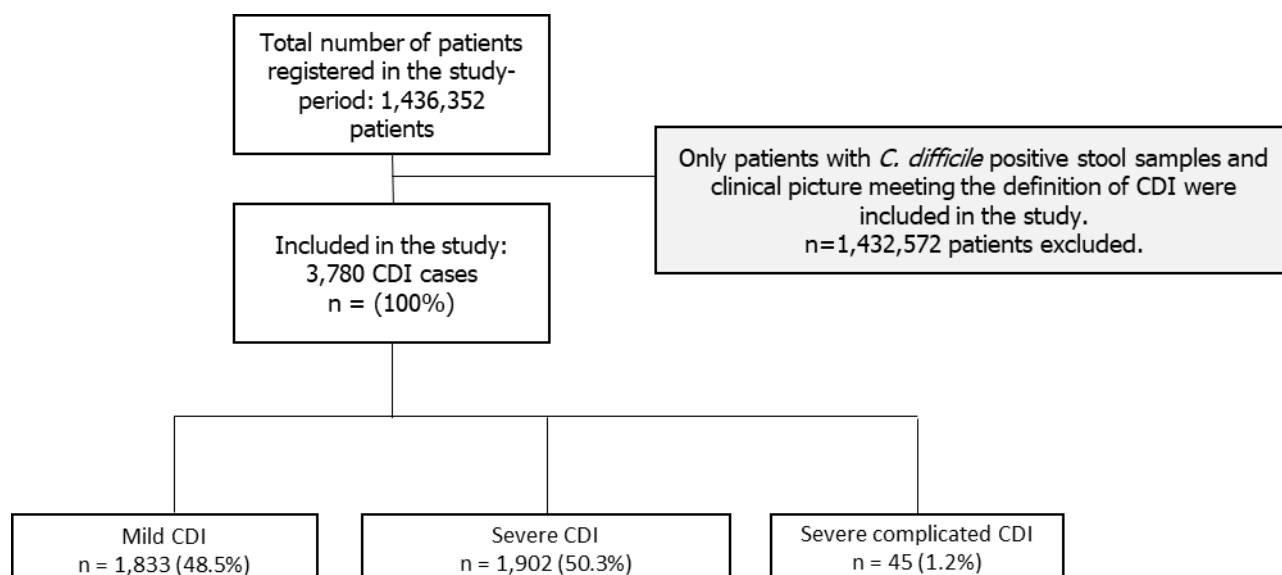


This supplementary material is given as supporting information alongside the article **Occurrence and trends of *Clostridioides difficile* infections in hospitalized patients: a prospective multicentre cohort study in six German university hospitals, 2016-2020**, on behalf of the authors, who remain responsible for the accuracy and appropriateness of the content. The same standards for ethics, copyright, attributions and permissions as for the article apply.

Supplementary Figure S1: Flow chart of CDI cases, stratified by severity



Supplementary Table S1: Assays used for microbiological testing for *C.difficile*

Method	Assays	Company
ELISA (GDH/Toxin A/B)	CDIF QUICK CHECK COMPLETE (Combined GDH/Toxin A/B Assay)	TECHLAB, Blacksburg, VA, USA
	RIDASCREEN® <i>Clostridium difficile</i> GDH	R-Biopharm, Pfungstadt, Germany
	RIDASCREEN® <i>Clostridium difficile</i> Toxin A/B	R-Biopharm, Pfungstadt, Germany
PCR	GeneXpert <i>C. difficile</i> /Epi test	Cepheid, Sunnyvale, CA, USA
	Meridian Bioscience™ illumigene™ <i>C. difficile</i> Test Kit	Meridian Bioscience, Cincinnati, OH, USA
Culture	CHROMID® <i>C. difficile</i> (Agar)	Biomerieux, Marcy-l'Étoile, France
	Cycloserine Cefoxitin Fructose Agar (CCFA)	Oxoid Ltd., Thermo Fisher Scientific, Wesel, Germany
	Schaedler agar (after alcohol shock)	Becton Dickinson, Heidelberg, Germany

Supplementary Table S2: Descriptive statistics of all CDI cases by hospital

Parameter	Category	Centre 1	Centre 2	Centre 3	Centre 4	Centre 5	Centre 6	p-value
		N (%) / median (IQR)	N (%) / median (IQR)	N (%) / median (IQR)	N (%) / median (IQR)	N (%) / median (IQR)	N (%) / median (IQR)	
CDI cases		1157 (100%)	594 (100%)	530 (100%)	560 (100%)	592 (100%)	347 (100%)	NA
Sex	Male	613 (53%)	322 (54.2%)	308 (58.1%)	262 (46.8%)	305 (51.5%)	179 (51.6%)	0.010
	Female	544 (47%)	272 (45.8%)	222 (41.9%)	298 (53.2%)	287 (48.5%)	168 (48.4%)	
Age		70 (58-79)	66 (56-77)	71 (61-80)	67 (57-77)	76 (66-83)	70 (59-80)	<0.001
In-hospital all-cause mortality	unknown	7 (0.6%)	6 (1.0%)	0 (0%)	3 (0.5%)	0 (0%)	0 (0%)	0.003
	Alive	1015 (87.7%)	506 (85.2%)	456 (86%)	508 (90.7%)	519 (87.7%)	316 (91.1%)	
	Dead	135 (11.7%)	82 (13.8%)	74 (14%)	49 (8.8%)	73 (12.3%)	31 (8.9%)	
Length of stay		22 (12-40)	27 (14-50)	18 (10-34)	21 (12-37)	18 (10-31)	13 (7-25)	<0.001
Recurrence	Initial Manifestation	71 (6.1%)	73 (12.3%)	58 (10.9%)	14 (2.5%)	41 (6.9%)	16 (4.6%)	<0.001
	Early Recurrence	939 (81.2%)	227 (38.2%)	457 (86.2%)	540 (96.4%)	535 (90.4%)	328 (94.5%)	
	Late Recurrence	23 (2%)	17 (2.9%)	4 (0.8%)	5 (0.9%)	14 (2.4%)	3 (0.9%)	
	Unknown	124 (10.7%)	277 (46.6%)	11 (2.1%)	1 (0.2%)	2 (0.3%)	0 (0%)	
Acquisition	Missing data	25 (2.2%)	27 (4.5%)	0 (0%)	23 (4.1%)	0 (0%)	1 (0.3%)	<0.001
	CA-CDI	64 (5.5%)	31 (5.2%)	66 (12.5%)	75 (13.4%)	62 (10.5%)	61 (17.6%)	
	HACO-CDI	286 (24.7%)	123 (20.7%)	120 (22.6%)	71 (12.7%)	112 (18.9%)	99 (28.5%)	
	HAHO-CDI	749 (64.7%)	401 (67.5%)	316 (59.6%)	363 (64.8%)	398 (67.2%)	153 (44.1%)	
	Unknown association CDI	33 (2.9%)	12 (2%)	28 (5.3%)	28 (5%)	20 (3.4%)	33 (9.5%)	
Ward type	ICU	259 (22.4%)	81 (13.6%)	32 (6%)	66 (11.8%)	43 (7.3%)	18 (5.2%)	<0.001
	Intermediate care	1 (0.1%)	35 (5.9%)	80 (15.1%)	7 (1.3%)	16 (2.7%)	25 (7.2%)	
	General ward	889 (76.8%)	478 (80.5%)	411 (77.5%)	487 (87%)	533 (90%)	292 (84.1%)	
	Others	8 (0.7%)	0 (0%)	7 (1.3%)	0 (0%)	0 (0%)	12 (3.5%)	
Ward specialty	Surgery	143 (12.4%)	139 (23.4%)	118 (22.3%)	109 (19.5%)	139 (23.5%)	40 (11.5%)	<0.001
	Internal medicine	825 (71.3%)	228 (38.4%)	378 (71.3%)	283 (50.5%)	306 (51.7%)	217 (62.5%)	
	Haematological/oncological	93 (8.0%)	188 (31.6%)	0 (0%)	127 (22.7%)	12 (2.0%)	58 (16.7%)	
	Other	96 (8.3%)	39 (6.6%)	34 (6.4%)	41 (7.3%)	135 (22.8%)	32 (9.2%)	
Year	2016	79 (6.8%)	23 (3.9%)	28 (5.3%)	26 (4.6%)	60 (10.1%)	24 (6.9%)	<0.001
	2017	281 (24.3%)	170 (28.6%)	149 (28.1%)	186 (33.2%)	173 (29.2%)	95 (27.4%)	
	2018	310 (26.8%)	200 (33.7%)	142 (26.8%)	128 (22.9%)	173 (29.2%)	101 (29.1%)	
	2019	335 (29%)	129 (21.7%)	145 (27.4%)	142 (25.4%)	142 (24%)	73 (21%)	
	2020	152 (13.1%)	72 (12.1%)	66 (12.5%)	78 (13.9%)	44 (7.4%)	54 (15.6%)	
Admission due to CDI	unknown	145 (12.5%)	9 (1.5%)	35 (6.6%)	1 (0.2%)	7 (1.2%)	0 (0%)	<0.001
	no	903 (78.1%)	534 (90.1%)	390 (73.6%)	523 (93.6%)	571 (96.5%)	233 (67.1%)	
	yes	108 (9.3%)	50 (8.4%)	105 (19.8%)	35 (6.3%)	14 (2.4%)	114 (32.9%)	
Distribution of symptoms at inclusion								
Symptom at inclusion: Diarrhoea	no	5 (0.4%)	3 (0.5%)	8 (1.5%)	4 (0.7%)	5 (0.8%)	9 (2.6%)	0.004
	yes	1152 (99.6%)	591 (99.5%)	522 (98.5%)	556 (99.3%)	587 (99.2%)	338 (97.4%)	

Symptom at inclusion: Toxic Megacolon	no	1157 (100%)	594 (100%)	529 (99.8%)	560 (100%)	592 (100%)	347 (100%)	0.293
	yes	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	
Symptom at inclusion: Colitis	no	1155 (99.8%)	591 (99.5%)	514 (97%)	556 (99.3%)	588 (99.3%)	337 (97.1%)	<0.001
	yes	2 (0.2%)	3 (0.5%)	16 (3%)	4 (0.7%)	4 (0.7%)	10 (2.9%)	
Symptom at inclusion: Ileus	no	1157 (100%)	594 (100%)	527 (99.4%)	560 (100%)	591 (99.8%)	347 (100%)	0.018
	yes	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	1 (0.2%)	0 (0%)	
Highest leukocytes/μl +/- 2 days of sampling		11240 (7260-16970)	9770 (4830-15250)	11300 (7800-15800)	9660 (5855-14575)	12400 (8220-17900)	9930 (5810-14990)	<0.001
Highest creatinine (mg/dl) +/- 2 days of sampling		1.15 (0.78-2.17)	1.19 (0.77-2.46)	1.2 (0.8-2.4)	1.04 (0.75-2.06)	1.2 (0.8-2.1)	1.2 (0.8-2.1)	0.186
Distribution of symptoms for severe complicated CDI								
Ileus associated with CDI ^a	unknown	126 (10.9%)	14 (2.4%)	101 (19.1%)	2 (0.4%)	0 (0%)	0 (0%)	<0.001
	no	1031 (89.1%)	577 (97.3%)	427 (80.6%)	557 (99.6%)	592 (100%)	347 (100%)	
	yes	0 (0%)	2 (0.3%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	
Toxic megacolon associated with CDI ^a	unknown	124 (10.7%)	14 (2.4%)	103 (19.4%)	2 (0.4%)	0 (0%)	0 (0%)	<0.001
	no	1028 (88.9%)	578 (97.6%)	423 (79.8%)	556 (99.6%)	591 (99.8%)	347 (100%)	
	yes	4 (0.3%)	0 (0%)	4 (0.8%)	0 (0%)	1 (0.2%)	0 (0%)	
ICU transfer due to CDI complications ^a	unknown	127 (11%)	38 (6.4%)	8 (1.5%)	3 (0.5%)	0 (0%)	0 (0%)	<0.001
	no	1022 (88.4%)	548 (92.4%)	518 (97.7%)	549 (98.4%)	592 (100%)	341 (98.3%)	
	yes	7 (0.6%)	7 (1.2%)	4 (0.8%)	6 (1.1%)	0 (0%)	6 (1.7%)	
Surgery due to CDI ^a	unknown	130 (11.3%)	35 (5.9%)	6 (1.1%)	3 (0.5%)	0 (0%)	0 (0%)	<0.001
	no	1023 (88.6%)	555 (94.1%)	522 (98.5%)	549 (99.1%)	592 (100%)	346 (100%)	
	yes	2 (0.2%)	0 (0%)	2 (0.4%)	2 (0.4%)	0 (0%)	0 (0%)	
Deceased due to CDI ^a	unknown	120 (10.4%)	29 (4.9%)	19 (3.6%)	0 (0%)	1 (0.2%)	1 (0.3%)	<0.001
	no	1028 (89.2%)	561 (94.6%)	508 (95.8%)	542 (99.3%)	591 (99.8%)	345 (99.4%)	
	yes	5 (0.4%)	3 (0.5%)	3 (0.6%)	4 (0.7%)	0 (0%)	1 (0.3%)	
Month	January	109 (9.4%)	66 (11.1%)	66 (12.5%)	62 (11.1%)	59 (10%)	35 (10.1%)	<0.001
	February	77 (6.7%)	64 (10.8%)	50 (9.4%)	45 (8%)	52 (8.8%)	32 (9.2%)	
	March	117 (10.1%)	49 (8.2%)	44 (8.3%)	46 (8.2%)	52 (8.8%)	41 (11.8%)	
	April	98 (8.5%)	49 (8.2%)	46 (8.7%)	49 (8.8%)	32 (5.4%)	31 (8.9%)	
	May	76 (6.6%)	55 (9.3%)	48 (9.1%)	66 (11.8%)	48 (8.1%)	36 (10.4%)	
	June	105 (9.1%)	62 (10.4%)	35 (6.6%)	48 (8.6%)	52 (8.8%)	34 (9.8%)	
	July	97 (8.4%)	42 (7.1%)	25 (4.7%)	31 (5.5%)	45 (7.6%)	23 (6.6%)	
	August	88 (7.6%)	38 (6.4%)	34 (6.4%)	41 (7.3%)	52 (8.8%)	17 (4.9%)	
	September	79 (6.8%)	31 (5.2%)	30 (5.7%)	41 (7.3%)	36 (6.1%)	15 (4.3%)	
	October	110 (9.5%)	49 (8.2%)	45 (8.5%)	23 (4.1%)	57 (9.6%)	27 (7.8%)	
	November	97 (8.4%)	50 (8.4%)	62 (11.7%)	52 (9.3%)	41 (6.9%)	28 (8.1%)	
	December	104 (9%)	39 (6.6%)	45 (8.5%)	56 (10%)	66 (11.1%)	28 (8.1%)	

^aEvaluated 14 days after diagnosis.

ICU, intensive care unit; CA-CDI, community-acquired CDI, HA-CDI, healthcare-acquired CDI; HAHO-CDI, healthcare-acquired healthcare-onset CDI; IQR, interquartil-range; NA, not applicable.

Supplementary Table S3: Full table with all CDI incidence and incidence densities by hospital

Parameter	Centre 1	Centre 2	Centre 3	Centre 4	Centre 5	Centre 6
Surveillance months	3263	2287	1942	3311	1112	1866
Patients	431588	180593.5	227256	310070	137614	149230
Patient days	1989449	1141172	909317	1285866	626747	847508
Case counts by acquisition						
CDI	1157	594	530	560	592	347
CA-CDI	64	31	66	75	62	61
HA-CDI	1035	524	436	434	510	252
HAHO-CDI	749	401	316	363	398	153
Mild CDI	539	302	252	306	260	174
Mild CA-CDI	28	12	32	41	26	26
Mild HA-CDI	488	262	210	237	224	124
Mild HAHO-CDI	363	202	165	201	182	80
Severe CDI	605	283	268	248	331	167
Severe CA-CDI	35	18	31	34	36	32
Severe HA-CDI	537	254	220	191	285	126
Severe HAHO-CDI	379	193	147	162	216	71
Severe complicated CDI	13	9	10	6	1	6
Severe complicated CA-CDI	1	1	3	0	0	3
Severe complicated HA-CDI	10	8	6	6	1	2
Severe complicated HAHO-CDI	7	6	4	0	0	2
Incidence per 100 patients, incidence densities per 10,000 pd (with 95% CI)						
CDI incidence	0.268 (0.247-0.284)	0.329 (0.292-0.356)	0.233 (0.206-0.254)	0.181 (0.160-0.196)	0.430 (0.382-0.466)	0.233 (0.199-0.258)
CA-CDI incidence	0.015 (0.010-0.019)	0.017 (0.010-0.024)	0.029 (0.020-0.037)	0.024 (0.017-0.030)	0.045 (0.031-0.058)	0.041 (0.028-0.053)
HA-CDI incidence	0.240 (0.219-0.255)	0.290 (0.256-0.316)	0.192 (0.167-0.211)	0.140 (0.122-0.154)	0.371 (0.326-0.404)	0.169 (0.141-0.191)
HAHO-CDI incidence	0.174 (0.156-0.186)	0.222 (0.192-0.245)	0.139 (0.118-0.155)	0.117 (0.101-0.130)	0.289 (0.250-0.319)	0.103 (0.081-0.120)
CDI incidence density*	5.82 (5.49-6.16)	5.21 (4.79-5.64)	5.83 (5.34-6.35)	4.36 (4.00-4.73)	9.45 (8.70-10.24)	4.09 (3.67-4.55)
CA-CDI incidence density*	0.32 (0.25-0.41)	0.27 (0.18-0.39)	0.73 (0.56-0.92)	0.58 (0.46-0.73)	0.99 (0.76-1.27)	0.72 (0.55-0.92)
HA-CDI incidence density*	5.20 (4.89-5.53)	4.59 (4.21-5.00)	4.79 (4.36-5.27)	3.38 (3.07-3.71)	8.14 (7.45-8.88)	2.97 (2.62-3.36)
HAHO-CDI incidence density	3.76 (3.50-4.04)	3.51 (3.18-3.88)	3.48 (3.10-3.88)	2.82 (2.54-3.13)	6.35 (5.74-7.01)	1.81 (1.53-2.12)
Mild CDI incidence	0.125 (0.110-0.136)	0.167 (0.141-0.187)	0.111 (0.092-0.125)	0.099 (0.084-0.110)	0.189 (0.158-0.213)	0.117 (0.093-0.135)
Mild CA-CDI incidence	0.006 (0.004-0.009)	0.007 (0.003-0.012)	0.014 (0.008-0.020)	0.013 (0.008-0.018)	0.019 (0.010-0.028)	0.017 (0.009-0.026)
Mild HA-CDI incidence	0.113 (0.099-0.124)	0.145 (0.121-0.164)	0.092 (0.076-0.106)	0.076 (0.063-0.087)	0.163 (0.134-0.186)	0.083 (0.064-0.099)
Mild HAHO-CDI incidence	0.084 (0.072-0.093)	0.112 (0.091-0.128)	0.073 (0.058-0.085)	0.065 (0.053-0.074)	0.132 (0.106-0.153)	0.054 (0.038-0.067)
Mild CDI incidence density*	2.71 (2.49-2.95)	2.65 (2.36-2.96)	2.77 (2.44-3.14)	2.38 (2.12-2.66)	4.15 (3.66-4.68)	2.05 (1.76-2.38)

Mild CA-CDI incidence density*	0.14 (0.09-0.20)	0.11 (0.05-0.18)	0.35 (0.24-0.50)	0.32 (0.23-0.43)	0.41 (0.27-0.61)	0.31 (0.20-0.45)
Mild HA-CDI incidence density*	2.45 (2.24-2.68)	2.30 (2.03-2.59)	2.31 (2.01-2.64)	1.84 (1.62-2.09)	3.57 (3.12-4.07)	1.46 (1.22-1.74)
Mild HAHO-CDI incidence density	1.82 (1.64-2.02)	1.77 (1.53-2.03)	1.81 (1.55-2.11)	1.56 (1.35-1.79)	2.90 (2.50-3.36)	0.94 (0.75-1.17)
Severe CDI incidence	0.140 (0.125-0.152)	0.157 (0.132-0.176)	0.118 (0.099-0.133)	0.080 (0.066-0.091)	0.241 (0.205-0.268)	0.112 (0.089-0.130)
Severe CA-CDI incidence	0.008 (0.005-0.011)	0.010 (0.005-0.016)	0.014 (0.008-0.019)	0.011 (0.006-0.015)	0.026 (0.016-0.036)	0.021 (0.012-0.030)
Severe HA-CDI incidence	0.124 (0.110-0.135)	0.141 (0.117-0.159)	0.097 (0.079-0.110)	0.062 (0.050-0.071)	0.207 (0.174-0.233)	0.084 (0.065-0.101)
Severe HAHO-CDI incidence	0.088 (0.076-0.097)	0.107 (0.087-0.123)	0.065 (0.051-0.076)	0.052 (0.041-0.061)	0.157 (0.129-0.179)	0.048 (0.033-0.060)
Severe CDI incidence density*	3.04 (2.80-3.29)	2.48 (2.20-2.79)	2.95 (2.60-3.32)	1.93 (1.70-2.18)	5.28 (4.73-5.88)	1.97 (1.68-2.29)
Severe CA-CDI incidence density*	0.18 (0.12-0.24)	0.16 (0.09-0.25)	0.34 (0.23-0.48)	0.26 (0.18-0.37)	0.57 (0.40-0.80)	0.38 (0.26-0.53)
Severe HA-CDI incidence density*	2.70 (2.48-2.94)	2.23 (1.96-2.52)	2.42 (2.11-2.76)	1.49 (1.28-1.71)	4.55 (4.03-5.11)	1.49 (1.24-1.77)
Severe HAHO-CDI incidence density	1.91 (1.72-2.11)	1.69 (1.46-1.95)	1.62 (1.37-1.90)	1.26 (1.07-1.47)	3.45 (3.00-3.94)	0.84 (0.65-1.06)
Severe complicated CDI incidence	0.003 (0.001-0.005)	0.005 (0.002-0.009)	0.004 (0.001-0.008)	0.002 (0.000-0.004)	0.001 (0.000-0.004)	0.004 (0.001-0.009)
Severe complicated CA-CDI incidence	0.000 (0.000-0.001)	0.001 (0.000-0.003)	0.001 (0.000-0.004)	0.000 (0.000-0.001)	0.000 (0.000-0.003)	0.002 (0.000-0.006)
Severe complicated HA-CDI incidence	0.002 (0.001-0.004)	0.004 (0.001-0.009)	0.003 (0.001-0.006)	0.002 (0.000-0.004)	0.001 (0.000-0.004)	0.001 (0.000-0.005)
Severe complicated HAHO-CDI incidence	0.002 (0.000-0.003)	0.003 (0.001-0.007)	0.002 (0.000-0.005)	0.000 (0.000-0.001)	0.000 (0.000-0.003)	0.001 (0.000-0.005)
Severe complicated CDI incidence density*	0.07 (0.03-0.11)	0.08 (0.04-0.15)	0.11 (0.05-0.20)	0.05 (0.02-0.10)	0.02 (0.00-0.09)	0.07 (0.03-0.15)
Severe complicated CA-CDI incidence density*	0.01 (0.00-0.03)	0.01 (0.00-0.05)	0.03 (0.01-0.10)	0.00 (0.00-0.03)	0.00 (0.00-0.06)	0.04 (0.01-0.10)
Severe complicated HA-CDI incidence density*	0.05 (0.02-0.09)	0.07 (0.03-0.14)	0.07 (0.02-0.14)	0.05 (0.02-0.10)	0.02 (0.00-0.09)	0.02 (0.00-0.09)
Severe complicated HAHO-CDI incidence density	0.04 (0.01-0.07)	0.05 (0.02-0.11)	0.04 (0.01-0.11)	0.00 (0.00-0.03)	0.00 (0.00-0.06)	0.02 (0.00-0.09)

* For HAHO-CDI, incidence density was calculated per 10,000 patient-days (pd). For total CDI, CA-CDI and HA-CDI the incidence was calculated per 100 patients, as we cannot record patient-days relevant to CDI onset for those cases. Nevertheless, we additionally calculated incidence densities per 10,000 pd (using pd of current hospital stay) for total CDI, CA-CDI as well as HA-CDI and showed them in supplement because they are reported frequently elsewhere.

Note: number of CDI with unknown CDI-association and missing values are not specified in this table, in total 154 (4.1%) cases are unknown association and in 76 cases (2%) we had missing values.

Supplementary Table S4: Full table with all CDI incidence and incidence densities in total and by specialty

Parameter	Total	Surgery	Internal Medicine	Haematology/Oncology	Other
Surveillance months	13,781	5,217	5,027	1,009	2,528
Patients	1,436,352	518,120	565,665	47,107	305,460
Patient days	6,800,059	2,464,959	2,702,231	418,634	1,214,235
Case counts by acquisition					
CDI	3,780	688	2,237	478	377
CA-CDI	359	45	259	16	39
HA-CDI	3,191	604	1,839	430	318
HAHO-CDI	2,380	531	1,275	348	226
Mild CDI	1,833	330	961	345	197
Mild CA-CDI	165	25	112	10	18
Mild HA-CDI	1,545	283	783	311	168
Mild HAHO-CDI	1,193	249	566	258	120
Severe CDI	1,902	348	1,247	128	179
Severe CA-CDI	186	18	142	5	21
Severe HA-CDI	1,613	315	1,033	116	149
Severe HAHO-CDI	1,168	278	697	87	106
Severe complicated CDI	45	10	29	5	1
Severe complicated CA-CDI	8	2	5	1	0
Severe complicated HA-CDI	33	6	23	3	1
Severe complicated HAHO-CDI	19	4	12	3	0
Incidence per 100 patients, incidence densities per 1,000 pd (with 95% CI)					
CDI incidence	0.263 (0.251-0.272)	0.133 (0.119-0.143)	0.395 (0.372-0.412)	1.015 (0.890-1.109)	0.123 (0.106-0.137)
CA-CDI incidence	0.025 (0.021-0.028)	0.009 (0.005-0.012)	0.046 (0.038-0.052)	0.034 (0.015-0.055)	0.013 (0.008-0.017)
HA-CDI incidence	0.222 (0.211-0.230)	0.117 (0.104-0.126)	0.325 (0.304-0.340)	0.913 (0.795-1.003)	0.104 (0.088-0.116)
HAHO-CDI incidence	0.166 (0.156-0.172)	0.102 (0.090-0.112)	0.739 (0.633-0.820)	0.074 (0.061-0.084)	0.225 (0.208-0.238)
CDI incidence density*	5.56 (5.38-5.74)	2.79 (2.59-3.01)	11.42 (10.42-12.49)	3.10 (2.80-3.43)	8.28 (7.94-8.63)
CA-CDI incidence density*	0.53 (0.47-0.59)	0.18 (0.13-0.24)	0.38 (0.22-0.62)	0.32 (0.23-0.44)	0.96 (0.85-1.08)
HA-CDI incidence density*	4.69 (4.53-4.86)	2.45 (2.26-2.65)	10.27 (9.32-11.29)	2.62 (2.34-2.92)	6.81 (6.50-7.12)
HAHO-CDI incidence density	3.50 (3.36-3.64)	2.15 (1.97-2.35)	4.72 (4.46-4.98)	8.31 (7.46-9.23)	1.86 (1.63-2.12)
Mild CDI incidence	0.128 (0.119-0.134)	0.064 (0.054-0.071)	0.170 (0.155-0.181)	0.732 (0.627-0.814)	0.064 (0.052-0.074)
Mild CA-CDI incidence	0.011 (0.009-0.013)	0.005 (0.003-0.007)	0.020 (0.015-0.024)	0.021 (0.007-0.039)	0.006 (0.003-0.009)

Mild HA-CDI incidence	0.108 (0.100-0.113)	0.055 (0.046-0.061)	0.138 (0.125-0.148)	0.660 (0.560-0.738)	0.055 (0.044-0.064)
Mild HAHO-CDI incidence	0.083 (0.076-0.088)	0.048 (0.040-0.054)	0.548 (0.457-0.619)	0.039 (0.030-0.047)	0.100 (0.089-0.109)
Mild CDI incidence density*	2.70 (2.57-2.82)	1.34 (1.20-1.49)	8.24 (7.39-9.16)	1.62 (1.40-1.87)	3.56 (3.33-3.79)
Mild CA-CDI incidence density*	0.24 (0.21-0.28)	0.10 (0.07-0.15)	0.24 (0.11-0.44)	0.15 (0.09-0.23)	0.41 (0.34-0.50)
Mild HA-CDI incidence density*	2.27 (2.16-2.39)	1.15 (1.02-1.29)	7.43 (6.63-8.30)	1.38 (1.18-1.61)	2.90 (2.70-3.11)
Mild HAHO-CDI incidence density	1.75 (1.66-1.86)	1.01 (0.89-1.14)	2.09 (1.93-2.27)	6.16 (5.43-6.96)	0.99 (0.82-1.18)
Severe CDI incidence	0.132 (0.124-0.139)	0.067 (0.058-0.075)	0.220 (0.203-0.233)	0.272 (0.209-0.323)	0.059 (0.047-0.068)
Severe CA-CDI incidence	0.013 (0.010-0.015)	0.003 (0.002-0.005)	0.025 (0.020-0.030)	0.011 (0.002-0.025)	0.007 (0.003-0.011)
Severe HA-CDI incidence	0.112 (0.105-0.118)	0.061 (0.052-0.068)	0.183 (0.167-0.194)	0.246 (0.187-0.295)	0.049 (0.038-0.057)
Severe HAHO-CDI incidence	0.081 (0.075-0.086)	0.054 (0.045-0.060)	0.185 (0.134-0.228)	0.035 (0.026-0.042)	0.123 (0.111-0.133)
Severe CDI incidence density*	2.80 (2.67-2.93)	1.41 (1.27-1.57)	3.06 (2.55-3.64)	1.47 (1.27-1.71)	4.61 (4.36-4.88)
Severe CA-CDI incidence density*	0.27 (0.24-0.32)	0.07 (0.04-0.12)	0.12 (0.04-0.28)	0.17 (0.11-0.26)	0.53 (0.44-0.62)
Severe HA-CDI incidence density*	2.37 (2.26-2.49)	1.28 (1.14-1.43)	2.77 (2.29-3.32)	1.23 (1.04-1.44)	3.82 (3.59-4.06)
Severe HAHO-CDI incidence density	1.72 (1.62-1.82)	1.13 (1.00-1.27)	2.58 (2.39-2.78)	2.08 (1.66-2.56)	0.87 (0.71-1.06)
Severe complicated CDI incidence	0.003 (0.002-0.004)	0.002 (0.001-0.004)	0.005 (0.003-0.007)	0.011 (0.002-0.025)	0.000 (0.000-0.002)
Severe complicated CA-CDI incidence	0.001 (0.000-0.001)	0.000 (0.000-0.001)	0.001 (0.000-0.002)	0.002 (0.000-0.012)	0.000 (0.000-0.001)
Severe complicated HA-CDI incidence	0.002 (0.001-0.003)	0.001 (0.000-0.003)	0.004 (0.002-0.006)	0.006 (0.001-0.019)	0.000 (0.000-0.002)
Severe complicated HAHO-CDI incidence	0.001 (0.001-0.002)	0.001 (0.000-0.002)	0.006 (0.001-0.019)	0.000 (0.000-0.001)	0.002 (0.001-0.004)
Severe complicated CDI incidence density*	0.07 (0.05-0.09)	0.04 (0.02-0.07)	0.11 (0.07-0.15)	0.12 (0.04-0.28)	0.01 (0.00-0.05)
Severe complicated CA-CDI incidence density*	0.01 (0.01-0.02)	0.01 (0.00-0.03)	0.02 (0.01-0.04)	0.02 (0.00-0.13)	0.00 (0.00-0.03)
Severe complicated HA-CDI incidence density*	0.05 (0.03-0.07)	0.02 (0.01-0.05)	0.09 (0.05-0.13)	0.07 (0.01-0.21)	0.01 (0.00-0.05)
Severe complicated HAHO-CDI incidence density	0.03 (0.02-0.04)	0.02 (0.00-0.04)	0.04 (0.02-0.08)	0.07 (0.01-0.21)	0.00 (0.00-0.03)

*For HAHO-CDI, incidence density was calculated per 10,000 patient-days (pd). For total CDI, CA-CDI and HA-CDI the incidence was calculated per 100 patients, as we cannot record patient-days relevant to CDI onset for those cases. Nevertheless, we additionally calculated incidence densities per 10,000 pd (using pd of current hospital stay) for total CDI, CA-CDI as well as HA-CDI and showed them in supplement because they are reported frequently elsewhere.

Note: number of CDI with unknown CDI-association and missing values are not specified in this table, in total 154 (4.1%) cases are unknown association and in 76 cases (2%) we had missing values.

Supplementary Table S5: Full table with all CDI incidences and incidence densities (95%CI) stratified by surveillance year

Parameter	2016	2017	2018	2019	2020
Surveillance months	749	3,726	3,705	3,736	1,865
Patients	79,900	407,044	388,468	381,962	178,979
Patient days	378,599	1,886,952	1,850,621	1,846,035	837,852
Median LOS (IQR)	20 (12-35)	19 (10-34)	22 (11-39)	21 (11-36)	21 (11-40)
Case counts by acquisition					
CDI	240	1054	1054	966	466
CA-CDI	17	118	77	100	47
HA-CDI	213	891	928	801	358
HAHO-CDI	164	625	700	616	275
Mild CDI	115	509	485	483	241
Mild CA-CDI	9	63	31	45	17
Mild HA-CDI	100	421	433	406	185
Mild HAHO-CDI	78	309	342	316	148
Severe CDI	124	530	561	466	221
Severe CA-CDI	8	55	44	51	28
Severe HA-CDI	112	456	489	385	171
Severe HAHO-CDI	85	310	355	293	125
Severe complicated CDI	1	15	8	17	4
Severe complicated CA-CDI	0	0	2	4	2
Severe complicated HA-CDI	1	14	6	10	2
Severe complicated HAHO-CDI	1	6	3	7	2
Incidence per 100 patients by specialty					
Internal medicine	0.193 (0.128-0.250)	0.144 (0.118-0.165)	0.129 (0.104-0.150)	0.118 (0.094-0.138)	0.118 (0.083-0.148)
Surgery	0.858 (0.448-1.275)	0.913 (0.698-1.089)	1.094 (0.849-1.294)	1.029 (0.790-1.224)	1.112 (0.783-1.397)
Haematology-oncology	0.105 (0.047-0.168)	0.151 (0.116-0.179)	0.137 (0.104-0.165)	0.094 (0.067-0.117)	0.103 (0.063-0.141)
Other	0.449 (0.351-0.528)	0.370 (0.329-0.402)	0.409 (0.364-0.442)	0.401 (0.357-0.435)	0.387 (0.325-0.435)
Incidence per 100 patients, incidence densities per 10,000 pd (with 95% CI)					
CDI incidence	0.300 (0.249-0.341)	0.259 (0.237-0.275)	0.271 (0.248-0.288)	0.253 (0.231-0.269)	0.260 (0.228-0.285)
CA-CDI incidence	0.021 (0.010-0.034)	0.029 (0.022-0.035)	0.020 (0.014-0.025)	0.026 (0.019-0.032)	0.026 (0.017-0.035)
HA-CDI incidence	0.267 (0.218-0.305)	0.219 (0.199-0.234)	0.239 (0.217-0.255)	0.210 (0.190-0.225)	0.200 (0.172-0.222)
HAHO-CDI incidence	0.205 (0.163-0.239)	0.154 (0.137-0.166)	0.180 (0.162-0.194)	0.161 (0.144-0.175)	0.154 (0.129-0.173)
CDI incidence density*	6.34 (5.56-7.19)	5.59 (5.25-5.93)	5.70 (5.36-6.05)	5.23 (4.91-5.57)	5.56 (5.07-6.09)

CA-CDI incidence density*	0.45 (0.26-0.72)	0.63 (0.52-0.75)	0.42 (0.33-0.52)	0.54 (0.44-0.66)	0.56 (0.41-0.75)
HA-CDI incidence density*	5.63 (4.90-6.43)	4.72 (4.42-5.04)	5.01 (4.70-5.35)	4.34 (4.04-4.65)	4.27 (3.84-4.74)
HAHO-CDI incidence density	4.33 (3.69-5.05)	3.31 (3.06-3.58)	3.78 (3.51-4.07)	3.34 (3.08-3.61)	3.28 (2.91-3.69)
Mild CDI incidence	0.144 (0.109-0.173)	0.125 (0.110-0.136)	0.125 (0.110-0.136)	0.126 (0.111-0.138)	0.135 (0.112-0.153)
Mild CA-CDI incidence	0.011 (0.004-0.021)	0.015 (0.011-0.020)	0.008 (0.005-0.011)	0.012 (0.007-0.016)	0.009 (0.004-0.015)
Mild HA-CDI incidence	0.125 (0.093-0.152)	0.103 (0.090-0.114)	0.111 (0.097-0.122)	0.106 (0.092-0.117)	0.103 (0.083-0.119)
Mild HAHO-CDI incidence	0.098 (0.069-0.122)	0.076 (0.064-0.085)	0.088 (0.075-0.098)	0.083 (0.070-0.092)	0.083 (0.065-0.097)
Mild CDI incidence density*	3.04 (2.51-3.65)	2.70 (2.47-2.94)	2.62 (2.39-2.86)	2.62 (2.39-2.86)	2.88 (2.52-3.26)
Mild CA-CDI incidence density*	0.24 (0.11-0.45)	0.33 (0.26-0.43)	0.17 (0.11-0.24)	0.24 (0.18-0.33)	0.02 (0.12-0.32)
Mild HA-CDI incidence density*	2.64 (2.15-3.21)	2.23 (2.02-2.45)	2.34 (2.12-2.57)	2.20 (1.99-2.42)	2.21 (1.90-2.55)
Mild HAHO-CDI incidence density	2.06 (1.63-2.57)	1.64 (1.46-1.83)	1.85 (1.66-2.05)	1.71 (1.53-1.91)	1.77 (1.49-2.08)
Severe CDI incidence	0.155 (0.119-0.185)	0.130 (0.115-0.142)	0.144 (0.128-0.157)	0.122 (0.107-0.134)	0.123 (0.101-0.141)
Severe CA-CDI incidence	0.010 (0.003-0.020)	0.014 (0.009-0.018)	0.011 (0.007-0.015)	0.013 (0.009-0.018)	0.016 (0.009-0.023)
Severe HA-CDI incidence	0.140 (0.106-0.169)	0.112 (0.098-0.123)	0.126 (0.110-0.138)	0.101 (0.087-0.111)	0.096 (0.076-0.111)
Severe HAHO-CDI incidence	0.106 (0.077-0.132)	0.076 (0.065-0.085)	0.091 (0.078-0.101)	0.077 (0.065-0.086)	0.070 (0.054-0.083)
Severe CDI incidence density*	3.28 (2.72-3.91)	2.81 (2.57-3.06)	3.03 (2.79-3.29)	2.52 (2.30-2.76)	2.64 (2.30-3.01)
Severe CA-CDI incidence density*	0.21 (0.09-0.42)	0.29 (0.22-0.38)	0.24 (0.17-0.32)	0.28 (0.21-0.36)	0.33 (0.22-0.48)
Severe HA-CDI incidence density*	2.96 (2.44-3.56)	2.42 (2.20-2.65)	2.64 (2.41-2.89)	2.09 (1.88-2.30)	2.04 (1.75-2.37)
Severe HAHO-CDI incidence density	2.25 (1.79-2.78)	1.64 (1.47-1.84)	1.92 (1.72-2.13)	1.59 (1.41-1.78)	1.49 (1.24-1.78)
Severe complicated CDI incidence	0.001 (0.000-0.007)	0.004 (0.002-0.006)	0.002 (0.001-0.004)	0.004 (0.002-0.007)	0.002 (0.000-0.006)
Severe complicated CA-CDI incidence	0.000 (0.000-0.005)	0.000 (0.000-0.001)	0.001 (0.000-0.002)	0.001 (0.000-0.003)	0.001 (0.000-0.004)
Severe complicated HA-CDI incidence	0.001 (0.000-0.007)	0.003 (0.001-0.006)	0.002 (0.000-0.003)	0.003 (0.001-0.005)	0.001 (0.000-0.004)
Severe complicated HAHO-CDI incidence	0.001 (0.000-0.007)	0.001 (0.000-0.003)	0.001 (0.000-0.002)	0.002 (0.000-0.004)	0.001 (0.000-0.004)
Severe complicated CDI incidence density*	0.03 (0.00-0.15)	0.08 (0.04-0.13)	0.04 (0.02-0.09)	0.09 (0.05-0.15)	0.05 (0.01-0.12)
Severe complicated CA-CDI incidence density*	0.00 (0.00-0.10)	0.00 (0.00-0.02)	0.01 (0.00-0.04)	0.02 (0.01-0.06)	0.02 (0.00-0.09)
Severe complicated HA-CDI incidence density*	0.03 (0.00-0.15)	0.07 (0.04-0.12)	0.03 (0.01-0.07)	0.05 (0.03-0.10)	0.02 (0.00-0.09)
Severe complicated HAHO-CDI incidence density	0.03 (0.00-0.15)	0.03 (0.01-0.07)	0.02 (0.00-0.05)	0.04 (0.02-0.08)	0.02 (0.00-0.09)

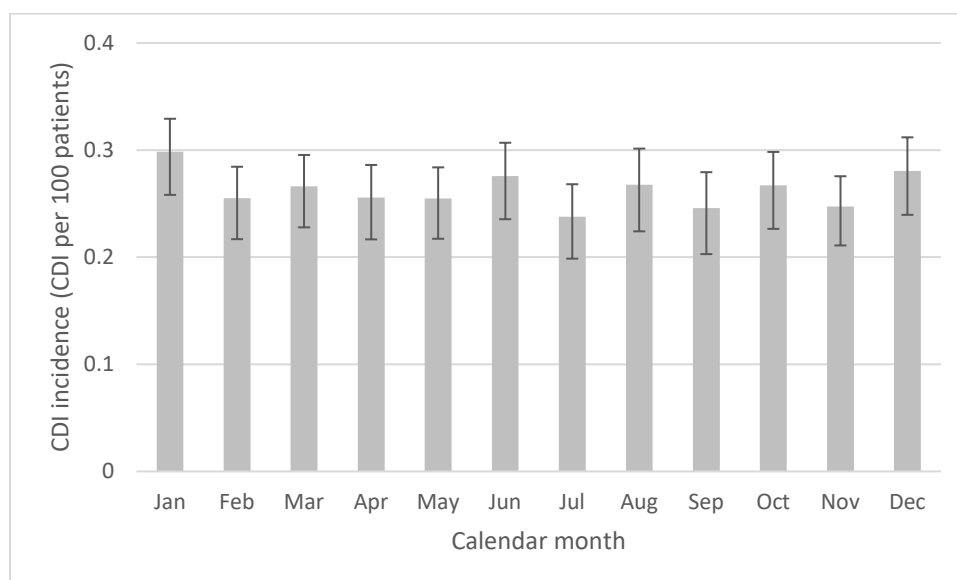
*For HAHO-CDI, incidence density was calculated per 10,000 patient-days (pd). For total CDI, CA-CDI and HA-CDI the incidence was calculated per 100 patients, as we cannot record patient-days relevant to CDI onset for those cases. Nevertheless, we additionally calculated incidence densities per 10,000 pd (using pd of current hospital stay) for total CDI, CA-CDI as well as HA-CDI and showed them in supplement because they are reported frequently elsewhere.

Note: number of CDI with unknown CDI-association and missing values are not specified in this table, in total 154 (4.1%) cases are unknown association and in 76 cases (2%) we had missing values.

Supplementary Table S6: Overall CDI incidence by surveillance month. No seasonality observable.

surveillance month	CDI incidence /100 patients (95% CI)
January	0.298 (0.258-0.329)
February	0.255 (0.217-0.284)
March	0.266 (0.228-0.295)
April	0.256 (0.217-0.286)
May	0.255 (0.217-0.284)
June	0.276 (0.235-0.307)
July	0.238 (0.199-0.268)
August	0.268 (0.224-0.301)
September	0.246 (0.203-0.279)
October	0.267 (0.226-0.298)
November	0.247 (0.211-0.276)
December	0.280 (0.240-0.312)

Supplementary Figure S2: Overall CDI incidence by surveillance month, Germany 2016 to 2020.

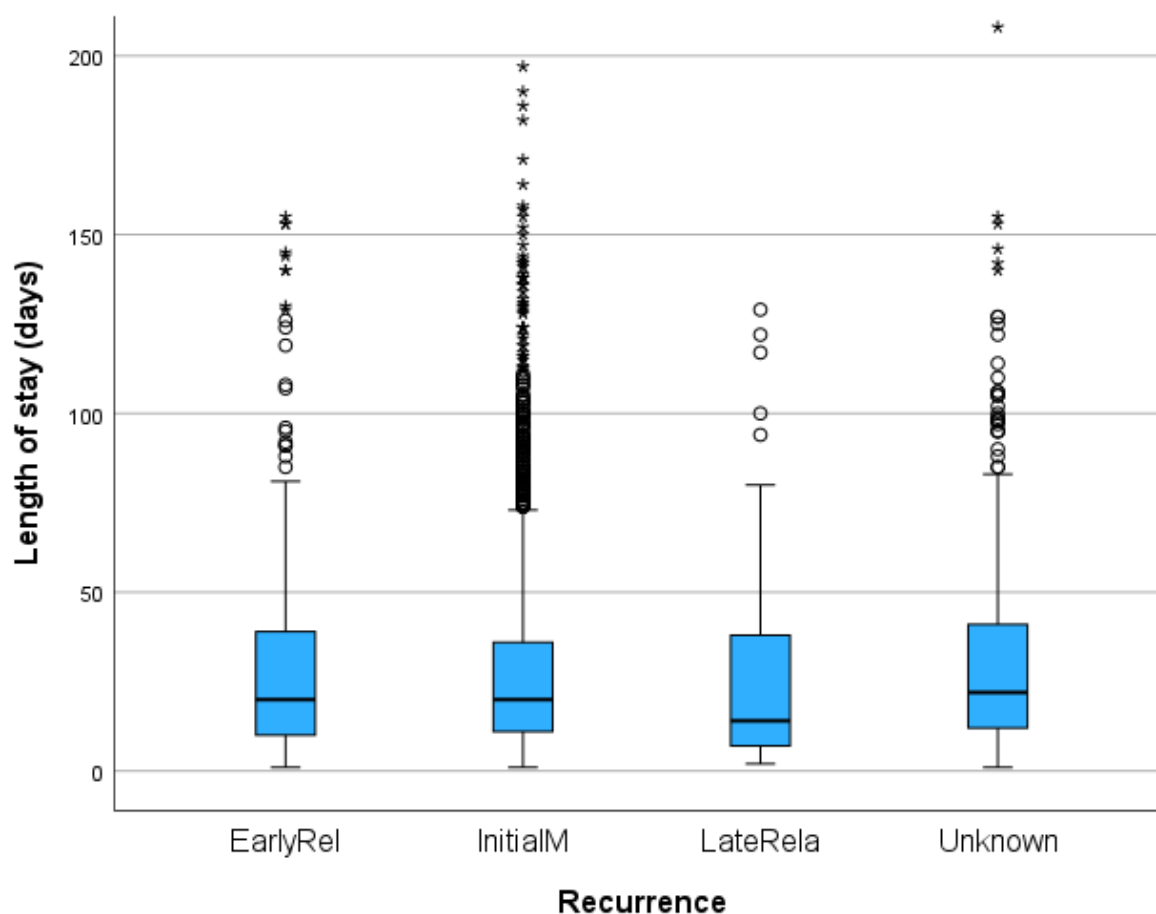


Supplementary Table S7: Length of stay (LOS) by recurrence.

Recurrence	LOS	LOS	p-value
	n	Med (IQR)	
Early recurrence	237	20 (10-39)	0.008
Initial manifestation	3026	20 (11-36)	
Late recurrence	66	14 (7-38)	
Unknown	415	22 (12-41)	

LOS, Length of stay; Med, median; IQR, interquartil-range; NA, not applicable.

Supplementary Figure S3: Length of stay (LOS) by recurrence.



EarlyRel: early recurrence (2-8 weeks after initial episode); InitialIM: initial manifestation/episode; LateRela: late recurrence (8-12 weeks after initial episode).

The horizontal line in each box indicates the median; whereas the top and bottom lines represent the 75th and 25th percentiles, respectively. Whiskers represent 1.5x IQR, each open circle represents one outlier, stars represent extreme outliers.