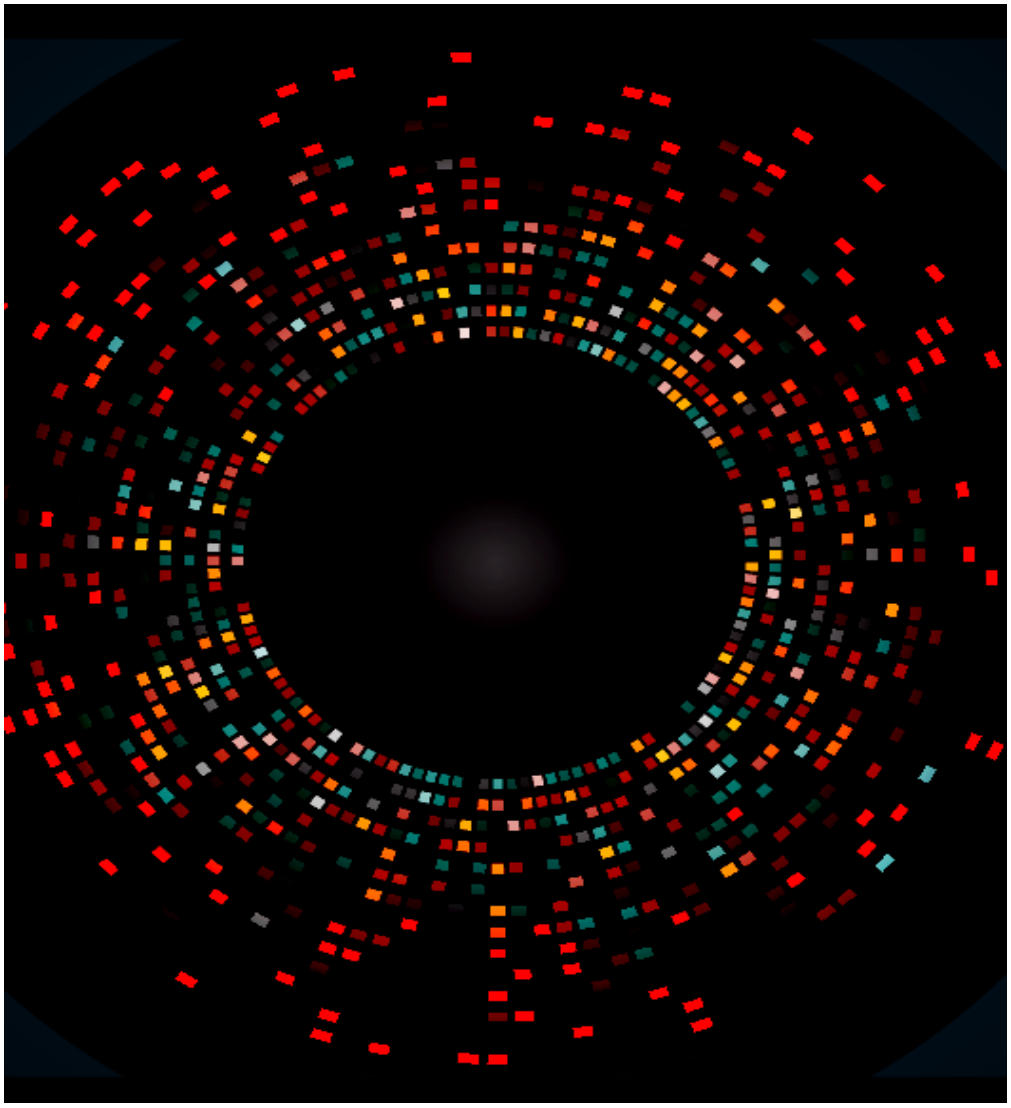
UK Health Security Agency

Clostridioides difficile ribotyping network (CDRN) for England and Northern Ireland

Report 2023 to 2025



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Introduction

Since the introduction of the *Clostridioides difficile* Ribotyping Network (CDRN) for England and Northern Ireland, coincident with the peak incidence of *C. difficile* infection (CDI) in England (and the UK), rates have fallen markedly (1). However, a subsequent period of relative stability of CDI rates in England ended during the COVID-19 pandemic; compared with pre-pandemic rates, CDI incidence has steadily increased in England by approximately 25%, particularly (but non-exclusively) driven by hospital onset cases (2). CDRN continues to respond to a major public health need, by providing a molecular epidemiological service that enhances our understanding of *C. difficile*, which is recognised as a global threat (3). CDI case fatality rates have also declined, notably in line with control of the epidemic ribotype *C. difficile* 027 (4 to 6). It is not possible to determine which interventions have been particularly responsible for the decreased incidence of CDI and associated deaths. However, it is plausible that access to the ribotyping and enhanced fingerprinting results provided by CDRN have facilitated improved local investigation and control of CDI cases, clusters and outbreaks. CDRN has certainly contributed to a much improved understanding of the epidemiology of CDI, and its scope or coverage is unrivalled worldwide.

Samples are submitted to CDRN according to local clinical need. We aim to provide results within 2 weeks of sample receipt. We believe that the timely data provided by CDRN has enabled healthcare institutions to respond to changes in CDI presentation and/or incidence. We encourage all hospitals to consider submitting samples according to the CDRN criteria so that they can be best placed to continue to prevent and control CDI.

Historically the CDRN has operated from a combination of the following participating laboratories:

- Leeds (Leeds General Infirmary) – Yorkshire and Humber; CDRN Reference Laboratory
- Birmingham (Heartlands Hospital) – West and East Midlands Regions
- Bristol – South West Region
- Cambridge (Addenbrooke's Hospital) – East of England Region
- Manchester (Manchester Royal Infirmary) – North West Region
- Southampton (Southampton General Hospital) – South East Region
- Belfast (Royal Victoria Hospital) – Northern Ireland Region

Due to centralisation efforts in Spring 2021, a full national CDRN service is now delivered from UKHSA CDRN Reference Laboratory at Leeds. The Royal Victoria Hospital Belfast has continued to support locations in Northern Ireland.

Accessing the service

The CDRN laboratories provide access to *C. difficile* culture and ribotyping according to standardised criteria for submission of faecal samples. The number of samples to be submitted to the CDRN per scenario should be agreed prospectively with respective regional microbiologists, or a microbiologist from the CDRN laboratory, according to the extent and severity of CDI cases. The CDRN aims to provide timely information to help optimise the management of *C. difficile* at a local level, with a turnaround time of less than 2 weeks (this includes the time to culture *C. difficile*). It is recommended that the CDRN service is used by hospitals and infection control teams in England to investigate the following scenarios:

- increased frequency of cases OR high baseline rates of CDI
- increased severity or complications of cases of CDI
- increased mortality associated with CDI
- increased recurrence rate of CDI

We believe that the CDRN service can help local teams to meet targets that have been set for reducing the incidence of CDI. Additionally, we collect, via a mandatory request form, antibiotic risk and outcome data that can be used to provide more detailed information about CDI at a national level. Some requests provide few such data, which hinders this aim, and we therefore encourage all users of the CDRN service to submit the data requested.

A full description of this service is available on the UKHSA webpages.

Enhanced DNA fingerprinting

Since late 2008, CDRN has offered an enhanced DNA fingerprinting (multilocus variable-number tandem-repeat analysis, MLVA) service. This can be used to characterise and improve the understanding of the transmission of epidemic *C. difficile* strains within healthcare institutions. Importantly, the method can provide a high level of discrimination among epidemic *C. difficile* ribotypes. For example, MLVA can distinguish more than 20 sub-types of *C. difficile* ribotype 027 (7). MLVA is far superior to most other fingerprinting methods, including pulsed field gel electrophoresis, for analysing closely related *C. difficile* strains (8). MLVA has similar discriminatory power, as a typing or fingerprinting method, to whole genome sequencing, although the latter method provides considerable additional genetic information (9).

Institutions should consider the use of the CDRN MLVA Enhanced Fingerprinting service to optimise the control and prevention of CDI. There is currently no charge for the enhanced fingerprinting service for NHS hospitals in England. Access to the service is controlled, in the first instance by regional microbiologists, given its high cost and need to balance availability with the scale of CDI challenge. MLVA is available via the Leeds laboratory.
The criteria used to access the enhanced fingerprinting service are:

- a hospital or trust with a high rate of CDI as identified with local commissioners

or:

- a hospital or trusts that is failing to meet its *C. difficile* target trajectory despite implementation and audit of control measures

or:

- a declared outbreak of CDI as agreed with the local Health Protection Unit

In addition:

- ribotyping carried out by CDRN must have confirmed the presence of a dominant *C. difficile* ribotype
- a plan should be in place of how results of *C. difficile* enhanced fingerprinting will contribute to the control of CDI
- infection control teams or consultant microbiologists will first need to agree with the regional microbiologist that use of the *C. difficile* enhanced fingerprinting service is merited
- numbers of samples or isolates to be examined will be agreed with the MLVA laboratory on a case-by-case basis, taking account of the scale of CDI challenge

A full description of this service is available on the UKHSA webpages.

Antibiotic susceptibility testing

In order to determine the epidemiology of the susceptibility to metronidazole, vancomycin and fidaxomicin of *C. difficile* isolates from CDI cases, periodic antimicrobial susceptibility was performed on strains received by the CDRN Reference Laboratory in Leeds until 2023. It is planned that a new susceptibility surveillance data program will soon become available aligned with the sentinel surveillance scheme.

Electronic requesting and reporting system

A dedicated electronic requesting and reporting system (ERS) continues to be available for NHS trusts to complete electronic request forms and receive test results electronically, as well as access archived historical results. The service is accessible via the NHS N3 secure network and users must securely register on the site before making requests.

The CDRN ERS can be accessed online. User guides can be found under the Help menu.

The electronic requesting and reporting system has been fully operational in all regions for several years and this service is completely electronic. The system employs heightened user notification via email, enabling faster reporting of results to assist outbreak investigation, and enhance data analysis capabilities.

We are collaborating with the UKHSA healthcare-associated infection surveillance team to streamline data collection. The aim is to enable different electronic data collection systems to communicate, and so minimise the duplication of data input by users of the different surveillance schemes.

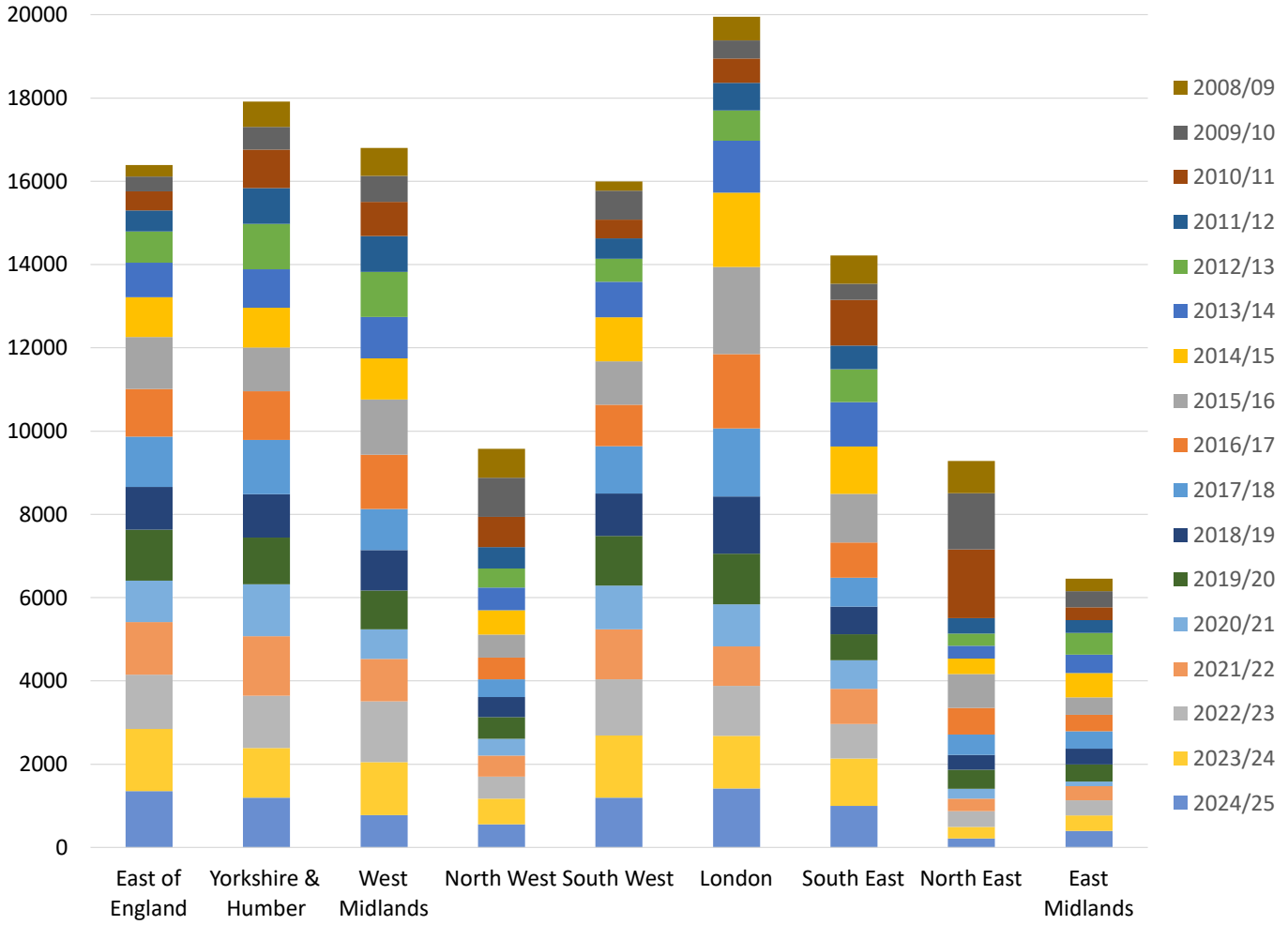
Results for 2023/2024 and 2024/2025

In financial years (FY) 2023 to 2024, and 2024 to 2025, CDRN processed 9,114 faecal samples from 130 healthcare facilities and 8,111 faecal samples from 133 healthcare facilities, respectively.

Data available during this period shows only minor regional differences in the number of samples submitted to the service, relative to those submitted in previous periods (Figure 1). Submissions from the East Midlands, North East and North West regions have been proportionally lower than from other regions.

On average, 70 and 61 samples were submitted to CDRN by each participating hospital in 2023 to 2024 and 2024 to 2025, respectively. On average, 60 samples were submitted to CDRN by each participating hospital in the previous 5-year period 2018 to 2023.

Figure 1. Distribution of CDRN samples submitted to the service (financial years 2008/2009 to 2024/2025)



Financial year	East of England	Yorkshire and Humber	West Midlands	North West	South West	London	South East	North East	East Midlands
2008/09	274	609	669	693	215	571	676	770	297
2009/10	356	542	623	942	699	435	385	1,350	388
2010/11	459	922	824	726	447	586	1,103	1,652	307
2011/12	504	867	860	517	491	657	566	374	308
2012/13	755	1,086	1,086	454	551	728	787	292	522
2013/14	827	924	989	547	857	1,247	1,066	307	444
2014/15	955	958	990	583	1,057	1,790	1,136	371	582
2015/16	1,243	1,052	1,325	555	1,043	2,092	1,172	810	414
2016/17	1,149	1,163	1,304	517	992	1,780	843	642	397
2017/18	1,210	1,304	991	427	1,137	1,640	699	494	424

Financial year	East of England	Yorkshire and Humber	West Midlands	North West	South West	London	South East	North East	East Midlands
2018/19	1,022	1,041	970	485	1,019	1,368	660	353	378
2019/20	1,224	1,122	933	521	1,196	1,216	622	459	405
2020/21	995	1,249	709	403	1,046	1,014	692	238	116
2021/22	1,265	1,428	1,018	500	1,204	944	839	297	334
2022/23	1,308	1,259	1,459	531	1,353	1,201	836	378	363
2023/24	1,491	1,192	1,269	618	1,489	1,270	1,133	277	375
2024/25	1,352	1,195	781	556	1,197	1,414	1,000	218	398

It should be noted that an epidemiological study took place in the North East region during 2009 to 2011, which accounts for the larger numbers of samples processed here in these years.

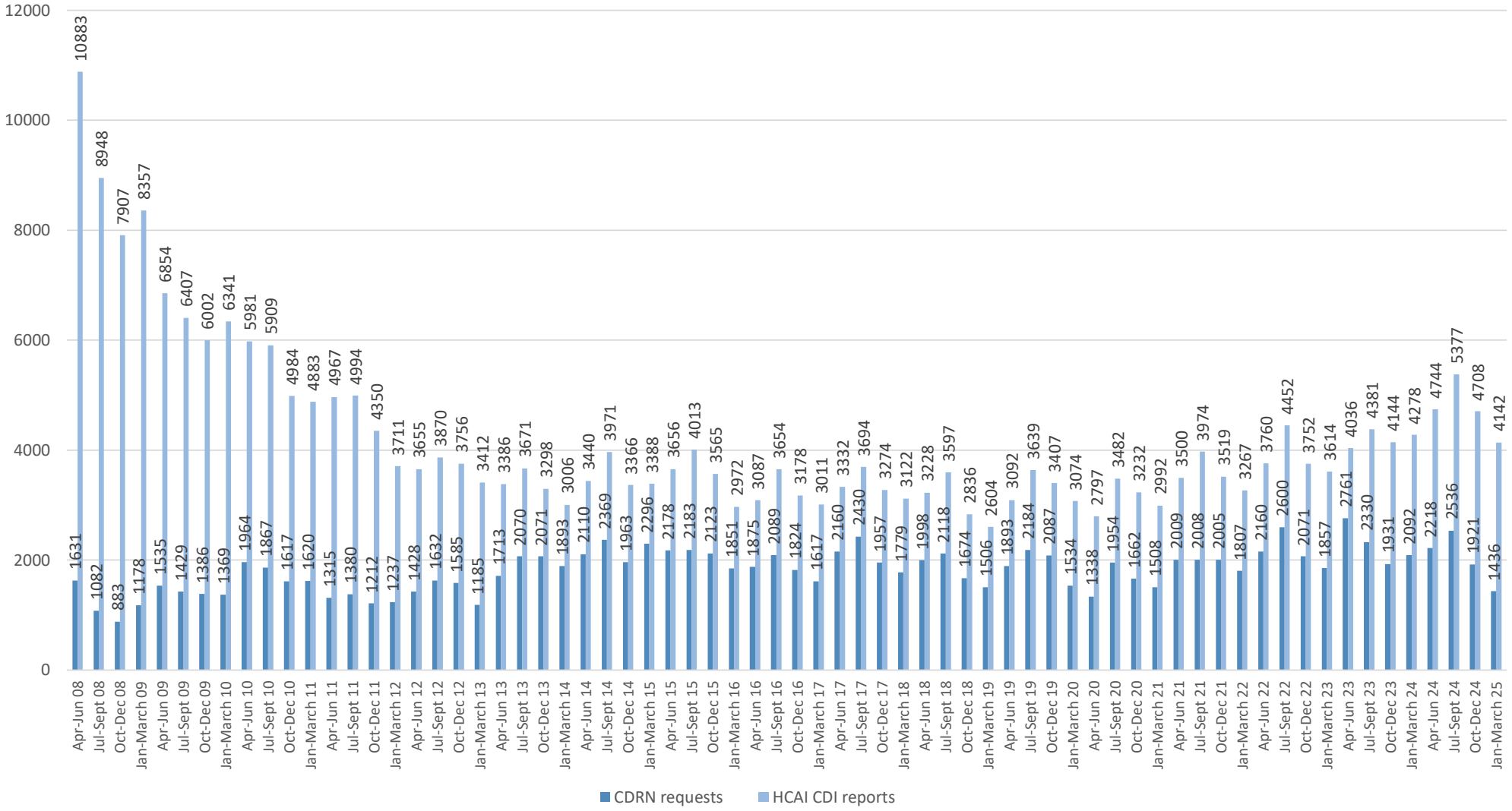
Proportion of mandatory CDI reported cases ribotyped

Figure 2 below shows the ribotyping sample submission to CDRN by quarter, expressed as the proportion of mandatory *C. difficile* (all reported cases) on the Mandatory HCAI Data Capture System (DCS) in England from April 2008 to March 2025.

The overall average annual proportion of *C. difficile* reported cases from whom samples were sent for ribotyping over the whole analysis period 2008 to 2025 was 47.7% (43.4% over the historical data period 2008/2009 to 2017/2018, 53.8% over the last 7 years (2018/2019 to 2024/2025), and 48.3% over the last 2 financial years (2023 to 2024, 2024 to 2025).

Usage of CDRN, expressed both in crude numbers and in terms of the proportion of all reported cases that are referred, has increased markedly since the service was launched. This data indicates that currently approximately one in every 2 reported cases of CDI are referred to CDRN for typing.

Figure 2. Proportion of HCAI CDI cases submitted for ribotyping to All Reported Cases of CDI to UKHSA (2008/09 to 2024/25)



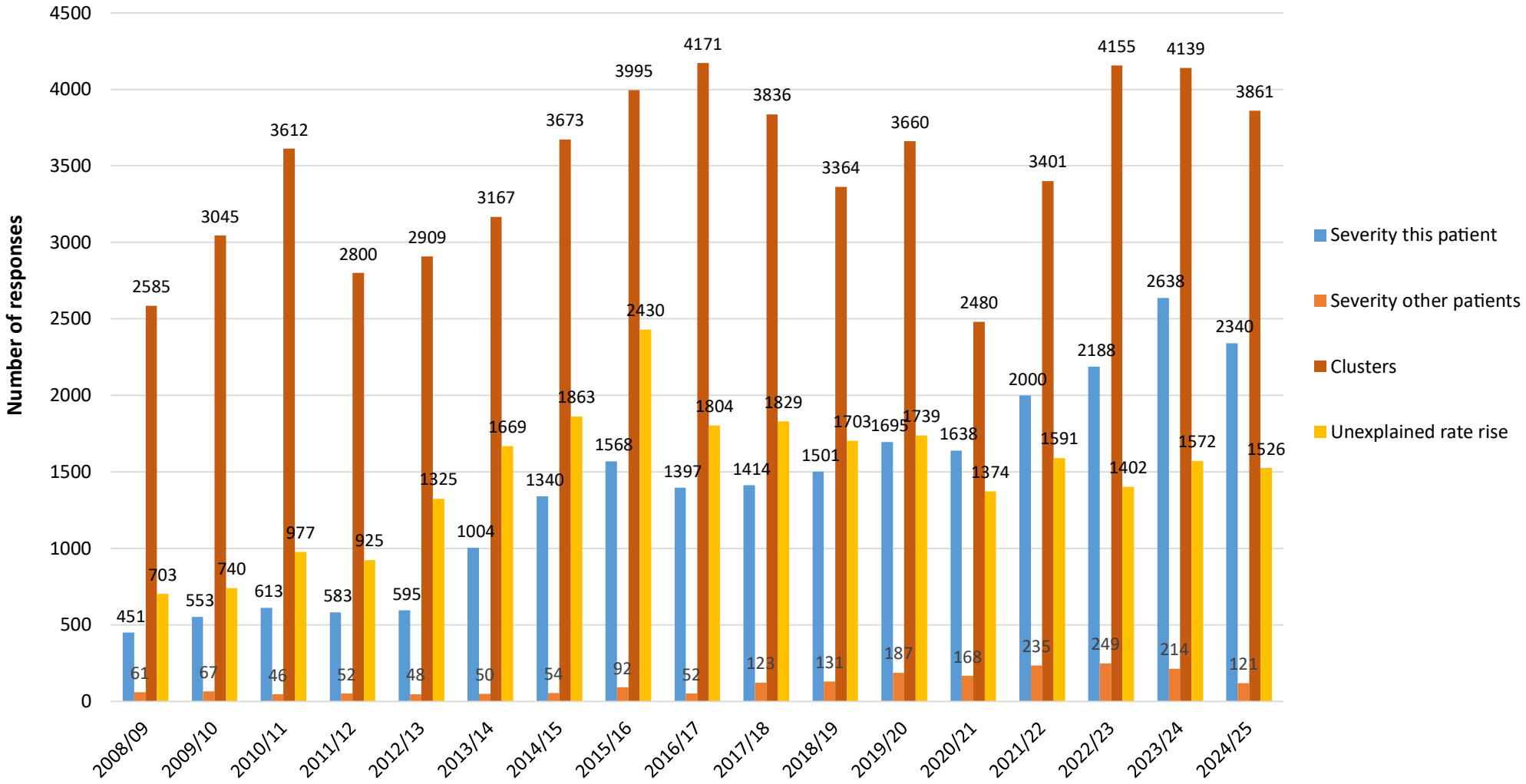
Reasons for sample submission to CDRN service

Samples submitted to CDRN are in response to clinical need. The reasons provided for sample submission are shown in Figure 3.

The most common reason cited for sample submission during the last 2 financial years (2023/2024 to 2024/2025), the last 7 years (2018/2019 to 2024/2025) and during the historical period (2008/2009 to 2017/2018) was clustering of cases (46.4%, 45.4% and 47.4% of all submissions cited this as a reason, respectively). Unexplained increase in CDI rate was cited as a reason for submission in 18.0% of cases during the last 2 years, 19.8% during the last 7 years, and in 20.0% during the historical period.

Notably, submissions associated with severity of symptoms of CDI in the affected patient and in other patients has increased to 27.7% during the last 7 years (13.3% historically, 30.8% last 2 years).

Figure 3. Reason for sample submission to CDRN (2008/09 to 2024/25)



C. difficile recovery rate

Table 1 shows *C. difficile* recovery rates for samples submitted to the service since 2008/09. This data excludes samples not processed or rejected (insufficient sample, duplicates and so on). There was a 29% increase between 2007/2008 and 2008/2009 in the proportion of faecal samples submitted to CDRN that were *C. difficile* culture-negative (that is, from 9.6% to 12.4%). This change may have reflected more false-positive samples (CDRN examines samples presumed to have tested toxin-positive at the source laboratory).

Notably, the *C. difficile* recovery rate progressively increased in the early CDRN years, and has remained stably high (at more than 91% since FY 2011/2012 and more than 93% since FY 2023/2024). This data is consistent with improved and then relatively effective laboratory diagnosis of CDI. Guidelines for the diagnosis of CDI were updated in 2025 (10).

Table 1. *C. difficile* recovery rate (financial years 2008/2009 to 2023/2025)

Year	Total samples	*C. difficile* growth	Recovery rate
2008/2009	4,774	4,175	87.45%
2009/2010	5,720	4,995	87.33%
2010/2011	7,026	6,202	88.27%
2011/2012	5,144	4,761	92.55%
2012/2013	5,830	5,523	94.73%
2013/2014	7,208	6,781	94.08%
2014/2015	8,124	7,609	93.66%
2015/2016	8,931	8,335	93.33%
2016/2017	7,880	7,405	93.97%
2017/2018	7,585	7,079	93.33%
2018/2019	6,717	6,272	93.38%
2019/2020	6,995	6,514	93.12%
2020/2021	5,664	5,198	91.77%
2021/2022	6,934	6,335	91.36%
2022/2023	7,686	7,116	92.58%
2023/2024	8,215	7,704	93.78%
2024/2025	7,347	6,976	94.95%

Ribotype distribution

Figure 5A indicates historic ribotype prevalence nationally, by quarter (April 2008 to March 2018). Ribotypes with more than 2% prevalence are shown separately (prevalence less than 2% are shown together in green, marked “sporadic”). Figure 5B indicates the most prevalent ribotypes (more than 5%) during the past 7 years (April 2018 to March 2025). Figure 5C indicates the most prevalent ribotypes (more than 5%) associated with severe CDI symptoms (that is, those samples where severity of symptoms of CDI in the affected patient was cited as the reason for submission). These data are displayed regionally in Figure 6.

Historically, there has been a striking decrease in the prevalence of *C. difficile* ribotype 027, and also in ribotypes 001 and 106, with ‘compensatory’ increases in other types. Data presented here would suggest that in some regions, ribotype 027 has almost completely disappeared (some persistence observed in the North West, albeit not for the latest reporting period 2023 to 2025, Figure 6). With increased sample submission to CDRN, such an effect may be expected to accompany an increase in the relative contribution of other ‘emergent’ *C. difficile* ribotypes to overall disease burden. Notably, the pattern of ribotypes in England has become markedly more heterogeneous (625 distinct ribotypes reported within last 7 years).

The relative prevalence rates for individual ribotypes have remained reasonably stable nationally and within regions between April 2018 and March 2025. Thus the recent increase in CDI incidence does not appear to be related to a change in relative ribotype prevalences (2). Overall, ribotypes 002, 015, 014, 005, 020, 023 and 078 have become, and remain the most prevalent types in England (11.4%, 10.6%, 10.2%, 9.1%, 6.3%, 5.4%, and 4.5%, respectively) during this period.

During the 2-year reporting period between April 2023 and March 2025, ribotypes 015, 002, 014, 005, 023 and 020 were also the most prevalent (11.3%, 11.2%, 10.1%, 9.6%, 6.2%, and 6.0%, respectively) types in England. Notably, these ribotypes are also those most commonly identified in patients with severe CDI symptoms.

A new emerging *C. difficile* strain ribotype 955 with 027-like characteristics remained a low prevalent type in England (0.23%) during the 2-year reporting period between April 2023 and March 2025 (with some persistence in the West Midlands, through to the last quarter of the 2-year reporting period, Figure 6) (11). (Also see Enhanced fingerprinting section).

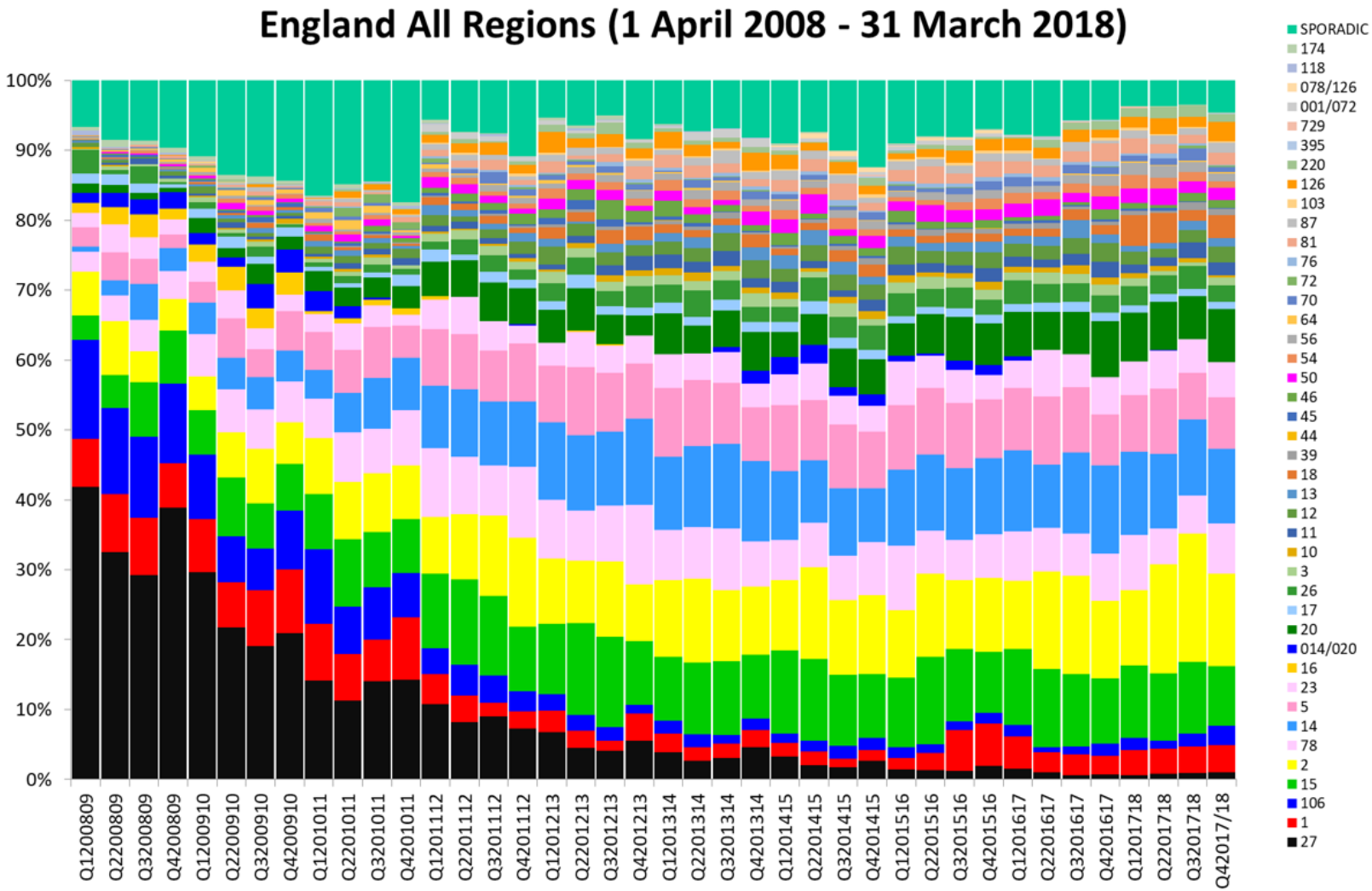
As part of the European, multicentre, prospective, biannual, point-prevalence study of *C. difficile* infection in hospitalised patients with diarrhoea (EUCLID), the largest *C. difficile* epidemiological study of its type, PCR ribotype distribution of *C. difficile* isolates in Europe was determined on 1,196 *C. difficile* isolates from diarrhoeal samples sent to the European coordinating laboratory in 2012 to 2013 and 2013 (from 2 sampling days) by 482 participating hospitals from 19 European countries (12). 125 distinct ribotypes were identified, with considerable intercountry

variation in ribotype distribution. Ribotypes 027 (19%), 001/072 (11%) and 014/020 (10%) were the most prevalent, followed by ribotypes 002, 140, 010, 078, 176 and 018 (each less than 5%). The prevalence of ribotypes 027 and 176, but not other epidemic strains, was inversely proportional to overall ribotype diversity (R2 = 0.717).

Importantly, there is increasing evidence that there are 2 distinct patterns of *C. difficile* ribotype spread (see Enhanced fingerprinting section).

Figure 5. Prevalence of *C. difficile* ribotypes in England (all regions) by quarter (April 2008 to March 2025); (A) April 2008 to March 2018 (more than 2% prevalence); (B) April 2018 to March 2025 (more than 5% prevalence); (C) April 2018 to March 2025 (more than 5% prevalence in patients with severe CDI)

A



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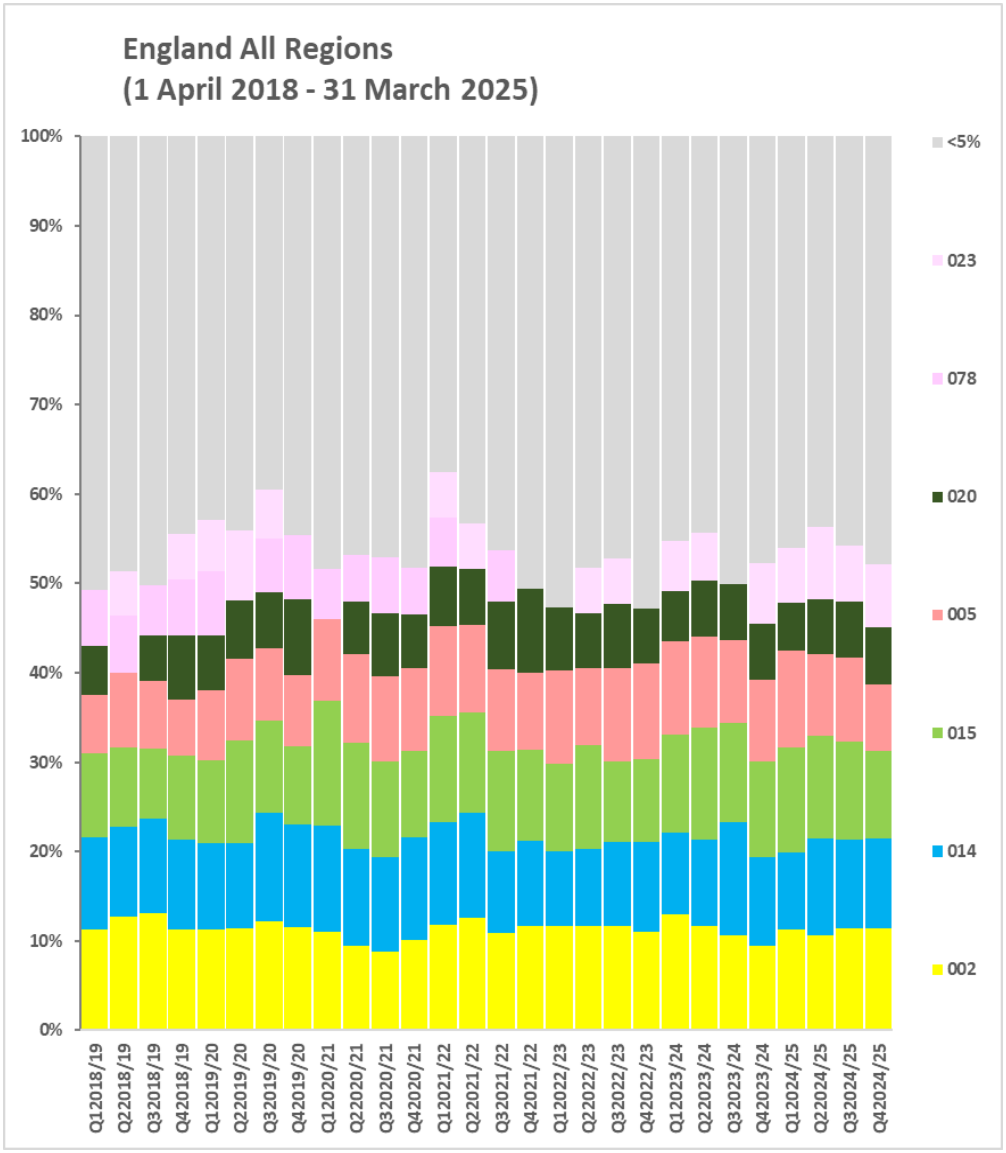
England All Regions
(1 April 2018 - 31 March 2025)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
<5%
023
078
020
005
015
014
002
Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
Q32020/21
Q42020/21
Q12021/22
Q22021/22
Q32021/22
Q42021/22
Q12022/23
Q22022/23
Q32022/23
Q42022/23
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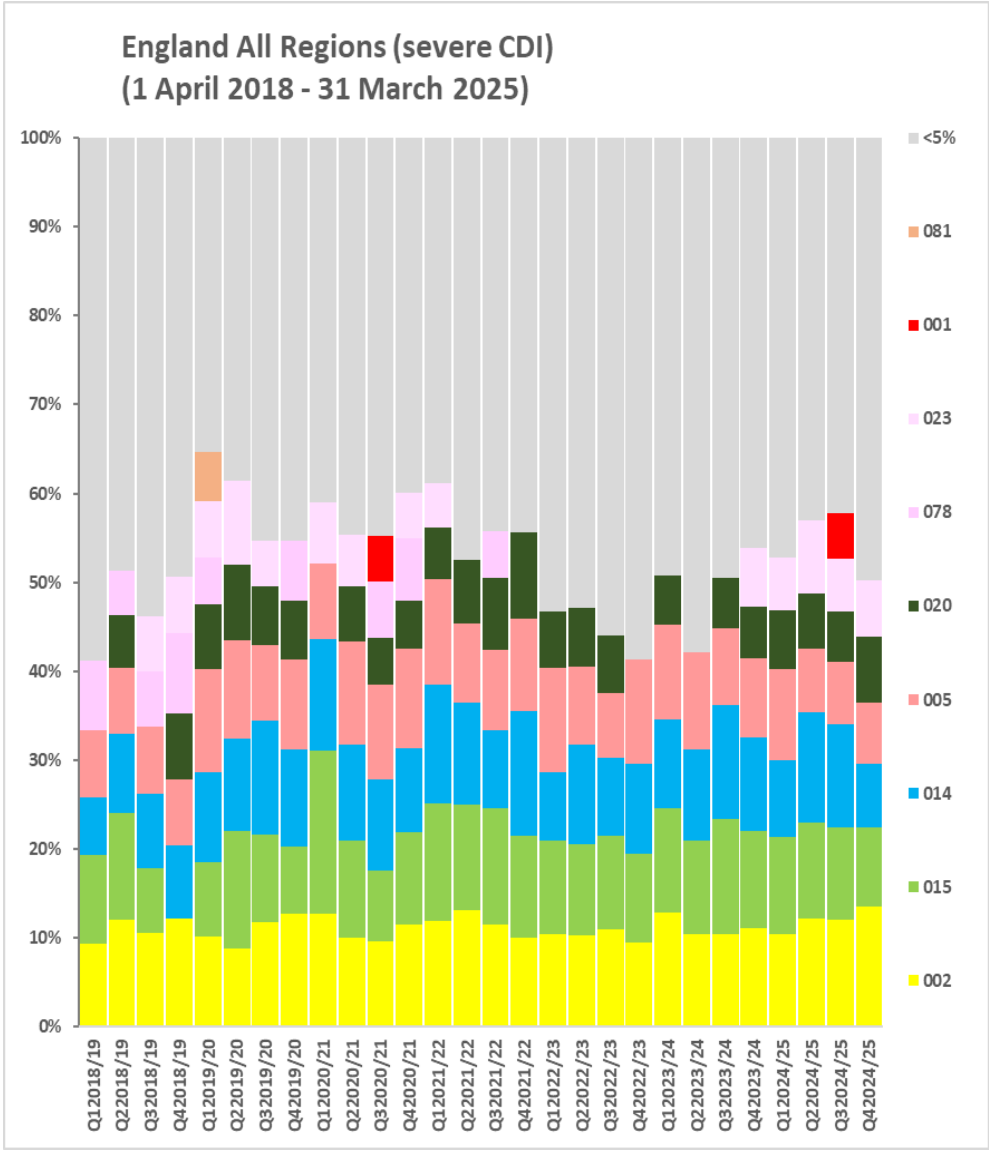
Q42024/25

C


England All Regions (severe CDI)
(1 April 2018 - 31 March 2025)
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
<5%
081
001
023
078
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002
Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
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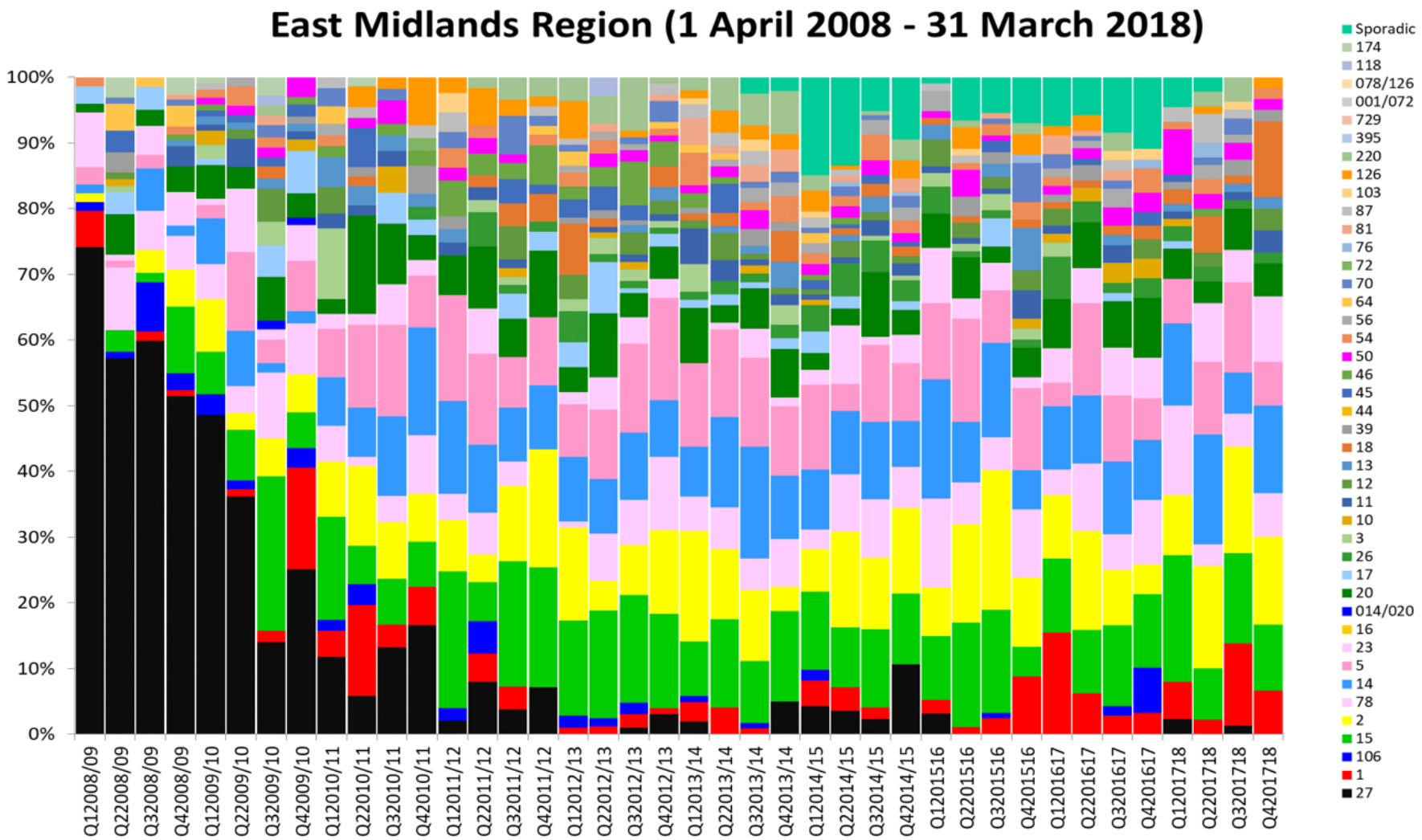
Q12023/24
Q22023/24
Q32023/24
Q42023/24
Q12024/25
Q22024/25
Q32024/25
Q42024/25

Figure 6. Distribution of PCR-ribotypes according to England region (April 2008 to March 2025); (A) April 2008 to March 2018 (more than 2% prevalence); (B) April 2018 to March 2025 (more than 5% prevalence); (C) April 2018 March 2025 (more than 5% prevalence in patients with severe CDI)

A



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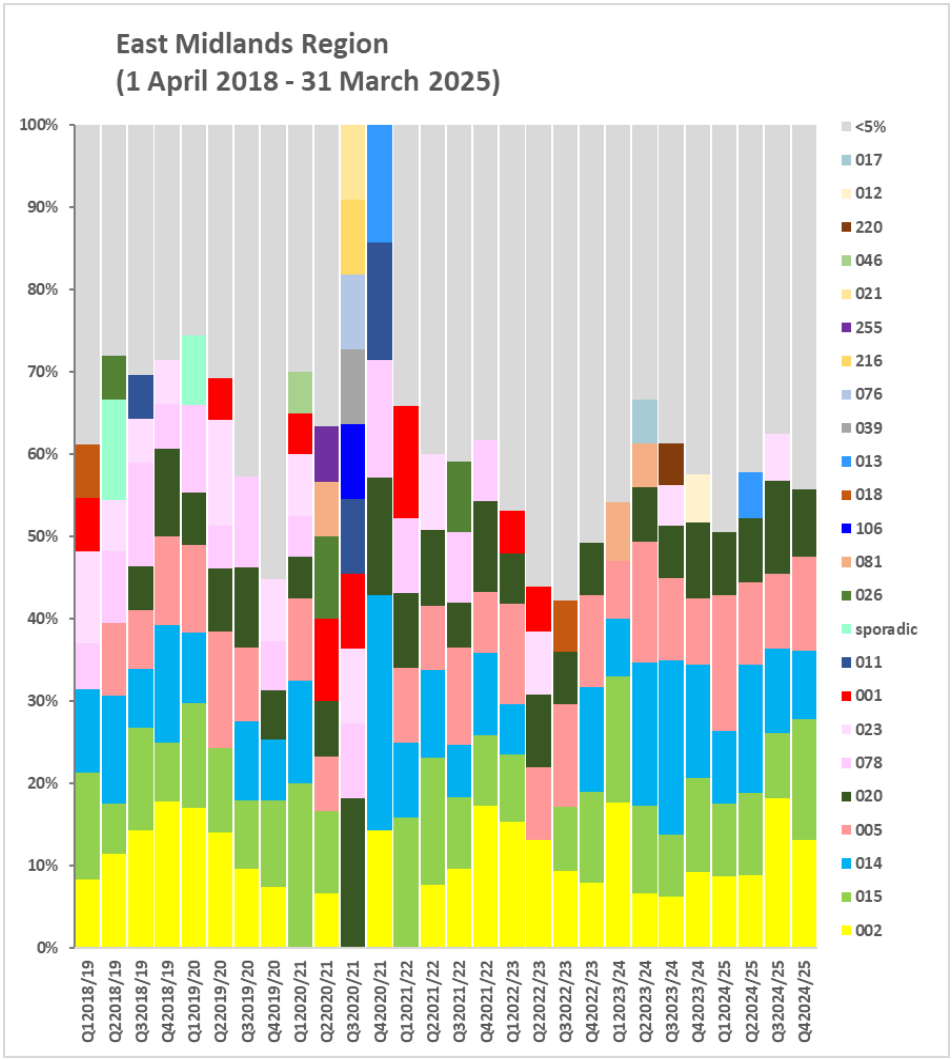
East Midlands Region
(1 April 2018 - 31 March 2025)
100%
90%
80%
70%
60%
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20%
10%
0%
Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
Q32020/21
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017
012
220
046
021
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081
026
sporadic
011
001
023
078
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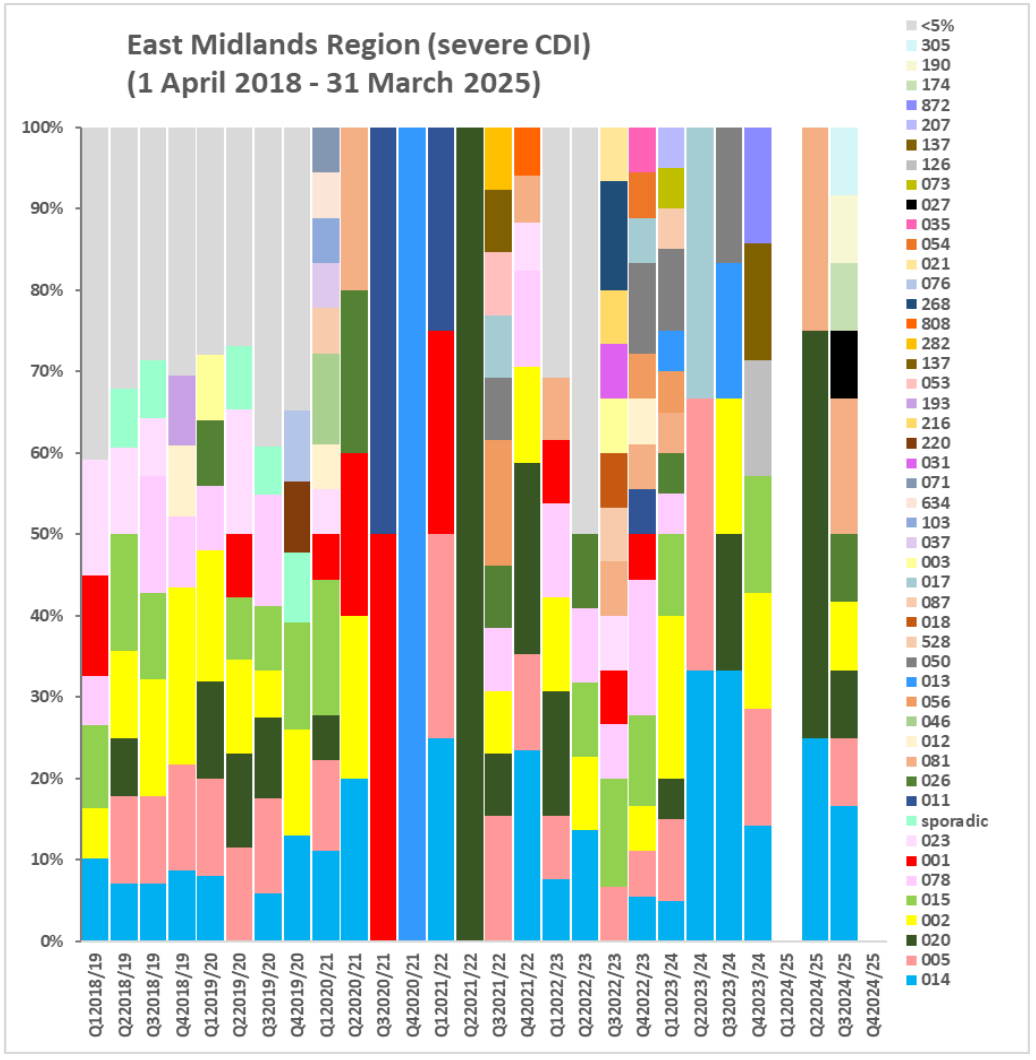
005
014
015
002

C


East Midlands Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
90%
80%
70%
60%
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30%
20%
10%
0%
Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
Q32020/21
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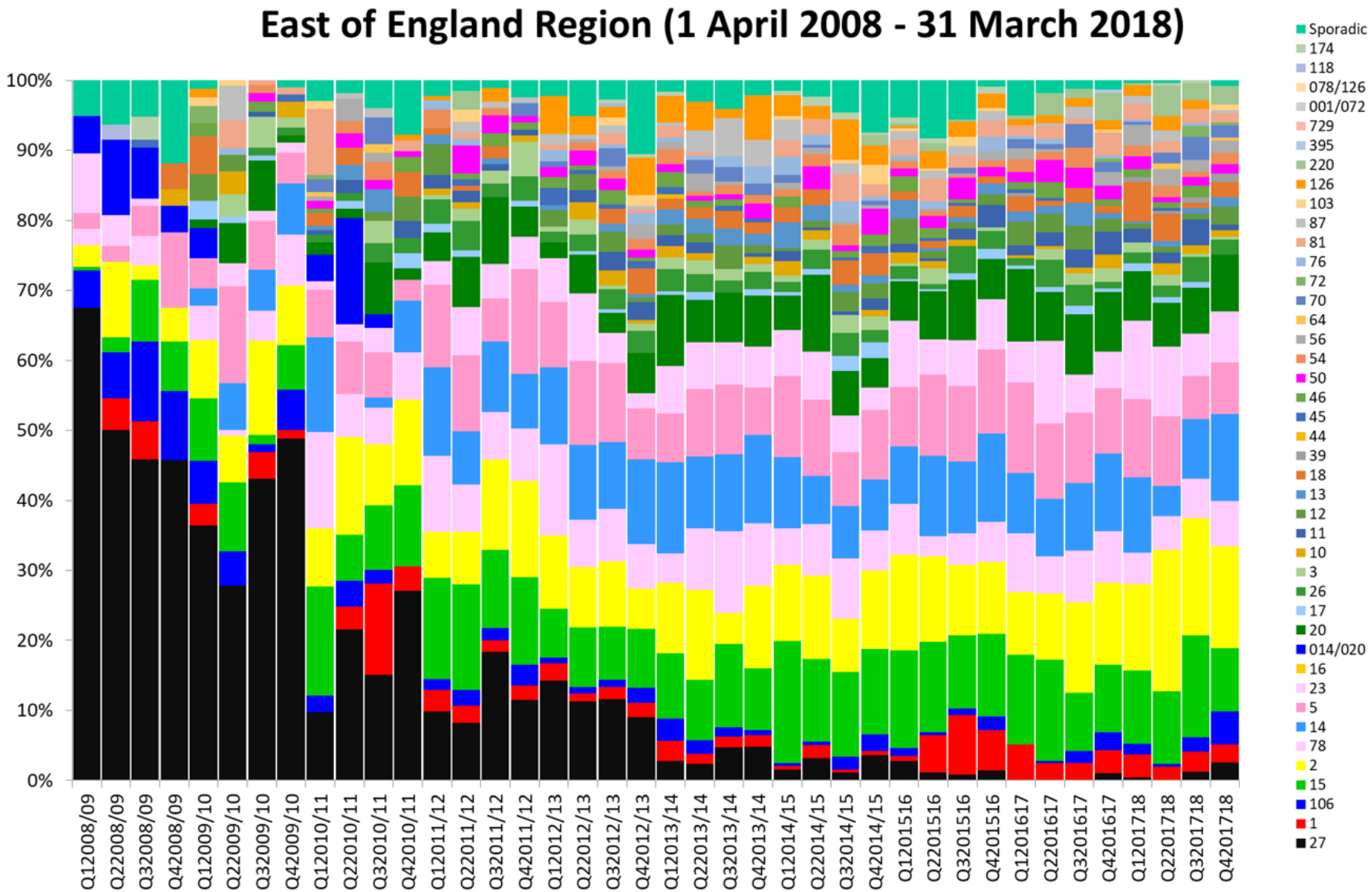
East of England Region (1 April 2008 - 31 March 2018)
100%
90%
80%
70%
60%
50%
40%
30%
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Q12008/09
Q22008/09
Q32008/09
Q42008/09
Q12009/10
Q22009/10
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Q42009/10
Q12010/11
Q22010/11
Q32010/11
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103
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76
72
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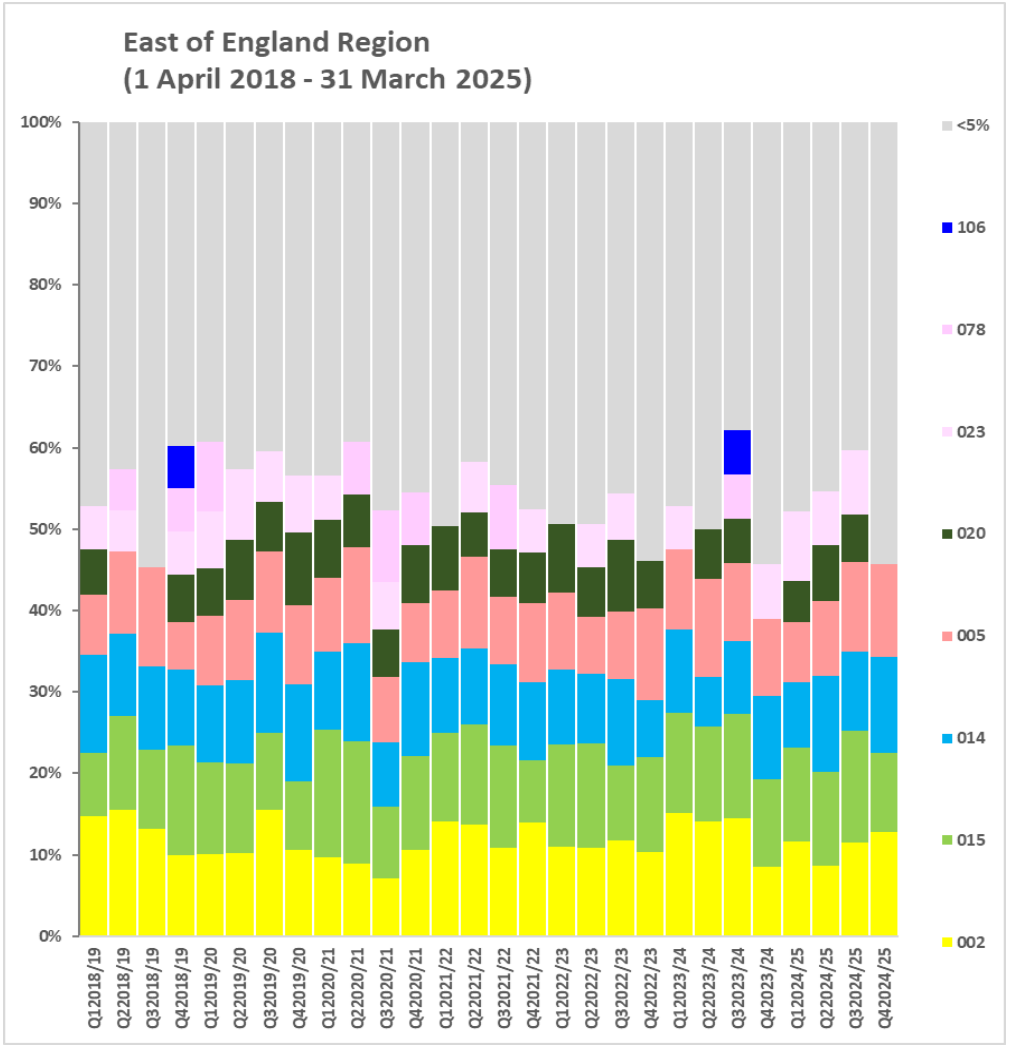
East of England Region
(1 April 2018 - 31 March 2025)
100%
90%
80%
70%
60%
50%
40%
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20%
10%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
Q32020/21
Q42020/21
Q12021/22
Q22021/22
Q32021/22
Q42021/22
Q12022/23
Q22022/23
Q32022/23
Q42022/23
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Q22023/24
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Q42023/24
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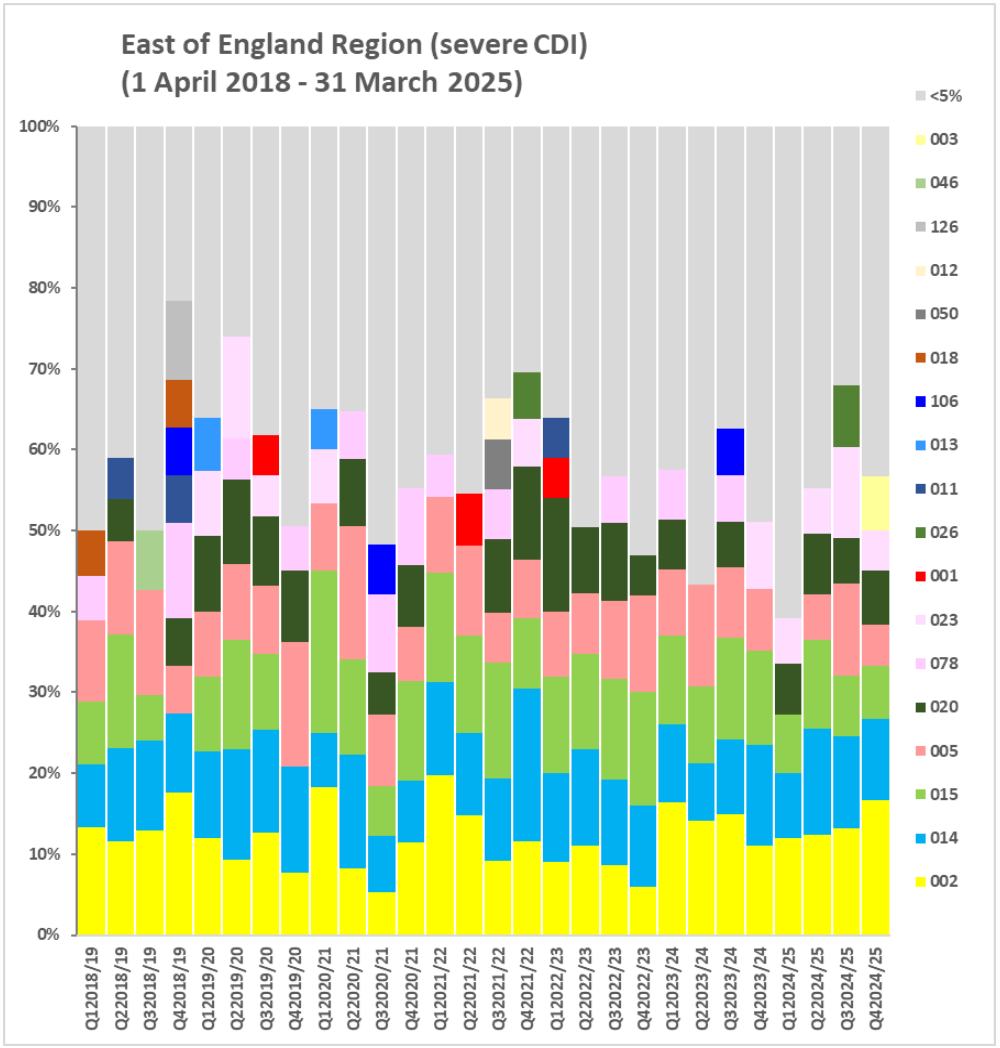
East of England Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
90%
80%
70%
60%
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40%
30%
20%
10%
0%
Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
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Q42021/22
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Q22023/24
Q32023/24
Q42023/24
Q12024/25
Q22024/25
Q32024/25
Q42024/25
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003
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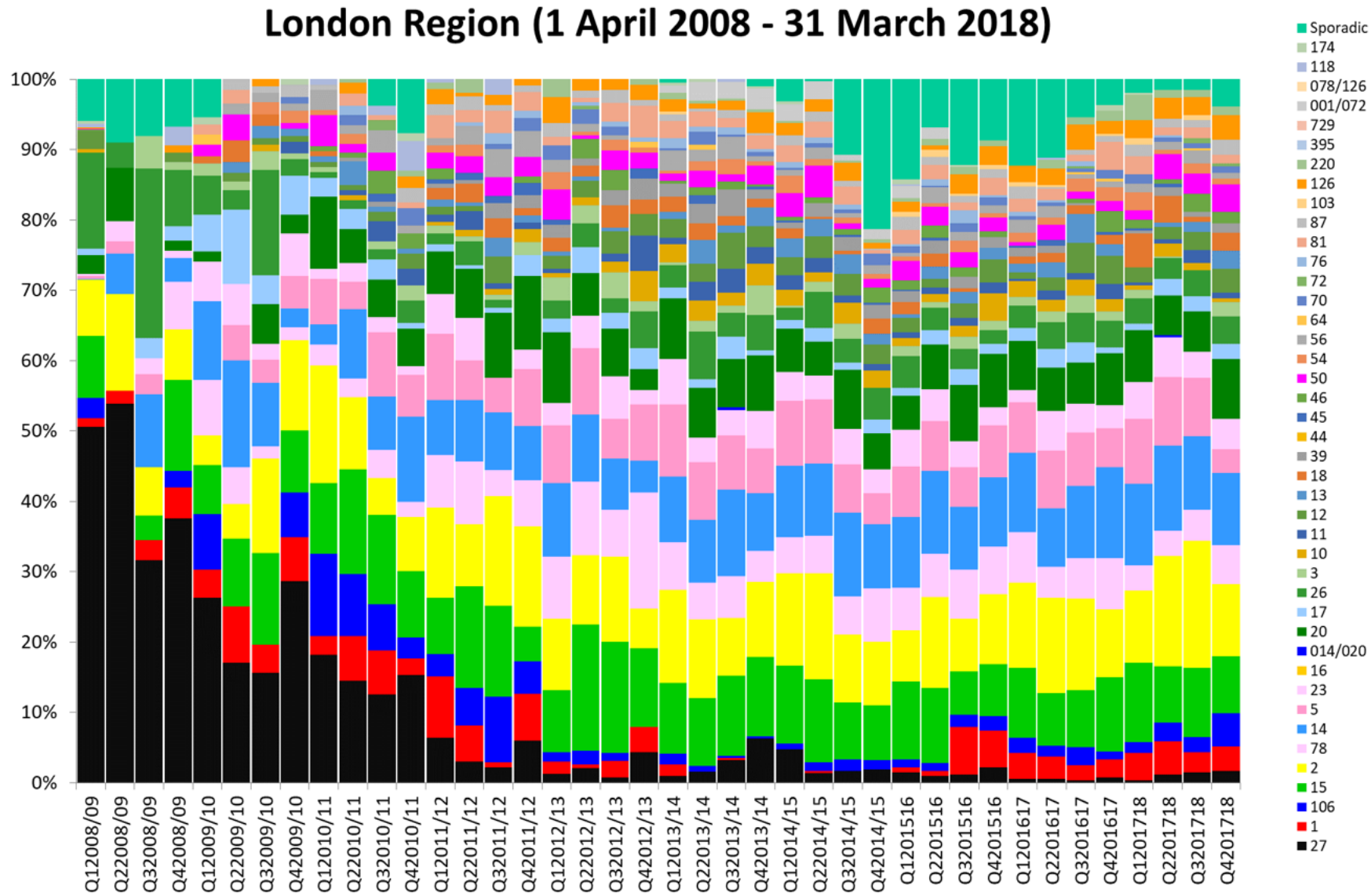
London Region (1 April 2008 - 31 March 2018)
100%
90%
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70%
60%
50%
40%
30%
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10%
0%
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Q22008/09
Q32008/09
Q42008/09
Q12009/10
Q22009/10
Q32009/10
Q42009/10
Q12010/11
Q22010/11
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Q12011/12
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Q42011/12
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Q22014/15
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Q42014/15
Q1201516
Q2201516
Q3201516
Q4201516
Q1201617
Q2201617
Q3201617
Q4201617
Q1201718
Q2201718
Q3201718
Q4201718
Sporadic
174
118
078/126
001/072
729
395
220
126
103
87
81
76
72
70
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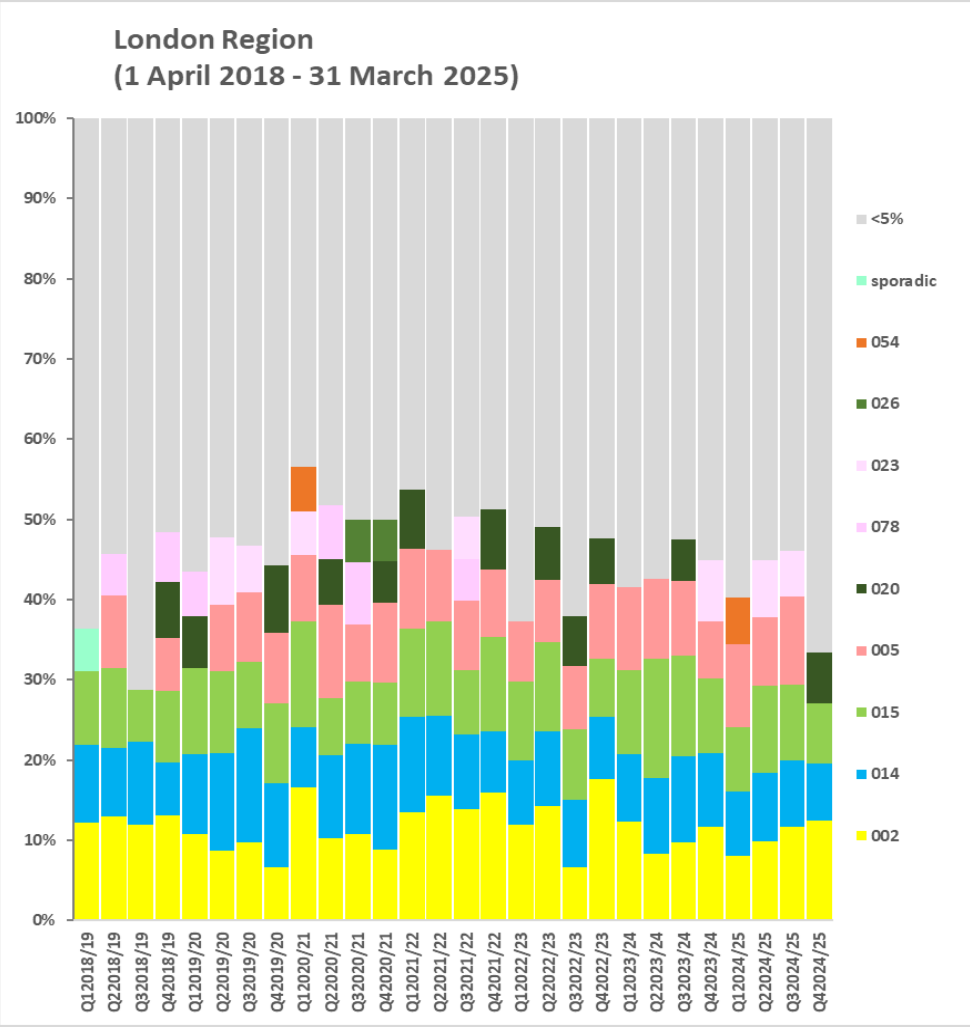
London Region
(1 April 2018 - 31 March 2025)
100%
90%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
Q32020/21
Q42020/21
Q12021/22
Q22021/22
Q32021/22
Q42021/22
Q12022/23
Q22022/23
Q32022/23
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Q12024/25
Q22024/25
Q32024/25
Q42024/25
<5%
sporadic
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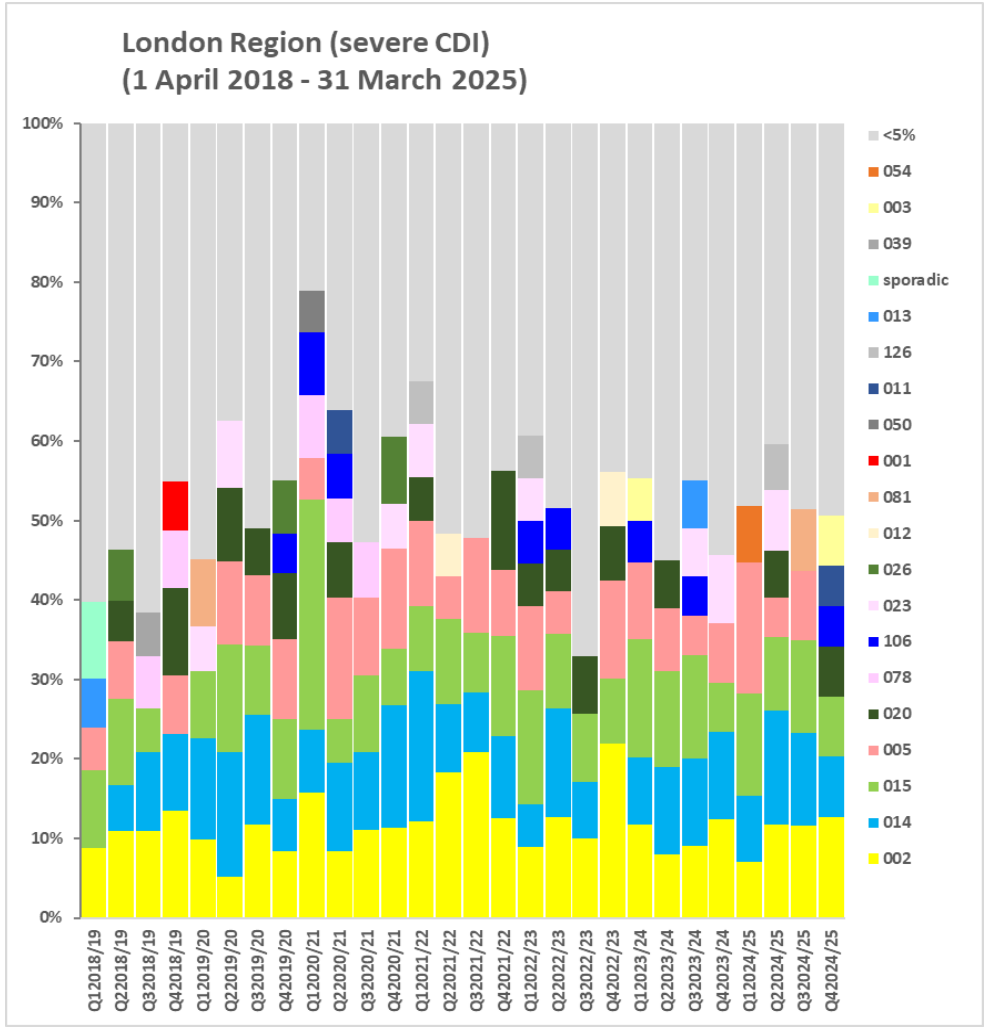
C


London Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
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Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
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Q12024/25
Q22024/25
Q32024/25
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<5%
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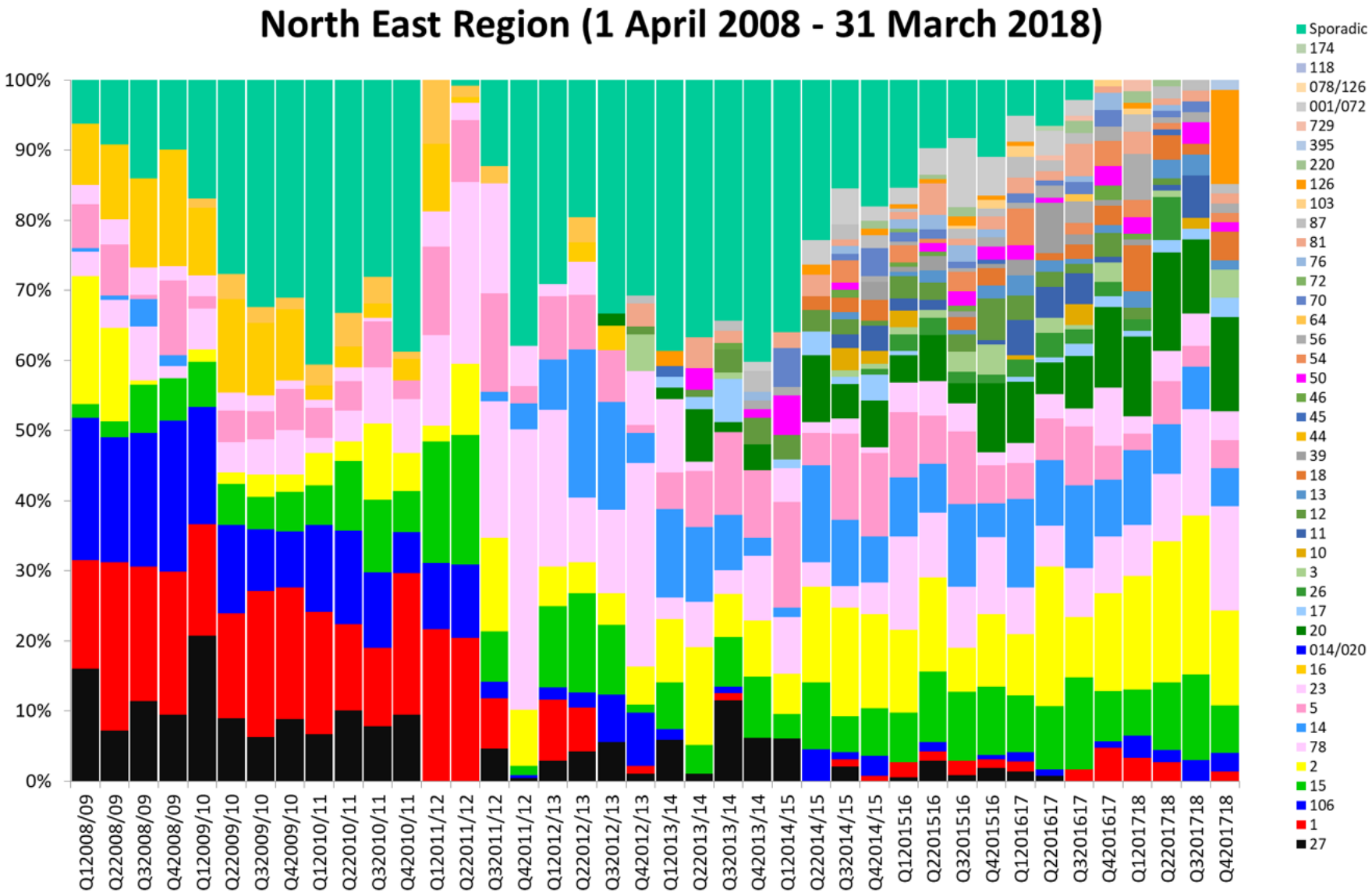
North East Region (1 April 2008 - 31 March 2018)
100%
90%
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Q12008/09
Q22008/09
Q32008/09
Q42008/09
Q12009/10
Q22009/10
Q32009/10
Q42009/10
Q12010/11
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Q22014/15
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Q42014/15
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Q2201617
Q3201617
Q4201617
Q1201718
Q2201718
Q3201718
Q4201718
Sporadic
174
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001/072
729
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70
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56
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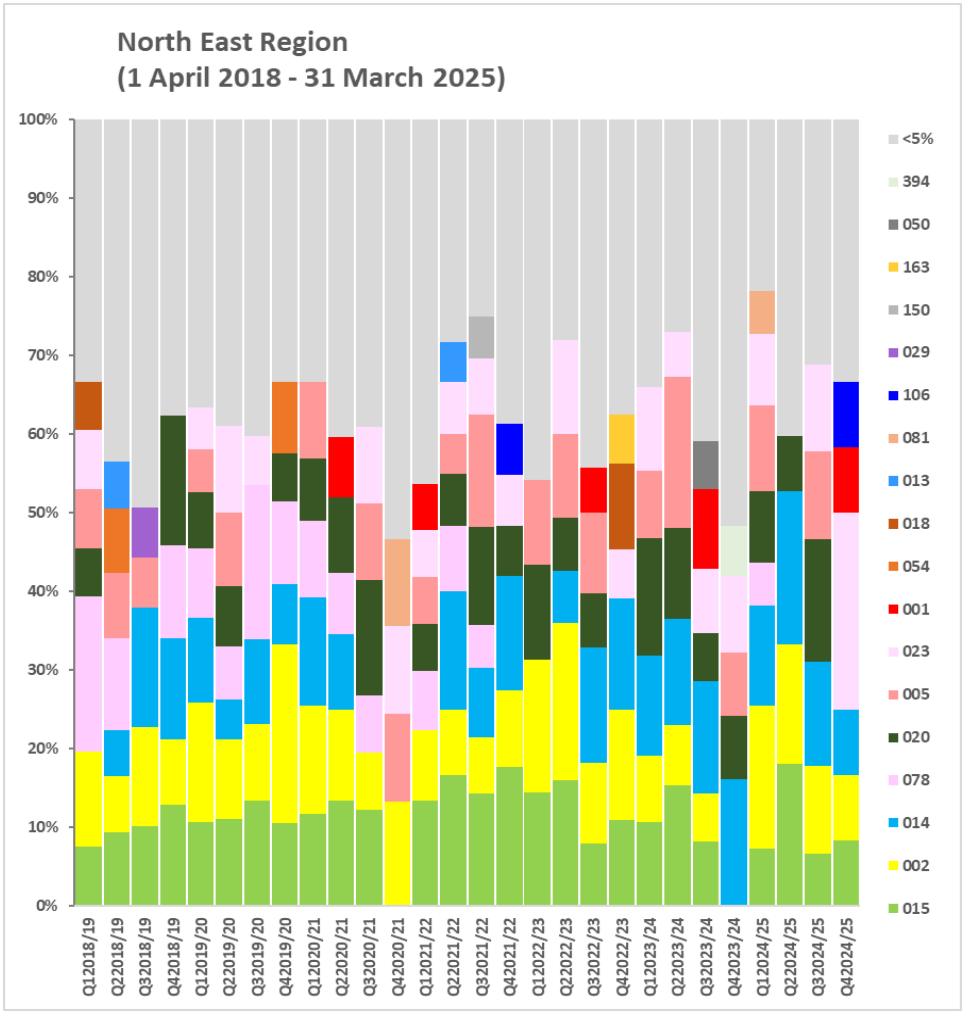
North East Region
(1 April 2018 - 31 March 2025)
100%
90%
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Q12018/19
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Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
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Q42021/22
Q12022/23
Q22022/23
Q32022/23
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Q42024/25
<5%
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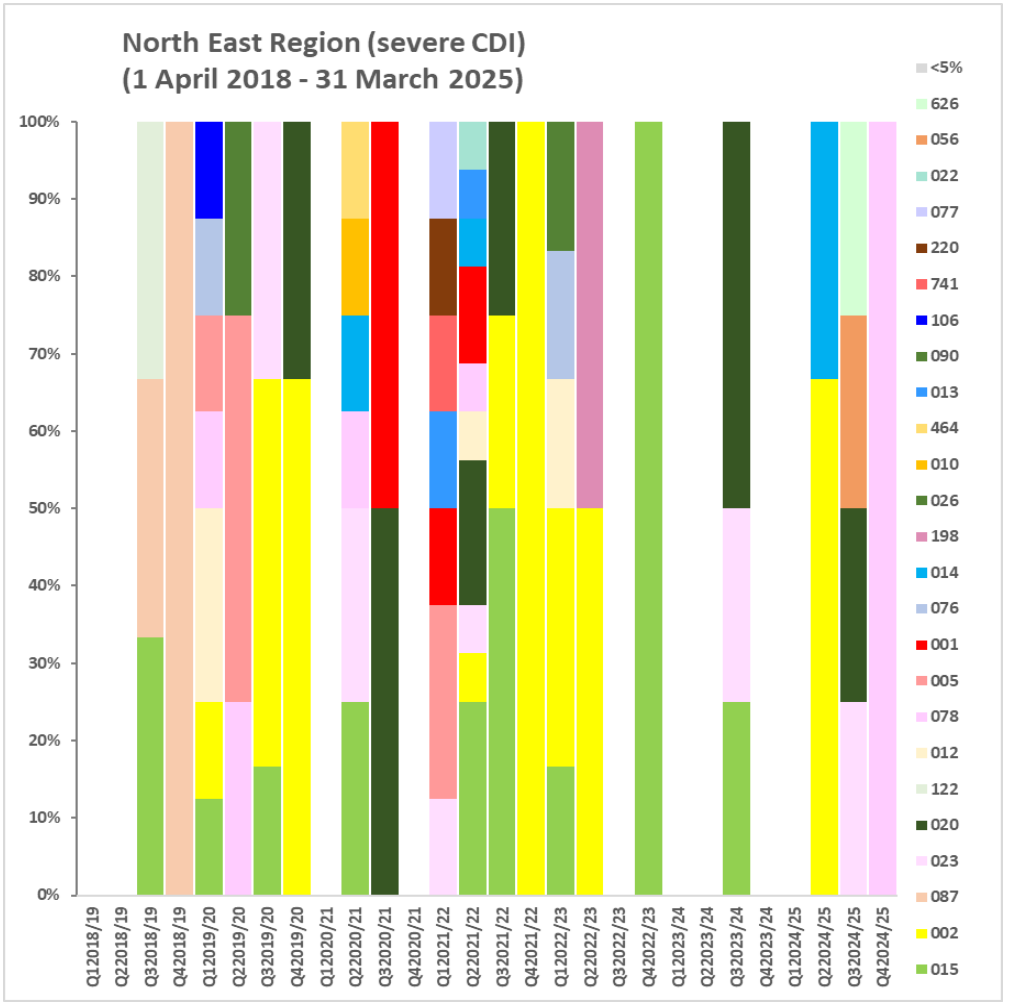
North East Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
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Q42022/23
Q12023/24
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Q32023/24
Q42023/24
Q12024/25
Q22024/25
Q32024/25
Q42024/25
<5%
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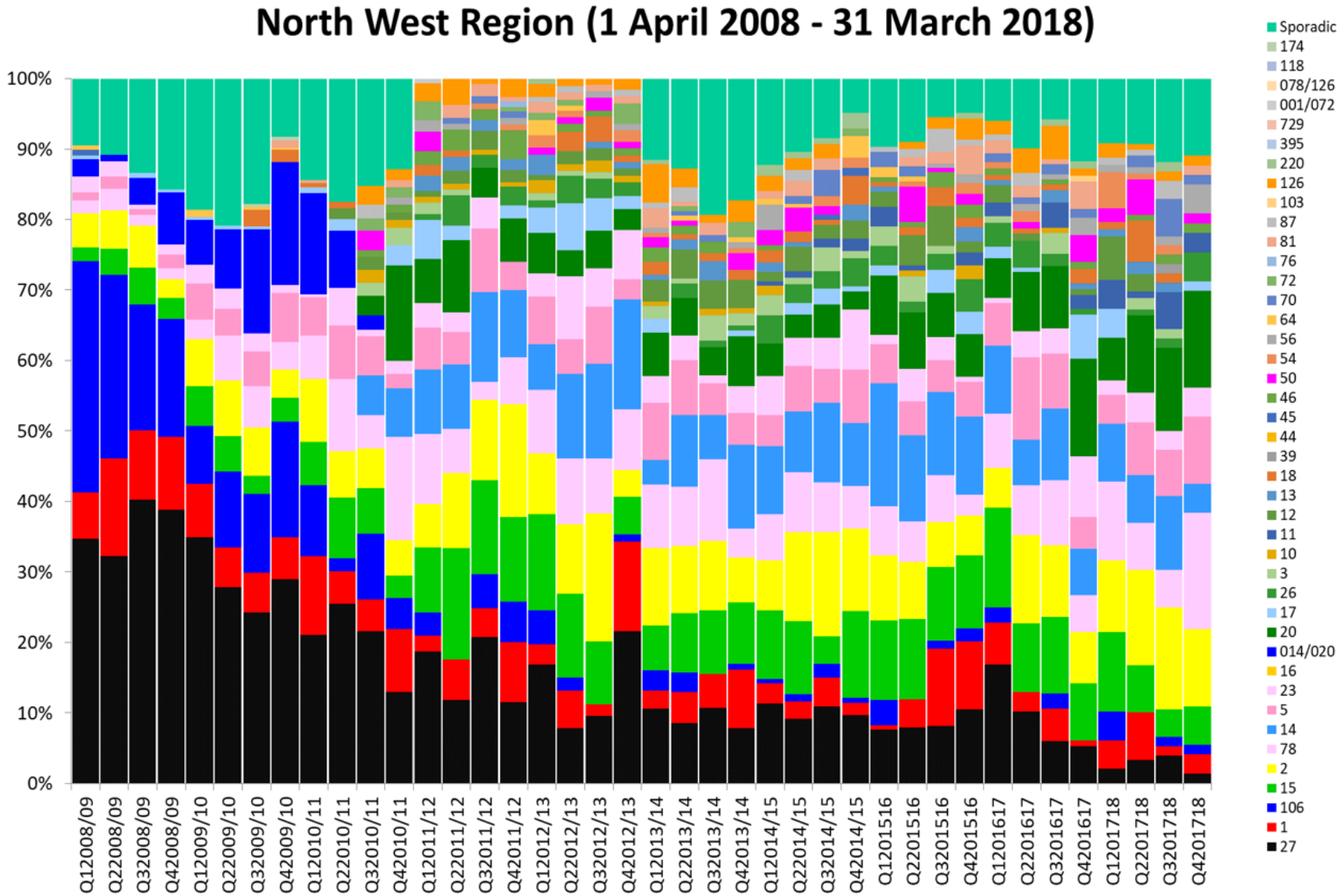
North West Region (1 April 2008 - 31 March 2018)
100%
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Q12008/09
Q22008/09
Q32008/09
Q42008/09
Q12009/10
Q22009/10
Q32009/10
Q42009/10
Q12010/11
Q22010/11
Q32010/11
Q42010/11
Q12011/12
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Q32011/12
Q42011/12
Q12012/13
Q22012/13
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Q42012/13
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Q42013/14
Q12014/15
Q22014/15
Q32014/15
Q42014/15
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Q4201516
Q1201617
Q2201617
Q3201617
Q4201617
Q1201718
Q2201718
Q3201718
Q4201718
Sporadic
174
118
078/126
001/072
729
395
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70
64
56
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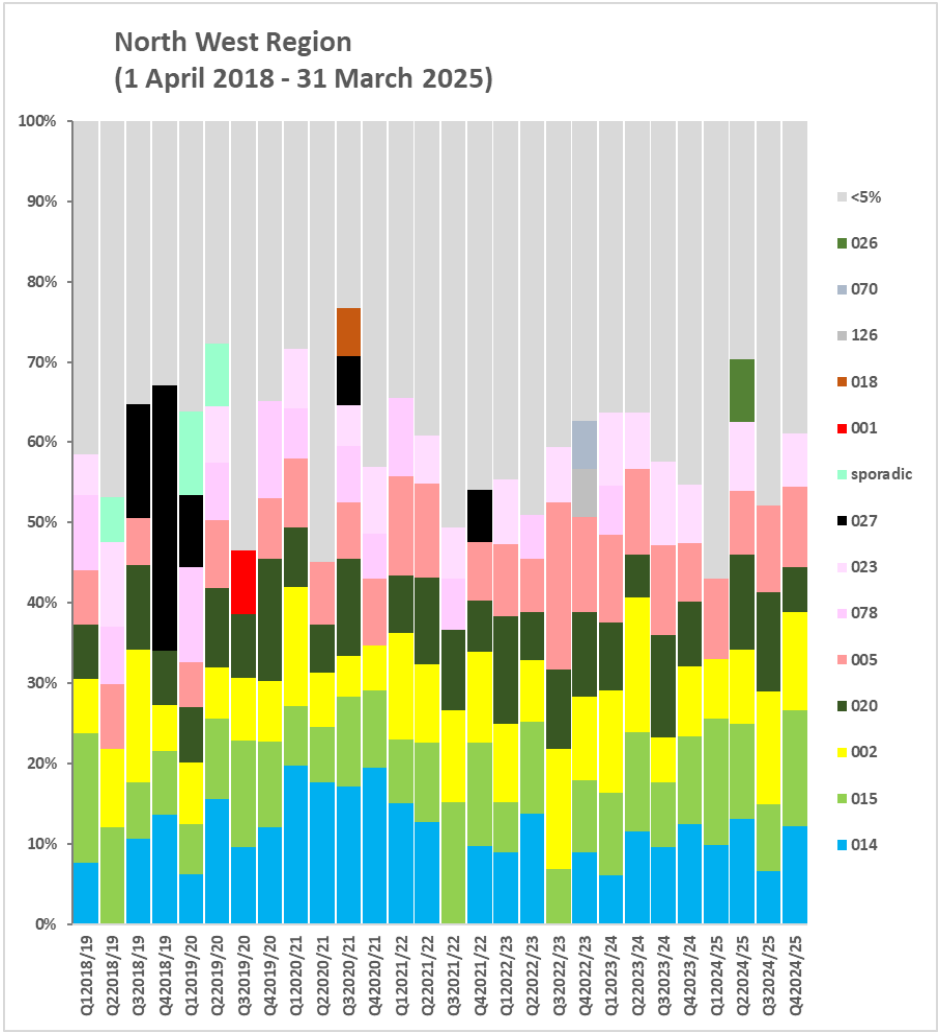
B


North West Region
(1 April 2018 - 31 March 2025)
100%
90%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
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Q42020/21
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Q42021/22
Q12022/23
Q22022/23
Q32022/23
Q42022/23
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Q32023/24
Q42023/24
Q12024/25
Q22024/25
Q32024/25
Q42024/25
<5%
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sporadic
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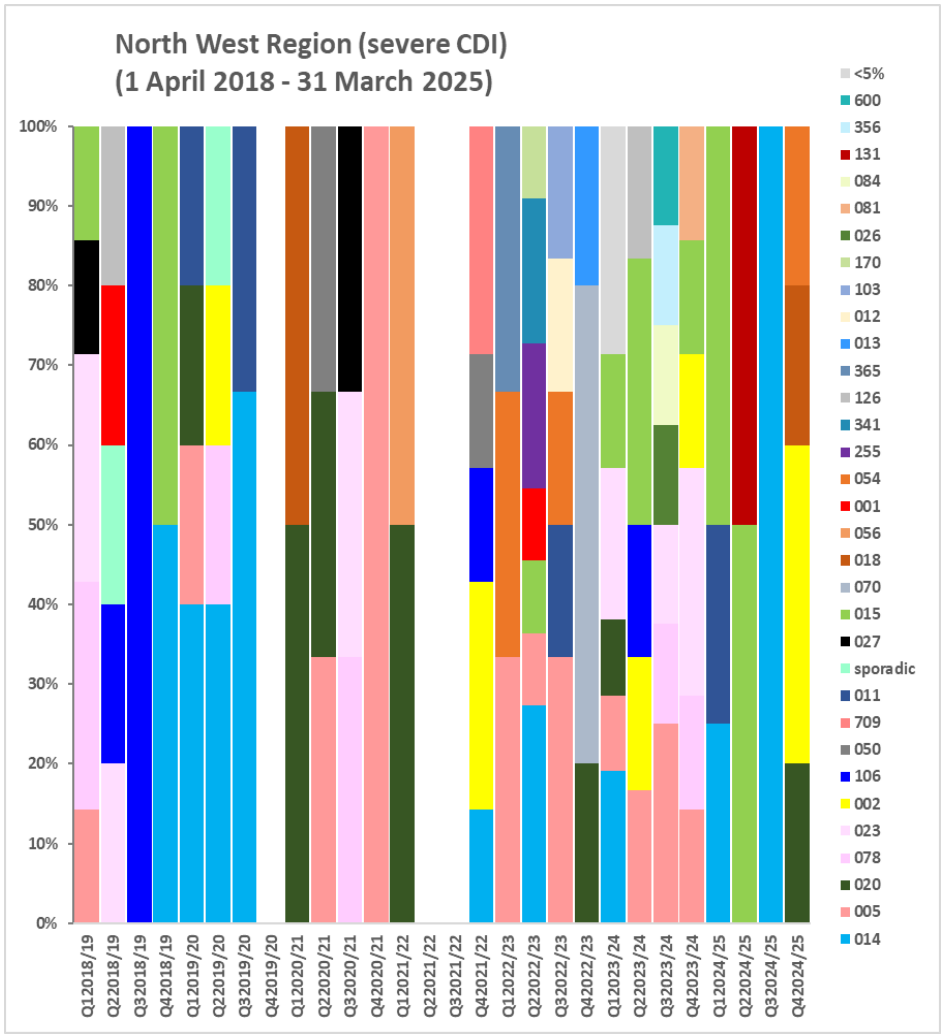
C


North West Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
90%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
Q32020/21
Q42020/21
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Q32023/24
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Q12024/25
Q22024/25
Q32024/25
Q42024/25
<5%
600
356
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084
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012
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365
126
341
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015
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sporadic
011
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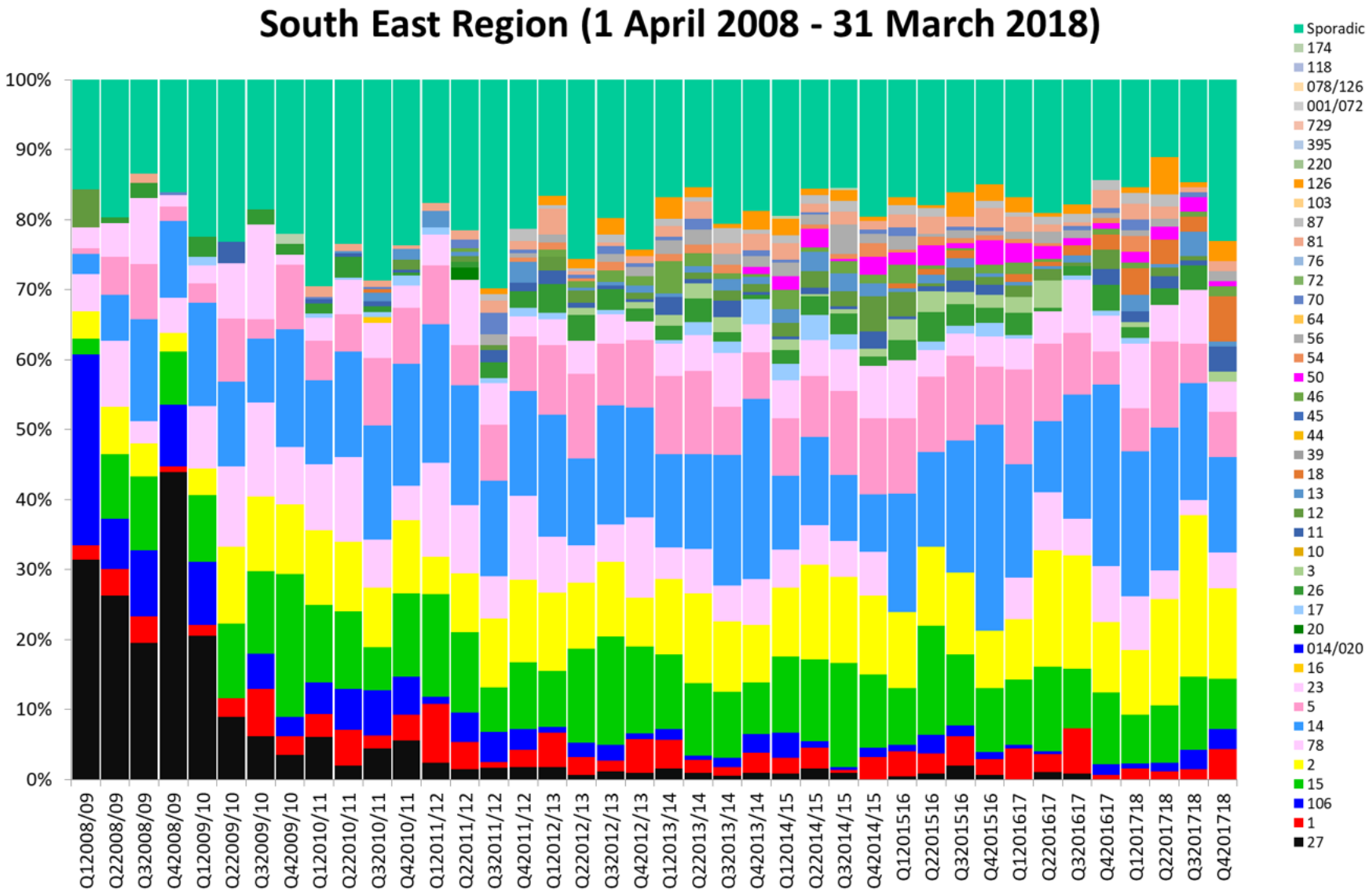
A


South East Region (1 April 2008 - 31 March 2018)
100%
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Q12008/09
Q22008/09
Q32008/09
Q42008/09
Q12009/10
Q22009/10
Q32009/10
Q42009/10
Q12010/11
Q22010/11
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Q12011/12
Q22011/12
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Q22012/13
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Q3201617
Q4201617
Q1201718
Q2201718
Q3201718
Q4201718
Sporadic
174
118
078/126
001/072
729
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103
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70
64
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46
45
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014/020
16
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106
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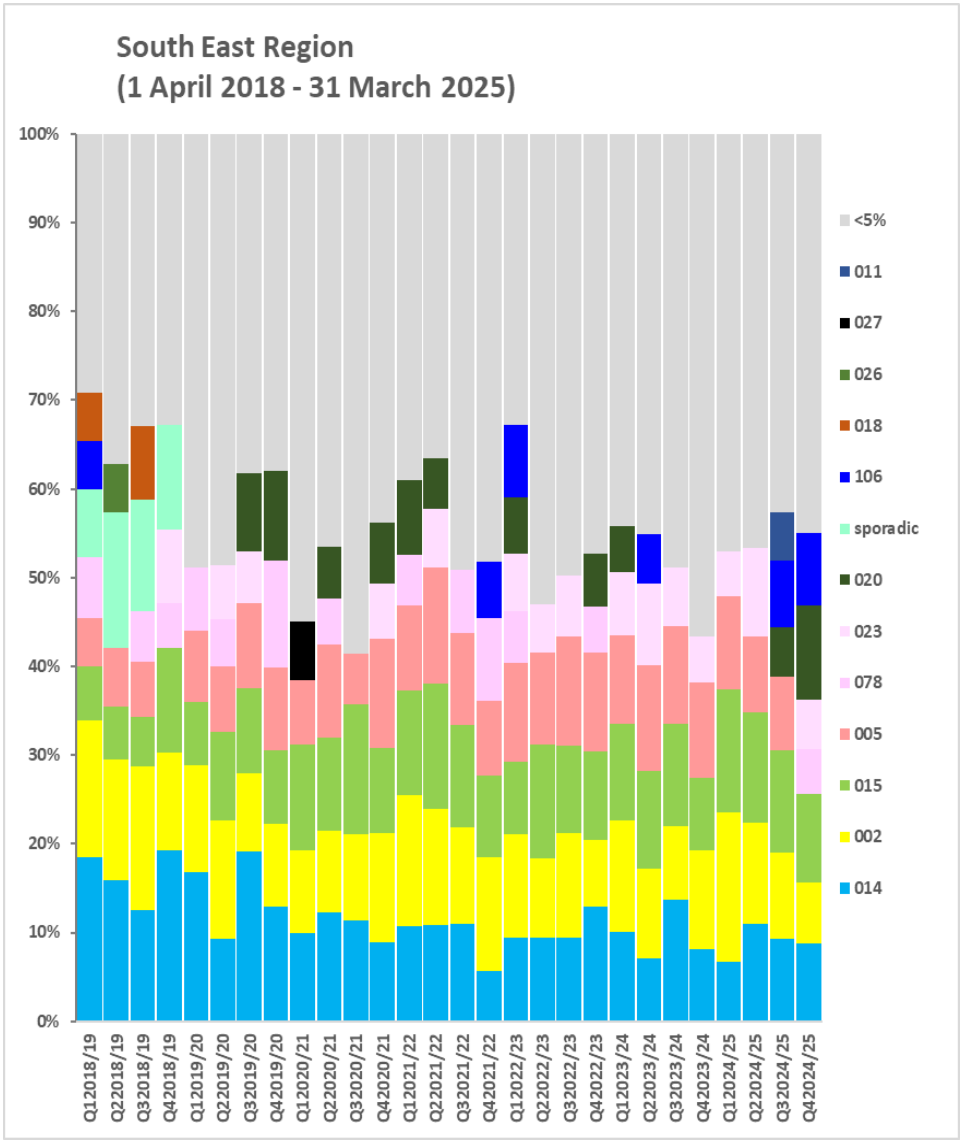
27

B


South East Region
(1 April 2018 - 31 March 2025)
100%
90%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
Q22020/21
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Q42020/21
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Q22022/23
Q32022/23
Q42022/23
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Q22024/25
Q32024/25
Q42024/25
<5%
011
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sporadic
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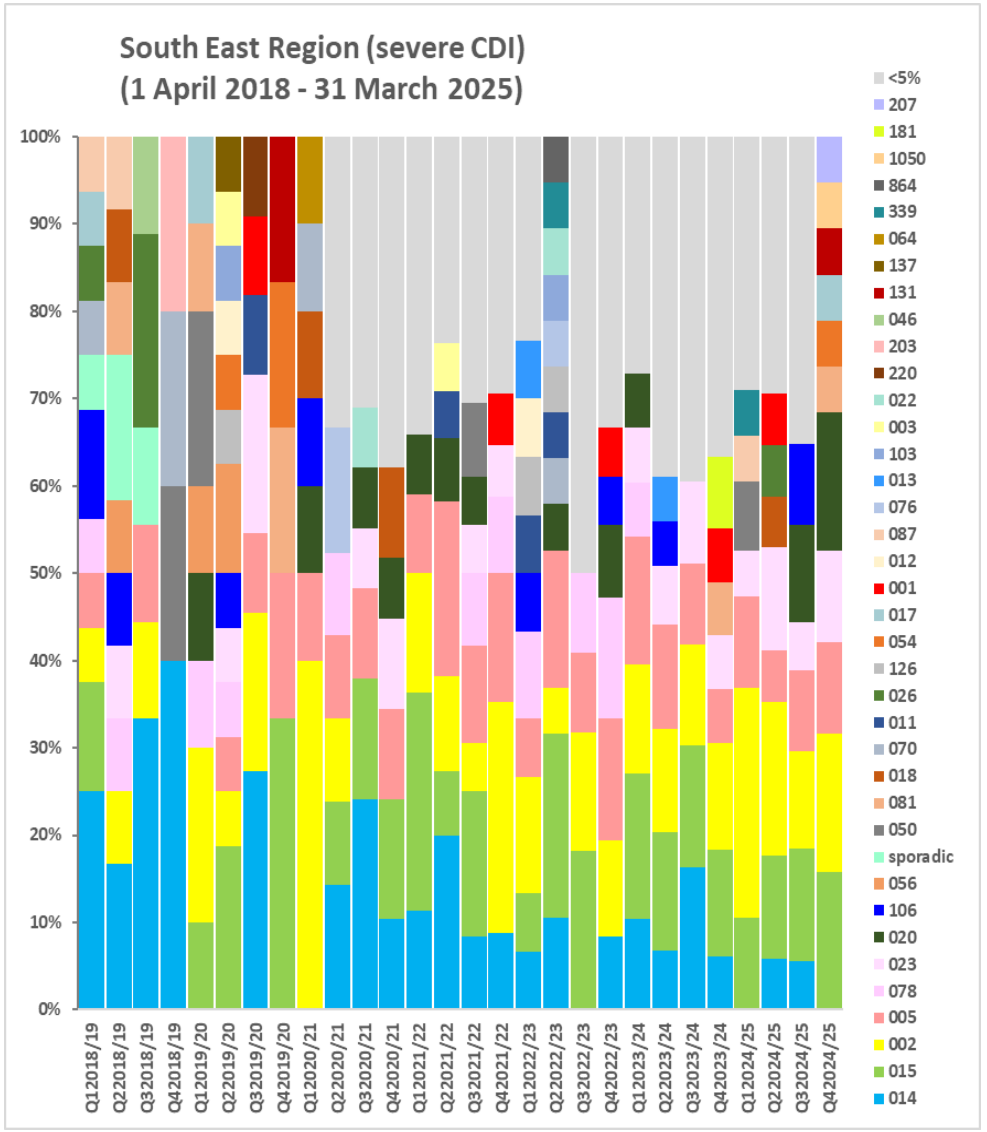
C


South East Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
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Q42022/23
Q12023/24
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Q12024/25
Q22024/25
Q32024/25
Q42024/25
<5%
207
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012
001
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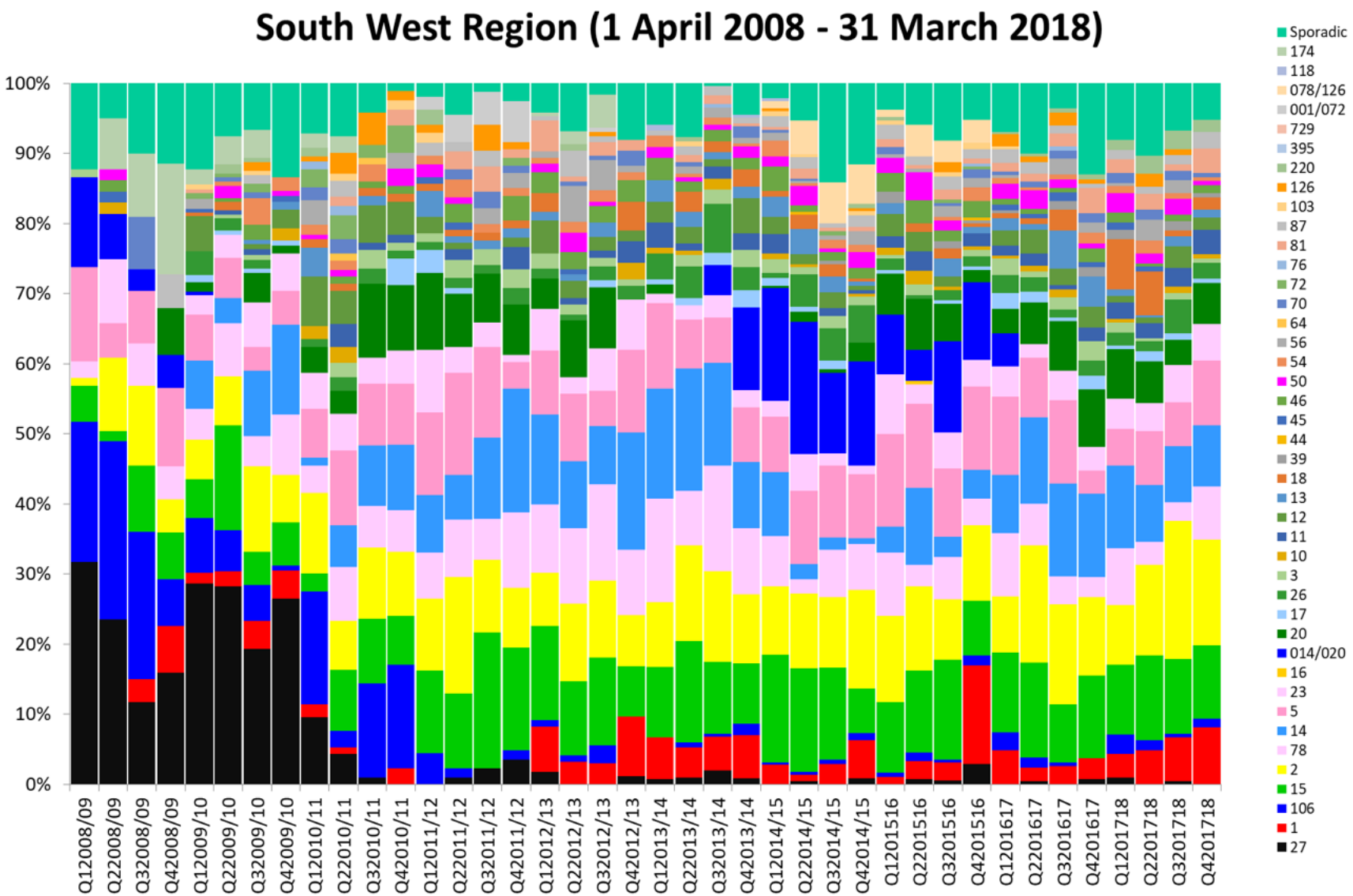
South West Region (1 April 2008 - 31 March 2018)
100%
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Q12008/09
Q22008/09
Q32008/09
Q42008/09
Q12009/10
Q22009/10
Q32009/10
Q42009/10
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Q1201617
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Q3201617
Q4201617
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Q2201718
Q3201718
Q4201718
Sporadic
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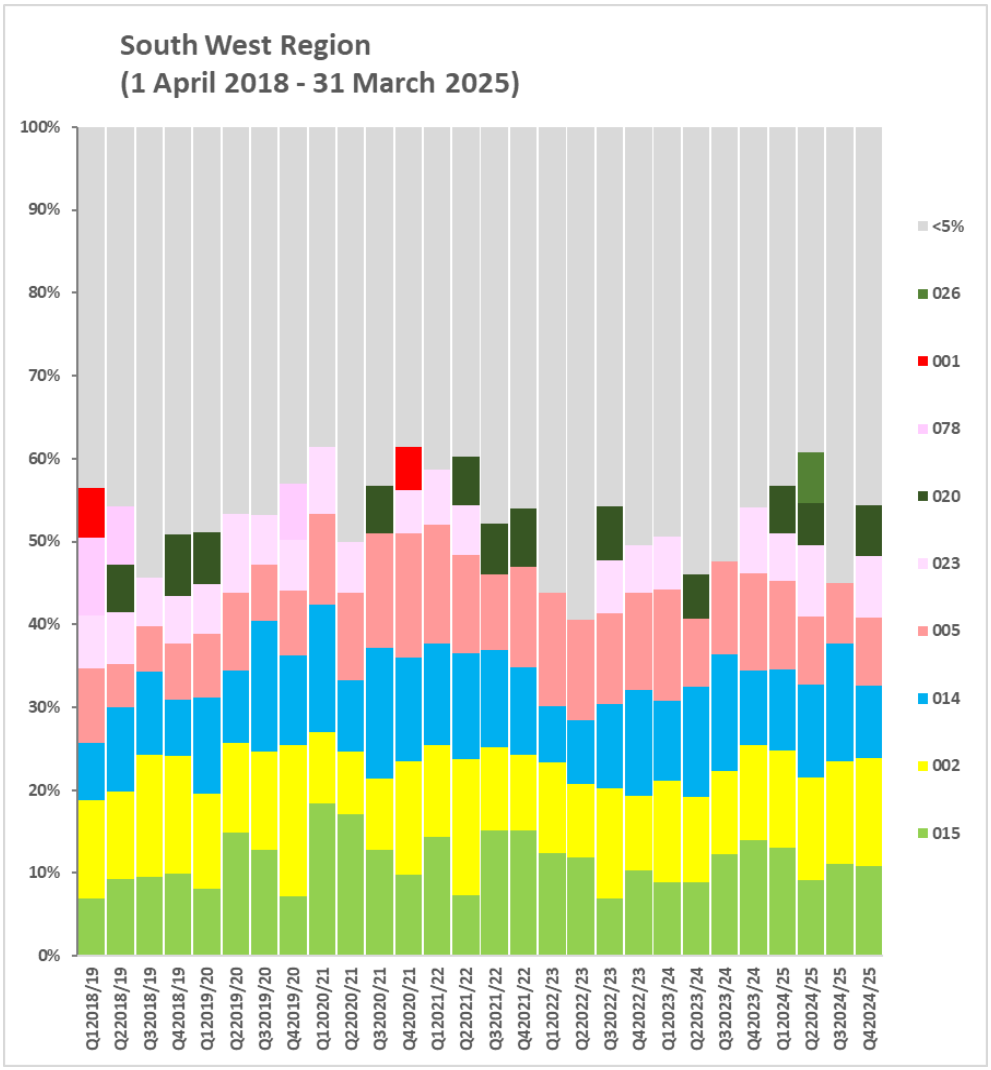
South West Region
(1 April 2018 - 31 March 2025)
100%
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Q12018/19
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Q22019/20
Q32019/20
Q42019/20
Q12020/21
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Q42022/23
Q12023/24
Q22023/24
Q32023/24
Q42023/24
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Q22024/25
Q32024/25
Q42024/25
<5%
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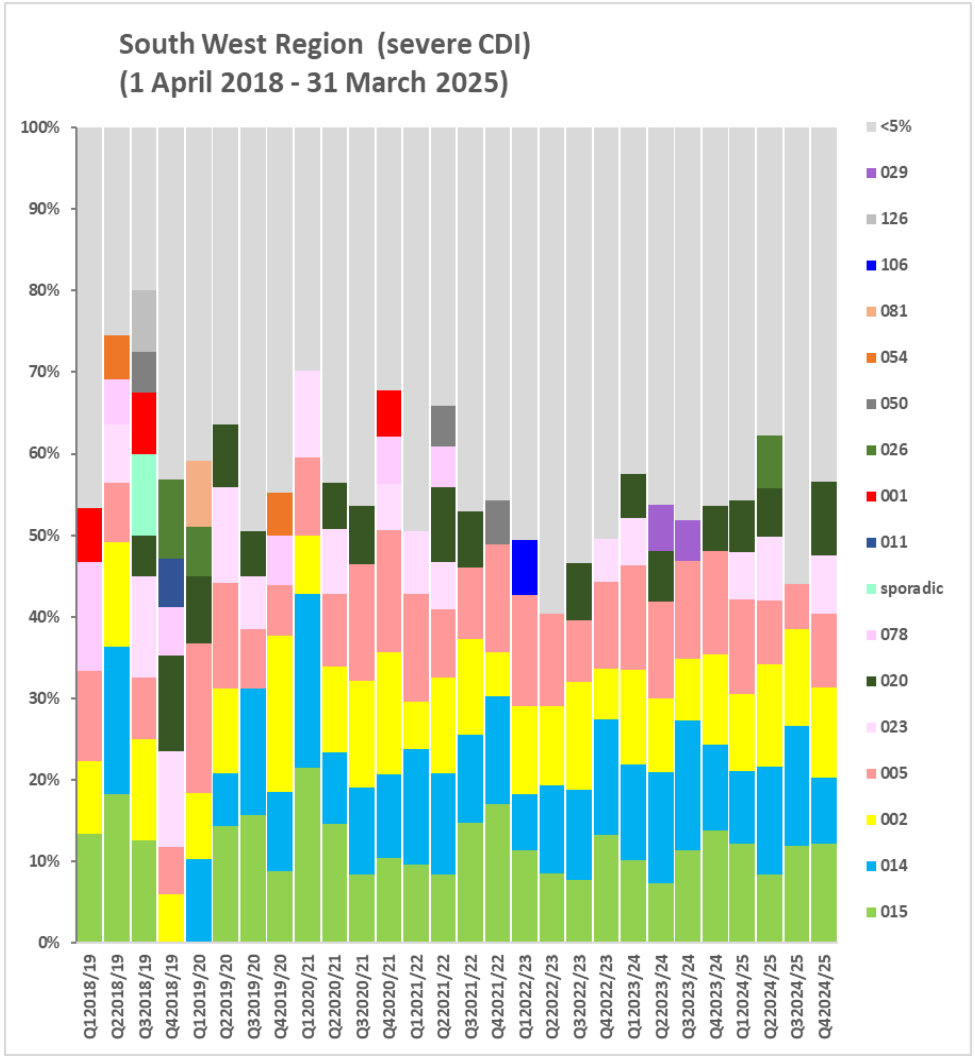
South West Region (severe CDI)
(1 April 2018 - 31 March 2025)
100%
90%
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Q12018/19
Q22018/19
Q32018/19
Q42018/19
Q12019/20
Q22019/20
Q32019/20
Q42019/20
Q12020/21
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Q42020/21
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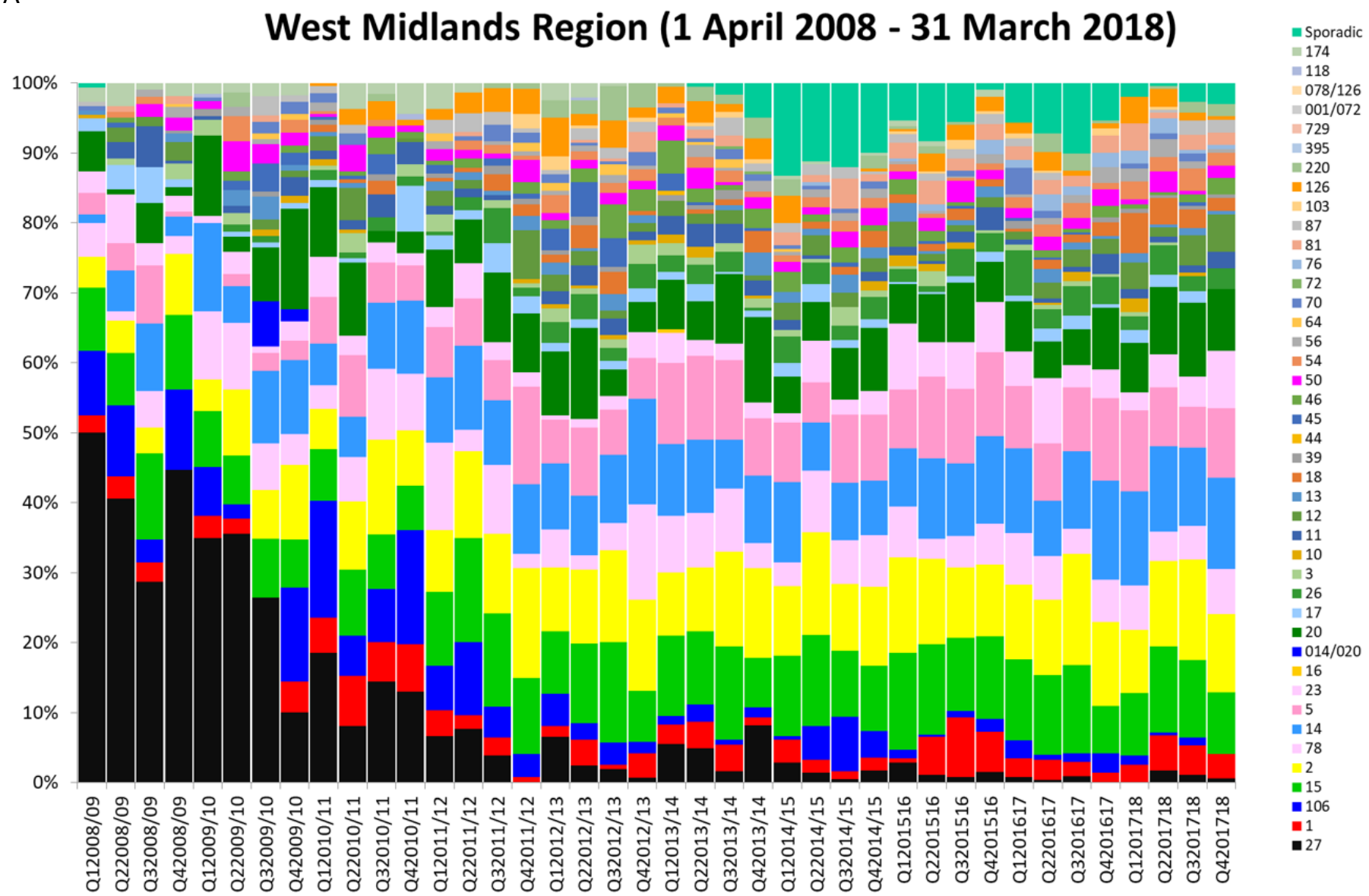
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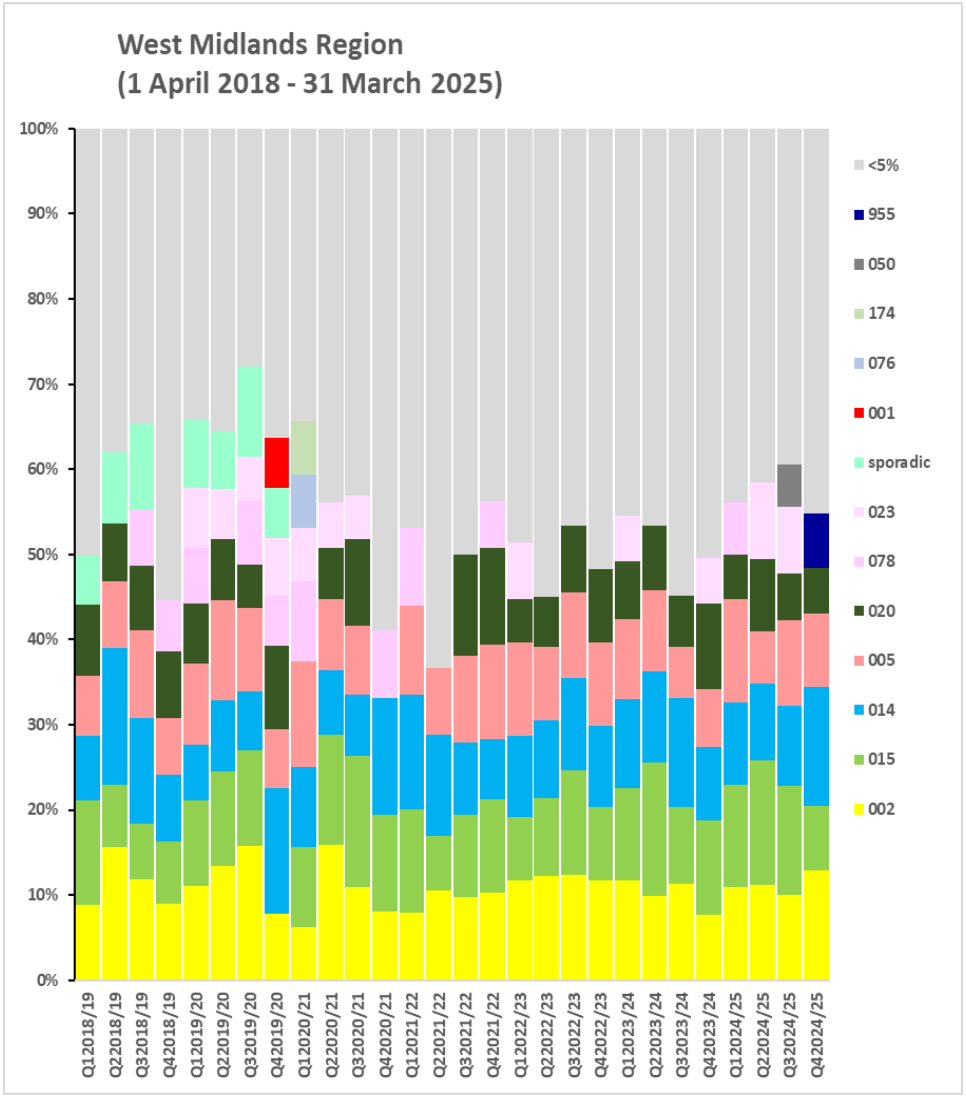
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Q22020/21
Q32020/21
Q42020/21
Q12021/22
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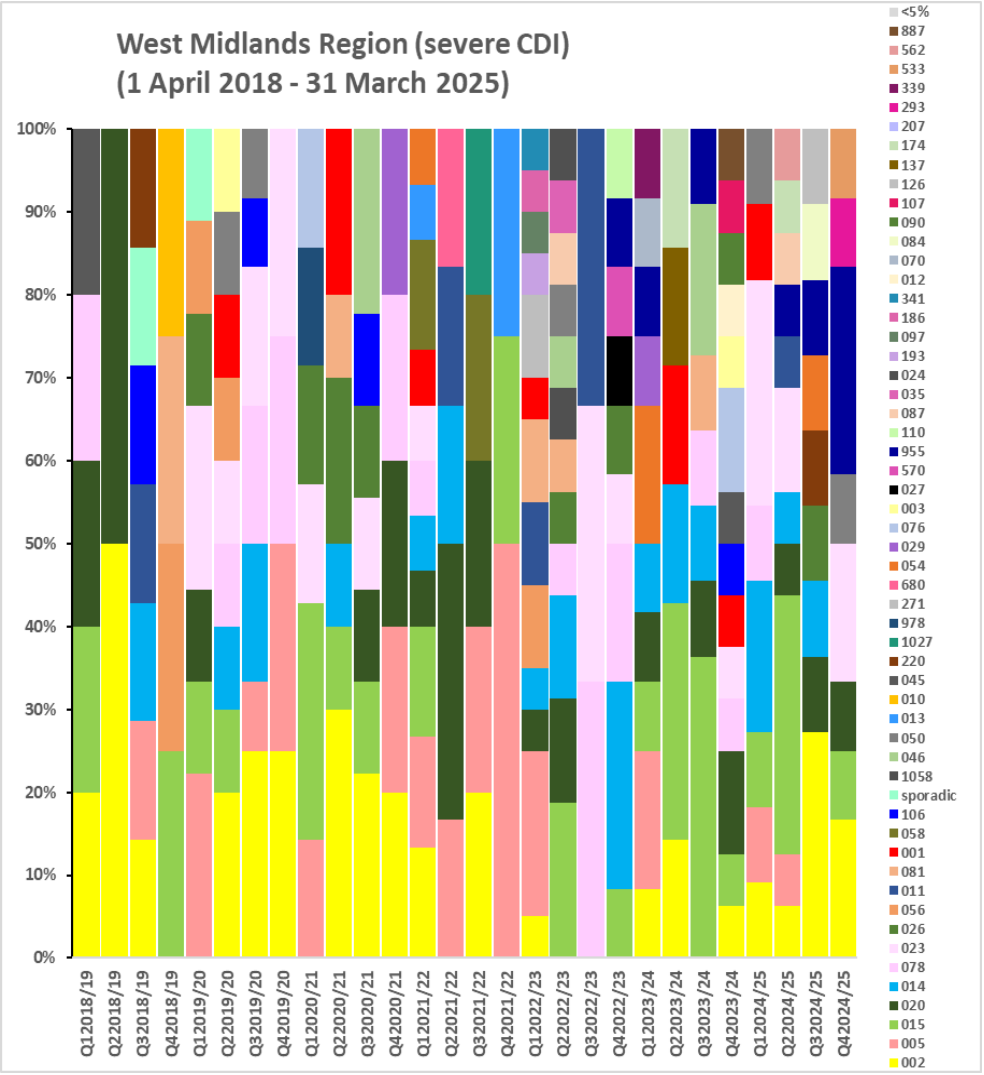
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Q12020/21
Q22020/21
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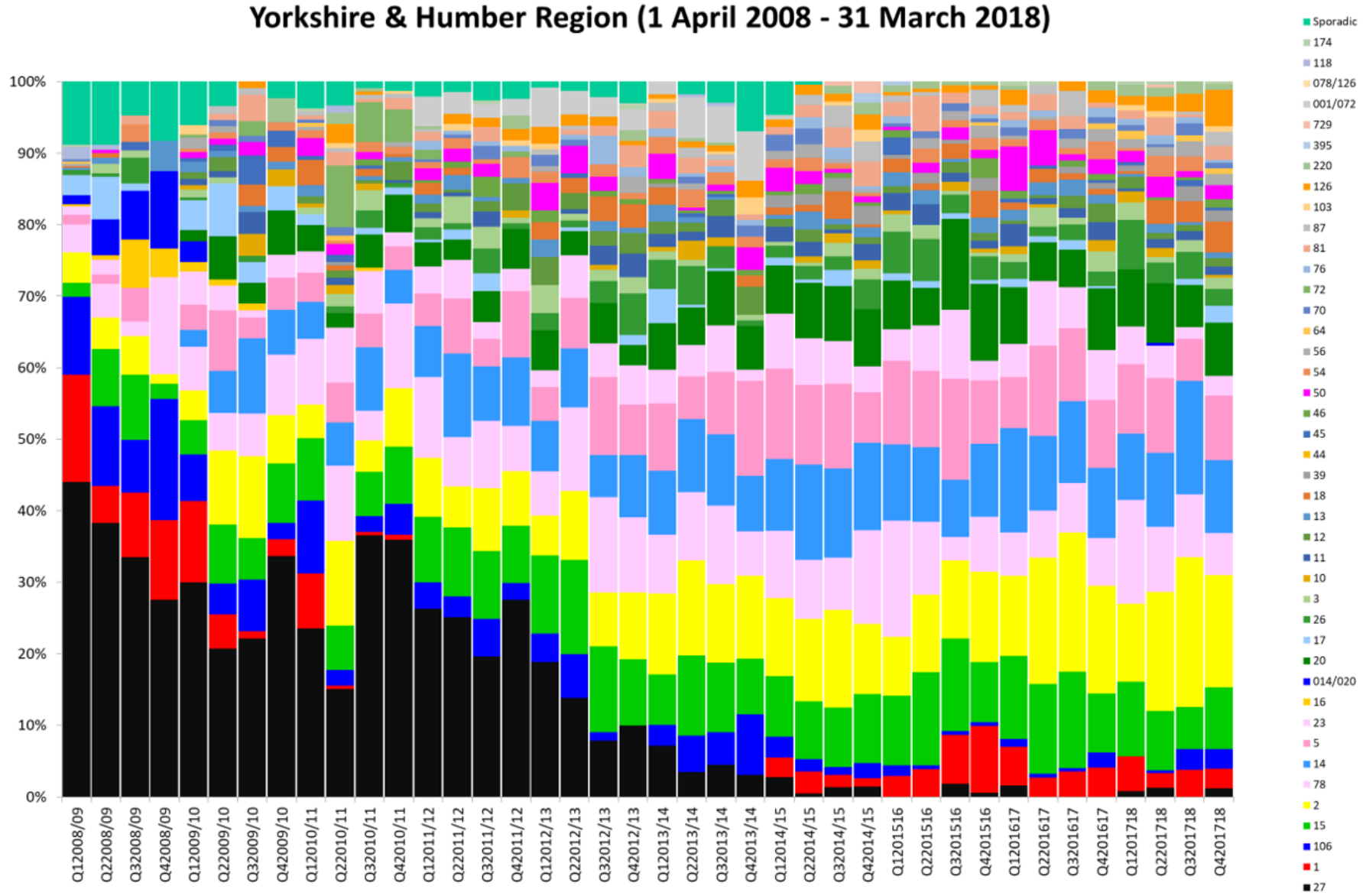
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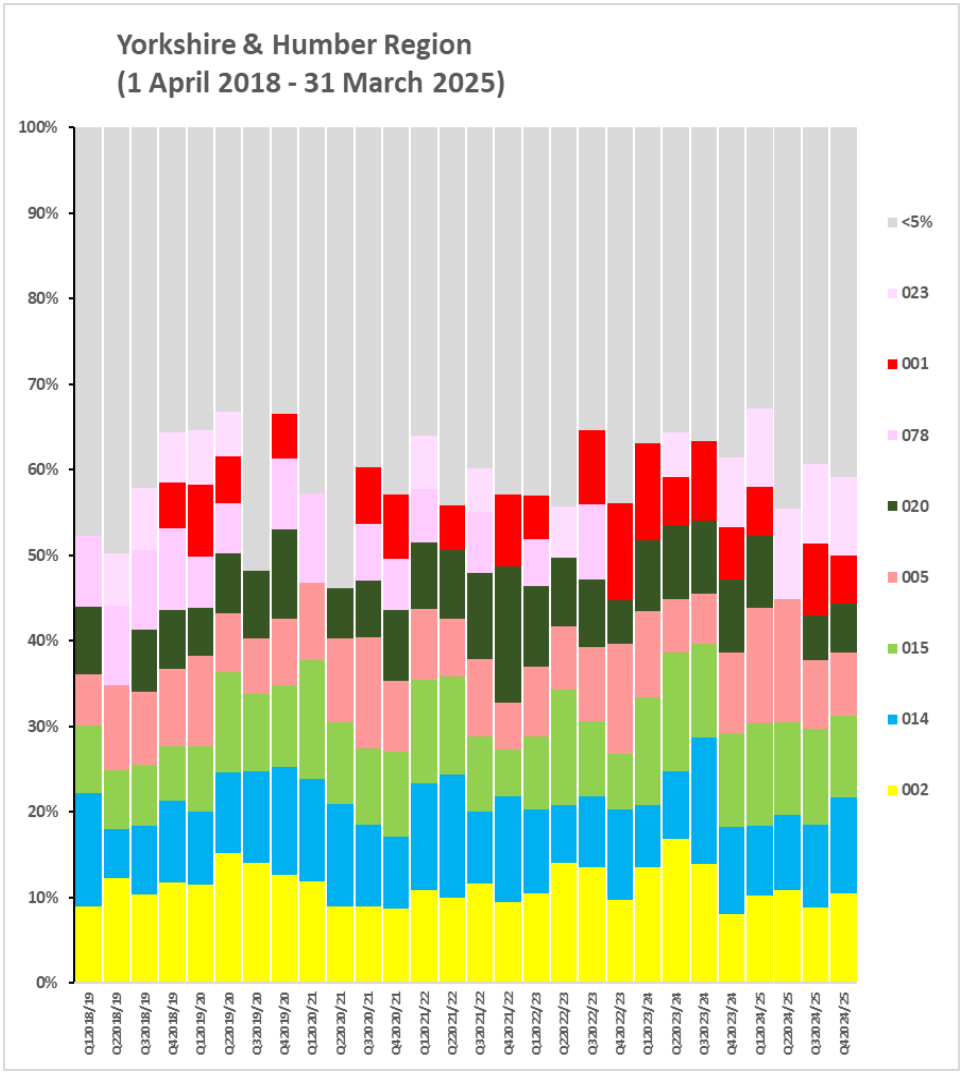
Yorkshire & Humber Region
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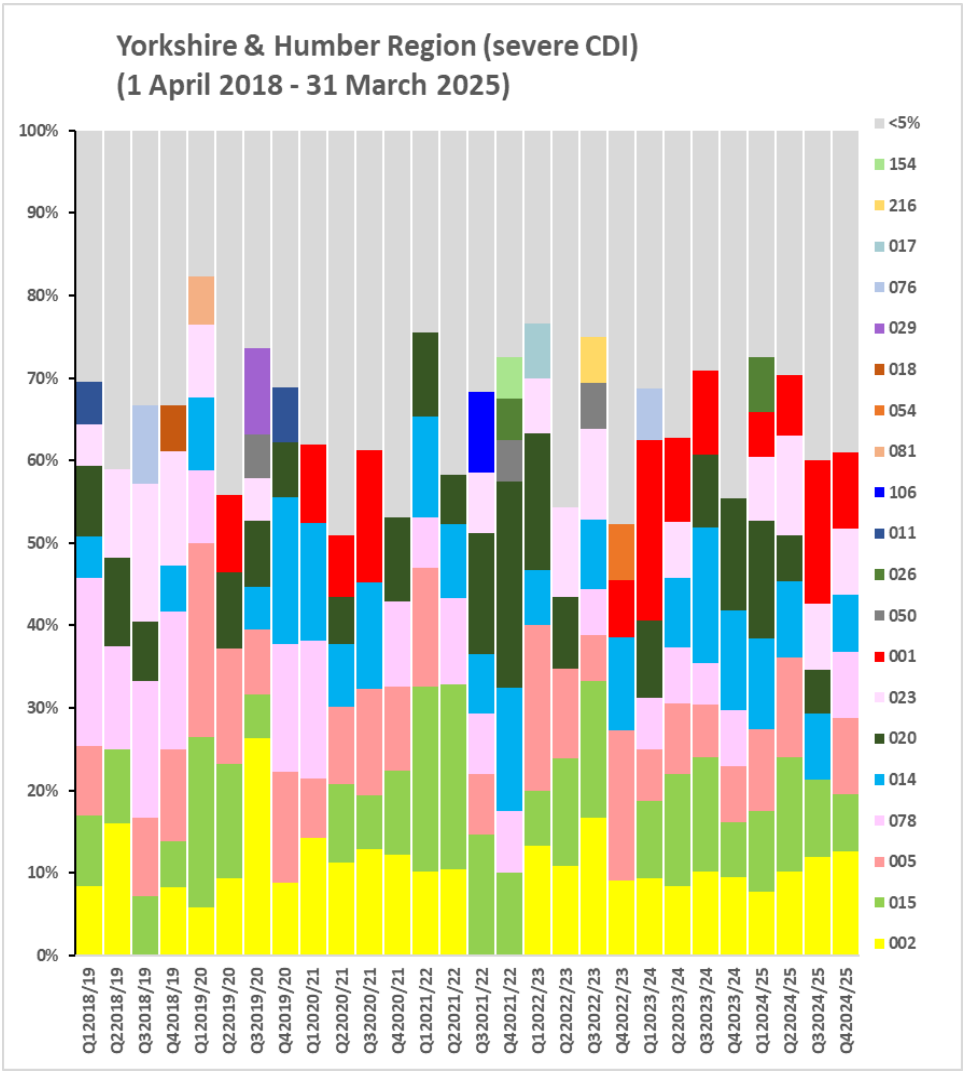
Yorkshire & Humber Region (severe CDI)
(1 April 2018 - 31 March 2025)
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Q32018/19
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Q12019/20
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Q12020/21
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Q32020/21
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Enhanced fingerprinting

CDRN has continued to provide access to enhanced fingerprinting (MLVA) to support investigations into potential CDI case clusters/outbreaks in hospitals, when PCR-ribotyping data alone are insufficient.

In financial years 2023/2024 and 2024/2025 CDRN performed 80 (202 isolates; range 2 to 8) and 61 (122 isolates; range 2 to 4) MLVA investigations, respectively. The most common ribotypes were 002, 955, 014, 005, 015 and 020 (featuring in 19, 15, 17, 18, 18 and 12 investigations, respectively).

An outbreak of CDI in England comprising 69 cases due to ribotype 955 (associated with 2 large hospital clusters in the Midlands region but detected at a total of 15 NHS trusts), occurred between September 2021 and July 2025. Notably, MLVA testing (contemporaneous to the outbreak) on isolates representative of all 15 affected NHS trusts, provided evidence to suggest that all cases except one originated from expansion of a single clone (later confirmed by WGS) (11).

CDRN originally published an analysis of enhanced fingerprinting (MLVA) investigations for potential CDI case clusters or outbreaks in hospitals in England (13). Notably, despite sharing a common ribotype, 19% of these potential CDI case clusters or outbreaks comprised unrelated isolates, and 34% contained a mixture of highly related and distinct isolates. These findings emphasise the value of enhanced fingerprinting to confirm or refute suspected CDI case clusters.

The utility of whole genome sequencing in comparison with MLVA for the examination of case clusters has been examined previously. These efforts were part of a UK-wide consortium, funded by the Wellcome Trust and MRC, between the University of Oxford, UKHSA (then PHE) and the Wellcome Trust Sanger Institute, to establish how revolutionary new technologies can be optimally integrated into medical microbiology (14). We examined *C. difficile* isolates from 61 suspected outbreaks affecting 2 to 41 patients in 31 UK hospitals (300 samples) using both 7-locus MLVA and WGS. Conclusions on whether potential outbreaks were confirmed were concordant in 58 out of 61(95%) of investigations (9). We completed a front-line service performance comparison of MLVA and WGS techniques. All isolates from MLVA-based cluster/outbreak investigations received by our testing laboratory over a period of 12 months were also subjected to WGS, in real time (15). 103 investigations (285 isolates (range 2 to 11 per investigation)) from 42 hospitals were examined. Outcome data generated by MLVA and WGS were concordant in 95 out of 103 (92%) investigations. Using current strain relatedness criteria, all investigations of discordant outcome involved instances where WGS discriminated further than MLVA. Results for investigations using MLVA and WGS were available in 2 and 5 days, respectively.

More recently, 624 *C. difficile* isolates from 19 countries underwent WGS, which demonstrated that 5 ribotypes had within-country clustering: ribotype 356, only in Italy; ribotype 018, predominantly in Italy; ribotype 176, with distinct Czech and German clades; ribotype 001/072, including distinct German, Slovakian, and Spanish clades; and ribotype 027, with multiple predominantly country-specific clades including in Hungary, Italy, Germany, Romania, and Poland.

By contrast, no within-country clustering was observed for ribotypes 078, 015, 002, 014, and 020, which is consistent with a Europe-wide distribution (16). This and other data support the existence of 2 distinct patterns of *C. difficile* ribotype spread, which are consistent with either predominantly healthcare-associated acquisition or Europe-wide dissemination via other routes/sources (for example, possibly via the food chain) (17, 18). Of interest, a recent large pan-European study identified a high *C. difficile* contamination of potatoes obtained from retail outlets in several countries, suggesting a possible source that could be agnostic of borders (19).

Overall, when applied to outbreak investigation of CDI, findings using MLVA and WGS are very similar, despite these techniques analysing different parts of the bacterial genome. WGS offers marginally higher levels of discrimination than MLVA. Although WGS analyses take longer than MLVA, processing times associated with both techniques remain relevant for hospital outbreak investigations. Notably, WGS provides additional data, such as antimicrobial susceptibility genotype and the presence or absence of virulence genes. WGS has also been successfully utilised as a novel surveillance tool to establish rates of *C. difficile* transmission between healthcare institutions, to facilitate targeted efforts in the reduction of CDI incidence (20). It is planned for CDRN to transition to using WGS instead of MLVA for the enhanced fingerprinting or investigation of *C. difficile*.

Sentinel Surveillance Scheme

This new scheme aims to provide robust national surveillance by focusing on sample submissions from a set of specific ‘sentinel’ hospital sites, which combine to intercept a significant proportion of the routes of *C. difficile* dissemination (when colonised or infected patients admitted to multiple facilities act as inter-hospital vectors).

This approach has been designed to identify newly circulating strains more rapidly, and close gaps in coverage that may exist using current surveillance methods.

This active surveillance has started by using isolates from 20 ‘sentinel sites’, identified by epidemiological modelling work (21, 22), which calculated that sampling from these sites will identify a circulating novel strain of C. difficile 27% faster than if using 20 randomly chosen sites. To enhance the information available per sample, the scheme provides participating sentinel sites with both *C. difficile* PCR-ribotyping and whole-genome sequencing-inferred relatedness data.

Sentinel samples are submitted to the *Clostridioides difficile* ribotyping network (CDRN) via the Electronic Requesting System. PCR-ribotyping is performed on sentinel samples and results are returned as for conventional CDRN services. Sentinel sites receive a quarterly report summarising the genetic relatedness of *C. difficile* isolates associated with their submissions.

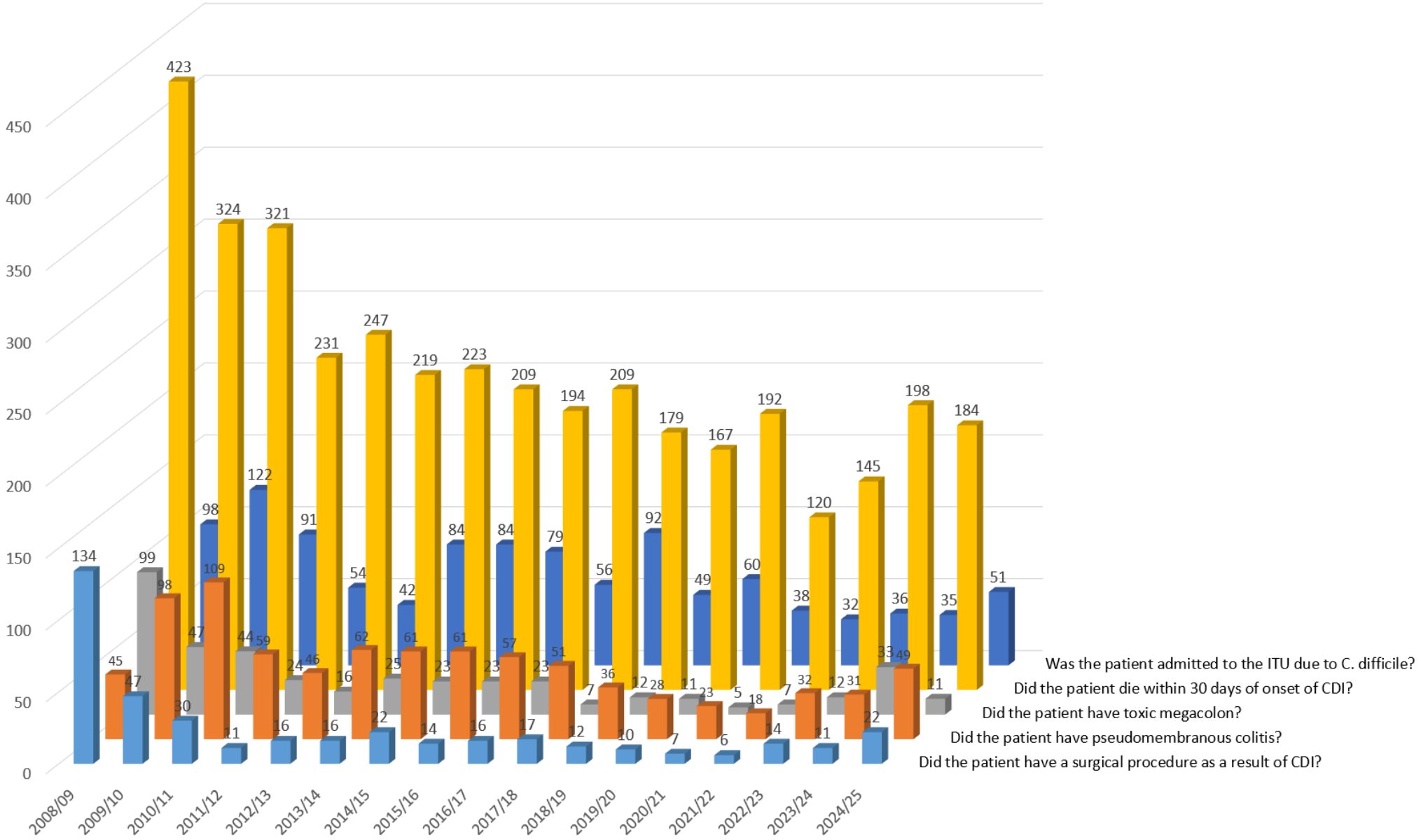
This scheme was launched in April 2025. For a full scheme description, see the Surveillance protocol for the CDRN.

Outcome data

In financial years 2023 to 2024 and 2024 to 2025, clinical follow-up data was available for approximately 53.5% and approximately 55% of cases, respectively, although some follow-up data (for example mortality and admission to ITU) was provided more commonly (42% and 48% of cases, respectively).

Clinical follow-up data is shown in Figure 7 (this is for all referred cases, regardless of culture result). The data should be interpreted with caution given the partial response rate. Numbers of deaths and cases associated with either toxic megacolon or requiring surgery declined between 2008 to 2009 and 2011 to 2012 and have remained approximately stable thereafter. These observations are consistent with control and declining incidence of ribotype 027 CDIs.

Figure 7. Outcome data provided at the time of CDRN request submission (2008/2009 to 2024/2025)



A detailed analysis of risk factors associated with CDI, outcomes and specific ribotypes was presented in the 2009 to 2010 CDRN report. Further detailed information can also be found in 2 peer-reviewed reports (23, 24).

Antibiotic exposure

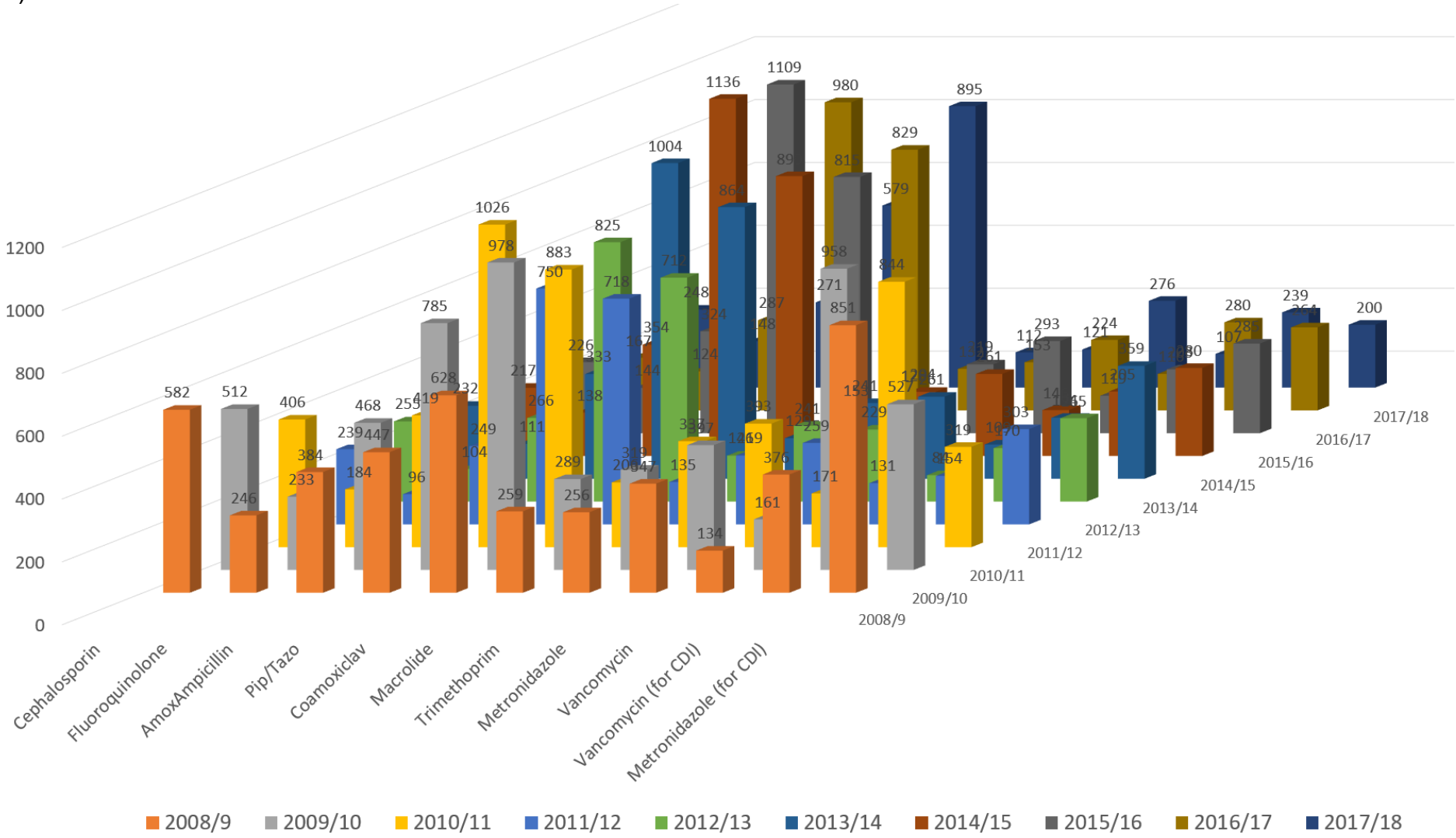
The interpretation of data on CDI risk associated with individual antibiotics is extremely difficult as commonly used agents may be reported as being associated with CDI more often than rarely prescribed antimicrobials, data often do not take into account duration of exposure or polypharmacy, and similarly may be confounded by other risks (patient age, co-morbidities and so on). Thus, the data in the following paragraphs need to be interpreted with caution; notably, the data should not be considered to be indicative of which agents actually caused CDI.

As in recent years, the most commonly reported antibiotics in financial years 2023 to 2024 and 2024 to 2025 were piperacillin-tazobactam (n=560, 516) and co-amoxiclav (n=683, 708) (Figure 8). It is noticeable that the most commonly recorded antibiotics have changed markedly over the 15-year period that CDRN has been in existence. In 2007 to 2008, cephalosporins were the most commonly cited agents, whereas these were uncommonly cited in subsequent reporting periods, and indeed have been numerically superseded by co-amoxiclav and piperacillin-tazobactam from 2008 to 2009 onwards. This data likely reflects real changes in prescribing of systemic antibiotics as one of the control measures for CDI.

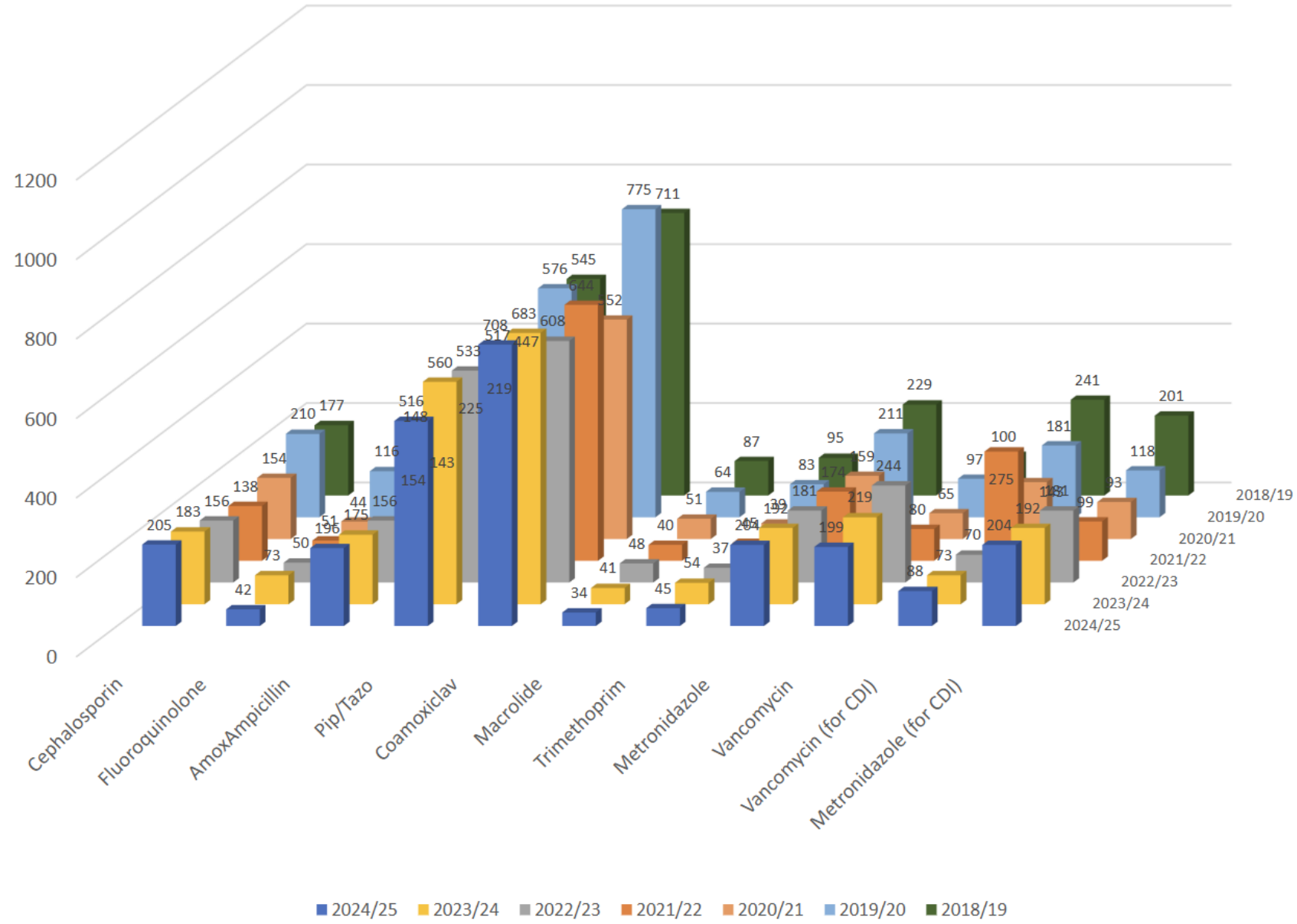
It is also noteworthy that in recent years there appears to have been a stable shift in the prescribing of CDI treatment antibiotics from metronidazole in favour of vancomycin (Figure 8). Such data is consistent with possible greater adherence to guidelines. Indeed, more recent evidence shows that vancomycin is superior to metronidazole for CDI treatment (25).

Figure 8. Reported antibiotics associated with CDI episodes (2008/2009 to 2024/2025) (A) April 2008 to March 2018; (B) April 2018 to March 2025

(A)



(B)


1200
1000
800
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400
200
0
Cephalosporin
Fluoroquinolone
AmoxAmpicillin
Pip/Tazo
Coamoxiclav
Macrolide
Trimethoprim
Metronidazole
Vancomycin
Vancomycin (for CDI)
Metronidazole (for CDI)
2018/19
2019/20
2020/21
2021/22
2022/23
2023/24
2024/25

Metronidazole, vancomycin and fidaxomicin susceptibility

Targeted surveillance, based on investigation of cases suspected to represent cross-infection, has identified reduced metronidazole and vancomycin susceptibility amongst epidemic ribotypes (26). Epidemic ribotypes with reduced metronidazole or vancomycin susceptibility were associated with location clusters, as determined by MLVA. This may indicate expansion or selection of strains with reduced susceptibility within epidemic ribotypes.

Antimicrobial susceptibility data on *C. difficile* from 2 European studies that included the UK (Closer and COMBACTE-CDI) is available in the literature (27 to 29).

Despite reports on vancomycin and fidaxomicin resistance in clinical *C. difficile* isolates in the literature, rates remain low, and are not associated with the UK (30 to 34). However, the reduced susceptibility to metronidazole in recently emergent PCR ribotype 955 highlights that, in line with current guidance, this antibiotic should not be used to treat CDI.

Summary

The *Clostridioides difficile* Ribotyping Network (CDRN) for England and Northern Ireland has for 15 years responded to a major public health need by providing a molecular epidemiological service that enhances our understanding of this pathogen. Since the introduction of CDRN the reports of *C. difficile* in England have fallen markedly, but have increased during the COVID-19 pandemic. Reports of deaths associated with CDI also started to decrease the year after CDRN commenced, which is likely due to enhanced control of the epidemic ribotype *C. difficile* 027. It is plausible that timely data provision by CDRN has enhanced the capacity of healthcare institutions and infection control and prevention teams to control CDI incidence.

Continued referral to CDRN will afford the greatest chance of identifying emergent *C. difficile* ribotypes. However, despite the approximately 75% decline in CDIs in England since 2007, the number of cases in England for which samples are submitted to CDRN has continued to increase (Figure 2), and now accounts for approximately half of all reported episodes. All NHS hospitals in England have been encouraged to submit samples, according to set CDRN criteria. However, the high proportion of all CDIs that are currently referred to CDRN for ribotyping indicates a high likelihood that these criteria are not being followed consistently.

It is appropriate that the function of CDRN is continually reviewed to ensure that the service is cost effective. We emphasise that all hospitals should submit samples according to the CDRN criteria (see Accessing the service section). Use of enhanced fingerprinting (and, in due course, WGS) is recommended to optimise the control and prevention of CDI following discussion with CDRN and UKHSA personnel (see Enhanced fingerprinting section).

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UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation health secure.

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