ORIGINAL ARTICLE

Impact of Hydrogen Peroxide Vapor Room Decontamination on *Clostridium difficile* Environmental Contamination and Transmission in a Healthcare Setting

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OBJECTIVE. To determine whether hydrogen peroxide vapor (HPV) decontamination can reduce environmental contamination with and nosocomial transmission of *Clostridium difficile*.

DESIGN. A prospective before-after intervention study.

SETTING. A hospital affected by an epidemic strain of *C. difficile*.

INTERVENTION. Intensive HPV decontamination of 5 high-incidence wards followed by hospital-wide decontamination of rooms vacated by patients with *C. difficile*–associated disease (CDAD). The preintervention period was June 2004 through March 2005, and the intervention period was June 2005 through March 2006.

RESULTS. Eleven (25.6%) of 43 cultures of samples collected by sponge from surfaces before HPV decontamination yielded *C. difficile,* compared with 0 of 37 cultures of samples obtained after HPV decontamination ($P < .001$). On 5 high-incidence wards, the incidence of nosocomial CDAD was significantly lower during the intervention period than during the preintervention period (1.28 vs 2.28 cases per 1,000 patient-days; $P = .047$). The hospital-wide CDAD incidence was lower during the intervention period than during the preintervention period (0.84 vs 1.36 cases per 1,000 patient-days; $P = .26$). In an analysis limited to months in which the epidemic strain was present during both the preintervention and the intervention periods, CDAD incidence was significantly lower during the intervention period than during the preintervention period (0.88 vs 1.89 cases per 1,000 patient-days; $P = .047$).

CONCLUSIONS. HPV decontamination was efficacious in eradicating *C. difficile* from contaminated surfaces. Further studies of the impact of HPV decontamination on nosocomial transmission of *C. difficile* are warranted.

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For nearly 30 years, *Clostridium difficile*–associated disease (CDAD) has affected a substantial proportion of hospitalized patients who receive antimicrobial therapy.[1] Although the incidence of CDAD began to increase in the 1990s,[2,3] the epidemiology of CDAD has changed significantly since 2000.[4,5] The emergence of the North American pulsed-field (NAP1) epidemic strain of *C. difficile,* which has enhanced virulence properties, has resulted in a dramatic increase in the incidence of CDAD and in the number of cases resulting in colectomy or death.[6,7]

In November 2004, a sudden increase in the incidence of CDAD at a 500-bed university-affiliated hospital, to 2.3 cases per 1,000 patient-days, was accompanied by an unprecedented number of patients with severe pseudomembranous colitis requiring colectomy.[8] *C. difficile* isolates recovered from stool samples from several affected patients were identified by the Centers for Disease Control and Prevention (Atlanta, GA) as the epidemic NAP1 strain. In late November 2004, control measures were implemented, including reminding physicians to avoid prescribing high-risk antimicrobial agents, performing *C. difficile* toxin assays more frequently, placing patients with CDAD in isolation, using contact precautions during patient care, using soap and water for hand hygiene after caring for patients with CDAD, and disinfecting rooms of patients with CDAD with a 1:10 dilution of household bleach (sodium hypochlorite). Despite these measures, the incidence of CDAD remained 1.4 cases per 1,000 patient-days, which was higher than the baseline level of fewer than 1.1 cases per 1,000 patient-days. As a result, we felt that evaluation of novel control measures

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that might reduce environmental contamination and transmission of *C. difficile* was warranted.

Because viable *C. difficile* spores are resistant to standard cleaning and disinfection practices, may contaminate environmental surfaces for prolonged periods, and contribute to transmission of the organism,[9-11] we evaluated a new method for terminal disinfection of rooms occupied by patients with CDAD. Hydrogen peroxide vapor (HPV) effectively kills *Clostridium botulinum* spores on hard surfaces in a laboratory setting.[12] Accordingly, we initiated a prospective, collaborative intervention trial to determine whether use of a commercial HPV decontamination system (Bioquell) decreases environmental contamination and nosocomial transmission of *C. difficile*.

METHODS

Study Population and Setting

We conducted a pre- and postintervention study at the Hospital of Saint Raphael, a 500-bed university-affiliated hospital in New Haven, Connecticut. The preintervention period was June 2004 through March 2005, and the intervention period was June 2005 through March 2006. Because there may be seasonal variation in the incidence of CDAD,[3] we compared the incidence of CDAD during the 10-month intervention period with the incidence during the same 10-month period in the preceding year. The study was approved by the Hospital of Saint Raphael's Infection Control Program, Quality Improvement Committee, and hospital administration.

Study Design

The 5 wards (A–E) with the highest incidence of CDAD were designated as "intensive-decontamination" wards. Three of these wards were cleaned of any visible dirt and temporarily vacated, and the entire units were subjected to HPV decontamination. On the other 2 wards, which could not be temporarily vacated, all patient rooms were similarly cleaned and individually decontaminated using HPV over a 2-week period. Once decontamination of the 5 intensive-decontamination wards was completed, individual patient rooms vacated by patients with CDAD throughout the hospital were terminally decontaminated on an ongoing basis.

Intervention

Before decontaminating any areas, personnel from the manufacturer of the decontamination system (Bioquell) conducted an engineering review in conjunction with the hospital's engineering department, with particular attention to heating, ventilation, and air conditioning systems. Each area was then cleaned to remove visible dirt and was decontaminated using HPV, as described by French et al.[13] Briefly, all heating, ventilation, and air conditioning ducts in the area to be decontaminated were sealed using tape. Special generators were used to convert 30% liquid hydrogen peroxide into HPV, which was injected into the enclosure until approximately 1 μm of hydrogen peroxide was deposited on exposed surfaces before being converted to oxygen and water vapor by catalytic converters. The time required for the entire process was 3–4 hours for a patient room and approximately 12 hours for an entire ward.

Microbiological Efficacy of HPV Room Decontamination

Premoistened cellulose sponges (Solar Biologicals) were used to collect 43 samples from multiple surfaces in 18 bathrooms and 17 associated rooms and to collect 8 samples from open ward areas before HPV decontamination. Thirty-seven matched, adjacent samples were collected immediately after HPV decontamination in 15 rooms, 14 bathrooms, and 8 open ward areas. In each room, a sponge was used to wipe approximately half the surface area of the bedrail, bed-raising buttons, nurse call button, intravenous pumps, the chair arm, the dresser, and the over-bed table. In the bathrooms, a sponge was used to wipe approximately half the surface area of the door handle, the sink, handrails, the shower, and the toilet. In the open ward areas, sites sampled included telephones, computer keyboards, bench tops, door handles, charts, and a soiled utility room. The total surface area wiped with each sponge was approximately 1 m^2. Matched 1-m^2 areas covering the remaining half of the items were wiped in the rooms and bathrooms sampled after HPV decontamination. All areas were cleaned of visible dirt with a detergent-based cleaning agent, and rooms that had been occupied by patients with CDAD were cleaned daily and after patient discharge with sodium hypochlorite solution (1,000 ppm).

The sponge samples were sent by express mail to the Centers for Disease Control and Prevention, where they were cultured for *C. difficile* by use of a quantitative method described elsewhere.[14] Biological indicators containing more than 1.0×10^6 *Geobacillus stearothermophilus* spores in Tyvek pouches (Apex Laboratories) were placed at the periphery of areas to be decontaminated. During the first 6 weeks of the trial, biological indicators were placed on wards and in individual patient rooms to determine the shortest HPV decontamination cycle times that reliably killed all biological indicators. Later in the trial, biological indicators were used to ensure the efficacy of HPV cycle times in other clinical areas. Biological indicators were cultured in nutrient broth at 60°C for 7 days; cultures were analyzed by infection-control laboratory personnel.

Presence of the Epidemic NAP1 strain

C. difficile isolates recovered from patients and from the environment during the first 2 months and last 2 months of the intervention period were forwarded to the Centers for Disease Control and Prevention for strain typing to determine whether the epidemic NAP1 strain was still present in the hospital during the intervention period. At the Centers for Disease Control and Prevention, isolates were characterized by toxinotyping and pulsed-field gel electrophoresis and by detecting binary

TABLE. Quantities of Antimicrobials Used During the Preintervention and Intervention Periods

Agent(s)	Quantity used, DDDs per 1,000 patient-days					
	Full comparison periods			Subperiods when epidemic strain was present[a]		
	Preintervention (Jun 2004 to Mar 2005)	Intervention (Jun 2005 to Mar 2006)	*P*	Preintervention (Nov 2004 to Mar 2005)	Intervention (Nov 2005 to Mar 2006)	*P*
All antibiotics	805.7	764.1	.10	814.6	766.4	.25
Proton pump inhibitors	300.4	298.9	.9	300.6	312.8	.83
All fluoroquinolones	158.9	146	.003	158	150	.12
Levofloxacin	138.5	140.5	.97	142.2	145.2	.60
Cephalosporins						
Second generation	10.2	7.5	.001	10.8	7.6	.02
Third generation	31.5	39.1	.21	31.6	41.4	.025
Fourth generation	32.0	29.7	.27	33	27.4	.11
Clindamycin	10.5	8.5	.07	9.8	7.6	.19

NOTE. DDD, defined daily dose.

[a] *Clostridium difficile* North American pulsed-field 1 (NAP1) strain.

toxin and deletions in the regulatory gene *tcdC,* using methods described elsewhere.[7]

Surveillance for CDAD

CDAD was considered to be present in patients with diarrhea and a stool enzyme immunoassay positive for *C. difficile* toxin A/B (Meridian Diagnostics). An electronic medical record review was performed by infection control personnel for each *C. difficile* toxin–positive patient identified retrospectively in the laboratory's computerized database from November 2003 through May 2005 and prospectively through laboratory-based surveillance during the intervention period. Each patient with CDAD was included only once—that is, repeated episodes were excluded.

New nosocomial CDAD cases were considered to be present in patients who had a positive *C. difficile* toxin test result for a sample obtained more than 72 hours after admission and in patients who were discharged to home within the preceding 3-month period and had a positive *C. difficile* toxin test result for a sample obtained within the first 72 hours after readmission. Patients who were discharged to an extended-care facility within the preceding 3-month period and who had a positive *C. difficile* toxin test result for a sample obtained within the first 72 hours after readmission were not considered to have nosocomial cases and were excluded from the analysis. The incidence of CDAD, expressed as the number of new nosocomial CDAD cases per 1,000 patient-days, during the intervention period was compared with that of the preintervention period.

Trends in Antimicrobial Use

The total quantity (in grams) of all oral and intravenous antimicrobial agents (excluding antifungal and antiviral agents) and proton pump inhibitors administered to inpatients from January 2004 through March 2006 was obtained from the hospital pharmacy database. On the basis of criteria published elsewhere,[15,16] the rate of consumption of antimicrobials and proton pump inhibitors was calculated (as the number of defined daily doses [DDDs] per 1,000 patient-days) for all antimicrobial agents combined; for second-, third-, and fourth-generation cephalosporins; for clindamycin; for all fluoroquinolones combined; for levofloxacin; and for all proton pump inhibitors combined.

Statistical Analysis

EpiInfo software, version 3.3.2 (Centers for Disease Control and Prevention), was used to compare dichotomous variables by use of χ^2 tests, and continuous variables were analyzed using the Mann-Whitney *U* test. To determine whether the incidence of CDAD was correlated with antimicrobial use patterns for the entire period from January 2004 through March 2006, simple linear regression methods were used. Multiple linear regression methods were used to determine whether CDAD incidence (dependent variable) was correlated with antibiotic use and a time variable (the pre-epidemic period [January 2004 through October 2004], the epidemic period before the intervention [November 2004 through May 2005], and the intervention period [June 2005 through March 2006]). The period was treated as a dummy variable.

RESULTS

From November 2003 through October 2004, the monthly incidence of new nosocomial CDAD cases remained relatively stable, ranging from 0.42 to 1.1 cases per 1,000 patient-days (Figure 1). The incidence increased to 2.3 cases per 1,000 patient-days in November 2004. After implementation of initial control measures in late November 2004, the incidence decreased, but by April 2005 it had not returned

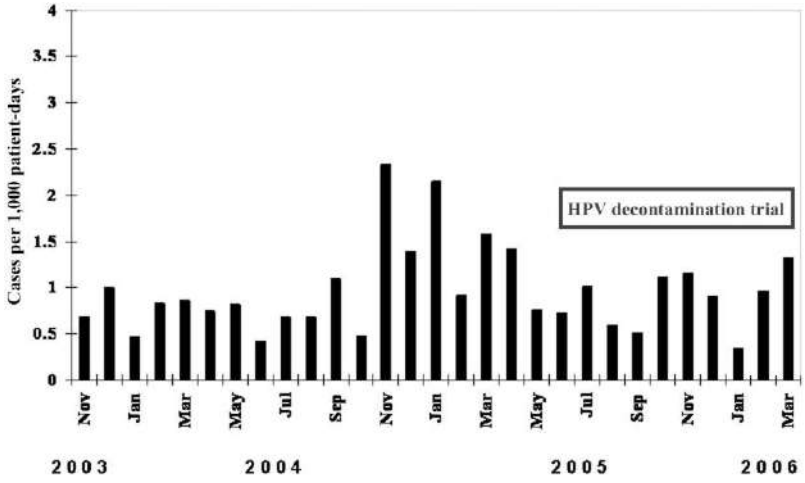

FIGURE 1. Hospital-wide incidence of nosocomial *Clostridium difficile*–associated disease, November 2003 through March 2006. HPV, hydrogen peroxide vapor.

to the baseline level of fewer than 1.1 cases per 1,000 patient-days.

Microbiological Efficacy of the HPV Process

C. difficile was cultured from 11 (25.6%) of 43 sponges used to sample surfaces before HPV decontamination but from 0 of 37 sponge samples obtained immediately after HPV decontamination (ie, recovery was below the detection limit of 6 colony-forming units [cfu] per sponge) ($P < .001$). The contaminated sites were 6 rooms, 4 bathrooms, and 1 soiled utility room. The highest concentration of *C. difficile* recovered before HPV decontamination was 1.3×10^3 cfu, from a sponge used to sample multiple surfaces in a room occupied by a patient with CDAD. Eighty-seven (91.6%) of 95 *G. stearothermophilus* biological indicators placed in patient rooms during the first 6 weeks of the trial to determine the shortest possible HPV cycle times yielded no growth. After cycle times were standardized, all 53 biological indicators yielded no growth on culture.

Presence of the Epidemic NAP1 Strain

Studies performed by the Centers for Disease Control and Prevention before the intervention documented the presence of the epidemic NAP1 strain of *C. difficile* in 5 patients with CDAD who were hospitalized in November and December 2004. Six of 21 patient and environmental isolates recovered during the first 2 months of the intervention period and 4 of 7 patient isolates recovered during the last 2 months of the intervention period were identified as the NAP1 strain of *C. difficile,* suggesting that the epidemic strain was present throughout the trial period.

Impact of the HPV Decontamination Trial on CDAD Incidence

During the intervention period, the mean incidence of new cases of nosocomial CDAD on each of the 5 intensive decontamination wards was lower than that during the preintervention period (Figure 2). For the 5 wards combined, the mean CDAD incidence decreased significantly, from 2.28 cases per 1,000 patient-days during the preintervention period to 1.28 cases per 1,000 patient-days during the intervention period ($P = .047$).

The hospital-wide CDAD incidence during the first 2 months of the intervention period, when most HPV decontamination was confined to the 5 high-incidence wards, was higher than that during the comparable months of the preintervention period (Figure 3). During 6 of the following 8 months of the intervention period, the CDAD incidence was lower than that during comparable months of the preintervention period. Overall, the mean hospital-wide incidence de-

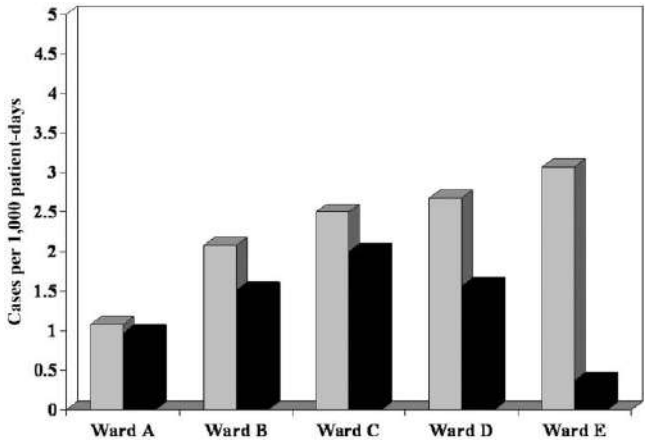

FIGURE 2. Incidence of nosocomial *Clostridium difficile*–associated disease on 5 wards (A–E) that underwent intensive hydrogen peroxide vapor decontamination, during the preintervention period (*gray bars;* June 2004 through March 2005) and the intervention period (*black bars;* June 2005 through March 2006).

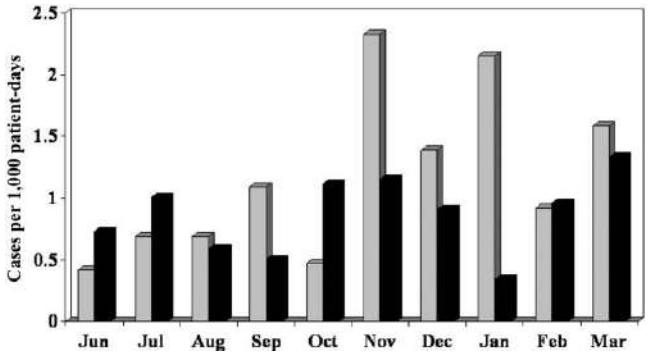

FIGURE 3. Hospital-wide incidence of nosocomial *Clostridium difficile*–associated disease, by month, during the preintervention period (*gray bars;* June 2004 through March 2005) and the intervention period (*black bars;* June 2005 through March 2006).

creased from 1.36 cases per 1,000 patient-days during the preintervention period to 0.84 cases per 1,000 patient-days during the intervention period, a reduction of 39% ($P = .26$). However, because the incidence of CDAD has been noted to be higher in institutions when the epidemic NAP1 strain is present,[6,7] it may not be appropriate to compare CDAD incidence for the period June through October 2004 of the preintervention period (before the epidemic strain was detected) with the incidence for the period June through October 2005 of the intervention period (when the epidemic strain was known to be present). If the analysis is limited to the months when the epidemic strain was known to be present both during the preintervention period (November 2004 through March 2005) and during corresponding months of the intervention period (November 2005 through March 2006), CDAD incidence decreased from 1.89 cases per 1,000 patient-days to 0.88 cases per 1,000 patient-days, a reduction of 53% ($P = .047$).

Trends in Rates of Antimicrobial Use

There were no significant differences in the overall quantity of antimicrobials used or in the quantity of proton pump inhibitors used during the 10-month intervention period, compared with during the 10-month preintervention period (Table). When compared with that during the preintervention period, the quantity of antimicrobial used during the intervention period was significantly less for all fluoroquinolones (158.9 vs 146.0 DDDs per 1,000 patient-days; $P = .003$) and for second-generation cephalosporins (10.2 vs 7.5 DDDs per 1,000 patient-days; $P = .001$). However, when the analysis was restricted to those months when the epidemic strain was known to be present, in both periods, only the quantity of second-generation cephalosporins used was significantly less during the intervention period, whereas the quantity of third-generation cephalosporins used was greater (both $P = .02$) (Table).

Simple linear regression analysis revealed a low but statistically significant correlation between the incidence of CDAD during the period January 2004 through March 2006 and the quantity of antimicrobial used for all antimicrobials combined ($r^2 = 0.20$; $P = .02$) and for fourth-generation cephalosporins ($R^2 = 0.22$; $P = .01$) but not for any of the following antimicrobials: all fluoroquinolones, levofloxacin, second-generation cephalosporins, third-generation cephalosporins, or clindamycin (data not shown). Multiple linear regression analysis that included the CDAD incidence, the quantity of antimicrobial used, and the time variable (preepidemic period, epidemic period before the intervention, and the intervention period) in the model revealed significant correlations between CDAD incidence and the quantity of antimicrobial used for all antimicrobials combined ($P = .02$) and for fourth-generation cephalosporins ($P = .001$).

DISCUSSION

Traditional measures recommended for control of CDAD in healthcare settings have included reducing the use of high-risk antimicrobial agents, placing patients with CDAD in private rooms, using contact precautions (gloves and gowns) for direct patient care, and hand washing after patient care.[17-19] Because routine cleaning with detergents may not reliably eradicate *C. difficile*—which may remain viable for weeks or months—from the environment, disinfection of the environment by use of sporicidal agents, such as sodium hypochlorite, has been recommended.[9,18,20-26] In the present study, we isolated *C. difficile* from 25.6% of the surfaces sampled; this finding is comparable to those of previous studies that have reported the frequency of *C. difficile* contamination in rooms of patients with CDAD to range from 20% to 49% of the surfaces sampled.[9-11,14,27-30] Contaminated medical equipment and other inanimate surfaces may come into direct contact with susceptible patients or may serve as sources of healthcare worker hand contamination.[11,31-35] Disinfection of the environment with sodium hypochlorite solutions, when used in combination with other control measures, has been shown to reduce transmission of *C. difficile*.[21,28] For example, switching from a quaternary ammonium disinfectant to sodium hypochlorite was associated with reduced transmission of *C. difficile* on a high-incidence ward.[21] Switching back to the quaternary ammonium disinfectant led to a rebound in the incidence of CDAD. However, disinfection of surfaces with sodium hypochlorite has not reduced *C. difficile* transmission in all settings in which it has been evaluated.[21,36,37]

In our study, HPV decontamination eradicated *C. difficile* from previously contaminated environmental surfaces. Previous studies have demonstrated that HPV decontamination is effective for killing methicillin-resistant *Staphylococcus aureus* and other organisms on contaminated surfaces in healthcare settings.[13,38] As in earlier studies, hospital staff did not report damage or malfunction of any of the medical equipment subjected to HPV decontamination in our study.[39,40] The HPV decontamination process used in this study appears to be safe for use in healthcare facilities, as long as the area to be decontaminated is appropriately sealed, hydrogen peroxide levels outside the area being decontaminated are closely monitored, and

levels within the decontaminated area are reduced to less than 1 ppm before allowing patients or healthcare workers to reenter. During the intervention period, hospital staff did not report any adverse effects attributable to the HPV decontamination process, among patients or personnel.

Another unique aspect of our trial was that we evaluated the potential impact of ongoing HPV decontamination of environmental surfaces on the incidence of nosocomial CDAD. At the beginning of the trial, 5 high-incidence wards were selected for intensive HPV decontamination efforts, because earlier experience has suggested that environmental disinfection may have the greatest impact in clinical areas where the incidence of CDAD is high.[21] During the intervention period, the incidence of nosocomial CDAD on the 5 intensive HPV decontamination wards was 44% lower than during the preintervention period ($P = .047$). HPV decontamination of rooms of patients with CDAD was associated with a 53% reduction in the hospital-wide incidence of nosocomial CDAD ($P = .047$) when analysis was limited to comparable months when the epidemic NAP1 strain was known to be present. We could not attribute these decreases to changes in other infection control measures during the trial period. Other control measures were implemented in November 2004 and continued thereafter through the end of the intervention period. A limited number of observations of compliance with hand hygiene and contact precaution policies, conducted in mid-December 2005, were compared with compliance rates observed in late 2004 and did not reveal improvements that might have contributed to the reduction in CDAD incidence (results not shown). Linear regression revealed very low, albeit statistically significant, correlations between the incidence of CDAD during the entire period between January 2004 and March 2006 and the quantity of antimicrobial used for all antimicrobials combined and for fourth-generation cephalosporins. Although significantly less of second-generation cephalosporins was used during the intervention period, the fact that these agents accounted for a very small proportion of all antimicrobial use suggests that the reduction in their use is unlikely to explain reduced CDAD incidence during the intervention period. Disappearance of the epidemic NAP1 strain from the hospital is not a potential explanation for the decreased incidence of CDAD, because this strain was confirmed to be present at the beginning and near the end of the intervention period.

An advantage of HPV decontamination technology is that medical equipment that either is difficult to disinfect or frequently escapes disinfection can be effectively decontaminated using HPV. Shortcomings of HPV decontamination technology include the inability to perform the procedure in rooms currently occupied by patients; the need for well-trained personnel and special equipment; the higher costs, compared with those associated with routine terminal room cleaning; and the longer turnaround times before vacated rooms are ready for occupancy by newly admitted patients.

The major limitation of our study was that we did not determine CDAD incidence rates on concurrent control wards where only traditional cleaning and disinfection procedures were used. As a result, we cannot exclude the possibility that some of the observed reduction in nosocomial CDAD incidence may have been due to "regression to the mean," a reduction in rates from high levels to lower levels that is not attributable to a specific intervention; this is supported by the low incidence of CDAD in May 2005 before the intervention began (Figure 1). However, the rate of CDAD is typically lower in the summer months and variable from month to month, so it is possible that May 2005 was a month of atypically low CDAD rates during the epidemic period. Another weakness was that the trial was conducted in a single university-affiliated hospital affected by the epidemic NAP1 strain. This may limit the extent to which our findings can be generalized.

To the best of our knowledge, our study is the first to assess the ability of HPV decontamination to reduce *C. difficile* environmental contamination and transmission in a healthcare setting. Our study found that the HPV decontamination process we used (Bioquell) was efficacious in eradicating *C. difficile* from contaminated surfaces in a hospital setting. Furthermore, HPV decontamination may have reduced transmission of *C. difficile* within the facility, although further studies are warranted to confirm this finding. We believe that HPV technology also warrants further evaluation in circumstances in which other pathogens (eg, *Acinetobacter* species) that survive for prolonged periods on environmental surfaces are causing ongoing transmission that is not controlled by traditional infection control measures. Because the costs of HPV decontamination are substantially greater than the costs of standard terminal cleaning by housekeeping personnel, additional studies of the cost-effectiveness of HPV decontamination in healthcare facilities are needed.

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