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The incidence of positive bloodstream and urine cultures in five Australian hospitals during the COVID-19 pandemic

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The incidence of positive bloodstream and urine cultures in five Australian hospitals during the COVID-19 pandemic

Running title

Incidence of HAI during COVID-19

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Introduction

The COVID-19 pandemic has seen an unprecedented increase in awareness and focus on infection prevention precautions, including hand-hygiene, cleaning, air quality, ventilation and correct use of personal protective equipment (PPE).[1] Recent research has documented that although standard precautions were adopted globally prior to the pandemic, deficits in implementation and compliance persist.[2-4] With an increased focus on infection prevention and control practices and processes in healthcare settings as a result of the pandemic, it could be hypothesised that this in turn may have a positive effect on reducing the overall risk of infection transmission in these settings. Conversely, hospitals and healthcare workers have been under enormous strain from COVID-19 and this may result in a reduced focus on preventing infections other than COVID-19.

Emerging research contains mixed results about the effect the COVID-19 pandemic has had on the rates of healthcare associated infections (HAIs). Substantial increases in central-line associated bloodstream infections (CLABSIs) and catheter associated urinary tract infections (CAUTIs) have been observed, along with an increase in contaminated specimens and potential reduction in local HAI reporting.[5-7] Researchers have suggested that this may be due to: resources shortages; influx of patients; changing recommendations; and general stress.[5-7] However, reductions in *Clostridioides difficile* have also been reported,[1,8,9] and generally a lower rate of multidrug resistant organisms - although this was in an area which was at the time not significantly affected by COVID-19 infections.[10] These have been attributed to the increased awareness and practice of standard precautions.[1,10,11]

The infection prevention challenges presented by COVID-19 are significant. To prepare for the admission and treatment of COVID-19 positive patients, a number of new and modified infection prevention initiatives have been implemented across healthcare sites. These include, but are not limited to: an overall heightened awareness of infection prevention; increase in education regarding PPE; increase in the use of PPE; increase in promotion of hand hygiene; changes to cleaning regimes; restriction in visiting hours; improvement in ventilation and limited patient movement.[12] Whilst the correct and appropriate use of PPE, adequate air quality, hand hygiene and cleaning are fundamental in every infection prevention program, the heightened awareness COVID-19 has introduced, may mean there is increased compliance and diligence. At the same time, whilst preventing the spread of COVID-19, these activities will also prevent many other types of infection. On the other hand, as emerging research is indicating, the increased stress on healthcare workers and organisations may increase HAIs,[13] particularly given evidence that increased glove use often leads to poor hand hygiene compliance.[14] There are also several reports of increases in

carbapenemase-producing Enterobacteriaceae in intensive care units in the context of COVID-19 and increased infection prevention activity related to non compliance with PPE, misuse of gloves, high antibiotic use and overwork.[15-18] The overall aim of this study is to explore if there has been any effect on HAI rates as a result of the increased infection prevention awareness brought about by COVID-19.

Methods

Study design

The study was a three-year retrospective review of inpatient laboratory data.

Setting and population

Data were sourced from five Australian hospitals from two different Australian jurisdictions (New South Wales and Victoria). These five hospitals consisted of four acute public hospitals (two Principal Referral Hospitals [Hospitals A and B]), and two Acute Group A hospitals [Hospitals C and D]) and one acute private hospital (Private Acute Group A [Hospital E]). Differences between these hospital types are detailed in Supplementary Table S1. Combined, these hospitals have over 2400 overnight beds and over 290,000 hospital admissions per year.

We constructed two cohorts; first, the pre-COVID-19 cohort, defined as inpatients who had specimens collected between January 2017 to February 2020, and second, the COVID-19 cohort, defined as inpatients who had specimens collected between March 2020 to March 2021, inclusive.

Data sources

Microbiology data were obtained from the laboratories of participating hospitals for the period of January 2017 through to March 2021 (inclusive) for positive bloodstream and urine cultures. For each positive culture, patient level data were collected, including age, gender, date of admission, date of specimen collection and name of organism. Positive cultures that were collected within 48 hours of admission, and repeat bloodstream cultures within 14 days, or urine cultures within 30 days, were excluded. To generate the incidence rate, monthly occupied bed day (OBD)[19] data were collected from each hospital for the same time period. To allow for uniform reporting of organisms, each organism reported from the source was categorised into a pathogen group (Supplementary Table S2).

Definitions

For the purposes of this study, we applied the following definitions for HAIs:

- Bloodstream infection (BSI): positive culture collected >48 hours post admission
- Urinary tract infection (UTI): positive culture collected >48 hours post admission

Statistical analyses

Interrupted time series (ITS) regression analyses with Newey-West autocorrelated errors [20] were carried out to assess differences in the log-transformed level and trend of HAI between the pre-COVID-19 and COVID-19 periods. The ITS models assessed the baseline rate of HAI (intercept), trend during the pre-COVID-19 interval (slope), the change in level of HAI, and the change in slope between the two time periods. Values with a response variable of zero had a small pseudo-count added to ensure the transformation was valid. Prior to analyses, model assumptions were evaluated through the inspection of autocorrelations and model residuals. Infection rates were also examined for potential seasonal trends, with no discernible seasonal trends detected. To ensure that the models accounted for the correct autocorrelation structure, Baum and Schaffer autocorrelation test for autocorrelation was used to test for up to 12 lags. Lags that had significant autocorrelations were incorporated into the model.[21] In all statistical analyses, nominal alpha level of 0.05 was used to interpret the results of significance tests.

To create the time series, the number of infections and number of OBD were aggregated by month. HAI rates were calculated as a ratio of the number of infections (numerator) in a given month to the corresponding number of OBD (denominator) and expressed as a rate per 10,000 admissions. We assessed changes in HAI rates overall, aggregated across hospitals, as well as changes in HAI rates for each hospital. We also assessed changes in the rates of BSI and UTI pooled across all sites and separately for each site. To assess the influence of individual sites on the overall HAI rates, jack-knife sensitivity analyses were undertaken by removing one hospital at a time and estimating ITS model for the rates pooled across the remaining hospitals.

Results

Positive culture data from all hospitals were collected on specimens taken between 1 January 2017 to 31 March 2021. All hospitals reported data on BSI and UTI.

A total of 9,685 positive cultures (1,988 bloodstream and 7,697 urine) from 8,194 patients were included in the final analysis. The overall median age of the patient cohort with positive UTI cultures was 74 (quartile range 60-84), and 65% (4,968/7,697) were female. The median age of the cohort with positive BSI cultures was 66 (quartile range 53-76) and 38% (757/1,988) were female. The mean monthly number of occupied bed days combined in the pre COVID-19 cohort was 75,317 compared to 73,157 for the COVID-19 cohort. All sites reported a notable drop in occupied bed days in April

2020, but by June 2020 numbers had returned to similar pre COVID-19 numbers (Supplementary Figure S1).

Hospital A contributed the most culture positive episodes with 4,792, followed by Hospital B 2,943 episodes, Hospital E 1,614 episodes, Hospital C 230 episodes and Hospital D 106 episodes. The unadjusted incidence rates for all HAIs in the pre-COVID-19 cohort was 25.5 per 10,000 OBDs (95%CI:24.9-26.1) and in the COVID-19 cohort was 25.1 per 10,000 OBDs (95%CI:24.1-26.1). (Table 1) Sensitivity analysis on the influence of each site on combined BSI and UTI infections demonstrated that hospital A had a significant downward influence in the pre-COVID-19 cohort (p=0.008), and Hospitals B and E had a significant upward influence on the COVID-19 cohort (p=0.009 and p<0.001 respectively. (Supplementary Figure S2).

Table 1 : Unadjusted incidence rates per 10,000 bed days.

	Pre-COVID-19 cohort (Jan 2017 – Feb 2020)		**COVID-19 cohort (Mar 2020 – Mar 2021)**	
	Number	Incidence per 10,000 OBDs (95%CI)	Number	Incidence per 10,000 OBDs (95%CI)
Bloodstream cultures	1,518	5.3 (5.0-5.6)	470	4.9 (4.5-5.4)
Urinary tract cultures	5,781	20.2 (19.7-20.7)	1,916	20.1 (19.2-21.1)
Total	7,299	25.5 (24.9-26.1)	2,386	25.1 (24.1-26.1)
Occupied bed days	*2,864,089*	--	*951,042*	--

Differences in laboratory reporting nomenclature, and small numbers of certain species, resulted in the grouping of several species for analysis, such as *Escherichia* species, *Staphylococcus* species and *Candida* species (Supplementary Table S2). *Escherichia* species were also the most frequent for BSI and UTI (Table 2).

Table 2: Frequency of most common organisms by infection type

Bloodstream infection (n=2,313[#])			Urinary tract infection (n=8,573[#])		
Organism	Number	%	Organism	Number	%
Escherichia species	339	14.7	*Escherichia* species	2556	29.8
Staphylococcus species	224	9.7	*Enterococcus* species	1258	14.7
Klebsiella species	203	8.8	*Candida* species	1206	14.1
Enterococcus species	200	8.6	*Pseudomonas* species	683	8
Candida species	176	7.6	*Klebsiella* species	647	7.5
VRE species	174	7.5	VRE species	423	4.9
MSSA	157	6.8	*Proteus* species	377	4.4
Enterobacter species	143	6.2	*Enterobacter* species	329	3.8
Pseudomonas species	140	6.1	*Staphylococcus* species	202	2.4

Time series analysis of pre COVID-19 cohort and COVID-19 cohort

Combined BSI and UTI by hospital

Hospital A demonstrated a significant increase in in the pre-COVID-19 cohort ($p<0.001$), and a significant decrease in the COVID-19 cohort ($p=0.004$) when combining both BSI and UTI data. Hospital D had a significant decrease in the COVID-19 cohort ($p=0.002$). There were no other significant trends identified, however Hospitals C and D had a slight decrease in the COVID-19 cohort, whilst Hospital B demonstrated an increase in the COVID-19 cohort.

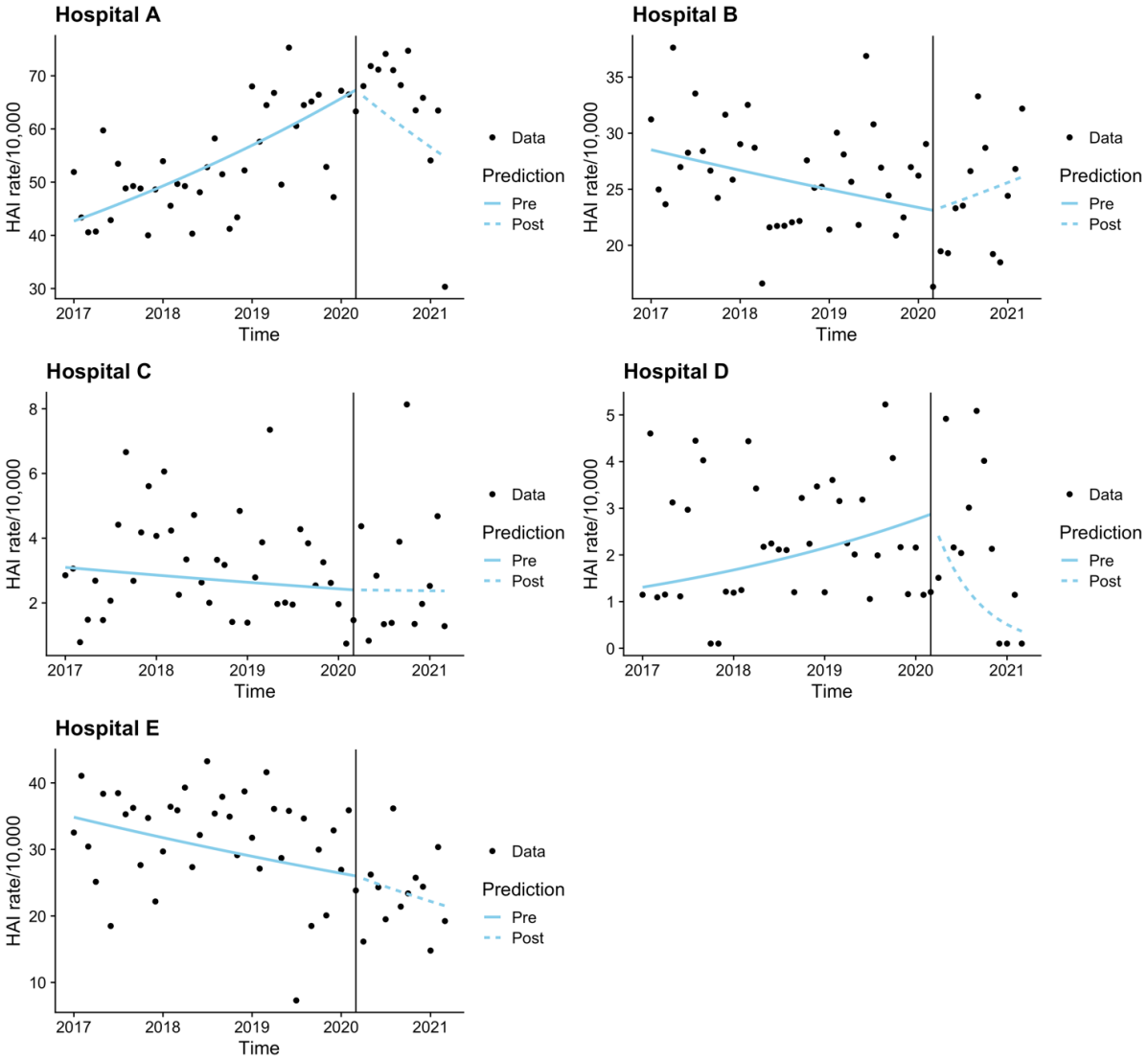

Figure 1: Time series analysis – Combined bloodstream infections and urinary tract infections by hospital

Bloodstream infections by hospital

When combing all BSI data, although a downward trend is noted in the COVID-19 cohort, it was not significant. Hospital A had significant increase in BSI in the pre COVID-19 cohort (p=0.028) and a significant decrease in the COVID-19 cohort (p=0.042). No other significant trends were identified, however Hospitals C, D and E all had downward trends in the COVID-19 cohort.

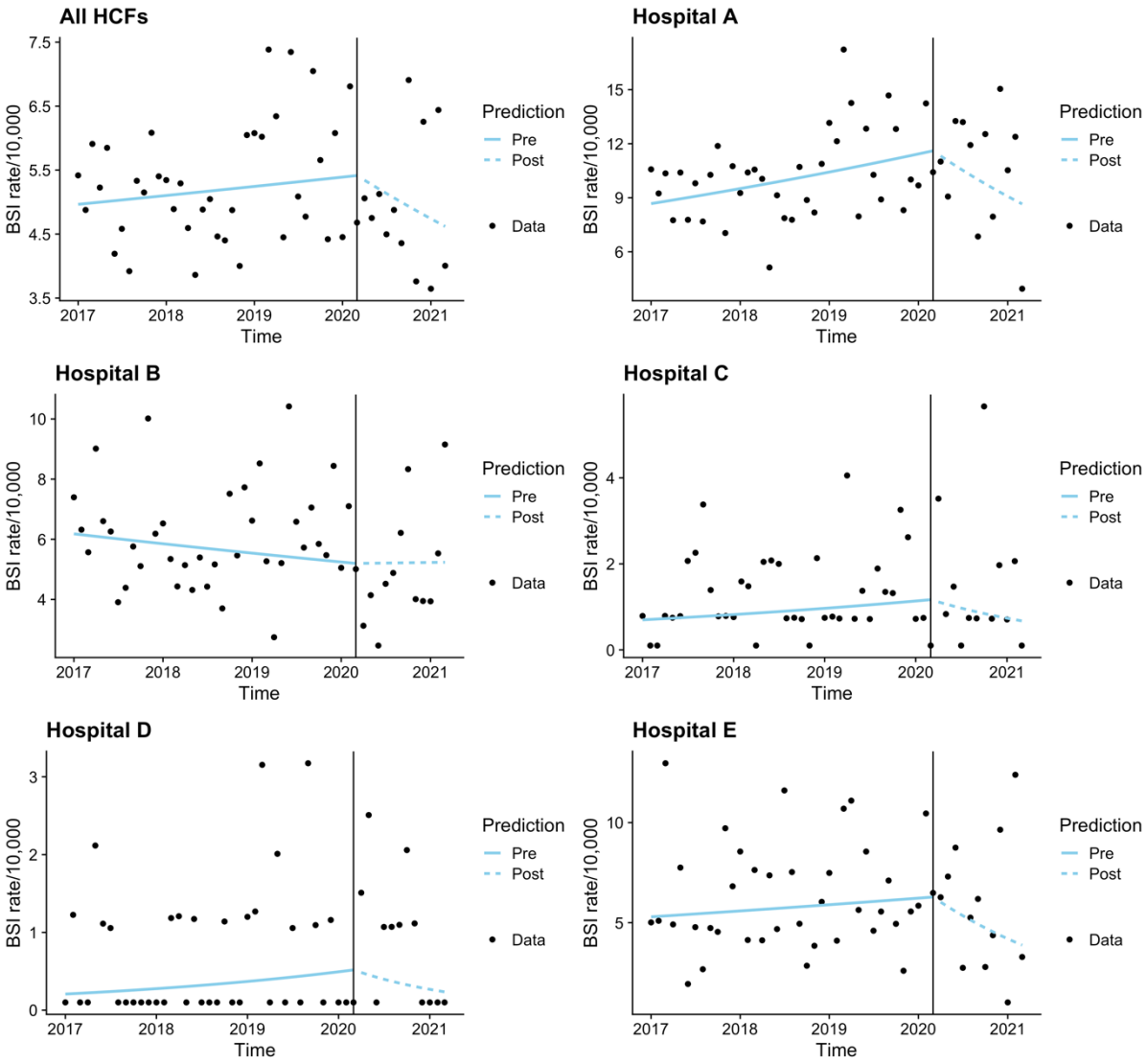

Figure 2: Time series analysis - Bloodstream infections combined and by hospital

UTI by hospital

There is a downward trend in the COVID-19 cohort when combining all hospitals UTI data, however it was not significant. Hospital A had a significant increase in the pre-COVID-19 cohort ($p<0.001$) and a significant decrease in the COVID-19 cohort ($p=0.005$). Hospitals B, C and D all demonstrated significant decreases in UTI in the pre-COVID-19 cohort ($p=0.026$, $p=0.043$ and $p=0.041$ respectively), whilst hospital B and C showed an increase in the COVID-19 cohort, and Hospitals D and E had a downward trend, none were significant.

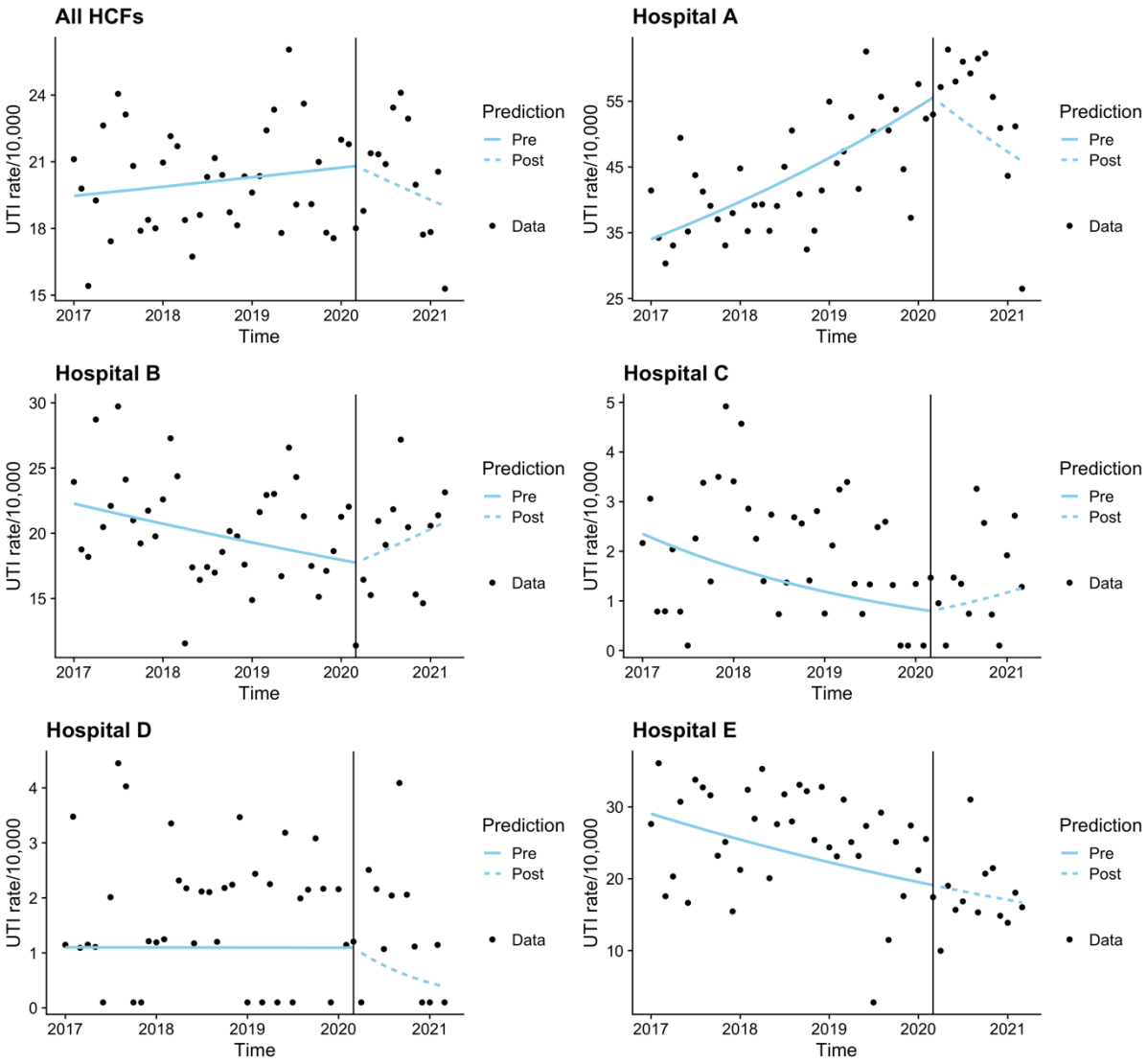

Figure 3: Time series analysis – Urinary tract infections combined and by hospital

Combined infections by state

Combining BSI and UTI data and grouping by state demonstrated that Victoria had a significant increase in the pre-COVID cohort (p=0.005) and a significant decrease in the COVID-19 cohort (p=0.011). No significant trends were identified in combined NSW data

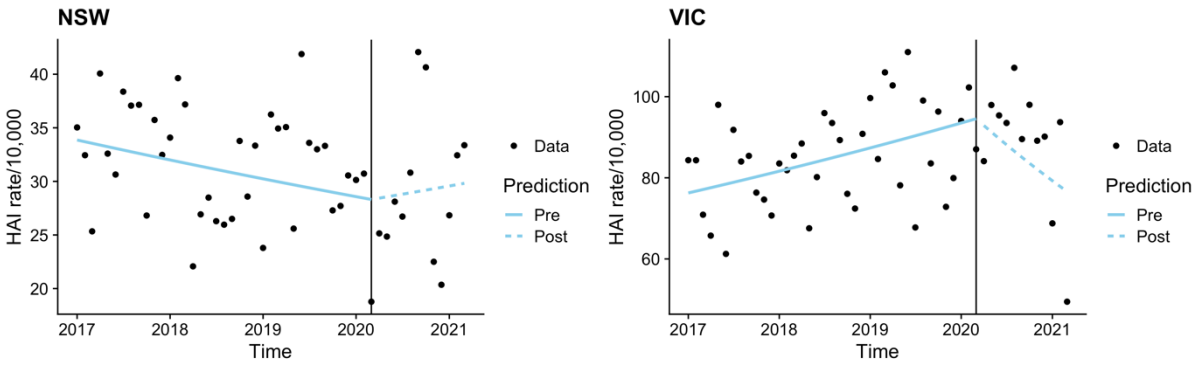

Figure 4: **Time series analysis – Bloodstream infections and Urinary tract infections combined by state**

Discussion

This is the first multicentred study exploring the impact of COVID-19 on healthcare associated infections in Australian hospitals using positive blood and urine cultures post 48 hours admission as a proxy marker, resulting in mixed findings that may have several explanations.

Australia's first case of COVID-19 was identified on 25th January 2020 in Victoria. By mid-March, Australia had closed its international borders, and towards the end of March 2020, States and Territories had implemented stay at home orders. By the end of 2020, there were approximately 28,500 cases Australia wide highlighted by two distinct peaks; nationally in March and April, and in Victoria in June to September.[22] There were also differences in the epidemiology between states. In this study, we reviewed data from Victorian and NSW hospitals only.

Victoria experienced Australia's largest COVID-19 wave in 2020 (Supplementary Figure S3) and implemented enhanced infection prevention measures prior to NSW. This may influence the decrease in HAIs in Victorian hospitals in this data (Hospitals A and E). According to the local epidemiology, hospitals implemented enhanced infection prevention and controls, limitations on visitors and a decrease in elective surgery at various times during the year, largely directed by the local authority. Furthermore, public sector hospitals had a higher burden of COVID-19 patients than the private sector which may have also influenced our data. The inpatient population also changed during 2020. A decrease in elective surgery facilitated the establishment of COVID-19 wards, capacity for intensive care beds increased, and the use of telehealth possibly enabled some patients to remain out of hospital. Staff were redeployed to areas of greatest need, and many staff were furloughed for periods of up to two weeks if they had COVID-19 or were a close contact. Whilst

enhanced infection prevention activity may be expected to reduce HAIs, the changes in patient populations and staff profile may in fact increase the risk of HAI.

Our mixed findings reflect the uncertainty of the effect COVID-19 has had on HAIs in other settings. Although there are numerous reports of increases in HAI,[6,23-30] and decreases,[31-35] variations in settings and methodology prevent comparisons between those findings and with our study.

There are a number of limitations with this study. Without a national HAI surveillance program in Australia, the effect of COVID-19 on HAIs nationally is unable to be estimated. As such, we have used proxy measures of HAI being positive cultures from blood and urine that were sampled greater than 48 hours post admission from five hospitals. We did not explore the triggers for taking cultures within each hospitals, therefore our results could have been influenced by differences in the practices of taking cultures between hospitals. However, we expect that practices for taking cultures within each individual hospital would have remained relatively stable during the study period. Although we had data from five hospitals, the number of positive cultures were relatively small. The period of data collection for the COVID-19 cohort was 13 months, which resulted in lower levels of statistical power to detect trends in the second study period compared with the first period. Finally, differences in reporting between the hospital laboratories meant that we had to report some groups at a genus level only, and data were not reviewed for potential contaminants.

Although the findings of this study are uncertain, such large and widespread increase in the awareness and implementation of infection prevention in hospitals nationally warrant further research. The COVID-19 pandemic has and will continue to have significant impact on healthcare in Australia, whilst much of the response is reactive, we must also continue to explore effectiveness of infection prevention and control measures and adapt as knowledge increases. Further larger studies that aggregate hospitals by state, and by hospital category, with time series analyses performed which consider the local epidemiology of COVID, may provide further insight on the effect of COVID on HAIs.

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Ethical Considerations

Ethics approval was granted by the Alfred Health Human Research Ethics Committee (68438). Informed consent was not possible given the retrospective accessing of large amounts of data, no identifying data was retained for analysis. Governance approvals were obtained where relevant for the participating hospitals.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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1.1. Supplementary File

1.2.

Table S1 - Australian hospital peer groups

Category	Definition
Principal referral hospitals	Provide a very broad range of services, including some very sophisticated services, and have very large patient volumes. Most include an intensive care unit, a cardiac surgery unit, a neurosurgery unit, an Infectious diseases unit and a 24-hour emergency department.
Public acute group A hospitals	Provide a wide range of services to a large number of patients and are usually in metropolitan centres or inner regional areas. Most have an intensive care unit and a 24-hour emergency department. They are among the largest hospitals, but provide a narrower range of services than *Principal referral* hospitals. They have a range of specialist units, potentially including bone marrow transplant, coronary care and oncology units.
Private acute group A hospitals	Private acute hospitals that have a 24-hour emergency department and an intensive care unit, and provide a number of other specialised services such as coronary care, special care nursery, cardiac surgery and neurosurgery.

Australian hospital peer groups. Health services series no. 66. Cat. no. HSE 170. (Canberra: AIHW) (2015).

Table S2- Pathogen Groups

Organism reported	Pathogen Group
Abiotrophia species	Abiotrophia species
Achromobacter species	Achromobacter species
Acinetobacter baumannii complex	Acinetobacter baumannii complex
Acinetobacter species	Acinetobacter species
Actinomyces neuii	Acinetobacter species
Actinomyces species	Acinetobacter species
Actinotignum (Actinobaculum) schaalii	Actinotignum species
Aerococcus sanguinicola	Aerococcus species
Aerococcus urinae	Aerococcus species
Aeromonas species	Aeromonas species
Aeromonas veronii species	Aeromonas veronii species
Aggregatibacter species	Aggregatibacter species
Anaerobic gram negative species	Anaerobic gram negative species
Anaerobic gram positive species	Anaerobic gram positive species
Bacillus species	Bacillus species
Bacteroides species	Bacteroides species
Bifidobacterium species	Bifidobacterium species
Burkholderia cepacia species	Burkholderia cepacia species
Burkholderia species	Burkholderia species
Burkholderia stabilis	Burkholderia species
Campylobacter species	Campylobacter species
Candida albicans	Candida species
Candida dubliniensis	Candida species
Candida glabrata complex	Candida species
Candida species	Candida species
Candida tropicalis	Candida species

Capnocytophaga species	Anaerobic gram negative species
Chryseobacterium species	Chryseobacterium species
Citrobacter amalonaticus	Citrobacter species
Citrobacter farmeri	Citrobacter species
Citrobacter freundii	Citrobacter species
Citrobacter freundii complex	Citrobacter species
Citrobacter koseri	Citrobacter species
Citrobacter species	Citrobacter species
Citrobacter youngae	Citrobacter species
Clavispora (Candida) lusitaniae	Candida species
Clostridium species	Clostridium species
Corynebacterium aurimucosum	Corynebacterium species
Corynebacterium durum	Corynebacterium species
Corynebacterium jeikeium	Corynebacterium species
Corynebacterium species	Corynebacterium species
Cryptococcus species	Cryptococcus species
Delftia species	Delftia species
Dermacoccus species	Dermacoccus species
Elizabethkingia species	Elizabethkingia species
Enterobacter cloacae	Enterobacter species
Enterobacter cloacae complex	Enterobacter species
Enterobacter species	Enterobacter species
Enterococcus avium	Enterococcus species
Enterococcus casseliflavus	Enterococcus species
Enterococcus faecalis	Enterococcus species
Enterococcus faecium	Enterococcus species
Enterococcus faecium (VRE)	VRE species
Enterococcus raffinosus	Enterococcus species
Enterococcus species	Enterococcus species

ESBL	ESBL
Escherichia coli	Escherichia species
Escherichia species	Escherichia species
Flavonifractor species	Flavonifractor species
Fusobacterium species	Fusobacterium species
Gemella species	Gemella species
Geotrichum species	Geotrichum species
Gordonia species	Gordonia species
Gram Negative Rod	Other GNR
Gram Positive Cocci	Gram positive species
Gram positive species	Other GPR
Granulicatella species	Granulicatella species
Haemophilus parainfluenzae	Haemophilus species
Haemophilus species	Haemophilus species
Hafnia alvei	Hafnia species
Hafnia species	Hafnia species
Helicobacter species	Helicobacter species
Klebsiella (Enterobacter) aerogenes	Enterobacter species
Klebsiella oxytoca	Klebsiella species
Klebsiella pneumoniae	Klebsiella species
Klebsiella species	Klebsiella species
Klebsiella variicola	Klebsiella species
Lachnoanaerobaculum species	Lachnoanaerobaculum species
Lactobacillus species	Lactobacillus species
Leclercia species	Leclercia species
Leptotrichia species	Leptotrichia species
Leuconostoc species	Leuconostoc species
Micrococcus species	Micrococcus species
Morganella morganii	Morganella species

Morganella species	Morganella species
MRSA	MRSA
MSSA	MSSA
Mycobacterium abscessus species	Mycobacterium abscessus species
Mycobacterium avium species	Mycobacterium avium species
Mycobacterium bovis	Mycobacterium species
Mycobacterium species	Mycobacterium species
Mycobacterium tuberculosis	Mycobacterium species
Neisseria flavescens species	Neisseria flavescens species
Neisseria species	Neisseria species
Nocardia species	Nocardia species
Other GNR	OTHER GNR
Other GPR	OTHER GPR
Pantoea species	Pantoea species
Parabacteroides species	Parabacteroides species
Paracraurococcus species	Paracraurococcus species
Parvimonas species	Parvimonas species
Peptostreptococcus species	Peptostreptococcus species
Pichia (C. krusei) kudriavzevii	Candida species
Prevotella species	Prevotella species
Proteus mirabilis	Proteus species
Proteus penneri	Proteus species
Proteus species	Proteus species
Proteus vulgaris	Proteus species
Providencia rettgeri	Providencia species
Pseudomonas aeruginosa	Pseudomonas species
Pseudomonas fluorescens	Pseudomonas species
Pseudomonas putida	Pseudomonas species
Pseudomonas species	Pseudomonas species

Raoultella ornithinolytica	Raoultella species
Raoultella planticola	Raoultella species
Raoultella species	Raoultella species
Raoultella terrigena	Raoultella species
Rhizopus microsporus	Rhizopus species
Ruminococcus species	Ruminococcus species
Saccharomyces cerevisiae	Saccharomyces species
Saccharomyces species	Saccharomyces species
Salmonella species	Salmonella species
Scedosporium species	Scedosporium species
Serratia marcescens	Serratia species
Serratia species	Serratia species
Shewanella species	Shewanella species
Sphingomonas species	Sphingomonas species
Staphylococcus aureus	MSSA
Staphylococcus aureus (MRSA)	MRSA
Staphylococcus capitis	MSSA
Staphylococcus epidermidis	Staphylococcus species
Staphylococcus haemolyticus	Staphylococcus species
Staphylococcus hominis	Staphylococcus species
Staphylococcus lugdunensis	Staphylococcus species
Staphylococcus saprophyticus	Staphylococcus species
Staphylococcus simulans	Staphylococcus species
Staphylococcus species	Staphylococcus species
Staphylococcus warneri	Staphylococcus species
Stenotrophomonas maltophilia	Stenotrophomonas species
Stenotrophomonas species	Stenotrophomonas species
Streptococcus agalactiae (Group B)	Streptococcus species
Streptococcus anginosus group	Streptococcus species

Streptococcus dysgalactiae	Streptococcus species
Streptococcus gallolyticus	Streptococcus species
Streptococcus infantarius	Streptococcus species
Streptococcus mitis group	Streptococcus species
Streptococcus pyogenes (Group A)	Streptococcus species
Streptococcus species	Streptococcus species
Trichosporon asahii	Trichosporon species
Trichosporon species	Trichosporon species
Ustilago species	Trichosporon species
Veillonella species	Veillonella species
VRE species	VRE species
Weissella species	Weissella species
Yeast species	Candida species
Yersinia species	Yersinia species

Figure S1 - Comparison of occupied bed days by month

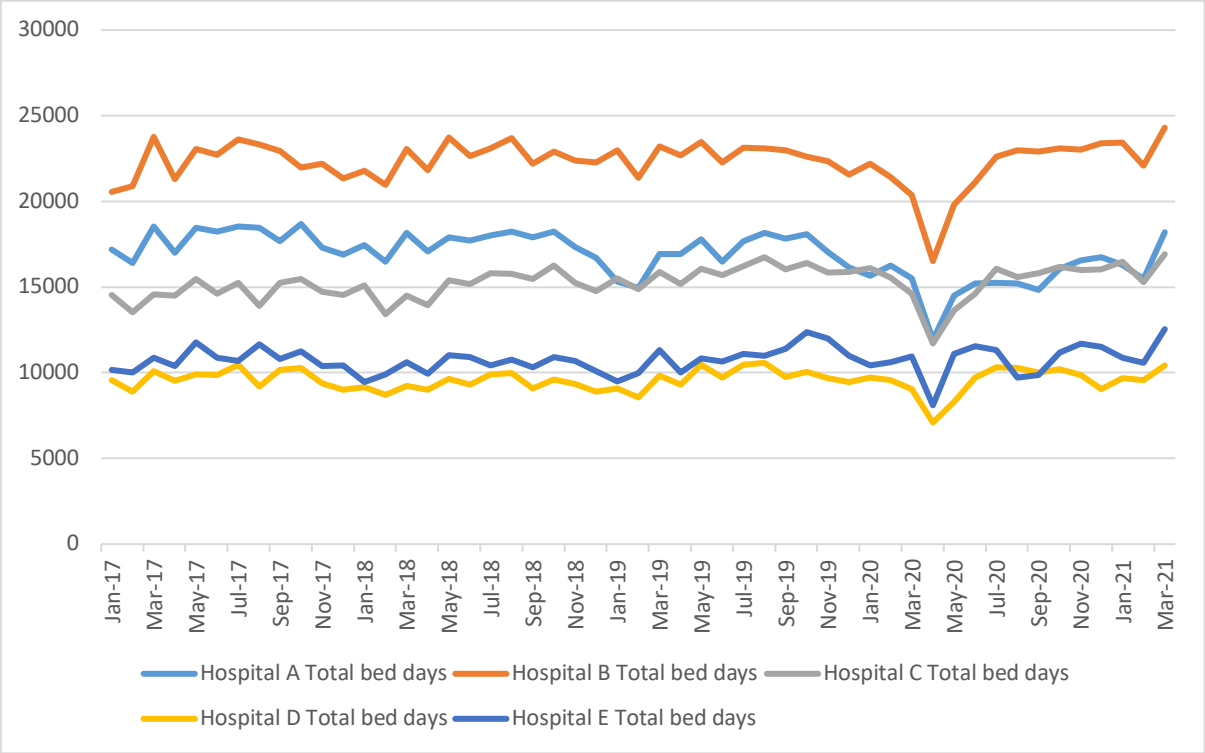

Figure S2: Jack-knife sensitivity analysis

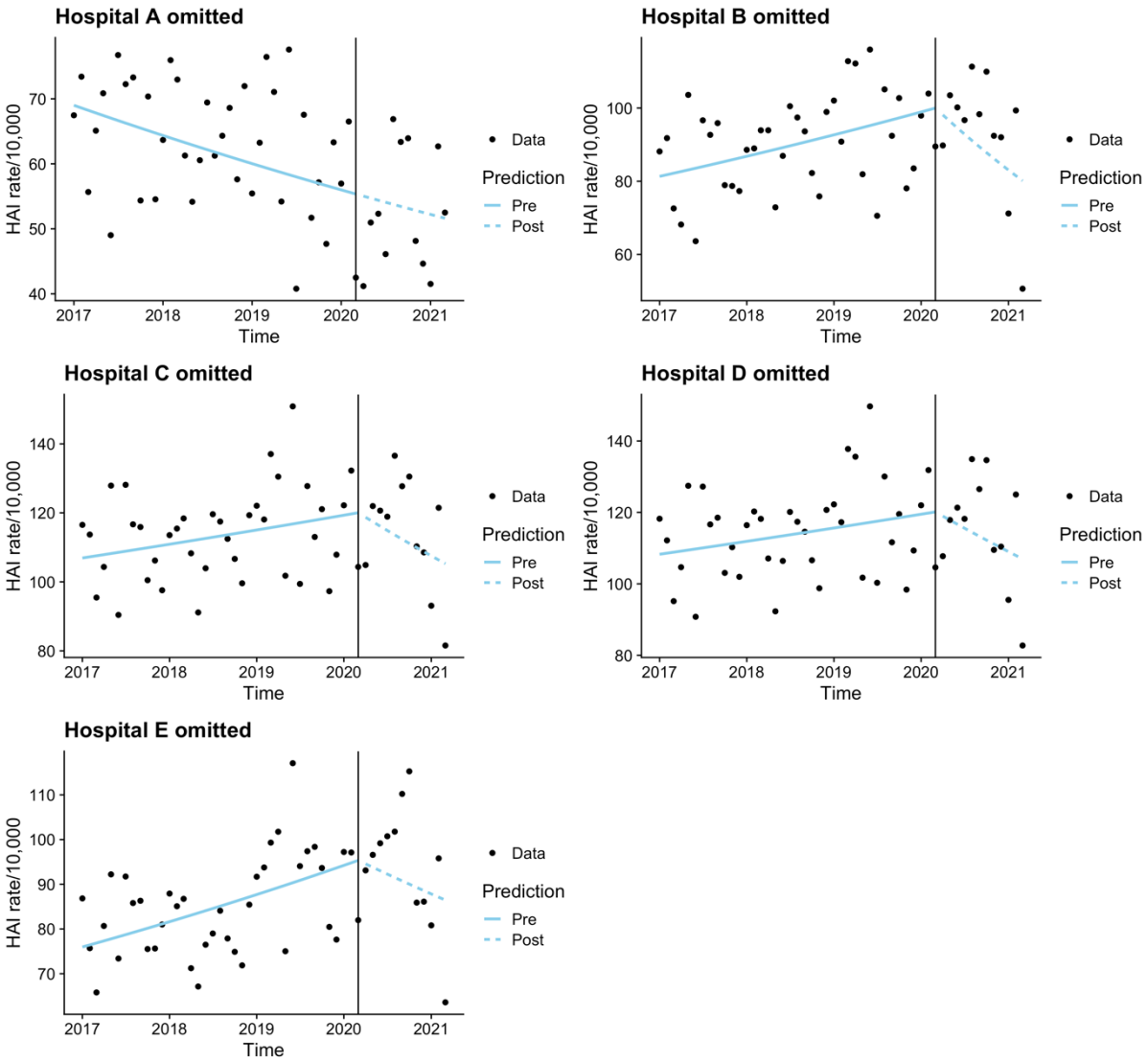

Figure S3: New cases and hospitalisations in Victoria and NSW