

# Agrobacterium species bacteraemia, Switzerland, 2008 to 2019: a molecular epidemiological study

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## Background and Objective

*Agrobacterium* species, a group of gram-negative, aerobic and motile environmental bacteria, are recognized as rare opportunistic human pathogens, which affect mostly immunocompromised patients or patients with other underlying diseases. The majority of reported cases with *Agrobacterium* spp. are bloodstream infections related to the use of central venous catheters (CVC)<sup>1,2,3</sup>. Infrequently, they are agents of bloodstream infections linked to healthcare-associated outbreaks<sup>1,2</sup>. It is unclear, however, if outbreaks also occur across larger geographic areas. Triggered by two local clusters from putative point sources<sup>4</sup>, our aim was to describe *Agrobacterium* spp. bacteraemia cases in Switzerland and explore their relatedness by a molecular epidemiological approach.

## Methods

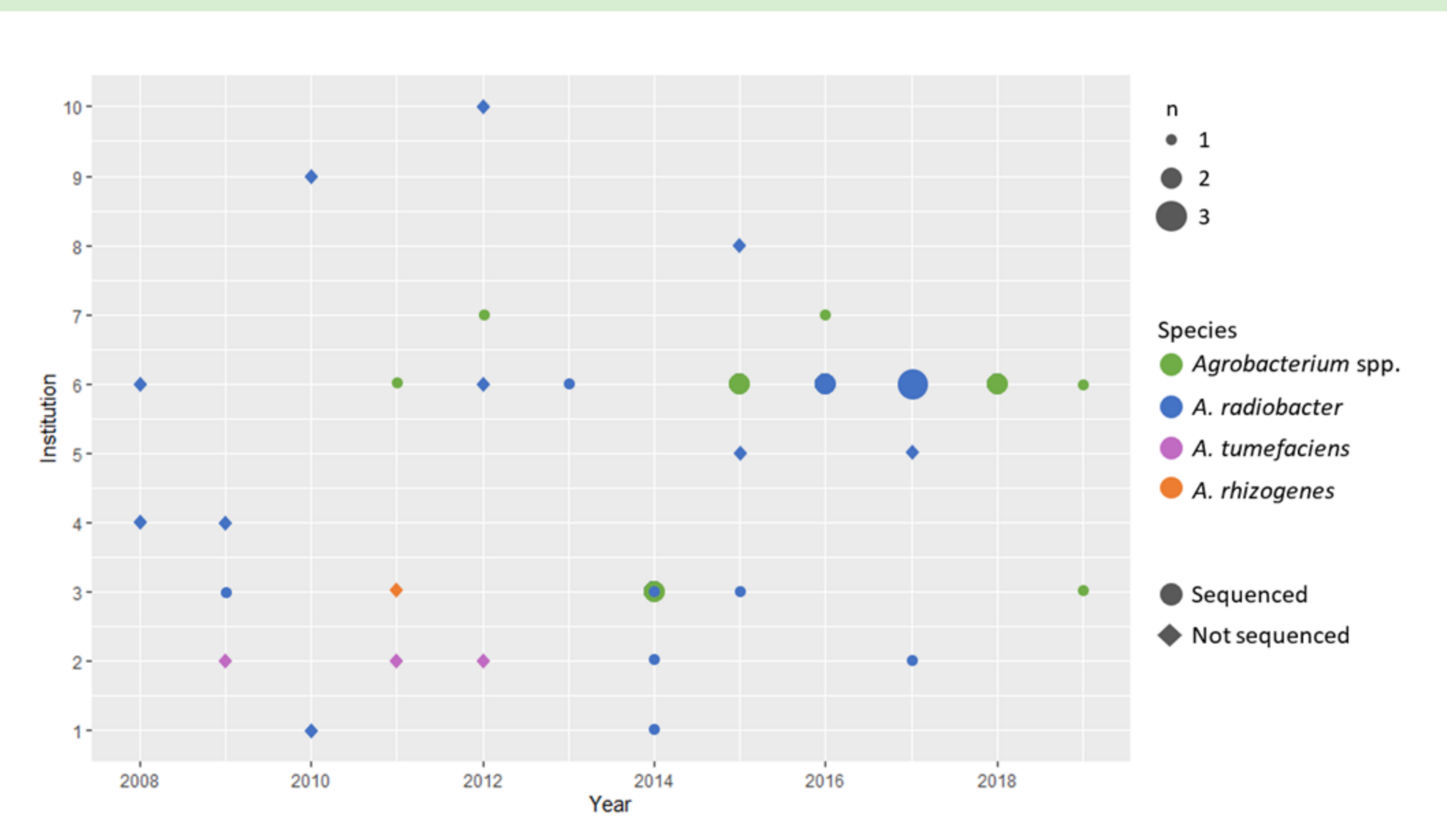
We performed a nationwide descriptive study of cases in Switzerland based on a prospective surveillance system (Swiss Centre for Antibiotic Resistance, anresis.ch), from 2008 to 2019. We identified patients with *Agrobacterium* spp. isolated from blood cultures and used a survey to collect epidemiologic information on the patients and antimicrobial susceptibility testing results. We performed whole genome sequencing (WGS) of available clinical isolates and determined their relatedness by single nucleotide polymorphism (SNP) variant calling analysis.

## Results I

We identified a total of 36 cases of *Agrobacterium* spp. from blood samples from the years 2008 to 2019, stemming from ten healthcare institution (Figure 1). According to the initial species identification by the originating microbiology laboratories, 22 (61%) were *A. radiobacter*, three were *A. tumefaciens*, and one was *A. rhizogenes*. In ten cases, the species was not identified beyond *Agrobacterium* spp. We saw a temporal-spatial accumulation of cases only in Institution 6 (Bern University Hospital, where the first outbreak was described).

## Figure 1: Overview of the 36 cases

We plotted the number of annual cases (x-axis) for all healthcare institutions (y-axis; 1-10) of *Agrobacterium* spp. bacteraemia and indicated availability for whole genome sequencing. Indicated are the initial presumptive species identifications by the originating microbiology laboratories, which may differ from the definite identification by WGS as shown in Figure 2.

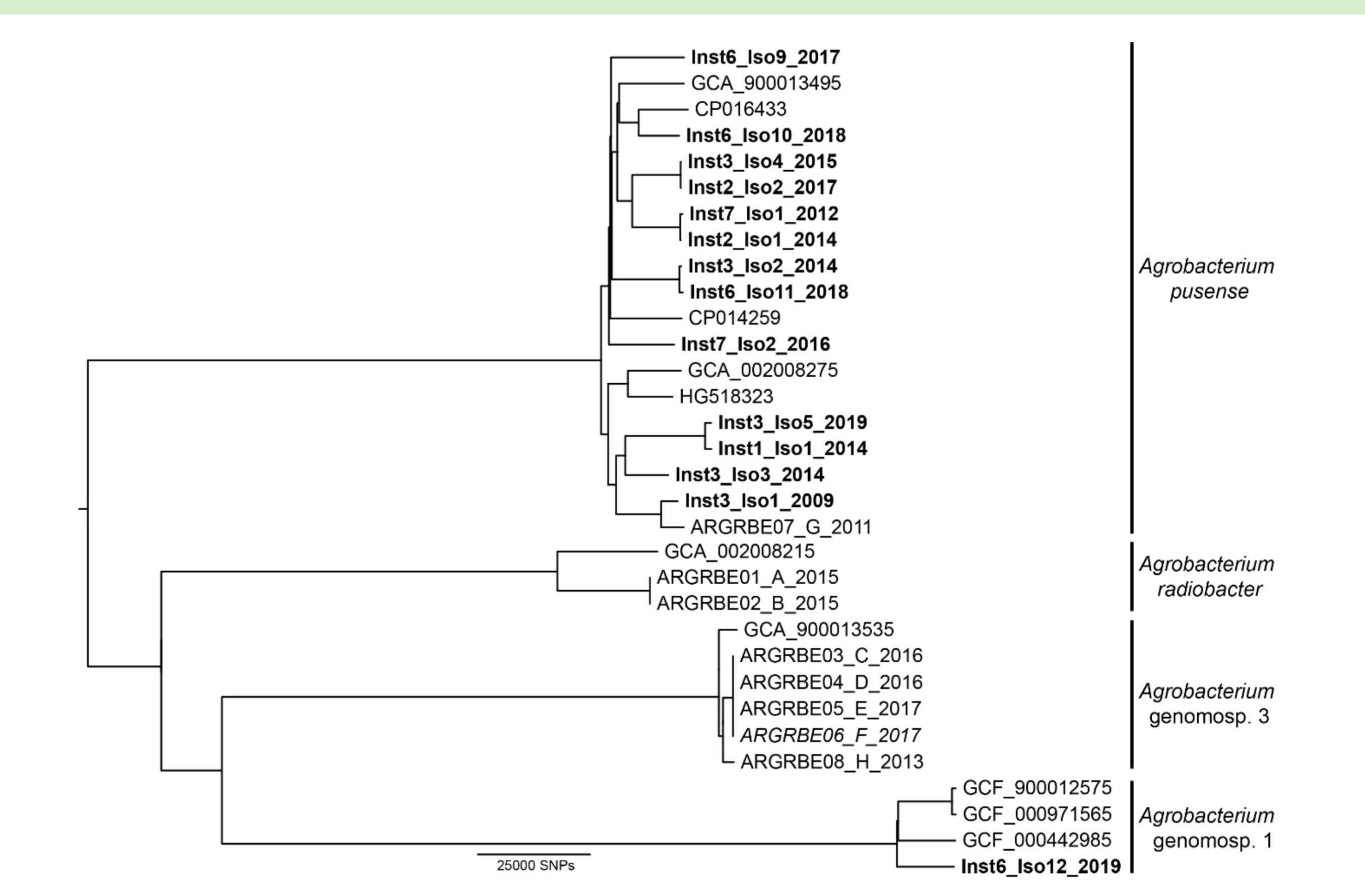


## Results II

WGS-based typing was performed on 22 available isolates, which accounts for 61% (22/36) of the cases included. A SNP phylogeny shows the relationships between isolates and reference genomes (Figure 2). It showed no clonal relationships between newly identified isolates or to those from the known clusters<sup>4</sup>, with all isolates outside these clusters being at least 50 SNPs apart.

## Figure 2: Whole genome SNP phylogeny of the 22 sequenced isolates relative to reference genomes.

The genome of isolate ARGBE06\_F was used as reference for the phylogeny (italics). Newly sequenced isolates are shown in bold. The previously described isolates<sup>4</sup> from the two clusters at Institution 6 are shown as AGRBE03\_C, AGRBE04\_D, AGRBE05\_E & AGRBE06\_F and as ARGREBE01\_A & ARGREBE02\_B. Scale bar indicates numbers of SNP differences between the isolates, across regions of the genome to which they map.



## Results III

Of the 36 cases included, antimicrobial resistance data was available for 29. Most isolates were resistant to tobramycin (88%) and ceftazidime (43%), followed by trimethoprim-sulfamethoxazole (33%) and ampicillin (29%). The isolates were uniformly susceptible to carbapenems and all but one were susceptible to fluoroquinolones.

## Conclusion

Healthcare-associated *Agrobacterium* spp. bacteraemia is infrequently detected and, given that it may stem from a point source, occurrence of multiple episodes should entail an outbreak investigation. Suspicion should be raised in particular if case patients underwent the same procedure in the same location, as common transmissions pathways with introduction from persistent point sources are possible.

With the help of the nation-wide surveillance system, we identified multiple cases of a rare pathogen and WGS revealed they were not related. Beyond the case of *Agrobacterium* species, the availability of national databases for pathogen queries can help to investigate rare pathogens and discover potential outbreaks.

## References

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