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## Brief Correspondence

# Benefits and Harms of Treatment of Asymptomatic Bacteriuria: A Systematic Review and Meta-analysis by the European Association of Urology Urological Infection Guidelines Panel

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### Abstract

People with asymptomatic bacteriuria (ABU) are often unnecessarily treated with antibiotics risking adverse effects and antimicrobial resistance. We performed a systematic review to determine any benefits and harms of treating ABU in particular patient groups. Relevant databases were searched and eligible trials were assessed for risk-of-bias and Grading of Recommendations, Assessment, Development and Education quality. Where possible, a meta-analysis of extracted data was performed or a narrative synthesis of the evidence was presented. After screening 3626 articles, 50 studies involving 7088 patients were included. Overall, quality of evidence ranged from very low to low. There was no evidence of benefit for patients with no risk factors, patients with diabetes mellitus, postmenopausal women, elderly institutionalised patients, patients with renal transplants, or patients prior to joint replacement, and treatment was harmful for patients with recurrent urinary tract infection (UTI). Treatment of ABU resulted in a lower risk of postoperative UTI after transurethral resection surgery. In pregnant women, we found evidence that treatment of ABU decreased risk of symptomatic UTI, low birthweight, and preterm delivery. ABU should be treated prior to transurethral resection surgery. In addition, current evidence also suggests that ABU treatment is required in pregnant women, although the results of a recent trial have challenged this view.

**Patient summary:** We reviewed available scientific studies to see if people with bacteria in their urine but without symptoms of urinary tract infection should be treated with antibiotics to eliminate bacteria. For most people, treatment was not beneficial and may be harmful. Antibiotic treatment did appear to benefit women in pregnancy and those about to undergo urological surgery.

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Clinical studies show that in most clinical situations, asymptomatic bacteriuria (ABU) has a low risk of progression to severe infection [1]. The benefit of treating ABU with antibiotics remains uncertain and requires clarification with the need for better antibiotic stewardship [2].

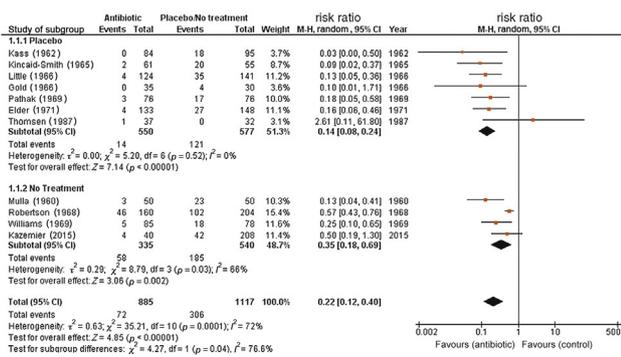
The aim of this systematic review was to synthesise evidence about benefits and harms of treating ABU in relevant patient groups. The review was undertaken as part of the European Association of Urology (EAU) Urological Infections Guideline 2017 update [3]. Data extraction, risk of bias (RoB) assessment using the Cochrane RoB Tool, and

quality assessment using the Grading of Recommendations, Assessment, Development and Education (GRADE) approach [4] were performed by two reviewers working independently. The detailed methods and additional results are described in the Supplementary material. Meta-analyses were performed on data extracted from 50 published trials recruiting 7088 patients (Supplementary Table 1).

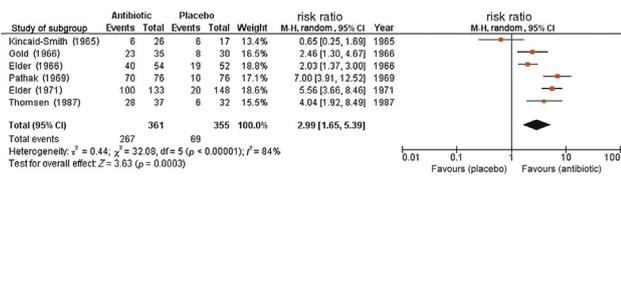
A single prospective, nonrandomised comparative study investigated the effect of treating ABU in adult, nondiabetic, nonpregnant women, and found no difference in the rate of

ABU treatment vs. no treatment/placebo in pregnant women

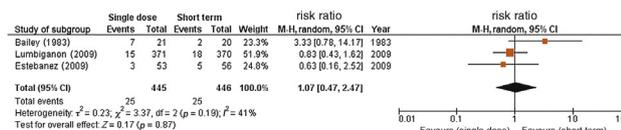
A. Symptomatic UTI



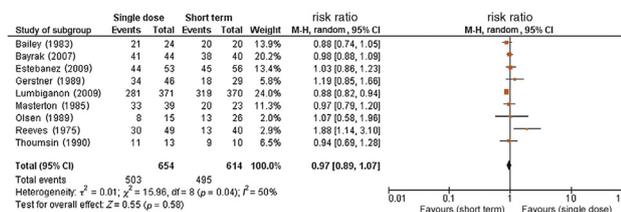
B. Resolution of ABU



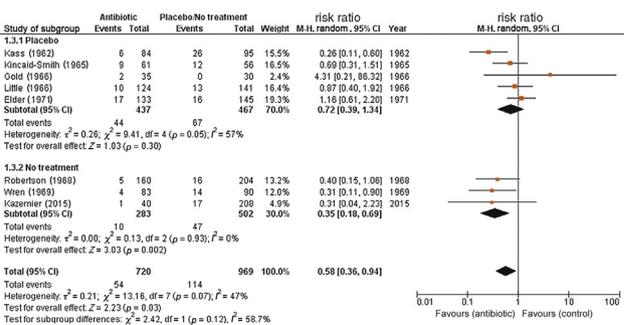
E. Symptomatic UTI



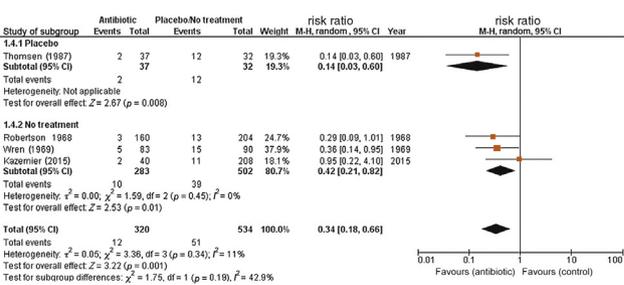
F. Resolution of ABU



C. Low birthweight

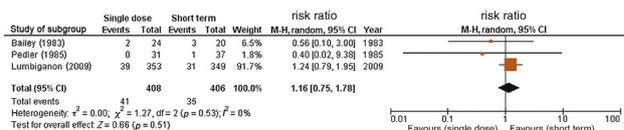


D. Preterm delivery



Single-dose versus short-course treatment in pregnant women

G. Preterm delivery



H. Side effects

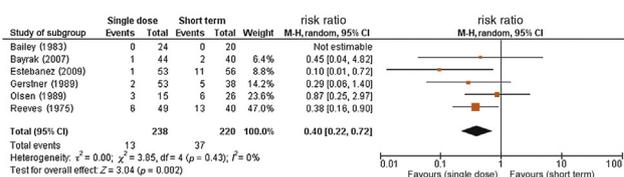


Fig. 1 – Forest plots on the effect of antibiotic treatment of ABU in pregnant women on (A) the rate of symptomatic UTI, (B) resolution of ABU, (C) rate of low birthweight, and (D) rate of preterm delivery; a comparison of single-dose versus short-term antibiotic treatment of ABU in pregnant women on (E) the rate of symptomatic UTI, (F) resolution of ABU, (G) rate of preterm delivery, and (H) rate of low birthweight. ABU = asymptomatic bacteriuria; CI = confidence interval; M-H = Mantel-Haenszel; UTI = urinary tract infection.

symptomatic urinary tract infection (UTI; very low-quality evidence; Supplementary Table 1).

One randomised controlled trial (RCT) comparing antibiotic treatment with no treatment of ABU in 673 women with recurrent symptomatic UTIs found that treatment increased the risk of subsequent symptomatic UTI episodes (risk ratio [RR] 0.28, 95% confidence interval [CI] 0.21–0.38; low-quality evidence; Supplementary Table 1).

A meta-analysis of 11 RCTs involving 2002 pregnant women with ABU found that antibiotic treatment significantly reduced the number of symptomatic UTIs (RR = 0.22, 95% CI 0.12–0.40; very low-quality evidence) compared with placebo or no treatment (Supplementary Table 1). Data from six RCTs involving 716 pregnant women showed benefit for antibiotic treatment in resolving ABU (RR = 2.99, 95% CI 1.65–5.39; very low-quality evidence). Data from eight RCTs with 1689 women showed reduction in risk of low birthweight (RR = 0.58, 95% CI 0.36–0.94; very low-quality evidence) and data from 44 RCTs with 854 women showed reduced risk of preterm delivery (RR = 0.34, 95% CI 0.18–0.66; low-quality evidence; Fig. 1A–D). A single recent trial of higher methodological quality did not find benefit for antibiotic treatment [5].

Nine RCTs compared a single dose with the standard short-course (2–7 d) treatment of ABU in pregnant women (Supplementary Table 1). Data from nine RCTs with 1268 women showed no difference in the rate of ABU resolution (RR = 0.97, 95% CI 0.89–1.07; very low-quality evidence). A meta-analysis of three RCTs with 891 women found no difference in the rate of symptomatic UTI

(RR = 1.07, 95% CI 0.47–2.47; low-quality evidence) and data from three RCTs with 814 women showed no difference in the rate of preterm delivery (RR = 1.16, 95% CI 0.75–1.78; low-quality evidence). One RCT with 714 women showed a higher rate of low birthweights using a single dose compared with short-course treatment (RR = 1.65, 95% CI 1.06–2.57; moderate-quality evidence). Single-dose treatment was associated with significantly fewer side effects compared with short-course treatment, based on the meta-analysis of data from six RCTs including 458 women (RR = 0.40, 95% CI 0.22–0.72; low-quality evidence; Fig. 1E–H).

One RCT including 105 patients with diabetes mellitus demonstrated that eradicating ABU did not reduce the risk of symptomatic UTI (RR = 1.05, 95% CI 0.66–1.66; low-quality evidence; Supplementary Table 1).

A meta-analysis of data from three RCTs with 208 postmenopausal women showed no benefit of antibiotic treatment compared with placebo or no treatment in reducing the rate of symptomatic UTI (RR = 0.71, 95% CI 0.49–1.05; very low-quality evidence; Fig. 2A) or resolving ABU (RR = 1.28, 95% CI 0.50–3.24; very low-quality evidence; Fig. 2B; Supplementary Table 1).

Meta-analyses of three RCTs with 210 elderly patients found no reduction in the rate of symptomatic UTI compared with placebo or no treatment (RR = 0.68, 95% CI 0.46–1.00; very low-quality evidence; Fig. 2C; Supplementary Table 1), and data from 328 patients in six RCTs showed no benefit for the rate of resolution of ABU (RR = 1.33, 95% CI 0.63–2.79; very low-quality evidence; Fig. 2D; Supplementary Table 1).

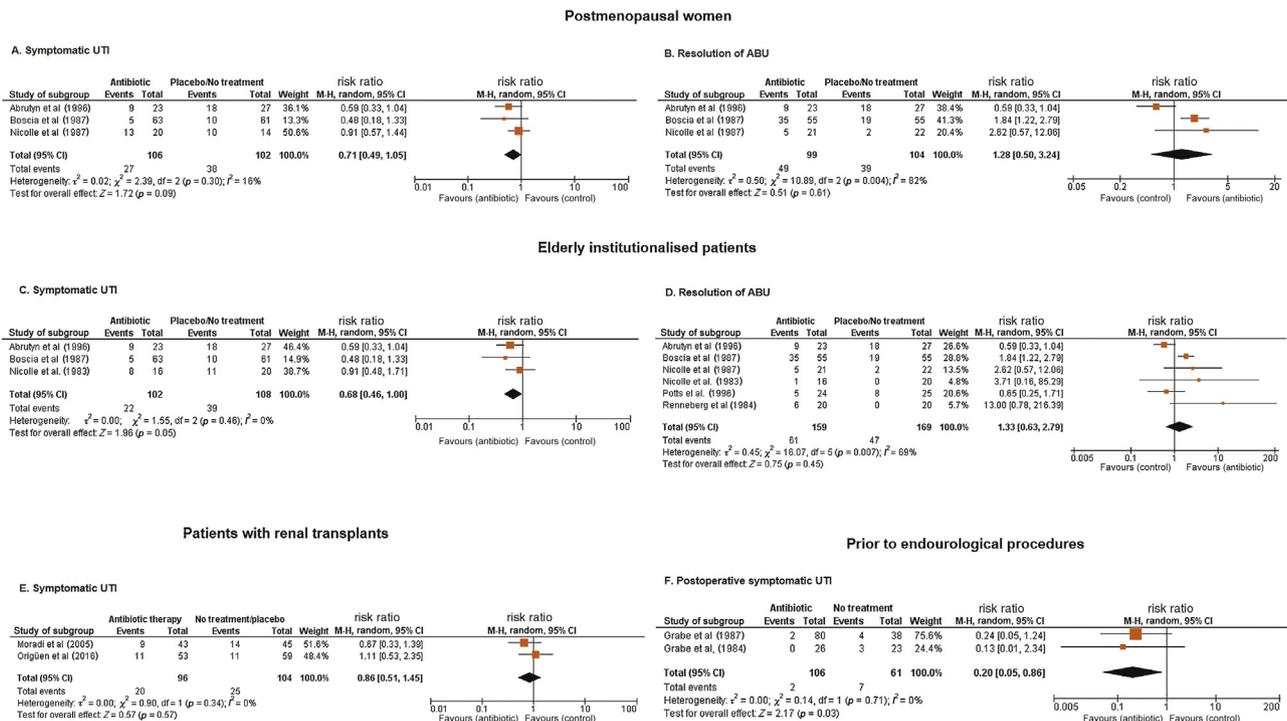


Fig. 2 – Forest plots on the effect of antibiotic treatment of ABU in postmenopausal women on the rate of (A) symptomatic UTIs and (B) resolution of ABU; in elderly institutionalised patients on the rate of (C) symptomatic UTI and (D) resolution of ABU; (E) in patients with renal transplants (E) the rate of symptomatic UTI; and (F) prior to transurethral endourological procedures with resection on the rate of postoperative symptomatic UTIs. ABU = asymptomatic bacteriuria; CI = confidence interval; UTI = urinary tract infection.

Two RCTs and two retrospective studies compared the effect of antibiotic treatment with that of no treatment in patients with renal transplants (Supplementary Table 1). A meta-analysis of the two RCTs did not show benefit in terms of reducing symptomatic UTIs (200 patients, RR = 0.86, 95% CI 0.51–1.45; very low-quality evidence; Fig. 2E). Furthermore, there were no significant differences in the rate of ABU clearance, graft loss, or change in renal function during longer-term follow-up.

Two RCTs and two prospective nonrandomised studies (Supplementary Table 1) including 167 patients compared the effect of antibiotic treatment with that of no treatment before transurethral resection. A meta-analysis of RCT data showed that treatment reduced the rate of postoperative symptomatic UTI (RR = 0.20, 95% CI 0.05–0.86; very low-quality evidence; Fig. 2F). Similarly, the rates of postoperative fever and septicaemia were significantly lower in patients who received antibiotic treatment compared with those receiving no treatment.

We identified one RCT (471 patients) and one multicentre cohort study (303 patients) comparing the treatment of ABU with no treatment prior to hip or knee arthroplasty (Supplementary Table 1). Neither of the studies showed benefit for antibiotic treatment regarding prosthetic joint infection (moderate-quality evidence). The cohort study reported no significant difference in the rate of postoperative symptomatic UTI (very low-quality evidence).

In the current era of increasing antibiotic resistance reducing unnecessary antibiotic usage is of utmost importance and is emphasised by all antibiotic stewardship programmes. Despite this clear message, treatment of ABU remains common practice. The demonstration of lack of benefit in most clinical situations shown by this thorough and methodologically robust systematic review and meta-analysis supports our recommendation of not to treat ABU [3]. ABU should only be treated prior to transurethral resection surgery. In addition, short-course treatment of ABU should continue to be recommended for pregnant women, although this is challenged by the results of a recent high-quality study finding no difference in neonatal outcomes [5].

**Author contributions:** Bela Köves had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Köves, Cai, Veeratterapillay, Pickard, Bartoletti, Bruyere, Wagenlehner, Pilatz, Geerlings, Lam, Bonkat, Wullt, Hoffman.

**Acquisition of data:** Köves, Cai, Veeratterapillay, Yuan.

**Analysis and interpretation of data:** Köves, Cai, Veeratterapillay, Seisen, Yuan, Lam, Wullt.

**Drafting of the manuscript:** Köves, Cai, Veeratterapillay, Seisen, Lam, Wullt.

**Critical revision of the manuscript for important intellectual content:** Seisen, Bartoletti, Bruyere, Geerlings, Wagenlehner, Pilatz, Lam, Bonkat, Wullt.

**Statistical analysis:** Köves, Cai, Veeratterapillay, Pradere.

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**Other:** None.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.eururo.2017.07.014>.

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