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Changes in Rectal Swab Surveillance Activity and Multidrug-Resistant Organism Colonisation Positivity Before and During the COVID-19 Pandemic in a Tertiary-Care Hospital

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Abstract

Background/Objectives: The COVID-19 pandemic may have disrupted hospital surveillance for multidrug-resistant organism (MDRO) colonisation. We assessed changes in rectal swab screening density and MDRO positivity in a tertiary-care hospital. **Methods**: We conducted a retrospective interrupted time-series study of adult hospital admissions and surveillance rectal swab requests in Barcelona, Spain, from January 2018 to December 2021, with March 2020 as the interruption point. Screening density was assessed using all eligible requests per 1000 patient-days, whereas positivity was analysed using patient-level deduplicated requests. Segmented regression models estimated immediate changes and changes in monthly trends. **Results**: Among 101,655 adult hospitalisation episodes, 19,931 requests were eligible for the screening-density analysis. The positivity analysis included 16,863 deduplicated requests, of which 3007 were positive. Although observed screening density increased from 20.02 to 28.29 requests per 1000 patient-days between periods, its estimated level at pandemic onset was lower than projected from the pre-pandemic trend (rate ratio [RR] 0.756, 95% confidence interval [CI] 0.595–0.961). This model-relative change was greater among patients aged ≥65 years than among those aged 18–64 years (ratio of RRs 0.721, 95% CI 0.583–0.890). MDRO positivity decreased (RR 0.512, 95% CI 0.412–0.637), followed by an upward change in the monthly trend (slope-change RR 1.026, 95% CI 1.010–1.042). **Conclusions**: Pandemic onset was associated with screening density below the level projected from the pre-pandemic trend and with reduced detected MDRO positivity. Changes in screening activity and patient selection may have influenced observed positivity, highlighting the importance of maintaining surveillance coverage during healthcare disruptions.

Keywords: antimicrobial resistance; multidrug-resistant organisms; rectal swab screening; COVID-19; interrupted time series; colonisation

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1. Introduction

Antimicrobial resistance (AMR) is a major global public health threat and remains a priority for healthcare systems worldwide. Global burden estimates have documented substantial mortality associated with bacterial AMR and projected further increases in the coming decades [1,2]. In hospital settings, multidrug-resistant organisms (MDROs), including resistant Gram-negative bacteria and vancomycin-resistant enterococci, are particularly relevant because they may colonise patients, spread within healthcare environments and contribute to subsequent healthcare-associated infections in high-risk populations.

Active surveillance using rectal swab screening is an important component of infection prevention and control programmes. Although rectal swabs detect colonisation rather than clinical infection, they provide information on the reservoir of selected MDROs among hospitalised patients and support early implementation of preventive measures. Maintaining surveillance activity is especially important in tertiary-care hospitals, where patients often have complex clinical conditions, prolonged hospital stays, exposure to invasive procedures and increased risk of MDRO acquisition.

The COVID-19 pandemic placed exceptional pressure on hospital systems. Hospitals reorganised staff, beds, care pathways and infection prevention activities to respond to large numbers of patients with COVID-19 [3–5]. These changes may have disrupted AMR surveillance and infection prevention programmes, as suggested by international reports describing interruptions or modifications in surveillance, prevention and control activities during the pandemic [6,7].

The length of hospital stay among patients with COVID-19 [8], together with changes in the volume and diagnostic composition of non-COVID-19 hospital admissions reported in Barcelona during the first pandemic year [9], may have influenced the population undergoing MDRO surveillance. Several studies have examined changes in antimicrobial resistance and antibiotic-resistant infections during the pandemic [10–12]. A time-series study conducted at the University Hospital of Modena assessed changes in antibiotic consumption and the incidence of resistant bloodstream infections during 2015–2021 [13]. However, apparent changes in MDRO detection may reflect both true epidemiological variation and modifications in screening intensity, making it important to evaluate testing activity and positivity together.

The present study aimed to quantify changes associated with the COVID-19 pandemic in MDRO rectal swab surveillance in a tertiary-care university hospital in Barcelona, Spain. Specifically, we assessed monthly changes in screening density, expressed as rectal swabs per 1000 patient-days, and in positivity for selected MDRO colonisation phenotypes detected through surveillance rectal swabs. Rather than assessing antimicrobial resistance in clinical isolates or infection outcomes, this study focuses on the activity of an indication-based hospital surveillance programme. Examining screening density alongside request-level positivity helps contextualise changes in detected MDRO colonisation when surveillance activity may itself vary over time.

2. Results

2.1. Study Population and Screening Activity

A total of 101,655 adult hospitalisation episodes contributed patient-days during the 2018–2021 study period. Characteristics of hospitalisation episodes and surveillance requests are summarised in Table 1.

Table 1. Characteristics of hospitalisation episodes and surveillance rectal swab requests at Clínic Barcelona, 2018–2021.

Variable	Pre-Pandemic	Pandemic	Overall
Hospitalisation episodes			
Adult hospitalisation episodes, *n*	53,424	48,231	101,655
Age 18–64 years, *n* (%)	29,821 (55.8%)	25,784 (53.5%)	55,605 (54.7%)
Age ≥65 years, *n* (%)	23,603 (44.2%)	22,447 (46.5%)	46,050 (45.3%)
Men, *n* (%)	24,918 (46.6%)	23,143 (48.0%)	48,061 (47.3%)
Women, *n* (%)	28,505 (53.4%)	25,083 (52.0%)	53,588 (52.7%)
Sex unknown, *n* (%)	1 (<0.1%)	5 (<0.1%)	6 (<0.1%)
Length of stay, days; median (IQR)	4 (2–8)	4 (2–9)	4 (2–8)
Patient-days, *n*	422,875	405,205	828,080
Eligible surveillance requests (screening density)			
Unique eligible rectal swab requests, *n*	8468	11,463	19,931
Positive requests, *n* (%)	2572 (30.4%)	1791 (15.6%)	4363 (21.9%)
Age 18–64 years, *n* (%)	4016 (47.4%)	5743 (50.1%)	9759 (49.0%)
Age ≥65 years, *n* (%)	4452 (52.6%)	5720 (49.9%)	10,172 (51.0%)
Men, *n* (%)	5303 (62.6%)	7429 (64.8%)	12,732 (63.9%)
Women, *n* (%)	3165 (37.4%)	4034 (35.2%)	7199 (36.1%)
Requests per 1000 patient-days	20.02	28.29	24.07
Requests per 100 admissions	15.85	23.77	19.61
Deduplicated requests (primary positivity)			
Unique deduplicated requests, *n*	6907	9956	16,863
Positive requests, *n* (%)	1692 (24.5%)	1315 (13.2%)	3007 (17.8%)
Negative requests, *n* (%)	5215 (75.5%)	8641 (86.8%)	13,856 (82.2%)
Age 18–64 years, *n* (%)	3275 (47.4%)	4923 (49.4%)	8198 (48.6%)
Age ≥65 years, *n* (%)	3632 (52.6%)	5033 (50.6%)	8665 (51.4%)
Men, *n* (%)	4307 (62.4%)	6409 (64.4%)	10,716 (63.5%)
Women, *n* (%)	2600 (37.6%)	3547 (35.6%)	6147 (36.5%)

Data are presented as *n* (%) or median (IQR), unless otherwise indicated. Hospitalisation episodes ($n = 101,655$) contributed patient-days during the study period. Requests were assigned to periods by laboratory request date. Age and sex distributions for surveillance requests use the corresponding request-level denominators (all eligible or deduplicated). Screening density is a descriptive crude rate and should be distinguished from the interrupted time-series (ITS) level change relative to the counterfactual projection. Descriptive *p*-values are omitted because repeated episodes or requests from individual patients may violate independence assumptions.

The original microbiological files contained 25,752 laboratory result records, corresponding to 23,700 unique laboratory requests. Of these, 3764 could not be linked to an eligible adult hospitalisation episode: 1255 had no matching patient identifier in the original admission database, 219 belonged to patients without an eligible hospitalisation episode, and 2290 were recorded outside the dates of an otherwise eligible hospitalisation episode. After linkage, 19,936 requests were identified, of which 19,931 had interpretable microbiological results and were included in the screening-density analysis (8468 pre-pandemic and 11,463 pandemic).

After applying the patient-level deduplication procedure based on the first observed detection of each microorganism–resistance combination, 16,863 unique requests were retained for the primary positivity analysis (6907 pre-pandemic and 9956 pandemic). Among these, 3007 requests (17.8%) were positive for at least one selected resistant microorganism: 1692 (24.5%) before the pandemic and 1315 (13.2%) during the pandemic. The remaining 13,856 requests were negative. The distribution of resistant organism groups among deduplicated surveillance requests by study period is presented in Supplementary Table S3.

The construction of the analytical datasets, including the distinction between microbiological result records, unique laboratory requests, and deduplicated requests, is summarised in Supplementary Table S1.

2.2. Impact of the COVID-19 Pandemic on Screening Density

Before March 2020, the fitted screening-density trend increased by approximately 3.4% per month (RR 1.034, 95% CI 1.023–1.046; $p < 0.001$). At pandemic onset, screening density was estimated to be 24.4% lower than the level projected under continuation of the pre-pandemic trend (RR 0.756, 95% CI 0.595–0.961; $p = 0.022$). This model-based comparison does not imply a decrease in observed screening activity between periods: crude screening density increased from 20.02 to 28.29 eligible requests per 1000 patient-days. No significant change in the subsequent monthly slope relative to the pre-pandemic trend was observed (RR 1.001, 95% CI 0.984–1.019; $p = 0.899$). The observed, fitted, and counterfactual trajectories are shown in Figure 1, with model estimates in Table 2.

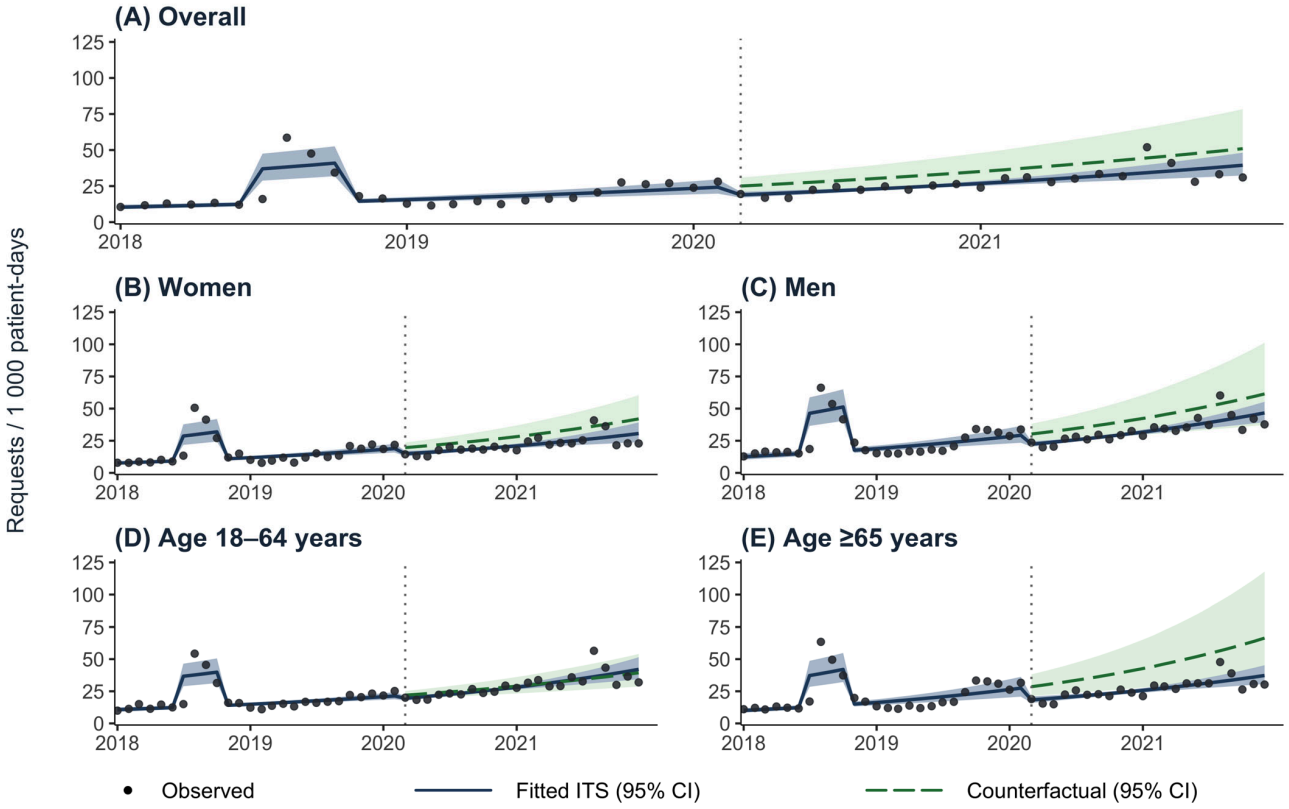


Figure 1. Monthly rectal swab screening density before and during the COVID-19 pandemic at Clínic Barcelona, 2018–2021. (**A**) Overall population; (**B**) women; (**C**) men; (**D**) patients aged 18–64 years; and (**E**) patients aged ≥65 years. Screening density is expressed as eligible unique surveillance requests per 1000 patient-days. Points represent observed monthly values; solid lines and shaded bands show fitted ITS estimates and 95% confidence intervals. Dashed lines and corresponding bands represent model-based counterfactual projections and 95% confidence intervals, assuming continuation of the pre-pandemic trend. The vertical dotted line indicates March 2020, the analytical interruption point.

Screening Density Stratified Analysis by Sex and Age

At pandemic onset, screening density was estimated to be below the corresponding counterfactual projections for both women (RR 0.757, 95% CI 0.596–0.962; $p = 0.023$) and men (RR 0.740, 95% CI 0.575–0.950; $p = 0.018$). However, the formal interaction analysis did not indicate a significant difference between sexes (ratio of RRs 0.977, 95% CI 0.864–1.104; $p = 0.706$).

Table 2. Interrupted time series analysis of MDRO rectal swab screening density and colonisation positivity at Clínic Barcelona, 2018–2021.

	Pre-Intervention Trend		Step Change		Post-Intervention Slope Change	
Subgroup	**RR (95% CI)**	***p*-Value**	**RR (95% CI)**	***p*-Value**	**RR (95% CI)**	***p*-Value**
Screening density						
Overall	1.034 (1.023–1.046)	<0.001	0.756 (0.595–0.961)	0.022	1.001 (0.984–1.019)	0.899
Sex						
Women	1.037 (1.027–1.046)	<0.001	0.757 (0.596–0.962)	0.023	0.998 (0.979–1.018)	0.853
Men	1.034 (1.020–1.048)	<0.001	0.740 (0.575–0.950)	0.018	1.001 (0.984–1.019)	0.888
ratio of RRs	0.998 (0.989–1.007)	0.596	0.977 (0.864–1.104)	0.706	1.003 (0.992–1.015)	0.592
Age Group						
18–64 years	1.028 (1.019–1.038)	<0.001	0.890 (0.754–1.051)	0.168	1.009 (0.992–1.025)	0.294
≥65 years	1.041 (1.026–1.056)	<0.001	0.641 (0.465–0.885)	0.007	0.994 (0.974–1.014)	0.537
ratio of RRs	1.012 (1.002–1.023)	0.019	0.721 (0.583–0.890)	0.002	0.985 (0.974–0.996)	0.011
MDRO colonisation positivity						
Overall	0.989 (0.978–1.000)	0.047	0.512 (0.412–0.637)	<0.001	1.026 (1.010–1.042)	0.001
Sex						
Women	0.991 (0.979–1.003)	0.149	0.480 (0.355–0.648)	<0.001	1.023 (1.004–1.043)	0.018
Men	0.987 (0.975–0.999)	0.038	0.532 (0.434–0.653)	<0.001	1.029 (1.012–1.047)	<0.001
ratio of RRs	0.996 (0.985–1.007)	0.492	1.109 (0.889–1.383)	0.359	1.006 (0.988–1.024)	0.527
Age Group						
18–64 years	0.990 (0.977–1.003)	0.140	0.467 (0.366–0.595)	<0.001	1.029 (1.010–1.048)	0.002
≥65 years	0.987 (0.976–0.999)	0.028	0.566 (0.440–0.727)	<0.001	1.025 (1.007–1.043)	0.005
ratio of RRs	0.997 (0.986–1.008)	0.604	1.212 (0.963–1.526)	0.102	0.996 (0.980–1.012)	0.611

RR, rate ratio; CI, confidence interval. Estimates are RR (95% CI) with corresponding *p* values. Pre-trend and slope effects are monthly. Step: immediate level change at March 2020. Comparison rows show ratios of RRs and formal pooled-model interaction tests. Screening density uses all 19,931 eligible requests; positivity uses 16,863 deduplicated requests. Group analyses are exploratory, with unadjusted *p* values. For sex, ratios of RRs compare men with women; for age, they compare patients aged ≥65 years with those aged 18–64 years.

By age group, the estimated immediate deviation below the projected pre-pandemic trajectory was greater among patients aged ≥65 years (RR 0.641, 95% CI 0.465–0.885; $p = 0.007$) than among those aged 18–64 years (RR 0.890, 95% CI 0.754–1.051; $p = 0.168$). This difference was supported by the age-by-intervention interaction (ratio of RRs 0.721, 95% CI 0.583–0.890; $p = 0.002$).

2.3. Impact of the COVID-19 Pandemic on MDRO Colonisation Positivity

Before March 2020, MDRO positivity among deduplicated surveillance requests showed a slight decreasing monthly trend (RR 0.989, 95% CI 0.978–1.000; $p = 0.047$). At pandemic onset, the ITS model estimated a significant immediate reduction in positivity of approximately 49% (RR 0.512, 95% CI 0.412–0.637; $p < 0.001$). This was followed by a significant upward change in the monthly slope relative to the pre-pandemic trend (slope-change RR 1.026, 95% CI 1.010–1.042; $p = 0.001$). The temporal trajectories are presented in Figure 2, with model estimates in Table 2.

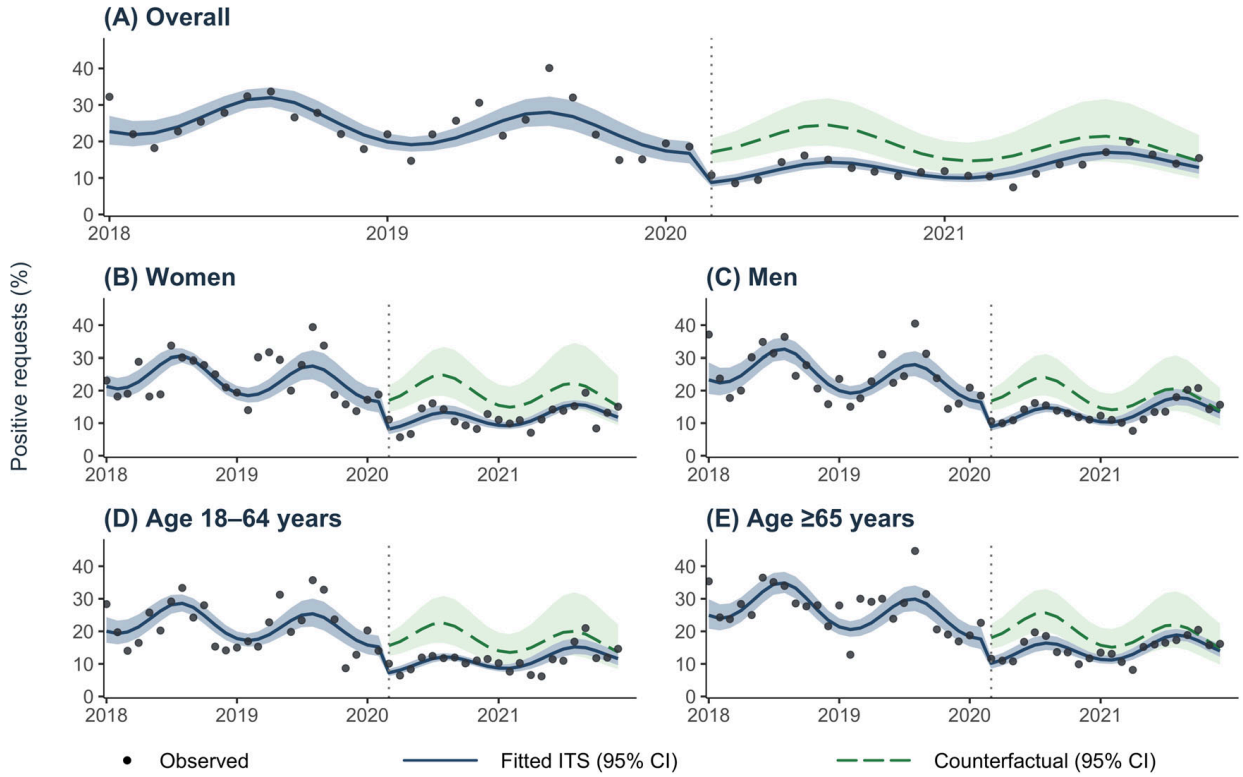


Figure 2. Monthly MDRO positivity among deduplicated rectal swab surveillance requests before and during the COVID-19 pandemic at Clínic Barcelona, 2018–2021. (**A**) Overall population; (**B**) women; (**C**) men; (**D**) patients aged 18–64 years; and (**E**) patients aged ≥65 years. Positivity is expressed as the percentage of deduplicated surveillance requests with at least one selected resistant microorganism detected. Points represent observed monthly values; solid lines and shaded bands show fitted ITS estimates and 95% confidence intervals. Dashed lines and corresponding bands represent model-based counterfactual projections and 95% confidence intervals, assuming continuation of the pre-pandemic trend. The vertical dotted line indicates March 2020, the analytical interruption point. The fitted ITS curves were obtained using negative binomial regression with a log link and annual seasonal harmonic terms. Heteroskedasticity- and autocorrelation-consistent (HAC) standard errors were calculated using a lag of two months.

MDRO Positivity Stratified Analysis by Sex and Age

At pandemic onset, positivity decreased significantly among both women (RR 0.480, 95% CI 0.355–0.648) and men (RR 0.532, 95% CI 0.434–0.653), with no significant difference in the immediate change between sexes (ratio of RRs 1.109, 95% CI 0.889–1.383; $p = 0.359$).

Similarly, significant immediate reductions were observed among patients aged 18–64 years (RR 0.467, 95% CI 0.366–0.595) and those aged ≥65 years (RR 0.566, 95% CI 0.440–0.727). However, the age-by-intervention interaction was not statistically significant (ratio of RRs 1.212, 95% CI 0.963–1.526; $p = 0.102$). Positive changes in the post-intervention slope relative to the pre-pandemic trend were observed across both sex and age subgroups.

2.4. Sensitivity Analyses

Sensitivity analyses supported the immediate reduction in detected MDRO positivity across alternative analytical definitions and model specifications (Supplementary Table S2). Similar results were obtained when all eligible surveillance requests were included (RR 0.518, 95% CI 0.423–0.635) and when positivity was analysed using logistic regression in the deduplicated dataset (OR 0.454, 95% CI 0.345–0.599). Admission-level analyses also showed immediate reductions, both when considering the first positive detection per admission (OR 0.471, 95% CI

0.364–0.609) and when analysing screened admissions with at least one positive surveillance request (OR 0.527, 95% CI 0.404–0.688).

For screening density, the estimated immediate level-change ratios were consistently below 1, although their magnitude and statistical significance varied across analytical specifications. The primary analysis yielded an RR of 0.756 (95% CI 0.595–0.961), whereas the analysis using deduplicated requests yielded an RR of 0.800 (95% CI 0.608–1.052), exclusion of March–April 2020 yielded an RR of 0.775 (95% CI 0.598–1.004), and restriction of the observation period to November 2018 onwards yielded an RR of 0.677 (95% CI 0.531–0.865). These estimates were directionally consistent but differed in statistical precision (Supplementary Table S2).

An additional sensitivity analysis examined positivity according to the timing of surveillance requests relative to hospital admission (Supplementary Table S5). Using admission calendar days 0–1 as a proxy for early screening, positivity among deduplicated requests decreased from 21.3% before the pandemic to 12.3% during the pandemic for early requests, and from 26.7% to 13.9% for later requests. ITS analyses showed immediate reductions in both groups (early: OR 0.576, 95% CI 0.375–0.885; later: OR 0.367, 95% CI 0.257–0.524). The interaction comparing later with early requests was not statistically significant (ratio of ORs 0.637, 95% CI 0.368–1.100; $p = 0.106$).

Analyses including all eligible requests also showed immediate reductions in both timing groups (early: OR 0.612, 95% CI 0.420–0.893; later: OR 0.343, 95% CI 0.245–0.479), with a statistically significant interaction (ratio of ORs 0.560, 95% CI 0.350–0.896; $p = 0.016$). Alternative classification using admission calendar days 0–2 yielded similar reductions, although the strength of evidence for differences between early and later screening depended on the analytical definition. Because collection times were unavailable, these categories represent calendar-day proxies rather than exact 48-h intervals or confirmed clinical screening indications.

3. Discussion

This study found that the onset of the COVID-19 pandemic was associated with an immediate screening-density level below that projected from the pre-pandemic trend, despite an increase in crude screening density between the study periods. The estimated deviation from the projected trajectory was greater among patients aged ≥65 years than among those aged 18–64 years. MDRO positivity among surveillance requests also decreased sharply at pandemic onset, followed by an upward change in the monthly trend relative to the pre-pandemic slope. These findings reflect changes in surveillance activity and detected colonisation positivity, rather than clinical infection incidence or confirmed patient-to-patient transmission.

The pronounced but transient increase in screening density observed in 2018 coincided with a known hospital outbreak and the associated intensification of rectal swab surveillance. This episode likely explains the short-term peak observed during the pre-pandemic period and reflects outbreak-driven surveillance activity rather than a sustained change in screening practice. Patient-level outbreak investigation data were not available for the present analysis.

The screening-density findings should be interpreted in light of the sensitivity analyses. Although the estimated immediate level-change ratios were consistently below 1, the magnitude and statistical precision of the estimates varied across analytical specifications. In particular, the confidence intervals included 1 when deduplicated requests were analysed or March–April 2020 was excluded, whereas the analysis restricted to November 2018 onwards supported a more pronounced deviation below the projected trajectory. Therefore, the evidence for an immediate change relative to the pre-pandemic trend was

sensitive to modelling decisions and should not be interpreted as a reduction in crude screening activity.

The significant age-by-intervention interaction indicates a greater immediate deviation below the projected pre-pandemic screening-density trajectory among patients aged ≥65 years. Because the models incorporated patient-days as an offset, this finding cannot be explained solely by differences in admission numbers. However, the available data do not allow us to determine whether this pattern reflected changes in adherence to screening indications, patient case-mix, or other operational factors. Differential screening activity may also have influenced observed positivity across age groups. These findings are consistent with reports of pandemic-related disruption of antimicrobial resistance surveillance and infection prevention and control activities [6].

The immediate reduction in MDRO positivity coincided with the introduction of strict infection prevention and control measures for SARS-CoV-2, including reinforced hand hygiene, masking, contact precautions and changes in patient flow. Previous studies have reported heterogeneous changes in healthcare-associated infections and MDRO outcomes during the COVID-19 pandemic. Reductions in selected infections or resistant organisms were observed in some settings [14–16], whereas other studies documented pathogen-specific and time-dependent variations [17,18]. Notably, Dabaja-Younis et al. reported increased carbapenem-resistant Enterobacterales despite reductions in other resistant organisms [17]. In our data, this pattern could reflect changes in colonisation detection, transmission opportunities, patient case-mix, or a combination of these factors.

The upward change in the post-intervention positivity trend may be compatible with several factors described in the literature, including changes in hospital antimicrobial consumption [10] and pandemic-related pressures on hospital infection prevention and MDRO control [19–22]. Previous research has also documented heterogeneous patterns of antimicrobial resistance during the COVID-19 pandemic [11]. However, these mechanisms could not be directly assessed using the available data. Importantly, this increase occurred after the marked immediate reduction in positivity observed at pandemic onset. Despite the subsequent increase, the fitted pandemic-period trajectory remained below the counterfactual projection based on continuation of the pre-pandemic trend. Thus, the observed post-intervention pattern is better interpreted as a partial rebound from the initial decline rather than as an increase above the level that would have been expected in the absence of the pandemic.

The study contributes most directly to the understanding of surveillance resilience. The distinction between all eligible rectal swab surveillance requests and the deduplicated dataset used for the primary positivity analysis, together with the age-stratified changes in screening density, highlights the importance of evaluating surveillance activity and detected MDRO positivity separately during periods of health-system disruption. Future surveillance evaluations should incorporate screening indications, patient-days, ward location and patient risk groups to assess whether surveillance coverage is maintained.

From a practical perspective, the findings support maintaining MDRO surveillance capacity during public health emergencies, consistent with recommendations to strengthen AMR surveillance and stewardship [23]. Evaluating the relationship between antimicrobial use, stewardship interventions and the observed trends would require antimicrobial consumption data, prescribing indicators and information on stewardship interventions, which were unavailable in this study [10].

Overall, these findings highlight the importance of evaluating surveillance systems not only in terms of MDRO detections, but also according to whether screening coverage is maintained across patient groups.

Limitations

This study has several limitations. First, it was based on retrospective surveillance rectal swabs and therefore measured gastrointestinal colonisation detected through screening, not clinical infection. Second, the study did not include clinical infection episodes, ward-level exposure, outbreak investigation data, antimicrobial use, device use, staffing measures or molecular typing; consequently, the analysis cannot confirm transmission pathways, antimicrobial selection pressure or clinical impact.

Third, screening was indication-based rather than universal. Although formal screening indications remained unchanged throughout the study period, adherence to these indications could not be systematically assessed and may have varied during periods of high clinical workload. Changes in the patients selected for screening could therefore have influenced both screening density and observed positivity independently of underlying MDRO colonisation prevalence. Although additional sensitivity analyses classified requests as early or later according to their timing relative to hospital admission, the available data contained calendar dates rather than exact collection times. Therefore, these classifications could not reliably distinguish admission screening from follow-up screening or establish an exact 48-h interval.

Furthermore, vancomycin-resistant enterococci (VRE) were detected incidentally on CHROMID CARBA SMART medium rather than through systematic selective VRE screening. Consequently, organism-specific VRE positivity estimates should be interpreted cautiously, as VRE ascertainment was not systematic during the study period.

A hospital outbreak in 2018 temporarily intensified screening activity and may have influenced the estimated pre-pandemic trend and corresponding counterfactual projection. Although the estimated immediate screening-density level changes were consistently below the counterfactual projections, their magnitude and statistical significance varied across sensitivity analyses. Accordingly, the screening-density findings should not be interpreted as a reduction in crude screening activity.

Finally, the greater immediate deviation below the projected screening-density trajectory among patients aged ≥65 years, supported by a significant age-by-intervention interaction, raises the possibility of differential ascertainment in positivity estimates. However, the corresponding interaction for the immediate change in positivity was not statistically significant. Consequently, changes in observed positivity cannot be assumed to reflect equivalent changes in underlying colonisation prevalence. This was also a single-centre study, which may limit generalisability to hospitals with different baseline epidemiology, screening policies or pandemic responses. Despite these limitations, the ITS design provides useful evidence on temporal changes in surveillance activity and detected colonisation positivity over the study period.

4. Materials and Methods

4.1. Study Setting and Design

The study used an ITS design [24,25] and was conducted at Clínic Barcelona, a 700-bed tertiary university hospital in Barcelona, Spain. The hospital admits adult medical, surgical and intensive-care patients. The study population included hospitalisation episodes of adults aged ≥18 years, with a length of stay of at least one day, that overlapped the study period from 1 January 2018 to 31 December 2021. This hospital-wide cohort was used to calculate patient-days and to provide the denominator for screening density. Laboratory data were restricted to surveillance rectal swabs; clinical samples from other sites were excluded.

4.2. Screening Policy and Microbiological Scope

The hospital maintained an institutional infection prevention and control programme that included active surveillance for selected resistant Gram-negative bacteria and methicillin-resistant *Staphylococcus aureus* (MRSA). During the study period, vancomycin-resistant enterococci (VRE) were not subject to dedicated selective screening but could be identified incidentally during the processing of surveillance samples, as detailed in Section 4.3.

According to the established surveillance protocol, screening was indicated upon admission and weekly thereafter for immunosuppressed patients, patients admitted to intensive care units, and referred patients. Screening was also indicated for patients readmitted with a documented history of multidrug-resistant organism colonisation. Furthermore, when at least one patient in a ward tested positive for a target organism, either through clinical or surveillance sampling, weekly screening was performed until no further positive detections were recorded for two consecutive weeks.

The formal indications for surveillance screening remained unchanged throughout the study period (2018–2021), including during the COVID-19 pandemic. However, adherence to these indications could not be systematically assessed using the available retrospective data.

The present study was restricted to rectal swabs collected for active surveillance of selected resistant microorganisms. Nasal swabs, environmental surveillance samples, and clinical specimens collected for diagnostic purposes were not included. Positive surveillance results were interpreted as detected colonisation rather than confirmed hospital acquisition or patient-to-patient transmission.

4.3. Microbiological Procedures

Rectal swab surveillance samples were processed using CHROMID® ESBL and CHROMID® CARBA SMART selective chromogenic media (bioMérieux, Marcy-l'Étoile, France), as part of the hospital's established surveillance programme. The broader institutional programme also included CHROMID® MRSA; however, MRSA surveillance was not considered in the present analysis.

Colonies growing on the selective media were identified by matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS), using a Microflex LT benchtop instrument (Bruker Daltonics, Bremen, Germany).

Antimicrobial susceptibility testing was performed by disc diffusion (Becton Dickinson, Heidelberg, Germany) on Mueller–Hinton agar [26]. Results were interpreted according to the EUCAST clinical breakpoint tables applicable in each study year (2018–2021) [27].

For Enterobacterales, antimicrobial susceptibility testing included ampicillin, amoxicillin/clavulanic acid, cefuroxime, cefoxitin, cefotaxime, ceftazidime, cefepime, aztreonam, piperacillin/tazobactam, imipenem, meropenem, ertapenem, gentamicin, amikacin, tobramycin, ciprofloxacin, temocillin and trimethoprim/sulfamethoxazole. For *Pseudomonas aeruginosa*, the agents included ceftazidime, cefepime, aztreonam, piperacillin/tazobactam, imipenem, meropenem, amikacin, tobramycin, ciprofloxacin, ceftazidime/avibactam and ceftolozane/tazobactam. For *Acinetobacter baumannii*, testing included ceftazidime, cefepime, aztreonam, piperacillin/tazobactam, imipenem, meropenem, amikacin, tobramycin, ciprofloxacin, ceftazidime/avibactam, ceftolozane/tazobactam and trimethoprim/sulfamethoxazole.

The principal agents relevant to the surveillance phenotypes were cefotaxime and ceftazidime for third-generation cephalosporin resistance in Enterobacterales; imipenem, meropenem and ertapenem for carbapenem resistance in Enterobacterales; and imipenem and meropenem for carbapenem resistance in *P. aeruginosa* and *A. baumannii*.

Resistance mechanisms were further characterised using NG-Test® CTX-M Multi and NG-Test® CARBA 5 immunochromatographic assays (NG Biotech, Guipry, France), which detect CTX-M-type extended-spectrum β-lactamases and KPC, IMP, VIM, NDM and OXA-48-like carbapenemases, respectively.

During the study period, vancomycin-resistant enterococci (VRE) were detected incidentally following growth on CHROMID® CARBA SMART plates, rather than through dedicated selective VRE screening. Suspected VRE isolates were confirmed using the GeneXpert system (Cepheid, Sunnyvale, CA, USA) to detect the *vanA* and *vanB* resistance genes. A dedicated selective VRE culture medium was introduced in 2023, outside the study period.

The microbiological screening procedures remained unchanged throughout 2018–2021, including during the COVID-19 pandemic.

4.4. Data Sources

Data were retrospectively extracted from the hospital information system and the laboratory information system, which routinely record hospital admissions and microbiological surveillance activity at Clínic Barcelona.

Hospital admission data included patient identifiers, sex, age, admission and discharge dates, and length of stay. Laboratory records included patient identifiers, rectal swab collection dates, laboratory request identifiers, microorganism identification, and antimicrobial resistance results.

Hospital and laboratory records were linked using patient identifiers and the temporal correspondence between laboratory request dates and eligible hospital admission episodes. As a single laboratory request could generate multiple microbiological result records, these records were consolidated at the request level before analysis.

The available analytical dataset did not include the clinical indication for each surveillance request, confirmed admission-versus-follow-up screening status, ward-level location, COVID-19 status, antimicrobial exposure, clinical infection episodes, or outbreak investigation records. However, hospital admission and laboratory request dates were available, allowing requests to be classified according to their timing relative to admission as a proxy for early versus later screening. Because exact collection times and screening indications were unavailable, this approach could not identify an exact 48-h interval or reliably distinguish admission screening from follow-up screening. Analyses stratified by the remaining unavailable clinical variables could not be performed.

Microbiological surveillance data preceding January 2018 were not available for retrieval. Therefore, previously documented colonisation before the start of the study could not be systematically identified.

The datasets were cleaned and processed in accordance with institutional data protection requirements. Only aggregated results are reported in this study.

4.5. Definitions

The surveillance targets included Enterobacterales resistant to third-generation cephalosporins or carbapenems, carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Acinetobacter baumannii*, and vancomycin-resistant enterococci (VRE). The antimicrobial agents relevant to these resistance phenotypes and their interpretation according to the annual EUCAST clinical breakpoint tables are described in Section 4.3. These organisms are collectively referred to as multidrug-resistant organisms (MDROs) for consistency with the institutional surveillance programme, although individual resistance phenotypes do not necessarily fulfil the formal definition of multidrug resistance [28].

The microbiological database contained individual laboratory results rather than exclusively unique rectal swab requests. A single laboratory request could generate multiple results corresponding to different microorganisms or resistance phenotypes. Accordingly, laboratory result records, unique requests, and microorganism–resistance detections were distinguished.

For the primary positivity analysis, the original patient-level deduplication rule was applied. The first observed positive calendar date for each distinct microorganism–resistance combination was identified for each patient during 2018–2021. Subsequent detections of the same combination were excluded, whereas first detections of additional combinations were retained. Distinct laboratory requests recorded on the same first positive date were also retained. Negative requests were included until the patient's first observed positive detection; subsequent negative requests were excluded.

For request-level positivity, each retained laboratory request was counted only once and classified as positive when at least one eligible first detection was recorded, irrespective of the number of microorganism–resistance combinations identified. For descriptive analyses, detections were additionally grouped into four categories: third-generation cephalosporin- or carbapenem-resistant Enterobacterales, carbapenem-resistant *Pseudomonas aeruginosa*, carbapenem-resistant *Acinetobacter baumannii*, and VRE.

The first observed positive result during the study period was not necessarily the patient's first-ever colonisation episode. Previous colonisation before January 2018 could not be excluded, and positive surveillance results were not interpreted as confirmed hospital acquisition or transmission.

4.6. Study Periods

The study covered 48 consecutive months, from 1 January 2018 to 31 December 2021. Two periods were defined for the ITS analysis: a pre-pandemic period comprising 26 months (January 2018–February 2020) and a pandemic period comprising 22 months (March 2020–December 2021).

March 2020 was selected as the intervention point because it marked the beginning of the major disruption to hospital organisation and healthcare delivery associated with the COVID-19 pandemic in Spain. The nationwide state of alarm was declared on 14 March 2020 [29]; however, as the surveillance data were aggregated monthly, 1 March 2020 was used as the analytical interruption point.

The pandemic period was modelled as a single intervention phase, although successive pandemic waves differed in hospital pressure and infection prevention and control measures. Accordingly, the estimated immediate level and subsequent slope changes should be interpreted as temporal associations with pandemic onset, rather than causal effects attributable to a specific pandemic wave or intervention.

A period of increased screening activity associated with a hospital outbreak in 2018 was also identified. To account for its potential influence on the pre-pandemic screening trajectory, the screening-density models included an indicator for July–October 2018. Additional sensitivity analyses examined the influence of the early outbreak period on the estimated intervention effects and counterfactual projections.

4.7. Statistical Analysis

Descriptive analyses were performed to characterise hospital admissions and rectal swab surveillance activity before and during the COVID-19 pandemic. Categorical variables were summarised as frequencies and percentages, and continuous variables as medians and interquartile ranges. Given the large sample size and the possibility of repeated admissions or screening requests from individual patients, descriptive compar-

isons were presented without conventional significance tests based on the assumption of independent observations.

Monthly surveillance outcomes were analysed using segmented ITS regression. The models included a continuous time variable, an indicator for the pandemic period beginning in March 2020, and a post-intervention time variable. These terms estimated the pre-pandemic monthly trend, the immediate level change associated with pandemic onset, and the change in monthly slope relative to the pre-pandemic trend, respectively.

Screening density was defined as the monthly number of eligible unique rectal swab requests per 1000 patient-days. All eligible requests were included in the primary analysis, irrespective of previous positive detections, to reflect surveillance activity without excluding repeated screening. Monthly patient-days, calculated from admission and discharge dates with the discharge date included, were used as the model offset. The original deduplicated dataset was additionally analysed as a sensitivity analysis.

MDRO positivity was defined as the proportion of deduplicated surveillance requests with at least one selected resistant microorganism detected. Each request contributed at most one positive result, irrespective of the number of microorganism–resistance combinations identified. Monthly positive-request counts were modelled using the logarithm of the corresponding number of deduplicated requests as an offset.

Count outcomes were analysed using generalised linear models with a logarithmic link and either a Poisson or negative binomial distribution. Model selection considered overdispersion, the Cameron–Trivedi test when available, and the Akaike information criterion. Screening-density models included an indicator for the period July–October 2018 to account for increased screening activity associated with a known hospital outbreak. Annual seasonality was modelled using sine and cosine terms with a 12-month period in the positivity models.

HAC covariance estimates were calculated using a Newey–West-type estimator [30] based on score contributions aggregated by calendar month, with Bartlett weights and a lag of two months. Residual autocorrelation was assessed using diagnostic plots and Ljung–Box tests.

Several sensitivity analyses were performed to assess the robustness of the findings. Screening-density and positivity models were repeated using alternative request-selection and deduplication strategies. Positivity was also analysed using binomial logistic regression at the swab-request level, first-detection definitions within individual hospital admissions, and the proportion of screened admissions with at least one positive surveillance request. The influence of the 2018 outbreak was assessed by restricting the observation period to November 2018 onwards. Additional analyses excluded March–April 2020 as a transition period. Observed and fitted trajectories were examined alongside model-based counterfactual projections to assess temporal patterns.

An additional sensitivity analysis examined whether changes in MDRO positivity differed according to the timing of surveillance requests relative to hospital admission. Requests recorded on admission calendar days 0–1 were classified as early screening, and subsequent requests as later screening. An alternative definition including admission calendar days 0–2 was also evaluated. Monthly positivity was analysed using pooled logistic ITS models incorporating interactions between screening-timing group and the time, intervention, and post-intervention slope terms, with annual seasonal harmonic terms and month-aggregated HAC standard errors using a two-month lag. Analyses were conducted using both all-eligible requests and the deduplicated dataset. Because exact collection times were unavailable, these classifications represented calendar-day proxies rather than exact 48-h intervals or confirmed clinical screening indications.

Differences in intervention effects by sex and age group (18–64 and ≥65 years) were assessed using pooled regression models incorporating interactions between subgroup membership and the time, intervention, and post-intervention slope variables. Formal interaction terms were used to evaluate effect modification, rather than comparing statistical significance between separately fitted subgroup models. Subgroup analyses were exploratory, and *p*-values were not adjusted for multiple comparisons.

Model coefficients were exponentiated and reported as rate ratios (RRs) or odds ratios (ORs), as appropriate, with 95% confidence intervals and two-sided *p*-values. Estimates were reported to three decimal places where required for interpretability. Counterfactual trajectories represented model-based projections assuming continuation of the estimated pre-pandemic trend without an interruption and were not interpreted as observed outcomes.

Statistical analyses were conducted using R version 4.2.3 (R Foundation for Statistical Computing, Vienna, Austria). Poisson and binomial logistic regression models were fitted using stats::glm(), and negative binomial models using MASS::glm.nb() (MASS version 7.3-58.2). Overdispersion was assessed using AER::dispersiontest() (AER version 1.2-15), and HAC covariance estimation used sandwich::estfun() and sandwich::bread() (sandwich version 3.1-1). Data management and visualisation were performed using dplyr version 1.1.4 and ggplot2 version 4.0.3. Additional sensitivity analyses and subgroup interaction estimates are presented in Supplementary Tables S2, S4 and S5.

5. Conclusions

In this tertiary-care hospital, the onset of the COVID-19 pandemic was associated with an immediate screening-density level below that projected from the pre-pandemic trend, despite an increase in crude screening density between study periods. The estimated deviation from the projected trajectory was greater among patients aged ≥65 years. MDRO positivity among surveillance requests also declined sharply at pandemic onset, followed by a partial rebound, although the fitted pandemic-period trajectory remained below the model-based counterfactual projection. These findings highlight the importance of maintaining surveillance coverage across patient groups during healthcare crises. Changes in observed positivity should be interpreted cautiously, as they may reflect differences in screening activity and patient selection rather than changes in underlying colonisation prevalence.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/antibiotics15111149/s1, Table S1. Selection flow and units of analysis. Table S2. Interrupted time-series sensitivity analyses of screening density and MDRO positivity. Table S3. Resistant organism groups among deduplicated surveillance requests, by period. Table S4. Formal subgroup interaction tests for screening density and MDRO positivity. Table S5. Sensitivity analyses of MDRO positivity by timing of surveillance requests relative to hospital admission.

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