Proposal for Conducting Sentinel Surveillance for Invasive *Escherichia coli* under the Minnesota Communicable Disease Rule (4605.7046)

Section: Emerging Infectious Disease Epidemiology and Response
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Introduction

This is a proposal for MDH to conduct sentinel surveillance for invasive *Escherichia coli* (*E. coli*) in two populations: (1) people of all ages and (2) infants under 90 days of age. Sentinel surveillance for people of all ages will be conducted in Hennepin and Ramsey Counties and for infants less than 90 days in hospital neonatal/pediatric intensive care units statewide. Invasive *E. coli* can affect anyone, but older adults, immunocompromised individuals, and neonates are at highest risk of infection. Sentinel surveillance will help describe the disease burden, epidemiology, and microbiology of invasive *E. coli* infections through a sample of Minnesotans and is critical in developing future prevention approaches, including informing vaccine development, in order to limit adverse health outcomes in the population.

Objectives of this proposed sentinel surveillance include:

1. Describe invasive *E. coli* infections including outcomes.
2. Understand health disparities in infected patients.
3. Characterize *E. coli* strains causing invasive disease.
4. Inform development of invasive *E. coli* public health interventions.
5. Monitor the success of prevention strategies.

Under part 4605.7046 of the Communicable Disease Reporting Rule, the Commissioner may select infectious diseases/syndromes and reporting sites for sentinel surveillance if specified criteria are met. The law states:

"Subpart 1. Disease Selection. The commissioner may select an infectious disease or syndrome for sentinel surveillance, other than a disease or syndrome for which general reporting is required under this chapter, if the commissioner determines that sentinel surveillance will provide adequate data for epidemiological purposes and the surveillance is necessary for

A. characterization of the pathogen;

B. monitoring vaccine effectiveness; or

C. achieving other significant public health purposes for a disease or syndrome that can cause serious morbidity or mortality.

Subpart 2. Site Selection. The commissioner shall select, after consultation with the sites, sentinel surveillance sites that have epidemiological significance to each disease or syndrome selected under subpart 1. In selecting the sites, the commissioner shall consider:

A. the potential number of cases at the site;

B. the geographic distribution of cases or potential cases in Minnesota, if indicated by the epidemiology of the disease or syndrome;

C. the epidemiology of the disease or syndrome; and

D. the overall impact of sentinel surveillance on a site and the benefit to public health in conducting sentinel surveillance at the site.

1. Disease Selection

Background on invasive *E. coli* infections

Invasive *E. coli* infections are infections that occur outside of the intestine (extraintestinal) and are identified from a body site that is normally considered "sterile" (e.g., blood, cerebral spinal fluid). Extraintestinal pathogenic *E. coli* is a leading cause of adult bloodstream infection and is the second most common cause of neonatal meningitis, infections that cause significant morbidity and mortality.[1] There is no surveillance system for invasive *E. coli* infection in Minnesota.

E. coli is a gram-negative bacillus found in the intestines of healthy humans and animals.[2,3] Although *E. coli* are a part of normal intestinal bacteria, there are strains capable of producing powerful toxins resulting in both intestinal and extraintestinal infections.[3] Intestinal *E. coli* infections such as those caused by *E. coli* O157:H7 or Shiga toxin-producing *E. coli* (STEC)[4] produce symptoms such as diarrhea, abdominal discomfort, nausea, and vomiting; these infections are currently reportable in Minnesota.[5] Extraintestinal pathogenic *E. coli* infections are different from intestinal infections and occur when these potential pathogens, which are normally found in the intestines of healthy individuals are found outside the intestinal tract and lead to infections of the urinary tract, bloodstream, soft skin and tissue, the lower respiratory tract, and other sites.[1] Urinary tract infection (UTI) is the leading source for *E. coli* bacteremia (invasive infection), accounting for more than 50% of cases. Other common sources of *E. coli* bacteremia are biliary tract infection[a] caused by bacteria ascending from the gastrointestinal tract and other intra-abdominal infections, which are predominantly complications of surgeries and procedures.[6] Extraintestinal *E. coli* is the leading cause of community-onset sepsis and bloodstream infections (invasive infection) in the United States.[2,6] Community-onset sepsis means the infection was acquired outside a hospital setting. It is a frequent cause of neonatal sepsis and meningitis, particularly among premature infants.

A. General Reporting Is Not Already Required for Extraintestinal Pathogenic *E.coli*

[a] The biliary tract includes the gallbladder and bile ducts inside and outside the liver.

The current reporting rule requires reporting of enteric *Escherichia coli* infections (all *E. coli* infections that cause enteric/intestinal symptoms, such as diarrhea, abdominal discomfort, nausea, and vomiting; including *E. coli* O157:H7, other Shiga toxin-producing (enterohemorrhagic) *E. coli*, enteropathogenic *E. coli*, enteroinvasive *E. coli*, enteroaggregative *E. coli*, and enterotoxigenic *E. coli*) must be reported to MDH within one working day. However, unlike established enteric E. coli reporting, sentinel surveillance would focus on extraintestinal pathogenic E. coli that is isolated from normally sterile sites. The risks and interventions for invasive e. coli infection are different from the pathogenesis of enteric infections.

B. Population-based sentinel surveillance will provide adequate data for epidemiological purposes, specifically characterization of the pathogen and achieving other significant public health purposes for a disease that can cause serious morbidity or mortality

Sentinel surveillance for invasive *E. coli* infections meets the criteria of Minnesota Rule 4605.7046, subpart 1because it will provide adequate data for epidemiological purposes including characterization of the pathogen for an infection that can cause serious morbidity or mortality.

Data will be adequate for epidemiologic purposes

Sentinel surveillance will provide adequate data for epidemiologic purposes. Case reports, clinical information, and bacterial isolates from cases identified through sentinel surveillance will provide adequate data to address gaps in our understanding of the epidemiology of invasive *E. coli* infection. Through sentinel surveillance, we will collect isolates from invasive *E. coli* cases and perform medical record reviews to collect demographic and clinical information. Combined, this approach will provide adequate data to address gaps in our understanding of the epidemiology of invasive *E. coli* infection. These knowledge gaps include understanding the burden of invasive *E. coli,* demographics of cases, underlying conditions of patients, and health disparities. Additional knowledge gaps involve clinical aspects of invasive *E. coli* infections including outcomes, antibiotic resistance, and the distribution of O serotypes associated with invasive illness. Knowledge gained from surveillance will help inform the development of appropriate prevention and control measures for invasive *E. coli*. Finally, this data will also provide a context for evaluating the effectiveness of future interventions, such as vaccines.

Invasive *E. coli* infections can cause serious morbidity and mortality

Invasive *E. coli* infection can affect anyone but the risk is increased for older adults, people who are immunocompromised (e.g., cancer, diabetes, HIV), pregnant people, and the very young (e.g., newborns and children).[7–9] In one study, the community burden of *E. coli* bloodstream infection was estimated to affect as many as 53,000 non-institutionalized people aged 65 or older each year.[10] Data from the National Healthcare Safety Network (2015-2017) found that among all hospital associated infections (HAIs) *E. coli* was the most prevalent and accounted for approximately 17.5% of pathogens reported.[11] Additionally, *E. coli* was found to be the most common pathogen causing community-onset sepsis in hospitalized adults admitted across 104 U.S. hospitals (2009-2015).[12] Finally, *E. coli* is one of

the most common causes of neonatal sepsis (sepsis in infants < 7 days of age) both nationally and in Minnesota.[13–15]

Morbidity and mortality from invasive *E. coli* infections are substantial, yet little is known about the type or distribution of *E. coli* virulence factors, or factors that promote an organism's ability to cause disease, among these cases. The case fatality rate among those with *E. coli* bloodstream infection ranges from 10-16% depending upon the population and geographic region studied. [9,16,17] Among neonates, meningitis (a substantial proportion which is caused by *E. coli*) results in a 10-15% mortality rate and survivors are at risk of long term neurologic impairment.[18] A potentially important virulence factor of invasive *E. coli* are the O-antigens, which occur on the lipopolysaccharide cell surface and are targeted by both the innate and adaptive immune systems. Over 180 O-antigen serotypes have been described.[19] Despite advances in genetic sequencing, there is limited data on the distribution of O-antigens associated with invasive *E. coli* infections.[19] Finally, recent data describe an increasing resistance to antibiotics among Enterobacterales (a group that includes *E. coli*) further adding to the need for more complete surveillance data.[13,20,21]

C. The surveillance is necessary for the characterization of the pathogen and to achieve significant public health purposes.

MDH does not have a systematic method for tracking invasive *E.coli* infection. Currently there are two surveillance systems that capture a small subset of invasive *E. coli* infections: infections caused by carbapenem (a specific class of antibiotics) resistant *E. coli* isolated from any body site, and sepsis among patients through the first seven days of life. The need for more comprehensive invasive *E. coli* surveillance is emphasized by the significant burden, morbidity, and mortality of invasive *E. coli* infection as well as gaps in knowledge. As proposed, sentinel surveillance for invasive *E. coli* infection will provide adequate data to address important knowledge gaps including burden, outcomes, underlying risk factors for illness, clinical course and outcomes, health disparities, distribution of virulence factors, and antibiotic resistance in Minnesota. Additionally, with vaccines in development, baseline data collected by sentinel surveillance will be useful in monitoring the effectiveness of future interventions.

2. Site Selection

A. MDH consulted with the selected sites

MDH consulted with infection preventionists and microbiologists from Minnesota health systems to introduce invasive *E. coli* sentinel surveillance and request feedback on the proposed surveillance protocols. We provided the justification and objectives for surveillance and described the work required by partners. The surveillance mechanisms will be consistent with existing systems in these facilities. MDH staff will be responsible for medical record reviews to complete case report forms. Partners will be responsible for the identification of cases and shipping of isolates to the MDH Public Health Laboratory, in addition to providing a line list of cases to MDH epidemiology staff.

Overall partners were supportive of establishing surveillance for invasive *E. coli* infection; many acknowledged the gaps in data and need for the surveillance. There were no issues or concerns raised by health care facilities or clinical laboratories. However, if concerns are raised in the future, we will work with partners to problem solve with them as in previous projects.

B. The sites have epidemiological significance to the disease selected.

The sites chosen for surveillance have epidemiological significance as Hennepin and Ramsey counties are the two most densely populated counties in Minnesota. In total, they comprise greater than 30 percent of the state's population and will contribute a representative sample of Minnesota residents. Within these two counties, there are approximately nineteen acute care facilities, including long-term acute care hospitals, transplant centers, an academic facility, trauma centers and a Veteran's Affairs hospital. While *E. coli* is a leading cause of neonatal sepsis, the overall burden of neonatal invasive infection is low. Therefore, hospital systems with neonatal intensive care units statewide were selected as surveillance sites since these facilities oversee the health of younger, high-risk patients who are the most likely to meet inclusion criteria. In summary, these sentinel surveillance sites were selected to obtain a large and representative sample of Minnesota residents in addition to increasing the surveillance sample for neonates < 90 days of age who are at high risk of invasive *E.coli* infection.

C. The following factors required under Minn. R. 4605.7046 subp. 2 were considered in selecting the sites:

a. Potential number of cases at the site

The incidence of invasive *E. coli* among adults and neonates in Minnesota is not well known; this is part of what we will learn through surveillance. MDH obtained preliminary data from three major health systems that conduct laboratory testing and identification of *E. coli* in the state. From September 2022 to December 2022, an estimated 635 cases of invasive *E. coli* were identified among Minnesota residents. We believe this number will be an under-estimate of the true surveillance burden. Our catchment area will include more than three health systems. Therefore, we anticipate approximately 250 cases per month including adult and neonatal cases. This sample size will be sufficient to identify rare clinical features or serotypes and to perform robust subgroup comparisons.

b. Geographic distribution of cases or potential cases in Minnesota, if indicated by the epidemiology of the disease or syndrome

The geographic distribution of invasive *E. coli* infections in Minnesota is unknown. However, because the risk of infection is associated with factors such as age or underlying condition, case numbers will correlate with population centers. Additionally, hospital systems with NICUs were selected because they

provide specialized care to a population that is high risk for invasive *E. coli* infection. In sum, sentinel sites were selected to maximize identification of invasive *E. coli* cases, particularly among those who are at highest risk.

c. Epidemiology of the disease or syndrome

Despite the substantial burden of invasive *E. coli* infections, no population-based data are available for Minnesotans. Previous studies have shown that invasive *E. coli* disease is the leading cause of community-onset sepsis and bloodstreams infections in the United States.[2,6] MDH continues to play an important role in describing the epidemiology of various diseases and invasive *E. coli* would not be different. As proposed, sentinel surveillance for invasive *E. coli* infection will provide adequate data to evaluate the incidence of invasive *E. coli,* describe demographics of patients and clinical aspects of invasive *E. coli* infections including outcomes, antibiotic resistance, describe the distribution of O serotypes associated with invasive illness, and identify health disparities. Additionally, with vaccines in development, data collected by sentinel surveillance will be useful in monitoring the effectiveness of future interventions.

d. Overall impact of sentinel surveillance on a site and the benefit to public health in conducting sentinel surveillance at the site

Very little is known about the epidemiology of invasive *E. coli* infection in Minnesota, and population-based national data are limited. Establishing sentinel invasive *E. coli* surveillance is critical to estimate the burden and risk factors of invasive *E. coli* infections, describe the strains causing invasive infections, understand important demographic or clinical features, and describe health disparities among cases. Additionally, MDH surveillance data will also contribute to regional and national descriptions of invasive *E. coli* infection epidemiology. Participating facilities will benefit from a greater understanding of the burden and epidemiology of invasive *E. coli* in Minnesota and nationally. Ultimately, this knowledge will inform prevention efforts and support health care providers in their efforts to prevent and control invasive *E. coli* infections as tools (e.g., vaccines) become available to do so. MDH will work to minimize the burden on sites by building on existing surveillance protocols and by providing epidemiologists to complete case report forms/chart reviews of cases. The key tasks of the health care entities are to identify cases and submit isolates to the MDH PHL.

CONCLUSION

The proposed sentinel surveillance of *E.coli* meets the requirements of subpart 1 and subpart 2 of Minnesota Rules, 4605.7046. The surveillance is needed and will benefit public health in Minnesota. Therefore, we request that the Commissioner approve this proposal.

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