Actionable Information for Antimicrobial Stewardship:
How data can combat antimicrobial-resistant bacteria in Veterans

Makoto Jones, MD, MSCI
HSR&D CDA Awardee
May 9, 2017
Discussant & Mentor: Michael Rubin, MD, PhD, MS

Acknowledgement

- VA HSR&D CDA funding
- Mentors: Michael Rubin (primary)
  - Matthew Samore
  - Charlene Weir
  - Tom Greene

  - Advisors
    - Matthew Goetz
    - Christopher Nielson

Poll Question #1

- When I say Antimicrobial Stewardship, you say?
  - HSR!
  - What's antimicrobial stewardship?

Poll Question #2

- Select the role that best describes you:
  - Steward
  - Clinician usually receiving advice from a steward
  - Clinician that's not heard of stewardship
  - Researcher interested in stewardship
  - Researcher that doesn't yet realize a latent interest in stewardship

Objectives

- Discuss what antimicrobial stewardship is
- Discuss what stewardship needs
- Outline cognitive needs of stewards
- Discuss antimicrobial effects
- Discuss decision support in complex systems

Poll Question #3

- At the dawn of modern medicine, there was no specialty of infectious diseases because
  - Cardiovascular and cerebrovascular disease, and cancer were the biggest killers
  - It lagged behind the other specialties in methods and discoveries
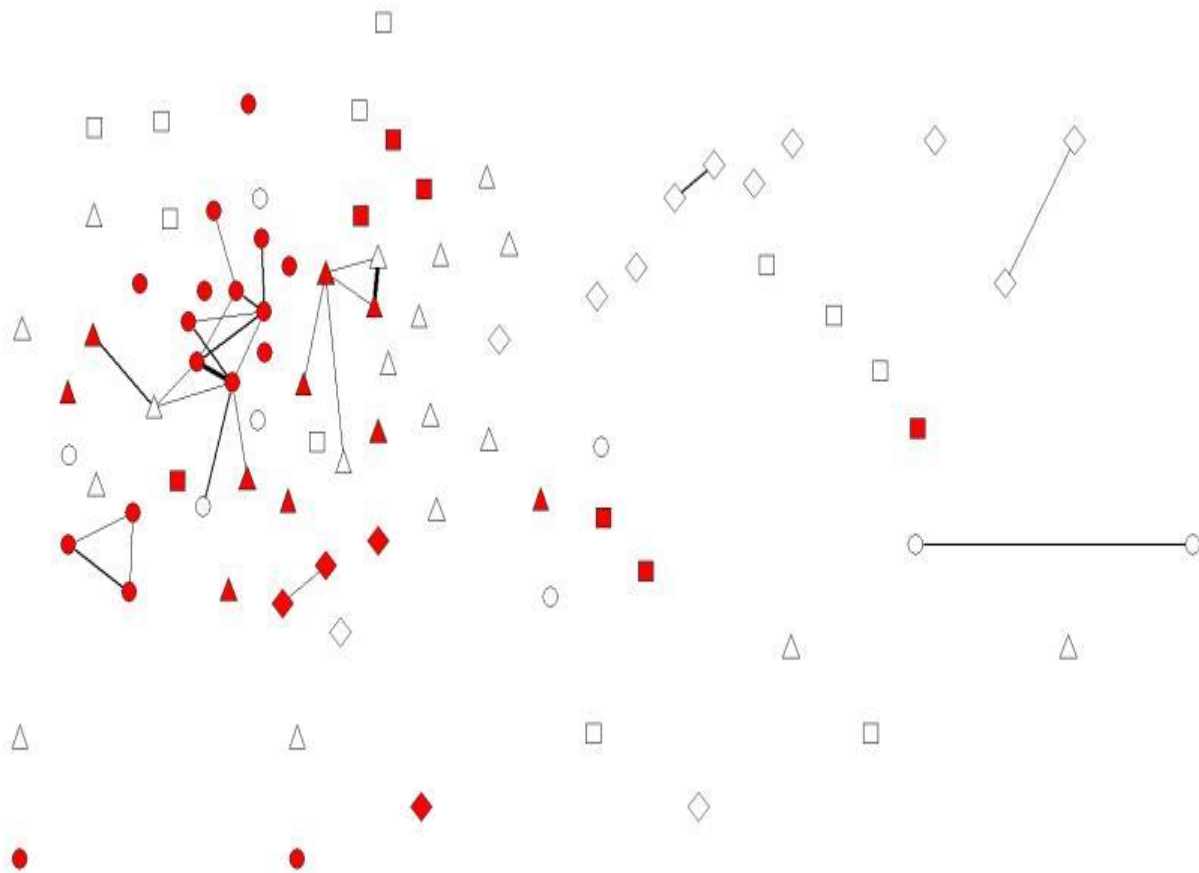 - Most of what everyone treated was infectious diseases

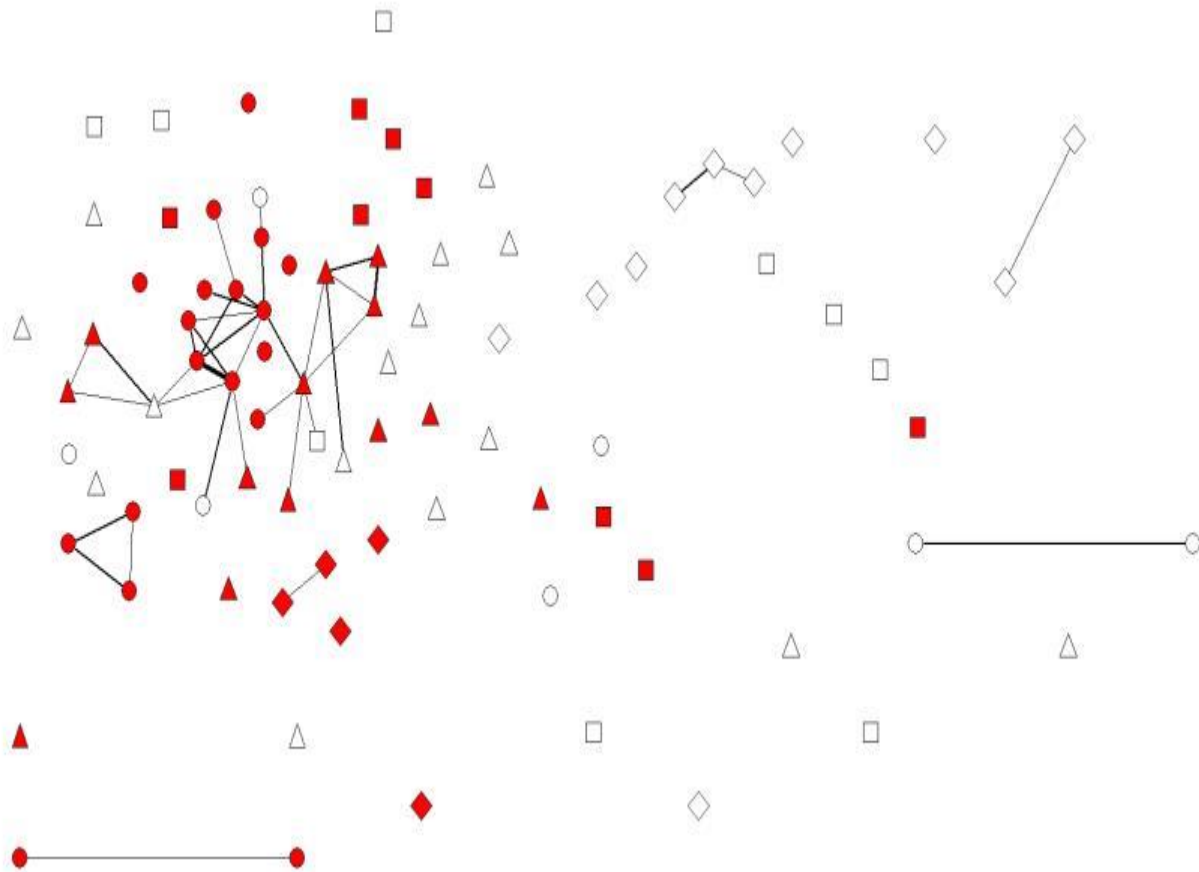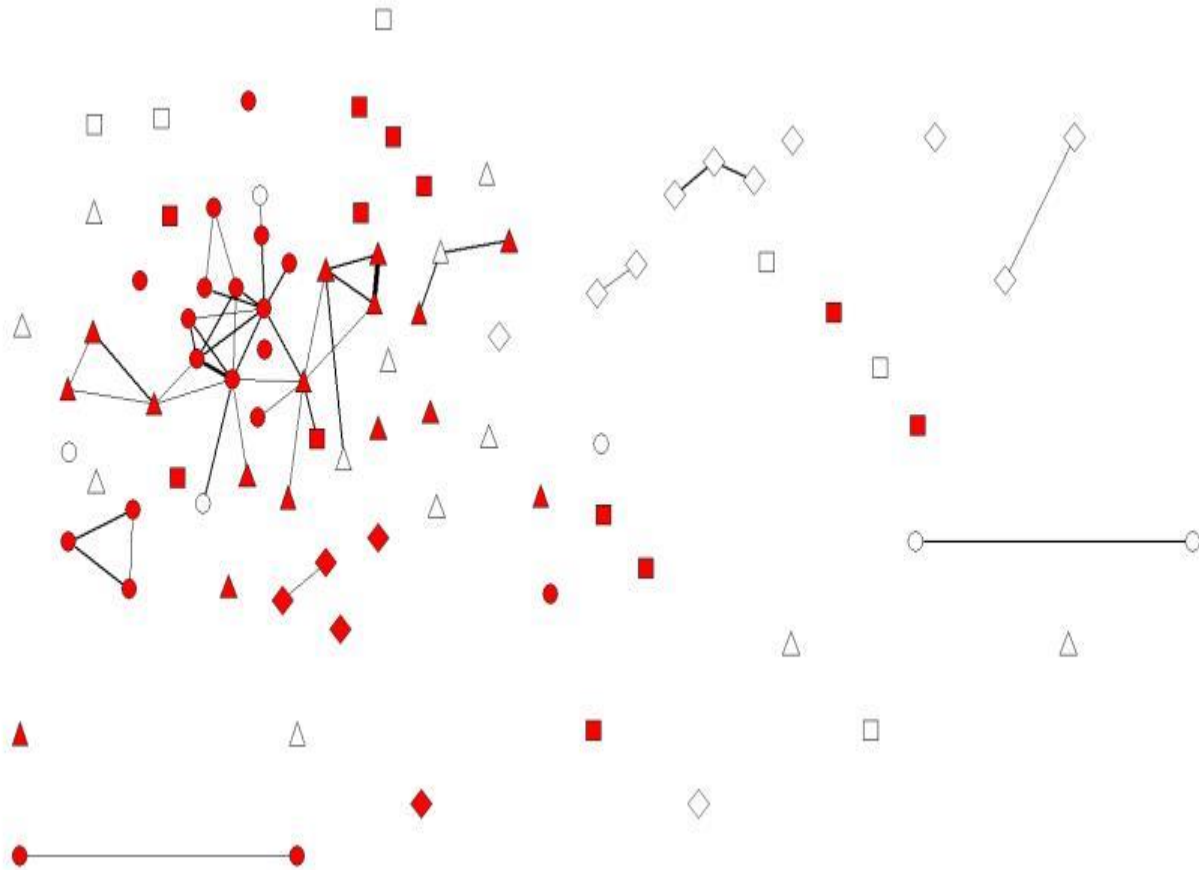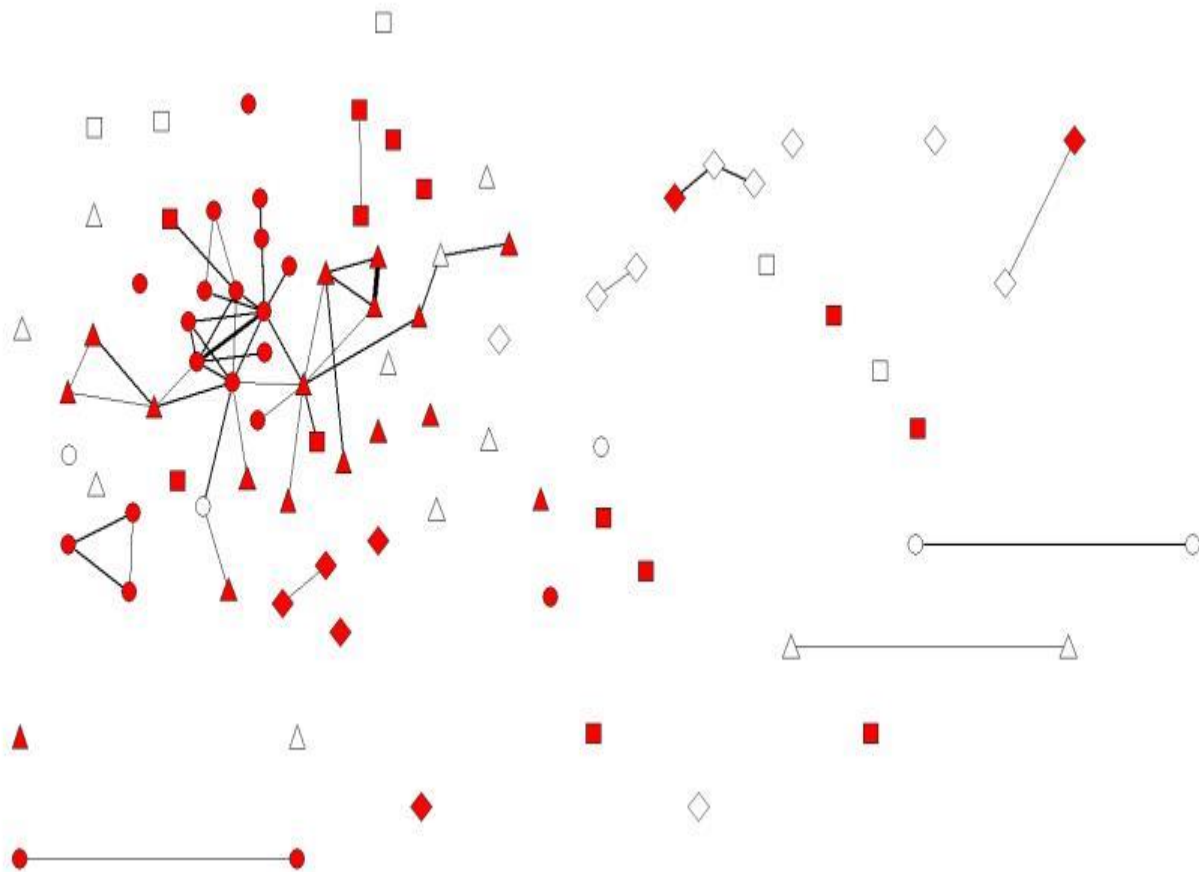# Movement of CRKP-positive patients in 2005 (or, one reason you should care)
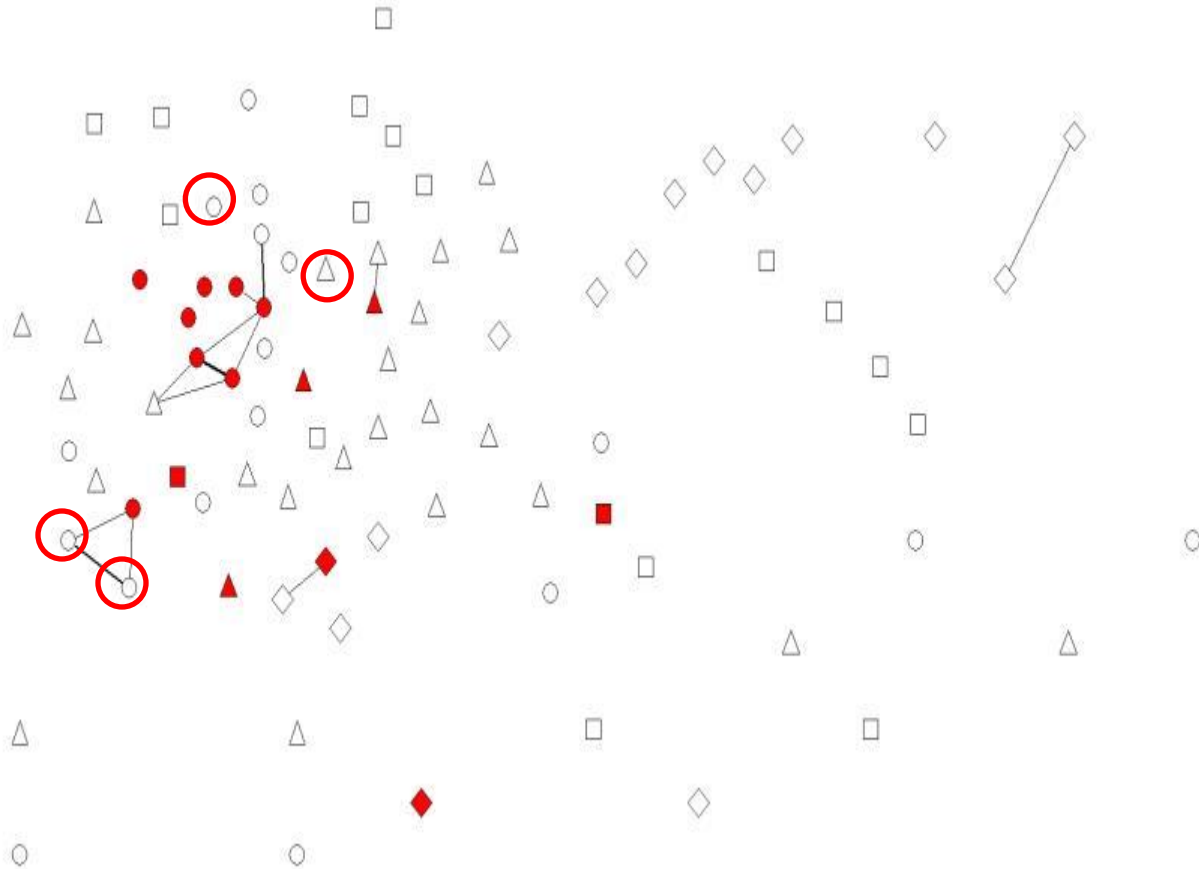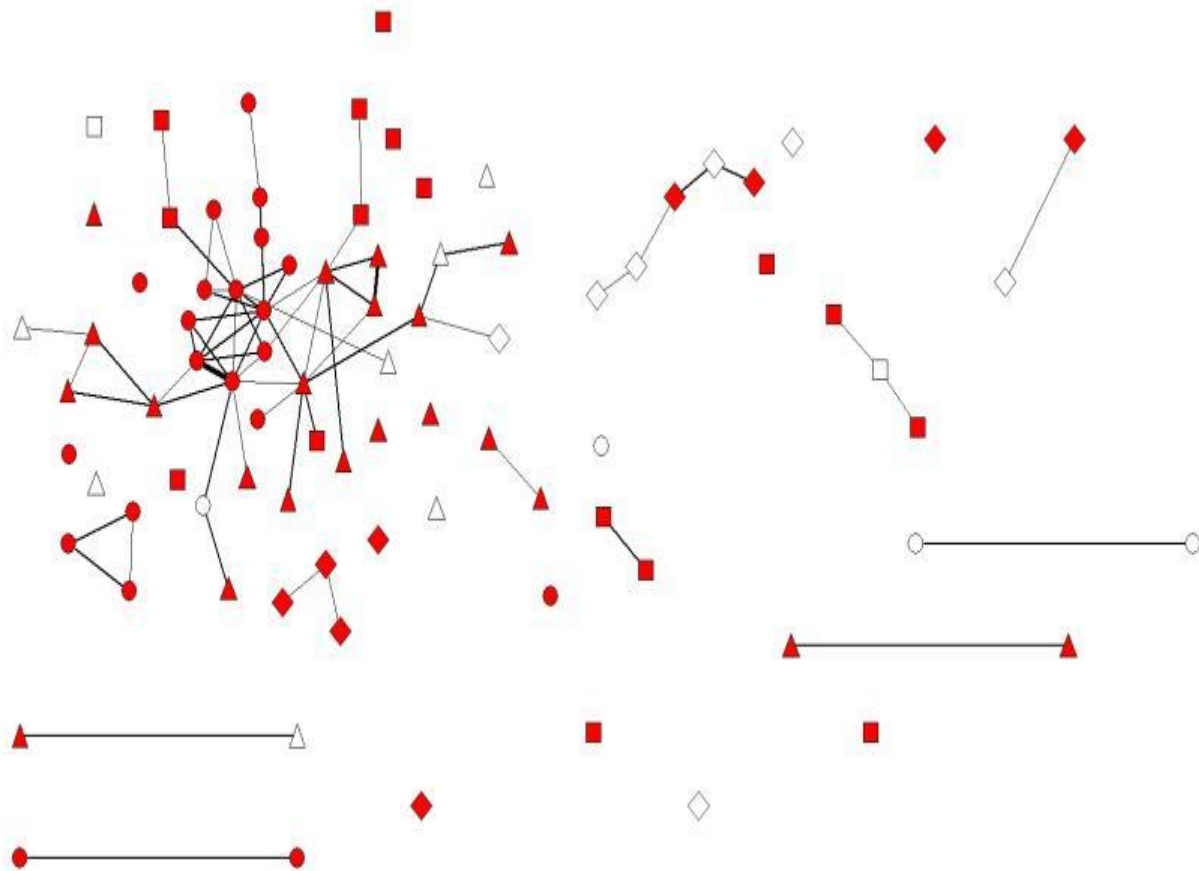
2006
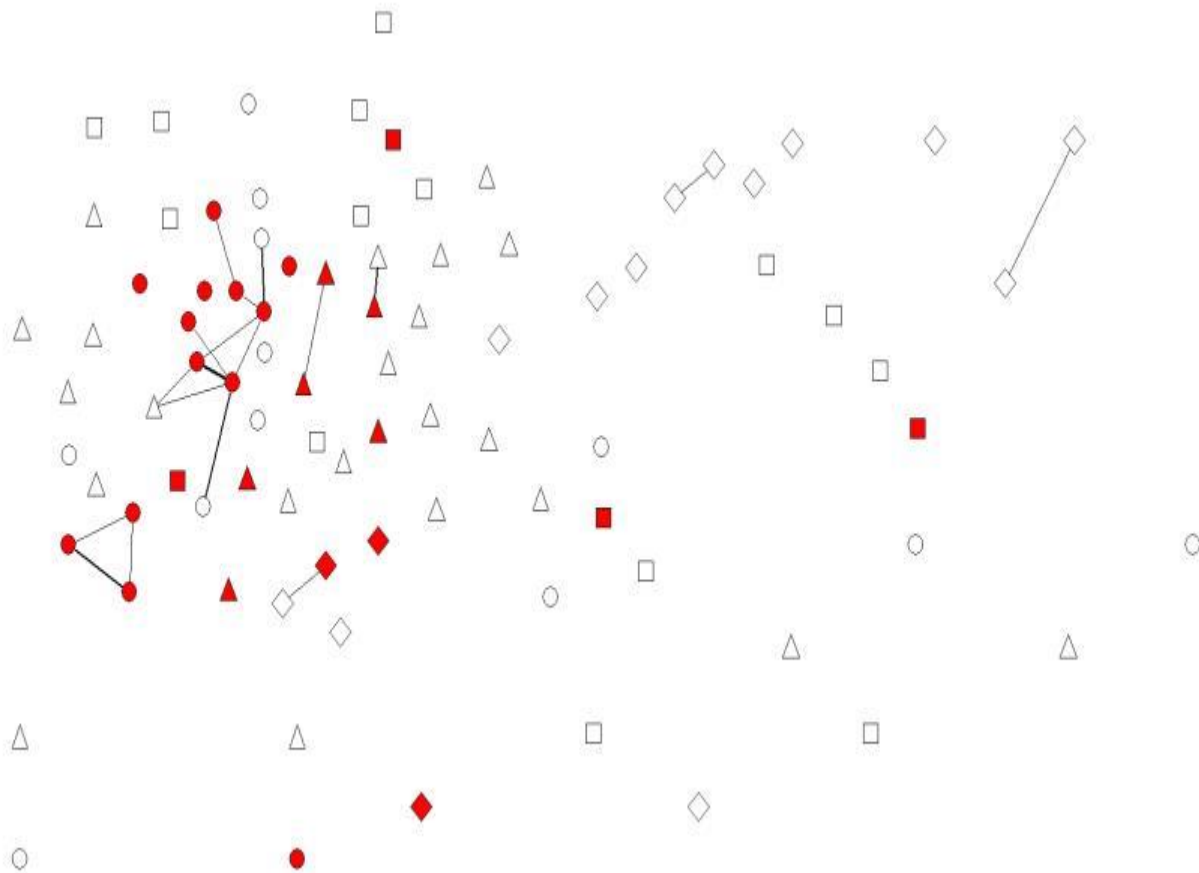
2007

2008

2009

2010

2011

2012
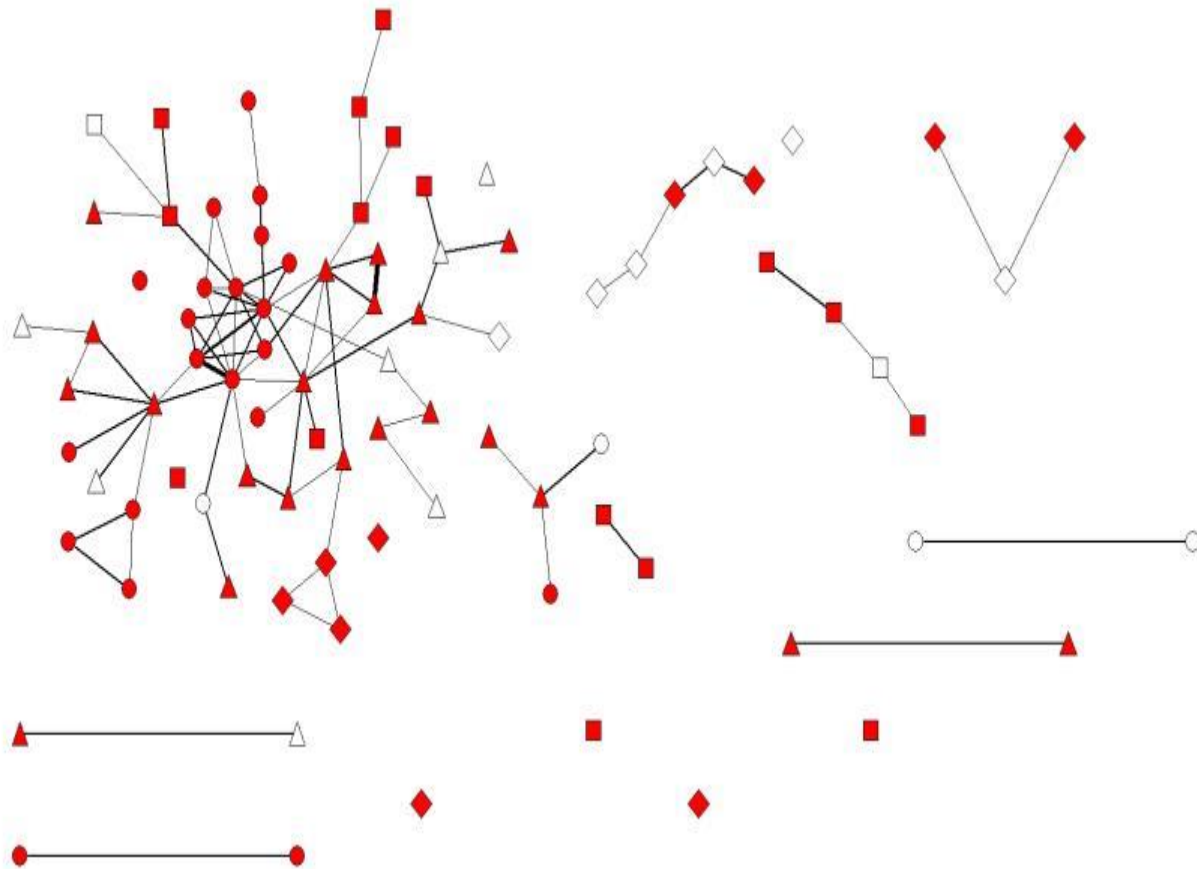
2013

Antimicrobial resistance, practice, outcomes, and stewardship

Getting on the antimicrobial bus
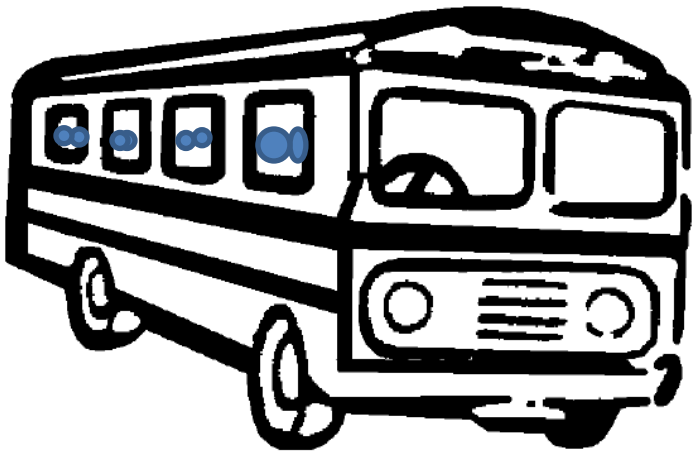
- Need to clarify goals[1]
- Need to clarify effects[2]
- Need to support decisions[3]
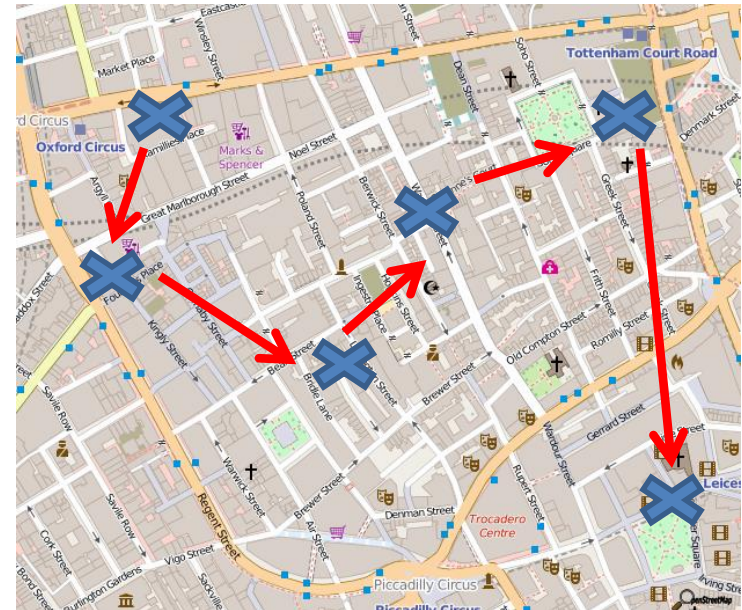
1. Whose goals?   2. Effects on me & on you.   3. By decision-maker perspective

What's the hold up?

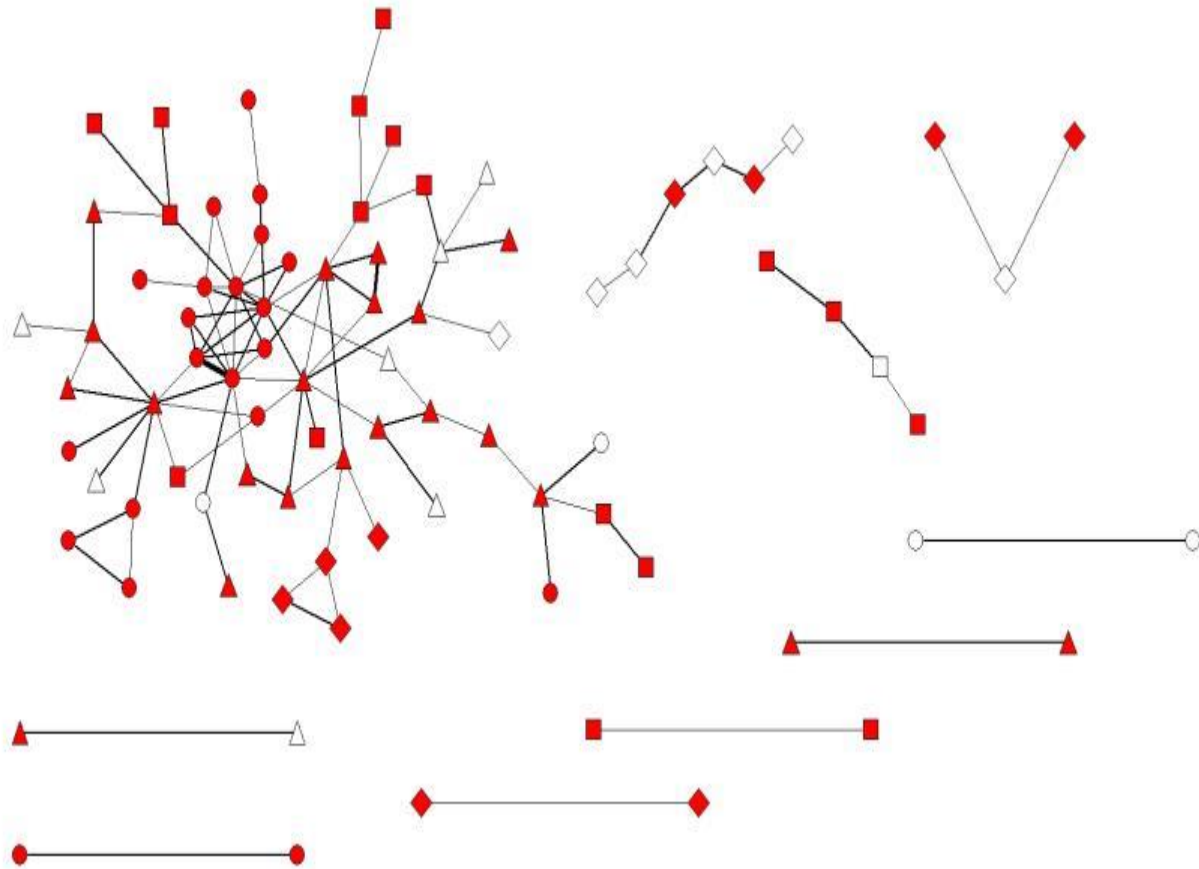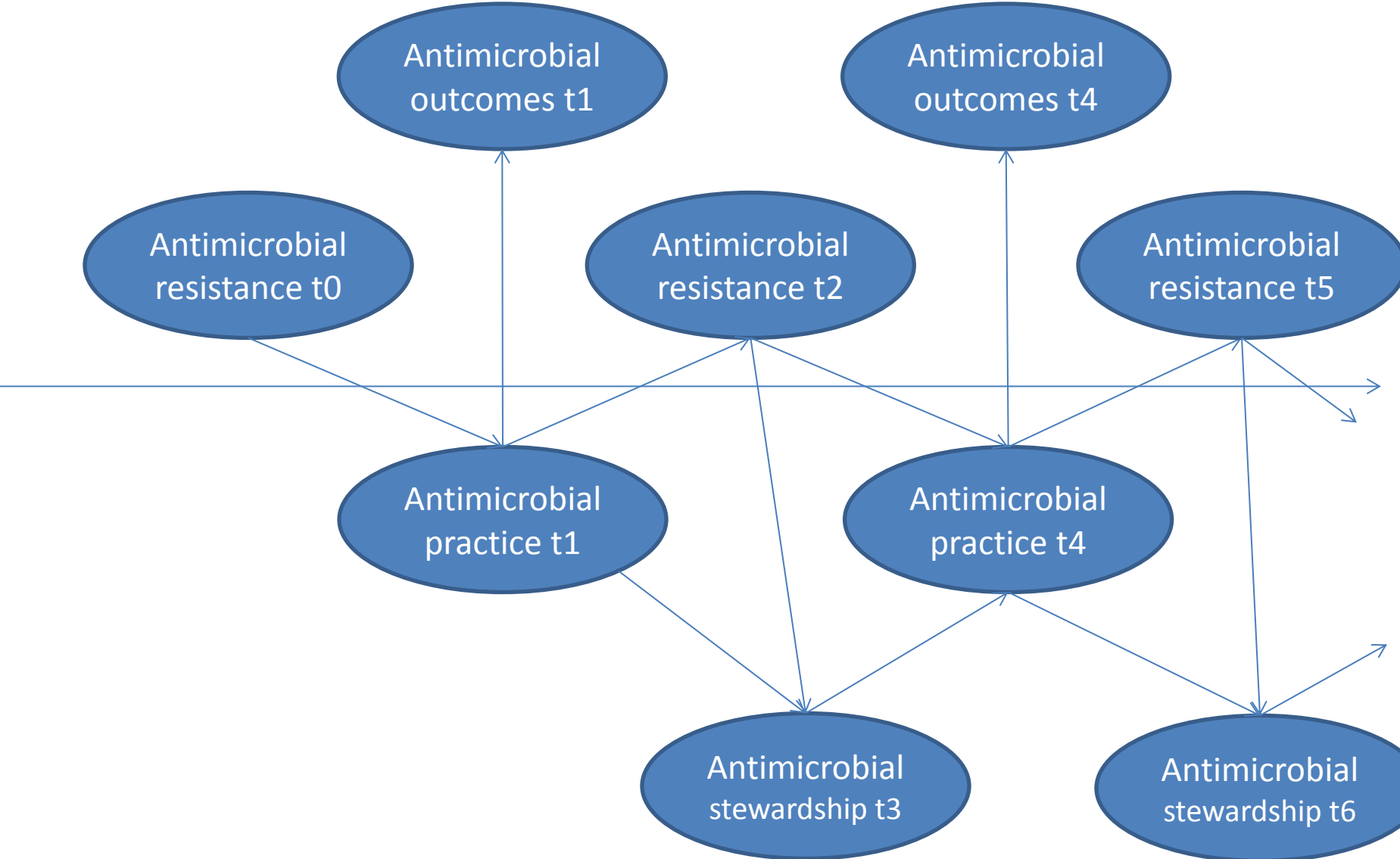Comparison of 41 IDSA guidelines using percentage distribution of quality of evidence underlying individual recommendations.
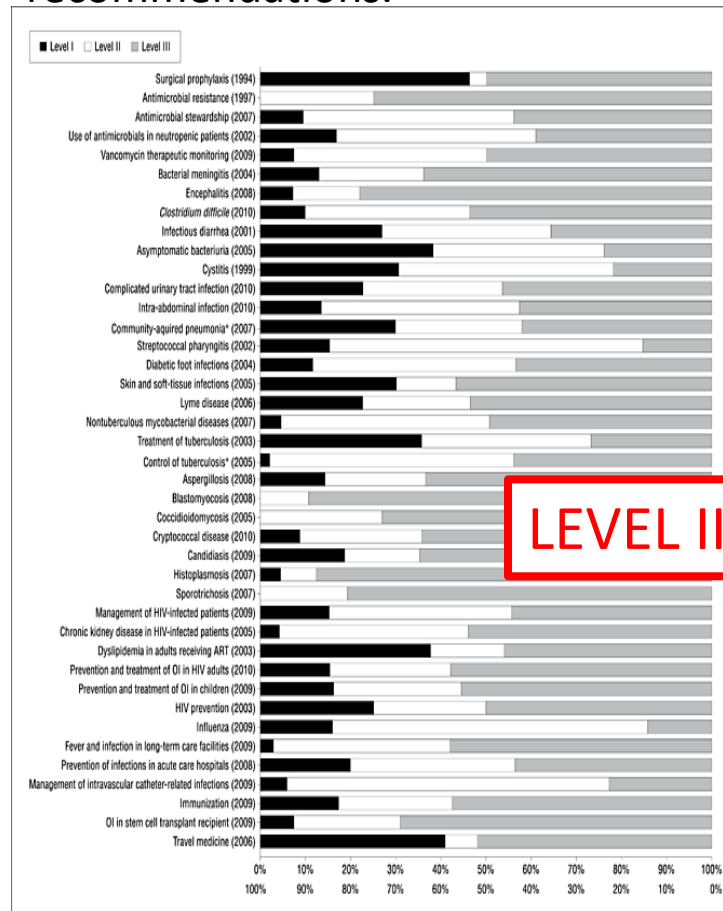
Level III, evidence from opinions of *respected* authorities based on clinical experience, descriptive studies, or reports of expert committees

Lee et Vielemeyer (2011). Arch Intern Med 171:18-22.

Swiss cheese model—why diversity *may* be good in antimicrobial stewardship
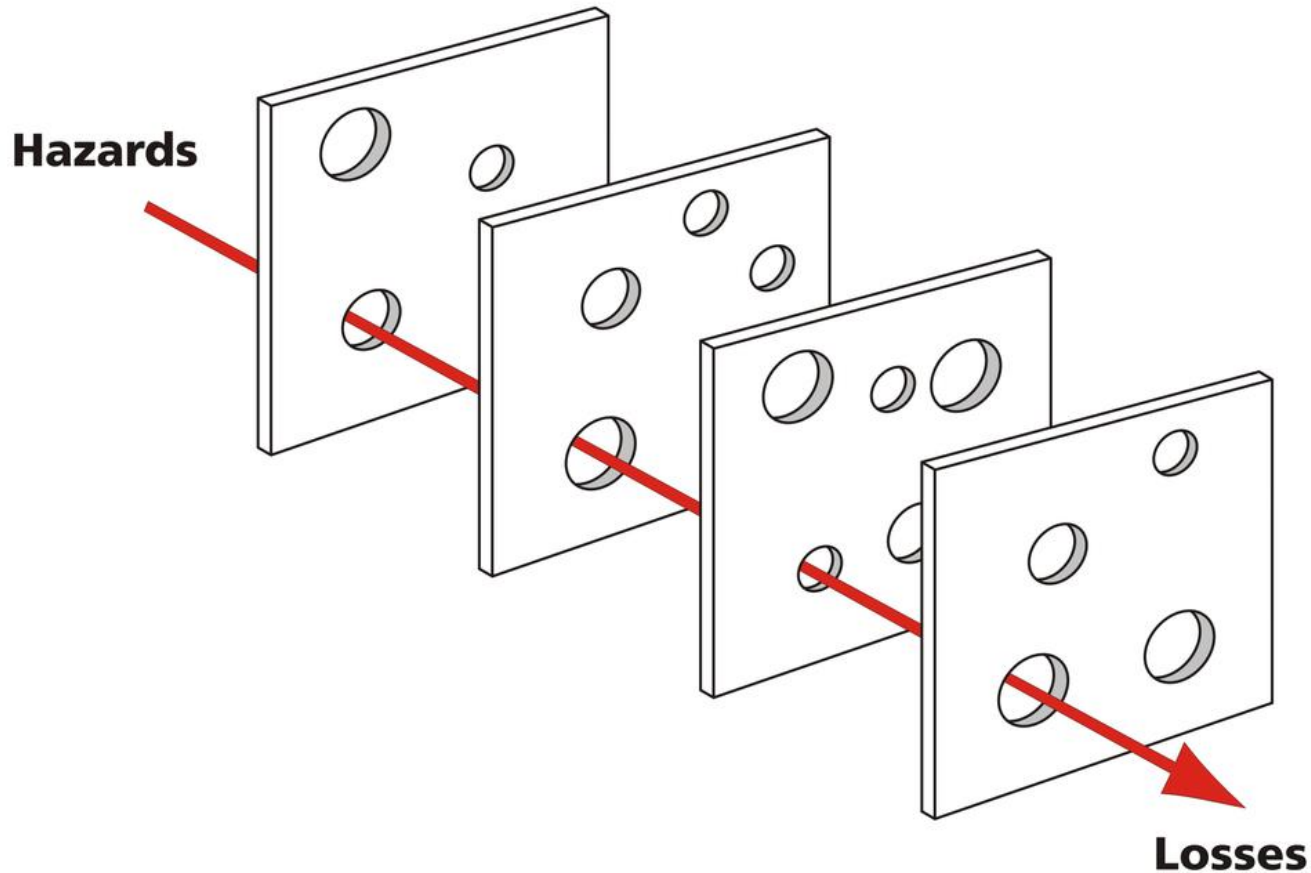
Specific Aims

1. Characterize the information needs and decision-making patterns of stewards when making antibiotic recommendations

2. Identify predictors of antibiotic coverage and emergence of resistance from local antibiotic use and resistance data

3. Develop a clinical decision-support system that nudges and prompts stewards to use local hospital data and test the influence on stewards

Semi-structured interviews based on Rasmussen's decision ladder

|	Construct	Explanation
1	Activation/ alert	Contexts, situations, and electronic triggers bring a potential problem to one's notice. Often these were social or embedded automatic work processes.
2	Appraisal/ interpretaton	What is the nature or "gist" of the problem? A common, systematic process was used to clarify the nature of the problem. The patient's acuity and the team's impression were the most vivid source of information. Chart review was performed when the details of the case did not fit a recognized pattern.
3	Information to act	What information do I need to act? Information on diagnosis, urgency, and team motivation and expertise were integrated to identify what to do. If the situation matched a protocol, they would use it directly, suggesting a mental shortcut or System 1 thinking in Dual Process Theory[2] parlance.
4	Activity/ action	Some have learned to avoid talking about resistance as a motivation or to use indirect narratives to negotiate the balance between resistance and treatment. Actions were taken to set up future "triggers" as part of the negotiation process as well as action in the future.
5	Expectation/evaluation	What more needs to be done? How has the patient responded? Many stewards noted that it is easier to make changes after 2-3 days of therapy. One steward expressed "if something happens [when recommending antibiotics or no antibiotics in the first few days] they're going to blame you from here to eternity."
6	Information gathering	Do I need more information to evaluate?
7	Information strategy	Where and how do I find the information that I need?

Triggering information

1

System 2

7

System 1

Inner triggering

2

6

3

5

4
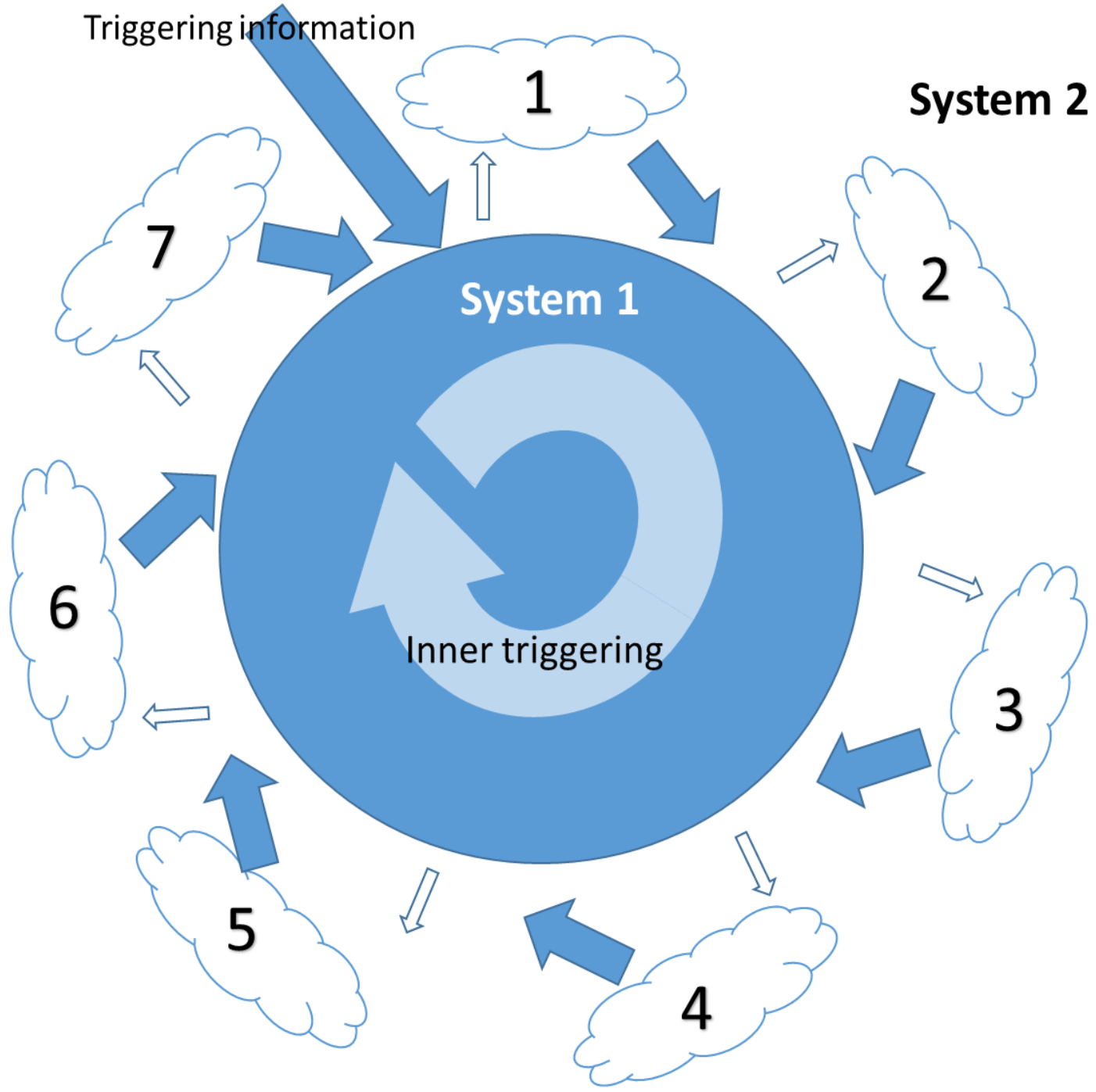
"Force fields"

- Diagnosis
- Severity of illness
- Culture
- Personal valuation of science
- Curiosity
- Bedside access
- Power
- Legitimacy
- Social influence
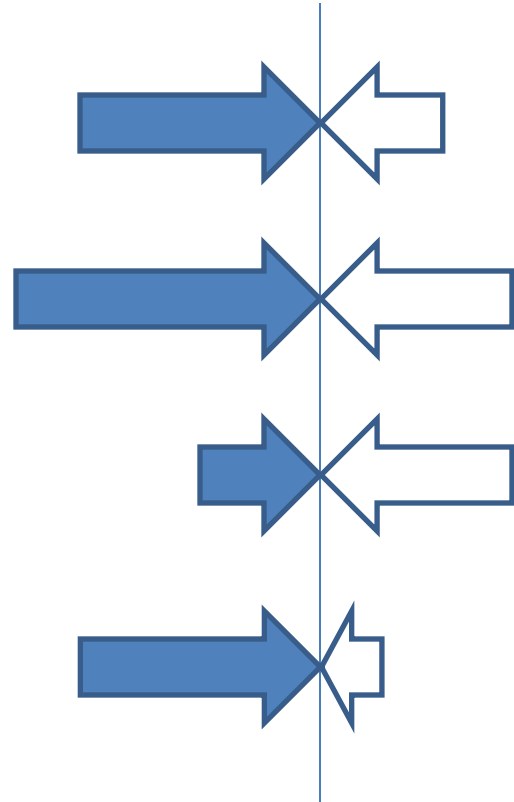
Examples

Construct	Example
Activation/alert	receive alert, phone call, consult; search for orders, review in COTS; might miss
Appraisal/interpretation	Dx->Abx->Guidelines->minimize resistance
Information to act	Labs, imaging, vitals-->hx, Rx, abx hx, allergies
Activity/ action	Make recommendation, concede, conversation, make follow-up plan, consult, go up the chain,
Expectation/ evaluation	follow-up labs, follow acceptance rates, look at the patient, develop metrics
Information gathering	is the information is inconsistent, incoherent
Information strategy	review the chart, call the team, see the patient

Predictors of coverage and resistance

DEALING WITH HUMAN CREATIVITY SO THAT YOU CAN DO QUANTITATIVE RESEARCH

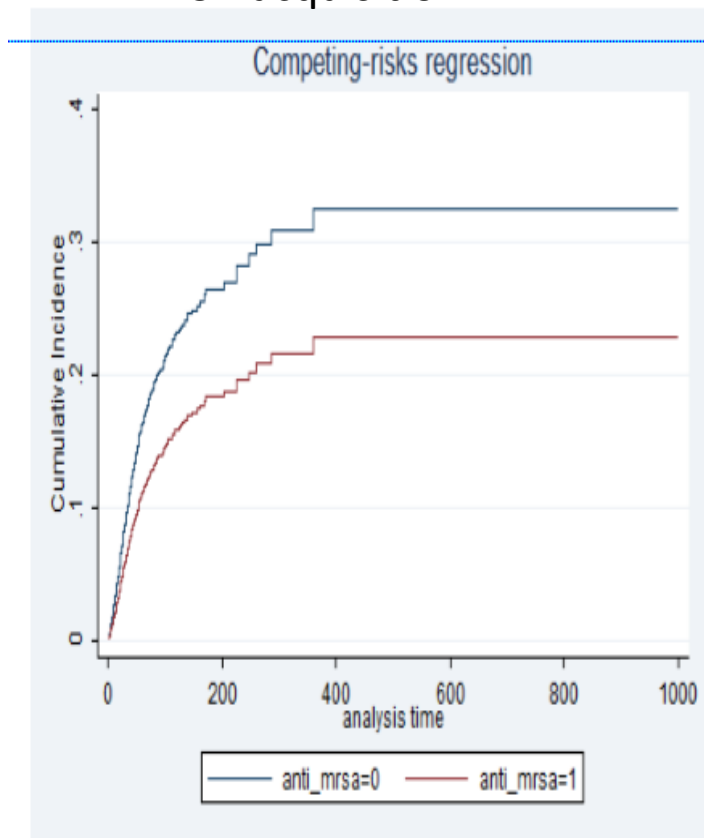# Understanding Potential for Vancomycin De-escalation

PMID:25103488
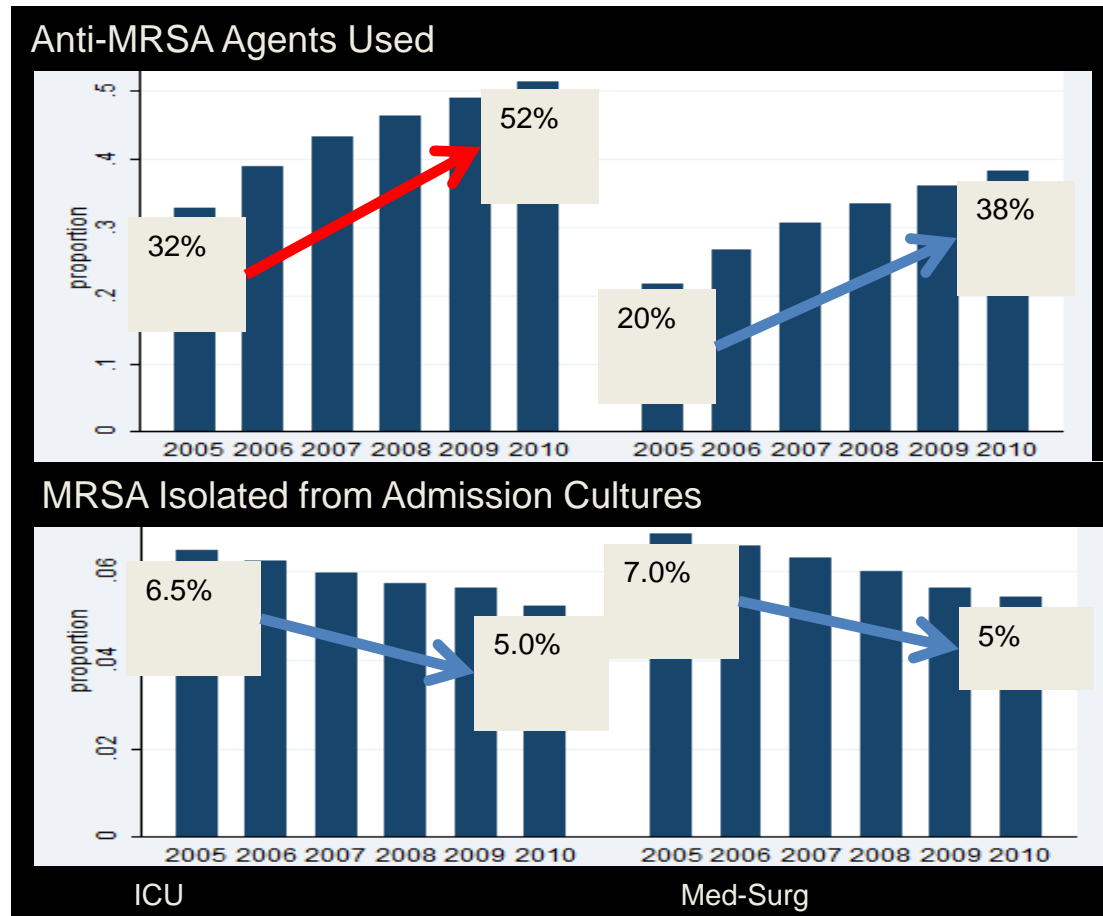
Matching weights analysis:
Initial choice of antibiotics on d4+ outcomes (cohort d4+)
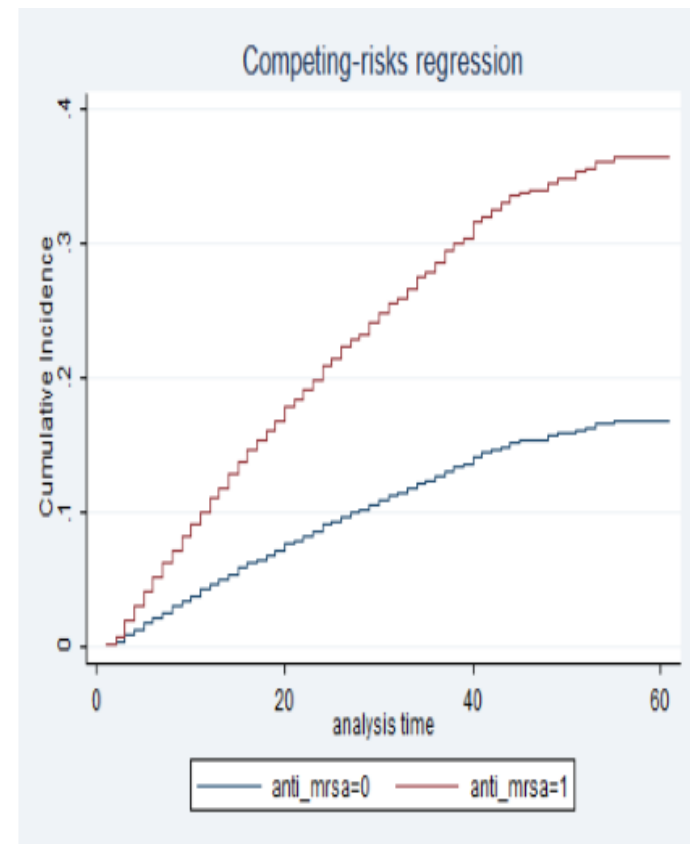
Impact of anti-MRSA antibiotics

Outcome	Unweighted	Weighted
MRSA Acquisition	1.3347 (95%CI 1.2063-1.4768)	1.1923 (95%CI 1.0390-1.3682)
Nosocomial MRSA	1.1661 (95%CI 0.9709-1.4005)	1.0460 (95%CI 0.8261-1.3243)

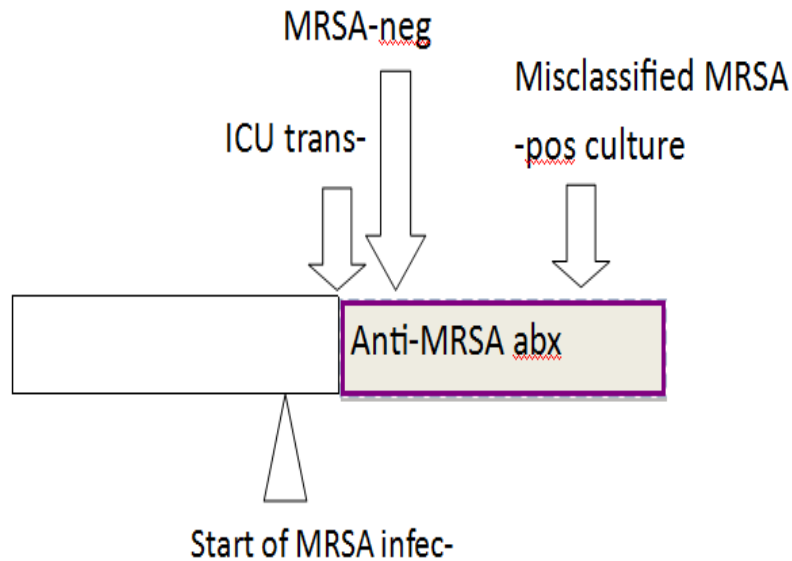# Anti-MRSA therapy and MRSA acquisition and MRSA-positive cultures

MRSA acquisition

MRSA+ cx
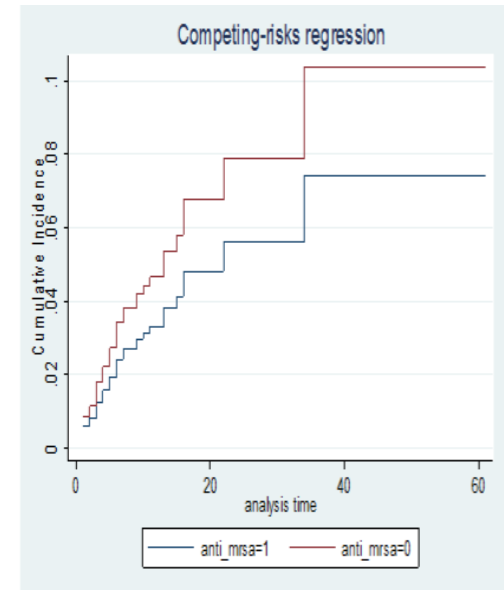
Misclassification of the exposure

MRSA+ cx among those Rx'd for ?CONS BSI

MRSA-neg

Misclassified MRSA

ICU trans-

-pos culture

Anti-MRSA abx

Start of MRSA infec-

Competing-risks regression

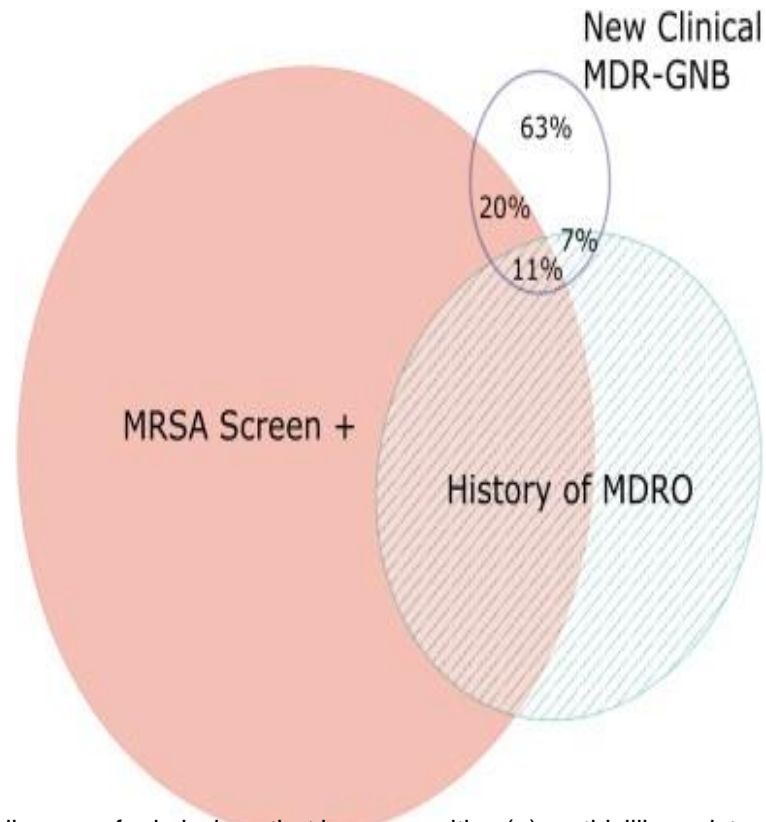 analysis time — anti_mrsa=1 — anti_mrsa=0

MRSA screens predict other MDRO

Fig 1. Euler diagram of admissions that have a positive (+) methicillin-resistant Staphylococcus aureus (MRSA) polymerase chain reaction hospital admission nares screen, have a history of a clinical multidrug-resistant organism (MDRO) (including MRSA, vancomyc...

Predicting CR-*Klebsiella*
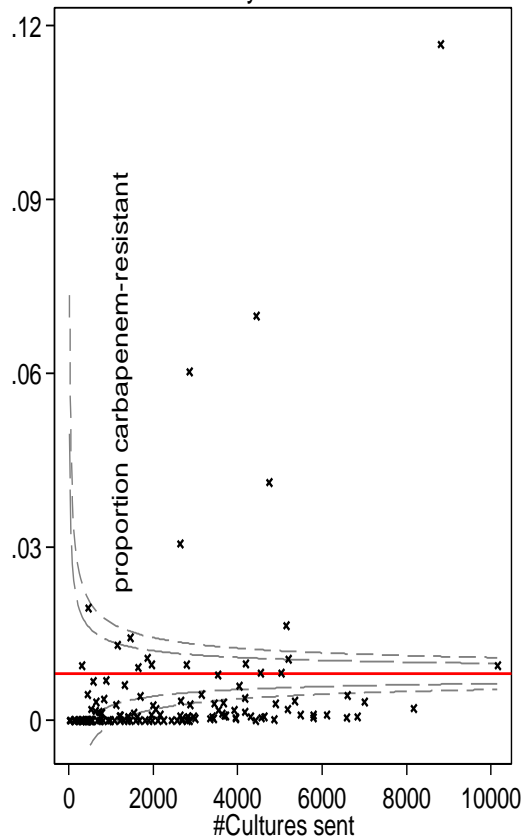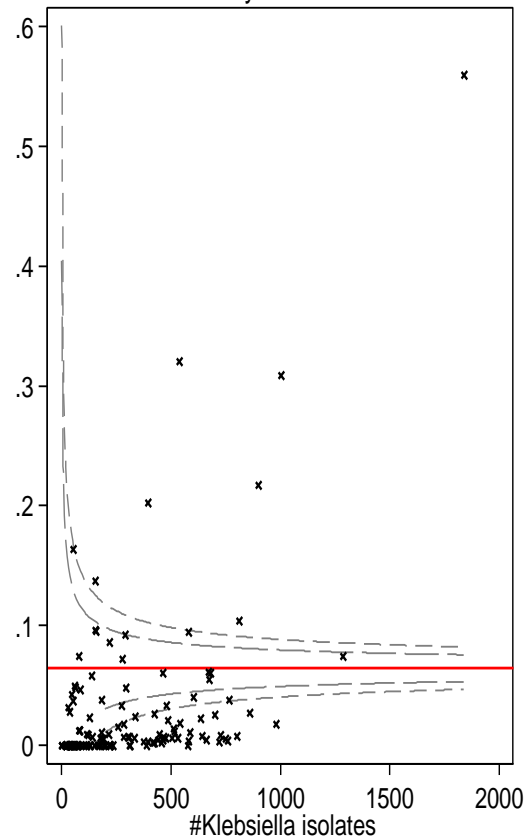
Table 2. Multi-variable model predicting CRK growth

**Non-susceptibility to an antibiotic in an organism that is not constitutively resistant.

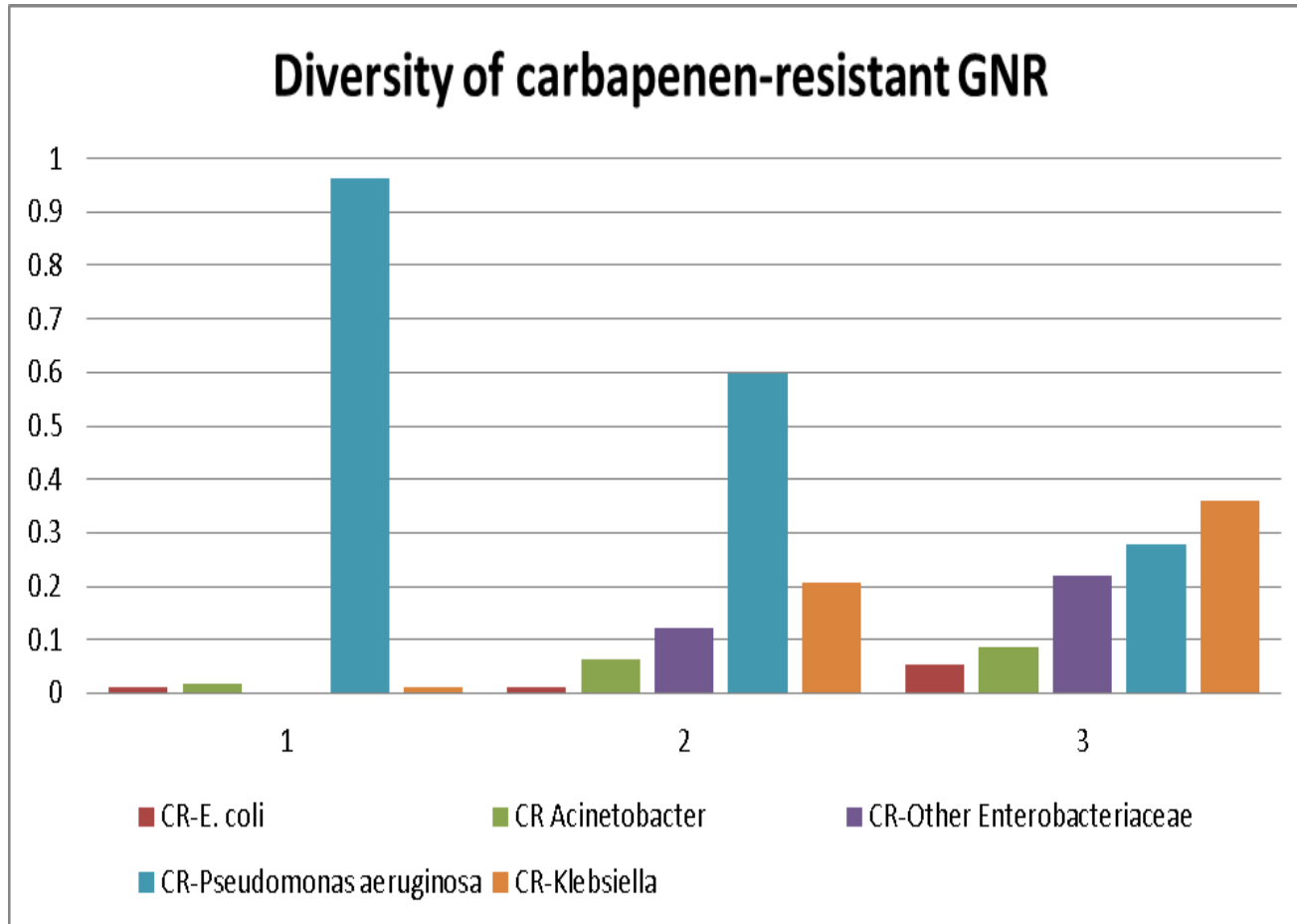| Factor	Odds ratio	95% CI
History of non susceptibility in the past year (any organism)**		
amikacin resistant	2.03	1.41-2.93
aztreonam resistant	1.45	1.06-1.97
cefepime resistant	1.68	1.21-2.34
fluoroquinolone resistant	1.37	1.09-1.71
carbapenem resistant	3.52	2.65-4.68
piperacillin/tazobactam resistant	1.45	1.07-1.97
non susceptible Klebsiella	6.15	2.87-13.18
Coded history of pneumonia from K. pneumoniae in the past year	3.31	2.05-5.34
History of positive urine nitrites in the past year	5.06	3.73-6.86
History of peripheral blood band neutrophils in the pasts year	1.92	1.23-2.99
History of culture and susceptibility test order in the past year	2.42	1.99-2.94
History of regular insulin order in the past year	2.00	1.3-3.06

Diversity of pathogens harboring carbapenem resistance at example stations

Diversity of carbapenen-resistant GNR

Legend:
- CR-E. coli
- CR Acinetobacter
- CR-Other Enterobacteriaceae
- CR-Pseudomonas aeruginosa
- CR-Klebsiella

Take away

- Antibiotics may have direct effects on patient acquisition of antibiotic-resistant organisms, as well as infections with them

- We can predict antibiotic-resistant organisms

- Need to work on understanding indirect effects on antibiotics and broadening to more organisms

Maxwell's demon and the quest for control
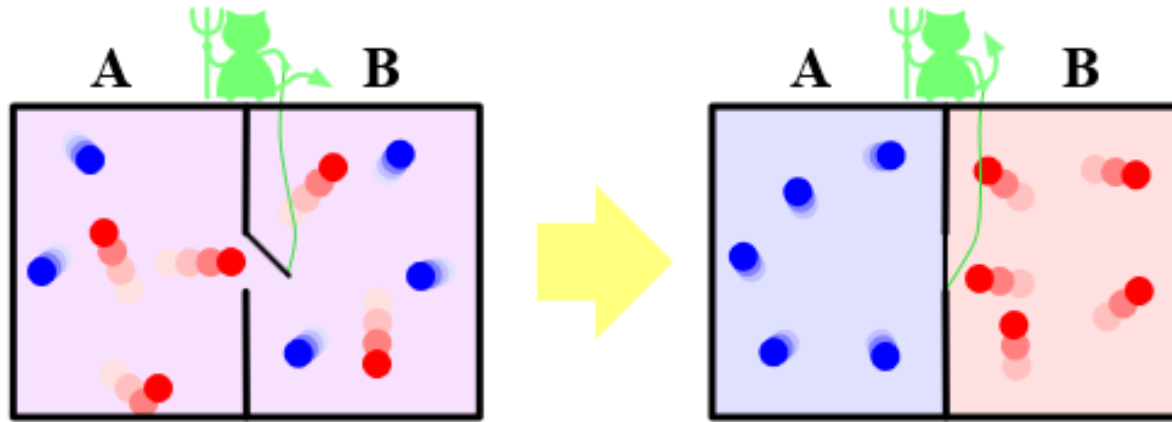
Data-Information-Knowledge
"Knowledge is heavy"—Cesar Hidalgo

Data

Knowledge

Information
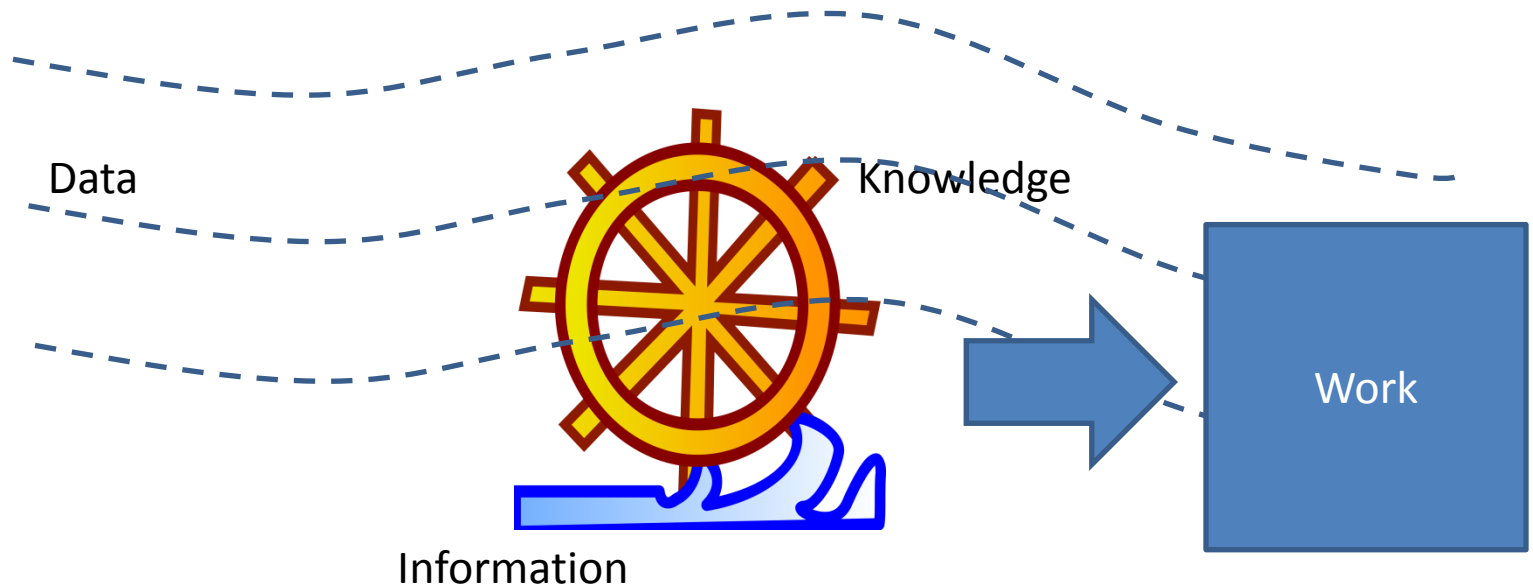
Work

The Cynefin Framework [adapted from Snowden (Cognitive Edge, 2010)]
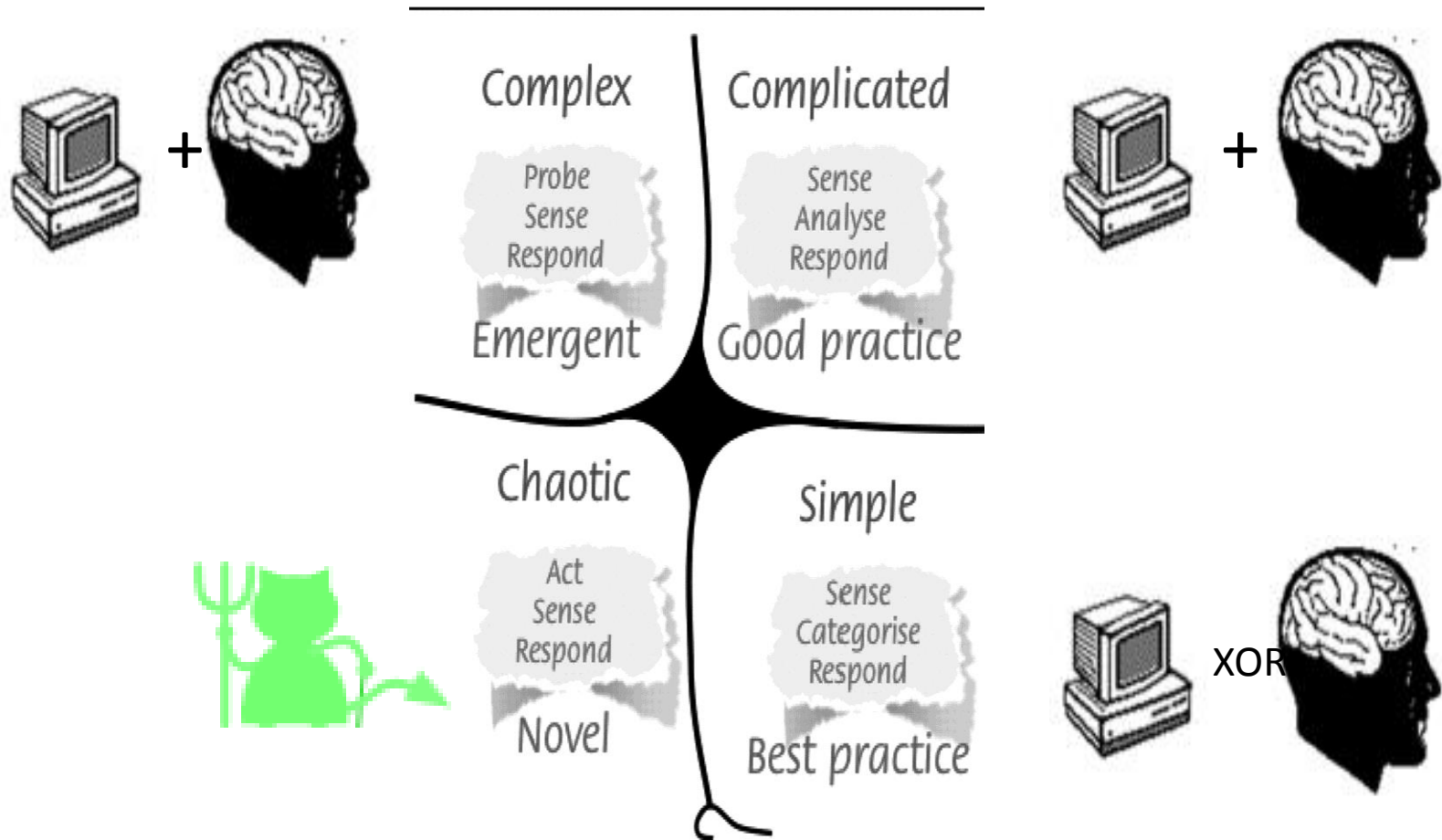
**Eric K. Van Beurden et al. Health Promot. Int.
2011;heapro.dar089**

Health Promotion International

Aggregate Antimicrobial Use

- Your antibiotic use is 589 AD/1000 DP
  - Is this good or bad?
  - Which part of it is good or bad?
  - If it's bad, how do I know what to fix?

Complicated

Sense
Analyse
Respond

Good practice

$$1,000 \frac{}{a + \qquad \qquad + \pi^2 d_A - \pi^2 d_0}$$

Relation between actual and adjusted, predicted antibiotic use
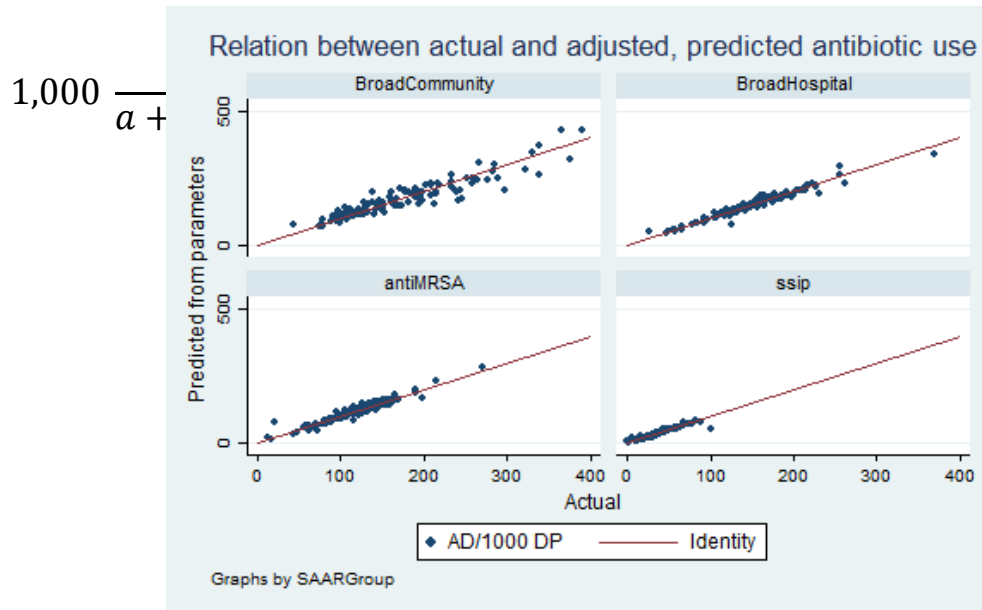
Aggregate Antimicrobial Use

- Your antibiotic use is 589 AD/1000 DP
  - Is this good or bad?
  - Which part of it is good or bad?
  - If it's bad, how do I know what to fix?

$$1{,}000\ \frac{a - ad_0 + 2\pi d_0 + \pi a d_0 - \pi^2 d_0}{a + b + d_A + a d_A - a d_0 - 2\pi d_A + 2\pi d_0 - \pi a d_A + \pi a d_0 + \pi^2 d_A - \pi^2 d_0}$$

SAARGroup	a	b	d0	dA	π	predicted AU	AU	drop P(admit abx) by 1%	drop P(start) by 1%	increase P(stop) by 1%
BroadHospital	5.5%	6.8%	15.8%	7.0%	6.9%	338.9	369.0	-12.4	-27.1	-17.0
BroadCommunity	5.9%	33.6%	13.5%	11.0%	10.8%	155.8	133.2	-4.8	-14.3	-3.1
antiMRSA	8.1%	12.9%	15.2%	6.9%	3.0%	279.9	271.5	-9.4	-21.4	-10.1
ssip	0.5%	28.7%	13.2%	12.0%	1.8%	22.1	21.5	-6.3	-20.6	-0.5

Complex antimicrobial decisions

Complex

Probe
Sense
Respond

Emergent

- What worked before will not necessarily now

- Not always a right answer

- Sometimes need more detailed (qualitative) information

- Requires thinking deeply
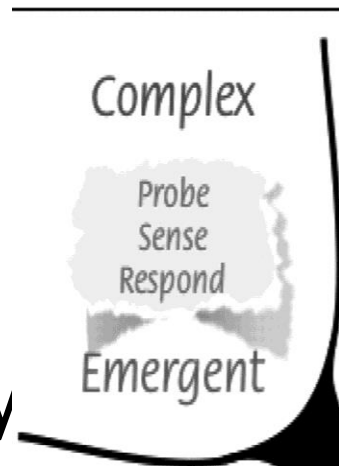
Themes from an antibiotic timeout intervention

- Captures and controls attention
- Enhances informed and deliberative reasoning
- Redirects decision direction by making inappropriate vancomycin and piperacillin/tazobactam discontinuation easier than continuation
- Fosters autonomy and improves team empowerment
- Limits use of emotion-based heuristics.

Stop and think more deeply

Makoto Jones, Jorie Butler, Christopher J. Graber, Peter Glassman, Matthew H. Samore, Lori A. Pollack, Charlene Weir, Matthew Bidwell Goetz

Think twice: A cognitive perspective of an antibiotic timeout intervention to improve antibiotic use

Stop and think

| Themes	Description
Captures and controls attention	*"Like as a resident you try to, of course, avoid unnecessary use of antibiotics regardless, so it's kind of like,* **it reminds us to think** *about it..."*
Enhances informed and deliberative reasoning	*"It makes you* **think twice.***"*
Redirects decision direction by making inappropriate vancomycin and piperacillin/tazobactam discontinuation easier than continuation	***"No, seriously, the fact that they handed me this form in the morning saying, oh, we're tracking your vanco usage made me not want to use it.***
Fosters autonomy and improves team empowerment	*"I think the template is good in that* **it forces the team to really discuss** *it."*
Limits use of emotion based heuristics.	*Clinician 1: "And when we speak to the pharmacist as well, if they're saying, well, I don't see why you're choosing this antibiotic; why don't you just choose this? We can say to them person to person, look, my concern...***my clinical concern is high enough** *I think they need more aggressive therapy at least for right now and usually they will agree to that because it's clinical judgment; it comes down to that so the template kind of does the same thing, so..."* *Clinician 2: "... You can say that about everybody and put everybody on vancomycin..."*

Information
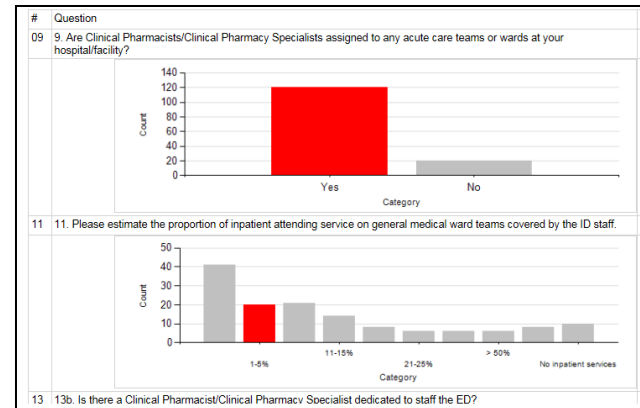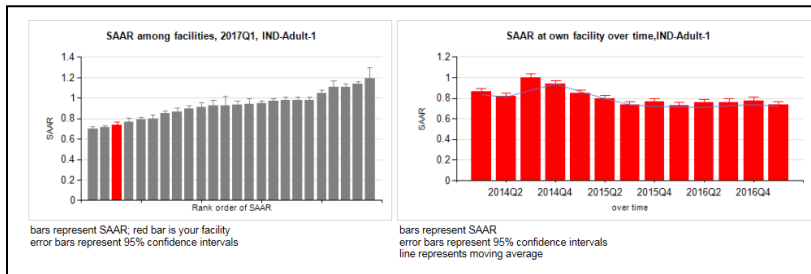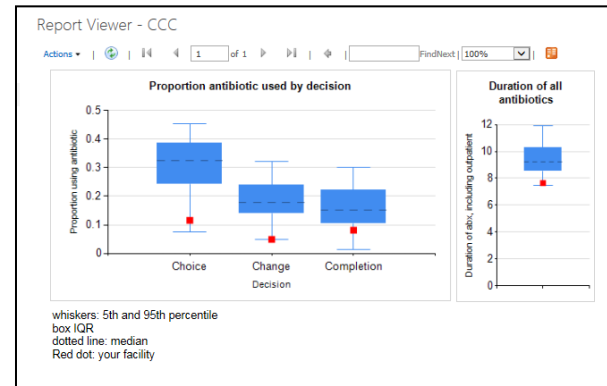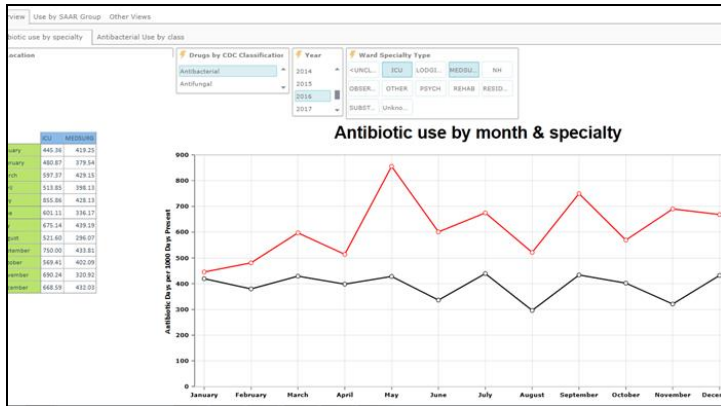
Actionable

- Contains all or nearly all of the contextual information necessary to make a decision
- Represents information that is of sufficient quality to act
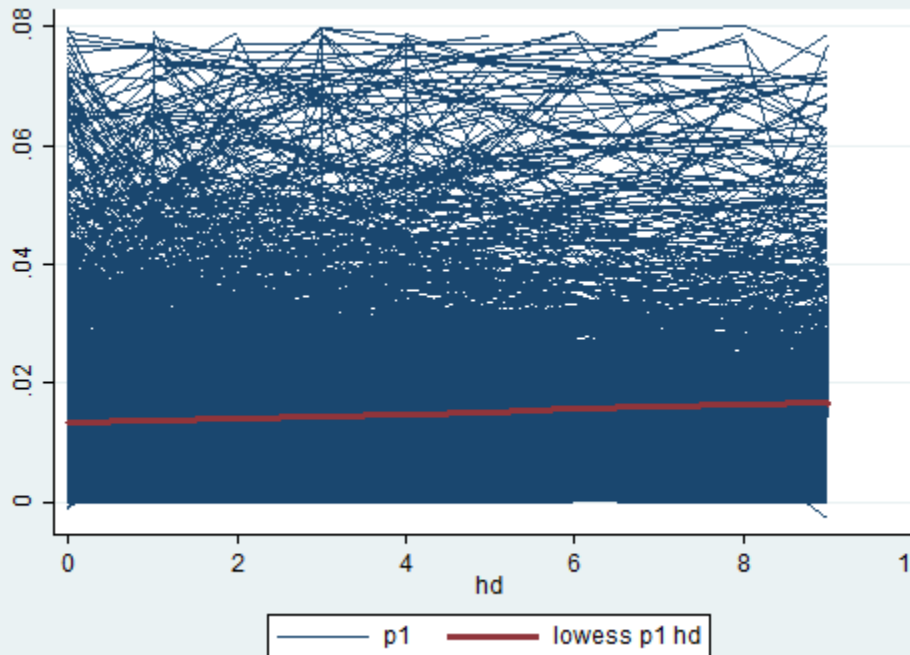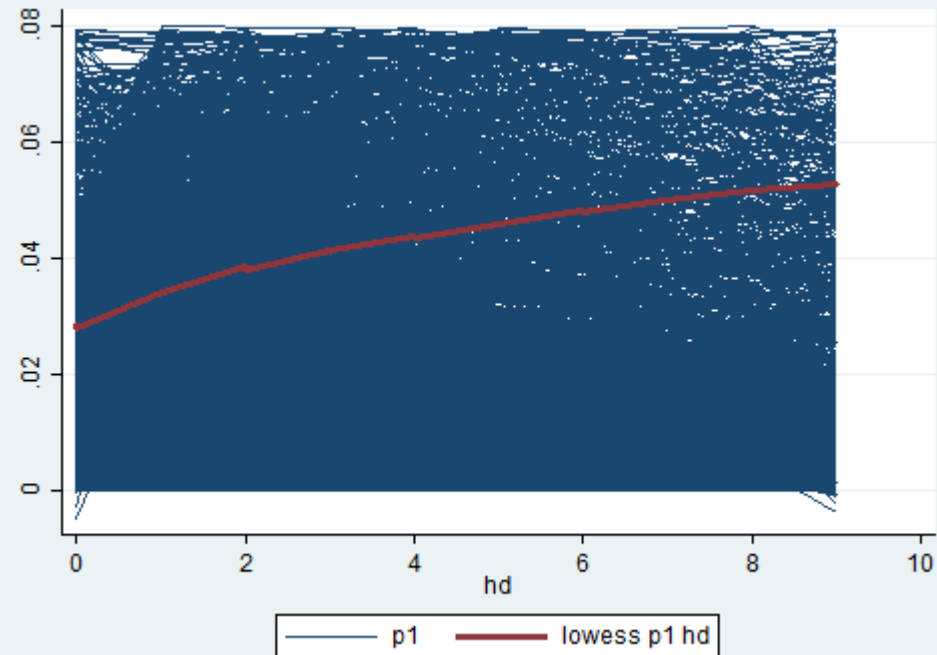
Pneumonia admissions order entropy
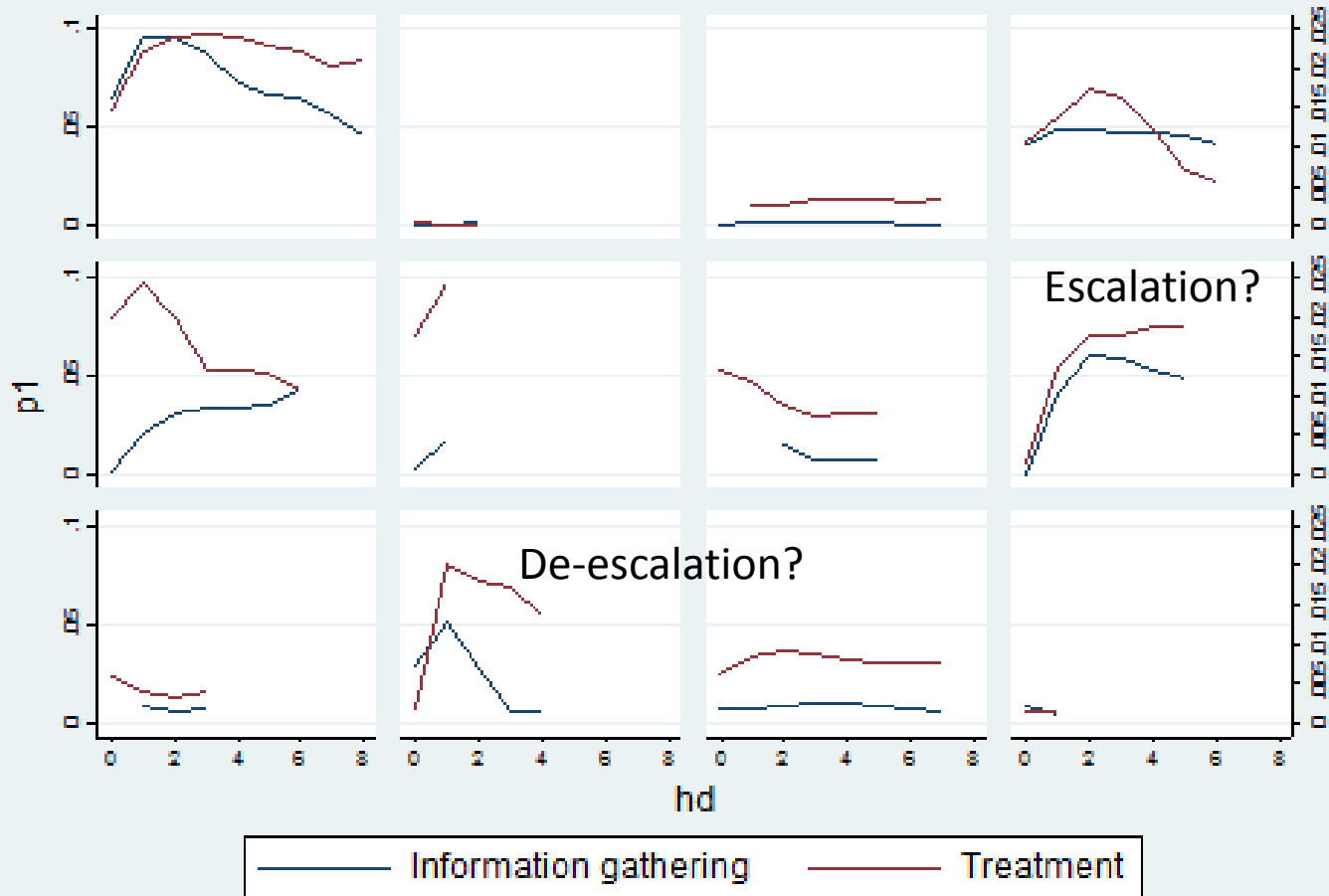
Graphs by inpatientsid

Information environment

Active treatment order entropy

Active information request order entropy

Information available and new information entropy not performed yet

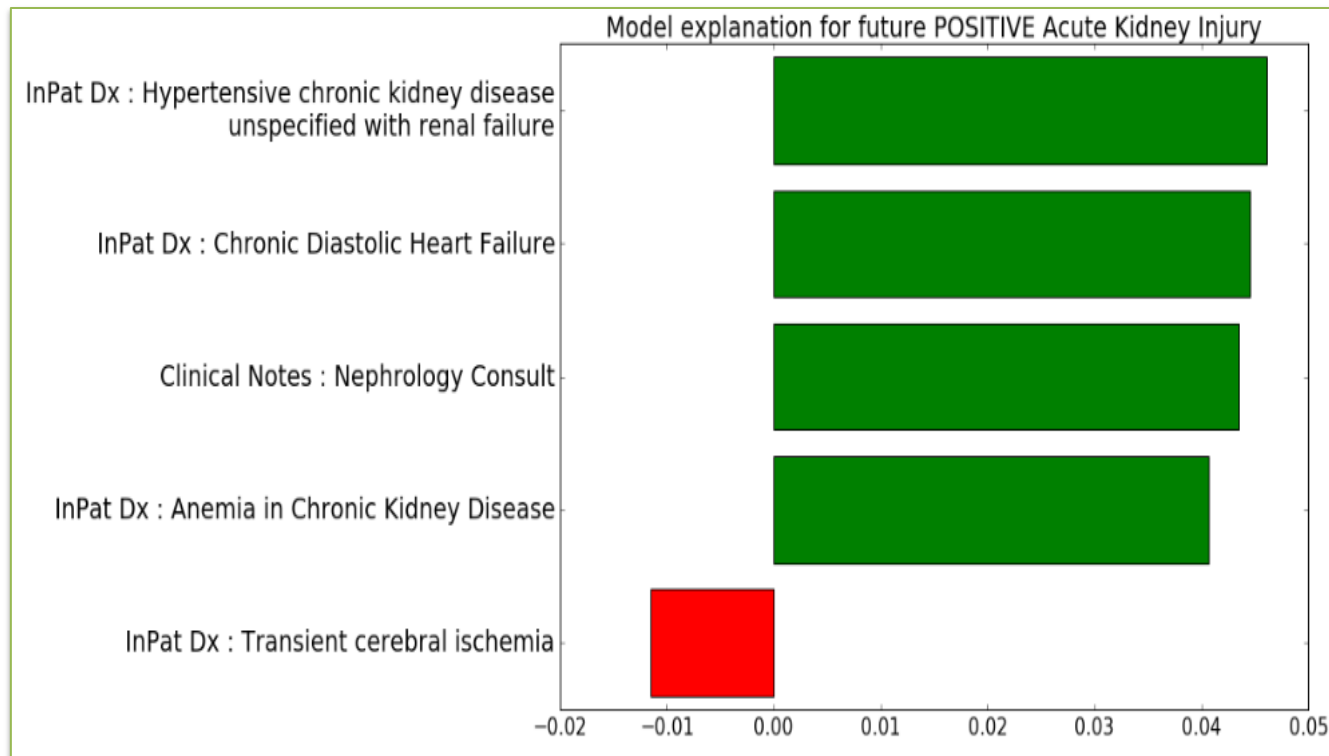# Future direction

- Data$\rightarrow$Information

- Information$\rightarrow$Knowledge

- Find information that interacts with knowledge to inform decision

- Present information so that it makes it easy to make the right decision

Resources

- Makoto Jones
  - makoto.jones@va.gov

Explaining Predictive Models

- State-of-the-art techniques, e.g., neural networks, are black box

- the example below estimates the predicted probability of future acute kidney injury at 83%

- New algorithms (LIME) facilitate interpretation of black box models

Model explanation for future POSITIVE Acute Kidney Injury

InPat Dx : Hypertensive chronic kidney disease unspecified with renal failure

InPat Dx : Chronic Diastolic Heart Failure

Clinical Notes : Nephrology Consult

InPat Dx : Anemia in Chronic Kidney Disease

InPat Dx : Transient cerebral ischemia

-0.02   -0.01   0.00   0.01   0.02   0.03   0.04   0.05

Representing "evidence," "data"

Model/Evidence

$$Y_i = g^{-1}(\beta_{0+}\beta_1 x_{1i} + \cdots + \beta_p x_{pi}) + \varepsilon$$

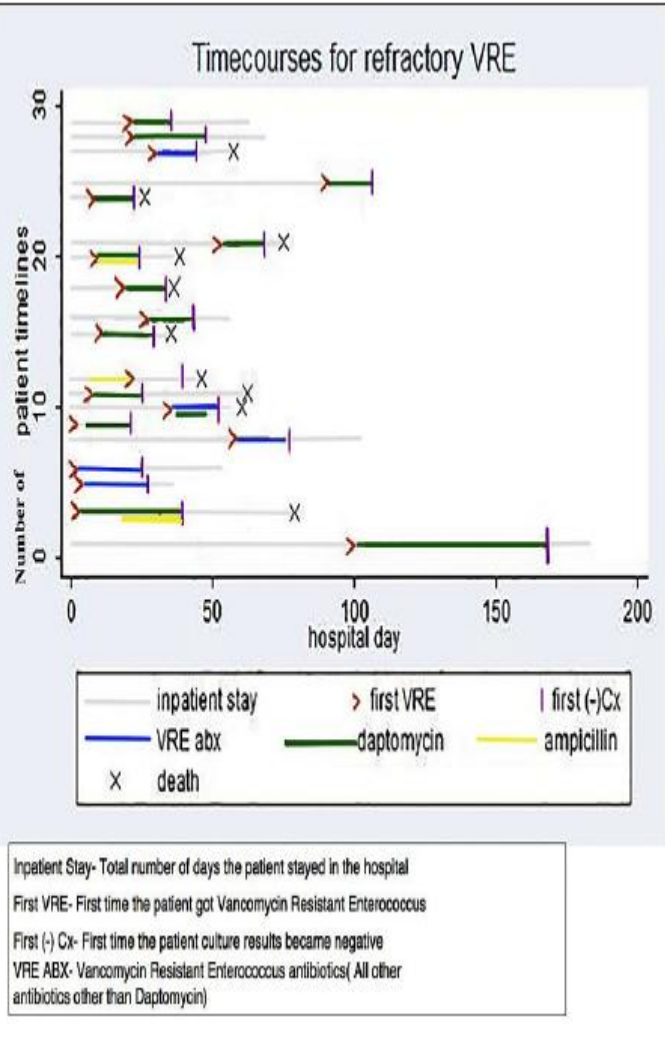Data/Context
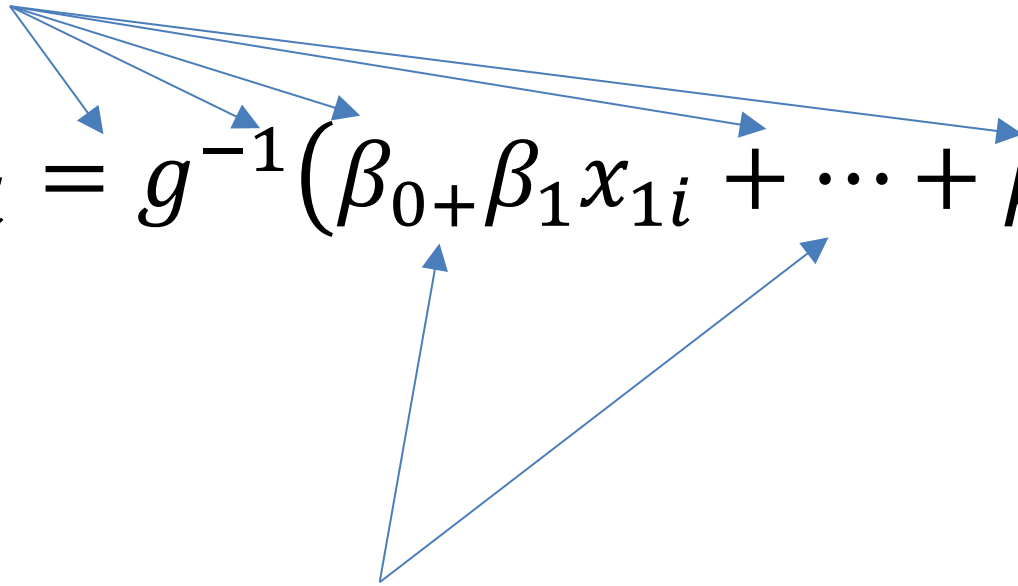
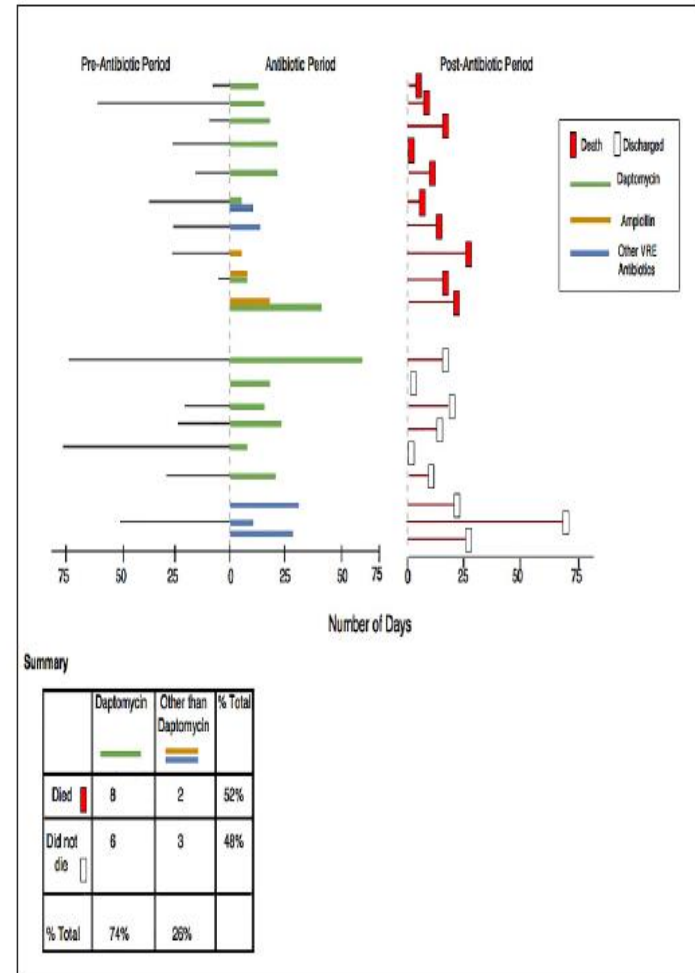# Veterans Like Mine

Fig. 1
Population information display

Fig. 3
Redesigned Population-based information display.

The naïve view
# (or the Greek Oracle Model)

Why didn't the Greek oracle model work?

- Performance expectancy
  - It took longer to do what physicians could already do
  - Things that weren't already obvious would have to be reviewed because of vulnerability to errors
- Effort expectancy
  - Took time to enter information, difficult to understand
- Social influence
  - No one "important" uses the system yet
- Facilitating conditions
  - Doesn't fit into workflow
- Attitude toward using technology
  - "Don't trust" the data; GIGO

New approach: "Fundamental theorem" of biomedical informatics— an aspiration, not a rule

Much, much less and selective input per patient
Much more short term memory
Reliable long term memory
Processing capability
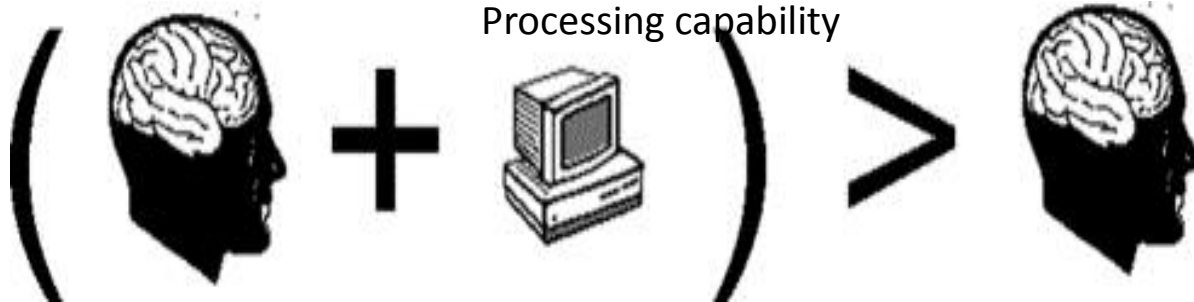
~gb/sec input that is always on
Short term memory: 3-7 items
Very large, unreliable long-term memory
Gargantuan subconscious processing capability

Make the computer do what the computer does best—not what the human does best.

Questions? Comments?

- Makoto Jones
  - makoto.jones@va.gov