Do nursing homes represent a reservoir of *Enterobacteriaceae* producing extended-spectrum β-lactamase (ESBLE) or carbapenemase (CPE) in a regional epidemic context in France? The CARBEHPAD study

N Hayatgheib, G Birgand, C Bourigault, C Legeay, V Guilloteau, S Perron, P Bemer, ME Juvin, Emmanuel Montassier, L de Decker, E Batard, D Lepelletier

*Bacteriology and Hospital Hygiene Department*  
*Nantes Teaching Hospital, Nantes, FRANCE*

*Mihar Laboratory*  
*Nantes University, Nantes, FRANCE*
Transparency Declaration

I haven’t received research grants and I ‘m not a paid consultant for this research
Facilities in the community with:
- Old population (residents)
- Long periods of life
- Frequent hospital transfers for acute cares and infection
- Probably represent a reservoir of enterobacteriaceae producing ESBL (ESBL-E) BUT carbapenemase (CPE)?

Prevalence of ESBL-E in nursing homes

<table>
<thead>
<tr>
<th>Country</th>
<th>ESBLs (%)</th>
<th>CPE (%)</th>
<th>source</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>17.3</td>
<td>0</td>
<td>RHC-arlin., 2016</td>
</tr>
<tr>
<td>Germany</td>
<td>27</td>
<td>0</td>
<td>Kleinkauf N et al., 2014</td>
</tr>
<tr>
<td>Ireland</td>
<td>40.5</td>
<td>_</td>
<td>Rooney PJ, et al., 2009</td>
</tr>
<tr>
<td>Italy</td>
<td>41.4</td>
<td>_</td>
<td>March A et al., 2010</td>
</tr>
<tr>
<td>Spain</td>
<td>26.6</td>
<td>4.1</td>
<td>Del Rosario-Quintana C et al., 2015_Ruiz-Garbajosa P et al., 2016</td>
</tr>
<tr>
<td>Netherlands</td>
<td>8.6</td>
<td>_</td>
<td>Platteel TN et al., 2013</td>
</tr>
<tr>
<td>Belgium</td>
<td>8.6</td>
<td>0</td>
<td>Ruiz-Garbajosa P et al., 2016</td>
</tr>
</tbody>
</table>
The two university hospitals of the Pays de la Loire Region have been concerned by large CPE outbreaks since 2013

In Nantes:
- The outbreak seems to be limited to the University Hospital with very few transfers of CPE carriers to nursing homes

In Angers:
- No limitation of CPE carriers at the beginning of the outbreak
- Transferred residents detected CPE positive during hospitalization
French context

• No French recommendations to perform systematic screening for ESBL-E or CPE digestive colonization in residents by rectal swab

• The control of the MDR or XDR microorganisms cross-transmission is based on standard precautions
Objectives of the study

• **Main objectives**
  - To measure the ESBLE and CPE prevalence among residents in nursing homes in the area of Nantes and Angers
  - To identify factors related to the host, drug exposure and hospitalization associated with CPE or ESBLE carriage among positive residents
Study design

POPULATION A
Unknown presence of CPE carrier resident
2 Nursing homes in Nantes: (312 residents)

POPULATION B
Presence of CPE carrier resident
4 Nursing homes in Angers: (130 residents)

289 residents were included (93%)
69 residents were included (53%)

178 residents (62%) were screened for ESBL and CPE digestive colonization
56 residents (81%) were screened for ESBL and CPE digestive colonization

Flow chart: inclusion of the study population

Multicenter point prevalence observational study
From June to August 2016
**Microbiological data collection**

- Stool sample in residents with fecal incontinence (*to make easy the sample collection*)
- Directly from the feces of the residents with a specific swab (Copan® or fecal swab®) by the assistant nurses
- Systematic checking of fecal matter presence before laboratory support
- Only one swab for both ESBLE and CPE detection
Microbiological analysis

• Screening with specific chromogenic agar culture medium appropriate to ESBL (ESBL-chromID®) and CPE (chromID CARBA-SMART ID®)

• Identification of colonies using mass spectrometry test (VITEK MS method, BioMérieux, FRANCE)

• Confirmation of the suspected resistance phenotype with MASTDISCS ESBL-test and MASTDISC-carbapenemase (BioMérieux, FRANCE)

• Phenotypic confirmation of ESBL production

• Molecular analysis by PFGE analysis using XbaI, SpeI and NotI digestion

BLSE (+) *E. coli*: Detecting the difference in diameter between a loaded disc to a 3GC (third generation cephalosporin) and a loaded disc to a C3G + ESBL inhibitor (Clavulanic acid)
Results

• 234 residents screened for CPE and ESBL-E digestive carriage / 447 residents included in the study

• None residents were colonized with EPC except the 5 carriers

• Global ESBL-E prevalence of 6.8% (16 residents / 234):
  ✓ Population A prevalence 7.9% (14 residents)
  ✓ Population B prevalence 3.6% (2 residents)
ESBL-E epidemiology

- All residents were colonized with only one strain
- The identification of strains cultured from stools were:
  - 11 (68.7%) *Escherichia coli*
  - 3 (18.7%) *Enterobacter cloacae*
  - 2 (12.5%) *Klebsiella pneumoniae*

*Strains used for molecular comparison*

Table. Relatedness among ESBL-producing isolates was investigated by **PFGE analysis** using XbaI, Spel and NotI digestion for *E. cloacae*, *K. pneumoniae* and *E. coli*

* Strains used for molecular comparison
ESBL-E risk factors (Population A)

<table>
<thead>
<tr>
<th>Factors</th>
<th>ESBL positive (n=14)</th>
<th>ESBL negative (n=164)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age – median (min-max)</td>
<td>88 (77-94)</td>
<td>86.5 (67-99)</td>
<td>0.702</td>
</tr>
<tr>
<td>Sex (men) – n(%)</td>
<td>3(21.4)</td>
<td>54(33)</td>
<td>0.376</td>
</tr>
<tr>
<td>GIR – median (min-max)</td>
<td>2 (1-4)</td>
<td>2 (1-6)</td>
<td>0.241</td>
</tr>
<tr>
<td>Infection – n(%)</td>
<td>0(0)</td>
<td>4 (2.4)</td>
<td>0.555</td>
</tr>
<tr>
<td>Antibiotic therapy</td>
<td>0(0)</td>
<td>5 (3.1)</td>
<td>0.508</td>
</tr>
<tr>
<td>Diabetes – n(%)</td>
<td>1(7.14)</td>
<td>19(12)</td>
<td>0.613</td>
</tr>
<tr>
<td>Dementia – n(%)</td>
<td>0(0)</td>
<td>2(1.22)</td>
<td>0.678</td>
</tr>
<tr>
<td>Indwelling urinary catheter – n(%)</td>
<td>1(7.14)</td>
<td>3(1.83)</td>
<td>0.189</td>
</tr>
<tr>
<td>At least one catheter – n (%)</td>
<td>3(21.43)</td>
<td>24(14.63)</td>
<td>0.496</td>
</tr>
<tr>
<td>Surgery intervention during the last month – n (%)</td>
<td>0(0)</td>
<td>0(0)</td>
<td>-</td>
</tr>
<tr>
<td>Hospitalization in the last 3 months –n (%)</td>
<td>0(0)</td>
<td>1(0.61)</td>
<td>0.770</td>
</tr>
</tbody>
</table>
Discussion

• **Strength of the study:**
  - Rigorous scientific approach (epidemiologic and microbiologic) with expert support
  - Analysis of fecal sample with few possibilities of false negative (swab directly in the feces)
  - A specific team to organize the data collection in the population A
  - Prevalence survey in an regional CPE outbreak context with transfers between nursing homes and University hospitals

• **Limitations:**
  - Size of the study sample:
    • Only 6 nursing homes (>500 nursing homes in the Pays de la Loire area)
    • All the residents in the selected nursing home were not screened (difficulty in applying the protocol) in Angers area without a specific team
  - No assessment of the compliance to standard precautions and isolation measures in nursing homes
Conclusion

• First survey of ESBL-E and CPE carriage in nursing homes in the region of Pays de la Loire in France
  • ESBL-E prevalence in the range expected at the national level
  • No risk associated with ESBL-E digestive carriage able to detect carriers
  • No clonal spread

• None CPE carrier or no secondary cases in this high risk population in contact with two regional CPE outbreaks
  • Very few ATB exposure
  • Low CPE relative abundance in the digestive flora
  • Low CPE spreaders

• Should we conclude that it is not necessary to screen residents in nursing homes for MDR colonization?

• These results must be confirmed by a largest prevalence study in our region
Acknowledgments

- Niki HAYATGHEIB and the Man-imal Master 2 degree team
- Dr. Gabriel BIRGAND for their scientific support
- Lab team
  - Pascale BEMER and Marie-Emmanuelle JUVIN) for their microbiological support and Niki training
  - Stéphane CORVEC for the molecular analysis and expertise
- All the HCWs and practitioners involved in the study in the 6 different nursing homes, particularly Paulette Cornu, infection control nurse in Nantes