

Enhanced detection of neonatal invasive infection clusters in South Africa using epidemiological and genomic surveillance data

Supplementary information

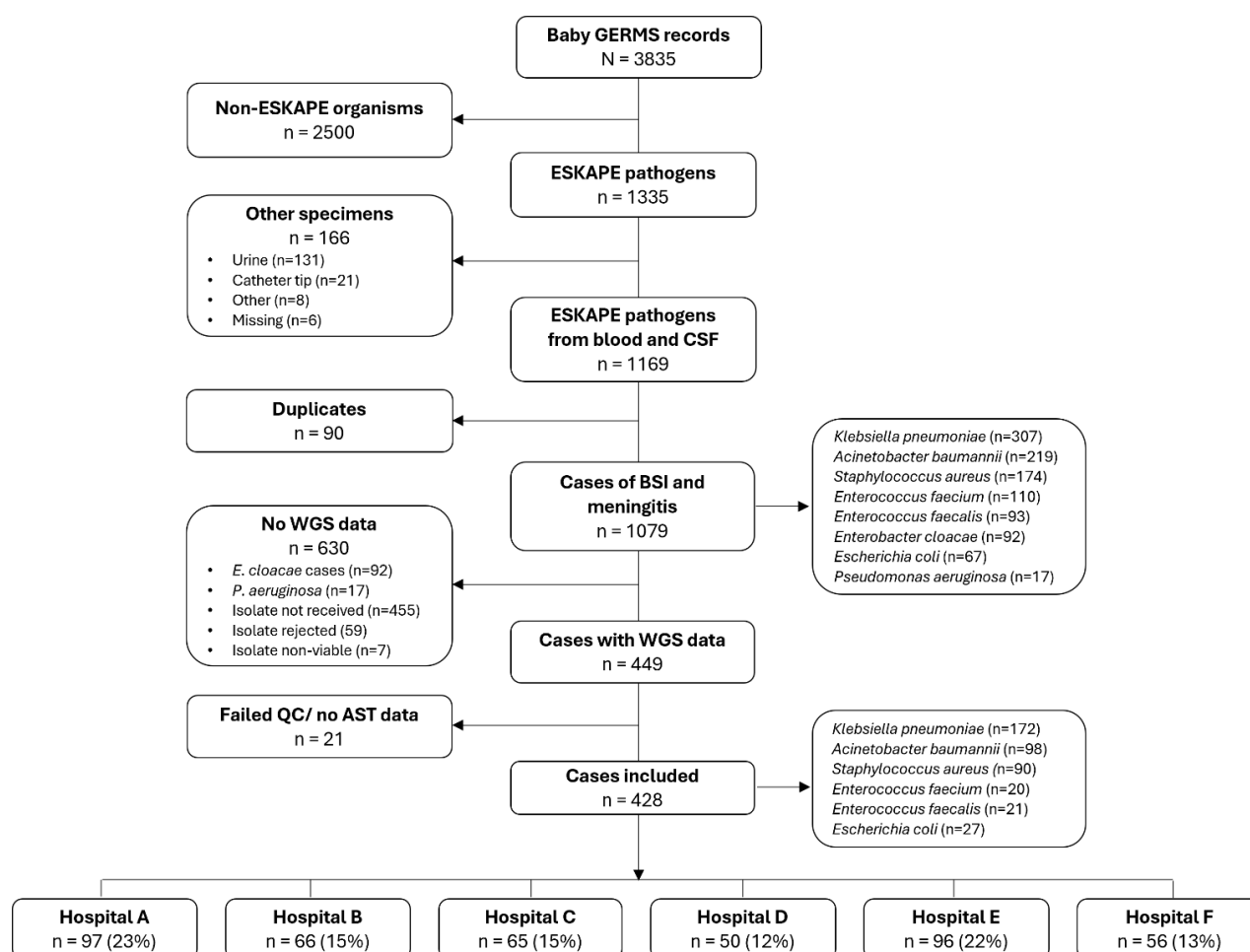


Fig S1: Cases of BSI and meningitis at six Baby GERMS-SA sentinel hospitals included in the study

Key; ESKAPE = *Enterococcus faecium* and *faecalis*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter cloacae* and *Escherichia coli*; CSF = Cerebrospinal fluid; BSI = bloodstream infection; WGS = Whole genome sequencing; QC = Quality control; AST = Antimicrobial susceptibility testing

Table S1: Odds of death by pathogen among patients with bloodstream infection or meningitis at six sentinel hospitals in South Africa, September 2019–October 2020, n=428

Pathogen	n	OR ^a (95% CI ^b)	p-value
<i>Staphylococcus aureus</i>	90	Ref	
<i>Klebsiella pneumoniae</i>	172	6.37 (2.14-18.96)	0.001
<i>Acinetobacter baumannii</i>	98	11.18 (3.63-34.35)	<0.001
<i>Escherichia coli</i>	27	4.6 (0.98-21.57)	0.053
<i>Enterococcus faecalis</i>	21	1.64 (0.27-9.93)	0.589
<i>Enterococcus aecium</i>	20	2.55 (0.41-16.11)	0.405

a: OR = odds ratio; b: CI = confidence interval

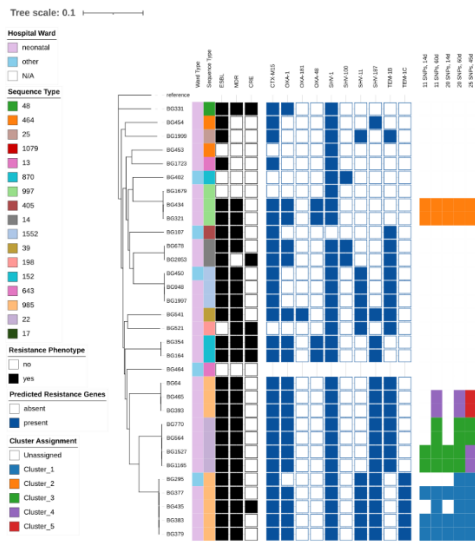
Table S2: Logistic regression model of factors associated with being in a SNP-EPI cluster at six sentinel hospitals in South Africa, September 2019–October 2020, n=428

Characteristic	Univariable			Multivariable		
	n	OR ^a (95% CI ^b)	p-value	n	aOR ^c 95% CI	p-value
Age (days)	424	0.98 (0.96-0.99)	0.002	196	0.98 (0.94-1.01)	0.300
Sex						
Female	191	Ref		90	Ref	
Male	221	0.85 (0.56-1.30)	0.400	106	1.1 (0.56-2.15)	0.800
HIV exposed						
No	148	Ref		124	Ref	
Yes	84	0.86 (0.48-1.52)	0.600	72	0.62 (0.30-1.26)	0.200
Gestation age (weeks)						
≤27	28	Ref		24	Ref	
28-31	70	0.89 (0.37-2.19)	0.800	56	0.68 (0.24-1.91)	0.500
32-36	70	0.74 (0.30-1.83)	0.500	60	1.05 (0.32-3.44)	>0.900
≥37	68	0.23 (0.08-0.62)	0.004	56	1.71 (0.13-4.10)	0.700
Weight (grams)^d						
≤1500	100	Ref		85	Ref	
1501-2499	52	1.14 (0.58-2.25)	0.700	47	0.91 (0.37-2.24)	0.800
≥2500	73	0.20 (0.09-0.44)	<0.001	64	0.20 (0.04-0.83)	0.033
Prior antibiotics^e						
No	41	Ref		38	Ref	
Yes	182	0.83 (0.41-1.72)	0.600	158	0.74 (0.32-1.72)	0.500
Exclusive breastfeeding						
No	334	Ref		112	Ref	
Yes	94	0.90 (0.54-1.48)	0.700	84	1.0 (0.48-2.11)	>0.900
Central line						
No	405	Ref		175	Ref	
Yes	23	1.51 (0.61-3.53)	0.400	21	2.3 (0.69-8.01)	0.200
Umbilical line						
No	388	Ref		165	Ref	

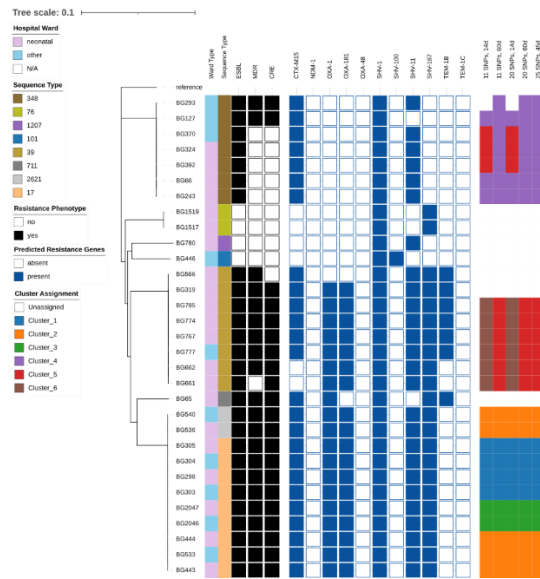
Yes	40	2.02 (1.03-3.90)	0.037	31	1.23 (0.47-3.22)	0.700
Peripheral line						
No	248	Ref		47	Ref	
Yes	180	0.97 (0.64-1.47)	0.900	149	1.40 (0.58-3.54)	0.500
Intubation						
No	370	Ref		155	Ref	
Yes	58	1.76 (0.99-3.09)	0.052	41	1.81 (0.78-4.27)	0.200

a: OR = odds ratio; b: CI = confidence interval; c: aOR = adjusted odds ration; d: Weight measured on specimen collection; e: Antibiotics in the last two weeks

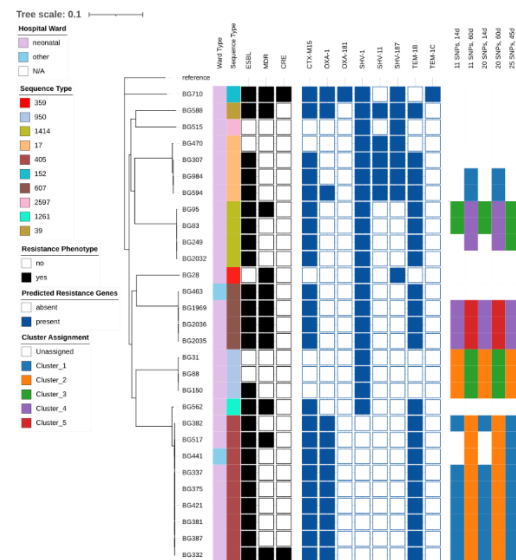
Hospital A



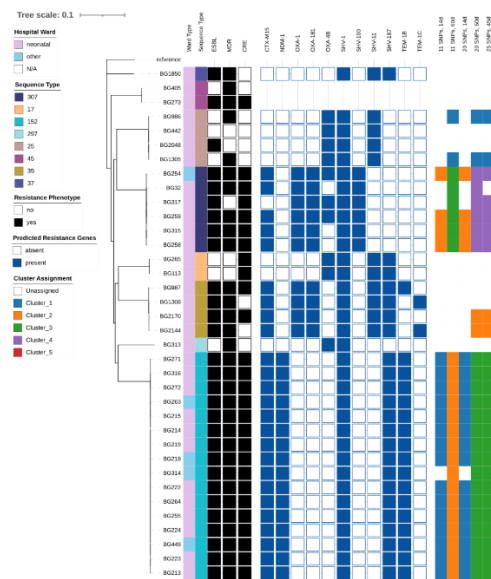
Hospital B



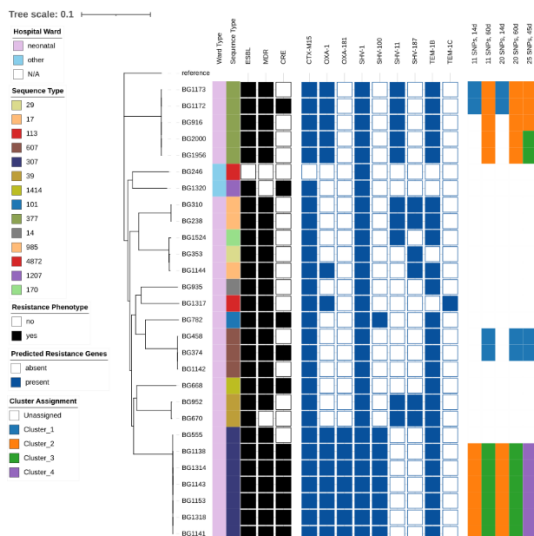
Hospital D



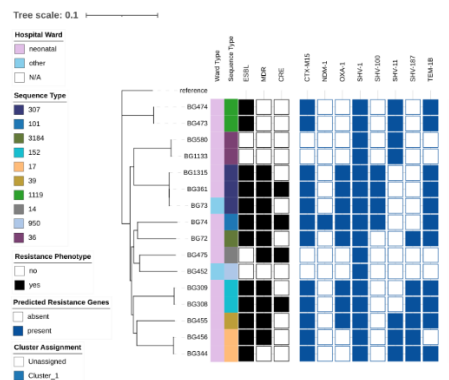
Hospital C



Hospital E



Hospital F



more antibiotic classes); CRAB = carbapenem-resistant *Acinetobacter baumannii* (defined as resistance to one or more carbapenem antibiotics).

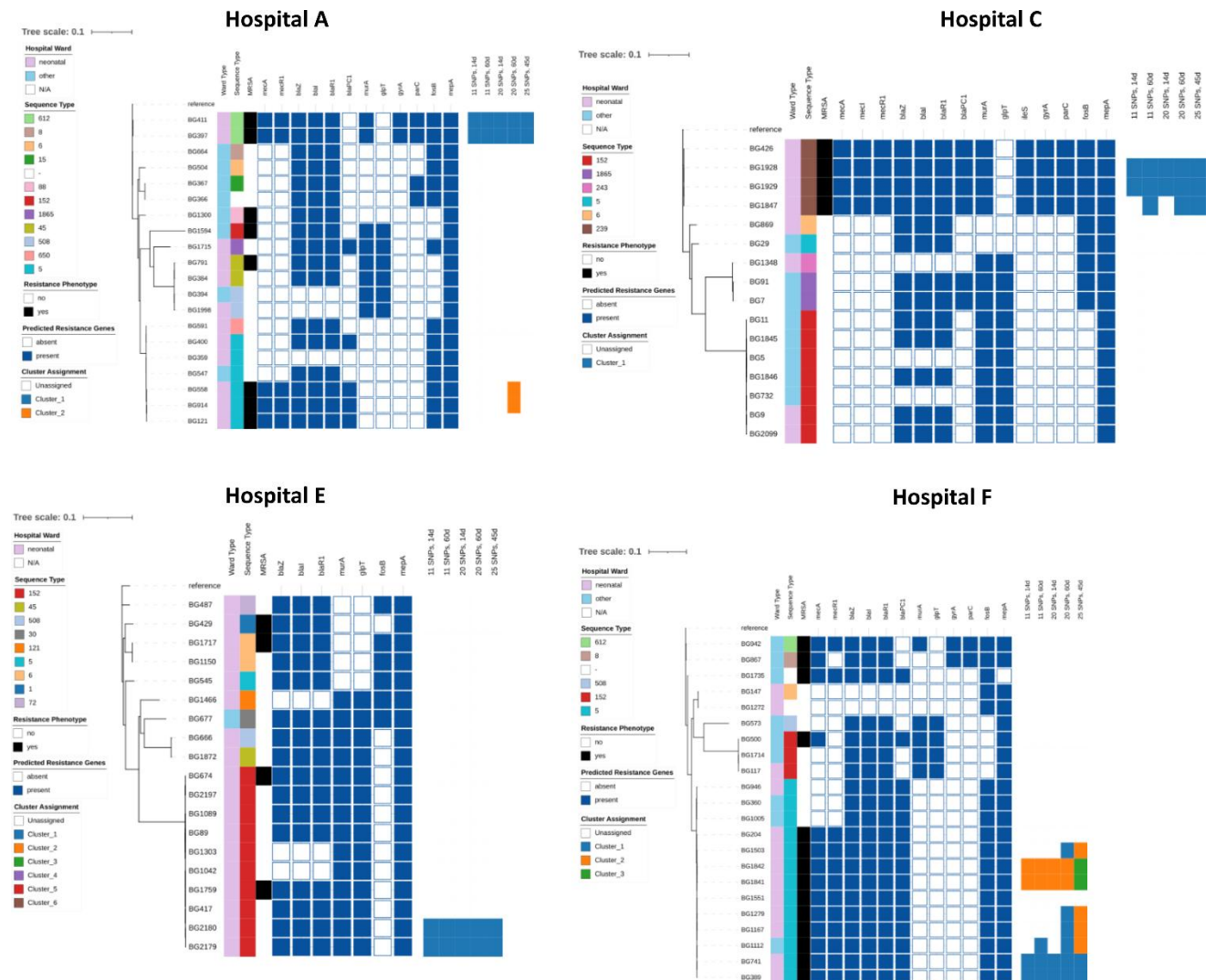


Fig S4: Phylogenetic trees showing selected phenotypic resistance and predicted genotypic resistance in *Staphylococcus aureus* isolates from case-patients at Hospital A, C, E and F. Key: MRSA = methicillin-resistant *Staphylococcus aureus* (defined as resistance to oxacillin or ceftazidime).

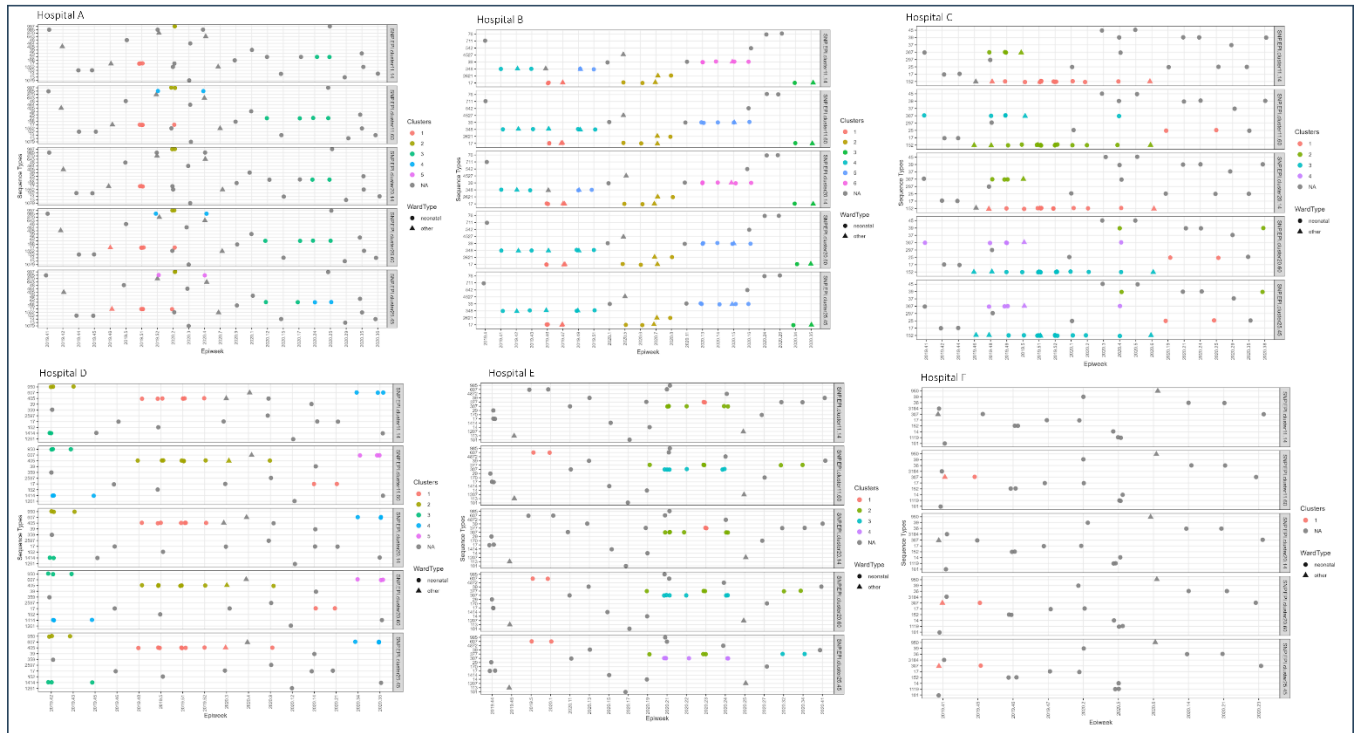


Fig S5: *K. pneumoniae* infection clusters detected in Hospital A to Hospital F by varying SNP-EPI criteria

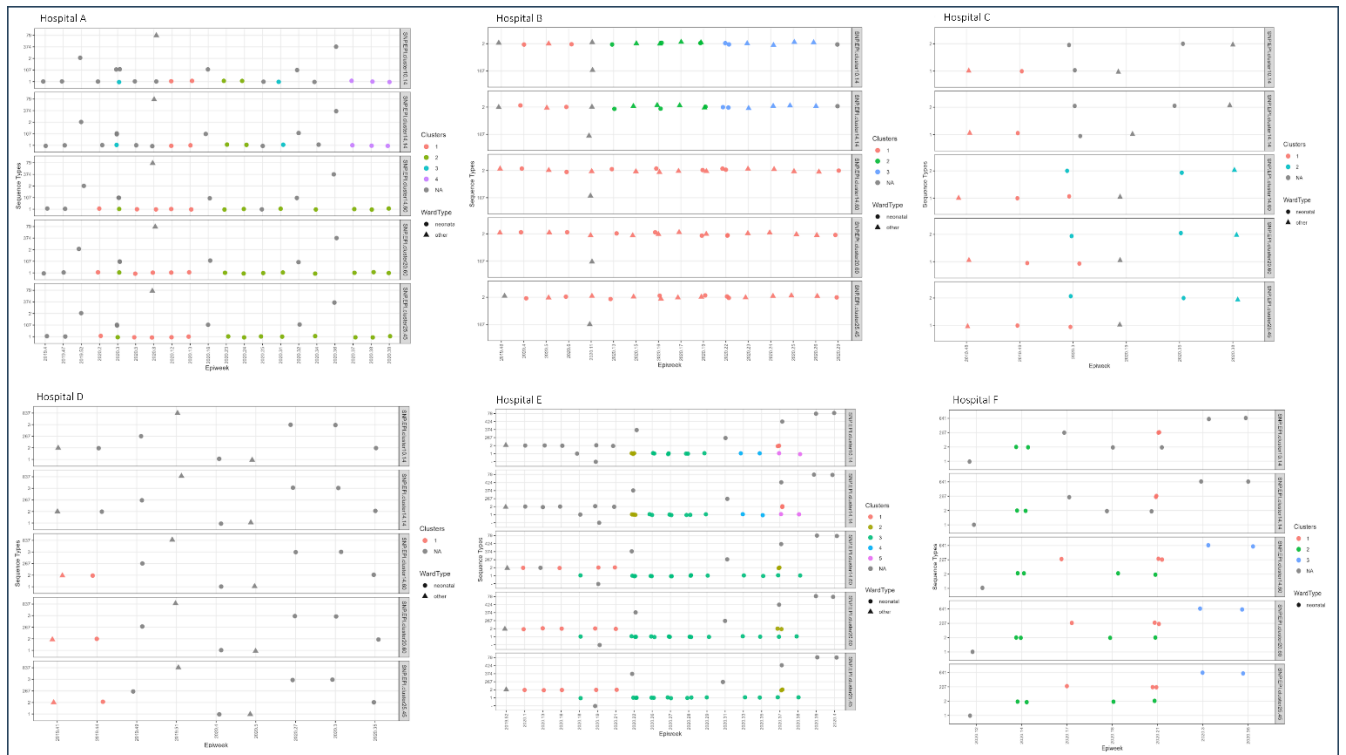


Fig S6 *A. baumannii* infection clusters detected in Hospital A to Hospital F by varying SNP-EPI criteria

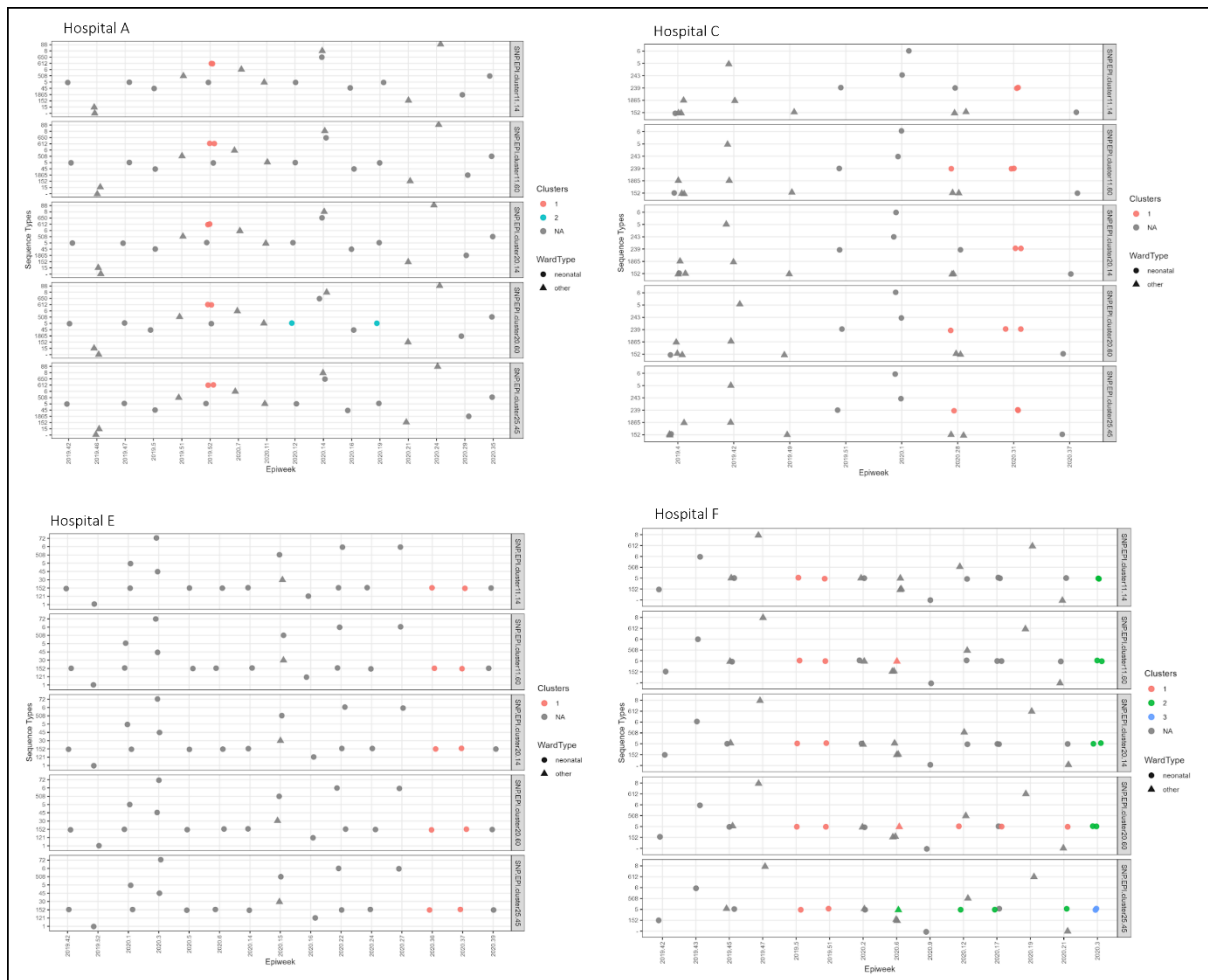


Fig S7: *S. aureus* infection clusters detected in Hospital A to Hospital F by varying SNP-EPI criteria