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# Journal of Hospital Infection



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# Efficacy of air cleaning units for preventing SARS-CoV-2 and other hospital-acquired infections on medicine for older people wards: a quasi-experimental controlled before-and-after study

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# SUMMARY

**Background:** Nosocomial infections are costly, and airborne transmission is increasingly recognized as important for spread. Air cleaning units (ACUs) may reduce transmission, but little research has focused on their effectiveness on open wards.

Aim: To assess whether ACUs reduce nosocomial severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), or other, infections on older adult inpatient wards.

Methods: This was a quasi-experimental before-and-after study on two intervention -control ward pairs in a UK teaching hospital. Infections were identified using routinely collected electronic health record data during 1 year of ACU implementation and the preceding year ('core study period'). Extended analyses included 6 months of additional data from one ward pair following ACU removal. Hazard ratios (HRs) were estimated through Cox regression controlling for age, sex, ward and background infection risk. The time that the ACUs were switched on was also recorded for Intervention Ward 2.

Findings: ACUs were initially feasible, but compliance reduced towards the end of the study (average operation in first vs second half of ACU time on Intervention Ward 2: 77% vs 53%). In total, 8171 admissions for >48 h (6112 patients, median age 85 years) were included. Overall, the incidence of ward-acquired SARS-CoV-2 was 3.8%. ACU implementation was associated with a non-significant trend of lower hazard for SARS-CoV-2 infection [HR core study period 0.90, 95% confidence interval (CI)  $0.53-1.52$ ; HR

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extended study period 0.78, 95% CI 0.53-1.14]. Only 1.5% of admissions resulted in other notable ward-acquired infections.

Conclusion: ACUs may reduce SARS-CoV-2 infection to a clinically meaningfully degree. Larger studies could reduce uncertainty, perhaps using a crossover design, and factors influencing acceptability to staff and patients should be explored further.

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## Introduction

Healthcare-associated infections are common and costly, due, in part, to prolonged hospital stays and excess mortality [\[1\]](#page-8-0). Hospitalized older adults are at higher risk of negative health outcomes [\[2](#page-8-1)[,3\]](#page-8-2), and this intensifies the system-wide strain on healthcare services, necessitating bed closures or cohorting patients. Additionally, nosocomial spread to healthcare workers (HCWs) can increase levels of absence, morbidity and mortality in HCWs [[4\]](#page-8-3).

Nosocomial spread accounted for an estimated 10-20% of infections in hospitalized patients during the first wave of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic [[5,](#page-8-4)[6\]](#page-8-5), consistent with experiences from past influenza seasons  $[7-10]$  $[7-10]$  $[7-10]$  $[7-10]$ . Additionally, respiratory viruses account for one-fifth of all healthcare-associated infections [\[1](#page-8-0)]. Infection prevention and control (IPC) measures directed against respiratory viruses prior to the SARS-CoV-2 pandemic focused predominantly on droplet or splash, as well as fomite, routes of spread. Airborne transmission [through the air via infectious respiratory particles (IRPs)] received less attention [\[11](#page-8-7)]. However, during the pandemic, evidence increasingly indicated that this is the dominant route of transmission for SARS- $Cov-2$  [[11](#page-8-7)-[13](#page-8-7)].

Air cleaning units (ACUs) can remove SARS-CoV-2 and other IRPs that remain suspended in the air [\[14\]](#page-8-8). Previous work has demonstrated the efficacy of ACUs and improved ventilation in reducing infections  $[15-24]$  $[15-24]$  $[15-24]$  $[15-24]$  $[15-24]$ . However, these studies were mainly restricted to operating theatres, isolation rooms and dressing rooms for burns patients [\[25\]](#page-8-10). Few studies have been conducted in the setting of an open ward, or with a focus on older adult inpatients.

This study aimed to assess whether the implementation of ACUs in older adult inpatient medical wards is feasible, and can reduce the incidence of nosocomial infections  $-$  either SARS-CoV-2 or other common nosocomial pathogens. It is part of the Addenbrooke's Air Disinfection Study [\[26](#page-8-11)].

## Methods

#### Study design

This quasi-experimental before-and-after controlled study was conducted within four wards in the Department of Medicine for the Elderly at Addenbrooke's Hospital, Cambridge, UK. ACUs were installed on two wards ('intervention wards'), with each ward having a corresponding 'control ward' to make two intervention-control ward pairs.

The 'core study period' ([Figure 1](#page-2-0)) for each ward pair included 12 months during ACU operation on the intervention wards and 12 months prior to ACU installation. When either ward in a ward pair was used as a coronavirus 2019 (COVID-19) isolation ward (due to short-term pandemic pressures), the ward pair was excluded. This only occurred for Ward Pair 2. The intervention was implemented in September 2021 for Ward Pair 1 and March 2022 for Ward Pair 2.

An 'extended study period' was also considered, which included data for 6 months post ACU removal for Ward Pair 1. This period was added (prior to unblinding of the statistical team) because there were few study-ward-acquired infections

<span id="page-2-0"></span>

Figure 1. Schematic of the study design, showing designation of the four study wards over time. Blue, control time period; orange, intervention time period; navy, extended time period (after intervention removed); transparent, excluded  $-$  data when either ward in a pair was designated as a coronavirus disease 2019 isolation ward were excluded from the study [this only occurred for Ward Pair 2 (30/10/ 2021 to 13/11/2022, 04/01/2022 to 15/02/2022 and 06/03/2022 to 01/05/2022 excluded)].

in the pre-ACU period, and it was within the remit of the existing study approval.

#### Study population

Patients (age  $>$ 18 years) were eligible for inclusion in this study if they were admitted to a study ward during the study period. Patients were assigned to control and intervention wards as per standard hospital bed management procedures that treated all four wards as suitable for the care of older adults presenting as emergencies, prioritizing older adults most likely to benefit from comprehensive geriatric assessment [[27](#page-8-12)]. One of the study wards was fitted with 10 cardiac monitors. Its patient intake differed slightly, but patients were still under the care of Geriatric Medicine. Patients requiring care led by a consultant cardiologist were cared for elsewhere, and were not included in this study.

# ACU intervention

Each intervention ward had two AeroTitan 3000 ACUs (Air Purity, Cambridge, UK) in the corridor, as space and electrical outlets allowed; and an AeroTitan 2000 ACU in each of four patient bays. Intervention Ward 2 used noisier 'Mk2' models with 20% higher fan speed compared with 'Mk1' models in Intervention Ward 1. The devices contained 'G4' grade prefilters, carbon filters and 'H13' grade high-efficiency particulate air filters, with ultraviolet C bulbs behind the filters primarily to disinfect the machine. Nominal air flows for AeroTitan3000 Mk1 and AeroTitan2000 Mk1 were usually 2250 $-$ 2550 m $^3$ /h and 1500 $-$ 1700 m $^3$ /h, respectively (see Section 1.1 in the online supplementary material for full specifications and locations). The ACUs were fully compliant with recently released NHS England guidance [[28\]](#page-8-13). The intervention wards were chosen pragmatically, particularly considering ease of installation in the existing ward environment.

The study protocol only allowed ACUs to be switched off during routine maintenance visits, but in practice they could be switched off by ward staff at any time. Data on the proportion of time that the ACUs were in operation were available for four of the units on Intervention Ward 2, enabling assessment of adherence to the protocol (see Section 1.2 in the online supplementary material).

The control wards contained no study ACUs. However, both the control and intervention wards occasionally had additional small ACUs placed on them by the hospital (see Section 1 in the online supplementary material). These were much less powerful than the study ACUs and were disregarded.

## Clinical outcomes

There were two primary outcomes of interest: (i) studyward-acquired SARS-CoV-2 infection; and (ii) a composite of other study-ward-acquired pathogens. The composite endpoint covered adenovirus, human metapneumovirus, influenza B, influenza A, parainfluenza, picornavirus, respiratory syncytial virus, norovirus, Clostridioides difficile, meticillin-resistant Staphylococcus aureus and meticillin-susceptible S. aureus. For both endpoints, study-ward-acquired infection was defined as cases diagnosed >48 h after admission to a study ward, with

no prior positive test for that pathogen during the hospital visit (see Section 2.1 in the online supplementary material for full specification of clinical outcomes).

All testing was undertaken as per normal clinical practice; no additional screening/testing was undertaken. The date and time of tests for all of the study patients throughout their hospital stay were extracted from electronic health records (EHRs), along with patient demographics, medical conditions, medications, physiological and biochemical test results, and visit details, as well as hospital-wide SARS-CoV-2 records (see Section 2.2 in the online supplementary material for the clinical data collected).

Several secondary outcomes were investigated: SARS-CoV-2 after 7 days on the ward, other infections identified through patients' culture results, antibiotic usage, deaths, and hospital re-presentations (see Section 2.1 in the online supplementary material for full specification of secondary outcomes).

#### Statistical analyses

Patients were excluded from the study if they were discharged or deceased within the first 48 h of admission to a study ward, or had a confirmed infection for that particular pathogen prior to 48 h post admission to the study ward during the same hospital visit (see Section 2.3 in the online supplementary material for full definition of study-ward visit).

The primary statistical analysis was pre-specified [[26\]](#page-8-11) in line with the quasi-experimental nature of the study design. The primary analyses were conducted with ward names deidentified, meaning the allocation of ACUs to the wards was blinded to the statistical team. Blinding of the patients and treating clinicians was not possible.

The pre-specified analysis was a Cox regression for the instantaneous hazard of infection adjusting for age, sex, ward and background infection risk (ward and hospital-wide for SARS-CoV-2, ward only for composite endpoint; see Section 2.4 in the online supplementary material for model details). The primary quantity of interest was the hazard ratio (HR) in the presence of an ACU compared with that in the absence of an ACU. Cox regression accounts directly for variation in patients' time at risk of infection due to varying length of stay on the ward, and the included co-variables helped account for variations in risk of infection [[29](#page-8-14)]. The robustness of the conclusions from the primary analysis was explored through a range of sensitivity analyses.

## Results

#### Feasibility and ACU operation

The ACUs on Intervention Ward 2 were initially switched on for the majority of the time ([Figure 2](#page-4-0)). However, they were switched off increasingly frequently during the second half of the intervention period (average operation 77% in first half vs 53% in second half). On Intervention Ward 1, anecdotally, the study team observed that ACUs were usually switched on during ward visits throughout the ACU period (e.g. for routine ACU maintenance or air sensor checking), although objective data were unavailable.

<span id="page-4-0"></span>

Figure 2. Weekly number of infections. Top panel: background severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infections in terms of the number of new hospital-acquired infections across the whole hospital each week. Bottom four panels: weekly number of SARS-CoV-2 and composite cases on each of the wards throughout the study. Blue bars, number of new SARS-CoV-2-positive tests after 48 h; yellow bars, weekly number of composite outcomes; green bars, overlap of yellow and blue bars (i.e. both SARS-CoV-2 and composite cases). Background colours represent whether the time period on that ward was a control period (light yellow), intervention period when ACU was present (light green), or excluded time period due to one of the ward pair being designated as a coronavirus disease 2019 isolation ward (purple). Numbers in brackets represent the total number of new SARS-CoV-2-positive tests after 48 h and new composite cases during that study period on each ward. The line graph superimposed on Intervention Ward 2 shows the percentage operation of the air cleaning unit.

#### Clinical outcomes

In total, there were 10,371 admissions (7443 unique patients) to a study ward during the study period, with 8171 admissions (6112 unique patients) lasting  $>$  48 h (3608 before, 3338 during and 1225 after ACU operation; Figure S2 in Section 3.1 in the online supplementary material). The patients were predominantly white British and had a median age of 85 years.

Patient characteristics were similar across the wards and time periods [\(Table I](#page-5-0) and Table S2, see Section 3.2 in the online supplementary material for breakdown by ward), including frailty, severity of acute illness and polypharmacy. Testing policies changed through time (Table S3, see Section 4.1 in the online supplementary material), but were always shared across wards, and implemented similarly within ward pairs (Table S4, see Section 4.2 in the online supplementary material). Intervention ward patients had a higher median length of stay (8.7 vs 6.6 days; [Table I](#page-5-0)), largely due to one of the control wards having a shorter median length of stay than the other wards throughout the study. However, the total person-days at risk was similar between the intervention and control wards [\(Table I\)](#page-5-0). There were slight differences in the proportion of patients with a primary reason for hospital stay of 'infectious diseases, immune system disorders and other healthcare contacts' (18% control, 23% intervention) and 'cardiac' (20% control, 11% intervention).

#### SARS-CoV-2

In total, 229 study-ward-acquired SARS-CoV-2 cases occurred during the core study period (35 cases before and 194 cases during ACU operation), with a further 68 cases in Ward Pair 1 after ACU removal [\(Figure 2](#page-4-0) and [Table II;](#page-5-1) Table S5, see Section 5.1 in the online supplementary material for breakdown by ward). Overall, incidence was 3.8% across study-ward stays >48 h. Weekly case numbers were very 'spikey' on all wards, and across time periods [\(Figure 2](#page-4-0)), but with a general increase over time. Visually, it is clear that the intervention did not eliminate SARS-CoV-2 'spikes'.

In Ward Pair 1, fewer cases occurred on the intervention ward compared with the control ward during the ACU period, but not before or after. In both wards in Ward Pair 2, most cases occurred in the second half of the ACU period. However, for much of this period, the ACUs were in operation for  $<$ 80% of the time, including in all weeks with spikes of four or more cases on the intervention ward [\(Figure 2\)](#page-4-0).

# <span id="page-5-0"></span>Table I

Patient characteristics for before, during and after the air cleaning units (ACUs) were in operation in the intervention and control wards (see Section 3.2 in the online supplementary material for a breakdown by individual ward and full category details)



IQR, interquartile range.<br><sup>a</sup> For all admissions on the ward >48 h, excluding the first 48 h of admission when patients were not 'at risk' of infection.

<sup>b</sup> Primary reason for hospital stay based on Healthcare Resource Group code, assigned after hospital discharge.<br>
<sup>c</sup> Score during hospital visit closest to ward start of patients with a score available (n.b. 41% of patie

e Number of different drugs administered in first 24 h of ward stay.

#### <span id="page-5-1"></span>Table II

Study-ward-acquired infections from before, during and after the air cleaning units (ACUs) were in operation across the intervention and control wards



SARS-CoV-2, severe acute respiratory syndrome coronavirus-2.

During the core study period, the estimated (adjusted) HR for infection in the intervention wards during ACU time periods, compared with the control wards, was 0.90 [95% confidence interval (CI)  $0.53-1.52$ ], with very wide CIs which overlap with an increase in hazard (see Section 5.2 in the online

supplementary material for estimates of all model coefficients). The estimated effect size is larger (HR 0.78, 95% CI  $0.53-1.14$ ) when including the 'extended study period', but the 95% CI still overlaps an increase in hazard. These findings were robust to excluding re-infections; altering the definition of ward-acquired infections to post 7 days on the ward; excluding patients with very long hospital stays; and allowing non-linearity in the effect of continuous variables (see Section 5.3 in the online supplementary material).

#### Composite infections

A total of 94 study-ward-acquired composite cases occurred during the core study period, with a further 29 cases in Ward Pair 1 after ACU removal, overall representing 1.5% of ward stays >48 h. Composite case numbers per week were generally low, but with a few 'spikes' and a slight upward trend over time [\(Figure 2](#page-4-0) and [Table II](#page-5-1)). The largest 'spike' was caused by a norovirus outbreak on Intervention Ward 2 near the end of the study ([Figure 2](#page-4-0)). As with SARS-CoV-2, it is clear visually that the intervention did not eliminate 'spikes' for the composite outcome. However, the ACU was in operation for only 35% of the time during the week of the largest 'spike' ([Figure 2](#page-4-0)).

Analysis of the composite endpoint prior to unblinding indicated that the pre-specified model, with no hospital-wide background infection risk, did not address confounding sufficiently to be scientifically robust, so only descriptive analysis is included (see Section 5.4 in the online supplementary material for model details).

#### Secondary outcomes

The number of new cultures was relatively stable across time periods within wards (Table S10 and Figure S7, see Section 6 in the online supplementary material). Overall, 61 unique species or genuses were first identified from patients' cultures  $>$ 48 h after admission to a study ward (Table S11, see Section 6.1 in the online supplementary material). The total bed-days lost decreased over time for all wards, but the number of new antibiotic-days post 48 h per person-days, deaths and representations showed no clear patterns over time or between wards (Table S10 and Figure S8, see Section 6 in the online supplementary material).

## **Discussion**

ACUs were initially a feasible, environmental intervention in older adult inpatient wards. However, during the last few months of the study, ACU machines on Intervention Ward 2 were increasingly not operational. In terms of efficacy, across both ward pairs, ACUs were associated with a non-significant trend of reducing ward-acquired SARS-CoV-2 infections (core study period: 10% lower hazard; extended study period: 22% lower hazard). In Ward Pair 1, SARS-CoV-2 infections followed a pattern consistent with ACUs reducing cases. Case numbers were lower on the intervention ward compared with the control ward in the 'during ACU' period, and higher or similar in the periods before and after. Ward Pair 2 did not show such a consistent pattern, which reduced the certainty of the findings. However, evaluation of Ward Pair 2 was limited by very few ward-acquired SARS-CoV-2 cases in the 'before ACU' time period, periods of exclusion due to one ward being an isolation ward, and low intervention compliance towards the end of the study. For example. ACUs were operational  $<80\%$  of the time for most weeks, including all weeks with spikes of four or more SARS-CoV-2 cases. The incidence of composite endpoint cases was very low, limiting analysis potential, but it is interesting to note the gradual increase in most endpoint infections over time. In contrast, the incidence of other secondary endpoint infections, identified through culture results, remained stable over time.

Low power was the main limitation of this study, as Ward Pair 2 faced some periods of exclusion. In addition, this study only considered patient cases and excluded HCWs, although HCWs were less likely to be impacted by the ACUs due to time spent off the wards. Additionally, although quasi-experimental, there were some differences between the control and 'intervention' populations and, despite adjustment of analyses, residual confounding remains possible. Testing protocols for SARS-CoV-2 and other infections also changed over time (see Section 4.1 in the online supplementary material), impacting detection of asymptomatic cases, although similarly for all wards. Blinding of bed managers, patients and treating clinicians was also not possible. However, the availability of ACUs was never part of hospital bed management policy, and patient characteristics were found to be stable across the different study phases through analysis of the comprehensive EHR data describing the study population. Therefore, there is no evidence that deployment of study ACUs altered ward allocation decisions. The strengths of this study were: the authors controlled for background SARS-CoV-2 infection risk over time; only those patients under the care of a consultant geriatrician were included; blinding of the analytical team was ensured; and the hypotheses and analyses were pre-specified.

A further strength of this work is that few studies examining ACUs have been conducted in the setting of an open ward or with a focus on older adults, who are particularly vulnerable to hospital-acquired infections. Other respiratory viruses will likely have similar transmission routes to SARS-CoV-2, and the potential reduction in SARS-CoV-2 observed in this study may be indicative of the impact that would be observed for respiratory viruses more generally. Whilst speculative, it is important to consider the potential impact in order to evaluate the case for further research. Over the short time-period of a median ward stay (7 days), a 22% reduction in hazard equates to approximately a 22% reduction in risk. Taking estimated impacts of additional NHS treatment costs, additional days in hospital, and percentage which are respiratory viruses [\[1](#page-8-0)], a crude calculation using 2016/2017 data suggests that a 22% reduction in nosocomial respiratory infections could save the NHS on the order of £105 million and 280,000 bed-days per year (see Section 7 in the online supplementary material). In addition, reducing nosocomial spread could alter the dynamics of epidemics and pandemics. Recently published modelling suggests that when community transmission is controlled by a community lockdown, released in a stepwise manner, reducing hospital transmission by 25% lowers the community prevalence of infection by more than half, similarly lowers the prevalence of infected HCWs, and reduces the total time that society spends in lockdown restrictions [[30](#page-8-15)]. Thus, the potential effect size observed in this study, with respect to ACUs and lower nosocomial transmission, could have a meaningful clinical and economic impact.

Historically, airborne transmission has received little attention from hospitals. Over 50% of the NHS estate has historic ventilation systems that fail to meet current technical guidance [[31](#page-8-16)], even including some newer built hospitals [[32](#page-8-17)]. ACU implementation may provide part of the solution. During commissioning of the ACU intervention, a large reduction in particulates during ACU operation was observed [\[33\]](#page-8-18), and other work, on a COVID-19 cohort ward in the study hospital, identified significant differences in airborne microbial genetic material between the on and off states of ACUs [[14\]](#page-8-8). Therefore, ACUs can alter the environment of a medical ward.

However, implementation strategies need to be considered carefully. To reduce infections, ACUs must not only remove IRPs when in operation, but  $-$  even more fundamentally  $-$  must be operational. There is no prior literature about feasibility or acceptability of ACUs in clinical environments. The present results showed a clear drop in ACU compliance in the latter half of the intervention phase of Ward Pair 2. The most likely reason is that the ACUs were increasingly switched off in the last few months of the study. An impact questionnaire of staff and patients indicated general acceptance of the ACUs but moderate noise disturbance, especially for respondents in Intervention Ward 2 [\[34\]](#page-8-19). The drop in compliance exemplifies the importance of acceptability of interventions, which can be complex to understand, change over time, and/or be specific to the clinical setting [\[34\]](#page-8-19). For example, it is interesting that the drop in compliance observed was preceded by cessation of asymptomatic COVID-19 screening and cohorting of COVID-19 patients at the study centre in the summer of 2022.

The large uncertainty in these estimates would be reduced by a larger study. Identifying a 22% hazard reduction in a simple single centre study with a 3.8% incidence rate would require a sample size of approximately 13,400 patients (see Section 8 in the online supplementary material), but this is highly dependent on incidence rate. Additionally, particularly given the variation between wards and between centres in background infection risk, a multi-centre crossover cluster randomized design would be preferable, which would require a more sophisticated sample size calculation. Including other hospitals and wards, or different types of implementation approaches could improve generalizability and help identify optimum implementation approaches.

In conclusion, this study found that ACUs were feasible on older adult inpatient wards, but compliance was lower at the end of the study. Despite this, a non-significant trend suggesting a lower hazard of SARS-CoV-2 infection with ACUs was observed. This was driven by data from Ward Pair 1, which showed a pattern of infection consistent with an ACU effect. Robust methods were in place to address confounding and minimize bias in this study, especially with respect to SARS-CoV-2, but it was not possible to exclude chance. Although this is a limitation, the potential effect size observed could be clinically meaningful if confirmed in larger studies. Acceptability of ACUs, or any other air cleaning intervention, and understanding factors important for compliance is also essential.

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#### Author contributions

RCB: data curation, methodology, investigation, formal analysis, writing  $-$  original draft, writing  $-$  review and editing. RJBG: conceptualization, data curation, methodology, formal analysis, writing  $-$  review and editing, supervision. CP: conceptualization, methodology, investigation, writing  $-$  review and editing. RT: conceptualization, investigation, writing  $-$  review and editing. TG: conceptualization, methodology, investigation, writing  $-$  review and editing. CJRI: conceptualization, methodology, writing  $$ review and editing. ACM: conceptualization; methodology, writing  $-$  review and editing. CBB: conceptualization, methodology, writing  $-$  review and editing. MB: conceptualization, methodology, investigation, project administration, writing  $-$  review and editing, funding acquisition. VLK: conceptualization, methodology, investigation, project administration, writing  $-$  original draft, writing  $-$  review and editing, supervision, funding acquisition.

#### Conflict of interest statement

CB is an expert witness in Module 3 of the UK COVID-19 Inquiry, and has received financial remuneration for his work in this capacity. MB and CP have undertaken work for FreshAirNHS, a non-profit campaigning organization advocating for airborne mitigations within the NHS; they have not received any financial remunerations for this work. ACM sits on the scientific advisory board of Cambridge Infection Diagnostics, and has received speaking fees from bio-Mérieux, Fischer and Paykel, ThermoFisher and Boston Scientific.

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#### Ethical approval

The AAirDS was approved by the NHS Health Research Authority and Health and Care Research Wales (IRAS ID

299336), and the Central Bristol Research Ethics Committee (REC Ref. No.: 22/SW/0010).

# Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jhin.2024.09.017>.

#### <span id="page-8-0"></span>References

- [1] [Guest JF, Keating T, Gould D, Wigglesworth N. Modelling the](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref1) [annual NHS costs and outcomes attributable to healthcare](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref1)[associated infections in England. BMJ Open 2020;10:e033367.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref1)
- <span id="page-8-2"></span><span id="page-8-1"></span>[2] [Watson A, Wilkinson TMA. Respiratory viral infections in the](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref2) [elderly. Ther Adv Respir Dis 2021;15:1753466621995050](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref2).
- [3] [Rubeshkumar P, Beer J, McClure V, Morgan M. Mortality amongst](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref3) [hospitalized COVID-19 cases by acquisition and pandemic wave in](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref3) [Wales, UK, February 2020](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref3)-[March 2022. J Hosp Infect 2024;](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref3)  $143:48 - 52.$  $143:48 - 52.$  $143:48 - 52.$
- <span id="page-8-4"></span><span id="page-8-3"></span>[4] [Appleby J. NHS sickness absence during the COVID-19 pandemic.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref4) [BMJ 2021;372:n471](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref4).
- [5] [Read JM, Green CA, Harrison EM, Docherty AB, Funk S, Harrison J,](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref5) [et al. Hospital-acquired SARS-CoV-2 infection in the UK's first](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref5) [COVID-19 pandemic wave. Lancet 2021;398:1037](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref5)-[8.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref5)
- <span id="page-8-5"></span>[6] [Knight GM, Pham TM, Stimson J, Funk S, Jafari Y, Pople D, et al.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref6) [The contribution of hospital-acquired infections to the COVID-19](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref6) [epidemic in England in the first half of 2020. BMC Infect Dis](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref6) [2022;22:556](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref6).
- <span id="page-8-6"></span>[7] [Yang K, Zhang N, Gao C, Qin H, Wang A, Song L. Risk factors for](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref7) [hospital-acquired influenza A and patient characteristics: a](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref7) [matched case](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref7)-[control study. BMC Infect Dis 2020;20:863](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref7).
- [8] [Huzly D, Kurz S, Ebner W, Dettenkofer M, Panning M. Character](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref8)[isation of nosocomial and community-acquired influenza in a](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref8) [large university hospital during two consecutive influenza sea](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref8)[sons. J Clin Virol 2015;73:47](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref8)-[51](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref8).
- [9] Fullana Barceló [MI, Asensio Rodriguez J, Artigues Serra F, Ferre](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9) [Beltran A, Salva D'agosto P, Almodovar Garcia M, et al. Epi](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9)[demiological and clinical characteristics of community-acquired](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9) [and nosocomial influenza cases and risk factors associated with](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9) [complications: a four season analysis of all adult patients](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9) [admitted in a tertiary hospital. Influenza Other Respir Viruses](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9) [2021;15:352](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9)-[60](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref9).
- [10] Martin D, Hönemann M, Liebert UG. Dynamics of nosocomial [parainfluenza virus type 3 and influenza virus infections at a large](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref10) [German university hospital between 2012 and 2019. Diagn](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref10) [Microbiol Infect Dis 2021;99:115244](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref10).
- <span id="page-8-7"></span>[11] [Jimenez JL, Marr LC, Randall K, Ewing ET, Tufekci Z,](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref11) [Greenhalgh T, et al. What were the historical reasons for the](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref11) [resistance to recognizing airborne transmission during the COVID-](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref11)[19 pandemic? Indoor Air 2022;32:e13070.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref11)
- [12] [Meyerowitz EA, Richterman A. SARS-CoV-2 transmission and](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref12) [prevention in the era of the delta variant. Infect Dis Clin North](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref12) [Am 2022;36:267](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref12)-[93](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref12).
- [13] [Meyerowitz EA, Richterman A, Gandhi RT, Sax PE. Transmission of](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref13) [SARS-CoV-2: a review of viral, host, and environmental factors.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref13) [Ann Intern Med 2021;174:69](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref13)-[79.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref13)
- <span id="page-8-8"></span>[14] [Conway Morris A, Sharrocks K, Bousfield R, Kermack L, Maes M,](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref14) [Higginson E, et al. The removal of airborne severe acute respi](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref14)[ratory syndrome coronavirus 2 \(SARS-CoV-2\) and other microbial](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref14) [bioaerosols by air filtration on coronavirus disease 2019 \(COVID-](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref14)[19\) surge units. Clin Infect Dis 2022;75:e97](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref14)-[101](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref14).
- <span id="page-8-9"></span>[15] [Hart D. Pathogenic bacteria in the air of operating rooms: their](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref15) [widespread distribution and the methods of control. Arch Surg](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref15) [1938;37:521](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref15)-[30](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref15).
- [16] [Hart D. Sterilization of the air in the operating room by bacter](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref16)[icidal radiant energy: results in over eight hundred operations.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref16) [Arch Surg 1938;37:956](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref16)-[72.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref16)
- [17] [Hart D. Bactericidal ultraviolet radiation in the operating room.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref17) [Twenty-nine-year study for control of infections. J Am Med Assoc](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref17) [1960;172:1019](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref17)-[28](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref17).
- [18] [Lowbury EJL. Air-conditioning with filtered air for dressing burns.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref18) [Lancet 1954;263:292](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref18)-[4.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref18)
- [19] [Bourdillon R, Colebrook L. Air hygiene in dressing rooms for burns](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref19) or major wounds. Lancet  $1946;247:601-5$  $1946;247:601-5$ .
- [20] [Shooter RA, Taylor GA, Ellis G, Ross JP. Postoperative wound](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref20) [infection. Surg Gynecol Obstet 1956;103:257](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref20)-[62.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref20)
- [21] [Wells WF, Wells MW, Wilder TS. The environmental control of](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref21) [epidemic contagion. An epidemiologic study of radiant dis](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref21)[infection of air in day schools. Am J Epidemiol 1942;35:97](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref21)-[121](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref21).
- [22] [Wells MW, Holla WA. Ventilation in the flow of measles and](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref22) [chickenpox through a community. J Am Med Assoc 1950;142:](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref22)  $1337 - 44.$  $1337 - 44.$  $1337 - 44.$  $1337 - 44.$
- [23] [Perkins JE, Bahlke AM, Silverman HF. Effect of ultra-violet irra](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref23)[diation of classrooms on spread of measles in large rural central](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref23) [schools preliminary report. Am J Public Health Nations Health](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref23) 1947:[37](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref23):529-37.
- [24] [Buonanno G, Ricolfi L, Morawska L, Stabile L. Increasing ven](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref24)[tilation reduces SARS-CoV-2 airborne transmission in schools: a](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref24) [retrospective cohort study in Italy's Marche region. Front Public](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref24) [Health 2022;10:1087087.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref24)
- <span id="page-8-10"></span>[25] Brady G, Bennin F, Koning RD, Tiwari M, Vindrola-Padros C, Morris D, et al. Interventions used to improve air flow in hospitals - a rapid review. medRxiv 2023. Available at: [https://www.](https://www.medrxiv.org/content/10.1101/2023.10.06.23296654v1) [medrxiv.org/content/10.1101/2023.10.06.23296654v1.](https://www.medrxiv.org/content/10.1101/2023.10.06.23296654v1)
- <span id="page-8-11"></span>[26] Keevil V, Goudie R, Butler M, Conway Morris A, Beggs C, Peters C, et al. Addenbrooke's Air Disinfection Study  $-$  implementation of air disinfection to prevent hospital acquired infections on inpatient wards for older people: a pragmatic controlled before-andafter study. 2022. Available at: [https://osf.io/j2esy.](https://osf.io/j2esy)
- <span id="page-8-12"></span>[27] [Ellis G, Gardner M, Tsiachristas A, Langhorne P, Burke O,](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref27) [Harwood RH, et al. Comprehensive geriatric assessment for older](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref27) [adults admitted to hospital. Cochrane Database Syst Rev](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref27) [2017;9:CD006211.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref27)
- <span id="page-8-13"></span>[28] NHS England. Application of high efficiency particulate air (HEPA) filter devices for air cleaning in healthcare spaces: guidance and standards. London: NHS England. Available at: [https://www.](https://www.england.nhs.uk/publication/application-of-hepa-filter-devices-for-air-cleaning-in-healthcare-spaces-guidance-and-standards/) [england.nhs.uk/publication/application-of-hepa-filter-devices-for](https://www.england.nhs.uk/publication/application-of-hepa-filter-devices-for-air-cleaning-in-healthcare-spaces-guidance-and-standards/)[air-cleaning-in-healthcare-spaces-guidance-and-standards/](https://www.england.nhs.uk/publication/application-of-hepa-filter-devices-for-air-cleaning-in-healthcare-spaces-guidance-and-standards/).
- <span id="page-8-14"></span>[29] R Core Team. R: a language and environment for statistical computing. Vienna: R Foundation for Statistical Computing. Available at: [https://www.R-project.org/.](https://www.R-project.org/)
- <span id="page-8-15"></span>[30] [Cooper BS, Evans S, Jafari Y, Pham TM, Mo Y, Lim C, et al. The](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref30) [burden and dynamics of hospital-acquired SARS-CoV-2 in England.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref30) [Nature 2023;623:132](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref30)-[8](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref30).
- <span id="page-8-16"></span>[31] Ralph M, Mills F. Engineering solutions to infection control. Birmingham NEC. Available at: [https://www.youtube.com/watch?](https://www.youtube.com/watch?v=HnhSVFWYIwE&list=PLXw6r9VD6y_5eDss8LyCfoJFbDzf1HlHD&index=20) [v](https://www.youtube.com/watch?v=HnhSVFWYIwE&list=PLXw6r9VD6y_5eDss8LyCfoJFbDzf1HlHD&index=20)=[HnhSVFWYIwE&list](https://www.youtube.com/watch?v=HnhSVFWYIwE&list=PLXw6r9VD6y_5eDss8LyCfoJFbDzf1HlHD&index=20)=[PLXw6r9VD6y\\_5eDss8LyCfoJFbDzf1HlHD&](https://www.youtube.com/watch?v=HnhSVFWYIwE&list=PLXw6r9VD6y_5eDss8LyCfoJFbDzf1HlHD&index=20)  $index=20.$  $index=20.$  $index=20.$
- <span id="page-8-17"></span>[32] Provisional Position Paper 5  $-$  History of Infections Concerns | Hospitals Inquiry. Available at: [https://www.hospitalsinquiry.](https://www.hospitalsinquiry.scot/inquiry-document/history-infection-concerns-hoic-queen-elizabeth-university-hospital-campus) [scot/inquiry-document/history-infection-concerns-hoic-queen](https://www.hospitalsinquiry.scot/inquiry-document/history-infection-concerns-hoic-queen-elizabeth-university-hospital-campus)[elizabeth-university-hospital-campus.](https://www.hospitalsinquiry.scot/inquiry-document/history-infection-concerns-hoic-queen-elizabeth-university-hospital-campus)
- <span id="page-8-18"></span>[33] [Butler MJ, Sloof D, Peters C, Conway Morris A, Gouliouris T,](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref33) [Thaxter R, et al. Impact of supplementary air filtration on aero](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref33)[sols and particulate matter in a UK hospital ward: a case study.](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref33) [J Hosp Infect 2023;135:81](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref33)-[9](http://refhub.elsevier.com/S0195-6701(24)00325-6/sref33).
- <span id="page-8-19"></span>[34] Love C, Street A, Riddell E, Goudie RJB, Brock RC, Thaxter R, et al. Acceptability of air cleaning units on inpatient wards: help for infection control or hindrance for ward occupants? J Hosp Infect 2024. <https://doi.org/10.1016/j.jhin.2024.09.010>.