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Associations between hospital structure, infection control and incidence of hospital-acquired viral respiratory infections: a 10-year surveillance study

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Abstract

Background Protecting patients from hospital-acquired viral respiratory infections is a major challenge, but the hierarchy of measures to achieve this is not yet completely clear.

Aim To describe the epidemiology of hospital-acquired viral respiratory infections and associations with structural hospital factors and adherence to infection control protocols.

Methods Retrospective cohort study conducted over 10 consecutive years (2014–2023) within 27 hospital wards in a 900-bed university hospital in Paris, France. All hospitalized adult patients who were tested for at least one virus on a respiratory sample during their stay were included. Structural factors (percentage of double occupancy rooms) and adherence to infection control protocols by healthcare workers (measured by consumption of alcohol-based hand sanitizer and of facemasks) were included as predictors in the model.

Main outcome and measure Incidence of hospital-acquired viral respiratory infections, defined by a positive PCR test for at least one respiratory virus, performed at least 5 days after hospital admission. Data were analyzed on ward-year aggregated data, with a linear mixed-effects model.

Findings Overall, 183 994 viral PCR tests were performed over the study period. Incidence of hospital-acquired viral respiratory infections was 0.57/1000 hospital-days. After adjustment on other factors (mean length of stay, use of PCR testing), incidence of hospital-acquired viral respiratory infections in a given ward was significantly associated with: the incidence of community-acquired viral respiratory infections among patients admitted to the ward (+ 0.10/1000 hospital-days per each additional point of incidence; $P < 0.001$), the number of double-occupancy rooms (+ 0.04/1000 hospital-days per each 10%-increase of double-occupancy rooms; $P = 0.03$) and masks consumption (+ 0.33/1000 hospital-days per 10 additional masks used per day; $P = 0.04$). Similar results were found for double-occupancy rooms (+ 0.01/1000 hospital-days per each 10%-increase of double-occupancy rooms; $P = 0.012$) in the sub-group analysis of influenza cases.

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Conclusion In a given hospital ward, the incidence of community-acquired cases and the proportion of double-occupancy rooms are independently associated with the incidence hospital-acquired viral respiratory infections.

Keywords Influenza viruses, Respiratory syncytial virus, SARS-CoV- 2, Healthcare-associated infections, Infection control

Introduction

Respiratory viruses are major disruptors of health system, as strikingly illustrated by epidemics of seasonal viruses [1, 2] and more recently, by the COVID- 19 pandemic [3, 4]. In healthcare settings, the burden of viral respiratory infections (VRI) is further aggravated by nosocomial transmission. Nearly one out of five hospitalized VRI was estimated to be of nosocomial origin for COVID-19 [5], and other respiratory viruses [6]. VRI are caused by viruses (i.e. influenza virus, rhinovirus, respiratory syncytial virus (RSV), metapneumovirus) that share common characteristics: transmission through droplets and aerosols [7, 8], evolution on an epidemic pattern with strong seasonality for some of them (in particular Influenza and RSV) [8], and existence of pauci- or asymptomatic forms, making it difficult to identify cases [9]. Hospital-acquired VRI (HA-VRI) have a negative impact on length of stay and hospital mortality in high-risk patients [10–12]. Multimodal prevention strategies against HA-VRI rely on both pharmaceutical and non-pharmaceutical interventions (NPI). The latter include hand hygiene [13–16] single room assignment and cohorting [17], facemask-wearing [13, 18–21] and identification of asymptomatic cases through routine testing [18, 22]. However, the relative impact of NPI on the incidence of HA-VRI at the hospital level is still undervalued [22–24].

Virological data collected in routine care are a major source of information on viral dynamics in hospital settings. These surveillance data could help informing on the impact of prevention policies. Based on data prospectively collected over a 10 years-period of time, this study aimed to: (1) describe the epidemiology of HA-VRI and community-acquired VRI (CA-VRI) before and during the COVID- 19 pandemic, and (2) estimate, in real-life conditions, the associations between structural factors (i.e., double occupancy rooms), infection control measures and the incidence of HA-VRI.

Methods

Study design and participants

This retrospective study occurred in the 900-bed, tertiary care, university-affiliated Bichat-Claude Bernard hospital in Paris, France. The hospital includes 21 adult medical and surgical wards (including lung and heart transplant units), three intensive care units, three rehabilitation care wards and one neonatology unit. All adult patients tested for at least one respiratory virus between 2014–01 -01 and 2023–06 -01 were included. Tests performed in healthcare workers or patients under 18 years of age, patients hospitalized for more than 365 consecutive days, or outpatient clinics, were excluded from subsequent analyses.

In a routine care context, testing was at the discretion of attending physicians. Briefly, before 2020, the strategy was mainly clinically driven, meaning that clinicians would order testing to patients with symptoms suggestive of VRI (fever, chills, cough, acute respiratory distress). From 2020, routine testing of SARS-CoV- 2 was additionally performed at admission in asymptomatic patients in most clinical wards, and repeated on a weekly basis in those hosting high-risk patients (immunocompromised, geriatric patients). In patients with clinical symptoms of VRI, the local policy strongly encouraged testing with wide multiplex PCR rather than with a monoplexe or duplex PCR. Data were extracted from the laboratory software (GLIMS®) in May 2023.

Data collection

For all PCR-tested patients, data included age, gender, ward, dates of hospital admission and discharge, and date of sample collection. A PCR test was considered positive if at least one respiratory virus target was detected. Based on the literature, we considered for all respiratory viruses a mean incubation period of 5 days [25, 26]. Consequently, if sampling had been performed ≥ 5 days after hospital admission, PCR-positive cases were categorized as HA-VRI, and otherwise as CA-VRI.

For each clinical ward and each year, incidences of HA-VRI and CA-VRI were calculated as the number of cases per 1000 hospital-days. The incidence of HA-VRI was the main outcome. Among explanatory variables, the incidence of CA-VRI (i.e., incidence of CA-VRI among patients admitted to the ward) reflected the pressure of exposure to VRI inside a specific ward, exerted by community cases. We also calculated two indicators of compliance to infection control policy: adherence to hand hygiene and use of facemasks. According to national recommendations, adherence to hand hygiene was evaluated by the annual alcohol-based hand sanitizer consumption index [27] (see Supplementary appendix,

Methods, page 2). The total volume of hand sanitizer used was extracted from the hospital pharmacy database. Annual facemask consumption was extracted from the hospital supply, and expressed as the number of masks consumed per hospital-day. The percentage of double-occupancy rooms in each ward was extracted from both hospital plans and direct observations. Overall, double-occupancy beds accounted for 40% of the total number of beds in the setting, and was stable over the study period. Details on data management and calculation of indicators are provided in the Supplementary appendix (Methods, page 2).

Virological analyses were performed and/or validated at the virological laboratory of Bichat-Claude Bernard Hospital, Paris, France. From winter 2018, point-of-care testing was also available in the emergency department, and results available in the virological laboratory database. Each PCR test detected 1–24 targets, depending on the diagnostic kit: influenza virus types A (IVA) and B (IVB), respiratory syncytial virus (RSV) types A and B, parainfluenza virus (PIV) types 1–4, human metapneumovirus (hMPV), adenovirus (AdV), bocavirus (BoV), seasonal coronaviruses (sCoV) types 229E, NL63, OC43 and HKU1, rhinovirus/enterovirus (HRV/EV) and SARS-CoV- 2. Diagnostic kits used, with corresponding performances and targets are detailed in the supplementary appendix (Table S1). Respiratory samples included nasopharyngeal swabs, sputum examinations, tracheal aspirations or bronchoalveolar lavages.

Statistical analyses

We first calculated the annual incidence of HA-VRI and CA-VRI (per 1000 hospital-days) expressed per ward and year, on the full database, which included hospital visits in conventional hospital wards, in day-care units, and the emergency department. A single patient could account for several PCR tests or hospital visits over the study period. In the case of repeated consecutive tests during the same hospital visit, only the first positive PCR test was considered. Data management of repeated data is detailed in the supplementary appendix (Methods, page 6).

Secondly, the impact of infection control measures on HA-VRI incidence was analyzed on a subset database, which included hospital stays in conventional wards, during years 2014 to 2022 (infection control indicators were not available for year 2023 at the time of data analysis). We used a Linear Mixed-Effects Model, using the lme4 (linear mixed-effects models using "Eigen" and S4 [28]) package. In the model, the outcome variable was the annual HA-VRI incidence per ward. A single observation corresponded to the incidence of HA-VRI for a given year, in a given ward. Individual variables (age, gender, length of stay), annual infection control indicators for the corresponding wards and years of sampling were included in the model as fixed effects. The hospital ward was included as a random effect. The model was weighted by annual ward activity. All variables were included in the multivariable model. The significance threshold was set at 0.05 for all statistical analyses. Missing data were managed with mean imputation. If no PCR was performed in a ward over a year, the incidence of HA-VRI and CA-VRI was set to zero. To evaluate effects of imputation on results, sensitivity analyses were performed excluding observations with missing data. Subgroup and sensitivity analyses were performed on influenza and SARS-CoV2 cases. In the subgroup analysis for influenza, we additionally set the incubation time to 3 days, meaning that cases were considered hospital-acquired if the test was positive ≥ 3 days after admission. As supplementary analysis we additionally computed a Poisson model to check consistency of our results. Conditions of application of the models and fitness are detailed in the Supplementary appendix (Results, page 15). All statistical analyses were computed with R Studio version 2022.12.0 (R Foundation for Statistical Computing, Vienna, Austria). Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines were followed. The Institutional Review Board of the Assistance Publique-Hôpitaux de Paris gave approval for the research project (IRB 00006477—CER- 2023–221).

Results

Participants

Over the study period, 646 263 admissions were reported in the hospital and 183 994 respiratory viral PCR tests were performed (Fig. 1). Of these, 139 299 PCR tests fulfilled the eligibility criteria. Management of repeated data resulted in suppression of 55 856 PCR tests, leading to keep 83 443 single hospital visits corresponding to 62 347 patients in the final database (i.e. 13% of hospital admissions over the study period).

Patients had a median age of 60 years (interquartile range, IQR = 39–75) and 50% were male ($n = 31\,475$). The median length of stay was 4 days (IQR = 1–12), and 70% ($n = 58\,299$) of PCR tests were performed within 24 h of admission. Conventional hospital stays were spread over 27 hospital wards.

Incidence of VRI

CA-VRI incidence was twice as high as HA-VRI incidence (Table 1). VRI incidence had continuously risen from 2014 to 2022, with a steeper incline for HA-VRI than CA-VRI (Fig. S1), in parallel with an increase in the

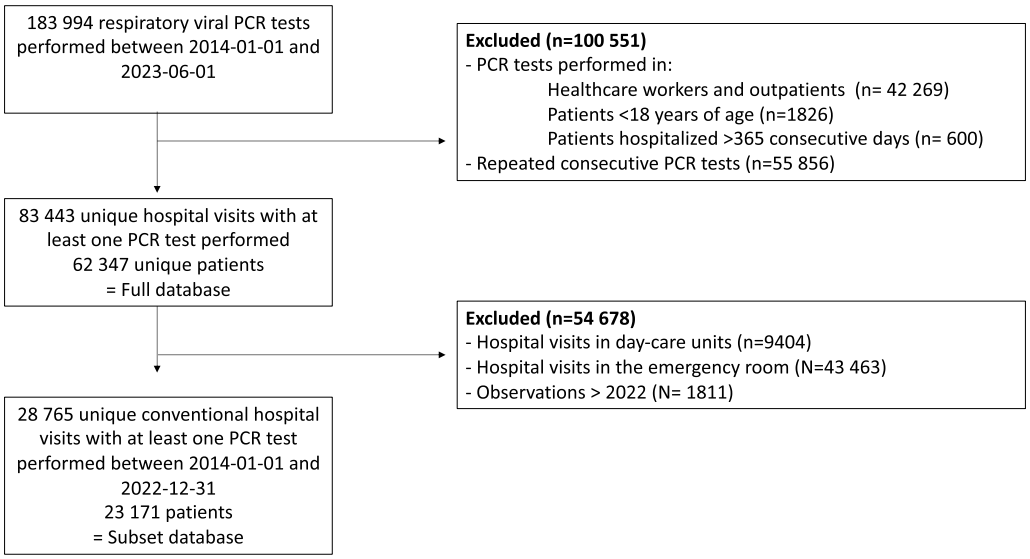

Fig. 1 Selection procedure of hospital visits included in the analysis. The full database included hospital visits in conventional hospital wards, day-care units, and in the emergency room. In case of repeated consecutive tests during the same hospital visit, only the first positive PCR test was considered. The subset database included only hospital stays in conventional wards, for years 2014–2022 (infection control indicators were not available for year 2023 at time of data analysis)

Table 1 Virus detected and incidence of community-acquired and hospital-acquired viral respiratory infections over 13 327 unique hospital visits (2014–2023)

	Total	**CA-VRI**	**HA-VRI**
	13 327	**11 009**	**2318**
Viruses			
SARS-CoV- 2	7260 (54.4%)	5995 (54.4%)	1265 (55.0%)
Rhinovirus/Enterovirus	1992 (15.0%)	1648 (15.0%)	344 (15.0%)
Influenza Virus	1783 (13.4%)	1543 (14.0%)	240 (10.0%)
Seasonal Coronavirus	606 (4.5%)	471 (4.3%)	135 (5.8%)
Respiratory Syncytial Virus	513 (3.8%)	418 (3.8%)	95 (4.05%)
Parainfluenza Virus	369 (2.8%)	274 (2.5%)	95 (4.05%)
Metapneumovirus	328 (2.5%)	274 (2.5%)	54 (2.3%)
Adenovirus	88 (0.7%)	69 (0.6%)	19 (0.8%)
Bocavirus	17 (0.1%)	12 (0.1%)	5 (0.2%)
Viral co-infections	371 (2.8%)	305 (2.8%)	66 (2.8%)
Incidence/1000 admissions ($_{95\%}$ CI)	12.9 (12.5–13.3)	9.0 (8.7–9.3)	3.9 (3.7–4.1)
Incidence/1000 hospital-days ($_{95\%}$ CI)	1.88 (1.83–1.94)	1.46 (1.41–1.51)	0.57 (0.54–0.60)

CA-VRI, Community-acquired Viral Respiratory Infections; HA-VRI, Hospital-acquired Viral Respiratory Infections; $_{95\%}$ CI, confidence interval

number of PCR tests performed (Fig. S2). Before 2020, the incidence of VRI followed a classical seasonal pattern for all viruses, except for rhinoviruses that were detected throughout the year. After 2020, detection of non-SARS-CoV- 2 viruses dramatically decreased until winter 2022 when a high incidence of influenza viruses, RSV and SARS-CoV- 2 was observed (Fig. 2). Community and hospital-acquired epidemics both followed a seasonal pattern. As illustrated in Fig. 3, the community epidemics seemed to constantly start before the nosocomial epidemic.

The positivity rate of PCR tests was 16% (13 327 positive tests/83 443 tests performed). Over 13 327 positive PCR tests, 2 318 (17%) corresponded to the definition of HA-VRI. The most frequent viruses were SARS-CoV- 2 (54%), followed by rhinovirus (15%) and influenza viruses (13%). The distribution of viruses was similar between CA-VRI and HA-VRI (Table 1).

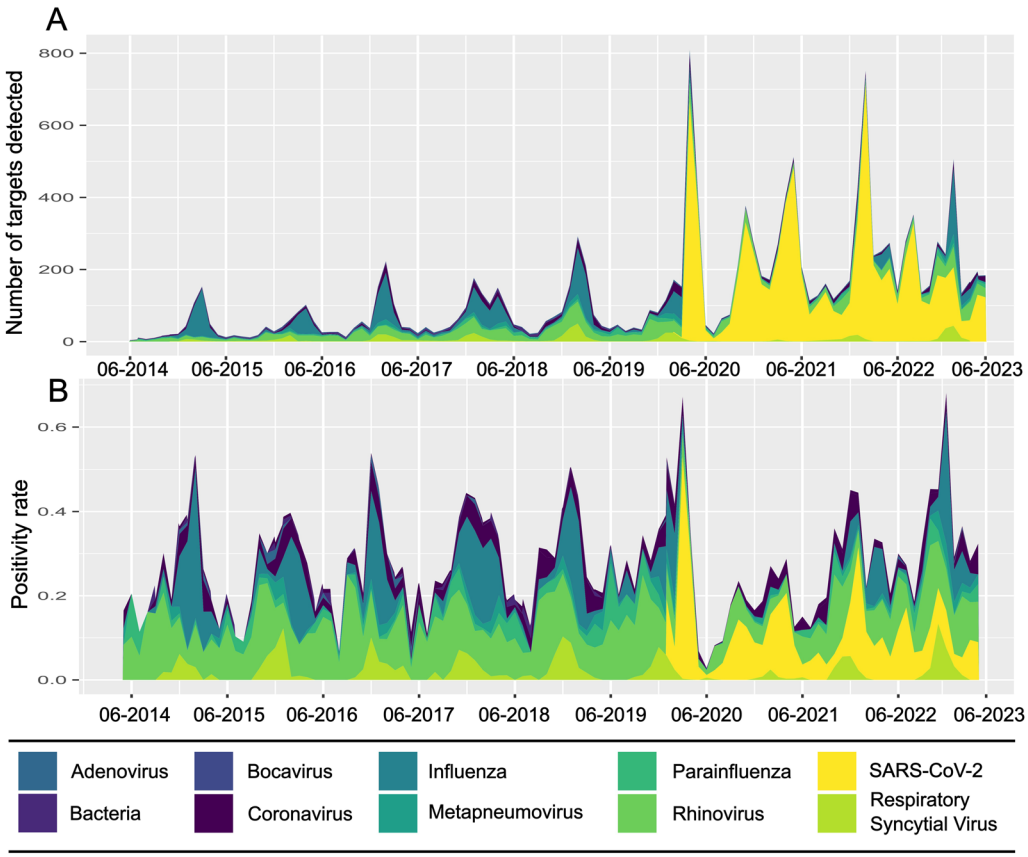

Fig. 2 Temporal trends of viral respiratory infections (2014–2023). **A**: Crude monthly number of targets detected. **B**: Positivity rate, calculated as the monthly number of positive tests over the total monthly number of targets tested

From 2020, 75% of positive PCRs were positive for SARS-CoV- 2.

Associations between infection control interventions and HA-VRI incidence

The subset database included 28 765 unique conventional hospital stays (Fig. 1), distributed over 27 wards for 9 consecutive years ([27 ×9] =243 single observations). In some wards and years (24/243 =9.9%), no PCR was performed and HA-VRI and CA-VRI incidences were set to zero. Six indicator values were missing (6/243 =2.5%), and were imputed to the mean. In the linear model, mean length of stay, CA-VRI incidence, PCR prescription incidence, percentage of double-occupancy rooms and masks consumption were statistically associated with HA-VRI incidence (Table 2). In the Poisson model, results were similar to the linear model with respect to length of stay, CA-VRI incidence, PCR prescription and double rooms (5% increase of HA-VRI for each extra 10 percentage points of beds in double rooms, $p = 0.02$), but mask and alcohol consumption were not significant ($p = 0.20$ and $p = 0.84$, Table S2). In the sensibility analysis on a subset database excluding imputed observations ($N = 216$), mean length of stay and CA-VRI incidence remained statistically significant. (Table S3).

Subgroup analyses

In the subgroup analysis of influenza cases, PCR prescription incidence and percentage of double-occupancy rooms were associated with influenza HA-VRI incidence, even after exclusion of imputed observations (Tables S4a and S4b). For SARS-CoV- 2, length of stay, CA-VRI incidence and percentage of double-occupancy rooms were associated with SARS-CoV- 2 HA-VRI incidence. CA-VRI incidence remained statistically associated with the incidence of HA-VRI after excluding imputed observations (Tables S5a and S5b).

Discussion

Our analysis, conducted over 10 consecutive years, showed an overall increase in the incidence of VRI over time, and a linkage between incidence of HA-VRI and CA-VRI. At a ward-level, we found an independent

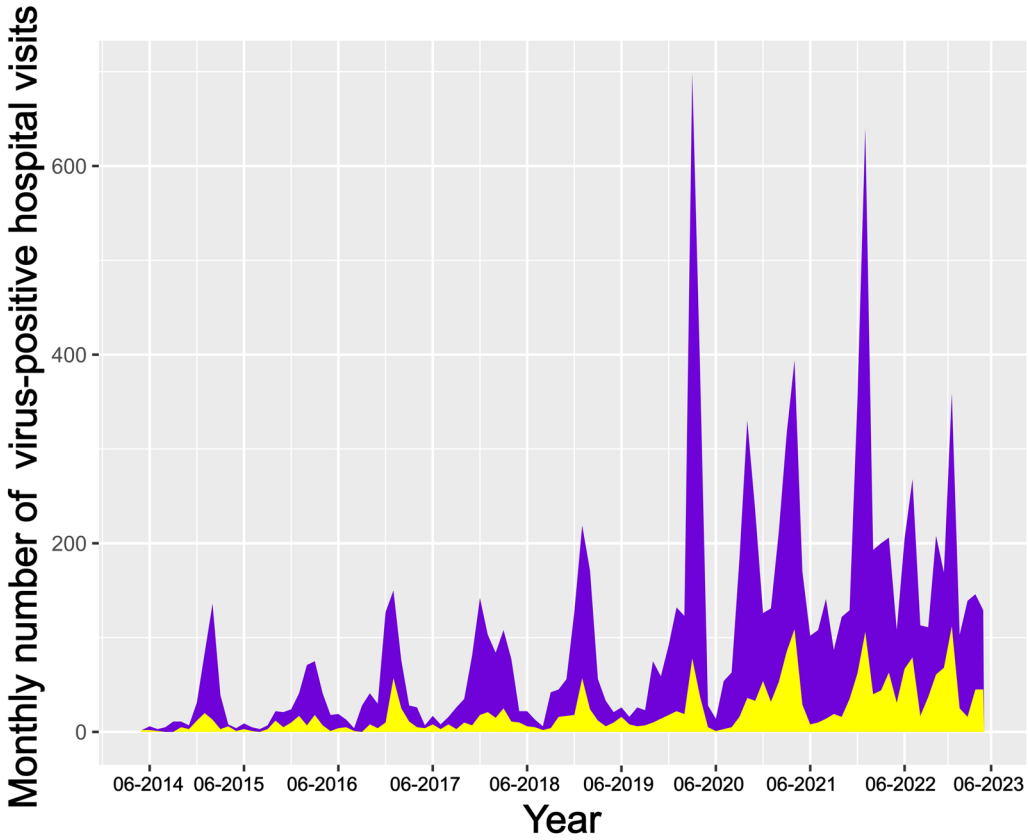

Fig. 3 Temporal trends of hospital-acquired (HA-VRI) and community-acquired (CA-VRI) viral respiratory infections (2014–2023). Data are expressed as the monthly crude number of unique hospital visits during which a HA-VRI (yellow) or a CA-VRI (purple) was diagnosed

Table 2 Predictors of incidence of Hospital-acquired Viral Respiratory Infections (HA-VRI). The outcome variable was the HA-VRI incidence per 1000 hospital-days, aggregated by ward and year. The analysis was performed on 243 ward-years. Individual variables (mean age, gender, length of stay), structural factors (percentage of single occupancy rooms) and annual infection control indicators (hand hygiene, mask use) in each ward and year of sampling were included in the model as fixed effects. Hospital ward was included as random effect. The model was weighted by annual ward activity. For each one-unit increase or decrease in the explanatory variable, the outcome (HA-VRI incidence expressed for 1000 hospital-days) increases or decreases by a factor indicated by the beta coefficient. For reference, the average incidence of HA-VRI was 0.57/1000 hospital-days. Of note, estimated effects report associations rather than causality, meaning that these predictors do not necessarily cause variations of HA-VRI incidence (see discussion section)

Explanatory variable	ß coefficient	Standard error	*p*-value	Estimated effect on HA-VRI incidence/1000 hospital-days
Mean age of patients in the ward	0.005	0.004	0.142	+ 0.005 per each additional year
Percentage of male patients in the ward	− 0.001	0.002	0.507	− 0.01 per each 10%-increase
Mean length of stay in the ward	0.005	0.001	0.001	+ 0.005 per each additional day
Incidence of CA-VRI in the ward/1000 hospital-days	0.100	0.027	< 0.001	+ 0.10 per each additional point of incidence of CA-VRI
Incidence of PCR testing in the ward/1000 hospital-days	0.007	0.002	0.007	+ 0.007 per each additional point of incidence of PCR testing
Percentage of double-occupancy rooms in the ward	0.004	0.002	0.030	+ 0.04 per each 10%-increase
Annual hand sanitizer consumption index (%) in the ward	0.004	0.002	0.052	+ 0.04 per each 10%-increase
Annual masks consumption/hospital-day in the ward	0.033	0.015	0.038	+ 0.33 per 10 additional masks consumed

HA-VRI, Hospital-acquired Viral Respiratory Infections

association between incidence of CA-VRI, percentage of double-occupancy rooms and incidence of HA-VRI with both linear and Poisson regressions.

The increase of VRI incidence over time has been reported before [6, 11], and is plausibly linked to the major increase of the number of PCRs performed over time, mainly driven by SARS-CoV- 2 tests from 2020 (Fig. S2). Moreover, improving access to reliable and rapid tests all over the study period (between 2014 and 2023) encouraged clinicians to use them, and probably changed indications for PCR testing, which impacted the proportions of CA-VRI and HA-VRI. A decrease of non-SARS-CoV- 2 respiratory viruses incidence in 2020/2021 [29, 30], and an extinction of some lineages (i.e. influenza B/Yamagata lineage) has been observed during the SARS-CoV- 2 pandemic [30, 31]. In 2022, our results show a co-circulation of SARS-CoV- 2, together with influenza and RSV (Fig. 3). We also observed a temporal linkage between HA-VRI and CA-VRI, as suggested by others [6].

As we move further away from the SARS-CoV- 2 pandemic, surveillance of community VRI has been gradually lifted. In this context, using data directly collected from hospital laboratories [32] could be an easy method to obtain real-time, fine-grain data on the epidemiological situation, to locally activate specific infection control interventions (for example universal masking in healthcare settings). Such strategy started to be implemented at a national scale during the 2023/2024 winter season in France, based on a combination of surveillance data collected and centralised from different sources (Santé Publique France: https://www.santepubliquefrance.fr/).

At a ward-level, CA-VRI incidence reflects the pressure of exposure to VRI inside the ward. This association between HA-VRI and CA-VRI suggests that specific prevention strategies may be useful in wards admitting a high rate of patients with CA-VRI. When community incidence is high, these could for example include universal masking of healthcare workers [18, 33], screening of patients before admission (in particular in double-occupancy rooms) [34], and even consider limiting occupancy of double rooms, if feasible. Feasibility and cost-effectiveness of such strategies should be further evaluated.

Hospitalization in a double room is a known individual risk factor for nosocomial acquisition of influenza [35, 36], and SARS-CoV- 2 [37–39]. Our results further emphasize that the percentage of double-occupancy rooms in a given ward is a structural predictor for HA-VRI after adjustment on other prevention strategies. According to the linear model, each 10%-increase of the percentage of double-occupancy rooms may be associated with in a + 7% increase of HA-VRI incidence. This result is consistent with a recent study showing that a higher proportion of beds in single rooms was associated with decreased transmission risk for SARS-CoV- 2 [40, 41]. In our study, this association was found despite a local policy strongly encouraging testing for respiratory viruses before admitting patients in double rooms [42]. It is difficult to draw formal conclusions on what would be an acceptable proportion of double-occupancy rooms in a healthcare facility. Still, our results suggest that, where possible, they should be discouraged for conception of future hospital facilities, as recently emphasized in the 2024 guidelines of the French Infection Control Society (www.sf2h.net).

Several limitations should be acknowledged. First, we used aggregated data, placing our analysis at a ward-level rather than a patient-level. This approach aimed at evaluating the global impact for each medical ward to include double rooms, while accounting for overall compliance to infection control protocols, including elements that are not directly measurable (disinfection of shared material, door closing, etc.). However, even if, to some extent, the random ward effect partially adjusted for the case mix of each ward, some patients-related potential confounding factors were not taken into account, which is an important limitation of our analysis. Second, we used imputation methods for some missing data. For infection control indicators, only six values were missing (6/243 = 2.5%), and we considered mean imputation as acceptable. Imputation may have impacted some of our results, but, for influenza cases, association between percentage of double rooms and incidence of HA-VRI was found even after exclusion of imputed observations. Third, there is still uncertainty on the duration of the incubation period for some viruses [6, 43, 44], which complicates definition of hospital-acquired cases [45]. We therefore performed subgroup analyses with different incubation times for influenza virus, which gave similar results. Additionally, because data were not available, we also based definition of HA-VRI on the date of PCR and not of symptoms onset. It is probable that the time between symptoms onset and testing was variable between wards, and this may also have led to classification bias for certain HA-VRI. Fourth, we did not detect infections occurring after hospital discharge and did not have data for non-PCR-tested patients, which may have led to an underestimation of the true burden of HA-VRI. Nevertheless, our local policy strongly encourages

patients' screening, via easy access to testing and to rapid results [46, 47]. Additionally, multiplex tests allow identification of viral infections (hMPV, sCoV, ect.) which would be undiagnosed when only monoplex PCR tests are being used. Our design also did not explore temporality, it is important to note that the positive association between mask consumption and HA-VRI may reflect an increase in mask consumption secondary to the detection of HA-VRI. Mask and AHR consumption could be colliders for HA-VRI and appropriate adjustment was limited by the nature of available data (Tables S6a, S6b and S7). Given that these factors are known to be associated with HA-RVI incidence, they can hardly be omitted from the model. Consequently, interpretation of coefficients for masks and alcoholic consumption should be cautious. More generally, like for all epidemiological studies, in particular performed on retrospective data, our study reports associations rather than causality, and these results should be confirmed with appropriate prospective interventional designs. Likewise, longer hospital stays could be responsible for higher incidence of HA-VRI, but HA-VRI could also result in an increased length of stay. The fact that alcohol sanitizer consumption was not a significant factor in the model is also questioning. Increased sanitizer consumption among staff may be a response to the increasing number of positive tests on the ward. Additionally, sanitizer consumption has its limitations since it does not allow for evaluating whether hand hygiene is being performed at the right time, using the correct technique, with the correct volume of sanitizer. But these practical consumption measures have the strong advantage of being standardized and reproducible, especially over a long study period. And last, the study was monocentric, which hampers the generalizability of our results. However, our data allowed comparisons within hospital wards with heterogeneous infection control practices, and over a 10-year period.

Conclusion

This 10-year surveillance study suggests that, at a ward level, high incidence of CA-VRI among admitted patients and high percentage of double-occupancy rooms may be independently associated with the risk of nosocomial transmissions of VRI in healthcare facilities. The linkage between CA-VRI and HA-VRI epidemics in healthcare settings also suggests that hospital laboratory data could be used as a real-time decision tool to implement interventions (i.e., universal masking, systematic screening at admission) during winter epidemic seasons.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13756-025-01543-4.

Supplementary file 1

Author contributions

Conceptualization: CS, QLH, AV, VM, IL, JCL, CC, SK Methodology: CS, QLH, SH, AV, VM, JCL, CC, SK Formal analysis: CS, SH, SK Writing original draft: CS, SK Writing review editing: CS, QLH, SH, AV, VM, DB, BV, NF, IL, JCL, DD, CC, SK.

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Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author SK.

Declarations

Ethics approval and consent to participate

The Institutional Review Board of the Assistance Publique-Hôpitaux de Paris gave approval for the research project (IRB 00006477—CER- 2023–221).

Competing interests

The authors declare no competing interests.

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