

***Consortium for
Interdisciplinary Research
to Reduce Antimicrobial
Resistance***

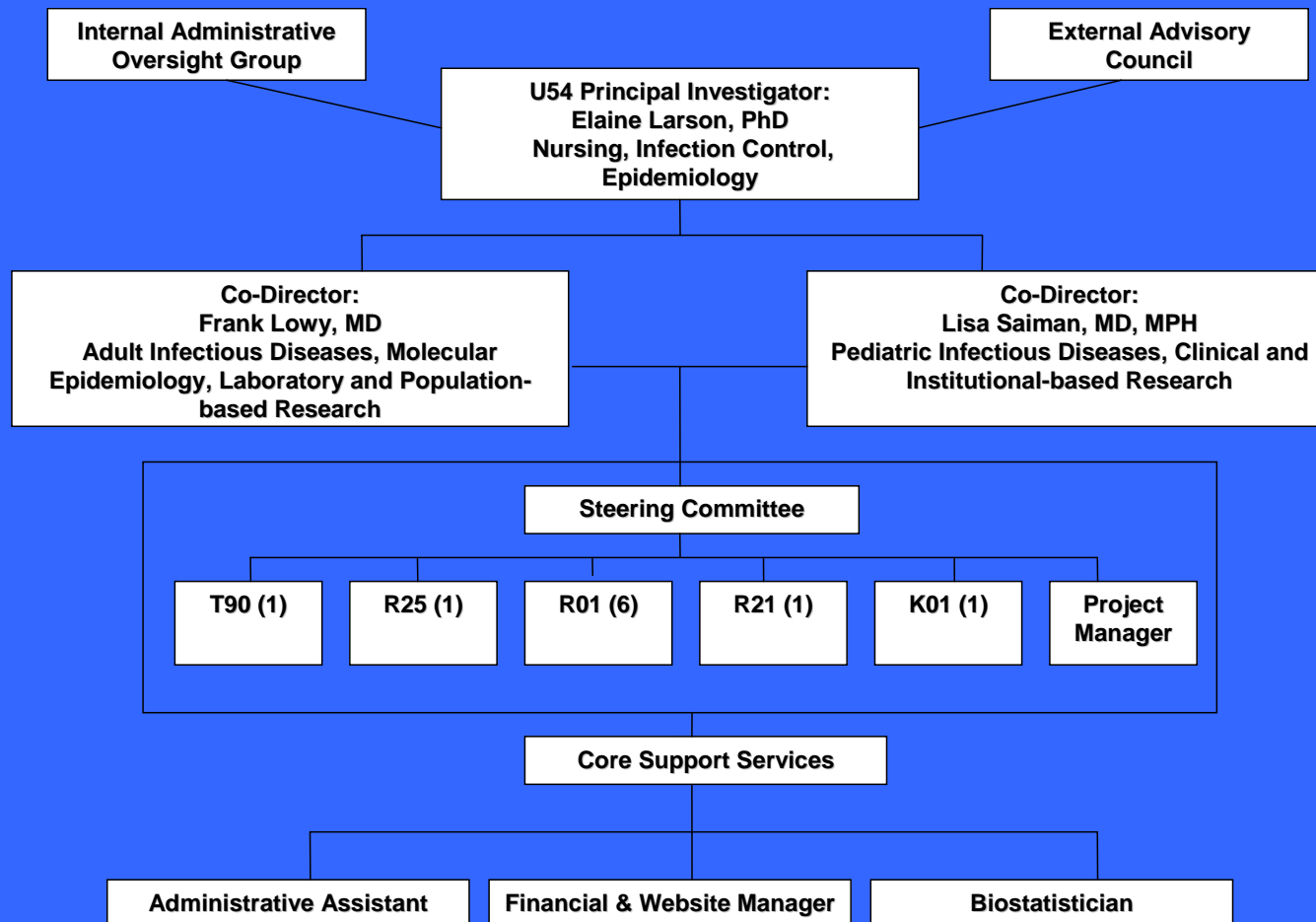
Co-Directors

Larson, Lowy, Saiman

Consortium Investigators

PI	Title	Mechanism
Larson	Consortium for Interdisciplinary Research to Reduce Antimicrobial Resistance (CIRAR)	U54
Gebbie	Training in Interdisciplinary Research to Reduce Antimicrobial Resistance (TIRAR)	T90
Bakken	Web-based Interdisciplinary Research Education and Collaboration (WIREd)	R25
Lowy	Transmission of <i>S. aureus</i> in medically underserved high-risk communities	R01 #1
Saiman	Improving antimicrobial prescribing practices in the neonatal intensive care unit	R01 #2
Stone	Effectiveness of antimicrobial resistance reduction practices in hospitals	R01 #3
Glied	Distribution of the costs of antimicrobial resistant infections	R01 #4
Tomasz	Drug resistance strategies evolving in staphylococci colonizing human populations	R01 #5
Lee	Metagenomic analysis of antibiotic resistance determinants	R01 #6
Currie	Electronic communication for antimicrobial management	R21
Razvi	Use of a web-based intervention for infection control in Cystic Fibrosis patients	K01

CIRAR Organizational Chart

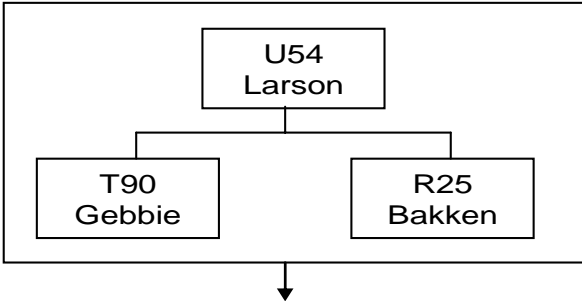


Interaction of CIRAR components, antimicrobial reduction strategies tested, and high risk populations studied

Horizontal Links

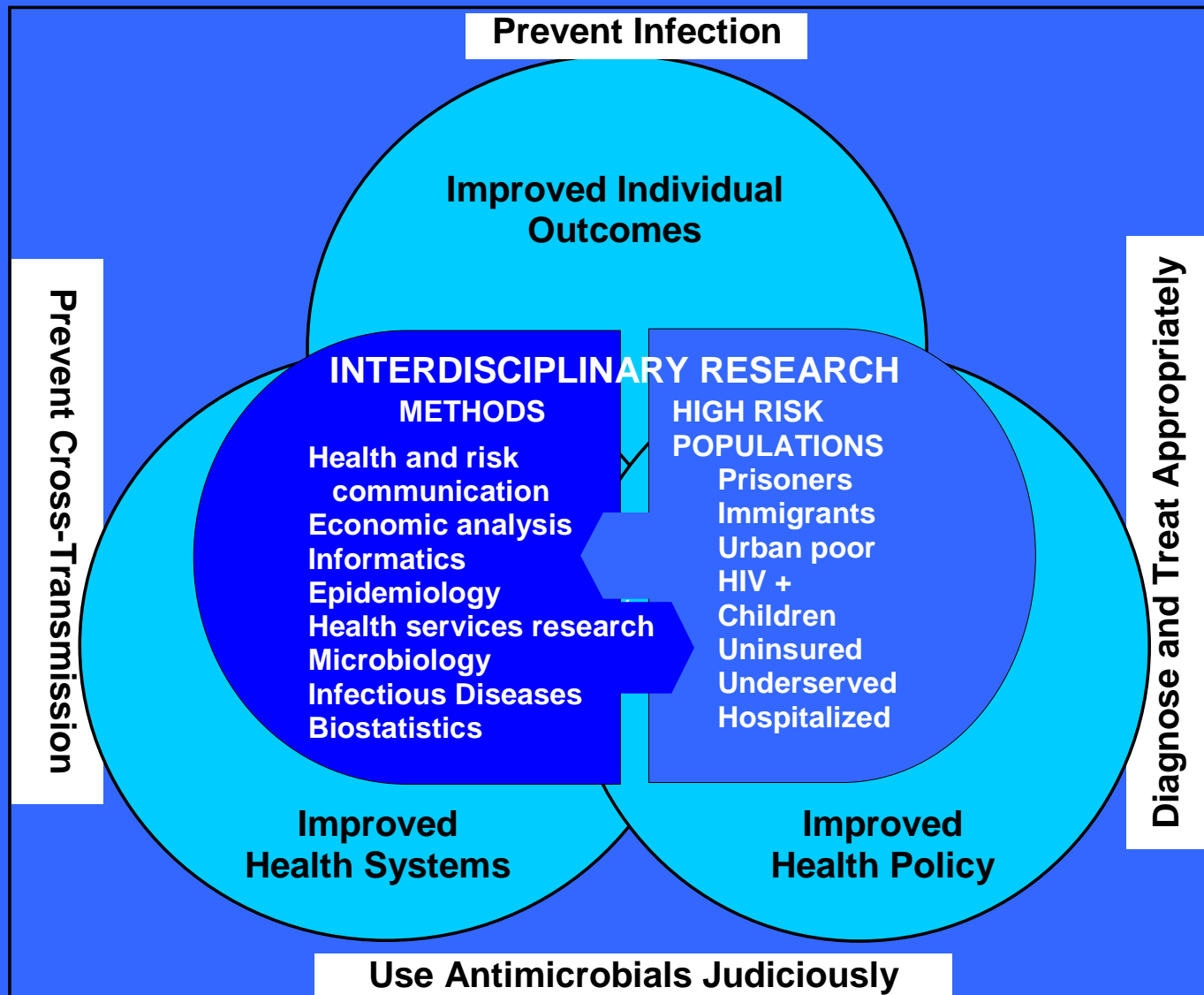
Vertically Integrated Projects

Antimicrobial Reduction Strategy				High Risk Populations/Settings					
Prevent Infection	Diagnose and Treat Rapidly	Use Antimicrobials Wisely	Prevent Transmission	Immigrants	Prisoners	Neonates / Children	HIV+	Hospital / ICU	
X			X	X	X		X		R01 #1 Lowy
X	X	X	X			X		X	R01 #2 Saiman
X	X	X	X					X	R01 #3 Stone
X			X					X	R01 #4 Glied
	X				X	X		X	R01 #5 Tomasz
	X		X			X		X	R01 #6 Lee
X		X	X			X		X	R21 Currie
X		X	X			X			K01 Razvi



= Interaction between components

Conceptual Underpinnings for CIRAR



Grant Deadlines

- **Pre-application**
 - **April 18, 2006**
- **Invitation to submit full proposal**
 - **October 2006**
- **Consortium application**
 - **December 19, 2006**
- **Budgeted start date**
 - **October 1, 2007**

Web-based Interdisciplinary Research Education and Collaboration (WIRED Collaboration)

- **PI: Suzzane Bakken, DNSc, RN**
 - (Nursing, Biomedical Informatics)
- **Mechanism: R25**
- **Collaborators:**
 - Kessin (Anatomy and Cell Biology)
 - Kukafka (Public Health, Biomedical Informatics)
 - Zimmerman (Dentistry, Biomedical Informatics)

Specific Aims

- Building upon the curriculum developed in the T90, the Web-based Interdisciplinary Research Education and Collaboration (WIRED Collaboration) project will design, implement, and evaluate a web-based approach to enhancing interdisciplinary research competency development and facilitating interdisciplinary communication related to the topic of antimicrobial resistance.

Methods

- **System design, implementation, and evaluation through iterative user-centered system life cycle techniques:**
 - Needs assessment – key stakeholders
 - Early prototype
 - Heuristic evaluation by usability experts
 - Prototype iteration
 - Usability testing with intended end-users
 - Prototype iteration
 - Pilot implementation and integration into InterTrial (NIH Roadmap and Clinical Translational Science Award)
 - Evaluation of pilot implementation – change in knowledge, skills, and attitudes; use (log analysis); ease of use, usefulness, overall satisfaction
 - System iteration
 - Implementation

Transmission of S. aureus in Medically Underserved High-Risk Communities

- **PI: Frank Lowy, MD**
 - (Adult Infectious Diseases, Molecular Epidemiology, Laboratory and Population-based Research)
- **Mechanism: R01**
- **Collaborators:**
 - **Elaine Larson** (Nursing, Infection Control, Epidemiology)
 - **Allison Aiello** (Epidemiology)
 - **Herminia de Lencastre** (Biology, Molecular Genetics)
 - **Alexander Tomasz** (Biological Chemistry)

Specific Aims

- Examine social networks of subjects from medically underserved populations (e.g., families from the Dominican Republic, HIV-infected subjects, men who have sex with men) within the community who are at increased risk for *Staphylococcus aureus* infections.
- Develop and test a network-based intervention strategy to prevent the development and spread of staphylococcal infections in these different high risk populations.

Methods - Aim 1

- Networks
 - Index case will have had an antecedent *S. aureus* infection. Study groups will include the following: 1) adults and children from the Dominican Republic in Columbia catchment area; 2) HIV infected subjects; and 3) Men who have sex with men.
- Contact tracing
 - Contacts of index cases will be identified, interviewed and cultured. Social network, spatial modeling and molecular strain typing techniques will be utilized to develop a model of how these strains penetrate into different communities extending beyond the initial exposure or risk group.
- Molecular epidemiologic analysis
 - *S. aureus* isolates will be characterized and compared by standard molecular typing techniques.

Methods - Aim 2

- A prophylactic intervention trial will explore the efficacy of two approaches – provision of educational material and a general set of instructions versus a more active intervention that involves identification of colonized subjects, environmental surveillance and eradication of colonization in all social network contacts.
- The endpoints will include prevention of infection and/or colonization with *S. aureus* in the network. A secondary endpoint will be to develop a community-based risk profile for individuals at particular risk for these infections.

Improving Antimicrobial Prescribing Practices in the Neonatal Intensive Care Unit (NICU)

- **PI: Lisa Saiman, MD, MPH**
 - (Pediatric Infectious Diseases, Epidemiology)
- **Mechanism: RO1**
- **Collaborators:**
 - Pediatrics
 - Microbiology
 - Biobehavioral medicine and adult learning
 - Pharmacy
 - Information technology
 - Biostatistics

Specific Aims

- **To assess potential Knowledge, Attitude, and Practice (KAP) barriers to implementing appropriate antimicrobial prescribing practices for late onset sepsis among neonatologists.**
- **To measure the impact of various interdisciplinary interventions on the antimicrobial prescribing practices of neonatologists.**
- **To compare the impact of the interventions on the antimicrobial resistance patterns of colonizing flora.**
- **To determine the cost effectiveness of the interventions studied.**

Methods

- **A multi-center study of university-affiliated, level III Neonatal ICUs will be performed.**
- **KAP Surveys will be developed to identify potential barriers to implementation of appropriate antimicrobial prescribing practices as outlined in the CDC 12 Step Program. Barriers to be explored will include extent of knowledge, presence of complex attitudes and belief systems, and the organizational climates of the participating NICUs.**
- **Interdisciplinary interventions including education, feed-back, and information technology will be developed and randomly assigned to the participating NICUs.**
- **Surveillance cultures to monitor colonizing flora will be obtained.**
- **A cost analysis will be performed.**

Effectiveness of Antimicrobial Resistance Reduction Practices in Hospitals

- **PI: Patricia Stone, PhD, RN**
 - (Nursing, Economics)
- **Mechanism: RO1**
- **Collaborators:**
 - Elaine Larson (Nursing)
 - Lisa Saiman (Epidemiology)
 - Dan Rabinowitz (Biostatistics)

Specific Aims

- Describe hospital processes related to preventing infections, diagnosing and treating infection prevention effectively, using antimicrobials wisely, and preventing transmission
- Determine setting characteristics (e.g., size, teaching status, region, staffing, device utilization) that predict consistency with evidence-based practice
- Estimate predictors of antimicrobial resistant hospital associated infection rates (specifically BSI, VAP and SSI).

Methods

- **Longitudinal Study**
- **Survey NHSN hospitals each year to ascertain specific process**
- **Link data to existing databases**
 - AHA
 - ARF
- **Infection data from NHSN**

Distribution of the Costs of Antimicrobial Resistant Infections

- **PI: Sherry Glied, PhD**
 - (Economics)
- **Mechanism: R01**
- **Collaborators:**
 - **Yoko Furuya (infectious disease medicine)**
 - **Joshua Graff Zivin (economist)**
 - **Sandra Hyman (epidemiology research nurse)**
 - **Clinical Data Warehouse**

Specific Aims

- **Estimate the hospital costs of hospital-acquired and community-acquired resistant infections**
- **Estimate who bears the economic burden of resistant infection**
- **Determine whether the economic costs of resistance extend to other patients, in addition to the resistant case**

Methods

- **Analysis of linked data across both Columbia and Cornell hospitals**
- **1) infection control \Rightarrow cost data \Rightarrow reimbursement and payer data**
 - **Compare resistant and non-resistant infection cases**
- **2) Index patient data \Rightarrow susceptible patient data \Rightarrow cost data**
 - **Compare susceptibles exposed to resistant and non-resistant infections**

Drug Resistance Strategies Evolving in Staphylococci Colonizing Human Populations

- **PI: Alexander Tomasz, PhD**
 - (Biochemistry)
- **Mechanism: R01**
- **Collaborators:**
 - Microbiology
 - Pediatrics
 - **Bioinformatics (Rockefeller University)**

Specific Aims

- Determine origin, chromosomal location and mode of spread of the beta-lactam resistance gene *mecA* and its carrier structure *SCCmec*
 - in *S. aureus*, *S. epidermidis* and *S. warneri* clones - recovered in CIRAR.
- Determine mechanisms of vancomycin resistance and tolerance in *S. aureus*, *S. epidermidis* and *S. warneri* clones identified in CIRAR.
- Determine the role of genetic background in the level of beta-lactam resistance in *S. aureus* clones circulating in CIRAR.
- Detect molecular level changes in the epidemic character of *S. aureus* clones during passage from one human host to another.

Methods

- DNA probes and sequencing will be used to identify variations in the SCC*mec* types and the putative origin of this carrier structure among various staphylococcal species.
- High resolution biochemical analysis of cell wall structure, electronmicroscopy and biochemical experiments will be used to determine the mechanism of decreased vancomycin susceptibility in *S. epidermidis* and *S. warneri*.
- Comparative DNA sequencing of highly resistant and isogenic low resistant MRSA will be used to identify determinants that appear to define oxacillin resistance level in MRSA.
- The high degree of polymorphism in the fibronectin binding protein and clumping factor genes will be used to identify changes at the surface of a *S. aureus* clone as it is passed from one human colonization site to another.

Metagenomic Analysis of Antibiotic Resistance Determinants

- **PI: Seok-Woo Lee, MS, DDS, PhD**
 - (Periodontics, CDM)
- **Mechanism: RO1**
- **Collaborators:**
 - **Katherine Chen (Obstetrics and Gynecology)**
 - **Panos Papapanou (Periodontics, CDM)**
 - **Bin Cheng (Biostatistics)**

Specific Aims

- **To identify both known and unknown antibiotic resistance determinants from oral, vaginal, and other microflora**
- **To globally assess the diversity and distribution of antibiotic resistance determinants among different bacterial populations**

Environmental sample

Metagenomic library construction

**Extract
DNA**



Clone



**Transform into a
host bacterium
(e.g. *E. coli*)**

Metagenomic library

**Metagenomic
analysis**

**screen for particular
sequences by PCR or
hybridization**

**random
sequencing**

**screen for
expression of
particular phenotypes**

Methods

- **Collection of microbial samples from different niches: oral, vaginal, and other areas**
- **Extraction of bacterial genomic DNA from the samples**
- **Construction of genomic library by inserting DNA into the *E. coli* vector**
- **Screening of the library for resistance based on expression or the known sequences**
- **Identification of already known or novel resistance determinants**

Significance

- **Allows identification and characterization of resistance determinants from uncultivable bacteria**
- **Provides a global view of the genetic diversity of antimicrobial resistance among different microbial populations in health and disease**
- **May lead to discovery of novel resistance mechanisms**
- **May lead to development of new antibiotic drugs inhibiting novel resistance mechanisms**

Electronic Communication for Antimicrobial Management

- **PI: Leanne Currie, DNSc, RN**
 - (Nursing, Informatics)
- **Mechanism: R21**
- **Collaborators:**
 - Philip Graham (Medicine, Epidemiology)
 - Lisa Saiman (Pediatric Infectious Diseases, Epidemiology)
 - Samiya Razvi (Pediatrics, CF)

Specific Aims

- **Aim 1: To evaluate adherence to a prescribing guideline**
 - **Sub Aim 1: To accurately represent guideline knowledge in the clinical information system**
- **Aim 2: To evaluate clinician perception of handoff communication (continuity of care)**
 - **Sub Aim 2: To automate interdisciplinary handoff communication related to the prescribing guideline**

Methods

- **Phase I - System Development**
 - **Guideline knowledge representation and integration into clinical information system**
 - **Automate interdisciplinary handoff communication**
- **Phase II - Evaluation**
 - **Evaluation of guideline adherence pre-post**
 - **Evaluation of perception of handoff communication pre-post**

Use of a Web-based Intervention for Infection Control in Cystic Fibrosis Patients

- **PI: Samiya Razvi, MD**
 - **(Pediatrics)**
- **Mechanism: K01**
- **Mentors: Lisa Saiman, MD, MPH; Lynne Quittell, MD**
- **Collaborators:**
 - **Medicine: Pediatric Pulmonology and Pediatric Infectious Diseases**
 - **Basic sciences: Microbiology**
 - **Behavioral Science**
 - **Nursing**
 - **Social work**
 - **Bio-informatics and Information Technology**

Specific Aims

- *Specific Aim I:*

To conduct a pre-intervention survey to assess baseline knowledge, attitudes and practices of patients with CF and their families regarding Infection Control recommendations.

- *Specific Aim II:*

To develop a focused educational intervention (reinforced by a web-based tool) for patients with CF and their families, in order to improve adherence to existing recommendations for hand hygiene, nebulizer cleaning and socialization with other patients with CF.

- *Specific Aim III:*

To evaluate the efficacy of the educational intervention and the web-based tool, in improving adherence by patients with CF and their families to the three specified recommendations for Infection Control in CF.

Methods

- ***Study population:***
 - Pediatric patients with Cystic Fibrosis and their families
- ***Design:***
 - Multi-center randomized clinical trial (full intervention group and a control waiting group)
- ***Study Intervention:***
 - Focused educational intervention with a web-based reinforcement strategy targeting each of the following recommendations for infection control in CF:
 - Hand hygiene
 - Nebulizer cleaning
 - Socialization with other persons with CF
- ***Primary outcome measure of the study:***
 - Adherence to the 3 specified recommendations in infection control by CF patients and their families

Conclusion

- **Questions?**
- **Feedback?**
- **Suggestions?**
- **Contact:**
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 - **cww2106@columbia.edu**
 - **(212) 342-4111**