What’s trending in the infection prevention and control literature? HIS 2012 -> HIS 2014

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Disclosures

I am employed part-time by Bioquell.
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- Ebola, MERS, Influenza
- Universal vs targeted interventions
- Faecal microbiota transplantation
- Whole genome sequencing
- CRE
- Environmental science
- What will be trending at HIS 2016?
MERS Google trends
MERS coronavirus
MERS-CoV is a respiratory viruses, so the most important route of transmission is likely to be droplet spread through close contact with infected individuals. However, airborne transmission cannot be ruled out (hence the CDC recommendation for airborne precautions). Recent data indicate that small droplet nuclei may be emitted most of the time by influenza infected patients, which justifies airborne precautions.¹

Ebola Google trends

- "First case" in America
- Declared global health emergency
‘...the greatest medical crisis in the world is about to happen.’

- Transmission routes ("it’s airborne")
- Role of quarantine
- PPE
- Lab safety

Ebola: transmission routes

- Direct contact with blood or body fluids incl. droplet sprays (through broken skin or mucous membranes)\(^1,2\)
- Indirect contact with contaminated environments\(^1-4\)

\[
R_0 = 2
\]
(Nishiura & Chowell\(^5\))

\(R_0\) significantly higher in non-survivors (2.36) than in survivors (0.66).\(^6\)

Surface survival: viruses with pandemic potential

<table>
<thead>
<tr>
<th>Virus</th>
<th>Survival time</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARS-CoV</td>
<td>Days to weeks(^1,2)</td>
</tr>
<tr>
<td>MERS-CoV</td>
<td>More than 2 days(^3)</td>
</tr>
<tr>
<td>Influenza</td>
<td>Hours to days(^1,4)</td>
</tr>
<tr>
<td>Ebola</td>
<td>Days to weeks* (^5-6)</td>
</tr>
</tbody>
</table>

* The study that reported survival times measured in weeks was performed at 4°C.\(^6\)

Game changer: Ebola transmission US / Spain

6 Oct 2014: Madrid, Spain

12 & 15 Oct 2014: Dallas, Texas, USA

13 cases -> 3 secondary transmissions
‘Politicisation’

Images: Temperature mapping, Quarantine, Passport
Ebola: PPE design, supply and training

Having the right PPE policy is only part of the solution – you also need to ensure PPE supply and that staff know how to don and doff safely.¹,²

The MSF ‘Buddy’ system has been designed for field settings, and may be useful in acute settings.¹,²

We probably need better designed PPE.³

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Image source: Controversies in HAI blog
CDC tightens PPE recommendations

Source: USA Today.
Prevention and control: theory and practise

Case-control study with 241 non-infected and 13 infected healthcare workers.

Targeted or universal interventions?

<table>
<thead>
<tr>
<th>Targeted</th>
<th>Universal</th>
</tr>
</thead>
<tbody>
<tr>
<td>aka ‘vertical’ or ‘go long’</td>
<td>aka ‘horizontal’ or ‘go wide’</td>
</tr>
<tr>
<td>• Screening</td>
<td>• Minimise invasive device use</td>
</tr>
<tr>
<td>• Isolation</td>
<td>• Hand hygiene</td>
</tr>
<tr>
<td>• Contact precautions</td>
<td>• Antimicrobial stewardship</td>
</tr>
<tr>
<td>• Decolonization of carriers</td>
<td>• Universal decolonization</td>
</tr>
<tr>
<td>• Targeted cleaning / disinfection</td>
<td>• General cleaning / disinfection</td>
</tr>
</tbody>
</table>

Examples of targeted and universal interventions (adapted from Wenzel & Edmond, via Septimus et al.).

# Universal chlorhexidine ± mupirocin

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Design</th>
<th>Intervention</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derde¹</td>
<td>ICU</td>
<td>Time series analysis</td>
<td>Universal CHG plus hand hygiene</td>
<td>Reduction in all MDROs and MRSA (but not VRE or ESBLs)</td>
</tr>
<tr>
<td>Climo²</td>
<td>ICU</td>
<td>Cluster RCT</td>
<td>Universal CHG</td>
<td>Reductions in MRSA / VRE acquisition and all BSI; BSI mainly CoNS</td>
</tr>
<tr>
<td>Milstone³</td>
<td>Paed ICU</td>
<td>Cluster RCT</td>
<td>Universal CHG</td>
<td>BSI reduced; mainly CoNS</td>
</tr>
<tr>
<td>Huang⁴</td>
<td>ICU</td>
<td>Cluster RCT</td>
<td>Universal CHG + mupirocin</td>
<td>Reduction in MRSA clinical isolates and all BSI; MRSA BSI not reduced</td>
</tr>
</tbody>
</table>

Universal chlorhexidine + mupirocin

74 US ICUs randomised.

'Selective’ digestive decontamination

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<thead>
<tr>
<th>Study</th>
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<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Jonge¹</td>
<td>ICU</td>
<td>RCT</td>
<td>SDD</td>
<td>Mortality and acquisition of MDR-GNR reduced</td>
</tr>
<tr>
<td>de Smet²</td>
<td>ICU</td>
<td>Cluster RCT</td>
<td>SDD or SOD</td>
<td>Both SOD and SDD reduced mortality</td>
</tr>
<tr>
<td>Oostdijk⁴</td>
<td>ICU</td>
<td>Cluster RCT</td>
<td>SDD v SOD</td>
<td>No significant difference in mortality, but SDD -&gt; more antibiotic resistance</td>
</tr>
<tr>
<td>Saidel-Odes⁴</td>
<td>Adults</td>
<td>RCT</td>
<td>SDD</td>
<td>Reduced, but did not eliminate CRE colonisation</td>
</tr>
</tbody>
</table>

‘Selective’ digestive decontamination

20 CRE colonized patients in each arm given gentamicin + polymyxin (SDD arm) or placebo (Control arm)

Universal decolonisation

‘…fighting antimicrobial resistance with more antimicrobials, although a necessary short-term strategy, is a long-term strategy destined to fail.’


ANTIBIOTICS ARE THE PROBLEM, NOT THE SOLUTION
Reduced CHG susceptibility

Proportion of BSI isolates with reduced susceptibility to chlorhexidine on units CHG daily bathing (n=28) or not (n=94).

Universal contact precautions (BUGG)

20 US ICUs randomised.

Harris et al. JAMA 2013;310:1571-1580.
Universal contact precautions (BUGG)

85% Compliance with glove and gown use in the BUGG study.¹

29% Compliance with correct glove and gown use in the real world.²

Universal contact precautions (BUGG)

1013 observations.

Dhar et al. ICHE 2014;35:213-221.
**Single rooms for all?**

<table>
<thead>
<tr>
<th>Single Rooms</th>
<th>Bays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reduced HCAI&lt;sup&gt;1-6&lt;/sup&gt;</td>
<td>Reduced risk of adverse events&lt;sup&gt;11-12&lt;/sup&gt;</td>
</tr>
<tr>
<td>Some patients more satisfied&lt;sup&gt;5-9&lt;/sup&gt;</td>
<td>Less social contact; isolation&lt;sup&gt;11-14&lt;/sup&gt;</td>
</tr>
<tr>
<td>Fewer “mix up” errors&lt;sup&gt;10-11&lt;/sup&gt; through uninterrupted patient contact</td>
<td>Reduced staffing levels and patient: HCW ratios&lt;sup&gt;14,15&lt;/sup&gt;</td>
</tr>
</tbody>
</table>


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### Universal MRSA screening – cost effectiveness

NHS decision makers will pay £30,000 per Quality Adjusted Life Year (QALY)\(^1\)

<table>
<thead>
<tr>
<th>MRSA rate</th>
<th>Cost-effective strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute</strong></td>
<td></td>
</tr>
<tr>
<td>High (2.8%)</td>
<td>All admissions to “high risk” units</td>
</tr>
<tr>
<td>Current (1.4%)</td>
<td>All admissions to “high risk” units</td>
</tr>
<tr>
<td>Low (0.7%)</td>
<td>All admissions to “high risk” units (with or without targeted screening of all admissions)</td>
</tr>
<tr>
<td><strong>Teaching</strong></td>
<td></td>
</tr>
<tr>
<td>High (2.6%)</td>
<td>All admissions to “high risk” units</td>
</tr>
<tr>
<td>Current (1.3%)</td>
<td>None</td>
</tr>
<tr>
<td>Low (0.7%)</td>
<td>None</td>
</tr>
<tr>
<td><strong>Specialist</strong></td>
<td></td>
</tr>
<tr>
<td>High (2.1%)</td>
<td>All admissions to “high risk” units</td>
</tr>
<tr>
<td>Current (1.0%)</td>
<td>All admissions to “high risk” units or universal screening with pre-emptive isolation of previous positives</td>
</tr>
<tr>
<td>Low (0.5%)</td>
<td>All admissions to “high risk” units or universal screening</td>
</tr>
</tbody>
</table>

Fecal microbiota transplantation Google trends (HIS 2012 to HIS 2014)

Note, I had to spell it ‘wrong’ (fecal v faecal) to detect a trend. Blasted Americans.
Fecal microbiota transplantation Google trends (2004 to present)

Note, I had to spell it 'wrong' (fecal v faecal) to detect a trend. Blasted Americans.
Faecal microbiota transplant for recurrent CDI

Patients with recurrent CDI randomised to FMT (n=16), vancomycin (n=12) or vancomycin + bowel lavage (n=13)

Introducing...the ‘crapsule’

Youngster et al. JAMA 2014 in press.
Whole genome sequencing Google trends (2004 to present)
Whole genome sequencing: *C. difficile*

All 1250 *C. difficile* isolates over 5 years from symptomatic cases typed by WGS. Only 35% of these had <2 SNVs compared with previous cases. The epidemiological links between these cases are illustrated below.

(How much CDI is hospital acquired?)

Relatedness of 56 hospital-acquired CDI cases to other *C. difficile* using MLVA (note, not WGS).

Whole genome sequencing: outbreaks

Transmission map based on epidemiological links only.

Transmission map based on epidemiological links + WGS.

Carbapenem resistant Enterobacteriaceae

Google trends (2004 to present)

CDC CRE Toolkit launched
CRE in the UK and USA
Invasive CR *K. pneumoniae* isolates (EARS-Net)
Invasive CR K. pneumoniae trends

CR K. pneumoniae invasive isolates

- Greece
- Italy
- UK

Year:
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
- 2011
- 2012

Percentage:
- 0%
- 10%
- 20%
- 30%
- 40%
- 50%
- 60%
- 70%
Colistin resistance in Italy

Survey of 191 CRE from 21 labs across Italy.

43%

Colistin resistant *K. pneumoniae*. Range = 10-80% for the 21 labs.

Monaco et al. 2014; Euro Surveill 2014;19 pii=20939.
Emergence of CPE in the UK

PHE AMRHAI, 24/01/14
Courtesy of Dr Neil Woodford
CRE in the USA

National survey of Enterobacteriaceae in 2001 (n=2,631) and 2011 (n=6,573).

CDC NHSN / NNIS data. MMWR 2013;62:165-170.
CRE in the USA – Long Term Acute Care (LTAC)

Point prevalence survey in 24/25 ICUs (n=910 patients) and 7/7 LTACs (n=391 patients) in the Chicago region.

CRE prevention & control

- Hand hygiene
- Antibiotic stewardship
- Active screening
- Cleaning / disinfection
- Contact precautions
- Topical CHX?
- SDD?
- Education?

<table>
<thead>
<tr>
<th>Type</th>
<th>n studies</th>
<th>Failure rate</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bundled intervention</td>
<td>75</td>
<td>28%</td>
<td>1.9</td>
</tr>
<tr>
<td>Single intervention</td>
<td>11</td>
<td>45%</td>
<td></td>
</tr>
</tbody>
</table>
Hospital cleaning Google trends (2004 to present)
Hydrogen peroxide vapour decontamination

Acquisition of MDROs in 6350 patients admitted to ICU rooms, stratified by the MDRO status of the prior room occupant, and disinfection method.

UV room disinfection
UV systems – what we know

1. UVC is fundamentally different to Pulsed-Xenon UV (PX-UV).\(^1\)
2. UV systems are more effective than conventional cleaning and disinfection.\(^2\-^3\)
3. UV systems are faster & easier, but less effective than HPV.\(^4\)
4. UV systems are less effective out of direct line of sight; using multiple room locations helps to mitigate this.\(^4\-^5\)
5. There’s some emerging evidence that UV room disinfection reduces transmission.\(^6\)

Time to ‘copperise’ our hospitals?

614 pts in 3 hospitals randomised to ‘copper’ or ‘non-copper’ ICU rooms

Hands vs. Environment

A model simulating the impact of improvements in hand or environmental hygiene on patient-to-patient transmission in a 20-bed ICU. Dotted line represents my not-very-scientific-extrapolations from eye-balling the data.

Barnes et al. Infect Control Hosp Epidemiol 2014; 35: 1156-1162
Biofilms on dry hospital surfaces

- Scanning electron microscopy identified biofilm on 5/6 dry hospital surfaces from an Australian ICU.
- MRSA was identified on three of the surfaces.

Could explain why vegetative bacteria can survive on dry hospital surfaces for so long

Be part of the reason why they are so difficult to remove or inactivate using disinfectants

Explain (to some degree) the difficulty in recovering environmental pathogens by surface sampling

Biofilms and biocide susceptibility

- Planktonic cells
- Up to 10x less susceptible
- Up to 1000x less susceptible
- Surface attachment
- Biofilm development and maturation
- Mature biofilm

Otter et al. *J Hosp Infect* in press.
Biofilms and surface survival

Survival of biofilm and non-biofilm forming *A. baumannii*. 

Espinal *et al.* *J Hosp Infect* 2012;80:56-60.
Google trends for all search terms (excluding viruses) (2004 to present)
Google trends for all search terms (2004 to present)
What will be trending at HIS 2016?

- Ebola, MERS, Influenza
- Universal vs targeted interventions
- Faecal microbiota transplantation
- Whole genome sequencing
- CRE (and friends) +
- Environmental science
- Cost effectiveness
And finally…what’s trending on Twitter?

- UK CMO recommends including antibiotic resistance on risk register (https://twitter.com/guardian/status/294218197928906752)
- UK CMO report mentions resistant bacteria “threat” (https://twitter.com/Reuters_Health/status/310907997553582080)
- USA FDA announcement on azithromycin safety profile (https://twitter.com/nytimeshealth/status/311700730899738624)
- USA CDC Antimicrobial Resistance Threat Report (https://twitter.com/marynmck/status/379986025860186112)

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