Should all patients harbouring ESBL-producing organisms be isolated?

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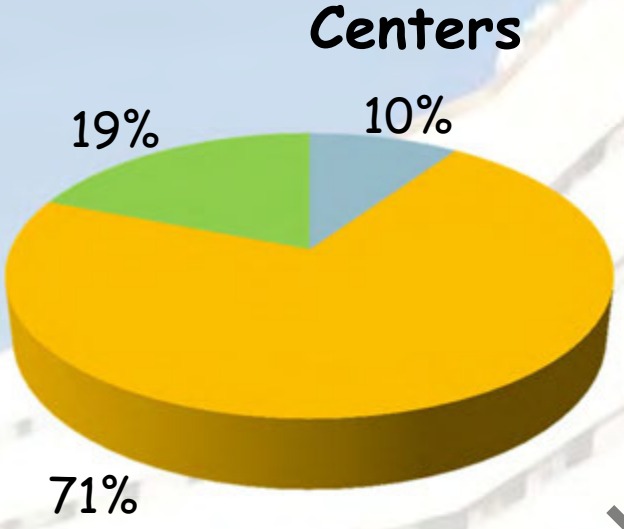
ESCMID COLLABORATIVE CENTRE

Red Española de Investigación en Patología Infecciosa REIPI

- Guidelines
- Evaluation of evidence
- Evidence-based vs epidemiology-based
- Conclusions

- Would you like your mother/father to share a hospital room with another patient who is colonised by ESBL-producing *K. pneumoniae*?
- What about ESBL-producing *E. coli*?
- What about your mother/father-in-law?

Informal survey among 30 worldwide colleagues
Isolation of patients harbouring ESBL producers



Organisms: only *Klebsiella*, only MDR
Units: ICU, NICU, Haematology
Others: "if possible"

Contact precautions (CDC)

- Who:
  - Patients colonised/infected with targeted MDRO
- Why
  - To prevent transmission of infectious agents spread by direct or indirect contact with the patient or the patient's environment
- How
  - Gown, gloves at entry and discarding before exiting
  - Patient transport
  - Care equipment and instrument/devices
  - Environmental measures

Siegel et al (HICPAC). Am J Infect Control 2007; 35: S65-164
Siegel et al (HICPAC). Am J Infect Control 2007; 35: S165-193

Contact precautions (CDC)

- A single room is preferred (IB).
  - Prioritize patients with conditions that facilitate transmission (stool incontinence, uncontained drainage) for single room (II)
- If not available: cohort (IB)
- If not possible:
  - Avoid sharing rooms with high risk patients (open wounds, (inmunocompromised) (II)
  - >3 feet (1 m) between beds (II)
  - Change protective attire and perform hand hygiene between patients (IB)

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Siegel et al (HICPAC). Am J Infect Control 2007; 35: S65-164
Siegel et al (HICPAC). Am J Infect Control 2007; 35: S165-193

Why isolation?

Why isolation?

Control of MDR gram negatives ESCMID guidelines (draft)

Outbreak setting

- CP: low/moderate quality evidence
- Isolation: low/moderate quality evidence
- Cohort patients: low quality evidence
- Cohort staff: low/moderate quality evidence

Endemic setting

- CP: low/moderate quality evidence
- Isolation: low/moderate quality evidence
- Cohort patients: no evidence available
- Cohort staff: no evidence available

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Cataldo et al. ECCMID 2012, O125
Data from E. Tacconelli

- Lack of evidence should not be interpreted as evidence against
  - Scarce or low quality studies
  - Different epidemiological situations
  - Bundles
  - Interpretation of evidence

Premises for CP/isolation efficacy

- Epidemiology
  - The colonised patients and/or their close environment must be key reservoirs
  - The organism must be efficiently transmitted by contact
  - Other reservoirs must not be important
- Once CP/isolation is decided
  - Compliance!!

Premises for CP/isolation efficacy

HOSPITAL A
Mostly 3-bed rooms
Low nurse:patient ratio
Low cleaning standards
Low adherence to hand hygiene

High probability of efficacy

HOSPITAL B
Mostly individual rooms
High nurse:patient ratio
High cleaning standards
High adherence to hand hygiene

Lower probability of efficacy

Tschuding-Sutter et al.
ECCMID 2012 O121

- No CP for ESBL producers
- High adherence to standard precautions

- Nosocomial transmission (PFGE): 2/133 (1.5%) contacts of colonised patients

Looking for evidence in infection control

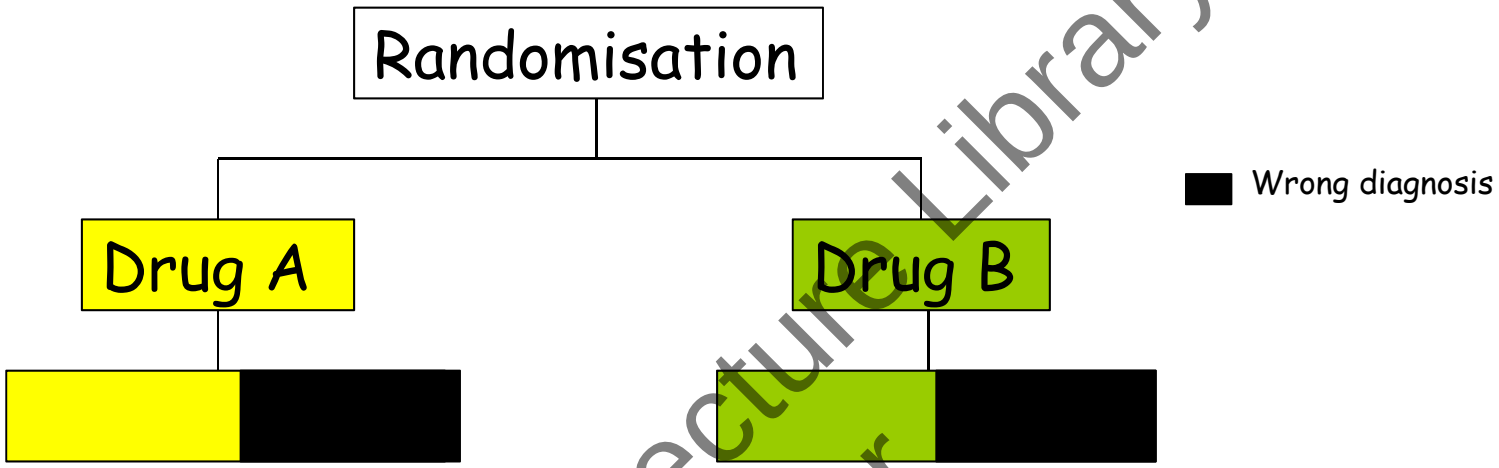
- Hierarchy in the design of studies
  - Randomized cluster trials
  - Quasi
    - Interrupted time series
    - Before-after
  - Outbreaks reports

Interpretation

- Eradication/control
  - Measures used were right to eliminate reservoir(s) and avoid transmission

    OR
  - Unrelated to measures
- No control
  - Measures are not useful

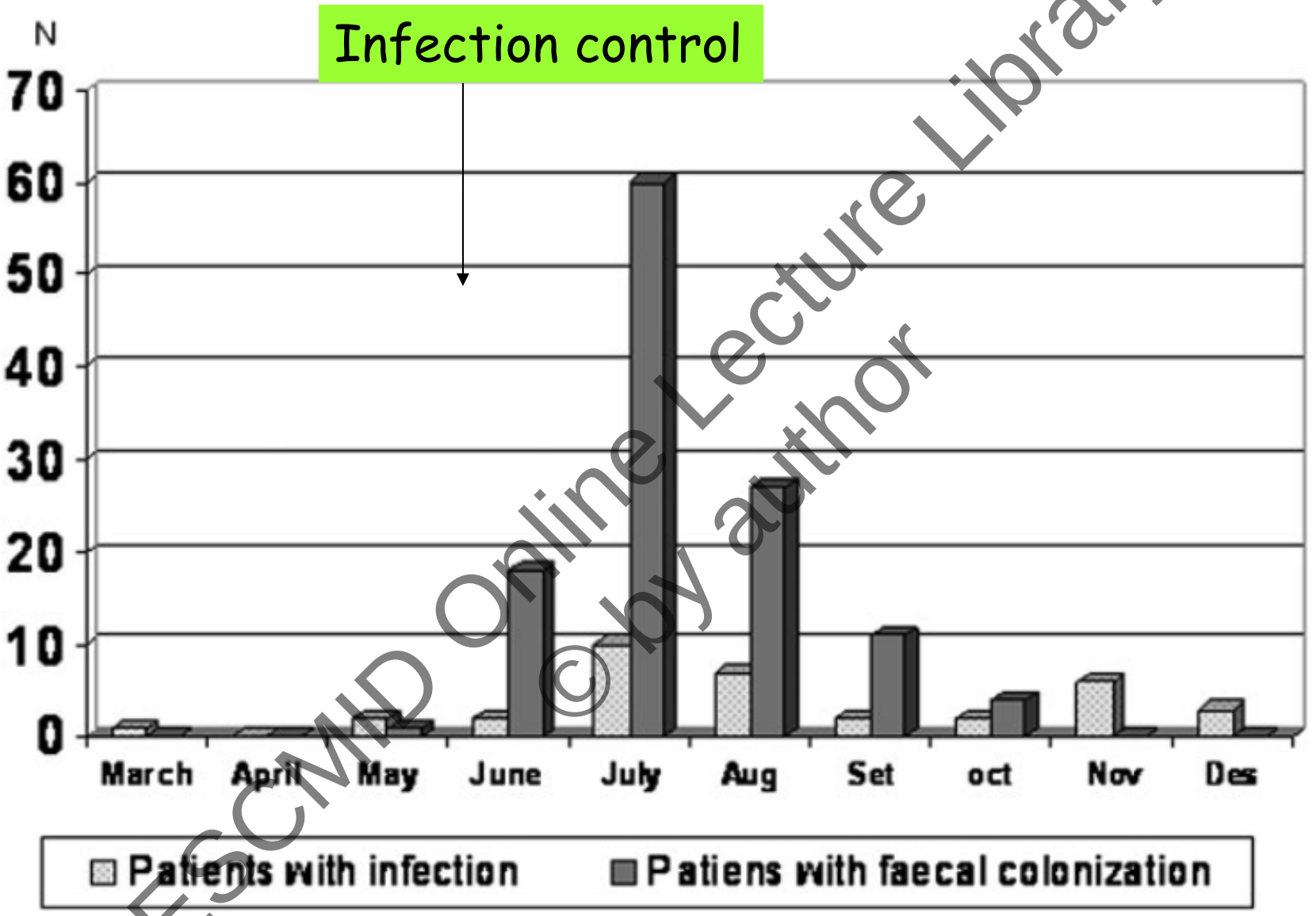
    OR
  - Measures were not the right ones or were not adequately performed



Non-differential bias

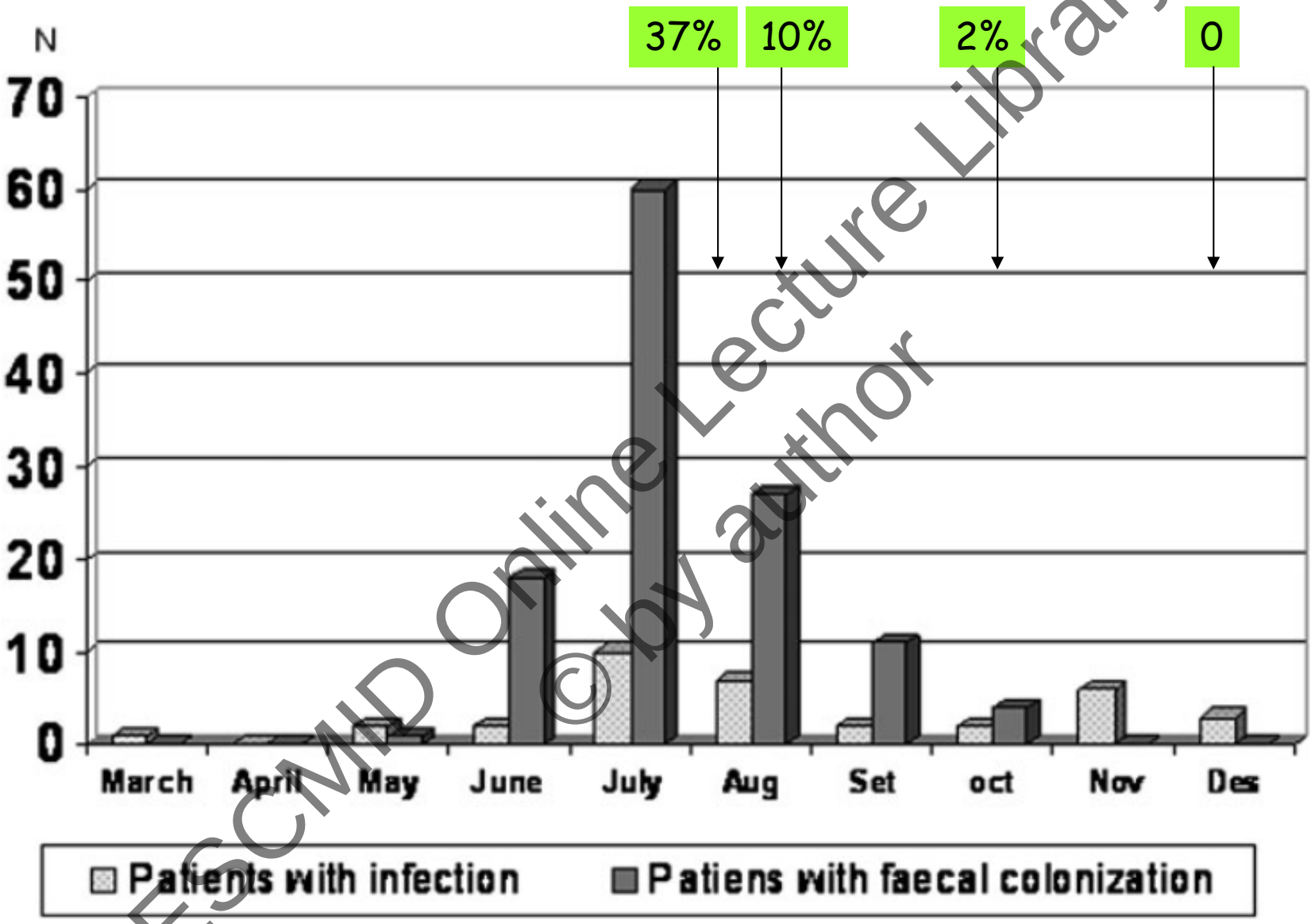
Studies on screening/contact precautions/isolation if patients or their close surfaces are not a key reservoir

Hospital wide clonal outbreak, ESBL-producing *K. pneumoniae*



Calbo et al, Clin Infect Dis 2011

Positive environmental samples in kitchen

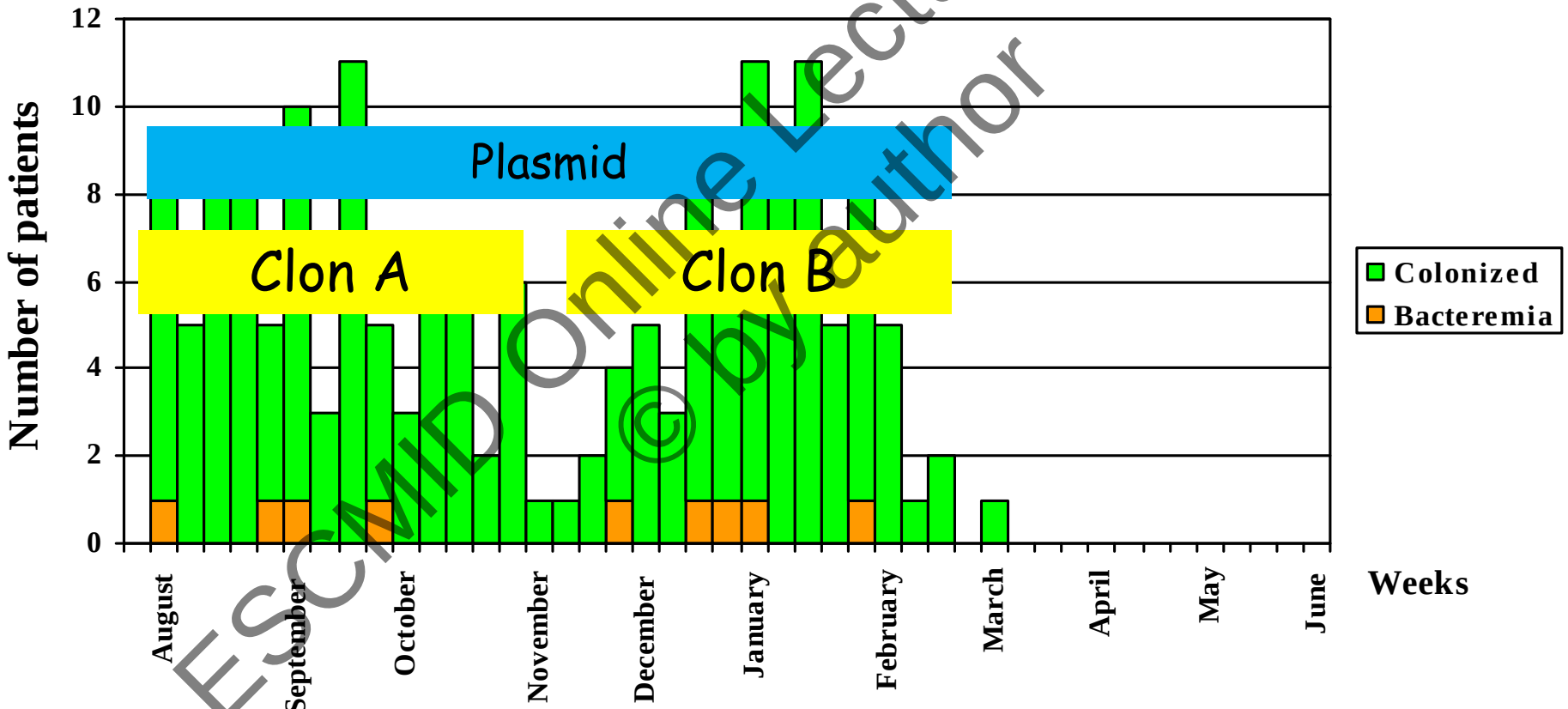


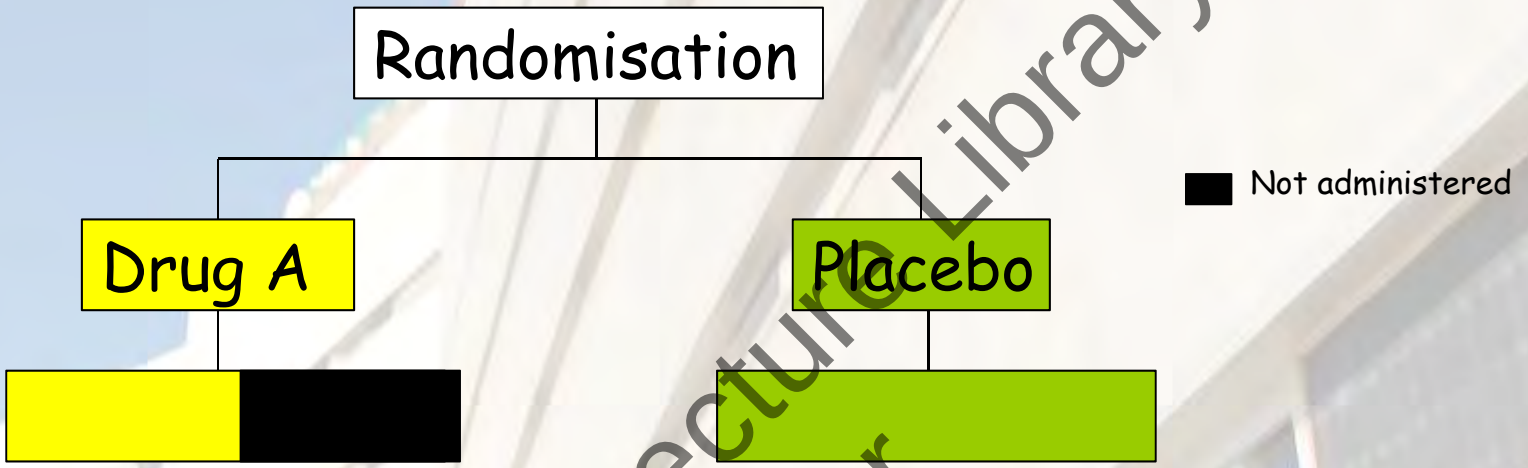
Calbo et al, Clin Infect Dis 2011

Eradication of an extensive outbreak in a neonatal unit caused by two sequential *Klebsiella pneumoniae* clones harbouring related plasmids encoding an extended-spectrum β-lactamase

C. Velasco [a,*], J. Rodríguez-Baño [b], L. García [b], P. Díaz [a], C. Lupión [b], L. Durán [c], A. Pascual [a,d]

J Hosp Infect 2009; 73: 157-163





Differential bias against Drug A

Studies on screening/contact precautions/isolation if adherence to measures is lower than predicted

Intervention to Reduce Transmission of Resistant Bacteria in Intensive Care

W. Charles Huskins, M.D., Charmaine M. Huckabee, M.S., Naomi P. O'Grady, M.D., Patrick Murray, Ph.D., Heather Kopetskie, M.S., Louise Zimmer, M.A., M.P.H., Mary Ellen Walker, M.S.N., Ronda L. Sinkowitz-Cochran, M.P.H., John A. Jernigan, M.D., Matthew Samore, M.D., Dennis Wallace, Ph.D., and Donald A. Goldmann, M.D., for the STAR*ICU Trial Investigators*

In a cluster-randomized trial, we evaluated the effect of surveillance for MRSA and VRE colonization and of the expanded use of barrier precautions (intervention) as compared with existing practice (control) on the incidence of MRSA or VRE colonization or infection in adult ICUs. Surveillance cultures were obtained from patients in all participating ICUs; the results were reported only to ICUs assigned to the

N Engl J Med 2011

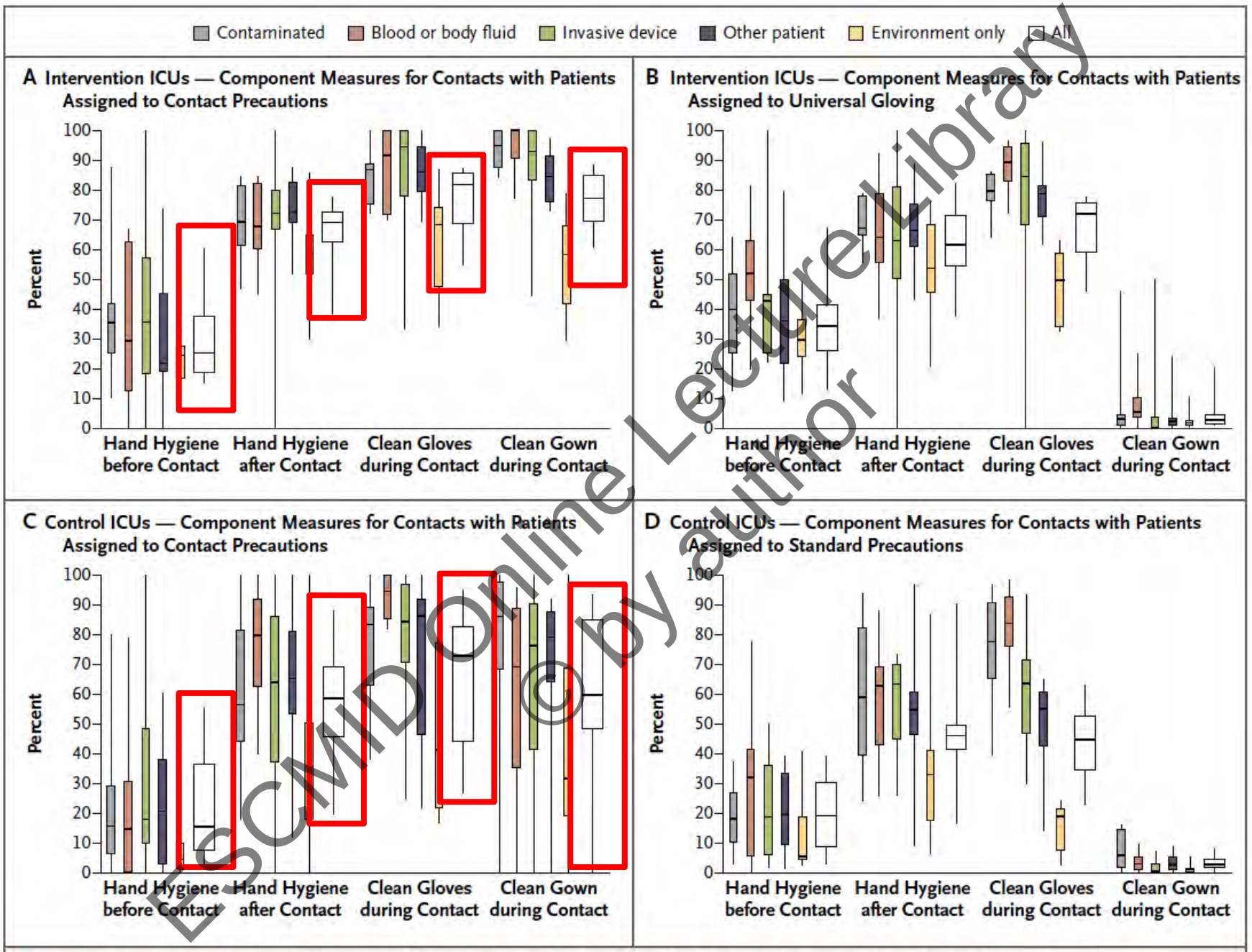


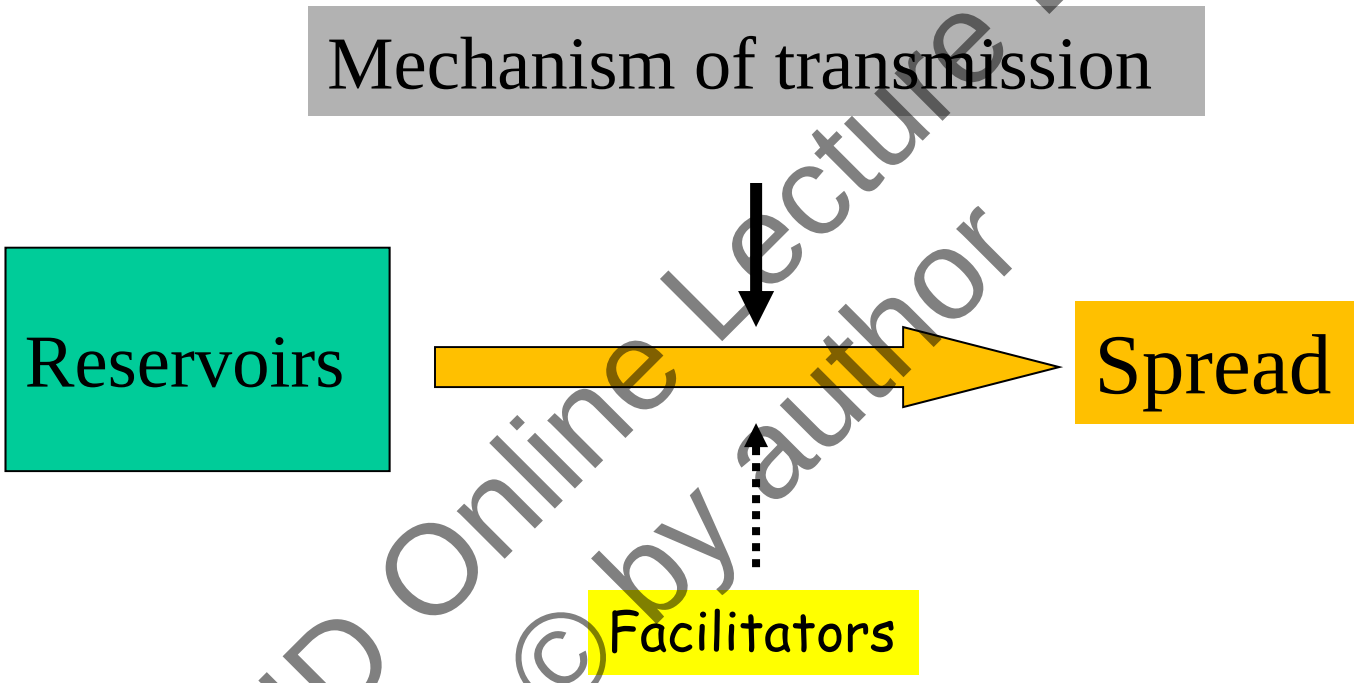
Figure 2. Use of Hand Hygiene, Gloves, and Gowns by Health Care Providers in Intensive Care Units (ICUs) during Contacts with Patients or Their Immediate Environment.

- Evidence-based approach

  vs

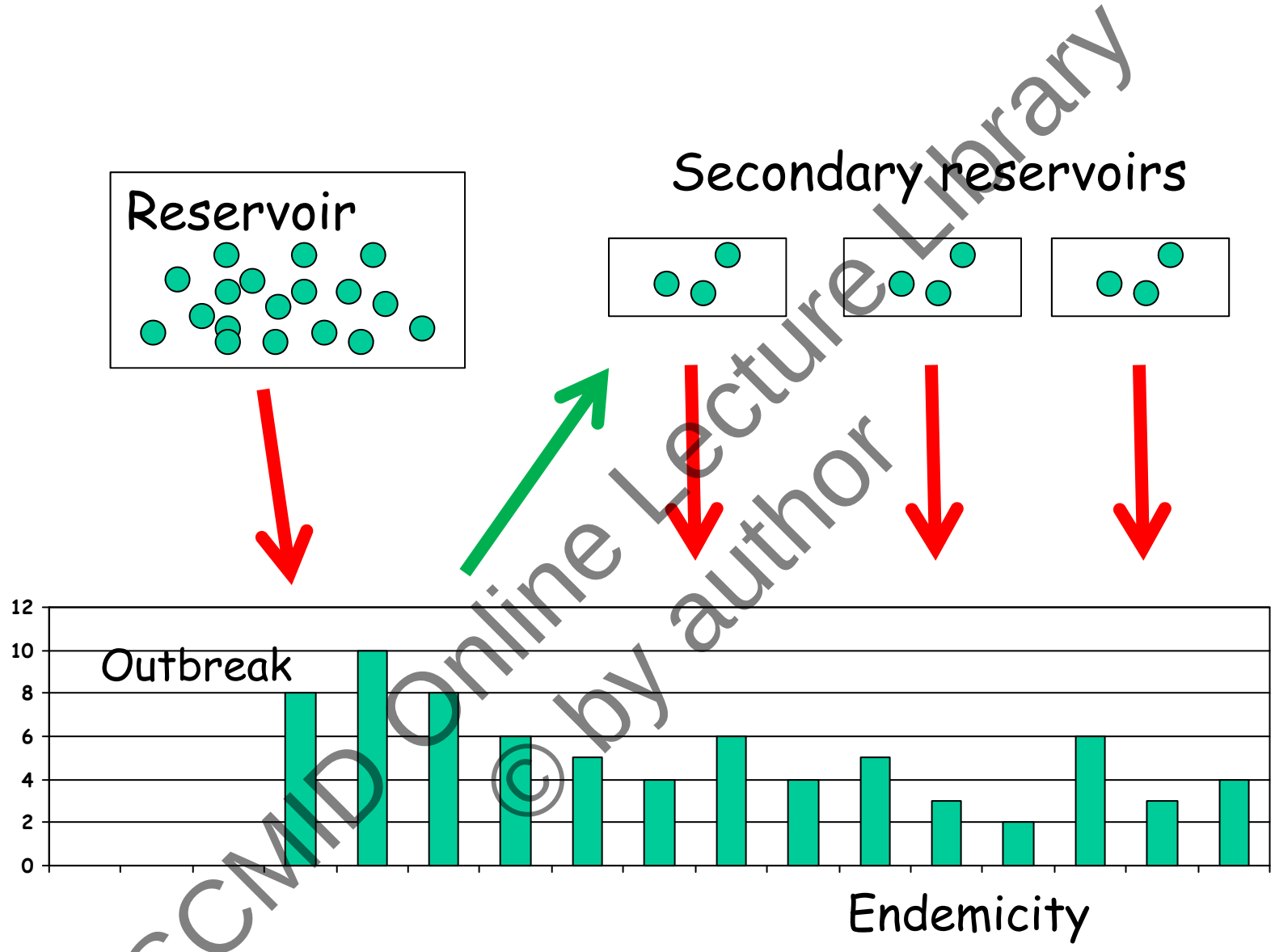
- Epidemiology based approach

Epidemiology of nosocomial pathogens



- Although the epidemiological behaviour may be quite predictable for specific organisms, surprises are not that rare…

- The hospital environment has probably be underestimated as a source for some enterobacteria (sinks…)



(ESBL-producing) *K. pneumoniae*

- Ability to cause wide and prolonged outbreaks
- Reservoirs
  - Gut of colonized patients
  - Environment underestimated?[1]
- Transmission: direct contact
  - Patient-to-patient[2] through the hands of HCW[3]
  - From environmental sources
- Antibotics: facilitators[4]

1. Gaillot JCM 1998. Cotton JHI 2000. Bagattini JAC 2006. Branger JHI 1997. Bureau-Chalot JHI 2004. Rogues JHI 2000. Szabo JCM 1999. Eisen JMC 1995. Hobson JHI 1996. Macrae JHI 2001. Borer, ICHE 2011. De Jong, ECCMID 2012. López-Cerero (unpublished). Domínguez (unpublished).
2. Harris CID 2007
3. Bagattini JAC 2006. Gupta ICHE 2004. Eisen JCM 1995. Hobson JHI 1996. Royle ADCFNE 1999. Abdel-Hady J Perinatol 2008
4. Asensio, CID 2000. Eveillard, ICHE 2002. Pessoa-Silva, JHI 2003. Lin, JHI 2003. Lee, ICHE 2004. Wiener, JAMA 1999. Piroth, CID 1998

E. coli as a nosocomial pathogen: the big unknown

- Reservoirs?
- Mechanisms of transmission?
- Outbreaks?

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How important is patient-to-patient transmission in extended-spectrum β-lactamase *Escherichia coli* acquisition

Anthony D. Harris, MD, MPH,[a,b] Mamuka Kotetishvili, PhD,[a] Simone Shurland, MS,[a] Judy A. Johnson, PhD,[b] J. Glenn Morris, MD, MPH,[a] Lucia L. Nemoy, MD,[a,b] and J. Kristie Johnson, PhD[a]
Baltimore, Maryland

Am J Infect Control 2007

Conclusion: Our data suggest that patient-to-patient is not an important cause of the acquisition of ESBL-producing *E. coli* colonization in the ICU setting.

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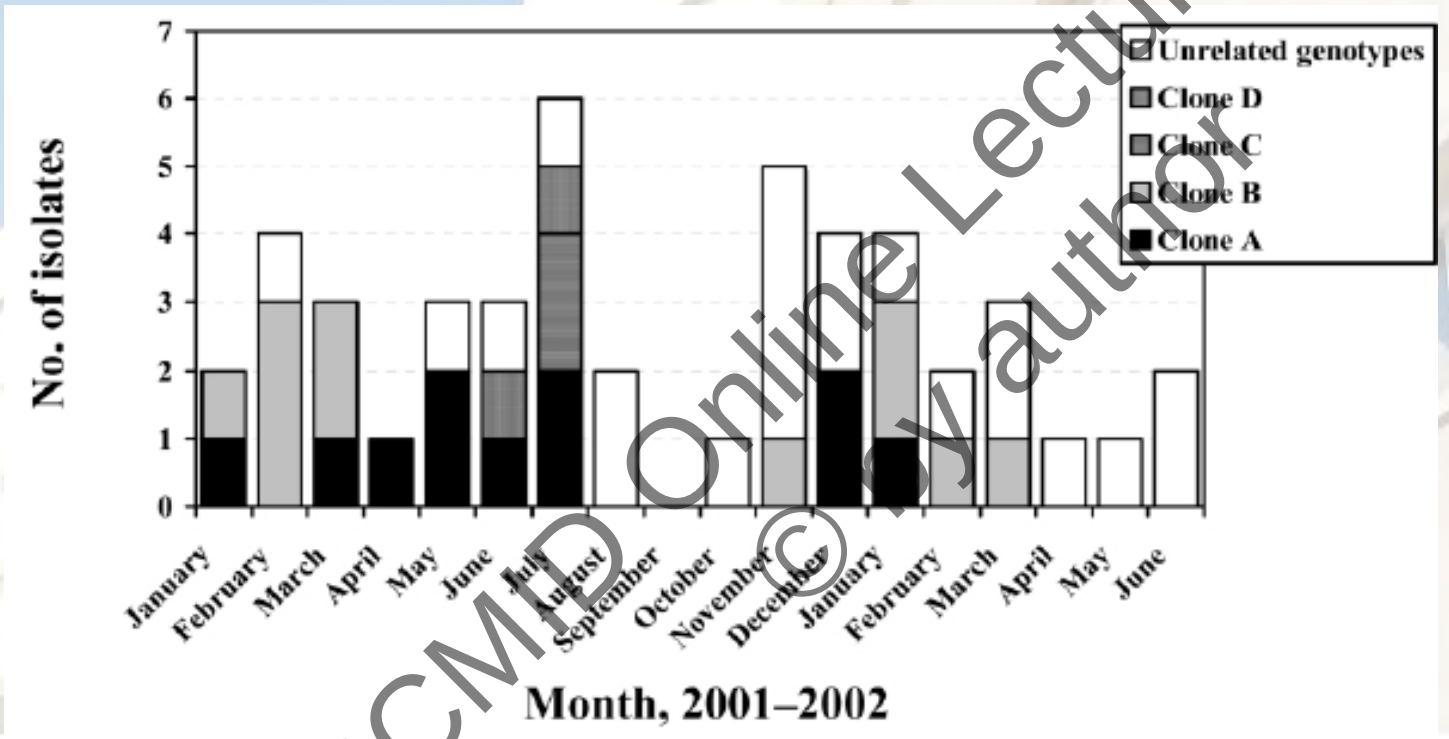
Nosocomial colonization/infection by ESBL-producing *E. coli*



Rodriguez-Baño et al, CID 2006; 42: 37-45

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Influx of Extended-Spectrum β-Lactamase–Producing Enterobacteriaceae into the Hospital

R. Ben-Ami,[1] M. J. Schwaber,[2] S. Navon-Venezia,[2] D. Schwartz,[3] M. Giladi,[1] I. Chmelnitsky,[2] A. Leavitt,[2] and Y. Carmeli[1,2]

Clinical Infectious Diseases 2006; 42:925–34

JOURNAL OF CLINICAL MICROBIOLOGY, July 2006, p. 2359–2366 Vol. 44, No. 7
0095-1137/06/$08.00+0 doi:10.1128/JCM.00447-06

Spread of *Escherichia coli* Strains with High-Level Cefotaxime and Ceftazidime Resistance between the Community, Long-Term Care Facilities, and Hospital Institutions

Jesús Oteo,[1] Carmen Navarro,[1] Emilia Cercenado,[2] Alberto Delgado-Iribarren,[3] Isabel Wilhelmi,[4] Beatriz Orden,[5] Carmen García,[1] Silvia Miguelañez,[1] María Pérez-Vázquez,[1] Silvia García-Cobos,[1] Belén Aracil,[1] Verónica Bautista,[1] and José Campos[1,6]*

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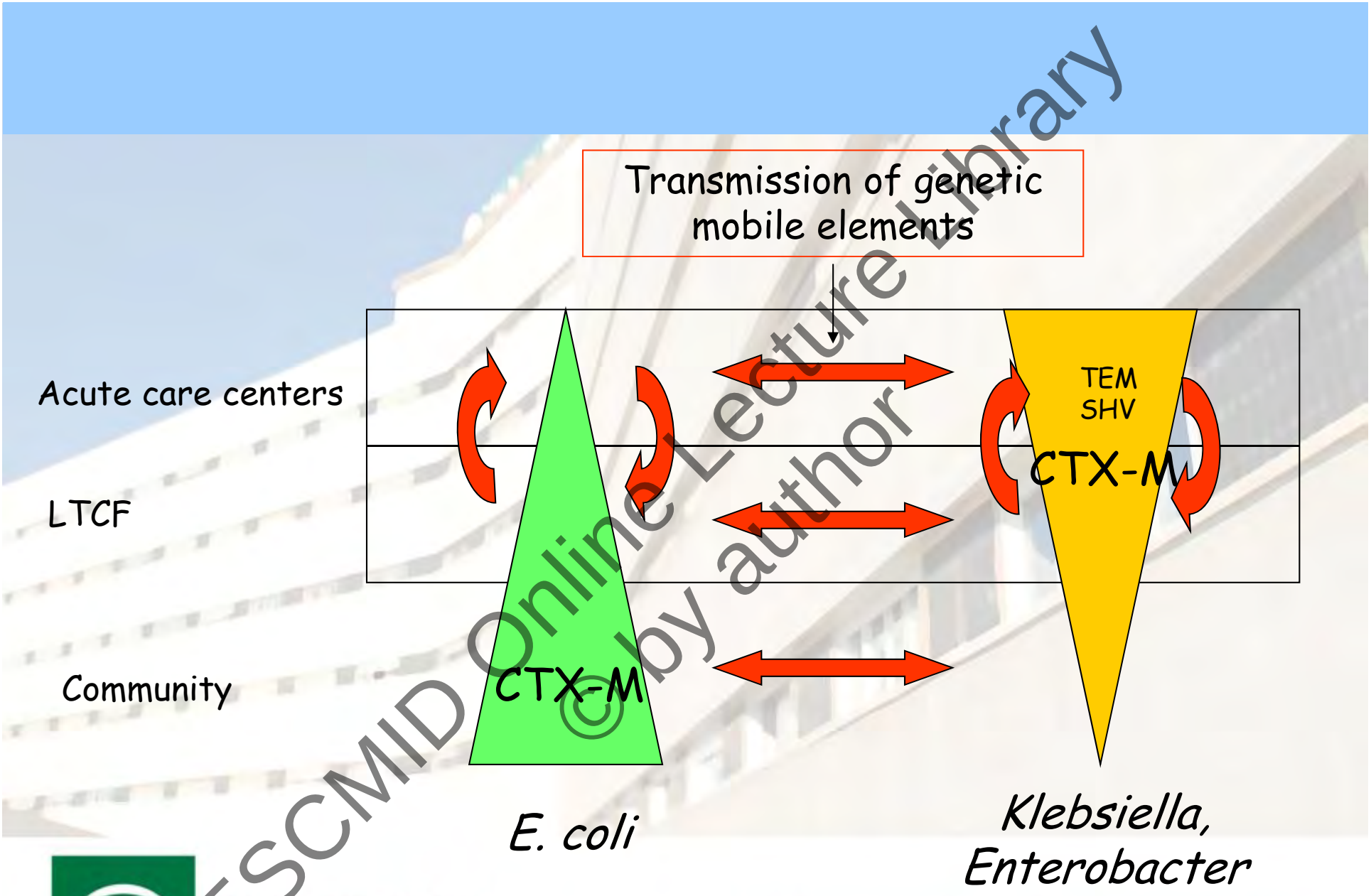
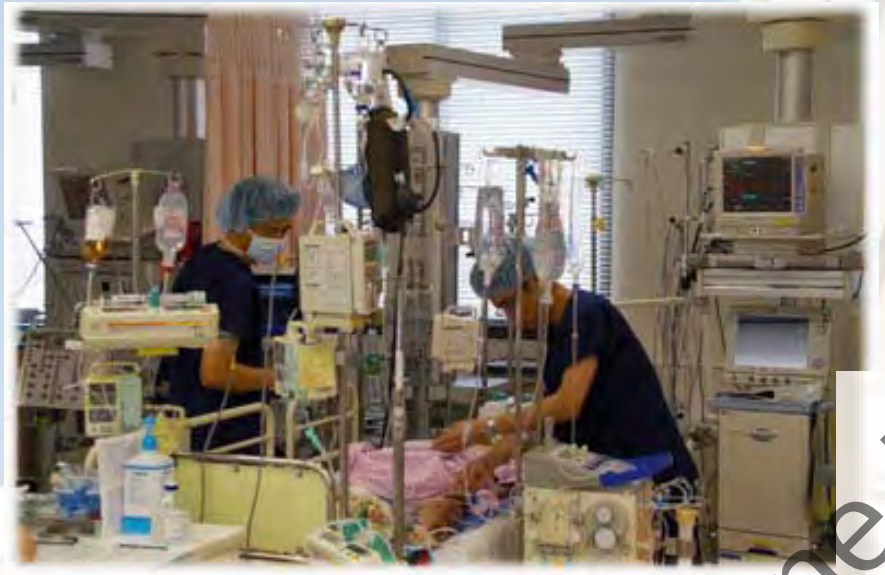


Are all colonized patients equally "dangerous"?



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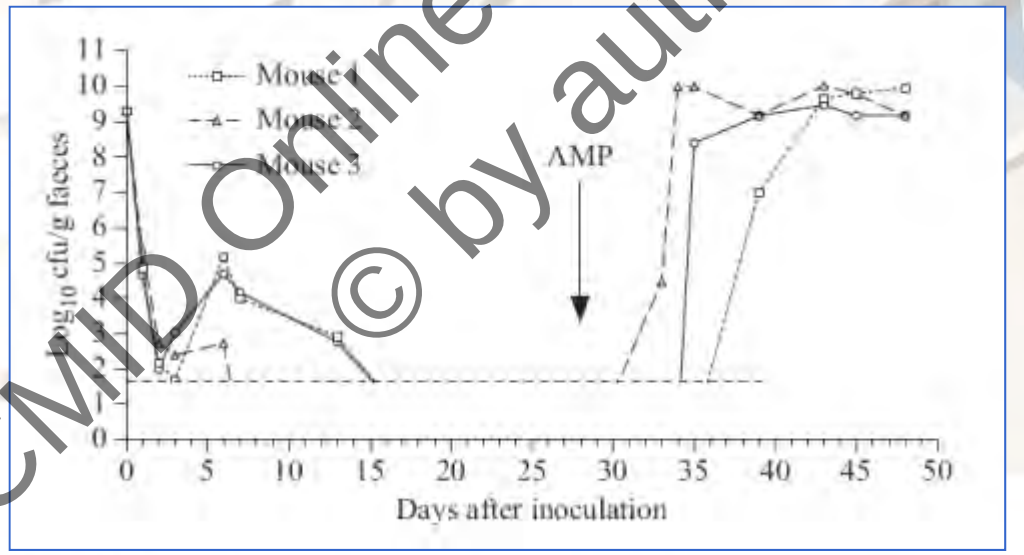
Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkn323

JAC

Transfer of antimicrobial resistance plasmids from *Klebsiella pneumoniae* to *Escherichia coli* in the mouse intestine

Susanne Schjørring, Carsten Struve and Karen A. Krogfelt*

- ESBL-producing *K. pneumoniae* (clinical isolate) colonized the intestine of mice



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Conclusions

- CP and isolation are key infection control measures for MDRO
- The efficacy if CP and isolation depends on the:
  - Epidemiologic behaviour of organism
  - Structural issues, cleaning and standard precautions
  - Adherence to CP measures
- The epidemiology of ESBL-producing organism would need to be characterised to decide/modify infection control practices
- It may be prudent to isolate ESBL-producing *K. pneumoniae* (and Enterobacter)
- It may not be necessary to isolate ESBL-producing *E. coli* (except if patient-to-patient transmission is suspected)

- If your mother/father needs to be hospitalised at Hosp Univ V Macarena…
  - Will be screened in the ICU
  - Will be isolated if colonised or infected by any ESBL-producing *Klebsiella*
  - Will not be isolated if ESBL-producing *E. coli*
  - Epidemiological data will be collected, and molecular typing performed if transmission is suspected

- Your mother/father in law too…