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Concise Communication

Clostridioides difficile infection across the lifespan: Estimation using life tables

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Abstract

Using a life tables approach with 2011–2017 claims data, we calculated lifetime risks of *Clostridioides difficile* infection (CDI) beginning at age 18 years. The lifetime CDI risk rates were 32% in female patients insured by Medicaid, 10% in commercially insured male patients, and almost 40% in females with end-stage renal disease.

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Clostridioides difficile is the most commonly identified cause of healthcare-associated diarrhea and increasingly recognized as an important pathogen in the community. The Centers for Disease Control and Prevention calculated an incidence of 101 of 100,000 persons in 2020 based on the Emerging Infections Program surveillance sites.[1] CDI recurs in 20%–30% of CDI patients and is associated with increased risk for hospitalization, healthcare costs, and death.[2]

Few databases are available to comprehensively determine risk of CDI across the age spectrum due to the fragmented system of US health insurance. Medicare data can be used to identify CDI among the permanently disabled or elderly. Health insurance data for younger adults is problematic for longitudinal analysis due to frequent changes in insurers associated with changing employers or employment status. A better understanding of CDI burden across the lifespan is needed to inform prevention strategies that can be applied to not just the elderly but also to younger persons.

To determine the US lifetime risk of CDI from a population perspective, we created multiple-decrement life tables using claims data from a collection of primarily employer-sponsored, commercially insured, nonelderly adults, Medicaid data for nonelderly adults from a number of states, and Medicare data for elderly persons. We separately calculated lifetime risk for commercially insured persons with 3 common chronic conditions, diabetes, heart disease, and end-stage renal disease, associated with increased risk of CDI.[3,4]

Methods

We used data from the 2010–2017 Medicare Chronic Condition Warehouse 5% sample for persons aged 65 and older and from the Merative® MarketScan Commercial and Multi-State Medicaid Databases for persons aged 18–64 years, as described previously.[3]

The first episode of CDI per person from 2011 to 2017 was identified using *International Classification of Disease, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis code 008.45 and ICD-10-CM diagnosis codes A04.71 and A04.72, as described previously.[3] We also focused on subgroups with chronic conditions known to be at higher risk of CDI and with published life tables available to calculate probability of survival until specific ages, including heart disease (congestive heart failure, valvular disorder, or coronary artery disease), diabetes, and end-stage renal disease with dialysis (see Supplementary Material online for references). Persons with these conditions were identified as previously described based on coding in the patient's first year of health insurance enrollment (beginning with 2011).[3]

CDI incidence was calculated by dividing the number of patients with codes for CDI by the person years (PY) of observation individually for 2017 and overall from 2011 to 2017 by type of insurer (commercial and Medicaid for those aged <65 years, and Medicare only versus Medicare + Medicaid in the elderly), sex, and age group. The number of patients with codes for CDI was determined similarly for the 3 chronic conditions of interest from 2012 to 2017 in the commercially insured and Medicare populations, and CDI incidence rates calculated from 2012 to 2017 by condition and sex.

Lifetime risks of CDI were estimated using a multiple-decrement life tables approach, in which a hypothetical cohort faces competing risks of either developing CDI or of mortality. Mortality risks by age and sex for the general population were an average of 2011–2017 rates, obtained from US life tables.[5] For each of the analyses in our table, we assumed that the full cohort began a starting interval (aged 18, 40, 45, 50, 55, 60, or 65 years, depending on the table) alive and without CDI. During a 5-year interval afterward, a portion of the cohort either developed CDI or was deceased, leading to smaller numbers in subsequent intervals.

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Table 1. Lifetime Risks of *Clostridioides difficile* Infection, 2011–2017 MarketScan and Medicare Data, by Sex and Source of Health Insurance

Sex	Source of Data	Age 18+, %	Age 40+, %	Age 45+, %	Age 50+, %	Age 55+, %	Age 60+, %	Age 65+, %
Male	Commercial	9.75	9.58	9.55	9.55	9.59	9.66	9.38
Male	Medicaid	28.16	27.73	27.58	27.33	27.10	27.00	25.93
Female	Commercial	13.46	12.83	12.70	12.58	12.45	12.30	11.62
Female	Medicaid	32.38	31.76	31.46	31.09	30.55	29.84	28.10
Chronic condition[a]								
Male	Dialysis	33.54						
Male	Diabetes		15.71					
Male	Heart disease		19.85					
Female	Dialysis	39.44						
Female	Diabetes		19.98					
Female	Heart disease		28.60					

[a]For the chronic conditions, the MarketScan commercial data were used for those aged 18–64 years, and Medicare data for those aged 65 years and older (both Medicare only and dually insured with Medicaid).

Mortality risks for the diabetes, dialysis, and heart disease cohorts were based on estimates in the literature.

Results

The lifetime risks of CDI at different ages by sex and insurance type are shown in Table 1. The cumulative probability of having had at least 1 CDI episode increased steadily with age in both men and women, regardless of insurer type (Supplementary Tables 1–4 online). The lifetime CDI risk beginning at age 18 years was highest in females insured by Medicaid (32.4%) and lowest in commercially insured males (9.8%). Using only the 2017 data, the lifetime CDI risks were lower in all 4 groups, ranging from 26.1% and 23.2% in females and males, respectively, insured by Medicaid, to 13.2% and 9.5% in commercially insured females and males, respectively (Supplementary Table 5 online).

For commercially insured persons starting at age 18 years, the lifetime CDI risk calculated using the 2012–2017 data in female patients undergoing dialysis was 39.4% versus 33.5% for male patients. The lifetime CDI risk in persons with heart disease beginning at age 40 years in female patients was 28.6% versus 19.9% in male patients. In patients with diabetes, this risk was 20.0% in female patients and 15.7% in male patients.

Discussion

In this analysis of lifetime risk of at least 1 episode of CDI in adult patients, the risk of CDI was higher in female patients than in male patients and was higher in persons insured by Medicaid compared to those commercially insured. It is well known that the risk of CDI increases with age, such that the lifetime CDI risk ≥10% was due primarily to disease in older persons. We previously reported higher incidence in younger and elderly persons insured by Medicaid compared to those insured by commercial plans and Medicare only.[3] We hypothesize that persons insured by Medicaid have greater CDI risk due to higher prevalence of many important comorbidities, resulting in greater antibiotic exposure.[3] A number of common comorbidities (eg, diabetes, asthma, chronic kidney disease) are associated with higher infection risk,[6–8] and patients with these comorbidities are more likely to be treated with antibiotics, even in the absence of recognized infection.[9] Higher risk of CDI in female patients has also been reported by several investigators.[10,11] We calculated lifetime risk for 2 common chronic conditions (heart disease and diabetes), and end-stage kidney disease treated with dialysis, known to be associated with increased burden of CDI. The lifetime risk of CDI in dialysis patients was almost 40% in female patients and 34% in male patients. Although the estimated lifetime risk was lower in patients with heart disease and diabetes, the burden was still much higher than in the general adult population.

A limitation of our study was the determination of CDI incidence based on ICD-9/-10 diagnosis codes, which may result in inaccuracy due to imperfect coding. Since the incidence of CDI has decreased in the past several years, our lifetime risk based on the number of persons with CDI from 2011 to 2017 may be an overestimate. To account for this possible overestimation, we separately calculated the lifetime risk of CDI using only the 2017 data, which (as expected) was lower, particularly for persons insured by Medicaid.

The CDI incidence we calculated in the elderly was restricted to the Medicare fee-for-service population and may not be generalizable to those insured by Medicare Advantage plans. Finally, some portion of the mortality risks reflects unobserved cases of CDI, leading to a small degree of imprecision, though "clean" life tables without such deaths are not available.

The high lifetime risks we calculated for persons insured by Medicaid and for persons with heart disease and end-stage renal disease treated with dialysis suggests that a high index of suspicion of CDI is warranted when these persons present with diarrheal disease. The high lifetime risks in these individuals also support the need for more broad-based preventive measures in these individuals, particularly development of an effective *C. difficile* vaccine.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2024.2

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Competing interests. Margaret A. Olsen reports receipt of grant funding from Pfizer in the past 36 months and personal fees from Pfizer for consulting work. Dustin Stwalley reports stock ownership in Abbvie, Inc, and Bristol-Myers Squibb. Erik R. Dubberke reports receipt of grant funding from Pfizer, Synthetic Biologics, and Ferring in the past 36 months and personal fees from Ferring, Rebiotix, Summit, Merck, Pfizer, and Seres. Holly Yu is an employee of Pfizer, Inc. All other authors report no conflicts of interest relevant to this article.

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