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Vital Signs: Preventing *Clostridium difficile* Infections

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Abstract, 1 figure , 2 tables omitted

Introduction

CLOSTRIDIUM DIFFICILE IS AN ANAEROBIC, spore-forming bacillus that causes pseudomembranous colitis, manifesting as diarrhea that often recurs and can progress to toxic megacolon, sepsis, and death. Infection is spread by the fecal-oral route; spores, the infective form, can persist on fomites and environmental surfaces for months. *Clostridium difficile* infection (CDI) often occurs in patients in health-care settings, where antibiotics are prescribed and symptomatic patients, an important source for transmission, are concentrated. From 2000 to 2009, the number of hospitalized patients with any CDI discharge diagnoses more than doubled, from approximately 139,000 to 336,600, and the number with a primary CDI diagnosis more than tripled, from 33,000 to 111,000.[1] Although the incidence of other health-care—associated infections has declined,[2] CDIs have increased and only recently plateaued.[1] Evidence-based guidelines for the prevention of CDIs in hospitals have been published.[3] However, because the evidence for many of these recommendations is weak[4] the degree to which they can prevent CDIs effectively across a range of hospitals is unknown, as is the relative burden of CDIs in nonhospital and hospital health-care settings.

Methods

In this investigation, three data sources were used to identify health-care exposures for CDIs, determine the proportion of CDIs occurring outside hospital settings, and assess whether prevention programs can effectively reduce CDIs. CDC's Emerging Infections Program conducted active, population-based surveillance for CDIs from eight diverse geographic areas in 2010.[5] Program surveillance coordinators received laboratory reports of positive stool *C. difficile* tests from residents of catchment areas. Cases were defined by a positive *C. difficile* test in a person without a positive test during the previous 8 weeks (repeat positive tests during this period suggest recurrence).[6] Medical records were reviewed to confirm the presence of symptoms consistent with CDI and to record all health-care exposures during the 12 weeks preceding specimen collection (i.e., minimum duration of antibiotic-induced susceptibility to CDI). CDIs were classified by the patient's location at the time of stool specimen collection and divided into three groups: (1) hospital-onset CDI, occurring in a hospitalized patient with a positive stool specimen collected more than 3 days after admission; (2) nursing home—onset CDI, occurring in a nursing home resident with a positive stool specimen collected at any time during their stay; and (3) community-onset CDI, occurring in an outpatient or an inpatient of any health-care facility with a positive stool specimen collected within 3 days (the median incubation period of *C. difficile*) after admission. Community-onset CDI cases were subcategorized based on previous health-care exposures during the 12 weeks preceding specimen collection; previous inpatient exposures took precedence over outpatient exposures when classifying cases.

A second data source was the National Healthcare Safety Network (NHSN) Multidrug-Resistant Organism and *Clostridium difficile* Infection module for laboratory-identified (LabID)-CDI events, which became available in March 2009.[7] Incident LabID-CDI events in NHSN are based on positive *C. difficile* test results from hospital patients who did not have a previous positive test result reported within that facility during the preceding 8 weeks. LabID-CDI events present on admission were defined by a positive stool specimen collected within the first 3 days of admission; a subset was delineated further if patients were discharged from the reporting hospital in the preceding 4 weeks, during which time previous hospitalization is most likely to influence the risk for CDI.[6,7] Rates of hospital-onset CDI cases were calculated per 10,000 patient-days.

The third set of data included early results from three state-led programs (Illinois, Massachusetts, and New York) similar to other programs in which hospitals collaborated with one another to prevent health-care—associated infec-

Key Points

Clostridium difficile infections (CDIs) increased several fold in the past decade and became more serious, but are nonetheless preventable.

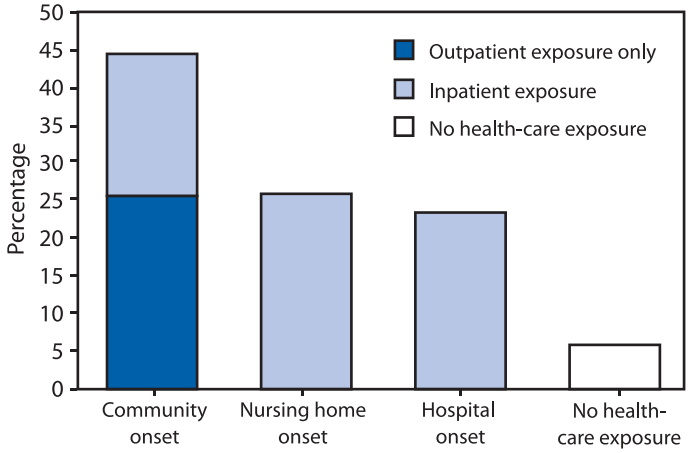
Of all CDIs, 94% are related to health-care exposures and are potentially preventable by reducing unnecessary antibiotic use and interrupting patient-to-patient transmission of *C. difficile*.

CDIs were reduced by 20% over approximately 21 months by 71 hospitals participating in prevention programs focused primarily on infection control strategies (e.g. early reliable detection, isolation, and enhanced environmental cleaning).

Of all health-care—associated CDIs, 75% have their onset outside of hospitals, and 52% of the CDIs treated in hospitals are present on admission; these infections are a potential source for intrahospital transmission.

More must be done to prevent CDIs by various stakeholders working together to expand prevention strategies, including a greater focus on antibiotic stewardship and extending prevention strategies in settings across the continuum of health-care delivery.

FIGURE. Percentage of *Clostridium difficile* infection (CDI) cases (N = 10,342), by inpatient or outpatient status at time of stool collection and type/location of exposures* — United States, Emerging Infections Program, 2010



tions[8] (in this case, hospital-onset CDIs). The three programs included a total of 71 hospitals focused on preventing CDIs during three different periods ranging from 19 to 22 months.* Although the systems for data collection and behavioral change strategies varied among programs, all three used CDC surveillance definitions[6] and focused primarily on infection control interventions to prevent transmission of *C. difficile*; the Massachusetts program did include antibiotic stewardship as a minor component. Using a negative binomial model, rates of hospital-onset CDI from hospitals participating in the three programs were compared between two same-calendar-month, 8-month periods (to control for seasonal variation in rates), one earlier and the other later in the conduct of each program.

Results

The Emerging Infections Program population under surveillance included persons in the catchment areas of 111 acute-care hospitals and 310 nursing homes. A total of 10,342 CDIs were identified; 44% of patients were aged <65 years. CDIs were classified by inpatient or outpatient status at time of stool collection and type/location of exposures (FIGURE). Overall, 94% of all CDIs were related to various precedent and concurrent health-care exposures; of these, 75% had their onset outside of hospitals. In addition, some cases occurred in patients who were exposed to multiple settings. For example, 20% of hospital-onset CDIs occurred in recent (i.e., <12 weeks) residents of a nursing home, and 67% of nursing home—onset CDI cases occurred in patients recently discharged from an acute-care hospital.

A total of 711 acute care hospitals in 28 states conducted facility-wide inpatient LabID-CDI event reporting to NHSN in 2010. A total of 42,157 incident LabID-CDI events were reported. Overall, 52% of LabID-CDI events were already present on admission to hospitals. The pooled rate of hospital-onset CDI was 7.4 per 10,000 patient-days, with a median hospital rate of 5.4 per 10,000 and an interquartile range of 6.2.

The pooled hospital-onset CDI rate across the three prevention programs declined 20%, from 9.3 per 10,000 patient-days during the early comparison period to 7.5 during the later comparison period (rate ratio: 0.80).

Conclusions and Comment

The incidence, mortality, and medical care costs of CDIs have reached historic highs.[1,3,9,10] The estimated number of deaths attributed to CDI, based on multiple cause-of-death mortality data, increased from 3,000 deaths per year during 1999-2000 to 14,000 during 2006-2007, with more than 90% of deaths in persons aged ≥65 years.[10] Recent excess health-care costs of hospital-onset CDI are estimated to be $5,042–$7,179 per case with a national annual estimate (limited to the subset of hospital-onset CDIs only) of $897 million to $1.3 billion.[11] Much of the recent increase in the incidence and mortality of CDIs is attributed to the emergence and spread of a hypervirulent, resistant strain of *C. difficile* that produces greater quantities of principal virulence toxins A and B and has additional factors enhancing its virulence.[9,12] Nonetheless, many of these infections can be prevented, as demonstrated by the 20% reduction in incidence of hospital-onset CDI among three state prevention programs conducted over approximately 21 months. In England, where a national campaign to publicly report and prevent CDIs was implemented in 2007 through an emphasis on antibiotic stewardship as well as infection control,[13] pooled hospital-onset CDI rates declined 56% during a 3-year period (2008-2011).[14] In the United States, the National Action Plan for Prevention of HAIs has targeted a 30% reduction of CDIs in acute-care hospitals by 2015.[15]

Principal recommendations to prevent CDI include improving antibiotic use, early and reliable detection of CDI, isolation of symptomatic patients, and reducing *C. difficile* contamination of health-care environmental surfaces.[3] Good antibiotic stewardship is an important aspect of quality health care that prevents CDI. Antibiotic use increases the risk for developing CDI by seven- to 10-fold while the patient is taking the antibiotic and for 1 month after discontinuation, and by approximately threefold for the subsequent 2 months.[16] CDC provides tools for facilities to develop antibiotic stewardship programs.†

To prevent transmission of *C. difficile*, early detection and isolation of patients with CDI is essential. Nucleic acid amplification tests can be as much as twice as sensitive as enzyme immunoassays and can detect CDI more accu-

rately when used in populations with an appropriate pretest probability (i.e., patients with more than three unformed stools in a 24-hour period without an identified cause).[3,17] Because of their increased sensitivity, nucleic acid amplification tests will yield higher hospital-onset CDI rates. Currently, 35% of NHSN hospitals are using nucleic acid amplification tests; risk adjustment will be necessary to compare rates accurately where diagnostic testing practices vary.

C. difficile frequently is transmitted between patients via hands of healthcare personnel transiently contaminated after contact with symptomatic patients or their surrounding environment. Glove use, with strict adherence to changing between patient contacts, is the best proven method for preventing hand contamination with *C. difficile* from symptomatic patients.[3,4] Health-care environmental services have a key role in reducing contamination that can directly transmit to patients or contaminate the hands of health-care personnel.‡ Because *C. difficile* spores resist killing by usual hospital disinfectants, an Environmental Protection Agency—registered disinfectant with a *C. difficile* sporicidal label claim§ should be used to augment thorough physical cleaning.

These findings emphasize how the risk for CDI from antibiotic exposure and transmission moves with patients across multiple health-care settings, leading to the interdependence of health-care settings in a region to lower their CDI rates. Because antibiotics disrupt the normally protective bacterial populations of the lower intestine in a manner that increases risk for CDI for 3 or more months, antibiotics received in one setting often predispose a patient to develop CDI in another. In contrast, because the incubation period is a median of only 2-3 days,[3] acquisition of *C. difficile* is overall more likely to have occurred in the setting where symptoms have their onset and CDI is diagnosed. Meanwhile, CDIs present on hospital admission are most often related to the care delivered in other inpatient or outpatient facilities; because they are an important source for intrahospital transmission, CDIs present on admission are a risk factor for higher hospital-onset CDI rates.[18]

The findings of this report are subject to at least six limitations. First, data on antibiotic exposure, which are important for targeting prevention efforts, were not available. An NHSN option designed to address this problem is undergoing piloting with electronic health record vendors.‖ Second, data on potential underlying temporal trends in prevention program hospitals were not available. Third, the various methods used to implement prevention strategies in the prevention hospitals were not described (e.g., staff training, assessment and feedback of compliance with isolation precautions, or adequacy of environmental cleaning). Although the pooled rate toward the end of these programs (7.5 per 10,000 patient-days) was similar to the rate across all NHSN hospitals in 2010 (7.4), the three programs started and ended at different rates, suggesting that locally tailored approaches to prevention might be beneficial. Fourth, the impact of ongoing CDI prevention initiatives under way during the early phase of evaluation also was not assessed. Fifth, the potential impact of any shifts in test sensitivity between different methods used (e.g., nucleic acid amplification versus enzyme immunoassay) was not assessed. Finally, in both the Emerging Infections Program and NHSN, the setting of onset was based on where the patient was located at the time of stool specimen collection; therefore, there might have been misclassification of cases if a marked delay occurred between onset of symptoms and stool specimen collection.

Because nearly 75% of all CDIs related to U.S. health care have their onset outside of hospitals, more needs to be done to prevent CDIs across all health-care settings. For its part, CDC is working to improve NHSN LabID-CDI event reporting for nursing homes as well as hospitals. Clinical document architecture specifications are available for electronic health record system vendors to use in enabling their systems to serve as electronic data sources for LabID-CDI event reporting to NHSN.¶ The option to report electronically will take on greater importance as increasing numbers of hospitals are required to report LabID-CDI events to NHSN. Currently, six states (California, Illinois, New York, Oregon, Tennessee, and Utah) mandate public reporting of facility-wide LabID-CDI events. Beginning in 2013, all hospitals participating in the Centers for Medicare and Medicaid Services' Inpatient Prospective Payment System Quality Reporting Program will be required to report facility-wide LabID-CDI events using NHSN to qualify for their 2015 annual payment update; public reporting of hospital rates will begin in 2014 at the Hospital Compare website.[19]

Clinicians and other health-care providers, as well as inpatient and outpatient health-care facilities, state and federal public health officials (e.g., the Partnership for Patients), and partner patient safety organizations, could benefit from increased collaboration in preventing CDIs. Such collaborations could broaden and enhance the use of prevention strategies and do so across the entire spectrum of U.S. health-care delivery. State health departments, working with regional quality improvement organizations, hospital associations, and other nongovernmental patient safety partners, are positioned uniquely to work across these multiple settings.# Given the emphasis of current health-care reform efforts to improve patient safety while reducing costs, now is an opportune time to begin to eliminate health-care—associated CDIs.

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*The Illinois prevention program, led by the Department of Public Health and the Iowa Foundation for Medical Care—Illinois (a health-care quality improvement organization headquartered in West Des Moines, Iowa), included 11 hospitals with complete data from the beginning of March 2010 through October 2011. The Massachusetts program, led by the Massachusetts Coalition for the Prevention of Medical Errors and the Massachusetts Department of Public Health, included 27 hospitals with complete data from January 2010 through September 2011. The New York program, led by the Greater New York Hospital Association and the United Hospital Fund in collaboration with the New York State Department of Health, included 33 hospitals with complete data from March 2008 through December 2009.
†Additional information available at http://www.cdc.gov/getsmart/healthcare/improve-efforts/clinicians.html.
‡Additional information available at http://www.cdc.gov/hai/toolkits/evaluating-environmental-cleaning.html.
§Additional information available at http://www.epa.gov/oppad001/cdif-guidance.html.
%Additional information available at http://www.cdc.gov/nhsn/psc_ma.html.
¶ Additional information available at http://www.cdc.gov/nhsn/cda_esurveillance.html.
#Additional information available at http://www.cdc.gov/hai/stateplans/haistateplans-map.html.

Notes From the Field: Use of Tetanus, Diphtheria, and Pertussis Vaccine (Tdap) in an Emergency Department—Arizona, 2009-2010

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BECAUSE OF AN INCREASING INCIDENCE of reported pertussis cases attributed to waning immunity among adults and adolescents, the Advisory Committee on Immunization Practices (ACIP) in 2005 recommended administration of a new, combined tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) for adolescents and adults aged 11-64 years.[1] ACIP recommended that they receive a single dose of Tdap to replace tetanus and diphtheria toxoid vaccine (Td) for booster immunization against tetanus and diphtheria if they had not previously received Tdap. Adults aged ≥65 years were to receive Td according to ACIP recommendations.[1] To learn whether these age-specific recommendations were being followed in an emergency department (ED), the charts of a sample of patients receiving tetanus vaccines at a large ED were reviewed.

The ED is part of an urban, academic center and has an annual volume of approximately 70,000 patient visits. Patients who received a tetanus booster during September 1, 2009–August 31, 2010, were identified through an inpatient pharmacy database. Orders placed through the computerized physician order entry system were used to determine which form of tetanus vaccine the physician ordered. Nursing documentation was reviewed to determine what vaccine was actually administered because, during the study period, the automated medication dispensary allowed access to both vaccine types when "tetanus" was entered. Records were stratified by month, assigned a random