UNIVERSITY OF LIVERPOOL

ANTIBIOTIC ACTION
THE ARMS RACE.

Recomandări privind depistarea precoce, managementul și controlul infecțiilor cu bacterii Gram-negative producătoare de carbapenemaze

Dr Dorina Timofte
Institute of Infection and Global Health
University of Liverpool

Intre timp…..

- Conferinta Societatii Romane de Microbiologie, 2015

- S-a conturat un **grup de lucru format din microbiologi si epidemiologi**

  - ✓ Comisia de Epidemiologie din Minister
  - ✓ SRE
  - ✓ SRM
  - ✓ Centre Universitare
  - ✓ Inst. Cantacuzino

- S-a trimis pentru consultare continutul ghidului "***Recomandări privind depistarea precoce, managementul și controlul infecțiilor cu bacterii Gram-negative producătoare de carbapenemaze***"

PLOS ONE

RESEARCH ARTICLE

Carbapenemase-Producing *Klebsiella pneumoniae* in Romania: A Six-Month Survey

Brandusa Elena Lixandru[1☯], Ani Ioana Cotar[1,2☯*], Monica Straut[1], Codruta Romanita Usein[1], Dana Cristea[1], Simona Ciontea[1], Dorina Tatu-Chitoiu[1†], Irina Codita[1], Alexandru Rafila[3], Maria Nica[4], Mariana Buzea[5], Anda Baicus[6], Mihaela Camelia Ghita[7], Irina Nistor[8], Cristina Tuchiluş[9], Marina Indreas[10], Felicia Antohe[11], Corinna Glasner[12], Hajo Grundmann[12], Aftab Jasir[2], Maria Damian[1]

Conclusions

This study shows the first detection of *K. pneumoniae* strains harbouring $bla_{\text{KPC-2}}$ and $bla_{\text{VIM-1}}$ genes in Romania. The carbapenemase most frequently detected is OXA-48, representing 79% of carbapenemase-producing *K. pneumoniae* strains. This carbapenemase was detected in isolates collected from patients hospitalized in all of the participating hospitals, and the PFGE results suggest the spread of a single clone in all sampled hospitals with outbreaks in two of them. Likewise, NDM-1 positive strains have also been identified in four hospitals and PFGE results indicate a similar epidemic dynamic as for OXA-48. Based on these findings Romania would assume a epidemiological stage 4 for OXA-48 and NDM-1 carbapenemases according to an international staging system.

Before starting this survey by self-assessment realized by the national expert in March 2013, the epidemiological stage 1 was established for carbapenemase-producing isolates from Romania. The present study allowed updating and upgrading the epidemiological stages for all investigated carbapenemases.

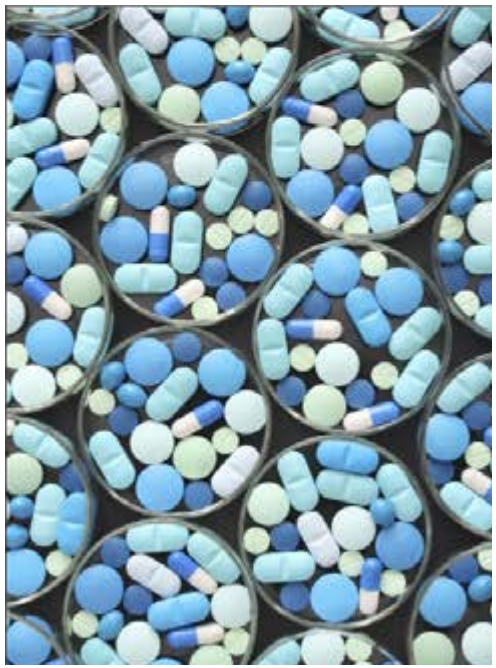
The results of this study show that for efficient monitoring of the rapidly evolving spread of carbapenemase-producing *K. pneumoniae* the development of a national management system for CPE through a dedicated surveillance program, the provision of references services, the

"*Antibiotic pipe-line is running dry*"

- Antibiotic stewardship:

  Utilizarea prudenta a antibioticelor

  - Prevenirea infectiilor associate asistentei medicale



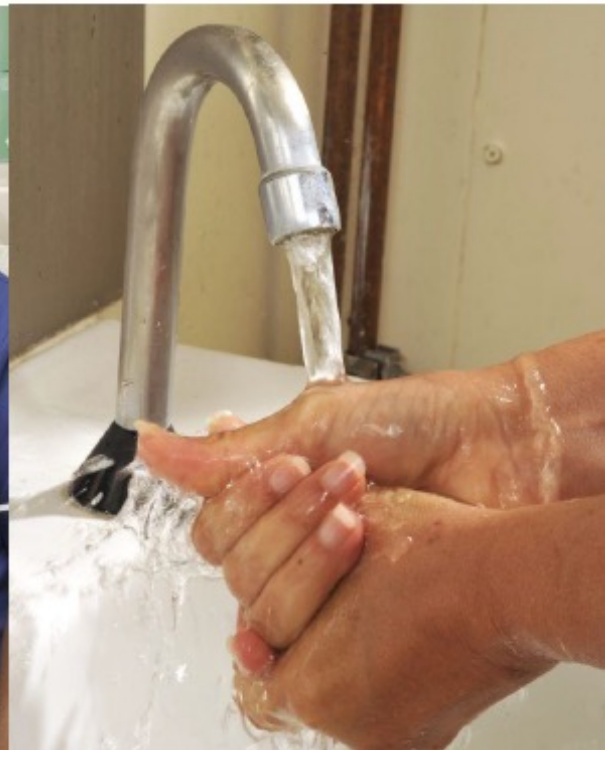
Sansele de reusita sunt mai mari atunci cand exista un cadru legal care sa reglementeze, dar mai ales sa sustina acest proces

Public Health England

Identificarea rapida a pacientilor colonizati/infectati permite:

- management corespunzator al pacientului
- implementarea masurilor de prevenirea transmiterii infectiilor

Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae



Continut

Secțiunea A – Destinată evaluarii pacientului la internare

Secțiunea B- Destinată specialistilor din laborator pentru detectia si raportarea bacteriilor Gram-negative producătoare de carbapenemaze.

Sectiunea C: Rolul igienii mainilor in prevenirea transmiterii bacteriilor cu rezistenta la carbapeneme

Sectiunea D. Destinată utilizării de către conducerea unitatilor medicale (comitete executive) in procesul de planificare și prevenire al infectiilor associate cu bacterii Gram-negative producătoare de carbapenemaze.

Secțiunea E - Destinată informării pacienților si publicului

Recomandări privind depistarea precoce, managementul și controlul infecțiilor cu bacterii Gram-negative producătoare de carbapenemaze

1.0 Introducere

- 1.1 Ce sunt bacteriile producatoare de carbapenemaze?
- 1.2 Ce rol au aceste recomandari?
- 1.3 Rezistență la carbapeneme – de ce este importanta?
- 1.4 Tări cu prevalență ridicată a bacteriilor Gram-negative producătoare de carbapenemaze.
- 1.4 Regiuni din Romania unde s-a evaluat prevalenta bacteriilor Gram-negative producătoare de carbapenemaze.

Secțiunea A – Destinată evaluarii pacientului la internare

- A.1 Diagramă privind admiterea si fluxul pacienților pentru evaluarea nivelului de risc privind portajul/infecțiile cu bacterii Gram-negative producătoare de carbapenemaze.
- A.2 Identificarea rapida a pacienților care pot fi colonizați/au o infecție cu bacterii Gram-negative producătoare de carbapenemaze.
- A.3 Considerații privind izolarea precoce a cazurilor suspicionate și/sau confirmate.
- A.4 Depistarea cazurilor suspecte care sunt/au fost in contact cu un pacient pozitiv/ confirmat.
- A.5 Tratamentul cu antibiotice și un punct de vedere asupra decolonizării.
- A.6 Introducerea precoce a masurilor de prevenire și control al infecțiilor cu bacterii Gram-negative producătoare de carbapenemaze.
- A.7 Măsuri de dezinfecție si decontaminare.
- A.8 Comunicarea informatiei la externarea pacienților sau transfer in alta unitate medicală.

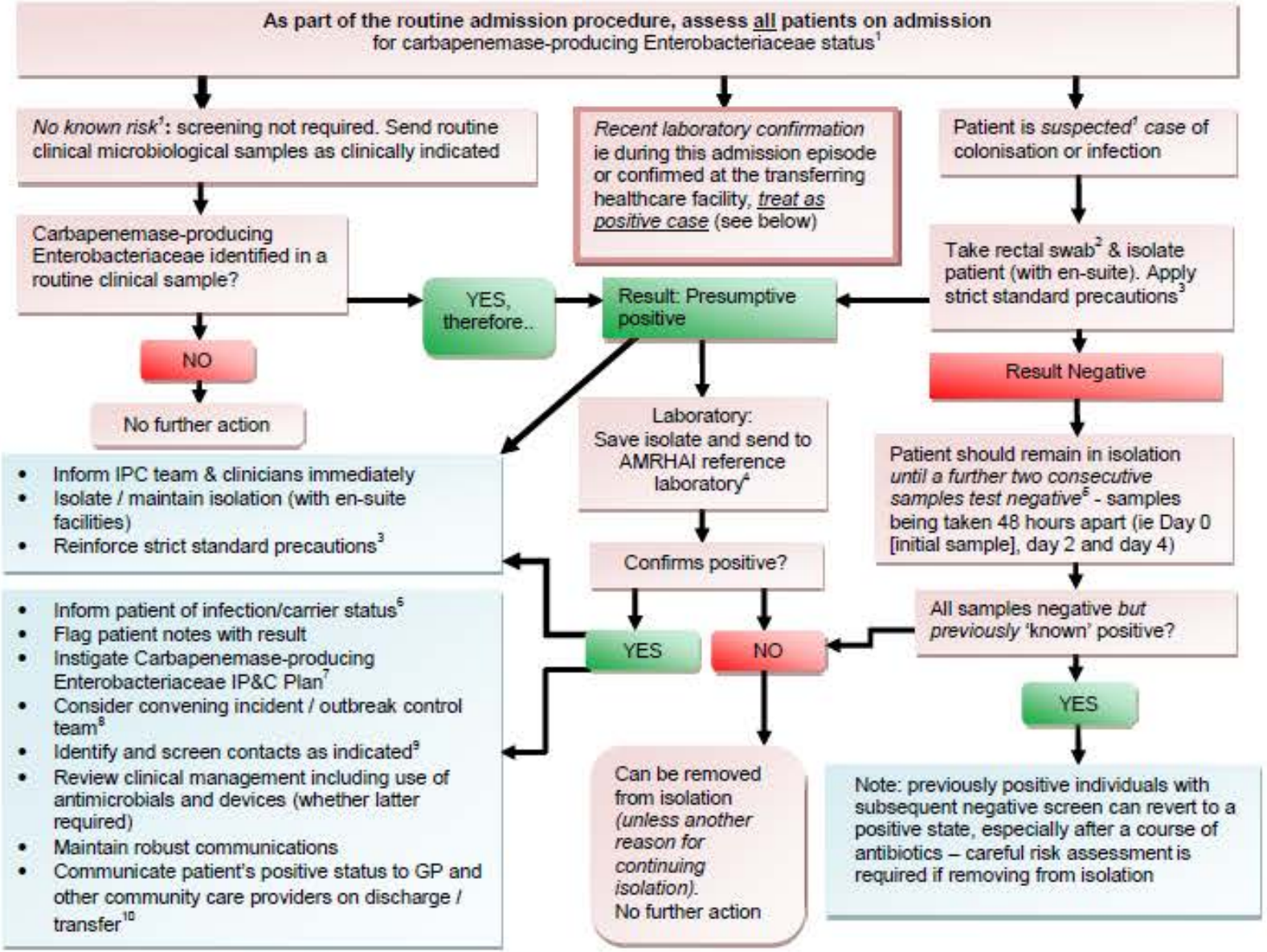
A.1 Acute trust – patient admission flow chart for infection prevention and control (IP&C) of carbapenemase-producing Enterobacteriaceae

As part of the routine admission procedure, assess all patients on admission for carbapenemase-producing Enterobacteriaceae status[1]

SECTIA CHIRURGIE

1. Spitalizati in oricare din spitalele din tara in ultimul an DA / NU
2. Spitalizati in afara Romaniei in ultimii doi ani DA / NU
3. Pacienti care au fost tratati anterior cu un antibiotic din grupa carbapenemelor (imipenem, ertapenem, meropenem) DA / NU
4. Pacienti care au fost anterior confirmati purtatori sau au avut o infectie cu un microorganism resistent la carbapeneme DA / NU

A.1 Acute trust – patient admission flow chart for infection prevention and control (IP&C) of carbapenemase-producing Enterobacteriaceae



Secțiunea A – Desti

- A.1 Diagramă privind ac nivelului de risc privind producătoare de carbap
- A.2 Considerații privind confirmate.
- A.3 Identificarea rapida bacterii Gram-negative
- A.4 Depistarea cazurilor pacient pozitiv/confirm
- A.5 Tratamentul cu anti
- A.6 Introducerea preco cu bacterii Gram-negati
- A.7 Măsuri de dezinfecț
- A.8 Comunicarea inforn unitate medicală.

A.3 Early isolation of suspected and laboratory-confirmed cases

KEY MESSAGE: If you have a suspected case or laboratory confirmed case[8] this step is needed to prevent spread within your organisation

If the patient already has laboratory-confirmed infection or colonisation with carbapenemase-producing Enterobacteriaceae *OR* meets the criteria for a suspected case (Card A.2) then:

Advise the patient (and relatives if appropriate) of the positive result or your suspicions (whichever applies) and your management plan – provide patient information leaflet (Card C.4)

AND

Immediately place the patient into a single room with en suite facilities and send screening samples (Card A.4)

AND

Apply strict standard precautions in all settings

Acute setting management advice

All suspected (including previously positive[9]) patients should be isolated until screening results are known. If the patient is **POSITIVE** on screening (Card A.4) for carbapenemase-producing Enterobacteriaceae or is a laboratory-confirmed case (colonisation or infection):

- they should remain in isolation for the duration of their hospital stay
- the hospital Carbapenemase-producing Enterobacteriaceae Management Plan (Card B.1) should be revisited
- comprehensive awareness raising of the plan should take place amongst staff including doctors, nurses, physiotherapists, domestics and others with patient contact

Strict standard precautions must be practiced (whether the patient has infection or colonisation) including:

- good hand hygiene (Card A.6)
- where any part of a staff uniform, not protected by an ordinary apron, is expected to come into contact with the patient, a long-sleeved disposable gown should be used eg when assisting movement for a dependent patient
- use of personal protective equipment (PPE) in line with standard precautions
- environmental cleaning and decontamination, with an enhanced focus on frequent cleaning of hand contact areas (Card A.7)

If **NEGATIVE** a further two negative samples need to be achieved and a risk assessment undertaken before removing from isolation (Card A.4).

Secțiunea B- Destinata specialistilor din laborator pentru detectia si raportarea bacteriilor Gram-negative producătoare de carbapenemaze.

- **B1.** Pentru detalii se recomanda consultarea documentului "*Ghid privind Enterobacteriaceae producătoare de carbapenemaze: diagnosticul, prevenirea transmiterii interumane și tratamentul infecțiilor produse*", site-ul Societătii Romane de Microbiologie, http://srm.ro/pdf/ghid%20carbapenemaze_final_23.09.2015.pdf

- **B2. Propunere**: introducerea unui protocol de lucru pentru screening-ului portajului intestinal;

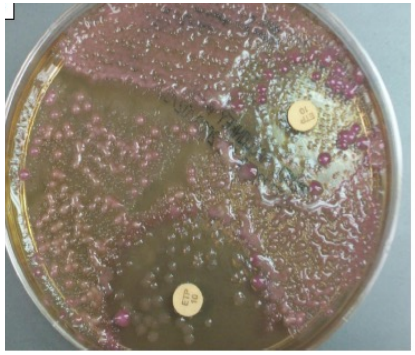
Protocol- screening colonizare intestinala

Tampon rectal/proba fecale

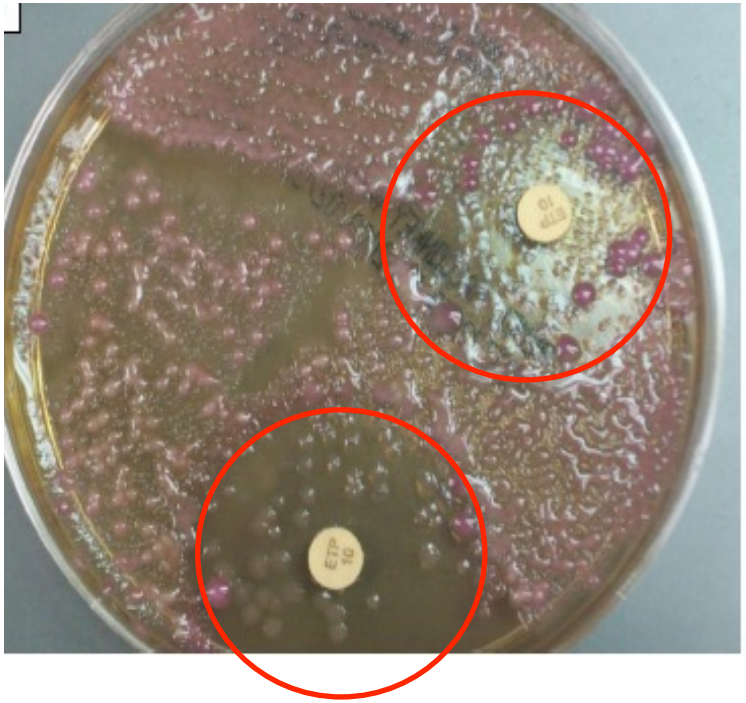
- 1. Trypticase soy broth (TSB) +meropenem (10µg
- Pasaj pe McConkey cu ertapenem si meropenem

- Medii cromogene

- Teste moleculare

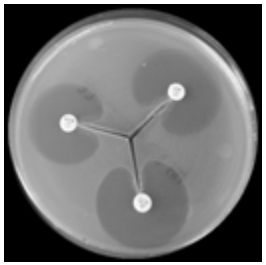


Teste de confirmare



1. Teste de sinergie intre carbapenem si un inhibitor al acestor enzyme;

2. Modified Hodge Test (MHT) or 'Cloverleaf' test



3. Carba-NP

4. Teste moleculare (PCR conventional sau Real-Time machines)

http://srm.ro/pdf/ghid%20carbapenemaze_final_23.09.2015.pdf

Public Health England

Examples of commercial 'real time' solutions

Company	Kit	Basis	Isolates	Samples	Family Coverage *	Platform	Time
Amplex	eazyplex SuperBug complete or eazyplex SuperBug CRE (CE-marked)	LAMP	Yes	"screening swabs"	KPC, OXA-48, VIM, NDM	Proprietary	15 mins (isolates) or 30 min (swabs)
Becton Dickinson	BD MAX CRE (RUO)	RT PCR	Yes	"clinical samples", screening swabs	KPC, OXA-48, NDM	Proprietary (Open)	2 h
bioMerieux	NucliSENS EasyQ KPC (RUO)	NASBA	Yes	stool samples, rectal swabs	KPC	Proprietary	3-4 h
Cepheid	GenXpert Carba-R (RUO)	RT PCR	Yes	rectal swabs	KPC, NDM, OXA-48, VIM, IMP	Proprietary	50 min
Check-Points	Check-Direct CPE (CE-marked)	RT PCR	Yes	rectal/perianal swabs	KPC, OXA-48, VIM, NDM	Multiple RT machines	2 h

e of alleles *within* the IMP, VIM and OXA-48 families varies between kits

“In house” PCR

Techne 3 Prime Base Personal Thermal Cycler, 18 x 0.5 ml

£2,280.00 from 2 shops

Techne 3 Prime Thermal Cyclers. Uses the Peltier effect - a chosen method for the most truste

Pcr-Thermal Cycler

£2,245.99 from Health and Care ★★★★☆ 83 seller reviews

Pcr-Thermal Cycler **Polymerase Chain Reaction** (PCR) is one of the most exciting techniques

Digital Thermal Pcr Machine Cycler Laboratory Product Labapp-81

£2,587.33 from eBay

Find Digital Thermal **Pcr Machine** Cycler Laboratory Product Labapp-81 on eBay in the catego

Edvocycler - Pcr Thermal Cycler Machine - Edv

£1,250.00 from ThinkSomeMore

EdvoCycler - **PCR** Thermal Cycler **Machine** - Edvotek #541The EdvoCycler™ is a stand alone

M, bla_{KPC},

a-

OXA-23,

oups

Consumabile (PCR mix + primeri = **0.2€/reactie**

Sectiunea C: Rolul igienii mainilor in prevenirea transmiterii bacteriilor cu rezistenta la carbapeneme

- Sectiune destinată echipelor de prevenire si control al infectiilor;

- WHO: *“5 momente pentru igiena mâinilor”*

C1. Introducerea celor « *5 momente pentru igiena mainilor* »- recomandate de Organiz

(WHO) report …. proper hand antisepsis is an extremely effective measure for reducing hospital-acquired infections, yet …….

*"**unacceptably low compliance with hand hygiene is universal in healthcare."***

WHO “5 momente pentru igiena mainilor”

OMS “Five moments’ pentru transmitere

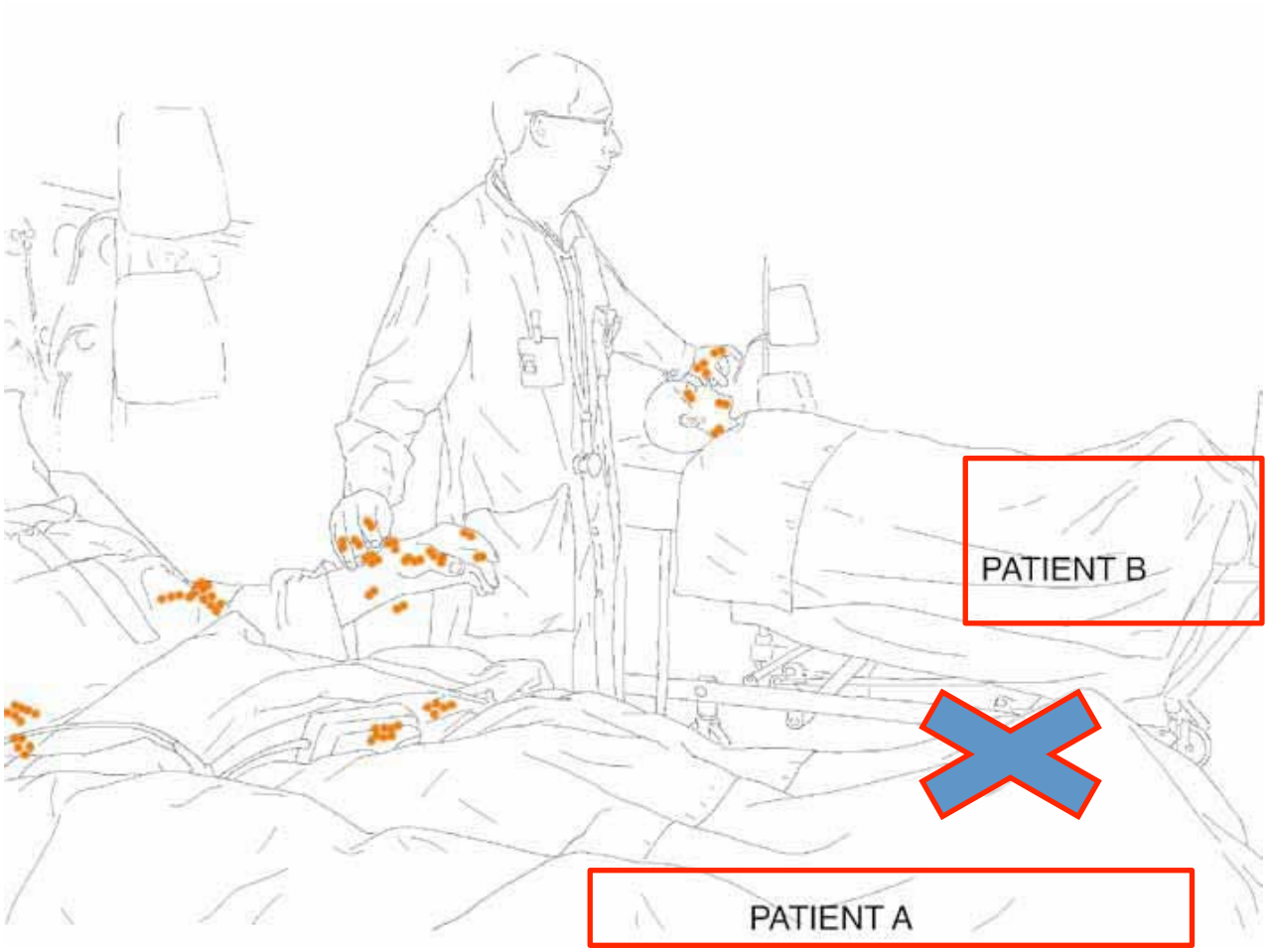
(1) Prezenta bacteriilor pe pielea pacientului (si in jurul sau)

(2) Transferul bacteriilor pe mainile personalului medical

(3)Bacteriile persista pe maini

Reprinted from Pittet, with permission from Elsevier.

(3) Lipsa igienizarii mainilor intre pacienti- duce l a cross-contaminare



Gelul cu alcool

- Mai multe studii au aratat o scadere a ratei infectiilor cu 30% in spitale unde este folosit frecvent;

- **Facilitarea accesului pacientilor la geluri cu alcool** si educarea lor – reducere cu 36% a ratei infectiilor;

Patient-centered hand hygiene: The next step in infection prevention

Timothy Landers, RN, PhD, Said Abusalem, RN, PhD, Mary-Beth Coty, RN, PhD, James Bingham, MS

Campania: “Spala-te pe maini” UK

-**A inceput in 2004** si a constat in:

- punerea la dispozitie a gelurilor cu alcool langa fiecare pat de spital

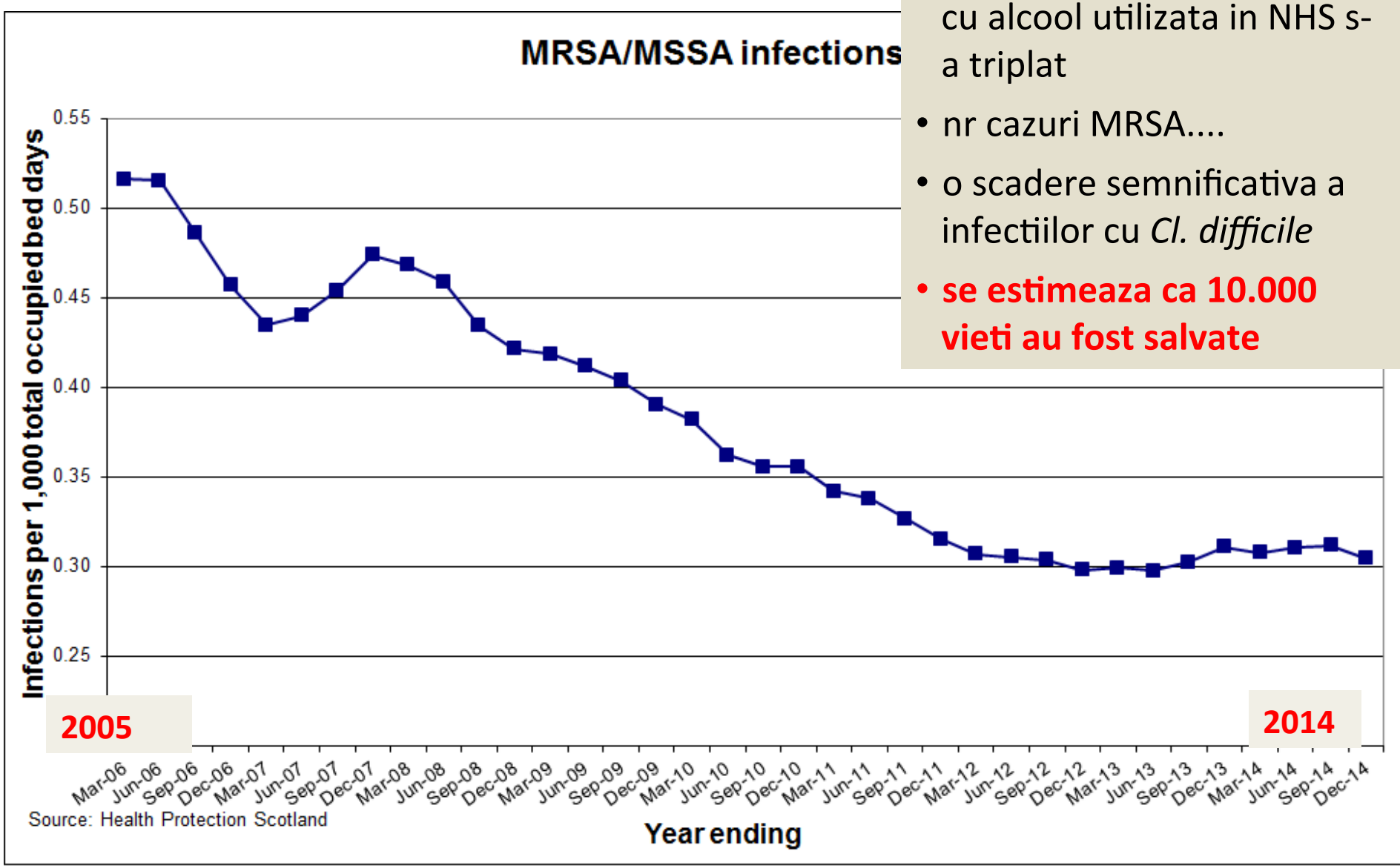
- afisarea de postere care re-amintesc personalului medical as se spele pe maini

- audit regulat si feed-back privind conformarea cu aceste masuri

- distribuirea de informatie scrisa pacientilor prin care erau informati ca au dreptul sa ceara personalului medical as se spele pe maini

Ca urmare:

- cantitatea de sapun si gel cu alcool utilizata in NHS s-a triplat
- nr cazuri MRSA....
- o scadere semnificativa a infectiilor cu *Cl. difficile*
- **se estimeaza ca 10.000 vieti au fost salvate**



CDC: costul total al infectiilor associate asistentei medicale in US este de $35 to $45 Billion,

Insa 70% din acestea pot fi prevenite

(a)

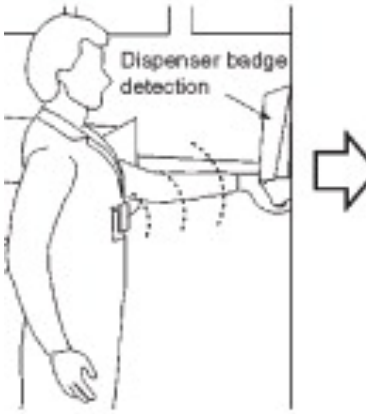


FIG. 1. A hand hygiene (HH) system working through a feedback loop with a wireless
healthcare worker (HCW) performs HH, and the radio signal emitted by the badge is de
detection of ...

A.R. Marra, M.B. Edmond

New technologies to monitor healthcare worker hand hygiene

Clinical Microbiology and Infection, Volume 20, Issue 1, 2014, 29–33

http://dx.doi.org/10.1111/1469-0691.12458

Forget to wash? Devices track hand washing adherence in hospitals

Maner
elibere
momer

Concentratia de etanol trebuie sa fie de cel putin 60% !!!

Secțiunea E - Destina
pu

Secțiunea E - Destinată infor

- E.1 *Bacteriile Gram-negat*
  carbapenemaze: Sunt colo
  înseamnă aceasta?

- E.3 *Bacteriile Gram-negat*
  carbapenemaze: Sunt per
  care este colonizat sau are

C.3 Carbapenemase-producing Enterobacteriaceae: I am colonised / have an infection – what does this mean?

What does 'carbapenemase-producing Enterobacteriaceae' mean?

Enterobacteriaceae are bacteria that usually live harmlessly in the gut of humans. This is called 'colonisation' (a person is said to be a 'carrier'). However, if the bacteria get into the wrong place, such as the bladder or bloodstream they can cause infection. Carbapenems are one of the most powerful types of antibiotics. Carbapenemases are enzymes (chemicals), made by some strains of these bacteria, which allow them to destroy carbapenem antibiotics and so the bacteria are said to be resistant to the antibiotics.

Why does carbapenem resistance matter?

Carbapenem antibiotics can only be given in hospital directly into the bloodstream. Until now, doctors have relied on them to successfully treat certain 'difficult' infections when other antibiotics have failed to do so. In a hospital, where there are many vulnerable patients, spread of resistant bacteria can cause problems.

Does carriage of carbapenemase-producing Enterobacteriaceae need to be treated?

If a person is a carrier of carbapenemase-producing Enterobacteriaceae (sometimes called CPE), they do not need to be treated. However, if the bacteria have caused an infection then antibiotics will be required.

How did I 'pick up' carbapenemase-producing Enterobacteriaceae?

Do ask your doctor or nurse to explain this to you in more detail. As mentioned above, sometimes this bacteria can be found, living harmlessly, in the gut of humans and so it can be difficult to say when or where you picked it up. However, there is an increased chance of picking up these bacteria if you have been a patient in a hospital abroad or in a UK hospital that has had patients carrying the bacteria, or if you have been in contact with a carrier elsewhere.

How will I be cared for whilst in hospital?

You will be accommodated in a single room with toilet facilities whilst in hospital. You may be asked to provide a number of samples, depending on your length of stay, to check if you are still carrying the bacteria. These will probably be taken on a weekly basis. The samples might include a number of swabs from certain areas, such as where the tube for your drip (if you have one) enters the skin, a rectal swab ie a sample taken by inserting a swab briefly just inside your rectum (bottom), and / or a faecal sample. You will normally be informed of the results within two to three days.

Secțiunea D

Destinată utilizării de către conducerea unitatilor medicale (comitete executive) in procesul de planificare și prevenire al infectiilor associate cu bacterii Gram-negative producătoare de carbapenemaze.

- D.1 Plan de management al circulatiei bacteriilor Gram-negative producătoare de carbapenemaze
- D.2 Propunere privind acțiunile pentru prevenirea și minimizarea răspândirii bacteriilor producătoare de carbapenemaze.
- D.3 Lista de verificare pentru conducerea spitalului/echipele de prevenire si control al infectiilor pentru gestionarea unui focar sau cluster-ul de cazuri cu colonizare sau infectie cu bacterii Gram-negative producătoare de carbapenemaze.
- D.4 Formularul de transfer intre sectii/unitati medicale - notificarea unui pacient colonizat sau infectat cu bacterii Gram-negative producătoare de carbapenemaze.

The International Collaborative Conference
in Clinical Microbiology & Infectious Diseases
"ICMID" Bahrain 2015

In association with

BSAC The British Society for Antimicrobial Chemotherapy

New Cross Hospital, Wolverhampton

Background - 2006

- Failing organisation
  - financially
  - HCAIs
- But clinically very good

UK Survey: "What are you most worried about if you have to go to an hospital and have a major intervention?

Answer "Most afraid that I will catch MRSA"

The International Collaborative Conference in Clinical Microbiology & Infectious Diseases "ICMID" Bahrain 2015

In association with

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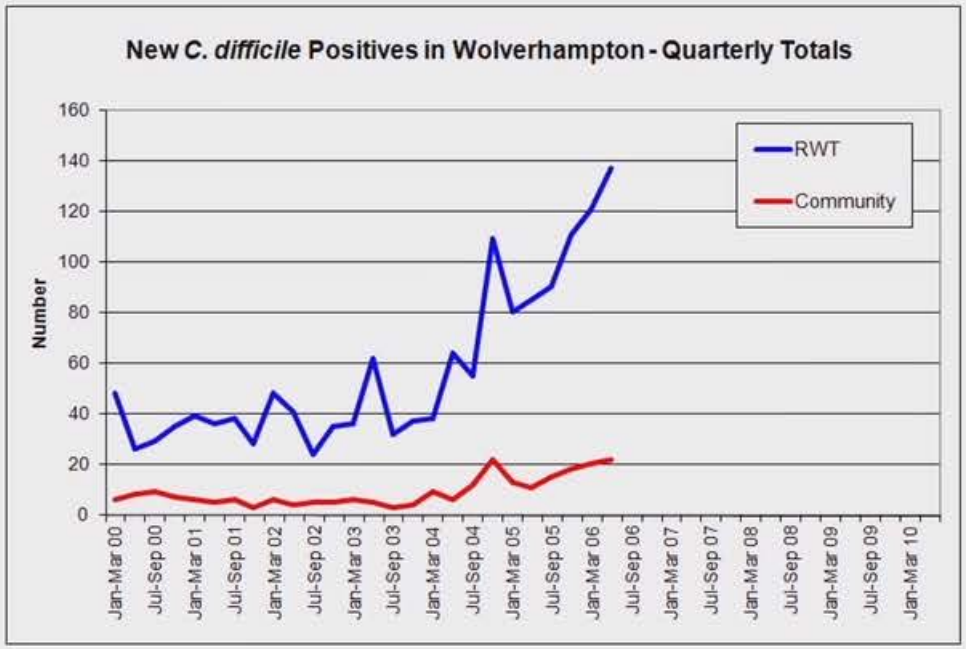


Background - Actions

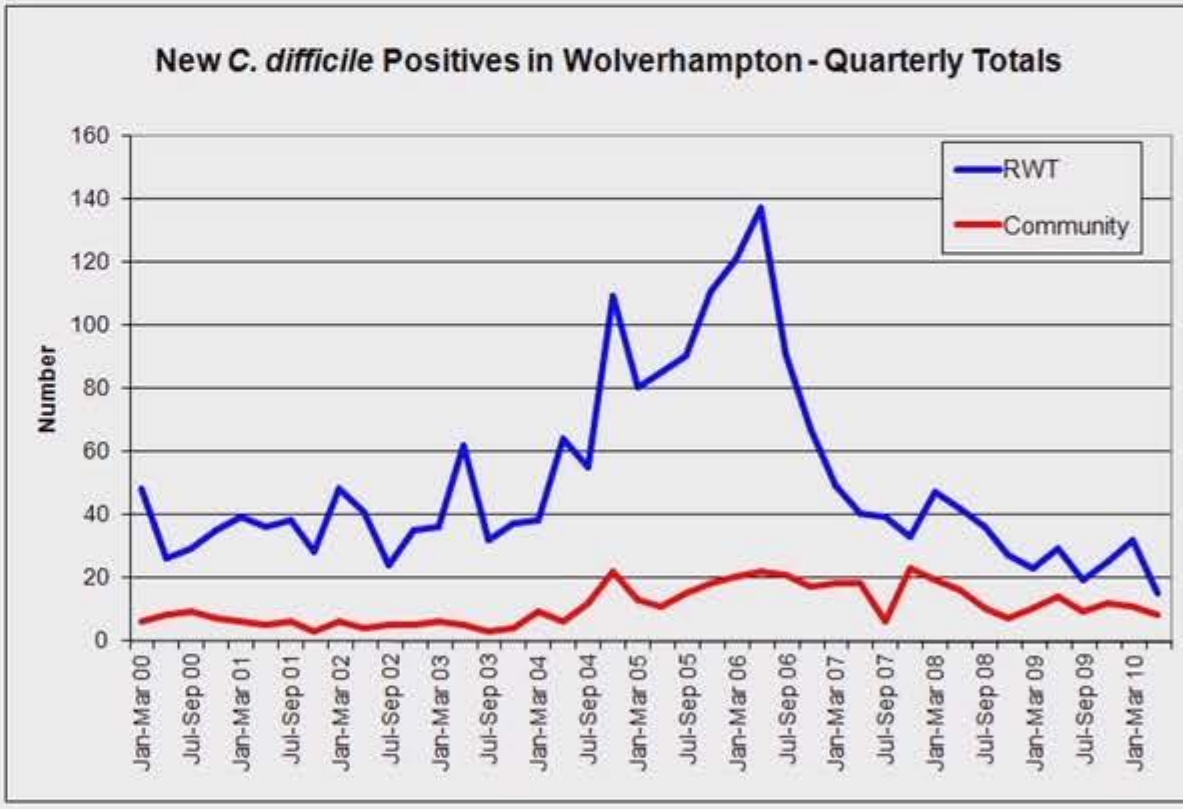
- Number one priority for organisation
- Organisation-wide strategy and actions
  - all-inclusive
- Implementation group (IPCC)
  - senior staff
  - can actually effect change
- Early win
  - gets doubters to believe
- Culture change
  - most difficult, but most effective component

1011

Days without an MRSA Bacteraemia

Conference

In association with



In association with

BSAC The British Society for Antimicrobial Chemotherapy

Consequences

- National and international recognition and awards
- Visits to or from many hospitals, organisations and countries
  - lots of discussions about what does and does not work

What Does Not Work

- Blame people who do not have the power to effect change for failure
- Ignoring local data and advice of local experts
- Clinicians who do not see it as 'their problem'

What Does Work? – Mortality Data

- 14 day all-cause mortality:
  - from MRSA bacteraemia = 33%
  - from MSSA bacteraemia = 25%
- 30 day all-cause mortality from *C. difficile* = 40% (2006) = 25% (2007)
- Comparing January to June 2006 with January to June 2007: just from MRSA, MSSA bacteraemias + *C. difficile*

= 106 fewer deaths

- What about other infections?
- Not just mortality: morbidity, length of stay, cost, litigation, coroner's court etc….

What Does Work?

- Senior management taking responsibility for performance and recognising their role in driving improvement

What does it work? CONCLUSIONS

- Involve everyone
  - All specialities
  - All grades of staff
  - Make it everyone's responsibility
- Feed back results at all levels
- Appropriate education and training at all levels
- Robust data
- Enthusiasm
- Imagination
- A bit of luck…

Va multumesc!