Supplementary Appendix

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Members of the Survey Team

In addition to the authors, the other members of the Emerging Infections Program (EIP) Healthcare-Associated Infections (HAI) and Antimicrobial Use Prevalence Survey Team are as follows: Sarah Jackson, MPH and Julie Duran, MPH (Colorado Department of Public Health and Environment, Denver, CO); Richard Melchreit, MD and Richard Rodriguez, MPH (Connecticut Department of Public Health, Hartford, CT); Lewis Perry, RN, MPH and Nancy White, RN, BSN, CIC (Georgia Emerging Infections Program, Atlanta, GA); Katie Richards, MPH (Maryland Department of Health and Mental Hygiene, Baltimore, MD); Jane Harper, BSN, MS, CIC, Jean Rainbow, RN, MPH, and Linn Warnke, RN, MPH (Minnesota Department of Health, St. Paul, MN); Joan Baumbach, MD, MPH, MS (New Mexico Department of Health, Santa Fe, NM); Cathy Concannon, MPH and Gail Quinlan, RN, MS, CIC (New York - Rochester Emerging Infections Program/University of Rochester, Rochester, NY); Margaret Cunningham, MPH, Valerie Ocampo, RN, MIPH, and Jennifer Tujo, RN, MSN, MPA, CIC (Oregon Public Health Authority, Portland, OR); and Matthew Crist, MD, MPH (Tennessee Department of Health, Nashville, TN).

Methods: Survey Conduct and Author Roles

The survey was supported through a cooperative agreement with the Emerging Infections Programs, with funds from the CDC's Division of Healthcare Quality Promotion, Division of Preparedness and Emerging Infections, and Office of Antimicrobial Resistance. There were no agreements concerning data confidentiality between the CDC and the authors (some of whom are U.S. federal government employees) or their institutions. All authors vouch for the accuracy and completeness of the data; the first two authors (Shelley Magill and Jonathan Edwards) performed and vouch for the accuracy of the data analysis.

The survey was designed and coordinated by Shelley Magill, Jonathan Edwards, Laura McAllister-Hollod, and Scott Fridkin, with input from other authors. Shelley Magill and Laura McAllister-Hollod developed and conducted survey training. Training in the use of the National Healthcare Safety Network (NHSN) HAI definitions was conducted with assistance from other CDC staff included in the "Acknowledgments" section (below). Survey activities, including data collection, were performed and supervised by EIP HAI and Antimicrobial Use Prevalence Survey Team members and individuals included in the "Acknowledgments" section. Authors participating in data collection include Wendy Bamberg, Meghan Maloney, Joelle Nadle and Deborah Thompson. Authors supervising survey activities and data collection in the EIP sites include Wendy Bamberg, Zintars Beldavs, Ghinwa Dumyati, Marion Kainer, Ruth Lynfield, Joelle Nadle, Susan Ray, Deborah Thompson, and Lucy Wilson. Shelley Magill wrote the first draft of the paper. All authors critically reviewed and provided comments on the first draft, and read and approved the final version. All authors agreed to publish the paper.

Methods: Patient Selection

To reduce the burden of survey activities on the hospital survey dates, the random selection of acute care inpatients to be surveyed in each participating hospital was performed through use of a randomly sorted acute care hospital bed number list. In advance of the survey date, each hospital submitted a list of its acute care inpatient units and the active, acute care bed numbers on those units to its EIP Team (EIPT). With the assistance of CDC project staff, EIPTs mapped each hospital's acute care inpatient units to appropriate NHSN location codes (e.g., adult medical intensive care unit, pediatric surgery ward, well newborn nursery, etc.). EIPTs randomly sorted each hospital's complete list of active, acute care bed numbers using a tool such as the Microsoft Excel® random number generator. This randomly sorted list was used by Primary Teams (PTs) to match acute care bed numbers to the identifiers of patients occupying those beds on the morning of the survey date, obtained from the daily inpatient census generated by PTs between midnight and 0800 hours. PTs and/or EIPTs reviewed medical records of patients matched to the randomly sorted bed number list, starting at the top of the bed number list and working down until the records of 75 patients had been reviewed in small and medium hospitals, or the records of 100 patients had been reviewed in large hospitals. PTs and/or EIPTs ensured that each patient matched to a sampled active, acute care bed number met eligibility criteria for the survey. Empty bed numbers on the randomly-sorted list or bed numbers occupied by ineligible patients (e.g., non-acute care patients) were replaced by proceeding down the list in order to other bed numbers until the target patient sample size was achieved.

Methods: *Clostridium difficile* Infection Definition

For surveyed patients with positive laboratory test results indicating *Clostridium difficile* infection (CDI) who did not meet one of the NHSN "Gastrointestinal" (GI) infection definitions, a prevalence survey-specific CDI infection definition was applied. This definition was consistent with laboratory aspects of previously published definitions[1] and case definitions for population-based surveillance,[2] and required a positive result for a laboratory assay for *C. difficile* toxin A and/or B, or a toxin-producing *C. difficile* organism, detected in a stool sample by culture or other means. The test specimen must have been collected after > 48 hours (or 3 calendar days) of hospitalization, with no evidence that CDI was present or incubating on admission to the survey hospital, or the test specimen could have been collected from the patient in an outpatient setting or during the first 48 hours (or 3 calendar days) of hospitalization when there was a previous stay in the survey hospital within 28 days prior to specimen collection and when there was no stay of >24 hours (or 2 calendar days) in another healthcare facility during the 28 days prior to specimen collection.

Methods: Use of Antimicrobial Therapy as a Screening Tool for Patients with HAIs

Patients were considered to be on antimicrobial drugs at the time of the survey if they were receiving or scheduled to receive an antimicrobial drug on the survey date or the calendar day prior to the survey date, as determined through review of paper or electronic medication administration records and operating room records. Dialysis patients were considered to be on antimicrobial drugs at the time of the survey if they received or were scheduled to receive antimicrobial drugs on the survey date or the calendar day prior to the survey date, or if they received vancomycin or aminoglycoside antibiotics in the 4 calendar days prior to the survey date.

EIPTs retrospectively reviewed the medical records of patients on antimicrobial drugs at the time of the survey, or for whom antimicrobial drug administration information was unknown at the time of the survey, to collect additional information about the rationale for antimicrobial drug use (Figure S1). For patients who were determined to be receiving antimicrobial drugs for treatment of active infections or for no documented rationale, the EIPTs performed additional medical record review to collect information on HAIs (Figure S1).

Methods: Analysis

To identify factors associated with HAI prevalence, we performed univariate and multivariable log-binomial regression modeling; those factors significantly associated with HAIs in univariate analyses (two-sided P value ≤ 0.05) were included in multivariable models. Factors significantly associated with HAIs in a multivariable model remained in the model. Different parameterizations of two factors—patient age and time from admission to survey date (TAS)—were evaluated to determine the model with the best fit, as determined by the likelihood ratio test and lowest Akaike Information Criterion score.

Because age and TAS were significantly associated with HAI prevalence and were the only two factors in the final regression model for which a corresponding variable was present in the Nationwide Inpatient Sample (NIS) dataset (patient age and hospital length of stay [LOS]), we created strata of age and TAS within which to convert predicted HAI prevalence from the regression model to incidence and generate HAI burden estimates. We used TAS as a proxy for hospital LOS, because actual hospital LOS data were available for only 51% of all surveyed patients. Although hospital admission dates were collected for all surveyed patients (since admission dates were known at the time of the survey), discharge dates were collected only for those patients for whom EIPTs performed retrospective medical record review to collect additional data (i.e., those patients receiving or scheduled to receive antimicrobial drugs at the time of the survey, or for whom antimicrobial drug information was not available at the time of the survey). To create proxy LOS categories, we extended the upper bound of TAS categories from the final regression model to the value of the mean hospital LOS for those patients within each TAS category for whom hospital LOS data were available.

Because of low numbers of HAIs in some individual age and TAS/proxy LOS categories, 3 of 6 age categories (≤0.125 years, 0.126-1 year, 2-26 years) and 2 of 6 proxy LOS categories (TAS 4 days and TAS 5-6 days) were collapsed into single categories (age 0-26 years and TAS 4-6 days) for the purposes of

estimating HAI burden in these groups of patients, resulting in 20 different age/LOS strata. The predicted HAI prevalence obtained from the regression model within each of the 20 age/LOS strata was converted to incidence as described in the main body of the manuscript.

Discussion: Limitations

Two additional limitations of our survey methods include: 1) use of antimicrobial therapy as a screening tool; and 2) the method for converting prevalence to incidence.

It is possible that we missed HAIs and underestimated HAI prevalence by using antimicrobial therapy as a screening tool to select medical records to review in detail to identify HAIs. Antimicrobial therapy has been evaluated by several investigators as a means of screening patients for HAIs. Older studies showed that antimicrobial therapy was relatively insensitive (41-86%) for identifying patients with HAIs; [3-6] however, in a more recent study[7] and in our own published[8] and unpublished experience, sensitivity exceeded 90%.

We converted HAI prevalence to incidence using the Rhame/Sudderth formula[9] to enable calculation of HAI burden estimates. Others have evaluated this formula in performing prevalence to incidence conversions, and have highlighted the challenges and limitations of this approach.[10, 11] In our survey, because hospital LOS data were available only for patients on antimicrobial therapy, the overall median hospital LOS used in calculating HAI burden may have been an overestimate; this would tend to result in the total number of patients with HAIs being larger than if hospital LOS data had been available for all surveyed patients. However, because using median hospital LOS data from the NIS in the calculations yielded similar results, we do not believe that our results represent a significant overestimate.

Acknowledgments

We would like to acknowledge the contributions of the following individuals: Deborah Godine, RN, CIC and Celeste Prothro, RN, MPH (California Emerging Infections Program, Oakland, CA); Katherine Allen-Bridson, RN, BSN, MScPH, CIC, Teresa Horan, MPH, Gloria C. Morrell, RN, MS, MSN, CIC, and Shirley Zhang, MSc (Centers for Disease Control and Prevention, Atlanta, GA); Cindy Gross, MT (ASCP), SM, CIC and Dee Higgins, RN, BSN (Georgia Emerging Infections Program, Atlanta, GA); Patricia Lawson, RN, MS, MPH, CIC, LaToya Forrester, MPH and Malorie Givan, MPH (Maryland Department of Health and Mental Hygiene, Baltimore, MD); Emily Hallberg, MPH (Minnesota Department of Health, St. Paul, MN); Monear Makvandi, MPH (New Mexico Department of Health, Santa Fe, NM); Barbara Mooney, BSMB, BSMT (ASCP), CIC (Infection Control Consultants of New Mexico, consultant through *HealthInsight* New Mexico, Albuquerque, NM); Mary Jaco, RN, MSN, CIC (consultant through *HealthInsight* New Mexico, Albuquerque, NM); Jennifer Salazar, LPN (*HealthInsight* New Mexico, Albuquerque, NM); Rebecca Tsay, MPH, MLS, and Anita Gellert, RN (New York - Rochester Emerging Infections Program/University of Rochester, Rochester, NY); Diane Roy, BS (Oregon Public Health Authority, Portland, OR); and Ellen Borchers, MSN, RN, Daniel Muleta, MD, MPH, Loretta Moore-Moravian, RN/BSN, COHN-S/CM, and Dana Jackson, RN, BSN (Tennessee Department of Health, Nashville, TN).

Figure S1. Medical record review process for surveyed patients.

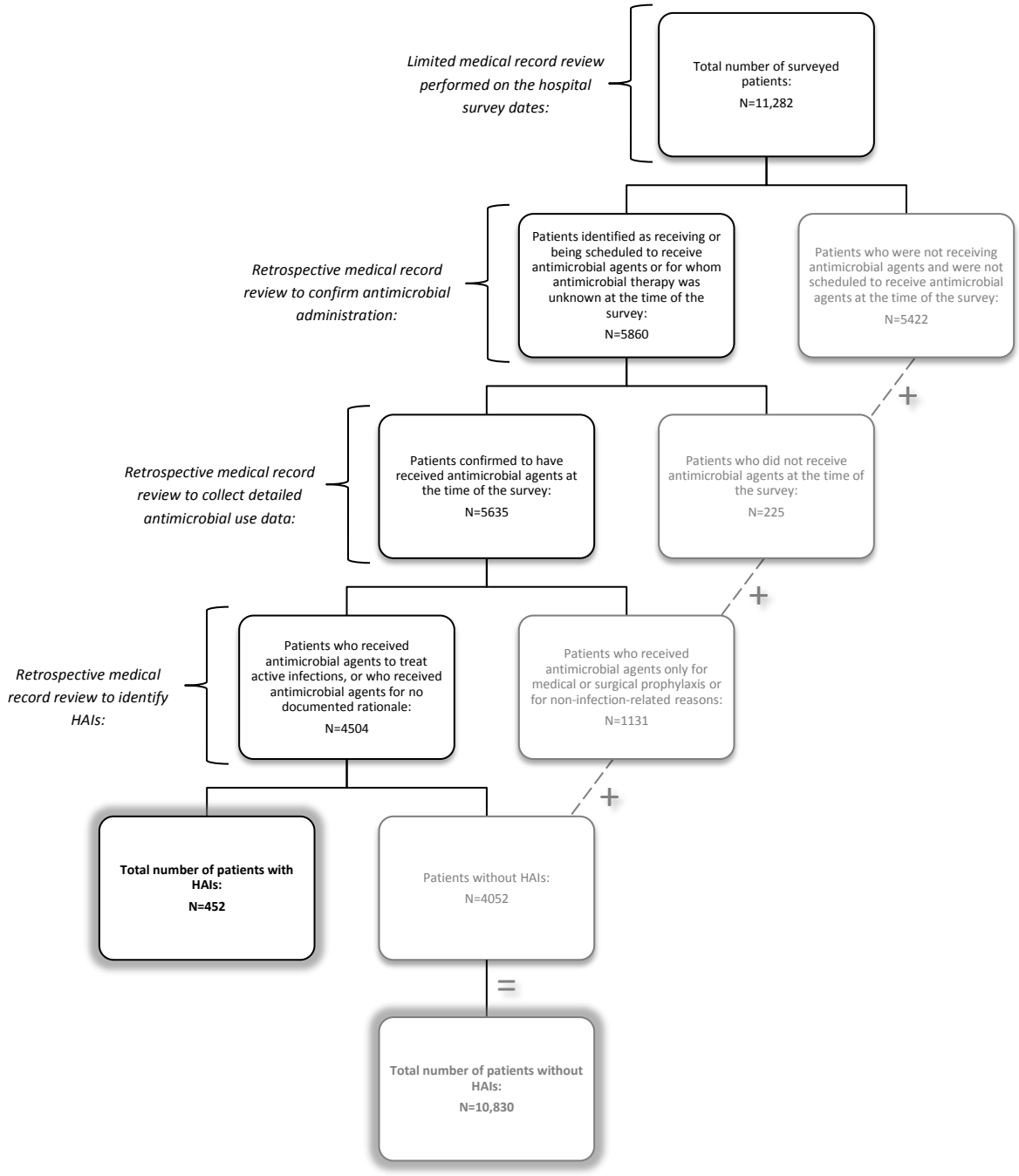

Table S1. Emerging Infections Program sites, survey catchment areas, participating hospitals and patients.

Site	Survey Catchment Area	No. of Hospitals (%)	No. of Patients (%)
California	3-county San Francisco Bay area	8 (4.4)	514 (4.6)
Colorado	5-county metropolitan Denver area	12 (6.6)	877 (7.8)
Connecticut	Entire state	13 (7.1)	945 (8.4)
Georgia	20-county metropolitan Atlanta area	22 (12.0)	1395 (12.4)
Maryland	Entire state	21 (11.5)	1372 (12.2)
Minnesota	Entire state	24 (13.1)	1358 (12.0)
New Mexico	Entire state	20 (10.9)	892 (7.9)
New York	9-county Western New York area	23 (12.6)	1545 (13.7)
Oregon	10-county metropolitan Portland and Eugene area	15 (8.2)	898 (8.0)
Tennessee	Entire state	25 (13.7)	1486 (13.2)
Total		***183 (100)***	***11,282 (100)***

Percentages may add up to >100 due to rounding.

Table S2. Factors independently associated with HAIs in multivariable log-binomial regression modeling.

Factor	Total No. of Patients	No. of Patients with HAIs	Unadjusted HAI Prevalence, percent	Adjusted Risk Ratio (95% CI)	P value
Age[a]					
≤0.125 yr	975	20	2.1	Ref	--
0.126–1 yr	226	21	9.3	2.12 (1.19 – 3.76)	0.01
2–26 yr	1070	33	3.1	2.20 (1.27 – 3.80)	0.005
27–64 yr	4567	180	3.9	2.40 (1.51 – 3.83)	<0.001
65–77 yr	2280	105	4.6	2.72 (1.69 – 4.38)	<0.001
>77 yr	2163	93	4.3	3.17 (1.97 – 5.12)	<0.001
Hospital size					
All others	9068	310	3.4	Ref	--
Large (≥400 beds)	2214	142	6.4	1.24 (1.03 – 1.49)	0.02
Patient location					
All other units	9575	296	3.1	Ref	--
Critical care unit	1707	156	9.1	1.31 (1.04 – 1.67)	0.02
Time from admission to survey date					
≤3 days	6850	44	0.6	Ref	--
4 days	835	16	1.9	2.59 (1.47 – 4.57)	0.001
5–6 days	1033	39	3.8	4.68 (3.05 – 7.19)	<0.001
7–8 days	665	50	7.5	8.86 (5.93 – 13.23)	<0.001
9–14 days	827	110	13.3	14.10 (9.89 – 20.09)	<0.001
≥15 days	1072	193	18.0	18.72 (13.29 – 26.37)	<0.001
Central line[b]					
No central line	9140	192	2.1	Ref	--
Present on survey date	2121	259	12.2	1.81 (1.48 – 2.21)	<0.001
Ventilator[c]					
No ventilator	10748	357	3.3	Ref	--
Present on survey date	527	95	18.0	1.53 (1.18 – 1.97)	0.001

[a]Missing for 1 patient without HAI.

[b]Missing for 20 patients without HAIs and 1 patient with HAI.

[c]Missing for 7 patients without HAIs.

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