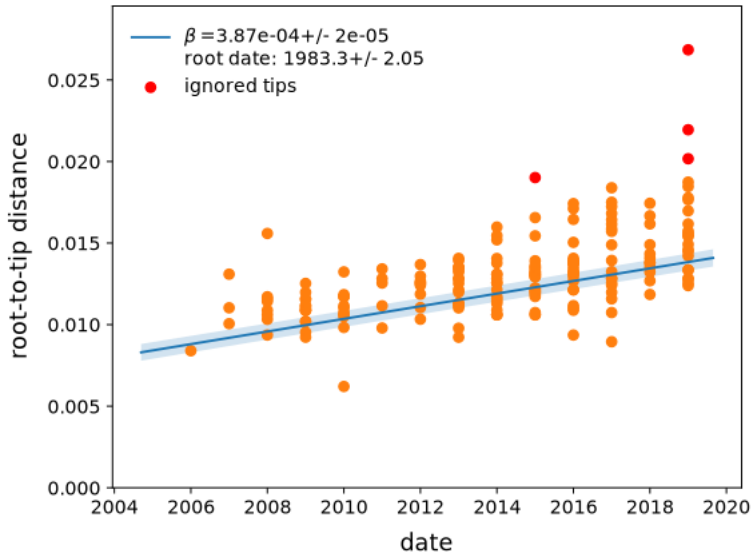
1. Methods

Time-scaled phylogenetic analysis

Root-to-tip regression analysis yielded a positive correlation coefficient of 0.36, indicating the data had sufficient temporal signal (Figure S1[A]). In addition, the substitution rate estimate with the correct sampling times (represented by the red line Figure S1 [B]) fell outside the distribution of date- randomised rate estimates in TreeTime (1), further suggesting the data had sufficient temporal signal for demographic analyses. TreeTime was used to estimate a substitution rate of 3.871e-04 (± 2.25e-05, one standard deviation) per site per year across the non-recombinant core SNP alignment, under a strict clock and using a least-squares approach while accounting for phylogenetic nonindependence (covariation). This corresponds to a substitution rate of 1.135e-06 (± 6.421e-08) when scaled to whole genome with an approximate core-genome size of 2.1 Mbp, in line with previous estimates for other *S. aureus* lineages (2–5). Minor rate variation was observed in the Bayesian analysis using the uncorrelated lognormal clock model. An inspection of the coefficient of rate variation, a measure of clocklike behaviour, revealed that this statistic was concentrated near zero, supporting a strict molecular clock model. The estimates for the substitution rate (1.507e-06, 95% HPD: 1.378e-06 – 1.648e-06), MRCA (1988.21, 95% HPD: 1985.11 - 1991.14) and the trajectory of the effective population size estimates were consistent with the strict clock model, thus the temporal analyses were reported using the simpler strict clock model.

A



B

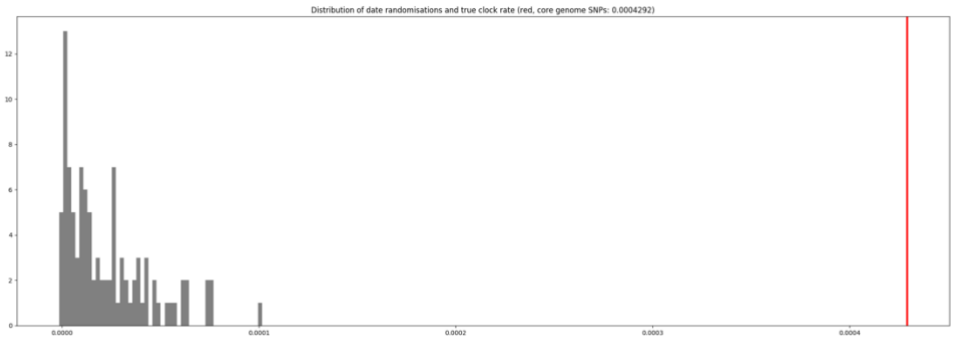


Figure S1. Temporal signal testing with a maximum-likelihood approach. (A) Regression analysis showing root-to-tip distance as a function of time. (B) Distribution of date-randomised substitution rate estimates in TreeTime.

TreeTime (1) was used as a "classical statistical" baseline prior to BEAST-2 analysis. The piece-wise coalescent estimate (Skyline, 20 grid points by default) was used to estimate the relative effective population size. Dating of the root suggested the most recent common ancestor (MRCA) of the lineage emerged in 1985.96 (90% maximum posterior bounds: 1981.61-1988.81) and the divergence of the MRSA clade had a mean of 1996.03 (90% maximum posterior bounds: 1994.89 - 1997.28; Figure S2). This analysis also indicated that the genetic diversity (effective population size) rapidly increased during the late 1990s, correlating with the acquisition of SCC*mec* (Figure S3).

Figure S2. Time-scaled maximum likelihood phylogeny (TreeTime) including 180 European CC1-MRSA- IV isolates (red) and 10 MSSA precursors (green) of the clone. Confidence intervals on internal nodes represent the 90% maximum posterior interval of node ages.

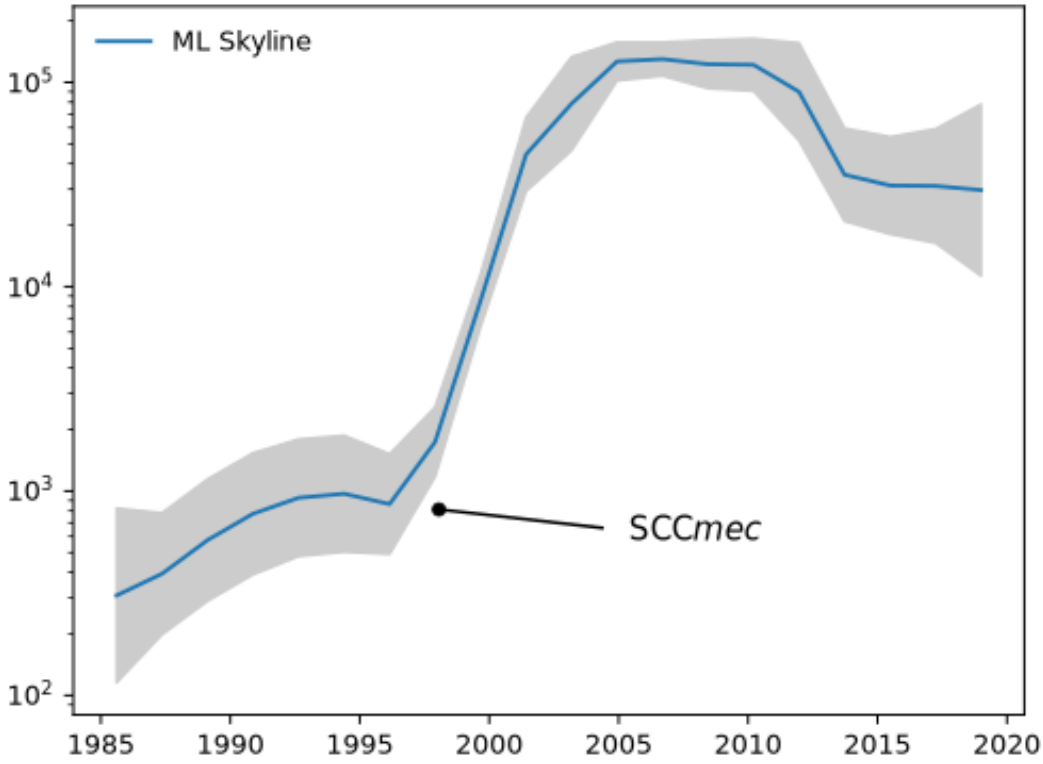


Figure S3. Maximum likelihood Skyline estimate of effective population size using a coalescent with 20 grid points in TreeTime. The blue line shows a rapid increase in effective population size in the late 1990s. Shaded regions correspond to 90% maximum posterior interval.

2. Results

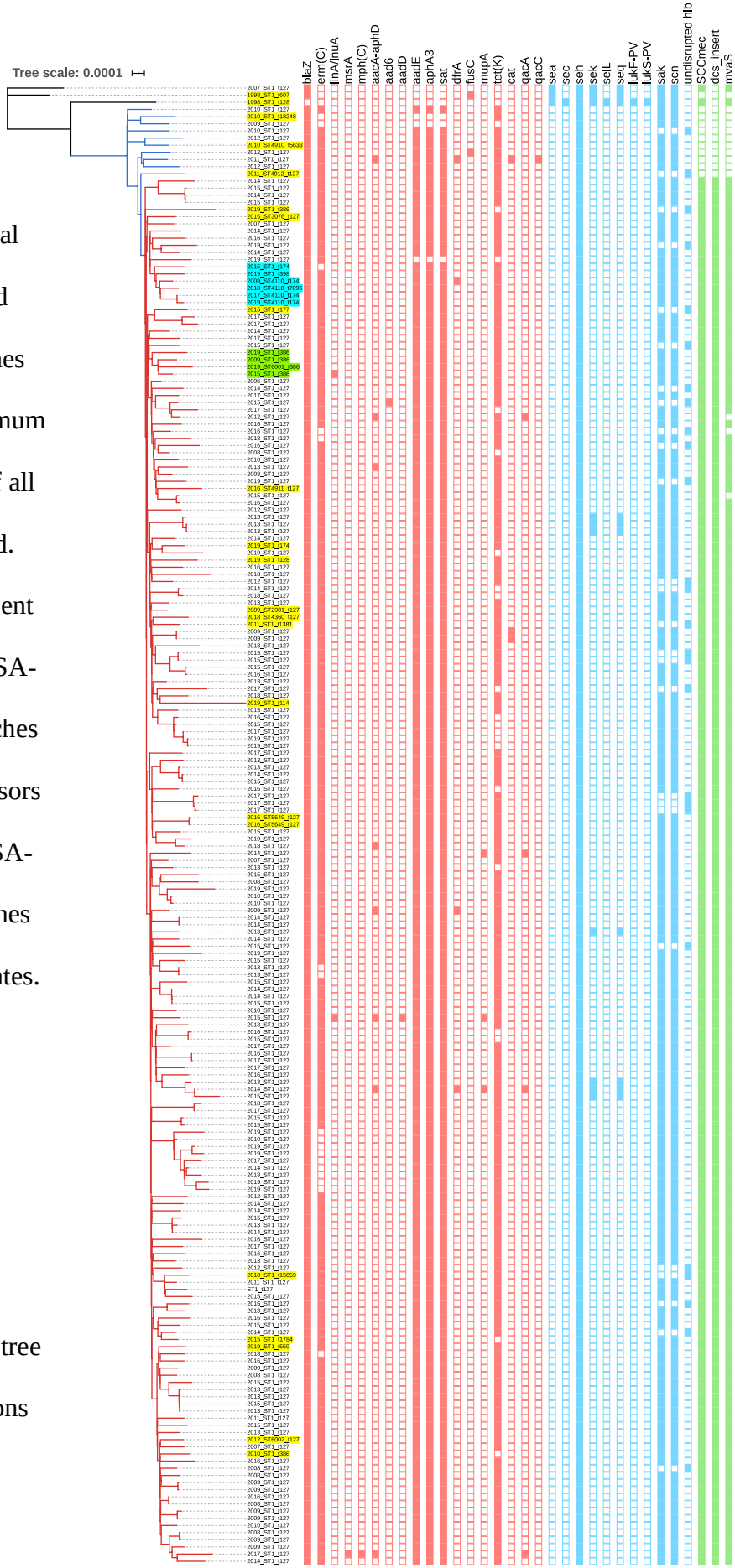


Figure S4. Antimicrobial resistance, virulence and SCC*mec*-associated genes mapped against a maximum likelihood phylogeny of all 207 isolates investigated. The red branches represent the European CC1-MRSA-IV clone, the blue branches represent MSSA precursors of European CC1- MRSA-IV, and the black branches represent outgroup isolates. The majority of isolates were identified as ST1-MRSA- IV-t127. Non-ST1/t127 isolates are highlighted in yellow, turquoise or green. The tree scale denotes substitutions per site.

3. References

1. Sagulenko P, Puller V, Neher RA. TreeTime: maximum-likelihood phylodynamic analysis. Virus Evol. 2018;4(1):vex042.
2. Stegger M, Wirth T, Andersen PS, Stegger M, Wirth T, Andersen PS, et al. Origin and evolution of European community-acquired methicillin-resistant *Staphylococcus aureus*. MBio. 2014;5(5):1–12.
3. Steinig EJ, Duchene S, Robinson DA, Monecke S, Yokoyama M, Laabei M, et al. Evolution and global transmission of a multidrug-resistant, community-associated methicillin-resistant *Staphylococcus aureus* lineage from the Indian subcontinent. MBio. 2019;10(6):e01105-19.
4. Duchêne S, Holt KE, Weill FX, Le Hello S, Hawkey J, Edwards DJ, et al. Genome-scale rates of evolutionary change in bacteria. Microb genomics. 2016;2(11):e000094.
5. van Hal SJ, Steinig EJ, Andersson P, Holden MTG, Harris SR, Nimmo GR, et al. Global scale dissemination of ST93: a divergent *Staphylococcus aureus* epidemic lineage that has recently emerged from remote Northern Australia. Front Microbiol. 2018;9:1453.
6. Bouckaert R, Vaughan TG, Barido-Sottani J, Duchêne S, Fourment M, Gavryushkina A, et al. BEAST 2.5: An advanced software platform for Bayesian evolutionary analysis. PLoS Comput Biol. 2019;15(4):e1006650.