ECDC Diphtheria Genomic Surveillance and the 2022-2023 European Diphtheria event

Andreas Hoefer (ECDC)

GenEpi-Biotrain - Focus on the Agents of Diphtheria **07/03/25**

Diphtheria in Migrants outbreak 2022

Diphtheria in Migrants 2022

1st case reported by Austria via the early warning and response system (EWRS) on **1 June 2022**

2nd case described in Swiss media

ECDC encouraged all EU/EEA countries to report recent detections of all cases through EpiPulse

Diphtheria in Migrants 2022

Population flux → more diphtheria?

Reaching pre-pandemic levels?

Corynebacterium ulcerans increase due to “pandemic-pets”

Early 7-gene multi locus sequence typing (MLST) information suggested similar sequence types (STs) were circulating

Microbiology group of ECDC requested reference/representative sequences

Diphtheria in Migrants 2022

Whole genome sequencing (WGS) data data of initial isolates confirmed high degree of identity among international cases

→ ECDC requested sequencing data via EpiPulse and Networks

→ Organised regular teleconferences with affected countries

→ Provided sequencing support to reduce turnaround times

Diphtheria in Migrants 2022

Diphtheria in Migrants 2022

As of 26 September 2022, 92 cases of diphtheria among migrants have been reported by seven European countries

66 of these cases presented with cutaneous diphtheria caused by *Corynebacterium diphtheriae*

All were toxigenic

Diphtheria in Migrants 2022

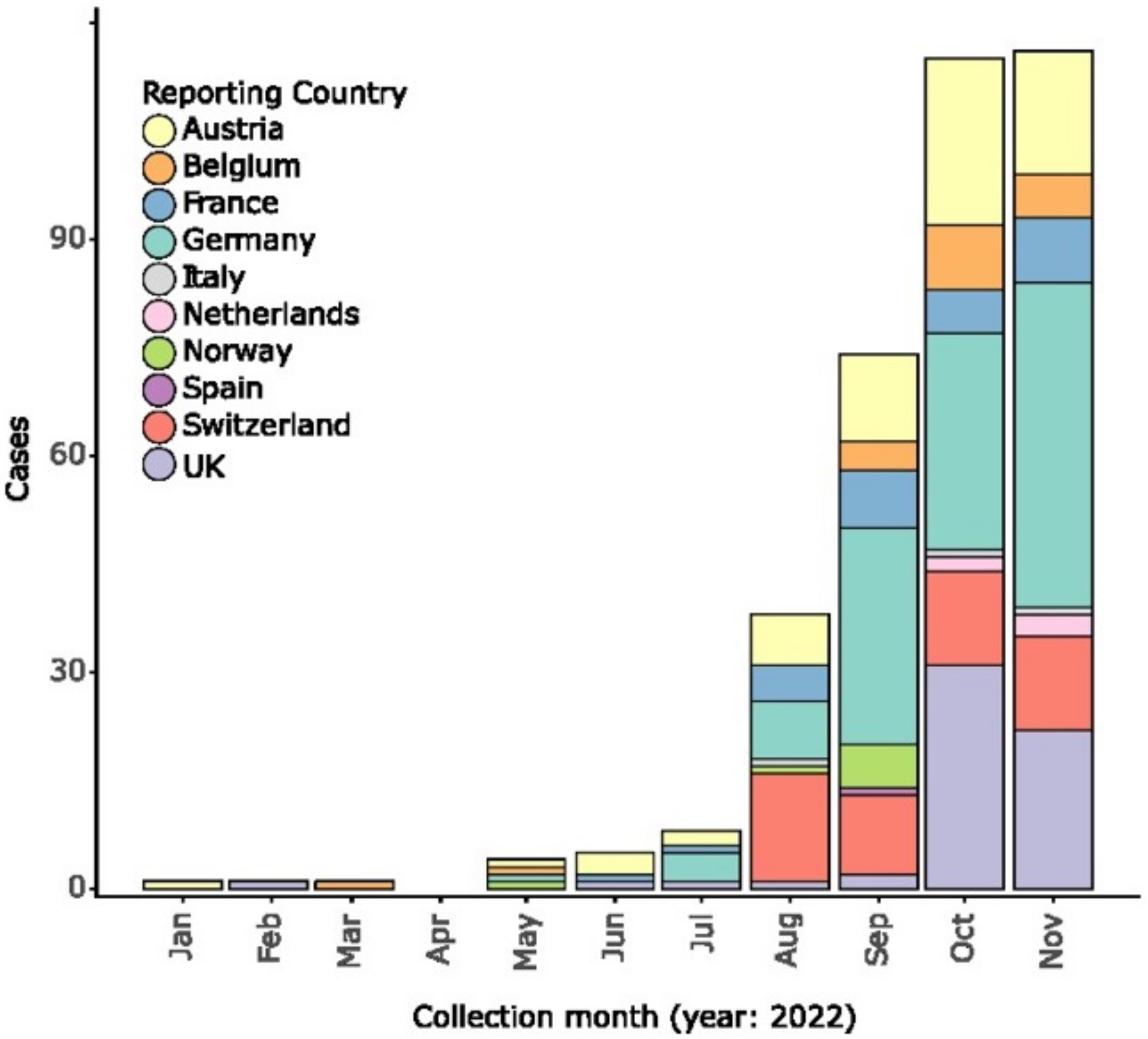
- Established a self-governed international consortium

Case definition:

- All cases of toxigenic *C. diphtheriae*
- Collected between 1 January and 30 November, 2022
- Affected countries (8 EU/EEA + Switzerland and UK)

Diphtheria in Migrants 2022

Number of cases detected by reporting countries over the study period



Total of 363 isolates in 362 individuals

Germany (118), Austria (66), UK (59), Switzerland (52), France (30), Belgium (21), Norway (8), The Netherlands (5), Italy (3), and Spain (1)

355/362 (98%) patients were male

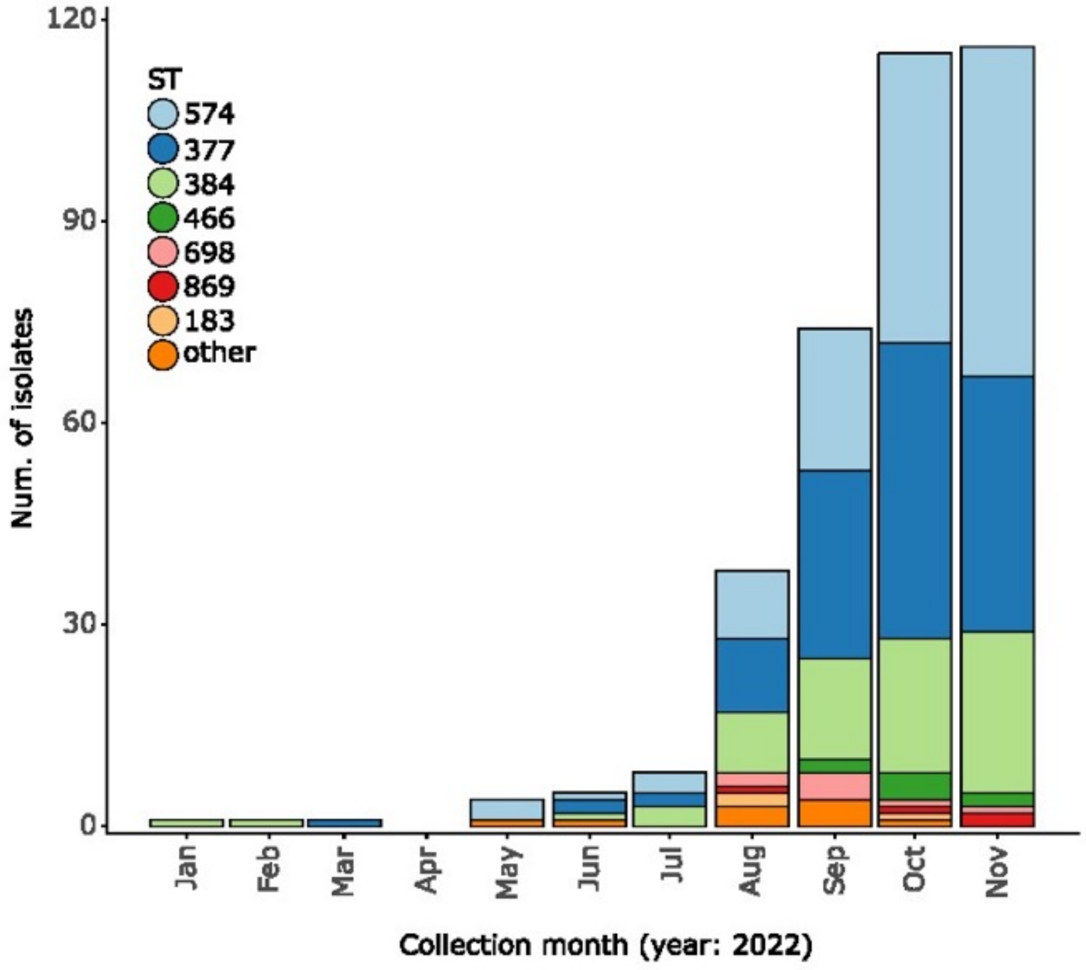
Median age of 18 years

96% had a recent migration history, and/or close contact with migrant populations

96% cases where clinical data was available, **268/346 (77%) were cutaneous**

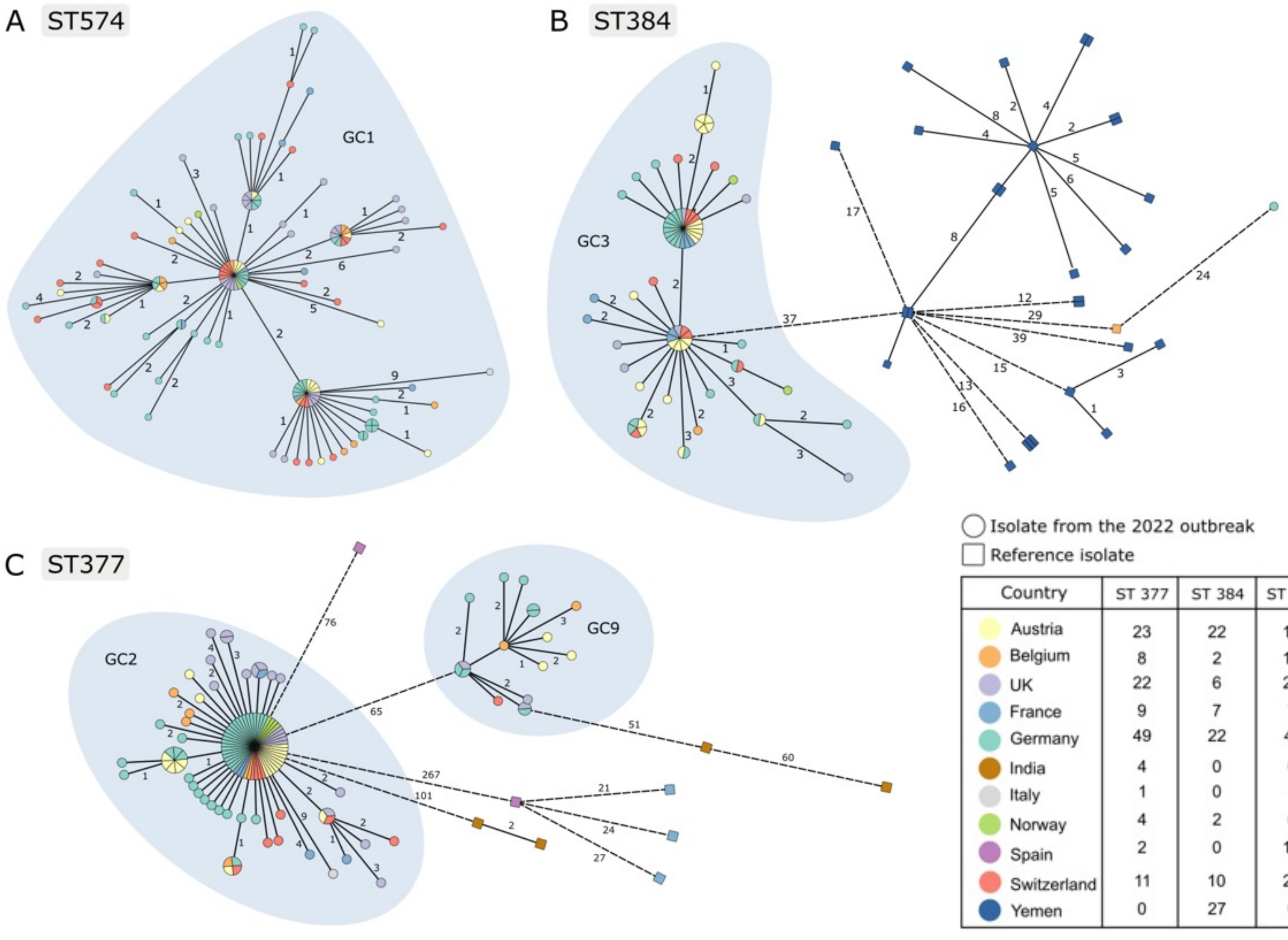
Diphtheria in Migrants 2022

Sequence types per month, 2022



Diphtheria in Migrants 2022

The genetic diversity of the four main genomic clusters (GC)



Isolate from the 2022 outbreak

Reference isolate

Country	ST 377	ST 384	ST 574
Austria	23	22	17
Belgium	8	2	10
UK	22	6	28
France	9	7	7
Germany	49	22	41
India	4	0	0
Italy	1	0	1
Norway	4	2	0
Spain	2	0	17
Switzerland	11	10	25
Yemen	0	27	0

Diphtheria in Migrants 2022

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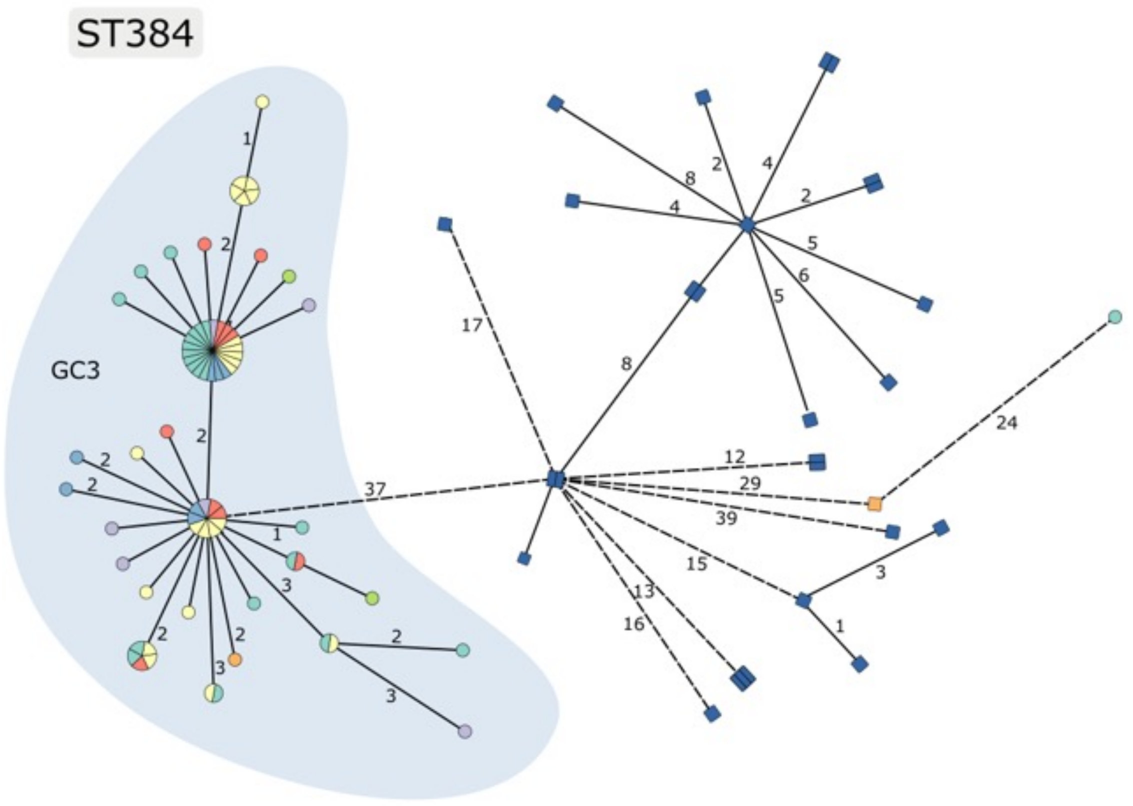

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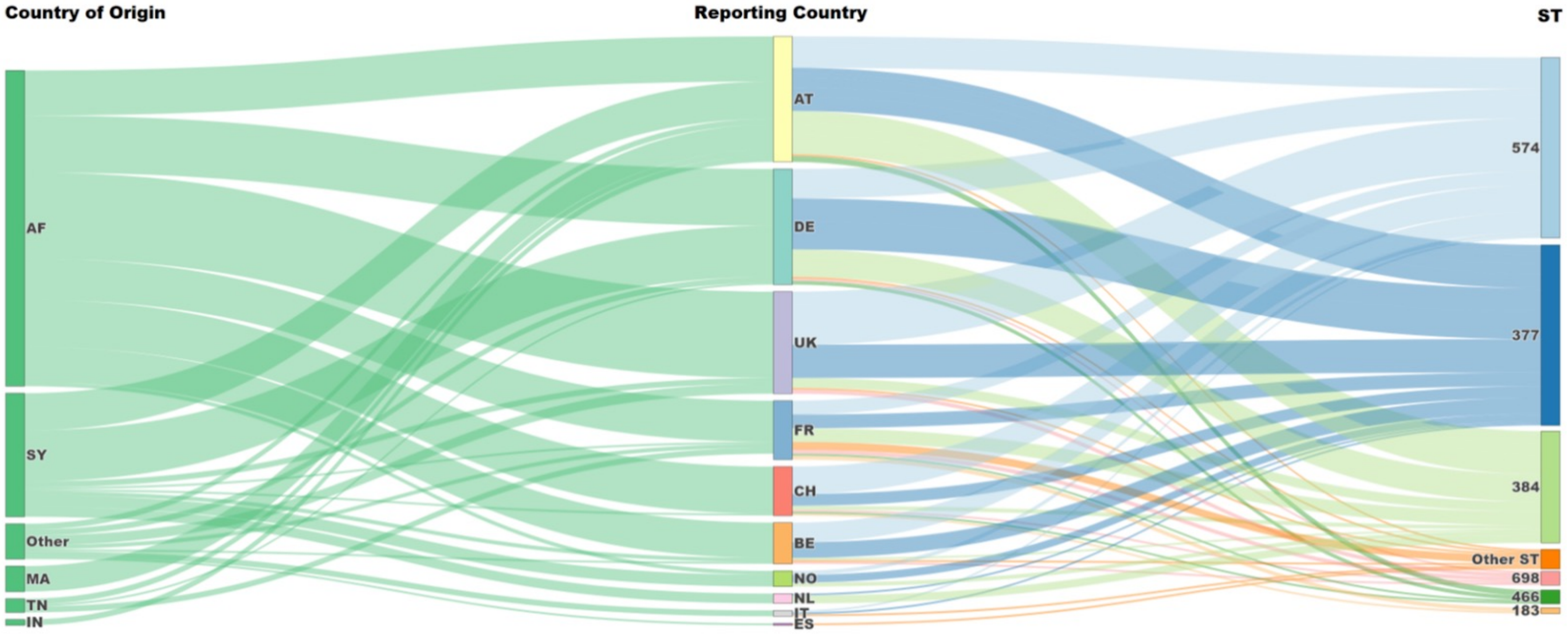
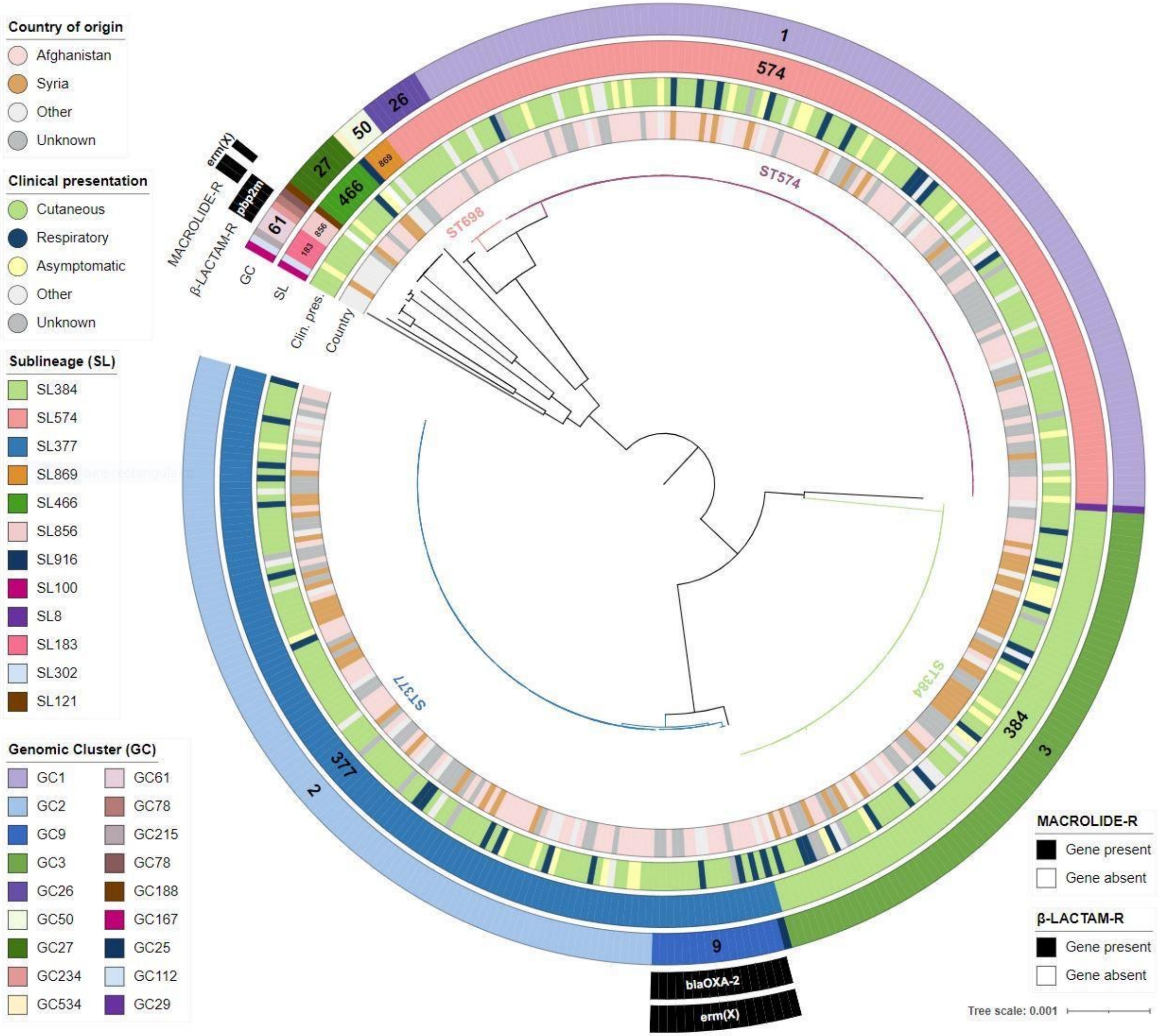
Diphtheria in Migrants 2022

Association of country of origin, country of reporting, and sequence types (STs)



Diphtheria in migrants 2022

Phylogenetic diversity of the 363 *C. diphtheriae* study isolates



Diphtheria in Migrants 2022

Conclusions:

- High genomic conservation of cases suggests epidemiological link/common source of infection
- Sustained foci of infection on migrant route to EU/EEA
- Secondary cases occurring in migrant centres in EU/EEA
    - Eventually also in vulnerable populations
- Concerning antimicrobial resistance (AMR) profile identified
- Need to stay vigilant and to further support international management of diphtheria

Diphtheria in Migrants 2022

Response activities:

- Raised public health and clinical awareness
- Screening of migrants in several countries
- Prophylactic antimicrobial treatment upon arrival
- International consortium → rapid sharing of genomic data to determine extent of outbreak
- Reference database of isolates to closely monitor situation
- Ongoing sequencing support
- Typical response options e.g. improved vaccination coverage etc

Possibilities of MTT/EpiPulse cases

MTT and EpiPulse cases

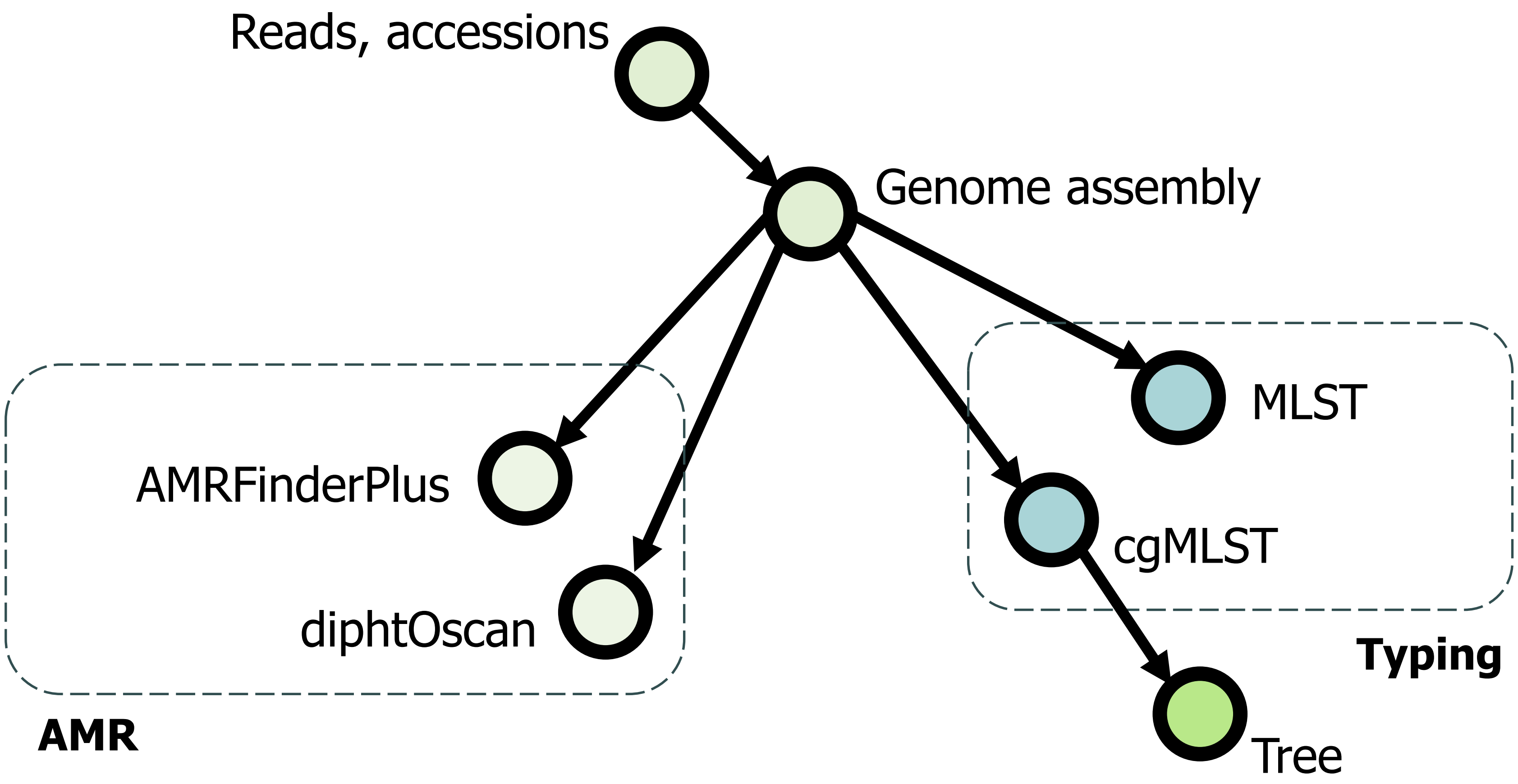
Among first pathogens to be rolled out in EpiPulse cases

Automated submission of sequencing data

Visualisation via Molecular Typing tool (MTT)

Drastically improved turnaround time

C. diphtheriae characterization on the MTT – First release



- This makes possible to upload a sequence, put it in context and get typing and AMR data. With these features we are able to track and characterize an outbreak as the one described here.
- Checking possible synergies with BIGSdb

Potential reemergence of VPDs

Potential reemergence of VPDs

- Consistent rise of previously 'eradicated'* vaccine preventable diseases
  - Internationally and EU/EEA
  - Fighting misinformation/disinformation/vaccine hesitancy globally

- Danger of complacency
  - Raise vaccination coverage among the population
    - Seroprevalence
    - Waning immunity
    - Public health communication encouraging vaccination

  - Global efforts to respond to diphtheria outbreaks in endemic regions
    - Ensure access to vaccination

*Eradicated in regions with large scale vaccination campaigns

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Phenotypic and genomic analysis of a large-scale *Corynebacterium diphtheriae* outbreak among migrant populations in Europe

Andreas Hoefer, Helena Seth-Smith, Federica Palma, Stefanie Schindler, Luca Freschi, Alexandra Dangel, Anja Berger, Joshua D'Aeth, Alexander Indra, Norman K. Fry, Daniel Palm, Andreas Sing, Sylvain Brisse, Adrian Egli, the 2022 European diphtheria Consortium

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Thank you