

Bond University
Research Repository



Uncomplicated urinary tract infection in women

Hoffmann, Tammy C; Bakhit, Mina; Del Mar, Chris

Published in:
BMJ

DOI:
[10.1136/bmj.n725](https://doi.org/10.1136/bmj.n725)

Licence:
CC BY-NC

[Link to output in Bond University research repository.](#)

Recommended citation(APA):
Hoffmann, T. C., Bakhit, M., & Del Mar, C. (2021). Uncomplicated urinary tract infection in women. *BMJ*, 372, Article n725. <https://doi.org/10.1136/bmj.n725>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

For more information, or if you believe that this document breaches copyright, please contact the Bond University research repository coordinator.

1
2
3 **10 minute consultation**
4

5 Uncomplicated Urinary Tract Infection
6

7 Tammy C Hoffmann¹

8 Mina Bakhit ¹

9 Chris Del Mar ¹
10

11 ¹ Institute for Evidence-Based Healthcare, Faculty of Health Sciences and Medicine, Bond
12 University
13

14 **Correspondence to:**

15 Tammy Hoffmann

16 Institute for Evidence-Based Healthcare
17 Faculty of Health Sciences and Medicine
18 University Drive
19 Bond University
20 Gold Coast, Queensland, Australia 4229
21

22 thoffmann@bond.edu.au

23 +61 7 5595 5522
24
25
26
27

28 **How this article was created**

29 We searched Medline and the Cochrane Library to identify published systematic reviews and
30 randomised controlled trials on the diagnosis and management of uncomplicated urinary
31 tract infections, including antibiotic benefits and harms, natural history of the condition, and
32 commonly used alternative treatments (cranberry, urinary alkalisers, non-steroidal anti-
33 inflammatory drugs). We included journal articles identified in the references of articles from
34 the initial search. We searched for relevant NICE guidelines on uncomplicated urinary tract
35 infections. We have referred to recent systematic reviews and meta-analyses but have cited
36 individual clinical studies where there is no higher quality of evidence.
37

38 **Contributorship and the guarantor**

39 TH and CDM conceived the article and are guarantors. All authors wrote and reviewed the
40 article and created the boxes.

41

42 **How patients were involved in the creation of this article**

43 We discussed the article with 2 women who have had uncomplicated urinary tract infections
44 and ensured that information was provided about whether alternatives to antibiotics work
45 and that contained Box 5 safety-netting information and prompted that written information be
46 provided.

47

48 **Conflicts of Interest**

49 TH and CDM have received funding from the Australian National Health and Medical
50 Research Council for research on reducing antibiotic resistance for acute infections and for
51 shared decision making, and from the Australian Commission on Safety and Quality in
52 Health Care for the development of shared decision making resources. MB has no
53 competing interests to declare.

54

55 **Licence**

56 “The Corresponding Author has the right to grant on behalf of all authors and does grant on
57 behalf of all authors, an exclusive licence (or non exclusive for government employees) on a
58 worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be
59 published in BMJ and any other BMJPGJL products and sublicences such use and exploit all
60 subsidiary rights, as set out in our licence (<https://authors.bmj.com/policies/#copyright>).”

61

62

63

64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100

Vignette/case and introduction

Your next patient is a 32 year old woman who thinks she has a urinary tract infection (UTI). She's passing urine more frequently, has suprapubic pain and dysuria. After two days, it hasn't improved.

This article will outline how to identify uncomplicated UTI in adult non-pregnant women (18-65 years) and discuss options with women to help them make an informed decision about its management.

What you should cover

Acute UTIs are very common community infections. They affect most women at least once in their life and far less prevalent among men.¹⁻³ Women with an acute UTI present with diverse symptoms that can be burdensome and impact their quality of life.^{4 5}

What questions you should ask

Take a history to determine risk factors for UTI and differentiate between uncomplicated UTIs and other causes of urinary symptoms. Recurrent UTI (when there are 3 or more UTIs within one year), asymptomatic bacteruria, or infection associated with an indwelling urinary catheter each require a different approach, not covered here. Symptoms and signs are described in box 1. Evidence from diagnostic studies supports the useful diagnostic value of commonly recognised symptoms such as dysuria, haematuria, nocturia, urgency and frequency, as well as those that decrease the probability that the patient has a UTI. Likelihood ratios of these symptoms are listed in box 2. However, no individual or combination of symptoms can make clinicians completely confident in diagnosing a UTI. Check for red flags suggestive of acute pyelonephritis or sepsis (box 3), which would require immediate management and/or referral to a hospital.

Is examination necessary?

In most cases of low-risk non-pregnant women with UTIs, clinical examination is not required, and the consultation can be safely conducted remotely. However, if the patient is systemically unwell and presents with any red flag symptom, arrange a physical examination. Assess the patient's vital signs (temperature, blood pressure, heart rate, and respiratory rate) for signs of systemic illness or sepsis and palpate the abdomen and the back for flank or suprapubic tenderness.

Box 1. Questions to ask

Is the patient experiencing:

- Burning pain while urinating (dysuria)?
- Urge to void immediately (urgency)?
- Passing urine more than usual at night (nocturia)? Or passing urine more frequently in general (frequency)?
- Cloudy urine visible to the naked eye or blood in the urine (haematuria)?

Vaginal discharge and/or vaginal irritation? (these symptoms are suggestive of a vaginal cause of urinary symptoms. Box 4 gives the most common differential diagnoses for UTIs.)

NICE Guidelines state that patients with 2 or 3 of these key symptoms (cloudy urine, dysuria or new nocturia) are indicative of a UTI.^{9 10} However a systematic review of 16 studies (3711 patients)¹¹ identified visible haematuria (rather than cloudy urine), along with dysuria or new nocturia, as one of the diagnostic symptoms suggestive of UTI.

Is there a history of:

- recent sexual activity? (UTIs are very common among sexually active women.⁶)
- previous UTI? (The majority of women with a UTI reported a history of UTI infection during the 12 months prior to the current episode.⁷)
- Using spermicidal agents or a diaphragm? (Spermicidal agents affect the vaginal flora and the diaphragm increase the levels of introital and periurethral colonization with bacteria.⁸)
- Current pregnancy? (UTIs are common during pregnancy)
- Diabetes? (UTIs are more frequent in patients with type 2 diabetes.⁶)

Box 2: Summary likelihood ratios (LR) of symptoms suggestive of an uncomplicated UTI^{11, 12}

Symptoms INCREASING the probability of UTI *

- Haematuria +LR 1.72 (95% CI 1.30 to 2.27)

Symptoms DECREASING the probability of UTI **

- A history of vaginal discharge +LR 0.3 (95% CI 0.1 to 0.9)

<ul style="list-style-type: none"> • Dysuria +LR 1.30 (95% CI 1.20 to 1.41) • Nocturia +LR 1.30 (95% CI 1.08 to 1.56) • Urgency +LR 1.22 (95% CI 1.11 to 1.34) • Frequency +LR 1.10 (95% CI 1.04 to 1.16) 	<ul style="list-style-type: none"> • A history of vaginal irritation +LR 0.2 (95% CI 0.1 to 0.9)
<p>* All values reported for threshold of $\geq 10^2$ CFU/ml, therefore probabilities at higher reference standards are lower.</p> <p>** Values reported for threshold of $\geq 10^5$ CFU/ml</p>	

103

104

Box 3: Red flags for acute pyelonephritis or sepsis	
Acute pyelonephritis^{6 13}	Sepsis¹⁴
<ul style="list-style-type: none"> • Flank pain (on the back, at and/or below level of ribcage) • Rigors or fever $>37.9^\circ\text{C}$ • Nausea/vomiting • New/different myalgia, flu-like illness 	<ul style="list-style-type: none"> • ≥ 21 breaths per minute • Heart rate: ≥ 91 beats per minute • Systolic blood pressure 91-100 mmHg or less than 90 mmHg (i.e. > 40 mmHg below normal) • Not passed urine in the past 12-18 hours or more • Behaviour changes (acute deterioration, altered behaviour or mental state)

Box 4: Common differential diagnoses of urinary symptoms¹²
<ul style="list-style-type: none"> • Vaginal infections (e.g., Trichomonas, Candida albicans, Gardnerella) • Vaginitis: post sexual intercourse, irritants • Sexually transmitted infections leading to pelvic inflammatory disease • Vulvovaginal atrophy

105

106 **What investigations might be needed?**

107 Urine dipstick tests are the most commonly used point of care test in primary care.¹⁵ For the
 108 laboratory diagnosis of UTI, dipstick results can modestly improve diagnostic precision, but
 109 cannot definitively rule out a UTI (Table 1).

110

Table 1. Investigations for uncomplicated UTI in 18-65 year old non-pregnant women ¹⁵					
Number of these symptoms present (Dysuria, new nocturia and cloudy urine / haematuria present)	Dipstick urinalysis			Possibility of UTI	Further testing
	Nitrite	Leukocyte	RBC		
2 or 3	May not be needed ¹⁰			Highly likely	urine culture typically not needed
1	+	-	+	Likely* ¹⁵	Send urine for culture ^t
	+	+	-		
	+	-	-	Likely**	
	-	+	+		
	-	+	-	Equally likely to other diagnosis	
	-	-	-	Less likely***	No indication for urine culture
<p>*Positive predictive value (PPV) of 92% (95% CI 86 to 96%), which is the probability that patients with a positive test have a UTI. Cut-off point on dipstick score ≥ 3 (NPV= 42%, 95% CI not reported).</p> <p>** Positive predictive value of 81% (95% CI= 77% to 84%). Cut-off point on dipstick score ≥ 2 (NPV =57%, 95% CI 52 to 62%)</p> <p>*** Negative predictive value (NPV) 76% (95% CI 66 to 84%) which is the probability that patients with a negative test truly do not have a UTI. Cut-off point on dipstick score ≥ 1</p> <p>Urine dipstick cut-off score is based on the sum of nitrite = 2, leucocyte = 1.5, RBC = 1.</p>					

[†] Growth cut-off thresholds used to define a UTI can vary (e.g. in some laboratories or countries, it may be $\geq 10^3$ CFU/ml, whereas $\geq 10^5$ CFU/ml in others). Culture results should also be interpreted with consideration of the severity of signs and symptoms.	
---	--

111

112 **What you should do**

113

114 ***Constructing a shared decision making conversation***

115 In this scenario there are typically two main options that are reasonable to consider:
116 immediate antibiotics or 'wait and see'/delayed prescribing. To enable the patient to make an
117 informed decision about the next steps, the clinician needs to explain both options to the
118 patient, along with the benefits and harms of each, and discuss the patient's preferences
119 before making a shared decision. An approach to this is suggested in box 5.

120

121 **What is the natural history of a UTI?**

122 There is uncertainty around the natural history of uncomplicated UTI, with few studies
123 examining this. In a systematic review of the placebo-controlled arms of three randomised
124 trials (346 placebo group participants), some women appeared to improve or become
125 symptom free spontaneously, with most improvement occurring in the first 9 days.¹⁶ Over the
126 first 9 days, the percentage of participants who were symptom free or reported improved
127 symptoms was reported as rising to 42% and by 6 weeks, the percentage was 36%. Some
128 women (39%) whose symptoms either failed to improve by 6 weeks or became worse over a
129 variable timespan, although the rate of serious complications was low with progression to
130 pyelonephritis was reported in one placebo participant in two of the trials. The low rate of
131 serious complications supports the practice of delayed prescribing, where the patient is
132 given a prescription but advised to wait to see whether symptoms self-resolve before
133 antibiotics are commenced.

134

135 An estimate of the mean duration of UTI symptoms is provided by an observational study of
136 women with suspected uncomplicated UTI.¹⁸ In the 511 women who had seen a clinician for
137 their symptoms and rated the initial problem as moderately bad or worse, the mean reported
138 symptom duration was 3.8 days. However, most of the sample took antibiotics, with only 17
139 participants (approximately 3%) who did not; their reported mean symptom duration was 4.9
140 days. In a related 5-arm randomised trial, a similar duration of moderately bad or worse
141 symptoms was reported: 3.5 days in the immediate antibiotic group and 4.8 days in the
142 delayed (by 48 hours) prescription group.¹⁹

143 **How long can you 'wait and see' for?**

144 The recommendation in the NICE guideline¹⁷ is to wait for 2 days before commencing
145 antibiotics. However, there is no evidence provided in support of this timeframe and it is
146 unclear whether the 2-day timeframe is from the start of symptoms or from first consultation.
147 The findings from the systematic review¹⁶ suggest a 2-day timeframe may be too short, with
148 few participants likely to have improved by then, although about a third may have improved
149 by 7–10 days. There appears to be a lot of uncertainty and variability in the spontaneous
150 recovery timeframe, and when ‘wait and see’ (delayed prescribing) is discussed with the
151 patient as an option this should include careful description of when to reconsult or
152 commence antibiotics (Box 5).

153 The option of a delayed prescription will be acceptable to many patients. In a cohort study in
154 Amsterdam, 37% of women who were asked by their general practitioner to delay antibiotic
155 treatment were willing to do so,²⁰ however no further details about how this option was
156 presented to patients are provided.

157 **What difference do antibiotics make?**

158 Surprisingly, we could not find a synthesis of antibiotic versus placebo randomised controlled
159 trials for uncomplicated UTI in women under 65 years and therefore no quantification of the
160 effect, perhaps because antibiotic treatment is the traditional management of uncomplicated
161 UTI. The extent to which they reduce recovery time, reduce the risk of progression to
162 pyelonephritis, and reduce the risk of recurrence is unknown and not presented in evidence-
163 based clinical practice guidelines.

164

165 For the antibiotics most commonly prescribed for UTI (e.g. nitrofurantoin, trimethoprim),
166 there does not appear to be synthesised evidence of their harms. For other antibiotics
167 commonly prescribed in primary care, commonly reported adverse effects include diarrhoea,
168 rash, and nausea.^{21 22} Candidiasis is also possible from antibiotic use. Another harm of
169 antibiotic use is the contribution to antibiotic resistance. This is already particularly a problem
170 for trimethoprim, with existing resistance rates of at least 30% of *Escherichia coli* isolates to
171 trimethoprim.²³ Patients with antibiotic-resistant *E. coli* UTI are significantly more like to
172 experience clinical response failure (odds ratio [OR] 4.19 (95% confidence interval 3.27 to
173 5.37); n = 2432 participants).²⁴

174

175 Despite being unable to quantify how much difference antibiotics make to UTI symptom
176 duration, they are effective in treating the infection. Refer to the current NICE guideline for
177 information about considerations about which antibiotic (guided by local antibiotic resistance
178 patterns, where possible), and recommended dosage and duration.¹⁷

179

180 **Other treatments**

181 There is little evidence to support the various over-the-counter medications that patients will
182 often have tried prior to a consultation or concurrently with antibiotics. A 2016 Cochrane
183 review of urinary alkalisers found no randomised trials.²⁵ There are no randomised trials of
184 cranberry for the treatment of uncomplicated UTI^{26 27} and a Cochrane review of cranberry
185 products found they did not prevent recurrent urinary tract infections in women any more
186 than placebo or no treatment (RR 0.86, 95% CI 0.71 to 1.04).²⁸

187

188 A systematic review of the effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs)
189 compared to antibiotics for uncomplicated UTI found five randomised trials.²⁹ For the
190 outcome of symptom resolution, three trials found that NSAIDs were inferior to antibiotics;
191 but two trials (smaller, with higher or unclear risk of bias) found no significant difference
192 between the arms. In the groups that received NSAIDs, the percentage of women with
193 symptom resolution by day 3 or 4 ranged from 39%-58%. In two of the three trials that
194 reported pyelonephritis, rates were slightly higher in the NSAID group (risk difference of 4
195 and 5 respectively).

196

197 **When to reconsult and when to refer**

198 Women with uncomplicated UTI without risk factors can be typically be assessed remotely.
199 Box 5 contains safety-netting information to advise patients about when to commence
200 antibiotics (if a delayed prescription was given) and/or reconsult and Box 3 lists the red flags
201 for acute pyelonephritis and sepsis which are likely to require hospital admission.

202

Box 5: Elements of a shared decision making conversation

A shared decision making discussion following the diagnosis of an uncomplicated UTI typically involves the following (although it may not be a simple linear process as presented here):

- **Outline that there is choice about the next steps** and a decision to be made; **invite** the patient to partner with you in the decision-making to the extent that the patient desires, and reassure any patient who feels overwhelmed or uncertain about the patient's involvement or how to proceed;
- **Elicit the patient's expectations about management of the condition.** This can include previously tried treatments and experiences, along with fears and concerns (including symptom severity and how it may impact daily tasks); this allows for

detecting and discussing misperceptions, where necessary, either now or later in the process);

- **Explain the options**

- Wait and see (this may involve providing a delayed prescription for antibiotics and clear information about when to use it)
- Commence antibiotics immediately

- **Discuss the benefits and harms of the options** (including their likely probability or size)

- Describe the natural course of an uncomplicated UTI and that for some women, it will resolve within about a week without taking antibiotics. Also explain that there is uncertainty about exact timeframes and whether your patient will be one of the women who gets better without antibiotics (and that if not, antibiotics may need to be commenced later).
- Discuss that antibiotics probably shorten the duration of symptoms, however by taking them, there is the risk of side effects and antibiotic resistance.
- Regardless of which option is chosen, provide advice on symptom management (e.g. paracetamol or ibuprofen)

- Provide the opportunity to **weigh up the benefits and harms of the options**, and consider them in the context of the patient's **preferences, values, and circumstances**

- **Explore if the patient has any questions**, is ready to make a decision, or needs further information, time, or the involvement of other people.

- Provide **safety-netting information** about when to commence antibiotics (if delayed prescription) and/or consult

- Nausea or vomiting
- Rigors
- Shivering, chills, and muscle pain
- Feeling confused or very drowsy
- Not passing urine all day
- Blood in the urine
- Temperature above 38°C
- Kidney pain in the back or under the ribs
- Worsening UTI symptoms
- If taking antibiotics, no improvement in UTI symptoms after 48 hours

- Provide written **patient information leaflet** with summary information³⁰

203

204 **What you need to know**

- 205 • In about a third of women, an uncomplicated UTI may resolve on its own within about
206 7-10 days, without the need for antibiotics
- 207 • The option of ‘wait and see’ (which typically involves providing a delayed
208 prescription) can be discussed as part of a shared decision making process within
209 the consultation
- 210 • Consider pyelonephritis or sepsis and hospital admission in patients who are
211 systemically unwell and have high fever, rigours, nausea/vomiting, flank pain, low
212 blood pressure, high heart rate, high respiratory rate, not passing urine for 12-18
213 hours, and behaviour change

214

215 **Education into practice**

216 How do you invite patients to share in the decision-making about management of their
217 uncomplicated UTI, including a discussion about their expectations?

218

219 How can you facilitate a balanced discussion about the benefits and harms of using
220 antibiotics immediately or adopting a ‘wait and see’ (delayed prescribing) approach?

221

222

223 **References**

- 224 1. McCormick A, Fleming D, Charlton J, Royal College of General Practitioners, Great
225 Britain Office of Population Censuses and Surveys, et al. Morbidity statistics from
226 general practice: fourth national study 1991-1992. London: H.M.S.O.; 1995.
- 227 2. Foxman B, Barlow R, D'Arcy H, Gillespie B, Sobel JD. Urinary tract infection: self-
228 reported incidence and associated costs. *Ann Epidemiol.* 2000 Nov;10(8):509-15.
- 229 3. Schappert SM. National ambulatory medical care survey: 1989 summary. *Vital*
230 *Health Stat* 13. 1992 Apr(110):1-80.
- 231 4. Bærheim KM, Anders. Peeing barbed wire: symptom experiences in women with
232 lower urinary tract infection. *Scand J Prim Health Care.* 1999;17(1):49-53.
- 233 5. Ellis AK, Verma S. Quality of life in women with urinary tract infections: Is benign
234 disease a misnomer? *J Am Board Fam Pract.* 2000;13(6):392-7.
- 235 6. Colgan R, Williams M, Johnson JR. Diagnosis and treatment of acute pyelonephritis
236 in women. *Am Fam Physician.* 2011 Sep 1;84(5):519-26.
- 237 7. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and
238 economic costs. *Dis Mon.* 2003 Feb;49(2):53-70.

- 239 8. Fihn SD, Boyko EJ, Chen CL, Normand EH, Yarbrow P, Scholes D. Use of spermicide-
240 coated condoms and other risk factors for urinary tract infection caused by
241 staphylococcus saprophyticus. Arch Intern Med. 1998 Feb 9;158(3):281-7.
- 242 9. National Institute for Health and Care Excellence. Clinical knowledge summaries:
243 urinary tract infection (lower) – women [Internet]. London: NICE; 2020 Oct. Available
244 from: <http://cks.nice.org.uk/urinary-tract-infection-lower-women>. Accessed: 06
245 January 2021.
- 246 10. Public Health England. Diagnosis of urinary tract infection: quick reference tool for
247 primary care for consultation and local adaptation [Internet]. London: PHE; 2020
248 May. Available from:
249 [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachm
250 ent_data/file/927195/UTI_diagnostic_flowchart_NICE-October_2020-FINAL.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/927195/UTI_diagnostic_flowchart_NICE-October_2020-FINAL.pdf).
251 Accessed: 06 January 2021.
- 252 11. Giesen LG, Cousins G, Dimitrov BD, van de Laar FA, Fahey T. Predicting acute
253 uncomplicated urinary tract infection in women: a systematic review of the diagnostic
254 accuracy of symptoms and signs. BMC Fam Pract. 2010 Oct 24;11(1):78.
- 255 12. Bent S, Nallamothu BK, Simel DL, Fihn SD, Saint S. Does this woman have an acute
256 uncomplicated urinary tract infection? JAMA. 2002 May;287(20):2701-10.
- 257 13. National Institute for Health and Care Excellence. Clinical knowledge summaries:
258 pyelonephritis – acute [Internet]. London: NICE; 2020 Nov. Available from:
259 <https://cks.nice.org.uk/topics/pyelonephritis-acute/>. Accessed: 06 January 2021.
- 260 14. National Institute for Health and Care Excellence. Sepsis: recognition, assessment
261 and early management [Internet]. London: NICE guideline; 2016 July 13 [updated
262 2017 Sep 13]. Clinical Guideline [NG51]. Available from:
263 <https://www.nice.org.uk/guidance/ng51>. Accessed: 06 January 2021.
- 264 15. Little P, Turner S, Rumsby K, Jones R, Warner G, Moore M, et al. Validating the
265 prediction of lower urinary tract infection in primary care: Sensitivity and specificity of
266 urinary dipsticks and clinical scores in women. Br J Gen Pract. 2010 Jul;60(576):495-
267 500.
- 268 16. Hoffmann T, Peiris R, Mar CD, Cleo G, Glasziou P. Natural history of uncomplicated
269 urinary tract infection without antibiotics: a systematic review. Br J Gen Pract. 2020
270 Oct;70(699):e714-e22.
- 271 17. National Institute for Health and Care Excellence. Urinary tract infection (lower):
272 antimicrobial prescribing [Internet]. London: Nice guideline; 2018 Oct 31 [updated
273 2019 Jul]. Clinical Guideline [NG109]. Available from:
274 <https://www.nice.org.uk/guidance/ng109/resources>. Accessed: 06 January 2021.

- 275 18. Little P, Merriman R, Turner S, Rumsby K, Warner G, Lowes JA, et al. Presentation,
276 pattern, and natural course of severe symptoms, and role of antibiotics and antibiotic
277 resistance among patients presenting with suspected uncomplicated urinary tract
278 infection in primary care: observational study. *BMJ*. 2010 Feb 5;340:b5633.
- 279 19. Little P, Moore MV, Turner S, Rumsby K, Warner G, Lowes JA, et al. Effectiveness of
280 five different approaches in management of urinary tract infection: randomised
281 controlled trial. *BMJ*. 2010 Feb 5;340:c199.
- 282 20. Knottnerus BJ, Geerlings SE, Moll van Charante EP, ter Riet G. Women with
283 symptoms of uncomplicated urinary tract infection are often willing to delay antibiotic
284 treatment: a prospective cohort study. *BMC Fam Pract*. 2013 May 31;14:71.
- 285 21. Hansen MP, Scott AM, McCullough A, Thorning S, Aronson JK, Beller EM, et al.
286 Adverse events in people taking macrolide antibiotics versus placebo for any
287 indication. *Cochrane Database Syst Rev*. 2019 Jan 18;1(1):CD011825.
- 288 22. Gillies M, Ranakusuma A, Hoffmann T, Thorning S, McGuire T, Glasziou P, et al.
289 Common harms from amoxicillin: A systematic review and meta-analysis of
290 randomized placebo-controlled trials for any indication. *CMAJ*. 2015 Jan
291 6;187(1):E21-E31.
- 292 23. Australian Commission on Safety and Quality in Health Care (ACSQHC). *Aura 2017:*
293 *Second Australian report on antimicrobial use and resistance in human health*
294 [Internet]. Sydney: ACSQHC; 2017. Available from:
295 [https://www.safetyandquality.gov.au/publications-and-resources/resource-](https://www.safetyandquality.gov.au/publications-and-resources/resource-library/aura-2017-second-australian-report-antimicrobial-use-and-resistance-human-health)
296 [library/aura-2017-second-australian-report-antimicrobial-use-and-resistance-human-](https://www.safetyandquality.gov.au/publications-and-resources/resource-library/aura-2017-second-australian-report-antimicrobial-use-and-resistance-human-health)
297 [health](https://www.safetyandquality.gov.au/publications-and-resources/resource-library/aura-2017-second-australian-report-antimicrobial-use-and-resistance-human-health). Accessed: 06 January 2021.
- 298 24. Van Hecke O, Wang K, Lee JJ, Roberts NW, Butler CC. Implications of antibiotic
299 resistance for patients' recovery from common infections in the community: a
300 systematic review and meta-analysis. *Clin Infect Dis*. 2017 Aug 1;65(3):371-82.
- 301 25. O'Kane DB, Dave SK, Gore N, Patel F, Hoffmann TC, Trill JL, et al. Urinary
302 alkalinisation for symptomatic uncomplicated urinary tract infection in women.
303 *Cochrane Database Syst Rev*. 2016 Apr 19;4(4):CD010745.
- 304 26. Gbinigie O, Allen J, Boylan AM, Hay A, Heneghan C, Moore M, et al. Does cranberry
305 extract reduce antibiotic use for symptoms of acute uncomplicated urinary tract
306 infections (CUTI)? Protocol for a feasibility study. *Trials*. 2019 Dec 23;20(1):767.
- 307 27. Jepson RG, Mihaljevic L, Craig J. Cranberries for treating urinary tract infections.
308 *Cochrane Database Syst Rev*. 1998 Oct 26;4(2):CD001322.
- 309 28. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections.
310 *Cochrane Database Syst Rev*. 2012 Oct 17;10(10):CD001321.

- 311 29. Carey MR, Vaughn VM, Mann J, Townsend W, Chopra V, Patel PK. Is non-steroidal
312 anti-inflammatory therapy non-inferior to antibiotic therapy in uncomplicated urinary
313 tract infections: a systematic review. *J Gen Intern Med.* 2020 Jun;35(6):1821-9.
- 314 30. National Institute for Health and Care Excellence. Endorsed resource - TARGET:
315 treating your infection - urinary tract infection (UTI) [Internet]. London: NICE
316 guideline; 2019 February. Clinical Guideline [NG15]. Available from:
317 [https://www.nice.org.uk/guidance/ng15/resources/endorsed-resource-target-treating-](https://www.nice.org.uk/guidance/ng15/resources/endorsed-resource-target-treating-your-infection-urinary-tract-infection-uti-4661131357)
318 [your-infection-urinary-tract-infection-uti-4661131357](https://www.nice.org.uk/guidance/ng15/resources/endorsed-resource-target-treating-your-infection-urinary-tract-infection-uti-4661131357). Accessed: 05 Jan 2021.
- 319