Incidence and Attributable Mortality of *Clostridioides difficile* Infection Among US Adults 18–64 Years of Age

Holly Yu,[1] Tamuno Alfred,[2] Jingying Zhou,[3] Jennifer Judy,[2]* Margaret A. Olsen[4]

[1]Pfizer Inc, Collegeville, PA, USA; [2]Pfizer Inc, New York, NY, USA; [3]Pfizer Inc, Peapack, NJ, USA; [4]Washington University School of Medicine, St. Louis, MO, USA

*Presenting author

For more information please contact:
Holly Yu
Pfizer Inc
500 Arcola Road
Collegeville, PA 19426, USA
Phone: (484) 865-3459
Email: Holly.Yu@pfizer.com

INTRODUCTION

- Life-threatening *Clostridioides (Clostridium) difficile* infection (CDI) affects nearly half a million individuals in the United States annually, with 0.7–8.9 deaths per 100,000 persons within 30 days of diagnosis.[1]
- Risk factors for CDI include advanced age and healthcare exposures that are common among the elderly, such as acute infections and hospitalization.[2-4]
- In 2019, the annual CDI incidence was reported at 58.3 per 100,000 persons for those 18–44 years of age and 93.4 per 100,000 for those 45–64 years of age compared with 257.3 per 100,000 population among those 65–70 years.[5]
  - In-hospital deaths ranged from 0.4% (among those 1–49 years of age) to 6% (among those 50–54 and ≥65 years of age).[5]
- Although the burden of CDI in individuals ≥65 years has been described,[6] studies on the burden of CDI for those <65 years of age are limited.

OBJECTIVE

- The goal of this study was to determine the annual incidence of CDI among patients 18–49 and 50–64 years of age, as well as mortality stratified by age group and hospitalization status among an adult population younger than 65 years enrolled in commercial health plans.

METHODS

- This retrospective cohort study used de-identified claims data from the Optum® Clinformatics® Data Mart, which includes complete medical and pharmacy claims information.
- CDI was defined by CDI diagnosis per International Classification of Diseases (ICD) 9th Revision diagnosis code 008.45 or ICD 10th Revision diagnosis code A04.7 or a combination of CDI diagnosis/testing with antibiotic prescription.
  - Cases occurring ≤60 days after prior CDI occurrences were excluded.
- Annual CDI incidence in 2012–2020 was evaluated among individuals who were aged 18–49 years and 50–64 years and enrolled in an Optum commercial plan by January 1 of the corresponding year.

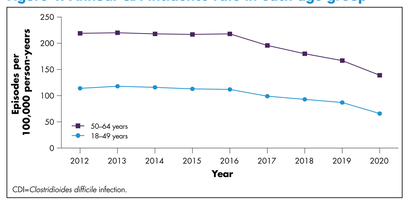
METHODS (continued)

  - Incidence rates were calculated as the number of CDI incident cases per 100,000 person-years of observation time.
- To assess CDI-attributable mortality, individuals with CDI (CDI+) diagnosed from 2016–2018 were matched 1:1 to non-CDI controls (CDI–) by the propensity score for CDI.
  - Propensity score matching was used to adjust for potential confounders (>60 variables) between groups for the mortality analysis. Logistic regression was used to develop the propensity score.
- All CDI+ and CDI– individuals were required to be continuously enrolled in the database for ≥12 months before the index date (ie, baseline period) through the earliest of 12 months follow-up or death.
  - Mortality was stratified by age group and hospitalization status.
- All study variables, including baseline and outcome measures, were analyzed descriptively.
- Standardized differences were calculated for each variable as the absolute difference in sample means divided by the estimate of the pooled standard deviation.

RESULTS

- CDI incidence was generally stable from 2012–2016 (217–220 and 112–118 episodes per 100,000 person-years in the 50–64- and 18–49-year age groups, respectively) before decreasing gradually between 2016 and 2020 to 139 episodes per 100,000 person-years (50–64-year age group) and to 66 episodes per 100,000 person-years (18–49-year age group; **Figure 1**).

Figure 1. Annual CDI incidence rate in each age group

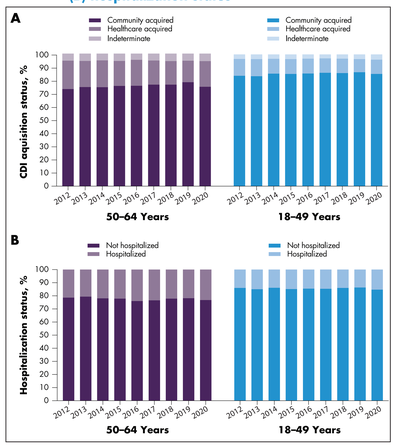


CDI=*Clostridioides difficile* infection.

  - During this period, most cases were community acquired and most patients were not hospitalized among both age groups (**Figure 2**).

RESULTS (continued)

Figure 2. Percentage of patients in each age group over time by (A) acquisition status and (B) hospitalization status



- Baseline demographics and clinical characteristics before and after propensity score matching are shown for the 50–64-year age group (**Table 1**) and 18–49-year age group (**Table 2**).
  - After matching, no meaningful differences were observed between the matched CDI+ and CDI– groups for both age groups.
- The CDI-attributable mortality rate at 12 months among the 50–64-year age group was higher than that in the 18–49-year age group.
- In the 50–64-year age group, CDI-attributable mortality increased through 12 months post-index, with larger attributable differences observed among patients who were hospitalized compared with those who were not hospitalized (**Figure 3**).
- In the 18–49-year age group, CDI-attributable mortality also increased through 12 months post-index, though to a lesser degree; larger attributable differences were observed among patients who were hospitalized compared with those who were not hospitalized (**Figure 4**; only data with n≥11 patients shown).

Table 1. Baseline Demographics and Clinical Characteristics of Patients in the 50–64-Year Age Group Before and After Propensity Score Matching*

	Before Matching			After Matching		
Characteristic	CDI+ n=6787	CDI– n=1,363,715	Std Diff	CDI+ n=6332	CDI– n=6332	Std Diff
Age, mean ± SD, y	57.2±4.2	56.6±4.1	0.2	57.2±4.1	57.2±4.1	<0.1
Age range, y, n (%)			0.2			0
50–54	1999 (29.5)	487,531 (35.8)		1859 (29.4)	1859 (29.4)	
55–59	2436 (35.9)	488,854 (35.8)		2293 (36.2)	2293 (36.2)	
60–64	2352 (34.7)	387,330 (28.4)		2180 (34.4)	2180 (34.4)	
Female, n (%)	4005 (59.0)	676,519 (49.6)	0.2	3749 (59.2)	3774 (59.6)	<0.1
Charlson Comorbidity Index score, mean ± SD	2.0±2.6	0.5±1.1	0.7	1.7±2.4	1.6±2.2	<0.1
Rx-risk score, mean ± SD	5.4±3.6	2.5±2.6	0.9	5.2±3.5	5.4±3.5	<0.1

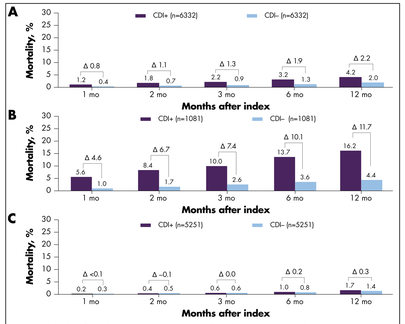
CDI+, *Clostridioides difficile* infection positive case; CDI–, *C difficile* infection negative control; Std diff, standardized difference. Std diff are presented as absolute values. Characteristics with absolute std diff ≤0.1 are considered acceptably balanced.
*A subset of >60 matching variables are listed here.

Table 2. Baseline Demographics and Clinical Characteristics of Patients in the 18–49-Year Age Group Before and After Propensity Score Matching*

	Before Matching			After Matching		
Characteristic	CDI+ n=7033	CDI– n=2,663,671	Std Diff	CDI+ n=6667	CDI– n=6667	Std Diff
Age, mean ± SD, y	36.1±9.2	34.6±9.2	0.2	36.2±9.1	36.1±9.2	<0.1
Age range, y, n (%)			0.2			0
18–29	1812 (25.8)	841,300 (31.6)		1686 (25.3)	1686 (25.3)	
30–39	2224 (31.6)	883,265 (33.2)		2124 (31.9)	2124 (31.9)	
40–49	2997 (42.6)	939,106 (35.3)		2857 (42.9)	2857 (42.9)	
Female, n (%)	4146 (59.0)	1,282,984 (48.2)	0.2	3946 (59.2)	4167 (62.5)	0.1
Charlson Comorbidity Index score, mean ± SD	0.9±1.7	0.2±0.6	0.5	0.8±1.6	0.7±1.5	<0.1
Rx-risk score, mean ± SD	3.8±3.1	1.2±1.8	1.0	3.6±3.0	3.6±3.0	<0.1

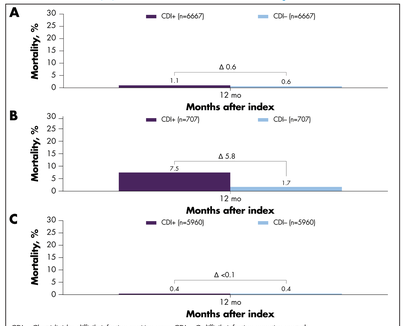
CDI+, *Clostridioides difficile* infection positive case; CDI–, *C difficile* infection negative control; Std diff, standardized difference. Std diff are presented as absolute values. Characteristics with absolute std diff ≤0.1 are considered acceptably balanced.
*A subset of >60 matching variables are listed here.

Figure 3. Mortality by CDI status in the 50–64-year age group by follow-up month for (A) the overall population, (B) those who were hospitalized, and (C) those who were not hospitalized



CDI+, *Clostridioides difficile* infection positive case; CDI–, *C difficile* infection negative control.
Δ is the CDI-attributable mortality as determined by the difference in mortality between CDI+ and CDI– groups.

Figure 4. Mortality by CDI status in the 18–49-year age group at 12 months for (A) the overall population, (B) those who were hospitalized, and (C) those who were not hospitalized*



CDI+, *Clostridioides difficile* infection positive case; CDI–, *C difficile* infection negative control.
Δ is the CDI-attributable mortality as determined by the difference in mortality between CDI+ and CDI– groups.
*Data are limited to the 12-month follow-up because only groups with n≥11 counts were included per licensing agreement with Optum.

CONCLUSIONS

- **As reported previously, both CDI incidence and attributable mortality among US individuals 18–64 years increased with age.[5]**
- **In both age groups, CDI cases treated in the hospital were associated with increased mortality.**
- **Identifying high-risk groups among non-elderly adults is warranted to develop better strategies to prevent CDI.**

REFERENCES

1. Lessa FC, et al. *N Engl J Med.* 2015;372:825-834.
2. Dubberke ER, et al. *PLoS One.* 2016;11:e0146822.
3. Olsen MA, et al. *BMC Infect Dis.* 2016;16:177.
4. Yu H, et al. *BMC Geriatr.* 2016;16:193.
5. US Centers for Disease Control and Prevention. Emerging Infections Program Healthcare-Associated Infections – Community Interface Report *Clostridioides difficile* infection, 2019. Available at: https://www.cdc.gov/hai/eip/Annual-CDI-Report-2019.html. Accessed September 8, 2022.
6. Yu H, et al. *Clin Infect Dis.* 2022:doi:10.1093/cid/ciac467.

ACKNOWLEDGMENTS

These studies were sponsored by Pfizer Inc. Medical writing support was provided by Erin P. O'Keefe, PhD, of ICON (Blue Bell, PA) and was funded by Pfizer.

DISCLOSURES

Holly Yu, Tamuno Alfred, Jingying Zhou, and Jennifer Judy are employees of Pfizer Inc, and may hold stock or stock options. Margaret A. Olsen reports grant funding and consulting work funded by Pfizer Inc.

Presented at IDWeek 2022; October 19–23, 2022; Washington, DC