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Incidence of urinary tract infections and antibiotic resistance in the outpatient setting: a cross-sectional study

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1 **Title: Incidence of urinary tract infections and antibiotic resistance in the outpatient**
2 **setting: A cross-sectional study**

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24

25 **Abstract**

26 **Purpose**

27 In 2012-2013, a cross-sectional survey was conducted in women visiting a general
28 practitioner for a urinary tract infection (UTI), to estimate the annual incidence of UTIs due to
29 antibiotic-resistant *Escherichia coli* (*E. coli*).

30 **Methods**

31 A sampling design (stratification, stages and sampling weights) was taken into account in all
32 analyses. Urine analyses were performed for each woman and centralised in one laboratory.

33 **Results**

34 Among 538 included women, urine culture confirmed UTI in 75.2% of cases. *E. coli*
35 represented 82.8% of species. Among *E. coli*, resistance (I + R) was most common to
36 amoxicillin (38% [95% confidence interval: 31.1–44.5]) and to trimethoprim/sulfamethoxazole
37 (18.1% [12.0–24.1]). Resistance to ciprofloxacin and cefotaxime was lower (1.9% in both
38 cases, [0.3–3.5]), as it was for nitrofurantoin (0.4 [0–1,0]) and fosfomycin (0). Extended-
39 spectrum β -lactamase (ESBL) represented 1.6% of *E. coli* [0.2–2.9]. Annual incidence rate of
40 confirmed UTI was estimated at 2,400 per 100,000 women [1,800–3,000]. Incidence rates of
41 UTI due to fluoroquinolone-resistant and ESBL-producing *E. coli* were estimated at 102 per
42 100,000 women [75–129] and at 32 [24–41], respectively.

43 **Conclusions**

44 ESBL had been found in a community population, and even though the rate was low, it
45 represents a warning and confirms that surveillance should continue.

46

47 **Key words:** urinary tract infection; *Escherichia coli*; antibiotic resistance; incidence; general
48 population; general practitioner.

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Introduction

Urinary tract infections (UTIs) are one of the most common community-onset infections. UTIs are often due to Enterobacteriaceae, in particular *Escherichia coli* (*E. coli*). *E. coli* accounts for 70–80% of positive urine cultures.[1] Enterobacteriaceae are part of the gut flora, which exposes those bacteria to selective pressure produced by antibiotic prescription.[2] An increasing prevalence of antimicrobial resistance is observed for UTIs.[2, 3] Since 2000, extended-spectrum β -lactamase (ESBL)-producing *E. coli* have emerged worldwide in both community and hospital settings.[4, 5] Unfortunately, ESBL-positive isolates are also commonly resistant to fluoroquinolone and trimethoprim/sulfamethoxazole, two antibiotics widely used to treat community-onset UTIs.[4] In France, the prevalence of antimicrobial resistance in UTIs due to *E. coli* has increased for inpatient and in faecal carriage among healthy subjects.[6, 7] For community-onset UTIs, French data are scant. Information about antibiotic resistance for uncomplicated UTIs is limited because they do not require systematic urine cultures.[8]

The aim of this study was to estimate the annual incidence of UTI caused by antibiotic-resistant *E. coli* among women visiting a general practitioner (GP) in France.

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70

71 **Materials and Methods**

72 Design and study population

73 The Drug Resistant Urinary Tract Infection (Druti) study was conducted in France between
74 January 2012 and February 2013 by the GPs of the Sentinelles network.[9] This was a
75 prospective, national observational survey. Eligible patients were female patients 18 years of
76 age and older visiting their GP for presumed UTI (i.e., complaining of at least one clinical
77 symptom of UTI—pain or bladder tenderness, pollakiuria or urinary urgency—for less than 7
78 days). Additional eligibility criteria included living in France at least 6 months in a year, not
79 being institutionalised (in hospital or nursing home) at the time of the study, having a good
80 understanding of the French language, not having cognitive disorders. Furthermore, women
81 recorded in the study as eligible even if they were not included, could not be eligible during 8
82 weeks after this registration. To be included, women had to agree to participate, not taken an
83 antibiotic in the past 7 days, have seen their GP in a working day for transportation of urine
84 samples (Monday, Tuesday, Wednesday and Thursday) and be able to provide a midstream
85 urine sample during the consultation. For each included patient, the GP administered a
86 questionnaire that was completed during the consultation. The questionnaire included
87 questions regarding the patient's demographic characteristics (age, household members and
88 nationality), clinical status (chronic diseases and comorbidities, particularly pregnancy,
89 urinary tract disorder, previous UTIs and urinary catheterisation) and other epidemiological
90 characteristic for ancillary studies. For example, hospitalization within 12 months before the
91 study was collected in the questionnaire to evaluate if it could be a risk factor for resistance.
92 To recover any missing data, within 2 weeks of inclusion, a trained investigator telephoned
93 the GP and patient to verify the information.

94 Concerning uncomplicated and complicated UTIs, various classifications are reported.[8, 10,
95 11] According to French recommendations, in 2008, cystitis were defined as local symptoms

96 (pain or bladder tenderness, pollakiuria or urinary urgency) and pyelonephritis were defined
97 as UTI with fever >38°C. Complicated UTI was defined as UTI occurring in a woman with
98 urinary tract anomalies, pregnant, aged 65 years and older or treated for a chronic disease
99 (diabetes, cancer or renal insufficiency).

100 Sample size

101 The sample size was calculated from a proportion of fluoroquinolone resistance of 18% from
102 Annual report of the European Antimicrobial Resistance Surveillance Network 2012 (EARS-
103 Net), with a precision of 4.5%, leading to the inclusion of 280 positive samples for *E. coli*. [12]
104 On the basis of a proportion of positive urine cultures of 70% and a proportion of *E. coli*
105 isolated from a positive sample of 77%, [1] it was necessary to include 520 urine samples.
106 Considering a median number of consultations for UTI of 16 per year per GP and a
107 proportion of eligible patients included of 34%, it was necessary to recruit 96 GPs to obtain
108 520 included patients.

109 Bacteriological analyses and definitions

110 For all urine cultures, bacterial identification and susceptibility testing were performed at the
111 same laboratory: the Department of Microbiology of Ambroise Paré University Hospital,
112 Paris. Bacteriological analyses and antimicrobial susceptibility testing were described
113 elsewhere. [13] They were conducted according to the recommendations of the French
114 Society of Microbiology and the European Committee on Antimicrobial Susceptibility
115 Testing. [14-17]. As previously described, ESBL was identified by specific polymerase chain
116 reaction (PCR) and sequencing. [17, 18]

117 Multidrug resistance (MDR) was defined as acquired resistance to at least three of the
118 following antimicrobial categories: penicillins, penicillins and β -lactamase inhibitors,
119 antipseudomonas penicillins and β -lactamase inhibitors, monobactams, carbapenems, non-
120 extended spectrum cephalosporins, extended-spectrum cephalosporins, anti-MRSA
121 (methicillin-resistant *Staphylococcus aureus*) cephalosporins, cephamycins,
122 aminoglycosides, tetracyclines, glycylicyclines, folate pathway inhibitors, fluoroquinolones,

123 phenicols, phosphonic acids and polymyxins (antimicrobial categories were dropped if
124 species had intrinsic resistance).[19]

125 Statistical analysis

126 The sampling design (stratification, stages and sampling weights) was taken into account in
127 all analyses to make inference to the population.[20] Collection of samples was based on
128 two-stage, stratified, random sampling. At the first stage, the sampling frame of all GPs in
129 France was stratified in five strata defined as five French inter-regions (North, East, West,
130 South-West, and South-East). GPs of the Sentinelles' network participating in the biological
131 sampling protocol were assumed to be selected from each stratum of a sampling frame using
132 simple, random sampling. This hypothesis means that each sampling unit (GPs participating
133 in the study) had, in each stratum, the same probability of being selected and saw the same
134 proportion of patients with UTI as other practitioners in France. At the second stage, GPs
135 proposed inclusion in the study and collected urine samples from all women matching the
136 eligibility criteria. Thus, the probability of inclusion at this stage was calculated for each
137 woman according to the number of women with a urine culture result, divided by the number
138 of eligible women consulted for a presumed UTI. Strata and stages were used to accurately
139 estimate associated variances. Sampling weights were post-stratified using the number of
140 consultations for GPs participating in the study compared with the number of consultations
141 for all GPs in France provided by the national health insurance system (CNAM).

142 For the descriptive analysis, we expressed the estimated proportions with 95% confidence
143 intervals (CIs) of the qualitative variables in the population. Incidences of UTI and UTI due to
144 antibiotic-resistant *E. coli* were estimated taking into account the sampling design. The
145 annual incidence rate was calculated as the incidence divided by the size of the French
146 female population over 18 (at the first January 2012: 25,862,849 women).[21] Categorical
147 variables were compared using the Pearson squared Chi² test, whereas the Student's *t*-test
148 was used to compare continuous data. A *p-value* of ≤ 0.05 was considered statistically
149 significant. Data were collected with EPI-Data and analysed with the R survey package[22]
150 or Stata.

151 Ethical considerations

152 The study obtained research authorisation from the French independent administrative
153 authority protecting privacy and personal data (CNIL), number 911,485, and from the local
154 human investigation committee of *Ile de France V*.

155

156

157 **Results**

158 Out of the expected 96 GPs, 87 GPs participated in the study (North: 13, East: 13, West: 14,
159 South-East: 26 and South-West: 21). In total, GPs saw 1,569 women with symptoms of UTI
160 (Fig. 1). Urine samples were collected for 538 included women. The three main reasons for
161 non-inclusion were unavailability for the transport of the urine sample (34%), lack of time of
162 the GP for inclusion (18%) and previous antibiotic treatment in the past 7 days (14%).

163

164 Mean age of the included women was 45 years old. The majority of participants had a history
165 of previous UTI (84% [95% CI: 80–88]), but few had recurrent UTIs (≥ 3 episodes in the past
166 12 months) (7% [5–10]). Clinical symptoms were pain or bladder tenderness in 93% [90–96]
167 of cases, pollakiuria in 92% [88–95], urinary urgency in 76% [69–82], flank or pelvic pain in
168 43% [36–51], hematuria in 23% [19–28] and fever in 7% [5–11]. Complicated UTIs
169 represented 23% [18–28] of UTI cases. Women treated for a chronic disease (diabetes,
170 cancer or renal insufficiency), pregnancy and urinary tract anomalies represented 6% [4-10],
171 3% [2-5], and 2% [1-4] of UTI cases, respectively. A quarter of the included women were
172 aged 65 years and older (16%, [11-22]). There were no women with chronic indwelling
173 urinary catheters, and only five women had had an intermittent urinary catheter in the last
174 month (1%, [0-4]).

175 Excluded women had less pollakiuria (91%), urinary urgency (64%) and flank or pelvic pain
176 (34%) (with $p = 0.03$, $p < 0.01$ and $p < 0.01$, respectively).

177 An empirical antibiotic treatment was prescribed in 97% cases [95–98].

178

179 Out of the 538 included patients, 393 (75.2%) had a positive urine culture. Among the 393
180 urine samples with significant bacteriuria, 421 bacteria were isolated: 366 urine samples
181 (93.1% [90.5–95.9]) had only one bacteria, 26 samples (6.6% [3.9–9.4]) had two bacteria
182 and one sample (0.3% [0.0–1.3]) had three different bacteria. The most common pathogen

183 was *E. coli* (82.8%), followed by *Proteus mirabilis* (4.3%) (Table 1). According to symptoms,
184 the rate of positive urine culture was not statistically different.

185
186 Among *E. coli*, resistance (I + R) was most common to amoxicillin (38%) and to
187 trimethoprim/sulfamethoxazole (18.1%). Resistance to ciprofloxacin was low (1.9%), as it
188 was to cefotaxime (1.9%) (Table 2). MDR concerned 20.4% [95% CI: 14.8–25.9] of *E. coli*
189 (64 isolates), and resistance to at least one antibiotic concerned 43% [95% CI: 36.0–49.5] of
190 *E. coli* (129 isolates). MDR *E. coli* were mainly resistant to amoxicillin (98.9% [95% CI: 91.7–
191 99.9]), trimethoprim/sulfamethoxazole (50.3% [95% CI: 33.1–67.4]) and fluoroquinolone
192 (15.3% [95% CI: 7.7–28.2]). Resistance rates were higher among older women except for
193 amoxicillin; however, those differences were not statistically significant (Table 3). No
194 differences in the distribution of resistance between the five regions have been shown (data
195 not shown).

196
197 Six *E. coli* produced classical ESBLs (1.6% [0.2–2.9]), of which three produced a CTX-M-1
198 ESBL, two a CTX-M-14 ESBL and one a CTX-M-15 ESBL. All ESBL *E. coli* were associated
199 with at least one of these following factors: hospitalisation, travel abroad or contact with a
200 traveller or previous antibiotic intake.

201
202 The annual incidence rate of confirmed UTI in general practice was estimated at 2,400 per
203 100,000 women in France [1,800–3,000], with an annual incidence rate of UTI due to *E. coli*
204 in general practice at 2,000 for 100,000 women [1,500–2,500] and with annual incidence
205 rates of UTI due to FQ-resistant *E. coli* and ESBL *E. coli* in general practice at 102 for
206 100,000 women [75–129] and 32 [24–41], respectively (Table 4).

207

208

209 **Discussion**

210 The present study permitted the updating of annual incidence rates of UTI in general practice
211 and provided actualised resistance rates in the community. It confirmed that FQ-resistant and
212 ESBL-producing *E. coli* are circulating in the community, still at a low rate. The study also
213 showed that a quarter of women visiting GP for presumed UTI had a negative urine culture.

214

215 It is difficult to compare our estimates of incidence of UTI with those previously published. In
216 Switzerland, incidence rates of visits to a GP for lower UTI has been estimated at 1.6 per 100
217 inhabitants per year, but that study was conducted among men and women.[23] Because
218 84% of the patients were women and because the denominator included men and women, a
219 lower rate than the one we estimated in women only was expected. In Canada, incidence
220 rates of UTI with positive urine culture has been estimated at 17.5 per 1,000 inhabitants per
221 year, an incidence still lower than our estimates, probably owing to the design of the study
222 based on passive surveillance (thus, excluding many uncomplicated cases of lower UTI).[24]

223

224 In the Antimicrobial Resistance Epidemiological Survey on Cystitis (ARESC), 74.6% of
225 patients had a positive urine culture, mostly *E. coli* (76.7% of the positive urine cultures).[11]

226 In ECO.SENS II, 72.1% of patients had a positive urine culture, mostly *E. coli* (74.2% of the
227 positive urine cultures).[25] However, both included only uncomplicated lower UTIs. Our
228 proportion of positive urine cultures is close to those found, but our proportion of *E. coli* is
229 higher than other studies because of patient characteristics: lower proportions of *E. coli* are
230 reported in studies based on complicated or recurrent UTIs and in routine samples versus
231 solicited ones.[1, 23] Available epidemiological data are mainly produced by passive
232 surveillance, based on data from clinical microbiology laboratories. Because standard care
233 for uncomplicated UTIs does not require a microbiological work-up,[26, 10] patients with
234 complicated UTIs, with comorbidity or recent antimicrobial exposure, or with healthcare-
235 related infections tend to be overrepresented in epidemiological studies based on passive

236 surveillance.[23, 27, 28] As a consequence, surveillance in community settings only based
237 on data from routine clinical microbiological laboratories overestimates antimicrobial
238 resistance. [23, 27, 28] Indeed, the European recommendations for antimicrobial resistance
239 surveillance stated that generating rates of resistance based on indiscriminate samples from
240 ambulatory patients would lead to an overestimate of the rates of resistance.[29] This has
241 been demonstrated in a recent study in which *E. coli* in UTIs showed higher susceptibility to
242 antibiotics in solicited samples collected with a specific protocol than in routine samples.[23]
243 Consequently, a recommendation of empirical antibiotic therapy for UTIs based on the
244 results of an epidemiological study conducted with a systematic collection of urine samples
245 would be more appropriate than a recommendation based on laboratory passive reporting.
246 Thus, the main interest of our study was to estimate, on a national scale, relevant
247 antimicrobial resistance rates among women seen by GPs for a presumed UTI.

248

249 In 2003–2006, the ARESC found resistance rates of *E. coli* isolated from uncomplicated UTIs
250 to be 17.6% for cefuroxime and 8.3% for ciprofloxacin in different European countries. In
251 France, the rates were 10.7% and 1.6%, respectively.[11] Resistance rates to ciprofloxacin
252 exceeded 10% in Italy, Russia, Spain and Brazil. More recent data from ECO-SENS II
253 (2007–2008) found resistant rates of *E. coli* isolated from UTIs at 1.2% for cefotaxime and
254 3.9% for ciprofloxacin in different European countries.[25] In our study, we observed lower
255 rates for cefuroxime (2%), cefotaxime (1.9%) and ciprofloxacin (1.9%).

256 Only six ESBL were identified from our samples (1.6%). Previously reported estimates in
257 France varied from no ESBL isolates among women visiting their GP for presumed UTI in
258 2008[30] to 1.83% of urine samples in a study based on passive surveillance.[23, 31] Even if
259 it is not possible here to detect a potential increase in the incidence of ESBL related to UTIs,
260 the fact that such bacteria are present in clinical samples of patients living in the community
261 represents a real warning. The high rate of resistance to trimethoprim/sulfamethoxazole or
262 high proportion of MDR *E. coli* also constitutes warnings. Comparing our results with those of
263 the ARESC study, trimethoprim/sulfamethoxazole resistance increased by seven points,

264 almost reaching the threshold of 20%.[11] This threshold represented the resistance
265 prevalence at which the agent is no longer recommended for empirical treatment of acute
266 cystitis.[32] In addition, the proportion of MDR *E. coli* based on the ECDC definition doubled
267 compared with the ARESC data, in which the same definition was used for MDR.[11, 19]

268

269 For other antibiotics, resistance rates were at the expected levels: low for fosfomycin and
270 nitrofurantoin and high for amoxicillin. The 38% resistance rate to ampicillin was very close to
271 the French ARESC results (39%), and thus the highest rate in Europe (except the
272 Netherlands).[11] The activity of amoxicillin is dramatically reduced; this antibiotic cannot be
273 used for empirical treatment of uncomplicated cystitis. Empirical antibiotics could be
274 fosfomycin or nitrofurantoin with susceptibility rates, in our study at 100% and 99.6%,
275 respectively. These rates were estimated in other European or American countries from 92%
276 to 100%.[11, 25, 33]

277

278 We are confident in our estimation of the actual antimicrobial resistance in UTI among
279 outpatients because of our use of a systematic collection of urine samples for all women
280 visiting their GP for presumed UTIs and taking into account the sampling design. The
281 sampling design and the post-stratification has corrected the bias due to drop-outs and
282 geographical repartition. Another strength of the study was the centralised urine analysis.
283 Finally, the prospective and standardised collection of data limited recall and information
284 bias.

285

286 The results of the present study should be interpreted taking into account the fact that the
287 population of the study were women visiting their GP for presumed UTI. The study does not
288 take into account women with UTI who do not consult a GP (e.g., visit to another specialist,
289 self-medication or spontaneous healing). Indeed, a US study estimated that only 50% of
290 UTIs had a medical visit.[34] Such data are not available in France. Another limitation is the

291 lack of results regarding pivmecillinam. This drug was not available in France at the time of
292 the study and thus was not tested in the laboratory.

293

294 Our results show that active surveillance of resistant UTIs in the community is required to
295 complete passive surveillance and healthcare-associated surveillance. ESBL had been found
296 in our community population and even though the rate was low, it represents a warning and
297 confirms that studies such as the one presented here should be repeated.

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301 **Competing interests: none**

302 The authors declare that they have no competing interests.

303 **Authors' contributions**

304 LR, SM, SV, TB, BC and TH conceived and designed the experiments. LR, SM, RB and BH
305 performed the experiments. SV, SM, AB, LR and YLS analysed the data. LR, SV, SM, AB,
306 YLS, BH, TB, BC and TH wrote the paper.

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313 Corporate foundation GPM, grants from French Urology Association during the conduct of
314 the study. They had no role in the study design, data collection, analyses, decision to publish
315 or preparation of the manuscript.

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318 **Tables**319 **Table 1: Distribution of pathogens in positive urine culture**

	<i>n</i>	Estimated proportion (% [95%CI]) *
Enterobacteriaceae	369	90.8 [86.1–95.6]
<i>Escherichia coli</i>	331	82.8 [77.0–88.6]
<i>Proteus mirabilis</i>	16	4.3 [1.6–7.1]
<i>Klebsiella pneumoniae</i>	7	2.1 [0.3–3.9]
<i>Citrobacter koseri</i>	7	1.8 [0.4–3.2]
<i>Klebsiella oxytoca</i>	5	0.6 [0.1–1.1]
<i>Enterobacter aerogenes</i>	1	0.2 [0.0–0.5]
<i>Enterobacter cloacae</i>	1	0.2 [0.0–0.5]
<i>Raoultella planticola</i>	1	0.1 [0.0–0.4]
Others	52	9.1 [4.4–13.9]
<i>Staphylococcus saprophyticus</i>	24	5.6 [2.8–8.3]
<i>Enterococcus faecalis</i>	15	4.6 [4.0–8.9]
<i>Streptococcus agalactiae</i>	7	2.0 [0.2–3.8]
<i>Staphylococcus aureus</i>	3	1.3 [0.0–3.0]
<i>Staphylococcus haemolyticus</i>	1	0.7 [0.0–2.2]
<i>Pseudomonas aeruginosa</i>	1	0.4 [0.0–1.3]
<i>Gardnerella vaginalis</i>	1	0.2 [0.0–0.7]

320 * Estimated proportion with the sampling design and 95% confidence intervals (CIs)

321 *n*: size in the study population

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323

324 **Table 2: Resistance rates among 331 *Escherichia coli* from urinary tract infection of**
 325 **women over 18 visiting a French GP in 2012–2013**

	S		I		R	
	<i>n</i>	Estimated proportion (% [95%CI])*	<i>n</i>	Estimated proportion (% [95%CI])*	<i>n</i>	Estimated proportion (% [95%CI])*
Amoxicillin	215	62.0 [55.5–68.9]	0	0.0	116	38.0 [31.1–44.5]
Amoxicillin/clavulanate	307	91.3 [87.9–94.6]	12	5.2 [2.1–8.4]	12	3.5 [1.5–5.5]
Cefuroxime	323	98.0 [96.4–99.7]	0	0.0	8	2.0 [0.3–3.6]
Cefotaxime	323	98.1 [96.5–99.7]	2	0.4 [0.0–0.9]	6	1.5 [0.1–3.0]
Ceftazidime	323	98.1 [96.5–99.7]	5	1.0 [0.0–2.1]	3	0.9 [0.0–2.1]
Carbapenems	331	100.0	0	0.0	0	0.0
Fosfomycin	331	100.0	0	0.0	0	0.0
Nitrofurantoin	328	99.6 [99.0–99.9]	0	0.0	3	0.4 [0.0–1.0]
Nalidixic acid	311	94.6 [92.1–97.1]	3	0.7 [0.0–1.7]	17	4.6 [0.2–7.1]
Ofloxacin	312	94.9 [92.6–97.3]	8	2.3 [0.8–3.8]	11	2.8 [1.1–4.4]
Ciprofloxacin	323	98.1 [96.5–99.7]	2	0.4 [0.0–0.9]	6	1.5 [0.1–3.0]
Aminoglycoside	327	98.7 [97.0–99.9]	0	0.0	4	1.3 [0.0–3.0]
Trimethoprim/sulfamethoxazole	278	81.9 [75.9–88.0]	2	0.3 [0.0–0.7]	51	17.8 [11.7–24.0]

326 * Estimated proportion with the sampling design and 95% CI

327 *n*: size in the study population; C3G: cephalosporin third generation; S: susceptible; I: intermediate; R:
 328 resistant)

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330

331 **Table 3: Resistance rates among 331 *Escherichia coli* from urinary tract infection of**
 332 **women over 18 visiting a French GP in 2012–2013, according to age**

	All women (n = 331)		Women <65 years old (n = 273)		Women ≥65 years old (n = 58)	
	n*	Estimated proportion (% [95%CI])**	n*	Estimated proportion** (% [95%CI])	n*	Estimated proportion** (% [95%CI])
Amoxicillin	116	38.0 [31.1–44.5]	95	38.4 [30.8–46.0]	21	34.2 [19.8–48.7]
Amoxicillin/clavulanate	24	8.7 [5.4–12.1]	20	9.1 [5.2–13.0]	4	6.5 [0.0–15.3]
Cefuroxime	8	1.9 [0.3–3.5]	6	1.4 [0.2–2.6]	2	4.9 [0.0–13.1]
Cefotaxime	8	1.9 [0.3–3.5]	6	1.4 [0.2–2.6]	2	4.9 [0.0–13.1]
Ceftazidime	8	1.9 [0.3–3.5]	6	1.4 [0.2–2.6]	2	4.9 [0.0–13.1]
Carbapenems	0	0.0	0	0.0	0	0.0
Fosfomycin	0	0.0	0	0.0	0	0.0
Nitrofurantoin	3	0.4 [0–1.0]	2	0.3 [0.0–0.8]	1	1.1 [0.0–3.3]
Nalidixic acid	20	5.4 [2.9–7.9]	15	4.5 [1.9–7.1]	5	10.5 [1.1–19.9]
Ofloxacin	19	5.1 [2.7–7.4]	14	4.1 [1.9–6.4]	5	10.5 [1.1–19.9]
Ciprofloxacin	8	1.9 [0.3–3.5]	6	1.8 [0.3–3.3]	2	2.8 [0.0–6.9]
Aminoglycoside	4	1.3 [0.0–3.0]	2	0.6 [0.0–1.4]	2	5.2 [0.0–15.8]
Trimethoprim/sulfamethoxazole	53	18.1 [12.0–24.1]	40	16.7 [10.5–22.9]	13	25.6 [11.6–39.6]

333 * *E. coli* were classified as being resistant when testing disclosed resistant or intermediate
 334 susceptibility to a particular antimicrobial agent

335 ** Estimated proportion with the sampling design and 95% CI

336 n: size in the study population; C3G: cephalosporin third generation.

337

338

339 **Table 4: Incidence rate of medical consultation for urinary tract infection (UTI) among**
 340 **women over 18 years old in mainland France, 2012–2013**

341

	Estimated incidence [95%CI]*	Estimated incidence rate per 100,000 ** [95%CI]*
Presumed urinary tract infection (UTI)	823,073 [623,614 – 1 040,532]	3,200 [2,400-4,000]
<i>Presumed uncomplicated cystitis</i>	576,151 [436,530– 728,372]	2,200 [1,700-2,800]
<i>Presumed complicated UTI</i>	189,307 [143,431 – 239,322]	730 [550-930]
<i>Presumed uncomplicated Pyelonephritis</i>	50,234 [25,172-75,297]	194 [97-291]
Confirmed UTI (positive urine culture)	626,046 [465,196 – 786,896]	2,400 [1,800-3,000]
<i>Uncomplicated cystitis</i>	463,274 [344,245– 582,303]	1,800 [2,200-1,800]
<i>Complicated UTI</i>	125,209 [93,039 – 157,379]	480 [360-610]
<i>uncomplicated Pyelonephritis</i>	34,587 [14,075– 55,099]	134 [54-213]
UTI due to <i>E. coli</i>	518,446 [381,981 – 654,911]	2,000 [1,500-2,500]
<i>UTI due to FQ-resistant E. coli</i>	26,441 [19,481 - 33,400]	102 [75-129]
<i>UTI due to C3G-resistant E. coli</i>	9,850 [7,258 – 12,443]	38 [28-48]
<i>UTI due to ESBL E. coli</i>	8,295 [6,112 – 10,479]	32 [24-41]

342 * Estimated size with the sampling design and 95% CI

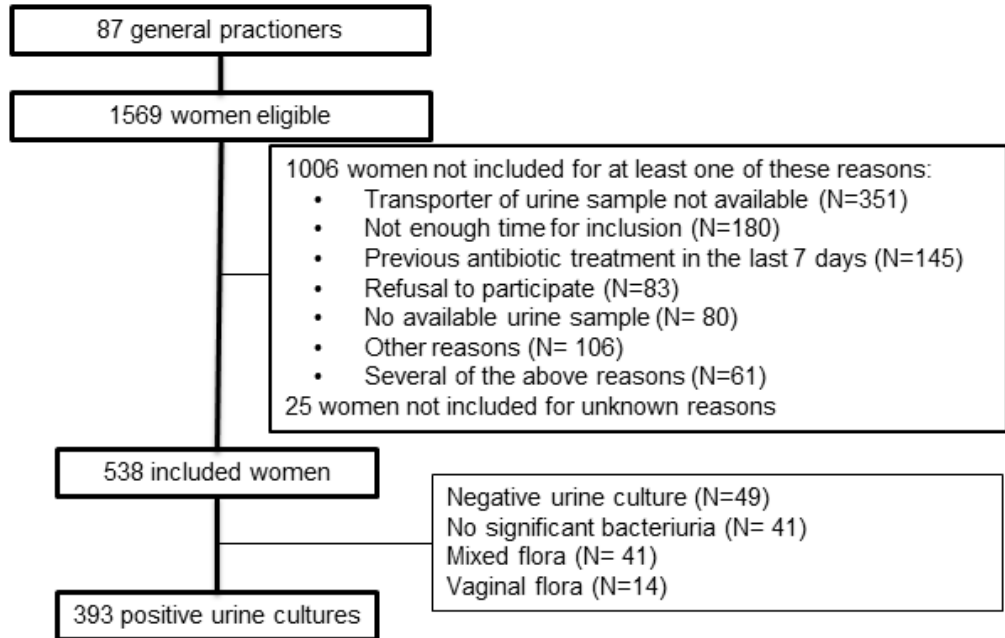
343 ** Estimated incidence rate in general practice per 100,000 women over 18 in mainland France per
 344 year

345 *E. coli*: *Escherichia coli* ESBL: Extended-spectrum β -lactamase; C3G: third generation cephalosporin;
 346 FQ: fluoroquinolone.

347

348 Figure

349 Figure 1: Flow chart



350

351

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