



LECTURE SERIES

Klebsiella pneumoniae
Genomic Epidemiology and
Antimicrobial Resistance

Seroepidemiology of *Klebsiella*

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Intended Learning Objectives

Specific objectives of this session:

1. Understand the relationship between K/O antigen diversity and *Kpn* population structure i.e. diversity within/between clones
2. Understand the diversity of K/O antigens among clinical *Kpn* isolates
3. Discuss key considerations for *Kpn* sero-epidemiology analyses

Outline

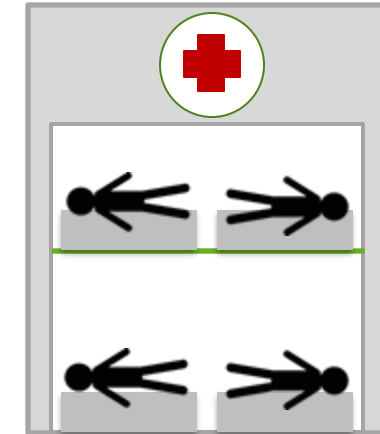
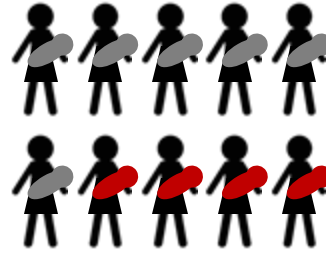
This session consists of the following elements

1. The *Kpn* vaccine value profile
2. Brief recap on *Kpn* K and O antigen genetics
3. K and O diversity in hypervirulent and multidrug resistant clones
4. K and O diversity in clinical *Kpn* collections:
 - Geographic differences
 - Temporal fluctuations
5. Meta-analysis of neonatal sepsis isolates
6. Sero-epi app
7. Summary

WHO *Kpn* vaccine value profile

Use cases:

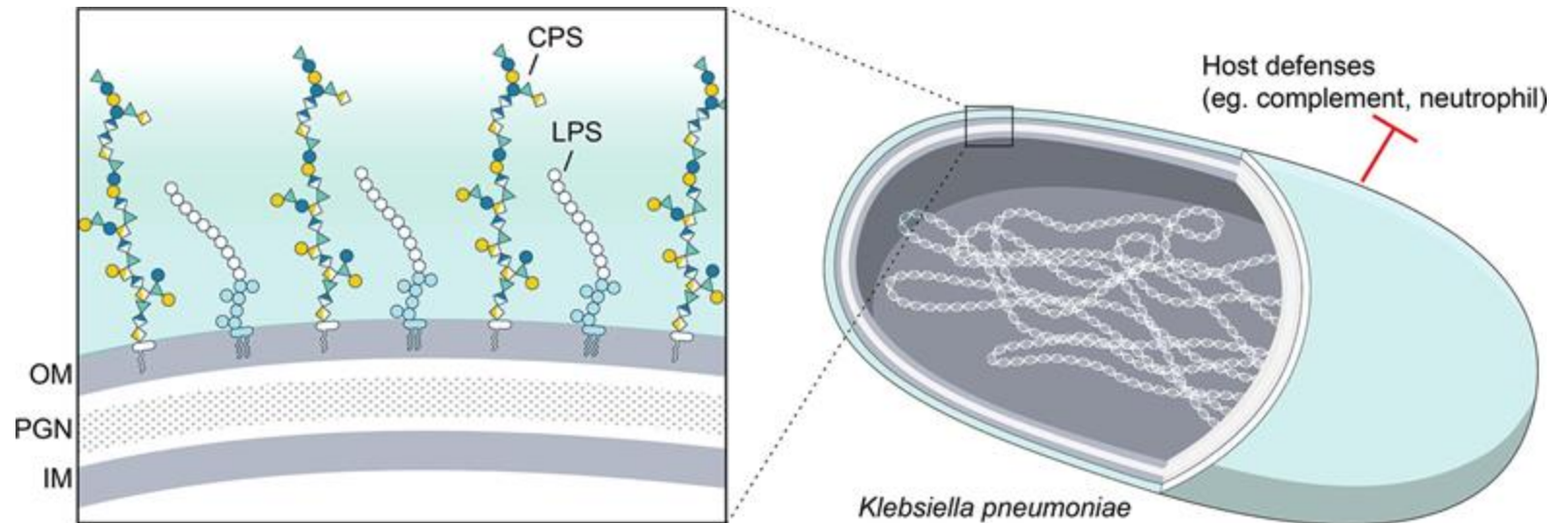
- Neonatal sepsis
- Adult HAIs



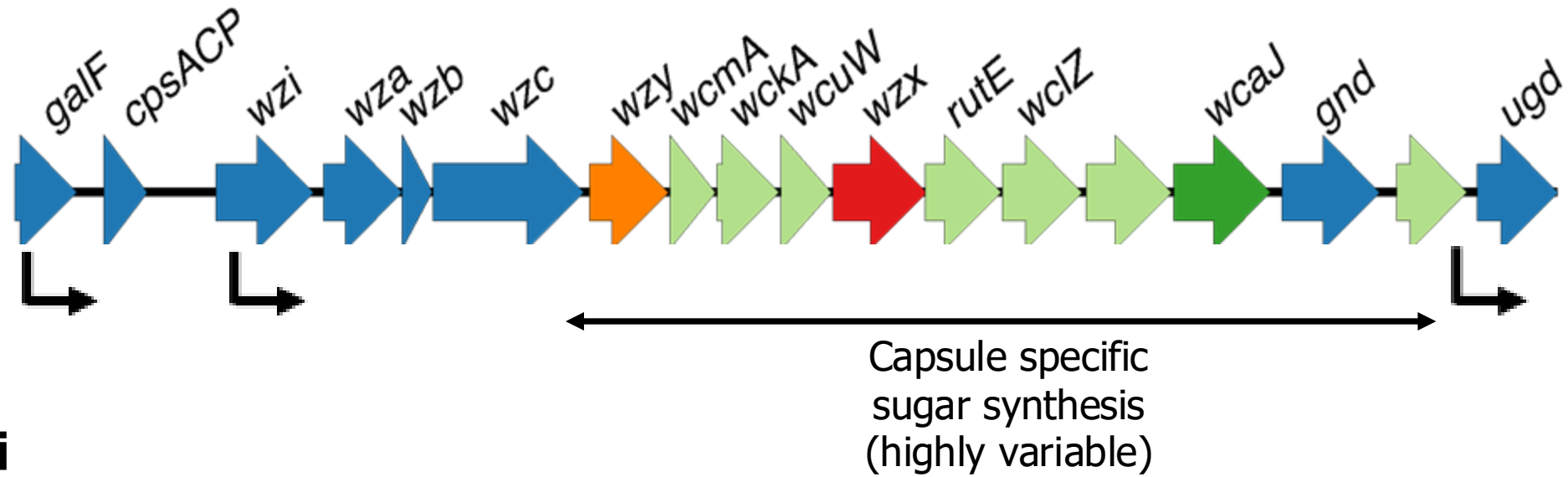
Major antigen targets:

- Capsule (K)
- Outer-LPS (O)

Coverage target:
≥70% infections



Klebsiella K loci are defined by unique gene content



**>160 K loci
defined to-date**

Common proteins
inc. core assembly
machinery

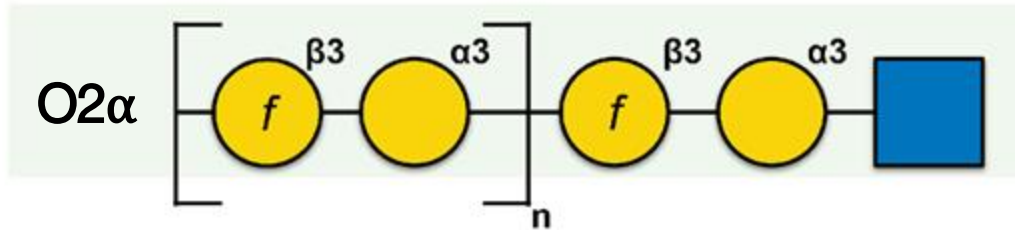
Wzy capsule repeat
unit polymerase

WbaP / WcaJ initiating
glycosyltransferase

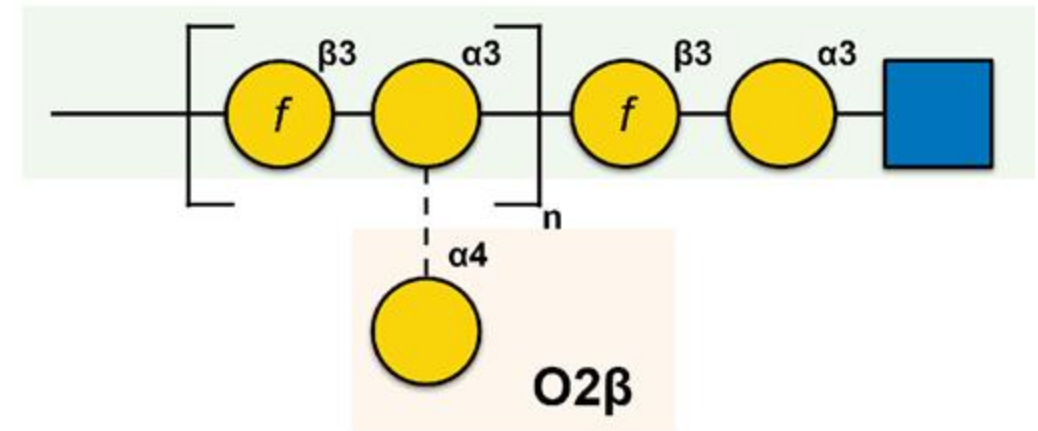
Wzx flippase

Other sugar synthesis
and processing

O types determined by O loci & additional genes



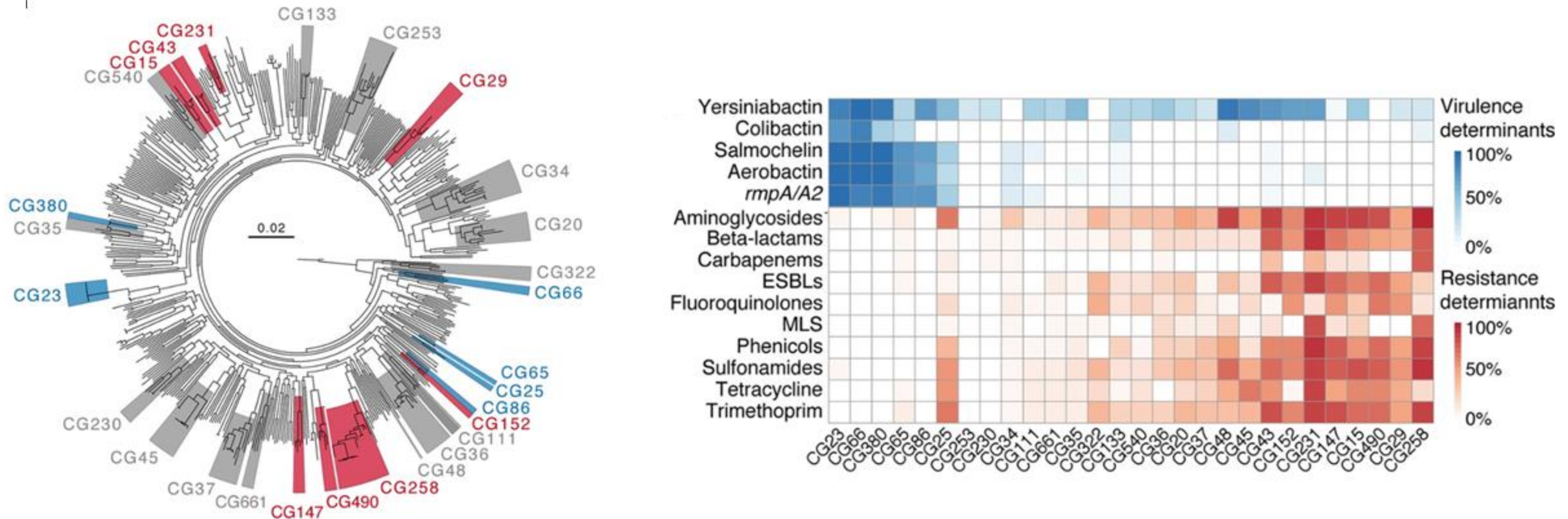
OL2 α



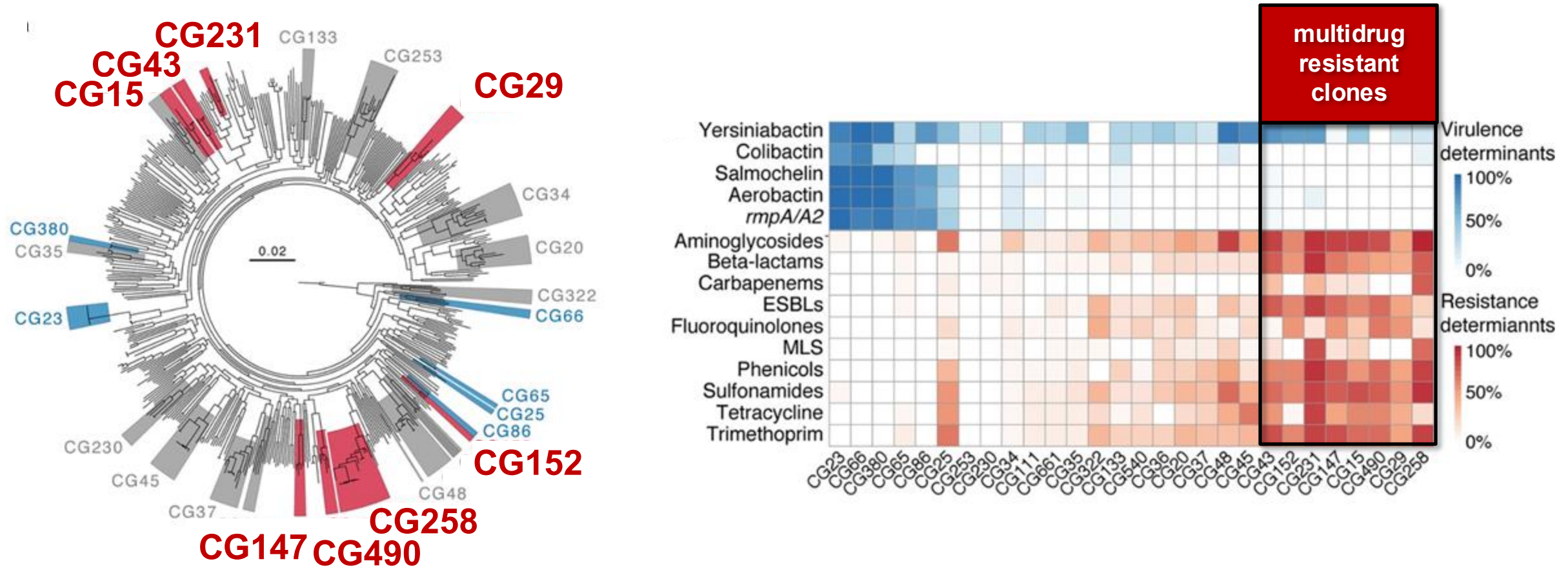
OL2 α + *gml2* β

**>20 combinations
identified to-date**

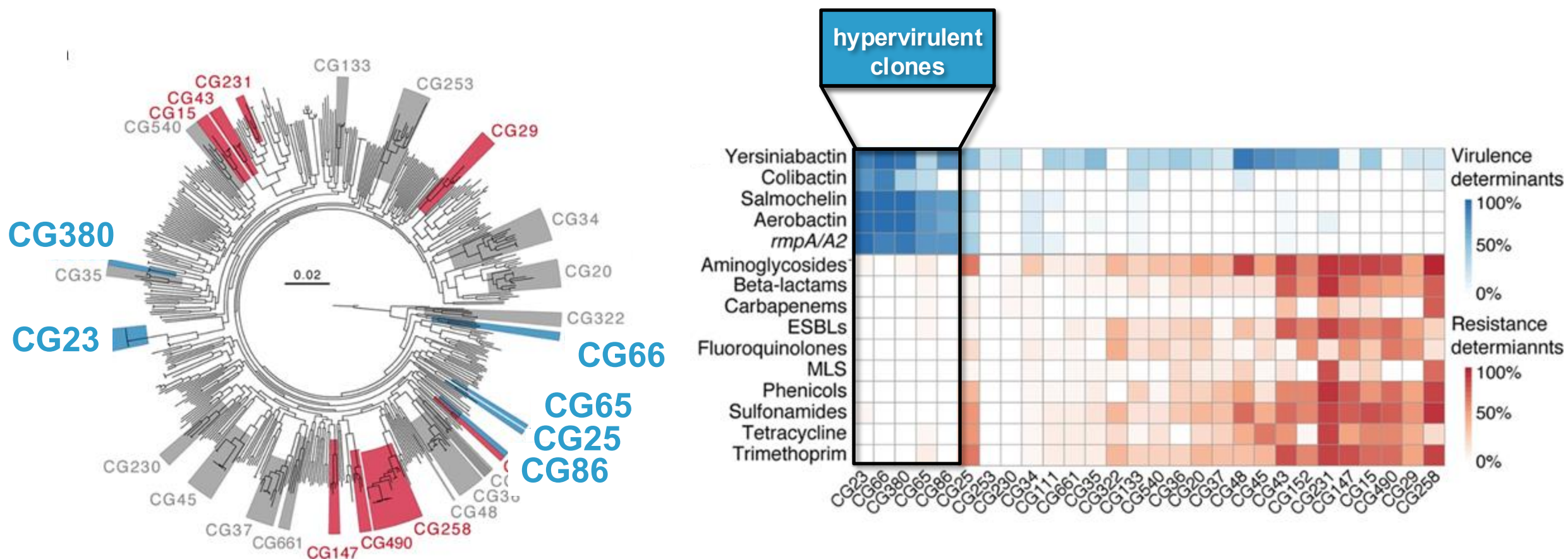
Distribution of AMR and virulence genes



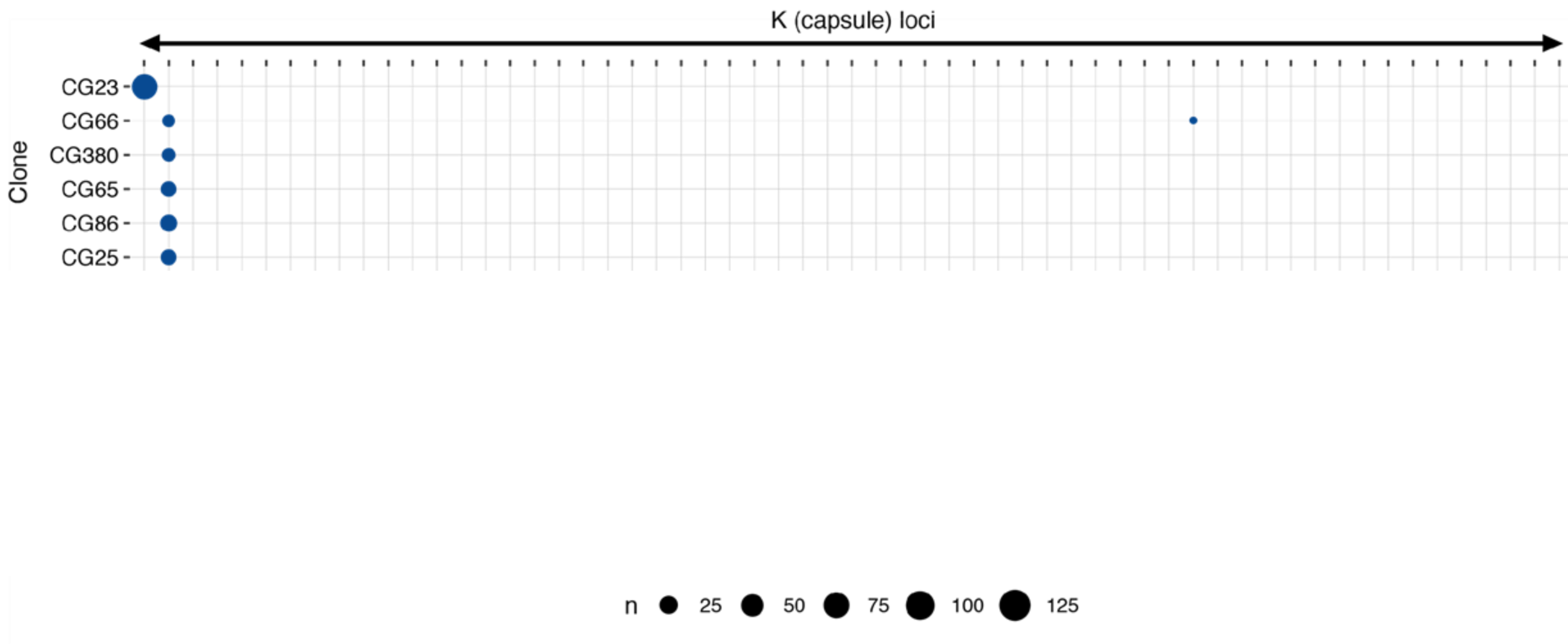
Distribution of AMR and virulence genes



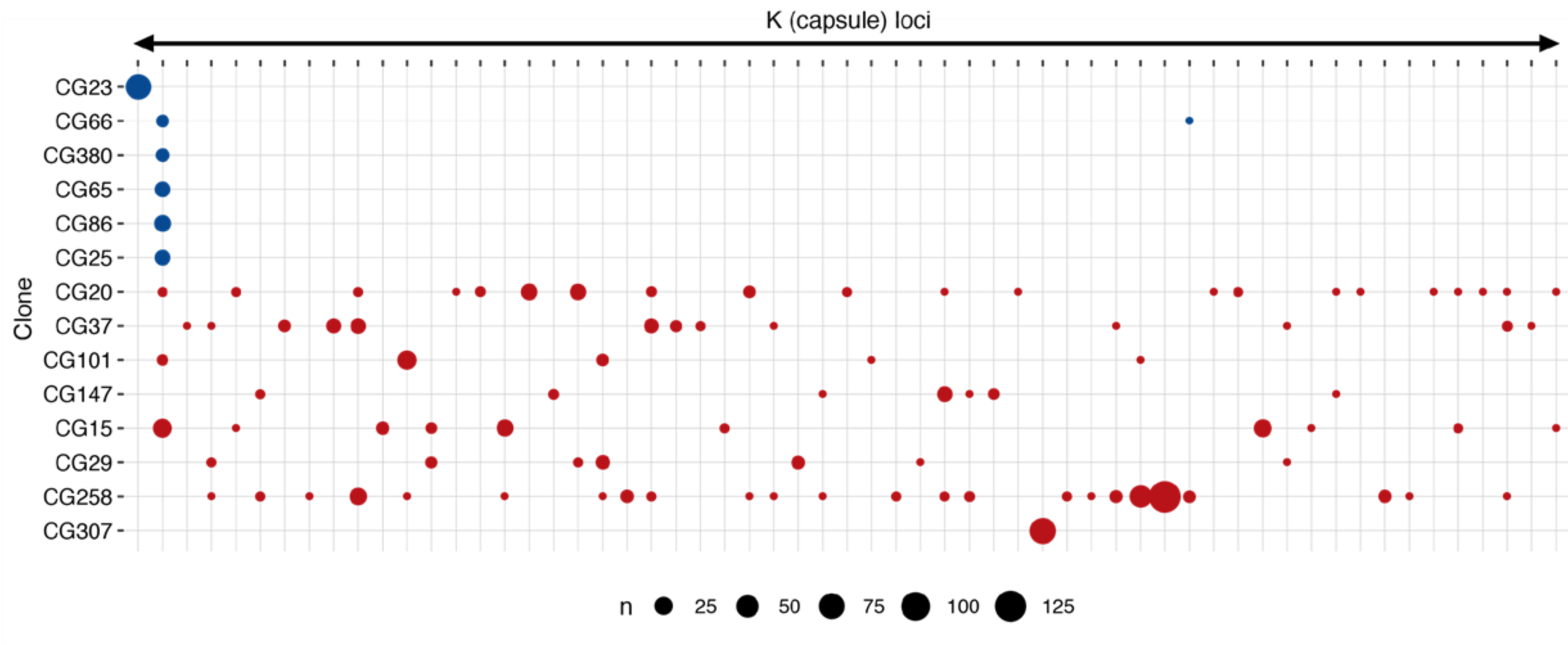
Distribution of AMR and virulence genes



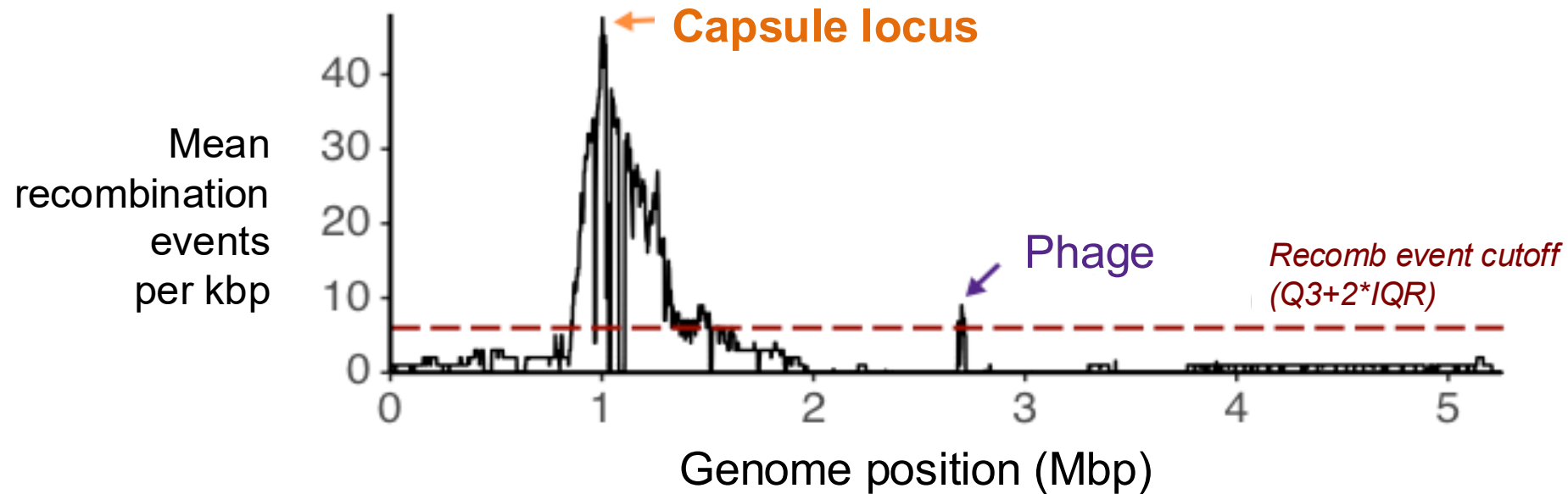
Hypervirulent clones carry either KL1 or KL2



MDR clones carry diverse K loci

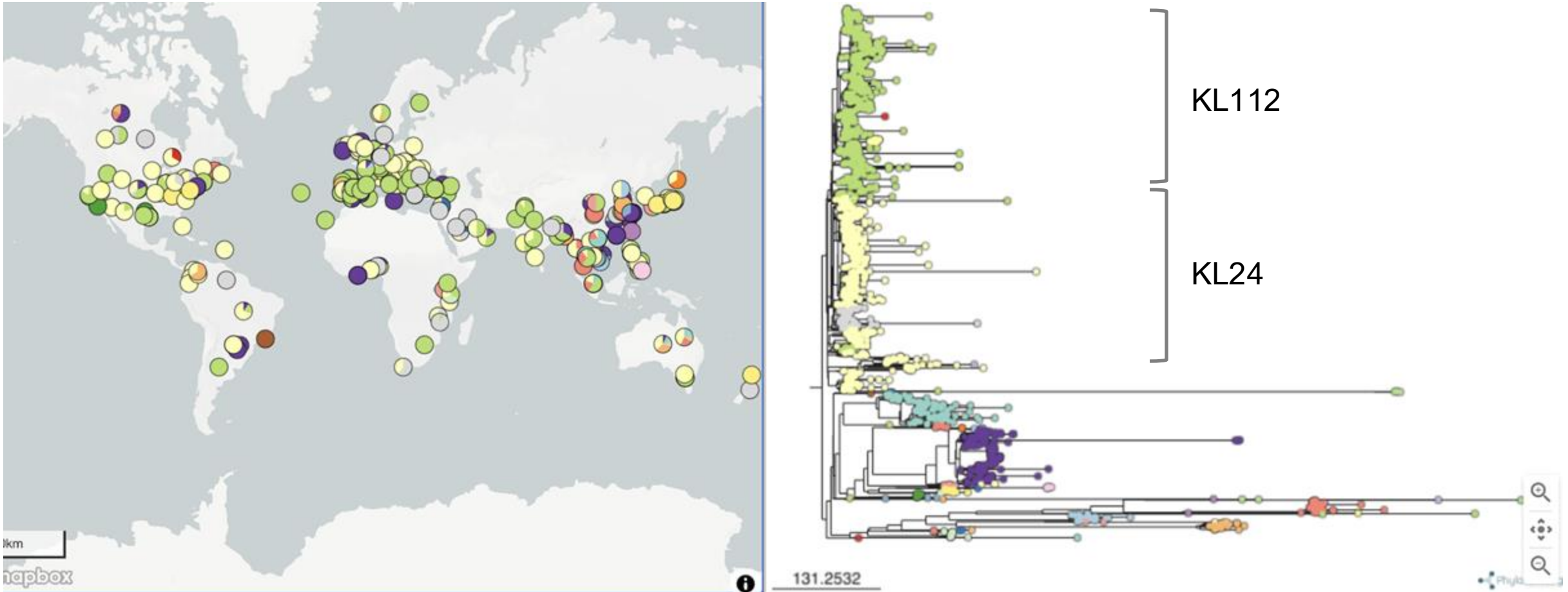


K locus is a recombination hotspot in MDR clones



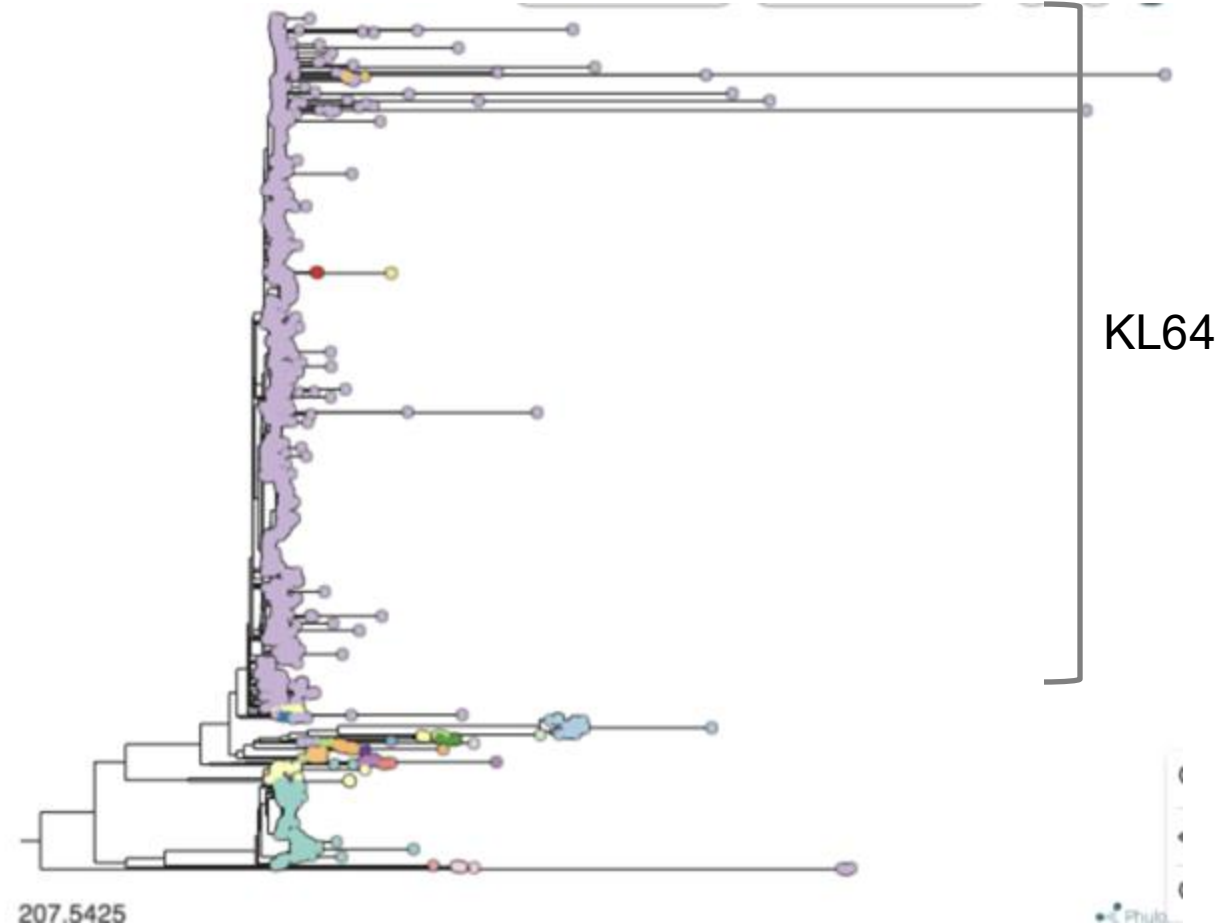
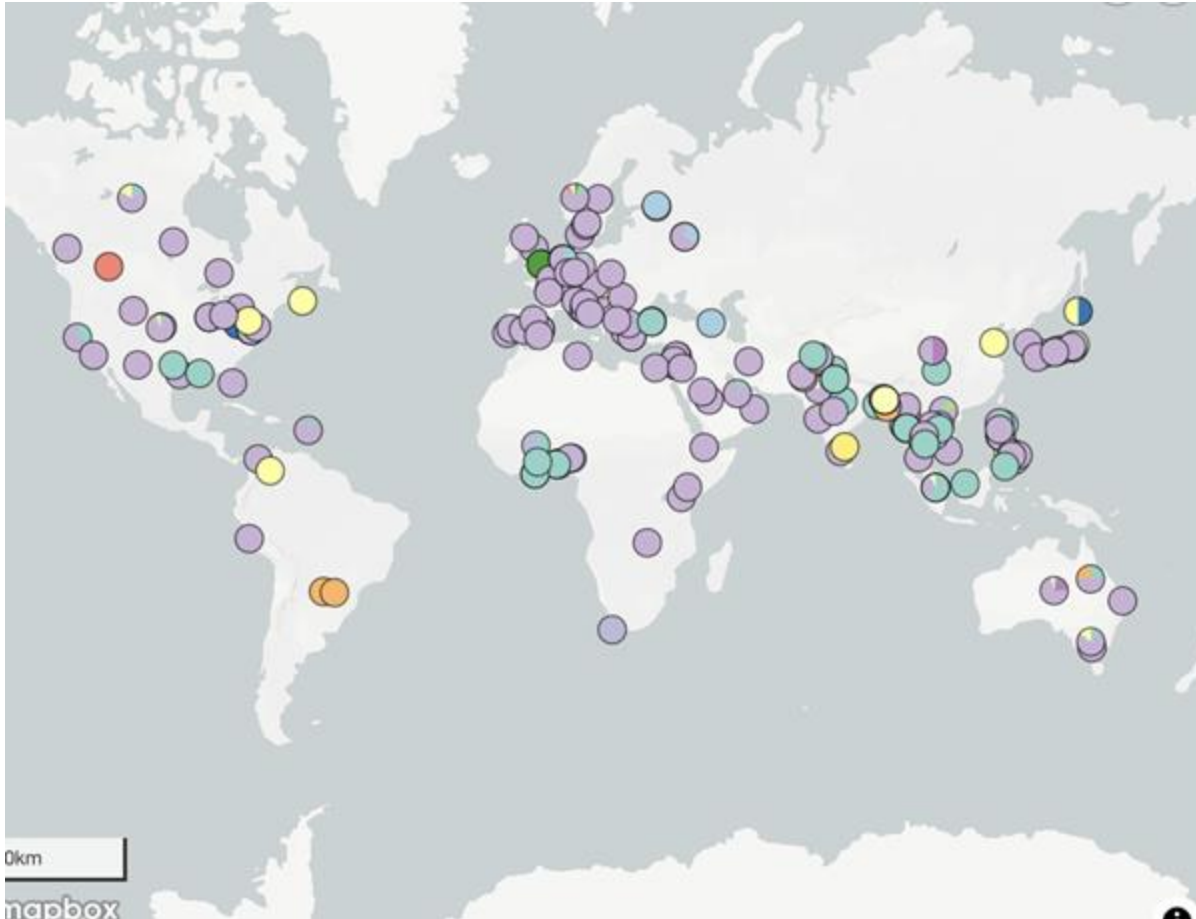
Some ST + KL combinations have proliferated

~1800 ST15 genomes, 1968-2023

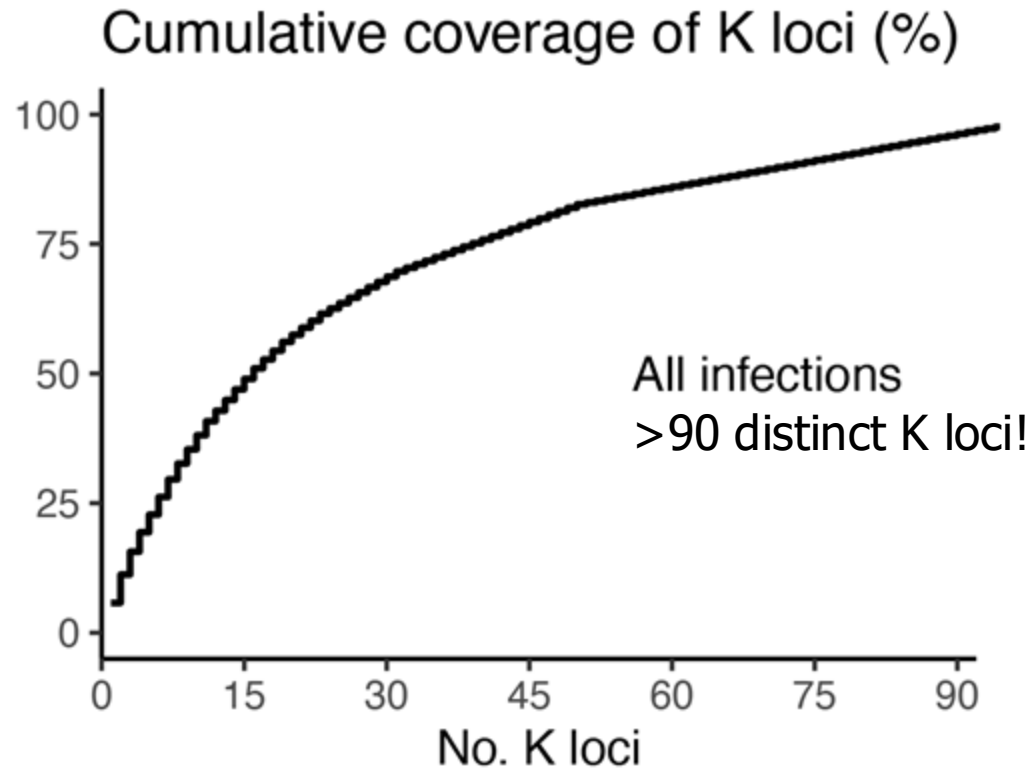


Some ST + KL combinations have proliferated

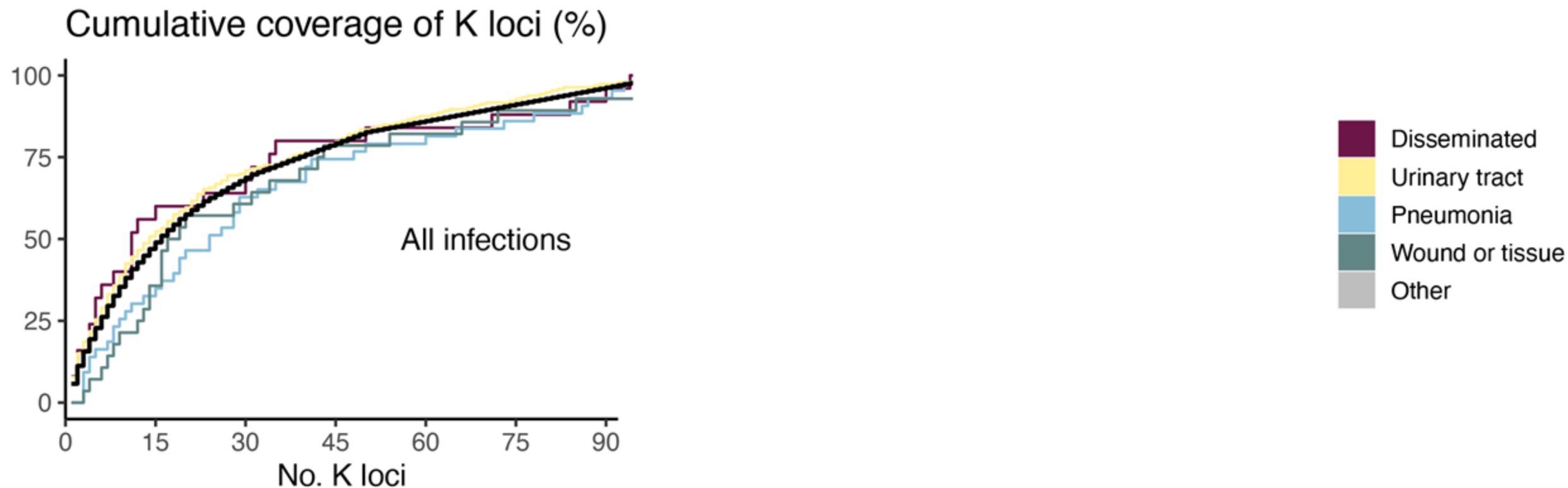
~2000 ST147 genomes, 2014-2023



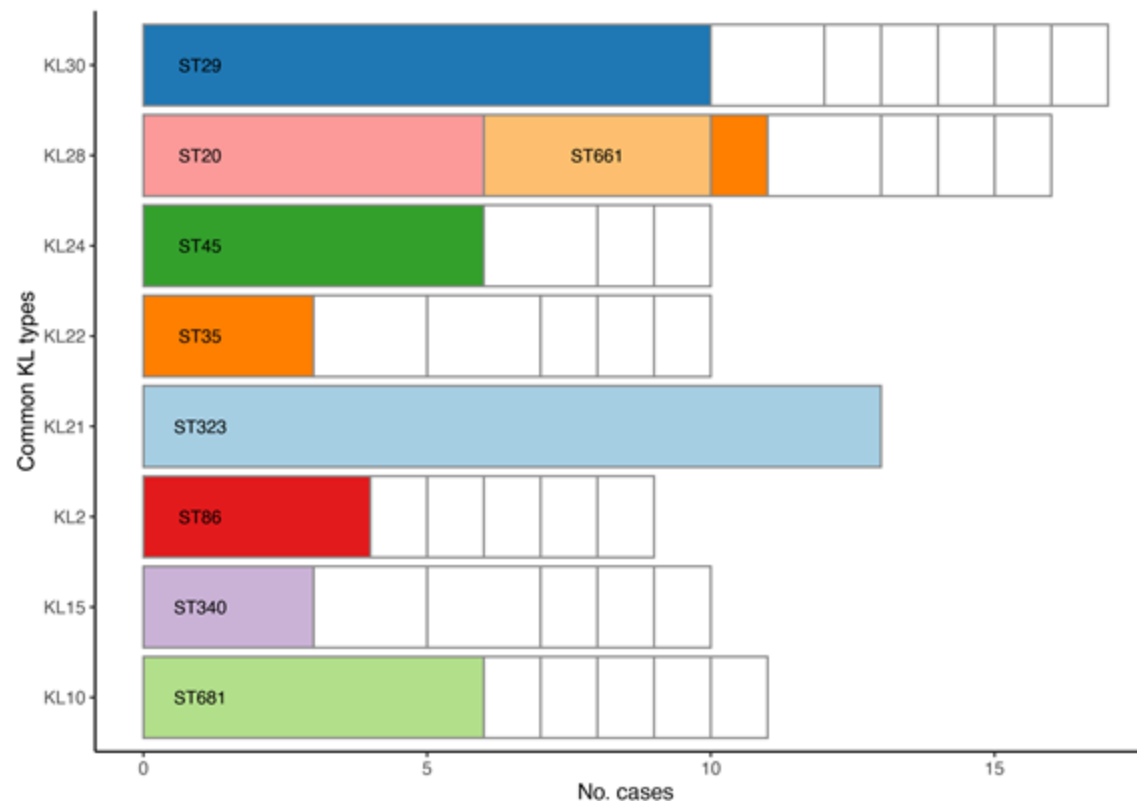
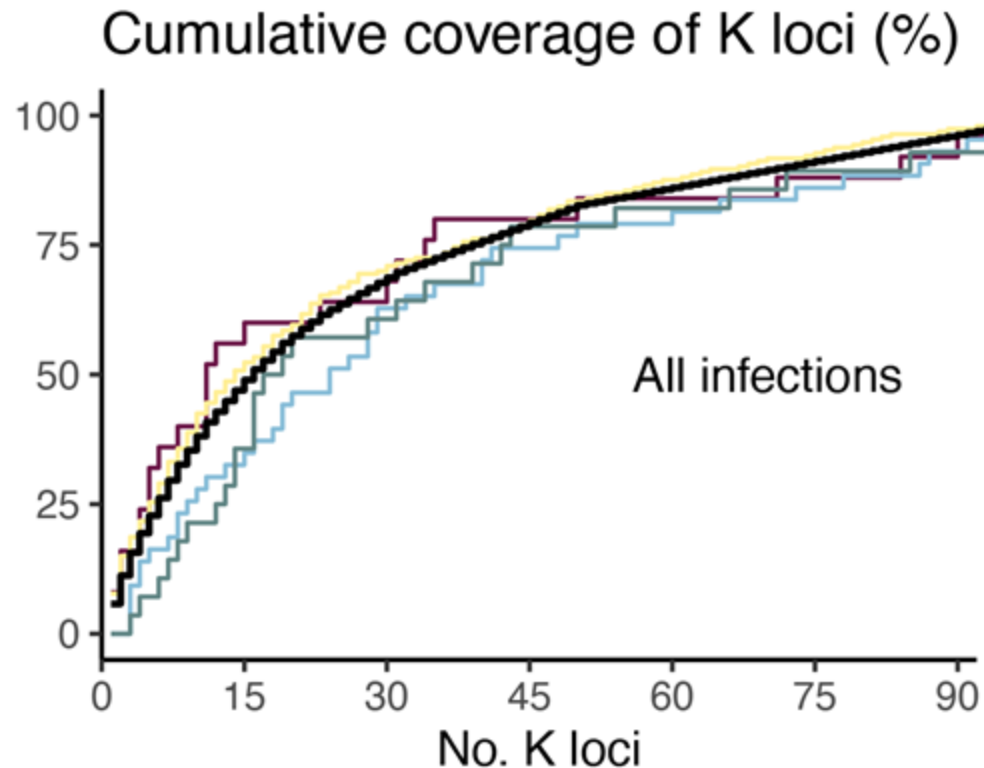
Substantial K diversity in 1 year of *Kpn* infections (n=294)



Diversity similar by infection type

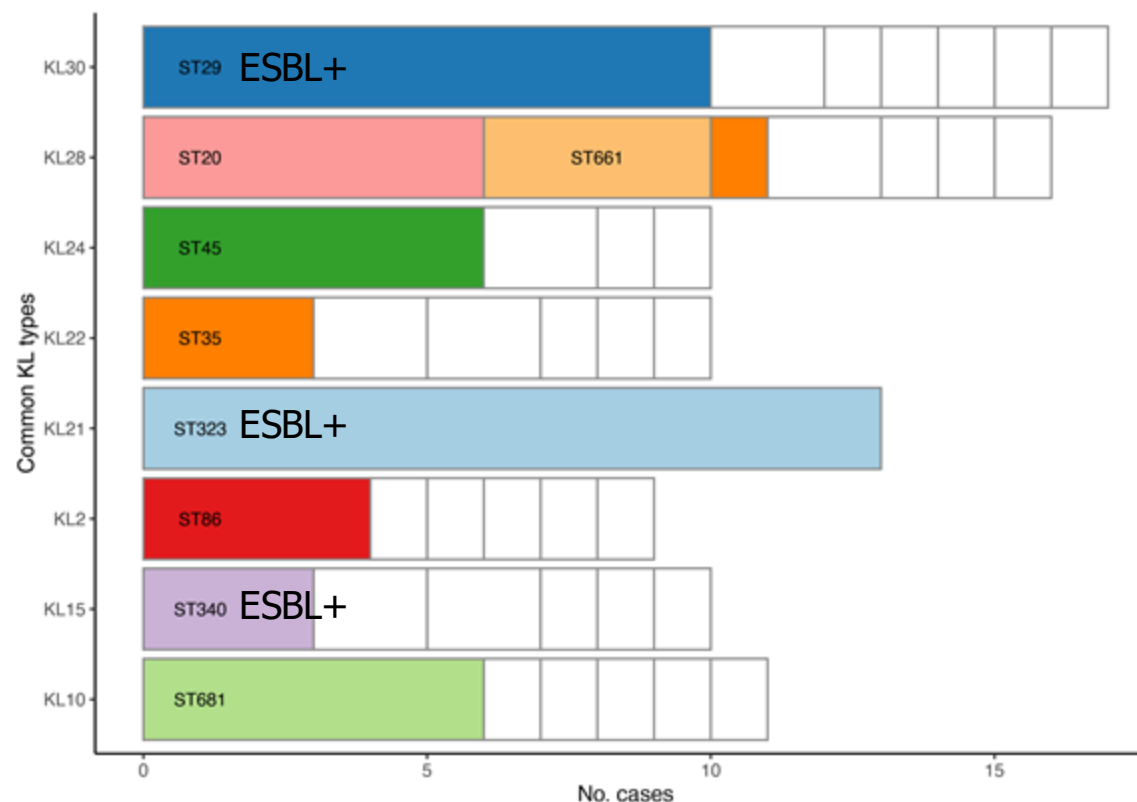
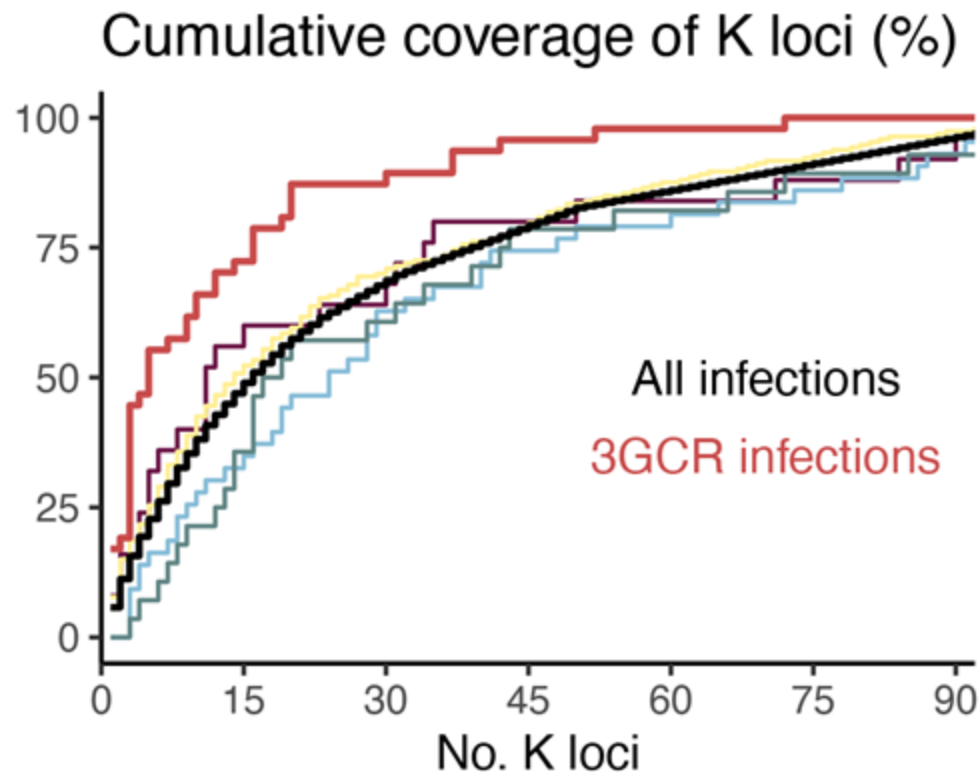


Common K loci associated with specific clones



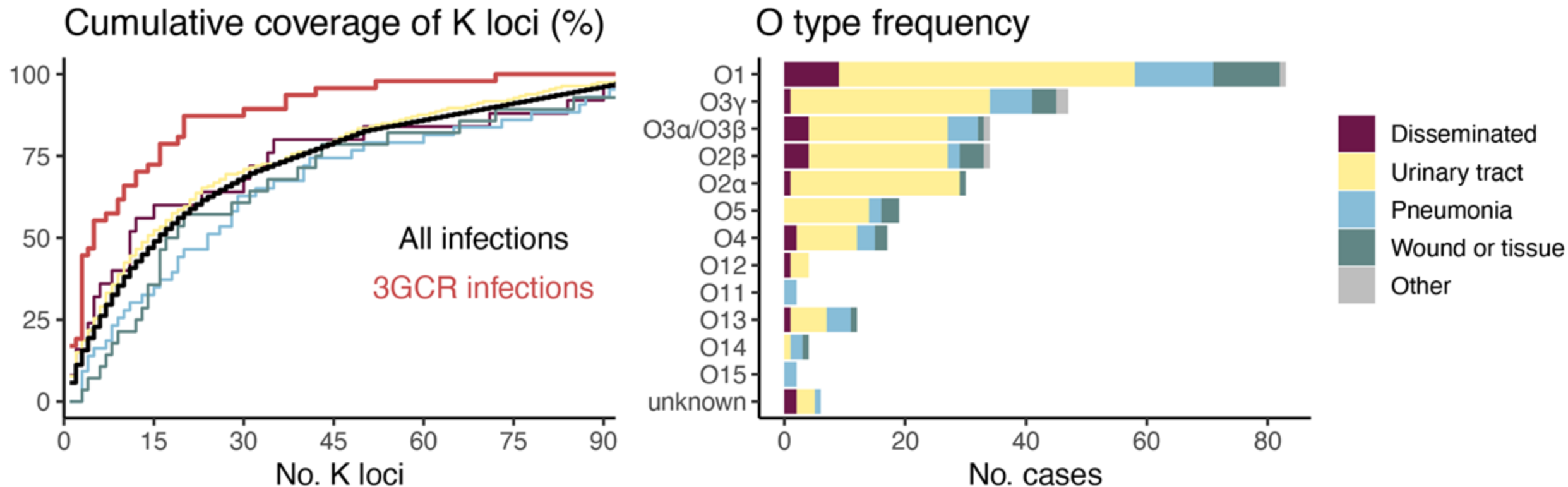
Note: few hypervirulent ST23 infections □ KL1 not common

Lower diversity among 3GCR resistant infections



Note: few hypervirulent ST23 infections □ KL1 not common

Comparable O diversity by infection type



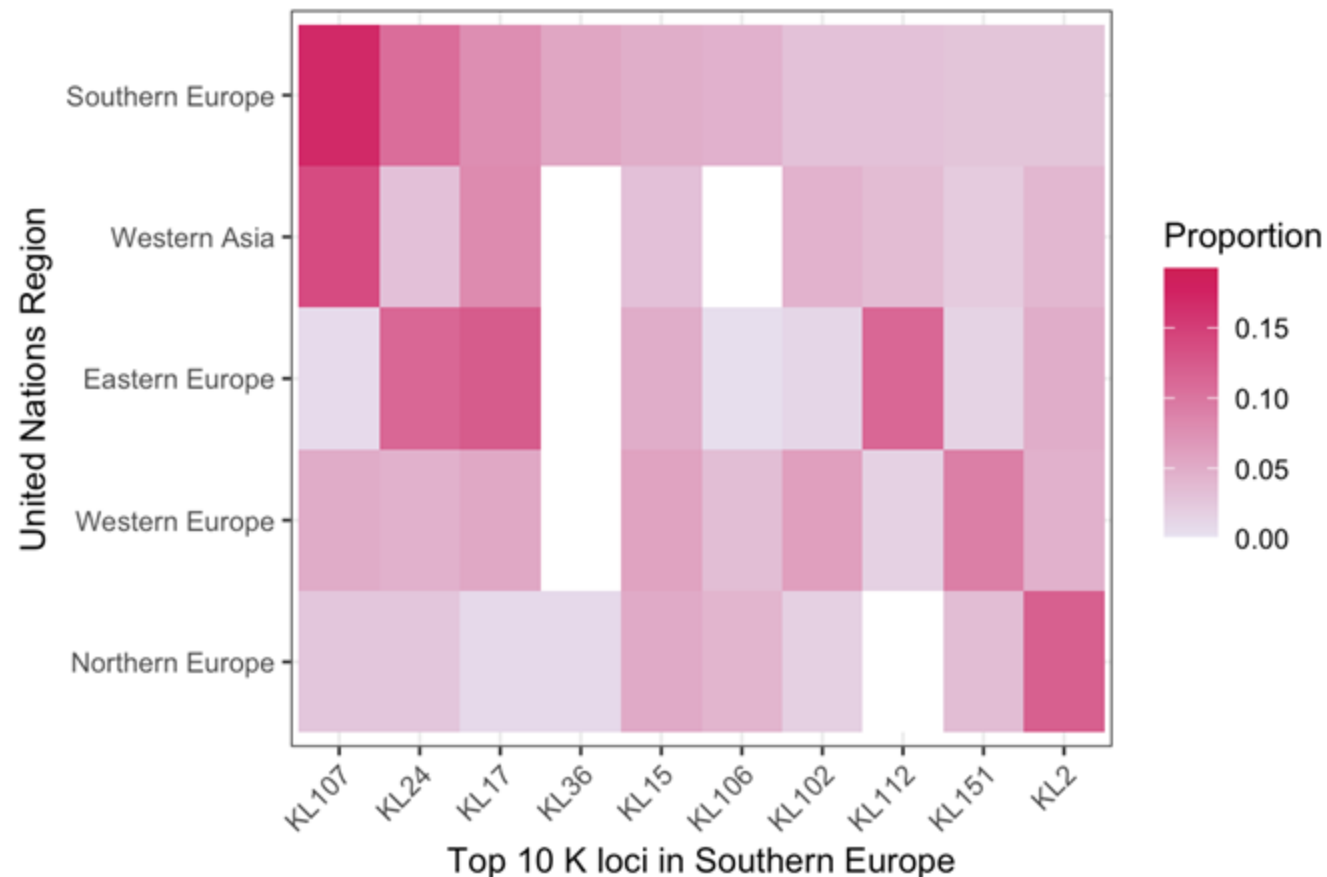
K frequencies differ by geography



KlebNET-GSP



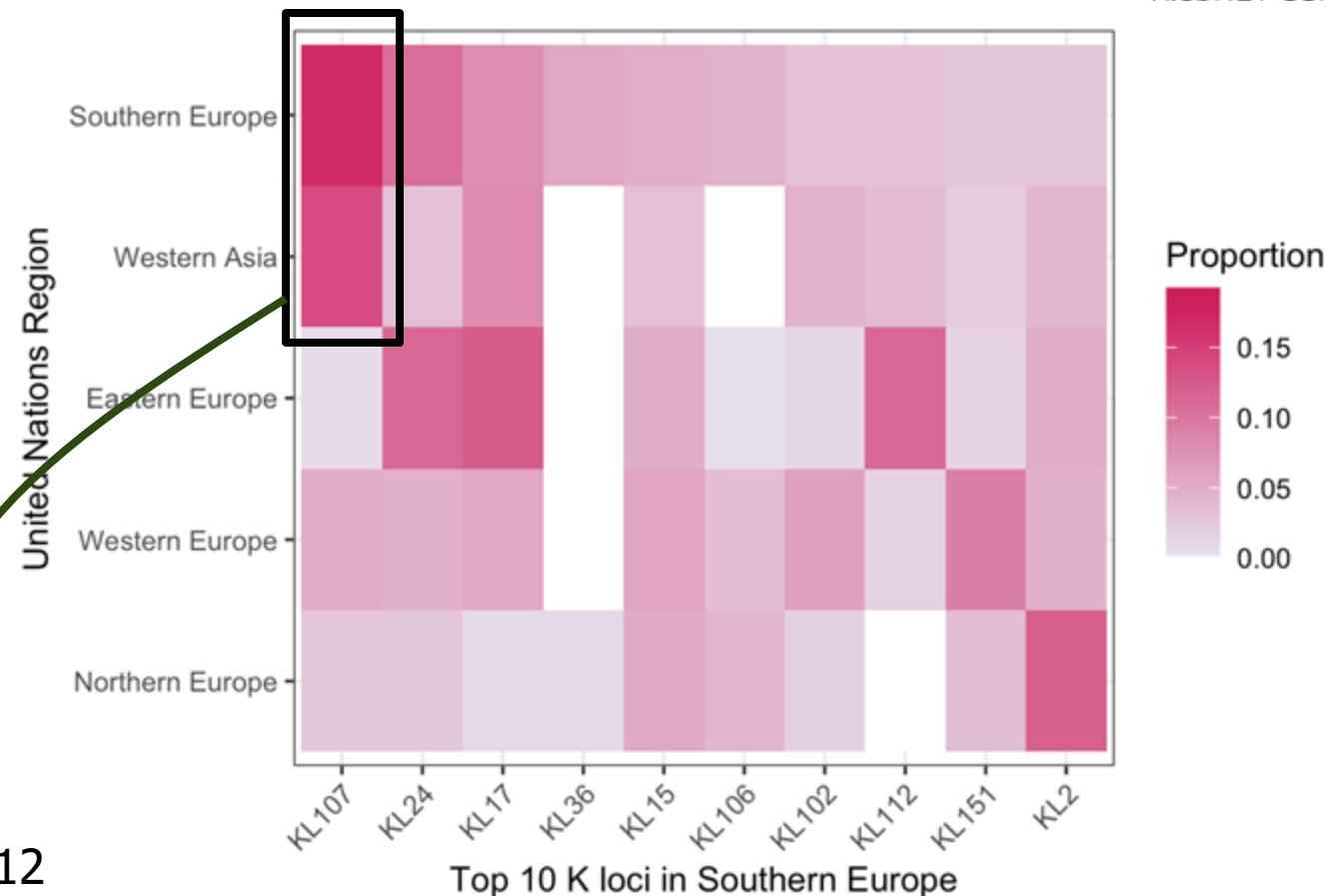
K frequencies differ by geography



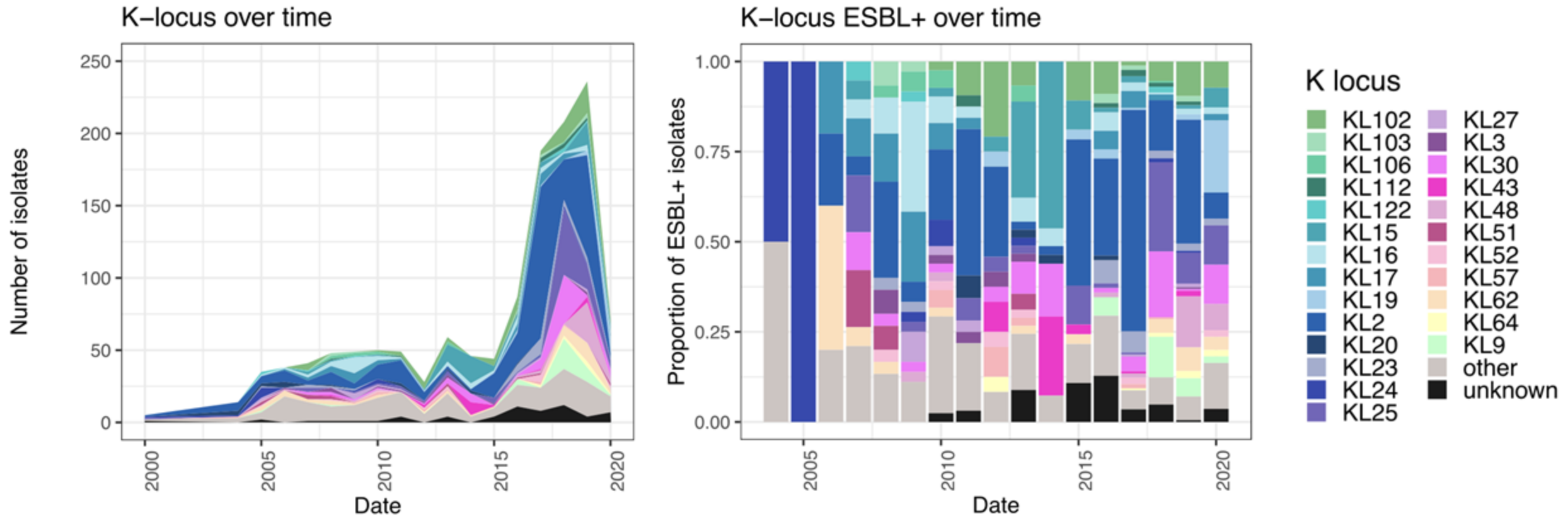
Geographic differences driven by clone associations



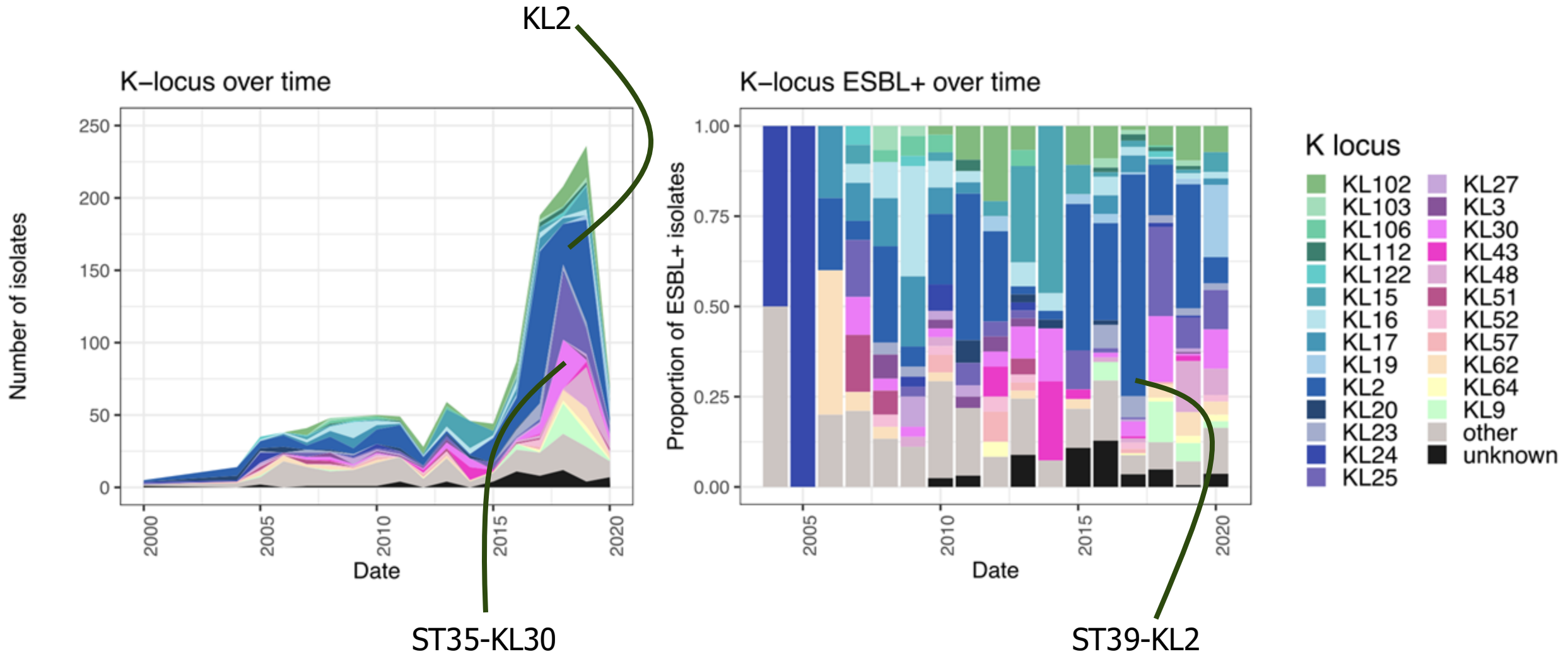
ST258 / ST512
(Italy and Israel)



K frequencies fluctuate through time



K frequencies impacted by successive clonal expansions



Considerations for robust *Kpn* sero-epidemiology analyses

Sampling:

- Large sample sizes
- Broad representation:
 - target infections
 - target geographies

Analysis approach:

- Account for sampling differences between sites
- Adjust for local clonal expansions

Kpn neonatal sepsis isolate meta-analysis



HUGE collaborative effort – 82 coauthors!

Bayesian prevalence estimates, adjusted for outbreaks

One WGS per infection



K loci and O types - Kaptive
ST and resistance score - Kleborate
Pairwise SNVs - Pathogenwatch

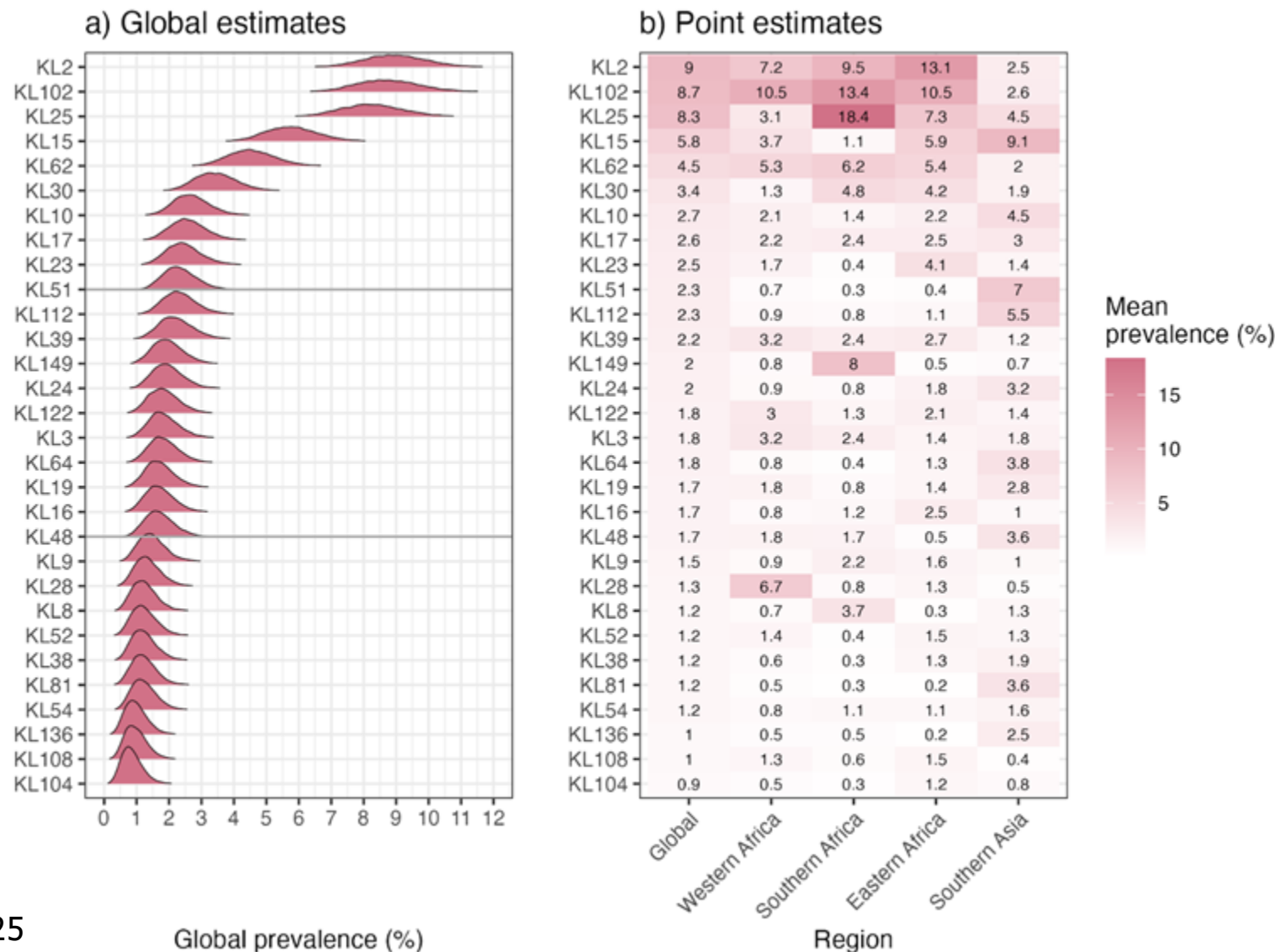


Cluster genomes ≤ 10 SNVs, same site, same year

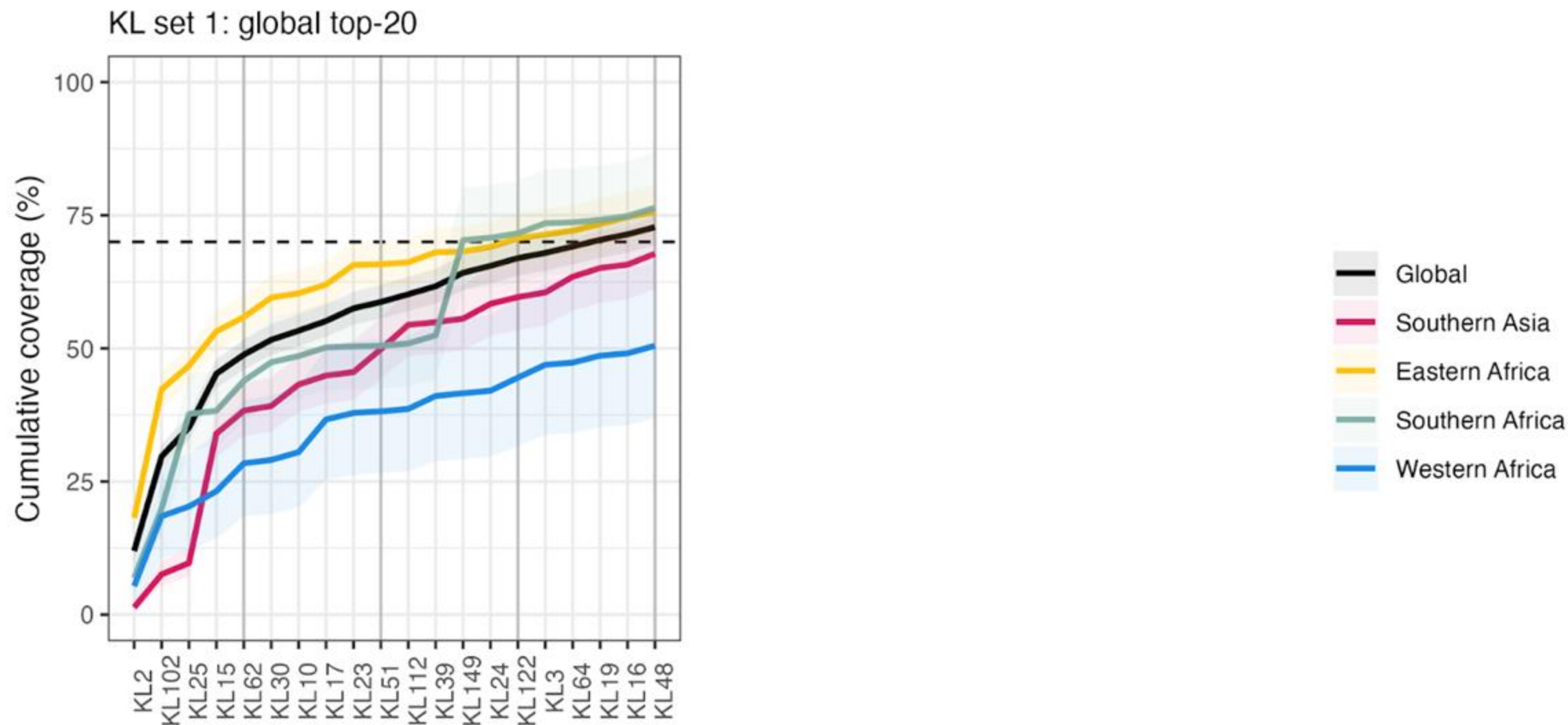


Bayesian prevalence estimates, global and regional
ESBL+, CP+, fatal cases

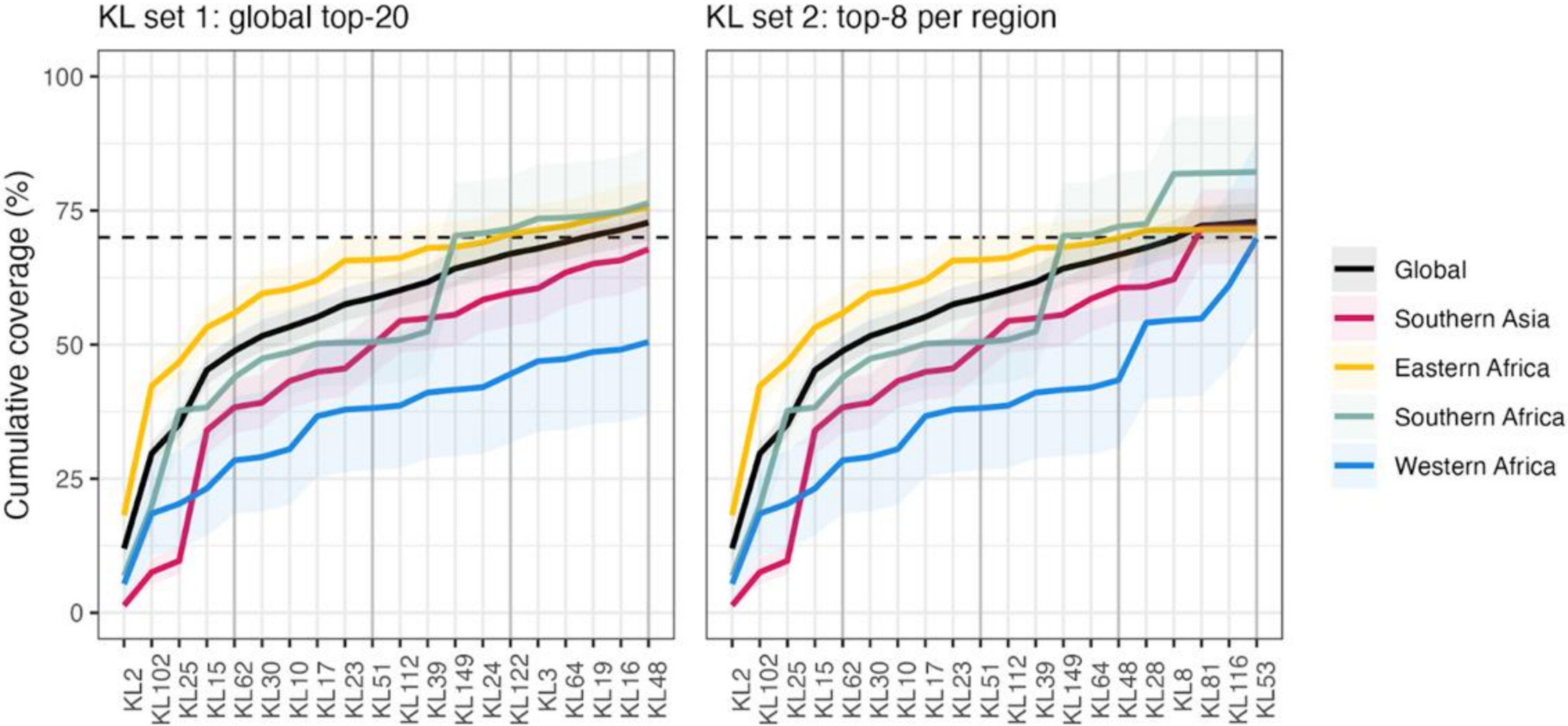
Bayesian prevalence estimates, adjusted for outbreaks



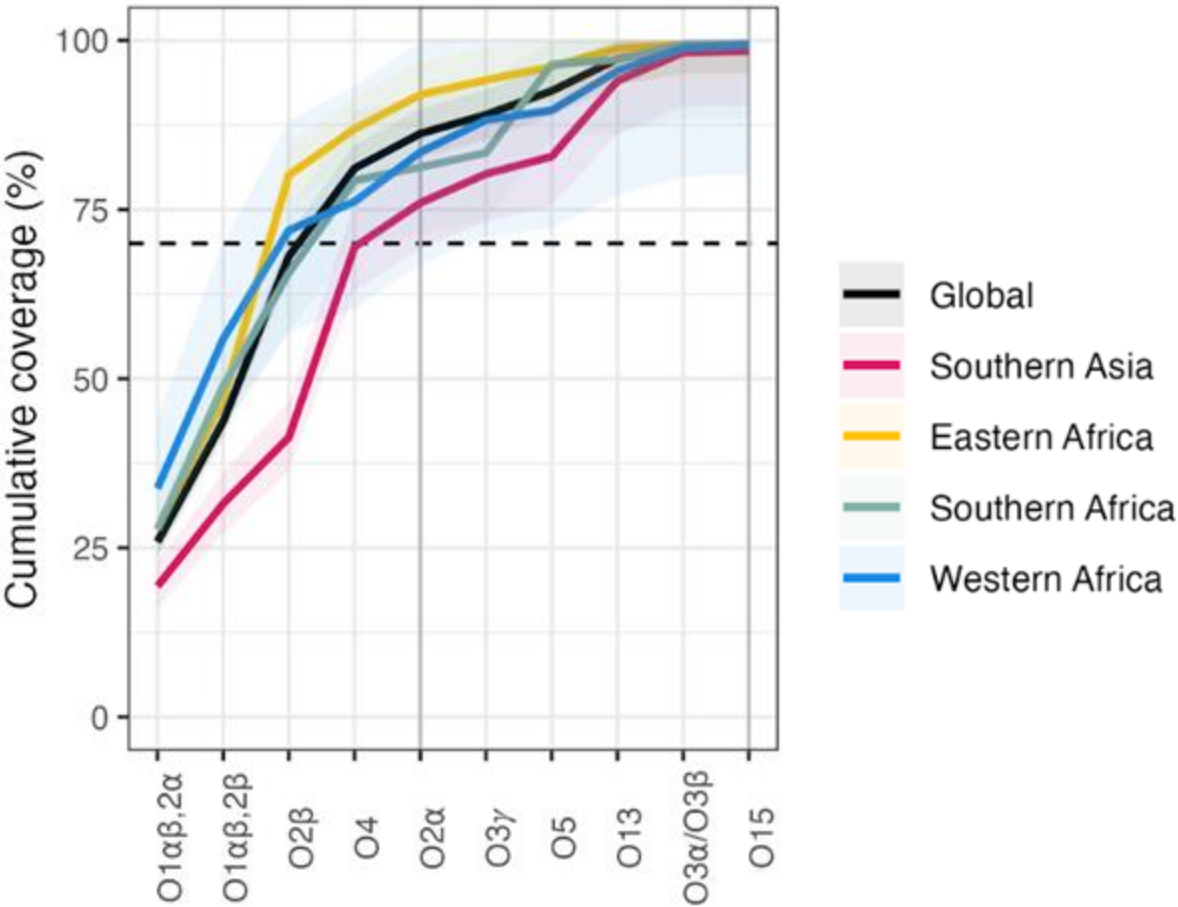
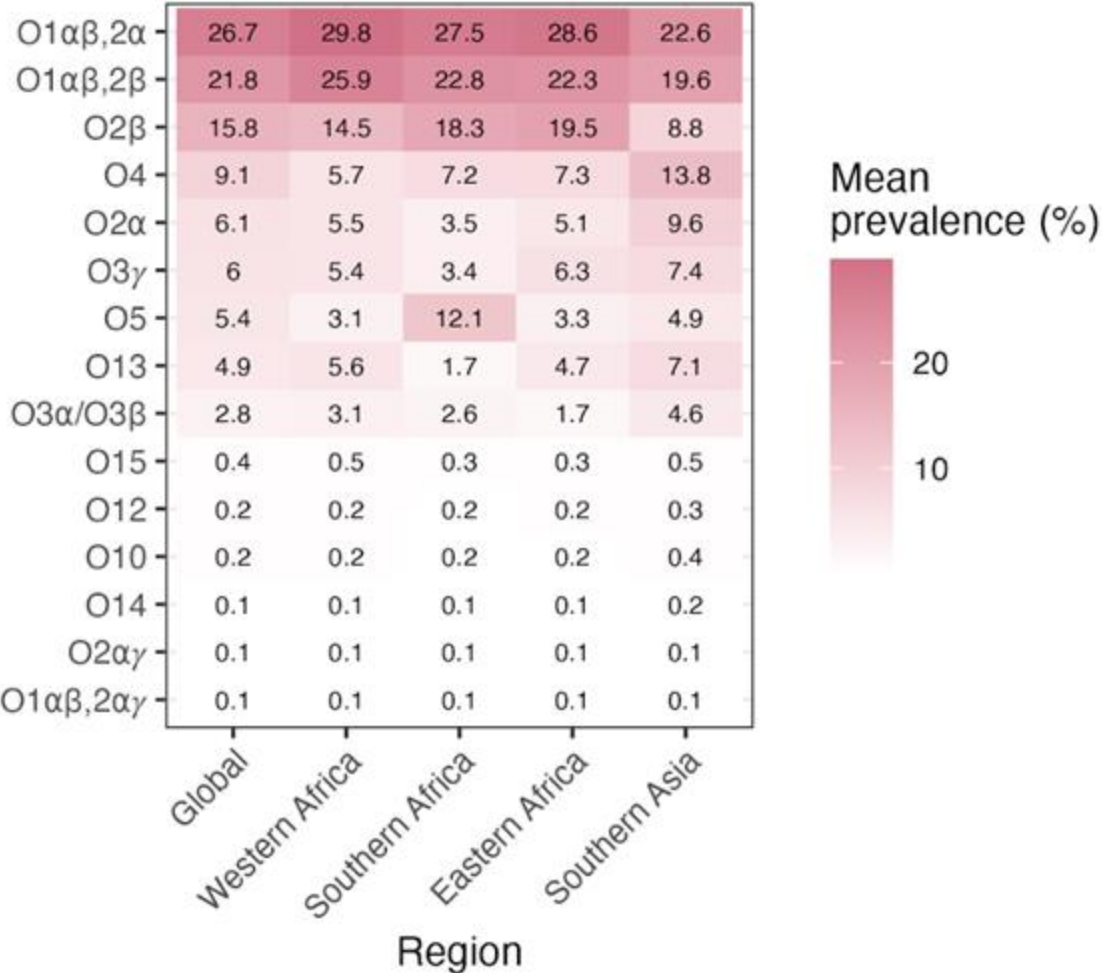
Cumulative coverage for top 20 K varies by region



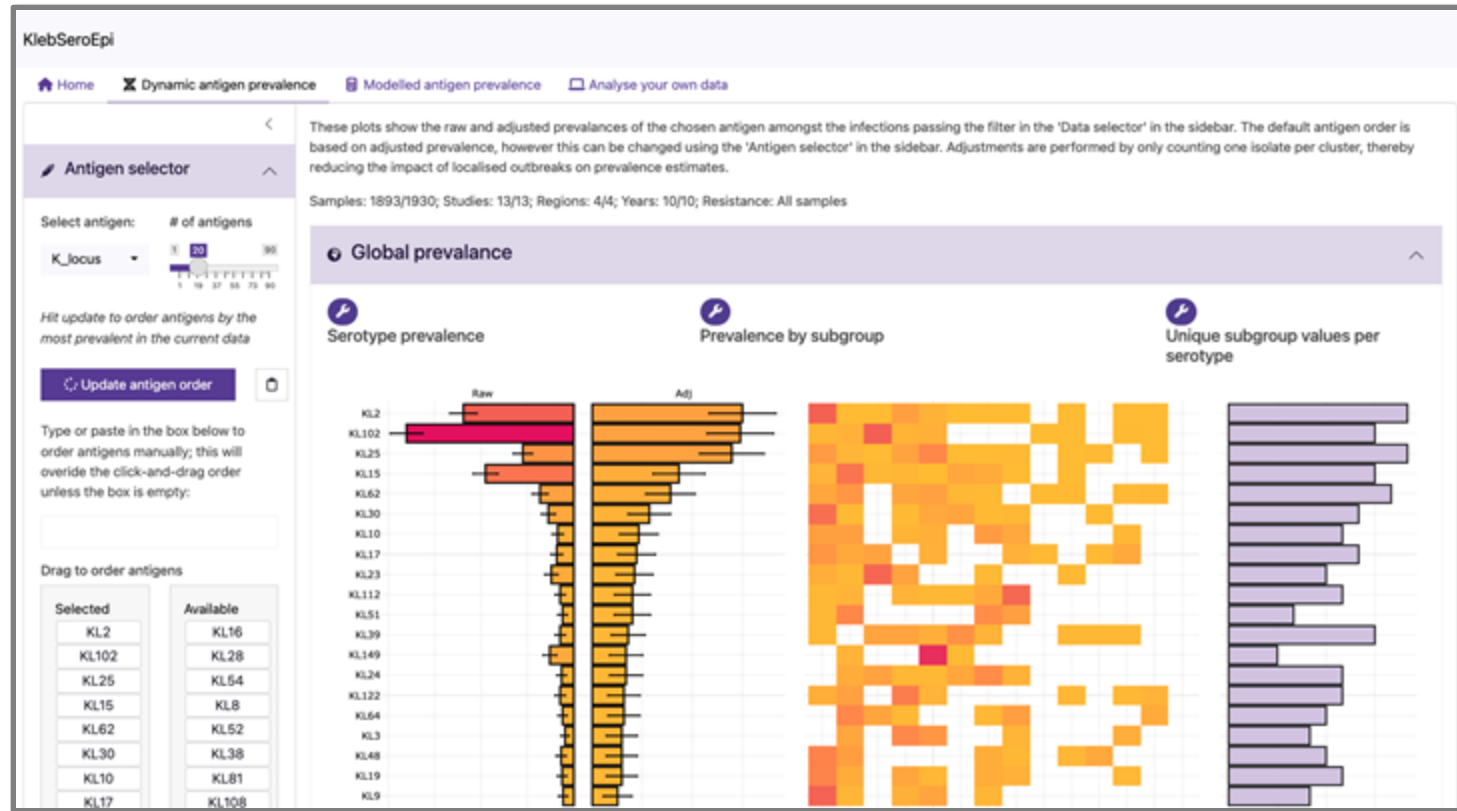
Can achieve $\geq 70\%$ coverage for all regions if select top loci from each



O types much less diverse, top 4 achieves ≥70% coverage in all regions



Sero-epi app for data exploration



<https://klebsiella.shinyapps.io/neonatal/>

In summary

List of learning points in this session:

- *Kpn* causing opportunistic human infections produce diverse K and O antigens
- MDR clones associated with diverse K and O loci, but some combinations have proliferated globally
- Hypervirulent clones (and infections) associated with KL1 and KL2
- K loci vary through space and time among opportunistic infections
- O types are less variable
- To prioritise antigens for vaccines and other interventions we need broadly representative data, and we need to adjust for localised clonal outbreaks
- Despite the extensive diversity it may be possible to produce a single anti-K vaccine with $\geq 70\%$ theoretical population coverage

Further reading

Specific further reading for this session

Stanton / Keegan *et al.* Distribution of capsule and O types in *Klebsiella pneumoniae* causing neonatal sepsis in Africa and South Asia: meta-analysis of genome-predicted serotype prevalence and potential vaccine coverage. *medRxiv* 2025
doi: <https://doi.org/10.1101/2025.06.28.25330253>

References

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