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# Is there evidence for a reservoir of Carbapenemase-producing *Enterobacteriaceae* in nursing homes and rehabilitation centers?

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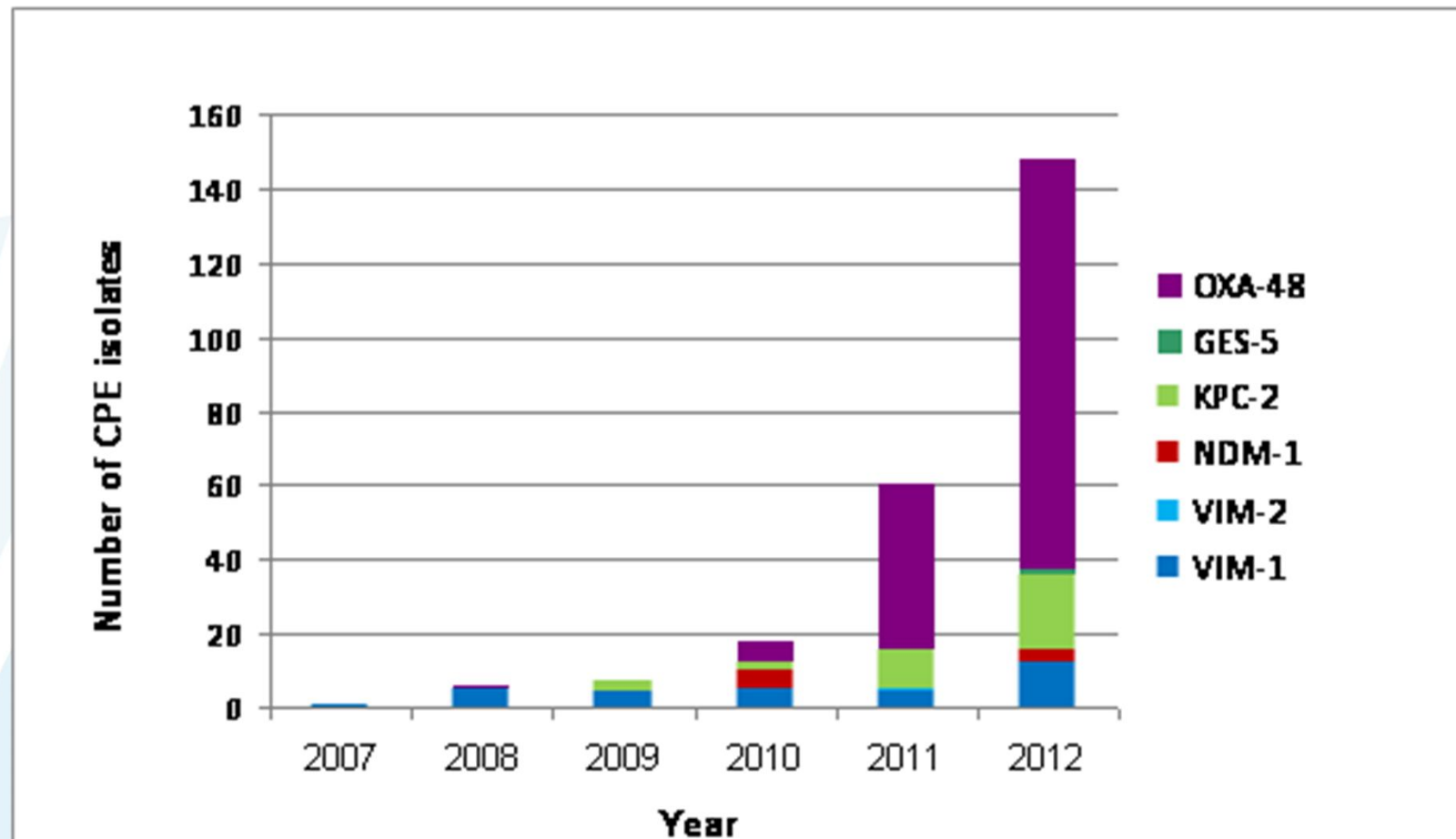
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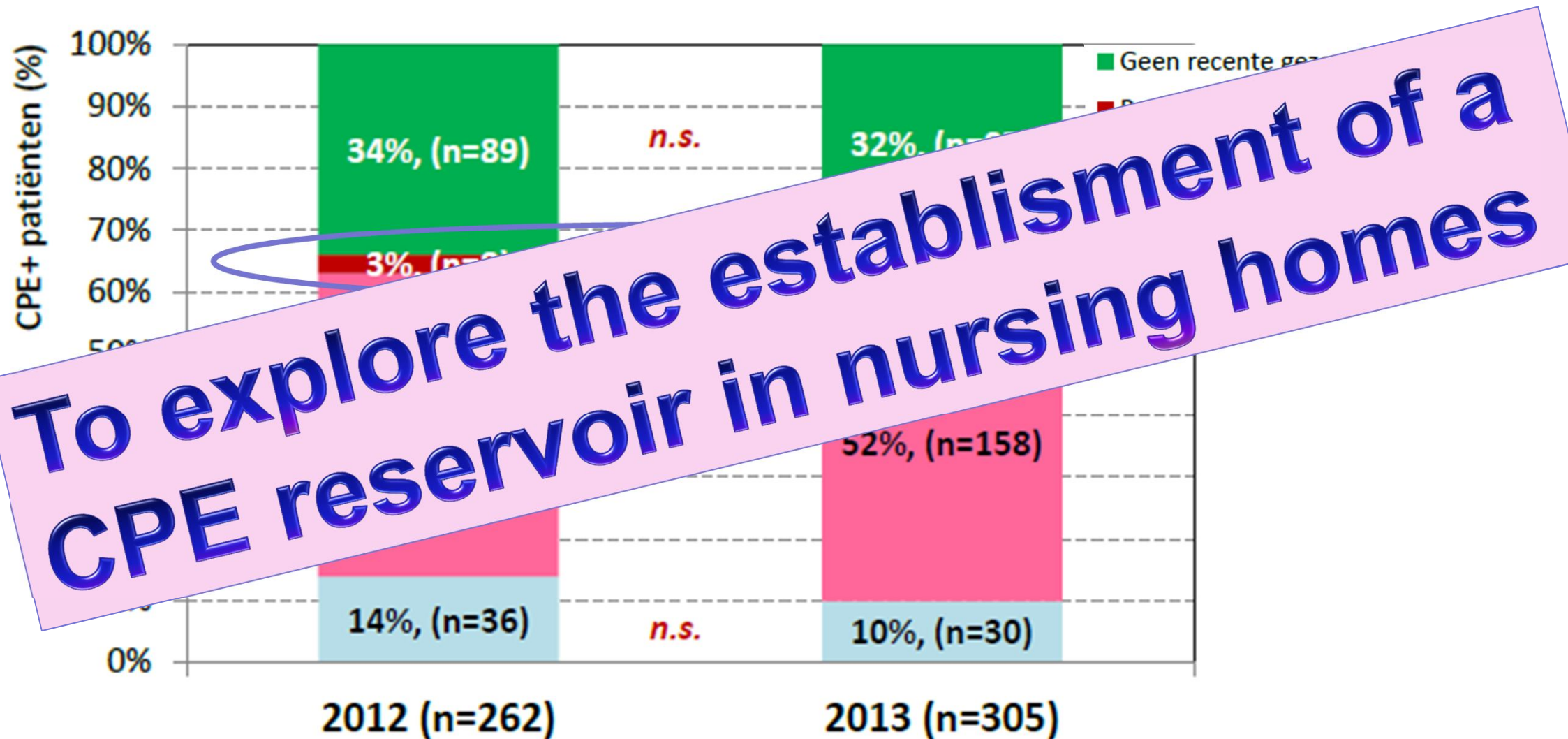
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- ↑ MDRO worldwide → public health concern
- Carbapenemase-producing *Enterobacteriaceae*



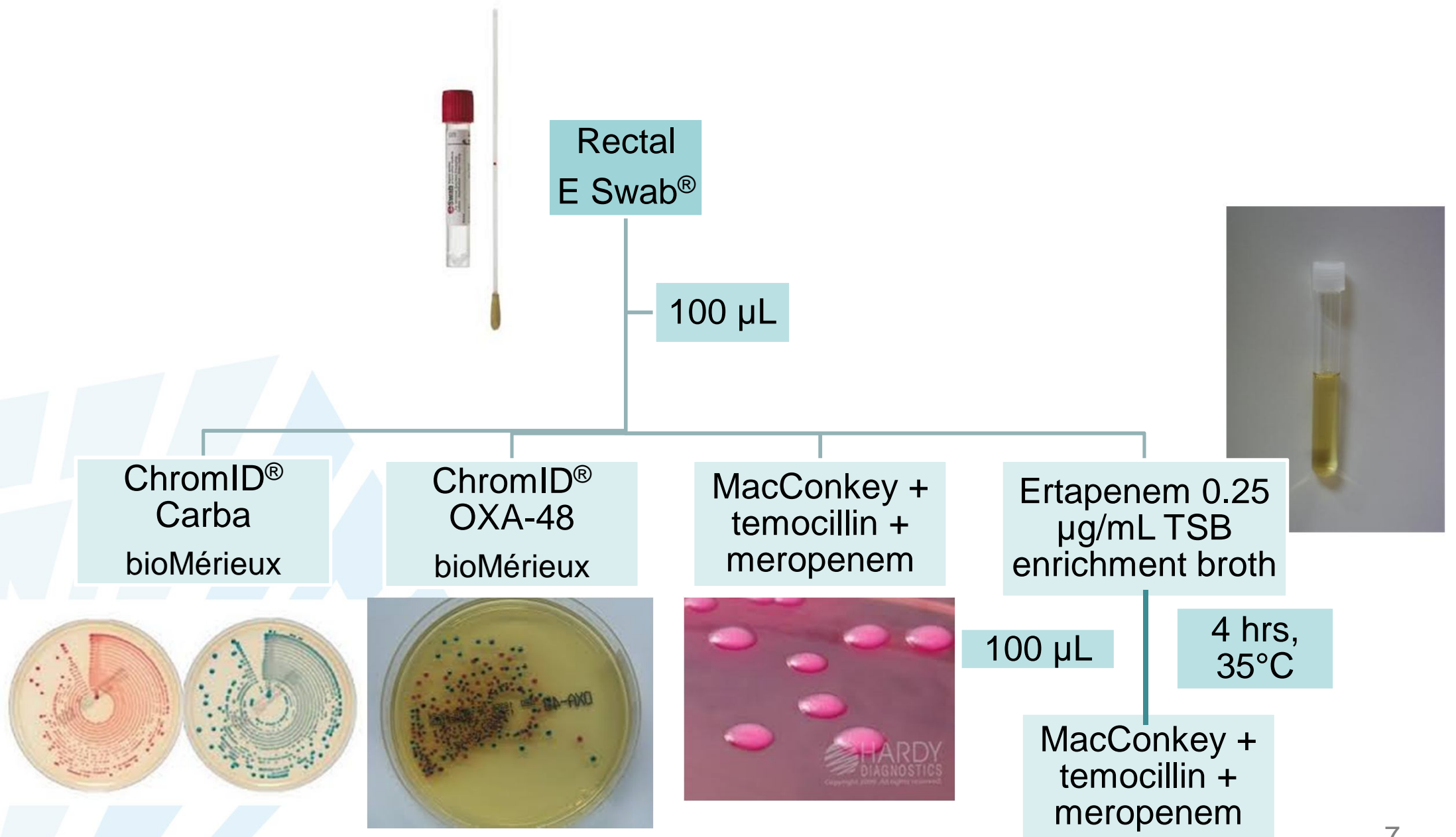
- Patient population



1. Establishment of a CPE reservoir in nursing homes and rehabilitation centers ?
2. Performance of different CPE culture methods and Check-*Direct*<sup>®</sup> CPE PCR
3. Risk factors for CPE

- Study population
  - 3 nursing homes (De Plataan, Populierenhof, Ter Vlierbeke (N=250))
  - 1 rehabilitation center (National MS center, Melsbroek (N=134))
- Screening protocol
  - Period: July 2013 – January 2014
  - Rectal E Swab<sup>®</sup>
  - Written informed consent (Study N° B322201214429)
  - Inoculation < 7 hrs

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- Screening protocol

- Reading: +24 hrs and + 48 hrs

- Species identification: Maldi-TOF MS (Bruker Biotyper)

- MacConkey: temocillin R (< 20 mm) – meropenem R (< 23 mm)

- Chromogenic media: all isolates

- Chromogenic media

- Semiquantitative growth

- Colour codes

- *Enterobacteriaceae*

- AST (Vitek<sup>®</sup> 2, AST-N205, bioMérieux)

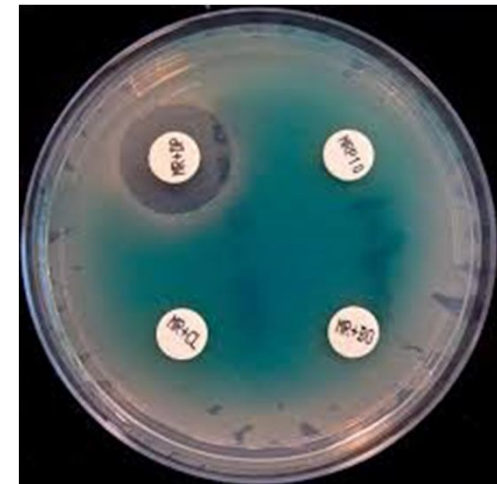
- Criteria

- Meropenem MIC  $\geq 0.5 \mu\text{g/mL}$   $\rightarrow$  Etest (bioMérieux)

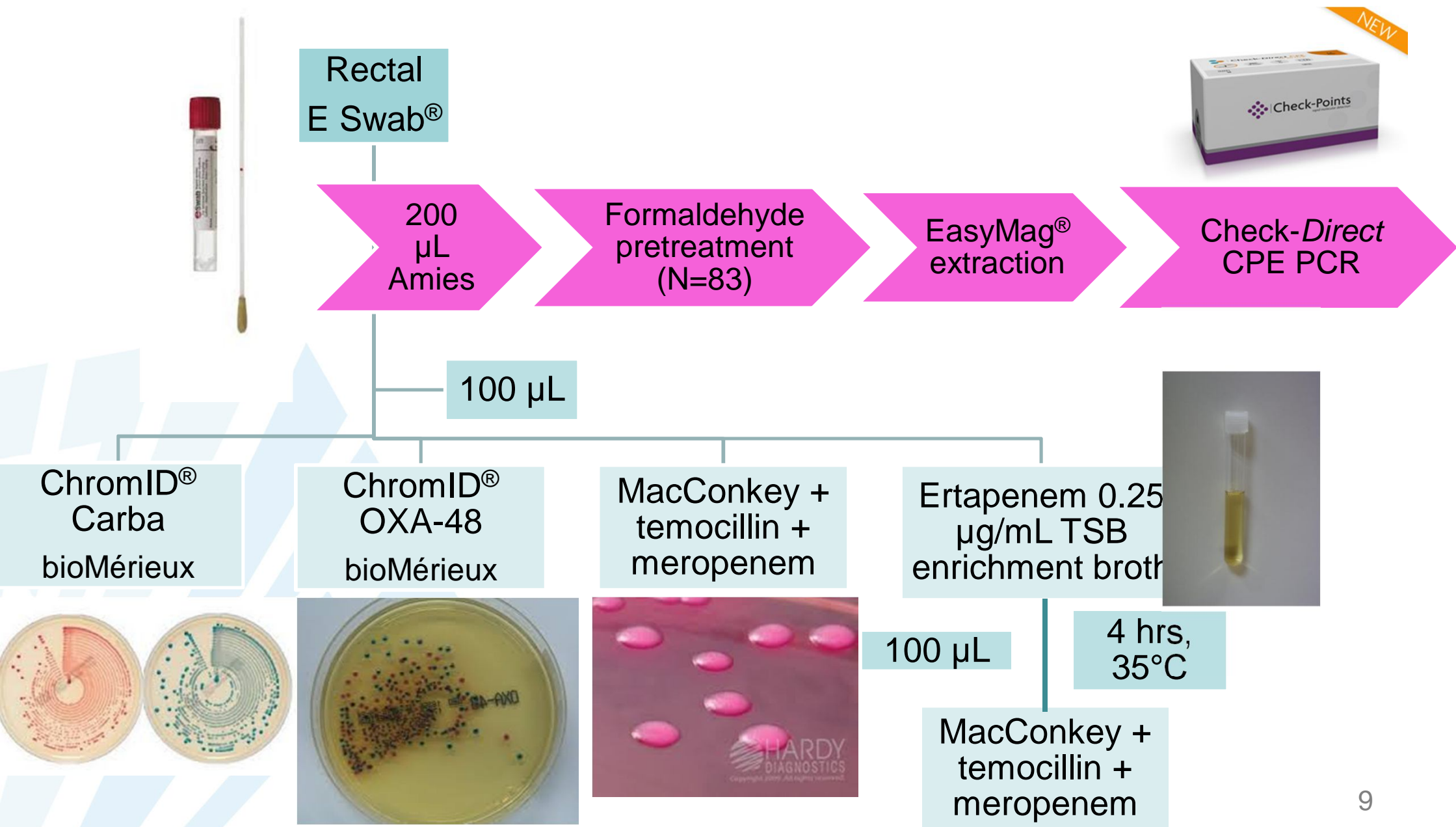
- + KPC/MBL confirmation test (Rosco Diagnostica)

- Temocillin MIC  $\geq 16 \mu\text{g/mL}$   $\rightarrow$  Etest (bioMérieux)

MBL disc diffusion







- Resident and patient characteristics
  - Questionnaire
    - Age
    - Gender
    - Residence
    - Length of residency at sampling time
    - Katz Index / Expanded Disability Status Score
    - Comorbidities
    - Antimicrobial therapy < 3 months
    - Colonization/infection MDRO
    - Stay in hospital or rehabilitation center < 6 months
    - Travel to foreign country < 12 months
    - Indwelling catheter

- Statistical analysis
  - Sensitivity and specificity
  - Gold standard: molecular CPE result on grown *Enterobacteriaceae* with meropenem MIC  $\geq 0,5 \mu\text{g/mL}$  +/- temocillin MIC  $\geq 16 \mu\text{g/mL}$

- Screening protocol
  - 261 residents/patients included (N=384)
  - 4 Eswabs: no growth on MacConkey → problematic pre-analytical phase
  - 20 *Enterobacteriaceae*
    - Colour codes on chromogenic agars

	Conform (N)	Not conform (N)
ChromID® Carba (bioMérieux)	5 ( <i>E. coli</i> , <i>Enterobacter</i> spp.)	3 ( <i>E. aerogenes</i> , <i>K. pneumoniae</i> , <i>C. freundii</i> )
ChromID® OXA-48 (bioMérieux)	1 ( <i>K. pneumoniae</i> )	0



**Table 1. No. species isolated after 24 hrs (a) and 48 hrs (b) of incubation**

(a)	ChromID® CARBA	ChromID® OXA-48	MacConkey - temocillin	MacConkey - meropenem	MacConkey after ertapenem enrichment - temocillin	MacConkey after ertapenem enrichment - meropenem
No. Isolates	24 hrs	24 hrs	24 hrs	24 hrs	24 hrs	24 hrs
<b>Enterobacteriaceae</b>	2	1	7	0	2	0
<i>Aeromonas</i> spp.	1	0	1	0	1	0
<i>Pseudomonas</i> spp.	81	8	42	0	49	2
<i>Stenotrophomonas</i> spp.	18	0	0	12	0	15
<i>Acinetobacter</i> spp.	1	2	22	0	21	0
<b>Other Gram-negatives</b>	1	0	0	0	0	0
<i>Arcobacter</i> spp.	0	1	0	0	0	0
<i>Enterococcus</i> spp.	1	2	5	0	4	0
<i>Lactobacillus</i> spp.	0	0	0	0	0	0
<i>Staphylococcus</i> spp.	0	0	0	0	0	0
<i>Candida</i> and <i>Geotrichum</i> spp.	1	0	0	0	0	0



**Table 1. No. species isolated after 24 hrs (a) and 48 hrs (b) of incubation**

<b>(b)</b>	ChromID® CARBA	ChromID® OXA-48	MacConkey - temocillin	MacConkey - meropenem	MacConkey after ertapenem enrichment - temocillin	MacConkey after ertapenem enrichment - meropenem
<b>No. Isolates</b>	48 hrs	48 hrs	48 hrs	48 hrs	48 hrs	48 hrs
<b>Enterobacteriaceae</b>	6	1	8	0	4	0
<i>Aeromonas</i> spp.	1	0	1	0	1	0
<i>Pseudomonas</i> spp.	110	18	52	0	54	2
<i>Stenotrophomonas</i> spp.	20	1	8	16	7	15
<i>Acinetobacter</i> spp.	3	12	25	0	25	0
<b>Other Gram-negatives</b>	2	4	0	0	0	0
<i>Arcobacter</i> spp.	0	1	0	0	0	0
<i>Enterococcus</i> spp.	1	11	69	8	50	6
<i>Lactobacillus</i> spp.	0	0	2	0	0	0
<i>Staphylococcus</i> spp.	0	18	0	0	0	0
<i>Candida</i> and <i>Geotrichum</i> spp.	12	11	15	11	1	1

- Screening protocol

- N = 255 PCRs (2 Eswabs: shortage of medium)
- N = 3: inhibited
- N = 250: negative
- N = 2: positive for OXA-48

1. *K. pneumoniae*: OXA-48 Ct-value 29.4 → **TRUE positive**
  - **Woman, 82 yrs, diabetes mellitus, known with CPE and MRSA, previous hospitalization (-3 mths) and amoxiclav treatment (-3mths)**
2. No *Enterobacteriaceae*: OXA-48 Ct-value 33.2 (not confirmed by NRC) → **FALSE positive**

<b>Table 3. Demographic and clinical characteristics of included residents (N=261)</b>		
<b>Female, no./No. (%)</b>	185/260	71
<b>Median age (years), (IQR\$)</b>	82.3	62.0-89.3
<b>Median length of stay (days), (IQR)</b>	302	15-1224
<b>Modified KATZ score, no./No. (%)</b>		
<b>Class O, complete autonomy</b>	15/175	8.6
<b>Class A</b>	21/175	12.0
<b>Class B</b>	48/175	27.4
<b>Class C, high level of dependency</b>	21/175	12.0
<b>Class Cd, high level of dependency</b>	70/175	40.0
<b>Expanded Disability Status Scale, no./No. (%)</b>		
<b>Assistance needed for walking (score 6)</b>	28/47	59.6
<b>Wheelchair but self-moving (score 7)</b>	9/47	19.2
<b>Bed patient, but with arm function (score 8)</b>	5/47	10.6
<b>Totally helpless bed patient (score 9)</b>	5/47	10.6
<b>Comorbidities, no./No (%)</b>	168/259	64.9
<b>Malignancy</b>	31/259	12.0
<b>Diabetes mellitus</b>	30/259	11.6
<b>Chronic renal insufficiency</b>	5/259	1.9
<b>Multiple Sclerosis</b>	69/259	26.6
<b>Cerebrovascular disease</b>	7/259	2.7
<b>Central nervous system disease</b>	12/259	4.6
<b>COPD</b>	10/259	3.9
<b>Trauma</b>	4/259	0.02

<b>Antimicrobials in previous 3 months, no./No. (%)</b>	<b>53/258</b>	<b>20.5</b>
Betalactams	25/53	47.2
Fluoroquinolones	5/53	9.4
Other	9/53	17.0
Not mentioned	14/53	26.4
<b>Previous infection with MDRO*, no./No. (%)</b>	<b>12/254</b>	<b>4.7</b>
MRSA	11/12	91.7
ESBL	1/12	8.3
CPE	1/12	8.3
<b>Hospitalization previous 6 months, no./No. (%)</b>	<b>45/257</b>	<b>17.5</b>
>7 days hospitalization, no./No (%)	33/43	76.7
Median No. days between hospital discharge and CPE screening, (IQR)	84.0	50.0-134.5
<b>Stay in revalidation center previous 6 months, no./No. (%)</b>	<b>29/260</b>	<b>11.2</b>
Median No. days between intake and CPE screening, (IQR)	123	93.0-156.5
<b>Long-term catheter, no./No. (%)</b>	<b>31/260</b>	<b>11.9</b>
Urinary, no./No. (%)	22/31	71.09
Gastro-enteric, no./No. (%)	7/31	22.6
Dialysis, no./No. (%)	2/31	6.5
Intrathecal pump, no./No. (%)	3/31	9.7
\$ IQR : interquartile range *MDRO : multi-drug resistant micro-organism		

**Table 4. Specificity of culture methods and PCR for CPE detection after (a) 24 hrs and (b) 48 hrs of incubation**

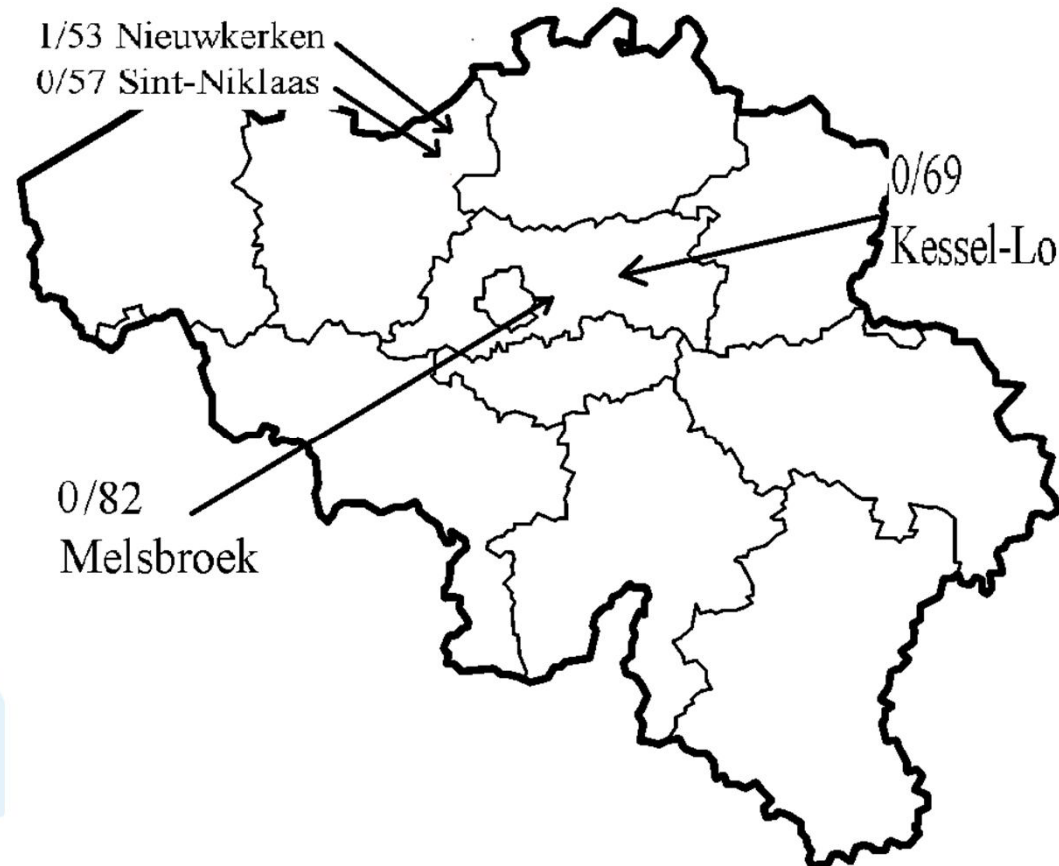
	ChromID CARBA (No. samples)	ChromID OXA-48 (No. samples)	MacConkey - temocillin (No. samples)	MacConkey - meropenem (No. samples)	MacConkey after ertapenem enrichment – temocillin (No. samples)	MacConkey after ertapenem enrichment – meropenem (No. samples)	Check-Direct CPE PCR (No. samples)
<b>(a) 24 hrs</b>							
True positive	0	1	1	0	1	0	1
False positive	2	0	6	0	1	0	1
True negative	254	256	250	256	255	256	250
False negative	1	0	0	1	0	1	0
Total	257	257	257	257	257	257	252
Specificity % (95% CI)	99.2 (98.1-100)	100 (100-100)	97.7 (95.8-100)	100 (100-100)	99.6 (98.8-100)	100 (100-100)	99.6 (98.8-100)
<b>(b) 48 hrs</b>							
True positive	0	1	1	0	1	0	NA
False positive	5	0	7	0	3	0	NA
True negative	250	256	249	256	253	256	NA
False negative	1	0	0	1	0	1	NA
Total	257	257	257	257	257	257	NA
Specificity % (95% CI)	98.0 (96.3-99.7)	100 (100-100)	97.2 (95.3-99.3)	100 (100-100)	98.8 (97.5-100)	100 (100-100)	NA

NA : not applicable

1. Establishment of a CPE reservoir in nursing homes and rehabilitation centers ?
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3. Risk factors for CPE



- This study: CPE prevalence: 0.39%



- Huang et al, 2013: 0.28% (0.13-0.44) CPE prevalence in Belgian hospitals

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## 2. Performance of different CPE culture methods and Check-*Direct*<sup>®</sup> CPE PCR

- Broth enrichment
- Prolonged incubation of agars (48 hrs)
- Overall performance of all culture methods (24 hrs) and Check-*Direct* CPE PCR
  - > 97% specificity

← no ↑ yield

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## 3. Resident and patient characteristics as risk factors

- Impossible to determine risk factors CPE (1 case)
- OXA-48 positive sample: patient with typical risk factors

- No confirmed CPE reservoir in nursing homes and rehabilitation centers
  - Additional surveillance studies on a larger scale are needed
- To confirm the role of chronic care settings as secondary CPE reservoirs



- Prof Glupczynski
- Nurses of nursing homes and MS center



Thank  
you!