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Impact of the SARS-CoV-2 pandemic on hospital robustness to the spread of antibiotic-resistant bacteria in a large German university hospital

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SUMMARY

Background: Patient transfers occur frequently between hospital departments and wards, and bring with them the risk of interdepartmental transmission of antibiotic-resistant bacteria (ARB). These bacteria form a risk to patients already susceptible to colonization and infection.

Aim: To assess the impact of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic on the intrahospital network of a large German university hospital.

Methods: Using data collected from the hospital between 2019 and 2023, a model was developed to represent an intrahospital transfer network with all patient movements between all wards by creating a time-sliced temporal network for each month. The network was described, and its robustness against the spread of ARB was assessed by simulating outbreaks between wards.

Findings: In April 2020, when many elective surgeries were cancelled due to the SARS-CoV-2 pandemic, the robustness of the network increased strongly in comparison with all other months. Despite the network being relatively stable over the study period, it was affected by an internal change in hospital structure due to a hospital merger.

Conclusion: The intrahospital transfer network was affected by external influences due to the SARS-CoV-2 pandemic, slowing down the potential spread of nosocomial pathogens. The network was generally stable and recovered quickly, although an internal force affected the structure of the network. A better understanding of the influence of patient transfers will help in the design of intervention strategies against the spread of antimicrobial resistance within hospitals.

Introduction

The burden of healthcare-associated infections is heavy worldwide, due, in part, to the high and increasing prevalence of antimicrobial resistance [1–4]. Patients admitted to hospitals are particularly susceptible to colonization by and

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infection with antibiotic-resistant bacteria (ARB) due to their frail condition, recent medical procedures, and the high level of antibiotic use in healthcare facilities [5,6]. While intensified infection prevention and control due to the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic have contributed indirectly to restricting the spread of ARB over the past few years [7,8], the prevalence of nosocomial ARB may also have been exacerbated by hospital disorganization and the increased use of antimicrobials in patients with coronavirus disease 2019 (COVID-19) [9–11].

Hospitals are by no means isolated entities, and are connected to the general population through their patients and staff, and to other healthcare institutions through shared patients. Taken together, these connections form a complete healthcare network, including all hospitals nationwide. Previous studies have underlined the importance of healthcare networks formed by the combined flows of patients that connect all hospitals within a country, and the role they may play in the global transmission pathway of ARB [12–15].

Along the same lines, wards within a single hospital are connected through the patients they share, and ward transfers may aid the transmission of ARB within the hospital. However, these transfer patterns are not stable over time, and external perturbations may cause changes in the network structure that could affect the spread of ARB across the hospital. One of the most recent large perturbations to health care was the COVID-19 pandemic; as elective surgeries were cancelled to free up beds in intensive care units, it is likely that transfers within the hospital changed.

This study investigated changes in the intrahospital transfer network of Universitätsklinikum Freiburg (UKF), Germany, between 2019 and 2023 by creating a time-sliced temporal network and simulating the spread of ARB among wards using the HospitalNetwork R package. This package standardizes the data cleaning and network reconstruction process, and has been used previously to predict the time span needed to spread a new pathogen in a given hospital network [16], and to show the correlation between hospital transfer networks and the prevalence of meticillin-resistant *Staphylococcus aureus* bacteraemia [12].

Methods

Detailed admission and discharge data were collected, together with information regarding the wards of stay, for each patient admitted to UKF in 2019–2023 using clinic databases. An intrahospital transfer network was then constructed to understand which wards were more connected, and therefore were capable of spreading a potential nosocomial pathogen more rapidly.

First, the data were divided into slices for each month, using the admission date as the inclusion criterion. This process was repeated for the 5-year study period, resulting in a total of 60 slices. The checkBase function within the HospitalNetwork R package was used to ensure that the data were ready for processing [17]. This function performs various checks, including data consistency, to ensure that the database is formatted correctly, and adjusts overlapping patient records.

Next, the network was created using the HospitalNetwork R package, delivering one network per time slice, 60 networks in total, including any admissions that occurred within 30 days of discharge from the previous ward as an interward transfer to account for the potential risk of re-introduction of ARB upon readmission. For each network, the instrength and indegree of the nodes were calculated, as well as the total number of connected wards in the network. Instrength was defined as the number of patients received by a focal ward from the other wards in the network, and indegree represented the number of wards from which a focal ward received patients.

Simulation

In order to assess the robustness of the intrahospital network against the spread of ARB in each month, a ward-based simulation of the potential spread of ARB was created, along the same line as Ciccolini *et al.* [16]. In short, each ward is considered to be affected by ARB or not, and the probability of a ward becoming affected is a function of the total number of received patients from affected wards as well as a transmission scaling parameter c:

$$P_i^{S\rightarrow I}(t) = c\sum_{j:H_j=I} w_{ij}\delta t$$

The expression $j{:}H_j{=}I$ indicates that the weight should be summed over all wards that have already been affected by the pathogen, and thus have state I. This equation approximates the actual probability as long as both the summed weight of the incoming connections and the transmission scaling factor c are small, and therefore $P<<1$. For higher values, one should use:

$$P_i^{S\rightarrow I}(t) = 1 - \prod_{j:H_j=I}(1-c)^{w_{ij}\delta t}$$

For each time step in the simulation, random number generating determined if non-affected wards became affected based on this probability. It was assumed that wards do not revert to an unaffected state, thus assuming indefinite colonization of the ward. The probability that a single patient transmits the disease from an affected ward to an unaffected ward (i.e. the transmission scaling factor c) was set at 0.001.

Each ward in each month's network was used 25 times as the starting point of the outbreak, resulting in 25 times N model realizations per time slice, with N being the total number of wards in the time slice network. Each simulation was run for 1000 time steps.

The robustness of the network is expressed as the median time required for the simulated pathogen to reach 25 wards from each of the starting wards. Per starting ward, the time to reach these 25 wards is taken as the median over all 25 simulation runs. A fixed number of wards (i.e. 25) was chosen instead of a percentage (e.g 50% of the wards), as the former better captures the speed of spread in different sized networks. This is important because some wards are sometimes disconnected from the network, or data are not available, influencing the size of the network. The number of wards chosen (i.e. 25) was selected to reflect the initial spread of the pathogen, but this is otherwise an arbitrary amount.

Furthermore, as UKF underwent structural changes during the study period by merging with Universitäts-Herzzentrum Freiburg – Bad Krozingen in April 2021, the number of wards that are interconnected increased, potentially influencing the analysis. The chosen definition of robustness enabled the authors to compare the values before April 2021 when they were less affected by the difference in network size. The exact value of the measure unit of time for this analysis is arbitrary, as it relates to the transmission parameter, and is meant to give a comparison of robustness between months.

Being aware of the addition of new wards from April 2021, they were identified and the dataset was split into an original dataset and a dataset excluding the new wards. New wards were defined as wards that existed in the dataset after June 2021, but did not exist before December 2020. The period from January 2021 to June 2021 was chosen as a transition period. The same descriptive statistics and analysis was performed on both datasets.

R Version 4.3.2 and the 'HospitalNetwork package were used to reconstruct the network.

Results

In total, 236,909 patients were admitted to UKF between 2019 and 2023, of which 76,679 were admitted on a single occasion, and 992,020 patient movements were observed during this period. There were 175 unique wards at UKF during the study period, with the number of wards admitting patients ranging from 110 to 153 per month (Table S1, see online supplementary material), of which 98—138 were connected in the network.

Within the whole dataset (Table S1, see online supplementary material), the number of wards was, on average, 118 until March 2021, and subsequently increased to an average of 143 from April 2021 onwards; the average number of patients until March 2021 was 9600, and this increased to 12,853 from April 2021. With an increase in patients and wards, the mean indegree and instrength per month were also higher after April 2021, averaging 5.88 and 7.02 wards, respectively (indegree), and 36.29 and 44.65 patients, respectively (instrength), before and after April 2021. The mean length of stay per month was relatively homogeneous over the years, with an average of 3.40 days. The lowest values in terms of number of patients and wards, and subsequently lowest measurements of connection, were seen in April 2020.

In order to identify the newly added wards, all wards that existed in the dataset before December 2020 were labelled as the original UKF wards, and all wards that existed in the dataset from June 2021 that were not original UKF wards were labelled as newly added wards. There were 136 original wards, 39 newly added wards, and six wards closed during the transition, resulting in 169 wards after the transition.

Table S2 (see online supplementary material) shows the descriptive statistics for the dataset without the newly added wards, and shows more homogeneous values: per month, the number of patients ranged from 7139 to 10,839 (mean 9783

Figure 1. Descriptive statistics for the complete dataset (blue line) and for the dataset including the original Universitätsklinikum Freiburg (UKF) wards alone (red line): (A) number of patients, (B) number of wards, (C) mean indegree (wards), (D) mean instrength (patients), and (E) mean length of stay (days).

patients); the number of wards ranged from 110 to 123 (mean 117 wards); the mean indegree ranged from 4.40 to 6.66 wards (mean 6.00 wards); the mean instrength ranged from 30.50 to 42.05 patients (mean 37.26 patients); and the mean length of stay ranged from 3.19 to 3.73 days (mean 3.44 days).

The comparison between the two datasets can be seen in the panels of Figure 1, where the blue lines correspond to the statistics of the complete data set and the red lines correspond to the statistics including the original UKF wards alone.

The total number of wards present in the dataset was 175; however, not all of them were connected to other wards. Table S3 (see online supplementary material) shows the number of months in which each ward was included as a node in the network, as well as the specific months of inclusion, for the dataset including all the wards and for the dataset including the original wards alone.

Regarding data including the complete dataset, it can be observed that the network was more robust in April 2020 (t=404) compared with any of the previous and subsequent months (mean values of 266 and 228, respectively) (Figure 2, blue line). Furthermore, it can be observed that from April 2021 onwards, and more evident from June 2021, robustness was lower than that observed in previous periods, with an average of 210. Other peaks in robustness corresponding to December 2020 and January 2021 (median values of 311 and 327, respectively), as well as relative peaks in January and February 2022, are also visible on the graph. The robustness of the network excluding the new wards shows the same peak in robustness in April 2020 (Figure 2, red line), as well as the peaks in December 2020, January 2021 and October 2022. However, the values in the months before and after April 2020 are similar.

These results are also visible in the mean proportion of wards affected at each time step of the simulation for each year using data including the original UKF wards alone, as well as when using the complete dataset (Figure 3 and Figure S1, see online supplementary material). The lower line in April 2020 indicates that it would take longer for the infection to spread in that month. The other lines are more compact, showing comparable robustness for all months in those years. When comparing network connectivity in April 2020 with previous months (Figure 4), it can be observed that the reduction in patient movement was occurring across most connections, while only a few ward pairs increased their connectivity.

Discussion

The findings of this study indicate that the intrahospital transfer network of UKF changed drastically during the COVID-19 pandemic, reflected in the higher robustness of the network against the spread of ARB in April 2020. During this month, the time required for a potential ARB outbreak to disseminate throughout the intrahospital network was longer compared with any of the other months under investigation. In light of the organizational changes to UKF brought about by the pandemic, it is plausible to suggest that the elevated robustness observed in April 2020 was a consequence of the restricted connections between the various departments, brought about by the suspension of elective surgeries and other deferrable procedures.

The intrahospital network of UKF remained relatively stable over the other months, returning quickly to previously observed robustness. However, from April 2021 onwards, a decline in robustness of the network was observed, indicated by more rapid dissemination of ARB in the simulation. A multitude of factors may have contributed to this observed change. Internal changes in structure, such as the opening of new wards and the formal merger between Universitäts-

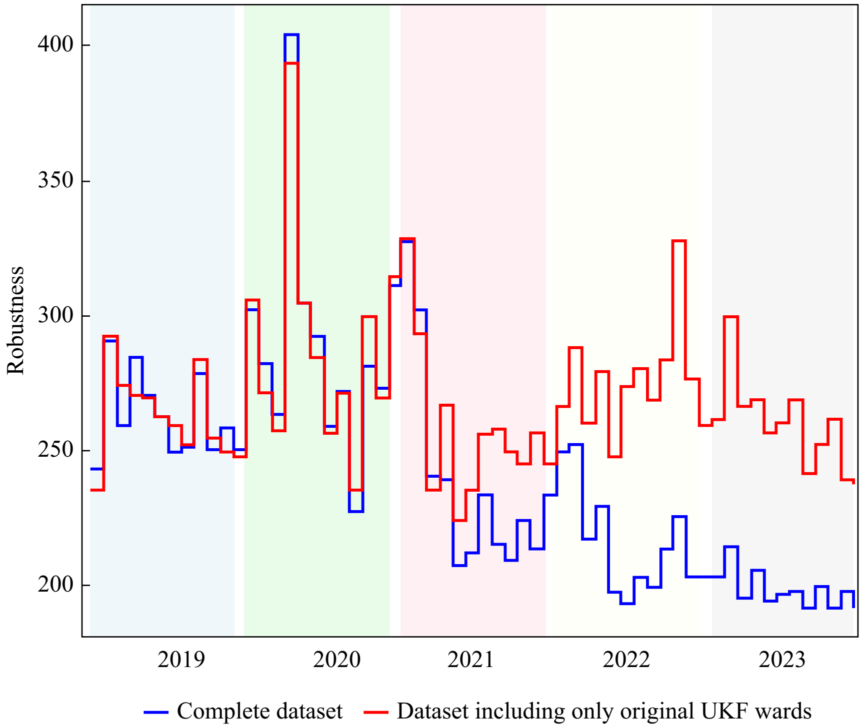

Figure 2. Robustness of the intrahospital network over the study period, with the blue line showing data for the complete dataset and the red line showing data for the original Universitätsklinikum Freiburg (UKF) wards alone.

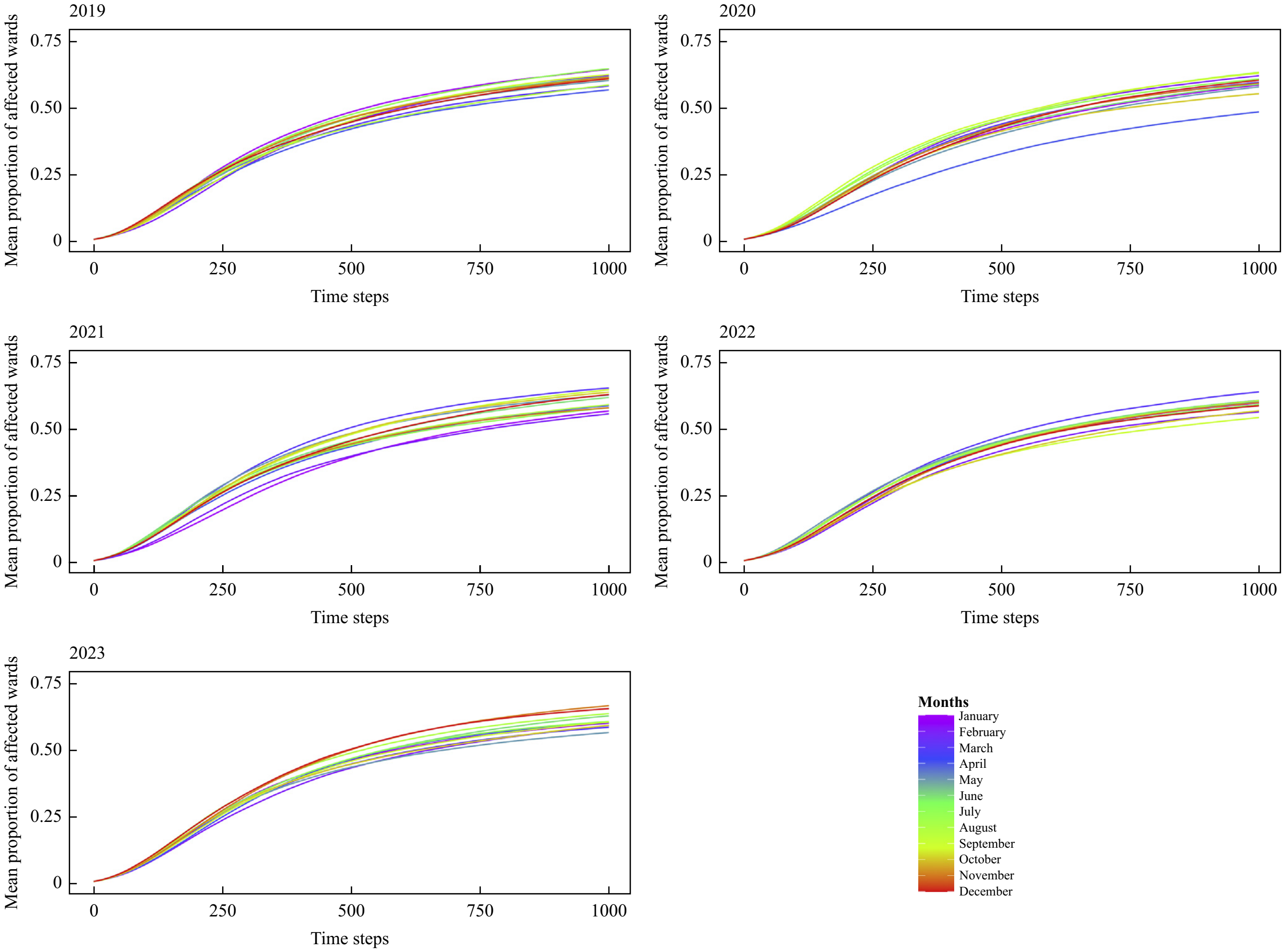

Figure 3. Mean proportion of wards affected at each time step of the simulation for each year of the dataset, coloured by month, based on the networks including the original Universitätsklinikum Freiburg wards alone.

Herzzentrum Freiburg – Bad Krozingen and UKF in April 2021, may have contributed to this phenomenon, although not all of the newly established 39 wards were integrated into the network to the same extent.

The inclusion of more connected departments could facilitate the spread of ARB through the exchange of patients between the different wards, increasing the vulnerability of the network vulnerability to ARB outbreaks [18,19]. Therefore, to compare the robustness of the network before and after the addition of new wards, the decision was made to analyse the data with new wards excluded from the analysis. Following this adjustment, no large difference was observed between the two periods before and after April 2021. Although the network was relatively stable to external forces over time, the internal force of the addition of new wards affected its structure. For this reason, it is important to highlight that the same networks should be compared for network analysis, otherwise the measurements could be biased by the network size.

A strength of this study lies in the analysis of transfer data for 5 years from one of the largest hospitals in Germany. By using network robustness as the primary metric, the authors were able to quantify the stability in risk of potential spread of ARB outbreaks in the hospital. This gives a clear indication of the influence of external forces on the robustness of the network, and opens up possibilities for using healthcare policies to make hospitals more robust against ARB outbreaks. Therefore, an understanding of intrahospital networks could have a significant impact on the strategies employed by hospitals to prevent the dissemination of ARB within and between wards [7].

The findings of this study may aid public health policy makers to strengthen infection control strategies by enhancing the resilience of hospital networks. This study suggests that intrahospital patient transfer patterns can influence the spread of nosocomial pathogens, and external factors, such as the cancellation of elective surgeries during the pandemic, can enhance network robustness by reducing patient movement. Policy implications could include optimized patient transfer protocols with more structured patient transfer pathways to limit unnecessary movement within hospitals. Furthermore, hospitals could employ predictive analytics to anticipate how patient transfers affect the spread of pathogens: real-time monitoring of transfers may help to detect risky patterns early. Implementing enhanced infection control measures, such as rigorous screening before transfers, dedicated transfer teams, and specialized cleaning protocols, may help contain

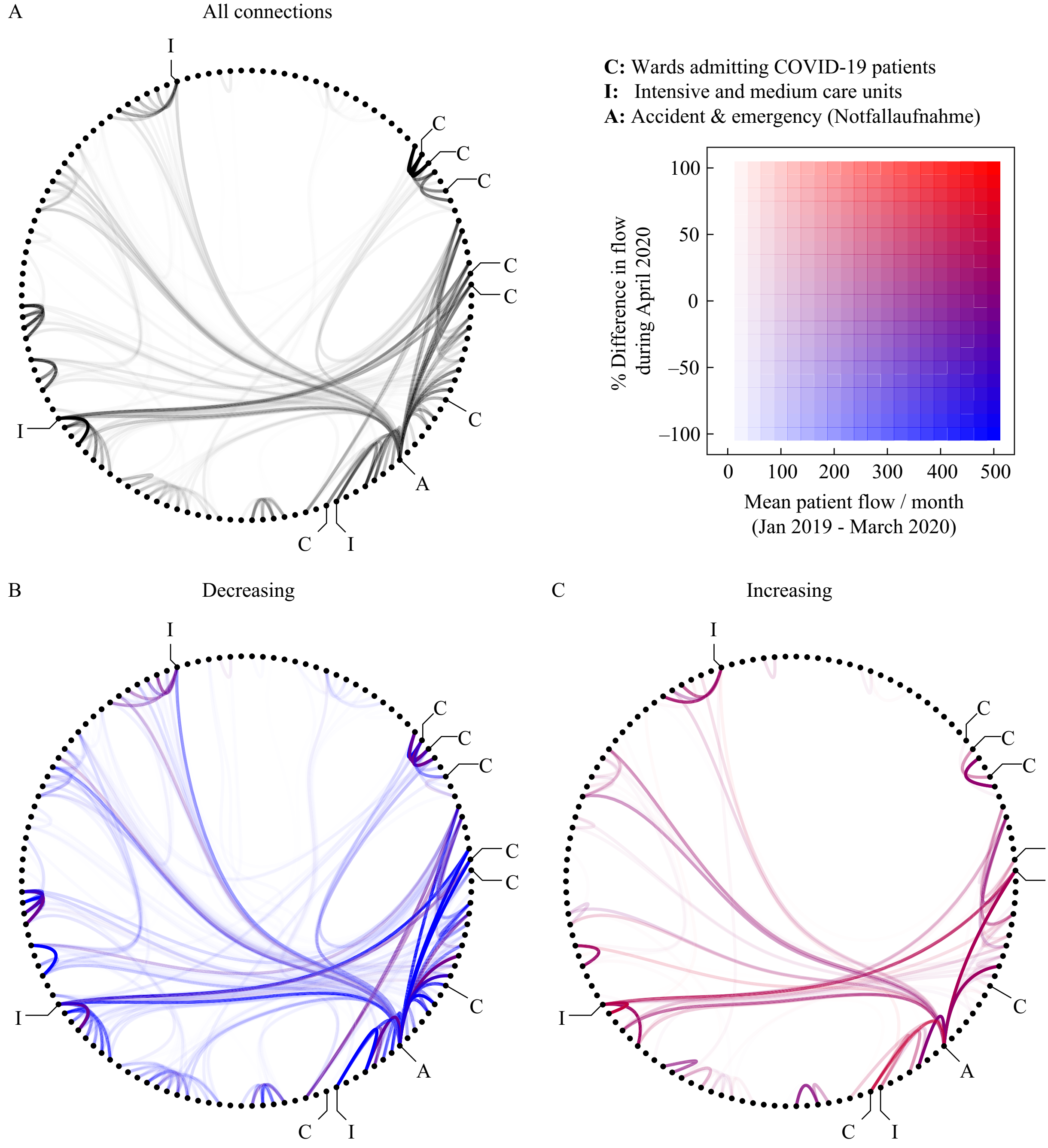

Figure 4. Changes in patient movements in the intrahospital network of Universitätsklinikum Freiburg in April 2020 compared with January 2019–March 2020. (A) Mean network for January 2019–March 2020, with each dot depicting a ward [with coronavirus disease 2019 (COVID-19) wards, intensive care units, and Accident & Emergency annotated], and connections coloured by the mean number of monthly patient movements between them. (B) Decreasing connections, coloured by their reduction. (C) Increasing connections.

potential outbreaks while maintaining essential hospital functions. If intrahospital transfers influence pathogen spread, interhospital patient movement may have similar effects; thus, a coordinated regional network approach, where hospitals collaborate to streamline transfers while reducing unnecessary movement, could further mitigate the risk of spread of antimicrobial resistance.

Network analysis is an effective tool to describe system behaviour, and can help identify opportunities for intervention with targeted improvements, such as locating and scaling resources strategically, streamlining transfers, and ultimately providing patient-centred approaches to drive increased value. While previous studies have shown that an intrahospital network was affected by the COVID-19 pandemic [20], the current study shows that this change was only temporary, at least for the studied hospital. Furthermore, the analysis also highlighted the impact of a change in internal structure and its importance when conducting this type of analysis.

Limitations

This study has a few limitations that need to be considered when interpreting its results. First, the study only used data on patient movements within the hospital, and not data on the occurrence of ARB infections on the wards. Robustness against the spread of ARB was based on simulated outbreaks, primarily because the spread of ARB occurs at a different time scale than the observed change in intrahospital network structure. The influence of the network changes can therefore not be observed in the incidence of ARB from a single hospital, unless the network changes last longer.

Furthermore, it should be noted that the analysed data were collected from a single hospital in Baden-Württemberg, Germany. Although the principle behind the study should be broadly applicable, the question remains to what extent the specific results apply to other hospitals or healthcare facilities. Nonetheless, the findings of this study could assist public health policy makers in the design of new strategies to prevent the spread of ARB infections.

In conclusion, with the data available for UKF, the network of connections between different patients in different departments was found to be relatively stable over the study period, except for April 2020. The likely influence of the SARS-CoV-2 pandemic, and particularly the hospital's policy in response to the first pandemic wave, caused the network to become temporarily more robust against ARB outbreaks. However, it returned rapidly to the normal values for UKF. Furthermore, the stability of the network may also have been influenced by differences in internal organization of the hospital, such as the hospital merger, resulting in lower robustness.

This study contributes to better understanding of the spread of antimicrobial resistance in hospitals. The added knowledge about network variation within hospitals will help public health regulators to design intervention strategies against the spread of antimicrobial resistance.

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Conflict of interest statement

None declared.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2025.04.032.

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