Thirty-day all-cause mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

April 2019 to March 2020
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Executive summary

In this analysis, we report the 30-day all-cause mortality following meticillin-resistant *Staphylococcus aureus* (MRSA), meticillin-susceptible *S. aureus* (MSSA) bacteraemia, Gram-negative (*Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa*) bacteraemia and *Clostridioides difficile* infections (CDI). 30-day all-cause mortality is a widely-used outcome for assessing risk of death. However, it should be emphasised that all-cause mortality is used in the analysis of this report, and thus not all deaths reported here will be attributable to these infections; many will be due to underlying medical conditions.

This report presents case fatality rates (CFR) and mortality rates (MR). CFR is the number of deaths as a percentage of all reported cases. This provides a measure for comparing survivability of different infections. In contrast, the MR is the number of deaths divided by the population at risk. This reflects the incidence of all-cause deaths following these infections in the population.

In 2019/20, the CFR were; MRSA bacteraemia (25.7%), *P. aeruginosa* bacteraemia (24.5%), MSSA bacteraemia (19.5%), *Klebsiella* spp. bacteraemia (19.1%), *E. coli* bacteraemia (14.3%) and CDI (13.5%).

The MR of 30-day all-cause deaths per 100,000 population for each infection covered in this report were; *E. coli* bacteraemia (10.7, n= 6,005 deaths), MSSA bacteraemia (4.1, n= 2,299 deaths), *Klebsiella* spp. bacteraemia (3.6, n= 2,042 deaths), CDI (3.1, n= 1,735 deaths), *P. aeruginosa* bacteraemia (1.8, n= 1,031 deaths) and MRSA bacteraemia (0.4, n= 201 deaths).

Between 2007/08 and 2019/20, there have been significant declines in the number of 30-day all-cause deaths for MRSA bacteraemia (1,354 to 201 deaths) and CDI (13,973 to 1,735 deaths) due to a decrease in incidence of these infections over the same period. In contrast, the number of deaths following MSSA bacteraemia (1,777 deaths in 2011/12 to 2,299 in 2019/20) and *E. coli* bacteraemia (5,163 deaths in 2012/13 to 6,005 in 2019/20) have increased, reflecting the continuing rise in incidence of these infections.

The overall trend in CFR of each infection has been a declining one, despite the increases in overall numbers for some, with statistically significant reductions in CFR between the current financial year and the start of mandatory surveillance of each infection - MRSA (2007/08 to 2019/20), *C. difficile* (2007/08 to 2019/20), MSSA (2011/12 to 2019/20), *E. coli* (2012/13 to 2019/20), *P. aeruginosa* (2017/18 to 2019/20) and *Klebsiella* spp. (2017/18 to 2019/20). This suggests that despite continued increases in incidence of infections like MSSA and *E. coli* bacteraemia, a greater proportion of
patients are surviving each type of infection over time. The CFR for the current financial year (2019/20) increased compared to the previous year (2018/19) for all infections except CDI; however, there was no statistical evidence of difference for these changes.

In 2019/20, the CFR of both hospital-onset and community-onset cases were highest in *P. aeruginosa* bacteraemia cases (28.4% and 22.3% respectively) and MRSA bacteraemia (29.2% and 24.1% respectively).

Overall, there were declining trends of CFRs of both hospital-onset and community-onset cases of each infection since the start of their surveillance schemes. However, the greatest reductions have been in MRSA (13.2% and 9.0% in hospital-onset and community-onset cases respectively) and CDI (9.7% and 10.7% in hospital-onset and community-onset cases respectively). The greater reduction in CFR of hospital-onset MRSA cases compared to community-onset cases could be due to the large reduction in the number of hospital-onset MRSA cases observed over time. Such cases have traditionally been associated with many co-morbidities resulting in poorer health outcomes. Therefore, the large reduction in hospital-onset MRSA cases would be accompanied by a considerable reduction in the total number of deaths following this infections. However, despite similarly large reductions in the number of hospital-onset CDI cases over time, the reduction in CFR of community-onset CDI cases was greater than that of hospital-onset CDI cases over the same period.
Introduction

Public Health England (PHE) has undertaken mandatory surveillance of key healthcare-associated infections (HCAIs) in England since 2001, when NHS acute trusts were mandated to report aggregate counts of *Staphylococcus aureus* bacteraemia (bloodstream infection) and the number that were meticillin-resistant *S. aureus* (MRSA). Case-level reporting was introduced for MRSA in 2005, and for *Clostridioides difficile* infections (CDI) in patients ≥2 years-old since April 2007. The mandatory surveillance programme was expanded to include meticillin-susceptible *S. aureus* (MSSA) and *Escherichia coli* bacteraemia in January and July 2011 respectively. In April 2017, *Klebsiella* spp. and *Pseudomonas aeruginosa* bacteraemia were also added to the surveillance programme [1].

Over time, the dominance of hospital-onset MRSA bacteraemia and CDI has declined with increasing proportion of community-onset cases. Also, a rising proportion of MSSA and Gram-negative bacteraemia are community-onset [1]. Since the composition of the patient population from both settings can vary, this publication investigates mortality outcomes by onset of infection, and by prior healthcare exposure for CDI. Due to the potential impact of HCAI on morbidity and mortality [2–4], monitoring trends in mortality is an important part of surveillance.

This report presents an analysis of 30-day all-cause mortality among MRSA, MSSA, *E. coli*, *Klebsiella* spp. and *P. aeruginosa* bacteraemia, and CDI patients. A separate report presents an analysis of the incidence of all reported cases of these same infections.
Methods

Data in this report are presented by financial year based on specimen dates (that is, collection date of first positive specimen) rather than when the patient died. It is therefore possible that a death occurred in a different financial year from the infection if the specimen date is sufficiently close to the end of the previous financial year. When the date of the blood culture (bacteraemia) or faecal sample (CDI) was taken is not known, the date when the sample was received in the laboratory for processing is used as a proxy. The counts of infections reported here are based on data extracted from the HCAI data capture system (HCAI DCS) on 23 June 2020. Patients’ mortality outcomes were traced on 26 August 2020. The extract covered MRSA bacteraemia and CDI cases between 1 April 2007 and 31 March 2020, MSSA bacteraemia cases between 1 April 2011 and 31 March 2020, *E. coli* bacteraemia cases between 1 April 2012 and 31 March 2020, and *P. aeruginosa* and *Klebsiella* spp. bacteraemia cases between 1 April 2017 and 31 March 2020. The number of infections and deaths presented here may differ from those in earlier publications due to late reports or inclusion of new reports since previous publications.

This report uses the same base data as PHE’s 2019/20 Annual HCAI Epidemiological Commentary [1]. Unlike the annual report, in this publication counts of infections and deaths within 30 days of specimen collection have been deduplicated (separately per infection) to a patient level. This means that a patient positive for 3 different types of infection within 30 days of their death is presented thrice – once per infection. This ensures that each patient can only have a single mortality outcome per infection. The most recent case in this 30-day window period is retained as the index, while earlier infections within the 30-day window are excluded from mortality figures. Percentage changes have been calculated using the raw data provided in the supplementary tables. A full description of the methods can be found in the Appendix.

Comparability with previous ONS publications on mortality

The Office for National Statistics (ONS) previously published data on deaths involving MRSA and *C. difficile* [5,6]. The ONS data on MRSA bacteraemia and CDI are not comparable to the data published here for several methodological reasons outlined in the Appendix. In summary, the ONS published data from England and Wales by calendar year, based on deaths which mention MRSA or *C. difficile* on the death certificate. By contrast, this publication includes data from England by financial year, with mortality calculated using all deaths occurring within 30 days of onset of MRSA bacteraemia or CDI. In addition, data are presented on deaths following MSSA and Gram-negative bacteraemia. The 2 outputs thus differ by geography, time period, source
of death information and range of pathogens covered. All deaths (all-cause mortality) occurring within 30 days of an infection report adopted is a common epidemiological convention. While it is not known if the deaths were attributable to the HCAIs, the use of all-cause fatality provides a consistent methodology to determine the temporal trends and reduces the subjectivity of cause of death or changes in priorities for death certification.

Interpreting case fatality rates

Case fatality rates (CFR) are a useful statistic to analyse the risk of death per case of a particular infection and are calculated as the number of deaths divided by the number of cases, multiplied by 100. Thus, if the ratio of deaths to cases remains constant over time so will the CFR, even if overall, there has been an increase or decrease in both the number of deaths and cases. By contrast the CFR will increase, if the number of deaths increases but the number of cases remains constant, or if the number of deaths remains constant but the number of cases decreases. Thus, the CFR facilitates comparison between clinical outcomes of diseases with differing incidence.

In addition to the CFR, this report includes 95% confidence intervals. These provide a range of values within which the true CFR is likely to lie. When confidence intervals for 2 or more different CFRs do not overlap then the true CFRs are not equal.

Interpreting mortality rates

Mortality rates (MR) are a measure of deaths in the population at risk. This contrasts with the CFR which shows the percentage of people with infections who die within 30 days. This is the risk of death if one has the infection. The MR is calculated as the number of deaths divided by a population estimate. The population estimate is based on England’s mid-year estimates [7]. For Hospital-onset cases, the population estimate used overnight admissions [8]. However, for Community-onset: Healthcare associated cases overnight and day admissions [9] have been used. These population estimates are the most readily available estimates which best represent the populations at risk.

Regression analysis

When comparing MR and CFR between infections, it is important to consider the patient-mix that different infections may have. Although we have presented crude CFRs and MRs by onset of infection and NHS commissioning regions, differences in mortality rates may be due to varying patient demographics (such as age and sex), and other unaccounted factors (for example comorbidities such as cancer, diabetes etc). Regression models controlled for age groups and patient sex as categorical variables were used to assess regional differences in MR (Poisson) and odds of death (Binomial).
P-values <0.05 were considered as providing at least some statistical evidence of non-random regional variation. For each model cases where the patient’s sex was reported as “unknown” were excluded.

An accompanying data table for this report can be found here.

Results

In 2019/20, there were a total of 84,830 cases of E. coli, Klebsiella spp., P. aeruginosa, MRSA and MSSA bacteraemia, and CDI in England. There were and 13,313 deaths within 30 days of taking a specimen (blood culture for bacteraemia, faecal sample for CDI). This gave a mortality rate (MR) of 23.8 deaths per 100,000 population (Table S0), and a case fatality rate (CFR) of 16% of all reported cases (Figure 2).

Figure 1: Number of deaths within 30 days of case detection by infection 2007/08 to 2019/20
Gram-negative bacteraemia

*Escherichia coli* bacteraemia

In 2019/20, 43,294 *E. coli* bacteraemia cases were reported in England. Information on mortality was available for 97% (n= 42,042) of these cases (Table S1). There were 6,005 deaths within 30 days of an *E. coli* bacteraemia which was a MR of 10.7 deaths per 100,000 population. The CFR was 14.3% of cases.

Overall, there was a declining trend in CFR starting from 16.8% in 2012/13 to 14.3 in the current financial year (2019/20), while the overall trend of MR increased from 9.7 per 100,000 population to 10.7 over the same period. The overall difference in CFR between 2012/13 and 2019/20 (-2.6%, p < 0.01) was statistically significant. However, the year-on-year difference in CFR was only statistically significant between 2012/13 and 2013/14 (-0.8%, p < 0.01), 2014/15 and 2015/16 (-0.8%, p < 0.01), 2015/16 and 2016/17 (-0.6%, p < 0.01) and 2017/18 and 2018/19 (-0.9%, p < 0.01).

There was a slight increase in CFR (13.9% to 14.3%) in CFR between the current and previous (2018/19) financial years. Additionally, there was a slight increase (10.4 to 10.7 deaths per 100,000 population) in MR over the same period.

**Variation by onset of bacteraemia**

In 2019/20, the MR of hospital-onset cases was 4.8 deaths per 100,000 bed-days (n= 1,665 deaths) compared to 4.6 (n= 1,585 deaths) in the previous financial year (2018/19) (Table S2 and Figure 3). Over the same period, the MR in community-onset
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Cases was 7.6 (n= 4,242 deaths, 2018/19) and 7.8 deaths per 100,000 population (n= 4,340 deaths, 2019/20) respectively.

Between 2012/13 and 2019/20, there was a decreasing trend of CFR in both hospital-onset and community-onset cases. In this period, the CFR of hospital-onset cases declined from 23.6% to 21.9%, while for community-onset cases it declined from 14.8% to 12.6% of cases (Table S2 and Figure 4). The CFR in 2017/18 (22.8%) was noticeably higher the previous financial years; an average of 1% higher than that of the 3 preceding financial years.

**Figure 3: 30-day all-cause mortality rate of *E. coli* bacteraemia by onset of bacteraemia; 2012/13 to 2019/20**

**Figure 4: 30-day all-cause case fatality rate of *E. coli* bacteraemia by onset of bacteraemia 2012/13 to 2019/20**
Variation by NHS commissioning region
Like the national trends, regional MR increased over time while regional CFR declined over the same period.

In 2019/20, regional MR ranged from 8.3 deaths per 100,000 population in London to 13.6 deaths per 100,000 population in North East and Yorkshire (Table S3 and Figure 5). Over the same period, CFRs ranged from 12.8% in London to 14.9% in Midlands (Table S3 and Figure 6).

For cases reported in 2019/20, regression analysis as described in the method section showed no strong evidence of a significant difference in most regional mortality rates (Appendix 3). There was no strong evidence to suggest a significant difference in regional odds of deaths after infection. (Appendix 4).

Figure 5: 30-day all-cause mortality rate of E. coli bacteraemia by NHS commissioning region 2012/13 to 2019/20

1 Strong evidence described as a statistically significant (p< 0.05) mortality rate ratio of ≥0.5.
2 Strong evidence described as a statistically significant (p< 0.05) odds ratio of ≥0.25.
Variation by age and sex
MR and CFR increased with age and was greater in male patients compared to female patients. However, both were greater in patients <1-year-old compared to those between 1-44 years-old (Table S4, Figure 7 and Figure 8).

In 2019/20, among male patients, the highest MRs were in the ≥85 year age group (210.9 deaths per 100,000 population) and 75-84 year age group (71.1, Figure 7), which equated to CFRs of 23.1% and 16.8% the cases respectively (Figure 8).

In 2019/20, among female patients, MR was; 116.0 per 100,000 population (≥85 year age group) and 43.5 (75-84 year age group). These equated to CFR of 19.1% and 13.5% of cases in respective age groups.

The MR in male patients <1-years-old was deaths per 100,000 population (% of cases) compared to (% of cases) in female patients.
Figure 7: 30-day all-cause mortality rate of *E. coli* bacteraemia by age and sex 2012/13 to 2019/20

Figure 8: 30-day all-cause case fatality rate of *E. coli* bacteraemia by age and sex 2012/13 to 2019/20
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**Klebsiella spp. bacteraemia**

In 2019/20, 11,016 *Klebsiella* spp. bacteraemia cases were reported in England. Information on mortality was available for 97% (n = 10,684) of these cases (Table S5). There were 2,042 deaths within 30 days of a *Klebsiella* spp. bacteraemia giving an 3.6 deaths per 100,000 population. The CFR was 19.1% of cases.

The lack of longer-term data collection for *Klebsiella* spp. makes it difficult to ascertain if the CFRs to date are part of a trend or variation around an average rate. The overall CFR for prior financial years were 20.2% (n = 1,895) in 2017/18 and 18.6% (n = 1,929) in 2018/19.

**Variation by onset of bacteraemia**

In 2019/20, the MR of hospital-onset cases was 1.9 deaths per 100,000 bed-days (n= 669 deaths) compared to 2.1 (n= 716 deaths) in the previous financial year (2018/19, Table S6 and Figure 9). Over the same periods, the MR in community-onset cases was 2.2 (n= 1,213 deaths) deaths per 100,000 population and 2.5 (n= 1,373 deaths) respectively. Although the increase in deaths following community-onset *Klebsiella* spp. cases for 2019/20 was higher than the previous years, it was a proportionate to the increase reported community-onset cases.

Between 2017/18 and 2019/20, the CFR of hospital-onset cases reduced consistently from 24.5% to 21.7%. In contrast, between the current and previous financial years, the CFR of community-onset cases increased from 16.7% to 18.1%.

Again, without longer-term data it is difficult to know whether these changes are part of a longer-term trend or variation around an average rate.

**Figure 9: 30-day all-cause mortality rate of *Klebsiella* spp. bacteraemia by onset of bacteraemia 2017/18 to 2019/20**

*deaths within 30 days of sample collection*
Figure 10: 30-day all-cause case fatality rate of *Klebsiella* spp. bacteraemia by onset of bacteraemia 2017/18 to 2019/20

Variation by NHS commissioning region

In 2019/20, regional MR ranged from 3.1 deaths per 100,000 population in Midlands to 4.3 deaths per 100,000 population in North East and Yorkshire (Table S7 and Figure 11). Over the same period, CFRs ranged 17.1% in London to 21.6% in South East (Table S7 and Figure 12).

Between 2017/18 and 2019/20, the South East region had the greatest increase in CFR (19.8% to 21.6%) and MR (3.1 to 4.0 deaths per 100,000 population).

For cases reported in 2019/20, regression analysis as described in the method section showed no strong evidence of a significant difference\(^3\) in most regional mortality rates (Appendix 3). There was no strong evidence\(^4\) to suggest significant differences in regional odds of deaths, except between South West and South East (OR: 1.34, p < 0.01) and North West (OR: 1.25, p = 0.03) (Appendix 4).

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3 Strong evidence described as a statistically significant (p< 0.05) mortality rate ratio of ≥0.5.
4 Strong evidence described as a statistically significant (p< 0.05) odds ratio of ≥0.25.
Variation by age and sex

In 2019/20, MR and CFR increased with age. The MR was greater in male patients while the CFR was greater in female patients (Table S8, Figure 13 and Figure 14).

Among male patients, the highest MRs were in the ≥85 years age group (68.9 deaths per 100,000 population) and 75-84 years age group (27.3) age groups, which equated to CFRs of 27.1% and 20.3% respectively.
In female patients of the same age groups the MRs were; 23.2 (≥85 years age group) and 12.5 (75-84 years age group). These were CFRs of 30.0% and 23.8% of all cases in those respective age groups.

The mortality rates in male patients <1-years-old was deaths per 100,000 population (% of cases) compared to (% of cases) in female patients.

**Figure 13:** 30-day all-cause mortality rate of *Klebsiella* spp. bacteraemia by age and sex 2017/18 to 2019/20
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

Figure 14: 30-day all-cause case fatality rate of *Klebsiella* spp. bacteraemia by age and sex 2017/18 to 2019/20

![Graph showing case fatality rate of Klebsiella bacteraemia by age and sex 2017/18 to 2019/20](image)

**Pseudomonas aeruginosa** bacteraemia

In 2019/20, 4,336 *P. aeruginosa* bacteraemia cases were reported in England. Information on mortality was available for 97% (n= 4,205) of these cases (Table S9). There were 1,031 deaths within 30 days of a *P. aeruginosa* bacteraemia, giving a MR of 1.8 deaths per 100,000 population. The CFR was 24.5% of cases.

The lack of longer-term data collection for *P. aeruginosa* makes it difficult to ascertain if the CFR observed to date are part of a trend or variation around an average rate. The overall CFR for prior financial years were 26.9% (n = 1,121) in 2017/18 and 24.1% (n = 977) in 2018/19.

**Variation by onset of bacteraemia**

In 2019/20, the MR of hospital-onset cases was 1.2 deaths per 100,000 bed-days (n= 430 deaths) compared to 1.2 (n= 396 deaths) in the previous financial year (2018/19) (Table S10 and Figure 15). Over the same period, the MR in community-onset cases was 1.0 (n= 581 deaths) deaths per 100,000 population and 1.1 (n= 601 deaths) respectively.

The CFR of hospital-onset cases was 29.9% of cases in 2017/18 and 28.4% in 2019/20. For community-onset cases, this was 25.2% in 2017/18 and 22.3% in 2019/20 (Table S10 and Figure 16).
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**Figure 15:** 30-day all-cause mortality rate of *P. aeruginosa* bacteraemia by onset of bacteraemia 2017/18 to 2019/20

**Figure 16:** 30-day all-cause case fatality rate of *P. aeruginosa* bacteraemia by onset of bacteraemia 2017/18 to 2019/20

**Variation by NHS commissioning region**

In 2019/20, regional MR ranged from 1.6 deaths per 100,000 population in South West to 2.1 deaths per 100,000 population in London (Table S11 and Figure 17). Over the same period, CFRs ranged from 23.4% in London to 26.6% in North West (Table S11 and Figure 18).
For cases reported in 2019/20, regression analysis as described in the method section showed no strong evidence of a significant difference\(^5\) in most regional mortality rates (Appendix 3). There was no strong evidence\(^6\) to suggest a significant difference in regional odds of deaths after infection. (Appendix 4).

**Figure 17: 30-day all-cause mortality rate of *P. aeruginosa* bacteraemia by NHS commissioning region 2017/18 to 2019/20**

![Graph showing 30-day all-cause mortality rate of *P. aeruginosa* bacteraemia by NHS commissioning region 2017/18 to 2019/20.]

**Figure 18: 30-day all-cause case fatality rate of *P. aeruginosa* bacteraemia by NHS commissioning region 2017/18 to 2019/20**

![Graph showing 30-day all-cause case fatality rate of *P. aeruginosa* bacteraemia by NHS commissioning region 2017/18 to 2019/20.]

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5 Strong evidence described as a statistically significant (p< 0.05) mortality rate ratio of ≥0.5.

6 Strong evidence described as a statistically significant (p< 0.05) odds ratio of ≥0.25.
Variation by age and sex

In 2019/20, MR and CFR increased with age. The MR was greater in male patients while the CFR was greater in female patients. However, the MR and CFR of patients <1-year-old were higher than those between 1-64 years-old (Table S12, Figure 19 and Figure 20).

In 2019/20, among male patients, the highest mortality rates were in the ≥85 years-old (31.1 deaths per 100,000 population) and 75-84 years-old (11.3) age groups, which were CFRs of 27.9% and 21.9% cases respectively.

In female patients of the same age groups, the MRs were; 11.1 (≥85 years-old) and 6.5 (75-84 years-old). These equated to CFRs of 39.7% and 36.1% of all cases in those respective age groups.

The MR in male patients <1-years-old was 3.7 deaths per 100,000 population (44.4% of cases) compared to 1.0 (15.0% of cases) in female patients.

Figure 19: 30-day all-cause mortality rate of *P. aeruginosa* bacteraemia by age and sex 2017/18 to 2019/20
Staphylococcus aureus bacteraemia

MRSA bacteraemia

In 2019/20, 814 MRSA bacteraemia cases were reported in England. Information on mortality was available for 96% (n= 782) of these cases (Table S13). There were 201 deaths within 30 days of an MRSA bacteraemia which was a MR of 0.4 deaths per 100,000 population. The CFR was 25.7% of cases.

There was a trend of declining MR beginning from 2.6 deaths per 100,000 population (n= 1,354) in 2007/08 to 0.4 in 2019/20. A similar trend is observed for the CFR, 38.9% in 2007/08.

Variation by onset of bacteraemia

Between 2007/08 and 2019/20, the MR and CFR declined in both hospital-onset and community-onset cases.

In 2019/20, the MR in hospital-onset cases was 0.2 deaths per 100,000 bed-days (n= 73 deaths) which was similar to the previous financial year (0.2, n= 67 deaths, 2018/19) (Table S26 and Figure 21).

Similarly, the MR in community-onset cases did not change between 2018/19 and 2019/20 – 0.2 deaths per 100,000 population in both.
Between 2007/08 and 2019/20, the CFR of hospital-onset cases declined from 42.4% to 29.2% respectively, while community-onset cases declined from 33.1% to 24.1% of cases (Table S14 and Figure 22) respectively.

**Figure 21: 30-day all-cause mortality rate of MRSA bacteraemia by onset of bacteraemia 2007/08 to 2019/20**

**Figure 22: 30-day all-cause case fatality rate of MRSA bacteraemia by onset of bacteraemia 2007/08 to 2019/20**

**Variation by NHS commissioning region**
Like the national trend, both regional MRs and CFRs declined between 2007/08 and 2019/20.
In 2019/20, regional MR ranged from 0.2 deaths per 100,000 population in South West to 0.5 deaths per 100,000 population in East of England (Table S15 and Figure 23). Over the same period, CFRs ranged 14.6% in South West to 32.6% in East of England (Table S15 and Figure 24).

For cases reported in 2019/20, regression analysis as described in the method section showed no strong evidence of a significant difference\(^7\) in most regional mortality rates (Appendix 3). There was no strong evidence\(^8\) to suggest a significant difference in regional odds of deaths after infection. (Appendix 4).

**Figure 23: 30-day all-cause mortality rate of MRSA bacteraemia by NHS commissioning region 2007/08 to 2019/20**

---

7 Strong evidence described as a statistically significant (p< 0.05) mortality rate ratio of ≥0.5.

8 Strong evidence described as a statistically significant (p< 0.05) odds ratio of ≥0.25.
Variation by age and sex

In 2019/20, MR and CFR increased with age and was greater in male patients compared to female patients (Table S16, Figure 25 and Figure 26).

Among male patients, the highest MR were in the ≥85 year age group (9.0 deaths per 100,000 population) and 75-84 year age group (3.4) age groups, CFRs 60.8% and 39.7% respectively.

In female patients, the mortality rates were also higher in older age groups; 3.2 (≥85 year age group) and 1.1 (75-84 year age group). These equated to CFRs of 52.8% and 30.6% of all cases in those respective age groups.

Compared to other infections covered in this report, there were relatively fewer deaths in patients <1-year-old compared to other age groups. In 2019/20, there was 1 death within 30-days following MRSA bacteraemia from male and female patients <1-year-old.
Figure 25: 30-day all-cause mortality rate of MRSA bacteraemia by age and sex 2007/08 to 2019/20

Figure 26: 30-day all-cause case fatality rate of MRSA bacteraemia by age and sex 2007/08 to 2019/20
MSSA bacteraemia

In 2019/20, 12,193 MSSA bacteraemia cases were reported in England. Information on mortality was available for 97% (n= 11,813) of these cases (Table S17). There were 2,299 deaths within 30 days of an MSSA bacteraemia which gave an MR of 4.1 deaths per 100,000 population. The CFR was 19.5% of cases.

Overall, there was an increasing trend in mortality rates from 3.3 deaths per 100,000 population in 2011/12 to 4.1 in 2019/20. However, the MR since 2015/16 has been relatively stable at annual average of 0.4 deaths per 100,000 population.

Variation by onset of bacteraemia

The MR in hospital-onset cases was relatively stable (1.9-2.2 deaths per 100,000 bed-days) between 2012/2013 and 2019/20 (Table S18 and Figure 27). For community-onset cases, the MR increased in each financial year from 2.0 deaths per 100,000 population in 2011/12 to 2.7 in 2018/19. This increased to 2.8 deaths per 100,000 population in 2019/20.

Between 2011/12 and 2019/20, the CFR of hospital-onset cases declined from 26.7% to 22.0%, while for community-onset cases it declined from 18.9% to 18.5% of cases (Table S18 and Figure 28).

Figure 27: 30-day all-cause mortality rate of MSSA bacteraemia by onset of bacteraemia 2011/12 to 2019/20
Figure 28: 30-day all-cause case fatality rate of MSSA bacteraemia by onset of bacteraemia 2011/12 to 2019/20

Variation by NHS commissioning region
In 2019/20, regional MR ranged from 2.8 deaths per 100,000 population in London to 5.5 deaths per 100,000 population in North East and Yorkshire (Table S19 and Figure 29). Over the same period, CFRs ranged from 16.2% in London to 21.2% in East of England (Table S19 and Figure 30).

For cases reported in 2019/20, regression analysis as described in the method section showed no strong evidence of a significant difference⁹ in most regional mortality rates (Appendix 3). There was no strong evidence¹⁰ to suggest significant differences in regional odds of deaths, except between North East and Yorkshire and London (OR: 1.26, p = 0.01) and South West (OR: 1.25, p = 0.02) (Appendix 4).

---

⁹ Strong evidence described as a statistically significant (p< 0.05) mortality rate ratio of ≥0.5.
¹⁰ Strong evidence described as a statistically significant (p< 0.05) odds ratio of ≥0.25.
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

**Figure 29:** 30-day all-cause mortality rate of MSSA bacteraemia by NHS commissioning region 2011/12 to 2019/20

**Figure 30:** 30-day all-cause case fatality rate of MSSA bacteraemia by NHS commissioning region 2011/12 to 2019/20

**Variation by age and sex**

In 2019/20, the MR and CFR increased with age however, MR was greater in male patients while CFR was greater in female patients. (Table S20, Figure 31 and Figure 32).
Among male patients, the highest MRs were in those ≥85 year age group (71.3 deaths per 100,000 population) and 75-84 year age group (29.5) age groups, CFRs 40.0% and 28.0% respectively.

In female patients, the MRs were also higher in older age groups; 34.8 (≥85 year age group) and 13.6 (75-84 year age group). These equated to CFR of 45.3% and 30.3% of all cases in those respective age groups.

The MR in male patients <1-years-old was deaths per 100,000 population (% of cases) compared to (% of cases) in female patients.

**Figure 31: 30-day all-cause mortality rate of MSSA bacteraemia by age and sex 2011/12 to 2019/20**
Clostridioides difficile infection

In 2019/20, 13,177 CDI cases were reported in England. Information on mortality was available for 98% (n= 12,893) of these cases (Table S21). There were 1,735 deaths within 30 days of a CDI case giving an MR of 3.1 deaths per 100,000 population. The CFR was 13.5% of cases.

There was a trend of declining MR beginning from 27.1 deaths per 100,000 population (n= 13,973) in 2007/08 to 3.1 in 2019/20. A similar trend was observed for the CFR from 26.3% in 2007/08 to 13.5% in 2019/20.

Variation by onset of infection
Between 2007/08 and 2019/20, MR and CFR declined in both hospital-onset and community-onset cases.

In 2019/20, there was an increase in the MR of hospital-onset cases (2.7 deaths per 100,000 bed-days, n= 945 deaths) compare to the previous financial year (2.5, n= 877 deaths; 2018/19) (Table S22 and Figure 33). Similarly, in community-onset cases, the MR fell from 2.5 deaths per 100,000 population 2018/19 to 2.7 in 2019/20.
Between 2007/08 and 2019/20, the CFR of hospital-onset cases declined from 30.2% to 20.5%, while for community-onset cases it declined from 20.2% to 9.5% of cases (Table S22 and Figure 34).

**Figure 33: 30-day all-cause mortality rate of CDI by onset of infections 2007/08 to 2019/20**

**Figure 34: 30-day all-cause case fatality rate of CDI by onset of infections 2007/08 to 2019/20**

**Variation by prior healthcare exposure**

The categorisation of CDI cases based on prior healthcare exposure began in 2017/18. In 2019/20, the MRs were: 3.1 deaths per 100,000 bed-days for Hospital-onset: healthcare-associated cases and 0.7 deaths per 100,000 bed-days plus day-admissions...
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

for Community-onset: healthcare-associated cases. In the same financial year, it was; 0.5 deaths per 100,000 population for Community-onset: community-associated cases, 0.3 for Community-onset: indeterminate association cases and < 0.1 for Community-onset: unknown healthcare association cases (Table S23).

The CFRs were; 20.2% for Hospital-onset: healthcare-associated cases, 10.7% for Community-onset: healthcare-associated cases, 7.0% for Community-onset: community-associated cases, 10.3% for Community-onset: indeterminate association cases and 10.2% for Community-onset: unknown healthcare association cases (Table S23; Figure 41).

**Figure 35: 30-day all-cause case fatality rate of CDI by prior healthcare exposure 2007/08 to 2019/20**

![Figure showing 30-day all-cause case fatality rate of CDI by prior healthcare exposure 2007/08 to 2019/20](image)

**Variation by NHS commissioning region**

In 2019/20, regional MR ranged from 2.1 deaths per 100,000 population in London to 4.4 deaths per 100,000 population in North West (Table S24 and Figure 36). Over the same period, CFRs ranged 12.2% in South West to 15.0% in North East and Yorkshire (Table S24 and Figure 37).

For cases reported in 2019/20, regression analysis as described in the method section showed no strong evidence of a significant difference\(^{11}\) in most regional mortality rates (Appendix 3). There was no strong evidence\(^{12}\) to suggest significant differences in regional odds of deaths, except between North East and Yorkshire and South West (OR: 1.32, \(p = 0.01\)) (Appendix 4).

---

\(^{11}\) Strong evidence described as a statistically significant (\(p < 0.05\)) mortality rate ratio of \(\geq 0.5\).

\(^{12}\) Strong evidence described as a statistically significant (\(p < 0.05\)) odds ratio of \(\geq 0.25\).
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

**Figure 36: 30-day all-cause mortality rate of CDI by NHS commissioning region 2007/08 to 2019/20**

[Graph showing mortality rates across different commissioning regions over different years]

**Figure 37: 30-day all-cause case fatality rate of CDI by NHS commissioning region 2007/08 to 2019/20**

[Graph showing case fatality rates across different commissioning regions over different years]

**Variation by age and sex**

The CDI surveillance only covers patients ≥2 years-old. The CFR following *C. difficile* infections increased with age. MR and CFR increased with age and was greater in male patients compared to female patients. (Table S25, Figure 38 and Figure 39).

Among male patients, the highest MRs were in the ≥85 year age group (58.7 deaths per 100,000 population) and 75-84 year age group (19.1) age groups, linked to 25.8% and 17.3% respectively.
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

In female patients, the MRs were also higher in older age groups; 41.9 (≥85 year age group) and 16.6 (75-84 year age group). These equated to CFRs of 19.9% and 13.7% of all cases in those respective age groups.

**Figure 38: 30-day all-cause mortality rate of CDI by age and sex 2007/08 to 2019/20**

**Figure 39: 30-day all-cause case fatality rate of CDI by age and sex 2007/08 to 2019/20**
**Discussion**

Over the surveillance period, the percentage of patients that died (CFR) following each infection covered by this report has declined (Figure 2) despite instances of increasing incidence of deaths (MR) in infections like *E. coli* and MSSA bacteraemia (Figure 1).

Between 2007/08 and 2019/20, the CFRs of MRSA bacteraemia and CDI declined by (13.2 % and 12.8 % respectively) which is indicative of the change in their epidemiology over the years. During this period, the incidence of these infections declined, and both have shown a shift from predominantly hospital-onset infections to predominantly community-onset cases. Since mortality and morbidity are often higher in hospital-onset (a proxy for healthcare-acquired) cases compared to community-onset cases, reductions in the former would be accompanied by reductions in the overall CFR of the infection as seen in MRSA bacteraemia cases (Figure 22, Figure 34; Table S14, Table S22).

The large decline in CFR following CDI may also be associated with reductions in infections caused by *C. difficile* ribotype 027, which was historically the predominant ribotype in England between 2007 and 2012, and has been associated with higher mortality compared to other ribotype [10].

The CFR of all infections covered in this report, except CDI, increased in the current financial year (2019/20) compared to the previous year (2018/19). These increases were relatively small, ranging from a difference of 0.4% in MSSA bacteraemia to a difference of 1.1% in MRSA bacteraemia over the same period. These changes in CFR, including that of CDI, were not statistically significant and so lack evidence to suggest that these changes are not part of a variation around an average CFR.

A substantial proportion of community-onset CDI cases will have had prior healthcare interactions, and thus are more likely to have a higher CFR associated with with healthcare associated infection, although greater likelihood of underlying conditions predisposing this group to increased risk of death can be discounted. CFR analysis confirmed higher CFR in the healthcare-associated cases with in Community-onset: healthcare-associated (10.7%) and Community-onset: community-associated (7.0%) in 2019/20 (Table S23; Figure 35).

There was a noticeable increase in the CFR of MRSA bacteraemia in 2012/13. This may be related to an excess in all-cause deaths associated with respiratory causes noted during the winter of 2012/13 [11]. However, this was set against the general downward trend observed in CFR. Furthermore, the confidence intervals for the CFR in 2012/13 overlap with those of the surrounding years; thus suggesting that differences between 2012/13 and surrounding years could have occurred by chance.
In general, for all pathogens, CFRs increased with age except in patients <1-years-old; where CFRs were usually higher than patients aged 1-14 years old, and in some cases compared to patients aged 15-44 years-old. Of note, is the relatively high CFR of *P. aeruginosa* bacteraemia in male <1-year-old patients - 44.4% (n= 12, MR: 3.7) compared to males of every other age group, and female patients of the same age group - 15.0% (n= 3, MR: 1.0). It is not possible to assess fatality rates in patients less than 2 years old with CDI as infections in this age group are not reported to PHE (see Appendix 1)

CFRs for CDI and *E. coli* bacteraemia were generally higher in male patients compared to female patients, while *Klebsiella* spp., MRSA, MSSA and *P. aeruginosa* bacteraemia were generally higher in female patients compared to male patients. Among MSSA and *P. aeruginosa* bacteraemia cases the CFR was always higher among females.

There were considerable regional differences in the mortality and case fatality rates of each infection covered in this report. For most of the infections covered in this report, the CFR in the northern regions was higher than those in the southern regions, which could suggest a demographic difference in underlying health conditions. Regression analysis revealed that, although in many instances there was no evidence of statistical differences in regional mortality rates and odds of death, in several instances there was a statistical difference between the odds of deaths in North East and Yorkshire and that of the South East.

In 2019/20, the largest CFR of infections covered in this report, were in MRSA and *P. aeruginosa* bacteraemia. The CFR of *E. coli* bacteraemia was relatively small compared to those for MRSA and *P. aeruginosa* bacteraemia. However, its higher incidence of infection, and deaths following infection (MR: 10.7 deaths per 100,000 population) compared to MRSA (MR: 0.4) and *P. aeruginosa* bacteraemia (MR: 1.8) highlights the public health burden of this infection. The continued increase in mortality rates following *E. coli* bacteraemia is of particular concern. In 2018/19, there were 5,798 deaths within 30 days of *E. coli* bacteraemia, over 4 times the number of deaths following MRSA bacteraemia at the start of mandatory surveillance (2007/08; 1,354) when MRSA bacteraemia cases were at its highest levels. Despite the high mortality rates, the CFR for *E. coli* bacteraemia remains low. Reducing the incidence rate of *E. coli* bacteraemia should have a concomitant effect of reducing the number of deaths from this infection.
Limitations

The analyses presented here are based on infections reported to PHE that could be linked to the NHS Spine to obtain mortality information. While most of infection reports had complete NHS numbers (required for linkage), for occasional reports the NHS Spine was not able to return patient information, for reasons such as the NHS number and date of birth not matching a record on the NHS Spine. Thus, there may be bias in the records with available mortality information, which may over- or under-estimate the number of deaths and associated CFRs, if the records without mortality information were for patients with a different likelihood of death. However, this effect on reported outcomes is to be low, since the linkage had a high degree of completeness, at around 96% of all cases.

Crude CFRs are presented and as such have not been adjusted for potential confounders such as age, gender or co-morbidities, which may affect comparisons over time, between regions and onset setting.

Due to data constraints, regional regression analysis could only be controlled for age and sex. Therefore, factors such as prior hospitalisation, healthcare interactions, co-morbidities, which are likely to be cofounders affecting mortality outcomes, have not been included in the regression analysis.

Finally, while analysis of 30-day all-cause fatality estimates the risk of death following an infection within a fixed time frame it does not provide insight into attributable mortality. However, it is difficult to ascertain attributable mortality in practice, due to clinical and diagnostic uncertainty encountered when trying to determine the exact cause of death in patients, particularly in those with multiple co-morbidities.

The ONS has historically published statistics on deaths involving MRSA and C. difficile; these statistics are not comparable with those presented here for the reasons highlighted in the Introduction.
Appendix

Appendix 1: Figures included in this report

Figure 1: Number of deaths within 30-days of case detection by infection
Figure 2: 30-day all-cause case fatality rate by infection
Figure 3: 30-day all-cause mortality rate of *E. coli* bacteraemia by onset of bacteraemia
Figure 4: 30-day all-cause case fatality rate of *E. coli* bacteraemia by onset of bacteraemia
Figure 5: 30-day all-cause mortality rate of *E. coli* bacteraemia by NHS commissioning region
Figure 6: 30-day all-cause case fatality rate of *E. coli* bacteraemia by NHS commissioning region
Figure 7: 30-day all-cause mortality rate of *E. coli* bacteraemia by age and sex
Figure 8: 30-day all-cause case fatality rate of *E. coli* bacteraemia by age and sex
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Figure 15: 30-day all-cause mortality rate of *P. aeruginosa* bacteraemia by onset of bacteraemia
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Figure 21: 30-day all-cause mortality rate of MRSA bacteraemia by onset of bacteraemia
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Figure 23: 30-day all-cause mortality rate of MRSA bacteraemia by NHS commissioning region
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and C. difficile infections

Figure 24: 30-day all-cause case fatality rate of MRSA bacteraemia by NHS commissioning region
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Figure 37: 30-day all-cause mortality rate of CDI by age and sex
Figure 38: 30-day all-cause case fatality rate of CDI by age and sex
Figure 39: 30-day all-cause case fatality rate of CDI by age and sex
Figure 40: Visualization of the 30-day mortality de-duplication methodology

Appendix 2: Tables in the accompanying data sheet

Table S1: 30-day all-cause case fatality rate of E. coli bacteraemia
Table S2: 30-day all-cause case fatality rate of E. coli bacteraemia by onset of bacteraemia
Table S3: 30-day all-cause case fatality rate of E. coli bacteraemia by NHS commissioning region
Table S4: 30-day all-cause case fatality rate of E. coli bacteraemia by age and sex
Table S5: 30-day all-cause case fatality rate of Klebsiella spp. bacteraemia
Table S6: 30-day all-cause case fatality rate of Klebsiella spp. bacteraemia by onset of bacteraemia
Table S7: 30-day all-cause case fatality rate of Klebsiella spp. bacteraemia by NHS commissioning region
Table S8: 30-day all-cause case fatality rate of Klebsiella spp. bacteraemia by age and sex
Table S9: 30-day all-cause case fatality rate of P. aeruginosa bacteraemia
Table S10: 30-day all-cause case fatality rate of P. aeruginosa bacteraemia by onset of bacteraemia
Table S11: 30-day all-cause case fatality rate of P. aeruginosa bacteraemia by NHS commissioning region
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

Table S12: 30-day all-cause case fatality rate of *P. aeruginosa* bacteraemia by age and sex
Table S13: 30-day all-cause case fatality rate of MRSA bacteraemia
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Table S15: 30-day all-cause case fatality rate of MRSA bacteraemia by NHS commissioning region
Table S16: 30-day all-cause case fatality rate of MRSA bacteraemia by age and sex
Table S17: 30-day all-cause case fatality rate of MSSA bacteraemia
Table S18: 30-day all-cause case fatality rate of MSSA bacteraemia by onset of bacteraemia
Table S19: 30-day all-cause case fatality rate of MSSA bacteraemia by NHS commissioning region
Table S20: 30-day all-cause case fatality rate of MSSA bacteraemia by age and sex
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Table S22: 30-day all-cause case fatality rate of CDI by onset of infection
Table S23: 30-day all-cause case fatality rate of CDI by prior healthcare exposure
Table S24: 30-day all-cause case fatality rate of CDI by NHS commissioning region
Table S25: 30-day all-cause case fatality rate of CDI by age and sex
Appendix 3: Age-sex adjusted regional mortality rate ratios

**E. coli bacteraemia**

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**Klebsiella spp. bacteraemia**

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Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

**P. aeruginosa bacteraemia**

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**MRSA bacteraemia**

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**MSSA bacteraemia**

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Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

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### Appendix 4: Age-sex adjusted regional odds ratios

#### *E. coli* bacteraemia

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#### *Klebsiella* spp. bacteraemia

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Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

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**P. aeruginosa bacteraemia**

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**MRSA bacteraemia**

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**MSSA bacteraemia**

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Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

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CDI

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Appendix 5: Detailed descriptions of methods

Data extraction; case reports and mortality outcomes

Data on MRSA, MSSA, *E. coli*, *Klebsiella* spp. and *P. aeruginosa* bacteraemia, and CDI were extracted on 23 June 2020 from the HCAI Data Capture System (DCS). Reports of CDI from patients aged <2 years at the time of specimen collection were excluded from all analyses because this data is not subject to mandatory surveillance, as carriage rates are high [12] with little evidence for disease [13]. Mortality estimates cover the first complete financial year after the start of the surveillance for each data collection; 2007/08 for MRSA bacteraemia and CDI, 2011/12 for MSSA bacteraemia, 2012/13 for *E. coli* bacteraemia and 2017/18 for *Klebsiella* spp. and *Pseudomonas aeruginosa* bacteraemia.

Mortality information was obtained by batch tracing the extracted MRSA, MSSA, and *E. coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa* bacteraemia, and CDI data against the NHS Spine; a central repository of patient demographic and medical information managed by the Health and Social Care Information Centre. Records were traced using the NHS number and date of birth (DOB). Only records that match on both the NHS number and the DoB can be successfully traced and have the potential for fatality information to be returned. These are referred to as “linked/traced reports” in this document and the accompanying datasheet. Within the HCAI DCS, NHS number and DOB are mandatory fields for entering and saving a case onto the surveillance system; users can enter “9”s in place of a valid NHS number if the NHS number is unknown, while 01/01/1900 is used for DoB if it is unknown. Only traced reports are considered when calculating CFR.\(^{13}\)

Records between 2007/08 and 2014/15 were originally traced on 04 July 2015; a secondary trace was conducted on all records from financial years’ 2013/14 to 2016/17 on 03 July 2017. Records after 2016/17, were traced in the same financial year they were published. Records from the most recent 3 financial years (2017/18, 2018/19 and 2019/20), and retrospective reports prior to these years which have not been included in previous reports were collectively traced on 26 August 2020. Where applicable, data revisions are made to previously traced records from 2017/18 and 2018/19 using the

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\(^{13}\) Some records had valid a NHS numbers and date of birth but failed to trace to the NHS Spine; this involved the following number of records across all reported financial years (and percentage of total records) for each infection: MRSA bacteraemia, 690 (3.7%); MSSA bacteraemia, 2,067 (2.2%); *E. coli* bacteraemia, 7,060 (2.3%); *Klebsiella* spp. bacteraemia, 603 (1.9%); *P. aeruginosa* bacteraemia, 242 (1.9%); CDI 6,646 (2.5%)
outcome of this re-trace. This retrace and/or addition of late reports may result in minor changes to previously published counts.  

Thirty-day all-cause deaths

For infection reports with a death reported in the NHS Spine, the time in days between specimen date and date of death was calculated to identify whether it was within the 30-day window included in the case fatality calculations. Bacteraemia reports with a date of death ≥2 days prior to the specimen date were excluded from the analysis. In publications prior to September 2018, CDI cases with dates of death ≥3 days were excluded however, since then, such cases have been included and are considered a 30-day all-cause death. On the HCAI DCS, MRSA, MSSA, *E. coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa* bacteraemia episode lengths are 14-days, and CDI is 28-days, therefore it is possible to have multiple cases within 30 days of a death. Where multiple records from the data collection (bacteraemia or CDI) had the same NHS number and date of birth within the 30-day fatality window, only the record with the specimen date closest to the date of death was used to calculate 30-day all-cause case fatality rates (CFR). This was done to prevent estimate bias by overestimating of the numbers of deaths. This deduplication algorithm was applied to both the 30-day fatality, traced and total number of reports to prevent an inflated count of deaths and reports.

Deduplication algorithm

Blood (faecal for CDI) sample with the earliest specimen date before the patient’s date of death was considered the index sample. However, if there was a bacteraemia positive post-mortem sample within 1 day after a patient’s date of death, and no other case was reported within 30 days prior to the patient’s date of death, that post-mortem sample is taken as the index sample and considered a 30-day all-cause death. This short period of allowance is included to account for the possibility of late reports and data entry errors. Post-mortem bacteraemia samples after this period of allowance are excluded and not included in either the denominator (linked cases) or numerator (30-day all-cause deaths) of CFR analyses.

In contrast, CDI positive post-mortem samples are included in CFR where applicable since they are subject to mandatory surveillance [1]. For the purpose of this report,

14 This involved the following number of new/updated reports for each infection in previous years’ where 30-day fatality status was updated from “yes” to from “no”: MRSA bacteraemia, 0 (0%); MSSA bacteraemia, 12 (< 1%); *E. coli* bacteraemia, 32 (< 1%); CDI 2 (< 1%)

15 There were 104 cases (< 1%) of CDI with dates of death ≥3 day prior to their specimen dates. These were included in the analysis and considered 30-day all-cause fatalities.

16 The following number of cases were excluded to ensure each patient had only one 30-day fatality: MRSA bacteraemia, 56 (< 1%); MSSA bacteraemia, 197 (< 1%); *E. coli* bacteraemia, 674 (< 1%); *Klebsiella* spp. bacteraemia, 82 (< 1%); *P. aeruginosa* bacteraemia, 41 (< 1%); CDI 368 (< 1%)
patients with a post-mortem CDI faecal sample are assumed to have died to on the same date as their most recent sample. If no other CDI positive sample was reported within 30 days prior to the patient’s date of death, these CDI positive post-mortem samples are taken as index cases and considered 30-day all-cause deaths.

For bacteraemia and CDI samples which could be linked to fatality records, the most recent sample was taken as an index sample. Bacteraemia and CDI positive samples with specimen dates before index samples but within a 30-day window period prior to the patient’s date of death are excluded as duplicates.

Deduplication is done at a data collection-level. This means that each data collection will have its own index sample if a patient tests positive for multiple infections covered in this report. Additionally, only duplicates of the same type of infection are excluded. For example, if a patient tests positive for MRSA, *E. coli* and CDI samples within 30-days of each other, they will be included in CFR calculation thrice; once for each data collection.
### Figure 40: Visualisation of the 30-day mortality de-duplication methodology

<table>
<thead>
<tr>
<th>Data collection</th>
<th>Patient</th>
<th>Mortality outcome</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteraemia</td>
<td>Patient 1</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>Patient 2</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>Patient 3</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>Patient 4</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>Patient 5</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>CDI</td>
<td>Patient 6</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>CDI</td>
<td>Patient 7</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>CDI</td>
<td>Patient 8</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>CDI</td>
<td>Patient 9</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>CDI</td>
<td>Patient 10</td>
<td>Yes</td>
<td>X</td>
</tr>
<tr>
<td>CDI/Bacteraemia</td>
<td>Patient 11</td>
<td>No</td>
<td>X</td>
</tr>
<tr>
<td>CDI/Bacteraemia</td>
<td>Patient 12</td>
<td>No</td>
<td>X</td>
</tr>
<tr>
<td>CDI/Bacteraemia</td>
<td>Patient 13</td>
<td>No</td>
<td>X</td>
</tr>
</tbody>
</table>

- **X**: Index sample
- **-->**: Retained sample
- **-->**: Excluded sample
- **P**: Retained post-mortem sample
- **-->**: Excluded post-mortem sample
- **>**: Date of death
- **>-**: 30-day all-cause mortality window period
- **->**: 1 day allowance for late report or data entry error (Bacteraemia and CDI)
- **-->**: 2 day allowance for late report or data entry error (CDI only)
- **-->**: 30-day deduplication window for cases with unknown mortality outcomes
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and *C. difficile* infections

**Case fatality rates (CFR)**

CFR was calculated by financial year (of the bacteraemia or CDI), region, age and gender; these were calculated for each organism as follows:

\[
30\text{ day all cause CFR} = \frac{\sum(30\text{ day all cause deaths})}{\sum(\text{traced reports})} \times 100
\]

Ninety-five percent CIs for CFR were calculated using the Pearson-Klopper method for a binomial distribution. These are included in the accompanying datasheet.

**Estimated total number of 30-day all-cause deaths**

An estimate of the number of deaths that might be observed in each period if all infection reports could have been linked to mortality records was calculated. This was done by multiplying the total number of deduplicated infection reports submitted to the HCAI DCS for a given financial year by the 30-day CFR (expressed as a proportion) and rounded to the nearest whole number. Care should be taken with interpretation of this data as it assumes the risk of death for those cases that could and could not be linked are the same. This information is included in the accompanying datasheet.

The estimated total number of 30-day all-cause deaths was calculated as follows:

\[
\text{Estimated total number of 30 day all cause deaths} = (\text{Deduplicated total reports}) \times (30\text{ day all cause CFR})
\]

**Change in CFR**

Changes in CFR were presented as percentage differences. For example, yearly changes in CFR of each infection are calculated as follows:

\[
\text{Percentage change} = (v_p - v_c)
\]

where

\[v_p = \text{CFR in financial year 1}, \ \text{and};\]
\[v_c = \text{CFR in financial year 2}\]

The P-values for these differences were calculated using the method described by Altman et al. [14].

95% confidence intervals for the difference in CFR were calculated using the Standard Error of the difference between 2 proportions:

\[
SE(p_1 - p_2) = \sqrt{\frac{p_1(1 - p_1)}{n_1} + \frac{p_2(1 - p_2)}{n_2}}
\]

\[
95\% \ CI = (p_1 - p_2) \pm 1.96 \times SE(p_1 - p_2)
\]
Regression analysis

Statistically significant differences in regional odds of death and mortality rates where assessed by multivariate regression analyses controlled for age and gender.

Sample calculation

Sample calculations for CFR (not including 95% CI), estimated total number of 30-day all-cause deaths, and percentage difference for MRSA in 2019/20 as shown below. Note that all calculations within the report use the raw figures found in the accompanying data sheet. Figures in this report are rounded to one decimal place:

\[
\text{30 day all cause } \text{CFR}_{\text{MRSA} \, 2019/20} = \frac{201 \text{ deaths}}{782 \text{ deduplicated traced reports}} \times 100 = 25.7\%
\]

\[
\text{Est. total number of deaths}_{\text{MRSA} \, 2019/20} = (811 \text{ mortality deduplicated DCS reports}) \times (0.257) = 209
\]

\[
\text{Percentage difference in CFR}_{\text{MRSA} \, 2007/08 \text{ to } 2019/20} = 38.9 - 25.7 = 13.2\% \text{ difference}
\]
Appendix 6: Summary of differences between Office for National Statistics and PHE fatality outputs

Table A1: Summary of differences in methodology between the ONS and PHE fatality publications

<table>
<thead>
<tr>
<th>Information</th>
<th>ONS</th>
<th>PHE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geography</td>
<td>England and Wales</td>
<td>England</td>
</tr>
<tr>
<td>Time period covered</td>
<td>Calendar year</td>
<td>Financial year</td>
</tr>
<tr>
<td>Mortality data source</td>
<td>Death registrations</td>
<td>NHS Spine reports of death</td>
</tr>
<tr>
<td>Deaths relating to</td>
<td>MRSA bacteraemia and C. difficile</td>
<td>MRSA, MSSA, <em>E. coli</em> bacteraemia and <em>C. difficile</em> infection</td>
</tr>
<tr>
<td></td>
<td>Mention of MRSA or <em>C. difficile</em> on the death certificate (where the patient need not have died from MRSA or <em>C. difficile</em>) and where MRSA or <em>C. difficile</em> were the underlying cause of death.</td>
<td>Deaths within 30 days of positive specimen of MRSA, MSSA or <em>E. coli</em> bacteraemia or <em>C. difficile</em> infection determined using data matched with the NHS Spine.</td>
</tr>
<tr>
<td>Denominator</td>
<td>All deaths in the given time period and population in the given time period (2 different denominators used)</td>
<td>All traced reports of MRSA, MSSA, <em>E. coli</em> bacteraemia or CDI in the given time period</td>
</tr>
</tbody>
</table>
Thirty-day mortality following MRSA, MSSA and Gram-negative bacteraemia and C. difficile infections

References

About Public Health England

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