... copy. to display th. medRxiv preprint doi: https://doi.org/10.1101/2024.08.01.24311290; this version posted August 3, 2024. The copyright holder for this preprint (which was not certified by peer review) is the author/funder, who has granted medRxiv a license to display the preprint in perpetuity. A It is made available under a ST Source 17 Blood 18 Fluid 80***** Tissue 🔲 117 🖈 Urine 203 Wound 375 Unknown/Other 412 AST 584 🔲 R 736 T 1471 1478 ★ S Other 🗌 NA 🚖 Emergent Lineage MILIMITINE ST Tree scale: 0.001 В Genome Length Antimicrobial Resistance Genes 3.4 Genome Length (MB) 15 3.2 No. of ARGs 3.0 10 2.8 5 2.6 0 51³¹⁵ <20⁵ STIAT A D Е **Plasmid Replicons** Virulence Genes 6 10 Vo. of Virulence Genes No. of Replicons Ŧ 5 İ 2 0 0 511478 €5T1A78 Ś

Figure S1: Genetic relatedness and genomic features of 710 VREfm isolates from UPMC. (A) The midpoint-rooted phylogenetic tree was constructed from a core genome alignment. Sequence types (ST) and isolation source are colored as indicated. Emergent lineages are noted by a black star. Antimicrobial susceptibility testing (AST) results for daptomycin (DAP) and linezolid (LNZ) were interpreted as resistant (R), intermediate (I), and susceptible (S). (B) Genome length, (C) presence of antimicrobial resistance genes, (D) presence of virulence genes, and (E) presence of plasmid replicons by main VREfm lineages. Averages of genomic features within each ST were compared to the average seen in the previously dominant ST17 lineage using a one-sided t-test. Asterisks indicate p-values <0.0045. Horizontal lines represent the average and error bars show the standard deviation for each group.



A

В

4,500

mobB

mobA



Figure S2: Bacteriocin prevalence and genomic context of bacteriocin T8. (A) Distribution of bacteriocins within 710 VREfm isolates from UPMC. Bacteriocins were identified using BAGEL4 with sequence identity and coverage thresholds of \geq 95%. (B) Bacteriocin T8-encoding rep11a plasmid from the ST117 isolate VRE38098. Bacteriocin T8 and immunity factor are highlighted in burgundy.

3,000

mobC

3,250

³,500

VRE38098_6 6,173 bp 1,500

750

CDS

Bacteriocin T8

Immunity Prote

2,750



Figure S3. Global population structure of 15,631 VREfm genomes from human sources.

Geographical distribution of VREfm genomes pulled from NCBI. The number of genomes from each country is shown from lowest (light grey) to highest (purple). Countries with >300 genomes are highlighted with the distribution of STs and vancomycin resistance operons.