FAVOURITE INFECTION CONTROL PUBLICATIONS 2016

IFIC – APECIH 2017

KATHRYN N. SUH, MD, FRCPC

29 SEPTEMBER 2017

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JOURNALS

- BMJ, BMJ Quality and Safety
- JAMA
- Lancet, Lancet Infectious Diseases
- MMWR
- New England Journal of Medicine
- American, Canadian, International Journals of Infection Control
- Infection Control and Hospital Epidemiology
- Journal of Hospital Infection

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY OCTOBER 2015, VOL. 36, NO. 10

ORIGINAL ARTICLE

Reconsidering Contact Precautions for Endemic Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant *Enterococcus*

Daniel J. Morgan, MD, MS;[1] Rekha Murthy, MD;[2] L. Silvia Munoz-Price, MD, PhD;[3] Marsha Barnden, RNC, MSN, CIC;[4] Bernard C. Camins, MD, MSc;[5] B. Lynn Johnston, MD, MSc;[6] Zachary Rubin, MD;[7] Kaede V. Sullivan, MD;[8] Andi L. Shane, MD, MPH, MSc;[9] E. Patchen Dellinger, MD;[10] Mark E. Rupp, MD;[11] Gonzalo Bearman, MD, MPH[12]

CONTACT PRECAUTIONS FOR MRSA AND VRE

- How many
  - Screen for MRSA? VRE?
  - Isolate MRSA? VRE?
  - Contact precautions?
  - If not, what?

CONTACT PRECAUTIONS FOR MRSA AND VRE

- Contact precautions (CP) recommended in guidelines from United States, Canada, United Kingdom and Ireland, others; but are they necessary?
- Review of the literature and survey
- No studies have looked at effect of CP alone for MRSA or VRE
- 48 studies: in combination with active surveillance cultures, CP or universal gown/glove use had controversial impact on MRSA rates
- 45 studies: of 5 in non-outbreak settings, no conclusive evidence for VRE control

- Downsides to CP:
  - Fewer patient visits by HCWs, increase in adverse events
  - Patient outcomes: depression, isolation
  - System: delayed admission / patient flow
- Several US centres have abandoned CP – focus on horizontal measures; long term outcomes to be seen (several reporting stable or lower rates)
- No evidence that strongly supports or rejects CP for MRSA
  - Need better, well controlled studies

Morbidity and Mortality Weekly Report

Investigation of the First Seven Reported Cases of *Candida auris*, a Globally Emerging Invasive, Multidrug-Resistant Fungus — United States, May 2013–August 2016

Snigdha Vallabhaneni, MD[1]; Alex Kallen, MD[2]; Sharon Tsay, MD[1,3]; Nancy Chow, PhD[1]; Rory Welsh, PhD[1]; Janna Kerins, VMD[3,4]; Sarah K. Kemble, MD[4]; Massimo Pacilli, MS[4]; Stephanie R. Black, MD[4]; Emily Landon, MD[5]; Jessica Ridgway, MD[5]; Tara N. Palmore, MD[6]; Adrian Zelzany, PhD[6]; Eleanor H. Adams, MD[7]; Monica Quinn, MS[7]; Sudha Chaturvedi, PhD[7]; Jane Greenko, MPH[7]; Rafael Fernandez, MPH[7]; Karen Southwick, MD[7]; E. Yoko Furuya, MD[8]; David P. Calfee, MD[9]; Camille Hamula, PhD[10]; Gopi Patel, MD[10]; Patricia Barrett, MSD[11]; Patricia Lafaro[12]; Elizabeth L. Berkow, PhD[1]; Heather Moulton-Meissner, PhD[2]; Judith Noble-Wang, PhD[2]; Ryan P. Fagan, MD[2]; Brendan R. Jackson, MD[1]; Shawn R. Lockhart, PhD[1]; Anastasia P. Litvintseva, PhD[1]; Tom M. Chiller, MD[1]

CANDIDA AURIS: AN EMERGING HAI?

- First described in 2009 in Japan; since, reports from many countries
  - High mortality, has caused outbreaks
  - Often resistant to antifungal therapy
  - Difficult for laboratories to identify
- 7 cases reported in US between 2013 and August 2016:
  - All with complex underlying medical problems
  - 5 candidemia; 4 deaths, all of whom candidemic
  - 5 initially misidentified

- In two instances, two patients admitted to same facility – not simultaneously for two, and not same units for any
  - Isolates for both pairs were analyzed by whole genome sequencing; in both, isolates were nearly identical (< 10 SNP difference)
- 5 isolates fluconazole resistant, 1 AmB and 1 echinocandin resistant
- Persistent patient colonization and documented environmental contamination – concerns for hospital reservoirs and potential for transmission

American Journal of Infection Control 44 (2016) 74-9

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Structure for prevention of health care–associated infections in Brazilian hospitals: A countrywide study

Maria Clara Padoveze PhD, RN, MSc [a,*],
Carlos Magno Castelo Branco Fortaleza MD, PhD, MSc [b], Carlos Kiffer MD, PhD, MSc [c],
Afonso Luís Barth PhD [d], Irna Carla do Rosário Souza Carneiro MD, PhD, MSc [e],
Heloisa Ilhe Garcia Giamberardino MD, MSc [f],
Jorge Luiz Nobre Rodrigues MD, PhD, MSc [g], Lauro Santos Filho MD, PhD, MSc [h],
Maria Júlia Gonçalves de Mello MD, PhD, MSc [i], Milca Severino Pereira PhD, RN, MSc [j],
Paulo Gontijo Filho MD, PhD, MSc [k], Mirza Rocha MD, PhD, MSc [l],
Eduardo Alexandrino Servolo de Medeiros MD, PhD, MSc [m],
Antonio Carlos Campos Pignatari MD, PhD [m]

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INFRASTRUCTURE FOR IPAC IN LMIC – BRAZIL

- Rates of HAIs often higher in LMIC – lack of resources, expertise
- Brazil: > 6000 hospitals; mandated to have IPCC (1997)
- Unclear what resources existed in Brazil – aim: identify IPAC resources across the country, 08/11 to 08/13
- Convenience sample of 10/26 states in all 5 regions of Brazil, accounting for 2/3 of all healthcare facilities; cluster sampling of HCFs by state and bed size, using 11 academic centres (reference centres)
- Evaluation of each HCF by trained IC nurses, using standardized forms; focused on specific components of IPCC, sterilization, hand hygiene, laboratory – on site visits: observations, interviews, review of processes

- Conformity index: proportion of no. of elements “in compliance” for a given component (desirable: > 0.75)
- Linear regression to assess correlation between CI and hospital size/ region
- 153 hospitals, both public and private; in general:
  - Smaller hospitals and those not in South / Southwest had lower CIs for all elements
  - Correlation between different elements of each area of focus
  - Laboratory: variable

- Author conclusions:
  - Smaller hospitals fill needs, but low complexity of care – how to best allocate resources?
  - Need for government (state) investment in IPAC – states have autonomous healthcare but should have more accountability for IPAC
  - Need for improved laboratory infrastructure / processes, and full implementation of HH infrastructure (directed by Brazilian regulation)
- Limitations
  - No assessment of IPAC staffing, activities

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY JANUARY 2016, VOL. 37, NO. 1

ORIGINAL ARTICLE

Transmission of *Clostridium difficile* During Hospitalization for Allogeneic Stem Cell Transplant

Mini Kamboj, MD;[1,2,3] Anna Sheahan, PhD;[1] Janet Sun, BS;[1] Ying Taur, MD, MPH;[2,3] Elizabeth Robilotti, MD, MPH;[1,2,3] Esther Babady, PhD;[4] Genovefa Papanicolaou, MD;[2,3] Ann Jakubowski, MD, PhD;[3,5] Eric Pamer, MD;[2,3] Kent Sepkowitz, MD[1,2,3]

IS *CLOSTRIDIUM DIFFICILE* HOSPITAL-ACQUIRED?

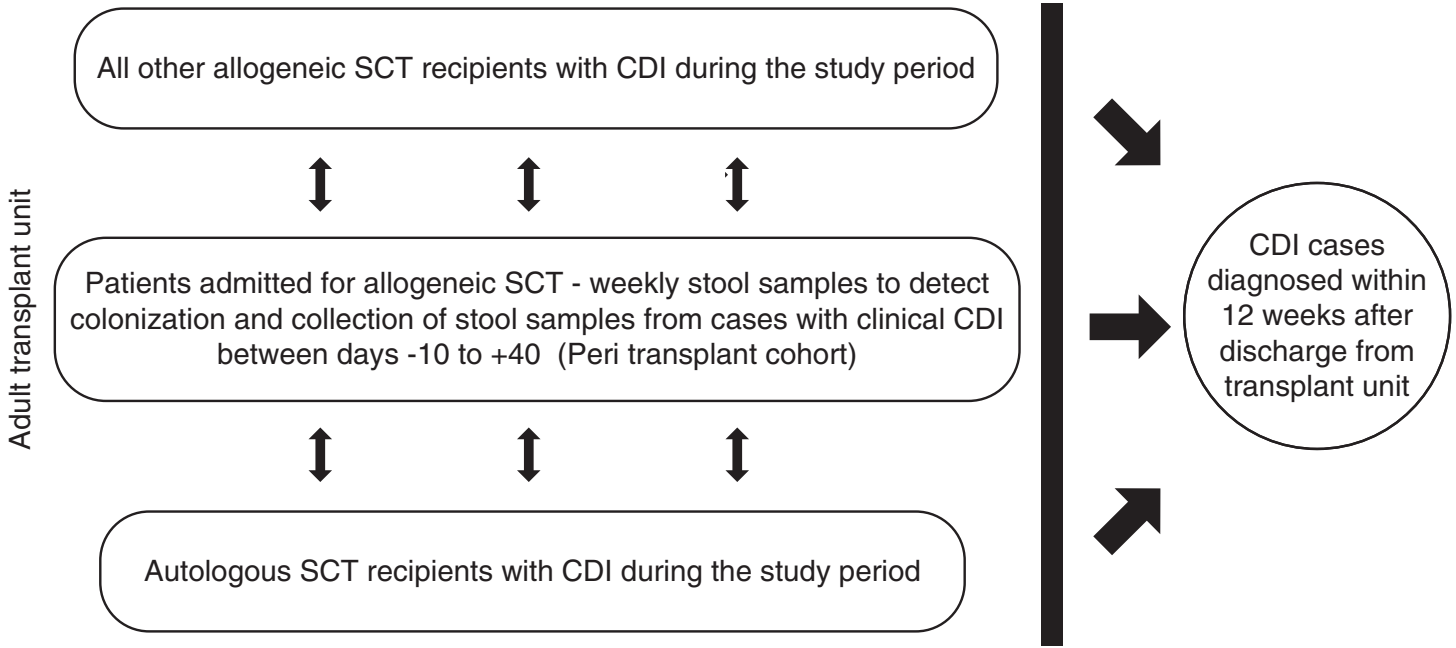
- *C. difficile* acquisition and transmission historically felt to be hospital-associated
- Eyre (2013), Oxfordshire UK: using WGS over 3.5 year period, identified that only 35% of cases were genetically associated with a previous case
  - Majority of cases acquired *C. difficile* from source other than infected patient - asymptomatic carriers or environment as reservoirs?

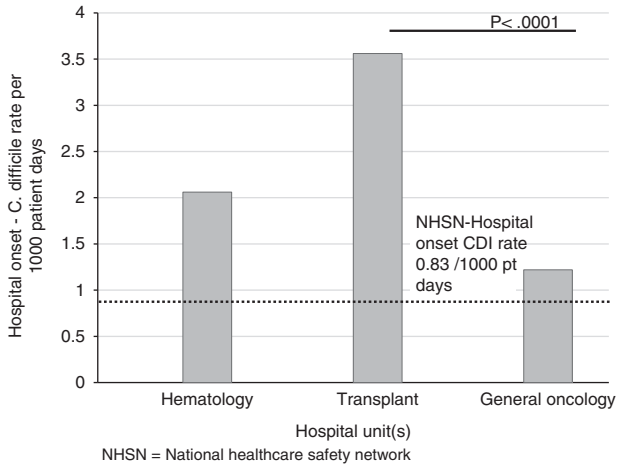
CDI IN STEM CELL TRANSPLANT PATIENTS, NYC

- CDI incidence 12.5-21% in SCT patients in previous studies – 15-25 fold higher than in general inpatient population
- Memorial Sloane Kettering Cancer Center, New York:
  - 471 bed cancer center with 29 bed SCT unit – private rooms, protective isolation for all patients
  - Screening cultures from 264 SCT patients (different study), CDI cases (hospital acquired up to 3 mos after discharge, or community acquired), recurrences (within 2 weeks of initial episode); 10/10 to 12/12

- 69/264 (26%) of screened patients colonized
  - 61 had specimen before SCT; 52 developed CDI around time of SCT, of whom 3 (6%) had relapse
  - 66 of 69 typed by MLST: 24 different types; **colonizing strain identical to infecting strain in those who developed CDI**

CLOSTRIDIUM DIFFICILE CASES





NHSN = National healthcare safety network

- 116 patients with CDI or colonization:
  - 99 CDI cases (84 HO, 15 CO) and 17 screened patients
- 102/116 available for typing:
  - 32 different MLST types
- Of 52 patients with CDI or colonization with MLST in whom CD was acquired in hospital, **only 17 (33%) could be explained by transmission in hospital**
- **26% colonized with CDI**

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Major Article

Assessment of terminal cleaning in pediatric isolation rooms: Options for low-resource settings

Angela Dramowski MD [a,*], Andrew Whitelaw MD [b], Mark F. Cotton MD, PhD [a]

[a] *Department of Paediatrics and Child Health, Division of Paediatric Infectious Diseases, Stellenbosch University, Cape Town, South Africa*
[b] *Department of Medical Microbiology, Stellenbosch University and the National Health Laboratory Service, Cape Town, South Africa*

ENVIRONMENTAL CLEANLINESS

- Role of environment well recognized in transmission of pathogens
- Standard guidelines / protocols do not exist in many LMIC facilities
- Aim: introduce monitoring of cleanliness (quality assurance)
- Stellenbosch, SA: Tygeberg Children's Hospital
  - 300 beds within a larger facility
  - High levels of antibiotic resistance – esp gram negatives

- Assessment by fluorescent marker, ATP and culture
  - Pre and post measurements, with feedback to housekeepers
- Improvement with objective measures:
  - Aerobic colony counts: mean 39 pre → 15 post ($p<0.001$)
  - ATP relative light units: 72+/- 40 pre → 23+/- 11 post ($p<0.001$)
  - Fluorescent marker: 22% pre → 61% post ($p<0.001$)
  - Sinks, mattresses, toilets, door handles problematic
  - Feedback using fluorescent markers was best received by housekeeping staff

- Quality assurance for environmental cleaning can be introduced into LMIC regions
  - In current setting, fluorescent marker easiest for cost, time, feasibility
  - Individual outcome can be sustained
- Limitations:
  - Measurement of outcomes not well defined
  - Unclear what degree of education provided to staff
  - Like most other studies, impact on HAIs was not assessed

MERS-CoV outbreak following a single patient exposure in an emergency room in South Korea: an epidemiological outbreak study

Sun Young Cho, Ji-Man Kang*, Young Eun Ha, Ga Eun Park, Ji Yeon Lee, Jae-Hoon Ko, Ji Yong Lee, Jong Min Kim, Cheol-In Kang, Ik Joon Jo, Jae Geum Ryu, Jong Rim Choi, Seonwoo Kim, Hee Jae Huh, Chang-Seok Ki, Eun-Suk Kang, Kyong Ran Peck, Hun-Jong Dhong, Jae-Hoon Song, Doo Ryeon Chung, Yae-Jean Kim*

Lancet 2016; 388: 994–1001

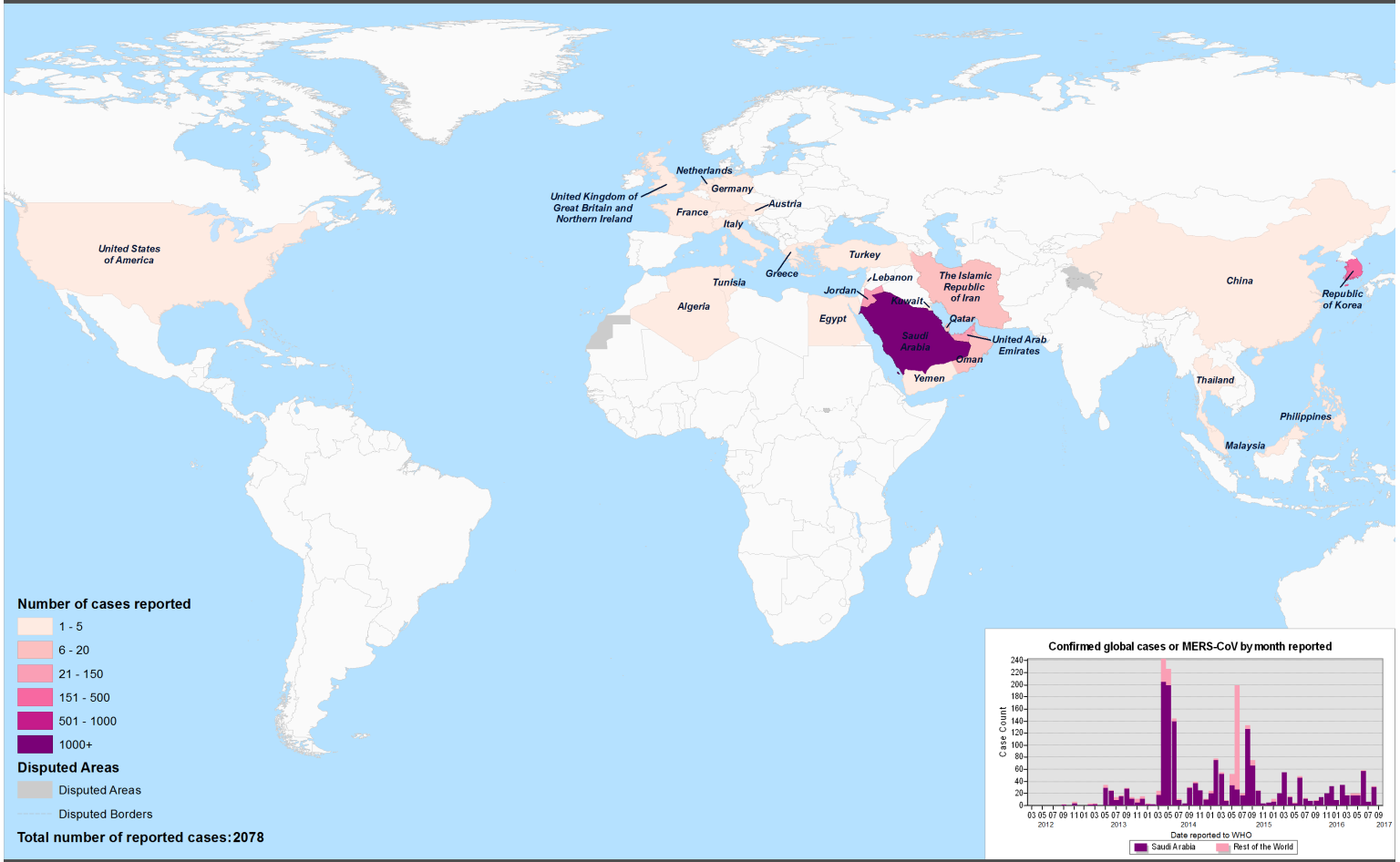
Summary

Background In 2015, a large outbreak of Middle East respiratory syndrome coronavirus (MERS-CoV) infection

MIDDLE EAST RESPIRATORY SYNDROME

- Coronavirus first described 2012 in Saudi Arabia
- WHO to date (September 2017):
  - 2081 laboratory confirmed cases in 27 countries
  - 82% of cases in Saudi Arabia
  - 722 deaths (~ 35%)
- Suspected low infectivity based on known epidemiology

CONFIRMED GLOBAL CASES OF MERS-COV 2012 - 2017



Map Scale (A3): 1:1,109,175,783
1 cm = 11,092 km
Coordinate System: GCS WGS 1984
Datum: WGS 1984
Units: Degree

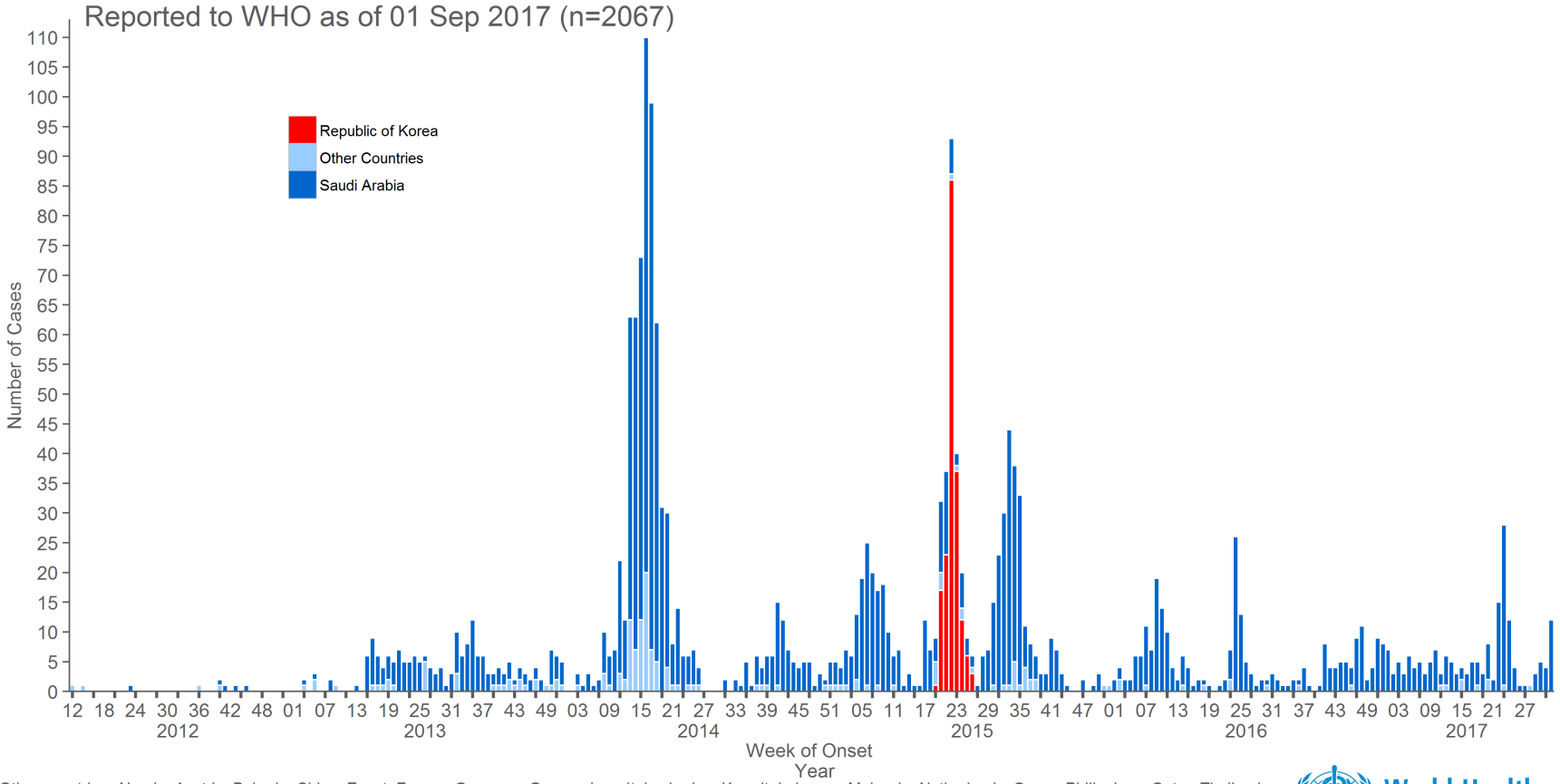
The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization

Map date:9/22/2017

World Health Organization

Confirmed global cases of MERS-CoV



Other countries: Algeria, Austria, Bahrain, China, Egypt, France, Germany, Greece, Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, Netherlands, Oman, Philippines, Qatar, Thailand, Tunisia, Turkey, United Arab Emirates, United Kingdom, United States of America, Yemen

Please note that the underlying data is subject to change as the investigations around cases are ongoing. Onset date estimated if not available.

World Health Organization

MERS IN KOREA

- 2 patients seen in ED of Samsung Medical Center, not recognized as possible MERS
  - 2000 bed tertiary care hospital – serves 50 million population
  - ED: 200 visits per day in 7 areas, average wait time 15 hours
- Patient exposures based on location:
  - Patients in same zone as index case
  - Patients with overlap at registration or in radiology
  - Patients in different areas of ED

- HCW exposures:
  - Direct contact with index (quarantined) or working in ED (surveillance)
- SMC outbreak provided an opportunity to assess risk of transmission based on exposure, not previously reported
- Confirmed case: lab confirmed by RT-PCR

- Patient 1: travel to Gulf area April 18-May 3; symptom onset May 11; presented to ED May 17, 18 (one of three facilities)
  - No transmission identified at SMC, but infected 28 others at other facility including Patient 14 between May 15-17
- Patient 14:
  - Admitted May 15-20, 21-25 at other facility; transfer to second facility May 25-27; left and presented to SMC May 27 – had not been notified of MERS contact (until May 29) – in ED for 54 hours

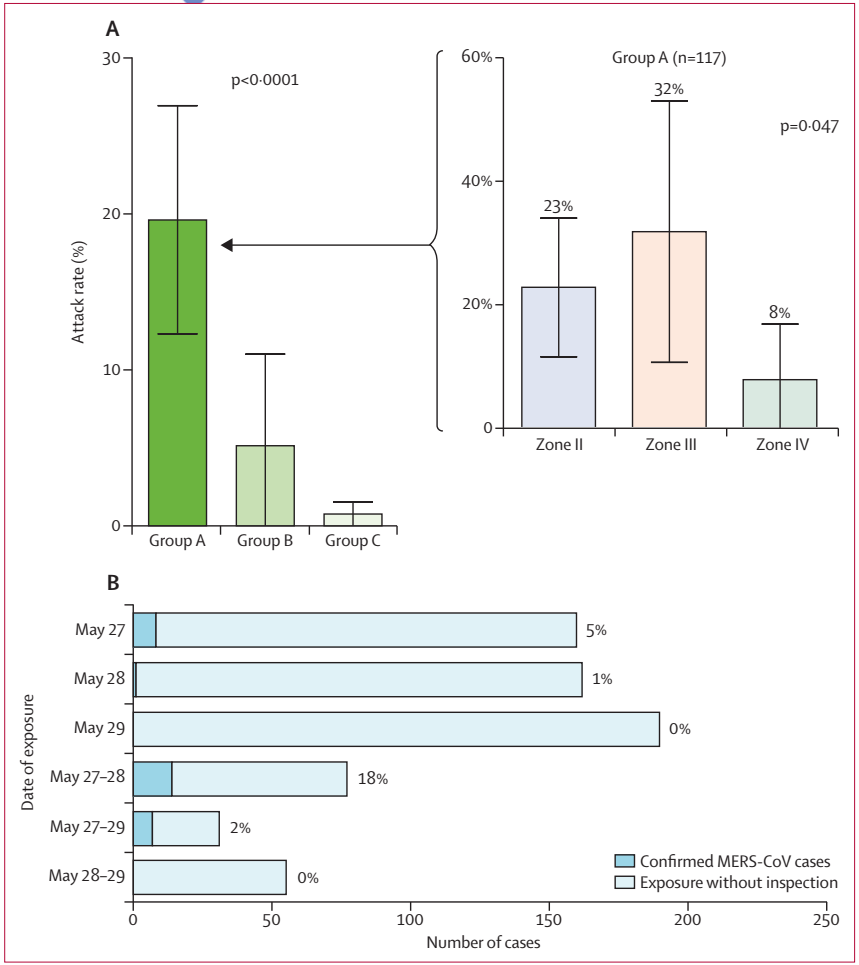


***Figure 3*: Attack rates (A) by groups of patient contacts and (B) by date of exposure**
Error bars represent 95% CI. MERS-CoV=Middle East respiratory syndrome coronavirus.

- 675 patient exposures
  - Overall attack rate 4% (20, 5, and 1% by exposure group)
- 683 visitor exposures
  - Overall attack rate 6% (combined with patients, 20, 5, and 2%)
- 218 HCW exposures
  - 5 infections (2%)
  - 3 not direct contacts
- Incubation periods:
  - Median 7d (5, 7, 11 by exposure group)

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY JULY 2016, VOL. 37, NO. 7

ORIGINAL ARTICLE

Improving Hand Hygiene Practices in a Rural Hospital in Sub-Saharan Africa

Ian C. Holmen, BA;[1] Celestin Seneza, MD;[2] Berthine Nyiranzayisaba, BS;[2] Vincent Nyiringabo, MD;[2] Mugisha Bienfait;[2] Nasia Safdar, MD PhD[3,4]

- Aim: to evaluate HH compliance with implementation of the WHO HH Toolkit in a small Rwandan hospital
- Quasi-experimental study at Gitwe Hospital – 160 bed private hospital with 12 physicians and 54 nurses serving population of 300,000:
  - Preparation, administration support
  - Baseline evaluation
  - Implementation
  - Evaluation

World Health Organization | Patient Safety

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- Baseline HH compliance audits using WHO methods, by trained observers
  - Audits of nurses and physicians in Medicine, Pediatrics, Maternity (29 rooms)
- Intervention: training and education (knowledge, attitudes, practice survey, didactic education, workplace reminders) and introduction of alcohol based hand rub (ABHR)

RESULTS

- 1 sink for 29 rooms; soap and water available, no towels
- Individual ABHR bottles for staff and physicians
- Baseline compliance 34.1% - increased to 68.9% 2-4 weeks later
  - Nurse and physician compliance both increased, across all 5 moments
  - ABHR used exclusively though technique not perfect
  - Knowledge scores increased from 41.3% to 78.4%

TABLE 1. Hand Hygiene Compliance at Baseline and Follow-Up, Gitwe Hospital, Rwanda

	Physician			Nurse		
Indication	Before, n/N (%)	After, n/N (%)	*P* Value	Before, n/N (%)	After, n/N (%)	*P* Value
Before touching a patient	65/104 (62.5)	95/110 (86.4)	<.001	5/63 (7.9)	25/50 (50.0)	<.001
Before a clean/aseptic procedure	6/19 (31.6)	21/27 (77.8)	0.002	0/12 (0)	26/43 (60.5)	<.001
After body fluid exposure risk	11/18 (61.1)	21/36 (58.3)	0.845	4/11 (36.3)	7/17 (41.2)	0.799
After touching a patient	50/77 (64.9)	67/78 (85.9)	0.002	13/49 (26.5)	41/69 (59.4)	<.001
After touching a patient's surroundings	18/51 (35.3)	30/34 (88.2)	<.001	8/124 (6.5)	26/57 (45.6)	<.001
Total	150/269 (55.8)	234/285 (82.1)	<.001	30/259 (11.6)	125/236 (53.0)	<.001

- Limitations:
  - Hawthorne effect?
  - Very short interval until evaluation – no measurements for sustained results
  - No infection control program in this hospital - ? feasibility elsewhere

Antimicrobial stewardship across 47 South African hospitals: an implementation study

*Adrian J Brink, Angeliki P Messina, Charles Feldman, Guy A Richards, Piet J Becker, Debra A Goff, Karri A Bauer, Dilip Nathwani, Dena van den Bergh, on behalf of the Netcare Antimicrobial Stewardship Study Alliance**

Lancet Infect Dis 2016; 16: 1017–25

Summary

Background The available data on antimicrobial stewardship programmes in Africa are scarce. The aims of this study were to assess the implementation of an antimicrobial stewardship programme in a setting with limited infectious

INTRODUCING STEWARDSHIP PROGRAMS

- Survey published in 2015: 14% of African respondents had antimicrobial stewardship program (ASP) in place
  - Absence of infectious diseases expertise identified as main barrier
- Aim: assess effect of implementing ASP in 47 private urban/rural hospitals in South Africa, using existing resources
  - Pharmacists, and one central quality coordinator / project manager
- Three phases of implementation:
  - Pre-implementation: baseline survey and training of hospital staff (10/09-01/11)
  - Simultaneous or stepwise introduction of 5 process measures, with daily rounding on patients receiving antibiotics (02/11-01/13)

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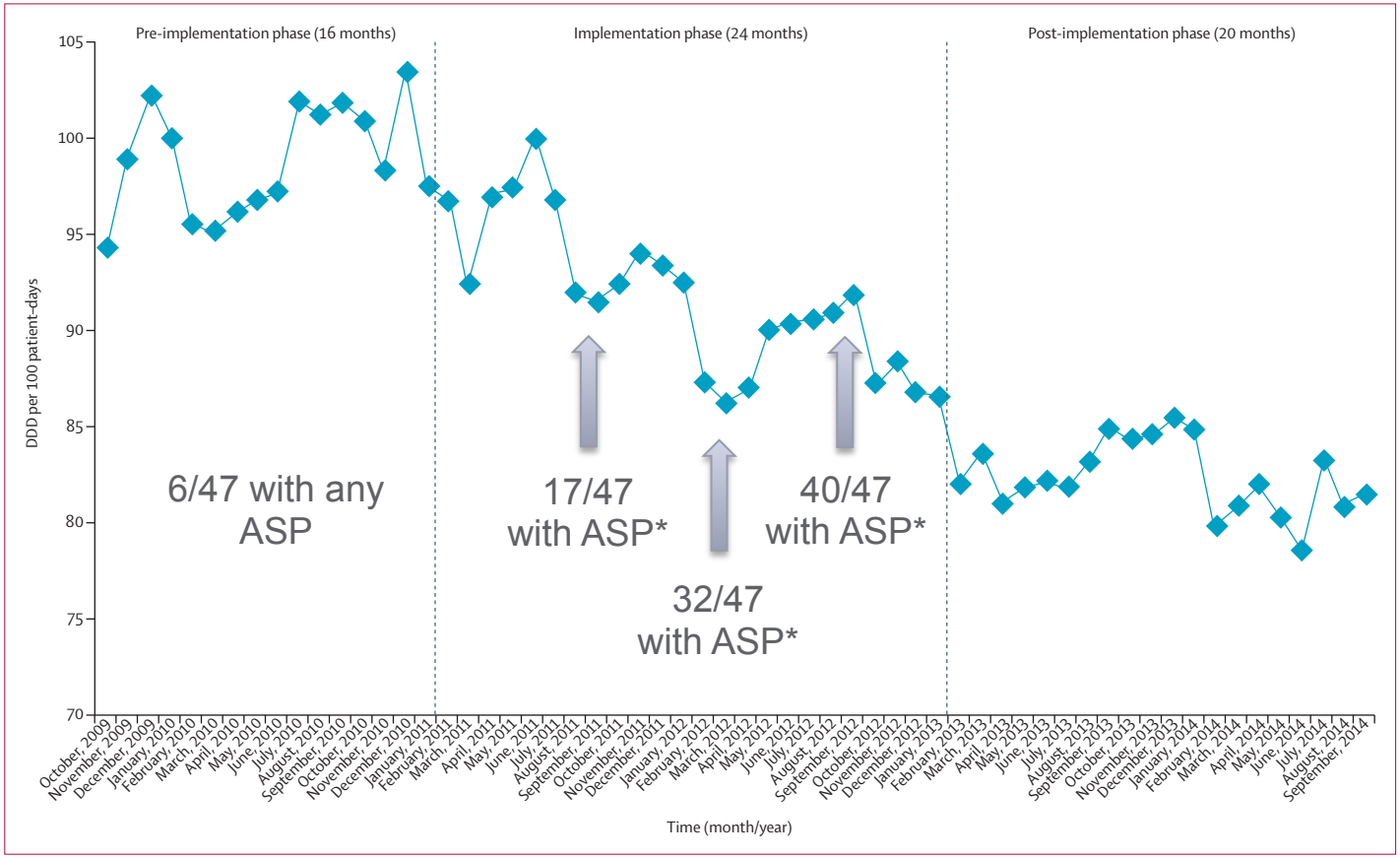
Howard P et al, J Antimicrob Chemother 2015

- Ongoing measurement and feedback, and ongoing learning (02/13-09/14)

- Improved implementation of stewardship activities, with overall reduction of 18.3/100 patient days of antibiotic use
- Pharmacist interventions in 1/15 patients; 39% related to duration of tx
- Demonstrates successful introduction of ASP without added resources or physician
  - Pharmacist driven success
  - Limitations: one health system, with no clinical outcomes
  - Expected plateau of efficacy – how to improve further? Behaviour change?



*all 5 interventions

***Figure 2*: Longitudinal cohort survey of mean antibiotic consumption for three phases of the Netcare antimicrobial stewardship model**
The entire study took place between Oct 10, 2009, and Sept 30, 2014, in 47 hospitals. Mean antibiotic consumption is measured in defined daily doses (DDDs) per 100 patient days.

Mitchell C, *et al*. *BMJ Qual Saf* 2016;**25**:466–474. doi:10.1136/bmjqs-2015-004134

ORIGINAL RESEARCH

Reducing the number and impact of outbreaks of nosocomial viral gastroenteritis: time-series analysis of a multidimensional quality improvement initiative

Caroline Mitchell,[1,2] Paul Meredith,[3] Matthew Richardson,[1,4]
Peter Greengross,[5] Gary B Smith[6]

- Norovirus – most common cause of gastrointestinal outbreaks in hospitals
  - Control is challenging: hand hygiene, environmental disinfection, early identification and isolation, restricting patient movement
- Portsmouth (UK) Hospitals Trust (National Health Service)
  - 5 hospitals, 1000 beds serving ~550 000 population
  - 7000 staff

- Multiple interventions:
  - Public health education campaign re: infection prevention (hand hygiene)
  - Enhanced IPAC activity for norovirus outbreaks: daily visits, enhanced cleaning, process audits, decluttering and ensuring supplies available
  - Building a new hospital (not feasible for most!)
  - Real time symptom assessment (nausea, vomiting, diarrhea) with electronic vital signs monitoring – early detection of symptoms and clustering of cases

- Comparing pre-intervention (1 yr) and post-intervention (4 yr) phases:
  - 62% reduction in norovirus cases (78 to avg 30 cases per year)
  - 91% reduction in outbreaks (2 or more cases on same unit) – from 21 to avg 2 annually
  - 88% reduction in days of disruption due to outbreaks (112 to avg 13)
  - 10% increase in hospital occupancy (81 to 91%)

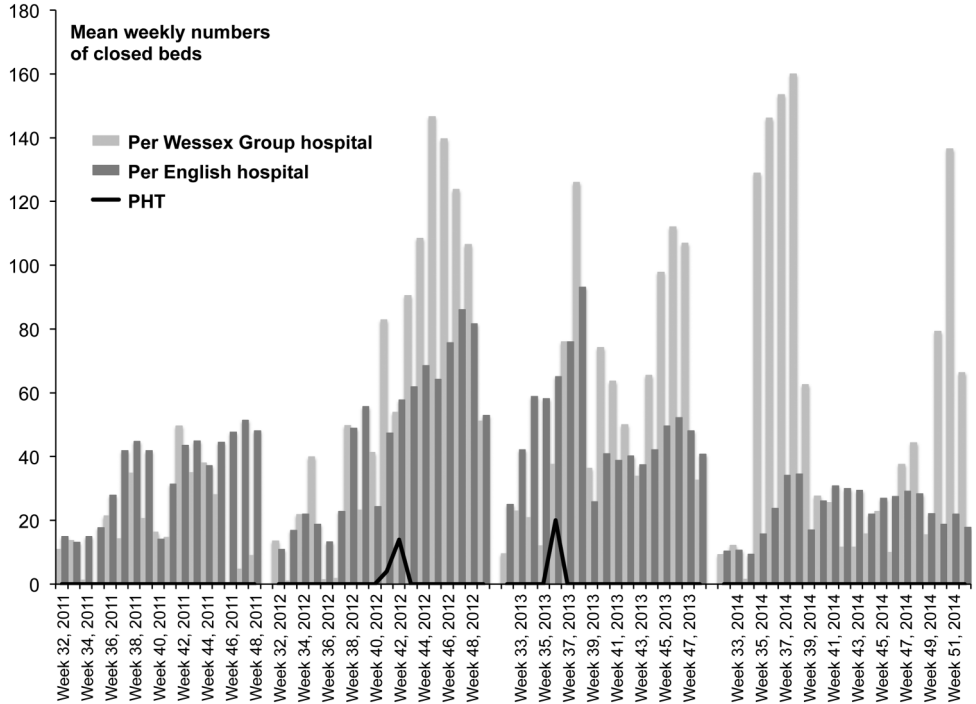


Figure 1 Mean weekly numbers of closed beds at Portsmouth Hospitals National Health Service Trust (PHT); the eight acute trusts in the former National Health Service South Central Strategic Health Authority; and all 158 acute trusts in England because of norovirus, as reported via Daily Winter Pressures Situation Reports during winter periods 2010/2011, 2011/2012, 2012/2013 and 2013/2014. Study weeks refer to fiscal weeks.

INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY SEPTEMBER 2016, VOL. 37, NO. 9

ORIGINAL ARTICLE

Personal Protective Equipment for Infectious Disease Preparedness: A Human Factors Evaluation

Tracey A. Herlihey, PhD;[1] Stefano Gelmi, BASc;[1] Christopher J. Flewwelling, MHSc;[1] Trevor N. T. Hall, MSc;[2] Carleene Bañez, BEng;[1] Plinio P. Morita, PhD;[1] Paul Beverley, AEMCA;[3] Joseph A. Cafazzo, PhD;[4,5] Susy Hota, MD[6,7]

HUMAN FACTORS AND PPE SELECTION

- How humans interact with the environment and system design
- Considerations for human factors during personal protective equipment (PPE) selection and use during Ebola virus disease preparations
- Usability testing and analysis of user feedback in 4 academic hospitals in Toronto, Canada – 2014
  - What we think is obvious or optimal is not, for users!
  - System design considerations – e.g. to avoid overheating, to create seals, reduce risk of cross contamination (disposal of equipment, one piece suits)
  - Environmental considerations – clean vs. soiled; physical layout

Journal of Hospital Infection 94 (2016) 23–29

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Review

Interventions to improve patient hand hygiene: a systematic review

J.A. Srigley [a,b,*], C.D. Furness [c,d], M. Gardam [e,f]

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INFECTION CONTROL & HOSPITAL EPIDEMIOLOGY APRIL 2016, VOL. 37, NO. 4

SHEA WHITE PAPER

Necessary Infrastructure of Infection Prevention and Healthcare Epidemiology Programs: A Review

Kristina A. Bryant, MD;[1a] Anthony D. Harris, MD, MPH;[2a] Carolyn V. Gould, MD, MSCR;[3] Eve Humphreys, MBA, CAE;[4] Tammy Lundstrom, MD, JD;[5] Denise M. Murphy, RN, BSN, MPH, CIC, FAAN;[6] Russell Olmsted, MPH, CIC;[7] Shannon Oriola, RN, BSN, CIC;[8] Danielle Zerr, MD, MPH[9]

Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis

Emelie C Schuts, Marlies E J L Hulscher, Johan W Mouton, Cees M Verduin, James W T Cohen Stuart, Hans W P M Overdiek, Paul D van der Linden, Stephanie Natsch, Cees M P M Hertogh, Tom F W Wolfs, Jeroen A Schouten, Bart Jan Kullberg, Jan M Prins

Summary

Background Antimicrobial stewardship is advocated to improve the quality of antimicrobial use. We did a systematic review and meta-analysis to assess whether antimicrobial stewardship objectives had any effects in hospitals and long-

Lancet Infect Dis 2016; 16: 847–56

- 14 stewardship objectives identified using Delphi procedure, from IDSA Guidelines, and from consensus meeting with professional societies in Netherlands
- 669 potentially relevant studies, of which 145 met inclusion criteria:
  - one of 4 patient outcomes (mortality / LOS in hospital, adverse events, cost, resistance rates)
  - data presented related to 9 (of 14) stewardship interventions
- Low quality evidence from 145 moderately-highly heterogeneous studies

	Definitions
Empirical therapy according to the guidelines	Empirical systemic antibiotic therapy prescribed according to local guide or national guidelines*
Blood cultures	Take at least two sets of blood cultures before starting systemic antibiotic therapy
Cultures from the site of infection	Take cultures from suspected sites of infection, preferably before starting systemic antibiotic therapy
De-escalation of therapy	Change to narrow-spectrum antibiotic or stop antibiotics as soon as culture results are available[10–13]
Adjustment of therapy to renal function	Adjustment of dose and dosing interval of systemic antibiotics
Switch from intravenous to oral therapy	Switch after 48–72 h, when the clinical condition of the patient is stable, oral intake and gastrointestinal absorption are adequate, and when sufficiently high concentrations in blood with a suitable oral antibiotic can be achieved[10,14,15]
Documented antibiotic plan	Documented antibiotic plan should include indication, drug name and dose, and administration route and interval, and should be included in the case notes at the start of systemic antibiotic treatment
Therapeutic drug monitoring	NA
Discontinuation of antibiotic therapy if infection is not confirmed	Discontinuation of empirical treatment based on lack of clinical or microbiological evidence of infection†
Presence of a local antibiotic guide	Local antibiotic guide present in the hospital and assessed for update every 3 years
Local antibiotic guide in agreement with national antibiotic guidelines	Corresponds for all features but can deviate on the basis of local resistance patterns
List of restricted antibiotics	Removal of specific antibiotics from the formulary or restriction of use by requiring preauthorisation by a specialist (infectious diseases or medical microbiology) or allowing use for only 72 h with mandatory approval for further use; studies in outbreak settings excluded
Bedside consultation	Formal consultation by an infectious disease specialist leading to written comments and advice on treatment based on physical examination and review of medical records (informal consultation, for example by telephone, does not count as bedside consultation)
Assessment of patients' adherence	NA

NA=not applicable. *All results extracted if both reported. †Studies only reporting on differences between discontinuing and continuing treatment were included, whereas those including more general reports on de-escalation of therapy (broad to narrower spectrum or stopping treatment based on culture results) were included in the review of de-escalation of therapy.

***Table 1*: Antimicrobial stewardship objectives included in systematic review**