Risk Factors for Invasive Methicillin-resistant *Staphylococcus aureus* (MRSA) among Patients Recently Discharged from Acute Care Hospitals through the Active Bacterial Core Surveillance for Invasive MRSA infections (ABCs MRSA)

Request for OMB Approval of a New Data Collection

April 2012

Revision Date: 02.05.2013

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Table of Contents for Part B:

Part B. Collections of Information Employing Statistical Methods

1. Respondent Universe and Sampling Methods

Cases will be identified through ABCs MRSA surveillance. A case for the surveillance is defined as isolation of MRSA from a normally sterile site in a surveillance area resident. Only cases identified as healthcare-associated community-onset (HACO), defined as cases with an initial MRSA culture from a normally sterile site obtained ≤3days after hospital admission and with a hospitalization in the 12 weeks prior to the initial MRSA culture, will be eligible to be included in the study. Only 2-3 hospitals in the following ABCs sites will be participating in the study: California, Connecticut, Georgia, Minnesota, New York, and Tennessee.

The estimated number of cases by ABCs site per year is shown below:

EIP SITES	**CA**	**CT**	**GA**	**MN**	**NY**	**TN**
HACO MRSA cases within 12 weeks after discharge > 18 years of age (N)	110	188	179	43	54	26
HACO MRSA Cases at participating facilities	33	45	27	12	23	10

An eligible case for the study is defined as a patient aged 18 years or older with a positive MRSA culture from a normally sterile site (e.g. blood, pleural fluid, joint, bone) within 3 days after hospital admission (community-onset) and who was discharged from an acute care hospital in the 12 weeks prior to this invasive MRSA episode.

Eligible cases for the study will be identified through routine ABCs MRSA surveillance. After an eligible case is identified, pertinent clinical information will then be abstracted

from the most recent hospitalization (i.e. the last hospitalization prior to initial MRSA invasive culture; also known as hospitalization of interest). Based on this information, EIP personnel will apply inclusion and exclusion criteria.

Inclusion Criteria for Cases:

1. An eligible case, and
2. Length of stay during hospitalization of interest > 3 calendar days (with admit = day 1)

Each person can be enrolled as a case only once during the study period; from the date of most recent hospitalization forward in the study period, a person enrolled as a case cannot serve as a control.

Exclusion Criteria for Cases:

1. Patient with medical record that is unavailable for review after three attempts to retrieve them, or
2. Patient admitted from or discharged to a prison, or
3. Patient who developed an invasive MRSA infection during hospitalization of interest, or
4. Patient where initial admission was to a non-acute care ward during hospitalization of interest, including psychiatric units, rehabilitative or skilled nursing units, or
5. Patient who has already been enrolled as a case, or
6. Patient who was not 18 years of age or older at the time of discharge from hospitalization of interest, or
7. Cases initially included based on medical record review who are found after phone interview to have had an additional hospitalization that lasted > 3 days in a **non-participating** acute care facility between discharge from hospitalization of interest and initial invasive MRSA culture. Enrollment of this case will result in misclassification of the hospitalization of interest.

If during a phone interview a case is found to have had an additional hospitalization that lasted >3days in a **participating** study facility, this case will be included in the study and

the hospitalization of interest will be rectified. For this case, a new medical abstraction form will need to be collected with information related to the previous hospitalization found during the interview (hospitalization of interest) and new control will need to be selected based on the date of the new hospitalization of interest.

Two controls will be identified for each case included in the study. Eligible controls will be randomly selected from a list of patients matched to each case on the following criteria:

- Hospital where case's most recent hospitalization occurred
- Date of hospital discharge on the same day or in the 29 days previous to the case's most recent hospital discharge date
- Age group

Administrative databases at participating hospitals will be used to generate a list of eligible matched controls. For each eligible control randomly selected from a list of potential controls, medical record will be reviewed to determine whether this eligible control should be included in the study.

Inclusion Criteria for Controls:

1) An eligible control,
2) Discharged alive from the matched hospital admission, just as all the case-patients were, and
3) Admitted to an acute care ward during hospitalization.

Exclusion Criteria for Controls:

1) Patient with length of hospital stay ≤3 calendar days (with admit=day 1), or
2) Patient where initial admission was to a non-acute care ward, including psychiatric units, rehabilitative or skilled nursing units, or
3) Patient with medical record that is unavailable for review after three attempts to retrieve them, or
4) Patient admitted from or discharged to a prison, or

5) Patient who developed an invasive MRSA infection in the 12 weeks after being discharged, or during the hospitalization of interest, or
6) Patient already enrolled as a control for another case, or
7) Patients who died between discharge date and matched-case initial invasive MRSA culture, or
8) Controls that meet inclusion criteria based on medical record review, but later are found during phone interview to have had an additional hospitalization that lasted > 3 days in an acute care facility between discharge from hospitalization of interest and the matched-case initial invasive MRSA culture.

A patient may not serve as a control more than once in the study; a person enrolled as a control cannot serve as a case.

We anticipate that a total of 450 patients (150 cases and 300 controls) will be contacted for a telephone interview annually. All these 150 cases and 300 controls will be further screened for eligibility, and, of those, we expect that 95 cases and 190 controls will be enrolled annually (refer to Part A).
Because the risk of HACO invasive MRSA infection varies with age, the following age groups will be used for matching:

AGE GROUP
18–30 years
31-40 years
41-50 years
51-60 years
61-70 years
71-80 years
>80 years

2. Procedures for the Collection of Information

ABCs MRSA surveillance officers are employees of the State Health Department or state agents. This staff will receive training by CDC and the EIP study principal investigator in study methods, data security, and patient confidentiality. All staff will undergo necessary ethics training by participating institutions as required by local policies.

Over a 1 year period, study personnel at each site will prospectively identify through routine ABCs MRSA surveillance eligible cases to be enrolled in the study. Cases and controls eligible for the study will have their medical records for the hospitalization of interest reviewed (appendix D), and those who meet study inclusion criteria and who provide verbal informed consent (refer to Appendix E, verbal consent) will be interviewed. Data will be abstracted from medical records using a standard data abstraction form (refer to Appendix C and D). Details on the hospitalization of interest (e.g. admit and discharge diagnoses, invasive procedures, placement of devices, discharge with an invasive device (such as a central vascular catheter [CVC]), antimicrobial exposures, MRSA infection or colonization status, chronic wounds, patient disposition at discharge, and outcome) will be collected. Microbiology records and infection control records will also be reviewed. Phone interview will be used to ascertain outpatient exposures that occurred from the time of hospital discharge to the onset of the invasive MRSA infection of interest. If a case cannot be reached after 8 phone attempts AND the case has an exposure period ≤ 3calendar days between the date of discharge from the hospitalization of interest and the date of the initial HACO MRSA culture, the health interview form will be completed using information available in the medical record associated with the HACO MRSA hospitalization, which is already being reviewed as part of the routine ABCs MRSA surveillance. The Phone Interview (refer to Appendix F) will include details on device maintenance and duration after discharge (e.g. CVC type, insertion site, duration, indication, number of lumens, use patterns, catheter care and bathing practices), outpatient surgical procedures, outpatient antimicrobial exposures, emergency room visits, type of wound care after discharge, training of caregivers, and patient functional status. Completed copies of coded abstraction forms and interviews will be faxed (if less than 10 completed forms), mailed or scanned and uploaded to a secure FTP site for

transmission to CDC on a monthly basis and data will be entered into a password protected database on a secure limited access server. No patient identifiers such as name, address, phone number, medical record number, and facility name will be sent to CDC.

Power Calculation:

A sample size calculation for a 1:2 matched case-control study was done using PASS software, 2008 (NCCS Statistical Software, Kaysville, Utah). A conservative sample size calculation was performed using a power of 0.80, an alpha of 0.05, and an estimated prevalence of intravascular catheterization (i.e. CVC) in control-patients of 7% to detect a matched odds ratio of 2.5 for cases compared to controls. The presence of CVC at the time of culture was used as the variable of interest because this is a main area where physicians can intervene to prevent invasive MRSA bloodstream infection. The estimated prevalence of CVC was based on a pilot study done in New York using similar population, but that only involved medical record review. Based on these numbers, a sample size of 190 cases (and, therefore, 380 controls) would be required as shown on the table below. For the sample size calculation, we used the prevalence of CVC found during the pilot study conducted in New York. In order for us to reach the target sample, two years of data collection will be necessary; 95 cases and 190 controls will be enrolled annually yielding to 190 cases and 380 controls at the end of two years.

Matched odds ratio	**2.0**
Cases (n)	190
Matched Controls (n)	380
Total Study Population	570

3. Methods to Maximize Response Rates and Deal with Nonresponse

This project is being conducted through the EIP infrastructure in which each of the participating sites has established relationships with laboratories and healthcare facilities within their defined catchment areas. Personnel at these sites have regular contact with the facilities and encourage all facilities and laboratories to participate. Audits of the clinical laboratories in the surveillance area will be performed 1-2 times per year by local EIP personnel to ensure complete ascertainment of cases. HIPAA regulation allows for the disclosure and use of protected health information for research purposes without individual authorization because criteria for a waiver were met. CDC personnel will not perform these audits. Completeness and correctness of data collected should be assessed and cross-checked regularly to identify and address issues with the data collection or the application of surveillance definitions to ensure response. CDC staff will perform site visits to the EIP ABCs MRSA participating sites on a yearly basis to evaluate compliance with standard operational procedures.

Each participating site will track response rates among eligible case- and control-patients. Basic demographic information such as age, gender and race will be recorded for all eligible subjects and used later to compare characteristics between respondents and non-respondents in order to test for any potential response bias.

4. Tests of Procedures or Methods to be Undertaken

To assess study feasibility and resources required for this prospective multi-site study. A pilot retrospective evaluation at one EIP ABCs MRSA site (Rochester, NY), that did not include interview of participants, was performed in September 2009. Preliminary findings suggested that patients discharged with chronic wounds or central venous catheters (CVC), as well as those with history of MRSA infection or colonization or hemodialysis are at increased risk of developing post-discharge MRSA infections.[7]

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Contact information for the statistician consulted for project design and data analysis is as follows:

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Data will be collected by EIP ABCs MRSA personnel, as described previously. Identification of the specific EIP ABCs MRSA surveillance officers who will participate in training and data collection activities is at the discretion of the participating EIP ABCs MRSA sites.