of 42 min for each hour for the remaining four hours. The total times during which the windows were kept closed and opened for the entire school day are t_{NV} = 122 min and t_{MA} = 178 min, respectively (including the 50 min and 10 min of window closing and opening periods related to the first hour). These new times resulted in a school-day average AER of about 1.3 h^{-1}. In light of this, the tentative opening and closing periods adopted for the first hour were too short to achieve the necessary AERs. For this reason, the quanta concentration in the first hour increases significantly. In the example, the actual AERs were considered constant during the entire school day; however, if the AERs at the end of each closing and opening periods do no match with the expected ones, for example due to variation in wind speed and direction, further corrections are needed for each hour.

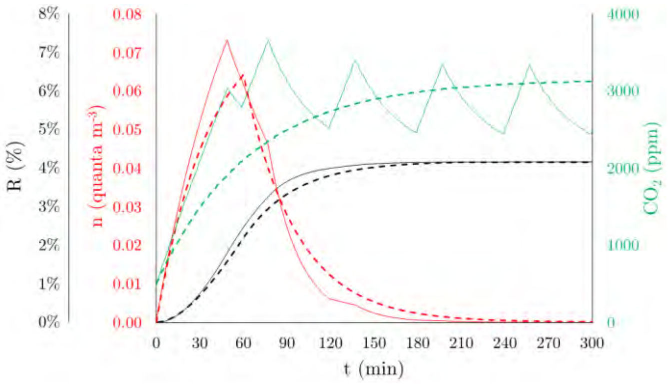

Figure 4 Trends of quanta concentration (n), individual risk (R), and indoor CO_2 concentration (CO_{2-in}) for the scenario T-60-S in the case of SARS-CoV-2 to guarantee a R_{event} < 1 through (a) mechanical ventilation system (constant AER = 0.8 h^{-1}; bold dotted lines) and (b) manual airing procedures corrected for actual AER (school-day average AER = 1.3 h^{-1} in the hypothesis of measured AER_{NV} and AER_{MA} of 0.15 and 2.0 h^{-1}, respectively; thin solid lines).

The procedure presented evaluates the required ventilation (using mechanical systems or manual airing) to reduce the spread of infectious diseases via the airborne route and proposed a control strategy to monitor and adjust such ventilation in naturally ventilated classrooms. By the way, to effectively reduce the transmission potential of a disease, the uncertainty of the event reproduction number (R_{event}) calculation should be taken into account. The estimation of this uncertainty (U_{Revent}) cannot be easily evaluated as it depends on several parameters and models adopted. Indeed, to assess the R_{event}, the following data are needed: quanta emission rate, deposition rate, inactivation rate, inhalation rate, room volume, air exchange rate, time of exposure. In our previous papers, we investigated the quanta emission rate, and we highlighted that uncertainty relates to the quality of data on viral load, infectious dose and particle volume. These data, at least for SARS-CoV-2, are not definitive (Abbas & Pittet, 2021; Gale, 2020; Watanabe et al., 2010) also due to the presence of different viral lineages (Alteri et al., 2021).

Regarding the deposition rate, it is mainly affected by the particle size (Chatoutsidou & Lazaridis, 2019). Adopting an average parameter, as typical of easy-to-use box models, results in additional uncertainty as well; similarly, there is limited data on the virus inactivation rate of SARS-CoV-2 (Fears et al., 2020; van Doremalen et al., 2020). With regards to the inhalation rate, it depends on the activity levels of the subject. In scientific literature, different IR values are reported for the same activity (Adams et al., 1993; Layton, 1993), confirming a significant variability. Finally, room volume and time of exposure could be considered as fixed values as well as the AER if provided employing a mechanical ventilation system. The uncertainty estimation would be even more complex for indoor environments without mechanical ventilation where manual airing procedures corrected based on the measured CO_2 values are put in place. The CO_2 measurements and the CO_2 mass balance equation's uncertainty to back-calculate the corrected AERs should be included in such a case. The uncertainty related to the CO_2 measurement is typically affected by the sensor accuracy, resolution, temperature effect, static pressure effect, dew-point effect, and probe positioning within the room (Mendes et al., 2015). CO_2 sensors should provide measurement data with an expanded accuracy of about 5% (Mendes et al., 2015; Sherman, Walker, & Lunden, 2014), but low-cost sensors may present more considerable uncertainties. To limit this problem it is possible to adopt a multi-points method instead of a two-point method. In light of this, the uncertainty of R_{event} is quite complex and beyond the current study's aims. Further studies are needed in view of improving the quantification of the virus transmission potential for different ventilation systems.

CONCLUSION

The aim of our study was to develop procedures able to support regulatory authorities in view of safely running schools during an airborne pandemic. The required ventilation to reduce the spread of infectious diseases via the airborne route was assessed for both mechanically and naturally-ventilated classrooms through virus mass balance equations. We also investigated the possibility to use CO_2 concentration as a proxy of a possible exceedance of a R_{event}<1 condition. The simulated scenarios show that adopting a CO_2 indoor concentration as a proxy for virus transmission is a misrepresentation; in fact, the dynamics of the virus-laden droplets and the occurrence of the virus emission may strongly differ from the exhaled CO_2 ones. As a result, CO_2 and virus concentrations present significantly different trends. Regarding seasonal influenza, due to the low emission rates typical of such virus, a negligible transmission potential via the airborne route in the classroom was found, even if it is in the presence of a low air exchange rate. Instead, for the SARS-CoV-2 virus, the required air exchange rates to guarantee a R_{event} < 1 can be very high for scenarios characterised by highly-emitting infected subjects, such as teacher giving lesson loudly speaking. These AERs may be even higher than those suggested by the indoor air quality technical standards. Due to this, mitigation solutions (for example, voice modulation in particular) are welcomed. To reduce virus transmission, ad-hoc procedures were defined in both mechanically- and naturally-ventilated classrooms. For mechanically-ventilated classrooms te procedure is straight-forward as long as the required AER to guarantee a R_{event}<1 is within the design capacity of the mechanical ventilation system.

On the contrary, in naturally-ventilated classrooms, a suitable manual airing procedure using a novel feedback control strategy was investigated and applied in the procedure. In these classrooms, manual airing cycles could increase the AER, but the required air exchange rate cannot be defined *a-priori*, and the condition of R_{event}<1 becomes a design parameter. We propose using the CO_2 indoor concentration as feedback to check the correct procedure and calculate the new AERs and time of window opening that are necessary to guarantee the condition R_{event}<1. In the light of the results found from this study, the authors believe that even though further efforts have to be performed in view of reducing the uncertainties of such models, , the suggested procedures can be adopted to minimise the contribution of school classroom environments to the spread of pandemics.

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Table 2 Scenarios taken into account to simulate the exposure to SARS-CoV-2 and seasonal influenza viruses in the classroom: emitting subjects, emission duration, and respiratory activity are summarised. Descriptions of the base scenarios and the possible mitigation strategies are reported.

Scenarios		Emitting subject	Emission duration (min), respiratory activity	Description
Base scenarios	T-60-LS	teacher	60 min, loudly speaking	Infected teacher giving lesson for the first 60 min of the school-day loudly speaking
	S-0-S	student	300 min, oral breathing	Infected student attending lessons for five hours (100% of the school-day) oral breathing
Voice modulation effect	T-60-S	teacher	60 min, speaking	Infected teacher giving lesson for the first 60 min of the school-day speaking (e.g. using a microphone)
Mask effect	T-60-LS-M	teacher	60 min, loudly speaking	Infected teacher giving lesson for the first 60 min of the school-day loudly speaking. Students and teacher wear a surgical mask.
Voice modulation & mask effect	T-60-S-M	teacher	60 min, speaking	Infected teacher giving lesson for the first 60 min of the school-day speaking (e.g. using a microphone). Students and teacher wear a surgical mask.