

Change in Distribution of *Clostridium difficile* NAP1 Strain in Patient Population in the North Suburbs of Chicago.

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Revised Abstract

Background: *Clostridium difficile* infection (CDI) is a significant healthcare concern worldwide, recognized as the most frequent etiologic agent of healthcare-associated infectious diarrhea in hospitalized adult patients. For the last few decades steady increase of CDI incidence along with higher morbidity and mortality has been associated with the emergence and rapid spread of NAP1 strain. NAP1 is implicated in many CDI outbreaks and possibly associated with increased morbidity and mortality. However, lately it has been noted that the prevalence of epidemic NAP1 strain is declining. The aim of this work was to determine any change in prevalence and distribution of NAP1 between 2013 and 2015.

Methods: NorthShore University HealthSystem is a 750 bed, 4-hospital system in the northern suburbs of Chicago. The Cepheid Xpert *C. difficile*/Epi test was used on all inpatient and outpatients with diarrheal stool to detect CDI. We compared the prevalence of NAP1 *C. difficile* strains during a 9 month period in 2013 (Period 1) to the same period in 2015 (Period 2). A nosocomial case was defined when disease was diagnosed ≥ 3 days hospital admission. Laboratory data was collected from the all patients by SoftLab reports. We analyzed differences using Fisher's exact test.

Results: In total, 8593 non duplicated stools were tested for *C. difficile*: 4180 in Period 1 and 4413 in Period 2. Compared data found the prevalence and incidence of NAP1 in inpatients were slightly lower in Period 2 (3% vs 2.1%, $p=0.01$ and 4% vs 2.5%, $p=0.02$, respectively). However, we did not observe significant differences in NAP1 distributions in nosocomial vs. non-nosocomial inpatients. The majority of NAP1 positive inpatients were not acquired nosocomially (75%). Interestingly, in Period 2 almost 60% of all NAP1 positives were detected in outpatients. The number of NAP1 positive outpatients was significantly increased compare to 2013 ($p=0.004$).

Conclusion: Our results indicate that distribution of *Clostridium difficile* NAP1 strain is shifting from hospital to the outpatient setting in our patient population. When determine trends in NAP1 disease it is important to consider both in- and outpatient CDI.

Introduction

Clostridium difficile infection (CDI) results from infection of the bowel by *Clostridium difficile*, a Gram-positive, spore-forming, obligate anaerobic bacterium. CDI clinical manifestation varies from self-limited diarrhea to life threatening colitis. For the last two decades CDI has re-emerged in healthcare facilities with nearly a 10-fold increase in mortality (1). It is presently diagnosed at the rate of several hundred thousand cases per year (2).

Currently, much health care-associated CDI in North America is attributed to the “hypervirulent” BI/NAP1/027 strain. Compared with non-epidemic strains, the characteristics of hypervirulent strains include increased transmissibility, toxin production, enhanced sporulation, greater toxin production, and increased resistance to antimicrobials and disinfectants (3). While *C. difficile* is increasingly resistant to a broad range of antibiotics, the NAP1 strain has recently acquired resistance to fluoroquinolones in addition to already prevalent clindamycin resistance (4).

Originally, CDI was associated with healthcare exposure and consumption of antimicrobials. However, currently the disease affects the population with virtually no contact with the healthcare setting. Also, lately it was noted that there are changes in the prevalence of epidemic NAP1 strain with declining trend (5).

The aim of this work was to determine the prevalence and distribution of NAP1 in the Chicagoland area.



Methods

NorthShore University HealthSystem is a 750 bed, 4-hospital system in the northern suburbs of Chicago. We compared the prevalence and incidence of NAP1 *C. difficile* strains during a 9 month period in 2013 (Period 1) to the same period in 2015 (Period 2) at all 4 hospitals. For the same 9 month period 2014 (Period 3) we collected the data only for 1 – 3 hospitals (in 2014 at hospital 4 NAP1 data was not collected due to the use of a non Epi test kit) and compared to Period 1 and 2 with adjusted data to the same three hospitals. All duplicated were removed. The Cepheid Xpert *C. difficile*/Epi test was used on all inpatient and outpatients with diarrheal stools to detect CDI. A nosocomial case was defined when disease was diagnosed at ≥ 3 days after hospital admission. Laboratory data was collected from the all patients by SoftLab reports. We analyzed differences using Fisher's exact test.

Results

Table 1. NAP1 results in stool specimens tested for CDI in 2013 – 2015

	All 4 hospitals					Three hospitals (1,2, and 3)						
	Total specimens tested for CDI, n	Total inpatient specimens, n	NAP1 positive				Total specimens tested for CDI, n	Total inpatient specimens, n	NAP1 positive			
			Outpatients, n	Inpatients, n	Nosocomial, %	Not nosocomial, %			Outpatients, n	Inpatients, n	Nosocomial, %	Not nosocomial, %
2015 (Apr - Dec)	4413	1657	60	44	25	75	3984	1368	49	36	27.8	72.2
2014 (Apr - Dec)							3786	1338	46	57	42.1	57.9
2013 (Apr - Dec)	4180	1919	51	82	24.4	75.6	3814	1534	48	68	23.5	76.5

Figure 1. 2013 – 2015: NAP1 Prevalence (%).

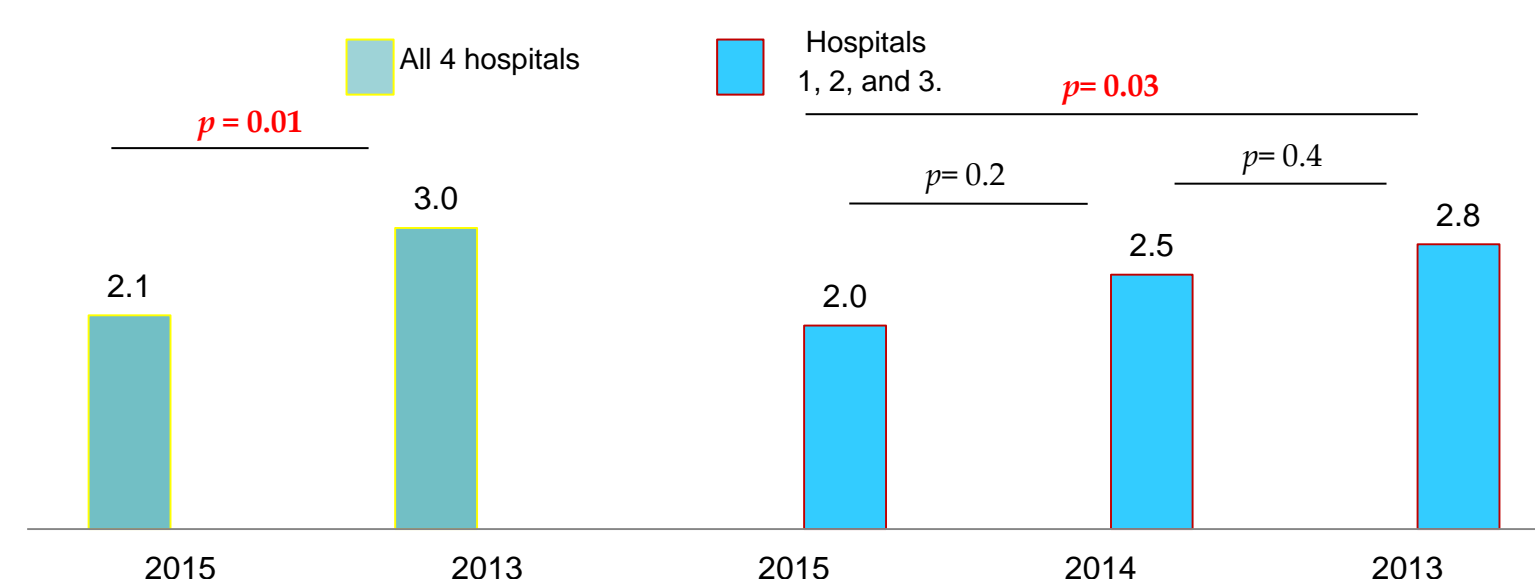


Figure 2. 2013 – 2015: NAP1 Incidence in inpatients (%).

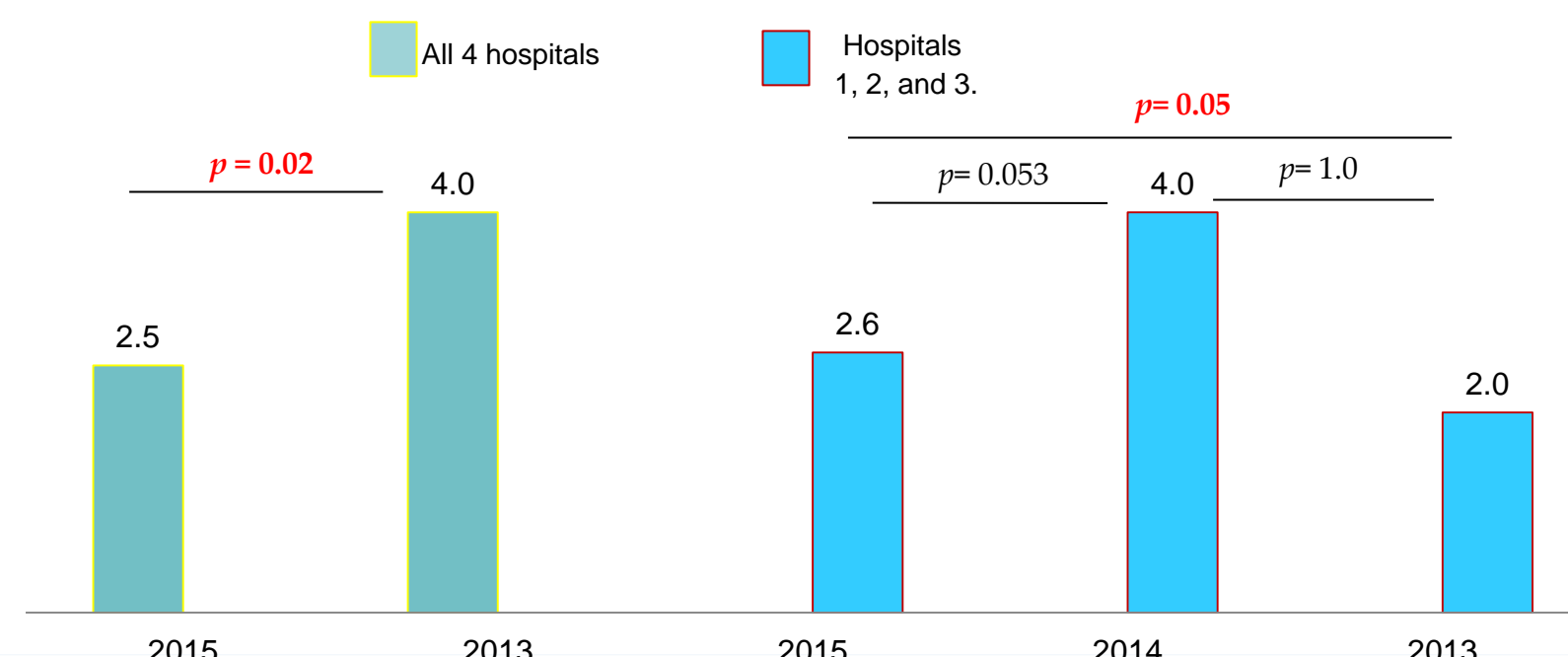


Figure 3. 2013 – 2015: NAP1 positive inpatients vs outpatients (n).

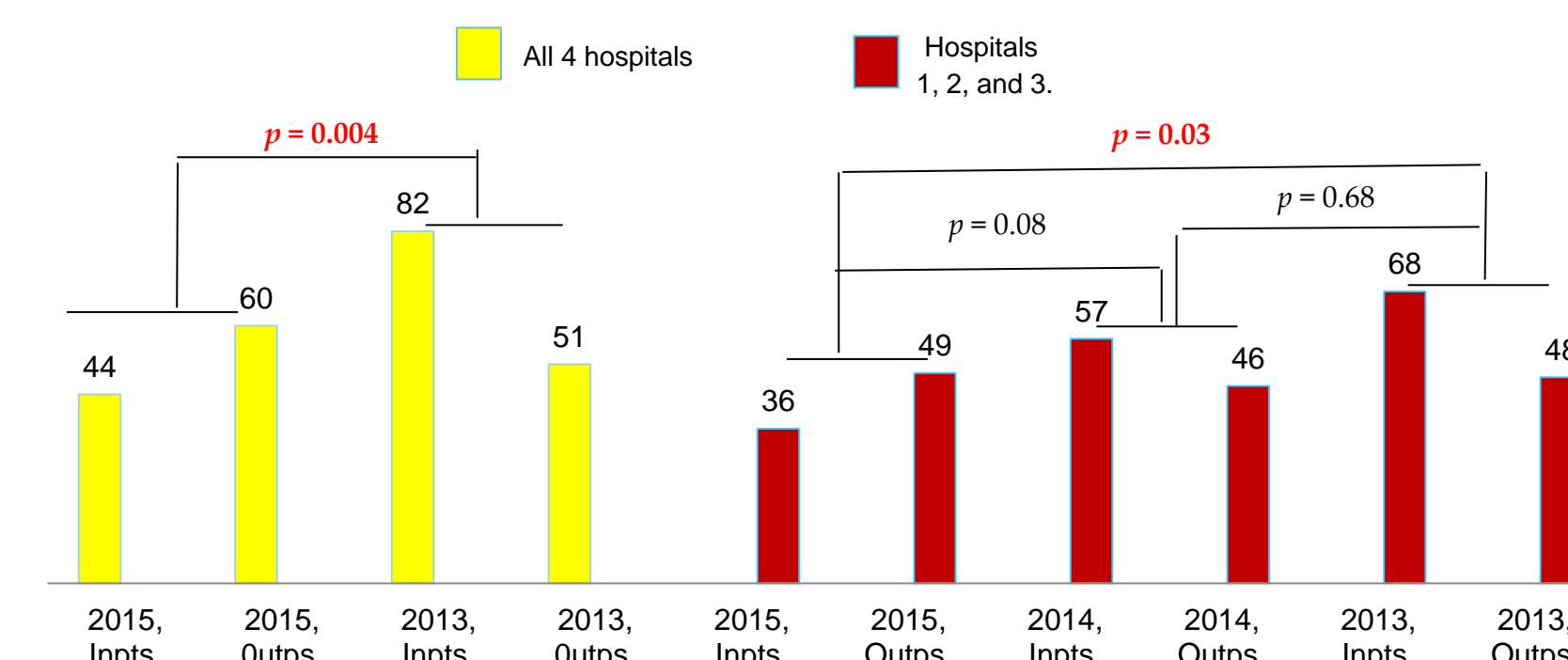
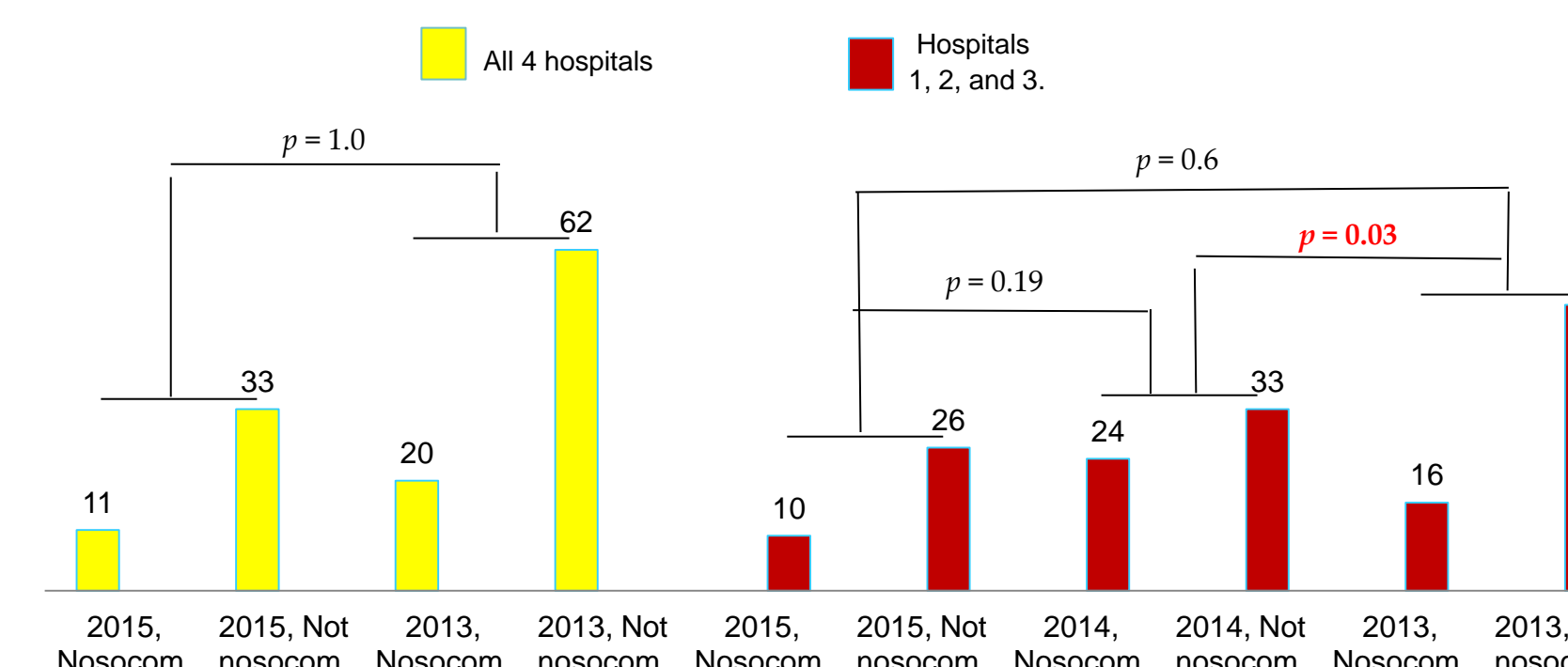


Figure 4. 2013 – 2015: Nosocomial vs not nosocomial in NAP1 positive inpatients (n).



Conclusions

- In 2015, the prevalence and inpatients incidence of *C. difficile* NAP1 strain were lower than in 2013.
- The distribution of *C. difficile* NAP1 strain in inpatient population in both settings (4 and 3 hospitals) was reduced to 2.7% in 2015 compare to 4.3% (2013 and 2014).
- Distribution of *Clostridium difficile* NAP1 strain is shifting from hospital to the outpatient setting.
- The number of NAP1 positive outpatients in 2015 was significantly increased compare to 2013 at all 4, and 3 hospitals ($p=0.004$ and $p=0.03$, respectively).
- In 2015, at all 4 and 3 hospitals, 58% of all NAP1 positives were detected in outpatients.
- The significant majority of NAP1 positive inpatients in 2015 and 2013 were not nosocomial (75%, $p<0.008$). However, pair-wise comparison of distribution of nosocomial and not nosocomial NAP1 strain in 2015, 2014, and 2013 did not show significant differences other than one observed between 2013 and 2014 ($p=0.03$).
- Possible explanation of drifting NAP1 strain into the community is rampant used of fluoroquinolones. However, further study is needed to determine this shift.

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