Table 1. Demographics for the CPRD/HES and CDC study populations

Characteristic	CPRD/HES population N (%)	CDC population* N (%)
Study population size	2,492,493 (100)	35,186 (100)
Sex		
Men	1,200,764 (48.18)	13,917 (39.55)
Women	1,291,729 (51.82)	21,269 (60.45)
Age (years)		
18–39	876,217 (35.15)	11,715 (33.29)
40–49	477,103 (19.14)	4,941 (14.04)
50–64	597,993 (23.99)	8,260 (23.48)
65–74	275,752 (11.06)	4,253 (12.09)
75+	265,428 (10.65)	6,017 (17.10)
Number of hospitalizations in previous 90 days		
0	2,465,563 (98.92)	31,267 (88.86)
1	23,324 (0.94)	3,020 (8.58)
2+	3,606 (0.14)	899 (2.55)
Length of stay (days)		
0	2,465,578 (98.92)	N/A
1–3	15,888 (0.64)	21,381(60.77)
4–9	5,422 (0.22)	10,394 (29.54)
10+	5,605 (0.22)	3,411 (9.69)
Number of antibiotic classes used in previous 90 days		
0	2,328,598 (93.42)	19,208 (54.59)
1	150,351 (6.03)	9,102 (25.87)
2	12,580 (0.50)	4,116 (11.70)
3	910 (0.04)	1,782 (5.06)
4	51 (0.00)	676 (1.92)
5+	3 (0.00)	302 (0.86)

*Data from Baggs et al.[6]

N: number of persons, %: percentage of persons in this category out of the total study population, CPRD: Clinical Practice Research Datalink database, HES: Hospital Episode Statistics database, CDC: US Centers for Disease Control and Prevention.

Table 2. Risk classification and *C. difficile* infection within 90 days or 365 days of index date with cut–off risk scores set to either 4 or 7 (sensitivity analysis)

	Cut–off value = 4				Cut–off value = 7			
	90 days		365 days		90 days		365 days	
	Case	Non–case	Case	Non–case	Case	Non–case	Case	Non–case
High–risk	480	1,621,077	1,290	1,620,267	394	335,023	983	334,434
Low–risk	10	870,926	42	870,894	96	2,156,980	349	2,156,727
Total	490	2,492,003	1,332	2,491,162	490	2,492,003	1,332	2,491,161
OR	25.79		16.51		26.42		18.16	
(95% CI)	(13.79–48.24)		(12.14–22.45)		(21.14–33.03)		(16.08–20.52)	
PPV	0.03		0.08		0.12		0.29	
NPV	99.99		99.99		100		99.98	
LR+	1.51		1.49		5.98		5.50	

High–risk: persons with a risk score ≥ 4 (cut–off value = 4) or ≥ 7 (cut–off value = 7); Low–risk: persons with a risk score < 4 (cut–off value = 4) or < 7 (cut–off value = 7); OR: odds ratio; CI: confidence interval; PPV: positive predictive value; NPV: negative predictive value; LR+: positive likelihood ratio.

Table 3. The study population by risk status and *C. difficile* infection status within 90 days of the index date

| Variable | Low–risk (risk score <7) | | High–risk (risk score ≥7) | |
| | Case (N = 96) | Non–case (N = 2,156,980) | Case (N = 394) | Non–case (N = 335,023) |
	n (%)	n (%)	n (%)	n (%)
Sex				
Men	46 (47.92)	1,065,758 (49.41)	166 (42.13)	134,794 (40.23)
Women	50 (52.08)	1,091,222 (50.59)	228 (57.87)	200,229 (59,77)
Age (years)				
18–39	12 (12.50)	875,769 (40.60)	5 (1.27)	431 (0.13)
40–49	13 (13.54)	472,429 (21.90)	5 (1.27)	4,656 (1.39)
50–64	33 (34.38)	557,364 (25.84)	22 (5.58)	40,574 (12.11)
65–74	38 (39.58)	251,418 (11.66)	36 (9.14)	24,260 (7.24)
75+	0 (0.00)	0 (0.00)	326 (82.74)	265,102 (79.13)
Previous hospitalization				
0	94 (97.92)	2,152,144 (99.78)	244 (61.93)	313,081 (93.45)
1	1 (1.04)	4,435 (0.21)	106 (26.90)	18,782 (5.61)
2+	1 (1.04)	401 (0.02)	44 (11.17)	3,160 (0.94)
Length of stay (days)				
0	94 (97.92)	2,152,147 (99.78)	244 (61.93)	313,093 (93.45)
1–3	2 (2.08)	4,228 (0.20)	21 (5.33)	11,637 (3.47)
4–9	0 (0.00)	605 (0.03)	20 (5.08)	4,797 (1.43)
10+	0 (0.00)	0 (0.00)	109 (27.66)	5,496 (1.64)
Previous antibiotics used (number of classes)				
0	89 (92.71)	2,080,266 (96.44)	286 (72.59)	247,957 (74.01)
1	6 (6.25)	73,556 (3.41)	88 (22.34)	76,701 (22.89)
2	1 (1.04)	3,031 (0.14)	16 (4.06)	9,532 (2.85)
3	0 (0.00)	120 (0.01)	3 (0.76)	787 (0.23)
4	0 (0.00)	7 (0.01)	1 (0.25)	43 (0.01)
5+	0 (0.00)	0 (0.00)	0 (0.00)	3 (0.00)

N: total number of cases or non–cases in this risk category; n: number of cases or non–cases in this category of the variable; %: (n/N) x100.

Antibiotics classes considered for inclusion: Aminoglycosides, 1st to 4th generation cephalosporins, fluroquinolones, vancomycin IV, betalatamase, penicillins, clindamycin, macorlides, sulfanomides antibiotics, carbapenhems, other antibiotics.

Table 4. Logistic regression for assessment of the association of risk factors assessed during the 90 days before *C. difficile* infection onset

Variable	CDI Case (N = 3,526) n (%)	CDI Non–case (N = 2,488,967) n (%)	Univariate analyses OR (95% CI)	Multivariate analysis Adjusted OR* (95% CI)
Age (years)				
18–39	118 (3.35)	825,446 (33.16)	Reference category	Reference category
40–49	118 (3.35)	472,152 (18.97)	1.75 (1.35–2.26)	1.67 (1.29–2.16)
50–59	417 (11.83)	600,870 (24.14)	4.85 (3.96–5.96)	3.84 (3.12–4.71)
60–74	614 (17.41)	294,380 (11.83)	14.59 (11.98–17.77)	7.96 (6.53–9.72)
75+	2,259 (64.07)	296,119 (11.90)	53.37 (44.35–64.22)	15.69 (13.00–18.95)
Hospitalized before				
0	878 (24.90)	2,431,332 (97.68)	Reference category	Reference category
1	1,736 (49.23)	48,703 (1.96)	98.70 (90.96–107.10)	47.76 (43.84–52.03)
2+	912 (25.87)	8,932 (0.36)	282.74 (257.13–310.91)	115.36 (104.36–127.51)
Length of stay (days)				
0	892 (25.30)	2,431,411 (97.69)	0.09 (0.08–0.11)	
1–3	125 (3.55)	31,460 (1.26)	Reference category	Not included in the adjusted
4–9	313 (8.88)	12,533 (0.50)	6.28 (5.10–7.74)	model
10+	2,196 (62.28)	13,563 (0.54)	40.75 (33.99–48.85)	
No. of antibiotics classes used				
0	2,348 (66.59)	2,278,820 (91.56)	Reference category	Reference category
1	897 (25.44)	188,347 (7.57)	4.62 (4.28–4.99)	2.07 (1.91–2.25)
2	241 (6.83)	20,203 (0.81)	11.58 (10.13–13.23)	3.34 (2.89–3.85)
3	35 (0.99)	1,508 (0.06)	22.53 (16.07–31.57)	4.94 (3.39–7.20)
4	4 (0.11)	85 (0.00)	45.67 (16.74–124.60)	7.30 (2.31–23.04)
5+	1 (0.03)	4 (0.00)	242.81 (27.14–2172.16)	70.31 (2.55–1934.91)

CDI: *Clostridium difficile* infection; OR: odds ratio; CI: confidence interval; N: number of cases or non–cases; n: number of cases (or non–cases) in this category; %: (n/N)x100.
Antibiotics classes considered for inclusion: Aminoglycosides, 1st to 4th generation cephalosporins, fluroquinolones, vancomycin IV, betalatamase, penicillins, clindamycin, macorlides, sulfanomides antibiotics, carbapenhems, other antibiotics.