

*MRSA in the Homeless:
Examples of social evolution and
future directions*

Timothy Landers, RN, PhD
Postdoctoral Research Fellow
Center for Interdisciplinary Research on Antimicrobial Resistance
(CIRAR)
School of Nursing, Columbia University

Microbiology of *Staphylococcus aureus*

- Gram positive pathogen
- Genetically controlled virulence factors
 - Promote bacteria adhesion
 - Produce various toxins
 - Modify host immune responses
- Acquires resistance to antibiotics
 - Mediated through genetic elements

Epidemiology of MRSA Infection

- Increasing social attention
- Public health threat
 - 31.8 Invasive Infections/100,000
 - 18,650 estimated deaths in 2005
- Changing population dynamics
 - Healthcare-Associated Infections
 - Community-Associated Infections
- Complex interaction of factors
 - Pathogen, Host, Environment

Pathogen

- Genetic variability
- Virulence Determinants
- Resistance Determinants



Environment

- Contaminated surfaces
- Crowded living conditions
- Selection pressure



Host

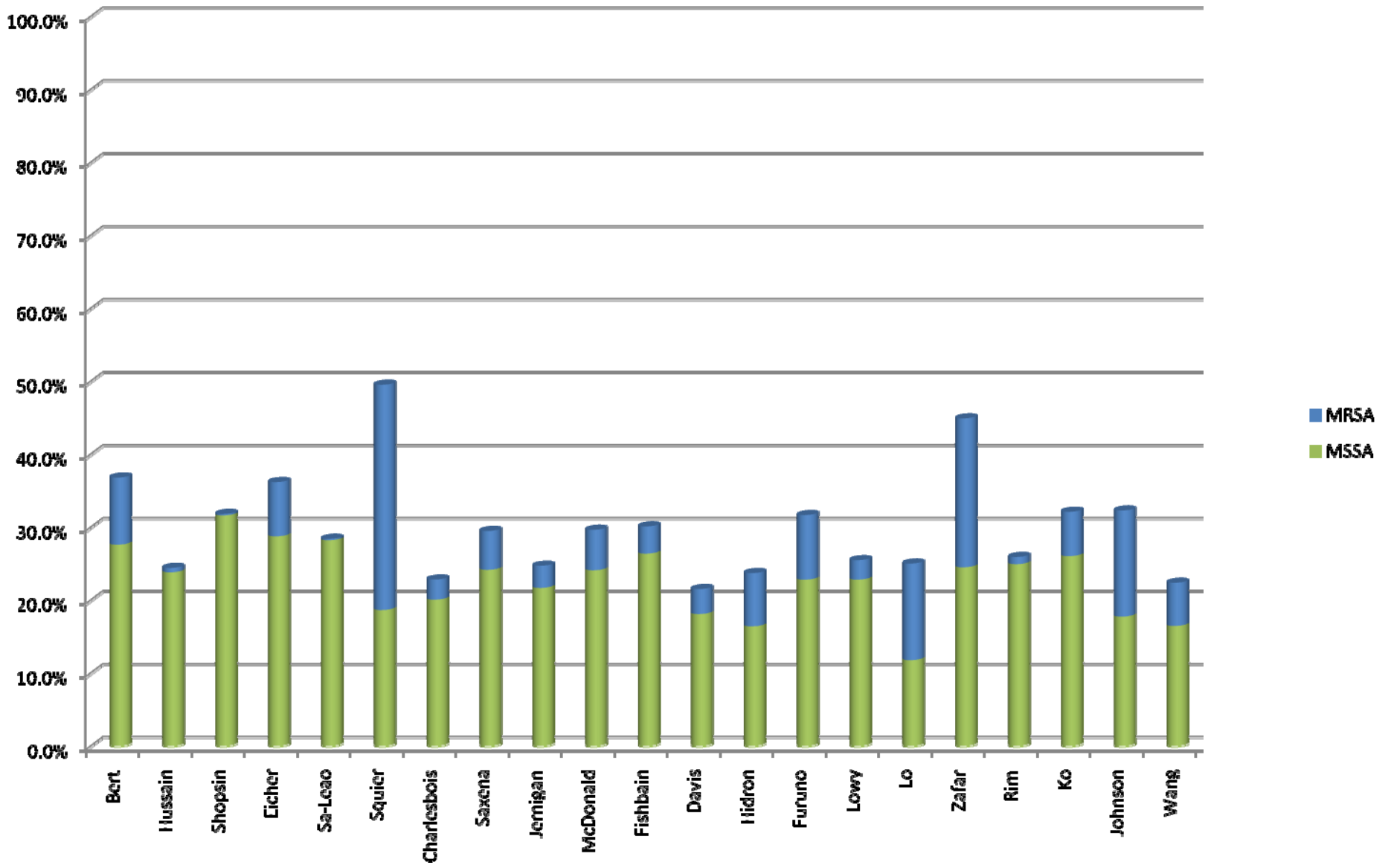
- Underlying health
- Immunity
- Colonization

Colonization vs. Infection

- Asymptomatic
 - Symbiotic (?)
 - Risk factors
 - Natural history poorly understood
- Symptomatic
 - Parasitic
 - Risk factors
 - Natural history well understood

Colonization

- Population estimates
 - SA 31.6% (95%CI, 29.8%-33.4%)
 - MRSA 0.84% (95% CI, 0.4%-1.2%)
1.3% (95% CI, 1.0%-3.5%)
- Higher MRSA colonization in some groups
 - Household contacts (20%)
 - Acutely ill patients (8-10%)
 - Indigenous Populations (15%)
 - Prisoners (25%)
 - Healthcare workers (4.7%)
 - Large Animal Veterinarians (15.6%)
 - Pig farmers (45%)



Surveillance – standard technique

Standard swab inserted in to anterior nasal mucosa

Other sites demonstrate variable recovery:

Axillary

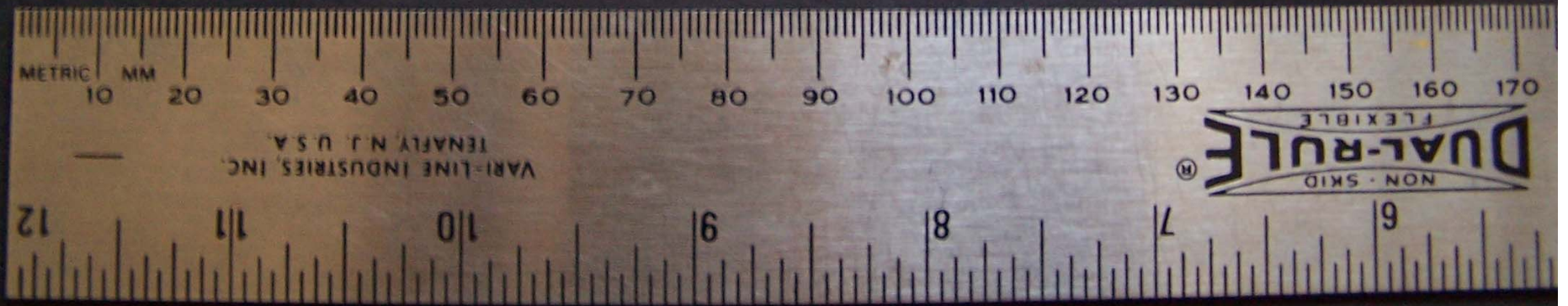
Inter-digital

Oral

Posterior pharynx

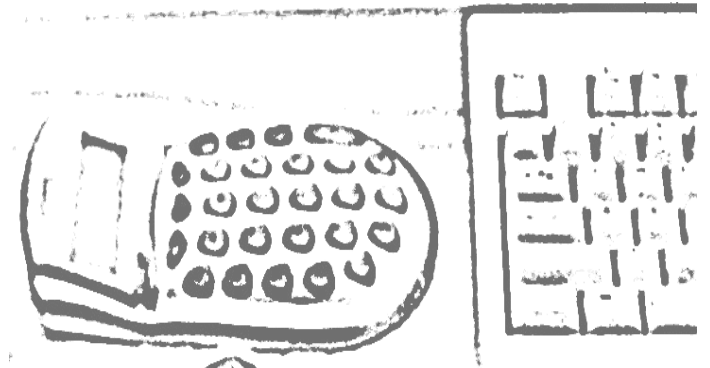
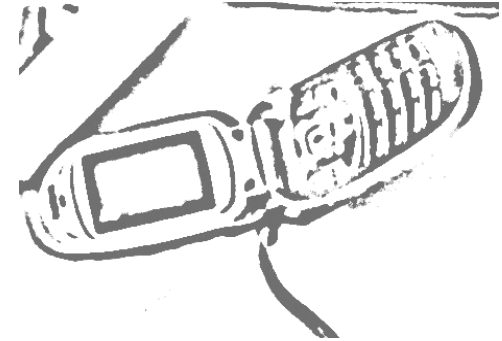
Rectal

Vaginal



Pilot Data

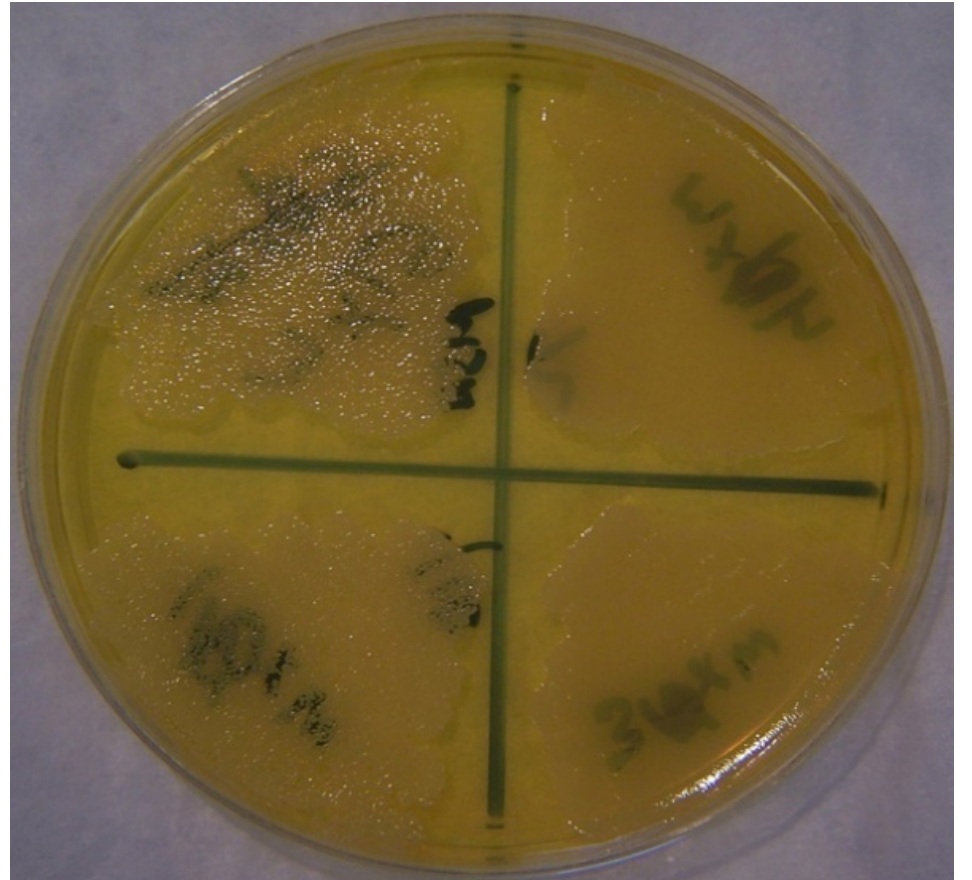
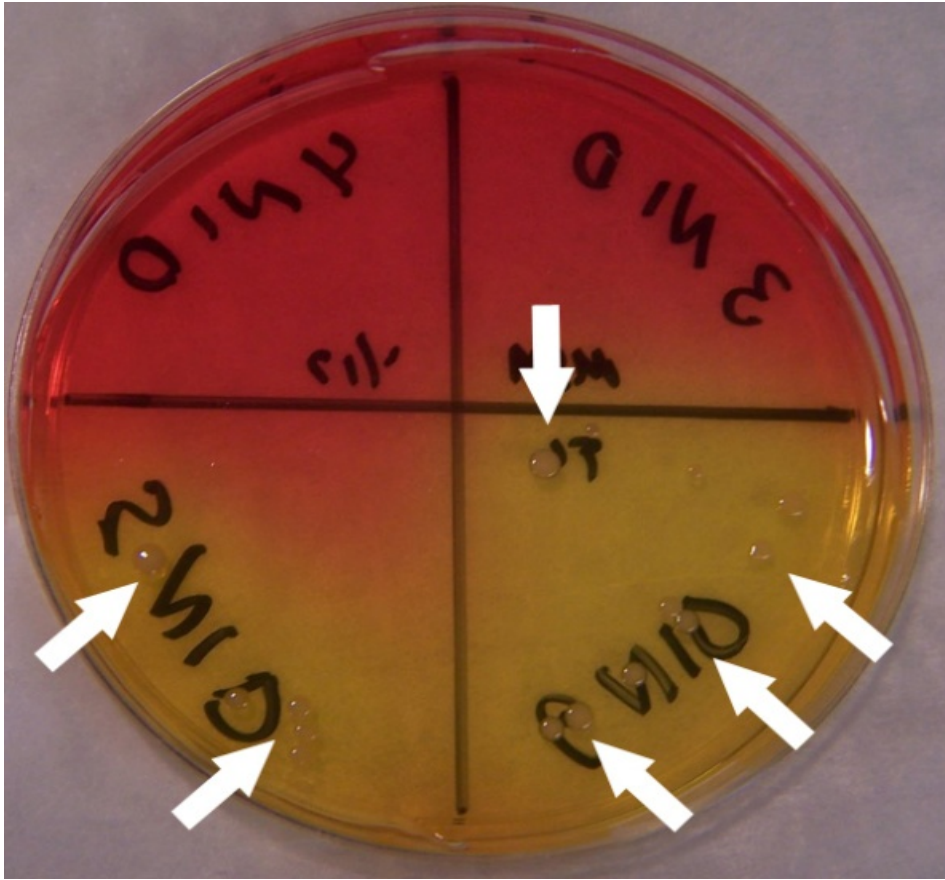
- Surface sampling
- Random order of swab types
 - Dacron, cotton, polyester
 - Wood, plastic, metal shaft
- Preincubation
- Pre-moistening of swab tip

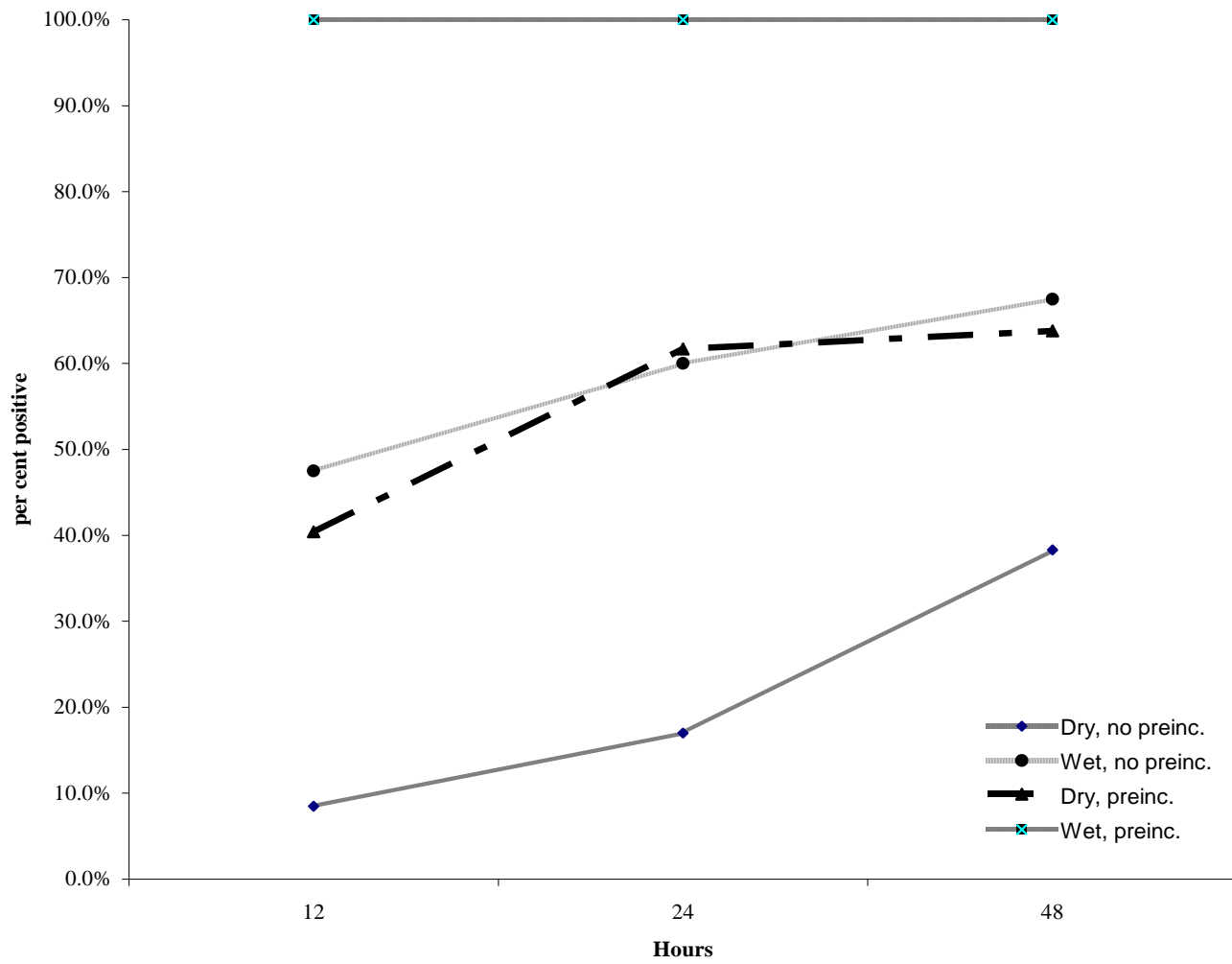




Flooring Test Sur F







Pilot data - summary

Improved recovery of SA from environmental surfaces with pre-moistened (“wet”) swabs.

Preincubation improves detection of SA from environmental surfaces

Host Risk factors

- Hospitalization
- LTC admission
- Catheters
- Recent Antibiotic Use
- Poor underlying health
- Chronic Disease
- Crowded living conditions
- Poor hygiene
- MRSA + family members
- Compromised skin
- High risk behaviors

Homelessness

- Estimates vary:

750,000

Point In Time

3,500,000

Homeless/year

13,500,000

Lifetime prevalence

- “lacks a fixed, regular, and adequate nighttime residence”
- Long-term vs. short-term
- Shelter users vs non-sheltered

Homelessness

- Poor access to hygiene facilities
- Crowded living conditions
- Access to fragmented healthcare system
 - Use of ER, multiple medication
- Comorbid conditions

Specific Aims

1. To determine the utility of a modified nasopharyngeal wash procedure compared with standard technique on detection of *Staphylococcus aureus* carriage in asymptomatic individuals
2. To examine risk factors for *S. aureus* and MRSA carriage in a population of at-risk homeless individuals.

Thank you for taking the time to complete this survey.

Age _____ years Male Female Black White Other

Weight _____ Height _____

What is the last grade in school that you finished?

In the past 3 months, have you been in the hospital overnight? Yes No

Which hospital? _____

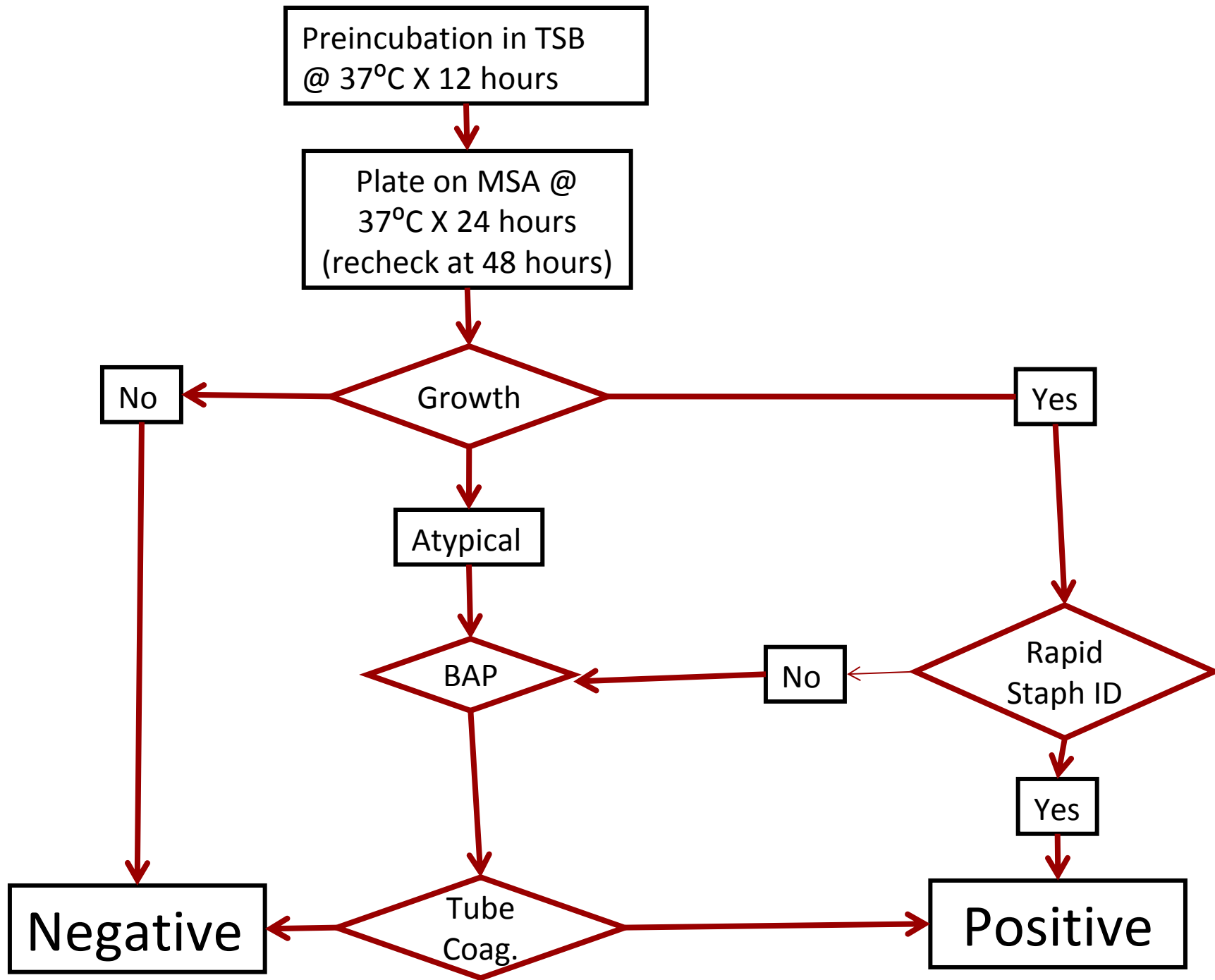
In the past 3 months, have you been to the Emergency Room? Yes No

In the past 3 months, have you taken a medication for infection like an Antibiotic? Yes No

Do you have any skin lesions, boils, bumps or infections? Yes No

In the past year, has anyone told you that you have a "Staff Infection?" (Staph Infection, Cellulitis) Yes No

Do you have any implants such as a pacemaker or artificial joint? Yes No



Sample

215 participants

- Mean age 41.7
- 74.3% black
- 18% white
- 77% Male
- Mean Height 67.9 inches
- Mean Weight

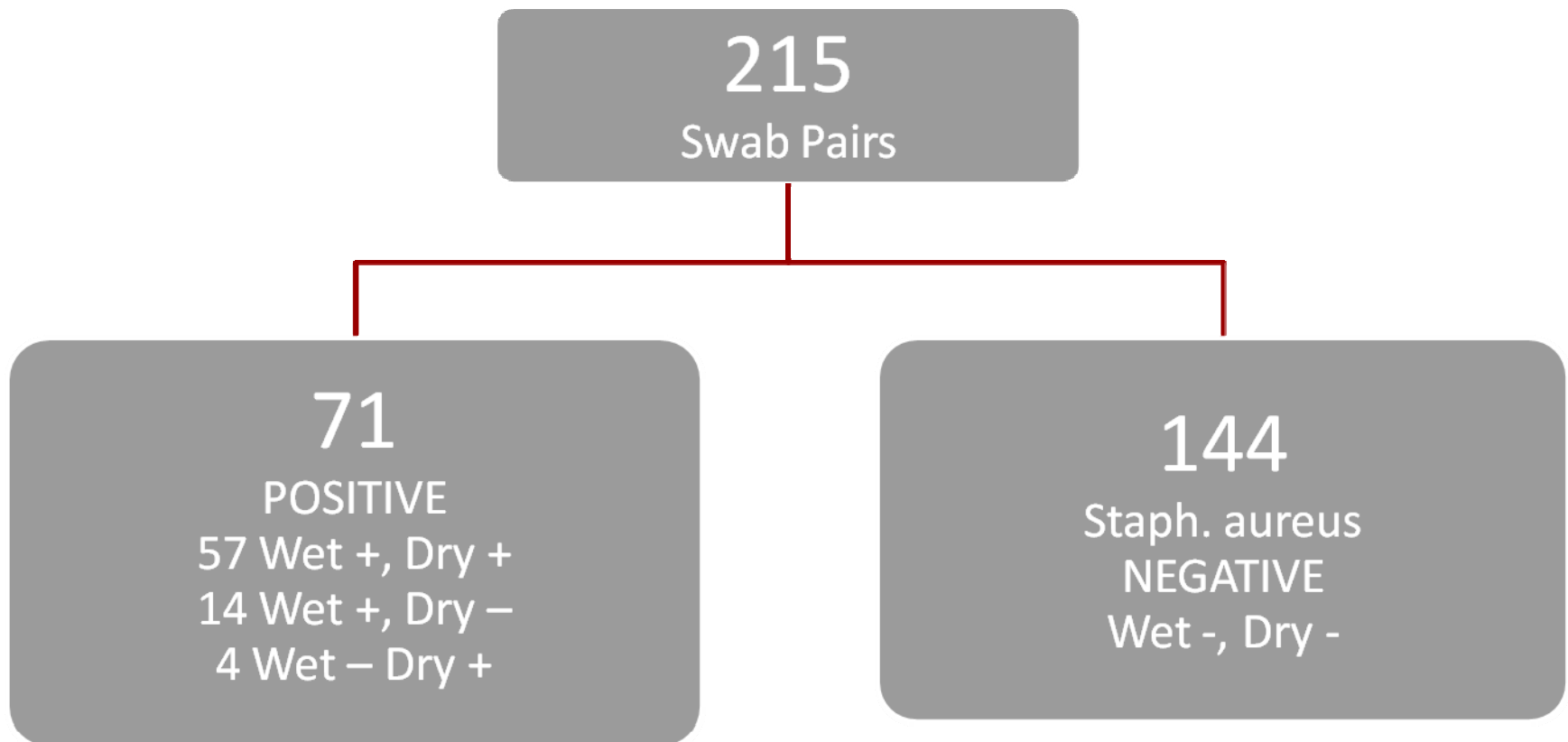
Results

- Overall SA prevalence 34.8% (75/215)
(95% CI 28.6% - 41.7%)

Results

- Overall SA prevalence 34.8% (75/215)
(95% CI 28.6% - 41.7%)
- Overall MRSA prevalence 25.1% (53/211)
(95% CI 19.5% - 31.6%)
- Among all identified SA, 74.6% were MRSA

All *Staph. aureus* Results



Paired Data Analysis

All SA

		Dry Swab	
		+	-
Wet Swab	+	57 (26.5%)	14 (6.5%)
	-	4 (1.9%)	140 (65.1%)

91.6% Agreement
86.3% Pos. Agreement
76% Chamberlain's PPA

Kappa = .804

McNemar's $\chi^2 = 4.5$ (1 df), $p = .015$, one-sided

OR = 3.5 (95% CI, 1.15, 10.63)

Results All SA

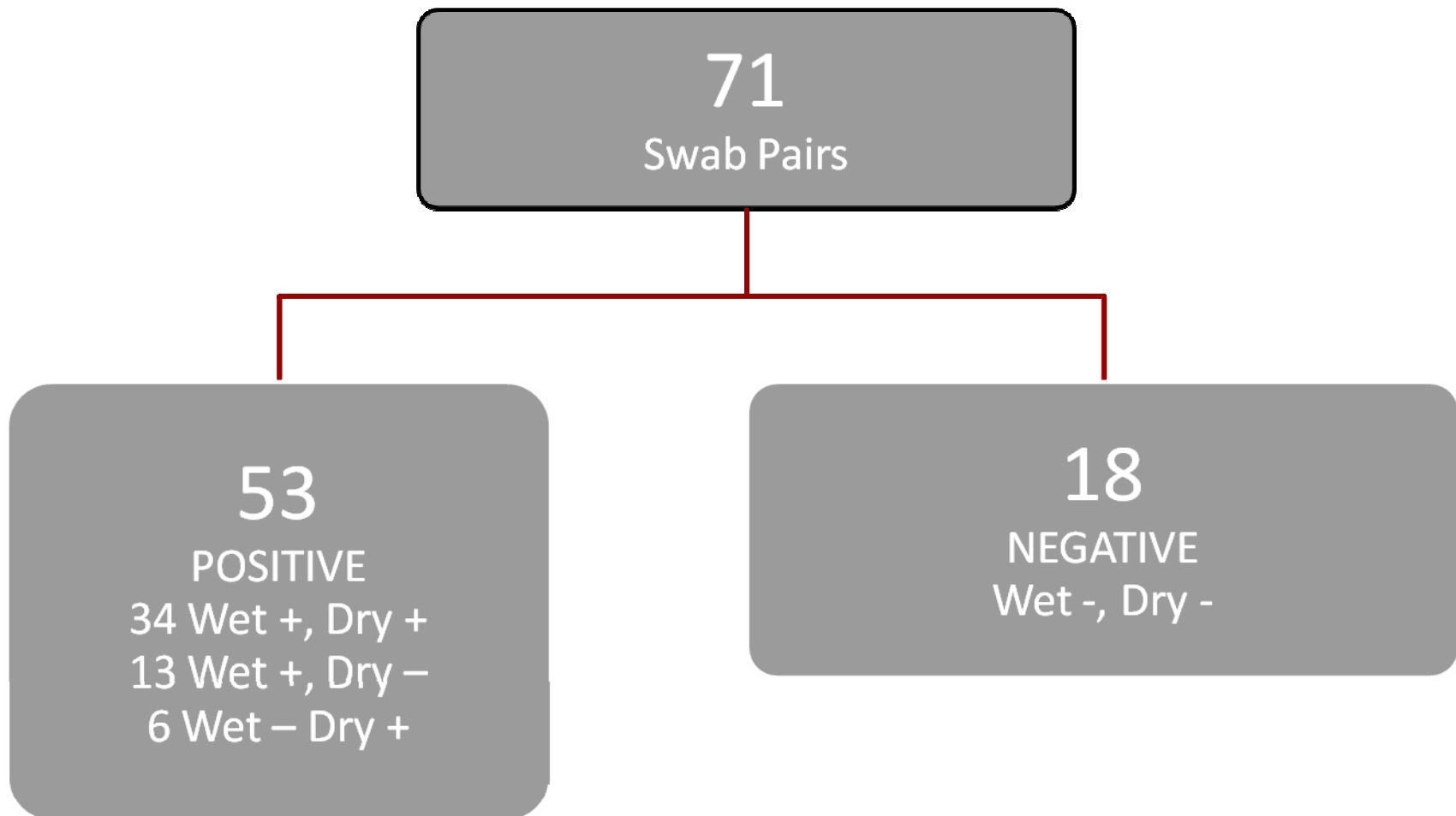
- Dry swab sensitivity 81.3%
- Wet swab sensitivity 94.7%
- Absolute difference 13.3%

- OR for Difference 4.07

- Relative True Positive Fraction 1.16
(95% CI 1.03-1.32)

Negative Predictive Value: 97.2%

MRSA Results



Paired Data Analysis All MRSA

		Dry Swab		
		+	-	
Wet Swab	+	34 (47.9%)	13 (18.3%)	73.2% Agreement
	-	6 (8.5%)	18 (25.4%)	78.2% Pos. Agreement
				64.2% Chamberlain's PPA

Kappa = .44

McNemar's $\chi^2 = 1.90$ (1 df), $p = .084$, one-sided

OR = 2.17 (95% CI, 0.82, 5.70)

Results MRSA

- Dry swab sensitivity 75.5%
- Wet swab sensitivity 88.7%
- OR for Difference 2.54
- Relative True Positive Fraction 1.18
(95% CI 1.13-1.22)

Negative Predictive Value: 94.3%

Univariable Risk Factors SA

Variable	No (%) of Subjects				OR 95% CI	P
	Positive (n=75)		Negative (n=140)			
Mean Weight	179.2		190.8			.05
Mean Height	68.0		67.8			.726
Recent Abx Use	13	(29.1%)	16	(12.3%)	2.09 (0.98-4.45)	.058
Implant	5	(6.7%)	5	(3.6%)	1.91 (0.54-6.84)	.317
Asthma	12	(16.0%)	12	(8.6%)	2.03 (.864-4.78)	.104
Alcoholism	6	(9.5%)	6	(4.3%)	2.33 (.754-7.22)	.141
Living w/ friend	3	(7.1%)	23	(18.9%)	0.33 (0.12-0.92)	.033
Homeless	43	(78.2%)	123	(78.8%)	0.782 (0.04-1.55)	.496

Univariable Risk Factors MRSA

Variable	No (%) of Subjects				OR 95% CI	P
	Positive (n=55)		Negative (n=156)			
Mean Weight	177.1		190.5			.042
Mean Height	67.3		68.0			.310
Recent Abx Use	13	(23.6%)	19	(12.3%)	2.21 (1.01-4.86)	.047
Implant	5	(9.1%)	5	(3.2%)	3.00 (.834-10.79)	.093
Asthma	8	(14.5%)	16	(10.3%)	1.49 (0.6-3.70)	.391
Alcoholism	7	(9.5%)	6	(4.3%)	2.66 (0.85-8.30)	.092
Living w/ friend	3	(7.1%)	23	(18.9%)	0.28 (0.08-0.98)	.046
Homeless	57	(76%)	112	(80%)	0.96 (0.46-2.03)	.918

Final Multivariable Model

Variable	Estimate	OR	95% CI	P
Recent Abx Use	1.004	2.729	(1.10-6.77)	.03
Living w/ friend	-1.734	.177	(0.04-0.72)	.016
Alcohol Abuse	1.638	5.144	1.238	.024

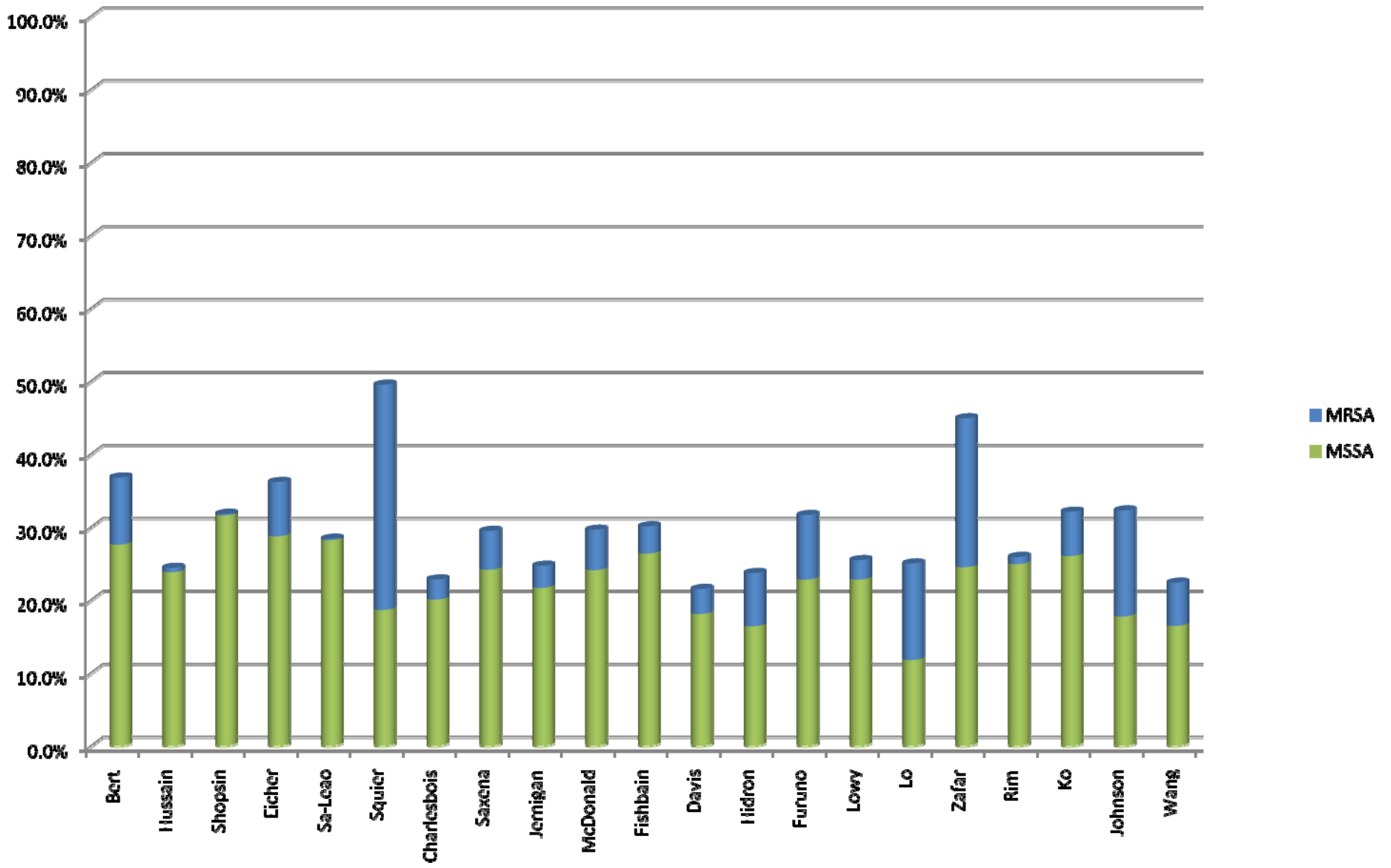
$$\text{OR (MRSA)} = e^{(-.985 + 1.004\text{AbxUse} - 1.734 \text{Liv_Friend} + 1.638\text{Dz_EtOH})}$$

-2 Log Likelihood 191.49, $r^2 = .088$, $p = .021$

Hosmer-Lemeshow Goodness of Fit $\chi^2 = 1.141$, $p = .565$

Conclusions & Implications

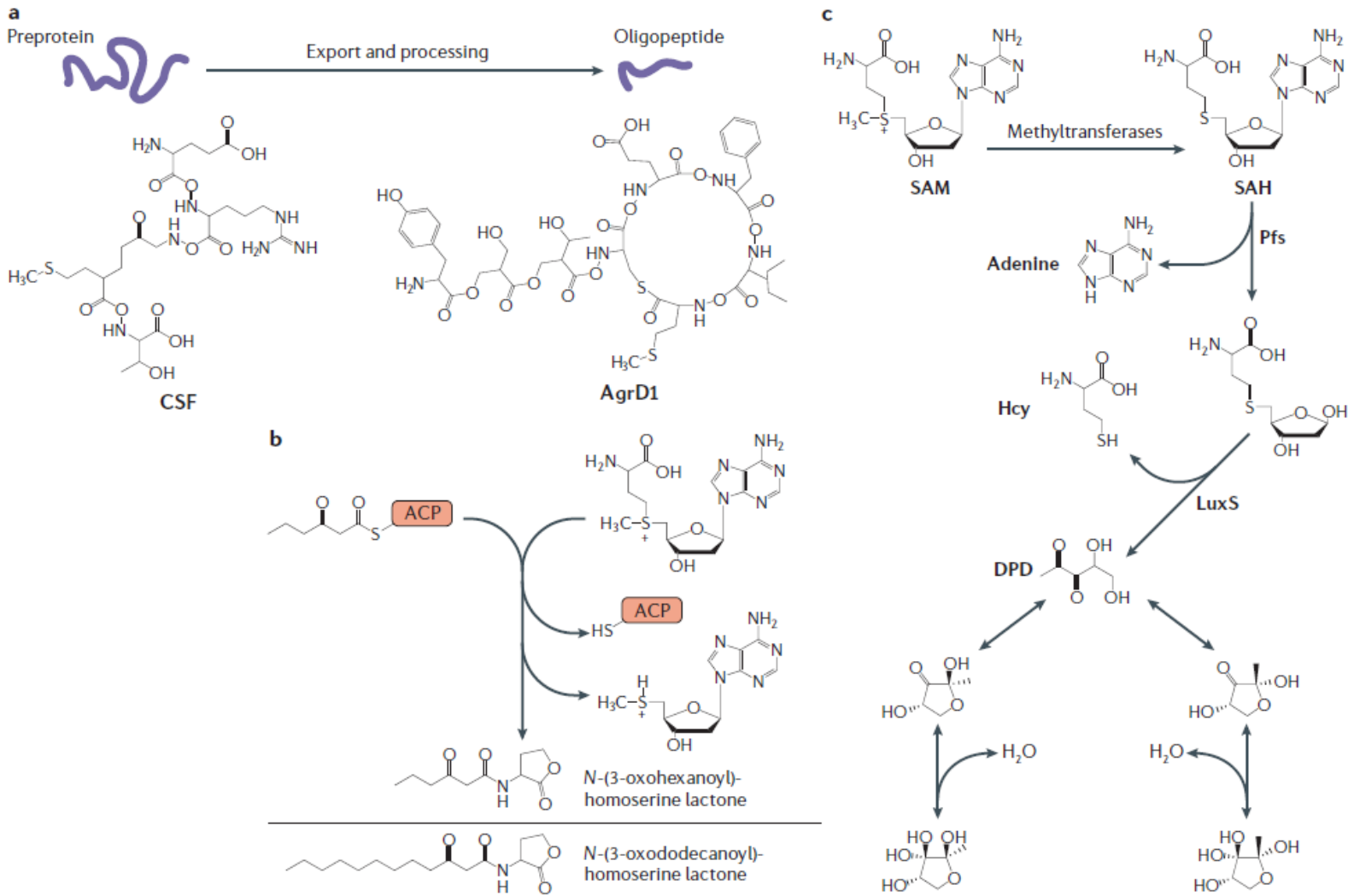
1. The modified saline rinse technique was shown to be superior to convention, dry swab collection for the detection of SA and MRSA.
2. Risk factors for MRSA colonization included a diagnosis of alcoholism, recent antibiotic use, while living with a friend decreased the odds of colonization.
3. The rate of SA colonization was similar to population estimates, but the rate of MRSA colonization was significantly higher.



Social Evolution in bacteria

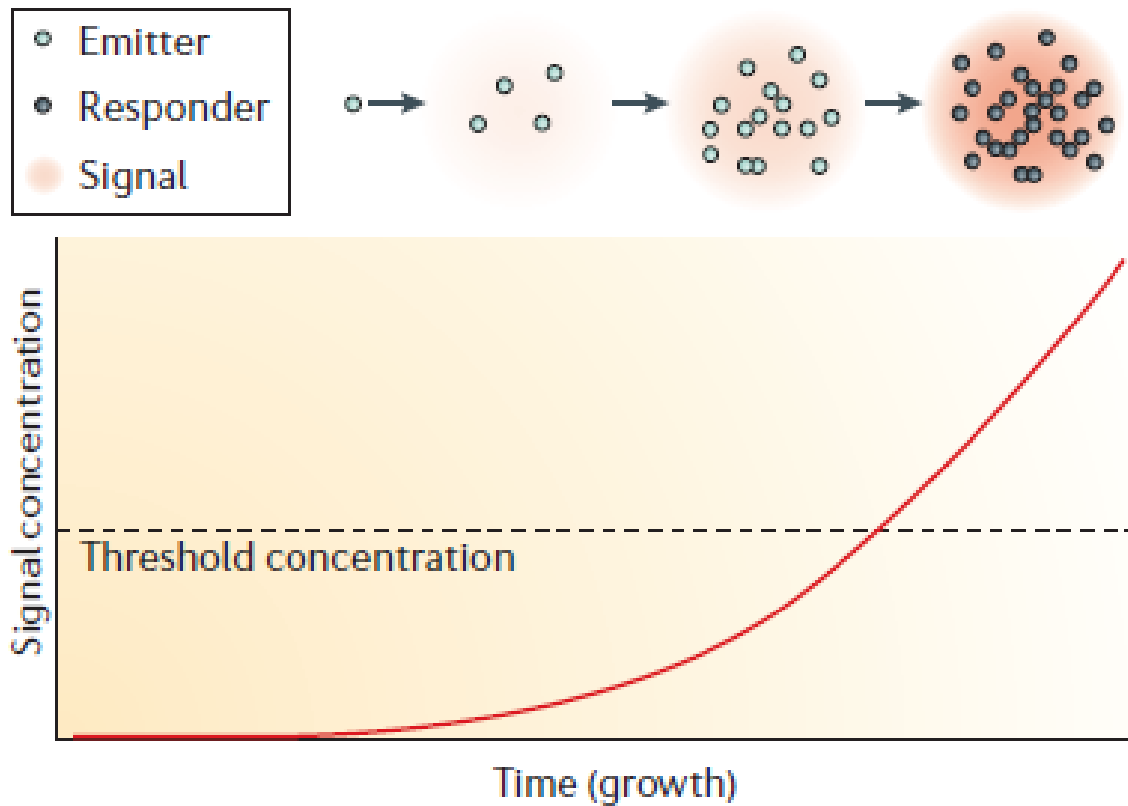
- Social behaviors
 - Cooperation
 - Communication
 - Synchronization
- Issues in social behavior
 - Public benefit
 - Relatedness
 - Cheats

Communication/Synchronization

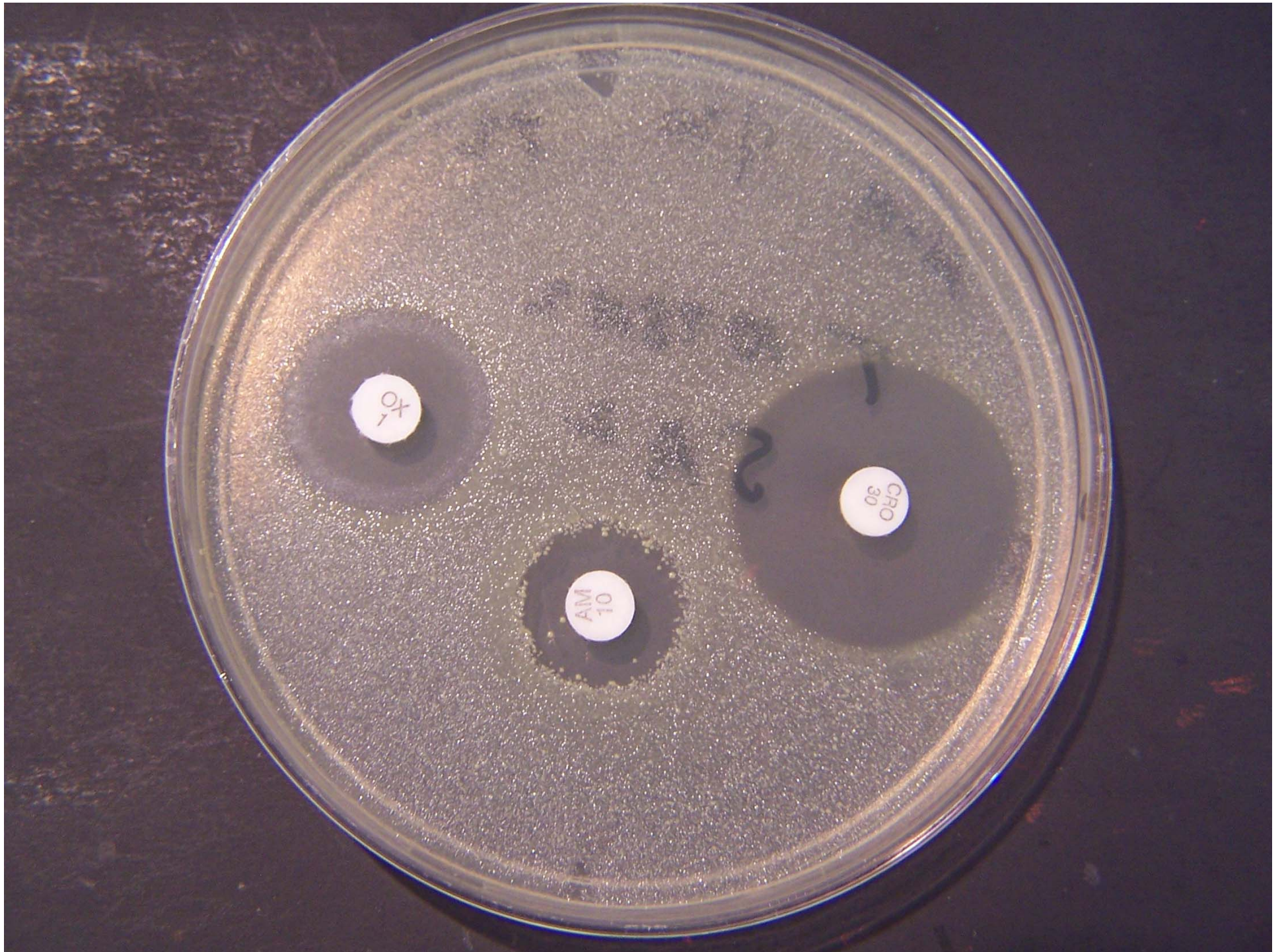


Source: Keller & Surret, 2006

Quorum sensing

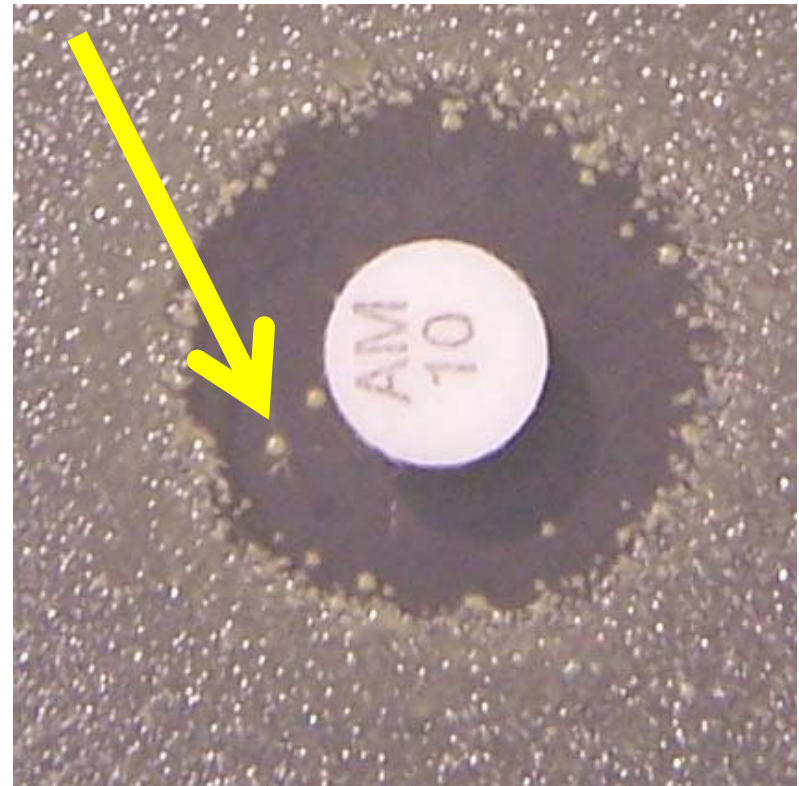


Source: Keller & Surret, 2006



Public Goods – enzymes

- Cost
- Benefits
 - Direct fitness benefit
 - Indirect fitness benefit



Relatedness

- Siblings $r = 0.5$
- Half siblings = 0.25

In population with N clones mixed equally,
average relatedness is

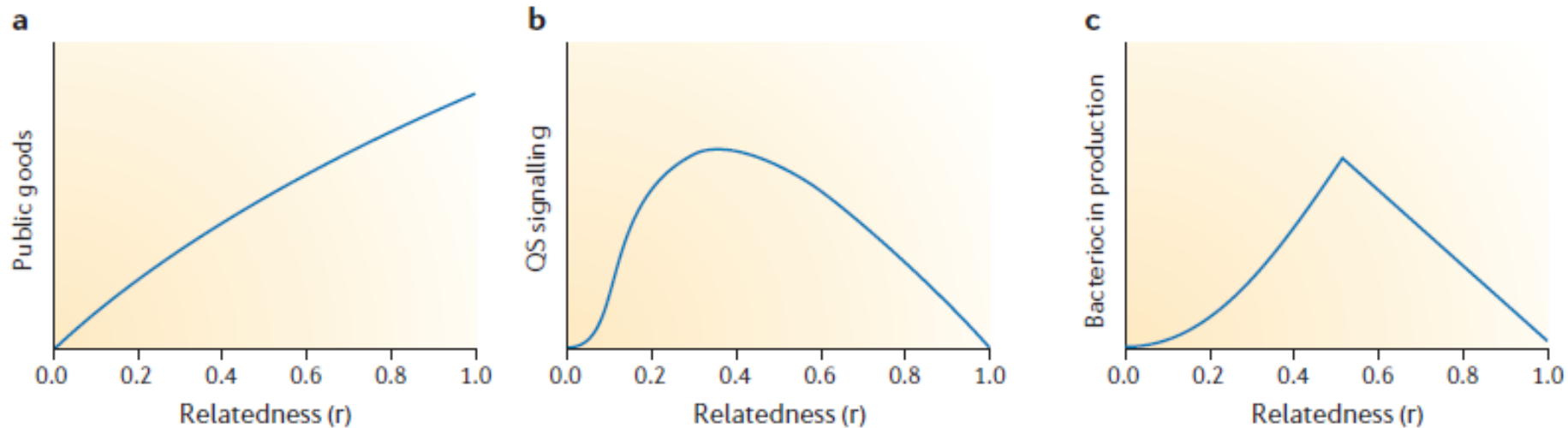
$$r = 1/N$$



Implications of relatedness in resource utilization

? *In high-relatedness populations*

? *In low relatedness (polyclonal) populations*



Source: West, Griffin, Gardner, Diggle, 2006

Implications of relatedness in resource utilization

? *In low dispersal (population viscosity)*

? *In high dispersal*

Altruistic behavior

- “Persistence”
 - Implications for antibiotic resistance
 - SCV *S. aureus*
- Hamilton’s Rule: Altruism is favored when

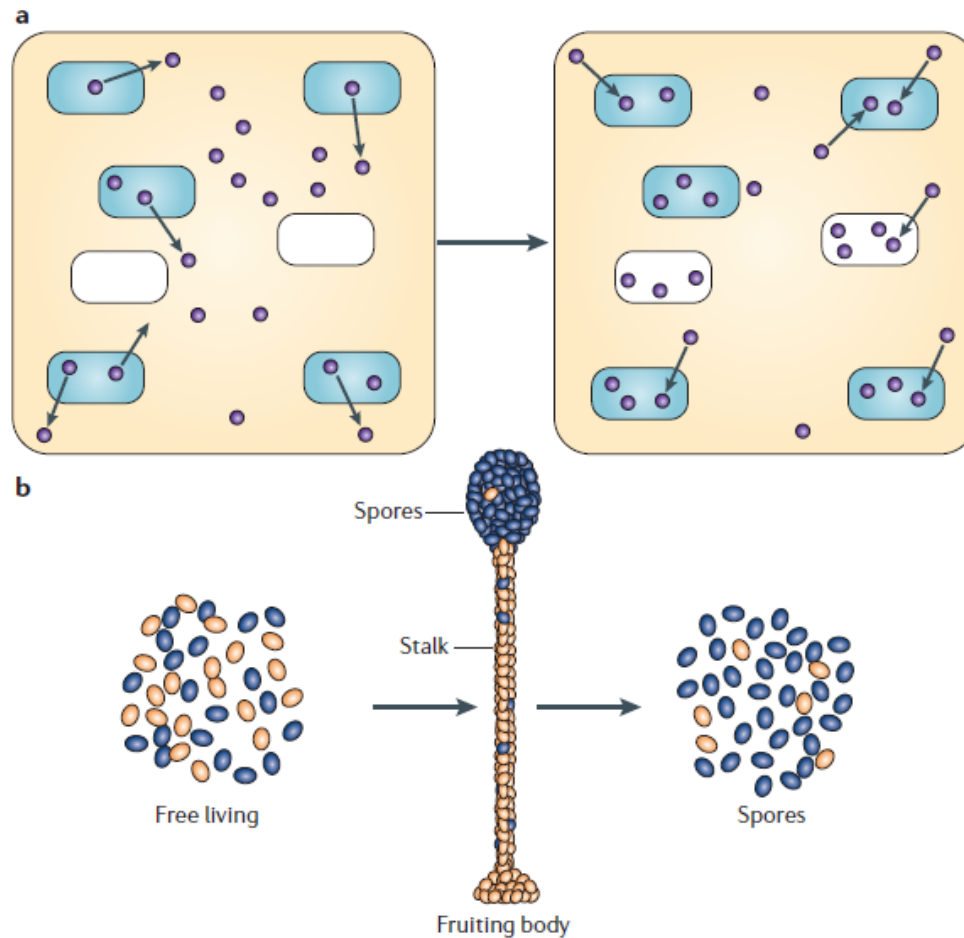
$$RB - C > 0$$

R = relatedness

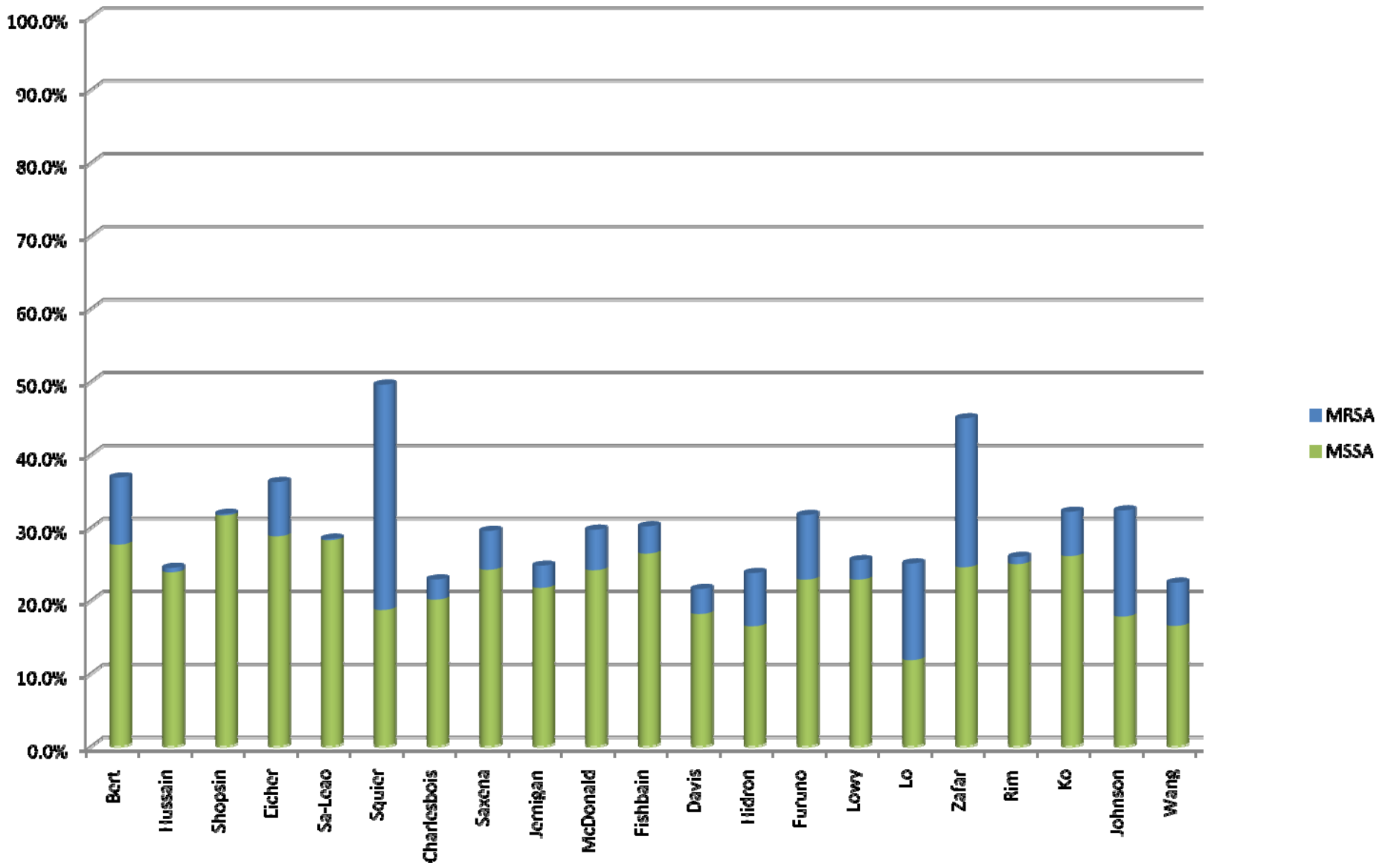
B = benefit

C = cost

Cooperative behavior and cheats



Source: West, Griffin, Gardner, Diggle, 2006



Social Evolution in bacteria

- Social behaviors
 - Cooperation
 - Communication
 - Synchronization
- Issues in social behavior
 - Public benefit
 - Relatedness
 - Cheats

Future Research

- Determine the impact of differential misclassification (variable sensitivity but fixed specificity) in estimation of OR
- Longitudinal Studies to examine the natural history of SA and MRSA colonization
- Examine the role of virulence factors in the natural history of colonization
- Utilize molecular techniques for identification of colonizing SA and MRSA strains
- Study the role of inanimate objects in transmission (fomite) as well as their use as a surrogate for colonization rates
- Group randomized trial of interventions to reduce transmission/colonization risk factors