Incidence of *Clostridioides difficile* infections among young and middle-aged adults: Veterans Health Administration

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**Abstract**

Objective: *Clostridioides difficile* infection (CDI) remains a significant public health concern, resulting in excess morbidity, mortality, and costs. Additional insight into the burden of CDI in adults aged <65 years is needed.

Design/Setting: A 6-year retrospective cohort study was conducted using data extracted from United States Veterans Health Administration electronic medical records.

Patients/Methods: Patients aged 18–64 years on January 1, 2011, were followed until incident CDI, death, loss-to-follow-up, or December 31, 2016. CDI was identified by a diagnosis code accompanied by metronidazole, vancomycin, or fidaxomicin therapy, or positive laboratory test. The clinical setting of CDI onset was defined according to 2017 SHEA-IDSA guidelines.

Results: Of 1,073,900 patients, 10,534 had a CDI during follow-up. The overall incidence rate was 177 CDIs per 100,000 person years, rising steadily from 164 per 100,000 person years in 2011 to 189 per 100,000 person years in 2016. Those with a CDI were slightly older (55 vs 51 years) and sicker, with a higher baseline Charlson comorbidity index score (1.4 vs 0.5) than those without an infection. Nearly half (48%) of all incident CDIs were community associated, and this proportion rose from 41% in 2011 to 56% in 2016.

Conclusions: The findings from this large retrospective study indicate that CDI incidence, driven primarily by increasing community-associated infection, is rising among young and middle-aged adult Veterans with high service-related disability. The increasing burden of community associated CDI in this vulnerable population warrants attention. Future studies quantifying the economic and societal burden of CDI will inform decisions surrounding prevention strategies.

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of younger age is more likely to be community associated, while for those that are older, HCF onset or HCF-associated is more likely.

Ample evidence has documented a rise in overall CDI incidence across the US since the start of the twenty-first century, a trend partially explained by both the emergence of hypervirulent strains and the increased use of highly sensitive methods for detection of C. diff, such as nucleic acid amplification testing. Whether these increases are also seen among those of younger age, and for community-associated CDI, warrants further investigation in the context of prevention and identification of opportunities for which to intervene.

More than 40% of CDI in the VHA patient population occurs among those aged <65 years. The objective of this study was to describe the epidemiology of CDI for the VHA population aged 18–64 years to better understand its occurrence among this vulnerable population whose disease burden may be a continuation of, or impacted by, experiences during active duty.

### Methods

A national, retrospective cohort study was conducted among patients aged 18–64 years as of January 1, 2011, with a VHA healthcare priority group rating of 1; at least 1 inpatient or 2 outpatient visits during calendar year 2011, and no evidence of CDI in the prior 90 days (October 1–December 31, 2010). As the single largest integrated healthcare system in the United States, the VHA of the Department of Veterans Affairs (VA) provides comprehensive services to veterans of the armed forces that can be followed across the care continuum, from the nonurgent outpatient clinic to the emergency department and subsequent hospitalization to postdischarge extended care in rehabilitation and nursing facilities. A higher healthcare priority group rating (groups 1–4) assigned at the time of enrollment indicates that the VHA will pay for a greater amount of an individual’s care; thus, patients with these ratings are more likely to use its services for most, if not all, of their needs, especially before becoming eligible for Centers for Medicare and Medicaid Services coverage.

Data for this study were extracted from the integrated databases of national clinical and administrative datasets of the VHA Corporate Data Warehouse (CDW) comprised of raw data delivered directly from VHA’s Veterans Health Information and Technology Architecture (Vista) unified electronic medical record (EMR) system. Standardization of the laboratory data was performed in accordance with previously established methods. Each patient is assigned a unique identification number that allows longitudinal follow-up.

The CDI episodes were identified by one of the following criteria: (1) a diagnosis code for CDI (ICD-9-CM 008.45 or ICD-10 A04.7) during an inpatient hospital stay or from an outpatient encounter accompanied by metronidazole, oral vancomycin, or fidaxomicin therapy within 14 days of diagnosis; or (2) the presence of toxin or toxin gene in a stool sample detected by enzyme immunoassay (EIA) or polymerase chain reaction (PCR). Duplicate episodes, those occurrences of either criteria within 14 days of one another as defined for the Centers for Disease Control and Prevention (CDC) laboratory identification definition, were excluded. Episodes were classified as HCF-onset; community-onset, HCF-associated; community-associated; or indeterminate according to Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) definition guidelines (Table 1).

The index date for the study cohort was defined as January 1, 2011. All patients were followed from the index date until the earliest of incident CDI, death, loss to follow-up, or December 31, 2016. Loss to follow-up was defined by a period of 2 consecutive years during which a patient was found to have no inpatient or outpatient visit and remained alive. Censoring occurred at the end of the calendar year during which she or he last had an encounter prior to the two-year period.

Demographic and clinical characteristics, including age, gender, race/ethnicity, region of care, healthcare utilization, Charlson comorbidity index score, and comorbidities (medical diagnoses), of patients with and without CDI were measured for the year prior to the index date (calendar year 2010) and compared using a standardized difference (SD) approach for which an absolute value > 10 may be indicative of a meaningful imbalance in a covariate between the 2 groups. The incidence of CDI was calculated as the number of patients with an incident, or first new, CDI episode acquired during the study period divided by the person-years of observation and reported for three age group stratifications of 18–34, 35–49, and 50–64 years to allow for additional granularity by age. To determine whether linear trends in the incidence of CDI, as well as the proportion of episodes identified as and incidence of community-associated CDI, differed significantly by age group over time, their interactions were included in the model. A significance level was set at 0.01 after Bonferroni adjustment to account for the overall and three age group stratifications.

### Table 1. Clostridioides difficile Infection Episode Definition per Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA) Classification

| Category                      | Definition                                                                                      |
|-------------------------------|-------------------------------------------------------------------------------------------------|
| Healthcare facility (HCF)-onset| Onset occurred during a hospitalization, or long-term care or skilled nursing facility stay, >48 h from admission |
| Community-onset, HCF-associated| Onset occurred in the community (outpatient setting) or during a hospitalization, or long-term care or skilled nursing facility stay, within 48 h of admission with a history of hospitalization, or long-term care or skilled nursing facility stay, during the previous 4 weeks |
| Community-associated          | Onset occurred in the community (outpatient setting) with no history of hospitalization, or long-term care or skilled nursing facility stay during the previous 12 weeks |
| Indeterminate                 | Onset occurred in the community (outpatient setting) or during a hospitalization, or long-term care or skilled nursing facility stay, within 48 hours of admission with a history of hospitalization, or long-term care or skilled nursing facility stay during the previous 4–12 weeks |
The study received institutional review board (IRB) approval from the Veteran’s IRB of Northern New England at the White River Junction VA Medical Center.

Results

Between 2011 and 2016, 1,073,900 patients met the study inclusion criteria (Fig. 1). Of these, 10,534 patients (1%) were identified as having a C. difficile infection (CDI). The proportion of episodes identified as outpatient onset rose across the study period, from 36% in 2011 to nearly 50% in 2016 (Table 2). Although the proportion of episodes identified by the presence of a positive test alone was relatively stable across the study period, the proportion with a positive test rose from 68% in 2011 to 84% in 2016.

The overall incidence rate was 177 CDIs per 100,000 person-years, steadily rising from 164 per 100,000 person-years in 2011 to 189 per 100,000 person-years in 2016. The proportion of episodes identified as outpatient onset rose across the study period, from 36% in 2011 to 49% in 2016 (Table 2). Although the proportion of episodes identified by the presence of a positive test alone was relatively stable across the study period, the proportion with a positive test rose from 68% in 2011 to 84% in 2016.

Table 2. *Clostridioides difficile* Infection Episode Characteristics

| Year | Total No. | Inpatient Onset No. | Outpatient Onset No. | Diagnosis + Treatment No. | Positive Test No. | \% No. | \% No. | \% No. | \% No. |
|------|-----------|---------------------|----------------------|--------------------------|------------------|--------|--------|--------|--------|
| All  | 10,534    | 6,092               | 4,442                | 1,603                    | 490              | 42.17  | 27.80  | 4.65   | 80.13  |
| 2011 | 1,752     | 1,115               | 637                  | 487                      | 81               | 63.64  | 36.36  | 4.62   | 67.58  |
| 2012 | 1,719     | 1,063               | 656                  | 314                      | 74               | 61.84  | 38.16  | 4.30   | 77.43  |
| 2013 | 1,807     | 1,081               | 726                  | 202                      | 93               | 59.82  | 40.18  | 5.15   | 83.67  |
| 2014 | 1,782     | 1,037               | 745                  | 211                      | 83               | 58.19  | 41.81  | 4.66   | 83.50  |
| 2015 | 1,722     | 916                 | 806                  | 181                      | 81               | 53.19  | 46.81  | 4.70   | 84.79  |
| 2016 | 1,752     | 880                 | 872                  | 208                      | 78               | 50.23  | 49.77  | 4.45   | 83.68  |

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The proportion of CDIs that were community-associated during the study period, nearly half (48%) were community-associated. The proportion of episodes identified as outpatient onset rose across the study period, from 36% in 2011 to 49% in 2016 (Table 2). Although the proportion of episodes identified by the presence of a positive test alone was relatively stable across the study period, the proportion with a positive test rose from 68% in 2011 to 84% in 2016.

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2016 (Fig. 3). Increases were observed for the 50–64 age group, from 35% to 52%, and 35–49 age group, from 56% to 64%, while a slight decrease was observed for the 18–34 age group, from 75% to 70%. The proportion of community-associated CDI decreased as age increased, from 72% of CDIs among patients aged 18–34 years to 44% of CDIs among those aged 50–64 years (Fig. 4).

In contrast, the proportion of all CDIs that were HCF-onset increased with age, from 11% in the youngest age group to 34% in the oldest.

Similarly, the incidence of community-associated CDI over time mirrored the rise of the proportion of this CDI type, up from 67 per 100,000 person years in 2011 to 105 per 100,000 person-years in 2016 (Fig. 5). Statistically significant increases were observed for all age groups, with the greatest increase occurring for the oldest age group (from 75 to 121 per 100,000 person years), as compared to the middle (from 51 to 85 per 100,000) and the youngest (from 60 to 71 per 100,000) age groups.

Except for the 2 younger age groups of the proportion of community-associated CDI, all linear slopes were statistically significant at the 0.01 level (18–34 years, $P = .72$ and 35–49 years $P = .06$) (Figure 3). In contrast, the only interaction term found to be statistically significant at the 0.01 level was of the proportion of community-associated CDI for the age group of 50–64 years, indicating its linear slope is significantly different from the other 2 age groups (Fig. 3).

Most patients were male (89%) and white (61%) (Table 3). Patients with a CDI were significantly older (mean, 55 vs 51 years; SD > 10), utilized more healthcare during the 6-year study period (mean, 7 vs 3 inpatient stays; SD > 10 and 117 vs 72 outpatient visits; SD > 10), and had a higher baseline Charlson comorbidity index score (mean, 1.4 vs 0.5; SD > 10) than those without a CDI.

**Discussion**

A substantial portion of CDI research efforts have focused on the incidence of and risk factors for infection among those that are 65 years and older as the disease burden disproportionately afflicts those of this age group. Undoubtedly an unintended consequence, this has resulted in a research gap among young and middle-aged adults that seems to have been acknowledged by the 2017 IDSA and SHEA clinical practice guideline update.1 Our study addresses this gap by estimating CDI incidence, and examining more closely this vulnerable population, among the VHA population aged 18–64 years using 6 years of rich, longitudinal VHA EMR data.

We observed a sustained increase in overall CDI incidence for this younger patient population between 2011 and 2016, a finding consistent with Reveles et al’s study that reported increasing CDI incidence for VHA enrollees from 2003 until 2013 and a subsequent decline in 2014.14 Several recent studies, including that by Reveles et al, that document a decline in HCF CDI include patients of any age, usually adults aged 18 years and older.13–15,22–25 As such, HCF CDI accounts for most episodes identified, ranging from 65% to 89% for those that defined both HCF and community-associated CDI. Declines in overall incidence, therefore, are not unexpected in populations for which the majority of episodes are HCF CDI, nor are comparisons between this study
and those published contradictory; rather, our findings suggest
trends in disease burden among those of younger age might differ
from those of older age.

Our results confirm that which is expected and perhaps inher-
ent to the infection definitions employed: with advancing age
comes deterioration of health and increasing healthcare contact,
implying that the proportion of HCF CDI is likely to be higher
for those of older age. We found that community-associated
CDI was more common than HCF-onset and HCF-associated
CDI among younger and middle-aged adults, and that the latter
increased with increasing age group as well. Similarly, Lessa
et al5 demonstrated differences in these proportions, for which

![Fig. 3. Proportion of incident (first new) Clostridioides difficile infection episodes classified as community-associated by year and age group. Bold values indicate P ≤ .01.](image1)

| Slope | Interaction |
|-------|-------------|
| 0.00  |             |
| 0.02  |             |
| 0.03  | 0.02        |
| 0.03  | 0.04        |

![Fig. 4. Incident (first new) Clostridioides difficile infection episodes by IDSA-SHEA classification and age group.](image2)
community-associated CDI was the predominant episode type among those aged 18–44 years, whereas HCF CDI accounted for 75% of CDIs among those ≥65 years.

In addition, we observed that the proportion of community-associated CDI increased during the study period, complementing the declines for HCF CDI noted by other recent studies. More striking, though, was the finding that while overall CDI incidence increased by 15% during our study period, the incidence of community-associated CDI rose by 20%. Again, the increase differs by age, however, and was more notable among the 2 older age groups in this younger population: we observed was a slight decline, marked by fluctuations over time, in the proportion for those aged 18–34 years. It is not clear whether this variation may be explained by limitations in the data source analyzed, as the low number of events, incompleteness of healthcare records, and undiagnosed infection might affect those in the youngest age group (<35 years) most. These findings are consistent with prior research by Reveles et al. that showed a gradual increase in the proportion of community-associated CDI for VHA patients aged 18 years and older from 2003 to 2014.15

Our results suggest that younger populations are not only at risk for community-associated CDI but also an important and perhaps expanding reservoir of C. diff. Although evidence of carriage rates by age is currently limited. Loo et al.16 found that the mean age of C. diff colonization on admission was lower than for those with an infection. Those aged 35–64 years are of interest given that such individuals are of working age, are raising children, and often have parents or other elder relatives to care for.27 Exposure to C. difficile from young children, as well as from frequent interactions with the healthcare system for both these children and aging parents/relatives, and the strain of caregiving itself, may augment the risk that an individual becomes colonized, with or without symptoms.1,8,27 This subsequently confers the risk of further transmission among and between individuals of all ages.

Most successful primary interventions to date have focused on protecting against symptomatic CDI and reducing transmission through enhanced antibiotic stewardship and infection prevention and control procedures in hospitals—the highest-risk setting. Durham et al.28 recently demonstrated that C. difficile transmission between healthcare settings and the community are interconnected, and the effects of community-based and hospital-based transmission on hospital-onset CDI are comparable.28 The findings from the present study and developments in our understanding of the interconnectedness of transmission underscore the need to account for such dynamics within and beyond healthcare settings when evaluating intervention and control strategies.29 Targeting C. diff in high-risk, high-contact settings, including community or ambulatory care facilities, such as through initiatives launched by CDC and United Hospital Fund to reduce outpatient antibiotic use, might serve as an effective approach to not only decrease primary CDI cases, but, perhaps just as importantly, reduce transmission of this pathogen to individuals with the greatest vulnerability and for whom outcomes tend to be more severe: those aged 65 years and older.30,31

Several potential limiting factors should be considered when interpreting the results of our study. As is common among retrospective cohort studies, misclassification bias may impact the design. Here, the definitions employed for episode identification have not been thoroughly validated and our data sources may be incomplete, such as for prescriptions filled outside VHA or laboratory results not recorded in structured data fields. Although diagnostic coding for CDI has been shown to have sufficient

Fig. 5. Incidence of community-associated Clostridioides difficile infection (CDI) per 100,000 person-years by year and age group. Bold values indicate P ≤ .01.
Table 3. Study Population Characteristics

| Variable                      | **Clostridioides difficile infection** |                       | **No Clostridioides difficile infection** |                       | St. Diff<sup>d</sup> |
|-------------------------------|---------------------------------------|------------------------|-------------------------------------------|------------------------|-----------------------|
|                               | No. (SD) | % (IQR) | No. (SD) | % (IQR) | No. (SD) | % (IQR) | No. (SD) | % (IQR) |
| Total Patients                | 10,534 | 0.98     | 1,063,366 | 99.02   |          |          |          |          |
| Age, ya<sup>a</sup>           | 55.4  | 10.2     | 60.0     | 51–62   | 51.1    | 12.3    | 55.0     | 43–62    | 37.6    |
| Gender Female                 | 1,065 | 10.11    | 115,489  | 10.86   |          |          |          |          |
| Male                          | 9,469 | 89.89    | 947,877  | 89.14   |          |          |          |          |
| Race                          |        |          |          |         |          |          |          |          |
| White                         | 7,104 | 67.44    | 645,436  | 60.70   |          |          |          |          |
| African-American              | 1,930 | 18.32    | 223,929  | 21.06   |          |          |          |          |
| Hispanic or Latino            | 561   | 5.33     | 74,870   | 7.04    |          |          |          |          |
| Other                         | 234   | 2.22     | 29,969   | 2.82    |          |          |          |          |
| Unknown                       | 705   | 6.69     | 89,162   | 8.38    |          |          |          |          |
| Region of care<sup>b</sup>   |        |          |          |         |          |          |          |          |
| East                          | 2,331 | 22.13    | 209,953  | 19.74   |          |          |          |          |
| Central                       | 2,855 | 27.10    | 268,591  | 25.26   |          |          |          |          |
| South                         | 2,813 | 26.70    | 341,819  | 32.14   |          |          |          |          |
| West                          | 2,277 | 21.62    | 224,342  | 21.10   |          |          |          |          |
| Other                         | 0     |          | 233      | 0.02    |          |          |          |          |
| Unknown                       | 258   | 2.45     | 18,428   | 1.73    |          |          |          |          |
| Healthcare utilization        |        |          |          |         |          |          |          |          |
| Patients with ≥1 hospitalization | 9,244 | 87.75    | 344,010  | 32.35   |          |          |          |          |
| Hospitalizations per patient<sup>c</sup> | 7.0 | 6.7 | 5.0 | 2.0–9.0 | 3.0 | 3.6 | 2.0 | 1.0–3.0 | 74.9 |
| Patients with ≥1 outpatient visit | 10,460 | 99.30 | 1,062,738 | 99.94 |          |          |          |          | -10.5 |
| Outpatient visits per patient<sup>c</sup> | 117.0 | 89.8 | 99.0 | 59–151 | 72.1 | 61.9 | 56.0 | 30–95 | 58.3 |
| Charlson Comorbidity Index score<sup>a</sup> | 1.4 | 1.6 | 1.0 | 0–2.0 | 0.5 | 1.0 | 0 | 0–1.0 | 14.2 |
| 0                             | 4,370 | 41.48    | 726,322  | 68.30   |          |          |          |          |
| 1                             | 2,195 | 20.84    | 195,255  | 18.36   |          |          |          |          |
| ≥2                            | 3,969 | 37.68    | 141,789  | 13.33   |          |          |          |          |
| Comorbidity                   |        |          |          |         |          |          |          |          |
| None                          | 1,677 | 15.92    | 357,580  | 33.63   |          |          |          |          |
| Any                           | 8,857 | 84.08    | 705,786  | 66.37   |          |          |          |          |
| Myocardial Infarction         | 216   | 2.05     | 7,403    | 0.70    |          |          |          |          |
| Congestive Heart Failure      | 714   | 6.78     | 19,504   | 1.83    |          |          |          |          |
| Cardiac Arrhythmia            | 931   | 8.84     | 31,967   | 3.01    |          |          |          |          |
| Valvular Disease              | 198   | 1.88     | 7,008    | 0.66    |          |          |          |          |
| Pulmonary Circulation Disorders | 184 | 1.75     | 4,937    | 0.46    |          |          |          |          |
| Peripheral Vascular Disorders | 682   | 6.47     | 18,528   | 1.74    |          |          |          |          |
| Hypertension                  | 5,406 | 51.32    | 348,378  | 32.76   |          |          |          |          |
| Chronic Pulmonary Disease     | 1,624 | 15.42    | 75,158   | 7.07    |          |          |          |          |
| Cerebrovascular Disease       | 548   | 5.20     | 18,947   | 1.78    |          |          |          |          |
| Other Neurological Disorders  | 633   | 6.01     | 25,400   | 2.39    |          |          |          |          |
| Paralysis                     | 383   | 3.64     | 6,667    | 0.63    |          |          |          |          |
| Diabetes                      | 3,732 | 35.43    | 209,679  | 19.72   |          |          |          |          |
| Renal Disease (incl. failure) | 1,214 | 11.52    | 23,922   | 2.25    |          |          |          |          |

(Continued)
sensitivity and specificity, we attempted to reduce the potential for misclassification by requiring that treatment accompany a diagnosis within a 14-day window, an approach established by prior studies, but that nevertheless may have resulted in overestimation of the incidence.2,32 Episodes identified by laboratory test result criteria align with widely accepted methods; however, by including PCR tests among those searched, misclassification of colonization rather than an episode of infection may have also resulted in overestimation of the incidence.1,19 Additionally, our data lack information about care received outside of the VHA system. To account for this, we included only patients with evidence of recent VHA healthcare utilization and a healthcare priority group rating of 1 in order to select for those that we assume are more likely to use its services and, therefore, have a more complete EMR. Although we found the included study population had, on average, 3 more outpatient visits per year than the VHA population meeting all criteria but with any healthcare priority group rating (Supplementary Table A online), non-VHA healthcare utilization has been shown to account for 15% of healthcare costs borne by individuals <65 years of age with a rating of 1, a proportion likely to have risen slightly towards the end of study period with the implementation of the Veterans Choice Program in 2014.33 Furthermore, the estimates of overall incidence and our classification of HCF-associated CDI may be underestimated due to the potential for fewer face-to-face encounters with the healthcare system and, subsequently, diagnostic testing.34

Finally, that we found slight differences in disease burden for the study population as compared to the VHA population aged 18–64 years with high service-related disability. The increasing burden of community-associated CDI in this vulnerable population warrants attention. Future studies quantifying the economic and societal burden of CDI will inform decisions surrounding prevention strategies.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2019.160.

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### Table 3. (Continued)

| Variable                          | No. (SD) | % (IQR) | No. (SD) | % (IQR) | St. Diff |
|----------------------------------|----------|---------|----------|---------|---------|
| Liver Disease                    | 792      | 7.52    | 21,986   | 2.07    | 25.7    |
| Peptic Ulcer Disease             | 97       | 0.92    | 3,119    | 0.29    | 8.1     |
| HIV/AIDS                         | 146      | 1.39    | 4,561    | 0.43    | 10.1    |
| Cancer (incl. non-metastatic)    | 876      | 8.32    | 40,655   | 3.82    | 18.9    |
| Metastatic Cancer                | 68       | 0.65    | 1,854    | 0.17    | 7.4     |
| Rheumatoid Arthritis/Collagen    | 249      | 2.36    | 11,715   | 1.10    | 9.7     |
| Hypothyroidism                   | 527      | 5.00    | 31,968   | 3.01    | 10.2    |
| Obesity                          | 1,535    | 14.57   | 107,433  | 10.10   | 13.6    |
| Weight Loss                      | 213      | 2.02    | 5,008    | 0.47    | 14.0    |
| Fluid and Electrolyte Disorders  | 883      | 8.38    | 16,004   | 1.51    | 32.1    |
| Coagulopathy                     | 274      | 2.60    | 5,898    | 0.55    | 16.5    |
| Deficiency Anemia                | 386      | 3.66    | 9,607    | 0.90    | 18.6    |
| Alcohol Abuse                    | 1,311    | 12.45   | 75,803   | 7.13    | 18.0    |
| Drug Abuse                       | 989      | 9.39    | 52,242   | 4.91    | 17.4    |
| Psychoses                        | 808      | 7.67    | 55,615   | 5.23    | 9.9     |
| Depression                       | 4,871    | 46.24   | 404,446  | 38.03   | 16.7    |
| Dementia                         | 37       | 0.35    | 772      | 0.07    | 6.1     |
| Inflammatory Bowel Disease       | 307      | 2.91    | 4,903    | 0.46    | 19.1    |

Variables are measured from the previous calendar year and are reported as of January 1, 2011. 
\[^a^\] mean (standard deviation; SD) and median (interquartile range; IQR) are reported instead of count and percentage; 
\[^b^\] East: CT, DE, IN, MA, MD, ME, MI, NH, NJ, NY, OH, PA, RI, VT; Central: AR, IA, IL, KS, LA, MN, MO, ND, NE, OK, SD, TX, WI; South: AL, Washington DC, FL, GA, KY, MS, NC, PR, SC, TN, VA, VI, WV; West: AK, AZ, CA, CO, GU, HI, ID, MT, NM, NV, OR, PI, UT, WA, WY; Other: AA, AE, AP, BC, EU, FM, FG, JA, MH, MX, NB, NF, MP, ON, PW; 
\[^c^\] Among those with at least one;
\[^d^\] Standardized difference (St. Diff), for which values indicative of a meaningful imbalance (>10 or <-10) between the two groups are bolded19.
use of facilities at the Veterans Affairs Medical Center, White River Junction, Vermont, USA. The content is solely the responsibility of the authors and does not necessarily represent the views of the US Department of Veterans Affairs or the US Government.

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