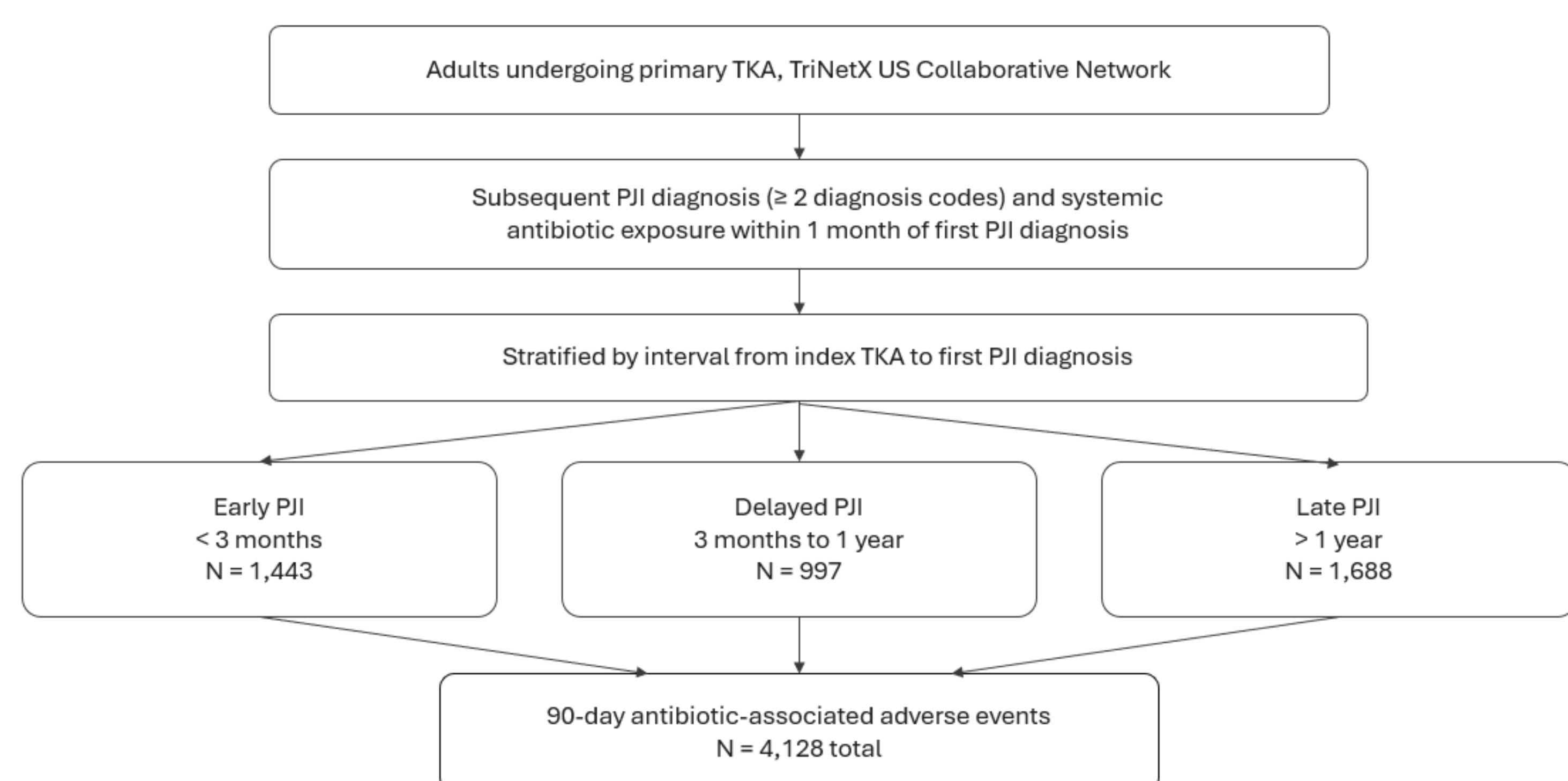


BACKGROUND

- Systemic antibiotics are essential for the treatment of periprosthetic joint infection (PJI) following total knee arthroplasty (TKA), but their short-term adverse-event burden remains incompletely characterized.
- Most PJI literature focuses on infection eradication, reoperation, and implant retention, while antibiotic-associated renal, hepatic, hematologic, gastrointestinal, allergic, and cardiac complications receive less attention.
- This study evaluated 90-day adverse events following systemic antibiotic treatment for TKA PJI and compared adverse-event profiles according to infection timing.

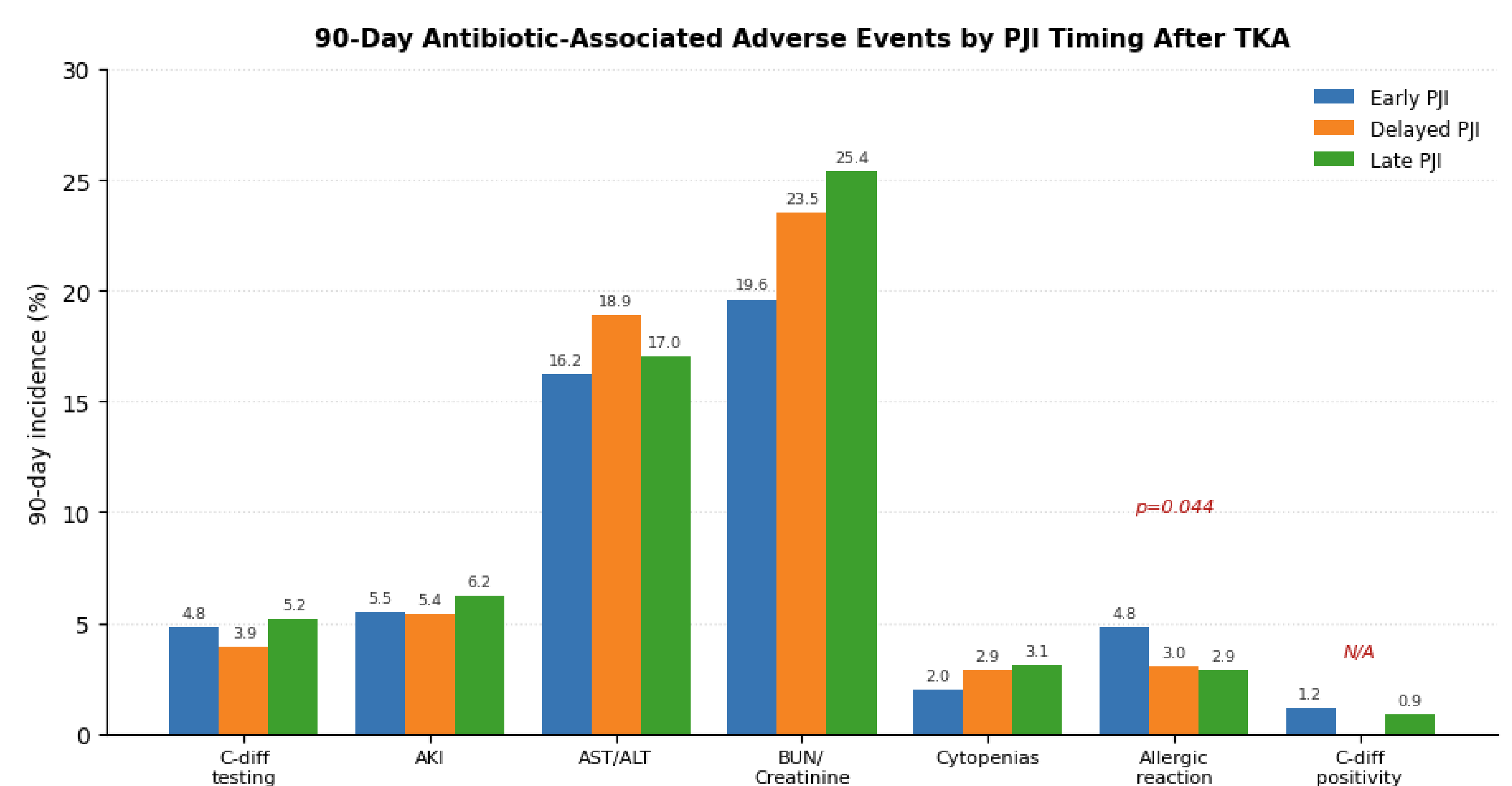
METHODS



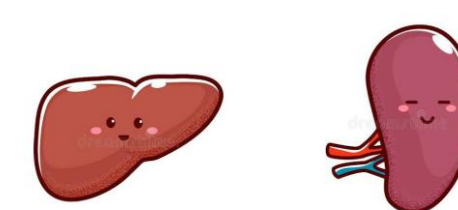
- A retrospective descriptive cohort study was performed using a federated, de-identified global electronic health record network.
- Adults undergoing TKA who subsequently developed PJI were identified using procedural and diagnosis codes.
- To improve diagnostic specificity, inclusion required:
 - ≥2 PJI diagnosis codes
 - Systemic antibiotic exposure within 1 month of the first PJI diagnosis.
- PJI was stratified by timing after the index TKA:
 - Early: <3 months
 - Delayed: 3 months to 1 year
 - Late: >1 year
- The primary analysis assessed 90-day adverse events after systemic antibiotic exposure, including: C. difficile testing and diagnosis-coded infection, acute kidney injury, elevated AST/ALT, elevated BUN/creatinine, hematologic abnormalities, allergic reactions, toxic liver disease, and cardiac events including long-QT syndrome/torsades de pointes.
- For each outcome, patients with that event before systemic antibiotic use were excluded from the corresponding at-risk population.
- As a secondary analysis, adverse-event rates were compared across early, delayed, and late PJI groups using Pearson chi-square testing.

RESULTS

- 4,128 patients met inclusion criteria:
 - 1,443 early PJI
 - 997 delayed PJI
 - 1,688 late PJI.
- Renal and hepatic laboratory abnormalities were the most common adverse events.
 - Elevated BUN/creatinine: 19.6% early, 23.5% delayed, 25.4% late
 - Elevated AST/ALT: 16.2%, 18.9%, and 17.0%, respectively.
- Acute kidney injury occurred in 5.5%, 5.5%, and 6.2% of early, delayed, and late PJI patients, respectively.
- C. difficile testing occurred in 4.8%, 4.0%, and 5.2%, while hematologic abnormalities occurred in 2.0%, 2.9%, and 3.1%.
- Most adverse events did not differ significantly by PJI timing.
- Allergic reactions were significantly more frequent in early PJI compared with delayed and late PJI (4.8% vs 3.0% vs 2.9%; $p=0.044$).
- Diagnosis-coded C. difficile infection, toxic liver disease, and cardiac events were infrequent or not reportable because of small cell counts.



CONCLUSION



- Among patients receiving systemic antibiotics for TKA PJI, renal and hepatic laboratory abnormalities were the most frequently recorded 90-day adverse events.
- Overall adverse-event profiles were generally similar across early, delayed, and late PJI.
- These findings demonstrate a measurable short-term morbidity associated with systemic antibiotic therapy and support consideration of treatment-related toxicity alongside infection control.
- This is particularly relevant because antibiotic treatment duration for PJI remains guided by limited high-quality evidence, reinforcing the need to balance efficacy with potential adverse effects.