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Monitors to improve indoor air carbon dioxide concentrations in the hospital: A randomized crossover trial

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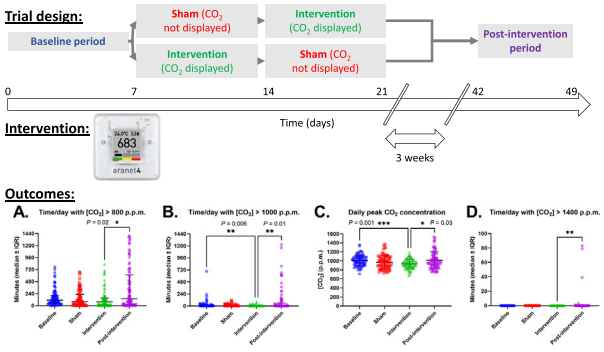
HIGHLIGHTS

- A randomized trial investigating CO_2 monitors to improve hospital room ventilation.
- CO_2 levels were >800 ppm 7.6% of the time pre-intervention.
- CO_2 levels were >800 ppm 5.4–5.7% during and 9.7% of time post-intervention.
- Worst CO_2 levels were observed in rooms housing couples.
- Staff reported cold discomfort as the main barrier towards increasing ventilation.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Ventilation has emerged as an important strategy to reduce indoor aerosol transmission of coronavirus disease 2019. Indoor air carbon dioxide (CO_2) concentrations are a surrogate measure of respiratory pathogen transmission risk.
Objectives: To determine whether CO_2 monitors are necessary and effective to improve ventilation in hospitals.
Methods: A randomized, placebo (sham)-controlled, crossover, open label trial. Between February and May 2021, we placed CO_2 monitors in twelve double-bed patient rooms across two geriatric wards. Staff were instructed to open windows, increase the air exchange rate and reduce room crowding to maintain indoor air CO_2 concentrations ≤800 parts per million (ppm).
Results: CO_2 levels increased during morning care and especially in rooms housing couples (rooming-in). The median (interquartile range, IQR) time/day with CO_2 concentration > 800 ppm (primary outcome) was 110 min (IQR 47–207) at baseline, 82 min (IQR 12–226.5) during sham periods, 78 min (IQR 20–154) during intervention periods and 140 min (IQR 19.5–612.5) post-intervention. The intervention period only differed significantly from the post-intervention period ($P = 0.02$), mainly due to an imbalance in rooming-in. Significant but small differences were observed in secondary outcomes of time/day with CO_2 concentrations > 1000 ppm and daily peak CO_2 concentrations during the intervention vs. baseline and vs. the post-intervention period, but not vs. sham. Staff reported cold discomfort for patients as the main barrier towards increasing ventilation.
Discussion: Indoor air CO_2 concentrations in hospital rooms commonly peaked above recommended levels, especially during morning care and rooming-in. There are many possible barriers towards implementing CO_2

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monitors to improve ventilation in a real-world hospital setting. A paradigm shift in hospital infection control towards adequate ventilation is warranted.
Trial registration: ClinicalTrials.gov Identifier: NCT04770597

1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has caused considerably morbidity and mortality worldwide, especially among frail older adults (De Smet et al., 2020). While vaccination protects against severe COVID-19, death and to some extent against transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, the virus which causes COVID-19), other mitigation strategies will likely continue to be required. Among such strategies, ventilation and purification of indoor air feature prominently (Allen and Ibrahim, 2021). Indeed, there is growing consensus and accumulating evidence for respiratory transmission or SARS-CoV-2, not only via larger droplets but also via smaller particles in aerosols, mainly in closed spaces (Greenhalgh et al., 2021; Meyerowitz et al., 2021; Morawska et al., 2021; Noorimotlagh et al., 2021; Tang et al., 2021).

One convenient surrogate parameter for ventilation in this context is the indoor carbon dioxide (CO_2) concentration (Rudnick and Milton, 2003). Humans exhale CO_2 at concentrations of almost 40,000 parts per million (ppm) (Rudnick and Milton, 2003) compared to outdoor concentrations which have increased in recent years to ~450 ppm (fluctuating between 400 and 500 ppm). Thus, the increase in CO_2 concentrations above outdoor levels mainly reflects the indoor concentration of human exhaled air. Under average circumstances, an indoor CO_2 concentration > 380 ppm above outside levels implies that inhaled air contains 1% exhaled air (Rudnick and Milton, 2003). In turn, this rebreathed fraction or "shared air" correlates with airborne microbial counts (Hiwar et al., 2021; Tavera Busso et al., 2020) and the basic reproductive number of respiratory infections (Du et al., 2020; Rudnick and Milton, 2003).

There is no universal agreement on optimal cut-offs for indoor CO_2 concentrations in general, or in the context of COVID-19 in particular. Regulatory bodies in several countries have proposed guidelines to maintain indoor CO_2 concentrations below values ranging from 800 to 1000 ppm (European Centre for Disease Prevention and Control, 2020; Superior Health Council of Belgium, 2020). One COVID-19 outbreak in a Dutch nursing home was associated with the use of an energy-saving CO_2-driven ventilation system, which maintained indoor CO_2 concentrations around 1000 ppm (de Man et al., 2021).

Modern hospitals, particularly operating and delivery rooms, intensive care units and microbiology laboratories, are equipped with superior heating, ventilation and air conditioning (HVAC) systems, which also remove particles via high-efficiency particulate air (HEPA) filters (Allen and Ibrahim, 2021). For normal patient rooms however, the recommended outdoor and total air change rates per hour are only 2 and 4–6, respectively (Allen and Ibrahim, 2021). While these rates may be sufficient to meet indoor air quality requirements under basal conditions (i.e. patients alone in their rooms), they may be temporarily insufficient when rooms are crowded by healthcare staff and/or visitors (Ramos et al., 2015; Tang et al., 2009). Indeed, physical distancing and limiting occupant density are challenging in hospitals, since patients (especially frail older adults) depend on caregivers. Moreover, opening windows in hospital may be avoided due to thermal and draft discomfort (Shajahan et al., 2019; Zhou et al., 2015) or risk of patient injury from falls out of open windows.

Few studies have reported indoor CO_2 concentrations in hospitals (Shajahan et al., 2019). Inappropriately high CO_2 concentrations were measured in hospitals without modern HVAC systems (Hwang and Park, 2020; Lee et al., 2020; Pereira et al., 2020; Zaman et al., 2021; Zhou et al., 2015). In contrast, excellent CO_2 values have been reported in COVID-19 wards without detectable airborne viral genomes (Vosoughi et al., 2021) and an Iranian intensive care unit (where viral genomes were still detected in $N = 2/14$ air samples) (Kenarkoohi et al., 2020). A French study found maximal CO_2 concentrations of 1121 to 1325 ppm in a hospital nursing care room and plaster room, respectively (Baures et al., 2018). In a Taiwanese four-bed intensive care unit room, CO_2 levels (range 828–1570 ppm) were above 1000 ppm during visitor hours 92% of the year (Tang et al., 2009). Another study from Taiwan reported that patient wards had the highest average CO_2 concentration (1063 ± 483 ppm, $N = 3$ hospitals) (Jung et al., 2015). Increases in CO_2 of almost 400 ppm above outside levels during working hours were observed in two chemotherapy units (Palmisani et al., 2021).

Thus, it is clear that despite guidelines for hospital HVAC systems and CO_2 targets in buildings, ventilation in hospital wards may be worse than commonly appreciated. More research is needed not only to provide a more detailed overview of indoor CO_2 fluctuations in hospital rooms, but even more so to define optimal strategies to maintain CO_2 below recommended maximum levels. One before-after implementation study reported an average CO_2 of 1211 ppm in a psychiatric nursing station, which decreased after an intervention to 997 ppm (Chang et al., 2013). Another recent study reported that monitors revealed insufficient ventilation (CO_2 up to 963 ppm) in clinical areas and guided implementation of effective mediation strategies (Lu et al., 2021).

CO_2 monitors are increasingly deployed and recommended (for example, in countries like Germany, Norway and Belgium (European Centre for Disease Prevention and Control, 2020)) to monitor ventilation and prevent aerosol transmission of SARS-CoV-2 in schools, offices and public buildings including hotels, bars and restaurants (Superior Health Council of Belgium, 2020). Some experts have called for the use of CO_2 monitors by nurses in hospitals and nursing homes too (Ahlawat et al., 2020). In schools, one controlled study showed that CO_2 warning devices improved the average daily CO_2 concentration in classrooms, whereas advice alone did not (Geelen et al., 2008). Other before-after observational studies in school settings support the effectiveness of CO_2 monitors (Wargocki and Da Silva, 2015) and other interventions to improve ventilation (Du et al., 2020; Rosbach et al., 2013; Sa et al., 2017). In the hospital environment, Yang et al. reported daily CO_2 peak concentrations > 1000 ppm, which could be mitigated using an integrated monitoring system, which alerted medical supervisors and automatically activated ventilation (Yang et al., 2014). However, randomized trials supporting the use of CO_2 monitors to improve ventilation, in any setting, remains lacking.

Given this background, we investigated (1) whether indoor air CO_2 exceeded threshold levels in double-bed hospital rooms, and (2) whether CO_2 monitors are feasible and effective to maintain indoor CO_2 concentrations below the commonest thresholds of 800 and 1000 ppm.

2. Methods

This report follows the Consolidated Standards of Reporting Trials (CONSORT) statement's extension to randomized crossover trials (see checklist in the Supplementary Data) (Dwan et al., 2019).

2.1. Setting

This single-center trial ran at the Geriatrics Department of Imelda general hospital in the rural area of Bonheiden, Belgium (Supplementary Fig. 1). A green environment surrounds the hospital and there is no traffic or other nearby CO_2 source. All rooms had type D ventilation (mechanical inlet, mechanical outlet) with the possibility to tilt the windows (fully open only by key), additional ventilation grilles, and recently had air-conditioning installed (cooling mode only).

Among general acute wards with standard air exchange rates, we selected the Geriatric Department for several reasons. First, bed occupancy rate in the department is typically >90%. Secondly, almost all patients require assistance from staff for activities of daily living such as washing, dressing, meals etc. Thirdly, geriatrics has higher staffing levels than other acute wards and many nursing students (occasionally up to 10/rotation/ward). All these elements increase room crowding.

On the other hand, many older patients have low levels of physical activity and thus low respiratory minute volumes. Visitors were allowed very restrictively due to the ongoing COVID-19 epidemic, typically only 1 h/week during most of the study period. Thus, older patient age and visitor restrictions may be associated with lower indoor CO_2 concentrations.

2.2. Trial design and randomization

The study design and protocol have been reported (Laurent and Frans, 2021). We performed a randomized, placebo (sham)-controlled, open label, crossover trial aimed to demonstrate superiority of the intervention. Between February 21st and May 2nd, 2021, we placed CO_2 monitors in twelve double-bed patient rooms across two geriatric wards. Following a baseline period, monitors were randomized 1:1 to an intervention or sham (monitor display visible or not) AB/BA crossover period. Three weeks later, post-intervention measurements were obtained. Each period lasted seven days (Fig. 1).

Thus, the study consists of four periods:

1. **Baseline (pre-intervention) period (duration 1 week)**: all monitors facing downwards, staff blinded to the CO_2 values.
2. **Sham period (duration 1 week)**: monitors facing downwards, staff blinded to the CO_2 values.
3. **Intervention period (duration 1 week)**: monitors facing forward, measurements visible to the clinical staff for one week.
4. **Post-intervention period (duration 1 week)**: after a three-week interval, the sensors are again installed in six double-bed rooms, with their display facing downwards and staff blinded to the measurements.

Given the open-label design, we chose the sham-control group to take potential observation bias (Hawthorne effect) and carryover effects (influence of the intervention on the sham periods due to lack of blinding) into account.

We randomized the six sensors to the sham/intervention or intervention/sham arm respectively (AB/BA crossover design), just before the end of the baseline period, using an online random sequence generator (1:1 ratio, $N = 1$ block size; https://www.random.org/sequences/?min=1&max=6&col=3&format=html&rnd=). Due to the nature of the intervention, allocation concealment is not possible. Investigators performing the analysis were also not blinded to allocation. However, the a priori statistical analysis plan (Laurent and Frans, 2021) and the availability of data for independent review by other scientists mitigates the risk of bias.

2.3. Intervention

This study used six Aranet4 Home® and one Airthings Wave Plus® monitor (measurement ranges 0–9999 ppm and 400–5000 ppm, respectively). Both monitors are commercially available in Europe and use non-dispersive infrared CO_2 sensors with ±3% accuracy reported by the manufacturer, and raw data logging with time stamps. The Aranet® sensors are factory-calibrated, recommended for use in schools by the Federation of European HVAC Associations, and have been shown to be reliable compared to research-grade instruments and to reflect ventilation rates in a clinical environment (Huang et al., 2021). The Airthings® instrument was used after the seven-day self-calibration period. When we cross-calibrated all devices, they displayed near-identical values. We also compared the CO_2 values from Aranet4 Home® to a professional indoor climate multimeter (Testo® 435-1) which again showed identical CO_2 values. The sensors were placed at a height between 1 and 2 m and not near the window or door.

Pilot data suggested that the highest CO_2 concentrations were observed in patient rooms, in line with previous literature (Baures et al., 2018). Compared to the Airthings Wave Plus®, Aranet4 Home® monitors were more responsive (a slight delay can be seen as an offset with the Airthings Wave Plus® sensor, Supplementary Fig. 2). We used the Airthings Wave Plus® to monitor outdoor CO_2 levels continuously during the trial.

At the start of the randomized sham/intervention period, clinical staff on each ward (nurses, nurse assistants, physiotherapists, occupational therapists, social workers etc.) were educated by the principal investigator on the purpose and methods of the trial and strategies to improve ventilation. Staff were instructed to maintain CO_2 levels ≤ 800 ppm. During the two-week sham/intervention period, staff were interviewed at least every three days regarding difficulties in achieving CO_2 targets, and additional solutions were sought to improve implementation. For example, in the intervention group, signs in the patient rooms alerted clinical staff to the ongoing experiment, CO_2 targets and strategies on how to improve ventilation (open window, increase HVAC ventilation rate, reduce room crowding). We also discussed with staff how they could improve ventilation to remove CO_2, or alter their care routines to prevent CO_2 accumulation.

2.4. Outcomes

Our primary hypothesis was that CO_2 monitors would record less time/day (in minutes) with elevated CO_2 levels (>800 ppm, primary

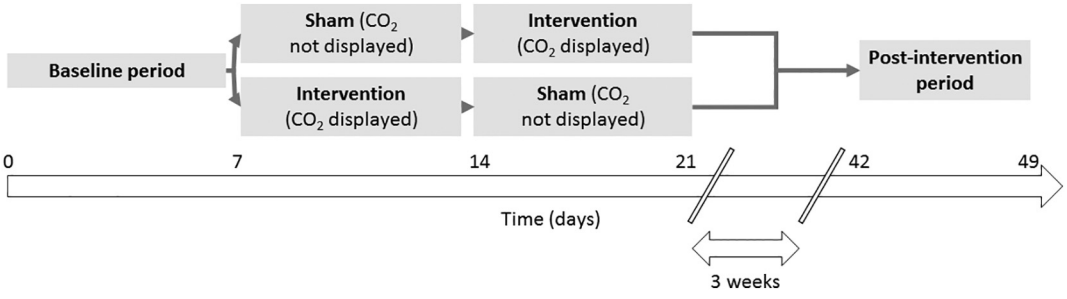

Fig. 1. Study design overview.

endpoint) during the intervention period, compared to the sham period. Secondary outcomes include the time with CO_2 > 1000 ppm or >1400 ppm (which are the built-in cut-off levels for orange and red warning lights on the Aranet® devices).

Following the two-week sham/intervention phase, an anonymous online survey was sent via e-mail to ward staff to collect quantitative feedback regarding feasibility and preference to use CO_2 monitors (using a 10-point Likert scale; predefined additional endpoints), as well as regarding their knowledge and behavior regarding ventilation and possible barriers towards implementation.

2.5. Statistical analysis

The four periods (baseline, sham, intervention and post-intervention) were analyzed by non-parametric Kruskal-Wallis test (because the residuals were not normally distributed) comparing the intervention period against the baseline, sham and post-intervention periods (3 comparisons). A priori, we assumed that if the intervention vs. baseline together with the intervention vs. post-intervention comparison would be significant (but not intervention vs. sham, which could be masked by carry-over effects), a pre-post effect of the intervention could be assumed.

The only exclusion criterion was incomplete occupancy: when the double-bed rooms were not fully occupied before 12 a.m., measurements from that day were excluded. Missing data were not planned to be imputated. Data were analyzed using the intention-to-treat principle, even though monitors in the sham group were occasionally noticed to be unblinded by staff during the study.

Statistical analyses were performed using GraphPad Prism v.9.1.1. Gaussian distribution of the data was assessed by the D'Agostino-Pearson (omnibus K2) normality test. Two-tailed, multiplicity-adjusted α below 0.05 was considered significant.

Due to lack of sufficient pilot data for robust power calculation, we assumed a conventional moderate effect size ($f = 0.25$). With an α error probability of 0.05, power of 0.95 and four groups, we calculated a total sample size of $N = 280$ measurements. With four groups, six sensors, two wards, seven days of measurements and expecting 15% excluded values due to unoccupied rooms ($N = 4 \times 6 \times 2 \times 7 \times 0.85 = 285.6$), our trial should be powered to detect a moderate effect size. Power calculation was performed using G*Power software version 3.1.9.7 (Kiel University, Germany).

2.6. Ethics and trial registration

On February 9th, 2021, our Institutional Ethical Committee decided that the study did not require informed consent since the design did not qualify as a human clinical trial according to applicable national and European regulations. Only basic demographic data about the room occupants (i.e. age and sex) as well as bed occupancy were collected anonymously via the electronic health records by the principal investigator. The head nurses of each ward provided verbal consent to participate voluntarily in the study, and all staff members were free to apply mitigation strategies to avoid high indoor CO_2 levels or proceed with usual care. There was no funding involved in this trial.

The trial protocol was registered with ClinicalTrials.gov on February 21st 2021 (and published on February 25th 2021), and later amendments were registered at: https://clinicaltrials.gov/ct2/show/NCT04770597.

3. Results

3.1. Study sample characteristics

During the study, rooms were occupied 95.2% of the time, yielding $N = 320/336$ days or 7680 h of data. Room occupants were 97 women and 30 men, mean age (±standard deviation) 86.6 ± 5.6 years. The median outdoor CO_2 concentration was 447 ppm (interquartile range [IQR] 424–470 ppm, see red dotted line in Supplementary Figs. 3–6).

3.2. Primary and secondary outcomes

CO_2 levels increased mainly during morning care or when couples were hospitalized together. In both circumstances, we noticed that not only windows but also room doors -the main ventilation inlet- were usually closed (see Supplementary Figs. 3–6). During the baseline period, we noticed that our staff never operated the air-conditioning system in the rooms, since they received no prior instructions how to do so.

The median (IQR) time/day with CO_2 concentration > 800 ppm (primary outcome) was 110 min (7.6% of the day; IQR 47–207 min, $P = 01511$ vs. intervention) at baseline, 82 min (5.7%, IQR 12–226.5 min, $P > 0.99$ vs. intervention) in the sham period, 78 min (5.4%, IQR 20–154 min) in the intervention period and 140 min (9.7%, IQR 19.5–612.5 min, $P = 0.0167$ by Dunn's multiple comparisons test) post-intervention (Fig. 2A).

The median time/day with CO_2 levels > 1000 ppm was 2 min (IQR 0–19, $P = 0.0064$ vs. intervention) at baseline, 0 min (IQR 0–20, $P = 0.2366$ vs. intervention) in the sham period, 0 min (IQR 0–2) during intervention and 0 min (IQR 0–57, $P = 0.0100$ vs. intervention) post-intervention (Fig. 2B). The median daily peak CO_2 concentration was 1010 ppm (IQR 926.5–1086, $P = 0.0010$ vs. intervention) at baseline, 964 ppm (IQR 846–1075, $P = 0.5143$) during the sham period, 932 ppm (IQR 861–1002) during intervention, and 977.5 ppm (IQR 873.5–1127, $P = 0.0298$) post-intervention (Fig. 2C). By Mann-Whitney U test, the differences in these three outcomes between the sham and intervention groups were not significant ($P = 0.77$, $P = 0.052$ and $P = 0.22$, respectively), confirming the results by the Kruskal-Wallis tests.

CO_2 concentrations exceeding 1400 ppm were only observed during the post-intervention period, for 3 min on one day in one room and for a total of 202 min over four days in another room (out of 12 total rooms, see Supplementary Fig. 6). By Kruskal-Wallis test, the medians differed significantly ($P = 0.0021$), and by Dunn's multiple comparisons test, the intervention period differed significantly from the post-intervention period ($P = 0.0055$) but not from the baseline and sham periods ($P > 0.9999$, Fig. 2D).

3.3. Other outcomes

Staff members ($N = 32$ anonymous survey respondents) gave high ratings (median 8/10) for feasibility and preference to use CO_2 monitors (Supplementary Fig. 7).

The main barriers for implementation were cold discomfort for patients ($N = 19$, 59%), lack of visibility and attention drawn by the monitors ($N = 5$) and risk that the patient would fall out of an open window ($N = 4$) (Fig. 3).

4. Discussion

Our findings show that indoor air CO_2 concentrations in our hospital commonly peaked above recommended levels, providing a rationale for widespread use of CO_2 monitors in patient rooms and clinical areas. These results are in line with previous reports in the literature (Baures et al., 2018; Chang et al., 2013; Jung et al., 2015; Pereira et al., 2020; Tang et al., 2009; Zhou et al., 2015) and are thus likely widely generalizable to many acute hospital wards worldwide. Of course, there are also many modern hospital wards with superior HVAC systems and excellent overall ventilation (as seen in intensive care units for example) (Kenarkoohi et al., 2020; Vosoughi et al., 2021).

Nosocomial transmission contributes to the incidence and mortality of COVID-19 (De Smet et al., 2020; Klompas et al., 2021). According to one estimate, ~11% of patients hospitalized with COVID-19, had

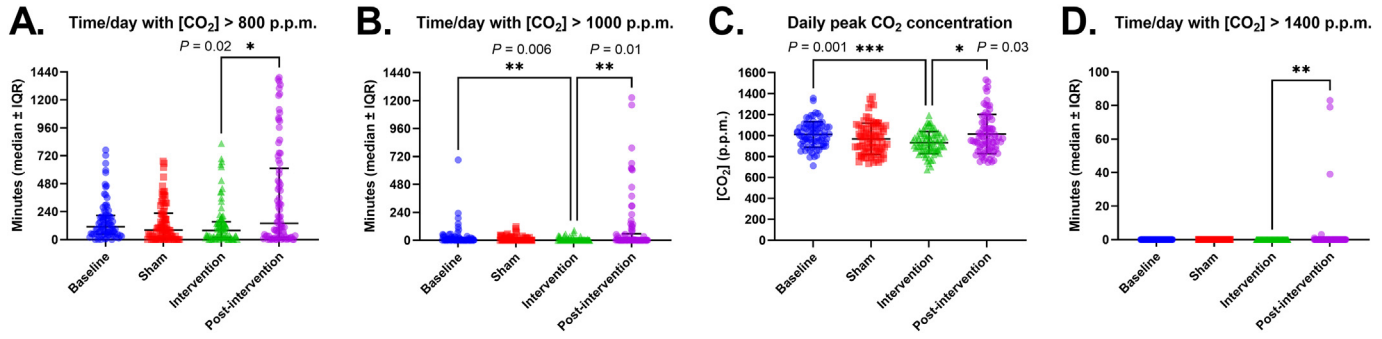

Fig. 2. Primary and secondary trial outcomes. A. The primary outcome of time/day (in minutes) with CO_2 concentration > 800 ppm. Secondary outcomes: B. Time/day (in minutes) with CO_2 concentration > 1000 ppm, C. daily peak CO_2 concentration, and D. Time/day (in minutes) with CO_2 concentration > 1400 ppm. Each point represents measurements from one 24 h period ($N = 77$, 82, 79 and 82 days in the baseline, sham, intervention and post-intervention period, respectively). Bars represent median and interquartile range. The intervention period was compared to the baseline, sham, and post-intervention period by Kruskal-Wallis test followed by Dunn's multiple comparisons test with multiplicity-adjusted *P* values as indicated.

hospital-acquired infection (Read et al., 2021). It is surprising how little attention has been paid to indoor CO_2 monitoring in hospitals during the pandemic, and prevention of nosocomial transmission of SARS-CoV-2 via the airborne route. While most attention concerning COVID-19 in hospital infection control has focused on traditional hand hygiene, surface disinfection and droplet precautions, a paradigm shift in hospital infection control towards a focus on improving ventilation ("air hygiene") is warranted (Greenhalgh et al., 2021; Morawska et al., 2021).

The use of CO_2 monitors did not affect our primary trial outcome, highlighting the many implementation barriers in a real-world hospital setting. Carryover effects might have influenced the results during the sham period. Still, key secondary outcomes showed significant (albeit small) improvements during intervention compared to baseline and post-intervention. These differences were driven mainly by situations of rooming-in (Supplementary Figs. 3 and 6). In these circumstances, couples in hospitals were noticed to spend prolonged time with their room door closed (especially at night), whereas the main inlet of fresh outside air in our (type D) balance ventilation system was located in the corridor (direction of air flow from the corridor into patient rooms). Thus, we identified hospital rooming-in as a situation of particular concern for aerosol transmission of COVID-19.

There is little doubt that monitors can measure CO_2 levels relatively cheaply and accurately in a hospital environment. However, like any technology, implementation requires nurses and other clinicians to look at the monitors and increase ventilation, e.g. by operating available HVAC systems, opening windows and/or altering their work routines (e.g., not washing two patients in the same room

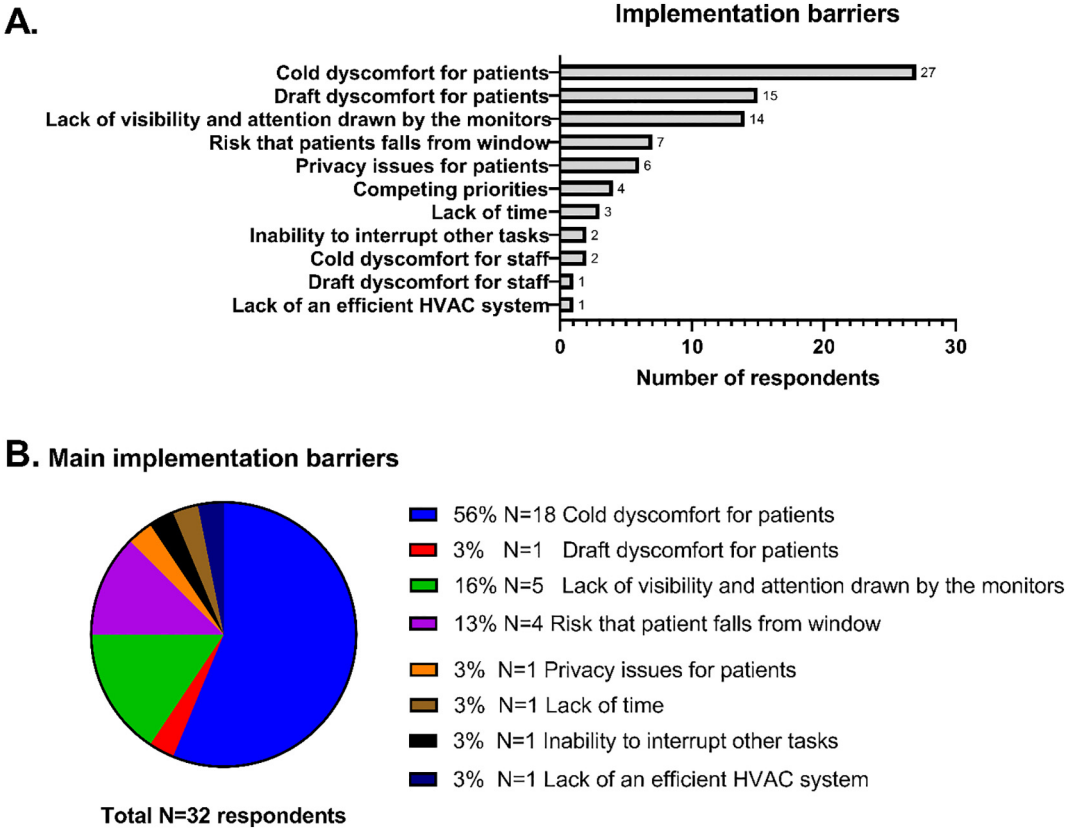

Fig. 3. Staff-reported barriers towards increasing ventilation using CO_2 monitors. A. Any implementation barriers identified by staff ($N = 32$) responding to post-study survey. B. The most important barrier indicated by each of the respondents. *HVAC* = heating, ventilation and air conditioning.

consecutively). Simply recommending monitors with the expectation that they by themselves maintain appropriate CO_2 levels in a clinical environment appears unrealistic. We identified significant barriers towards implementation, mainly patients complaining from cold and draft discomfort from increased ventilation as well as lack of attention drawn by the monitors. Indeed, nurses and other clinical staff have many other responsibilities and may resist alterations in their work routines e.g. due to privacy concerns from leaving the door open while giving a bed bath to a patient behind a curtain, or concern that windows must remain closed to prevent patients from falling out. Further coaching and training staff in using CO_2 monitors and applying ventilation strategies may be required to obtain sustained behavioral changes (perhaps using a "CO_2 steward"), ideally in combination with engineered solutions like CO_2-driven ventilation (Yang et al., 2014). In any case, the risks for healthcare workers and patients of insufficient indoor air quality in hospitals should not continue to be ignored.

Our study has several limitations, mainly due to its single-center, open-label design. A major limitation is that our trial is not designed nor powered to determine whether CO_2 monitors reduce the risk of hospital-acquired infections including COVID-19. Moreover, CO_2 is an excellent though imperfect proxy of respiratory infection risk. Mask wearing, HEPA filters, loud vocalization or physical distancing for example, affect pathogen transmission risk (Bazant and Bush, 2021; Miller et al., 2021) without influencing CO_2 levels, while metabolism (i.e., respiratory quotient) influences CO_2 production independent of exhaled air volume.

5. Conclusions

To the best of our knowledge, this is the first randomized trial investigating the use of CO_2 monitors in the hospital environment. At least during this short-term intervention, the use of CO_2 monitors did not affect the primary outcome, although significant but small reductions in secondary outcomes were observed. Staff generally reported positive attitudes towards using CO_2 monitors although several possible barriers towards manually improving ventilation in the real-world hospital setting were identified. Further research is required to determine the clinical significance of indoor CO_2 concentrations, and to define optimal strategies to achieve target CO_2 levels in hospitals.

Data availability statement

Following publication, all data supporting this manuscript will be made available to established investigators upon simple request.

Ethics approval statement

The study protocol was reviewed and approved by the Institutional Review Board of Imelda Hospital, Bonheiden, Belgium.

Patient consent statement

Not applicable.

Clinical trial registration

ClinicalTrials.gov Unique Identifier NCT04770597

CRediT authorship contribution statement

Conceptualization: Laurent, Frans. *Resources*: Laurent, Frans. *Data curation*: Laurent. *Formal analysis*: Laurent. *Investigation*: Laurent, Frans. *Project administration and supervision*: Laurent. *Writing - original draft*: Laurent. *Writing - review & editing*: Laurent, Frans. *Approval of the final manuscript*: Laurent, Frans.

Declaration of competing interest

Dr. Laurent has received consultancy and lecture fees from Alexion, Amgen, Kyowa Kirin, Menarini, Orifarm, Sandoz, Takeda, UCB and Will Pharma, all unrelated to this work. Dr. Frans reports no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.151349.

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