

**Title:** Rising Injection-Related Infections Amid Declining Overdose Deaths in the Southeast

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**Background:** Although opioid overdose deaths have recently stabilized or declined in parts of the southeastern United States, injection-related infections (IRIs) continue to rise. This evolving syndemic of substance use disorder (SUD) and infectious complications is often under-identified due to limitations in ICD-10 coding, provider documentation variability, and underreporting of injection drug use. Consequently, health systems lack reliable tools to quantify IRI burden and evaluate trends.

**Objectives:** To develop and validate an ICD-10–based algorithm to accurately identify four IRI phenotypes (endocarditis, vertebral osteomyelitis/epidural abscess, bacteremia & deep infections, and skin & soft tissue infections (SSTI)) and to quantify its diagnostic performance against gold-standard manual chart review.

**Methods:** We conducted a retrospective analysis of a multi-hospital electronic medical record dataset within a single health system from January 1, 2023 to January 1, 2025. Phenotype-specific ICD-10 codes for IRI diagnoses were combined with SUD-related ICD-10 codes and temporally linked evidence of SUD using an iterative modeling approach. Validation was performed through blinded manual chart review by two independent reviewers using predefined adjudication criteria. Inter-rater reliability was assessed using Cohen’s kappa. Algorithm performance was summarized using positive predictive value (PPV).

**Results:** The algorithm identified 710 true positive, 158 suspected positive, and 175 false positive encounters. Strict PPV was 68%, and inclusive PPV was 83%. Inter-rater reliability was strong ( $\kappa = 0.86$ ). Over the study period, IRI encounters increased, while opioid overdose admissions remained stable.

**Conclusions:** Injection-related infections are rising despite stabilization of overdose admissions in this southeastern health system. A validated ICD-10 algorithm enables scalable identification of IRIs without reliance on structured data fields or natural language processing.

**Recommendations:** This validated algorithm may strengthen public health surveillance, inform resource allocation, support addiction medicine integration and infectious disease service planning, and enable health system–level monitoring of injection-related infection trends as the opioid crisis evolves beyond overdose mortality alone.

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