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## **FUrTIHF: French Urinary Tract Infections in Healthcare Facilities**

French Urinary Tract Infections in Healthcare Facilities: 5-year historic cohort 2014-2018

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5 **Abstract**

6 **Background:** Urinary tract infections (UTIs) are common and diverse. Even when not severe  
7 UTIs regularly lead to hospitalization, but their hospital burden remains unknown. This study  
8 aimed to estimate the national incidence of hospitalized UTIs in France.

9  
10 **Materials/methods:** an historic 5-year cohort of adult patients hospitalized with UTIs in  
11 France was performed on the medico-administrative databases using an ICD-10 code  
12 algorithm built by a multidisciplinary team. The performance parameters were estimated  
13 blindly, by reviewing 1,122 cases, medical reports as the gold standard, giving a global  
14 predictive positive value of 70.4% [95%CI 66.6-74.1]. The national incidence of UTIs was then  
15 estimated.

16  
17 **Results:** 2,083,973 patients with UTIs were hospitalized over the period, giving an adjusted  
18 incidence rate ~900 cases/100,000 inhabitants, stable over the period, higher in female and  
19 increasing with age; 1.2% was device-associated UTIs. Unspecific acute cystitis represented  
20 almost 2/3 of cases (63.5%); followed by pyelonephritis (23.6%) and prostatitis (12.4%).  
21 More than 3/4 of patients had at least one comorbid condition (76.8%).

22  
23 **Conclusions:** This national cohort study is the first to date to estimate the incidence of UTI-  
24 related hospitalizations in France. UTIs represent a substantial burden of care. Further  
25 analysis will provide data for more informed goal-of-care discussion targeting each type of  
26 UTI, their management and outcomes.

27

## 28 INTRODUCTION

29 Urinary tract infections (UTIs) are the most common bacterial infection, [1] and a major  
30 source of healthcare-associated infections (HAI) [2–4], leading to significant morbidity and  
31 cost [5]. In a French study across 34 Emergency medical services, UTIs were the second  
32 commonest infectious disease (ID) (20.4%) after respiratory tract infections among  
33 admissions [6]. Moreover, UTIs correspond to 36% of HAIs outside of intensive care units  
34 [4,7,8], even though 72% of UTIs are currently non–device-associated [9].

35 UTIs are diverse in their clinical presentation, clinical course and management. UTIs can be  
36 characterized (i) by the site of infection (cystitis, pyelonephritis, prostatitis, or kidney abscess)  
37 [10], or (ii) by microbial aetiology [11]. Information on the burden of UTIs in acute  
38 healthcare settings is sparse. The aim of this study was to measure trends in the national  
39 incidence of UTIs in hospitalized adults in France over a 5-year cohort study, validating and  
40 using a hospital discharge algorithm as a new computerized tool for detection and  
41 surveillance.

42

43

## 44 MATERIALS & METHODS

### 45 *Data source*

46 A population-based cohort study was carried out from January 1<sup>st</sup> 2014, to December 31<sup>st</sup>  
47 2018, using national data collected from French Diagnosis-related groups (F-DRG = PMSI,  
48 *Programme de Médicalisation des Systèmes d'Information*). This national medico-  
49 administrative database is based on the mandatory notification of each hospital stay for all  
50 French public or private healthcare settings. All hospitalization information is coded in a  
51 hospital stay summary using the International Classification of Diseases tenth revision (ICD-  
52 10) and the current French procedure terminology. As all patients are assigned a unique

53 identification number, the same individual can be followed over time, allowing robust  
54 epidemiological studies at the national level [12–15].

### 55 *Study population and case definition*

56 The study population included all adult patients ( $\geq 18$  years old) hospitalized with UTIs in  
57 France during the study period. UTIs in children were excluded due to their different clinical  
58 presentation and care pathway. Outpatient stays ( $< 24$  hours) were excluded. A  
59 multidisciplinary team of infectious disease (ID) specialists, urologists and epidemiologists  
60 built an algorithm according to the coding summary and the current French procedure  
61 terminology featuring the discharge summary, to select patients with UTIs over the 5-year  
62 period. The case definition was based on the presence of at least one specific ICD-10  
63 diagnostic code for UTI as a main diagnosis or secondary diagnosis in their summary  
64 extracted from the national PMSI database (case definition - Appendix). Device-associated  
65 UTIs were defined by the presence of specific ICD-10 diagnostic code for infection due to a  
66 prosthesis, implant or urinary tract graft. A sensitivity analysis was performed on three  
67 different algorithms, based on the different codes and their position in the summary. Finally,  
68 the most robust case definition was selected to be assessed and validated.

### 69 *Validation of the case definition*

70 We first validated the algorithm using a sample of hospital charts from 6 public and private  
71 volunteer hospitals. For each hospital, 200 medical records were selected: 100 corresponding  
72 to the UTI detection algorithm and 100 randomly selected among hospitalizations without any  
73 UTI coded in the same hospital and units. This selection was performed via an automated  
74 extraction module. All available data, including clinical, bacteriological data and the various  
75 radiological examinations were used to check the UTI diagnosis. Among the 1,200 medical  
76 charts selected, 78 could not be analyzed (no computer files, no hospital record, etc.) giving a  
77 validation sample of 1,122 medical charts reviewed. The medical chart review was performed

78 by an ID specialist or a urologic in charge of the patient, reading the complete medical report  
79 and blinded to the hospital discharge database (HDD) case definition criteria. Sensitivity (Se),  
80 specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were  
81 calculated with their 95% confidence intervals (CIs). Eventually, 401 of 415 HDD cases were  
82 true positives giving a PPV of 70.4%  $_{95\%CI}$  [66.6%-74.1%]; with 538 true negatives, the NPV  
83 was 97.5% [96.2%-98.8%]. Case definition sensitivity was 95.1% [95.1% – 98.1%] and  
84 specificity was 76.1% [72.6%-79.6%].

#### 85 *Statistical analyses*

86 We estimated the overall incidence of UTIs and by type stratified by age and sex, as the  
87 number of hospital admissions attributed to UTIs divided by the total national population  
88 recorded during the last French census as reported by the National Institute of Statistics and  
89 Economic Studies. The yearly in-hospital incidence of UTI was calculated as the number of  
90 hospital admissions attributed to UTIs divided by the French population during the same  
91 study year. The hospital mortality rate for UTI was calculated as the number of deaths that  
92 occurred among hospitalized UTI patients.

93 Results were analyzed according to the type of UTI (kidney abscess, prostatitis,  
94 pyelonephritis, cystitis and other urinary infections, corresponding to unspecified code N390).  
95 We described the characteristics of the patient (demographics: age, sex, type of ITUs, device-  
96 associated infections using the specific code T835, microbiology, mortality, and lethality),  
97 and the UTI length of stay. As patients could have multiple hospitalizations over the study  
98 period, we defined a single episode as all hospital stays occurring within four consecutive  
99 weeks; if separated by more than 4 weeks, they were considered as different infection  
100 episodes. The re-hospitalization rate was defined as the number of patients readmitted to the  
101 hospital over four weeks after the first admission for the same pathology divided by the total  
102 number of hospitalizations for UTIs.

103 Continuous variables were expressed as mean  $\pm$  standard deviation (SD), while qualitative  
104 variables were expressed as frequency and percent; Statistical analyses were performed using  
105 SAS version 9.1 for Microsoft Windows (SAS Institute, Cary, NC).

106 *Ethical approval*

107 Our study involved the reuse of previously recorded and anonymized data. The study fell  
108 within the scope of the French Reference Methodology MR-005 (number #0615171019  
109 subscribed by Tours University Hospital), which requires neither information nor non-  
110 opposition of the included individuals. Access to anonymous file in the DRG databases was  
111 approved by the French National Commission for Data Protection and Liberties. No consent  
112 was needed from the patients involved in this retrospective study.



## 113 RESULTS

114 From 2014 to 2018, 2,279,604 UTI-related hospitalizations occurred in France; 1,125,056  
115 cases of cystitis and other urinary tract infections, 230,134 cases of prostatitis, 414,906 cases  
116 of pyelonephritis, 8,893 kidney abscesses and 22,634 device-associated infections (Figure 1).  
117 In 2018, of the 10.7 million hospital stays in France, 474,642 met the UTI case definition,  
118 giving a yearly frequency of 4.4% of overall French hospitalizations. The distribution of  
119 UTIs was: 63.5% cystitis and other urinary infections, prostatitis 12.4%, pyelonephritis  
120 23.6% and kidney abscess 0.5%. Overall, 1.2% of UTIs were device-associated.

121 The yearly UTI incidence rate was 900/100,000 inhabitants, with a stable trend over time in  
122 females (1,070/100,000 females) and a slight increase in males (712/100,000) (Figure 2).

123 Cases of cystitis were the more prevalent UTIs (yearly incidence of 5,533/100,000), followed  
124 by pyelonephritis (2,060/100,000), especially in females, whereas prostatitis was retrieved in  
125 males (incidence 1,163/100,000) (Figure 3). The results showed that 1,801,623 distinct  
126 patients were hospitalized with a UTI over the study period. Patient demographics and  
127 hospitalization characteristics are described in Table 1.

128 Excluding prostatitis, all types of UTIs occurred mainly in females (overall SR M/F=0.59).  
129 The proportions of women with cystitis, pyelonephritis and renal abscess were 69.3%, 78.3%  
130 and 66.9%, respectively. UTIs predominantly affected the elderly  $\geq 70$ , especially for cystitis  
131 (70.2%) and prostatitis (62.3%) (Figure 4). Pyelonephritis affected younger people between  
132 18 and 39 years (17.3%). Renal abscesses occurred in patients of all ages. Among the  
133 2,279,604 UTI hospitalizations, 5.3% were admitted to the intensive care unit. Renal abscess  
134 were reported in 11,191 hospital stays, representing the longer mean length of stay (14.5  
135 days), and more frequently associated with an admission to the intensive care unit (8.3%)  
136 (Table 1). A large majority of patients had at least one comorbid condition. The most

137 frequent were metabolic diseases (diabetes mellitus and obesity; 12.0%) and cancer and  
138 chemotherapy (11.3%).

139 Device-associated infections represented 22,634 patients over the 5-year period, mainly in  
140 older men (55.3%). The average length of stay was 19.2 days, and the number of admissions  
141 to the intensive care unit was 11.5% of hospitalizations with device-associated infections. The  
142 hospital mortality rate during hospitalization with UTIs in France was 48/100,000 inhabitants  
143 per year. Regarding the case fatality, 7.2% of patients with UTIs died during their  
144 hospitalization (4.1% during a hospital stay with kidney abscess, 7.6% for cystitis and other  
145 infections, 5% for prostatitis and 5% for pyelonephritis). For device-associated infections,  
146 mortality increased to 9.5%.

147 The most common microorganisms coded in the hospital stays for UTIs were *Escherichia coli*  
148 (45.3% for kidney abscess, 50% for cystitis, 42.5% for prostatitis, and 55.5% for  
149 pyelonephritis), *Klebsiella pneumoniae*, *Proteus* spp., *Staphylococcus* spp., and *Enterococcus*  
150 *faecalis* (Table 2).

151

## 152 **DISCUSSION**

153 Urinary tract infection is a common disease, though epidemiological knowledge remains  
154 sparse. This study is the first estimation to date of incidence of UTI-related hospitalizations in  
155 France, using a computerized tool via an HDD algorithm. The yearly UTI incidence rate was  
156 estimated at 900/100,000 inhabitants, higher in females and older patients, stable over the 5-  
157 year period. The mortality and case fatality rates within UTI-related hospital stays were non-  
158 negligible, even though patients could have died with a UTI occurring during a hospital stay  
159 for management of another disease, representing a key point to compare with the international  
160 literature in the near future. Of note, we focused on adult inpatients, due to the differences  
161 from children and from outpatient UTIs.

162 Using the HDD databases, the incidence of UTI-related hospitalizations in France was  
163 computerized after validation of the HDD algorithm following the review of more than 1,100  
164 medical charts. Performance parameters were estimated at a large multicentric scale, in  
165 several centres to take into account the possible coding variability over a large panel of acute  
166 care settings over the whole country. Indeed, hospital stays are coded by various healthcare  
167 practitioners, giving a coding variation depending on the coder profile [12,13]. While the PPV  
168 was not as high as expected (70%), sensitivity was over 95%. This could be explained by the  
169 use of imprecise codes or by the fact that hospitalized cases of cystitis are difficult to define  
170 clinically (true infection, soiling, catheter-associated inflammation, etc.). Indeed, classifying  
171 asymptomatic bacteriuria versus cystitis is already difficult in clinical practice, and hence  
172 probably even harder to be clinically characterized by an algorithm. Indeed, these situations  
173 rely on each physician's assessment, and the scope of the diagnosis varies widely according to  
174 the healthcare practitioner and their specialty: a surgeon will not have the same judgment as  
175 an ID specialist for instance [12,16,17]. Hence, an algorithm could not replace the clinical  
176 assessment, especially when the situation is clinically complex [12,16]. We hypothesized that

177 bacteriuria occurred without any flank pain or fever and as the code for asymptomatic  
178 bacteriuria does not exist, cystitis was often chosen. The high number of cases of cystitis  
179 found in men in our study could probably represent simple male urinary colonization in a non-  
180 negligible proportion of cases.

181 Our study highlights the burden of UTIs in France, with almost 500,000 hospital stays  
182 meeting the UTI case definition in France in 2018 and remaining stable over time. Simmering  
183 *et al.* showed a 52% increase in incidence between 1998 and 2011[18]. In our study, 1.2%  
184 were device-associated UTIs, corresponding to 22,634 patients over the 5-year period. A large  
185 proportion of patients had at least one medical condition, such as metabolic disease or cancer  
186 and chemotherapy, suggesting that the prevention of UTIs must be integrated into a global  
187 management of hospitalized patients. Infections associated with implanted devices were more  
188 likely to occur in an elderly population, which may explain the length of hospitalization, or  
189 patients staying in hospital for long periods of time are more likely to suffer urinary tract  
190 infections. Prevention must therefore take into account all the modifiable factors found. In a  
191 recent study, Strassle *et al.* showed that the following conditions were associated with an  
192 increased risk of non–device-associated urinary tract infection: peptic ulcer disease (HR, 2.25;  
193 95% CI, 1.04–4.86), immunosuppression (HR, 1.48; 95% CI, 1.15–1.91), trauma admissions  
194 (HR, 1.36; 95% CI, 1.02–1.81), total parenteral nutrition (HR, 1.99; 95% CI, 1.35–2.94) and  
195 opioid use (HR, 1.62; 95% CI, 1.10–2.32) [19]. Further analyses targeting a specific type of  
196 UTI would need to be performed in order to study the French risk factors. In line with other  
197 studies, the main UTI causative organisms were found to be conventional urological  
198 microorganisms, in particular *E. coli* [20].

199 This study had several limitations. Firstly, cystitis and other imprecise UTIs ranked first,  
200 representing a wide and varied category of symptoms and preventing further analyses; a next  
201 step will be to focus on the more specific categories of UTIs represented by prostatitis, acute

202 pyelonephritis or kidney abscess. In that spectrum, the performance parameters of the UTI  
203 algorithm varied widely according to the HDD definition considered, especially in terms of  
204 PPV [12,21]. As the HDD is primarily a financial tool, the reported codes could be mainly  
205 financially valued codes, while those more informative than financial, such as contextual  
206 codes, are not[12,22]. Another explanation could be the lack of coding training of the  
207 clinicians in charge of coding the hospital stays, using incorrect or imprecise coding, or the  
208 fact that hospitalized cystitis are difficult to define clinically (true infection, soiling, catheter-  
209 associated inflammation, etc.), though the coding along with the medical chart review are not  
210 accurate and reliable [12,16]. Cystitis was the most frequent UTI managed during  
211 hospitalization. Even though no cases of cystitis may have been hospitalized, the code  
212 “cystitis” was found in hospitalized patients. The detection algorithm, however, detected  
213 almost all patients (96.6% sensitivity). The method used in this study did not allow a detailed  
214 examination of microbiological results. Thus we were unable to ascertain antibiotic  
215 susceptibility data as part of this first step of national surveillance.

216

217 This study design and validation process did, however, open up prospects for new specific  
218 studies: further investigations may focus on specific urological infections such as prostatitis  
219 and acute pyelonephritis, studying patient profiles, risk factors and types of stay. Analysis of  
220 the factors associated with a fatal outcome or a type of surgery would be possible. **Moreover,**  
221 **healthcare-associated UTIs could be analyzed separately, and focusing on one type of UTIs**  
222 **could allow accurate comparisons with the European Center of Diseases Control prevalence**  
223 **points [4,8]. Indeed, reliable and accurate studies using automated and validated tools do**  
224 **already exist in the field of HAI, such as surgical site infections in orthopedics [12,15,21].**  
225 This innovative algorithm could also be used to perform accurate medico-economic analyses.

226 Using this validated algorithm, epidemiological data adjusted for PPV have been presented  
227 for the first time to date and used to estimate the incidence of UTI-related hospitalizations in  
228 France. UTIs are very commonly associated with medical or surgical hospital stays,  
229 representing a substantial burden of care. Further analyses using the algorithm targeting one  
230 of the UTIs, however, should provide data for more informed goals-of-care discussions,  
231 especially regarding the procedures performed and their outcomes. This automated tool may  
232 help target UTI surveillance in acute care settings and prevention, especially in device-  
233 associated UTIs.

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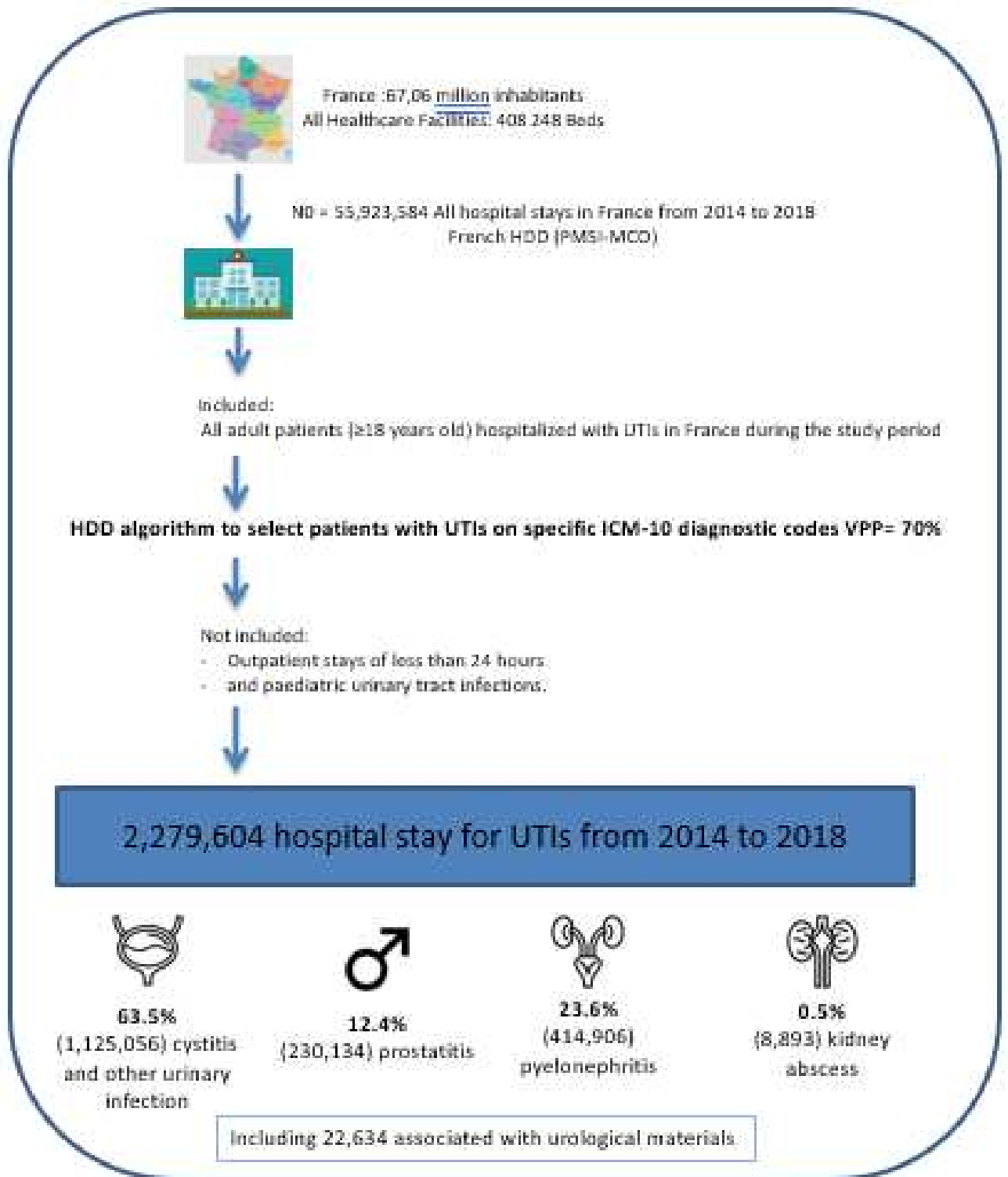
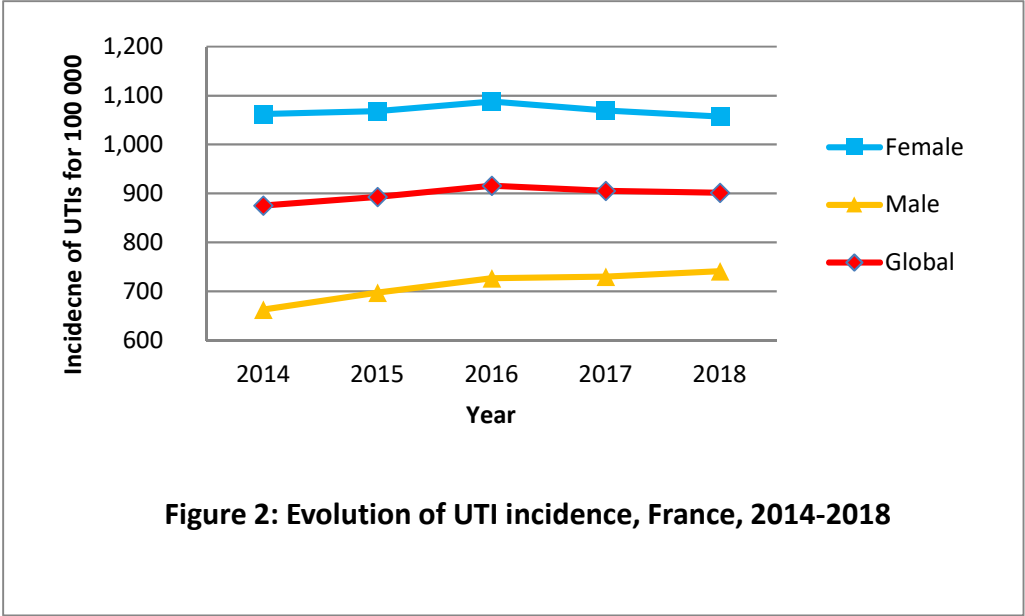
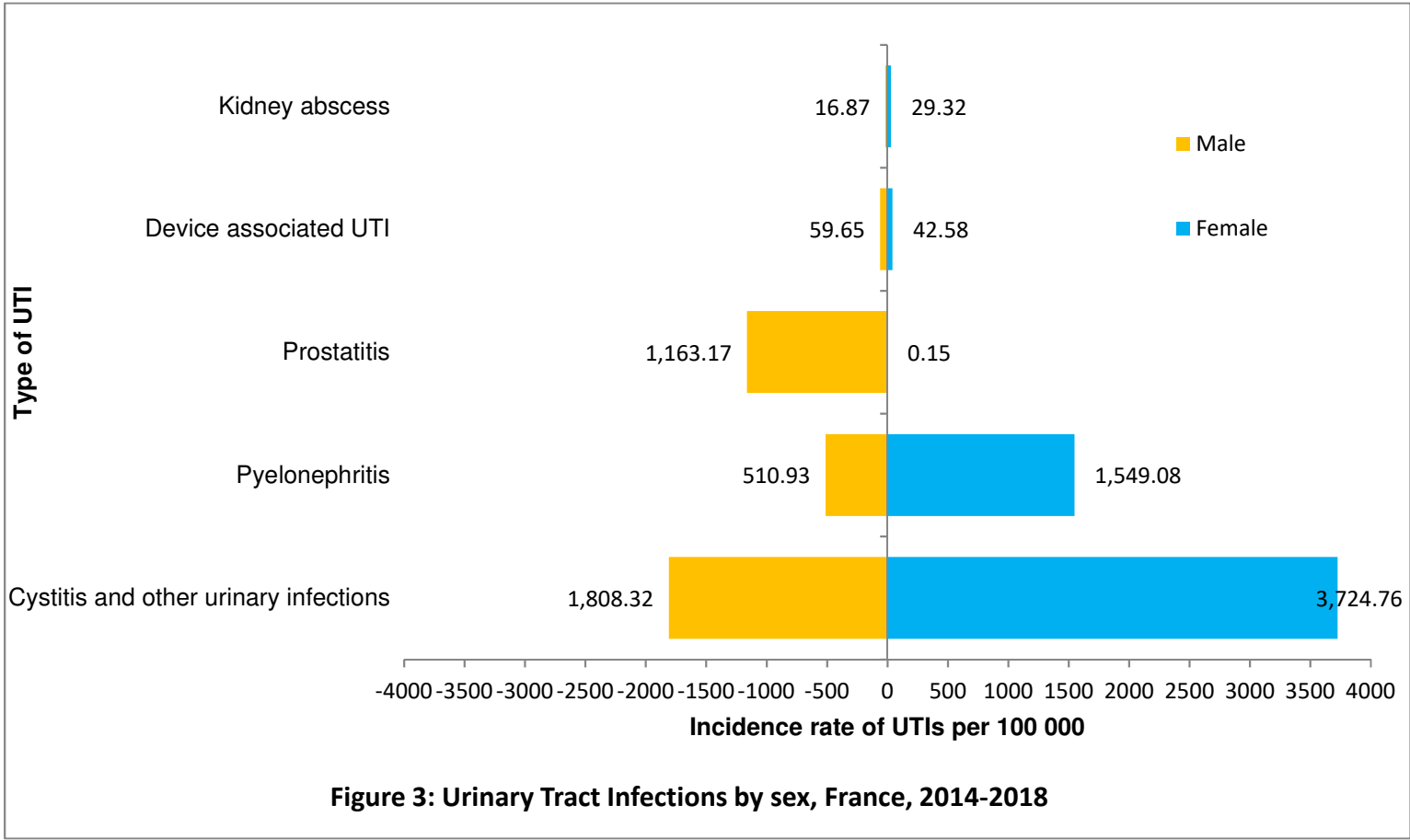


Figure 1: Selection algorithm of urinary tract infection (UTI) cases according to ICD-10, 2014-2018. ICD-10: International classification of Diseases, tenth Revision

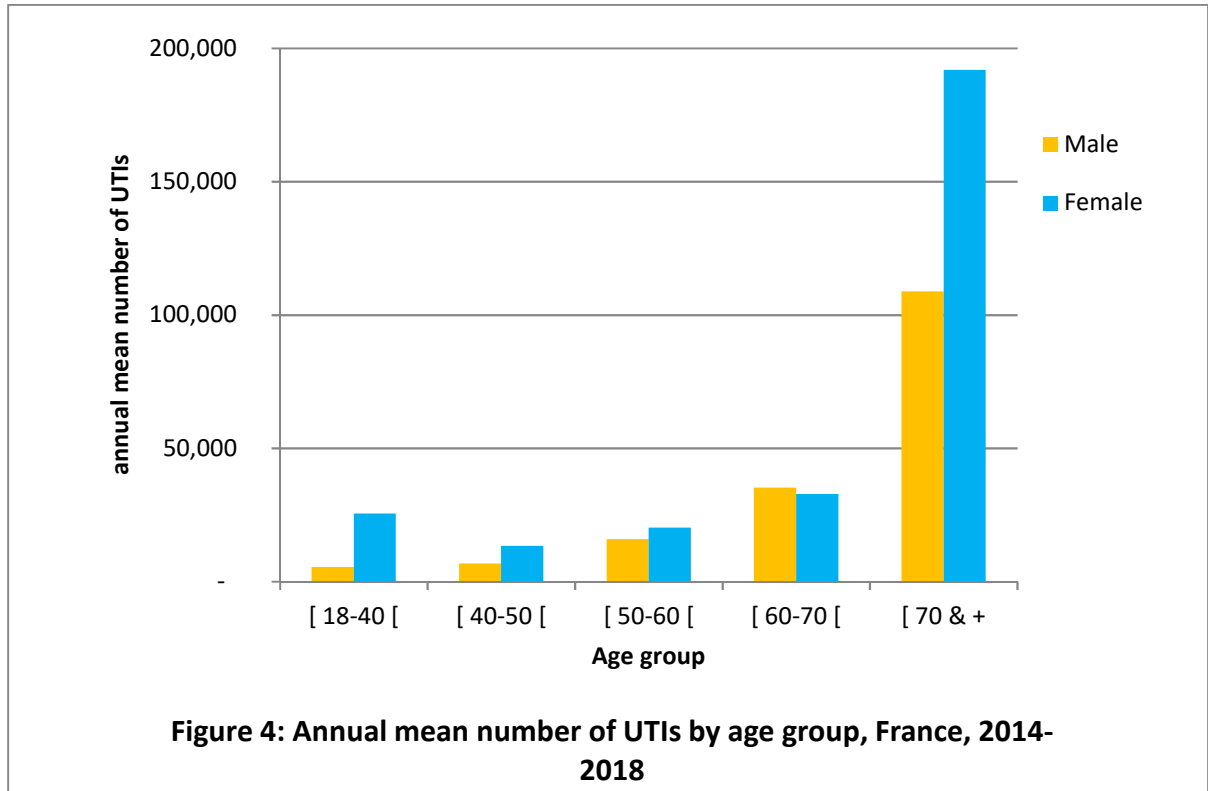


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