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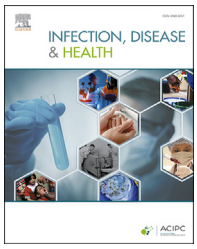

Research paper

Unexpected benefit of COVID-19 hospital restrictions: Reduction in patients isolating with multidrug resistant organisms after restrictions were lifted

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Abstract *Background:* During the COVID-19 pandemic, measures to prevent microorganism transmission were implemented across hospitals, including wearing compulsory surgical masks, minimising non-urgent procedures and restricting visitors. Previously, concerns have been raised that MRO-associated deaths could rise during a future pandemic through superimposed bacterial infections, inappropriate antibiotic use and reduced focus on preventing MRO infections.
Methods: In the state of Queensland, Australia with a population of 5 million, only a short first wave of coronavirus cases occurred and restrictions were quickly scaled back. This presented a natural experiment of pre-, during and post-COVID-19 restriction timings to evaluate the effectiveness of heightened prevention measures on multidrug resistant organism (MRO) infections. Patient isolation days and MRO types were collected weekly from routine infection control reports, at a large public hospital, from 28th January 2020 to 24th July 2020. In this interrupted time series design, we employed Poisson mixed effect regression modelling to evaluate the difference in incidence of patient isolation days between time periods.
Results: Compared to pre-COVID, patient isolation days reduced during COVID restrictions (incidence rate ratio 0.65, 95%CI: 0.59, 0.70; $p < 0.001$) and increased again post-COVID

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restrictions, but did not return to pre-COVID levels (0.87, 95%CI: 0.80, 0.95; p = 0.001). The efficiency of isolating patients improved after COVID-19 with fewer bed closures required.
Conclusion: Heightened infection control awareness, hand sanitation and mask wearing after COVID-19 restrictions were lifted appear to effectively prevent common hospital-acquired MRO infections.

Highlights

- Post COVID-19 restrictions, patient isolation days decreased by 0.87 (0.80, 0.95; p = 0.001).
- Post COVID-19, patient non-isolation room days decreased by 0.60 (0.47, 0.76; p < 0.001).
- Improved isolation efficiency for patients with MROs post COVID-19 restrictions.
- Decrease in patient isolation days was evident across all but one MRO type (VRE VAN-b).

Introduction

Termed an 'invisible pandemic', multidrug resistant organisms (MRO) causing infections in healthcare settings are a growing problem worldwide and result in 700,000 deaths globally each year [1]. Infections with MROs are more difficult to treat, and are associated with poorer outcomes for patients such as increased morbidity, length of stay, additional treatment and increased costs to the health care system [1]. Managing MRO aims to minimise MRO transmission through surveillance and by creating barriers between contacts. Hospitals enact this through targeted measures such as alerts and notification systems, isolating patients, hand hygiene practices and wearing personnel protective equipment. During the Coronavirus Disease 2019 (COVID-19) pandemic, several additional infection control measures were implemented across hospitals to prevent viral transmission. These included compulsory surgical masks, delaying surgeries and increasing the use of telehealth.

In Queensland Australia the first COVID-19 wave peaked in late March with around 78 cases per day. The wave was small compared with elsewhere in the world with Queensland only having 10+ cases per day for 28 days from mid-March 2020 [2]. On 23rd March 2020, Brisbane hospitals elevated their response by reducing hospital service capacity [3]. During the height of the COVID-19 response, 67% of outpatient appointments were conducted via phone or videoconferencing [4] and 50% of all elective surgery activity was suspended [5]. Due to international and interstate border closures along with 'stay at home' orders, the surge of COVID-19 patients in Brisbane was avoided. On the 1st June 2020, reduced patient capacity orders were reversed but universal mask wearing and hand sanitation stations across all facilities remained [5].

Previously, concerns have been raised that MRO-associated deaths could rise during a future pandemic through superimposed bacterial infections, inappropriate antibiotic use and reduced focus on preventing MRO infections [6]. However, a study during the COVID-19 pandemic showed the prolonged use of intensive preventive measures could decrease MRO burden [7]. To inform this further, here we describe a natural experiment, based on the COVID-19 experience in Brisbane, analysing pre-, during and post-COVID-19 restrictions, to evaluate the effectiveness of heightened prevention measures on MRO infections.

Methods

Study population

The study hospital is an 834-bed tertiary/quaternary facility in Brisbane with 163 isolation beds. Hospital policy is to isolate patients in single-bed isolation rooms if detected with any of: vancomycin-resistant *Enterococcus (VRE)* VanA resistance, VRE VanB resistance, carbapenem-resistant *Acinetobacter baumannii (CRAB)*, carbapenemase-producing/carbapenem-resistant *Enterobacterales (CPE/CRE)*, Extended spectrum beta-lactamase producing *Klebsiella pneumoniae* (ESBL-KP), methicillin-resistant *Staphylococcus aureus* United Kingdom strain 15/hospital strain (MRSA UK15/HS) and carbapenem resistant *Pseudomonas aeruginosa* (CRP). Risk based surveillance is undertaken with high risk wards screened regularly.

Data

Data were collected on 'patient isolation days' defined as the number of days where a patient was isolated due to harbouring one or more of the MROs of concern. Ward locations were collected for each patient in isolation from 28th January to 24th July 2020 (129 days), excluding weekends and public holidays. In each ward, the number of single-bed isolation rooms vary between 2 and 6, and when filled, patients are isolated in multi-bed rooms (hereafter called non-isolation rooms). Prioritising patients with viral pathogens limits the single-bed isolation rooms available to patients with MROs. 'Patient isolation days' include patients isolated in either dedicated single rooms or non-isolation rooms. Monthly occupied bed day reports were used to assess patient capacity.

Table 1 Average number of patients isolating per day pre-, during and post-COVID-19 restrictions.

Ward	Pre COVID-19 (1285 isolation days, 39 collection days, 28th January – 20th March 2020, average of 1007 OBD[b])	During COVID-19 restrictions (953 isolation days, 47 collection days[a], 26th March – 1st June 2020, average of 862 OBD[b])	Post COVID-19 restrictions (1103 isolation days, 35 collection days[a], 7TH June – 24th July 2020, average of 1002 OBD[b])
Infectious Diseases	6.59 (3.01)	0.79 (0.93, $p < 0.001$)	2.49 (1.15, $p < 0.001$)
Renal/General Medicine	3.18 (1.12)	1.47 (1.02, $p < 0.001$)	2.49 (1.15, $p = 0.010$)
Respiratory	3.00 (0.92)	0.53 (0.69, $p < 0.001$)	0.46 (0.61, $p < 0.001$)
Vascular	2.97 (0.78)	0.96 (1.28, $p < 0.001$)	3.57 (1.29, $p = 0.017$)[c]
Colorectal	2.49 (1.00)	0.96 (0.51, $p < 0.001$)	1.66 (0.94, $p < 0.001$)
Haematology/Bone marrow transplant	2.46 (1.41)	3.32 (1.48, $p = 0.008$)	3.49 (1.69, $p = 0.006$)[c]
Orthopaedics/Trauma	1.69 (1.58)	0.26 (0.53, $p < 0.001$)	2.03 (0.86, $p = 0.266$)
Offsite	1.26 (0.55)	1.53 (0.72, $p = 0.053$)	0.31 (0.47, $p < 0.001$)
Endocrinology/Rheumatology/ General Medicine	1.15 (1.11)	0.98 (1.07, $p = 0.461$)	0.94 (1.06, $p = 0.407$)
Cancer Care	0.87 (1.00)	0.36 (0.70, $p = 0.007$)	1.11 (0.72, $p = 0.241$)
Gynaecology	0.82 (0.60)	1.26 (1.41, $p = 0.076$)	1.00 (1.03, $p = 0.357$)
Urology	0.77 (0.58)	0.00 (0.00, $p < 0.001$)	0.00 (0.00, $p < 0.001$)
Burns	0.67 (0.93)	0.36 (0.49, $p = 0.054$)	2.14 (0.73, $p < 0.001$)
Upper GI/General Surgery	0.64 (0.78)	0.55 (0.72, $p = 0.588$)	0.97 (0.75, $p = 0.067$)
Emergency and Trauma Centre	0.64 (1.18)	0.17 (0.43, $p = 0.013$)	0.29 (0.79, $p = 0.137$)
Geriatric Evaluation and Management	0.62 (0.54)	0.70 (0.69, $p = 0.525$)	0.80 (0.41, $p = 0.105$)
Intensive Care	0.59 (0.85)	0.74 (0.99, $p = 0.443$)	0.74 (0.89, $p = 0.451$)
Cardiology	0.56 (0.79)	0.47 (0.86, $p = 0.593$)	0.71 (0.86, $p = 0.436$)
Short stay surgical	0.54 (1.05)	0.40 (0.77, $p = 0.496$)	1.31 (0.90, $p = 0.001$)
Neurosurgery	0.33 (0.48)	1.11 (0.37, $p < 0.001$)	0.34 (0.54, $p = 0.936$)
early patient intervention centre	0.31 (0.52)	0.17 (0.48, $p = 0.207$)	0.11 (0.32, $p = 0.062$)
Ear, nose & throat	0.28 (0.86)	0.66 (0.60, $p = 0.019$)	0.60 (0.69, $p = 0.086$)
Other	0.26 (0.64)	0.11 (0.31, $p = 0.158$)	0.06 (0.24, $p = 0.085$)
Stroke	0.18 (0.60)	0.23 (0.52, $p = 0.653$)	0.20 (0.41, $p = 0.866$)
Maternity	0.08 (0.27)	0.13 (0.34, $p = 0.450$)	0.11 (0.32, $p = 0.590$)
Intensive Care Nursery	0.00 (0.00)	0.00 (0.00, $p =$ n/a)	0.57 (0.92, $p < 0.001$)
MRO type			
MRSA -UK15/HS	7.54 (1.59)	2.62 (2.01, $p < 0.001$)	5.68 (2.35, $p < 0.001$)
VRE-VAN A	7.10 (2.15)	3.16 (1.78, $p < 0.001$)	4.28 (1.84, $p < 0.001$)
VRE-VAN B	6.36 (1.51)	5.78 (2.09, $p = 0.149$)	9.03 (3.02, $p < 0.001$)
ESBL - KP	6.23 (2.18)	4.88 (1.51, $p < 0.001$)	4.98 (1.94, $p = 0.008$)
CRP	2.36 (0.99)	1.54 (1.09, $p < 0.001$)	1.90 (0.67, $p = 0.018$)
CPE/CRE	1.64 (0.78)	0.68 (0.71, $p < 0.001$)	1.43 (0.78, $p = 0.222$)
PCP	0.95 (1.57)	0.12 (0.33, $p < 0.001$)	0.00 (0.00, $p < 0.001$)
CRAB	0.64 (0.78)	0.12 (0.33, $p < 0.001$)	0.28 (0.51, $p = 0.015$)
VRE-VAN A&B	0.13 (0.47)	0.14 (0.35, $p = 0.892$)	0.03 (0.16, $p = 0.192$)
Other	0.00 (0.00)	0.02 (0.14, $p =$ n/a)	0.00 (0.00, $p =$ n/a)

Abbreviations: OBD = occupied bed days; GI = gastrointestinal; n/a = not applicable; *VRE* = vancomycin-resistant *Enterococcus*, CRAB = Carbapenem-resistant *Acinetobacter baumannii; CPE* Carbapenemase-Producing *Enterobacterales*; CRE = carbapenem-resistant *Enterobacterales*; ESBL – KP = Extended spectrum beta-lactamase *Klebsiella pneumoniae*; MRSA Methicillin-resistant *Staphylococcus aureus*; UK15 = United kingdom strain 15; HS = hospital strain; CRP = carbapenem resistant *Pseudomonas*; PCP = *Pneumocystis* pneumonia.

[a] Six days between restriction periods were not included in analysis in order to let the prevention measures impact patients.

[b] Monthly occupied bed days were: January – 1008; February – 1011; March –1002; April – 837; May – 853; June – 1159; July – 853.

[c] With VRE Van-b removed from analysis no difference between scenarios were present.

Analysis

In this interrupted time-series design, a Poisson mixed-effect regression analysis was employed to evaluate the difference in patient isolation days between the pre-, during and post-COVID-19 restriction time periods. Ward was used as the random effect in the Poisson mixed effect regression to account for potential clustering effect at this level, and isolation events were offset by the occupied bed days to calculate incidence rate ratios (IRR). We also assessed the subset of non-isolation room patient days. The time periods comprised 39 days in pre-; 47 days during; and

35 days post-COVID-19 restrictions. We hypothesized immediate decreases (level change) in outcomes and no continued decrease over time (i.e., slope change). The validity of the Poisson mixed-effect model was evaluated by inspecting the model residuals and the presence autocorrelation. All statistical analyses were conducted using Stata v15.0 software (StataCorp, College Station, TX).

Results

In total there were 1285 patient isolation days in the pre-, 856 during and 998 post-COVID-19 restriction time periods (Table 1). The rate of patient isolation was substantially lower during COVID-19, with isolation during this period being approximately two-thirds of that observed pre-COVID-19 (IRR = 0.65; 95%CI: 0.59, 0.70; $p < 0.001$) Compared to pre-COVID-19, there was a decrease in patient isolation days post COVID-19 restrictions with an IRR of 0.87 (95%CI: 0.80, 0.95; $p = 0.001$) (Fig. 1). In the non-isolation room subset, we found 200 patient isolation days pre-, 58 during and 117 post-COVID-19 restriction time periods. Compared to pre COVID-19, there were decreases in non-isolation room days with IRRs of 0.17 (95%CI: 0.12, 0.25; $p < 0.001$) during COVID-19 restrictions and 0.60 (95%CI: 0.47, 0.76; $p < 0.001$) post COVID-19 restrictions (Fig. 1).

Patient isolation days attributed to VRE VAN-b were uniquely not impacted during COVID-19 restrictions and increased after restrictions were lifted (Table 1). Patient isolation days decreased in both during and post-COVID-19 restriction periods across five wards, while increases in VRE VAN-b led to increased isolation days in Haematology and Vascular wards (Table 1).

Discussion

We identified an overall decrease in the number of patients isolating with MROs during the COVID-19 restrictions that subsequently rose after the restrictions were lifted but did not return to pre-COVID-19 levels. This decrease was evident across all but one MRO type. We highlight improved isolation efficiency with the continued decrease in non-isolation room use for isolating patients with MROs. If maintained post pandemic, this improved isolation efficiency could save AU$54,692 per month in hospital costs [8] through reducing closure of multi-bed rooms.

Three studies have investigated the heightened precautions associated with COVID-19 and its impact on incidence of MROs. An Italian study found a significant reduction in the incidence of total MRO infections during the pandemic compared to previous years [7]. Similar to our study, no changes in detection of *Enterococcus faecium* infections were identified during COVID-19 restrictions. Also similar to our findings, in a Belgian study, no differences in the acquisition rate of MROs in the intensive care unit (ICU) were found before and during the COVID-19 pandemic [9]. This may be explained by the heightened prevention measures already occurring for patients within an ICU. Within an Italian geriatric population, increased MRO bloodstream infections and mortality were identified in a post COVID-19 outbreak period [10]. However, the small selective sample size (83 cultures) and incomplete screening limits the generalizability of these results. We conclude from these studies that a holistic approach is required to understand the impact of COVID-19 precaution measures, rather than within a specific ward.

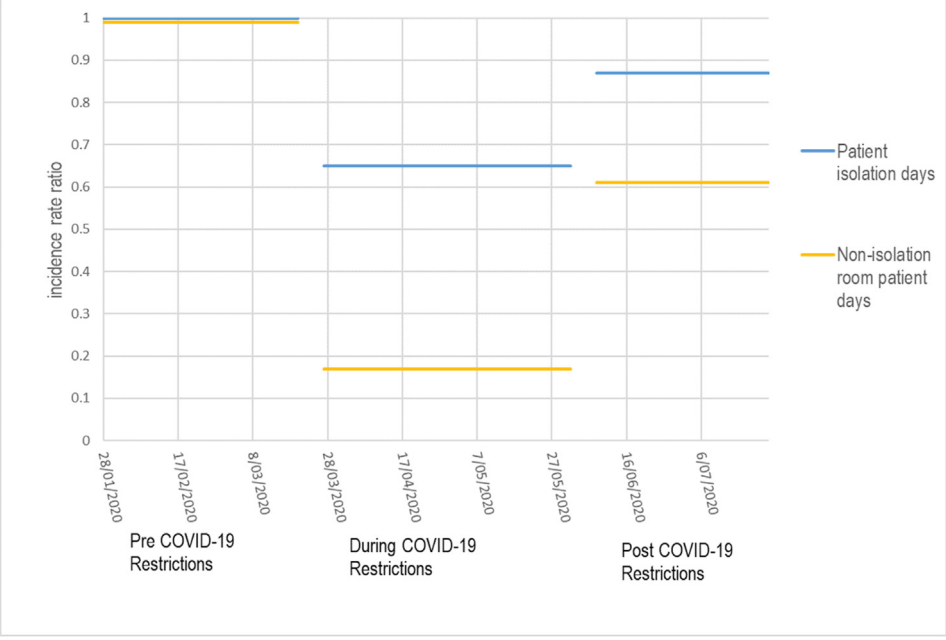

Figure 1 Incidence rate ratios for MRO isolation days and isolation days in non-isolation rooms (pre-COVID is the referent). Note: The Incidence rate ratio of isolation days is represented in blue and the subset non-isolation room patient days in orange. The incidence rate ratio was estimated from the interrupted time series analysis. Pre COVID-period is between 28th of January to 22nd of March 2020. The During COVID-19 restriction period is between 26th March and 1st June 2020. The post COVID-19 restrictions period was between 7th June to 24th July 2020.

The limitations of this study were the lack of patient-level data and brevity of data collection to further explore this topic. We cannot rule out the impact of changes in patient case mix or other service-line factors (e.g, volume of transplants) that may affect the susceptibility of patients to MROs. Seasonality was not included in the interrupted time-series design, although the impact should be minimal with influenza season not occurring. Balanced against these limitations, was access to patient isolation data before, during and after a COVID-19 wave at a large public hospital.

We have shown a hospital committed to reduced microorganism transmission, as occurred during COVID-19 pandemic, can immediately reduce the MRO burden, with potential ongoing improvements in MRO prevention and patient isolation efficiency.

Ethics

No patient information was collected during this study, hence patient consent was not required. Data collected in this study was approved by the QIMR Berghofer Medical Research Institute Human Research Ethics Committee (P2353) and the Queensland Government Public Health Act Human Research Ethics Committee (RD007427).

Authorship statement

Thomas Elliott: Conceptualization, Methodology, Formal analysis, Writing - Original Draft.

Cameron Hurst: Formal analysis, Writing - Review & Editing.

Michelle Doidge: Resources, Investigation.

Trish Hurst: Resources, Investigation.

Patrick NA Harris: Supervision, Writing - Review & Editing.

Louisa G Gordon: Conceptualization, Writing - Original Draft, Writing - Review & Editing, Supervision.

Conflict of interest

No author had any conflicts of interest.

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Provenance and peer review

Not commissioned; externally peer reviewed.

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