Appendix

Table 3

*Evidence Synthesis Table*

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| Studies | Design | Sample | Outcome/Findings |
| Cost-Effectiveness Analysis of Fosfomycin for Treatment of Uncomplicated Urinary Tract Infections in Ontario.  Perrault L, et al. (2017) | Cost-minimization analysis, meta-analysis | Data were obtained from Physician Services (2016), Ontario Case Costing Initiative, and Pharma Stat provincial data. | The analysis revealed that the cost per patient for uncomplicated UTI treatment is similar for all 4 antibiotics, from $96.19 for sulfonamides to $105.12 for fosfomycin. Fosfomycin has lower resistance profile, safe, effective and offers a single dose regimen for treatment of uUTI, associated with high degree of compliance. |
| Cost-effectiveness of antibiotic treatment of uncomplicated urinary tract infection in women: a comparison of four antibiotics.  Sadler S, et al. (2017) | Systems review, network meta-analysis  Probabilistic economic and deterministic sensitivity analyses. | The systemic review identified 11 studies that formed a connected evidence network meta-analysis. | Based on recent estimates of trimethoprim resistance rates in England, a single 3 g dose of Fosfomycin is likely the most cost-effective treatment option for uncomplicated UTIs in women. |
| Cost-effectiveness and budget impact of the management of uncomplicated urinary tract infection by community pharmacists.  Sanyal et al. (2019) | Prospective Study of community pharmacists in New Brunswick between June 2017 and April 2018.  Probabilistic analysis to evaluate impact of treatment strategies on cost and quality-adjusted-life-months (QALMS)  Cost-utility analysis | The systemic review identified 11 studies that formed a connected evidence network meta-analysis. | The community pharmacist-initiated and guided management was less costly and gave comparable QALMs compared to family and emergency physicians in prescribing Nitrofurantoin, TMP-SMX, or Fosfomycin for the treatment of uncomplicated UTIs. |
| Qualitative Analysis of Primary Care Provider Prescribing Decisions for Urinary Tract Infections  [Grigoryan](https://pubmed.ncbi.nlm.nih.gov/?term=Grigoryan+L&cauthor_id=31248119) et al. (2019) | Qualitative semi-structured interviews and thematic analysis. | 18 primary care providers practicing in two family medicine clinics in a large urban area in Texas, between July 2017 and November 2017. | Few providers relied on IDSA guideline in the treatment of uncomplicated UTIs. |
| Antibiotic Prescribing in New York State Medicare Part B Beneficiaries Diagnosed with Cystitis Between 2016 and 2017  Yu et al. (2020) | Retrospective, cohort study of Medicare Part B enrollees in New York State. | There were 23,981 and 26,677 prescriptions written for cystitis across NYS in 2016 and 2017. | TMP-SMX, and Fosfomycin prescription and B lactamase prescriptions increased, and fluoroquinolone use decreased in both older female and male adults.  The study suggests widespread prevalence of fluoroquinolone and B lactamase prescribing needs outpatient antimicrobial stewardship. |
| Effect of 5-Day Nitrofurantoin vs Single-Dose Fosfomycin on Clinical Resolution of Uncomplicated Lower Urinary Tract Infection in Women: a Randomized Clinical Trial  Huttner et al. (2018) | Multinational, open-label, analyst-blinded, randomized clinical trial | 513 non-pregnant women aged 18 years and older with symptoms of acute uncomplicated cystitis was conducted in Geneva, Switzerland from October 2013 to April 2017. Participants were recruited at hospital units and outpatient units. | 5-day Nitrofurantoin significantly has higher clinical and microbiological resolution than single-dose Fosfomycin, with few gastrointestinal adverse events of nausea and vomiting for both groups. |
| Preferential Use of Nitrofurantoin Over Fluoroquinolones for Acute Uncomplicated Cystitis and Outpatient Escherichia coli Resistance in an Integrated Healthcare System.  Pedela RL, et al. (2017) | Retrospective pre-intervention post-intervention study. | Urban setting in Colorado, 477-bed hospital, emergency department and urgent care department, eight community health clinics, and 15 school-based clinics.  study included 5,714 adults treated for acute cystitis and 11, 367 outpatient E. coli isolates. | After a change in the institutional guidelines, there was an immediate 26% reduction in Fluoroquinolone use and stabilization in Fluoroquinolone resistant E. coli. There was an increased use of Nitrofurantoin use without a change in nitrofurantoin resistance. |
| Evaluation of the trends and appropriateness of fluoroquinolone use in the outpatient treatment of acute uncomplicated cystitis at five family practice clinics.  Robinson, et al. (2019) | Retrospective Study | 19-64 YO women seen at five family medicine clinics and prescribed nitrofurantoin, ciprofloxacin, or levofloxacin for uncomplicated cystitis | Of the 567 women included in the study, 395 were given Nitrofurantoin and 172 were given Fluoroquinolones. 343 or 86.8% and 18 or 10.5% were appropriately prescribed Nitrofurantoin and fluroquinolones, respectively. For women inappropriately Fluoroquinolones, 15 or 87.8% lack contraindication to Nitrofurantoin. |
| Fosfomycin Trometamol versus Comparator Antibiotics for the Treatment of Acute Uncomplicated Urinary Tract Infections in Women: A Systematic Review and Meta-Analysis.  Cai T et al. (2020) | Systematic Review and meta-analysis | 15 RCTs were included, with a total of 2,295 female patients older than 18 years old | Fosfomycin trometamol is associated with high patient compliance and is as effective and safe in comparison to comparator antibiotic in the treatment of acute uncomplicated cystitis. |
| Improvement in adherence to antibiotic duration of therapy recommendations for uncomplicated cystitis: a quasi-experimental study.  Giancola SE, et al. (2019) | Quasi-experimental study | Women aged 18-64 years who were prescribed Nitrofurantoin, SMT-TMX, or ciprofloxacin within seven days of encounter at five family medicine clinics. | Clinics which received education, with revised EHR, increased adherence from 22.1% to 58.8%; *P*<0.01. Revising/adding default prescribing instructions to targeted antimicrobials and their DOT in an EHR, and in-service, increased clinician adherence to uncomplicated cystitis first-line antibiotic DOT guidelines. |
| Treatment Effect of Nitrofurantoin for a Non-Inferiority Trial in Uncomplicated Urinary Tract Infection.  Mitrani-Gold FS, et al. (2020) | Systemic literature review and meta-analysis. | Search resulted in a total of 2048 publications. Of these 76 met eligibility criteria. After inclusion and exclusion, twelve studies, including 11 trials were included in meta-analysis. | The corresponding treatment effect estimate for Nitrofurantoin supports the conservative non-inferiority margin of 12.5% and is consistent with the recently published FDA guidance. |