WHO Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities

Prof. M. Lindsay Grayson, University of Melbourne, Australia

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Rationale for CRE-CRAB-CRPsA Recommendations

- Concern about the burden of illness associated with CRE-CRAB-CRPsA infection/colonisation = urgent priority
### Rationale for CRE-CRAB-CRPsA Recommendations

#### Reasons

- CRE-CRAB-CRPsA infection is associated with high morbidity and mortality
- CRE-CRAB-CRPsA transmission associated with high potential to cause outbreaks
- Key CR mechanism - a mobile resistance gene - readily transmitted between various intestinal bacterial species

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  - Duration of colonisation and subsequent risk for infection can be long
  - Can have substantial psychological implications for colonised patients
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- Long-term consequences of CRE-CRAB-CRPsA acquisition can be severe
  - Duration of colonisation and subsequent risk for infection can be long
  - Can have substantial psychological implications for colonised patients
- Current lack of effective treatments for infected and/or colonised patients
- CRE-CRAB-CRPsA are highlighted as the top critical priority pathogens
  - WHO publication *Prioritization of pathogens to guide discovery, research and development of new antibiotics for drug-resistant bacterial infections*
- Cost impact of colonisation and infection with CRE-CRAB-CRPsA on healthcare systems is high
  - Potentially threatening the stability of health care systems in both the short and long term
  - IPC is critical to control these costs and resource implications
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**Reasons**

- CRE-CRAB-CRPsA infection is associated with high morbidity and mortality
- CRE-CRAB-CRPsA transmission is associated with high potential to cause outbreaks

**Note:**

- Prevention and control of CRE-CRAB-CRPsA should be seen in the context of the broader priority to implement effective IPC for the prevention of all HAI and the strengthening of health care service delivery

- Importance of good antimicrobial stewardship - not included in these GLs, but critical

- Cost impact of colonisation and infection with CRE-CRAB-CRPsA on health care systems is high
  - Potentially threatening the stability of health care systems in both the short and long term
  - IPC is critical to control these costs and resource implications

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**Key staff**

- **Dr. Benedetta Allegranzi**
- **Dr. Matthias Egger**

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Experts who served on the GDG

- George L. Daikos (Laikon and Attikon Hospitals, Greece)
- Petra Gastmeier (Charité Universitätsmedizin, Germany)
- Neil Gupta (CDC, USA)
- Ben Howden (University of Melbourne and Austin Health, Australia)
- Bijie Hu (Chinese Infection Control Association, People’s Republic of China)
- Kushlani Jayatilleke (Sri Jayewardenapura General Hospital, Sri Lanka)
- Marimuthu Kalisvar (Tan Tock Seng Hospital and National University of Singapore)
- Anna-Pelagia Magiorakos (European CDC, Sweden)
- Shaheen Mehtar (Infection Control Africa Network; Stellenbosch University, South Africa)
- Maria Luisa Moro (Agenzia Sanitaria e Sociale Regionale, Italy)
- Babacar Ndoye (Infection Control Africa Network, Senegal)
- Folasade Ogunsola (College of Medicine, University of Lagos, Nigeria)
- Fernando Otaiza (Ministry of Health, Chile)
- Pierre Parneix (Société Française d’Hygiène, Hôpital Pellegrin, France)
- Mitchell J. Schwaber (National Center for Infection Control, Tel Aviv University, Israel)
- Sharmila Sengupta (Medanta - The Medicity Hospital, India)
- Wing-Hong Seto (WHO Collaborating Centre, Hong Kong, China)
- Nalini Singh (Children's National Medical Center; George Washington University, USA)
- Evelina Tacconelli (University Hospital Tübingen, Germany)
- Maha Talaat (CDC Global Disease Detection Programme, Egypt)
- Akeau Unahalekhaka (Chiang Mai University, Thailand).

WHO Guidelines on Best Practices and Procedures to Prevent and Control the Spread of Carbapenem-resistant Enterobacteriaceae (CRE), *Acinetobacter baumannii* (CRAB) and *Pseudomonas aeruginosa* (CRPsa) in health care

Background evidence:
Systematic Review on Best Practices and Procedures to Prevent and Control the spread of CRE, CRAB and CRPsa in health care

REPORT

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### Study characteristics

*Figure 1. Flowchart*

<table>
<thead>
<tr>
<th>Total Abstracts screened</th>
<th>9247</th>
</tr>
</thead>
<tbody>
<tr>
<td>From electronic databases</td>
<td>5048</td>
</tr>
<tr>
<td>From conference</td>
<td>4199</td>
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</table>

Abstracts potentially including:

- **CRE**: 9247
- **CRE** Full-text references screened: 183 (152 from electronic databases; 31 abstracts from conferences)
- **Included references**: 48

- **CRAB**: 1426
- **CRAB** Full-text references screened: 126 (122 from electronic databases; 4 abstracts from conferences)
- **Included references**: 34

<table>
<thead>
<tr>
<th>EPOC</th>
<th>Non-EPOC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* After removing duplicates

---

### Included studies according to WHO region

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>CRE</th>
<th>CRAB</th>
<th>CRPsA</th>
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<tbody>
<tr>
<td></td>
<td>EPOC</td>
<td>Non-EPOC</td>
<td>EPOC</td>
</tr>
<tr>
<td>Africa</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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<td>4</td>
<td>14</td>
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<tr>
<td>Eastern Mediterranean</td>
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<td>-</td>
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<tr>
<td>Europe</td>
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<td>17</td>
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<td>Western Pacific</td>
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<td>1</td>
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# Included studies according to study designs

<table>
<thead>
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<th>CRE</th>
<th>CRAB</th>
<th>CRPsA</th>
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<tbody>
<tr>
<td></td>
<td>EPOC</td>
<td>Non-EPOC</td>
<td>EPOC</td>
</tr>
<tr>
<td>Randomized controlled trials</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Non-randomized controlled trials</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Controlled before-after studies</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Interrupted time series</td>
<td>11</td>
<td>1</td>
<td>5</td>
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<tr>
<td>Before-after case counts</td>
<td>-</td>
<td>14</td>
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<td>Longitudinal studies</td>
<td>2</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Mathematical modelling studies</td>
<td>-</td>
<td>3</td>
<td>-</td>
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<tr>
<td>Non-controlled before-after studies</td>
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<td>15</td>
<td>-</td>
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<td><strong>Total</strong></td>
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</table>

# Included studies according to study scope/setting

<table>
<thead>
<tr>
<th>Study scope/setting</th>
<th>CRE</th>
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<th>CRPsA</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>EPOC</td>
<td>Non-EPOC</td>
<td>EPOC</td>
</tr>
<tr>
<td>National</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Regional/State</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Hospital</td>
<td>6</td>
<td>12</td>
<td>2</td>
</tr>
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<td>ICU</td>
<td>2</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Neonatal ICU</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Other Units: Haematology</td>
<td>-</td>
<td>8</td>
<td>-</td>
</tr>
<tr>
<td>Other Units: Burns</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LCTFs</td>
<td>1</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
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<td>35</td>
<td>5</td>
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</table>
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### Included studies according to study outcome

<table>
<thead>
<tr>
<th>Study outcome</th>
<th>CRE</th>
<th>CRAB</th>
<th>CRPsA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EPOC</td>
<td>Non-EPOC</td>
<td>EPOC</td>
</tr>
<tr>
<td>Incidence of infection</td>
<td>8</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Prevalence of infection</td>
<td>5</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Incidence of bloodstream</td>
<td>2</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of colonization</td>
<td>9</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Prevalence of colonization</td>
<td>1</td>
<td>13</td>
<td>-</td>
</tr>
<tr>
<td>Incidence of &quot;cases&quot;</td>
<td>1</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>(colonization or infection)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>35</td>
<td>5</td>
</tr>
</tbody>
</table>

*Note: A number of studies reported multiple outcomes and are therefore listed more than once*

### Findings according to impact of intervention on CRE-CRAB-CRPsA outcomes in EPOC studies

The results of the EPOC studies for CRE, CRAB and CRPsA were each reported separately according to outcome and (1) change in slope (i.e. trend) using an autoregressive integrated moving average model (ARIMA) and (2) change in level (i.e. immediate change after intervention implemented). Using segmented regression analysis. These are the EPOC-recommended analyses for integrated time-series data. In order to present the EPOC-recommended analysis, we contacted authors of all potential EPOC interrupted time-series studies for raw data and re-analysed 12 of the 17 included EPOC studies. These results can be seen in Table 6. These and the results reported by authors can be seen in detail in Table 9.

### Table 6. Results by outcome of EPOC-recommended analysis for change in slope (i.e. trend) and level (i.e. immediate change) from pre-intervention to post-intervention periods

<table>
<thead>
<tr>
<th>Study</th>
<th>Interventions package</th>
<th>Slope change ( \beta )</th>
<th>Level change ( \beta )</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNn</td>
<td>Yes</td>
<td>-0.52 (0.01), -0.72</td>
<td>-0.71 (0.55), -0.72</td>
</tr>
<tr>
<td>Bn</td>
<td>Yes</td>
<td>-0.7 (0.01), -1.2</td>
<td>-0.91 (0.55), -0.92</td>
</tr>
<tr>
<td>Gb</td>
<td>Yes</td>
<td>-0.6 (0.01), -0.8</td>
<td>-0.81 (0.55), -0.82</td>
</tr>
<tr>
<td>Cb</td>
<td>No</td>
<td>-0.5 (0.01), -0.6</td>
<td>-0.7 (0.55), -0.72</td>
</tr>
<tr>
<td>Gb</td>
<td>Yes</td>
<td>-0.6 (0.01), -0.8</td>
<td>-0.81 (0.55), -0.82</td>
</tr>
</tbody>
</table>

*Note: A number of studies reported multiple outcomes and are therefore listed more than once*
Findings of the EPOC studies

Table 9. Summary characteristics of EPOC studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Study design and setting</th>
<th>Main interventions</th>
<th>Timing</th>
<th>Patients admitted</th>
<th>Reported Pre-intervention results</th>
<th>Reported Post-intervention results</th>
<th>Reanalyzed results using EPOC technique</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben-David</td>
<td>2010</td>
<td>Israel</td>
<td>Carbenems resistant Enterobacteriaceae</td>
<td>2010</td>
<td>1,000 patients with clinical isolates</td>
<td>0.5 cases per 10,000 patient-days</td>
<td>0.1 cases per 10,000 patient-days</td>
<td>Change in rate: 0.4 (0.1-0.7)</td>
<td>Clear description of 150 cases</td>
</tr>
</tbody>
</table>

Table 10. Risk of bias assessment of EPOC studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention independent of other changes</th>
<th>Shape of intervention effect specified</th>
<th>Interventions unlikely to affect data collection</th>
<th>Knowledge of allocated interventions prevented</th>
<th>Incomplete outcome data addressed</th>
<th>No selective outcome reporting</th>
<th>No other risk of bias</th>
<th>Risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben-David, ICHE 2010</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Borer, ICHE 2011</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Campbel, ICHE 2016</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Chellin, A, ICHE 2011</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>De Fissis, ICHE 2016</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Enkada, ICHE 2014</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Figari, E, ICHE 2014</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Hadler, ICHE 2016</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Khs et al., ICHE 2011</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Schaller, ICHE 2016</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
<tr>
<td>Veale, ICHE 2016</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>High</td>
</tr>
</tbody>
</table>

Legend: * Low risk of bias, ** High risk of bias.
Table 11. GRADE evidence profile for the EPOC studies

<table>
<thead>
<tr>
<th>CRE (n=11)</th>
<th>n/a</th>
<th>n/a</th>
<th>n/a</th>
<th>n/a</th>
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</thead>
<tbody>
<tr>
<td># of Studies (Design)</td>
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<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
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<tr>
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<td>Serious</td>
<td>Not Serious</td>
<td>n/a</td>
</tr>
<tr>
<td>Indirectness</td>
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<td>Not Serious</td>
<td>Serious</td>
<td>Not Serious</td>
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<td>Serious</td>
<td>Not Serious</td>
<td>n/a</td>
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<tr>
<td>Publication bias</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Outcome: Incidence of CRE infection
- Seven out of eight studies reported a significant negative change in slope from pre- to post-intervention.
- Four studies reported a significant negative change in level (immediate change in outcome after intervention) out of seven which calculated this measure.
- Four studies reported a significant negative change in the outcome according to the ARIMA (coefficient) out of seven which calculated this measure.

Outcome: Incidence of CRE bloodstream infection
- Both studies reported a significant negative change in slope from pre- to post-intervention.
- One study reported a significant negative change in level (immediate change in outcome after intervention).
- One study reported a significant negative change in the outcome according to the ARIMA (coefficient).

Outcome: Prevalence of CRE colonization
- The study only reported a significant negative change in level (immediate change in outcome after intervention).
- The other two measures were non-significant (i.e., slopes and ARIMA coefficient).

Quality: Low

Global guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities

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The panel recommends that multimodal IPC strategies should be implemented to prevent and control CRE-CRAB-CRPsA infection or colonisation; and that these should consist of at least the following:

- Hand hygiene
- Surveillance (particularly for CRE)
- Contact precautions: gowns, gloves, and patient isolation
- Patient cohorting or single room isolation
- Environmental cleaning

*(Strong recommendation, very low to low quality of evidence)*

---

**Recommendation 1:**

Implementation of multimodal IPC strategies

Key Remarks

- Majority of studies from settings with a high prevalence of CRE-CRAB-CRPsA
  - But the IPC principles outlined were equally valid in all prevalence settings.
- Control of large outbreaks was recognized to be very costly
  - All studies were all undertaken in high- to middle-income countries
  - Concerns regarding cost implications of outbreaks and affordability in other settings.
WHO Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities
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Recommendation 1: Implementation of multimodal IPC strategies

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• Although the evidence = acute care facilities, similar IPC principles apply in all healthcare settings

• Implementing this REC-1 may be complex - requiring a multidisciplinary approach

• Good quality microbiological laboratory support is critical.

Recommendation 1: Implementation of multimodal IPC strategies

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• Control of large outbreaks was recognized to be very costly
  – All studies were all undertaken in high- to middle-income countries
  – Concerns regarding cost implications of outbreaks and affordability in other settings.

• Although the evidence = acute care facilities, similar IPC principles apply in all healthcare settings

• Implementing this REC-1 may be complex - requiring a multidisciplinary approach

• Good quality microbiological laboratory support is critical.

• Education/training and monitoring, audit and feedback are critical to make any multimodal strategy successful

• Daily patient bathing with chlorhexidine – insufficient evidence to be recommended

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The panel recommends that hand hygiene best practices according to the WHO Guidelines on hand hygiene in health care should be implemented.

*(Strong recommendation, very low quality of evidence)*

**Recommendation 2:**

Importance of good hand hygiene compliance for control of CRE-CRAB-CRPsA

- As noted in the WHO “Guidelines on Core Components of Infection Prevention and Control Programmes at the National and Acute Health Care Facility Level”, hand hygiene compliance and consumption of alcohol-based hand-rub (ABHR) is very dependent on appropriate product placement and availability
  - Adequate resources are therefore necessary to ensure these features are met.
- Important to monitor hand hygiene compliance
- Beneficial impact of good hand hygiene compliance dependent on effective implementation strategies with local adaptation

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Recommendation 3:
Surveillance of CRE-CRAB-CRPsA infection and surveillance cultures for asymptomatic CRE colonization

The panel recommends that:

1. Surveillance of CRE-CRAB-CRPsA infection should be performed

2. Surveillance cultures for asymptomatic CRE colonization should be performed, guided by local epidemiology (outbreaks vs endemic settings) and risk assessment.
   – Populations to be considered for such surveillance include:
     • Patients with previous CRE colonization
     • Patient contacts of CRE colonized/infected patients and
     • Patients with history of recent hospitalization in endemic CRE settings

(Strong recommendation, very low quality of evidence)

Recommendation 3:
Surveillance of CRE-CRAB-CRPsA infection(s)

Key Remarks

• Surveillance (i.e. clinical monitoring and laboratory assessment of clinical samples) of CRE-CRAB-CRPsA infection is essential

• In some settings (e.g. LMICs) laboratory testing for carbapenem resistance among potential CRE-CRAB-CRPsA isolates may not be available or routine
  – Unanimous view - testing for carbapenem resistance in these pathogens should now be considered as routine in all microbiology laboratories
### Recommendation 3:

**Surveillance of CRE-CRAB-CRPsA infection(s)**

**Key Remarks**

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- In some settings (e.g. LMICs) laboratory testing for carbapenem resistance among potential CRE-CRAB-CRPsA isolates may not be available or routine
  - Unanimous view - testing for carbapenem resistance in these pathogens should now be considered as routine in all microbiology laboratories
- Surveillance of CRE-CRAB-CRPsA infection needed to define the local epidemiology of these pathogens
  - Identify patterns
  - Better allocate resources to areas of need
  - Reviewing demographics, exposures, and locations of patients can help a facility understand where, when, and which patients are getting sick to better prevent and control infections

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### Recommendation 3:

**Surveillance cultures for asymptomatic CRE colonization**

**Key Remarks**

- Information regarding a patient’s CRE colonization status does not (yet) constitute routine standard of care provided to patients by health systems
  - But information critical in an outbreak situation or high risk situations for CRE
  - Surveillance CRE culture results for colonization may not have immediate benefit to the screened patient, but instead contribute to the overall IPC response to CRE
  - Information regarding CRE colonization status could potentially have important beneficial effects on the antibiotic treatment plan for screened patients with subsequent CRE infection.
Information regarding a patient’s CRE colonization status does not (yet) constitute routine standard of care provided to patients by health systems. But information critical in an outbreak situation or high risk situations for CRE. Surveillance CRE culture results for colonization may not have immediate benefit to the screened patient, but instead contribute to the overall IPC response to CRE. Information regarding CRE colonization status could potentially have important beneficial effects on the antibiotic treatment plan for screened patients with subsequent CRE infection.

This recommendation should always apply in an outbreak situation (and also ideally in endemic settings). Extensive discussion re. resource limitations (esp. LMICs) = prioritization of resources. No one single best surveillance approach - decision should be guided by the local epidemiology, and likely clinical.

**Recommendation 3:**

*Surveillance cultures for asymptomatic CRE colonization*

**Key Remarks**

- Surveillance screening based on a patient risk assessment (i.e. higher risk of CRE acquisition, the potential risk posed to others in their environment). Categories to be considered:
  - Patients with a previously known history of CRE colonization or infection
  - Epidemiologically-linked contacts of newly identified patients with CRE colonization or infection (this could include patients in the same room, unit or ward)
  - Patients with a history of recent hospitalization in regions where the regional epidemiology of CRE suggests an increased risk of CRE acquisition (e.g. hospitalization in a facility with known or suspected CRE).
  - Patients who, based on the epidemiology of their admission unit, may be at increased risk of CRE acquisition and infection (e.g. immunosuppressed patients, and those admitted to ICUs, transplantation services, or haematology units etc.)
**Recommendation 3:**

**Surveillance cultures for asymptomatic CRE colonization**

**Key Remarks**

- Surveillance cultures - feces best > rectal swab > perianal swab
  - Minimum one culture necessary; >1 better
- Take surveillance as soon as possible after hospital admission or risk exposure
  - Prompt processing
- Optimal frequency of testing uncertain – commonly, on-admission, then weekly

**Recommendation 3:**

**Surveillance cultures for asymptomatic CRE colonization**

**Additional Remarks**

- Surveillance activities could involve potential harms or unintended consequences for the patient with ethical implications, including:
  - A sense of cultural offensiveness or stigma associated with obtaining a rectal swab or providing a fecal specimen
  - Potential discrimination of colonized or infected patients
  - HOWEVER – key mitigation measures are available and should be implemented
Surveillance cultures for asymptomatic CRE colonization

Additional Remarks

- Surveillance activities could involve potential harms or unintended consequences for the patient with ethical implications, including:
  - A sense of cultural offensiveness or stigma associated with obtaining a rectal swab or providing a fecal specimen
  - Potential discrimination of colonized or infected patients
  - HOWEVER - key mitigation measures are available and should be implemented

- Ethical obligation to reduce the burden of CRE - larger public good
- Ethical burdens associated with this:
  - personally identifiable information - risk of disclosure
  - discrimination
  - potential risks with rectal swabs
  - perhaps no direct benefit to patient
- Safeguards to be provided to protect the patients:
  - ongoing monitoring for ethical burden (discrimination, clinical harms),
  - making all patients aware of surveillance protocol to generate awareness
  - identification of vulnerable patients

- Insufficient evidence on surveillance cultures for CRAB and CRPsA colonization to extend the recommendation to these two microorganisms
  - Sometimes beneficial - depends on the clinical setting, epidemiological stage (for example, outbreak) and body sites
  - Optimal microbiological methods for CRAB-CRPsA surveillance cultures for colonization require further research
WHO Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, 
Acinetobacter baumannii and Pseudomonas aeruginosa in health care facilities
Prof. M. Lindsay Grayson, University of Melbourne, Australia
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Recommendation 4:
Contact precautions

The panel recommends that:
Contact precautions should be implemented when providing care for patients colonised or infected with CRE-CRAB-CRPsA

(Strong recommendation, very low to low quality of evidence)

Key Remarks

Recommendation 4:

Contact precautions

- “Contact precautions” = WHO definition of contact precautions – namely, the use of gowns, gloves, PPE, dedicated equipment, appropriate patient placement, limiting transport/movement of patients; use of disposable or dedicated patient-care equipment; and prioritizing cleaning and disinfection of patient rooms
- Contact precautions should be considered a standard of care for patients colonized or infected with CRE-CRAB-CRPsA in the vast majority of health systems
- HCW education regarding the principles of IPC and monitoring of contact precautions is crucial

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WHO Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in health care facilities

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- Contact precautions should be considered a standard of care for patients colonized or infected with CRE-CRAB-CRPsA in the vast majority of health systems

- HCW education regarding the principles of IPC and monitoring of contact precautions is crucial

- Pre-emptive isolation/cohorting and use of contact precautions may be necessary in some situations, until the results of surveillance cultures for CRE-CRAB-CRPsA are available
  - Patients with a history of recent hospitalization in regions where the local epidemiology of CRE suggests an increased risk of CRE acquisition

- Clear communication regarding a patient’s colonization/infection status - important

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**Key Remarks**

- Inform patients of need for PPE practices to facilitate acceptance
- Ethical burdens associated with this:
  - Reduced contact with health care providers
  - Discrimination
  - Resource constraints in material resource leading to poor management of patients
- Safeguards to be provided to protect the patients:
  - Active engagement of patients in the contact precaution decision
  - ? Patients under contact precautions receive priority services to mitigate potential harms

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The panel recommends that:

Patients colonised or infected with CRE-CRAB-CRPsA should be physically separated from non-colonised/infected patients using:

1) single room isolation, or
2) cohorting with patients with the same resistant pathogen.

*(Strong recommendation, very low to low quality of evidence)*

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**Key Remarks 1**

- Inconsistent use of the terms “isolation” and “cohorting.” Standard definition used:
  - *Isolation:* Patients should be placed in single-patient rooms (preferably with own toilet facilities) when available. When single-patient rooms are in short supply - cohort
  - *Cohorting:* Grouping together patients who are colonized or infected with the same organism to confine their care to one area and prevent contact with other patients

- Purpose of isolation – to separate colonized/infected patients from non-colonized/non-infected patients

- Strongest evidence for CRE colonization/infection
  - But also likely to be effective for CRAB and/or CRPsA

- Patient isolation = some potentially negative unintended consequences
  - But that these can be minimized so as to outweigh these concerns

- Patient isolation - should always apply in an outbreak situation
Inconsistent use of the terms “isolation” and “cohorting.” Standard definition used:

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Purpose of isolation: separate colonized/infected patients from non-colonized/non-infected patients

Strongest evidence for CRE colonization/infection - But also likely to be effective for CRAB and/or CRPsA

Patient isolation - some potentially negative unintended consequences - But that these can be minimized so as to outweigh these concerns

Patient isolation should always apply in an outbreak situation

**Key Remarks 1**

Recommendation 5:
- Inform patients of need for isolation to facilitate acceptance
- Ethical burdens associated with this:
  - Reduced contact with health care providers
  - Discrimination
  - Resource constraints in material resource leading to poor management of patients
  - Depression/ anxiety in the patient
- Safeguards to be provided to protect the patients:
  - Active engagement of patients in the isolation decision; psychological support
  - Patients under contact precautions receive priority services to mitigate potential harms

Single rooms may not be possible in endemic situations - Particularly in low-income settings where resources and facilities are limited

Some evidence to support the use of dedicated health care workers to exclusively manage isolated/cohorted patients - Although there may be some feasibility issues
The panel recommends that:

Compliance with environmental cleaning protocols of the immediate surrounding area (i.e. “patient zone”) of patients colonised or infected with CRE-CRAB-CRPsA should be ensured

(Strong recommendation, very low quality of evidence)

Recommendation 6:
Environmental Cleaning

Key Remarks

- The “patient zone” = the patient and his/her immediate surroundings
  - Includes all inanimate surfaces that are touched by or in direct physical contact with the patient such as the bed rails, bedside table, bed linen, infusion tubing, bedpans, urinals and other medical equipment.
  - Contamination is likely in toilets and items found nearby
- The optimal cleaning agent for environmental cleaning protocols for CRE-CRAB-CRPsA has not yet been defined
  - A number (n=3) studies used hypochlorite (gen. a concentration of 1000 ppm)
Environmental Cleaning

Key Remarks

- The “patient zone” = the patient and his/her immediate surroundings
  - Includes all inanimate surfaces that are touched by or in direct physical contact with the patient such as the bed rails, bedside table, bed linen, infusion tubing, bedpans, urinals, and other medical equipment.
  - Contamination is likely in toilets and items found nearby
- The optimal cleaning agent for environmental cleaning protocols for CRE-CRAB-CRPsA has not yet been defined
  - A number (n=3) studies used hypochlorite (gen. a concentration of 1000 ppm)
- Educational programs for hospital cleaning staff – crucial
  - Multimodal strategies to implement environmental cleaning essential – including institutional policies, structured education, monitoring compliance with protocols
- Assessment of cleaning efficacy by performing environmental screening cultures - worthwhile in some settings
- In some outbreak situations, temporary ward closures necessary to allow for enhanced cleaning

Recommendation 6:

Surveillance cultures of the environment for CRE-CRAB-CRPsA may be considered when epidemiologically indicated

(Conditional recommendation, very low quality of evidence)
Surveillance cultures of the environment for CRE-CRAB-CRPsA colonization/contamination

Key Remarks

- Correlation of environmental surveillance culture results to the rates of patient colonization/infection with CRE-CRAB-CRPsA should be undertaken with caution and depend on an understanding of the local epidemiology and resources
- Based on expert opinion (and only limited available data), surveillance cultures of the general environment were considered most relevant to CRAB outbreaks
- Outbreaks of CRPsA colonization/infection - more commonly associated with environmental CRPsA contamination involving water and waste-water systems such as sinks and faucets

Recommendation 8:
Monitoring, Audit and Feedback

The panel recommends:
Monitoring of the implementation of multimodal strategies and feedback of results to health care workers and decision-makers

(Strong recommendation, very low to low quality of evidence)
**Recommendation 8:**

**Monitoring, Audit and Feedback**

**Key Remarks**

- Monitoring, audit and feedback of IPC interventions - fundamental component of any effective intervention - esp. for CRE-CRAB-CRPsA
- Appropriate training of HCWs who undertake monitoring – crucial
  - Is a key component of all IPC educational programs
- All components of the multimodal strategy intervention should be regularly monitored, including hand hygiene compliance
- Monitoring, audit and feedback of multimodal strategies are a key component of all IPC educational programmes
- IPC monitoring should encourage improvement and promote learning in a non-punitive institutional manner

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**Planned dissemination and implementation of the Guidelines**

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Conclusions

- New CRE-CRAB-CRPsA Guidelines now available
- IPC interventions – the key to controlling CRE-CRAB-CRPsA in healthcare settings
- Implementation will be a challenge, but is necessary
WHO Guidelines for the prevention and control of carbapenem-resistant Enterobacteriaceae, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in health care facilities

Prof. M. Lindsay Grayson, University of Melbourne, Australia

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Learn more about WHO’s IPC work at: [http://www.who.int/infection-prevention/en/](http://www.who.int/infection-prevention/en/)

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