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MAJOR ARTICLE

Effectiveness and Safety of Antibiotics in Kidney Transplant Recipients With Asymptomatic Bacteriuria: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Background. Asymptomatic bacteriuria (ASB) is generally systematically screened and treated with antibiotics in kidney transplant recipients (KTRs). We aimed to explore the role of antibiotic therapy in management of ASB in KTRs.

Methods. Randomized controlled trials conducted through 10 May 2023 were searched on Ovid MEDLINE, Web of Science, PubMed, and Cochrane CENTRAL. We used inverse variance random-effects models for all meta-analyses; for rare outcomes, we used the Mantel-Haenszel method. ROB-2 criteria were used to assess the risk of bias.

Results. We identified 4 randomized controlled trials (including 478 participants). Antibiotic therapy, compared with no therapy, nonsignificantly increased the risk of acute pyelonephritis by 19% (relative risk, 1.19 [95% confidence interval (CI)], .72–1.94; $I^2 = 0\%$) and that of symptomatic urinary tract infection (UTI) by 18% (1.18 [.78–1.78]; $I^2 = 28\%$). The risks of all-cause mortality (relative risk, 1.56 [95% CI, .54–4.52]), graft loss (0.80 [.20–3.19]), graft rejection (0.89 [.46–1.70]), hospital admission due to symptomatic UTI (0.92 [.48–1.76]), symptomatic UTI caused by a multidrug-resistant organism (1.31 [.63–2.74]), *Clostridioides difficile* diarrhea (0.75 [.23–2.42]), and serious adverse events (1.20 [.75–1.91]) did not differ significantly between groups, nor did the change in serum creatinine level from baseline to the end of the study (mean difference, 0.40 mg/dL [95% CI, −.05 to .85 mg/dL]). No significant differences were demonstrated in any outcomes between antibiotic therapy and no-therapy arms across subgroup and sensitivity analyses.

Conclusions. Current evidence does not support routine screening and treatment of posttransplant ASB in KTRs.

Keywords. antibiotic; asymptomatic bacteriuria; kidney transplantation; pyelonephritis; urinary tract infection.

Asymptomatic bacteriuria (ASB) is defined as the presence of bacteria in the urine when there are no symptoms of urinary tract infection (UTI), such as fever, chills, painful urination, abdominal pain, or blood in urine. Up to 51% of kidney transplant recipients (KTRs) experience bacteriuria in the first 3 years after kidney transplantation, and the incidence of UTIs, as the most common complication and a significant source of morbidity in KTRs, ranges from 6% to 83% depending on the diagnostic criteria [1–3]. Acute pyelonephritis is the most serious form of UTI and may result in sepsis and acute graft dysfunction in this patient population [4].

Despite the absence of solid evidence, ASB is systematically screened for and treated with antibiotics in many kidney transplant centers, with the presumption that eradication of ASB can reduce the risk of acute pyelonephritis and symptomatic UTI [5]. Clinicians are also concerned that clinical manifestations

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of posttransplant pyelonephritis may be masked due to graft denervation and use of immunosuppressive medications [6]. Nevertheless, it remains unclear whether antibiotic treatment of ASB effectively prevents progression to acute pyelonephritis or symptomatic UTI and thereby improves patient and graft outcomes. In addition, antibiotic exposure has well-known ramifications, such as emergence of antimicrobial resistance and antibiotic-associated adverse events [6, 7].

To date, 1 Cochrane review and 2 systematic reviews and meta-analyses have assessed the effects of antibiotics versus no therapy in KTRs with ASB. In the Cochrane review, published by Coussement et al in 2018 [6], only 2 studies were included (1 randomized controlled trial [RCT] and 1 quasi-RCT); the authors concluded that the results of 3 RCTs ongoing at the time of this review may help resolve existing uncertainties. In a more recently published systematic review and meta-analysis [3], a total of 5 studies (4 RCTs and 1 quasi-RCT) were included. The results of that study suggested that antibiotic treatment of KTRs with ASB does not reduce the incidence of subsequent symptomatic UTI or provide any benefit to graft outcomes. Antibiotic treatment was also found to present an uncertain risk for the emergence of multidrug-resistant (MDR) bacteria. This systematic review and meta-analysis had important limitations. First, the authors asserted that no subgroup analyses could be performed due to the paucity of data. Furthermore, the study lacked some critical sensitivity analyses (eg, analysis of RCTs excluding KTRs with ureteral catheters) and included some inaccurate data regarding the number of study participants from whom MDR bacteria were isolated during follow-up. Similarly, another systematic review and meta-analysis evaluating 9 studies (4 RCTs, 1 quasi-RCT, and 4 observational studies) indicated no clinical benefit of antibiotic therapy for ASB in KTRs [8].

We performed the current systematic review and meta-analysis of RCTs evaluating antibiotic therapy versus no antibiotic therapy in KTRs with ASB at any time point after transplantation. We also aimed to investigate the outcomes in several preplanned subgroup and sensitivity analyses. We hypothesized no significant difference between antibiotic therapy and no antibiotic therapy for all patients and both subgroups.

METHODS

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [9]. We registered our protocol at PROSPERO (International Prospective Register of Systematic Reviews) (CRD42023430397; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=430397) (accessed 20 August 2024). There were no changes in our protocol until we finished conducting the systematic review.

Population, Intervention, Comparator, and Outcomes

The participants/populations were adults with end-stage kidney disease who were recipients of a first or subsequent cadaveric or living donor kidney transplant and who had ASB. The interventions or exposures were antibiotics, and the comparators/controls received placebo or no antibiotic. The outcomes were the incidences of acute pyelonephritis and symptomatic UTI.

Literature Searches

A thorough search of Ovid MEDLINE, Web of Science, PubMed, and Cochrane CENTRAL was conducted through 10 May 2023 to identify studies according to inclusion/exclusion criteria. Literature search strategies are presented in the Supplementary Materials. We included all languages and did not restrict by publication year.

Selection of Studies and Data Extraction

We included RCTs comparing antibiotic therapy with no antibiotic therapy or placebo for ASB in recipients of a first or subsequent cadaveric or living donor kidney transplant. RCTs assessing pregnant women, patients with graft loss before randomization and those awaiting any urological procedure in which mucosal bleeding is anticipated were excluded, as were quasi-RCTs. Three investigators (U. A., K. K., and S. C.) independently selected studies by applying the prespecified inclusion/exclusion criteria after the literature search; disagreements were resolved by a fourth reviewer (A. T. A.). Data extraction was performed by 3 reviewers (U. A., K. K., and S. C.) using a predefined standard data extraction form and was checked by another researcher (A. T. A.). A member of the systematic review team (L. H. T.) contacted the authors of primary studies to obtain any missing data relevant to the current review and meta-analysis; authors of primary studies were also asked to check extracted data for completeness and correctness.

Primary and Secondary Outcomes, and Definitions Used

The co–primary outcomes were the incidences of symptomatic UTI and acute pyelonephritis. To identify ASB in asymptomatic women and men, previous definitions or those adapted by the authors were used [6, 10]. In 3 of the included RCTs [11–13], ASB was defined as isolation of a single bacterial species at 10^5 colony-forming units (CFUs)/mL in a urine specimen from a patient without UTI symptoms. In contrast, Origüen et al [14] required 2 consecutive urine specimens with isolation of the same bacterial strain in quantitative counts $\geq 10^5$ CFUs/mL in women, whereas a single clean-catch voided urine specimen was adequate for diagnosis of ASB in male patients. Symptomatic UTI was defined as the isolation of a bacterial species from a patient with symptoms such as fever, chills, dysuria, abdominal pain, and blood in the urine. We used the thresholds of urinary bacterial growth (in CFUs per milliliter)

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from the included RCTs to define symptomatic UTI. Acute pyelonephritis was defined by the presence of fever with bacteriuria and/or bacteremia and ≥1 of the following criteria: chills, allograft tenderness, or cystitis. MDR bacteria were defined as being nonsusceptible to ≥1 antibiotic in ≥3 antimicrobial categories [15].

Secondary outcomes included all-cause mortality, graft loss (including death with a functioning allograft), graft rejection (either clinically suspected and treated or histopathologically proven), change in the estimated glomerular filtration rate (eGFR) from baseline to the end of follow-up, change in the serum creatinine level (in milligrams per deciliter) from baseline to the end of follow-up, hospital admission due to symptomatic UTI, number of persistent or relapsing ASB episodes (with persistence defined as an episode caused by the same bacterial species with similar antimicrobial susceptibility profile and relapse as recurrence after clearance of the initial bacteriuria episode), symptomatic UTI caused by an MDR organism during follow-up, a second episode of ASB caused by an MDR organism during follow-up, severe adverse events, and *Clostridioides difficile* diarrhea.

Assessment of Risk of Bias and Certainty of Evidence

The overall risk of bias (RoB) assessment was independently performed by 2 reviewers (A. T. A. and L. H. T.) using the RoB 2.0 tool [16]; disagreements were resolved by a third reviewer (A. V. H.). The certainty of evidence was described per outcome using the GRADE method, and its assessment covered 5 aspects: RoB, inconsistency, indirectness, imprecision, and publication bias [17]. The certainty of evidence was described in a summary of findings table, created using GRADEpro GDT software (version 2020) [18].

Statistical Analysis

We primarily used inverse variance random-effects models for all meta-analyses; for rare outcomes (incidence <10% of individuals), we used the Mantel-Haenszel method. Between-study variance (τ^2) was calculated using the Paule-Mandel method. Effects on dichotomous outcomes were described with relative risks (RRs) and their 95% confidence intervals (CIs); effects on continuous outcomes, with mean differences (MDs) and their 95% CIs. We explored the heterogeneity among study effects with Cochran *Q* tests and I^2 statistics. For I^2 statistics, 30%–60% indicates moderate heterogeneity; >60%, high heterogeneity; and >75%, substantial heterogeneity. All statistical analyses and pooling were performed using R software v.4.0.2 (www.r-project.org).

Four preplanned subgroup analyses were performed to explore possible sources of heterogeneity: time from transplantation to ASB (<12 vs ≥12 months), baseline eGFR at study inclusion (<40 vs ≥40 mL/min), type of bacteria causing initial ASB episode (*Escherichia coli* vs others), and presence of antimicrobial resistance against ≥2 of the 3 antibiotics (trimethoprim-sulfamethoxazole, ciprofloxacin, and third-generation cephalosporins) in bacteria identified in the initial ASB episode. We also performed 2 post hoc subgroup analyses based on reviewers' suggestions (time from transplantation to ASB [<6 vs ≥6 months] and sex [male vs female]). Significant subgroup effects had *P* for interaction values <.1. A post hoc sensitivity analysis was performed to include only RCTs (n = 3) that randomized patients after ureteral catheters were removed. Other sensitivity analyses were carried out by repeating all analyses using fixed-effects models.

RESULTS

Study selection is illustrated in Figure 1. Four trials met our inclusion criteria; all were investigator initiated and compared antibiotics versus no therapy in KTRs with ASB [11–14]. Only 1 trial included KTRs who were early after transplantation and had ureteral catheters. All trials reported the incidences of acute pyelonephritis and symptomatic UTI. While Coussement et al [11] included KTRs ≥2 months after transplantation, when they developed ASB, the 3 other trials systematically included patients after transplantation (Table 1). Therefore, in these trials, not all participants developed ASB during the trial follow-up [12–14]. Other characteristics of included trials are depicted in Table 1.

The RoB of the included RCTs is depicted in Figure 2. For symptomatic UTI, the RCT by Sabé et al [12], was at high RoB due to measurement of outcome, and the 3 remaining trials had some concerns of bias in the deviations from the intended intervention and selection of the reported results. For pyelonephritis, all RCTs had some concerns of RoB due to the deviations from the intended intervention, and selection of the reported results. The certainty of evidence was heterogeneous across RCTs, ranging from very low to moderate across primary and secondary outcomes (Table 2).

Overall, the systematic review included 234 patients randomized to the antibiotic arm and 244 to the no-therapy arm. For the primary outcome analysis, antibiotic therapy increased acute pyelonephritis risk nonsignificantly, by 19% (n = 478; RR, 1.19 [95% CI, .72–1.94]; $I^2 = 0\%$) (Figure 3). In the per-protocol analysis, albeit not reaching statistical significance, the risk of acute pyelonephritis was higher in patients who were treated for ASB than in those who were not (n = 409; RR, 1.43 [95% CI, .62–3.27]; $I^2 = 25\%$) (Supplementary Figure 1). Similarly, antibiotic therapy nonsignificantly increased the risk of symptomatic UTI risk, by 18% (n = 478; RR, 1.18 [95% CI, .78–1.78]; $I^2 = 28\%$) and 27% (n = 409; RR, 1.27 [.67–2.39]; $I^2 = 55\%$) in intention-to-treat (Figure 4) and per-protocol (Supplementary Figure 2) analyses, respectively.

Regarding secondary outcomes, the following risks and MDs did not differ significantly between groups: all-cause mortality

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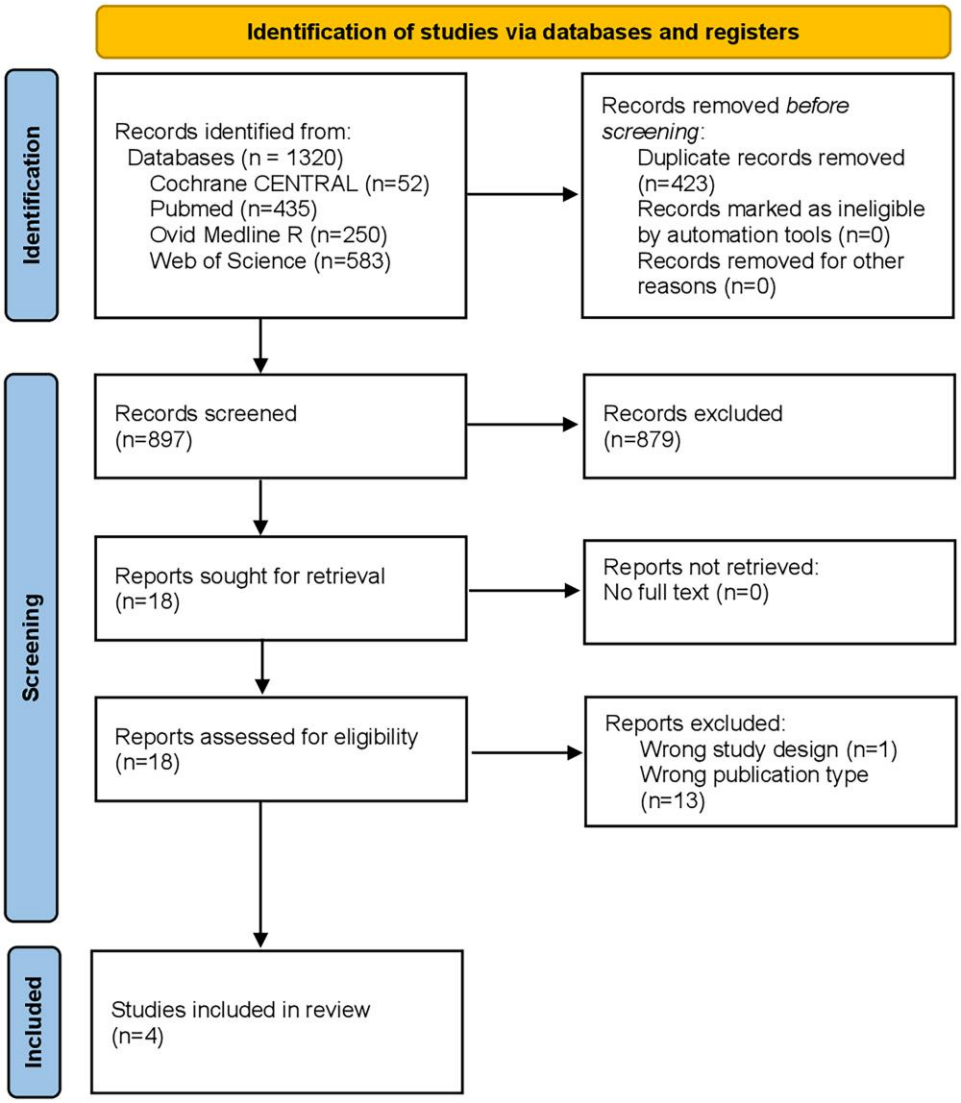

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram for systematic review and meta-analysis, demonstrating the identification, screening, and inclusion of studies.

(n = 478; RR, 1.56 [95% CI, .54–4.52]; $I^2 = 0\%$) graft loss (n = 398; RR, .80 [.20–3.19]; $I^2 = 0\%$), graft rejection (n = 478; RR, 0.89 [.46–1.70]; $I^2 = 0\%$), hospital admission due to symptomatic UTI (n = 478; RR, 0.92 [.48–1.76]; $I^2 = 6\%$), persistent or relapsing ASB episodes (n = 452; RR, 0.86 [.69–1.06]; $I^2 = 34\%$), incidence of a second episode of ASB caused by an MDR organism (n = 267; RR, 0.98 [.54–1.79]; $I^2 = 46\%$), symptomatic UTI caused by an MDR organism (n = 206; RR, 1.31 [.63–2.74]; $I^2 = 0\%$), change in serum creatinine level from baseline to end of study (n = 308; MD, 0.40 mg/dL [95% CI, −.05 to .85 mg/dL]; $I^2 = 66\%$), change in eGFR from baseline to end of study (n = 357; MD, −2.77 mL/min/1.73 m^2 [95% CI −6.25 to .70 mL/min/1.73 m^2], $I^2 = 78\%$), serious adverse events (n = 478; RR, 1.20 [.75–1.91]; $I^2 = 0\%$), and *C difficile* diarrhea (n = 478; RR, 0.75 [.23–2.42]; $I^2 = 0\%$) (Supplementary Figures 3–13). The results of the sensitivity analyses including patients randomized after removal of ureteral catheters were consistent with those from the main analyses (Supplementary Figures 14 and 15). The same trends were seen when a fixed-effects model was used in place of a random-effects model in all analyses (data not provided).

The results of predefined subgroup analyses (time from transplantation to ASB [<12 vs ≥12 months]), baseline eGFR [<40 vs ≥40 mL/min], ASB due to *E coli* versus other organisms, and antimicrobial resistance against ≥2 of the following: trimethoprim-sulfamethoxazole, ciprofloxacin, and third-generation cephalosporins) are presented in the Supplementary Materials (Supplementary Figures 16–23), along with those requested by the reviewers (time from transplantation to ASB (<6 vs ≥6 months) and sex (male vs female) (Supplementary

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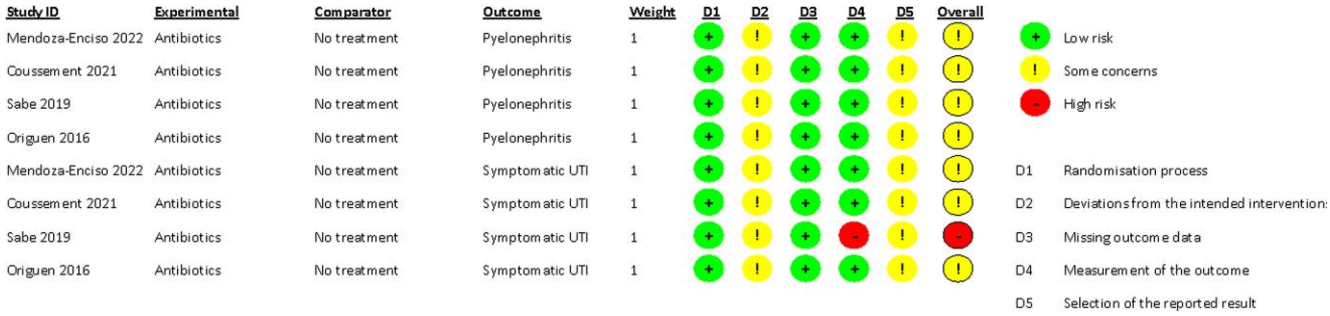

Figure 2. Review of authors' judgments about each risk-of-bias item for each of the 4 included randomized controlled trials [11–14]. Abbreviation: UTI, urinary tract infection.

Figures 24–27). No significant effects of antibiotic therapy were detected in any of the subgroups, in terms of pyelonephritis or symptomatic UTI.

DISCUSSION

In this systematic review and meta-analysis, which included data on 478 participants from 4 randomized trials, antibiotic treatment of KTRs with ASB had no significant protective effect on subsequent acute pyelonephritis and symptomatic UTI. Furthermore, antibiotic therapy had uncertain effects on symptomatic UTI caused by MDR bacteria, serious adverse events, *C difficile* diarrhea, and persistent or relapse ASB episodes. There was no evidence that antibiotic treatment of KTRs with ASB improves patient and graft function outcomes (eg, change in eGFR, graft loss, or acute graft rejection), hospitalization due to symptomatic UTI, or the all-cause mortality rate. The results of the sensitivity and subgroup analyses were parallel with those of the main analyses.

Observational studies published between the 1970s and 1980s reported high incidences of ASB in KTRs, particularly within the first few months after kidney transplantation [10]. Many KTRs with ASB also developed symptomatic UTI with detrimental impacts on graft function [19]. This impelled many clinicians to screen for and treat posttransplant ASB with the assumption that this strategy may reduce the risk of subsequent symptomatic UTI and improve long-term patient and graft outcomes [20]. However, the posttransplant risk of UTI has probably been modified by advances in the management of KTRs, including the introduction of routine antibiotic prophylaxis in the perioperative period, earlier removal of indwelling urinary devices, and long-term antibiotic prophylaxis to prevent opportunistic infections (eg, *Pneumocystis jirovecii* pneumonia) [6]. With these changes having the potential to help prevent symptomatic UTI and ASB [21], more recent retrospective studies indicated that few ASB episodes result in symptomatic UTI, without any major impact on graft function and patient outcomes [22, 23]. Supporting international guidelines that recommend against systematically treating ASB in KTRs [10, 24–26], our meta-analysis of 4 randomized trials did not find any significant benefit of antibiotic therapy in this population. Although the prevalence of persistent or relapse ASB was numerically lower in patients allocated to antibiotic therapy, this microbiological effect did not translate into a clinically relevant benefit (ie, less frequent acute pyelonephritis and symptomatic UTI). In addition, antimicrobial therapy for ASB includes an uncertain risk for the development of MDR bacteria (ie, symptomatic UTI caused by MDR bacteria) and serious adverse events.

The great majority of participants from the primary studies included in our meta-analysis were randomized after removal of urinary catheters. As a consequence, it remains unclear whether or not antibiotic treatment for ASB occurring before removal of these devices can be useful in preventing acute pyelonephritis or symptomatic UTI [3]. Of the evaluated RCTs, only a single trial explored the effect of antibiotic treatment of ASB before removal of the ureteral catheter during the early posttransplant period. That trial found the incidences of acute pyelonephritis (15% for antibiotic vs 2.5% for no treatment; $P = .04$) and symptomatic UTI (25% vs 10%, $P = .07$) to be higher in the antibiotic group [13], but it was limited by its size; further RCTs are needed to determine the effects of systematically treating ASB in the first weeks after kidney transplantation, before removal of urinary catheters. Furthermore, the optimal duration of antibiotic therapy in ASB should be investigated if the clinical benefit of antibiotic therapy is revealed in this patient population.

The strengths of our systematic review include the comprehensive search strategy, the prespecified eligibility criteria and screening process, and the participation of the principal investigators from the primary studies, who validated and completed the data extracted from their studies. In addition, the availability of individual data from each RCT allowed us to perform clinically relevant subgroup and sensitivity analyses, which enhanced the transparency and reliability of our results. Such

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Table 1. Characteristics of Included Randomized Controlled Trials

Authors	Study Design	Country	Population	Antibiotic Therapy Group/No-Therapy Group: Patients in ITT Analysis, No.	Female Sex, No.	Age, Mean (SD), y	Primary Kidney Disease, No.	Follow-up Duration	Stratification[a]	Primary Outcome
Coussement et al [11]	Open label, multicenter (n = 13)	France and Belgium	Adult KTRs (aged ≥18 y) who had ASB within ≥2 mo after transplant and with urinary catheters removed; exclusion criteria: bladder and/or ureteral catheter, pregnancy, combined transplant, major increase in immunosuppression, neutropenia, ESRD requiring dialysis, recurrent allograft pyelonephritis, use of antibiotics at time of ASB episode, nonfunctioning native bladder, urinary surgery within 2 mo before randomization	100/99	77/74	60.2 (11.5)/ 60.1 (11.6)	Glomerular disease, 24/26; polycystic kidney disease, 17/16; TIN, 17/0; vascular nephropathy, 0/13	12 mo	1:1; 10-d Antibiotic therapy vs no antibiotic therapy	First episode of symptomatic UTI during follow-up
Sabé et al [12]	Open label, multicenter (n = 2)	Spain	Adult KTRs (aged ≥18 y) within first year after transplant and with urinary catheters removed; exclusion criteria: bladder and/or ureteral catheter	41/46	26/25	61.0 (11.5)/ 60.1 (11.4)	Previous KT, 11/0; diabetes, 9/8; glomerular disease, 6/0; unknown, 0/12; polycystic kidney disease, 0/9	12 mo	1:1; 5–7-d Antibiotic therapy vs no antibiotic therapy	First episode of acute pyelonephritis during follow-up
Mendoza-Enciso et al [13]	Open label, single center	Mexico	Adult KTRs (aged ≥18 y) within first 2 mo after transplant; exclusion criteria: urological complications and removal of ureteral catheter	40/40	12/15	29.9 (10.5)/ 29.7 (10.4)	Unknown, 36/35; glomerular disease, 3/3; WT, 1/ 0; diabetes, 0/1	63 d	1:1; 5-d Antibiotic therapy vs no antibiotic therapy	ASB and time before development of UTI or acute pyelonephritis during first 2 mo after transplant
Origüen et al [14]	Open label, single center	Spain	Adult KTRs (aged ≥18 y) with ≥1 ASB episode >2 mo after transplant; exclusion criteria: bladder and/or ureteral catheter, pregnancy, kidney-pancreas transplant, graft loss within first 2 mo after transplant, previous diagnosis of ASB >2 mo after transplant but before randomization	53/59	25/28	55.4 (14.5); 53.0 (15.8)	Diabetes, 15/11; polycystic kidney disease, 11/ 0; glomerular disease, 10/14; nephroangiosclerosis, 0/8	24 mo	1:1; 3–7-d Antibiotic therapy vs no antibiotic therapy	First episode of acute pyelonephritis during follow-up

Abbreviations: ASB, asymptomatic bacteriuria; ESRD, end-stage renal disease; ITT, intention-to-treat; KT, kidney transplant; KTRs, KT recipients; TIN, tubulo-interstitial nephritis; UTI, urinary tract infection; WT, Wilms tumor.

[a]For antibiotic therapy, the choice of agent, dosing, and route of administration were left to the discretion of the treating physician.

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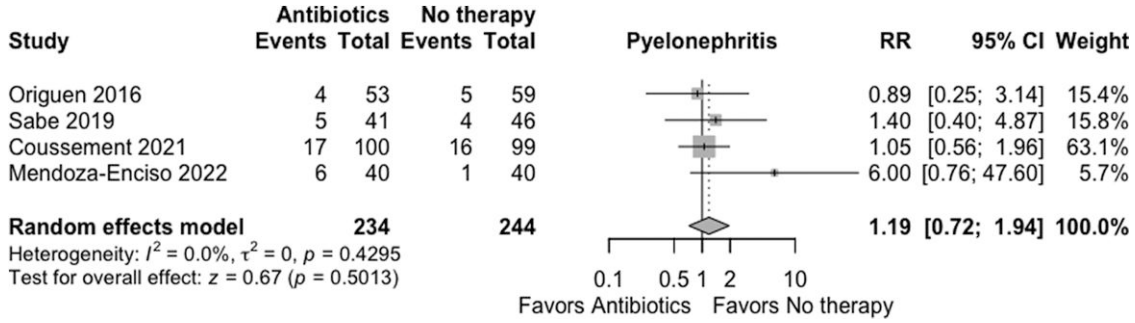

Figure 3. Forest plots from random-effects meta-analysis comparing the incidences of acute pyelonephritis between antibiotic and no-therapy groups [11–14]. Abbreviations: CI, confidence interval; RR, relative risk.

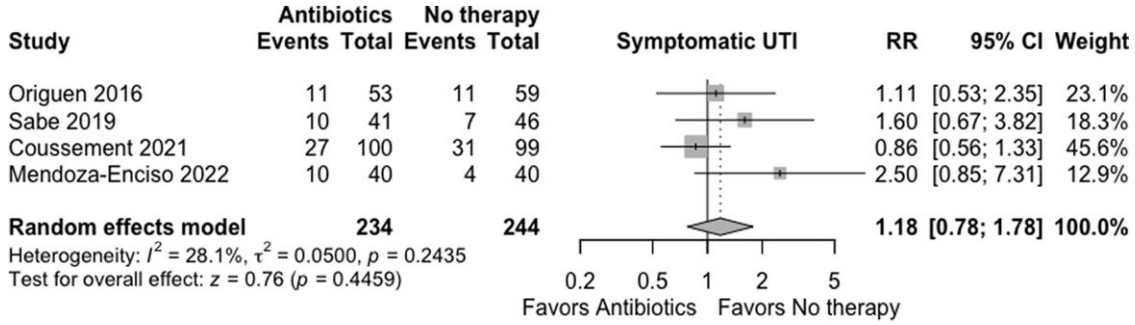

Figure 4. Forest plots from random-effects meta-analysis comparing the incidences of symptomatic urinary tract infection (UTI) between antibiotic and no-therapy groups [11–14]. Abbreviations: CI, confidence interval; RR, relative risk.

detailed sensitivity and subgroup analyses could not be performed in the previous systematic review and meta-analyses due to the paucity of data. Finally, all primary trials were limited by their relatively small size (80–199 participants per trial). Hence, this meta-analysis increases our confidence that antibiotics probably do not improve patient outcomes, including for relatively rare events such as pyelonephritis, which is less common than symptomatic UTI and therefore difficult to assess in small trials.

Our work has several limitations. First, the estimated effects of antibiotic therapy for preventing acute pyelonephritis and symptomatic UTI were relatively imprecise and compatible with either clinically relevant benefits or harms. This mainly stemmed from the limited number of patients enrolled in each trial, ranging from 80 to 199. Second, as symptomatic UTI can be subjectively reported, a number of biases may have influenced the measurement of this end point in the original RCTs. In addition, its impact on graft and patient outcome is minimal when not associated with other complications. Third, the great majority of the trials did not blind participants, recruiters, or trial statisticians. Since symptoms of UTI may be subjective, lack of blinding may augment the risk of biasing the results, particularly for patients within the first months after kidney transplantation. Fourth, compliance to the intervention arm was limited in the majority of the RCTs included. For this specific reason, we also performed per-protocol analysis for co–primary outcomes (ie, acute pyelonephritis and symptomatic UTI), even though it may have a larger estimated treatment effect than intention-to-treat analysis and the balance gained by randomization may be lost with per-protocol analysis.

Fifth, the types, doses, and durations of antibiotics used in the antibiotic group were very heterogeneous across the trials. It can be assumed that types and doses of antibiotics used for treatment of ASB episodes are not uniform, mainly due to heterogeneities in the types of bacteria and their resistance profiles. The duration of antibiotic treatment for ASB in the included studies ranged from 3 to 10 days. It can be argued that 3 days of antibiotic treatment may not be sufficient to eradicate the bacteriuria in this population and that 10 days of antibiotic treatment may be relatively long among asymptomatic patients. While a 10-day duration may have covered potential cases of asymptomatic graft pyelonephritis, it may also have facilitated the emergence of resistant bacteria. Similarly, the duration of follow-up varied significantly between included studies, which might have affected the results. The short follow-up period in the study by Mendoza-Enciso et al [13] may be

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Table 2. Summary of Findings: Certainty of Evidence per Outcome of Treatment With Antibiotics Versus No Treatment for Asymptomatic Bacteriuria in Kidney Transplant Recipients

Outcome	RR (95% CI)	Anticipated Absolute Effects (95% CI)			Certainty of Evidence
		No Treatment	Antibiotic Treatment	Difference	
Symptomatic UTI assessed based on urinary symptoms associated with positive urine culture (follow-up, 2–24 mo; n = 478; 4 RCTs)	1.18 (.78–1.78)	21.7%	25.6% (16.9%–38.7%)	3.9% (–4.8% to 16.9%)	⨁⨁◯◯ Low
Pyelonephritis assessed based on fever associated with bacteriuria and/or bacteremia and ≥1 of the following: chills, allograft tenderness, or cystitis (follow-up, 2–24 mo; n = 478; 4 RCTs)	1.19 (.72–1.94)	10.7%	12.7% (7.7%–20.7%)	2.0% (–3% to 10%)	⨁⨁⨁◯ Moderate
All-cause mortality rate assessed using data from patient records and clinical follow-up (follow-up, 2–24 mo; n = 478; 4 RCTs)	1.56 (.54–4.52)	2.0%	3.2% (1.1%–9.3%)	1.1% (–0.9% to 7.2%)	⨁⨁⨁◯ Moderate
Change in eGFR assessed based on serum creatinine measurements calculated with CKD-EPI equation (follow-up, 12–24 mo; n = 357; 3 RCTs)	–	Mean change in eGFR, 2.4828 mL/min/1.73 m^2	Mean change in eGFR, 1.0477 mL/min/1.73 m^2	MD, –2.77 mL/min/1.73 m^2 (–6.25 to 0.7)	⨁◯◯◯ Very low
Change in serum creatinine levels assessed based on serum creatinine levels at baseline and end of follow-up (follow-up, 12–24 mo; n = 308; 3 RCTs)	–	Mean change in creatinine levels, –0.2244 mg/dL	Mean change in creatinine levels, –0.1484 mg/dL	MD, 0.4 mg/dL (–0.05 to 0.85 mg/dL)	⨁⨁◯◯ Low
Graft loss assessed by monitoring transplanted graft function with clinical evaluations and laboratory tests (follow-up, 12–24 mo; n = 398; 3 RCTs)	0.80 (.20–3.19)	2.0%	1.6% (.4%–6.3%)	–0.4% (–1.6% to 4.3%)	⨁⨁⨁◯ Moderate
Graft rejection assessed using clinical, laboratory, and pathological evaluations (follow-up, 2–24 mo; n = 478; 4 RCTs)	0.89 (.46–1.70)	7.4%	6.6% (3.4%–12.5%)	–0.8% (–4% to 5.2%)	⨁⨁⨁◯ Moderate
Hospital admission due to symptomatic UTI (follow-up, 2–24 mo; n = 478; 4 RCTs)	0.92 (.48–1.76)	8.6%	7.9% (4.1%–15.1%)	–0.7% (–4.5% to 6.5%)	⨁⨁⨁◯ Moderate
Persistent or relapse ASB episodes (follow-up, 2–24 mo; n = 452; 4 RCTs)	0.86 (.69–1.06)	52.3%	45.0% (36.1%–55.5%)	–7.3% (–16.2% to 3.1%)	⨁⨁◯◯ Low
Symptomatic UTI caused by MDR bacteria (follow-up, 2–24 mo; n = 206; 4 RCTs)	1.31 (.63–2.74)	10.5%	13.7% (6.6%–28.7%)	3.2% (–3.9% to 18.2%)	⨁⨁⨁◯ Moderate
Clostridioides difficile diarrhea (follow-up, 2–24 mo; n = 478; 4 RCTs)	0.75 (.23–2.42)	2.0%	1.5% (.5%–5%)	–0.5% (–1.6% to 2.9%)	⨁⨁⨁◯ Moderate
Second ASB episode caused by MDR bacteria (follow-up, 2–24 mo; n = 267; 3 RCTs)	0.98 (.54–1.79)	35.2%	34.5% (19%–63%)	–0.7% (–16.2% to 27.8%)	⨁⨁◯◯ Low

Abbreviations: ASB, asymptomatic bacteriuria; CI, confidence interval; CKD-EPI, Chronic Kidney Disease–Epidemiology; eGFR, glomerular filtration rate; MD, mean difference; MDR, multidrug-resistant; RCTs, randomized controlled trials; RR, relative risk; UTI, urinary tract infection.

associated with underestimation of the rates of persistent or recurrent ASB episodes and symptomatic UTI. Finally, the results from our meta-analysis cannot be extrapolated to pediatric patients and recipients of combined transplants. Nonetheless, there is no strong reason to assume that antibiotic treatment of posttransplant ASB would be more beneficial in recipients of combined transplants (eg, kidney and pancreas transplants) than in KTRs.

In conclusion, current evidence does not support routine screening and treatment of posttransplant bacteriuria in KTRs. Given that KTRs within the first 2 months after kidney transplantation are usually severely immunocompromised and often have a ureteral catheter facilitating the ascent of bacteria from the lower urinary tract to the kidney graft, well-conducted large-scale trials are needed to determine the effects of antibiotic treatment in KTRs who develop ASB within the first 2 months after transplantation.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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