

## **SUPPLEMENTARY DATA FOR MANUSCRIPT:**

### **Comparison of strategies to reduce meticillin resistant *Staphylococcus aureus* rates in surgical patients: a controlled multicentre intervention trial**

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Figure A1: Nosocomial meticillin resistant *Staphylococcus aureus* isolation rates from clinical specimens by hospital

**Table A1: Methicillin resistant *Staphylococcus aureus* screening methods used in study centres in the screening and decolonisation arm and combined arm**

Study arm	Hospital	Chromogenic medium used	Minimum time to detection (days)*	Months during intervention phase test used†	Molecular assay used	Total assay time (hours)*	Months during intervention phase test used‡
Screening and decolonisation	2	BBL CHROMagar (BD Diagnostics)	1.72	1 to 12	GeneOhm (BD Diagnostics)	2 to 3	1 to 10
					GeneXpert (Cepheid)	<1.5	7 to 12
	3	BBL CHROMagar (BD Diagnostics)	1.72	1 to 12	GeneXpert (Cepheid)	<1.5	6 to 12
	5	BBL CHROMagar (BD Diagnostics)	1.72	1 to 12	GeneOhm (BD Diagnostics)	2 to 3	10 to 12
	6	BBL CHROMagar (BD Diagnostics)	1.72	1 to 12	GeneXpert (Cepheid)	<1.5	8 to 12
Combined	4	MRSA Select (Bio-Rad Laboratories)	1.35	1 to 12	GeneOhm (BD Diagnostics)	2 to 3	1 to 12
	7	ChromID (bioMérieux)	1.65	1 to 12	Not used	-	-

\*From Malhotra-Kumar S, Haccuria K, Michiels M, et al. Current trends in rapid diagnostics for methicillin-resistant *Staphylococcus aureus* and glycopeptide-resistant enterococcus species. *J Clin Microbiol* 2008;46:1577-87.

†Screening for methicillin resistant *Staphylococcus aureus* occurred during all study phases for centres in the combined arm using existing local methods.

‡For the screening and decolonisation arm, molecular assays were introduced during the latter part of the intervention phase. In one centre in this arm (Hospital 2) a locally available molecular assay was used from the commencement of the intervention phase.

**Table A2: Study characteristics by study period and study arm**

Characteristic	Baseline phase	Intervention phase	Washout phase
Duration (months)	6 to 7*	12	6
Total admissions (n)	33 608	63 810	29 332
Enhanced hand hygiene	18 379	34 996	16 413
Screening and decolonisation	6692	12 279	6615
Combined	8537	16 535	6304
Total patient-days (n)	264 035	496 975	249 119
Enhanced hand hygiene	150 757	286 667	135 745
Screening and decolonisation	57 754	112 971	58 473
Combined	55 524	97 337	54 901
Total surgical procedures (n)	27 768	49 747	22 123
Enhanced hand hygiene	13 227	25 003	12 706
Screening and decolonisation	5400	9963	5074
Combined	9141	14 781	4343
Surgical procedures in clean surgery wards (n)†	12 916	21 463	8787
Enhanced hand hygiene	5160	9102	4693
Screening and decolonisation	1310	2551	1185
Combined	6446	9810	2909
Surgical procedures in other types of surgery wards (n)†	14 852	28 284	13 336
Enhanced hand hygiene	8067	15 901	8013
Screening and decolonisation	4090	7412	3889
Combined	2695	4971	1434
Mean patient-to-nurse ratio (SD)‡	6.55 (3.78)	6.67 (3.59)	6.87 (4.18)
Enhanced hand hygiene	6.46 (2.35)	6.73 (2.11)	6.99 (2.57)
Screening and decolonisation	7.68 (5.11)	7.96 (4.74)	8.31 (5.52)
Combined	4.65 (1.62)	4.14 (1.17)	3.96 (1.30)
Total number of patients MRSA positive on admission (%)§	269 (0.8)	724 (1.1)	228 (0.8)
Enhanced hand hygiene	167 (0.9)	272 (0.8)	136 (0.8)
Screening and decolonisation	40 (0.6)	259 (2.1)	13 (0.2)
Combined	62 (0.7)	193 (1.2)	79 (1.3)
Number of patients MRSA positive on admission by clinical culture (%)	65 (0.2)	85 (0.1)	41 (0.1)
Enhanced hand hygiene	32 (0.2)	46 (0.1)	30 (0.2)
Screening and decolonisation	31 (0.5)	27 (0.2)	11 (0.2)
Combined	2 (0.02)	12 (0.1)	0 (0)
Number of patients MRSA positive on admission by screening swab (%)	204 (0.6)	639 (1.0)	187 (0.6)
Enhanced hand hygiene	135 (0.7)	226 (0.6)	106 (0.6)
Screening and decolonisation	9 (0.1)	232 (1.9)	2 (0.03)
Combined	60 (0.7)	181 (1.1)	79 (1.3)

MRSA, methicillin resistant *Staphylococcus aureus*.

\*Baseline phase was 6 months in six hospitals and 7 months in four hospitals (two in the screening and decolonisation arm and one hospital in each of the enhanced hand hygiene and combined arms).

†Clean surgery wards included cardiothoracic, neuro-, orthopaedic, plastic, and vascular surgery. Other types of surgery wards included abdominal, general, and urological surgery.

‡Calculated by dividing the mean patient load by mean number of nurses working on the ward at a given time (averaged over day, evening, and night shifts).

§By screening or clinical culture.

**Table A3: Multiple segmented multilevel logistic regression model showing factors associated with monthly hand hygiene compliance rates\***

Variable	Adjusted odds ratio	95% CI	p Value
Baseline phase			
Trend	1.04	0.98 to 1.10	0.24
Intervention phase			
Change in level	1.19	1.01 to 1.42	0.04
Change in trend	1.03	0.97 to 1.09	0.30
Washout phase			
Change in level	1.17	0.82 to 1.68	0.39
Change in trend	0.91	0.85 to 0.97	0.004
Professional category			
Physician	1.00	-	-
Nurse	1.37	1.28 to 1.46	<0.001
Auxiliary nurse	1.27	1.16 to 1.39	<0.001
Other	1.11	0.99 to 1.24	0.06
Indication for hand hygiene			
Before touching patient	1.00	-	-
Before clean/aseptic procedure	1.20	1.09 to 1.32	<0.001
After body fluid exposure	4.95	4.47 to 5.48	<0.001
After touching patient	2.79	2.60 to 3.00	<0.001
After touching patient surroundings	1.52	1.41 to 1.65	<0.001
Patient-to-nurse ratio (per 1-unit increment)†	0.91	0.89 to 0.94	<0.001
MRSA colonisation pressure‡			
0 to 0.7%	1.00	-	-
0.8 to 3.2%	0.86	0.79 to 0.94	<0.001
3.3 to 8.2%	0.90	0.81 to 1.01	0.07
>8.2%	0.78	0.68 to 0.90	<0.001

MRSA, meticillin resistant *Staphylococcus aureus*.

\*Random effects for intercepts at the hospital and ward levels and random baseline trends at the hospital level were all statistically significant, though baseline trends and intercepts showed no evidence of correlation.

†Calculated by dividing the mean patient load by mean number of nurses working on the ward at a given time (averaged over day, evening, and night shifts) for each month.

‡Calculated by dividing the patient-days of subjects known to be colonised or infected with meticillin resistant *Staphylococcus aureus* by the total number of patient-days in the ward in any given study month. This variable was divided into quartiles for the analysis.

**Table A4: Full model results for the multiple segmented multilevel Poisson regression models showing adjusted incidence rate ratios for changes in level and trend of nosocomial meticillin resistant *Staphylococcus aureus* rates\***

Variable	MRSA clinical isolates (per 100 susceptible patients)			Total MRSA infections (per 100 admissions)			MRSA surgical site infections (per 100 procedures)		
	aIRR	95% CI	p Value	aIRR	95% CI	p Value	aIRR	95% CI	p Value
Baseline phase									
Trend	0.97	0.89 to 1.06	0.55	1.00	0.90 to 1.11	0.98	1.02	0.90 to 1.16	0.75
Intervention phase									
Change in level									
Enhanced hand hygiene	1.44	0.96 to 2.15	0.08	1.28	0.79 to 2.06	0.31	1.25	0.70 to 2.23	0.45
Screening and decolonisation	0.87	0.49 to 1.57	0.65	0.97	0.49 to 1.92	0.94	0.79	0.35 to 1.79	0.58
Combined	1.63	0.96 to 2.75	0.07	1.17	0.62 to 2.20	0.63	1.33	0.59 to 3.00	0.49
Change in trend									
Enhanced hand hygiene	0.99	0.91 to 1.09	0.88	0.99	0.89 to 1.10	0.84	0.98	0.86 to 1.12	0.75
Screening and decolonisation	0.94	0.85 to 1.05	0.26	0.93	0.82 to 1.05	0.27	0.90	0.78 to 1.04	0.16
Combined	0.88	0.79 to 0.98	0.02	0.90	0.80 to 1.02	0.10	0.86	0.74 to 1.01	0.06
Washout phase									
Change in level	1.90	0.91 to 3.95	0.09	1.52	0.66 to 3.51	0.32	1.90	0.69 to 5.27	0.21
Change in trend	1.02	0.91 to 1.15	0.74	1.00	0.88 to 1.15	0.95	0.95	0.80 to 1.12	0.53
Patient-to-nurse ratio (per 1-unit increment)†	1.01	0.94 to 1.08	0.87	1.01	0.93 to 1.09	0.84	1.04	0.96 to 1.14	0.33
Calendar month									
January	1.00	-	-	1.00	-	-	1.00	-	-
February	0.83	0.54 to 1.28	0.41	0.89	0.53 to 1.50	0.67	0.76	0.40 to 1.45	0.41
March	1.16	0.78 to 1.72	0.47	1.49	0.94 to 2.35	0.09	1.34	0.76 to 2.37	0.31
April	0.93	0.61 to 1.43	0.75	1.16	0.70 to 1.90	0.57	0.81	0.42 to 1.55	0.52
May	1.19	0.78 to 1.83	0.42	1.33	0.80 to 2.21	0.27	1.31	0.71 to 2.41	0.39
June	1.40	0.92 to 2.12	0.11	1.40	0.84 to 2.33	0.19	1.45	0.79 to 2.64	0.23
July	1.31	0.86 to 1.99	0.21	1.44	0.88 to 2.38	0.15	1.52	0.83 to 2.77	0.17
August	1.20	0.78 to 1.84	0.40	1.14	0.67 to 1.94	0.63	1.22	0.65 to 2.30	0.54
September	1.40	0.92 to 2.13	0.11	1.39	0.84 to 2.32	0.20	1.41	0.77 to 2.58	0.27
October	0.89	0.59 to 1.34	0.58	1.06	0.65 to 1.72	0.81	1.19	0.67 to 2.10	0.55
November	1.04	0.70 to 1.55	0.85	1.13	0.70 to 1.82	0.63	1.11	0.62 to 1.98	0.72
December	1.29	0.87 to 1.90	0.21	1.34	0.84 to 2.14	0.23	1.33	0.75 to 2.35	0.32
Surgical subspecialty									
Orthopaedics	1.00	-	-	1.00	-	-	1.00	-	-
Vascular	2.91	1.44 to 5.88	0.003	2.07	0.98 to 4.37	0.06	1.90	0.73 to 4.92	0.19
Cardiothoracic	1.10	0.52 to 2.34	0.80	1.16	0.55 to 2.45	0.70	1.35	0.55 to 3.27	0.51
General	1.65	0.70 to 3.89	0.26	1.92	0.81 to 4.55	0.14	2.06	0.72 to 5.88	0.18
Abdominal	1.51	0.69 to 3.29	0.30	1.44	0.67 to 3.13	0.35	1.30	0.52 to 3.27	0.58
Urology	0.82	0.33 to 2.05	0.67	0.63	0.24 to 1.64	0.34	0.90	0.29 to 2.86	0.87
Neurosurgery	0.79	0.22 to 2.78	0.71	0.85	0.23 to 3.07	0.80	0.53	0.10 to 2.71	0.44
Plastic surgery	0.75	0.13 to 4.41	0.75	0.59	0.08 to 4.38	0.60	0.54	0.06 to 4.51	0.57
Baseline HH compliance rate (per increment from 0 to 100%)	1.56	0.32 to 7.53	0.58	1.11	0.20 to 6.06	0.91	1.29	0.18 to 9.27	0.80

MRSA, methicillin resistant *Staphylococcus aureus*; aIRR, adjusted incidence rate ratio; HH, hand hygiene.

\*Methicillin resistant *Staphylococcus aureus* was defined as nosocomial if it was isolated from specimens collected more than 48 hours after admission or within 30 days (or 12 months for infections of prosthetic devices) after discharge from the surgical ward. The model used a lagged dependent variable to account for autocorrelation and accounted for overdispersion. Random effects for intercepts at the hospital and ward levels and random baseline trends at the hospital level were all significant, and baseline trends were negatively correlated with intercepts (i.e. hospitals with higher baseline MRSA rates tended to have larger decreases in baseline rates).

†Calculated by dividing the mean patient load by mean number of nurses working on the ward at a given time (averaged over day, evening, and night shifts) for each month.

**Table A5: Full model results for the multiple segmented multilevel Poisson regression models showing changes in nosocomial meticillin resistant *Staphylococcus aureus* rates for the subgroup analysis of clean surgery only\***

Variable	MRSA clinical isolates (per 100 susceptible patients)			Total MRSA infections (per 100 admissions)			MRSA surgical site infections (per 100 procedures)		
	aIRR	95% CI	p Value	aIRR	95% CI	p Value	aIRR	95% CI	p Value
Baseline phase									
Trend	1.05	0.93 to 1.18	0.41	1.10	0.94 to 1.28	0.23	1.11	0.93 to 1.33	0.26
Intervention phase									
Change in level									
Enhanced hand hygiene	1.31	0.75 to 2.30	0.34	1.06	0.52 to 2.16	0.88	1.09	0.47 to 2.53	0.83
Screening and decolonisation	0.87	0.41 to 1.85	0.71	1.03	0.39 to 2.69	0.96	0.92	0.29 to 2.92	0.89
Combined	1.79	0.86 to 3.74	0.12	1.15	0.44 to 2.96	0.78	1.21	0.39 to 3.73	0.75
Change in trend									
Enhanced hand hygiene	0.89	0.78 to 1.01	0.06	0.88	0.75 to 1.04	0.13	0.89	0.73 to 1.07	0.21
Screening and decolonisation	0.85	0.74 to 0.97	0.02	0.83	0.69 to 0.99	0.04	0.81	0.66 to 1.00	0.05
Combined	0.82	0.71 to 0.95	0.01	0.84	0.70 to 1.00	0.06	0.84	0.68 to 1.03	0.10
Washout phase									
Change in level	3.01	1.05 to 8.63	0.04	2.21	0.61 to 8.04	0.23	2.59	0.59 to 11.46	0.21
Change in trend	0.96	0.81 to 1.15	0.67	0.91	0.73 to 1.12	0.37	0.86	0.67 to 1.09	0.21
Patient-to-nurse ratio (per 1-unit increment)†	0.99	0.91 to 1.07	0.73	0.99	0.90 to 1.09	0.81	0.99	0.88 to 1.12	0.90
Calendar month									
January	1.00	-	-	1.00	-	-	1.00	-	-
February	1.06	0.54 to 2.07	0.86	1.58	0.66 to 3.81	0.31	1.22	0.45 to 3.28	0.69
March	1.13	0.60 to 2.16	0.70	1.68	0.72 to 3.95	0.23	1.51	0.60 to 3.84	0.38
April	1.32	0.68 to 2.57	0.41	2.12	0.89 to 5.03	0.09	1.52	0.57 to 4.09	0.41
May	2.00	1.06 to 3.76	0.03	3.07	1.34 to 7.04	0.01	2.61	1.04 to 6.52	0.04
June	2.34	1.25 to 4.39	0.01	3.33	1.43 to 7.74	0.01	3.06	1.22 to 7.65	0.02
July	2.19	1.16 to 4.15	0.02	3.20	1.35 to 7.57	0.01	2.94	1.14 to 7.59	0.03
August	2.25	1.18 to 4.26	0.01	2.80	1.18 to 6.65	0.02	2.77	1.08 to 7.10	0.03
September	2.35	1.26 to 4.39	0.01	2.88	1.24 to 6.72	0.01	2.89	1.15 to 7.26	0.02
October	1.49	0.81 to 2.73	0.20	2.66	1.20 to 5.90	0.02	2.39	1.00 to 5.72	0.05
November	1.70	0.93 to 3.09	0.09	2.52	1.12 to 5.67	0.03	1.86	0.75 to 4.62	0.18
December	1.96	1.06 to 3.60	0.03	2.44	1.06 to 5.66	0.04	2.02	0.80 to 5.08	0.14
Surgical subspecialty									
Orthopaedics	1.00	-	-	1.00	-	-	1.00	-	-
Vascular	2.14	1.00 to 4.58	0.05	1.57	0.70 to 3.54	0.27	1.29	0.50 to 3.33	0.60
Cardiothoracic	1.22	0.55 to 2.72	0.62	1.25	0.58 to 2.68	0.57	1.51	0.68 to 3.38	0.31
Neurosurgery	0.72	0.21 to 2.40	0.59	0.87	0.22 to 3.42	0.84	0.78	0.17 to 3.62	0.75
Plastic surgery	0.57	0.11 to 3.03	0.51	0.50	0.07 to 3.88	0.51	0.53	0.07 to 3.83	0.53
Baseline HH compliance rate (per increment from 0 to 100%)	2.07	0.45 to 9.53	0.35	1.37	0.29 to 6.53	0.69	2.15	0.34 to 13.60	0.42

MRSA, meticillin resistant *Staphylococcus aureus*; aIRR, adjusted incidence rate ratio; HH, hand hygiene.

\*Meticillin resistant *Staphylococcus aureus* was defined as nosocomial if it was isolated from specimens collected more than 48 hours after admission or within 30 days (or 12 months for infections of prosthetic devices) after discharge from the surgical ward. Clean surgery included cardiothoracic, neuro-, orthopaedic, plastic, and vascular

surgery subspecialties. The model used a lagged dependent variable to account for autocorrelation and accounted for overdispersion. Random effects for intercepts at the hospital and ward levels and random baseline trends at the hospital level were all significant, and baseline trends were negatively correlated with intercepts (i.e. hospitals with higher baseline MRSA rates tended to have larger decreases in baseline rates).

†Calculated by dividing the mean patient load by mean number of nurses working on the ward at a given time (averaged over day, evening, and night shifts) for each month.



**Table A6: Multiple segmented multilevel Poisson regression models showing nosocomial meticillin resistant *Staphylococcus aureus* rates in the washout phase by study arm**

Variable	MRSA clinical isolates (per 100 susceptible patients)			Total MRSA infections (per 100 admissions)			MRSA surgical site infections (per 100 procedures)		
	aIRR	95% CI	p Value	aIRR	95% CI	p Value	aIRR	95% CI	p Value
Baseline phase									
Trend	0.96	0.89 to 1.05	0.41	0.99	0.89 to 1.09	0.81	1.02	0.90 to 1.15	0.80
Intervention phase									
Change in level									
Enhanced hand hygiene	1.37	0.90 to 2.07	0.138	1.21	0.74 to 1.98	0.44	1.23	0.68 to 2.23	0.50
Screening and decolonisation	1.03	0.42 to 2.48	0.95	0.99	0.36 to 2.74	0.99	0.86	0.26 to 2.90	0.81
Combined	2.29	1.14 to 4.61	0.020	2.10	0.88 to 4.99	0.093	1.57	0.52 to 4.72	0.42
Change in trend									
Enhanced hand hygiene	1.01	0.92 to 1.11	0.77	1.01	0.91 to 1.13	0.83	0.99	0.86 to 1.13	0.85
Screening and decolonisation	0.94	0.81 to 1.08	0.37	0.95	0.81 to 1.11	0.52	0.89	0.73 to 1.09	0.27
Combined	0.84	0.74 to 0.96	0.008	0.83	0.71 to 0.97	0.020	0.84	0.70 to 1.02	0.081
Washout phase									
Change in level									
Enhanced hand hygiene	1.43	0.64 to 3.21	0.39	1.11	0.44 to 2.78	0.82	1.68	0.55 to 5.07	0.36
Screening and decolonisation	3.16	0.50 to 19.96	0.22	1.93	0.24 to 15.78	0.54	2.76	0.22 to 34.28	0.43
Combined	8.65	1.20 to 62.29	0.032	13.31	1.38 to 128.72	0.025	4.43	0.19 to 102.38	0.35
Change in trend									
Enhanced hand hygiene	1.05	0.92 to 1.21	0.44	1.04	0.90 to 1.21	0.58	0.97	0.80 to 1.16	0.71
Screening and decolonisation	0.98	0.73 to 1.32	0.90	0.93	0.64 to 1.34	0.70	0.90	0.58 to 1.40	0.64
Combined	0.89	0.57 to 1.39	0.62	0.90	0.57 to 1.43	0.66	0.86	0.42 to 1.74	0.67

**Table A7: Exploratory analysis using multiple segmented multilevel Poisson regression models including interventions implemented by centres as covariates in the model\***

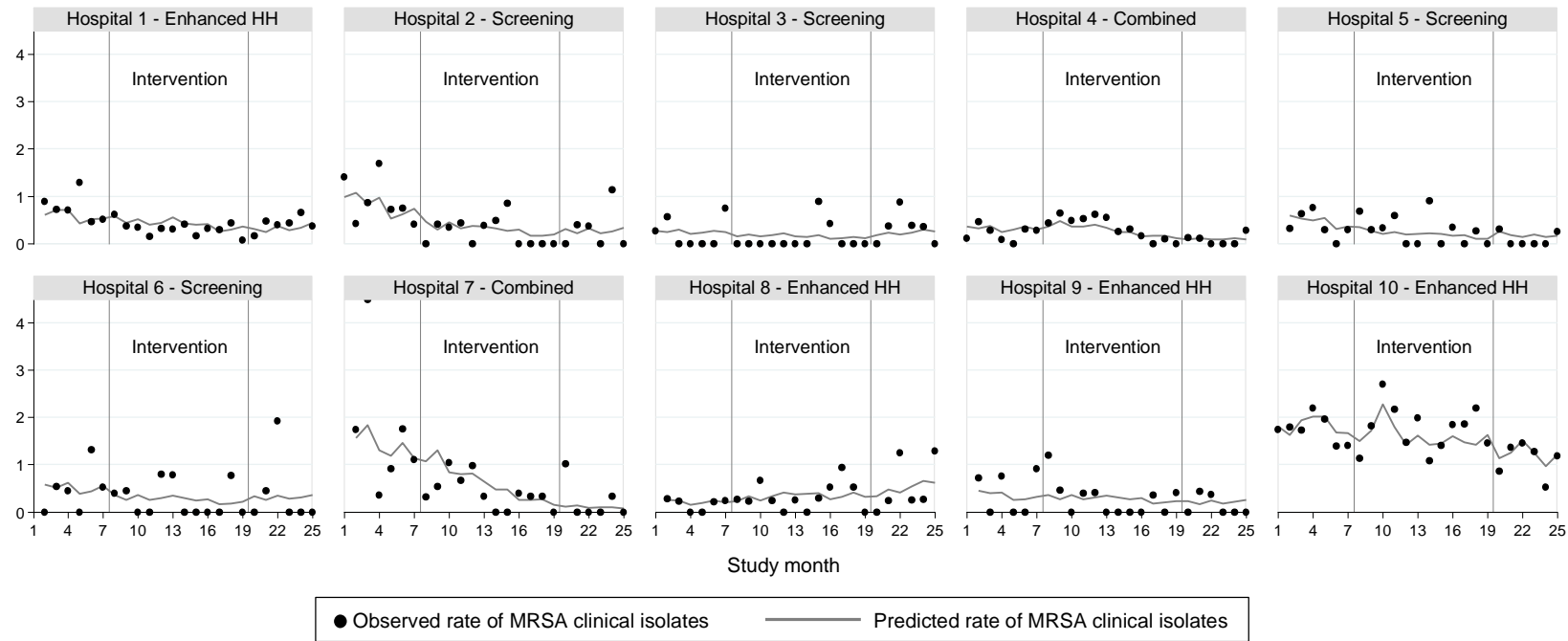
Variable	MRSA clinical isolates (per 100 susceptible patients)			Total MRSA infections (per 100 admissions)		
	aIRR	95% CI	p Value	aIRR	95% CI	p Value
Baseline phase						
Trend	1.00	0.95 to 1.05	0.92	1.00	0.95 to 1.06	0.92
Hand hygiene promotion						
Change in level	1.05	0.87 to 1.27	0.63	1.03	0.83 to 1.28	0.80
Change in trend	0.98	0.92 to 1.04	0.47	0.99	0.92 to 1.06	0.68
MRSA screening						
Change in level	0.71	0.40 to 1.26	0.24	0.95	0.49 to 1.84	0.88
Change in trend†	0.91	0.85 to 0.98	0.01	0.92	0.85 to 0.99	0.03

MRSA, meticillin resistant *Staphylococcus aureus*; aIRR, adjusted incidence rate ratio.

\*The models used a lagged dependent variable to account for autocorrelation and adjusted for staffing (patient-to-nurse ratios), seasonal effects, type of surgical ward, and baseline hand hygiene compliance rates. The model also accounted for overdispersion. Random effects for intercepts at the hospital and ward levels and random baseline trends at the hospital level were all significant, though there was no evidence that baseline trends significantly correlated with intercepts.

†Each additional month with x% compliance with admission screening would be associated with a reduction in the MRSA isolation rate by a factor of  $\text{aIRR}^{x/100}$ .

**Figure A1** Nosocomial meticillin resistant *Staphylococcus aureus* isolation rates from clinical specimens by hospital



The solid dots represent the observed meticillin resistant *Staphylococcus aureus* (MRSA) rates while the lines represent the predicted MRSA rates based on the regression models. MRSA, meticillin resistant *Staphylococcus aureus*; HH, hand hygiene.