

Compared lethality rates of *Clostridium difficile* infections at the local, regional and national levels in France

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Dear Sir,

In December 2013, we reported a *Clostridium difficile* (CD) outbreak caused by the hyper-virulent ribotype 027 in the Provence-Alpes-Côte d'Azur (PACA) area, southeastern France [1]. Sixty-one patients were hospitalized from March 2013 to April 2014 in the four university hospitals of Marseille (Timone, Conception, North and Sainte-Marguerite) for CD 027 infection, with a mortality of 43% [2]. Following this outbreak, we developed an automated epidemiological surveillance system for CD cases.

Clostridium difficile is associated with an elevated lethality worldwide [2–4]. This lethality has gradually increased, exceeding that of many other bacterial species. In the present retrospective study, from January 2012 to December 2015, we compared the lethality rates of CD isolated in enterocolitis and the three most common bacterial pathogens isolated from any specimen (*Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*) in the university hospitals of Marseille, in the PACA area, France. The analysed data include the numbers of

patients infected by each of the four above-mentioned bacterial species and the associated lethality for patients over 65 years old. The data at the Marseille and regional levels were obtained using our epidemiological surveillance system whereas national data were obtained by the medical information service in Timone hospital (National Data obtained by *Convention de droit d'usage des données* PMSI, N° d'agrément 2015-111111-88-46). Duplicates were removed. For a given patient, only the first infection caused by a given microorganism was registered. We calculated the annual lethality rates (for the years 2012 to 2015) by dividing the number of deaths by the number of patients affected by the respective bacterial species by each year. All data collection and descriptive epidemiological analyses were performed in EXCEL.

Within Marseille university hospitals, we observed a stable lethality rate of *E. coli* urinary-tract infections between 2012 and 2015 (3.6%–5.6%, Table 1). For *E. coli* bacteraemia, the lethality increased from 2012 to 2014 (11.8%–18.3%, Table 1) and decreased in 2015 (10.7%). For *S. aureus* bacteraemia, the lethality decreased constantly from 22.9% in 2012 to 19.1% in 2014 (Table 1) then increased in 2015 (20.3%). For *P. aeruginosa* bacteraemia the lethality increased from 2012 (28.6%) to 2013 (31.7%), then decreased in 2014 (23.1%) and increased in 2015 (30.4%; Table 1). The CD lethality rate was lower in 2012 (10.6%) than in other years and reached a peak of 18.3% in 2013 (1.7-fold increase) and then decreased in 2014 (17.9%) and 2015 (12.4%).

At the PACA level, in 2012, 2013 and 2014, the lethality rate of CD infections was also lower than those of other pathogens (Table 1). At the country level, the highest lethality rate in 2012 and 2013 was that of *P. aeruginosa*, which was slightly higher than that of *C. difficile*.

When considering the evolution of lethality rates over time (Table 1), we observed that CD-related mortality had the greatest variation among bacterial pathogens in Marseille and PACA, which may be explained by the 2013–2014 CD 027 outbreak [2]. We also observed a great reduction in CD-related lethality in 2015, although non-significant (two-sided Pearson's chi-square test, $p = 0.09$). This reduction followed the implementation of systematic faecal microbiota transplantation for patients hospitalized in Marseille university hospitals with CD 027 infections [2].

Together, these results confirmed that CD is a major life-threatening bacterial pathogen, especially for the elderly, like *P. aeruginosa*. This confirms what was previously observed in our region [1,5] and also in northern France and other countries [6,7]. The rapid decrease in the lethality of CD infections in Marseille university hospitals (18.3% to 12.4%) and the PACA

TABLE 1. Number of deaths and lethality rate of infection caused by *Clostridium difficile* and the three most common bacterial pathogens in Marseille university Hospitals, Provence-Alpes-Côte d'Azur region and France from January 2012 to December 2015

Bacterial species	Marseille University Hospitals			PACA Region			France		
	Number ^a of patients	Number of deaths	Lethality rate	Number of patients	Number of deaths	Lethality rate	Number of patients	Number of deaths	Lethality rate
2012									
Global mortality ^b	30 890	1581	5.1	339 182	19 037	5.6	3 502 943	215 945	6.2
<i>Clostridium difficile</i>	47	5	10.6	566	86	15.2	7500	1288	17.2
<i>Escherichia coli</i> bacteraemia	136	16	11.8	1146	298	26.0	10 752	2575	23.9
<i>Escherichia coli</i> UTI	380	21	5.5	8 562	688	8.0	97 357	5891	6.1
<i>Staphylococcus aureus</i> bacteraemia	105	24	22.9	660	238	36.1	8131	2539	31.2
<i>Pseudomonas aeruginosa</i> bacteraemia	28	8	28.6	324	131	40.4	3028	1176	38.8
2013									
Global mortality ^b	31 723	1583	5.0	347 520	19 220	5.5	3 588 311	215 303	6.0
<i>Clostridium difficile</i>	142 [*]	26 [*]	18.3	710	142	20.0	8461	1511	17.9
<i>Escherichia coli</i> bacteraemia	133	22	16.5	1201	313	26.1	11 574	2923	25.3
<i>Escherichia coli</i> UTI	478	17	3.6	9023	642	7.1	103 746	6549	6.3
<i>Staphylococcus aureus</i> bacteraemia	104	21	20.2	687	222	32.3	7988	2669	33.4
<i>Pseudomonas aeruginosa</i> bacteraemia	41	13	31.7	333	122	36.6	3155	1168	37.0
2014									
Global mortality ^b	32 335	1559	4.8	356 108	19 427	5.5	3 695 116	216 734	5.9
<i>Clostridium difficile</i>	148	27	18.2	914	175	19.1	8883	1580	17.8
<i>Escherichia coli</i> bacteraemia	197	36	18.3	1365	310	22.7	13 069	3095	23.7
<i>Escherichia coli</i> UTI	534	29	5.4	9679	733	7.6	110 565	6939	6.3
<i>Staphylococcus aureus</i> bacteraemia	173	33	19.1	771	269	34.9	8350	2774	33.2
<i>Pseudomonas aeruginosa</i> bacteraemia	52	12	23.1	404	126	31.2	3325	1158	34.8
2015									
Global mortality ^b	32 555	1645	5.1	N/A	N/A	N/A	3 836 118	229 608	6.0
<i>Clostridium difficile</i>	153 [*]	19 [*]	12.4	N/A	N/A	N/A	11 336	1972	17.4
<i>Escherichia coli</i> bacteraemia	242	26	10.7	N/A	N/A	N/A	21 901	4152	19.0
<i>Escherichia coli</i> UTI	1 111	62	5.6	N/A	N/A	N/A	114 962	7507	6.5
<i>Staphylococcus aureus</i> bacteraemia	143	29	20.3	N/A	N/A	N/A	11 481	3608	31.4
<i>Pseudomonas aeruginosa</i> bacteraemia	56	17	30.4	N/A	N/A	N/A	4301	1483	34.5

UTI, urinary tract infection.
^{*}p 0.09, not significant.
^aNational Data obtained by: *Convention de droit d'usage des données PMSI, N° d'agrément 2015-111111-88-46.*
^bIncludes all causes of death, infectious or not.

region can be explained by the introduction of new treatment for all patients in PACA, the faecal microbiota transplantation [5].

Our study demonstrated that the CD-related lethality was similar in Marseille university hospitals and at the regional and national levels and was lower than those caused by *P. aeruginosa* or *S. aureus*. CD remains a major public health concern. Moreover, our results should encourage hospitals to extensively survey CD infections by the implementation of automatic monitoring systems, and also by developing rapid screening procedures to identify and isolate infected patients and healthy carriers upon hospitalization.

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