Antimicrobial-resistant organisms - Transmission investigation

Multidrug-resistant organisms (MDROs) pose a serious and growing threat to public health, particularly in healthcare settings such as intensive care units (ICUs). One of the most concerning MDROs is Methicillin-resistant *Staphylococcus aureus* (MRSA), a bacterium that can cause life-threatening bloodstream, skin and soft tissue, and surgical site infections.

Researchers at Rush University Medical Center aimed at studying how MRSA spreads in the hospital's ICUs[1]. They sampled patients, healthcare workers, medical equipment, and the environment. In total, they obtained 413 MRSA bacterial isolates and performed whole-genome sequencing to analyze their genetic relationships.

In the following exercises, you will analyze genomic and epidemiological data to help interpret their findings, identify how MRSA spreads, and brainstorm strategies to control it.

Exercise 1 (10 min)

You will analyze an **SNV (single nucleotide variant)** matrix, which shows the genetic differences between MRSA samples. Each cell in the matrix represents the number of SNVs between two isolates. By identifying groups of isolates that are genetically very similar (below a certain SNV threshold), you can define transmission clusters—groups of bacteria likely linked by recent spread. These clusters help us understand how MRSA is moving within and between ICUs. For this analysis, we will focus on 54 samples that appear to be part of transmission clusters.

In the given R code in file **workshop_amr_session.Rmd**:

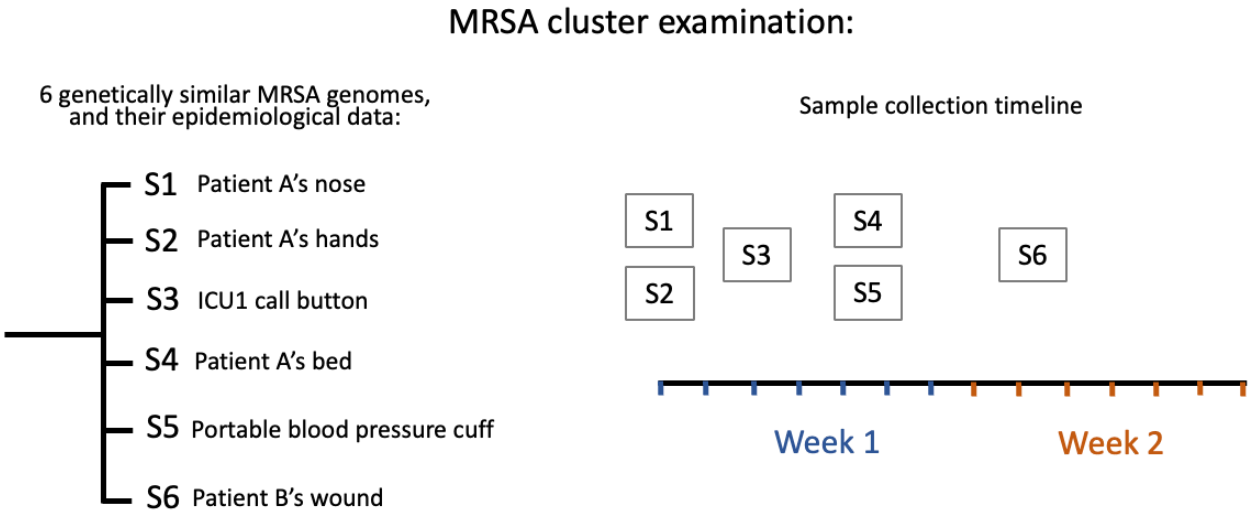
a) Set an SNV threshold of 40 SNVs in the RMarkdown file.
b) Run the code to generate a heatmap (blue indicates more similarity, i.e., fewer SNVs).
c) How many clusters can you identify?
d) What does it mean if multiple MRSA samples are genetically very similar?
e) Change the threshold to 10 SNVs, how does this affect your results? Now change it to 400 SNVs, how many clusters are there now? How might the selected threshold affect findings?

If you cannot run the R code, you can do the exercise using this Shiny App:
https://publichealthanalyticsmodeling.shinyapps.io/workshop_amr_session_shiny/

Exercise 2 (15 min)

Now we will focus on a specific cluster (named **cluster C** by the researchers) to try and understand where transmission might have occurred. You will find that this cluster has 6 samples, isolated from medical equipment and two patients that were in different intensive care units:

You have epidemiological data for these samples including at what point of the study they were taken and where they were collected:



Since these bacteria are genetically very similar, this suggests a possible transmission event. Based on the epidemiological data above, discuss the following questions with your research team (your table):

a) Where was the first sample isolated? Where was the last sample isolated?
b) What does the presence of the intermediate sample on a *portable blood pressure cuff* suggest about how transmission may have occurred?
c) What are possible routes through which the bacteria could have spread from *ICU 1 to ICU 2*? Consider factors such as healthcare staff, equipment movement, patient transfers, and shared spaces.
d) What additional data or testing would you need to confirm the direction of transmission and identify potential sources of contamination?

Exercise 3 (10 min)

The hospital administrators heard about your interesting research findings and want to ask your team about infection prevention strategies to help reduce potential transmission events in the future. Discuss with your team how you would answer their questions:

a) What hospital policies could be implemented or improved to prevent similar events?
b) How could routine genomic surveillance of MRSA isolates help detect potential transmission events earlier?
c) What additional epidemiological data would help confirm transmission routes?
d) The hospital has recently started a program where healthcare workers wash their hands before and after patient contact. How could you use genomic surveillance to evaluate the effectiveness of this measure? What additional epidemiological data would be helpful?

[1]Kyle J Popovich, Stefan J Green, Koh Okamoto, Yoona Rhee, Mary K Hayden, Michael Schoeny, Evan S Snitkin, Robert A Weinstein, MRSA Transmission in Intensive Care Units: Genomic Analysis of Patients, Their Environments, and Healthcare Workers, *Clinical Infectious Diseases*, Volume 72, Issue 11, 1 June 2021, Pages 1879–1887, https://doi-org.ezp-prod1.hul.harvard.edu/10.1093/cid/ciaa731