

# Engaging Scientists, Clinicians, Community Health Workers and Patients to Conduct a CER Study of Home-based Interventions to Reduce CA-MRSA Recurrence and Household Transmission

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# Disclosure

- I do not have financial or other relationships with the manufacturer(s) of any commercial product(s) or provider(s) of any commercial service(s) discussed in this educational activity.
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  - NHLBI, NIDDK, NIMH, **NCATS**
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  - Hepatitis Foundation International/Merck
  - Leukemia and Lymphoma Society
  - March of Dimes
  - New York Academy of Sciences/Sackler Institute for Nutrition Science
  - Opioid Post-Marketing Requirements Consortium (OPC)/Campbell Alliance (Purdue Pharma, LP; Actavis; Endo Pharmaceuticals; Janssen Pharmaceuticals; Mallinckrodt, LLC; Pfizer; Rhodes Pharmaceuticals, LP; Roxane Laboratories; and Zogenix)
  - **Unilever**

# CDN N<sup>2</sup>-PBRN : Building a Network of Safety Net PBRNs

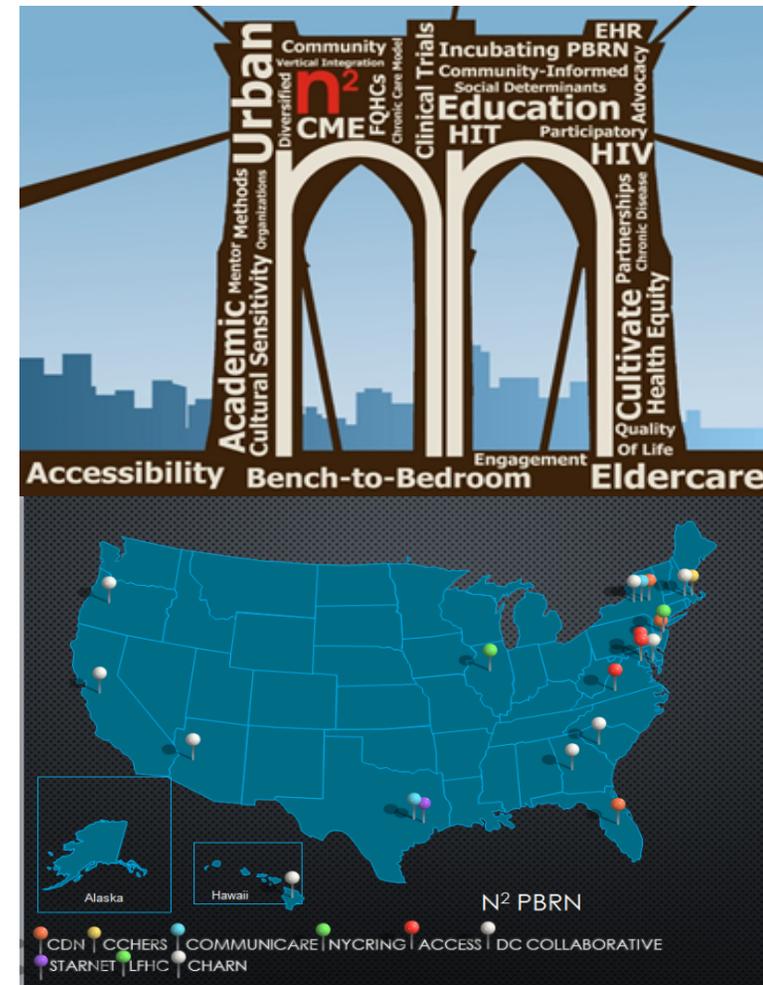
## ► A collaboration among:

- Access Community Health Network (ACCESS)
- Alliance of Chicago (ALLIANCE)
- Association of Asian Pacific Community Health Organization (AAPCHO)
- Center for Community Health Education Research and Service (CCHERS)
- **Clinical Directors Network (CDN) [Lead PBRN]**
- Community Health Applied Research Network (CHARN)
- Fenway Institute (FENWAY)
- New York City Research and Improvement Group (NYCRING)
- Oregon Community Health Information Network (OCHIN)
- South Texas Ambulatory Care Network (STARNet)
- University of Florida (ONE FL)

Funded by AHRQ Grant: P30 HS 021667

Principal Investigator: Jonathan N. Tobin, PhD (CDN)

Program Officers: Rebecca A. Roper, MS, MPH & Theodore G. Ganiats, MD - AHRQ PBRN Initiative



- **9 Established PBRNs**
- **3 "Incubator" PBRNs**
- **600+ Practices**
- **4.5 million patients**





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## *The Rockefeller University*

- Unique structure
  - 82 heads of labs
  - 100+ year tradition of translational research
  - 40 bed JCAHO-accredited research-only hospital
  - AAHRPP-accredited
- 250 protocols
  - 80% investigator - initiated
  - 20% phase I, II, III or device trials
- Center for Clinical Translational Science 2006 -
  - Community Engaged Research Core

THE ROCKEFELLER UNIVERSITY HOSPITAL  
CENTER FOR CLINICAL AND TRANSLATIONAL SCIENCE

# Shirish Balachandra, MD (CDN/Urban Health Plan FQHC) and Maria Pardos, MD PhD (Rockefeller) Case Study of MRSA Infection Recurrence

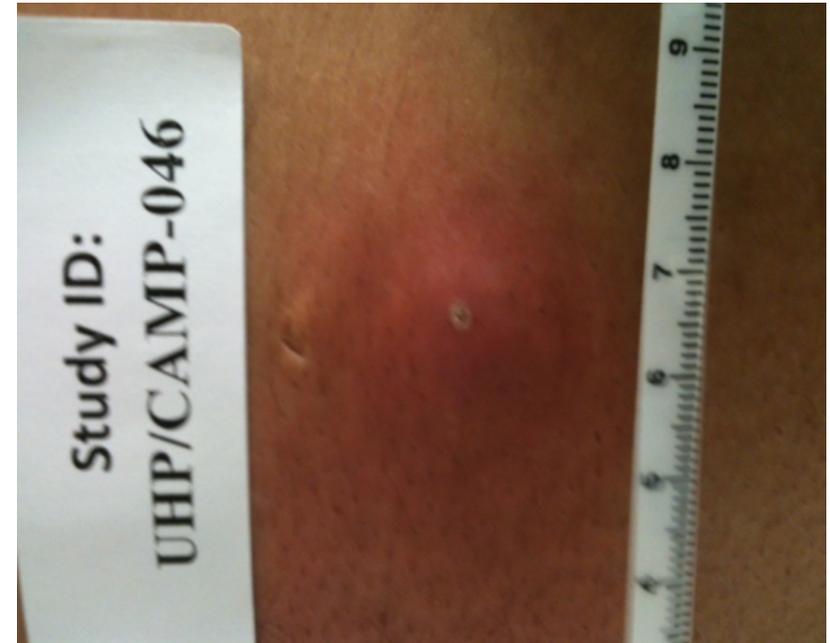
MICROBIAL DRUG RESISTANCE  
Volume 21, Number 2, 2015  
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DOI: 10.1089/mdr.2014.0283

**(T3 Clinician Investigator Expertise/Interest)**

## Recurrent Furunculosis Caused by a Community-Acquired *Staphylococcus aureus* Strain Belonging to the USA300 Clone

Shirish Balachandra,<sup>1,\*</sup> Maria Pardos de la Gandara,<sup>2,\*</sup> Scott Salvato,<sup>1</sup> Tracie Urban,<sup>1</sup> Claude Parola,<sup>1</sup>  
Chamanara Khalida,<sup>3</sup> Rhonda G. Kost,<sup>4</sup> Teresa H. Evering,<sup>4</sup> Mina Pastagia,<sup>4</sup> Brianna M. D'Orazio,<sup>3</sup>  
Alexander Tomasz,<sup>2</sup> Herminia de Lencastre,<sup>2,5</sup> and Jonathan N. Tobin<sup>3,4</sup>

**Background:** A 24-year-old female with recurrent skin and soft tissue infections (SSTI) was enrolled as part of a multicenter observational cohort study conducted by a practice-based research network (PBRN) on community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA). **Methods:** Strains were characterized by pulsed-field gel electrophoresis (PFGE), *spa* typing, and multilocus sequence typing. MRSA strains were analyzed for SCCmec type and the presence of the Panton-Valentine leukocidin (PVL) and arginine catabolic mobile element (ACME) using PCR. **Results:** In the first episode, *S. aureus* was recovered from the wound and inguinal folds; in the second, *S. aureus* was recovered from a lower abdomen furuncle, inguinal folds, and patellar fold. Molecular typing identified CA-MRSA clone USA300 in all samples as *spa*-type t008, ST8, SCCmecIVa, and a typical PFGE pattern. The strain carried virulence genes *pvl* and ACME type I. Five SSTI episodes were documented despite successful resolution by antibiotic treatment, with and without incision and drainage. **Conclusions:** The source of the USA300 strain remains unknown. The isolate may represent a persistent strain capable of surviving extensive antibiotic pressure or a persistent environmental reservoir may be the source, possibly in the patient's household, from which bacteria were repeatedly introduced into the skin flora with subsequent infections.



**RECURRENT FURUNCULOSIS IN A COMMUNITY ACQUIRED *S. aureus* INFECTION CAUSED BY A STRAIN BELONGING TO THE USA300 CLONE OF MRSA**

**Abstract**  
A 24-year-old female with recurrent skin and soft tissue infections (SSTI) was enrolled as part of a multicenter observational cohort study conducted by a practice-based research network (PBRN) on community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA). The patient had recurrent furunculosis and abscesses involving the inguinal folds, lower abdomen, and patellar fold. Molecular typing identified CA-MRSA clone USA300 in all samples as *spa*-type t008, ST8, SCCmecIVa, and a typical PFGE pattern. The strain carried virulence genes *pvl* and ACME type I. Five SSTI episodes were documented despite successful resolution by antibiotic treatment, with and without incision and drainage. The source of the USA300 strain remains unknown. The isolate may represent a persistent strain capable of surviving extensive antibiotic pressure or a persistent environmental reservoir may be the source, possibly in the patient's household, from which bacteria were repeatedly introduced into the skin flora with subsequent infections.

**Microbiology Methods**  
Sampling of infectious etiologies: The patient was treated with antibiotics and drainage. The source of the USA300 strain remains unknown. The isolate may represent a persistent strain capable of surviving extensive antibiotic pressure or a persistent environmental reservoir may be the source, possibly in the patient's household, from which bacteria were repeatedly introduced into the skin flora with subsequent infections.

**Results**  
Molecular typing: The patient was treated with antibiotics and drainage. The source of the USA300 strain remains unknown. The isolate may represent a persistent strain capable of surviving extensive antibiotic pressure or a persistent environmental reservoir may be the source, possibly in the patient's household, from which bacteria were repeatedly introduced into the skin flora with subsequent infections.

**Clinical Presentation**  
Chronology of the case: The patient was treated with antibiotics and drainage. The source of the USA300 strain remains unknown. The isolate may represent a persistent strain capable of surviving extensive antibiotic pressure or a persistent environmental reservoir may be the source, possibly in the patient's household, from which bacteria were repeatedly introduced into the skin flora with subsequent infections.

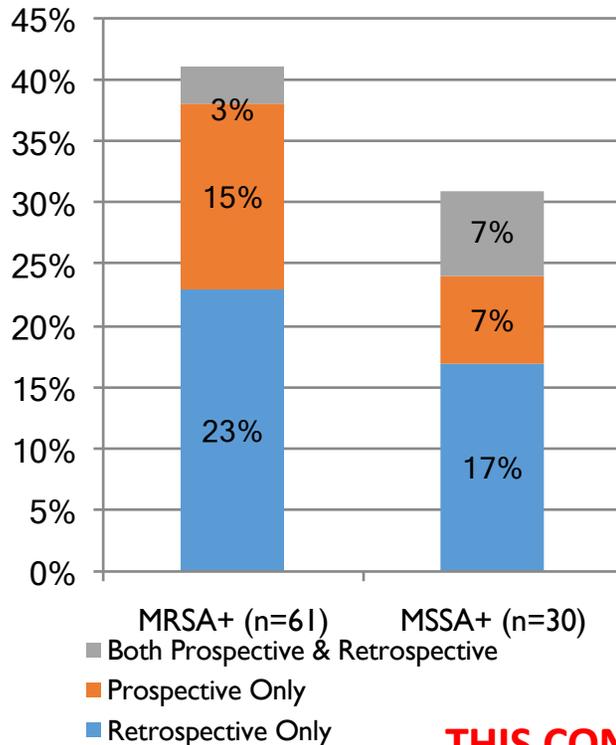
**Conclusions & Next Steps**  
The source of the USA300 strain remains unknown. The isolate may represent a persistent strain capable of surviving extensive antibiotic pressure or a persistent environmental reservoir may be the source, possibly in the patient's household, from which bacteria were repeatedly introduced into the skin flora with subsequent infections.

**Funding**  
The study was supported by the Rockefeller University Hospital and the Center for Clinical and Translational Science.

# CAMP1 Findings:

## Convergence of CER/PCOR Interests

### S. aureus Recurrence (n=91)



- **Patients:** Responses from the RPPS patient focus group indicated that many patients participated in the CAMP study in order to contribute to knowledge about CA-MRSA transmission and recurrence. Outcomes that patients were most concerned about include: **recurrence**, pain and inability to work.
- **Clinicians:** “[It is assumed that] colonization is ongoing, because we’ve had **patients return with recurrent infections**. ...If you just use systemic antibiotics, the nasal colonization persists. Another question to consider is if the source is in the house. We can take all measures to decolonize the person but if the infection is still in the house (pet, towel, sheets, etc), then it’s a huge factor.” – Dr. Balachandra
- **Laboratory Investigators:** “Does the MRSA **recurrent** phenotype reflect a single or multiple genotypes?”
- **Clinical Investigators:** **31%** of MRSA+ wounds and **28%** of MSSA+ wounds are **recurrent**

**THIS CONVERGENCE OF INTERESTS LED US TO FOCUS ON LABORATORY & CLINICAL CORRELATES OF INFECTION RECURRENCE AND TO PRIORITIZE THE STUDY OF PREVENTION OF INFECTION RECURRENCE**

# INFECTION VS COLONIZATION: RESERVOIRS

## *Staphylococcus aureus* in the Community: Colonization Versus Infection

Maureen Miller<sup>1</sup>, Heather A. Cook<sup>2</sup>, E. Yoko Furuya<sup>2</sup>, Meera Bhat<sup>2</sup>, Mei-Ho Lee<sup>2</sup>, Peter Vavagiakis<sup>3</sup>, Paul Visintainer<sup>1</sup>, Glenny Vasquez<sup>2</sup>, Elaine Larson<sup>4</sup>, Franklin D. Lowy<sup>2,5\*</sup>

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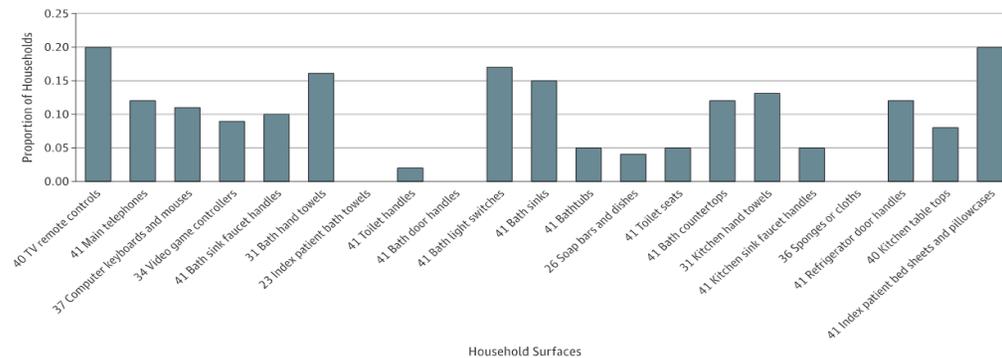
The lack of association between *S. aureus* nasal colonization and serious skin infection underscores the need to explore alternative venues or body sites that may be crucial to transmission. Moreover, the magnitude of colonization and infection within the household suggests that households are an underappreciated and substantial community reservoir.

### Original Investigation

## Contamination of Environmental Surfaces With *Staphylococcus aureus* in Households With Children Infected With Methicillin-Resistant *S aureus*

Stephanie A. Fritz, MD, MSCI; Patrick G. Hogan, MPH; Lauren N. Singh, MPH; Ryley M. Thompson; Meghan A. Wallace, BS; Krista Whitney, MD; Duha Al-Zubeidi, MD; Carey-Ann D. Burnham, PhD; Victoria J. Fraser, MD

Figure. Proportion of Households Contaminated With an Environmental Strain Type of *Staphylococcus aureus* Correlating With the Participants' Baseline Colonizing or Infecting Strain Type, by Household Surface



Repetitive sequence-based polymerase chain reaction queries the entire chromosome but is not specific to the *mecA* gene; thus, a methicillin-resistant

determined by whether the surface was available for testing and whether there was at least 1 baseline isolate (colonizing or infecting strain) obtained from the

# EFFECTIVE INTERVENTIONS TO PREVENT INFECTION

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JUNE 13, 2013

VOL. 368 NO. 24

## Targeted versus Universal Decolonization to Prevent ICU Infection

Susan S. Huang, M.D., M.P.H., Edward Septimus, M.D., Ken Kleinman, Sc.D., Julia Moody, M.S., Jason Hickok, M.B.A., R.N., Taliser R. Avery, M.S., Julie Lankiewicz, M.P.H., Adrijana Gombosev, B.S., Leah Terpstra, B.A., Fallon Hartford, M.S., Mary K. Hayden, M.D., John A. Jernigan, M.D., Robert A. Weinstein, M.D., Victoria J. Fraser, M.D., Katherine Haffner, B.S., Eric Cui, B.S., Rebecca E. Kaganov, B.A., Karen Lolans, B.S., Jonathan B. Perlin, M.D., Ph.D., and Richard Platt, M.D., for the CDC Prevention Epicenters Program and the AHRQ DECIDE Network and Healthcare-Associated Infections Program\*

Universal decolonization resulted in a significantly greater reduction in the rate of all blood stream infections than either targeted decolonization or screening and isolation.

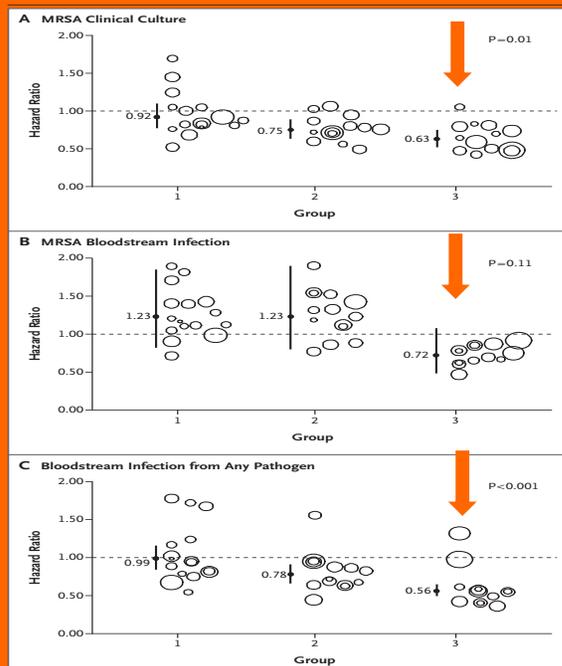


Figure 2. Effect of Trial Interventions on Outcomes.

Shown are group-specific hazard ratios and 95% confidence intervals (indicated by vertical lines) for outcomes attributable to the intensive care unit. Results are based on unadjusted proportional-hazards models that accounted for clustering within hospitals. Analyses were based on the as-assigned status of hospitals. Panel A shows hazard ratios for clinical cultures that were positive for methicillin-resistant *Staphylococcus aureus* (MRSA) infection, Panel B hazard ratios for MRSA bloodstream infection, and Panel C hazard ratios for bloodstream infection from any pathogen. Bubble plots of hazard ratios (predicted random effects or exponentiated frailties) from individual hospitals relative to their group effects are shown. The size of the bubble indicates the relative number of patients contributing data to the trial.

# CAMP2 Specific Aims

- **Aim 1:** To evaluate the **comparative effectiveness of a CHW/Promotora-delivered home intervention** (Experimental Group) as compared to Usual Care (Control Group) on the primary patient-centered and clinical outcome (SSTI recurrence rates) and secondary patient-centered and clinical outcomes (pain, depression, quality of life, care satisfaction) **using a two-arm randomized controlled trial (RCT)**
- **Aim 2:** To understand the **patient-level factors** (CA-MRSA infection prevention knowledge, self-efficacy, decision-making autonomy, prevention behaviors/adherence) and **environmental-level factors** (household surface contamination, household member colonization, transmission to household members) that are associated with differences in SSTI recurrence rates
- **Aim 3:** To understand **interactions of the intervention with bacterial genotypic and phenotypic** variables on decontamination, decolonization, SSTI recurrence, and household transmission
- **Aim 4 [Exploratory]:** To explore the **evolution of stakeholder engagement and interactions** among patients and other community stakeholders with practicing community-based clinicians and academic laboratory and clinical investigators over the duration of the study period

# CAMP1 & CAMP2 Stakeholders and Partners

## The Rockefeller University

Barry Collier, MD  
 Rhonda G. Kost, MD  
 Alexander Tomasz, PhD  
 Herminia de Lencastre, PhD  
 Maria Pardos de la Gandara, MD, PhD  
 Marilyn Chung, BA  
 Cameron Coffran, MS  
 Joel Correa da Rosa, PhD  
 Kimberly Vasquez, MPH  
 Teresa Evering, MD, MS  
 Mina Pastagia, MD, MS  
 Maija Neville-Williams, MPH

## CDN

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 Anthony Rhabb  
 Cynthia Mofunanya  
 Jessica Ramachandran  
 Uma Siddiqui

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 Jessica Ramachandran, MBBS  
 \*Van Johnson

## Coney Island Hospital

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 Slava Gladstein, DO  
 Rosalee Nguyen, DO, MS  
 \*Ronnett Davis

## Community Healthcare Network

Satoko Kanahara, MD  
 Katrina Adams

## Academic Stakeholders

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 Christopher Mason, PhD  
*Weill Cornell Medical College*  
 Eric Lofgren, PhD  
*Washington State University College of Veterinary Medicine*  
 Susan Huang, MD, MPH  
*University of California Irvine*

## NYU Lutheran Family Health Centers

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 Paula Clemons, PA  
 Jason Hyde, MA  
 Jasbir Singh, MBBS  
 \*Keenan Millan

## Open Door Family Medical Center

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 Asaf Cohen, MD

## Urban Health Plan

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 Shirish Balachandra, MD  
 Claude Parola, MD  
 Tracie Urban, RN  
 \*Brenda Gonzalez

## Hudson River Health Care

Carmen Chinae, MD  
 Nancy Jenks, NP

## Manhattan Physician's Group

Ronda Burgess, RN

## PCORI Project Officers

Anne Trontell, MD, MPH  
 Jess Robb

## Denny Moe's Superstar Barbershop

\*Dennis "Denny Moe" Mitchell

## \*Patient/Community Stakeholders

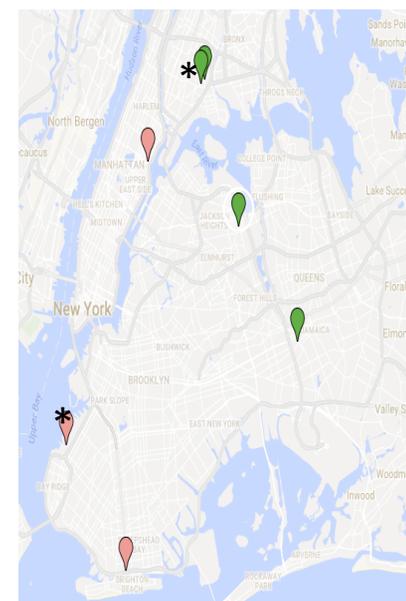
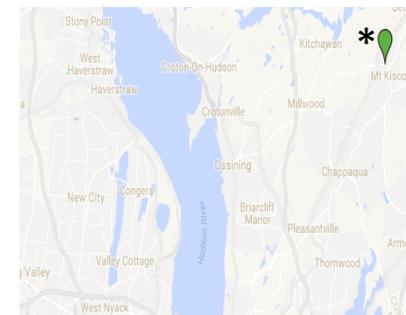
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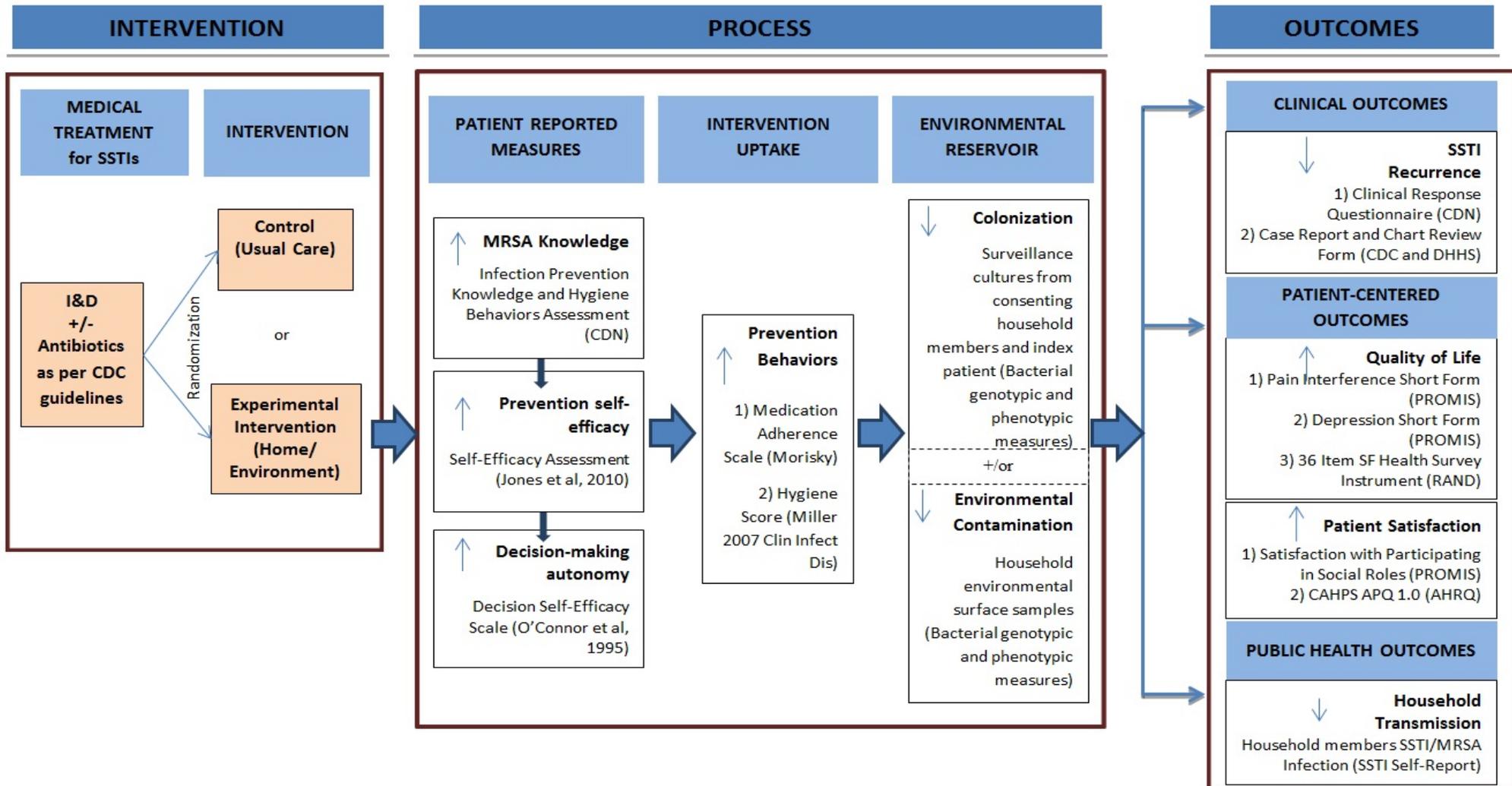
*AHRQ Grant # P30 HS 021667*



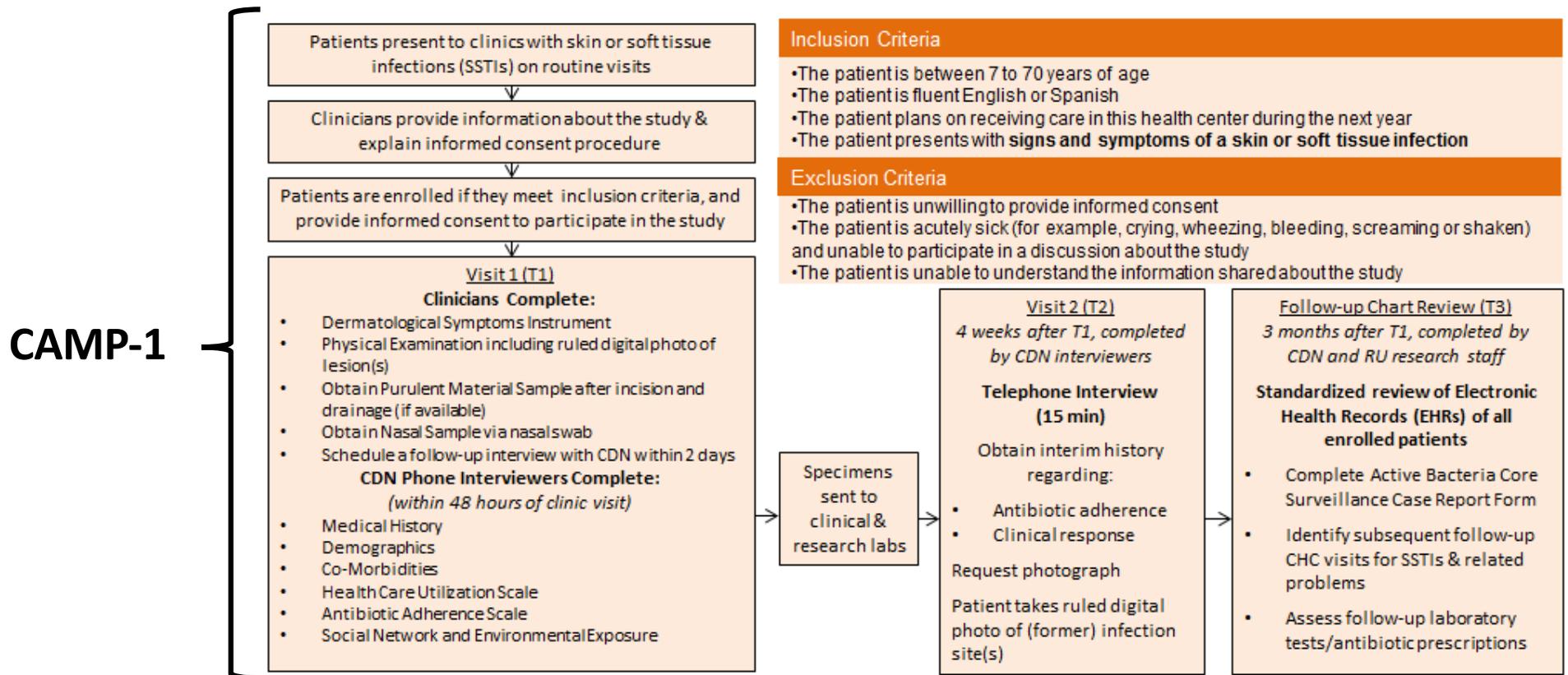
- Community Health Centers
- Community Hospitals
- \* Participated in Previous MRSA Studies



# CAMP2 Logic Model



# CAMP1 and CAMP2 Study Designs



- CAMP-2**
1. Home visits with Community Health Workers/Promotoras (patient and household assessment/swabs) [Exp + UC]
  2. Patient and household member decolonization [EXP]
  3. Household decontamination [EXP]

# CAMP2 Research Design

## CDC Guidelines:

Incision & Drainage  
± Oral Antibiotics

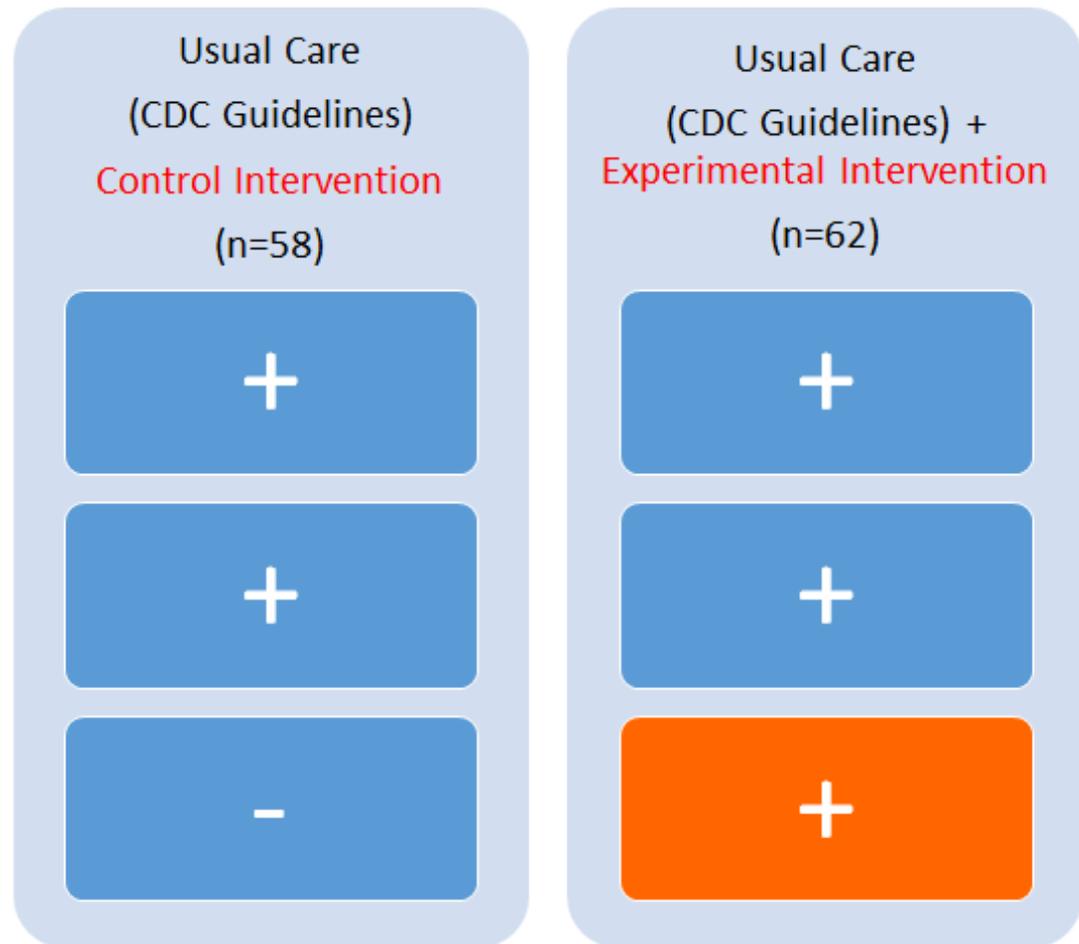
**Assessment of Household  
Environmental Contamination &  
Household Members  
Colonization**

## Patient & Household Members

- Decolonization  
**Home Environment**
- Environmental  
Decontamination

*(after S. Huang, 2014)*

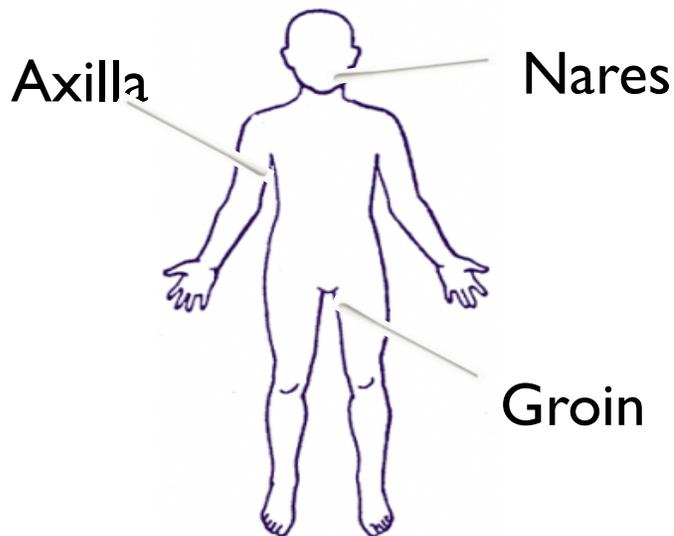
- 1) Nasal Mupirocin
- 2) Chlorhexidine Baths on Skin
- 3) Chlorine Bleach Cleaning of Household Surfaces



# Home Visit Assessment: Household Surface Sampling

Collected from index patients (n=278), consenting household members, and home environment surfaces.

**Index Patients and Household Members**  
(n=3 per participant)  
Baseline and 3-Months



**Environment**  
(n=13 surfaces per household)  
Baseline and 3-Months

Swab Category	
Front doorknob	Kitchen floor
TV remote	Bathroom sink handle
Telephone	Hair brush
Kitchen light switch	Toilet seat
Kitchen countertop	Bedroom floor
Refrigerator door handle	Favorite child's toy (non-plush)
Kitchen sink handle	

# CONSORT Diagram UPDATE 6 MONTH TIMEPOINT

**Enrollment**  
(thru 11/25/2017)

Assessed for eligibility (n=602)

Excluded based on eligibility criteria (n=181)

- Declined to participate (n=141)
- Not meeting inclusion criteria (n=40)
  - Over or under age limit (n=10)
  - On antibiotics (n=3)
  - Acutely ill (n=3)
  - Did not speak English or Spanish (n=7)
  - Does not meet probable diagnostic criteria for CA-MRSA (n=7)
  - No lesion to culture (n=4)
  - Not planning to continue receiving care at site (n=6)

Consented; Baseline Visit  
Conducted  
(n=421)

Excluded based on negative  
lab result (n=235)

Randomized (n=186)

**Allocation**

Allocated to Usual Care Group (n=89)

- Received allocated intervention (n=58)
- Did not receive allocated intervention (n=31)

Allocated to Experimental Group (n=97)

- Received allocated intervention (n=62)
- Did not receive allocated intervention (n=35)

3-Month Home Visit

- Complete (n=47)
- Pending (n=7)

3-Month Home Visit

- Complete (n=50)
- Pending (n=8)

6-Month Interview and Chart Review

- Complete (n=)
- Pending (n=)

6-Month Interview and Chart Review

- Complete (n=)
- Complete (n=)

# Results: Baseline Demographic Data

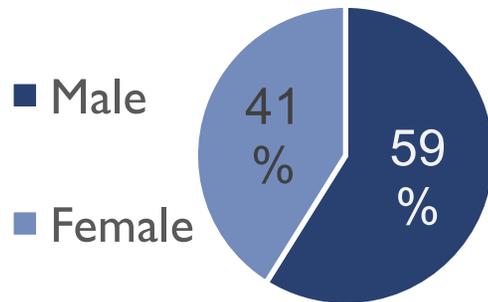
We have recruited **421 patients with SSTIs** to participate;

**44.1%** (n=186) have been **eligible** for the study

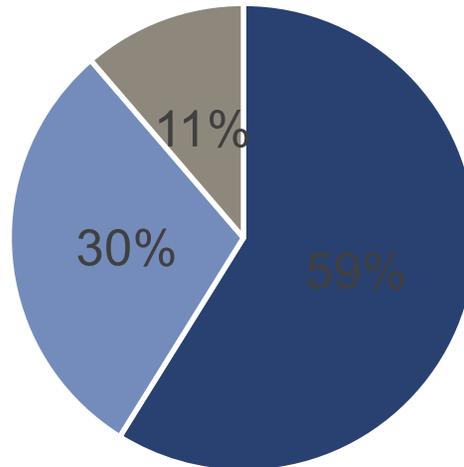
[Wound culture: MRSA+ (22.3%) or MSSA+ (22.3%)]

120 baseline home visits and 95 three-month home visits have been completed

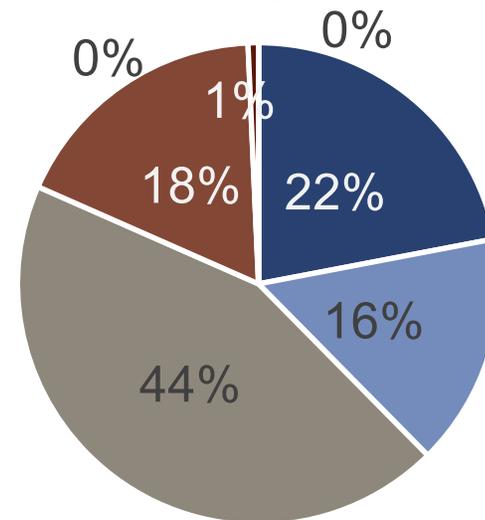
### Gender



### Ethnicity



### Race



### Age

Mean: 38 ± 14.9 years

Range: 9 – 70 years

■ Hispanic or Latino

■ Not Hispanic or Latino

■ Prefer not to Answer

■ Black or African American

■ More than one race

■ Prefer not to answer

■ White

■ American Indian or Alaska Native

■ Asian

■ Native Hawaiian or Other Pacific Islander



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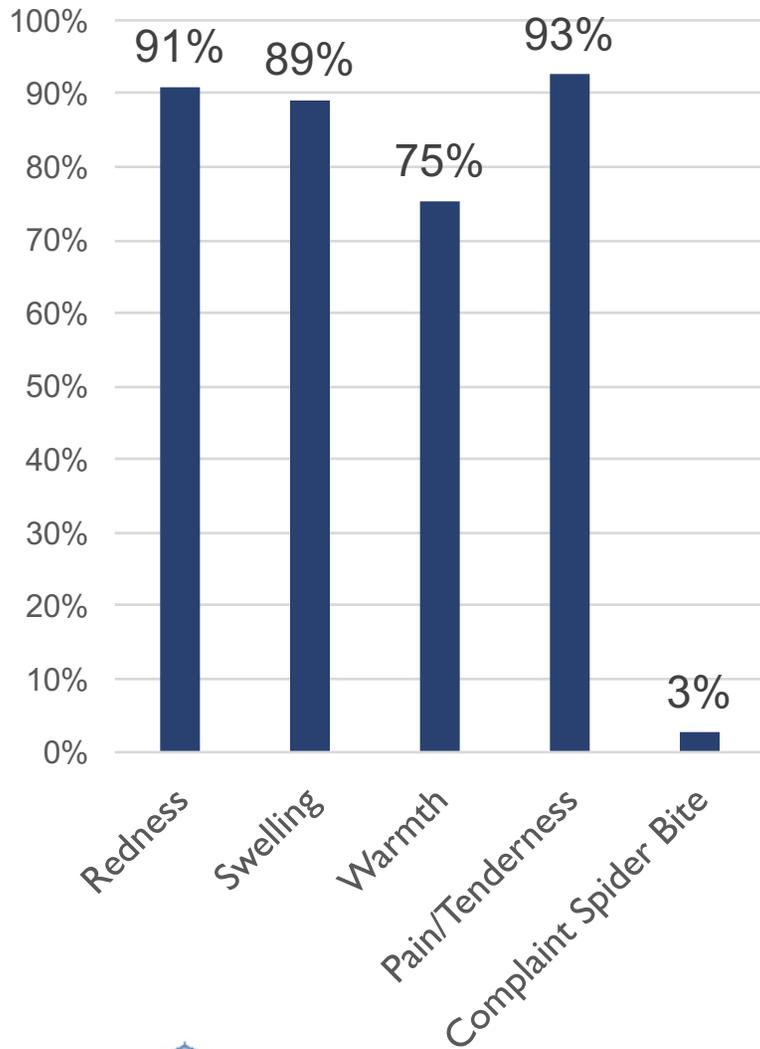
CLINICAL DIRECTORS NETWORK

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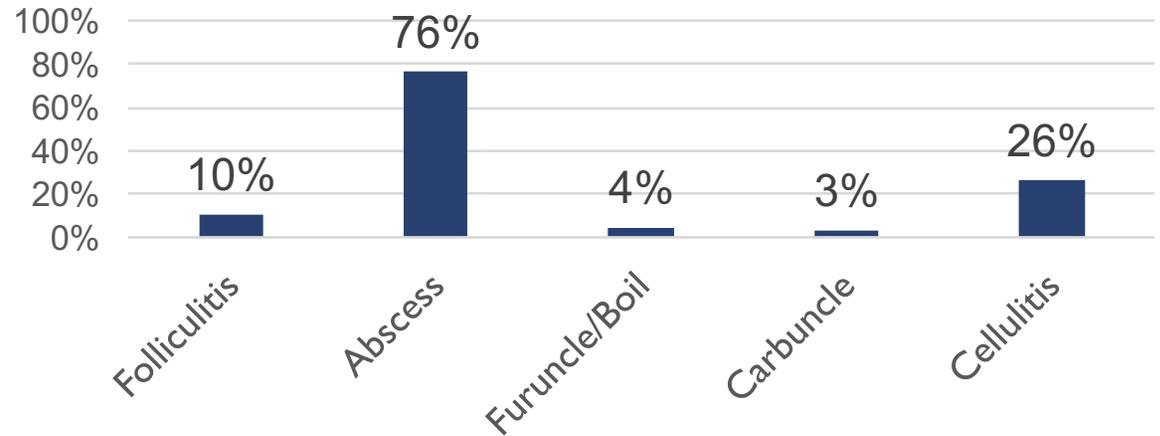
# Results: Baseline Clinical Data

## Dermatological Symptoms and Treatment (n=186)

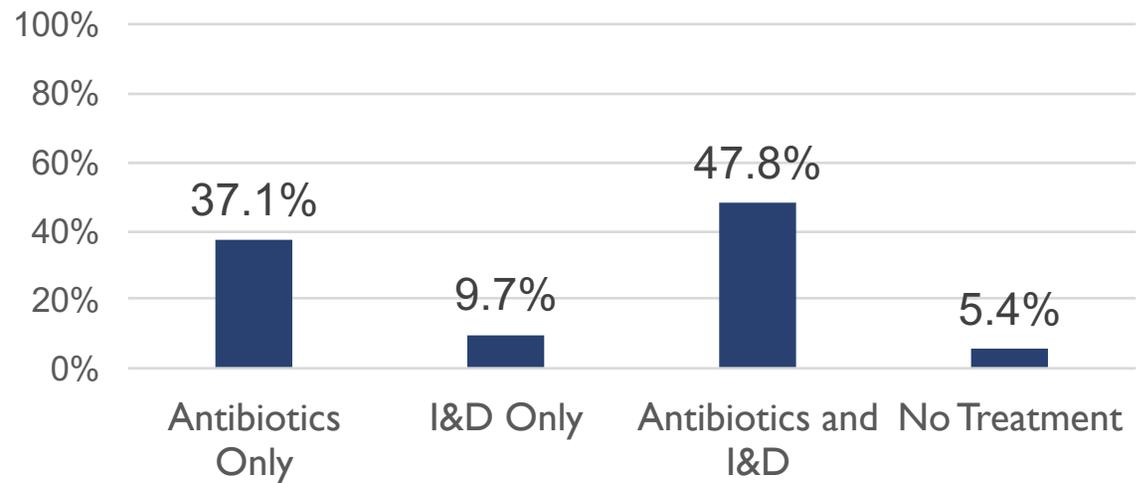
Signs and Symptoms of SSTI



Lesion Type



Treatment



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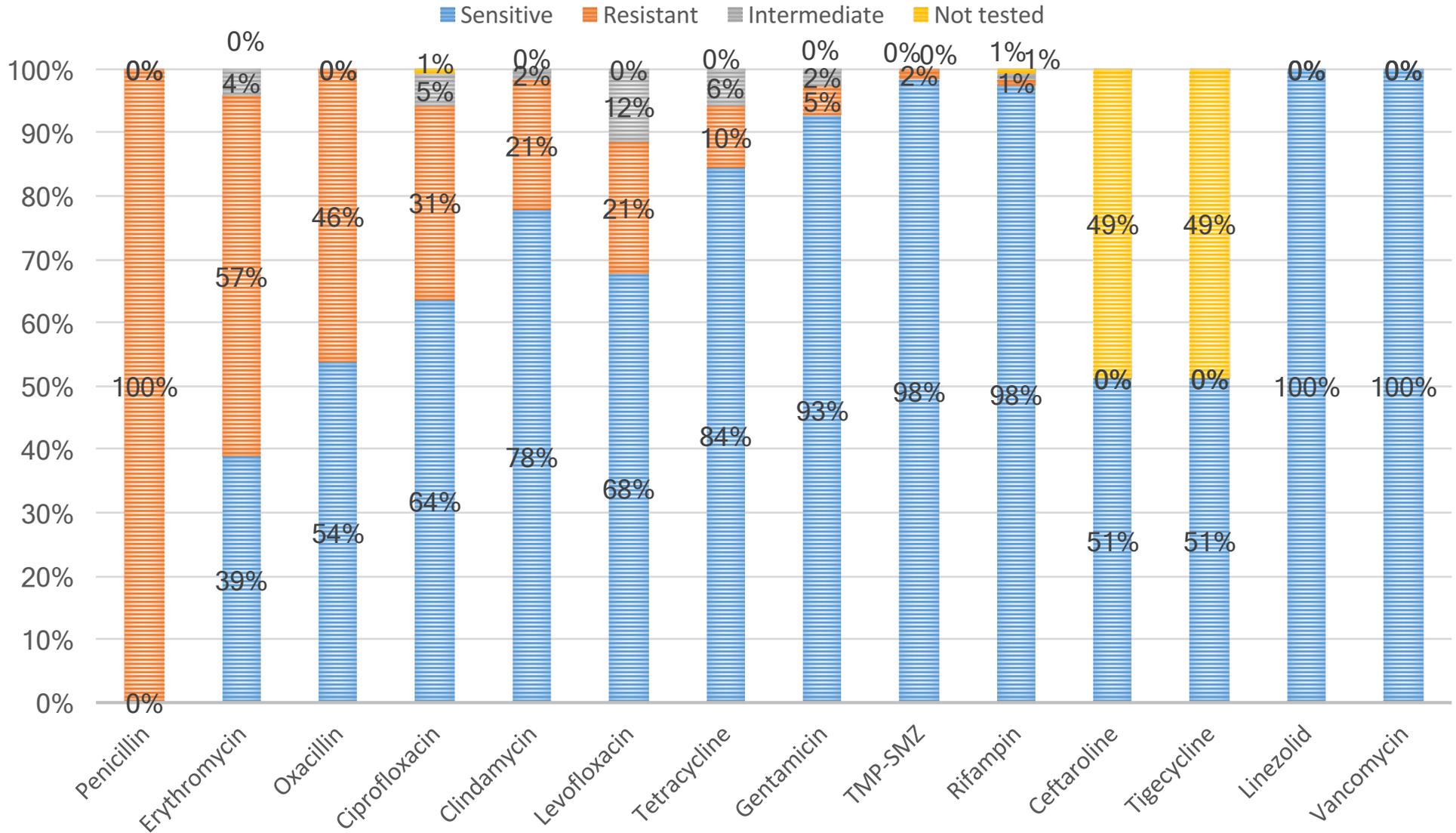
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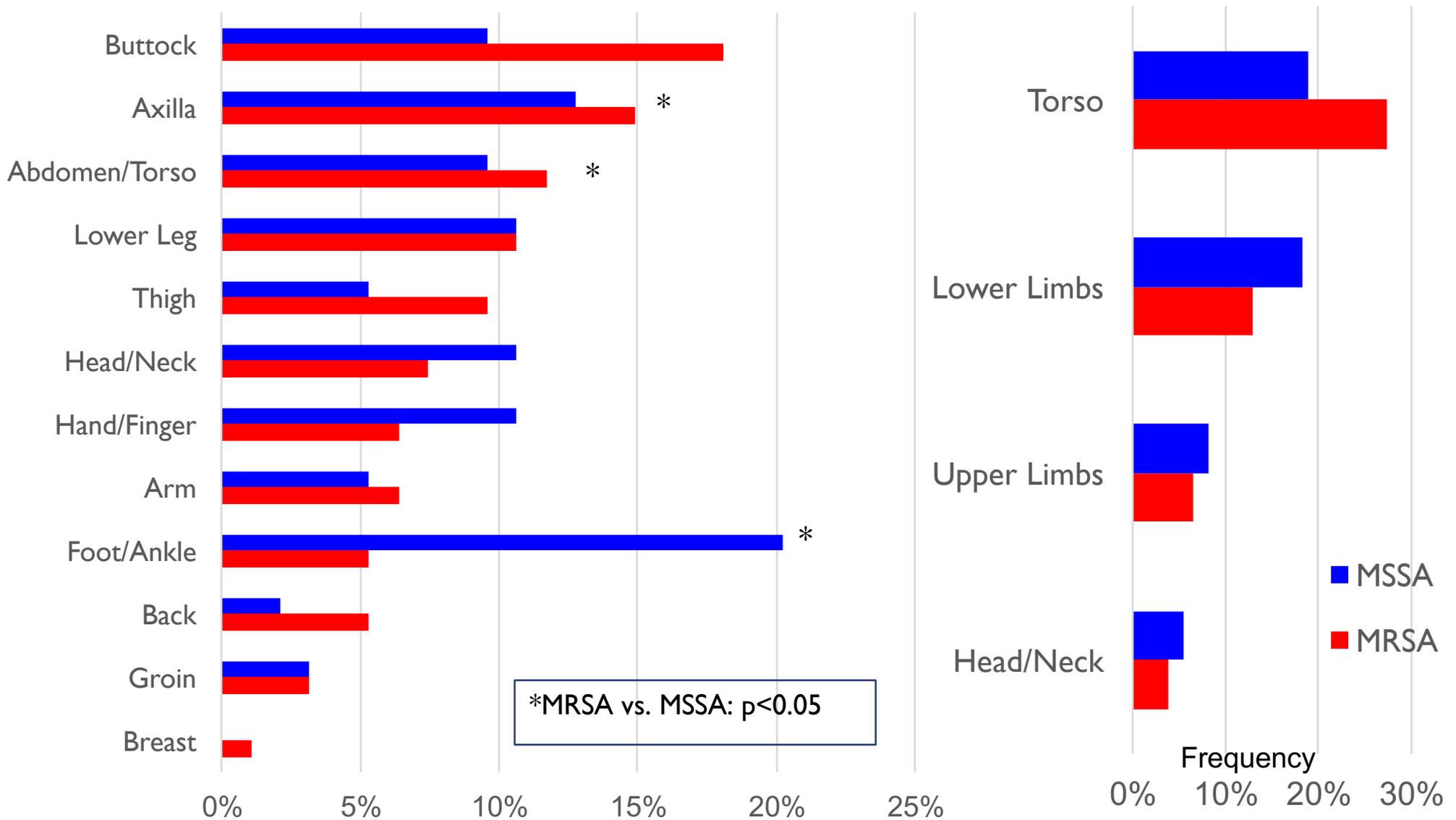
# Results: Baseline Microbiological Data

## ANTIBIOTIC CULTURE & SENSITIVITY (n=121)



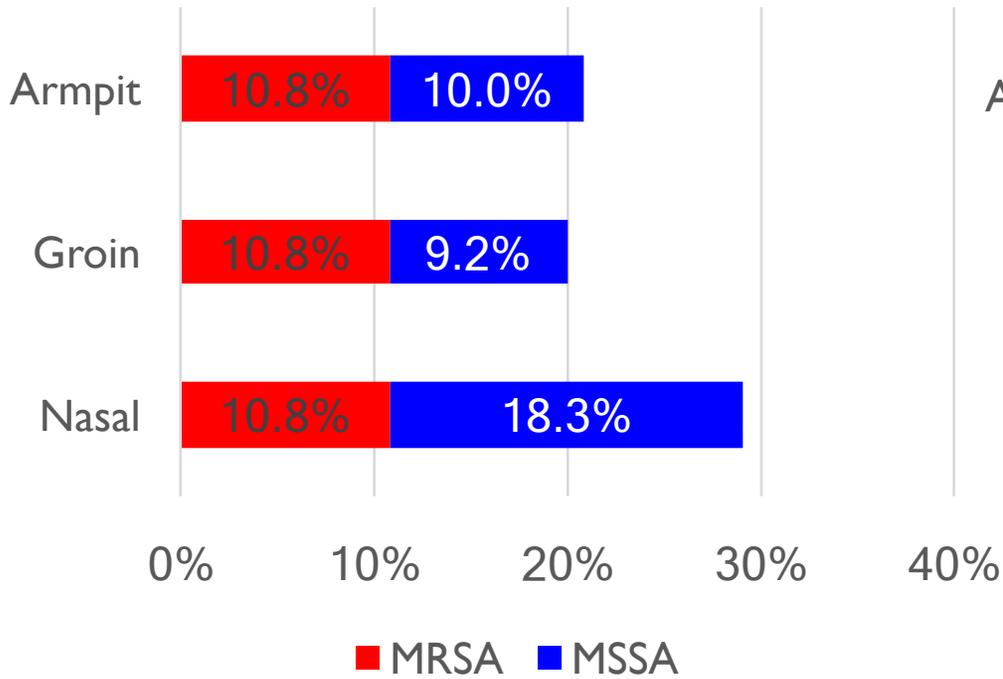
# Results: Baseline Data – Staph Infection

Comparison of Proportions of Infected Body Sites between MRSA and MSSA Infection

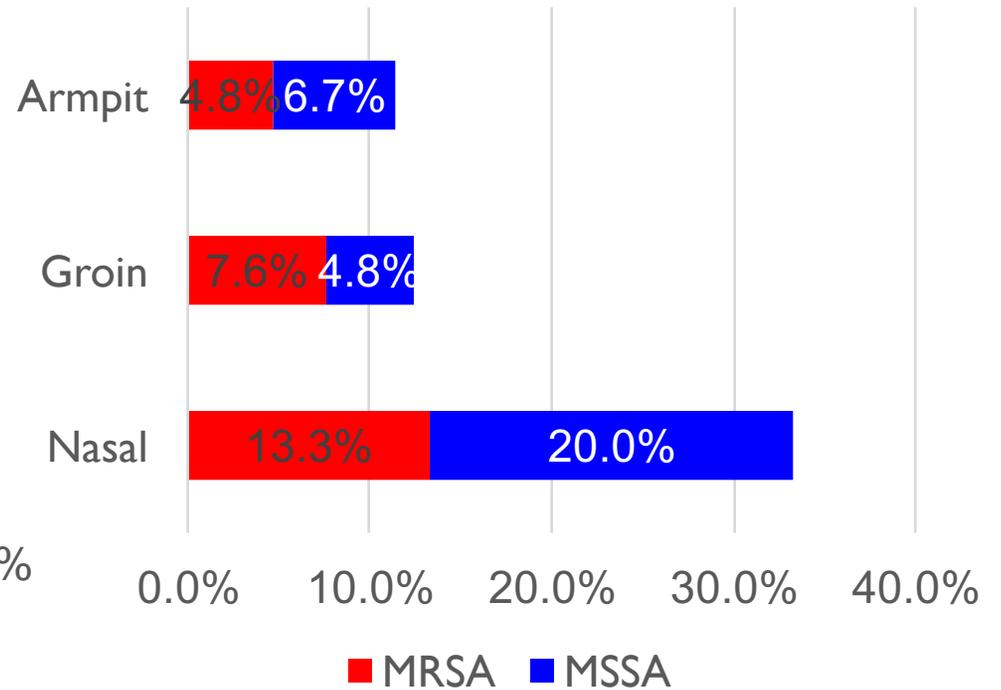


# Results: Baseline Data – Staph Colonization

Index Patient S. aureus Positivity Rate (n=120)



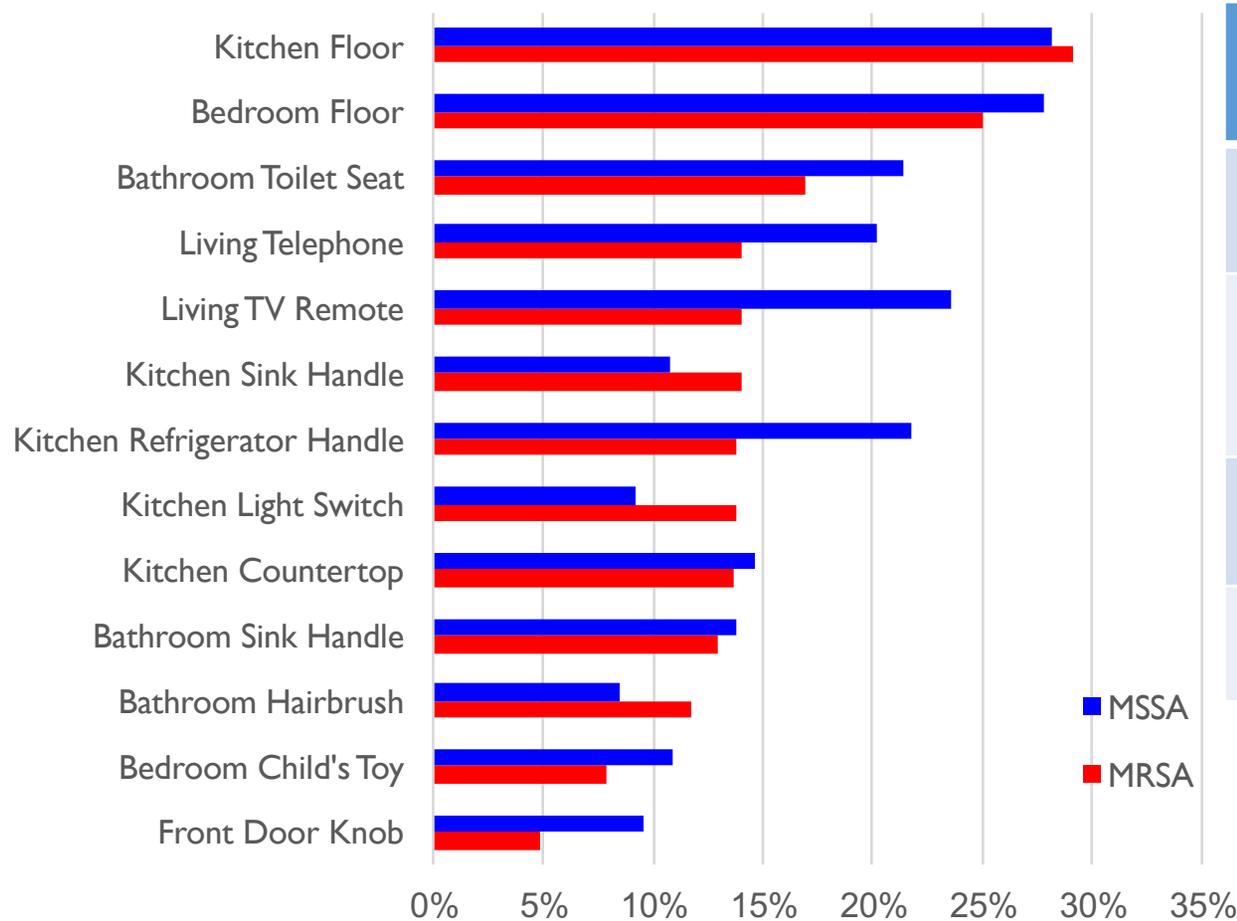
Household Member S. aureus Positivity Rate (n=105)



# Results: Baseline Data – Staph Contamination

Surface contamination similar between MRSA and MSSA (15% vs 17.2%, respectively;  $p=0.22$ ). MRSA and MSSA contamination were most prevalent on the Kitchen Floor, Bedroom Floor, and Toilet Seat.

Surface Contamination with MRSA or MSSA



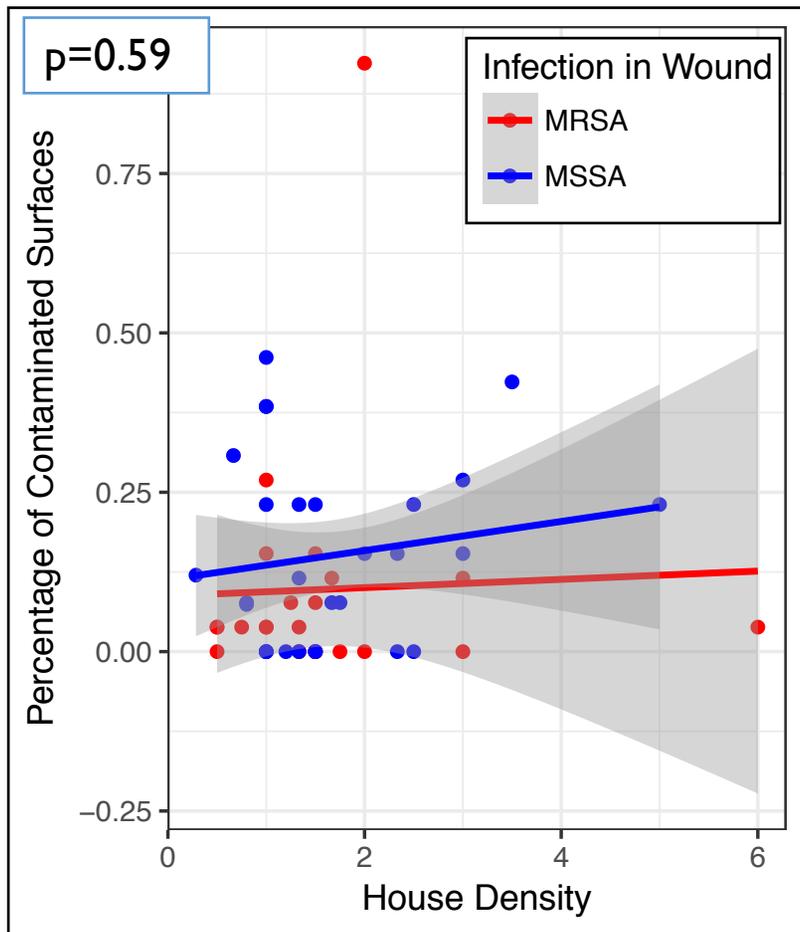
## Household Contamination Score (n=120)

No Contamination (0 surfaces)	46.2%
Moderate Contamination (1-3 surfaces)	36.1%
High Contamination (>4 surfaces)	17.6%
Mean: $1.64 \pm 2.36$	
Range: (0, 12)	

# Results: Baseline Housing Density & Contamination

- The relationship between infection type and household density may be confounded by birthplace, since non-USA born participants had both significantly higher household density and MSSA positivity

Household Density vs. Surface Contamination



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Household Density and Wound Infection Type vs. Birthplace

	Household Density		Infection Type	
	Low	High	MRSA	MSSA
Non-USA	58.0%	42.0%	40.0%	60.0%
USA	57.3%	42.7%	57.3%	42.7%

Household Density= # residents/# rooms; median=1.37

Birthplace vs. Infection Type: P=0.0502

Household Density vs. Infection Type, controlling for Birthplace:  
MRSA: P=0.56; MSSA: P=0.55

# Summary of Baseline Colonization & Contamination Results

- 47.5% of 120 index patients and 38.1% of 105 household members were positive for *S. aureus* colonization in one or more body sites
- 53.8% of households had at least one surface contaminated with *S. aureus* (MRSA: 44.3%, MSSA: 55.7%)
- MRSA and MSSA surface contamination showed similar patterns of contamination, most common in the kitchen (38.5%) and bathroom (23.3%), followed by bedroom (15.4%), living room (15.4%) and entryway (7.7%)
- Those who were not born in the USA had a higher proportion of MSSA infection as compared to those born in the USA ( $p=0.05$ )
- There are high levels of colonization and contamination of surfaces in households of patients with confirmed MRSA/MSSA SSTIs suggesting the importance of these reservoirs for controlling infections



# CA-MRSA Project (CAMP) Rockefeller-CDN-CHC Team

*Bi-Directional Community Engaged Research Partnership*



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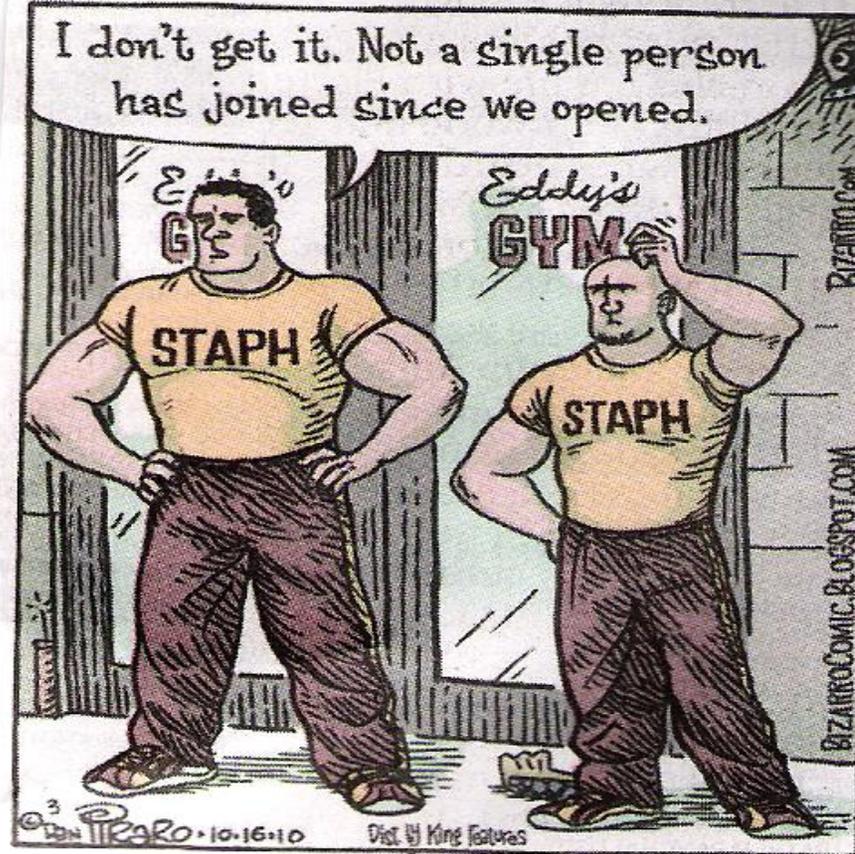
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## BIZARRO



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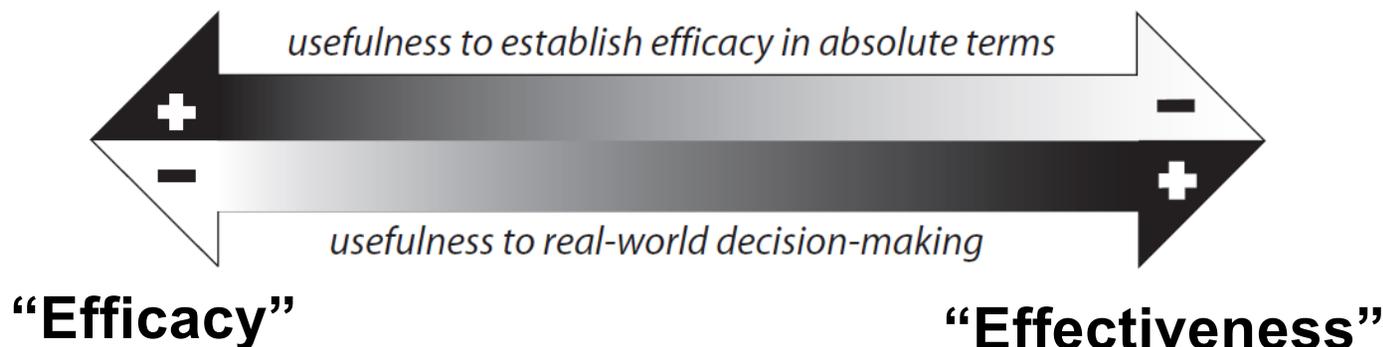
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# PBRNs & Full Spectrum Translational Research Studies

**Tightly Controlled Studies  
in Academic Centers**

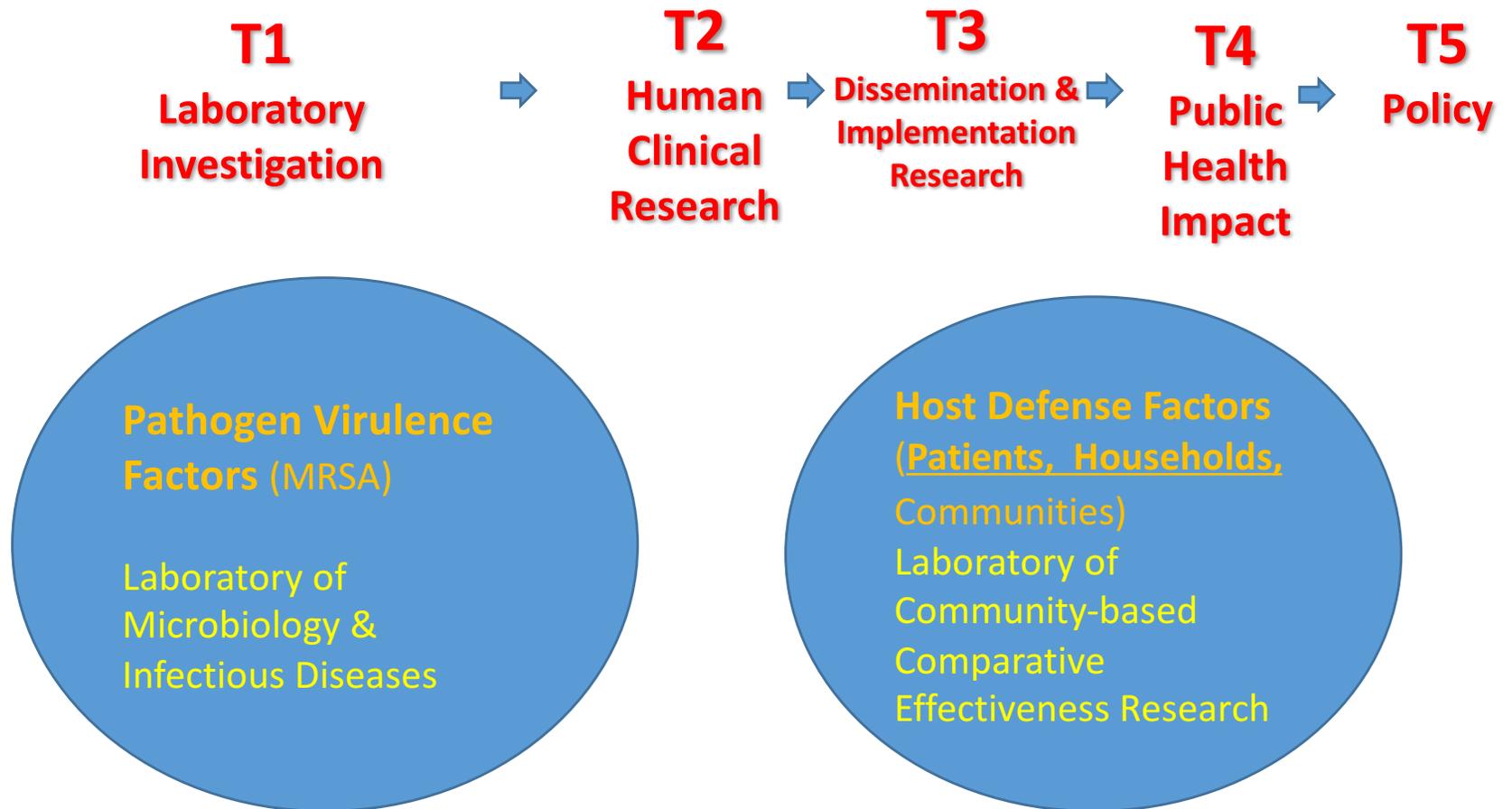
**Studies in Real Life  
Community Settings**



**Rockefeller/CDN Model:  
To Simultaneously Study Effectiveness and Mechanisms  
so as to Answer the Questions:**

- 1) What works?** [Comparative Clinical Effectiveness]
- 2) For whom does it work?** [Heterogeneity of Tx Effects/Precision Medicine]
- 3) How does it work?** [Mechanisms]

# Translational Research, NIH “Blue Highways” & The Rockefeller/CDN Model



# T<sub>5</sub>: Translation into Policy

Reducing Antibiotic Resistant Bacteria (ARBs) and Antibiotic Resistant Gene Fragments (ARGs) in the Environment

- Antibiotic Stewardship
  - Clinical
  - Livestock
- Livestock/Feed/Antibiotics
  - Food Supply
- Environmental Waste Management
  - Soil microbiome
  - Water microbiome

# T<sub>5</sub>: Why is this Important?



## MRSA has been recovered from:

- Companion Animals/Pets (dogs, cats)
- **HUMANOSIS ↔ ZONOSIS**
- Farm/Food Animals (cows, pigs)
- **Livestock Acquired MRSA (LA-MRSA)**
  - Meat (beef, pork)
  - Dairy (cow milk)
  - Fish (tilapia)
- Aquaculture
- Occupational Settings (healthcare, veterinarians, agriculture, livestock, fishermen, athletes)
- Environment (high touch surfaces, public transportation, soil, water table,
- Ocean, Lakes, Wastewater pools





# Clonal Distribution of Nasal and Wound Isolates, MRSA and MSSA Results



## Molecular Types of Methicillin-Resistant *Staphylococcus aureus* and Methicillin-Sensitive *S. aureus* Strains Causing Skin and Soft Tissue Infections and Nasal Colonization, Identified in Community Health Centers in New York City

María Pardos de la Gandara,<sup>a</sup> Juan Antonio Raygoza Garay,<sup>b</sup> Michael Mwangi,<sup>b</sup> Jonathan N. Tobin,<sup>c,d</sup> Amanda Tsang,<sup>c,e</sup> Chamanara Khalida,<sup>f</sup> Brianna D'Orazio,<sup>f</sup> Rhonda G. Kost,<sup>d</sup> Andrea Leinberger-Jabari,<sup>d</sup> Cameron Coffran,<sup>d</sup> Teresa H. Evering,<sup>d</sup> Barry S. Collier,<sup>g</sup> Shirish Balachandra,<sup>g</sup> Tracie Urban,<sup>g</sup> Claude Parola,<sup>g</sup> Scott Salvato,<sup>g</sup> Nancy Jenks,<sup>f</sup> Daren Wu,<sup>g</sup> Rhonda Burgess,<sup>h</sup> Marilyn Chung,<sup>g</sup> Herminia de Lencastre,<sup>a,i</sup> Alexander Tomasz<sup>a</sup>

Laboratory of Microbiology and Infectious Diseases, The Rockefeller University, New York, New York, USA<sup>a</sup>; Department of Biochemistry and Molecular Biology, Penn State University, University Park, Pennsylvania, USA<sup>b</sup>; Clinical Directors Network (CDN), New York, New York, USA<sup>c</sup>; The Rockefeller University Center for Clinical and Translational Science, New York, New York, USA<sup>d</sup>; Urban Health Center, Bronx, New York, USA<sup>e</sup>; Hudson River Health Care, Peekskill, New York, USA<sup>f</sup>; Open Door Family Medical Center, Ossining, New York, USA<sup>g</sup>; Manhattan Physicians Group—125th Street Clinic, New York, New York, USA<sup>h</sup>; Laboratory of Molecular Genetics, Instituto de Tecnologia Química e Biológica (ITQB/UNL), Oeiras, Portugal<sup>i</sup>

In November 2011, The Rockefeller University Center for Clinical and Translational Science (CCTS), the Laboratory of Microbiology and Infectious Diseases, and Clinical Directors Network (CDN) launched a research and learning collaborative project with six community health centers in the New York City metropolitan area to determine the nature (clonal type) of community-acquired *Staphylococcus aureus* strains causing skin and soft tissue infections (SSTIs). Between November 2011 and March 2013, wound and nasal samples from 129 patients with active SSTIs suspicious for *S. aureus* were collected and characterized by molecular typing techniques. In 63 of 129 patients, the skin wounds were infected by *S. aureus*: methicillin-resistant *S. aureus* (MRSA) was recovered from 39 wounds and methicillin-sensitive *S. aureus* (MSSA) was recovered from 24. Most—46 of the 63—wound isolates belonged to the CC8/Panton-Valentine leukocidin-positive (PVL<sup>+</sup>) group of *S. aureus* clone USA300: 34 of these strains were MRSA and 12 were MSSA. Of the 63 patients with *S. aureus* infections, 30 were also colonized by *S. aureus* in the nares: 16 of the colonizing isolates were MRSA, and 14 were MSSA, and the majority of the colonizing isolates belonged to the USA300 clonal group. In most cases (70%), the colonizing isolate belonged to the same clonal type as the strain involved with the infection. In three of the patients, the identity of invading and colonizing MRSA isolates was further documented by whole-genome sequencing.

TABLE 1 Distribution of *S. aureus* isolates grouped by clonal complex

MLST	No. of isolates				
	Total	Wound		Nasal	
		MRSA	MSSA	MRSA	MSSA
CC8	69	34	12	17	6
CC30	12	2	4	1	5
CC5	6	1	2	1	2
CC15	6	0	2	0	4
CC121	3	0	1	0	2
ST72	2	1	0	0	1
CC1	1	0	0	0	1
CC45	1	0	1	0	0
CC88	1	1	0	0	0
CC97	1	0	0	0	1
CC152	1	0	1	0	0
CC398	1	0	1	0	0
Total	104	39	24	19	22

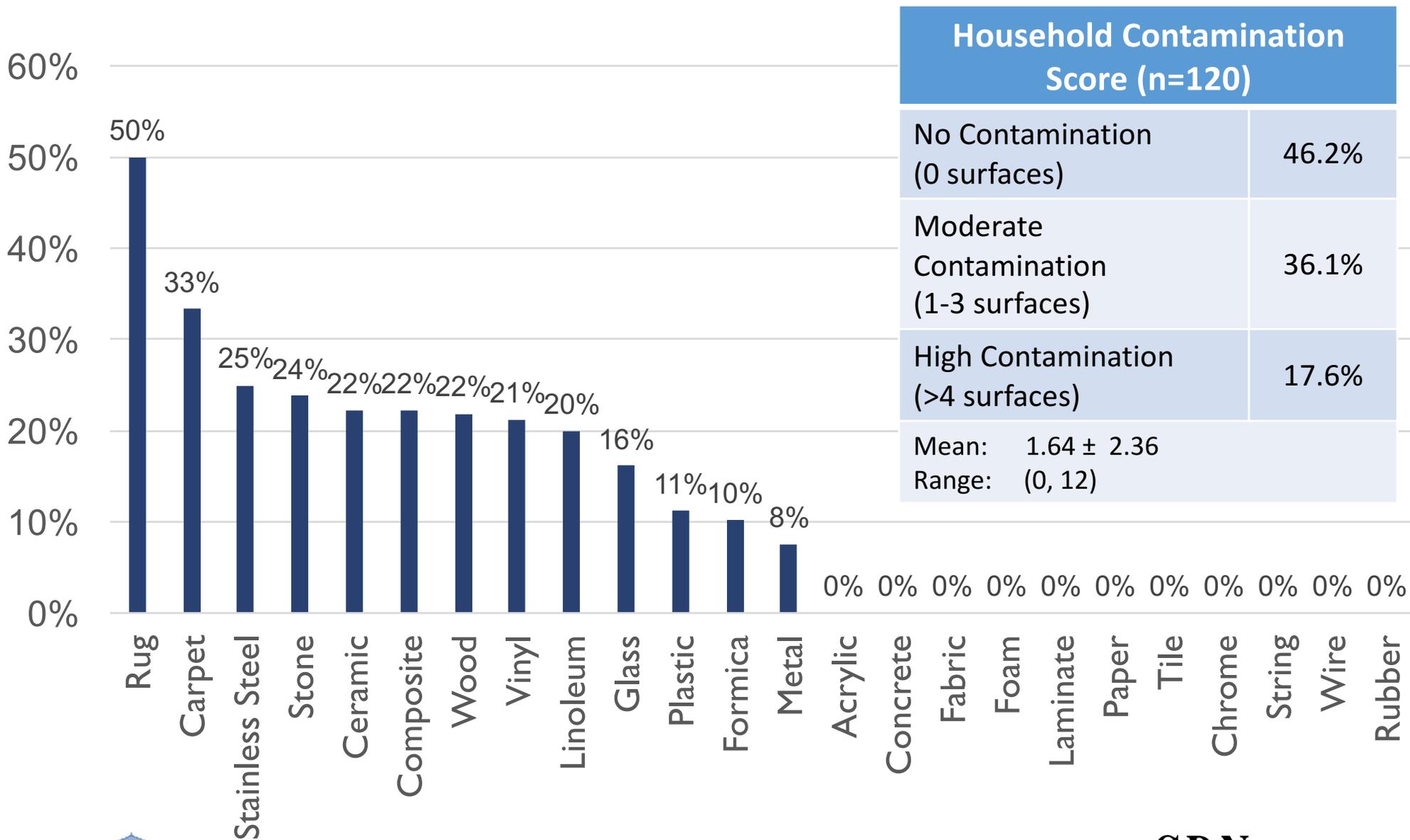
TABLE 2 Distribution of wound isolates belonging to clonal complex CC8

<i>S. aureus</i> type and clone type	No. of wound isolates
MRSA	
USA300 (t008/ST8/SCCmecIVa/PVL <sup>+</sup> /ACME <sup>+</sup> )	21
Other <i>spa</i> types	7
PVL <sup>-</sup>	0
ACME <sup>-</sup>	2
Other	4
Total	34
MSSA	
USA300-like (t008/ST8/PVL <sup>+</sup> /ACME <sup>+</sup> )	3
Other <i>spa</i> types	1
PVL <sup>-</sup>	0
ACME <sup>-</sup>	4
Other	4
Total	12

Pardos de la Gandara M et al. 2015. Molecular types of methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *S. aureus* strains causing skin and soft tissue infections and nasal colonization, identified in community health centers in New York City. *J Clin Microbiol* 53:2648–2658. doi:10.1128/JCM.00591-15.

# Results: Baseline Data – Staph Contamination

## Contamination with MRSA or MSSA by Surface Material



### Household Contamination Score (n=120)

No Contamination (0 surfaces)	46.2%
Moderate Contamination (1-3 surfaces)	36.1%
High Contamination (>4 surfaces)	17.6%

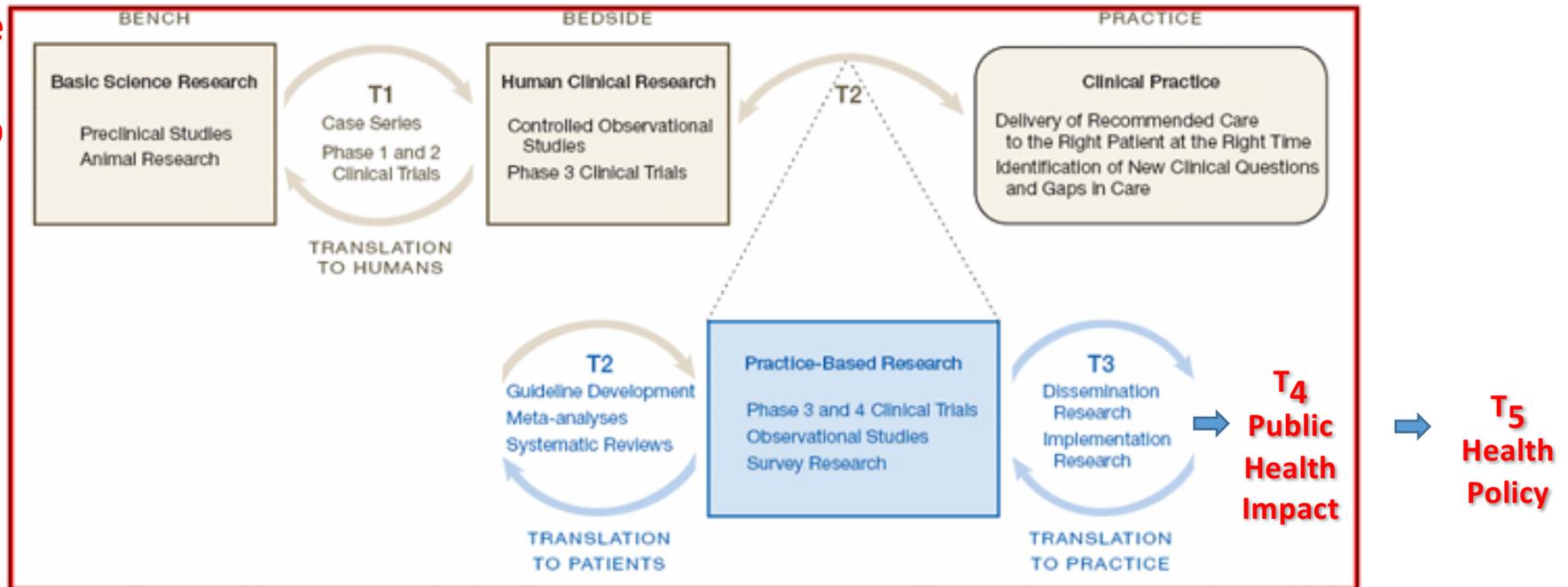
Mean: 1.64 ± 2.36  
Range: (0, 12)

# Translational Research & NIH “Blue Highways”

SOURCE: Westfall, et al., “Practice-Based Research—“Blue Highways” on the NIH Roadmap” *JAMA* 2007; 297: 403-406

What made the partnership work:

T<sub>0</sub> Basic Science →



▪**Aim 3:** To understand interactions of the intervention with bacterial genotypic and phenotypic variables on decontamination, decolonization, SSTI recurrence, and household transmission

▪**Aim 2:** To understand patient-level factors (CA-MRSA infection prevention knowledge, self-efficacy, decision-making autonomy, prevention behaviors/adherence) and environmental-level factors (household surface contamination, household member colonization, transmission to household members) associated w/ diffs in SSTI recurrence rates

▪**Aim 1:** To evaluate the comparative effectiveness of a CHW/Promotora-delivered home intervention (Experimental Group) as compared to Usual Care (Control Group) on the primary patient-centered and clinical outcome (SSTI recurrence rates) and secondary patient-centered and clinical outcomes (pain, depression, quality of life, care satisfaction) using a two-arm randomized controlled trial (RCT)

▪**Aim 4** To explore the evolution of stakeholder engagement and interactions among patients and other community stakeholders with practicing community-based clinicians and academic laboratory and clinical investigators over the duration of the study period



# Conclusion:

## We are Hunting an Important Microbe which serves as a Metaphor for the Best of Medicine and the Worst of Medicine

### MRSA: Elusive & Rapidly Spreading & Mutating Bacteria

Multiple clones

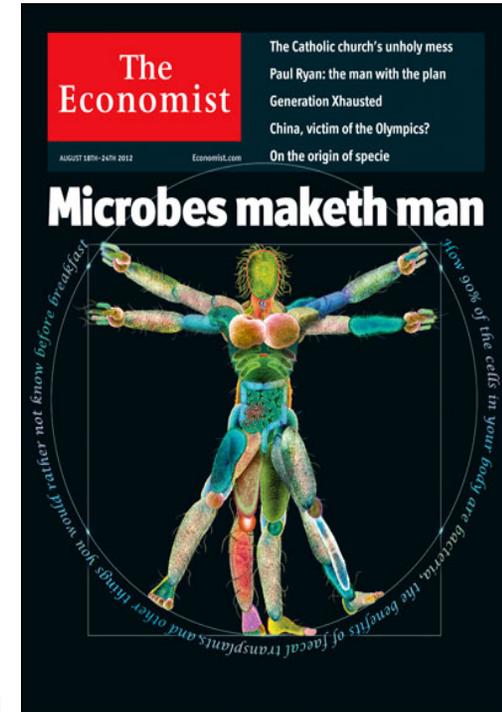
Different phenotypes

Geographic heterogeneity

- Inappropriate Antibiotics Prescribing by Clinicians
- Inadequate Antibiotic Medication Adherence by Patients
- Differential Access to Care and Pharmaceuticals
- Increasing Concentrations of Antibiotics by Pharmaceutical Manufacturing and Animal Husbandry Practices that are Flooding the Environment and Food Supply
- Antibiotic Stewardship by the Health Care and Agriculture/Food Industries

### MRSA Project: A Model System of *in-vivo/in-situ* Research that combines

- Clinical and Public Health Surveillance
  - Clinical Practice/Community-based Comparative Effectiveness Research
  - Health and Environmental Policy
  - Embedded Mechanistic Research about Evolution of Antibiotic Resistance
- Interactions of microbial genomics & evolution with the health care system & environment



Microbiome

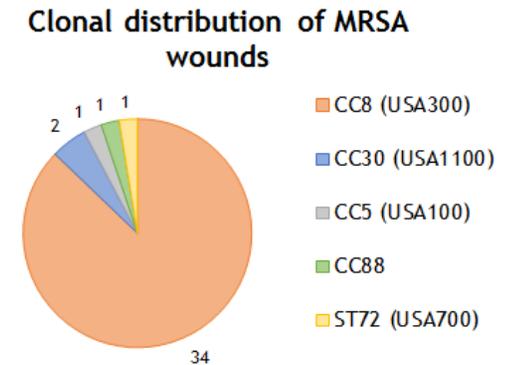
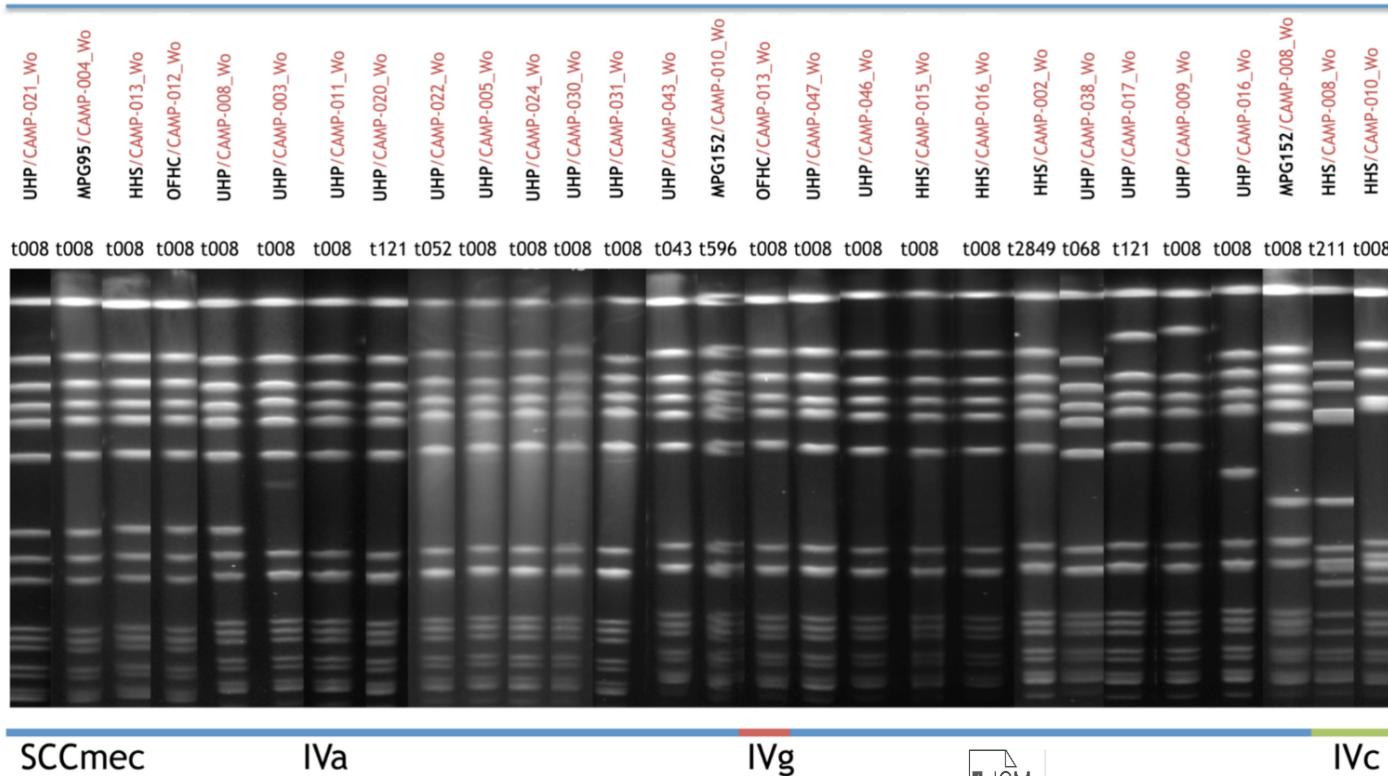
# Community-Associated Methicillin-Resistant *Staphylococcus aureus* (CA-MRSA) Surveillance Network CA-MRSA Project (CAMP1)

## Goals:

1. Define the incidence of CA-MRSA in New York area Community Health Centers (CHCs)
2. Insure that CHCs clinicians have the training to provide optimal care to patients with CA-MRSA
3. Identify the substrains of MRSA responsible for the infections
4. Assess the relationship between MRSA colonizing a patient's nose and the MRSA causing the clinical infection
5. Build a respectful, enduring, bidirectional partnership and network infrastructure for conducting and disseminating future studies

# CA-MRSA Molecular Epidemiology: (T1 Laboratory Investigator Expertise/Interest)

## Molecular profile of USA 300 MRSA wound isolates



All MRSA wound isolates belonging to the USA 300 clone (ST 8) were:

- *pvl* +
- ACME type I



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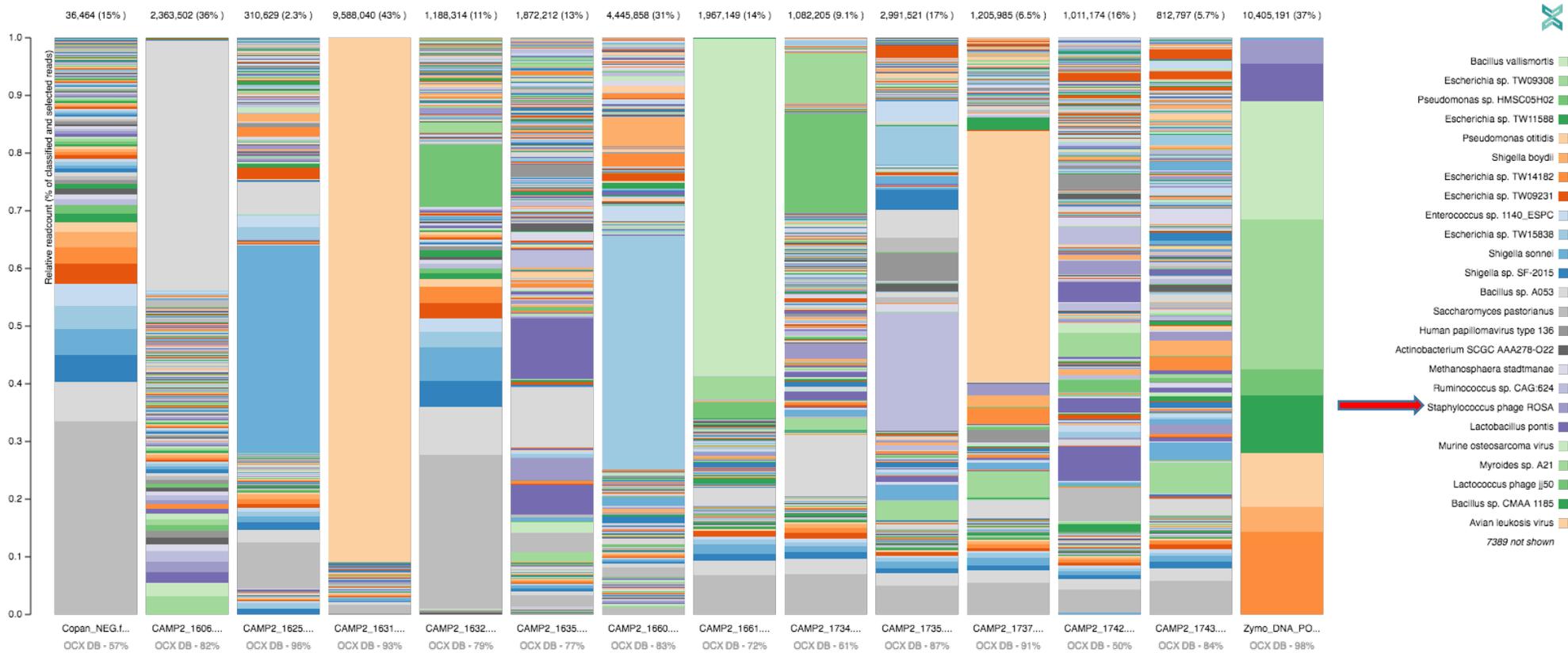
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# Environmental Samples vs. Isolates: So many species where to begin...



One Codex: A Sensitive and Accurate Data Platform for Genomic Microbial Identification, Samuel S Minot, Niklas Krumm, Nicholas B Greenfield  
 bioRxiv 027607; doi: <https://doi.org/10.1101/027607>