Food-borne infections are prevalent globally, with an average of approximately 95,000 laboratory-confirmed cases per year in Europe caused by the gram-negative, facultative anaerobic *Salmonella* spp. (1). The bacterium has a diverse genetic repertoire with over 2500 serovars encompassed within the *S. enterica* subspecies *Enterica*, accounting for 99% of human and animal infections spread via the faecal-oral route.

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Genomic Analysis of *Salmonella* Virchow and Antimicrobial Resistance in the UK associated with travel to Africa

Queen Mary
University of London

[1&2]Aman Zahra, [1]Marie Anne Chattaway
[1]Salmonella Reference Unit, UK Health Security Agency, 61 Colindale Avenue, London, NW9 5EQ
[2] Queen Mary University of London, Mile End Road, London, E1 4NS

INTRODUCTION

Food-borne infections are prevalent globally, with an average of approximately 95,000 laboratory confirmed cases per year in Europe caused by the facultative anaerobic *Salmonella* spp. (1). This includes *S.* Virchow, which has frequently shown resistance to a broad range of antibiotics.

The Salmonella Reference Unit (SRU) within the Gastrointestinal Bacteria Reference Unit (GBRU) at the UK Health Security Agency (UKHSA) receives presumptive *Salmonella* isolates from laboratories across England and Wales as *Salmonella* spp. are notifiable organisms under national legislation (2). The implementation of Whole Genome Sequencing (WGS) by the SRU in 2014, also provides the chance to screen for emerging antimicrobial resistance (AMR) threats (3). Africa is known to have a high salmonellosis burden, yet limited routine genomic data is available on the different serovars and population structure of *Salmonella* from this continent. At UKHSA, recent travel history can be used for sentinel surveillance to infer circulating strains from African countries being imported into the UK and allow comparison against the global incidence using databases like Enterobase and Core genome Multilocus sequence Typing (cgMLST)(4).

This research aimed to provide a better understanding on the incidence, population structure and AMR of S. Virchow infections within England in relation to travel to Africa.

METHODS

1. Data was provided by the SRU that had been collected between 2004-2021 from patients with travel to Africa within 28 days of generating symptoms. Of the 699 isolates, a total of 114 *S.* Virchow isolates from 681 patients had WGS data.
2. Analysis included; determining demographics of patients, understanding burden of *S.* Virchow infections in the UK associated with travel to different parts of Africa and assessing impact of Sars-Cov-2 on *Salmonella* cases between 2019-2020.
3. WGS data from 2014 -2021 was analysed using cgMLST via Enterobase to identify genetic relatedness of strains and detect any potential outbreaks.
4. Antimicrobial resistance determinants were detected using GeneFinder and mapped against travel to understand importation of potential resistance and detect MDR strains.

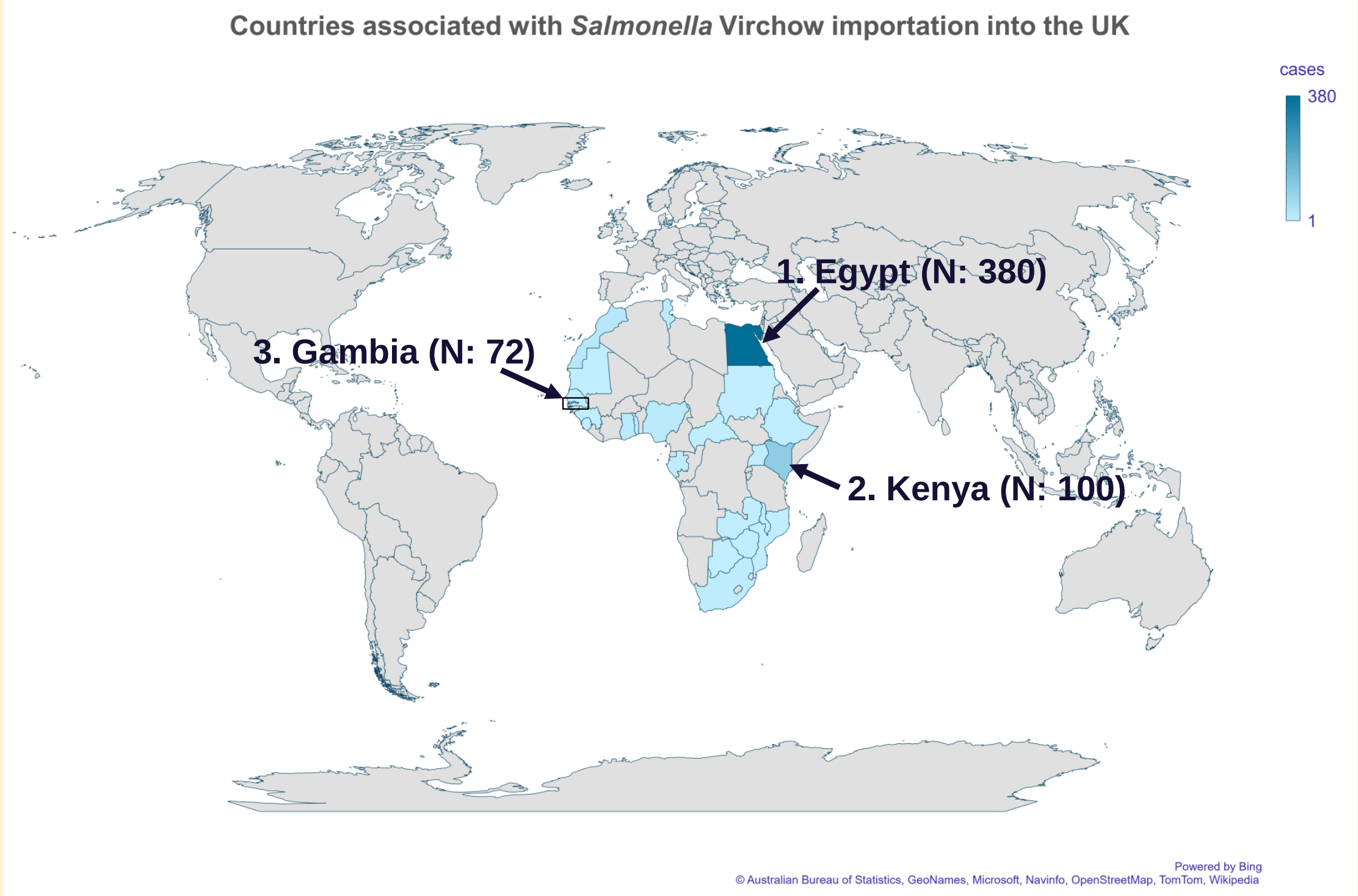

Figure. 1 Map of African countries associated with importation of the 699 isolates of *Salmonella* Virchow detected in the UK between 2004 to 2021 with the top 3 countries (Egypt, Kenya, Gambia) with highest cases of importation shown

RESULTS

S. Virchow was the third most common *Salmonella* spp. serovar being imported into the UK in association with travel to African countries. 55% of the patients were female and 45% male, with the most common age group being 20-29 and 40-45 for both genders.

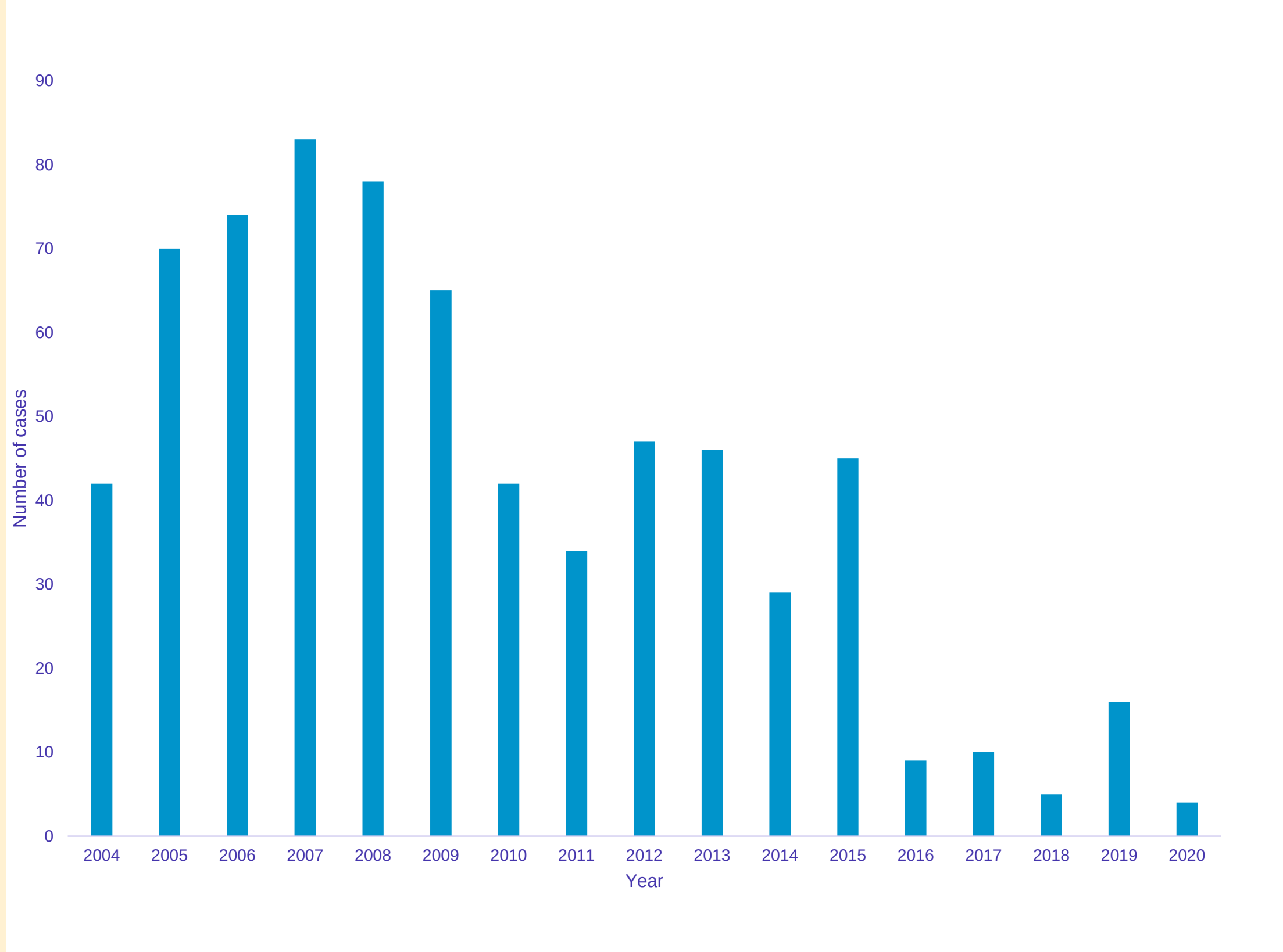

Figure. 2 Yearly cases between 2004 to 2020 of *Salmonella* Virchow detected in the UK related to travel to Africa showing cases were highest in 2007 before fluctuating until 2015 and decreasing to below 20 cases per year until 2020

Importation of cases in the UK were linked to travel from 25 African countries. The countries associated with the highest incidence of infection were; Egypt (N: 380), Kenya (N: 100), and Gambia (N: 72) (Figure 1).
The number of isolates received in 2020, when COVID lockdown and further restrictions started, showed a 75% decrease compared to 2019 (Figure 2).

AMR genomic analysis showed 55% of isolates received between 2014 and 2020 had a minimum of one resistance marker, with 18% showing multiple drug resistance (MDR). WGS analysis detected resistance determinants against different antibiotics (Figure 3).

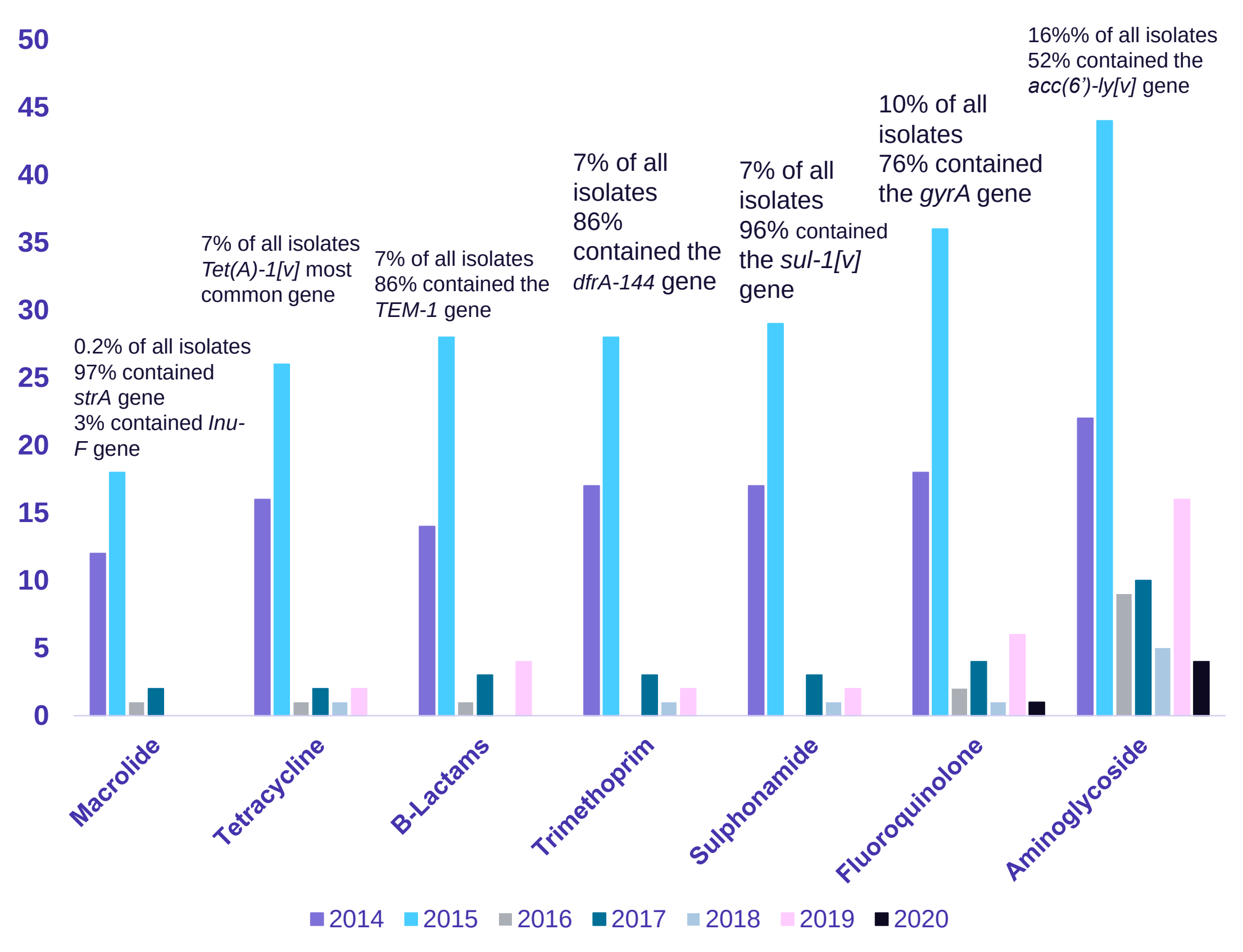

Figure. 3 Number of resistance genes detected against different antimicrobials from 2014-2020 using Whole Genome Sequencing analysis showing peak in 2015 and a dramatic decrease

Genomic Analysis

- cgMLST population structure analysis showed 25 cases fell into hierarchal cluster 5 (HC5) 1298 and 10 cases were HC5_7734, mainly associated with travel to Egypt but some cases were associated with travel to Ghana and South Africa (Figure 4)
- Highest number of HC5_1298 cases were imported into the UK in 2015, increasing from 2014 and highlight a potential outbreak during this period in Egypt
- Cases from the HC5_1298 cluster were later detected in the UK in 2019 from Egypt, indicating this may be an endemic strain and still circulating in the country (Figure 4)
- The smaller HC5_7734 cluster had 9 cases from Egypt (with 1 unspecified isolate listed as from the ‘African continent’)
- HC5_7734 cases were first detected in 2014 and last detected in 2017

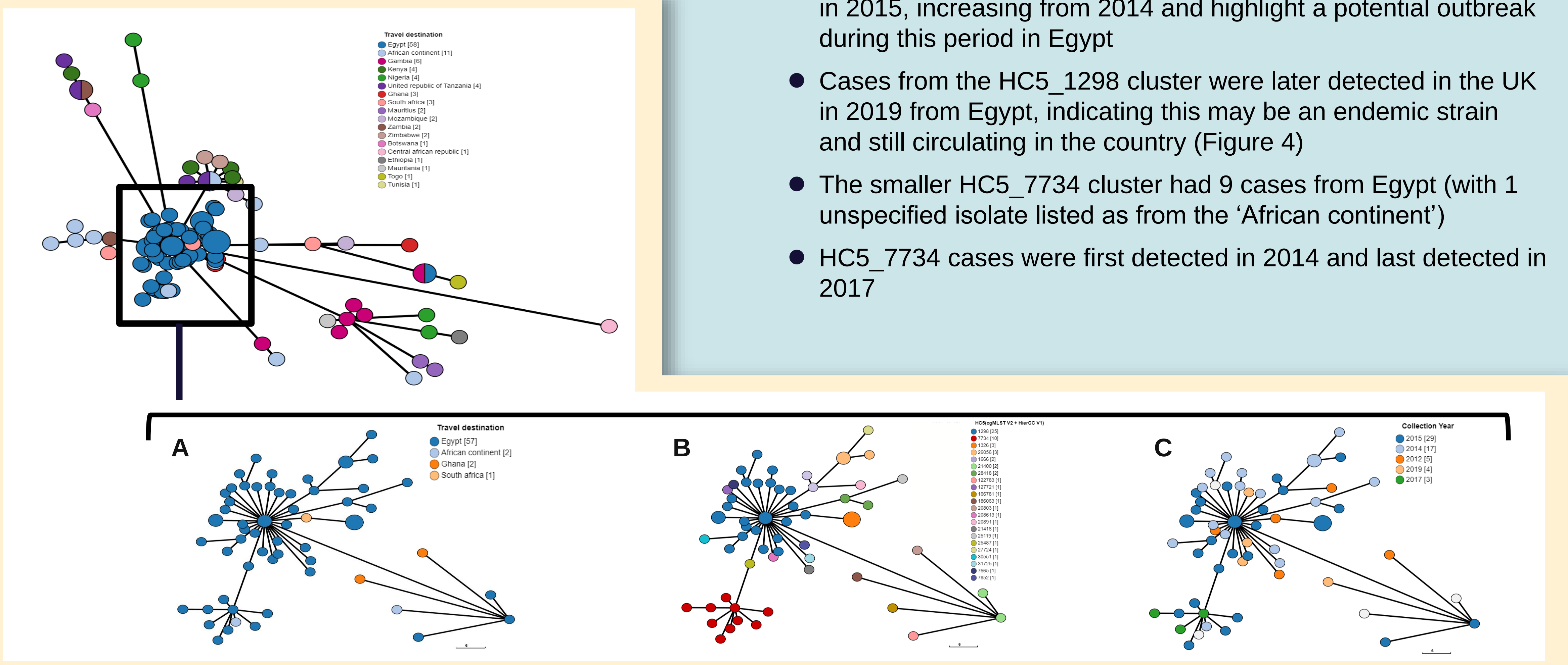

Figure. 4 cgMLST tree analysis of all *S.* Virchow cluster in the UK related to travel to Africa between 2014-2020, categorized into cgMLST trees by; travel destinations (A), Hierarchical cluster 5 clones (B) and years of collection (C). Identifying an potential outbreak of cases falling within the HC5_1298 cluster in Egypt in 2015 with further detection in 2019 and another HC5_7734 cluster detected in Egypt between 2014-2017

DISCUSSION

Results show that there are multiple clones circulating in Africa, that have been imported into the UK. The data from this study allows understanding on the possible origins of strains, supporting surveillance purposes and permitting comparisons against global databases when detecting outbreaks. However, further global comparisons is needed to confirm.

Analysing genomics to assess AMR only allows a prediction that resistance is expressed but further experiments to test the strains phenotypically can be conducted to better understand expression of resistance. AMR peaked in 2015 but data maybe skewed due to the potential outbreak.

The dramatic decrease of cases from 2015 onwards, maybe due to the increased efforts in African countries to control *Salmonella* spp. incidence in collaboration with the Welcome Trust and the Bill and Melinda Gates Foundation (5).

The 75% decrease in cases between 2019 and 2020 can be attributed to the impact of travel restrictions because of the Sars-Cov-2 pandemic. Less travel meant less importation of infections into the UK from Africa but does not infer that *S.* Virchow infections in Africa has decreased.

It must be considered that not all cases are reported by patients to healthcare professionals, therefore the true number of cases from importation is expected to be higher.

CONCLUSIONS

- S. Virchow is the third most common *Salmonella* spp. serovar imported into the UK linked to travel to Africa, this could be due to the outbreak detected in Egypt in 2015.
- Importation was mainly linked to travel from Egypt, Kenya and Gambia with sporadic invasive cases
- The number of cases decreased from 2019 to 2020 as a result of travel restrictions due to the Sars-Cov-2 pandemic
- 55% of cases detected contained a minimum of 1 resistance determinant with 18% indicating multiple drug resistances, but further work is required to understand the expressions of resistance.
- The true incidence of infection related to *S.* Virchow is expected to be higher
- This study identified a potential outbreak of HC5_1298 strains in Egypt in 2015 that maybe endemic due to later detection of same strain in 2019
- Further Genomic analysis to compare data globally would confirm if circulating clones are endemic to Africa or globally distributed

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