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Permalink https://escholarship.org/uc/item/1kf561fk

Journal NEJM Evidence, 3(5)

ISSN 2766-5526

Authors

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Publication Date 2024-04-23

DOI 10.1056/evidoa2300342

Supplemental Material

https://escholarship.org/uc/item/1kf561fk#supplemental

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A Trial of Automated Outbreak Detection to Reduce Hospital Pathogen Spread

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Abstract

Background:

Detection and containment of hospital outbreaks currently depend on variable and personnelintensive surveillance methods. Whether automated statistical surveillance for outbreaks of health care-associated pathogens allows earlier containment efforts that would reduce the size of outbreaks is unknown.

Methods:

We conducted a cluster-randomized trial in 82 community hospitals within a larger health care system. All hospitals followed an outbreak response protocol when outbreaks were detected by their infection prevention programs. Half of the hospitals additionally used statistical surveillance of microbiology data, which alerted infection prevention programs to outbreaks. Statistical surveillance was also applied to microbiology data from control hospitals without alerting their infection prevention programs. The primary outcome was the number of additional cases occurring after outbreak detection. Analyses assessed differences between the intervention period (July 2019 to January 2022) versus baseline period (February 2017 to January 2019) between randomized groups. A post hoc analysis separately assessed pre-coronavirus disease 2019 (Covid-19) and Covid-19 pandemic intervention periods.

Results:

Real-time alerts did not significantly reduce the number of additional outbreak cases (intervention period versus baseline: statistical surveillance relative rate (RR)=1.41, control RR=1.81; difference-in-differences, 0.78 (95% CI, 0.40 to 1.52; P=0.46). Comparing only the prepandemic intervention with baseline periods, the statistical outbreak surveillance group was associated with a 64.1% reduction in additional cases (statistical surveillance RR=0.78, control RR=2.19, difference-in-differences, 0.36 (95% CI, 0.13 to 0.99)). There was no similarly

observed association between the pandemic versus baseline periods (statistical surveillance RR=1.56, control RR=1.66; difference-in-differences, 0.94 (95% CI, 0.46 to 1.92)).

Conclusions:

Automated detection of hospital outbreaks using statistical surveillance did not reduce overall outbreak size in the context of an ongoing pandemic.

Word count: 249

Trial Registration Number: NCT04053075

Background

Health care-associated infections are a leading cause of preventable morbidity and mortality.¹ Some of these infections are attributed to outbreaks resulting from transmission of microorganisms to patients from health care personnel, other patients, or contaminated surfaces or equipment.² Despite the critical importance of early identification of hospital-associated outbreaks to limit their spread,³⁻⁵ there is currently no standardized approach for detecting outbreaks, and a substantial majority of outbreaks are missed.^{6,7} Many hospitals rely on detection of temporal or spatial (unit-based) clustering of a limited number of prespecified multidrug-resistant organisms or a limited number of procedure-related infections. Hospitals often use arbitrary criteria such as three or more patients with a hospital-onset organism in the same unit over a 2-week period.⁷⁻¹¹ Decisions about when to intervene and which infection control responses to implement also vary widely between hospitals and even within hospitals over time.⁶

We developed a statistically based outbreak detection tool by integrating WHONET,^{12,13} an analytics software program for microbiology data, and SaTScan, a disease surveillance software. The latter tool implements space-time scanning statistical methods to detect clusters.¹⁴⁻²³ The resulting WHONET-SaTScan allows automated real-time identification of statistically unusual groupings of hospital-onset pathogens that accounts for hospital location, antimicrobial susceptibility pattern, and historical prevalence of each pathogen.

WHONET-SaTScan has been used by hospitals to improve and streamline outbreak detection.^{7,24} In the current study, we assessed whether implementation of the statistical surveillance tool, coupled with a standardized response protocol, could reduce the size of outbreaks.

Methods

We designed and conducted a two-group cluster-randomized trial with a 24-month baseline period (February 2017-January 2019), a phase-in period (February 2019-July 2019), and a 30-month intervention period (July 2019-January 2022).

Recruitment of Hospitals and Eligibility Criteria

Recruitment of hospitals occurred within the HCA Healthcare system, a system of community hospitals accounting for 5% of U.S. hospitalizations. Eligibility criteria included having at least 2 years of pretrial (prebaseline) microbiology data in the HCA Enterprise Data Warehouse so that the statistical surveillance tool could account for the historical prevalence of hospital pathogens when detecting outbreaks.

Intervention

Hospitals randomized to the statistical outbreak surveillance group implemented the automated WHONET-SaTScan tool with real-time alerting of infection prevention programs during the intervention period. All hospitals continued prior processes for routine outbreak detection. In addition, hospitals in both groups adopted a standardized outbreak response protocol (see the protocol provided with the full text of this article) for any outbreaks detected during the intervention period, whether the outbreak was detected by WHONET-SaTScan (intervention group) or usual means (both groups). The protocol required a progressively intensive sequence of mitigation strategies as outbreak cases accrued.

WHONET-SaTScan was also implemented retrospectively for the baseline period in all hospitals, as well as prospectively in control hospitals during the intervention period without alerting their infection prevention programs. An outbreak was determined based on the recurrence interval, which estimates the likelihood that a cluster of hospital-onset pathogens would occur by chance.^{7,24} We defined an outbreak as occurring when the recurrence interval

for an organism exceeded 200 days, meaning that the observed number, location, and distribution of cases would be expected to occur by chance less frequently than once every 200 days. The threshold of 200 was selected to balance sensitivity of outbreak detection with an acceptable number of false-positive signals to which an infection prevention program would be able to respond. Outbreaks could have as few as two patients.

We used finalized microbiology results for a broad set of bacteria and fungi previously associated with hospital outbreaks for specimens obtained more than 2 days after admission until discharge, including available species and antimicrobial resistance patterns.²⁴ Only first isolates of a specific organism per patient were included. We excluded surveillance cultures because practices varied between and within hospitals over time. Scan statistic expectations for species, resistance profiles, and hospital locations were derived from each hospital's prior 2 years' rolling data.^{7,24} Hospital-onset isolates were attributed to the patient's hospital location 2 days before specimen collection.²⁵ We searched for outbreaks within hospital units and groups of related units specified by the infection prevention program before the start of the trial.

In the statistical outbreak surveillance group, the signaling of outbreaks was integrated into HCA's infection prevention platform (TheraDoc[®]) to facilitate alerting and annotation in the daily workflow of infection preventionists. When an alert was received or if an outbreak was detected by routine methods, the infection preventionist was expected to initiate the outbreak response protocol. Each additional case that extended the outbreak prompted another alert that called for a more rigorous response.

Coaching calls with local infection prevention teams in the control and statistical outbreak surveillance groups were held at least quarterly during the intervention period to discuss the outbreak response protocol and encourage adherence. Assessment of adherence was based on infection preventionists' implementing program-directed interventions and reporting their assessments of selected response measures such as hand hygiene, contact precaution

adherence and environmental cleaning. A complete response was defined as completing 3 weeks of an intervention with three weekly assessments. A timely response was defined as an intervention which began within 4 days of an alert. Additional details are defined in the response protocol provided with the full text of this article.

Study Outcomes

The primary outcome was the number of additional cases identified after the first outbreak signal detected by the statistical surveillance tool, regardless of whether the signal was reported to the infection prevention team (statistical outbreak surveillance group, intervention period) or not (control group for both periods and intervention group for the baseline period). The prespecified secondary outcome was outbreak duration, defined as the number of days from the initial signal through the last outbreak case (last case considered part of the outbreak based on the predetermined statistical threshold). Because there are no standard processes for routine outbreak detection, we limited the analyses to outbreaks detected by the statistical surveillance tool in both arms.

Randomization

Hospitals were randomized in a 1:1 ratio. We used aggregated baseline hospital data to establish similar hospital pairs based on key baseline hospital characteristics including census, length-of-stay, comorbidity score (Elixhauser),²⁶ and baseline outbreak rates (size and duration) to improve balance across the groups. Pairing was done using the Goldilocks Approach.^{27,28} We then randomly assigned one hospital of each pair to each group.

Data Collection and Outcome Assignment

Output from WHONET-SaTScan plus associated information including hospital name, unit(s), organism, alert date and alert type (matching by species or species plus antimicrobial susceptibility pattern), specimen type, and date of specimen collection were obtained from

HCA's data repositories. Infection preventionists provided the same information for routinely detected outbreaks and recorded the information on study forms. Study staff tracked the response to each routinely identified outbreak (both groups) or automated outbreak detection tool alert (statistical outbreak surveillance group). There were no competing infection prevention interventions in either group in the trial, other than changes that might have been introduced or practices that were reinforced in follow-up to recognized outbreaks.

Trial Oversight

The Harvard Pilgrim Health Care Institute institutional review board provided centralized oversight with waiver of consent. M.A.B. takes full responsibility for the conduct of the study and its publication. M.A.B., N.V. and K.K. had full access to the data and K.K. was responsible for all statistical analyses. M.A.B, S.S.H., R.P., K.K. and N.V. drafted the manuscript. All authors contributed to the acquisition, analysis and/or interpretation of the data; critically revised the manuscript and approved the final version.

Statistical Analysis

Analyses were conducted using generalized linear mixed models with a negative binomial distribution, accounting for the correlation of outbreaks within each hospital. Model terms included group, trial period (baseline or intervention), and an interaction term between trial period and group. The assessment of trial success was determined by the significance of the interaction term, which assessed whether the difference in outbreak size between the baseline and intervention period differed significantly between the two groups. Similar methods were used for the secondary outcome of outbreak duration. Data from the phase-in period were excluded from all analyses.

Adjusted models accounted for organism type (Gram-positive, Gram-negative, and fungi or mycobacteria), size of outbreak at first signal, and signal location (single unit or multi-unit).

Analyses were performed using SAS software, version 9.4 (SAS Institute) and R statistical software, version 4.2.0 (R Project for Statistical Computing).

Two post-hoc analyses were undertaken. First, to account for the potential impact of the Covid-19 pandemic during the intervention period, we performed separate analyses for the "pre-Covid-19" intervention period (July 2019-June 2020) and the "Covid-19" intervention period (July 2020-January 2022), defined based on the date when Covid hospitalizations began to increase at participating hospitals based on HCA inpatient data.²⁹ Second, we assessed whether the probability that a hospitalized patient was part of an outbreak differed in the statistical outbreak surveillance versus the control group using a logistic regression generalized linear mixed model, accounting for frequency and size of outbreaks. Because we did not control for multiple testing, the only reported P value is for the primary outcome. All other analyses report only the point estimates with 95% confidence intervals which should not be used to draw causal inferences.

Results

Study Participants

82 hospitals in 16 states were randomized (Figure 1). Three hospitals withdrew due to divestment from HCA: one in the statistical outbreak surveillance group (14 months into the intervention period), and two control hospitals (24 and 26 months into the intervention period). There were more than 2.5 million admissions in each group, including baseline and intervention periods (Table 1).

Outbreak Characteristics

Statistical Outbreak Surveillance

The outbreak detection software identified 419 outbreaks (2.6 per hospital/year) in the baseline period and 647 outbreaks (3.2 per hospital/year) in the intervention period (Table 2).

Approximately one-third of outbreaks were Gram-positive pathogens (baseline 32.7%, intervention 29.4%) and two-thirds Gram-negative pathogens (baseline 62.8%, intervention 66.2%). The median (IQR) size of the outbreak at first signal was 2 patients (2-4) during the baseline and 3 patients (2-5) during the intervention period.

Routine Surveillance

During the intervention period, routine outbreak detection methods identified 23 outbreaks (10 in the statistical outbreak surveillance group (0.10 per hospital/year) and 13 in the control group (0.13 per hospital/year)). Nine of the 23 routinely detected outbreaks were also identified by automated outbreak detection, and the majority (7 of 9) signaled before being detected by routine methods. Of the 14 outbreaks that were not detected by the automated statistical surveillance tool, 3 were based on non-clinical screening tests which were excluded from the statistical surveillance algorithm. Another 3 outbreaks included patients in units not considered to be related by the infection prevention program prior to the start of the trial and were therefore not analyzed together. Only one of the remaining 8 outbreaks that were not identified by automated methods progressed by one case after initial identification.

Outcomes

For the primary trial outcome (unadjusted as-randomized analysis), the statistical outbreak surveillance group had 1.41 times as many additional cases after the initial outbreak signal in the intervention period compared to the baseline, while the control group had 1.81 times as many. This means that the statistical outbreak surveillance group had 22.4% fewer additional cases than the control group, or 0.78 (95% CI, 0.40 to 1.52; P=0.46) additional outbreak cases in the intervention versus the baseline period compared to the control group, a difference that was not statistically significant (Table 3, Figure 2).

After adjustment for organism type, number of isolates in the first signal, and unit location, the statistical outbreak surveillance group had 1.11 times as many additional cases after the initial outbreak signal in the intervention period compared to the baseline, while the control group had 1.65 times as many. This means that the statistical outbreak surveillance group had 0.67 (95% CI, 0.36 to 1.26) as many additional outbreak cases in the intervention versus the baseline period compared to the control group, or 32.5% fewer additional cases with a confidence interval from 64% fewer cases to 26% additional cases (Table 3).

For the secondary outcome, unadjusted and as-randomized analyses found a relative decrease (0.79 days, 95% CI, 0.50 to 1.24) in outbreak duration in the intervention versus the baseline periods with the control group, though with a wide confidence interval around that estimate.

In the post hoc analysis, the statistical outbreak surveillance group had 0.36 (95% CI, 0.13 to 0.99) as many additional cases in the pre-Covid-19 period compared to the control group, i.e., 64.1% fewer additional cases, relative to baseline. In the Covid period, this group had 0.94 (95% CI, 0.46 to 1.92) or 5.9% fewer additional cases.

We performed additional post hoc analyses (Table 3). The risk that a hospitalized patient would be part of an outbreak in the statistical outbreak surveillance group in the intervention period relative to baseline was 0.64 (95% CI, 0.56 to 0.73) compared to the control group. Thus the relative odds of an individual being in an outbreak in our data set was about a third smaller in the statistical outbreak surveillance group compared to the control group, comparing the intervention period to baseline. The same comparison was 0.43 (95% CI, 0.35 to 0.53) when using only the pre-Covid intervention period data and 0.71 (95% CI, 0.62 to 0.82) using the Covid intervention period data. However, because these were post-hoc analyses, we cannot attribute these differences directly to the automated outbreak surveillance system.

During the pandemic, using nonsystematic qualitative data from convenience samples of interviews with hospital personnel, many of the infection prevention programs noted that they were too busy with urgent pandemic needs to optimally respond to outbreaks, and the infection prevention completion and return of outbreak response protocol forms were highly limited, resulting in an inability to assess the degree of intervention response.

Discussion

Automated statistical surveillance for outbreaks using microbiology data and a space-time scan statistic to alert infection prevention personnel to respond to an outbreak in progress did not significantly reduce the overall size or duration of outbreaks in this large cluster-randomized trial. The Covid-19 pandemic began one-third of the way through the intervention period and may have affected the outcomes of this trial. It also created unforeseen challenges that adversely affected infection prevention response and practice nationally due to overwhelming responsibilities, staff distractions, supply shortages, and disruptions in usual infection prevention protocols. Nationally, the pandemic resulted in markedly increased rates of health care-associated infections, antibiotic-resistant pathogens, and outbreaks.²⁹⁻³¹

In a post-hoc analysis of the intervention period prior to the Covid-19 pandemic, we observed a smaller number of outbreak cases after alerting the infection prevention team in the statistical outbreak surveillance group, with 64.1% fewer additional cases after the initial outbreak alert compared to the control group relative to the baseline. During the Covid-19 pandemic, this relatively lower number of additional cases was erased, although the risk that a hospitalized patient would be part of an outbreak was lower at 28.6%. The lower rate of outbreaks in the statistical outbreak surveillance group during the intervention period may have been due to improved adherence to infection prevention following outbreak response.

In the absence of automated statistical outbreak detection, the 82 participating hospitals would have found only 23 outbreaks using routine methods over 2.5 years. The control group hospitals were unaware of 96.3% of the outbreaks found by retrospective automated surveillance of their microbiology data. This failure to recognize most outbreaks has been previously shown and is not surprising since routine outbreak detection is usually limited to the tracking of a few antibiotic-resistant pathogens even though several hundred pathogens are known to cause hospital outbreaks.^{6,7,24} Moreover, a large proportion of outbreaks identified through hospital routine surveillance was actually not statistically unusual compared to the hospitals' own baseline data as only 39.1% of routinely-detected outbreaks overlapped with statistically-detected outbreaks. Among the outbreaks that were detected by both routine and statistical methods, the automated detection tool signaled earlier for most outbreaks, suggesting that such a tool is not only more comprehensive, but more timely.

The greatest limitation of the trial was the unanticipated Covid-19 pandemic that began 12 months into the trial, diverting infection preventionists' attention to pandemic-related activities. Although the automated outbreak detection tool identified more outbreaks during the pandemic, personnel who would ordinarily have responded to the alerts were often unable to take action because of other patient care responsibilities. Second, because the statistical outbreak surveillance relied on two years of baseline data, the pandemic changes to patient case mix and admission volume may have affected the performance of the statistical outbreak detection tool in ways we could not anticipate. Third, we set the parameters of the statistical surveillance tool to detect outbreak set an unexpected rise in positive cultures of a single pathogen, so a multi-pathogen outbreak would not be captured. Finally, we recognize that many outbreaks did not enlarge after the first signal; therefore, time and effort was expended on responding to a proportion of statistical outbreaks that will resolve spontaneously. The response protocol, however, was tailored to ensure that the initial response to an outbreak targeted observed

deficiencies in basic infection prevention and control activities, such as hand hygiene or environmental cleaning, which meant that effort was spent on needed activities.

Although statistical surveillance for outbreak detection did not reduce overall outbreak size in this trial, it was interrupted by the Covid-19 pandemic, which limited the bandwidth of infection prevention programs for non-Covid outbreak response. Coupled with a standardized response to outbreak detection, this approach to enhanced outbreak detection may improve containment during non-pandemic settings.

Funding for this study was provided by CDC, grant number CDC U54CK000484. Support for HCA Healthcare's participation in the study was provided in kind by HCA. The views expressed in this publication represent those of the authors and do not necessarily represent the official views of CDC nor HCA nor any affiliated entities.

Acknowledgements:

We thank the unit staff and leadership, infection prevention programs, nurse & medical directors, microbiology laboratories, and administrative leadership at all of the participating hospitals for their commitment and dedication to this trial: CJW Medical Center - Chippenham Campus, CJW Medical Center - Johnston Willis Campus, Colleton Medical Center, Doctor's Hospital Sarasota, Eastern Idaho Regional Medical Center, Eastside Medical Center, Fairview Park Hospital , Garden Park Medical Center, Grand Strand Medical Center, HCA Florida Brandon Hospital, HCA Florida Fawcett Hospital, HCA Florida Gulf Coast Hospital, HCA Florida JFK Hospital, HCA Florida JFK North Hospital, HCA Florida Lake Monroe Hospital, HCA Florida Largo Hospital, HCA Florida Lawnwood Hospital, HCA Florida Memorial Hospital, HCA Florida Northside Hospital, HCA Florida Ocala Hospital, HCA Florida Orange Park Hospital, HCA

Florida Raulerson Hospital, HCA Florida South Shore Hospital, HCA Florida St. Lucie Hospital, HCA Florida Trinity Hospital, HCA Florida West Hospital and ER, HCA Florida West Marion Hospital, HCA Houston Clear Lake, HCA Houston Healthcare Conroe, HCA Houston Healthcare Kingwood, HCA Houston Mainland, Heart Hospital of Austin, Henrico Doctors' Hospital - Forest, Henrico Doctors' Hospital - Parham, Lake City Medical Center, Las Palmas Medical Center, Lee's Summit Medical Center, LewisGale Hospital - Montgomery, Los Robles Hospital and Medical Center, Medical Center Lewisville, Medical City Alliance, Medical City Arlington, Medical City Dallas, Medical City Denton, Medical City Fort Worth, Medical City McKinney, Medical City North Hills, Menorah Medical Center, Methodist Hospital, Methodist Hospital Northeast, Methodist Stone Oak Hospital, MountainView Hospital, North Suburban Medical Center, Ogden Regional Medical Center, Overland Park Regional Medical Center, Parkland Medical Center, Portsmouth Regional Hospital, Presbyterian St. Luke's Medical Center, Redmond Regional Medical Center, Regional Medical Center of San Jose, Research Medical Center, Reston Hospital Center, Retreat Doctors' Hospital, Rio Grande Regional Hospital, Riverside Community Hospital, Rose Medical Center, Sky Ridge Medical Center, Spotsylvania Regional Medical Center, St. David's Georgetown Hospital, St. David's Medical Center, Summerville Medical Center, Swedish Medical Center, Trident Medical Center, TriStar Centennial Medical Center, TriStar Greenview Regional Hospital, TriStar Horizon Medical Center, TriStar Southern Hills Medical Center, TriStar Summit Medical Center, Valley Regional Medical Center, Wesley Medical Center, Wesley Woodlawn Hospital, West Valley Medical Center

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 Table 1: Characteristics of Statistical Outbreak Surveillance versus Control Populations

| | Baseline | e Period | Intervention Period | | |
|-----------------|----------------|----------------|---------------------|----------------|--|
| | 24-M | onths | 30-Months | | |
| | | Statistical | | Statistical | |
| | Control | Outbreak | Control | Outbreak | |
| | N (%) | Surveillance | N (%) | Surveillance | |
| | | N (%) | | N (%) | |
| Admissions | 1,154,982 | 1,123,851 | 1,446,854 | 1,458,601 | |
| Age (median | 58 (32.0-73.0) | 56 (31.0-72.0) | 58 (32.0-73.0) | 56 (32.0-72.0) | |
| (IQR)) | 00 (02.0 70.0) | 00 (01.072.0) | 00 (02.0 70.0) | 30 (32.0-72.0) | |
| Male | 499,585 (43.4) | 487,842 (43.6) | 642,729 (44.5) | 648,992 (44.6) | |
| Race | | | | | |
| White | 827,424 (71.6) | 785,409 (69.9) | 1,017,301 (70.3) | 996,468 (68.3) | |
| Black | 153,924 (13.3) | 170,210 (15.1) | 196,654 (13.6) | 229,501 (15.7) | |
| Other | 71,981 (6.2) | 48,464 (4.3) | 84,017 (5.8) | 65,406 (4.5) | |
| Unknown | 101,653 (8.8) | 119,768 (10.7) | 148,882 (10.3) | 167,226 (11.5) | |
| Hispanic/Latino | 181,526 (15.7) | 141,759 (12.6) | 248,148 (17.2) | 195,943 (13.4) | |
| Primary | | | | | |
| Insurance | | | | | |
| Medicare | 522,046 (45.2) | 493,617 (43.9) | 632,231 (43.7) | 614,756 (42.1) | |
| Commercial | 281,164 (24.3) | 279,776 (24.9) | 349,076 (24.1) | 360,513 (24.7) | |
| Medicaid | 225,139 (19.5) | 222,600 (19.8) | 287,289 (19.9) | 298,188 (20.4) | |
| Other | 126,633 (11.0) | 127,858 (11.4) | 178,258 (12.3) | 185,154 (12.7) | |

| 4 (3.0-6.0) | 4 (3.0-6.0) | 4 (3.0-6.0) | 4 (3.0-6.0) |
|----------------|---|---|--|
| | | | |
| | | | |
| | | | |
| 2 (0.0-4.0) | 2 (1.0-4.0) | 2 (1.0-4.0) | 3 (1.0-4.0) |
| | | | |
| 291,854 (25.3) | 290,663 (25.9) | 388,784 (26.9) | 401,017 (27.5) |
| 167,989 (14.5) | 157,656 (14.0) | 225,073 (15.6) | 222,739 (15.3) |
| 69,722 (6.0) | 70,919 (6.3) | 93,805 (6.5) | 97,795 (6.7) |
| 54,306 (4.7) | 51,962 (4.6) | 92,329 (6.4) | 94,798 (6.5) |
| 0 (0.0) | 0 (0.0) | 65,566 (4.5) | 80,864 (5.5) |
| | 2 (0.0-4.0) 291,854 (25.3) 167,989 (14.5) 69,722 (6.0) 54,306 (4.7) | 2 (0.0-4.0) 2 (1.0-4.0) 291,854 (25.3) 290,663 (25.9) 167,989 (14.5) 157,656 (14.0) 69,722 (6.0) 70,919 (6.3) 54,306 (4.7) 51,962 (4.6) | 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (1.0-4.0) 2 (1.0-4.0) 2 (0.0-4.0) 2 (0.0-4.0) 2 (0.0-4.0) 2 (0.0-4.0) 2 (0.0-4.0) 2 (0.0-4.0) 167,989 (14.5) 157,656 (14.0) 225,073 (15.6) 69,722 (6.0) 70,919 (6.3) 93,805 (6.5) 54,306 (4.7) 51,962 (4.6) 92,329 (6.4) |

a. Elixhauser comorbidity count score is based on the summed count of comorbidities using diagnostic codes. Scores can range from 0-38, with higher numbers indicating greater illness.²⁶

 Table 2 – Characteristics of Outbreaks Under Statistical Outbreak Surveillance versus

Routine Care, by Study Period

| | Baseline Period | | Intervention Period | | |
|-------------------------|-----------------|--------------|---------------------|--------------|--|
| | 24-Months | | 30-Months | | |
| Outbreak Characteristic | | Statistical | | Statistical | |
| | Control | Outbreak | Control | Outbreak | |
| | N (%) | Surveillance | N (%) | Surveillance | |
| | | N (%) | | N (%) | |
| Total Outbreaks | 191 | 228 | 349 | 298 | |
| Outbreaks per Year per | | | | | |
| Hospital | 2.3 | 2.8 | 3.4 | 2.9 | |
| Outbreaks per 10,000 | 1.7 | 2.0 | 2.4 | 2.0 | |
| Admissions | | 2.0 | | 2.0 | |
| Organism | | | | | |
| Gram Positive | 63 (33.0%) | 74 (32.5%) | 110 (31.5%) | 80 (26.8%) | |
| Gram Negative | 118 (61.8%) | 145 (63.6%) | 226 (64.8%) | 202 (67.8%) | |
| Fungi & Mycobacteria | 10 (5.2%) | 9 (3.9%) | 13 (3.7%) | 16 (5.4%) | |
| Outbreak Location | | | | | |
| Non-ICU | 126 (66.0%) | 116 (50.9%) | 185 (53.0%) | 132 (44.3%) | |
| ICU and ICU/Non-ICU | 65 (34.0%) | 112 (49.1%) | 164 (47.0%) | 166 (55.7%) | |
| Outbreak Units | | | | | |
| Single unit | 109 (57.1%) | 139 (61.0%) | 260 (74.5%) | 196 (65.8%) | |
| Related units | 82 (43.0%) | 89 (39.0%) | 89 (25.5%) | 102 (34.2%) | |
| Total Size of Outbreak | | | | | |
| 2 Patients | 87 (45.5%) | 109 (47.8%) | 145 (41.5%) | 128 (43.0%) | |

| 3-5 Patients | 64 (33.5%) | 81 (35.5%) | 107 (30.7%) | 108 (36.2%) |
|-------------------|-------------|-------------|-------------|-------------|
| 6-10 Patients | 36 (18.8%) | 30 (13.2%) | 72 (20.6%) | 43 (14.4%) |
| >10 Patients | 4 (2.1%) | 8 (3.5%) | 25 (7.2%) | 19 (6.4%) |
| Total Duration of | | | | |
| Outbreak | | | | |
| 1-2 Days | 25 (13.1%) | 27 (11.8%) | 38 (10.9%) | 32 (10.7%) |
| 3-5 Days | 20 (10.5%) | 24 (10.5%) | 40 (11.5%) | 27 (9.1%) |
| 6-10 Days | 18 (9.4%) | 25 (11.0%) | 33 (9.5%) | 30 (10.1%) |
| >10 Days | 128 (67.0%) | 152 (66.7%) | 238 (68.2%) | 209 (70.1%) |

Table 3 – Impact of Statistical Outbreak Surveillance Versus Routine Care, Overall and by

| Pre-Covid a | and Covid | Subsets ^a |
|-------------|-----------|----------------------|
|-------------|-----------|----------------------|

| | | Statistical | | | | | |
|--------------------------------------|--|---------------------|-------------------|---------|--|--|--|
| Analysis | Control | Outbreak | | | | | |
| | | Surveillance | | | | | |
| | Relative Rate | Relative Rate | | | | | |
| | (CI) | (CI) | Overall | | | | |
| | (Intervention | (Intervention | Difference in | P-Value | | | |
| | Period to | Period to | Differences | | | | |
| | Baseline Period) | Baseline Period) | | | | | |
| | Outbreak Cases | s After First Alert | | | | | |
| | (Primary | Outcome) | | | | | |
| Overall | 1.81 (1.11, 2.96) | 1.41 (0.88, 2.24) | 0.78 (0.40, 1.52) | 0.46 | | | |
| Pre-Covid Subset | 2.19 (1.16, 4.14) | 0.78 (0.36, 1.73) | 0.36 (0.13, 0.99) | | | | |
| Covid Subset | 1.66 (0.98, 2.81) | 1.56 (0.96, 2.54) | 0.94 (0.46, 1.92) | | | | |
| Adjusted ^b | 1.65 (1.04, 2.61) | 1.11 (0.72, 1.72) | 0.67 (0.36, 1.26) | | | | |
| | Duration of Outbreak After First Alert | | | | | | |
| | (Secondar | y Outcome) | | | | | |
| Overall | 1.12 (0.81, 1.56) | 0.88 (0.64, 1.21) | 0.79 (0.5, 1.24) | | | | |
| Pre-Covid Subset | 1.19 (0.78, 1.8) | 0.9 (0.49, 1.66) | 0.76 (0.36, 1.59) | | | | |
| Covid Subset | 1.09 (0.76, 1.56) | 0.88 (0.63, 1.23) | 0.8 (0.5, 1.31) | | | | |
| Patient Risk of Being in an Outbreak | | | | | | | |
| | (Post Hoc Outcome) | | | | | | |
| | Odds Ratio (CI) | Odds Ratio (CI) | Odds Ratio (CI) | | | | |

| Overall | 1.94 (1.76, 2.13) | 1.24 (1.13, 1.36) | 0.64 (0.56, 0.73) | |
|------------------|-------------------|-------------------|-------------------|--|
| Pre-Covid Subset | 1.25 (1.10, 1.43) | 0.54 (0.46, 0.63) | 0.43 (0.35, 0.53) | |
| Covid Subset | 2.36 (2.14, 2.60) | 1.68 (1.53, 1.85) | 0.71 (0.62, 0.82) | |

^a All analyses are unadjusted and as randomized unless otherwise specified

^b Adjusts for organism type, number of isolates in the first signal, unit location

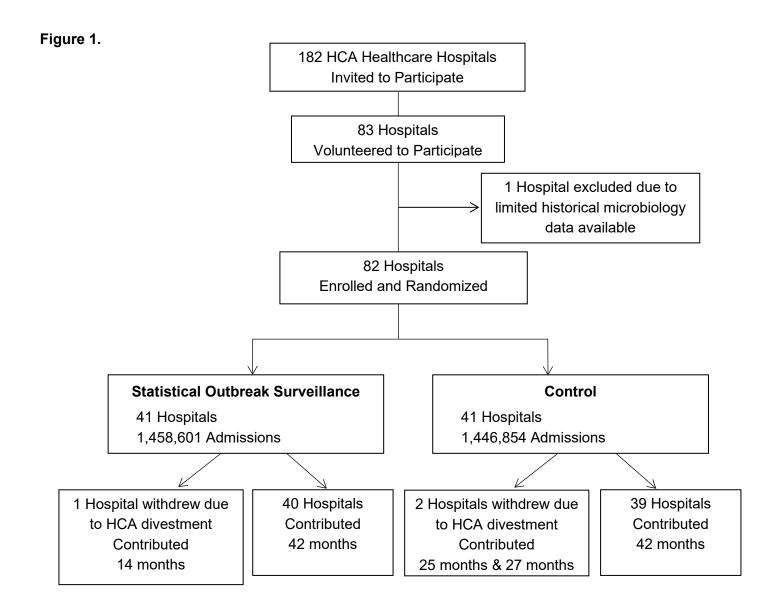


Figure 1. CONSORT Diagram of Eligibility, Recruitment, and Randomization of Hospitals

in the Trial

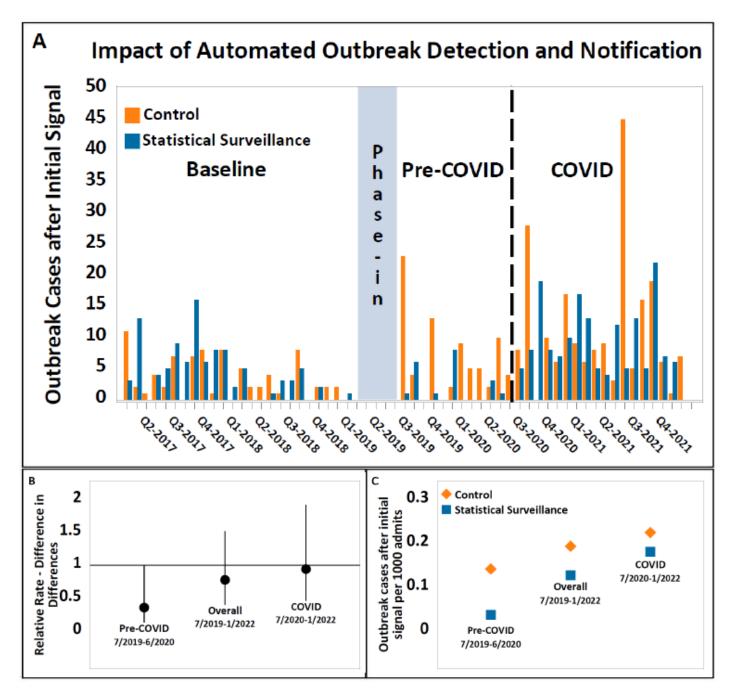


Figure 2. Impact of Outbreak Detection and Notification

Panel 2A shows the additional outbreak cases occurring after the initial outbreak signal. The Control group cases (orange) and Statistical Outbreak Surveillance group cases (blue) are shown as bar graphs by month of year. The figure includes the baseline and intervention periods, and a dotted line between June 30 and July 1, 2020 distinguishes pre-Covid from Covid pandemic conditions. Panel 2B demonstrates the relative reduction (black dot with 95% CI) in additional outbreak cases in the intervention versus baseline period comparing the Statistical Outbreak Surveillance group to the Control group. The panel includes the total intervention period and the pre-Covid and Covid time periods. Panel 2C demonstrates the outbreak cases after the initial signal per 1,000 admissions, comparing the Statistical Outbreak Surveillance group (blue) and the Control group (orange). The figure shows the total intervention period (overall) and the pre-Covid and Covid time periods.