The Infection control at ECCMID 2017

http://www.eccmidlive.org/

Gabriel Birgand
Saturday, 22 April 2017

• Implementing infection control and antimicrobial stewardship interventions in your hospital
• Which mathematical models for antimicrobial resistance?
• Innovation in infection control
Session EW005 - Implementing infection control and antimicrobial stewardship interventions in your hospital

http://www.eccmidlive.org/#!contentsessions/22169
Navigating the published literature - what level of evidence is needed before implementing an intervention in your hospital?

Eli Perencevich, MD MS
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PI and Director, VA HSR&D Center of Innovation (COIN)
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Implementing infection control and antimicrobial stewardship interventions in your hospital

Objectives

- At the conclusion of this talk, you should be able to

  1. Categorize studies into high, moderate or low quality
  2. Identify factors other than level of evidence of effectiveness that would influence implementation
  3. Describe how Publication Bias might influence decision-making around specific interventions
Implementing infection control and antimicrobial stewardship interventions in your hospital

### Infection Prevention Situations

<table>
<thead>
<tr>
<th></th>
<th>No Evidence</th>
<th>Equipoise – Pro/Con Sessions</th>
<th>Proven – In Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outbreaks</strong></td>
<td>++</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td><strong>Endemic Problems</strong></td>
<td>-</td>
<td>+</td>
<td>+++++</td>
</tr>
<tr>
<td><strong>Preventing Future Outbreaks and Problems</strong></td>
<td>-</td>
<td>?</td>
<td>+++</td>
</tr>
</tbody>
</table>
Why did I show you all of this?

☐ Some interventions are **VERY difficult** to study

☐ Example: BBE, influenza vaccination of HCW, universal gloving
  - Because **acquisition** harder to detect than infection
    - Cost, multiple swabs,
    - Impacts power calculations, study design (e.g. cluster-randomized, quasi studies)
    - More likely to be underpowered and thus falsely negative

☐ Maybe observational or QE evidence is all we’ll ever have

#EW0021
Additional Difficulties with Acquisition

- Patients who acquire or become colonized with a new pathogen:
  - Most will not develop an infection
  - If they do become infected, it will be after discharge or at another hospital

- Most care about preventing infections and avoiding mortality, not acquisition
Implementing infection control and antimicrobial stewardship interventions in your hospital

Magical Evidence Pyramid

For more info...
http://guides.lib.usf.edu/ebp/levels_of_evidence

#EW0021
Which abstracts are likely to be published?

- “Positive” results (RR = 1.30; CI 1.14-1.47)
- Oral vs. poster (RR = 1.28; CI 1.09-1.49)
- Higher quality of abstracts (RR = 1.30, CI 1.00-1.71)

FOR MORE INFO...
Cochrane Database Syst Rev. 2007 Apr 18;(2):MR000005

#EW0021
Conclusion: When can we implement?

- Evidence one piece of puzzle
- Gauging the level of evidence is difficult in control/stewardship
  - Situation: Outbreak, Endemic
  - Acquisition vs infection
- Tools available to help
  - GRADE: economic, side-effects
- Publication Bias
Evaluation of new interventions targeting HAI - before, during and after implementation

Walter Zingg, PD, MD
# Evaluation of new interventions targeting HAI

## Key components (ECDC – SIGHT)

1. An effective infection control programme in an acute care hospital must include at least: one full-time specifically trained IC-nurse ≤ 250 beds; a dedicated physician trained infection control; microbiological support; data management support.

2. To make sure that the ward occupancy does not exceed the capacity for which it is designed and staffed; staffing and workload of frontline health-care workers must be adapted to acuity of care; and the number of pool/agency nurses and physicians minimized.

3. Sufficient availability of and easy access to material and equipment and optimized ergonomics.

4. Use of guidelines in combination with practical education and training.

5. Education and training involves frontline staff, and is team- and task-oriented.

6. Organizing audits as a standardized (scored) and systematic review of practice with timely feedback.

7. Participating in prospective surveillance and offering active feedback, preferably as part of a network.

8. Implementing infection control programmes follow a multimodal strategy including tools such as bundles and checklists developed by multidisciplinary teams and taking into account local conditions.

9. Identifying and engaging champions in the promotion of a multimodal intervention strategy.

10. A positive organizational culture by fostering working relationships and communication across units and staff groups.

## Core components (WHO)

- **An IPC programme with a dedicated, trained team should be in place in each acute health care facility for the purpose of preventing HAI and combating AMR through IPC good practices.**

- **In order to reduce the risk of HAI and the spread of AMR, the following should be addressed: (1) bed occupancy should not exceed the standard capacity of the facility, (2) health care worker staffing levels should be adequately assigned according to patient workload.**

- **At the facility level, patient care activities should be undertaken in a clean and/or hygienic environment that facilitates practices related to the prevention and control of HAI, as well as AMR, including all elements around the WASH infrastructure and services and the availability of appropriate IPC materials and equipment.**

- **Evidence-based guidelines should be developed and implemented for the purpose of reducing HAI and AMR. Education and training of the relevant health care workers on guideline recommendations and monitoring of adherence with guideline recommendations should be undertaken to achieve successful implementation.**

- **At the facility level, IPC education should be in place for all health care workers by utilizing team- and task-based strategies that are participatory and include bedside and simulation training to reduce the risk of HAI and AMR.**

- **Regular monitoring/audit and timely feedback of health care practices should be undertaken according to IPC standards to prevent and control HAI s and AMR at the health care facility level. Feedback should be provided to all audited persons and relevant staff.**

- **Facility-based HAI surveillance should be performed to guide IPC interventions and detect outbreaks, including AMR surveillance with timely feedback of results to health care workers and stakeholders and through national networks.**

- **At the facility level, IPC activities should be implemented using multimodal strategies to improve practices and reduce HAI and AMR.**

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*Zinng W Lancet Infect Dis 2015;15:212*

*Storr J Antimicrob Resist Infect Control 2017*
Evaluation of new interventions targeting HAI

- Structures/activities
  - Organisation/staffing
  - Surveillance/feedback

- Resources/management
  - Organisation/staffing
  - Bed occupancy/workload

- Implementation
  - Material/devices/ergonomics
  - Guidelines
  - Team- and task-oriented education and training
  - Multimodal strategies
  - Engagement of champions

- Organisational culture
  - Creating a positive organisational culture
Evaluation of new interventions targeting HAI

Implementation
- Material/devices/ergonomics
- Guidelines
- Team- and task- oriented education and training
- Multimodal strategies
- Engagement of champions

Structures/activities
- Organisation/staffing
- Surveillance/feedback

Resources/management
- Organisation/staffing
- Bed occupancy, workload

Organisational culture
- Creating a positive organisational culture
Evaluation of new interventions targeting HAI
Source of the intervention

Perception of key stakeholders about whether the intervention is externally or internally developed

Adaptability

Core component – adaptive periphery (package)
(One size dose NOT fit all)

Complexity

“Perceived” difficulty of the intervention

Cost

Costs of the intervention and costs associated with implementing that intervention including investment, supply, and opportunity costs.
Implementation process...

Four components in common: planning, engaging, executing, evaluating

The four process activities are not meant to be sequential
Evaluation of new interventions targeting HAI
Evaluation of new interventions targeting HAI
Session EW015
Which mathematical models for antimicrobial resistance?

http://www.eccmidlive.org/#!contentsessions/22160
Which mathematical models for antimicrobial resistance?

Guillaume Béraud:
More data? Better data?
Which mathematical models for antimicrobial resistance?
Two ways, one conclusion

• Two ways:
  – Knowing how many individuals are in each compartment, we can deduce transmission characteristics.
  – Knowing transmission characteristics, we can deduce how many individuals are in each compartment.

• But we always need DATA
Which mathematical models for antimicrobial resistance?

Big data and infectious diseases

- Data available.
- Not so big compared to onco-genomics or theoretical physics.
- Will allow understanding of infectious disease dynamics without a priori.
- Big data already successfully used in marketing and meteorology.
Big data for infectious diseases surveillance

• Incredibly powerful
• But some failure (Google Flu Trends and a new pandemic virus), notably when only based on digital data.
• The solution: Combining digital big data and traditional laboratory based surveillance

➢ InfluenzaNet offers voluntary reported data and could be combined with data from traditional surveillance system (Sentinelle)
Which mathematical models for antimicrobial resistance?

But, challenges remain

- Integration with existing tools
- Representativeness & bias:
  - More digital data available coming a young man in New-York than a newborn in Botswana
  - Integration of data on zoonotic diseases
- Data volatility: A data stream not specifically designed for infectious diseases surveillance may not persist.
- « Big data hubris »:
  - An overload of data is not an excuse for a lack of rigorous analysis.
  - Data without model are not better than model without data
- Managing data volume
  - Better organization of data is still beneficial, along with better models to exploit it.
The greatest challenge

- A paradigm shift is needed
- Physicians should refine the way they approach infectious diseases
- Find and treat the most prominent bacteria identified is not enough, anymore
Which mathematical models for antimicrobial resistance?

Data vs. Models

- Models without data are purely speculative, and may prove that dragons and unicorns exist.
- But data without models are useless, a waste of time and money.
- The next speaker will confirm...
Which mathematical models for antimicrobial resistance?

ECCMID, Vienna, April 2017

Which mathematical models for antimicrobial resistance?

Niel Hens: Better models? A bird’s eye view

VAXINFECTIO
Vaccine & Infectious Disease Institute
University of Antwerp

UHasselt
I-BioStat
KU Leuven

Interuniversity Institute for Biostatistics
and statistical Bioinformatics

#EW0066
Which mathematical models for antimicrobial resistance?

Mathematical Modelling

• Purposes:
  – prediction: requires the inclusion of known complexities and population-level heterogeneity
  – understanding: investigating the factors that drive dynamics

• Building a model presents a trade-off:
  – accuracy: reproduce what is observed and predict future dynamics
  – transparency: ability to understand how model components influence the dynamics and interact
  – flexibility: ease of adapting the model to new situations
Which mathematical models for antimicrobial resistance?

Mathematical Modelling

• Limitations:
  – models present a simplification of reality
  – chance events of infectious disease transmission hinder perfect prediction

• A good model:
  – suited to its purpose: simple as possible, but no simpler
  – balance accuracy, transparency, flexibility
  – parametrisable from available data (see Guillaume and Lulla)
Which mathematical models for antimicrobial resistance?

Mathematical Modelling

• Deterministic or compartmental models (SIR model -> Guillaume)
• Stochastic models
• Meta-population models
• Network models
• Agent-based models
• Within and/or between-host models
Which mathematical models for antimicrobial resistance?

Model Issues: Biological plausibility

- ≠ detailed and complex
- informing models by parameters estimated from data & informing models by estimating/calibrating the model to data
- don’t put your eggs in one basket
- question the literature
  - the bodyguard principle (known in statistics)
  - assumptions
Conclusion & discussion

- Mathematical and statistical models, if properly used, offer valuable instruments to understand mechanisms of antibiotic use and resistance
- Interdisciplinary research
  - Example: Methusaleem grant awarded to Herman Goossens (Vaxinjecto, UAntwerpen) and Geert Molenberghs (CenStat, UHasselt)
- Lulla Opatowski will present several examples

Opatowski et al. (Current Opinion in ID, 2011)
Which mathematical models for antimicrobial resistance?

Better use of existing data with new modelling approaches?

A series of applications

Lulla Opatowski
Université de Versailles St Quentin / Institut Pasteur / Inserm
Paris, France
Which mathematical models for antimicrobial resistance?

Outline: three illustrations

- Models assessing antibiotic strategies
- Models analyzing complex interactions between antimicrobials
- Models integrating detailed contact network
Antibiotic strategies

• **Idea:** optimized antibiotic patterns may slow the evolution and spread of resistant strains

• **In hospitals:**
  – **Cycling:** *empiric use >2 classes of antibiotics is alternated over time*
  – Antibiotic restrictions

• **In the community, modulate dose and duration**
  – Individual impact shown *in-vitro* and *in-vivo* in PK-PD modelling studies
  – Rarely collected in surveillance systems (focused on global consumption)

Ball, 2007; Nicolau, 2008; Mattoes, 2004; Olofsson, 2007; Drusano, 2004;
Which mathematical models for antimicrobial resistance?

Influence of PCV and antibiotic campaign in the trends of meningitis incidence?

1) Potential effect of antibiotic exposure
   A- Selective pressure of ATB on resistant (R) strains?
   B- Resistance associated fitness cost: S strains are more epidemic? More Pathogenic?

2) Potential effect of vaccine
   A- Selective pressure of PCV on Non-Vaccine (NV) strains?
   B- Differences in competitiveness between V and NV strains: NV strains are more epidemic? More pathogenic?

Test hypotheses by constructing a series of mechanistic models
Which mathematical models for antimicrobial resistance?
General conclusions

- *Mathematical model make it possible to explore the different complexity levels (including antimicrobials, populations and microorganisms)*

- Models (even theoretical ones) can help assessing the ecological impact of control measures on bacterial resistance

- Confrontation of models to data is a unique opportunity to
  - Test mechanistic hypotheses and understand better the mechanisms at stake
  - Characterize strains intrinsic specifies (epidemiicity, virulence etc.)

- To understand better bacterial resistance, more data will be required
Session EW008 - Innovation in infection control

http://www.eccmidlive.org/#!contentsessions/22171
Yehuda Carmeli
#EW0033
Modelling spread of pathogens in your hospital
Nico Tom Mutters
#EW0034
How to prioritize infection control measures in the local setting - cost incentives
How to calculate infection control costs and convince your hospital administration to spend the money

Bart Gordts, MD, MBA
Ziekenhuisnetwerk Antwerpen (ZNA)
🌐 bart.gordts@zna.be
Traditional motivation for IC intervention

1. Cost of the (MRSA) infection
2. Selection and effectiveness of the intervention
3. Cost of intervention
4. Expected reduction in incidence
5. Expected cost savings
How to calculate IC costs

Management response

Cost of the (MRSA) infection
unrealistic in our country unrealistic in our finance system

Selection and effectiveness of the intervention
other possibilities? why most costly ones?

Cost of intervention
much higher in our baseline situation Expected reduction in incidence

Expected cost savings
Many materials, staff and indirect costs are only theoretically saved, not in true life!

To compete successfully for the scarce resources in healthcare, IC practitioners need to substantiate economic as well as medical benefit of their programs.
How to calculate IC costs

Burden of HA-infections

Extent
- Prevalence / incidence / risk factors

Impact
- Medical
  - Mortality
  - Morbidity
- Economical
  - Patient
  - Hospital
  - Healthcare system
  - Society
# How to calculate IC costs

## Impact of nosocomial infections on different stakeholders

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Hospital</th>
<th>Social security</th>
<th>Society</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Traditional</td>
<td>DRG</td>
<td>Traditional</td>
<td>DRG</td>
</tr>
<tr>
<td>mortality</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>In-hospital morbidity</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Ambulatory morbidity</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Incapacity</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>+++</td>
</tr>
<tr>
<td>Increased LOS</td>
<td>++</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>+</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Isolation room</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
</tbody>
</table>
How to calculate IC costs

How to evaluate the preventability of HAI?

- Comparing infection ratio to standard (benchmarking)
- Case – control / cohort studies
- Mathematical modelling
- Comparing infection ratio before and after multi-modal intervention
- Case per case evaluation of preventability
- All exogenous cross infections (proven) are preventable
How to calculate IC costs

Categories in classical cost calculation

Financial result

- Cost
  - Investment
    - direct spending
    - depreciation
  - Staff (salaries)
    - marginal cost
  - Outsourcing
  - Consumables
    - disposables
    - medication

- Revenue
  - marginal billing increase
  - Maintained income with decreased purchases
# How to calculate IC costs

## Ranking of top-10 activities generating yearly MRSA cost

<table>
<thead>
<tr>
<th>Rank</th>
<th>Activity</th>
<th>Cost 2007</th>
<th>Proportion of cost</th>
<th>Cumulated proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Isolation Decolonization</td>
<td>€ 314,41</td>
<td>27,6%</td>
<td>27,6%</td>
</tr>
<tr>
<td>2</td>
<td>Screening Lab Process (PCR)</td>
<td>€ 197,23</td>
<td>17,3%</td>
<td>44,9%</td>
</tr>
<tr>
<td>3</td>
<td>Isolation Nurse Contact</td>
<td>€ 183,65</td>
<td>16,1%</td>
<td>61,0%</td>
</tr>
<tr>
<td>4</td>
<td>Screening Taking Samples (Culture)</td>
<td>€ 85,40</td>
<td>7,5%</td>
<td>68,5%</td>
</tr>
<tr>
<td>5</td>
<td>Isolation Visitors</td>
<td>€ 74,51</td>
<td>6,5%</td>
<td>75,0%</td>
</tr>
<tr>
<td>6</td>
<td>Screening Lab Process (Culture)</td>
<td>€ 67,59</td>
<td>5,9%</td>
<td>80,9%</td>
</tr>
<tr>
<td>7</td>
<td>Isolation Antibiotic</td>
<td>€ 57,50</td>
<td>5,1%</td>
<td>86,0%</td>
</tr>
<tr>
<td>8</td>
<td>Isolation Prep IC Inform</td>
<td>€ 44,58</td>
<td>3,9%</td>
<td>89,9%</td>
</tr>
<tr>
<td>9</td>
<td>Screening Lab Reception Processing</td>
<td>€ 32,06</td>
<td>2,8%</td>
<td>92,7%</td>
</tr>
<tr>
<td>10</td>
<td>Isolation Patient Transport</td>
<td>€ 28,43</td>
<td>2,5%</td>
<td>95,2%</td>
</tr>
</tbody>
</table>
How to calculate IC costs

I. Background and motivation

II. Description of the problem
   - Definition, extent, morb. & mort., financial & operational burden, indicators

III. Proposed interventions

Strategy
- Qualitative and quantitative targets
- Cost benefit/effectiveness
- Implementation (who, what, when...)

Uniform lab method
Universal screening
Presumptive isolation
Compliance isolation
Prompt AB treatment
Systematic decontamination
Controlling emerging MDR outbreaks: can we help by tracking MDR bacteria through links with travel insurance companies?

Vincent Jarlier, MD, PhD
Bacteriology & Hygiene
Pitié Salpêtrière hospital, Paris, France
Central Infection control team
Direction of Medical affairs
Assistance Publique – Hôpitaux de Paris

VJarlier 2017
Controlling emerging MDR outbreaks

% of index cases leading to 2ary cases: CPE versus VRE
AP-HP 2010-2015

CPE: 8 % VRE: 21 %

Fournier, Jarlier 2017 submitted

p < 10^{-3}
Controlling emerging MDR outbreaks

% of 2ary cases depending on the type of measures implemented within the first 2 days after admission
AP-HP 2010-2015

Fournier, Jarlier 2017 submitted

Cohorting + dedicated staff 4%
Contact isolation 14%
Standard precaution 44%
p < 10^{-3}
Learning infection control via games – does it work?

Dr. AG Venier, MD, PhD, Bordeaux, France
HAI prevention centre - CCLIN Sud-Ouest

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Games?

- **A serious game** is a game designed for a primary purpose other than pure entertainment.

- **Gamification** is the use of game design elements in non-games contexts making use of the potential ability of games.

- **Principles of a game**
  - Objective + Rules + Means

- **Why do we play?**
  - To have fun
  - To learn and grow
  - To overcome challenges
  - To interact with other people

Cugelman B. *JMIR serious games* 2013/ Abdulla El-Hilly A. *JMIR serious games* 2016/ Wattanasontorn V. *Entertainment computing* 2013
Serious games – CCLIN Sud-Ouest experience

- 2012 …*Sarcoptes invasion* (scabies)
- 2013 …*Flu.0* (Flu)
- 2014 …*Dojo résistance* (XDR bacteria)
- 2015 …*Code Name UTI* (urinary tract infection)
- 2017 …*I control* (universal precautions)


#EW0037
## Results

264 physicians (213 fellows), 62 senior nurses, 577 nurse students

Rate given to the game 7.9/10

<table>
<thead>
<tr>
<th></th>
<th>Physicians / Senior nurses</th>
<th>Nurse students</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before the game</td>
<td>After the game</td>
</tr>
<tr>
<td>Seasonal flu = benign disease</td>
<td>156 (48%)</td>
<td>113 (35%)</td>
</tr>
<tr>
<td>Flu vaccination of health care workers = useful</td>
<td>302 (93%)</td>
<td>322 (99%)</td>
</tr>
<tr>
<td>I know the indications of the antiviral treatment</td>
<td>201 (62%)</td>
<td>280 (86%)</td>
</tr>
<tr>
<td>I feel well prepared to face a flu case</td>
<td>257 (79%)</td>
<td>309 (95%)</td>
</tr>
<tr>
<td>Well prepared to perform rapid flu diagnostic test</td>
<td>95 (29%)</td>
<td>280 (86%)</td>
</tr>
</tbody>
</table>

p = 0.001
Learning IPC via games

Results

95% learnt at least one key point

Two key points
52% Physicians, senior nurses
82% Nurse students

Three Key points
16% Physicians, senior nurses
45% Nurse students
How to use games for infection control

- Choose the correct game for the correct population
- Check the users’ context is ok

- Use them!
  - During a learning session, in a multiple tool strategy, for a special day
  - Voting keypads/ Computers/ Smartphone

- Don’t be overconfident
  - Games can’t exert massive influence across all contexts
  - So… add briefing + debriefing +/- synthetic cognitive information
Public engagement and fight against antimicrobial resistance

Dr Kirsten Schaffer
Department of Microbiology
St Vincent’s University Hospital, Dublin
kirsten.e.schaffer@ucd.ie
Why is public engagement important?

How can we improve public engagement?
Why is public engagement important?

1. Significant knowledge gaps and misconceptions about antimicrobial resistance by the public
2. Public engagement to help increase pressure on stakeholders!
3. To improve prescriber-patient interactions
‘AMR’ means nothing to people – they can’t even guess at what it stands for

When we ask about ‘AMR’ and ‘antimicrobial resistance’ we just get blank faces all round – even when we’ve just been talking about resistance more generally.

I need a dictionary for that.
F, 40-60, no education past 16 years old, Manchester

That sounds like something made up.
M/F, 18-25, not at university, London
It’s only when it feels direct, personal and relevant that people take note

My world

Our world

The world

If resistance feels part of my world (me/my family) or to a lesser extent our world (my community) it starts to matter

When it feels like a ‘the world’ issue it just doesn’t hit home

If you walk around blind to everything big it’s the best way.

M/F, 25-50, Mixed, Birmingham
The findings of the research do seem to have some relatively far-reaching implications

As we reflect on what we’ve learnt, the following four things stand out:

1. The current language needs to change – AMR is meaningless and ‘antibiotic resistance’ does not take people to the right place.

2. The focus of the resistance ‘story’ for the general public needs to shift away from macro factors such as number of deaths, cost to the economy and epidemics/pandemics.

3. **There is a need for a communications campaign for the public which makes the issue feel real and relevant, so that the tide of opinion is behind taking action.**

4. Doctors (and dentists) are key – while more research may be needed it appears there is a need for a behaviour change programme for doctors which provides clear guidelines and targets around when to prescribe antibiotics, and advice on how to manage patients.
‘First, we need a *global public awareness campaign* to educate all of us about the problem of drug resistance, and in particular children and teenagers. I see this as an urgent priority....’
Public engagement

Iconic Symbols

Advertisement campaign
Public engagement

Smartphone applications

- One fifth of smartphone users have health apps on their phone
- No apps available to actively involve the user in their antibiotic prescriptions
- Difficulty: to get users to use apps

1. Micallef et al, Clinical Infectious Diseases 2016;63(1):140–1
Evelina Tacconelli
#EW0039
Optimize infection control using antimicrobial stewardship
Session OS024 –
Confronting the threat of resistance in Gram-negatives
Colonization sites in carriers of multidrug-resistant Gram-negative bacteria

• **Objective:** to investigate the epidemiology of colonisation sites in patients colonized with ESBL

• **Results:**

• **Conclusions:**
  – Follow-up cultures of MDR-GNB carriers should include, in addition to rectal swabs, a culture from the site where the MDR-GNB was initially found.
Impact of contact precautions on nosocomial acquisition of ESBL E. coli in a high-risk setting

• **Objective:** Clinical effectiveness of contact isolation of patients colonised with ESBL-EC with co-resistance to fluorquinolones

• **Method:**
  – Screened for intestinal ESBL colonisation within 72 h of admission, weekly thereafter and before discharge
  – 2 sites with contact precautions and 2 without

• **Result:**
  – CP-sites: 1.8% (1.2- 2.5%) ESBL-EC acquisition & 11.4% (9.8-13.0%) intestinal ESBL-EC colonisation
  – NoCP-sites: 3.8% (2.8-4.8%) & 14.2% (12.4-16.1%)
  – 5 events of Kp ESBL likely patient-topatient transmission in NoCP-sites and 1 event in CP-sites

Lena Biehl #OS0102
Quantifying the impact of antimicrobial usage on the nosocomial acquisition of ESBL colonization

- **Objective:** To determine the relative importance of nosocomial transmission of ESBLs compared to selection following antimicrobial usage.
  - **Method:** Markov chain Monte Carlo data augmentation algorithm,
    - General medical and surgical wards from three European countries
    - Colonisation data were derived from rectal swabs from 10,035 patients (3,468 on antibiotic therapy) on admission and discharge,

- **Results:**
  - 10% of colonization on ward admission in all settings,
  - 27% (Romania), 18% (Italy) and 31% (Serbia) colonization at some point in their ward stay.
  - Cross-transmission: 47% (95%CI: 42 – 49) in Italy, 61% (60 – 63) in Romania and 70% (64 – 71) in Serbia.
  - Patients exposed to antimicrobials were found to have an increased rate of ESBL acquisition, though no difference in transmissibility was found compared to patients free from antimicrobials.

Van Kleef OS0103
Decontamination of 3rd-generation cephalosporin- and carbapenem-resistant Gram negative bacteria in ICU patients

- **Objective:** Selective Digestive Decontamination (SDD), Selective Oropharyngeal Decontamination (SOD) and chlorhexidine [1% or 2%] mouthwash (CHX) eradicates carriage with 3GCE CR-GNB) in the oropharynx and rectum.

- **Method:** Data from 6 of 13 European ICUs participating in an ongoing cluster RCT comparing SDD, SOD and CHX
  - Rectum and respiratory tract samples obtained twice weekly

- **Results:** 2.681 patients enrolled in the clinical study
  - 620 (27,8%) 3GCE & 248 patients (11,1%) CR-GNB from rectum
  - 306 (11,7%) and 220 patients (8,4%) from respiratory tract
  - IRR: 2,67 (1,80-3,99) for 3GCE & 2,49 (1,40-4,41) for CR-GNB for SDD
  - IRRs not statistically significantly different from SC for CHX and SOD
  - IRRs 3GCE: 2,00 (1,27-3,13) and 1,83 (1,16-2,87) for SOD and SDD
  - IRRs for CR-GNB were not statistically significantly different from SC for SDD, SOD and CHX.

Wittekamp OS024
What is the minimal intervention bundle to stop a CRE outbreak

- **Objective:** Evaluated the minimal infection control (IC) intervention bundle required to curtail the epidemic

- **Results:**
  - 2005-2008: 19.8% reaching a peak quarter 15
  - Quarter 18: drop following implementation of patients and staff cohorting
  - Quarter 27: decrease following surveillance on admission for patients at risk, high-risk departments, carbapenem restriction, a hospital-wide hand hygiene campaign including observations and feedback

Carbapenem consumption increased from 26 to 43 DDD/1000 HD between 2005-2012, dropping thereafter to 26 DDD/1000 HD in 2016.

*Khetam Hussein OS024*
• **Objective:** To describe the ventilator-associated events (VAE) prevalence and related variables in European Intensive care units (ICU) using the new definitions proposed by the U.S. Centers for Disease Control.

• **Results:** 460 patients included
  
  – Mechanical ventilation was initiated in 200 (48%) at the ICU, 76 (18%) in the OR, 71 (17%) in other hospital wards and 66 (16%) outside.
  
  – 442 episodes of VAE were detected in 131 (28.4%) patients;
  
  – 1st cause of VAE was IVAC in 206 (56.4%).
  
  – IVAC group: 169 (82%) cases met the CDC criteria for possible pneumonia but only 37 (18%) fulfil criteria for probable pneumonia.
  
  – Mortality in the ICU was of 29.4%.
  
  – Patients at the VAE group had a higher ICU mortality when compared to NO VAE patients. (10.7% versus 3.2%) p=0.008, (RR 1.71, 95% IC 1.008-2.918).

Sergio Ramirez OS0106
Polymyxin applied to the respiratory tract fails to prevent Acinetobacter-associated VAP

- **Objective:** to estimate the effect of topical polymyxin toward preventing Acinetobacter associated VAP
- **Method:** A meta-analysis and meta-regression of 42 studies
- **Results:**
  - Mean AAVAP is 4.9% and 3.7% for control groups [C] and intervention groups [I] of 20 topical PM studies versus 2.7% for the AAVAP benchmark
  - Membership of the following are significantly correlated with each of VAP and AAVAP:
    - Trauma ICU (positively)
    - North American ICU (negatively),
    - topical PM intervention group was not significantly correlated.

James Hurley #OS0107
Acetic acid decontamination of sink drains to prevent spread of multi-resistant

P. aeruginosa on a haematology ward.

• **Objective:** to investigate whether acetic acid (described by Aspelund et. al.1) can be used to decontaminate sink and shower drains from MDR P. aeruginosa.

• **Method:** 51 sink and shower drains from the hematology ward treated with a 25% acetic acid solution three times per week.
  – Selection of drains was sampled weekly for culture

• **Results:** 1st screening yielded a total of 10 P. aeruginosa positive drains (seven sink drains and three shower drains)
  – After 5 weeks of acetic acid treatment: the number of positive drains decreased by half, and after 6 weeks all drains were negative
  – Next round of sampling: again the presence of P. aer in 2 drains.
  – 1 P. aeruginosa strains that was cultured after weeks of negative cultures was identical to the strain detected earlier in that same drain

• **Conclusion:** Treatment of sink and shower drains three times a week with acetic acid led to clearance of a MDR P. aeruginosa from contaminated drains.

Rosa Van Mansfeld #OS0108
Objective: systematic review and meta-analysis of published literature to assess the effectiveness of combined antimicrobial-stewardship (AMS) and hand-hygiene interventions

Results: 31 studies reporting 9050857 patient-days
   - the implementation of AMS+HH showed a 70% reduction in the IR of studied pathogens (Incidence Rate Ratio (RR) 0,30; 95% confidence interval (CI): 0,16-0,55; p < 0,05; I²=84%).
   - The 26 studies which did not contemporarily implement HH showed a significant effect of 20% (IRR 0,80; 95% CI: 0,68-0,93; p < 0,05; I²=97%).
   - Sensitivity analysis did not change the effects of the estimates

Conclusions: Combination of AMS+HH measures (education and audit) has a superior effect than the implementation of AMS alone on the reduction of IRs of AMR bacteria and C. difficile in hospitalized patients.
Association between contact precautions and symptoms of depression and anxiety: meta-analysis

• **Objective:** contact precautions have been associated with depression and anxiety; however, the magnitude of association is not known

• **Method:** systematic review

• **Results:** 11 studies evaluated the association between contact precautions and depression or anxiety with a control group not under contact precautions

  – 4 (36%) found a significant association between contact precautions and increased depression and anxiety,
  
  – 5 (46%) did not find statistically significant associations,
  
  – 2 (18%) found significant increases in depression but not anxiety among contact precautions patients

  – Pooled the 5 studies: contact precautions were associated with significantly higher levels of depression (pooled mean difference=2.36; 95% confidence interval [CI]=0.76, 3.97) and anxiety (pooled mean difference=2.21, 95% CI=0.74, 3.67).

Marin Schweizer #OS0110
OS039 - *Clostridium difficile* infections: epidemiology and outcome
Multivariate analysis of factors affecting *C. difficile* infection rates; the more you look, the more you find, but should you believe what you see?

- **Objective:** To describe the impact of multiple factors on CDI rates using a multivariate model.
- **Method:** 40 institutions/hospitals in each of five countries
  - Data on the size and type of institution, *C. difficile* testing methodology, monthly numbers of tests performed and monthly patient bed days
- **Results:** Italian institutions (average 11.8/10,000pbds), acute/primary hospitals (12.3), small institutions (16.7), and those institutions using methods that do not detect toxin (10.7)
  - Winter peaks in CDI rates were only seen in those institutions using standalone toxin detection methods
  - Multivariate analysis testing method (*p* = 0.045), type of institution (*p* = 0.003) and the testing density (*p* = <0.001) remained significant predictors of CDI rate.
  - The sizes of the effects indicated that testing density has the biggest impact on CDI rates.

Kerrie Davies #OS0221
Local-area socioeconomic status is associated with \textit{Clostridium difficile} infection rates

- **Objective:** to investigate how socioeconomic status was correlated with C. difficile infection.

- **Methods:**
  - Cases are mapped geographically primarily based on the location of the patient’s General Practitioner (GP) to Clinical Commissioning Groups (CCGs),
  - compared with socioeconomic status measured by average Index of Multiple Deprivation (IMD)

- **Results:** 14,120 CDI cases 2015/16 (26.0 cases/100,000 population)
  - Rates per CCG ranged from 8.3 per 100,000 to 54.8.
  - Deprivation associated with age-standardised rates of CDI
  - After adjusting for sex, or antibiotic items prescribed higher levels of deprivation remained associated with higher CDI rates
  - Higher levels of antibiotic prescribing per CCG showed an association with higher age-standardised rates of CDI ($\beta = 0.14$, 95% CI = 0.00 - 0.28, $p = 0.049$).
A cluster of *Clostridium difficile* infections caused by a binary toxin-producing new PCR ribotype 826

- **Context:** outbreak management we identified a cluster of 8 CDI episodes in 5 patients within a 4-month period at a gastro-intestinal surgical ward in the Netherlands

- **Method:** PCR ribotyping, MLVA typing, toxinotyping and antimicrobial susceptibility testing

- **Result:** CDI incidence rate from 3.3 per 10,000 patient days to 19.8 per 10,000 patient days
  - The new strain was assigned as ribotype 826 by the UK Ribotyping Reference laboratory
  - closely related “hypervirulent” ribotype 078
  - resistant to ciprofloxacin and moxifloxacin

Monique Crobach OS0223
Clinical outcomes following hospitalization with *Clostridium difficile*

- **Objective:** Explore hospital inpatients in terms of recurrence of CDI, mortality, readmissions to hospital and length of stay
- **Methods:** 3304 CDI cases and 9516 controls
- **Results:**
  - 58% of cases were female, 22% aged 85+, 29% of cases were from the most deprived quintile compared to 27% of controls.
  - At 2 months: 22% of cases died before discharge vs 9% of controls,
  - CDI cases had an estimated additional length of stay of 10.3 days
  - Hazard ratio (HR) of death: 2.2 (95% CI 1.9, 2.5)
  - 14% recurred within 90 days.
  - age 85+ vs under 65: HR for recurrence = 1.9 (95% CI 1.9, 3.3)
  - Among those that recurred 371 survived and 29% had a second recurrence within one year of the second infection with the majority occurring within 90 days of the second infection.
  - 59% were readmitted within 6 months. Few readmissions were directly related to the CDI infection.
EU-wide surveillance of *C. difficile* provides opportunity to assess outcomes of ribotype 027 infections

- Preliminary data sent to ECDC until March 2016 were used to assess the characteristics/outcomes of RT027 CDI at European level.
- Results: data for 123 hospitals in 20 (65%) of 31 EU/EEA countries
  - 1,055 CDI cases were reported (median HACDI incidence: 3.0/10,000 patient-days)
  - RT027 (n=79; 42%), RT014/020/077 (n=16; 8%) and RT001/072 (n=8; 4%). RT027 CDI cases were only reported by Hungary (n=58/85 cases), Poland (n=17/31) and Slovenia (n=4/24).

---

Table: Association between PCR ribotype 027 *C. difficile* infection and infection characteristics/outcomes, in EU/EEA hospital incidence surveillance data, 1 January – 31 March 2016.

<table>
<thead>
<tr>
<th>Characteristic/outcome</th>
<th>PCR Ribotype (^a)</th>
<th>Univariate analysis</th>
<th>Multivariable analyses (^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RT027</td>
<td>non-RT027</td>
<td>Odds Ratio (95%CI)</td>
</tr>
<tr>
<td>Recurrent case</td>
<td>12</td>
<td>62</td>
<td>1.80 (0.75–4.30)</td>
</tr>
<tr>
<td>Healthcare-associated case</td>
<td>71</td>
<td>79</td>
<td>1.95 (0.81–4.69)</td>
</tr>
<tr>
<td>High-incidence hospital (^c)</td>
<td>27</td>
<td>79</td>
<td>7.7 (3.15–18.9)</td>
</tr>
<tr>
<td>Complicated course of infection</td>
<td>10</td>
<td>71</td>
<td>1.99 (0.74–5.31)</td>
</tr>
<tr>
<td>In-hospital death</td>
<td>14</td>
<td>77</td>
<td>1.14 (0.52–2.48)</td>
</tr>
</tbody>
</table>

\(^a\) All cases reported in the 'enhanced' surveillance option that had named the detected *C. difficile* PCR ribotype; \(^b\) Individual multivariable multi-level mixed effects models for the association of RT027 with each characteristic/outcome, within each country that reported ≥1 RT027, i.e. Hungary, Poland and Slovenia. Each model contains the characteristic/outcome, age, McCabe score and gender; \(^c\) Incidence of healthcare-associated *C. difficile* infection ≥75th percentile for the entire EU/EEA dataset; RT: *C. difficile* PCR ribotype; 95%CI: 95% confidence interval.
Objective: We investigated whether whole-genome sequencing (WGS) of consecutive C. difficile isolates from six English hospitals over one year (2013-14)

Results:

- 453/973 (46.6%) sequenced samples were faecal-toxin-positive. The most common ribotypes were 014, 015, 005, 002, 020, and 078; only 2% were ribotype 027.
- Faecal-toxin-positive patients were more likely to have a linked prior source identified, OR, vs toxin-negative) = 1.6 (95% CI 1.1-2.4, p=0.02).
- Faecal-toxin-positive and toxin-negative patients were similarly infectious in terms of being a potential transmission donor, OR = 1.0 (0.7-1.5, p=0.97)
- 51/337 (15%, 95% CI 11-19%) faecal-toxin-positive cases >90 days after the study started were genetically linked to another faecal-toxin-positive case.
- Greatest proportion of cases genetically related to a prior case, 31% (22-41%), lowest, 0% (0-9%).
Clostridium difficile diversity across Europe from whole-genome sequencing

- **Objective:** we investigate the extent of Europe-wide diversity within each RT

<table>
<thead>
<tr>
<th>Ribotype</th>
<th>n</th>
<th>Countries found in</th>
<th>Within mean SNPs</th>
<th>Between mean SNPs</th>
<th>Overall mean SNPs</th>
<th>Within: across country SNP ratio</th>
<th>Expected ratio, 95% confidence interval (from permutation)</th>
<th>Compatible with random European distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>020</td>
<td>33</td>
<td>9</td>
<td>64</td>
<td>54</td>
<td>55</td>
<td>1.20</td>
<td>0.75-1.25</td>
<td>Yes</td>
</tr>
<tr>
<td>014</td>
<td>80</td>
<td>13</td>
<td>121</td>
<td>126</td>
<td>124</td>
<td>0.96</td>
<td>0.90-1.09</td>
<td>Yes</td>
</tr>
<tr>
<td>002</td>
<td>44</td>
<td>11</td>
<td>71</td>
<td>77</td>
<td>76</td>
<td>0.92</td>
<td>0.89-1.09</td>
<td>Yes</td>
</tr>
<tr>
<td>015</td>
<td>29</td>
<td>7</td>
<td>247</td>
<td>277</td>
<td>269</td>
<td>0.89</td>
<td>0.84-1.10</td>
<td>Yes</td>
</tr>
<tr>
<td>078</td>
<td>31</td>
<td>9</td>
<td>81</td>
<td>92</td>
<td>90</td>
<td>0.88</td>
<td>0.71-1.31</td>
<td>Yes</td>
</tr>
<tr>
<td>027</td>
<td>216</td>
<td>10</td>
<td>48</td>
<td>88</td>
<td>77</td>
<td>0.55</td>
<td>0.95-1.04</td>
<td>No</td>
</tr>
<tr>
<td>001</td>
<td>119</td>
<td>14</td>
<td>103</td>
<td>244</td>
<td>186</td>
<td>0.42</td>
<td>0.84-1.16</td>
<td>No</td>
</tr>
<tr>
<td>176</td>
<td>21</td>
<td>3</td>
<td>7</td>
<td>19</td>
<td>14</td>
<td>0.36</td>
<td>0.77-1.18</td>
<td>No</td>
</tr>
<tr>
<td>018</td>
<td>34</td>
<td>7</td>
<td>31</td>
<td>159</td>
<td>84</td>
<td>0.19</td>
<td>0.50-1.55</td>
<td>No</td>
</tr>
<tr>
<td>366</td>
<td>18</td>
<td>1</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

- **Conclusions:** Two distinct patterns of *C. difficile* RT spread were observed. RT027 and RT001

- RT078, previously associated with pig-farming, and RT015, RT002, RT014 and RT020 had evidence of Europe-wide dissemination, consistent with spread via other routes/sources, e.g. for RT078 possibly the food chain

David Eyre OS0227
Clostridium difficile infection in the Asia-Pacific region

- severity appeared milder, and mortality and recurrence were lower, than in North America and Europe
- This is likely because molecular types of C. difficile in Asia differed from other regions of the world

Deirdre Collins OS0228
Objective: to determine, if the usage of metabolomics might help to predict patients at greater risk of recurrent CDI.

Methods: Recurrent CDI cases (n=47), which originated in healthcare facilities or the community in Ireland vs matched controls.

Results: Distinct faecal metabolite profiles were identified among the two groups.

Conclusions: The determination of faecal metabolite profiles using NMR spectroscopy may be a useful tool to identify patients, who are more likely to develop recurrent CDI and might benefit from drugs, such as fidaxomicin.

- Only propionate levels were significantly different between the two groups.
Hospital-onset diarrhoea prevalence, aetiology and management in the United Kingdom: the HOODINI study

• **Objective:** service-evaluation across the NHS to determine the prevalence, aetiology and management of Healthcare onset Diarrhea

• **Results:** 230/4955 eligible patients on 141 wards had HOD (crude point-prevalence 4.6%; 95%CI 4.1-5.3%).
  
  – 125/230 (54%) were receiving antimicrobials,
  
  – 195/230 (85%) were taking other medication that can cause diarrhoea (laxatives in 65%).
  
  – Only 75 (33%) of patients had CDI testing, 9 were faecal toxin positive (4%); a further 3 had norovirus.
  
  – Patients had not reported diarrhoea to staff in 10% (22/230) cases;
  
  – HOD was not documented in 50% of medical notes.
  
  – Only 80 patients (35%) had evidence of a medical assessment of the diarrhoea.

<table>
<thead>
<tr>
<th>Hospital type</th>
<th>Point-prevalence</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DGH</td>
<td>2.9%</td>
<td>2.3,3.6%</td>
</tr>
<tr>
<td>Specialist</td>
<td>10.0%</td>
<td>4.2,21.9%</td>
</tr>
<tr>
<td>Teaching</td>
<td>6.1%</td>
<td>5.3,7.1%</td>
</tr>
</tbody>
</table>

Damian Mawer OS0230
Sunday, 23 April 2017
SY049 - Transmission of plasmid-borne resistance - a new paradigm for infection control?
Transmission of plasmid-borne resistance

The role of conjugative plasmids in the nosocomial spread of antimicrobial resistance in Gram-negatives
What is the evidence?

Roberto Melano, PhD.

Symposium
Transmission of plasmid-borne resistance
A new paradigm for infection control?
27th ECCMID – Vienna, Austria
April 23rd, 2017
Transmission of plasmid-borne resistance
Transmission of plasmid-borne resistance

K. pneumoniae → same PFGE pattern and same MLST ST277 (related to ST258) → inter-patient transmission

Both patients share the same room (2 days) Hosp. 2


#SY0265
Transmission of plasmid-borne resistance

Colorectal cancer surgery in a large hospital in Italy

Patient traveled back, hospitalized in a large tertiary hospital in Wenzhou, Eastern China

Intra-abdominal abscesses → *K. pneumoniae*, *E. coli* and *E. faecalis*
Blood culture → *K. pneumoniae* and *E. coli*
Abscess specimen → *E. coli* and *E. faecalis* (one week later)

All *K. pneumoniae* and *E. coli* → I or R to AMP, SAM, CFZ, EPM, IPM, and TZP, but S to 3GC and 4GC and to ATM

PCR assays revealed that they all carried *bla*$_{OXA-48}$
Transmission of plasmid-borne resistance

Characterization of Multiple NDM-1-Producing Enterobacteriaceae Isolates from the Same Patient
Nathalie Tijet, a David Richardson, b,c,d Gregory MacMullin, a Samir N. Patel, a,n Roberto G. Melano n,s,f

- A 65 year-old man hospitalized in India with a UTI, complicated by the development of a large sacral decubitus ulcer

- Presented to the Emergency Department of a community hospital (ON, Canada) with fever and generalized weakness

- Blood culture → MDR E. coli GN568 TIG 5 (with which the patient was treated and recovered)

- Two weeks after treatment, his fever recurred
  Blood culture → ESBL-producing K. pneumoniae
  Urine culture → E. cloacae GN574 (only TIG 5) and P. stuartii GN576 (TIG 5, SXT 5 and CIP 5)

PublicHealthOntario.ca


#SY0265
Transmission of plasmid-borne resistance
In conclusion...

- Outbreak strains are traditionally defined as isolates of the same species that are epidemiologically, phenotypically and genetically related.

- However, “plasmid outbreaks” would show indistinguishable (or highly related) plasmids in unrelated bacterial strains and species in the same patient, highlighting the existence of epidemic plasmids and horizontal gene transfer.

- Very often they belong to plasmid families with very efficient conjugative systems (e.g. IncI1 and IncN), or showing broad host range (e.g. IncA/C, IncL/M).

- These plasmids can be stably maintained independently of their harboured resistance genes (e.g. presence of toxin-antitoxin systems).
Horizontal transfer of antimicrobial resistance in patients and the environment

ECCMID 2017
Session: Transmission of plasmid-borne resistance - a new paradigm for infection control?

University of Virginia
Amy Mathers, MD
April 23rd, 2017
Transmission of plasmid-borne resistance

Very suspicious epidemiology
Plasmid genomics slightly complicated

- Both isolates PacBio sequenced
- Chromosome differs by 3 SNVs
- $bla_{KPC}$ plasmids almost identical except for 14 kb of additional DNA in the environmental plasmid
  - KPC Gene
  - Transposon carrying KPC

169 kb IncFIB/IncFII plasmid
43 kb RepA pKPC_UVA01
12.5 kb segment of plasmid DNA
1.5 kb segment

Isolated January
Isolated March

#SY0266
Transmission of plasmid-borne resistance

Incidence of KPC-producing Bacteria by Species in our institution

Perirectal surveillance begins

#SY0266
Transmission of plasmid-borne resistance

Structural diversity of pKPC_UVA01

Initial results simply WRONG:
- Many different plasmids involved
- Plasmid structures NOT conserved
Transmission of plasmid-borne resistance

Enhanced interventions to stop patient to patient transmission worked but...

Use of CRE toolkit stopped transmission of related Gram negative drug resistant organisms but saw multispecies KPC-producers persist

Enfield K et al. 2014 Inf Contr Hosp Epi. 35(7):810-7.
Transmission of plasmid-borne resistance

When we looked, we found KPC in the sink drains
Transmission of plasmid-borne resistance

Dissection of a sink trap

**Raoultella ornithinolytica**

IncN 72kb backbone
Tn4401b-2/Tn5403
Tn5403 3.6 kb

**Citrobacter freundii**

Incl/M 86kb backbone
Tn4401b-1

Patient isolate from October 2012
Transmission of plasmid-borne resistance

Goal: Prevent transmission of $bla_{KPC}$ positive organisms from sink traps to patients

Two Lines of Attack

1. Avoid using the *sink countertop* for patient care items
2. Eliminate or reduce KPC-producing bacteria in *sink traps*
   - Remove drains, P-traps and overflow
   - Apply bleach, $H_2O_2$ or ozone **to keep from coming back**
Transmission of plasmid-borne resistance

Results: PacBio

Patient 2: K. pneumoniae

Patient 2: S. marcescens

Nov 2013 - Patient carried KPC-positive K. pneumoniae and S. marcescens

Room: K. pneumoniae

Feb 2014 - Patient goes into room with newly replaced sink trap
10 days later - K. pneumoniae with three bla\textsubscript{KPC} plasmids isolated from sink trap

→ Plasmid transfer from KPC-Sm to KPC-Kp likely occurred within patient

Oral Abstract presented by Anna Sheppard
Conclusions

- Plasmid exchange in the environment may not be what we suspect
- Real-world examples of plasmid mediated transmission with environmental involvement are complicated
- These findings reveal more questions than answers to tracking complex bacterial evolution
- Great deal of unknowns remain with what to do with waste water environment
Is there enough evidence from research on plasmid-encoded antimicrobial resistance to change infection control guidelines?

Surbhi Malhotra-Kumar

Laboratory of Medical Microbiology
Vaccine & Infectious Disease Institute
University of Antwerp, Belgium
Transmission of plasmid-borne resistance

Nosocomial transmission, especially in LTCFs…!

Transmission dynamic for exposed contacts

Pediatric and adult inpatients in Basel hospital 2008 – 2010

<table>
<thead>
<tr>
<th></th>
<th>Klebsiella</th>
<th>E.coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>Index patient</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Exposed patient</td>
<td>24</td>
<td>88</td>
</tr>
<tr>
<td>Transmission events</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Contact precautions</td>
<td>78%</td>
<td>25%</td>
</tr>
<tr>
<td>Incidence</td>
<td>13.8/1000J.</td>
<td>5.6/1000J.</td>
</tr>
</tbody>
</table>

Long term care facilities or rehabilitation centers

9 nursing homes in Sweden, 560 participants
October-november 2008

15 ESBL positive patients in 7/9 nursing homes
14/15 ESBLs = E.coli

Hilly M et al, Clin Infect Dis 2012

Andersson H et al, Scandinavian Journal of Infectious Diseases, 2012
Transmission of plasmid-borne resistance

Movement of ESBL genes across enterobacterial genera: within hospital spread

Transmission of ESBL CTX-M resistance

E. Coli ST131 CTX-M15
  Early 2000’s

CTX-M

ESBL-Enterobacter
Nowadays

ESBL-K. pneumoniae

Transfer of an Escherichia coli ST131 multiresistance cassette has created a Klebsiella pneumoniae-specific plasmid associated with a major nosocomial outbreak

Linus Sandegren1, Marius Linkevicius1, Birgitta Lytys1, Ása Melhus1 and Dan I. Andersson1

- blaCTX-M-15-encoding multiresistance cassette integrated in the pKPN3 K. pneumoniae plasmid backbone
- recombination points in an IS26 element!
Host–specific IS-mediated plasmid deletions underlie adaptive evolution in new clinical bacterial hosts

- Plasmid gene reduction consistently targeted the conjugation machinery
  - Compensatory mechanism to decrease biological cost of plasmid carriage

- Radical restructuring narrows the plasmid host range by constraining its dissemination
  - Tradeoff between horizontal and vertical plasmid transfer

- In the right host background, makings of a potential MDR superbug!!

Usefulness of contact precautions

What are the precautions?

• **Vertical approach**
  - Active surveillance culture
  - **Contact precautions** for colonized/infected patients
  - Decolonization of patients with specific MRB

• **Horizontal approach**
  - **Standard precautions/hand hygiene**
  - Universal decolonization (Chlorhexidine bathing)
  - Universal use or gloves/gowns
  - Antimicrobial stewardship
  - Environmental cleaning and disinfection

   - Hand hygiene after a contact with the environment
   - Single room or cohorting
   - Signaling
   - Screening in case of outbreaks

   - Hand hygiene
   - Gloves & apron if projection risk
   - Mask if aerosolization risk
In conclusion

- Settings with high MDR-GNB (ESBL-E.coli/CR-KPN) colonization pressure, extended hospital stay and close contact between vulnerable patients may serve as amplification platforms to accelerate transmission events.
- Impact of MDR-GNB loads on transmission events remains unclear
- There are potentially more transmissible and virulent strains that may require contact precautions
- The contribution of transmission of plasmids rather than strains to ongoing ESBL/Carbapenemase-transmission is currently elusive.

• ➔ Such considerations may favor contact precautions for patients colonized or infected with MDR-GNB
In conclusion (2)

- When abandoning contact precautions for carriers, a few pre-requisites need to be fulfilled:
  - high compliance with standard precautions including hand hygiene
  - ongoing surveillance and early detection of nosocomial MDR-GNB outbreaks
  - if possible, sporadic molecular typing of infection isolates to exclude ongoing nosocomial transmission of virulent and presumably highly transmissible ESBL-E.coli ST131-H30 and ST258-KPN clones
IN SILICO DETECTION AND TYPING OF PLASMIDS USING WHOLE-GENOME SEQUENCE DATA

applications in infection control

Henrik Hasman
Statens Serum Institut
Copenhagen
Transmission of plasmid-borne resistance

PLASMID TYPING

- Plasmid size
- Restriction Fragment Length Polymorphism (RFLP)
  - Typing of conserved elements (replicons, tra genes)
  - Complete sequencing

In silico
Transmission of plasmid-borne resistance

PLASMID DESIGN 101

Origin of transfer (oriT)
Replicase
Origin of replication (ori)
Replicon
Resistance plasmid
Resistance
virulence
bacteriocins
Plasmid transfer
Plasmid maintenance and stability

#SY0268
Transmission of plasmid-borne resistance

Hierarchical Approach

- Replicon (PlasmidFinder)
- Scaffold specific genes (pMLST)
- Shared resistance genes (ResFinder, ARG-ANNOT, SRST2)
- Full plasmid sequences (WGS alignment?)
Transmission of plasmid-borne resistance

Illumina MiSeq system

DNA (Chromosome or plasmid)
Replicon
AMR

De novo assembly

Including data from other plasmids and the chromosome

Repetitive element (IS or transposons)

#SY0268
CONCLUDING REMARKS

- Plasmid typing is an important first step to follow plasmid epidemiology
- The 2. generation WGS technology is not optimal for full plasmid typing
- SMRT sequencing platforms are often required for full assembly
- … but still require extensive lab- and laptop efforts to complete the task
- Comprehensive plasmid databases need to be created….and updated
SY084 - Surgical site infection prevention worldwide
The basis for the new WHO global guideline – systematic assessment of risks and the burden of SSI around the world

Petra Gastmeier
Institute of Hygiene and Environmental Medicine
Charité – University Medicine Berlin
SSI burden in low-/middle-income countries
Systematic review 1995-2010

Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis
Benedetta Allegranzi, Sepideh Bagheri Nejad, Christophe Combescure, Wilco Graafmans, Homa Attar, Liam Donaldson, Didier Pittet

57 articles investigating SSI
Allegranzi B et al. Lancet 2011;377:228-41
SSI burden in low-/middle-income countries
Systematic review 1995-2010

**Figure 5:** Cumulative incidence of surgical-site infections overall (A) and according to wound classification (B) in developing countries, 1995-2008.

Box plots contain results for first and third quartile. Medians are indicated as a black line. Whiskers indicate lower and upper limits of distribution. Incidence is reported as surgical-site infection episodes, either per 100 surgical patients or per 100 surgical procedures.

Allegrenzi B et al. Lancet 2011;377:228-41
#SY0442

## Surgical site infection prevention worldwide

### Seasons as risk factor for SSI in other studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of surgery</th>
<th>Season</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manian et al., 1998</td>
<td>Neurosurgery</td>
<td>April-Sept.</td>
</tr>
<tr>
<td>Gruska et al., 2013</td>
<td>Spine surgery</td>
<td>Summer</td>
</tr>
<tr>
<td>Kane et al. 2014</td>
<td>Total joint arthroplasty</td>
<td>July-Sept.</td>
</tr>
<tr>
<td>Durkin et al. 2015</td>
<td>15 procedures</td>
<td>Summer</td>
</tr>
<tr>
<td>Schröder et al. 2015</td>
<td>Colon surgery</td>
<td>Summer</td>
</tr>
</tbody>
</table>

**Summer: higher bacterial burden on the patient’s skin during warm and humid months -> perspiration**
Volume effect

Impact of department volume on surgical site infections following arthroscopy, knee replacement or hip replacement

Meyer et al. BMJ Qual Saf 2011; 20:1069-74

Figure 1 Surgical site infection rate by department volume per year.
Volume effect

Original Article

Surgical Site Infections

Volume-Outcome Relationship and Year-to-Year Stability of Performance Rankings

Michael S. Calderwood, MD, MPH,*† Ken Kleinman, ScD,‡ Susan S. Huang, MD, MPH,§ Michael V. Murphy, BA,† Deborah S. Yokoe, MD, MPH,* and Richard Platt, MD, MSc†

Claim based surveillance data from US hospitals 2005-2011:
Risk factors: CABG: < 50 per year
Hip arthroplasty < 200 per year

Calderwood et al. Med Care 2017; 55:79-85

#SY0442
Summary: Risks and burden of SSI around the world

- Robust SSI data from Europe and North America, with SSI as the most frequent HAI in Europe
- Improving data from low and middle income countries with much higher SSI rates
- High burden of SSI (58 DALYs per 100,000 inhabitants in Europe)
- Some well known risk factors
- Some risk factors should be further investigated
- Preventing surgery if possible
Translating recommendations into practice – effective implementation strategies and tools across settings with different levels of resources

Prof. B. Allegranzi
IPC Global Unit
SDS, HIS, WHO HQ

27th ECCMID, Vienna 23 April 2017
Surgical site infection prevention worldwide

WHO SSI Prevention Guidelines
- 27 systematic reviews & meta-analysis
- 29 recommendations on 23 topics
- 30 core chapters

Key updates on:
- Timing & duration of surgical ATB prophylaxis
- ATB use with drains
- S. aureus carriers’ decolonization
- Glucose control
- Normovolemic
- Oxygenation
- Wound irrigation
- Antimicrobial sutures
& A LOT MORE....

Abstracts presented at 26th ECCMID, Amsterdam 2016
The Lancet Infectious Diseases & official launch, 3 November 2016

#SY0443
SSI prevention throughout the patient journey

WHAT’S THE SOLUTION?
A range of precautions - before, during and after surgery - reduces the risk of infection

BEFORE SURGERY
- Ensure patients bathe or shower
- Do not shave patients
- Only use antibiotics when recommended
- Use chlorhexidine alcohol-based antiseptic solutions to prepare skin
- Surgical scrub technique: hand wash or alcohol-based handrub

DURING SURGERY
- Limit the number of people and doors being opened
- Ensure all surgical equipment is sterile and maintain asepsis throughout surgery

AFTER SURGERY
- Do not continue antibiotics to prevent infection - this is unnecessary and contributes to the spread of antibiotic resistance
- Check wounds for infection and use standard dressings on primary wounds

World Health Organization
WHO Recommendations for SSI Prevention for the Preoperative Period

- Carriers’ decolonisation with mupirocin
- MBP & use of oral antibiotics
- Hair removal
- SAP optimal timing
- Surgical hand preparation
- Surgical site skin preparation

- Perioperative immunosuppressive agents
- Enhanced nutritional support
- Preoperative bathing
- Antimicrobial skin sealants

SAP: surgical antibiotic prophylaxis

Launched on 3 November 2016
WHO Recommendations for SSI Prevention for the Intraoperative Period

- Perioperative oxygenation
- Normothermia
- Normovolemia
- Glucose control
- Drapes and gowns
- Wound protection devices
- Incisional wound irrigation
- Prophylactic negative pressure wound therapy
- Antimicrobial-coated sutures
- Laminar flow

Launched on 3 November 2016
WHO Recommendations for SSI Prevention for the Postoperative Period

- Surgical antibiotic prophylaxis prolongation
- Advanced dressing
- Antimicrobial prophylaxis in presence of a drain

Launched on 3 November 2016
Surgical site infection prevention worldwide

Mapping two implementation strategies

Critical point: implementation, whatever way you look at it, means that there are key elements for success, whatever these elements are called – these two strategies are similar and have demonstrated success.

1. WHO HAND HYGIENE MULTIMODAL IMPROVEMENT STRATEGY & The 4 E’s: An action-oriented implementation model (Pronovost et al)
In other words...

1. Build it
   (system change)

2. Teach it
   (training & education)

3. Check it
   (monitoring & feedback)

4. Sell it
   (Reminders & communications)

5. Live it
   (culture change)

Surgical site infection prevention worldwide

The Surgical Unit-based Safety Program (SUSP) approach

Patient safety culture improvement (CUSP):
- Science of safety education
- Staff safety assessment
  - Leadership
  - Learning from defects
  - Team work & communications

Infection prevention best practices identified according to local staff assessment

Improvement of the patient safety climate

Reduction of:
- Surgical site infections
- Surgical complications

World Health Organization

JOHNS HOPKINS MEDICINE
Lessons learned and conclusions

- Use multimodal strategies (not just checklists & bundles)
- Have a step-wise action plan
- Map recommendations acc to surgical patient journey
- Empower teams and involve front-line staff
- Engage leadership
- Let teams take the lead on adaptation
- Catalyze collective and individual ownership
- Use data to create awareness
- Award teams and work with a safety culture spirit

World Health Organization

#SY0443
KN080 - The role of intestinal microbiota to combat antimicrobial-resistant bacteria
Role of the intestinal microbiota in defense against antimicrobial-resistant bacteria.

Eric G. Pamer, M.D.
Infectious Diseases Service, Memorial Hospital
Immunology Program, Sloan-Kettering Institute
Lucille Castori Center for Microbes, Inflammation and Cancer
Memorial Sloan-Kettering Cancer Center
VRE Domination of the GI tract occurs in some patients following allogeneic hematopoietic stem cell transplantation and is associated with VRE bacteremia.

Intestinal microbiota diversity decreases following allo-HSCT.

Taur et al. (2012) Clinical Infectious Diseases
Loss of microbiota diversity following allo-HSCT is variable.
Transplant-related mortality is markedly reduced in patients with a diverse microbiota following engraftment.

Log-rank
P = 0.003

Low Diversity
(Inverse Simpson < 2)

Medium diversity
(Inverse Simpson 2–4)

High diversity
(Inverse Simpson > 4)

Number at Risk
High diversity 26
Medium diversity 20
Low Diversity 34

Time, post-engraftment (years)

Probability of Transplant Related Death

0%
25%
50%
75%
100%

Different antibiotics: disparate duration of susceptibility to *Clostridium difficile* infection.

![Graphs showing relative abundance over days post-antibiotic cessation for Ampicillin, Clindamycin, and Fluoroquinolone](image)

*Buffie et al. (2015) Nature 517:205*
Protection against \textit{C. difficile} mediated by four commensal bacterial species: \textit{B. intestihominis}, \textit{Blautia hansenii}, \textit{Pseudoflavonifractor capillosus} and \textit{C. scindens}.

"Normal" microbiota eliminates persistent VRE

- Amp – 1 week
- No Antibiotic

VRE in Fecal Samples

- Untreated
- 2 weeks post-infection + Feces

Microbiota composition

- PBS
- Fecal pellet

Ubeda et al. (2013) Infection and Immunity
7 bacterial taxa can mediate colonization resistance against VRE.

**7-mix**

- *Blautia producta*
- *Clostridium bolteae*
- *Eubacterium dolichum*
- *Blautia_unclassified*
- *Akkermansia muciniphila*
- *Parabacteroides distasonis*
- *Bacteroides sartorii*

---

**Graph**

- Days: -4, -3, -2, -1, 0, 1, 3, 6/8
- Ampicillin
- 7-mix
- VRE
- Fecal sample

---

**Log_{10} (VRE CFU g^{-1} feces)**

- **d1**
- **d3**
- **d6/8**

**L.o.D.**

Caballero et al. 2017, Cell Host & Microbe, in press
Co-coculture of VRE with *B. producta* inhibits VRE growth.

![Graph showing](image)

*In vitro* VRE co-culture

- **VRE** (CFU/mL)
- **Time (hours post-inoculation)**
- **LOD**

Sohn Kim, MSKCC

#KN0434
Cell-free supernatant from *B. producta* inhibits VRE.
*Blautia producta* inhibitor has broad activity against Gram-positive bacteria.

*in vitro* culture of various species

Sohn Kim, MSKCC
Variable inhibition of VRE by different *B. producta* strains.

*in vitro* VRE co-culture

- **B. producta** (MSKCC)
- **B. producta** (Clostridiales VE-202-06)
- negative control

Sohn Kim, MSKCC
Distinct consortia of obligate anaerobic bacterial species provide resistance against different intestinal pathogens.

**Clostridium scindens**
- Blautia hansenii
- Pseudoflavonifractor capillosus
- Barnesiella intestinhominis

**Clostridium difficile**

**Blautia producta**
- Clostridium bolteae
- Bacteroides sartorii
- Parabacteroides distasonis

**Enterococcus faecium**

**Blautia producta**
- Clostridium hathewayi
- Clostridium ramosum
- Clostridium saccharogumia

**Listeria monocytogenes**
Microbiota-mediated defense against antibiotic-resistant bacterial infections.

Microbial populations in the gut stimulate antimicrobial mechanisms that reduce the ability of pathogens to colonize the gut.

Complex microbial networks in the gut provide colonization resistance; the indirect and direct mechanisms remain incompletely defined.

Microbiota-mediated modification of bile acids contributes to host resistance to intestinal pathogens.

Microbiota diversity predicts survival following allogeneic hematopoietic stem cell transplantation.

Reconstitution of mucosal bacterial populations following antibiotic therapy using FMT or specific commensal microbes provides an alternative approach to treat and prevent infections in an era of decreasing antibiotic susceptibility.
OS098 - New frontiers in reducing SSI
Objective: to provide guidance and pragmatic recommendations for patients that may aid in the optimal prevention of SSI.

Results: nine essential components of perioperative care that can influence SSI prevention

- Areas for action: Staphylococcus aureus (MSSA) screening and decolonization, smoking, hair removal, hand hygiene, body temperature, showering, diabetes mellitus, wound care and prevention of multi drug resistant organisms (MDRO) transmission

- Patient information leaflet:
  - If you are undergoing high risk surgery including cardiothoracic and orthopedic surgery ask the healthcare worker (HCW) for a nasal screening test, to identify MSSA carriage; quit smoking > 4 weeks before your surgery;
  - If hair is to be removed at the planned incision site using a razor, speak up - if necessary,
  - Hair should only be removed with an electrical clipper;
  - Shower or bathe with either soap or an antiseptic agent the night before and/or in the morning before the surgery;
  - Preserve warm body temperature by taking a hot shower shortly prior to the surgery and stay under the covers after the shower;

Veronica Weterings OS098
Not all heater-cooler units are equal - different risk for contamination with M. chimaera during open-heart surgery

- **Objective:** the contamination of and risk from HCUs of different manufacturers has not yet been systematically assessed.

- **Methods:** Three types of HCUs (3T, HCU30 and HCU40) from two different manufacturers were in use during the surveillance.
  - Monthly water samples from the patient- and cardioplegia-circuit as well as air samples next to the operation field before and while operating were obtained

- **Results:** contamination with M. chimaera was found in the water of all 3T and HCU30 units
  - aerosolisation of M. chimaera was detected with 3T but not HCU30
  - Despite intensified disinfection procedures, M. chimaera grew in 2/42 water samples from 3T HCUs in 2015

Only HCU40 remained negative for M. chimaera in water and air sampling

<table>
<thead>
<tr>
<th>Heater-cooler units</th>
<th>Samples with detection of M. chimaera (n/total)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2014</td>
</tr>
<tr>
<td>3T</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>8/47</td>
</tr>
<tr>
<td>Air</td>
<td>22/43</td>
</tr>
<tr>
<td>HCU30</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>7/12</td>
</tr>
<tr>
<td>Air</td>
<td>0/4</td>
</tr>
<tr>
<td>HCU40</td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>na</td>
</tr>
<tr>
<td>Air</td>
<td>na</td>
</tr>
</tbody>
</table>

na = not applicable
Optimal timing of antimicrobial prophylaxis in cardiac surgery: an analysis of 15'873 patients

**Objective:** We analyzed data on cardiac surgery to better define the optimal timing of SAP

**Methods:** We used generalized additive models to describe time varying effects to predict SSIs.

- Variables such as antibiotic class (limited to 1./2. generation cephalosporins, vancomycin, and combinations thereof), timing of SAP and baseline patient and procedural characteristics were used to adjust risk in the models.

**Results:**

- 15’873 cases with documented SAP times (median=45 minutes; IQR 33-60) were enrolled with an SSI incidence of 5.7% (n=902)
- SSI risk in cardiac surgery patients was approximately constant within the 120 minutes time interval before incision
Semi-automated surveillance of deep surgical site infections after cardiothoracic surgery

- This study presents an algorithm that relies on routine care clinical data to retrospectively classify patients as having a low or high probability of a deep SSI after cardiothoracic surgery.
- **Results:** This study included 2590 procedures, of which 25 (1.0%) were complicated by a deep SSI (22 sternal infections, 3 harvest site infections).
  - An algorithm based on a combination of revision surgery, cultures, antibiotics and mortality resulted in 113 patients classified as having a high probability and a PPV of 22.1%, while maintaining 100% sensitivity.
  - Workload reduction, this means it suffices to manually assess 22.1% of the 512 medical charts currently evaluated in routine surveillance and 4.4% of all medical charts.
Preoperative oral antibiotic prophylaxis reduces SSI after elective colorectal surgery

- Oral antibiotic prophylaxis (OAP = tobramycin and colistin) preceding colorectal surgery was recently introduced with the objective to further reduce SSIs.
- **Results:** 352 patients in the control period and 1,135 patients in the treatment period.
  - 50 patients (14.2%) in the control period developed a deep SSI or died within 30 days after surgery, versus 91 patients (8.0%) in the treatment period (OR 0.53, 95% CI 0.36 – 0.76)
  - Mortality decreased from 3.4% to 2.2% (OR 0.64; 95% CI 0.32 – 1.28) and deep SSIs from 11.3% to 6.3% (OR 0.50, 95% CI 0.34 – 0.75).
  - Multivariate analysis: use of OAP was significantly associated with a decrease in the incidence of deep SSI and/or mortality (OR 0.55, 95% CI 0.37 - 0.81).
  - Decrease in anastomotic leakage (control period 7.6%; treatment period 4.5%; OR 0.57, 95% CI 0.35 - 0.92) and median length of hospital stay (control period: 9 days; treatment period: 8 days, p<0.001)
Effectiveness of decontamination measures in the prevention of surgical site infection in spinal surgery

- **Objective:** to evaluate the role of decontaminations measures in the prevention of spinal SSI.
- **Methods:** 5 days of nasal mupirocine application with chlorexidine cutaneous application before surgery
- **Results:** 4613 in Beaujon with 272 SSI and 701 patients in GPEH with 39 SSI.
  - Incidence of SSI decreased significantly from 7.3% to 4.5% (p=0.003) then to 3% (p<0.001) in Beaujon, and from 8.27% to 3.9% (OR=2.2, p=0.017) in GPEH.

Bouyer Benjamin OS0514
This study assessed the Staphylococcus aureus (S. aureus) infection risk among German T2DM patients undergoing an orthopedic surgery.

**Methods:** Cumulative S. aureus incidence (based on ICD-10 codes) was calculated for the index inpatient hospitalization stay and for 30, 90, 180, and 365 days after index surgery.
Risk factors for *S. aureus* SSI after orthopedic surgery in a French university hospital

- **Objective:** to evaluate risk factors for *S. aureus* SSI after orthopedic surgery in a French University Hospital.

- **Methods:** A case-control study nested within a prospective cohort of patients undergoing orthopedic surgery (hip arthroplasty, knee arthroplasty, revision of hip arthroplasty, revision of knee arthroplasty, osteosynthesis)

- **Results:** 7438 selected interventions, 137 (1.84%) SSI were identified; 50 (0.67%) were only due to *S. aureus* – 35 (70%) infections were deep and 8 (16%) were organ/space. A total of 46 (92%) SSI were due to methicillin-sensitive *S. aureus* and 4 (8%) to methicillin-resistant *S. aureus*

  - 46 *S. aureus* SSI were matched to 91 controls

  - Multivariable analysis: smoking (odds-ratio (OR) 8.35, 95% CI 1.17-59.60), and NNISS score of one or more (OR 5.77, 95% CI 1.75-19.05). Bathing one or two times with antiseptic soap prior to intervention was protective (OR 0.26, 95% CI 0.12-0.65) against *S. aureus* SSI.

Caroline Landelle OS0516
SY093 - Best infection control practices in a culturally diverse world
Core elements for successfully implementing infection control – What do I have to ask my hospital director?

Andreas Voss, MD, PhD
Clinical Microbiology & ID
Professor of Infection Control
CWZ and Radboud umc
Nijmegen, The Netherlands

Nothing to disclose
Best infection control practices in a culturally diverse world

ECDC Core Competencies

- Programme management
- Quality improvement
- Surveillance and investigation HAIs
- Infection control activities

Generating money or convincing administrators is nowhere in it

Core competencies for infection control and hospital hygiene professionals in the European Union. Stockholm: ECDC; 2013
Best infection control practices in a culturally diverse world

Two questions to answer

What can I do to convince my hospital director?

What do I have to ask my hospital director?
Best infection control practices in a culturally diverse world

What can I do to convince my hospital director?

1. Convince your administration that "we" have a problem
2. The "business case for IPC"
3. Ensure your "mission" is known
4. Show that IPC is more than "saving costs"
5. Choose best things to do with your "fixed budget"
6. Never waist a good outbreak or public health crisis
The business case for ICP (SHEA guideline)

1. Frame the problem + create hypothesis about solutions
2. Create interest by meeting with key stakeholders
3. Determine local costs of intervention, costs that can be avoided by reducing HAI, and attributable and variable costs
4. Calculate financial impact and other health benefits
5. Communicate the possibilities of the BC
6. Prospectively collect cost and outcome data

adjusted from 9 point SHEA guideline
Best infection control practices in a culturally diverse world

Cost-effectiveness is not the only key to your administrator’s heart...

- Safe care = better care
- Corner-stone in preserving antibiotics
- Stimulate general preventive measures e.g. flu-shot
- Engage in visible actions e.g. hand hygiene action that get picked-up by press
- Educate not only HCWs, but patients and the public
- Try to evaluate patients satisfaction with regard to IPC

#SY0479
5. Choose best things to do with your “fixed budget”

- Task differentiation
- Link-nurse system
- Prioritize high prevalence units/problems
  - actually choose “priorities” you really don’t do!
  - turf unwanted tasks (e.g. needle-stick accidents to occupational health)
  - invent new positions in professional guidelines (DSMH/DSRD)
- Invest in better software and automation (e.g. surveillance)
- Engage clinicians (e.g. surgeons in charge of SSI improvement)
Best infection control practices in a culturally diverse world

What do I have to ask my hospital director?

1. Structure and position in organization
2. Access to all data sources
3. Use of rapid diagnostic tests & typing
4. Moral support (by administration and medical director)
5. Finance CME including (non-ICP) education
6. Freedom and support to implement new idea’s
Best infection control practices in a culturally diverse world
2. Access to all data sources

Access to:

- All departments (requested and un-requested)
- All patient files
- OR systems
- Complication registration systems
- Census data of the hospital
- Facility services and medical technique reports
Best infection control practices in a culturally diverse world

- Behavior
- Patient participation
- Transmission prevention
  - Hand hygiene, Environmental control
- Surveillance
- Guidelines
Control of multi-drug Gram-negative bacteria in Low & middle-income countries
High impact interventions without much resource

Nalini Singh, MD, MPH
Professor Pediatrics, Global Health & Epidemiology
George Washington University, Washington DC
Global hand hygiene promotion – how to reach the top at low cost?

Walter Zingg, PD, MD
Best infection control practices in a culturally diverse world

Diagnostic Microbiology Challenges in Infection Prevention Across the World

Daniel Diekema, MD, D(ABMM)
Director, Division of Infectious Diseases

University of Iowa Hospitals & Clinics

University of Iowa Health Care

Research funding from bioMérieux
Outline

• Define essential elements of lab support for IP

• Key challenges to effective lab support
  – Limitations of existing technology
  – Obstacles to realizing potential of tech advances

• Future directions
  – Bringing technologic advances to the point-of-care
  – Strengthening regional/national lab networks
What is “good quality....support”? 

• Timely organism detection and reporting
  – Accurate ID and AST (if applicable)

• Cumulative data availability
  – Regularly updated, accessible to providers
  – Susceptibility + pathogen incidence

• Access to molecular typing/advanced testing
  – Regional and national referral laboratories
The future: NGS and metagenomics

- **Next-generation sequencing**: DNA-sequencing methods that produce more data in a shorter time, with less manual intervention, than previous methods.

- **Metagenomics**: Analyzing all genetic material in a sample, without separating genomes or culturing.

- **Metagenomic whole genome sequencing**: Applying WGS to a metagenomic sample—DNA is extracted from a sample, producing a mixture of genomes, which are subjected to WGS en masse.
Emerging diagnostic technologies: Speed, accuracy, sensitivity

• Mass spectrometry (MALDI-TOF)
  – Matrix-assisted laser desorption/ionization-TOF

• **Nucleic acid amplification/detection (NAAT)**
  – PNA-FISH, PCR approaches (microarrays, multiplex)

• Magnetic resonance
  – Applied directly to sample after short amplification step

• Automated microscopy + FISH
  – “Rapid phenotypic testing”
Microarrays: changing a paradigm

1. Recognize syndrome
2. Formulate Diff Dx
3. Send tests for most likely etiologies
4. Make diagnosis
5. Send tests for less likely etiologies

SYNDROMIC TESTING
Summary:
Diagnostic microbiology challenges for IP

• Provide the essential support:
  – Timely organism detection and susceptibility
  – Cumulative data availability/feedback
  – Access to molecular typing/advanced testing

• Bring this essential support close to the POC

• Strengthen the laboratory response network
Monday, 24 April 2017
Eyes for the invisible

The regional healthcare networks
Think in networks - modern resistance prevention and control

Network of health care institutions

Construct from Electronic Medical Records

England: NHS-Hospital Episode Statistics (HES)
Netherlands: National Medical Registry (LMR)

Record all patient movements between hospitals
Shows the easiest routes for AMR to travel through the patient flow
Epidemiological significance of contact networks

- Deviates from random mixing of individuals
  - Assumed by many models of disease spread
- Not all possible routes exist
  - Network structure can influence spread
  - Network position of individual relates to risk
- How do we measure network structure and position of individuals?
  - Taking into account the entire network
Think in networks - modern resistance prevention and control

Networks structure

Measuring the properties of the entire network

- Clustering or cliqueness
- Community structure

- Diameter
  - Based on shortest paths between nodes
  - Longest distance
Network metrics
Centrality (degree, strength)

Degree

- The number of other nodes it is connected to

Strength

- The total weight of all connections with other nodes
- For weighted networks
Think in networks - modern resistance prevention and control

Effect of direct connections in the network: Difference in risk far and near hospitals

High prevalence hospitals far away pose little risk

More likely to receive colonised patients from nearby hospitals

Total expected CPE introductions to hospitals in the regions from:
- the same hospital
- other hospitals in the region
- Manchester region
- other regions

Confirmed CPE isolates / 100,000 admissions

Expected introductions

Oxford Biomedical Research Centre, MRC, Newton Fund, Bill and Melinda Gates Foundation, NERC, Public Health England, Department of Health, National Institute for Health Research
Think in networks - modern resistance prevention and control

Network vs geographical distance

Geographically close by: ranked, short distance

Geographically far away: all same (long) distance

Indirect connections offer many routes between hospitals

Outside primary affected region, AMR can arrive from anywhere, unexpectedly
Think in networks - modern resistance prevention and control
Regional control

Hospitals need to be aware of what is happening in their neighbouring hospitals
They share the AMR problems, through their shared patients
All health care institution within a region
Region defined by the patient sharing network
Need to be open about AMR situation, even the small ones.
Keep an eye out for any potential route, not just from ‘problem hospitals’
Think in networks - modern resistance prevention and control

Epidemiology of the spread of antimicrobial resistance within healthcare networks

Hajo Grundmann, University Medical Centre Freiburg, Germany
Think in networks - modern resistance prevention and control

Co-creative regional networks on antimicrobial resistance: A real life example

Alex W. Friedrich
Medical Microbiology and Infection Prevention
University Medical Center Groningen
Netherlands
Think in networks - modern resistance prevention and control

Network epidemiology

Network of patient transfer

- Undirected.
- Vertices are care units.
- Edge width (logarithmic) shows number of transfers

Applying the G. Lawyer algorithm:
G. Lawyer, Max Planck Institute for Informatics, Scientific Reports 5 : 2015
Understanding the influence of all nodes in a network
"The expected force is a novel measure of a node’s influence. It summarizes the size, density, and diversity of the node’s neighborhood. The measure is derived from epidemiology, and represents the expected force of infection generated by each node."

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Think in networks - modern resistance prevention and control

Transmission risk profiling of a hospital

- No infection control (high-risk period)
- 59 UMCG wards: 1 year movements
- Per-patient transmission probability: 1%

Outbreak development within hospital

- Analysis of patient transfer throughout the wards by using Brockmann-Heilig algorithm
- Calculation of time distance to occurred transmission on ward (red) (transmission wave)

Ciccolini et al. 2013
Think in networks - modern resistance prevention and control

Next-Hub-analysis for efficient outbreak screening

525 patients screened in 5 next-hub-wards and 7 non-hub wards

<table>
<thead>
<tr>
<th></th>
<th>ESBL-KPNEU</th>
<th>Outbreak-strain</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hubs:</strong></td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td><strong>Non-hubs:</strong></td>
<td>9</td>
<td>1</td>
</tr>
</tbody>
</table>

p<0.001

1. Hub analysis for identifying carriers in hospital
2. Typing necessary to differentiate outbreak
3. 8 patients identified and isolated without relation to outbreak

Relatedness of UMCG wards on basis of transmission jumps
OS120 - Antimicrobial resistance in long-term care facilities
• **Objective:** to estimate the burden of HAIs and antimicrobial use

• **Results:** In HALT, 61,932 residents were recruited in 722 LTCFs in 28 EU/EEA countries.
  
  – Prevalence of HAIs (residents with ≥1 HAI) was 2.4%; the prevalence of antimicrobial use (residents receiving ≥1 antimicrobial agent) was 4.3%.
  
  – In HALT-2: 77,264 residents were recruited in 1,181 LTCFs in 19 EU/EEA countries.
    
    • Prevalence of HAIs was 3.4%. We estimated that on any given day, >116,000 residents in EU/EEA LTCFs have an HAI. The prevalence of antimicrobial use was 4.4%.
    
    – Our results suggest that the burden of HAIs in LTCFs is higher in LTCFs than in acute care hospitals
HAI, antimicrobial use and indicators of infection prevention in LTCF in EU; point prevalence surveys 2010/2013

Size and national representativeness of participating LTCFs


Analysis: data aggregated for ‘nursing homes’ + ‘residential homes’ + ‘mixed facilities’

Source: ECDC HALT and HALT-2 reports. Key: + mean; * National representativeness of LTCF sample

Pete Kinross OS120
Prevalence of HAIs in LTCFs in EU/EEA countries, HALT (2010) and HALT-2 (2013)

HALT (2010): 2.4%\(^a\) of residents

- Bulgaria
- Cyprus
- Germany
- Lithuania
- Hungary
- Croatia
- Sweden
- the Netherlands
- Estonia
- Luxembourg
- France
- Poland
- Belgium
- UK - Scotland
- Greece
- Malta
- UK - England
- Slovenia
- Austria
- Spain
- Ireland
- Italy
- Czech Republic
- Denmark
- UK - Northern Ireland
- UK - Wales
- Finland
- Portugal

HALT-2 (2013): 3.4%\(^a\) of residents

- Croatia
- Slovenia
- Sweden
- Hungary
- Germany
- Denmark
- Italy
- UK - Wales
- Belgium
- Finland
- Malta
- Norway
- Ireland
- Czech Republic
- Greece
- UK - England
- Netherlands
- UK - Northern Ireland
- Portugal

\(^a\) crude mean; *poor national representativeness of LTCF sample
Antibiotic prescribing in long-term care facilities in Slovenia, a point prevalence study

- **Objective:** to investigate the prevalence and practice of antimicrobial prescribing in LTCF in Slovenia, and hence identify targets for quality improvement.

- **Methods:** point prevalence study was conducted between April and June 2016. We invited 117 Slovenian LTCF, counting 20224 residents.

- **Results:** 317 residents out of 13022 (2.4%, median: 1.9%, min-max: 0-7.6%) received antibiotics.
  - The most common were respiratory tract infections (RTI) (42.7%), followed by urinary tract infections (UTI) (33.3%) and skin and skin structure infections (19.6%).
  - Correlation between the age of 80 and above and antibiotic treatment ($p=0.0425$, Chi2 test, OR=1.33).
  - Advanced dementia was not significantly correlated with antibiotic.
  - wheelchair was also not significantly correlated.
  - Correlation between immobility and antibiotic treatment ($p<0.01$, $\chi^2$ test, OR=1.62).

Lea Ušaj OS0579
Antibiotic prescribing in long-term care facilities in Slovenia, a point prevalence study

317 residents out of 13022 received antibiotics on the day the survey was conducted.

Prevalence: 2.4%
(min-max per LTCF: 0-7.6%)

Lea Ušaj OS0579
## Prevalence of colonisation with multidrug resistant bacteria in patients receiving antibiotic treatment.

<table>
<thead>
<tr>
<th>Multidrug resistant bacteria</th>
<th>n (% of residents receiving antibiotics)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>11 (4.5%)</td>
</tr>
<tr>
<td>ESBL</td>
<td>39 (15.8%)</td>
</tr>
<tr>
<td>CRE</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>VRE</td>
<td>0</td>
</tr>
</tbody>
</table>

- Prevalence of colonisation with multidrug resistant bacteria in UMC Ljubljana in 2015:
  - MRSA: 0.5% of patients,
  - ESBL: 1.3% of patients,
  - CRE: 0.006% of patients

http://www.intranet.kclj.si/admin/dokumenti/00001668-00002ces-kazalniki_intranet_wob_06.html

Lea Ušaj OS0579
The burden of colonization and infection by CPE in the neuro-rehab setting: 4-year experience

- **Objective:** to assess the burden of CPE colonization and infection in a neuro-rehabilitation hospital.
- **Methods:** All patients were screened for CPE rectal colonization on admission and every 2 weeks.
- **Results:** 2841 patients were screened; mean length-of-stay was 78 days.
  - CPE rectal colonization on admission in 258 patients (9%),
  - in-hospital acquisition in 206 (7.9%).
  - incidence of in-hospital acquisition of CPE rectal colonization and CPE-BSI were 9 and 2.9 cases/10,000 patient-days, respectively.

<table>
<thead>
<tr>
<th>Patients admitted</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPE carriers–n°(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On admission</td>
<td>124 (19)</td>
<td>119 (16.5)</td>
<td>100 (13.5)</td>
<td>121 (16.6)</td>
</tr>
<tr>
<td>During hospitalization</td>
<td>66 (10)</td>
<td>68 (9.4)</td>
<td>56 (7.5)</td>
<td>68 (9.3)</td>
</tr>
<tr>
<td>In-hospital CPE colonization/10,000 patient-days</td>
<td>58 (9.8)</td>
<td>51 (7.8)</td>
<td>44 (6.4)</td>
<td>53 (8)</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>9.2</td>
<td>7.9</td>
<td>9.3</td>
</tr>
</tbody>
</table>
The burden of colonization and infection by CPE in the neuro-rehab setting: 4-year experience
The burden of colonization and infection by CPE in the neuro-rehab setting: 4-year experience

INCIDENCE OF CPE COLONIZATION AND BSI

- CPE -
- CPE+ acquired during hospitalization
- CPE+ on admission

Incidence of colonization (n*/1000 patient-days)

Incidence of CPE-BSI (n*1000/patient-days)

2012: 0.42, 2013: 0.29, 2014: 0.14, 2015: 0.32, 2016: 0.29

Sara Tedeschi OS0580
The burden of colonization and infection by CPE in the neuro-rehab setting: 4-year experience
The impact of a CPE clearance protocol and contact-precaution discontinuation on prevalence and risk of acquisitions in postacute care hospitals

- **Objective:** to assess the impact of the clearance policy implemented in PACH on the burden of CRE isolation and the risk of CRE acquisition among non-carriers.
- **Methods:** cross-sectional prevalence surveys
- **Results:** The proportion of patients with a history of CRE carriage was 27.7% (668/2483).
  - 50% (341/688) of carriers completed the clearance protocol (CCCP) and contact precautions were discontinued.
  - 13.7% (47/341) were found to be CRE positive compared with 40.1% (139/347) of the carriers who had remained on contact precautions.
  - The risk of carriage among CCCP was 26% during the first year after initial positive culture compared with 9.8% among patients who were screened after at least one year.
  - Among those without history of carriage, CRE prevalence decreased from 15.5% (86/545) in 2011 to 0.98% (6/611) in 2015.
  - The presence of CCCP on the ward was not associated with increased risk for CRE carriage among those without history of carriage.
SY152 - Explaining differences in resistance rates
Explaining differences in resistance rates

Weather, Climate and Antimicrobial Resistance

David N. Fisman, MD MPH FRCP(C)
Dalla Lana School of Public Health
University of Toronto

ECCMID Annual Meeting
Vienna, Austria, April 21-25, 2017
Explaining differences in resistance rates

Outline

2. Gram-negative infections, climate, seasonality, and geography.
3. Antimicrobial resistance, climate, seasonality, and geography.
Explaining differences in resistance rates

Is it really the season?

• Establishing causal links between environmental factors and disease occurrence may be difficult when the disease is seasonal.
• Relationships may be confounded by underlying factors:
  — e.g. increased incidence during certain types of weather might just reflect population risk behaviour
  — Correlation necessary but not sufficient
• Aggregation of exposures may lead to “ecological fallacy”.
• “Forced” aggregation via structure of PH data.

[Slide courtesy of Laura Kinlin and Alexander White]

David Fisman #SY0761
Summertime Seasonality of GNR

<table>
<thead>
<tr>
<th>Infecting organism, by class</th>
<th>Incident Rate Ratio (95% CI)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Spring (N = 54,742 admissions)</td>
<td>Summer (N = 56,167 admissions)</td>
<td>Fall (N = 55,214 admissions)</td>
</tr>
<tr>
<td>Gram-positive bacteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus species</em></td>
<td>0.95 (0.88–1.03)</td>
<td>0.91 (0.84–0.98)</td>
<td>0.88 (0.81–0.95)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>0.99 (0.91–1.08)</td>
<td>1.04 (0.95–1.13)</td>
<td>1.02 (0.94–1.12)</td>
</tr>
<tr>
<td>Gram-negative bacteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Acinetobacter baumannii</em></td>
<td>1.05 (0.90–1.23)</td>
<td>1.21 (1.04–1.41)</td>
<td>1.05 (0.89–1.23)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>0.98 (0.88–1.10)</td>
<td>1.28 (1.16–1.42)</td>
<td>1.06 (0.96–1.18)</td>
</tr>
<tr>
<td><em>Enterobacter cloacae</em></td>
<td>1.28 (1.12–1.48)</td>
<td>1.46 (1.27–1.67)</td>
<td>1.21 (1.04–1.39)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>1.02 (0.93–1.11)</td>
<td>1.12 (1.03–1.22)</td>
<td>1.02 (0.93–1.12)</td>
</tr>
</tbody>
</table>

NOTE. In winter (the comparator season), there were 52,471 admission. There were 218,394 admissions to the hospital. Seasons were defined as follows: winter, January–March; spring, April–June; summer, July–September; fall, October–December. Overdispersed Poisson generalized linear models were used, while controlling for long-term time trends by use of natural cubic splines, with degrees of freedom chosen on the basis of Akaike’s information criterion. CI, confidence interval.

* Calculated with the χ² test with 3 degrees of freedom.

[Perencevich et al., ICHE 2008]
Reproducibility of Observation

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Author [reference]</th>
<th>Seasonality</th>
<th>Correlation with temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>Eber [4]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Al Hassan [6]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Chazan [7]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>Eber [4]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Anderson [8]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Al Hassan [9]</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>Al Hassan [10]</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Eber [4]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

[Richet, Clin Micro Infect 2012]
# Explaining differences in resistance rates

## Healthcare-Associated Infection

### TABLE 2. Seasonality in healthcare-associated infections and correlation with temperature

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Author [reference]</th>
<th>Seasonality</th>
<th>Correlation with temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacter cloacae</td>
<td>Perencevich [15]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>Perencevich [15]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>Perencevich [15]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Perencevich [15]</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>Retaillau [16]</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>McDonald [17]</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Gales [18]</td>
<td>Yes</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Christie [19]</td>
<td>Yes</td>
<td>–</td>
</tr>
</tbody>
</table>

[Richet, Clin Micro Infect 2012]
Figure 5. Mean monthly fraction of bloodstream infections due to Gram-negative bacteria (Y-axis) plotted against latitude by study site (black circles).

https://doi.org/10.1371/journal.pone.0114548
http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0114548
Why Would GNR Infections Be Temperature-Sensitive?

• Temperature-sensitive replication of environmentally abundant microbes?
  – Direct effects of temperature on growth, abundance of nutrients? (Legionella) → Increased contamination, increased inoculum sizes?
  – Host factors? Vectors? (flies, as in campylobacter?).

• But HCA BSI also seem increased, even in high-income areas with climate controlled hospitals.
  – Sinks (Pseudomonas/Aeromonas)? Air conditioners?
Impact on Resistance Within GNR

- GNR increasingly MDR so temperature sensitivity/summertime seasonality could impact ARO burden.
- Could temperature or season directly impact resistance within GNR species?
- Enhanced growth, reduced generation times $\rightarrow$ speed Darwinian selection.
- Effect of temperature on gene transfer.
Explaining differences in resistance rates

ARO in E. coli, U.S.

[Derek MacFadden et al., submitted]
What Explains Differences in Resistance Rates?
Economics

Ramanan Laxminarayan
ECCMID
April 2017
Explaining differences in resistance rates

Rising incomes drive antibiotic consumption

Per capita total antibiotic use, retail sector, 2005-2010

Source: Based on data obtained under license from IMS Health MIDAS™ (January 2005-December 2010); IMS Health Incorporated. All Rights Reserved.
Explaining differences in resistance rates

Antibiotic use per capita by income in selected countries, 2010

Source: Van Boeckel et al. 2014 (based on IMS MIDAS) and World Bank 2015
Explaining differences in resistance rates

Total antibiotic consumption in selected countries, 2000 and 2010

Van Boeckel et al. 2014 (based on IMS MIDAS)

R Laxminarayan #SY0762
Explaining differences in resistance rates

Non-prescription use of antimicrobials is common

Figure 2: Frequency of non-prescription use of antimicrobials in the general population based on published works. In small areas, countries with similar frequency of non-prescription antimicrobial use have been grouped.

Morgan et al, Lancet ID, 2011

R Laxminarayan #SY0762
Explaining differences in resistance rates

The flu season is a key driver of antibiotic consumption – when people can afford antibiotics

Van Boeckel et al, Lancet Inf Dis, 2014
Decision fatigue increases inappropriate prescribing

Relative to the first hour of a session, the adjusted odds ratios of antibiotic prescribing in the fourth hour was 1.26 (95% CI, 1.13–1.41)

Linder et al, JAMA IM, 2014
Explaining differences in resistance rates

What happens when antibiotics are provided free?

Table 2: Average Percentage Change in prescriptions 1 year into the program

<table>
<thead>
<tr>
<th></th>
<th>Percentage Change Before and After</th>
<th>Diff-in-Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment Group</td>
<td>Control Group</td>
</tr>
<tr>
<td>All Antibiotics</td>
<td>7.67 (0.40)</td>
<td>2.74 (0.31)</td>
</tr>
<tr>
<td>Covered Antibiotics</td>
<td>11.73 (0.43)</td>
<td>4.62 (0.31)</td>
</tr>
<tr>
<td>Not-covered Antibiotics</td>
<td>-8.75 (0.66)</td>
<td>-4.76 (0.39)</td>
</tr>
<tr>
<td>No-equivalent Antibiotics</td>
<td>-4.76 (0.82)</td>
<td>-0.32 (0.56)</td>
</tr>
</tbody>
</table>

Note: The changes before the program are calculated using data from November 2005 to October 2006, and the changes after the program are based on data from November 2006 to October 2007.

Overall increase in antibiotic prescriptions as well as substitutions to covered antibiotics from not-covered antibiotics.

Li and Laxminarayan, *Health Economics*, 2013

R Laxminarayan #SY0762
Explaining differences in resistance rates

Drug Binge
China consumes half the world’s antibiotics, with the majority administered to animals

<table>
<thead>
<tr>
<th></th>
<th>Humans</th>
<th>Animals</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>77,760</td>
<td>84,240</td>
</tr>
</tbody>
</table>

162,000 of antibiotics used in total

Antibiotics consumed (metric tons) in 2013

Bloomberg
Explaining differences in resistance rates

The rich pay with their wallets, the poor with their lives

Developed world cost per course of therapy

- Linezolid
- Vancomycin
- Gemifloxacin
- Amox./Clav.
- Ceftriaxone
- Levofloxacin
- Ciprofloxacin
- Azithromycin

Developing world

- Cotrimoxazole
- Amoxicillin
- Chloramphenicol
- Tetracycline

Notes: *Chloramphenicol is not available in developed world—price is therefore estimated. †Ceftriaxone and ciprofloxacin may be available in some tertiary settings in developing world.

Antimicrobial resistance:
How does culture influence differences in rates?

Peter Collignon AM
Infectious Diseases and Microbiology, The Canberra Hospital.
Professor, Canberra Clinical School,
Australian National University
Exec Director, ACT Pathology
Globally, water is the major risk for spread of resistant bacteria.
Explaining differences in resistance rates

**Box 2. Indicators of Weak Governance of Antimicrobials**

- Globally, WHO estimates that only 50% of antibiotics are used correctly.
- Of the 150 million prescriptions for antibiotics written by U.S. doctors every year, fully 50 million were not necessary, according to a study released in May 2016 by the U.S. Centers for Disease Control and Prevention (CDC).
- In many countries, antibiotics can be bought over-the-counter from pharmacies, grocery stores, and street vendors.
- Up to 60% of the antimicrobials used in Africa and Asia may be substandard; counterfeit drugs have infested markets in these and other regions.
- Public data on use of, and trade in, antimicrobials are lacking or poor, indicating weak governance of a high-value public asset. Estimates of global annual use in agriculture range considerably, from 63,000 tons to over 240,000 tons.
Explaining differences in resistance rates

Policy effect on Over counter sale restriction had a reduction in consumption of 24%
Very strong statistical evidence as predictors of higher antibiotic consumption

- Human development index (HDI),
  - a composite measure of education, health and income was the best predictor of higher antibiotic consumption
- density of private health establishments,
- percentage of urban population,
- lower levels of illiteracy,
- life expectancy,
- lower percentage of population between 15 years old,
- higher Gini coefficient (i.e., income inequality),
- lower density of Government run health establishments,
- higher population density,
- larger population,
- higher GDP per capita,
- Higher proportion female
Significant determinants of antibiotic consumption in Europe

- The population income
  - More income then more usage
- demographic structure
- density of general practitioners and their remuneration method
  - more income incentive for practitioners, the more are prescribed

“Although countries with higher levels of bacterial resistance exhibited significantly higher levels of per capita antibiotic use, ceteris paribus, the responsiveness of antibiotic use to changes in bacterial resistance was relatively low.”
Explaining differences in resistance rates

Resistence versus control of corruption in EU

Note: Average Antibiotic Resistance is from EARS-Net Database of the European Centre for Disease Prevention and Control.
Explaining differences in resistance rates

Corruption in healthcare sector and antibiotic consumption

Fig. 1. Corruption in the health sector and antibiotic use in the European regions, N = 117. Regions with fewer than 50 respondents were excluded. Source: European Quality of Government Index 2013 and Special Eurobarometer 338.
Explaining differences in resistance rates
If Poor Governance/corruption

• People will bend or break rules
  – Higher antibiotic use than recorded
  • People/Agriculture
• Disposal of waste
  – Drugs, animals and sewage
• Water contamination
• Infection control
• Supplies more often defective or not there
Explaining differences in resistance rates

Antibiotic resistance

- Factors other than usage are very important
  - Water
  - Governance
  - Corruption
  - Rule of law
  - Government competence
  - education
  - Income
  - Socio-economic status
  - Literacy
  - Private sector medicine proportion
  - Culture
Tuesday, 25 April 2017
ME160 - Game changers in infection control - personal experiences of discoveries that have changed clinical practice
Game changers in infection control

Staphylococcus aureus, my Odyssey
Jan Kluytmans

University Medical Center Utrecht & Amphia Hospital, Breda
Game changers in infection control

What is the source?

- Preoperative nasal cultures had been taken
- Why?
- Case-control study
  - Cases: patients with S. aureus infection after CT surgery
  - Controls: patients from the same population without S. aureus infection
Game changers in infection control

Results

- 40 cases, 120 controls
- Mortality
  - cases: 10.0%, controls 0.8%

<table>
<thead>
<tr>
<th>Nasal carriage</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9.6</td>
<td>3.9 - 23.7</td>
</tr>
</tbody>
</table>

All available pairs were identical

Prospective surveillance

Intranasal mupirocin for reduction of *Staphylococcus aureus* infections in surgical patients with nasal carriage: a systematic review

Miranda M. L. van Rijen¹*, Marc Bonten², Richard P. Wenzel³ and Jan A. J. W. Kluymans¹,⁴
**Game changers in infection control**

### Surgical Patients: Carriers

<table>
<thead>
<tr>
<th>Study</th>
<th>Mupirocin ( n/N )</th>
<th>Control ( n/N )</th>
<th>RR (random) ( 95% ) CI</th>
<th>Weight %</th>
<th>RR (random) ( 95% ) CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia</td>
<td>1/31</td>
<td>3/34</td>
<td></td>
<td>4.76</td>
<td>0.37 [0.04, 3.33]</td>
</tr>
<tr>
<td>Kalmeijer</td>
<td>2/95</td>
<td>5/86</td>
<td></td>
<td>8.93</td>
<td>0.36 [0.07, 1.82]</td>
</tr>
<tr>
<td>Perl</td>
<td>17/430</td>
<td>34/439</td>
<td></td>
<td>72.38</td>
<td>0.51 [0.29, 0.90]</td>
</tr>
<tr>
<td>Konvalinka</td>
<td>5/130</td>
<td>4/127</td>
<td></td>
<td>13.93</td>
<td>1.22 [0.34, 4.44]</td>
</tr>
</tbody>
</table>

Total (95% CI): 686

Test for heterogeneity: \( \chi^2 = 1.92, \) df = 3 (\( P = 0.59 \)), \( I^2 = 0\% \)

Test for overall effect: \( Z = 2.43 (P = 0.02) \)

### Surgical Patients: Non-carriers

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Mupirocin ( n/N )</th>
<th>Control ( n/N )</th>
<th>RR (random) ( 95% ) CI</th>
<th>Weight %</th>
<th>RR (random) ( 95% ) CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kalmeijer</td>
<td>3/220</td>
<td>3/213</td>
<td></td>
<td>18.46</td>
<td>0.97 [0.20, 4.74]</td>
</tr>
<tr>
<td>Perl</td>
<td>28/1454</td>
<td>21/1447</td>
<td></td>
<td>75.58</td>
<td>1.33 [0.76, 2.33]</td>
</tr>
<tr>
<td>Garcia AM</td>
<td>0/65</td>
<td>3/61</td>
<td></td>
<td>5.96</td>
<td>0.13 [0.01, 2.55]</td>
</tr>
</tbody>
</table>

Total (95% CI): 1739

Test for heterogeneity: \( \chi^2 = 2.36, \) df = 2 (\( P = 0.31 \)), \( P = 15.3\% \)

Test for overall effect: \( Z = 0.23 (P = 0.81) \)
# Game changers in infection control

**Table 2. Relative Risk of Hospital-Acquired Staphylococcus aureus Infection and Characteristics of Infections (Intention-to-Treat Analysis).**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mupirocin–Chlorhexidine (N = 504)</th>
<th>Placebo (N = 413)</th>
<th>Relative Risk (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S. aureus infection</strong></td>
<td>17 (3.4)</td>
<td>32 (7.7)</td>
<td>0.42 (0.23–0.75)</td>
</tr>
<tr>
<td>Source of infection†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endogenous</td>
<td>12 (2.4)</td>
<td>25 (6.1)</td>
<td>0.39 (0.20–0.77)</td>
</tr>
<tr>
<td>Exogenous</td>
<td>4 (0.8)</td>
<td>6 (1.5)</td>
<td>0.55 (0.16–1.92)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Localization of infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep surgical site‡</td>
<td>4 (0.9)</td>
<td>16 (4.4)</td>
<td>0.21 (0.07–0.62)</td>
</tr>
<tr>
<td>Superficial surgical site‡</td>
<td>7 (1.4)</td>
<td>13 (3.5)</td>
<td>0.45 (0.23–1.11)</td>
</tr>
<tr>
<td>Lower respiratory tract</td>
<td>2 (0.4)</td>
<td>2 (0.5)</td>
<td>0.82 (0.12–5.78)</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>1 (0.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bacteremia</td>
<td>1 (0.2)</td>
<td>1 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Soft tissue</td>
<td>2 (0.4)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
Cost-effectiveness

- Cost reduction per treated carrier was
  - €2841 in cardio-thoracic surgery  N= 1600 (400)
  - €955 in orthopedic surgery  N= 2600 (650)

Van Rijen et al. Plos One 2012;7:e43065

- Annual savings Amphia hospital
  1.8 Million Euro
Discussion

• Why did it take 25 years before this method was included in an international guideline?
• How much evidence do we need?
• What about different surgical procedures?
• Is it ethical to stop an intervention that you strongly believe in, based on circumstantial evidence, in a population with hardly any complications that the intervention is aiming at?
Game changers in infection control

Persuasion

- Organism Typing for Success

L.E. Nicolle
University of Manitoba
Winnipeg, MB  CANADA
Persuasion

Evidence essential:
- high quality,
- local

Other professionals may try to discredit evidence:
- be convinced yourself
- acknowledge limitations

Organism typing for precision and clarity is often compelling evidence
#SY0820 Worldwide outbreak linked to heater-cooler units in cardiac surgery
Epidemiology of heater-cooler-linked outbreaks

- Risk if more than 2h of HCU
- Concentration of droplet higher than water in the tank

*M. chimaera* aerosolization in the OR: Pathogenesis of disseminated infection

- All patients to date with *disseminated* infections have implants (valves, vascular grafts, LVADs)
- High inoculum (long bypass time, direction of exhaust, OR air handling) results in contamination of implant, leads to biofilm formation on an intravascular device
- Chronic granulomatous inflammatory response to near-continuous seeding of the bloodstream by a low virulence organism that is otherwise easily contained

Daniel J. Diekema #SY0820
MAC Outer Membrane Favors Persistence in Water Systems

- Lipid-rich hydrophobic barrier
- Resistant to common disinfectants
  - Chlorine, chloramine, ozone
- 1,000 times more resistant than industry standard for disinfection (*E. coli*)
  - 5 seconds vs. 2 hours at 1 ppm chlorine
- Form thick biofilms, enhance resistance
  - 10,000 CFU/cm² in biofilm

### Epidemiology of heater-cooler-linked outbreaks

**M. chimaera clinical experience**
52 cases from 3 case series (US, UK, EU)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of cases</td>
<td>52</td>
</tr>
<tr>
<td>Earliest sentinel surgery</td>
<td>2008</td>
</tr>
<tr>
<td>Male</td>
<td>83%</td>
</tr>
<tr>
<td>Age, y (mean, range)</td>
<td>60 (1-83)</td>
</tr>
<tr>
<td>Prosthetic cardiovascular material</td>
<td>90%</td>
</tr>
<tr>
<td>Duration from surgery to symptom onset in months, mean (range)</td>
<td>17 (1-72)</td>
</tr>
<tr>
<td>Crude mortality at time of publication or presentation of cases</td>
<td>48%</td>
</tr>
</tbody>
</table>

Appenheimer AB et al. IDWeek 2016, #2392, October 29, 2016.
Diagnostic considerations

• If exposed and with unexplained symptoms:
  - Fatigue, fever, night sweats, weight loss, surgical site
  - Exam: ? HSM, surgical site, joint involvement, ophtho exam
  - Labs: CBC/diff, chem 7, LFTs, CRP, UA, AFB blood/other cx
• Cytopenias, elevated LFTs, AKI, chorioretinitis
  - Often seen at presentation with disseminated disease
• Cultures require mycobacterial lab expertise
  - Take several weeks to turn positive
  - ID as “MAC” by probe, few labs can do species ID
  - Culture blood (>=2 sets) and any involved site
  - “Screening” AFB blood cultures (asymptomatic) not indicated
Epidemiology of heater-cooler-linked outbreaks

• Prevention
  – Disinfection not enough, manufacturer guidance not enough
  – Wall water system is an alternative

Diagnostic considerations

• If exposed and with unexplained symptoms:
  – Fatigue, fever, night sweats, weight loss, surgical site
  – Exam: ? HSM, surgical site, joint involvement, ophtho exam
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SY195 - How medical overuse drives healthcare costs and antimicrobial resistance
Prevention of infectious disease through limiting overuse of devices

Prof. Stephan Harbarth
Infection Control Programme
University of Geneva Hospitals
How medical overuse drives healthcare costs and antimicrobial resistance

Topics

• General introduction
• Catheter-associated UTI
• Catheter-related BSI
• Mechanical ventilation and VAP
How medical overuse drives healthcare costs and antimicrobial resistance

HCWs’ mobile phones

- **MRSA:**
  - 52%+ mobile phones
  - 38%+ HCW hands
- **ESBL:**
  - 38%+ mobile phones
  - 40%+ HCW hands
- **Cleanliness:**
  - 90% of HCWs never cleaned their phone

(Courtesy of A. Voss)


Stephan Harbarth #SY097
How medical overuse drives healthcare costs and antimicrobial resistance

Duration of postoperative urinary catheter use and risk of UTI

Retrospective cohort study
USA 2001
2965 hospitals
35 904 patients

86% perioperative catheter
50% of these > 2 days

Beyond Infection: Device Utilization Ratio as a Performance Measure for Urinary Catheter Harm

Mohamad G. Fakhri, MD, MPH,1,2 Carolyn V. Gould, MD, MScCR,3 Barbara W. Trautner, MD, PhD,1,5 Jennifer Maddings, MD, MSc,6 Russell N. Olmsted, MPH, CIC7 Sarah L. Krein, RN, PhD,7 Sanjay Saint, MD, MPH8

- **Key concept**: To advocate use of the device utilization ratio (DUR) as an additional performance measure for potential urinary catheter overuse and harm

Analysis: Device Utilization (DUR) Ratio

\[
\text{DU Ratio} = \frac{\text{# Indwelling catheter days}}{\text{# Patient Days}}
\]

DU Ratio measures the proportion of total patient-days in which indwelling urinary catheters were used

Indwelling catheter use is necessary for CAUTI. Therefore reducing your facility/location's catheter device utilization rate, may lead to reduced CAUTI rates.
Are physicians aware of which of their patients have indwelling urinary catheters?

Many of them don’t seem to be aware... so remind them!

<table>
<thead>
<tr>
<th>Provider unaware of catheter [n (%)]</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All providers</td>
<td>88 / 319 (28%)</td>
</tr>
<tr>
<td>Medical students</td>
<td>8 / 39 (21%)</td>
</tr>
<tr>
<td>Interns</td>
<td>19 / 88 (22%)</td>
</tr>
<tr>
<td>Residents</td>
<td>28 / 104 (27%)</td>
</tr>
<tr>
<td>Attending physicians</td>
<td>33 / 88 (38%)</td>
</tr>
</tbody>
</table>

Prevention of Catheter-Associated Urinary Tract Infection (CA-UTI)

Two main principles

Avoid unnecessary catheterization

Limit the duration of catheterization
How medical overuse drives healthcare costs and antimicrobial resistance

**Unjustified CVC use**

- Hospital-wide cross-sectional survey
- 320 patients, 74 CVCs, 62 (19%) Pts (46 ICU, 28 non ICU)

![Bar chart showing total CVC days and Unjustified CVC days for ICU and Non ICU patients with p=0.007]

**Bundle components to reduce catheter-associated bloodstream infections:**

- Hand hygiene
- Maximal sterile barrier precaution at insertion
- Skin antiseptic with alcohol-based chlorhexidine-containing products
- Subclavian access as the preferred insertion site
- Standardized catheter care using a non-touch technique
- Respecting the recommendations for dressing change
- Daily review of line necessity

**References**

Eggimann P. Lancet 2000; 35: 290
How medical overuse drives healthcare costs and antimicrobial resistance

**Ventilator-associated pneumonia (VAP)**

- Most common infection in the ICU
- Affects approx. 15% of ventilated patients
- Daily hazard peak: day 5

---

**The basic rules of VAP prevention**

- Do not intubate, unless necessary
- Extubate, as soon as possible

---

E Tejerina et al, J Crit Care 2006

Stephan Harbarth #SY097
How medical overuse drives healthcare costs and antimicrobial resistance

Take home messages

- Invasive devices: Less is more
- Physicians should first consider safety and not patient/nurse comfort
- Develop and implement reminders about catheter indications and removal

Urinary Cath: ABCDE

- Adherence to general infection control principles is important (e.g., hand hygiene, surveillance and feedback, aseptic insertion, proper maintenance, education).
- Bladder ultrasound may avoid indwelling catheterization.
- Condom catheters or other alternatives to an indwelling catheter such as intermittent catheterization should be considered in appropriate patients.
- Do not use the indwelling catheter unless you must!
- Early removal of the catheter using a reminder or nurse-initiated removal protocol appears warranted.
Medical Overuse, Choosing Wisely and other intervention to reduce overuse

Dan Morgan MD, MS

ECCMID April 2017

Chief Hospital Epidemiologist, Associate Professor
Epidemiology and Public Health/Infectious Diseases
University of Maryland School of Medicine &
VA Maryland Healthcare System
Uncertainty in medicine

“Uncertainty is generally suppressed and ignored, consciously and subconsciously”

BECOMING A PHYSICIAN
Tolerating Uncertainty — The Next Medical Revolution?
Arabella L. Simpkin, B.M., B.Ch., M.M.Sc, and Richard M. Schwartzstein, M.D.

Once it struck me what quality went to form a Man of Achievement . . . when a man is capable of being in uncertainties, mysteries, doubts, without iterative and evolutionary nature of clinical reasoning — is the very antithesis of humanistic, individualized patient-centered care. We believe that a shift toward seem, intuitively, to have been designed to tolerate ambiguity and denies that rec
How medical overuse drives healthcare costs and antimicrobial resistance

Uncertainty leads to variation in practice

• ~30% of care is estimated to be overuse
• The majority of patients experience overuse


Daniel Morgan #SY0972
How medical overuse drives healthcare costs and antimicrobial resistance

Why is overuse important?

- Patient safety (avoiding harms and treating more appropriately)—C. difficile and MDROs

- Patient satisfaction (lessen burden of care)

- Artificial elevation of rates, problems with measures, costs
How medical overuse drives healthcare costs and antimicrobial resistance

Overuse Increases Spending
Many practices without strong evidence

Effectiveness of 3000 treatments as reported in randomised controlled trials selected by Clinical Evidence. This does not indicate how treatments are used in healthcare settings or their effectiveness in individual patients.
How medical overuse drives healthcare costs and antimicrobial resistance

Providers often don’t understand testing

“If a test to detect disease whose prevalence is 1 out of 1000 has a false positive rate of 5 percent, what is the chance that a person found to have a positive result actually has the disease?”

Prior to testing
- Abstract testing numbers
- Initial likelihood of disease 1/1000 (0.1%)

Test specificity 95%

Reality after testing
- True positives, 2%
- False positives, 99%

Physician perceptions
- False positives, 5%

Casscells et al NEJM 1978, Manrai et al JAMA IM 2014; Gigerenzer 2003
Overdiagnosis

- Diagnosis of disease that will never cause symptoms or problems
- Atypical cells that will never cause disease

Fatal Retraction
Not all cancers are lethal—despite the fear the name evokes. Although doctors often can't tell for certain which individual tumors are destined to be deadly, a growing number of studies suggest that many found at early stages may be so slow-growing they are unlikely to be fatal. Some recent estimates of this 'overdiagnosis' rate in common cancers:

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Overdiagnosis Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>60%</td>
</tr>
<tr>
<td>Breast</td>
<td>30%</td>
</tr>
<tr>
<td>Thyroid</td>
<td>90%</td>
</tr>
<tr>
<td>Skin</td>
<td>90%</td>
</tr>
<tr>
<td>Lung*</td>
<td>18%</td>
</tr>
</tbody>
</table>

* Refers only to lung cancers detected by low-dose CT scans

Sources: American Cancer Society (Prostate); New England Journal of Medicine (Breast); The BMJ (Thyroid); Journal of the American Medical Association and Lancet Oncology (Skin); JAMA Internal Medicine (Lung)

Wall Street Journal 2014; Esserman et al. JAMA 2013
Contact Precautions

Con
• adverse events, satisfaction & depression
• Cause fewer visits
• Are a bother, $
• Don’t prevent infections

Pro
• Improve hand hygiene
• Decreases contamination & may decrease infections
How medical overuse drives healthcare costs and antimicrobial resistance

Overdiagnosis of *C. difficile*

- 1416 pts tested, only Tox reported
- 131 Tox+
- Additional 162 PCR+ (tox-)
  - Minimal use of Rx

>100% overdiagnosis of *C. difficile* with PCR

<table>
<thead>
<tr>
<th>Outcome</th>
<th>C difficile Positive</th>
<th>C difficile Negative</th>
<th>P Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C difficile-Related Complication or Death Within 30 d, No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complication&lt;sup&gt;b&lt;/sup&gt;</td>
<td>10 (7.6)</td>
<td>3 (0.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Death&lt;sup&gt;c&lt;/sup&gt;</td>
<td>11 (8.4)</td>
<td>0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Complication or death</td>
<td>18 (13.7)</td>
<td>3 (0.3)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Polage et al JAMA IM 2015

Daniel Morgan #SY0972
How to improve overuse
Choosing wisely

- Lists of things not to do...per physician societies
- >250

Don’t do imaging for low back pain within the first six weeks, unless red flags are present.

Don’t obtain a urine culture unless there are clear signs and symptoms that localize to the urinary tract.

Don’t place, or leave in place, urinary catheters for incontinence or convenience or monitoring of output for non-critically ill patients (acceptable). Antibiotics should not be used for apparent viral respiratory illnesses (sinusitis, pharyngitis, bronchitis).

Don’t prescribe oral antibiotics for uncomplicated acute external otitis.
Understand and communicate limitations in therapy

- absolute benefits >> Relative
- Do providers understand benefits
- Shared-decision making

When **2,000** People Take a Daily Aspirin for Two Years:

<table>
<thead>
<tr>
<th>Heart attacks are not prevented</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 heart attacks are not prevented</td>
</tr>
<tr>
<td>1 Heart Attack is Prevented</td>
</tr>
</tbody>
</table>

Would shared decision making help in stewardship?

NYT 2015
How medical overuse drives healthcare costs and antimicrobial resistance

Diagnostic stewardship

- Many HAIs dependent on a clinical syndrome or additional tests
- Make testing more appropriate to prevent false positives
- Urine culture, blood cultures, *C. difficile* PCRs
Conclusions

- Much medical care is useful and being cared for is important
- Overuse is common & harmful
- Field of Overuse can help Infectious disease—i.e. Shared Decision Making/Choosing Wisely
- Stewardship should extend to testing
- Infectious disease understands overuse and can inform other fields