Phenotype Pseudocode for Community Associated Methicillin-resistant *Staphylococcus aureus* (CA-MRSA)

**Background:**

Methicillin-resistant *Staphylococcus aureus* now represents the most common cause of skin and soft tissue infections (SSTIs) in the U.S. Community-associated MRSA (CA-MRSA) has replaced healthcare associated strains in many communities. CA-MRSA strains express increased virulence factors leading to increased tissue destruction and more severe infections. Genetic host factors are suspected as a risk factor for recurrent infection with CA-MRSA, with an increased prevalence in younger, healthier populations.

We propose development of an algorithm to identify patients infected with CA-MRSA for subsequent genome wide association study (GWAS). As many patients with CA-MRSA are diagnosed clinically and treated empirically this algorithm aims to more narrowly define cases as patients with culture-confirmed MRSA infections. In particular our target cohort is to identify the population of younger, healthier patients with MRSA SSTIs as at highest likelihood of having a genetic predisposition to infection with CA-MRSA. Comparison patients (“controls”) will be defined as confirmed MRSA-screen negative patients.

We will implement the algorithm across multiple institutions to achieve adequate power for GWAS with a goal of at least 1500 cases and 1500 controls.

Our emphasis is on isolating a potential genetic association (host), and leveraging data captured routinely in EHRs shapes our algorithm definition to:

* Err on the side of specificity over sensitivity.
* Focus on data elements which are likely to be reliably captured in EHRs

This approach may require fewer data sources, but where that data is available, can allow us to define cases according to the CDC’s clinical definition of CA-MRSA, listed below. We may not be able to abide by this criteria 100%, but we will do the best we can with available EHR data:

•Diagnosis of MRSA was made in the outpatient setting or by a culture positive for MRSA within 72 hours after admission to the hospital.

•No medical history of MRSA infection or colonization.

•No medical history in the past year of:

* Hospitalization
* Admission to a nursing home, skilled nursing facility, or hospice
* Dialysis
* Surgery

•No permanent indwelling catheters or medical devices that pass through the skin into the body.

**Algorithm:**

**Refer to the Appendix of Definitions below for the details on what to search for the numbered footnotes.**

**Case Definition:**

**1: General Inclusion Criteria:**

All patients, aged 0 to 89.

**2: caMRSA Case Criteria:**

**2a: Gold standard MRSA definition:**

Bacteria culture-confirmed MRSA2

AND

Culture drawn in the outpatient (including emergency department) setting, or within 72 hours of admission as an inpatient.

AND

With site of infection classified as a SSTI (skin and soft tissue infection).3 In particular, this focus on a particular infection syndrome/site is more likely associated with a host genetic risk factor.

**OR**

**2b: Silver standard MRSA definition:**

Diagnosis of MRSA (see ICD-9 codes below)

|  |  |  |
| --- | --- | --- |
| icd9\_cd | dx\_dsc | base\_dx\_dsc |
| 038.12 | Methicillin resistant staphylococcus aureus septicemia | Septicemia |
| 041.12 | Methicillin resistant Staphylococcus aureus in conditions classified elsewhere and of unspecified site | Bacterial infection in conditions classified elsewhere and of unspecified site |
| 482.42 | Methicillin resistant pneumonia due to Staphylococcus aureus | Other bacterial pneumonia |

AND

SSTI diagnosis within +/- 7 days of that diagnosis

**3: Case Exclusions:**

AND

No antecedent inpatient hospitalization in the prior 1 year before MRSA infection.

**Non-case (AKA control) definition:**

**Inclusion Criteria**

Patients, aged 0 to 89, who receive routine primary care within your study site defined as >= 2 visits with a primary care provider over a minimum of a 3 year continuous period of enrollment1.

AND

No prior h/o of positive MRSA screen2

AND

No prior h/o SSTI3

AND

No prior h/o MRSA infection4

**Appendix of Definitions**

1. Continuous enrollment:

Implementations of “continuous enrollment” may vary by institution. We are using the same definition as was used for other phenotypes starting with Group Health’s Zoster phenotype where the following was stated:

Continuous enrollment is defined at Group Health as a period of enrollment in a Group Health-administered insurance or integrated health care plan for at least 5 years, allowing interruptions or gaps in coverage of up to three months. Gaps of this size are allowed because they typically represent administrative data inconsistencies rather than actual interruptions in access to care.

Sites may implement continuous enrollment in whatever manner they deem to be consistent with continuous enrollment, including use of more granular rules. For example, Mayo Clinic’s continuous enrollment rules incorporate patient age and gender into the calculation. This is sensible because younger men receiving regular care at Mayo Clinic tend to have fewer encounters than women of the same age or older men.

1. Bacterial culture results for MRSA screen:
   1. Find the following or similar keywords in the text results of a bacterial culture lab test (methicillin OR oxacillin are the only 2 antibiotics for which to search):
      1. MRSA: this was only screenings at NU so was not used at NU, but at other sites may be different
      2. Methicillin-resistant *Staphylococcus aureus*
      3. '"STAPHYLOCOCCUS AUREUS" AND "OXACILLIN RESISTANT"'

AND

* 1. “present” or “positive” or other affirmative mention (unqualified by negation, uncertainty, or historical reference) for cases
  2. “absent” or “negative” or other negative mention for controls

1. SSTI:
   1. For cases:
      1. Must have the following or similar keywords in the text results of a bacterial culture lab test, such as skin, wound, boil, abscess, but also recognizing that anatomic sites (e.g. foot/hand/leg/buttock, etc.) are also typically classified as an SSTI. Thus, keywords we used are:

* SKIN
* WOUND
* BOIL
* ABSCESS
* FOOT
* HAND
* LEG
* BUTTOCK
* BREAST
* CARBUNCLE
* FURUNCLE
* FINGER
* TOE
* CELLULITIS
* IMPETIGO
* SUBCUTANEOUS
* HAIR
* HYDRADENITIS
* ~~NOSE~~
* ~~NASAL~~
  + 1. else, if cannot search this text, must have 1 of the ICD-9 codes from Table 1 below, within 1 week of the MRSA positive culture
  1. For controls:
     1. Exclude if any of the above list of keywords for cases is found in the text result of a lab test
     2. AND use the ICD-9 codes in Table 1 as exclusions if they occurred at any time:

**Table 1**: from McCaig, et al.: Staphylococcus aureus–associated Skin and Soft Tissue Infections in Ambulatory Care (<http://wwwnc.cdc.gov/eid/article/12/11/06-0190-t1>)

|  |  |
| --- | --- |
| Diagnosis | ICD-9-CM code |
| Inflammatory disease of breast | 611 |
| Carbuncle and furuncle | 680.\* |
| Cellulitis and abscess of finger and toe | 681.\* |
| Other cellulitis and abscess | 682.\* |
| Impetigo | 684.\* |
| Unspecified local infection of skin and subcutaneous tissue | 686.9 |
| Other specified diseases of hair and hair follicles | 704.8 |
| Hydradenitis | 705.83 |

1. History of MRSA infection: use ICD-9 codes 041.12, 482.42, 482.41, 038.12, V02.54, V12.04, V09.0. Search anywhere there are diagnosis codes, and also in the problem list. If you have text in your problem list, please also search for MRSA that way.

**Additional desired variables:**

We will also capture the following variables to define our study cohort:

* Demographics:
  + Age
    - at time of infection for cases
    - at time of last continuous enrollment visit for controls
    - current age for both?
  + Gender
  + Race & ethnicity
  + optionally Home address (where allowed by IRB, for geocoding, or instead GeoID)
* optionally, History (y/n) or number of prior MRSA infections, for ex., using the line list from infection control
* History of dialysis (y/n)
* Diabetes status (y/n) : either type 1 or 2 diabetes mellitus, by T2DM algorithm &/or use 250.x ICD-9 codes
* Where possible, also note prior stay in a long term care facility/nursing home in the last year before MRSA infection5

1. Use whatever coded data you have to determine if in a nursing home, or use text search for generic or proper names of area nursing homes, esp. within Social Work/case management notes, e.g.:

* Generic names:
  + NH
  + NSH
  + nursing home
  + SNF
  + skilled nursing facility
  + Hospice
  + NHC
* Proper names such as:
  + Cumberland Manor,
  + Ida Culver House,
  + etc.