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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 1st 2014, to December 31st
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 (≥ 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 ≥ 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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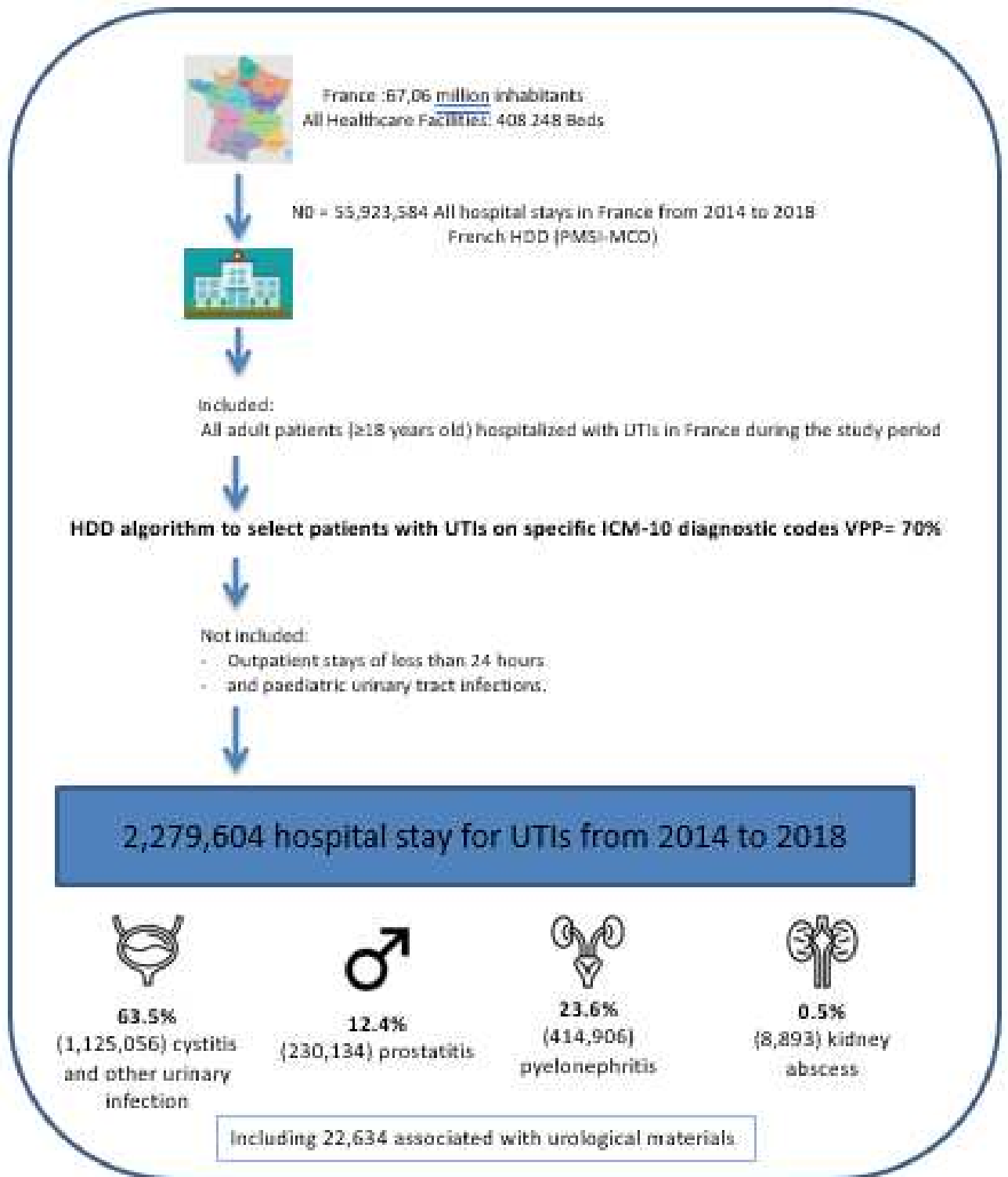
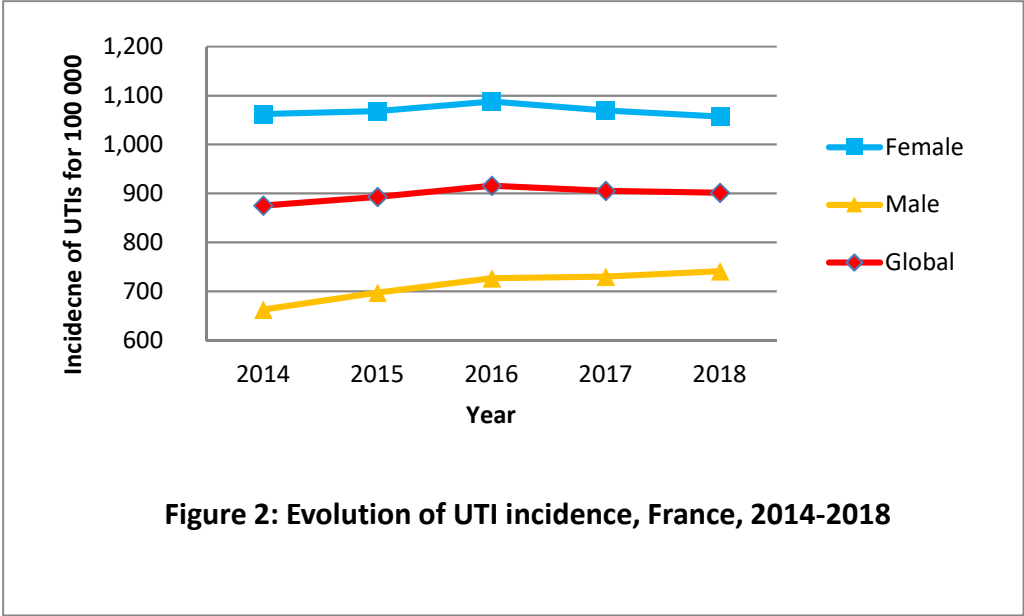
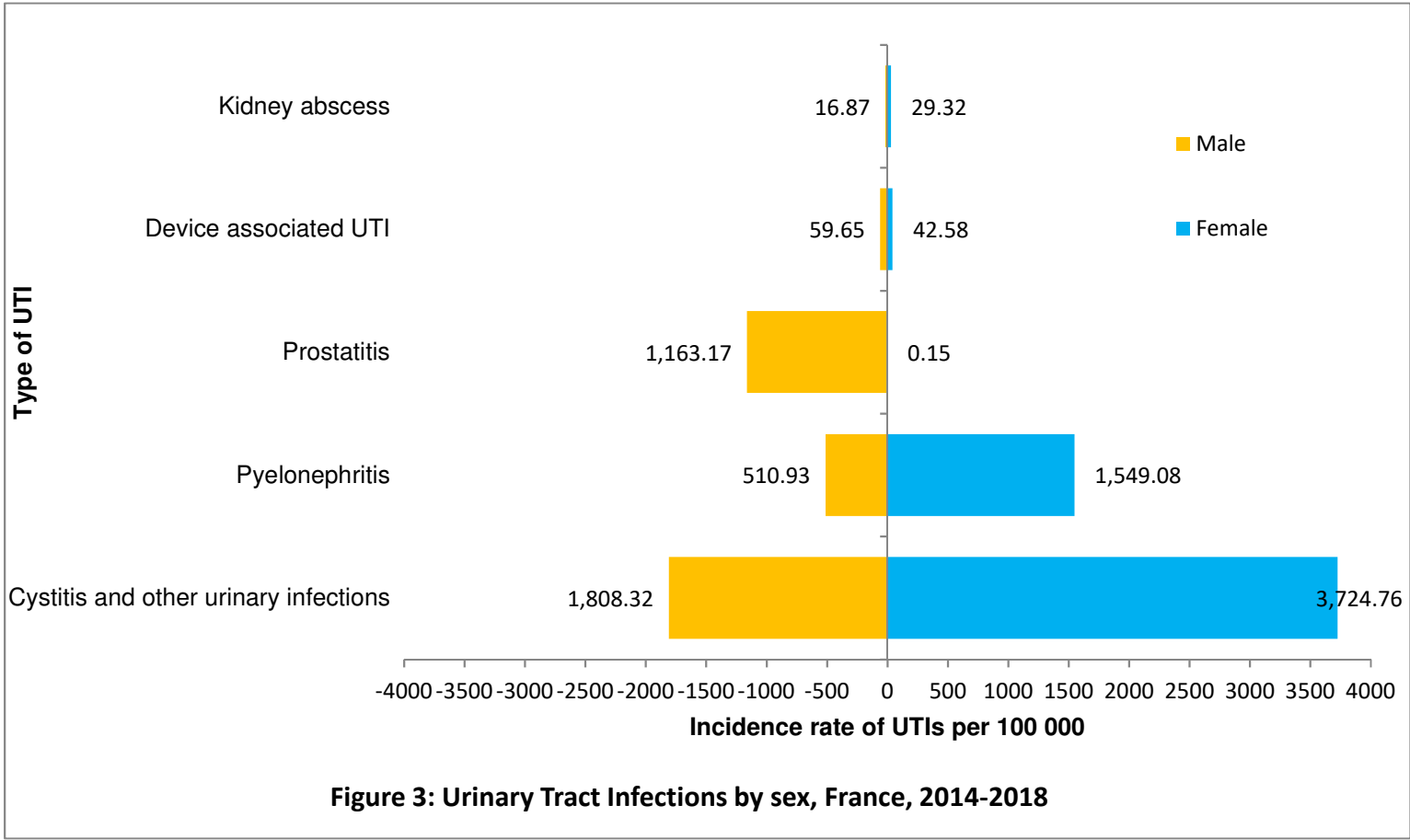


Figure 1: Selection algorithm of urinary tract infection (UTI) cases according to ICD-10, 2014-2018. ICD-10: International classification of Diseases, tenth Revision

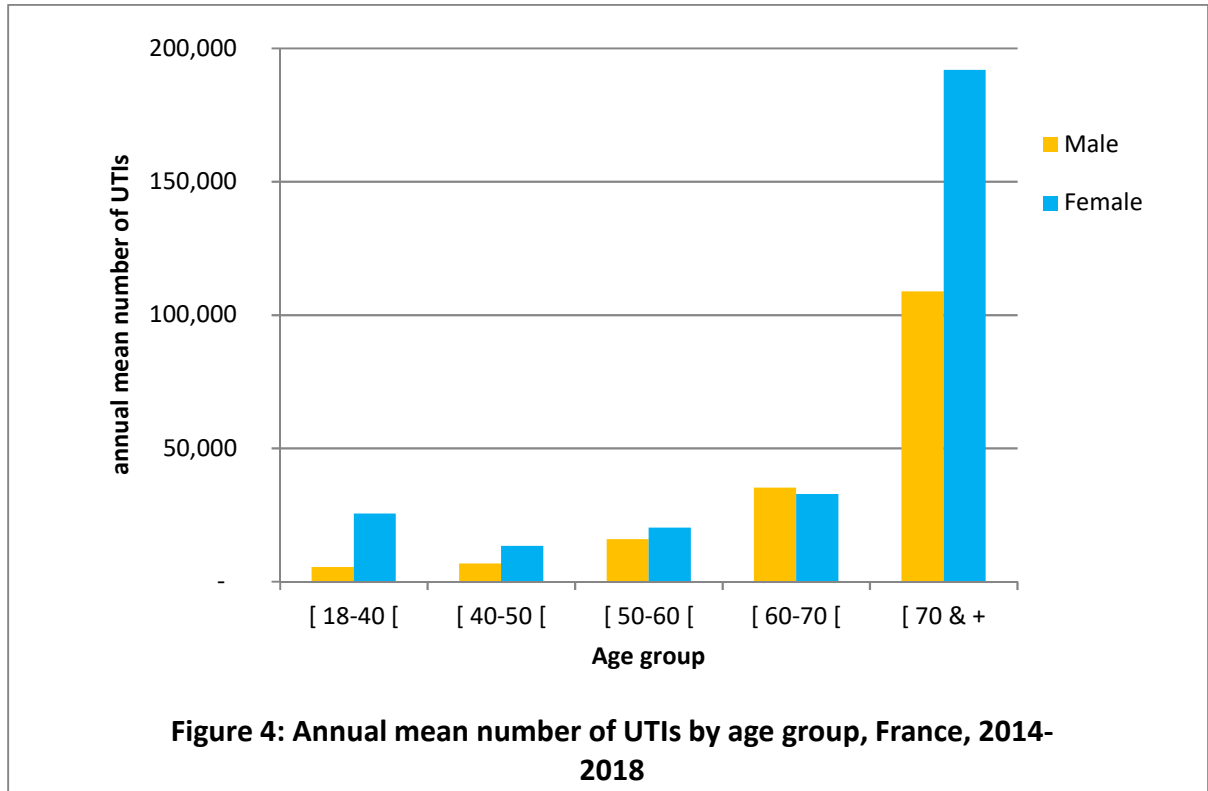


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