VII Congresso GdS SIN Neonatologia e Sviluppo Cure essenziali nei paesi a basse risorse

"IN CAMMINO PER IL MONDO: NEONATOLOGIA SENZA CONFINI"

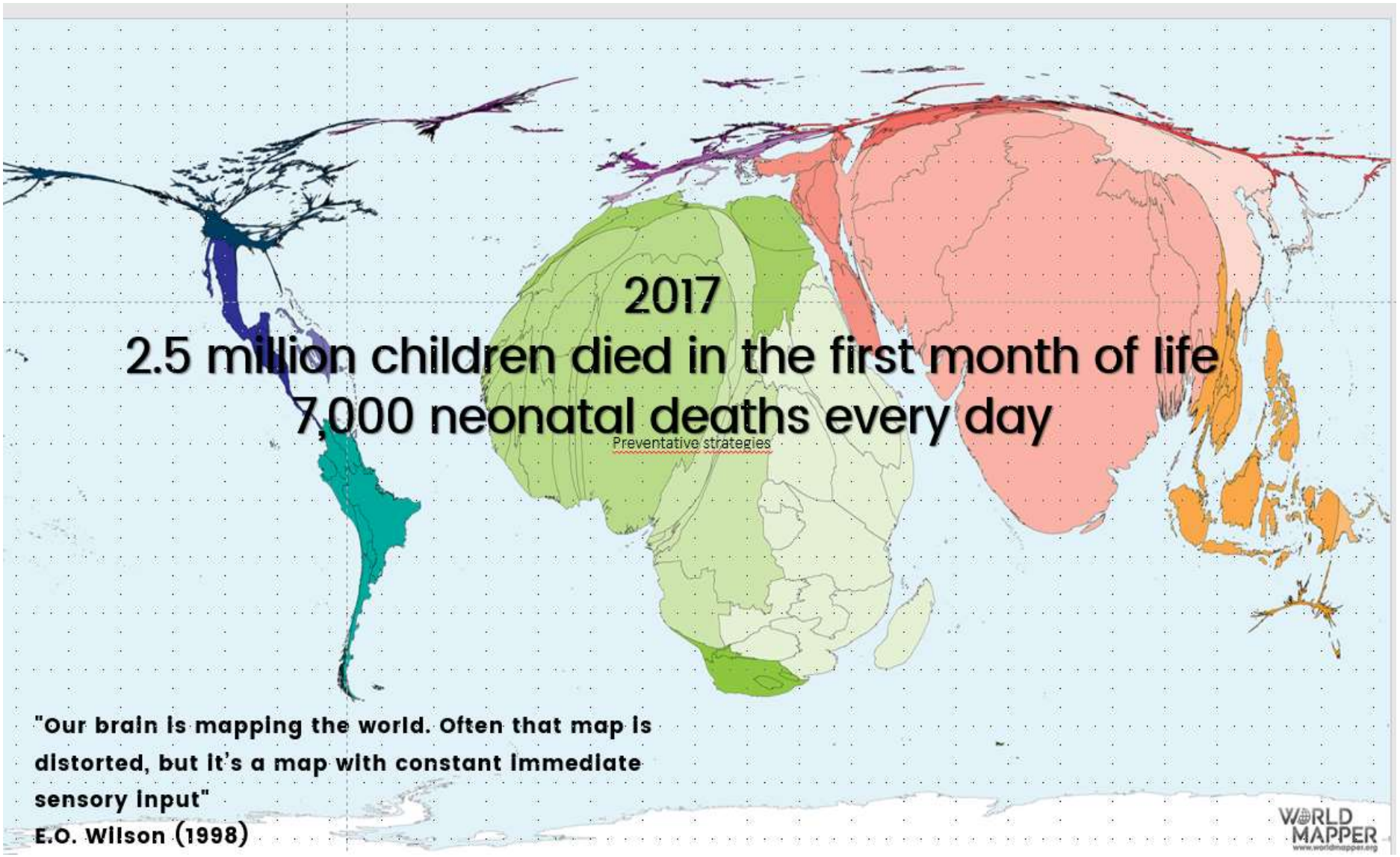
18/19 Ottobre 2019 Aula magna Az. Osp. Univ. Meyer/Firenze

PKG

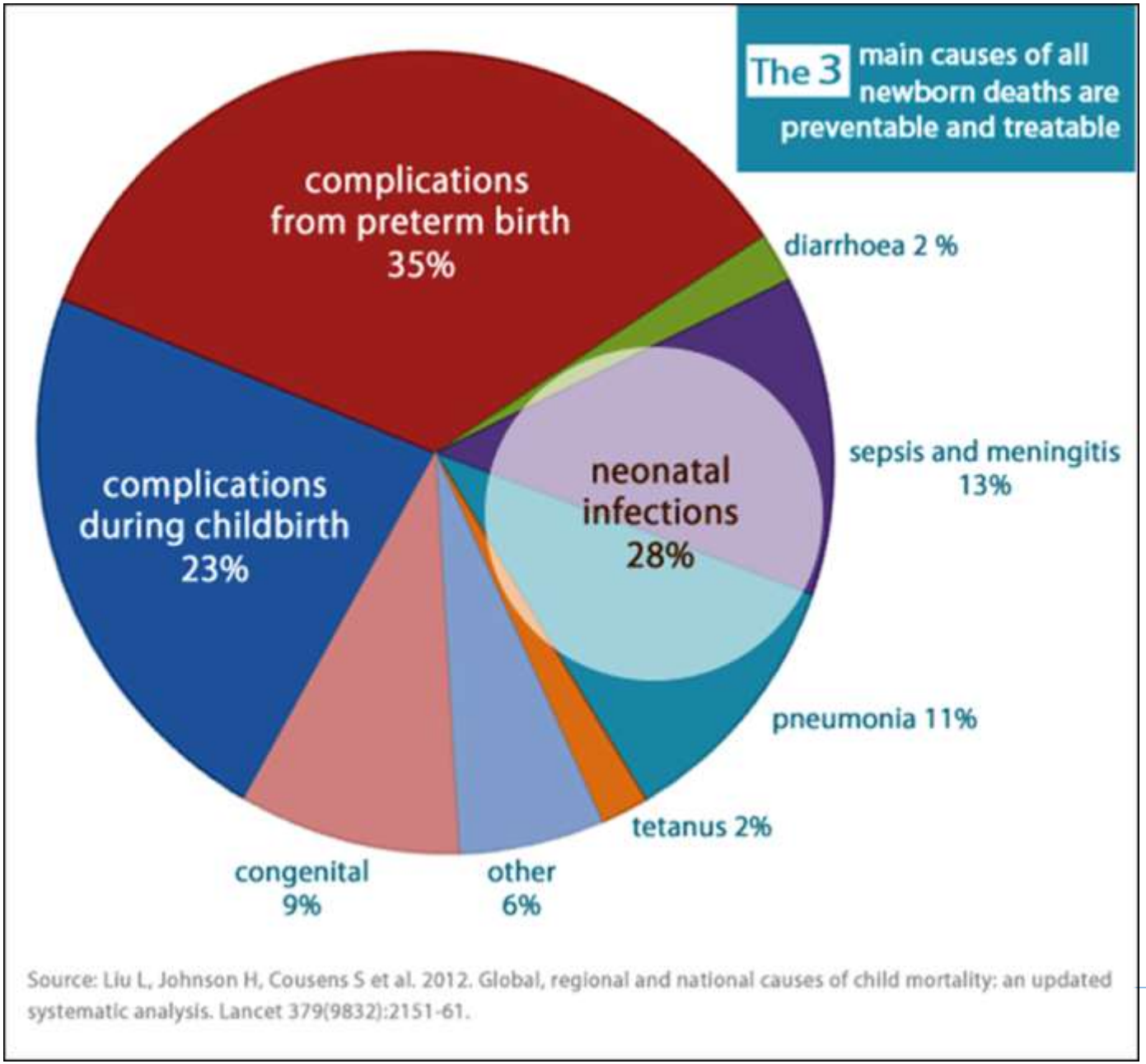
Strategies to prevent infections in the ward and appropriate use of antibiotics

Dr.ssa Barbara Perrone

Dr.ssa Lucia Tubaldi



WHO, Global Health Observatory 2018

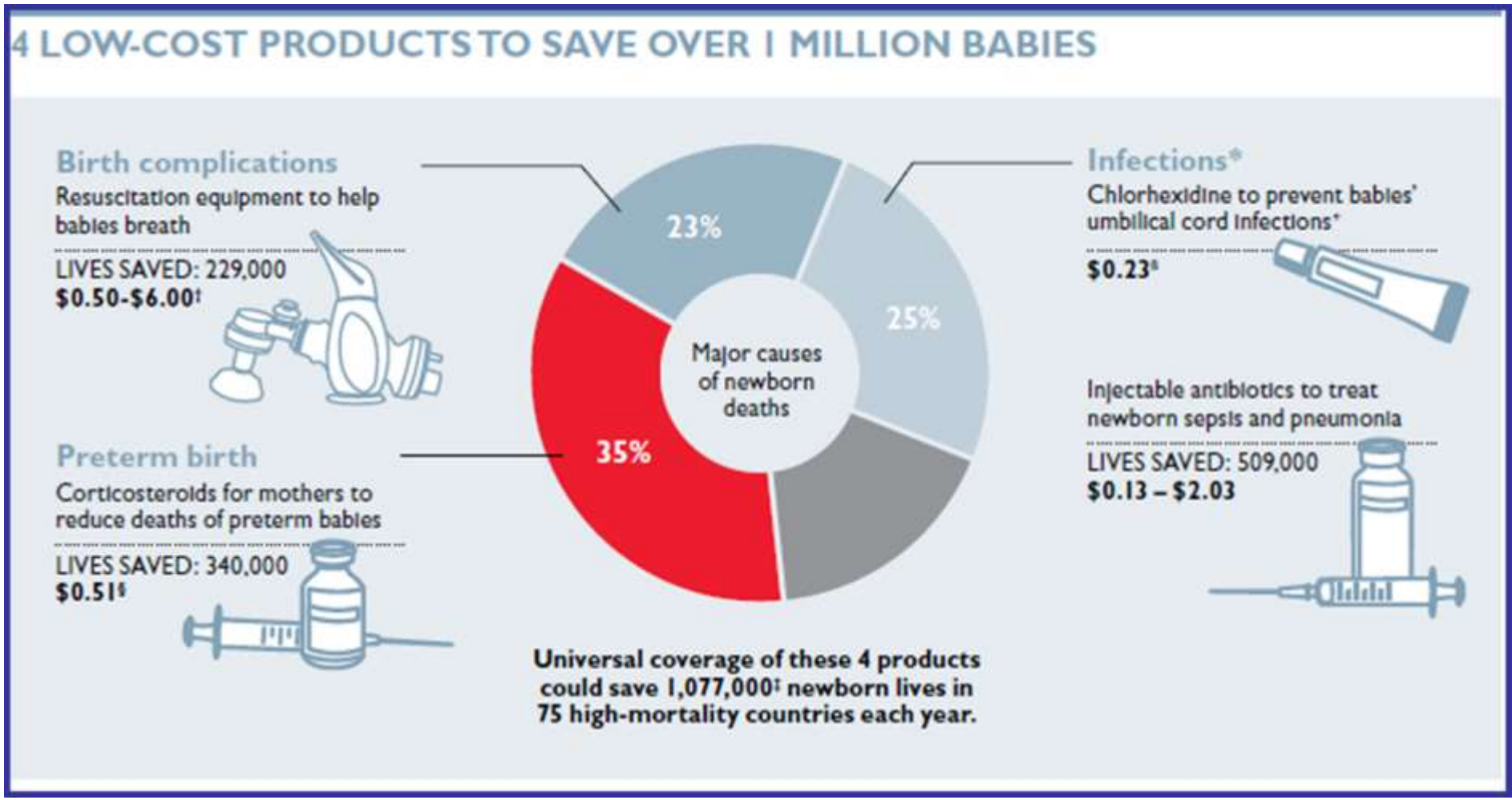


Neonatal Mortality rate:

28/1000 in Sub-Saharan Africa

25/1000 in Southern Asia

WHO, Global Health Observatory 2018



Every Newborn Study Group, The Lancet 2014

“Newborn survival rates potentially increase 44% when handwashing and clean birthing kits are in place.”

Blencowe et al. 2010

Timing of acquisition of infections

- During pregnancy

  Transplacental
  Through amniotic fluid

  Antenatal preventive measures and controls

- At birth

  Through the mother's blood
  Through the genital secretions
  Cord-cutting and care

  Safe and clean delivery

- After birth

  Usual routes: respiratory, orofecal, etc
  Nosocomial infections:
  hand to hand,
  contamination of surfaces or the equipment,
  invasive procedure

  Prevention of nosocomial infections
  Early recognition and treatment of acquired neonatal infections

Definition of Healthcare Associated Infections (HAI)in newborns

Infection Prevention and Control at Neonatal Intensive Care Units 2018

- Replaces the formerly used “nosocomial” or “hospital” infection because evidence has shown that these infections can affect patients in any setting where they receive health care.
- **HAI starts on or after the 3rd day of admission to the health facility or on the day of or the day after discharge from the facility.**
- Infections occurring on the day of birth/admission or the day after are not health care-associated infections.

Newborns' susceptibility to infections

Newborns are more susceptible to infections than older children due to a number of factors

- Immunology of the neonate: immunocompromised, immature, ineffective and inadequate levels of antibody Immature immune system
- Fragile skin barrier
- Permeable intestinal mucosa
- Manipulation, invasive procedures
- Comorbidities (congenital condition)

Gomella 2004

Newborn risk factors that increase the risk of infection

- Pre-term birth
- Low birth-weight (ELBW>VLBW)
- IUGR -Small for age
- Perinatal asphyxia
- Resuscitation
- Hypothermia

Gomella 2004

Care-related risk factors that increase the risk of infection

- Intensive care stay

  -Increasing use of invasive medical devices and procedures (parenteral nutrition, mechanical ventilators, central intravenous lines)

  -Inadvertent contamination of prepared supplies/pharmaceuticals (IV fluid, infant formula, general medications)

  -Increased length of stay
- Poor implementation of hand washing policy
- Suboptimal cleaning, disinfection and sterilization practices
- Inadequate treatment with antibiotics

  Antibiotic resistance due to overuse of broad-spectrum antibiotics

Allegranzi et al. 2011

Care-related risk factors that increase the risk of infection

- **Overcrowding and Understaffing**
- Contact with colonized/ infected family, visitors, or healthcare workers
- Proximity of colonized neonates
- **No contact with the mother**
- **Artificial feeding**

Allegranzi et al. 2011

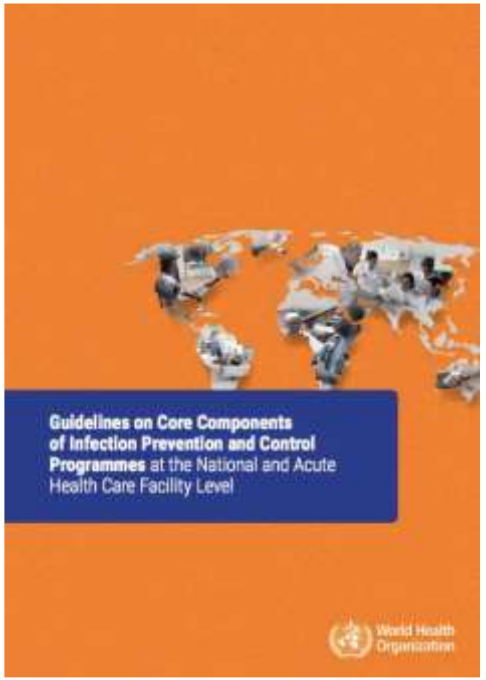
Healthcare acquired infections

Rates of HAI in newborns are 20 times higher in resource-limited settings compared to developed country context, with **inadequate environmental hygiene** and **low adherence to infection prevention and control** cited as potential explanations

Allengranzi et al, 2011

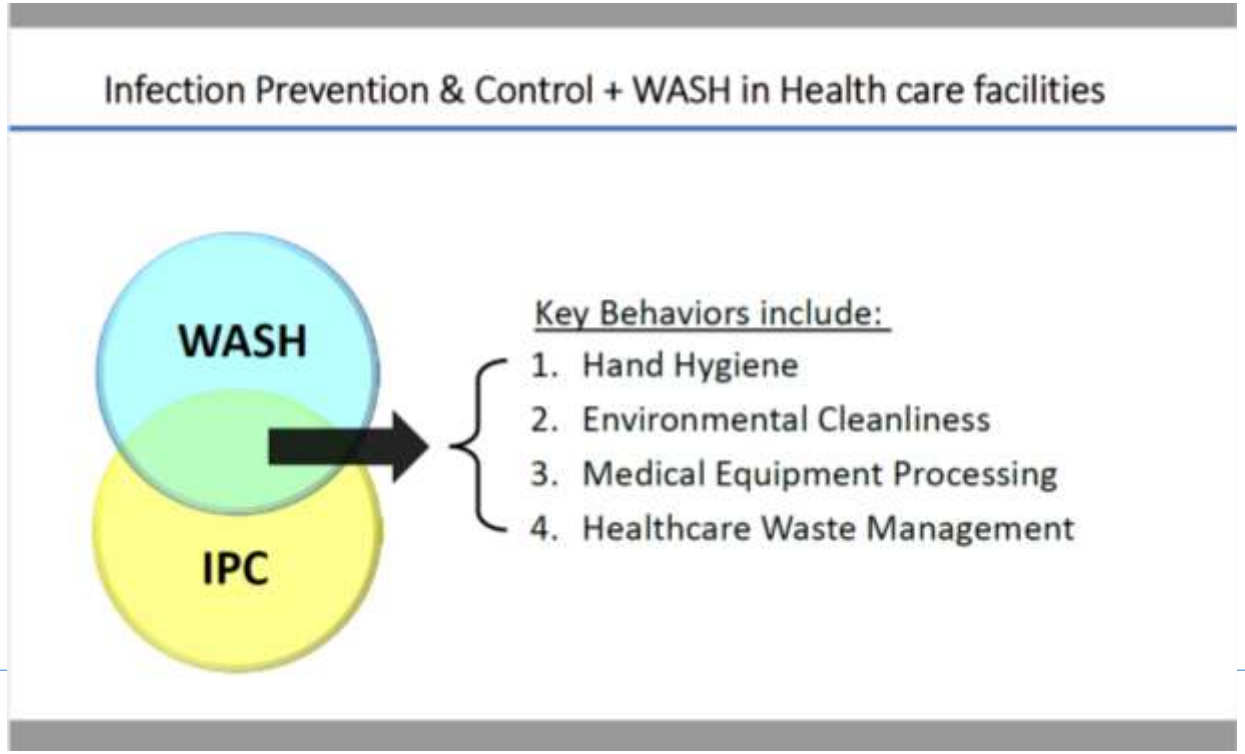
Infection Prevention & Control

- Infection Prevention and Control are the measures that a healthcare facility undertakes to prevent **harm** caused by infection to patients and healthcare workers.
- These measures include hygiene and environmental cleanliness as well as needle safety, personal protective equipment and healthcare waste management.



Source: WHO (2016)

Improving infection prevention and control **(IPC)** and water, sanitation, and hygiene **(WASH)** is one of the five objectives in the World Health Organization's (WHO) AMRGlobal Action Plan.



Situation in healthcare facilities in low and middle income country

WASH

- 38% of HC facilities do not have water sources
- 19% do not have improved toilets
- 35% do not have water and soap or alcohol base and rub for hand washing
- Up 90% of health workers do not adhere to recommeded hand hygiene practice

IPC

- In Africa up to 20% of women a wound infection of caesearen section
- Hospital born babies in low income setting are at a higher risk of being affected by neonatal sepsis ,with infection rate 3-to 20 time higher than in high-income setting
- On overage 15% of patiens will acquired at least one infection in acute care hospitals

New WHO Guidelines on Core Components of IPC and implementation tools.

Many early neonatal infections can be prevented by

- avoiding unnecessary separation of the newborn from the mother e.g. baby unit
- good basic hygiene and cleanliness during delivery (e.g. chlorhexidine cream for all maternal vaginal examinations)
- hand-washing before handling the infant
- appropriate umbilical cord care
- appropriate eye care
- give prophylactic antibiotics only to neonates with documented risk factors for infection

Many late neonatal infections are acquired in hospitals. These can be prevented by:

- **exclusive breastfeeding**
- strict procedures for hand-washing or alcohol hand rubs for all staff and for families before and after handling infants
- **using Kangaroo mother care** and avoiding use of incubators for preterm infants. If an incubator is used, do not use water for humidification (where Pseudomonas will easily colonize) and ensure that it was thoroughly cleaned with an antiseptic.
- strict sterility for all procedures
- clean injection practices
- **removing intravenous drips when they are no longer necessary**

Hand hygiene

- Most effective method for reducing health care associated infections (Larson *et* al Clin Infect Dis 1999)
- Higher rates of hand hygiene compliance = lower rates of central line bloodstream infection (Edqards JD *et al.* Pediatr Infect Dis 2002)
- CDC published guidelines for hand hygiene in health care settings in 2002
- Recent analysis of implementation of these guidelines had no effect on hand hygiene compliance rates (mean, 56.6%) Larson EL *et al*. Am J Infect Control 2007
- Educational programmes and multidisciplinary QI teams – effective in increasing compliance with hand hygiene (J Hosp Infect 2007)
- In May 2009, the World Health Organization published new consensus recommendations for hand hygiene.categorized according to grading system

Use of gloves

- The use of gloves does not replace the need for hand hygiene (IB).
- Wear gloves when it can be reasonably anticipated that contact with blood or other potentially infectious materials, mucous membranes, or nonintact skin will occur (IC).
- Remove gloves after caring for a patient. Do not wear the same pair of gloves for more than 1 patient (IB).
- Change or remove gloves during patient care if moving from a contaminated body site to either another body site (including nonintact skin, mucous membrane, or medical device) within the same patient or the environment (II)

A week of action to help raise awareness of when gloves should and shouldn't be worn and how to protect the skin on your hands

PEDIATRICS®

Strategies for Prevention of Health Care–Associated Infections in the NICU

Richard A. Polin, Susan Denson, Michael T. Brady and THE COMMITTEE ON FETUS AND NEWBORN and COMMITTEE ON INFECTIOUS DISEASES

Pediatrics 2012;129;e1085; originally published online March 26, 2012;
DOI: 10.1542/peds.2012-0145

epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England

H.P. Loveday, J.A. Wilson, R.J. Pratt, M. Golsorkhi, A. Tingle, A. Bak, J. Browne, J. Prieto, M. Wilcox

World Health Organization

Doing Saves Lives

Prevent Infections

- Decontaminating Cleaning Sterilisation and Disinfection of Commonly used Equipement MNCH

- Clening What When and How

Decontaminating Cleaning Sterilisation and Disinfection of Commonly used Equipment MNCH

Equipment		**Decontamination** is the first step in handling used items it reduces risk of Viruses especially hepatitis and HIV	**Cleaning** removes all visible blood, body fluids and dirt	**Sterilisation (Autoclave /Pressure Pot)** destroys all microorganisms including endospores	**High-Level Disinfection (if sterilisation not possible)** destroys all viruses bacteria parasites fungi and some endospores
	**Delivery table**	Wipe off with 0.5% chlorine solution. Including legs after each delivery	Wash with soap and water. Rinse with clean water, air dry	**No**	**No**
	Other operating or exam tables trolleys	Wipe off with 0.5% chlorine solution. As above	Wash with soap and water if organic material remains after decontamination.	**No**	**No**
	**Blood pressure cuff**	If contaminated with blood or body fluids, wipe with gauze pad or cloth soaked with 0.5% chlorine solution.	If soiled, wash with soap and water. Rinse with clean water, air or towel dry.	**No**	**No**
	**Stethoscope**	Wipe with gauze pad soaked in 60–90% alcohol after each use	If soiled, wash with soap and water. Rinse with clean water, air or towel dry.	**No**	**No**
	**Thermometer** (Keep oral and rectal thermometers Separate)	No	Wipe with disinfectant solution (soap and 0.5% chlorine). Rinse with clean water, air dry	**No**	**No**
	**Delivery Instruments and other surgical instruments**	Soak in 0.5% chlorine solution for 10 minutes prior to cleaning. rinse or wash immediately	Using a brush, wash with soap and water. Rinse with clean water. If to be sterilized, air or towel dry and wrap in packs or individually	**Dry heat** for 1 hour after reaching 170°C (340°F) , or **Autoclave** at 121°C (250°F) and 170°C (340°F) 106 kPa (15 lbs/in) for 20 minutes (30 minutes if wrapped). For sharp instruments: Dry heat for 2 hours after reaching 160°C (320°F).	Steam or boil for 20 minutes. Chemically high-level disinfect by soaking for 20 minutes. Rinse well with boiled water and air dry before use or storage.
	**Ambu bags and CPR face masks**		Wash all parts in warm water using mild detergent. Rinse to remove all detergent . Leave items to air dry	**Steam autoclave** in distilled water at 136 °C and 2 kg/cm for 10-20 minutes **Chemical Disinfection** with activated glutaraldehyde or CIDEX solution following manufacturers instruction Rinse in clean 500 mls water leave immersed for 60minutes Rinse again Repeat	Boil all parts in boiling water for at least 10 minutes
	Neonatal Suction New type Penguin	Open head part and empty remaining suctioned matter.	Wash and scrub all parts in soapy water flush water through nozzle and head and make sure all visible contamination removed	Steam autoclaving 136 C and 2 kg/cm2 for 10-20 minutes Chemical disinfection with activate glutaraldehyde in accordance with manufacturers instructions. Rinse in clean water and immerse for 1 minute Dry and keep clean till next use	Boiling in water **minimum of 10 minutes**
	**Old type Rubber Suction bulb:** (-very difficult to clean and normally recommended for single newborn)	Soak in a 0.5% chlorine solution for 10 minutes prior to cleaning.	Rinse and wash immediately	no	no
	**Scales**			no	no
	**Fixed**	Wash if soiled . Wipe with 0.5% chlorine solution.			
	Hanging	Same as for BP cuff		no	no

Cleaning What When and How		
What	**When**	**How**
Floors	**Twice daily or more as needed**	**Use a clean, wet mop and fresh detergent solution. A disinfectant cleaning solution should be used when contamination is present**
Sinks	**Daily or more often as needed**	**Scrub with a separated mop, cloth or brush and a disinfectant cleaning solution**
Lamps, chairs, table and counters	**Daily or when visibly dirty**	**Damp dusting – wipe with a cloth dampened in a fresh detergent solution**
Walls, windows, ceilings and doors	**Weekly or when visibly dirty**	**Clean using a damp cloth – wipe with a cloth dampened in a fresh detergent solution**
Procedure and Examination Rooms	**After every procedure, and whenever visibly soiled**	**Wipe horizontal (flat) surfaces, equipment, and furniture used for the procedures with a disinfectant cleaning solution. Linen or paper on the examination table should be changed after each patient. Clean blood or other body fluid spills as described above.**
Toilets and latrines	**Wash at least three times daily and as needed**	**Scrub frequently with separate mop, cloth or brush and a disinfectant cleaning solution**
Operating room	**At the beginning of every day**	**All flat (horizontal) surfaces (table, chairs, etc.) should be wiped with a clean, moist cloth to remove dust that may have collected overnight**
	Between every case	**Wipe all surfaces and mattress pads with a disinfectant cleaning solution; Wipe all flat surfaces that have come in immediate contact with a patient or body fluids with a disinfectant cleaning solution.**
	At the end of every day	**Total cleaning or terminal cleaning (mopping floors and scrubbing all surfaces from top to bottom) of the operating room should be done at the end of each day (Remember to clean door handles, light switches etc.)**
Cleaning equipment (mops, brushes,	**Between each use**	**If contaminated, decontaminate in 0.5% chlorine solution; Clean in soap or detergent and water; Sun dry until completely dry before next use**

General Rules For Cleani Surfaces and Floors [6]

SCRUBBING is the best way to re dirt, debris and microorganisms;

ALWAYS clean before any disinfe process because dirt, debris and o materials reduce the effectiveness many chemical disinfectants;

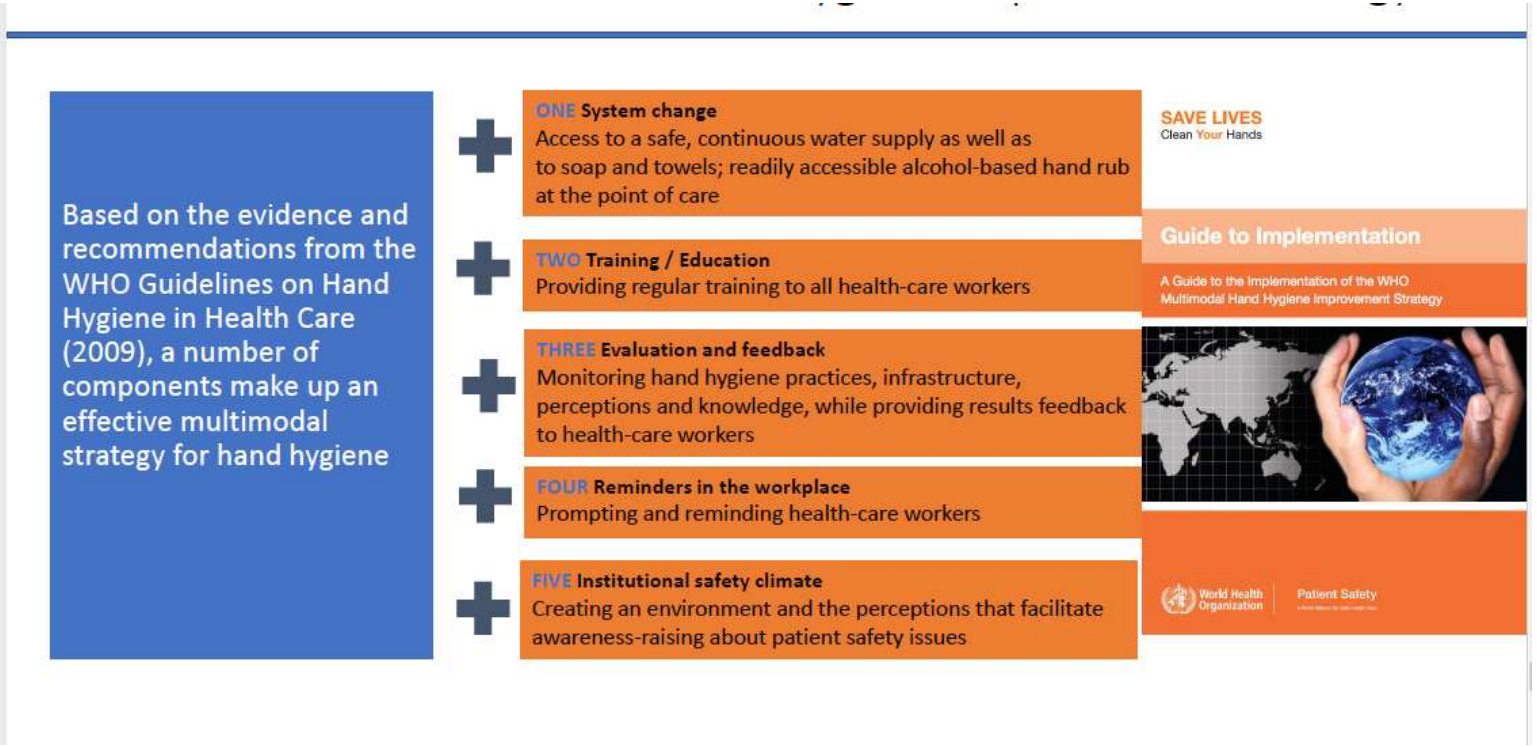
START cleaning from the least soi areas to the most soiled areas anc high to low areas , so that the dirt debris fall on the floor and will be cleaned up last of all.

AVOID dry sweeping, mopping ar dusting to prevent dust, debris an microorganisms from getting into and landing on clean surfaces. Airl fungal spores can cause fatal infec

FOLLOW MIXING INSTRUCTIONS (dilution), when using disinfectant too much or too little water can re the effectiveness

ROUTINE cleaning is necessary tc maintain a standard of cleanliness prevent spread of infections. Schedules and procedures should routine, posted on the wall and ch by in charges

What is the WHO Multimodal Hand Hygiene Improvement Strategy?



What is the WHO Multimodal Hand Hygiene Improvement Strategy?

Health Education/Motivational Programs

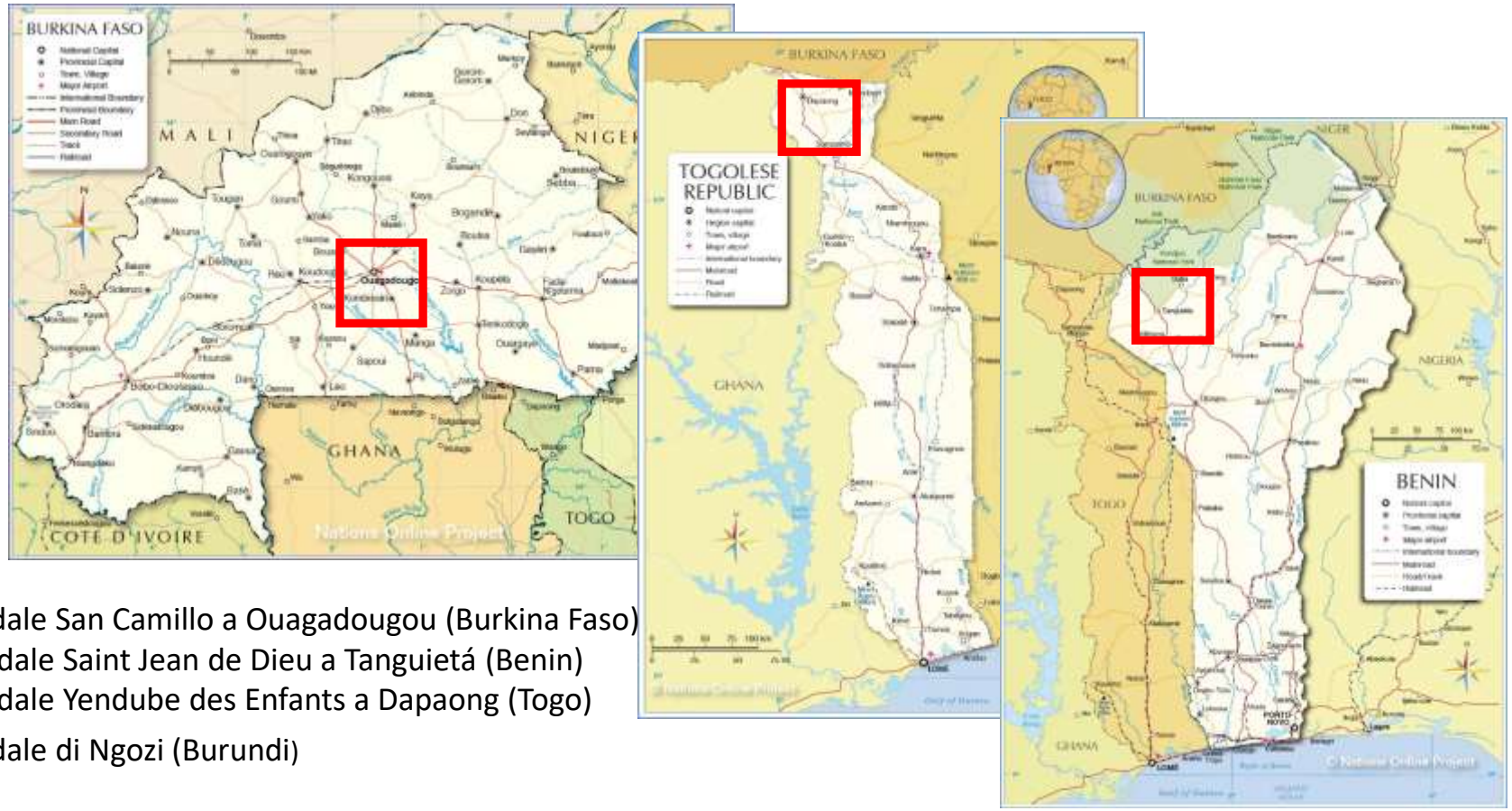
- In hand hygiene–promotion programs for health care workers, focus specifically on factors currently found to have a significant influence on behavior and not solely on the type of hand hygiene product.
  The strategy should be multifaceted and multimodal and include education and senior executive support for implementation (IA)
- Monitor health care workers' adherence to recommended hand hygiene practices and provide them with performance feedback (IA).

Administrative Measures to Improve Hand Hygiene

WHERE IN AFRICA?

l'Ospedale San Camillo
a Ouagadougou (Burkina Faso)
l'Ospedale Saint Jean de Dieu
a Tanguietá (Benin)
l'Ospedale Yendube des Enfants
a Dapaong (Togo)
l'Ospedale di Ngozi (Burundi)

WHERE IN AFRICA?



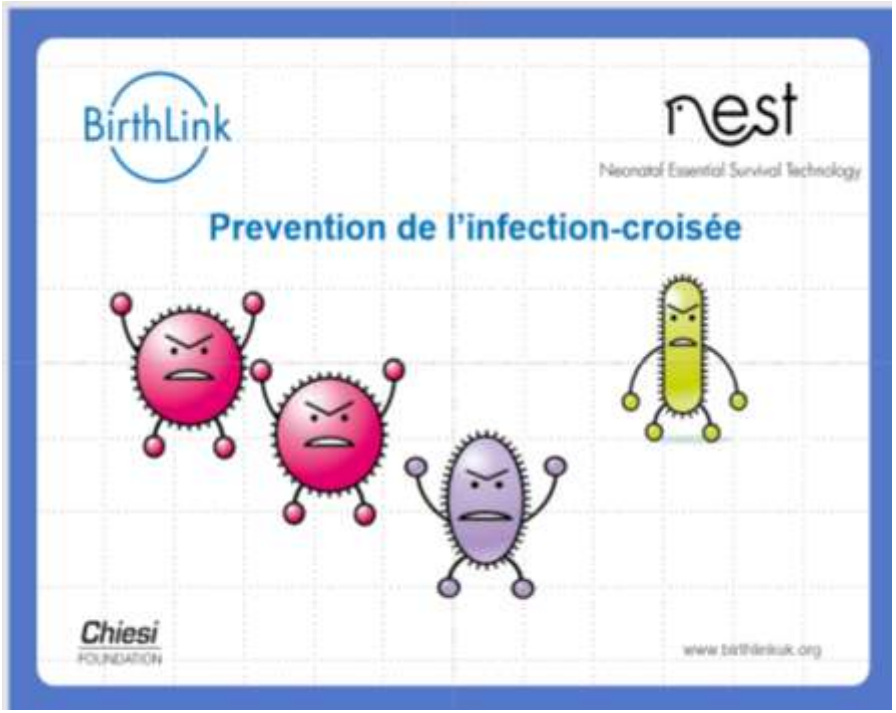
l'Ospedale San Camillo a Ouagadougou (Burkina Faso)
l'Ospedale Saint Jean de Dieu a Tanguietá (Benin)
l'Ospedale Yendube des Enfants a Dapaong (Togo)
l'Ospedale di Ngozi (Burundi)


Da una riflessione sulle ineguaglianze di accesso a cure neonatali adeguate nelle diverse regioni del mondo nasce il
MODELLO NEST
nest
Neonatal Essential Survival Technology
Chiesi
FOUNDATION


Il NEST ha l'obiettivo di contribuire alla riduzione della mortalità neonatale attraverso il miglioramento della qualità dell'assistenza ai neonati in Paesi a basso e medio reddito, con particolare attenzione alla cura dei bambini prematuri, patologici e di basso peso.
nest

Formazione in aula

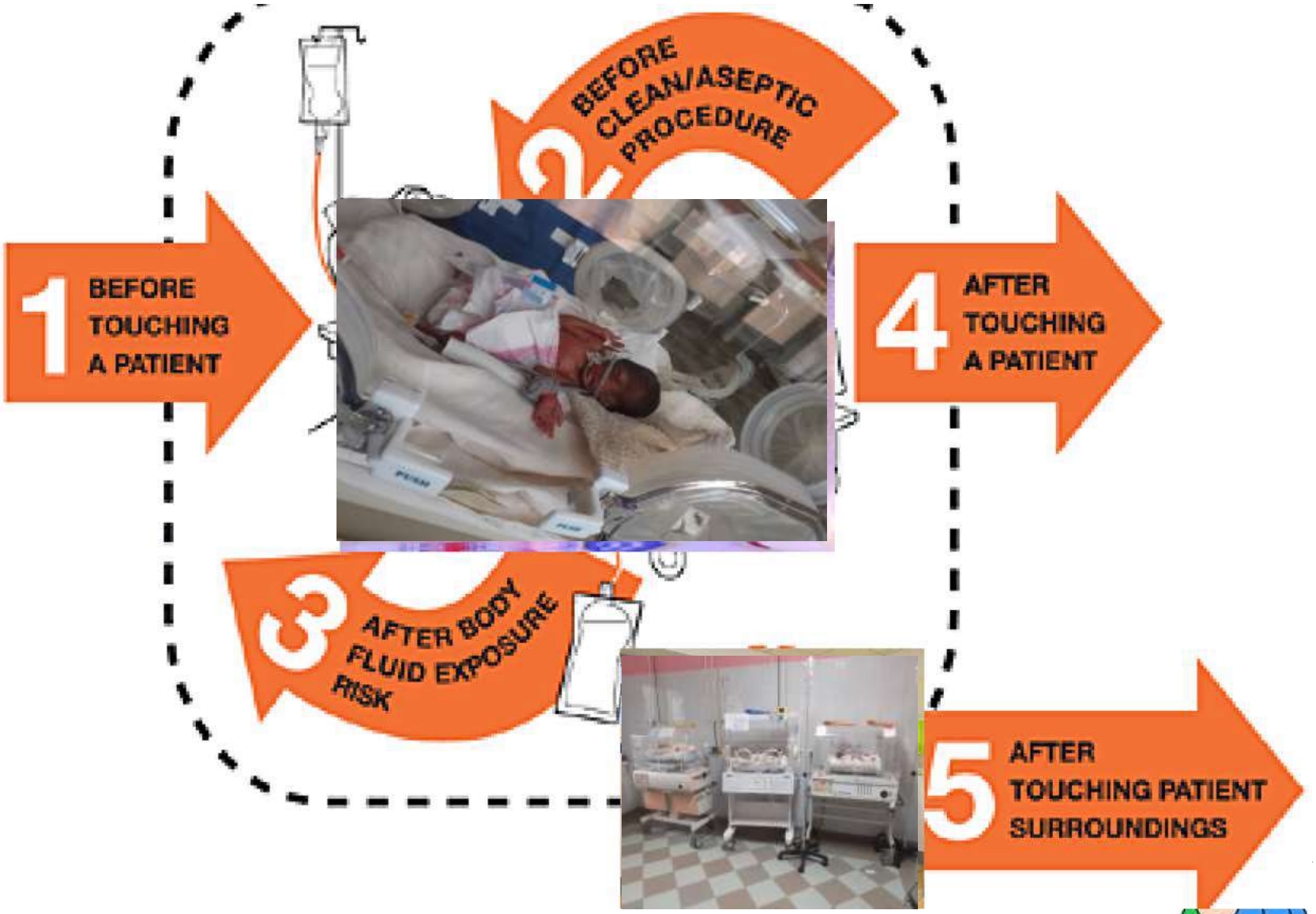
Moduli formativi



Formazione sul campo

Principes généraux Incubateurs et lits médicalisés doivent être démontés dans toutes leur parties.

Démonter les plans sous-jacent le matelas comme le manuel d'utilisation l'indique


1
BEFORE
TOUCHING
A PATIENT
2
BEFORE
CLEAN/ASEPTIC
PROCEDURE
3
AFTER BODY
FLUID EXPOSURE
RISK
4
AFTER
TOUCHING
A PATIENT
5
AFTER
TOUCHING PATIENT
SURROUNDINGS

Le lavage des mains
Comment ?

Laver vos mains au savon et à l'eau lorsqu'elles sont visiblement souillées.
Sinon, utiliser la friction hydro-alcoolique pour l'hygiène des mains.

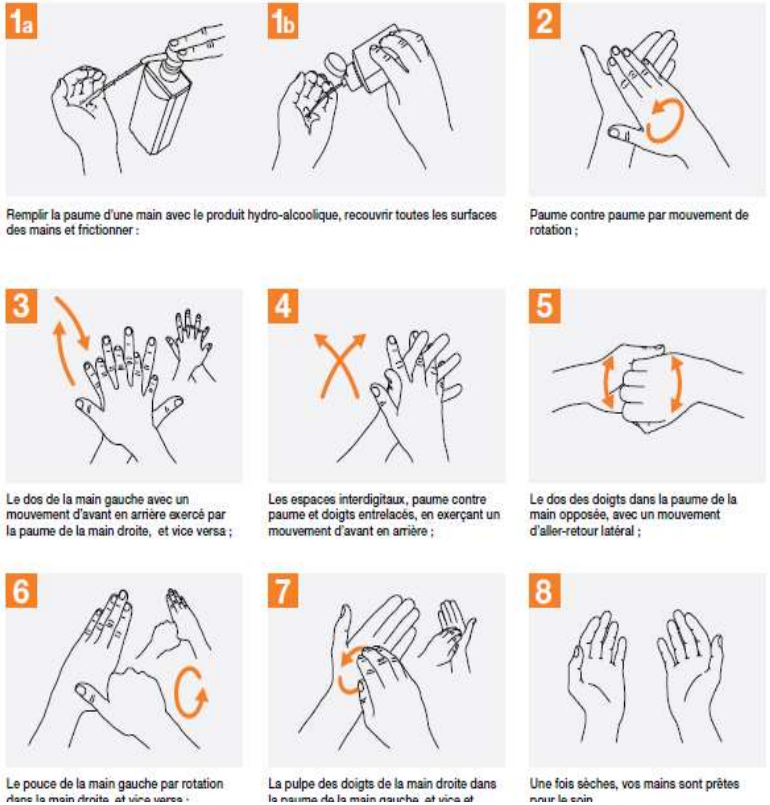
Durée de la procédure : 40-60 secondes

Organisation mondiale de la Santé | Sécurité des patients | SAVE LIVES Clean Your Hands

La friction hydro-alcoolique
Comment ?

Utiliser la friction hydro-alcoolique pour l'hygiène des mains !
Laver vos mains au savon et à l'eau lorsqu'elles sont visiblement souillées.

Durée de la procédure : 20-30 secondes



[Chanson Les mains propres]

In cammino per il mondo: neonatologia senza confini

SIN Società Italiana di Neonatologia


Le lavage des mains
Comment ?


Le lavage des mains
Comment ?


SAVE LIVES


Optima

Esperienza nella Neonatologia di Ngozi(Burundi) Osservatore esterno

- unico osservatore non conosciuto all'interno della "grande sale" della neonatologia durata complessiva di 7 ore in 6 sessioni pre e post formazione(2017)
- Le osservazioni sono state effettuate seguendo le linee guida dell'OMS con lo scopo di rilevare l'aderenza alle pratiche d'igiene delle mani.
- Durante ogni osservazione è stato rilevato il numero di opportunità che gli operatori sanitari - medici, infermieri e stagisti infermieri - hanno avuto per lavarsi le mani nonché il numero di volte e la modalità in cui questo è avvenuto.


GLOBAL HEALTH MEDIA PROJECT
Newborn Care Series
Cleaning Resuscitation Equipment

Criticità rilevate

- Utilizzo del telefonino …..e le APP !!?
- Disinfezione dei dispositivi condivisi: sonda del saturimetro-termometro-fonendoscopio-Ambu e mascherine etc..
- ***E le formiche??***

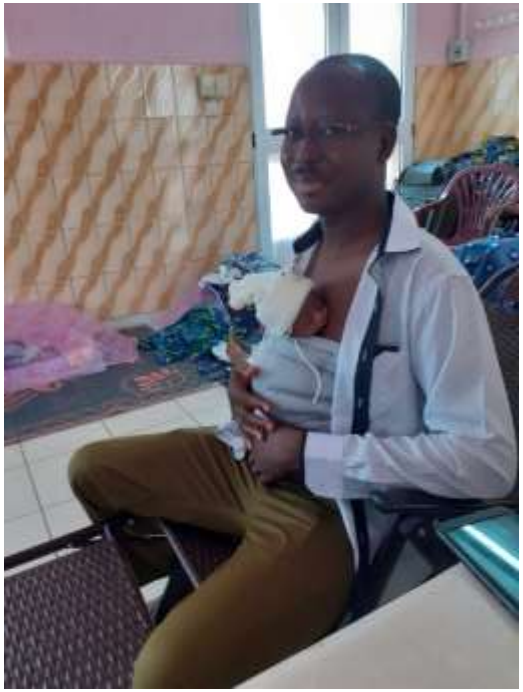
Kangaroo mother care and exclusive breastfeeding

se qualcuno ha ancora dei dubbi su chi vince la partita …

VS


manutenzione
efficienza
P5210065.JPG
polvere, urine, sangue, zanzare (morte)

Kangaroo Mother/Father Care challenge



Peer help

Formazione KMC

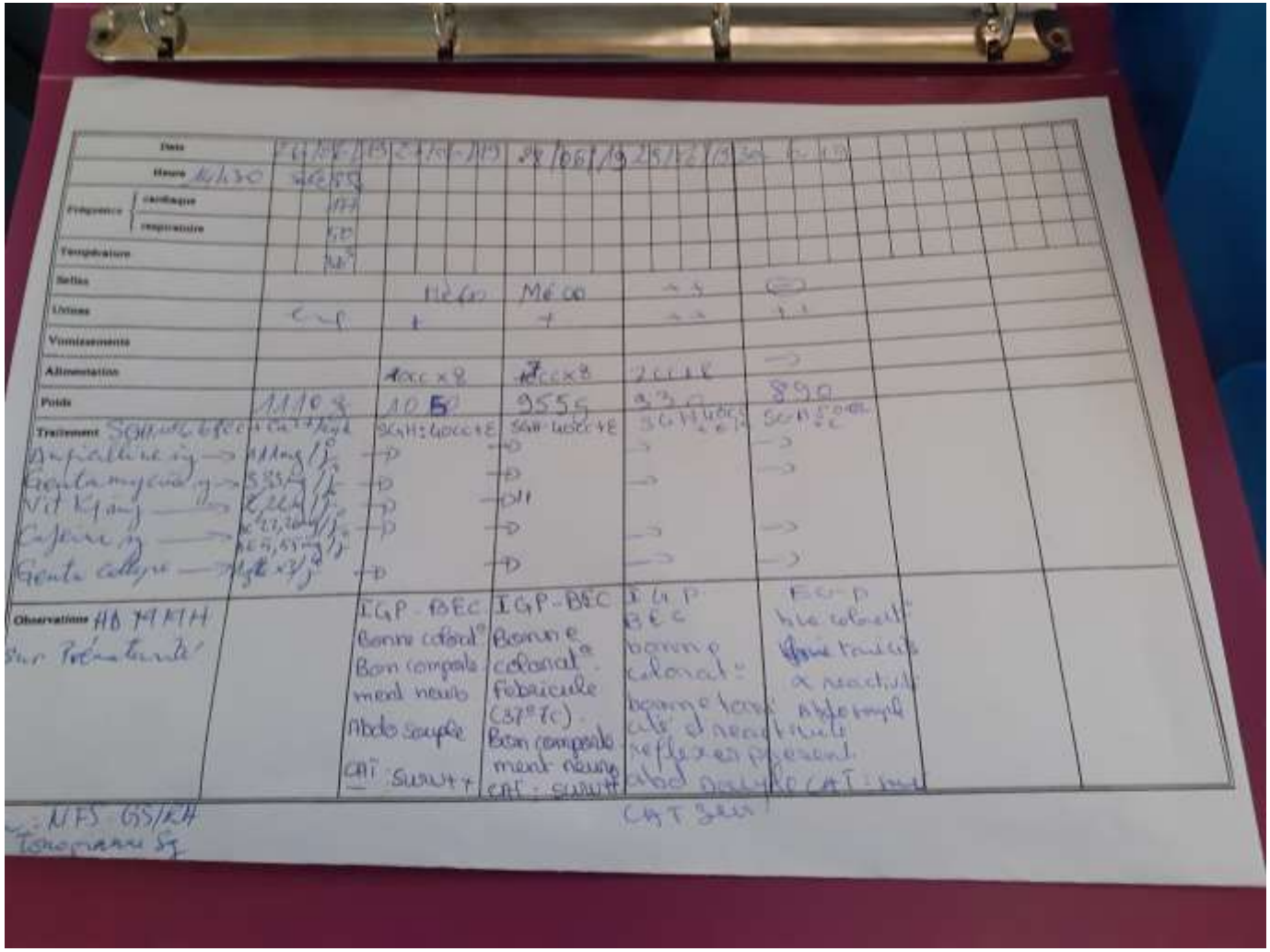
KMC intermittent

Quando la mamma non è sempre in reparto

Family centered newborn care

- Parents are part of the care team
- Emerging as an important feature of NICU care
- Creates unique Infection Prevention and control challenges

Nutritional Emergency



Recommandation for parenteral nutrition and fluids

	Starting Dose (1 giorno di vita)	Target
Energia Kcal/kg/die	≥ 45-55	90-120
Aminoacidi g/kg/die	≥ 1.5	3.5
Glucosio mg/kg/die	4-8	8-10
Lipidi g/kg/die	1-2	< 4
Calcio mg/kg/die	32-80	100-140
Fosforo mg/kg/die	31-62	77-108

Minimal Enteral Feeding (< 25ml/kg/die) con **latte materno o donato** in prima giornata, se neonato stabile e salvo controindicazioni

Table 1
Recommended parenteral fluid and electrolyte intake during the first days of life in neonates (Phase I of adaptation).[e]

	Days after birth				
	Day 1	Day 2	Day 3	Day 4	Day 5
Fluid intake[a] (ml/kg/d)					
Term neonate	40–60	50–70	60–80	60–100	100–140
Preterm neonate >1500 g	60–80	80–100	100–120	120–140	140–160
Preterm neonate 1000–1500 g	70–90	90–110	110–130	130–150	160–180
Preterm neonate <1000 g	80–100	100–120	120–140	140–160	160–180

Nutritional emergency

« In assenza di alimentazione parenterale solo l'alimentazione enterale completa permette di fornire i nutrimenti e le calorie necessarie

L'alimentazione enterale deve essere considerata al pari di una terapia

un neonato che non riceve almeno 110-120 kcal/kg/die (140 - 160 ml/kg/die di latte materno) va incontro a malnutrizione che apre la porta all'infezione

Quando l'alimentazione trofica è tollerata (dopo 3 giorni)si può calcolare individualmente la progressione giornaliera di latte materno (30ml o più) in modo da sospendere l'infusione di liquidi il più presto possibile »

Prof Rouvinez

Bed strenght and human resources

unicef for every child

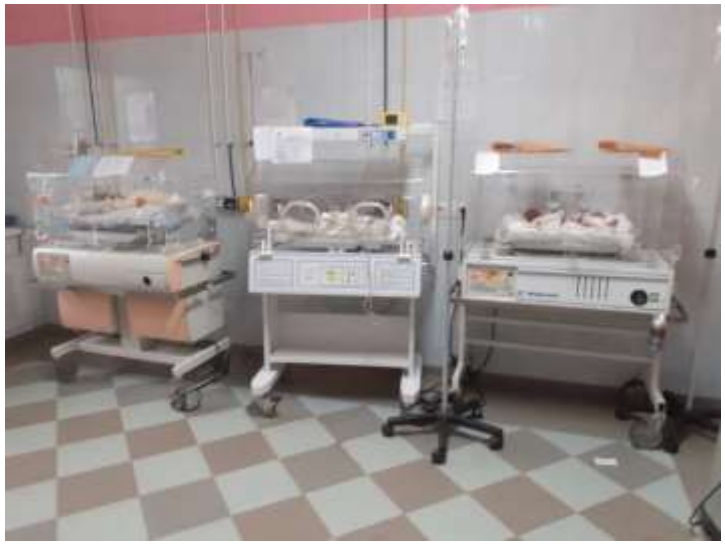
Infection Prevention and Control at Neonatal Intensive Care Units 2018

Spacing for Facilities with Newborns- 1

Type of design	Newborn nursery	Special care unit	NICU
Multi-patient rooms	• 2.2 square meters (24 net square feet) per infant • 1 meter (3 feet) between bassinets	• 11.2 square meters (120 net square feet) per infant • 2.4 meters (8 feet) between incubator /warmer/bassinet/ crib • Aisles > 1.2 meters (4 feet) wide	
Single patient rooms	2.2 square meters (24 net square feet), at least 1 meter (3 feet) in all directions between cribs	• > 14 square meters (150 net square feet)	> 14 square meters (150 net square feet) • 2.4 meter (8 feet) wide aisles • Space should be added for sinks, desks, cabinets, computers, and corridors

SIN SOCIETÀ ITALIANA DI NEONATOLOGIA

Too many neonates per unit



Recommendations for Nurse British Association of Perinatal Medicine Service Standards for hospitals providing neonatal care 2010

- Intensive care unit 1:1 –1:2patients
- High Dependency unit: 1:2-3patients
- Special Care Baby Units 1:3-4patients

«il numero minimo di infermiere per neonato in patologia neonatale deve essere di 1:8 senza differenze tra giorno e notte.

ma tutti gli ospedali in LIC lavorano su 2 turni di servizio al giorno e non 3 come in Italia e questo sembra difficilmente modificabile.

un medico esperto nella cura del neonato presente in ospedale 24-7 con 1 medico reperibile»

Appropriate use of antibiotics

«The cost-effective use of antimicrobials which maximizes clinical therapeutic effect,
while minimizing both drug-related toxicity
and the development of antimicrobial resistance.»
WHO 2001

«The access and excess dilemma»

General access to antibiotics to treat infections is a fundamental right to reduce child mortality.

At the same time, integrated, cross-sectoral approaches to infectious disease control, global antibiotic stewardship, sanitation and universal health care are needed.

The Lancet Infectious diseases 2013, The Lancet 2016, JOGH 2019

Risk associated with empirical administration of broad-spectrum antibiotics in neonatal care units

- Alteration of gut colonization
- Increasing risk of Candida colonization and invasive candidiasis
- Increased risk of death before discharge
- Emergency of resistant strains

Use of third generation cephalosporins or carbapenems are associated with an increased risk of invasive candidiasis (OR 2.2). *Pediatrics 2006, Clin perinat 2012*

The concurrent use of cefotaxime with ampicillin during the first three days after birth is associated with an increased risk of death, compared with the concurrent use of gentamicin. *Pediatrics 2006*

Overuse of third-generation cephalosporins favors the emergence of ESBL-producing strains of Gram-negative bacteria. *Curr Infect Dis Rep 2014*

Adverse effects of prolonged courses of empirical antibiotic treatment in neonatal care unit

Recent cohort studies show an association between the duration of empirical antibiotic therapy and:

- Mortality
- Necrotizing enterocolitis
- Late onset sepsis

Each additional day of antibiotic therapy was associated with a 7% increase in the odds of NEC and 16% of death. *Pediatrics 2009*

Antibiotic exposure for > 10 days resulted in a threefold increase in the risk of NEC. *J Pediatr 2011*

Prolonged antibiotic therapy (≥ 5 days) initiated on the day of birth was independently associated with LOS and the composite outcome of LOS, NEC or death. *J Pediatr 2011*

The effectiveness of antibiotics is declining worldwide, by ever-higher rates of their use and selection pressure for resistance

Resistant clones, eg. **meticillin-resistant Staphylococcus aureus (MRSA), Escherichia coli ST131, Klebsiella ST258 are disseminated rapidly worldwide**.

This spread is facilitated by interspecies gene transmission, poor sanitation and hygiene in communities and hospitals, misuse and overuse of antibiotics, and the increasing frequency of global, travel, trade, and disease transmission.

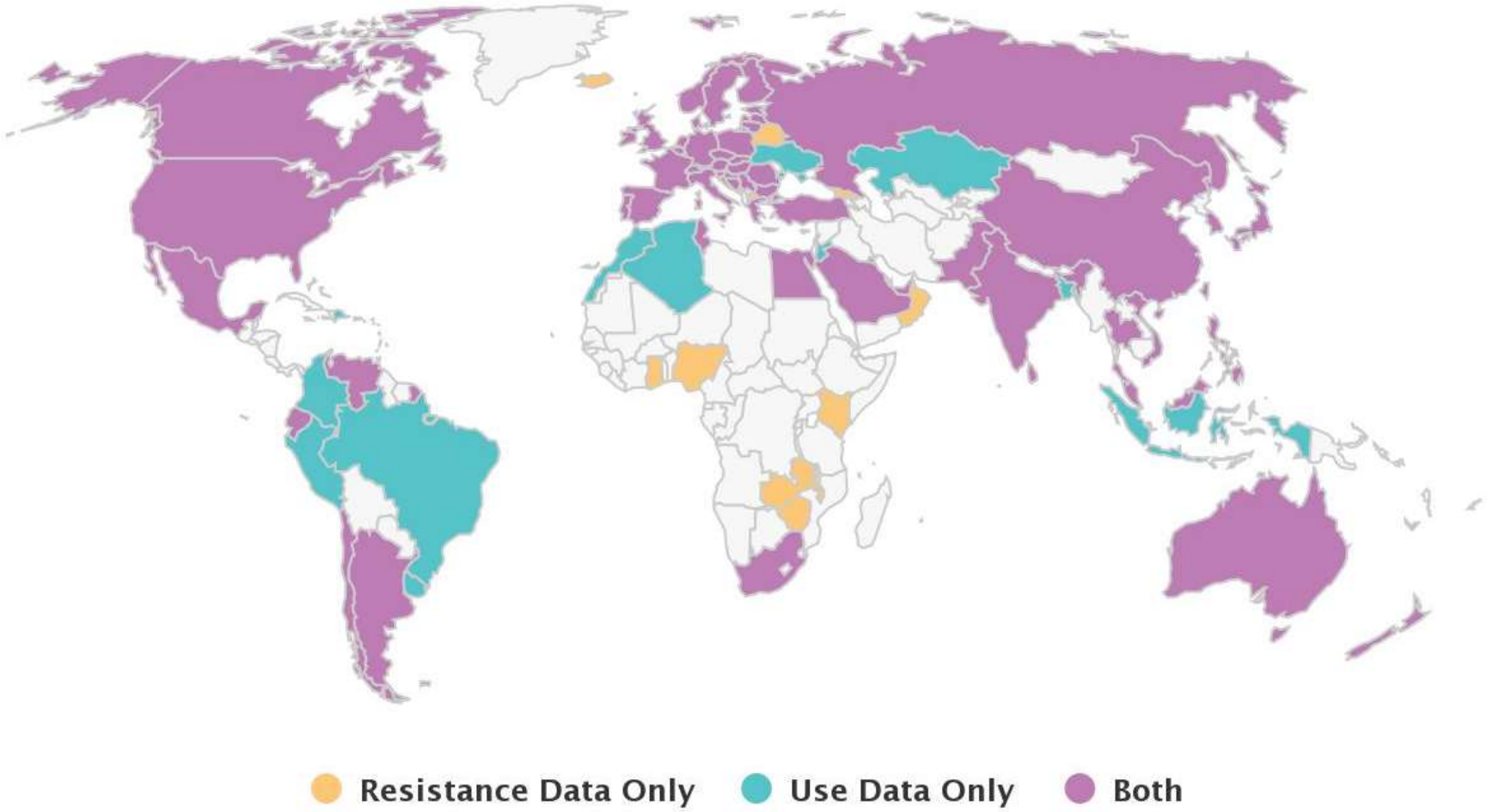
In low and middle-income countries antibiotic use is increasing.

Solving the challenge of providing effective antibiotics requires **balancing access and resistance**.

The Lancet Infectious Diseases Commission 2013

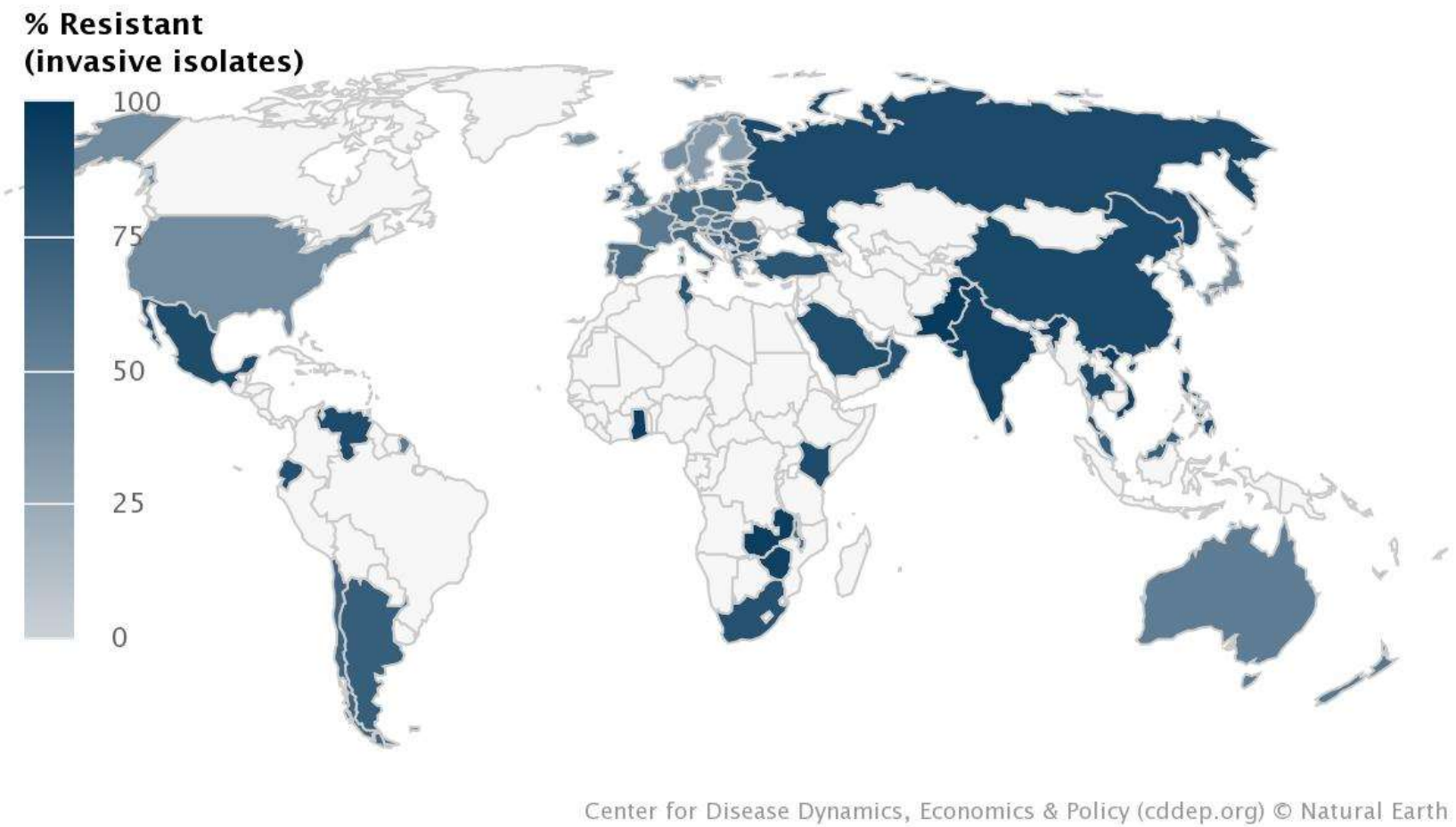
Global epidemiology of antibiotic resistance and use

ResistanceMap Data Availability



ResistanceMap.org

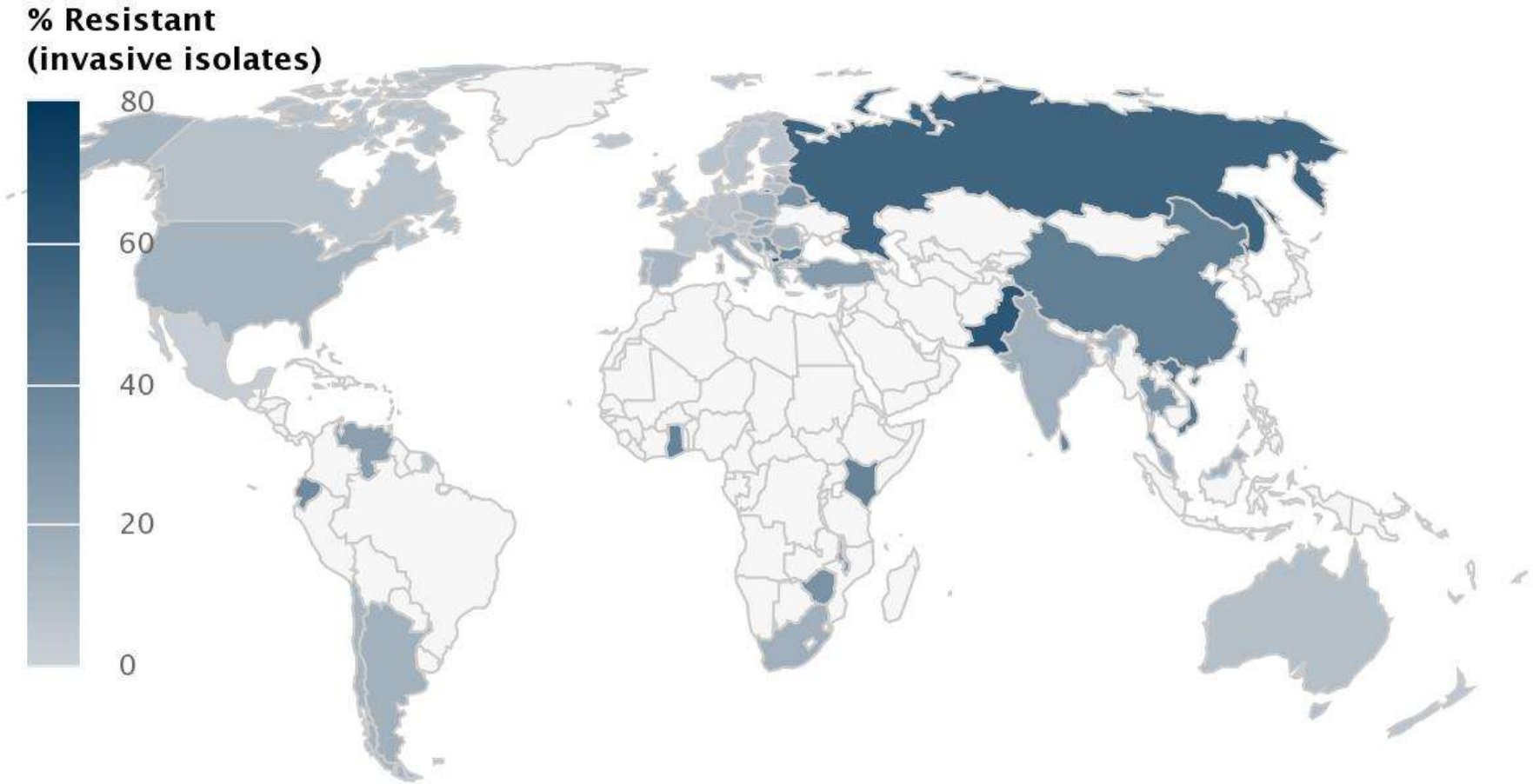
Antibiotic Resistance is spreading worldwide



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

Resistance of *Escherichia coli* to Aminoglycosides



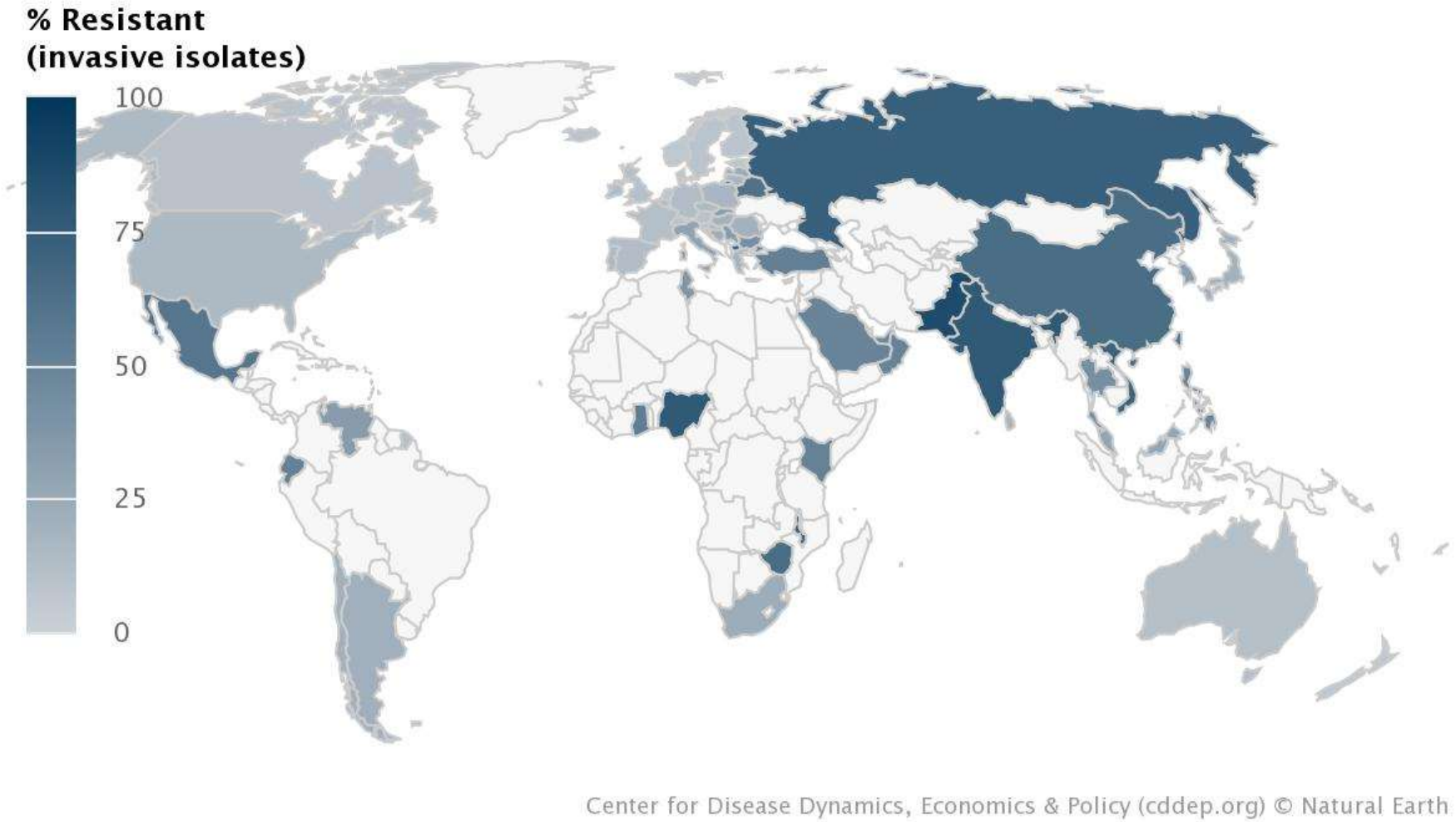
Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

SIN

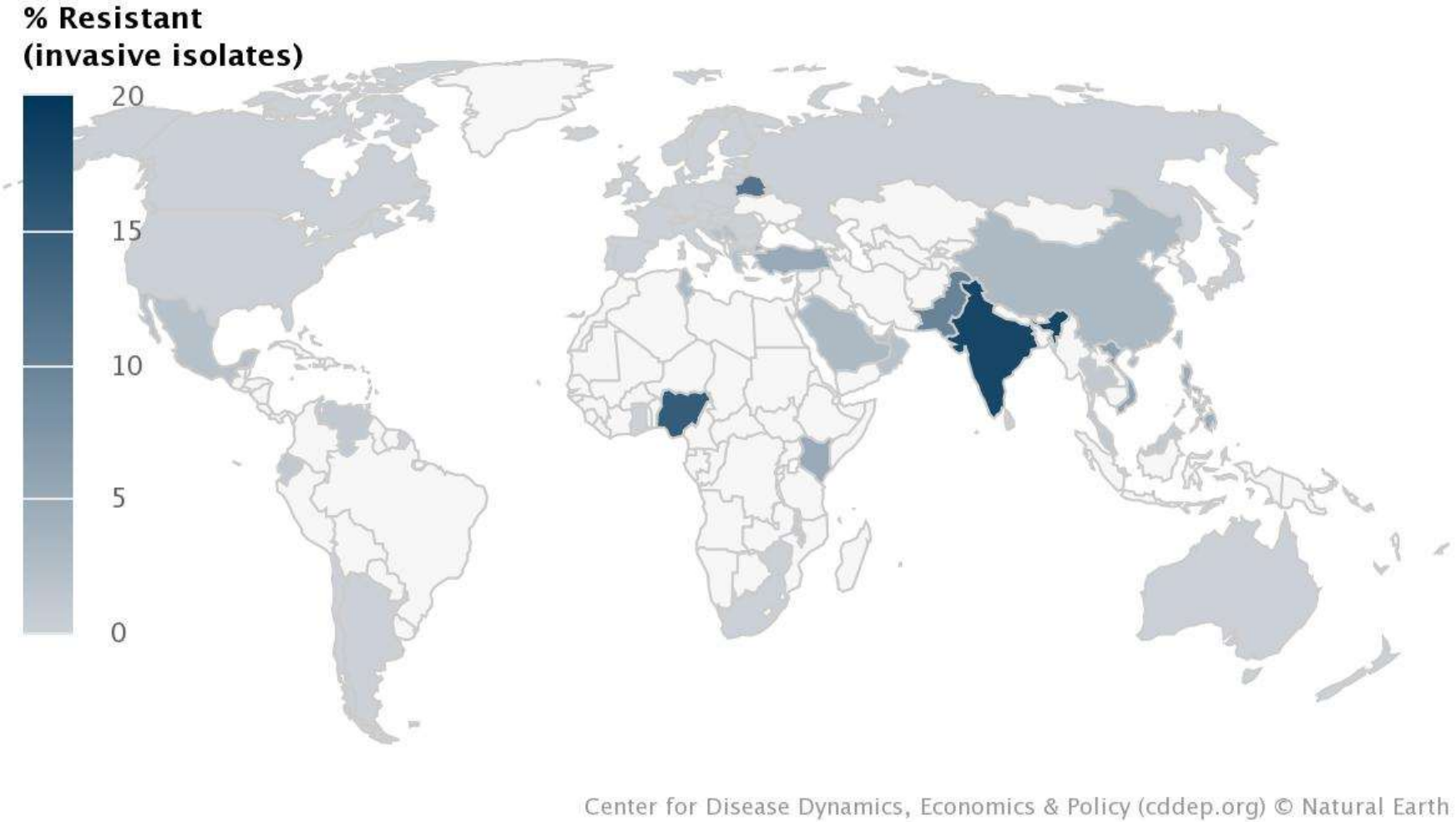
Resistance of *Escherichia coli* to Cephalosporins (3rd gen)



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

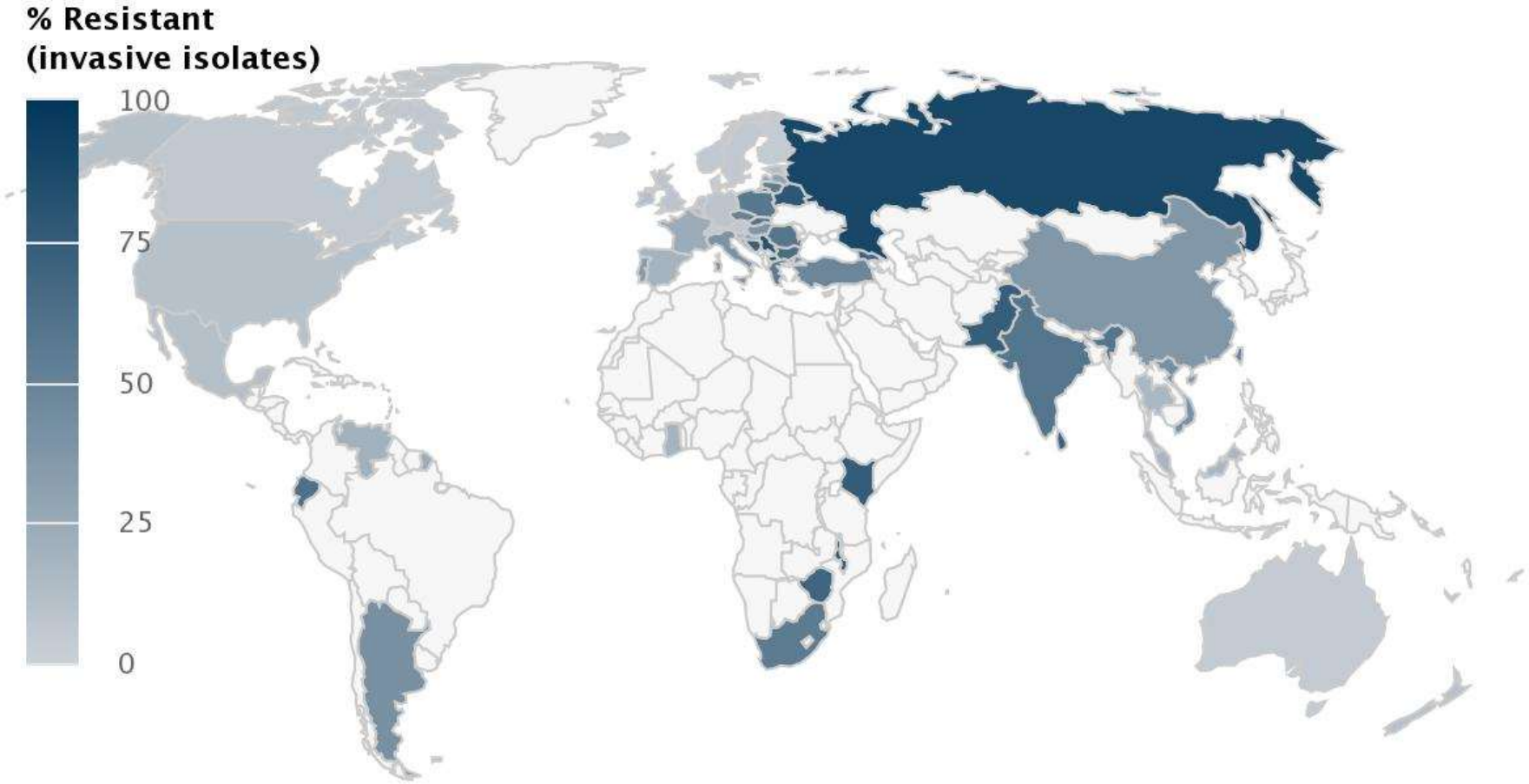
Resistance of *Escherichia coli* to Carbapenems



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

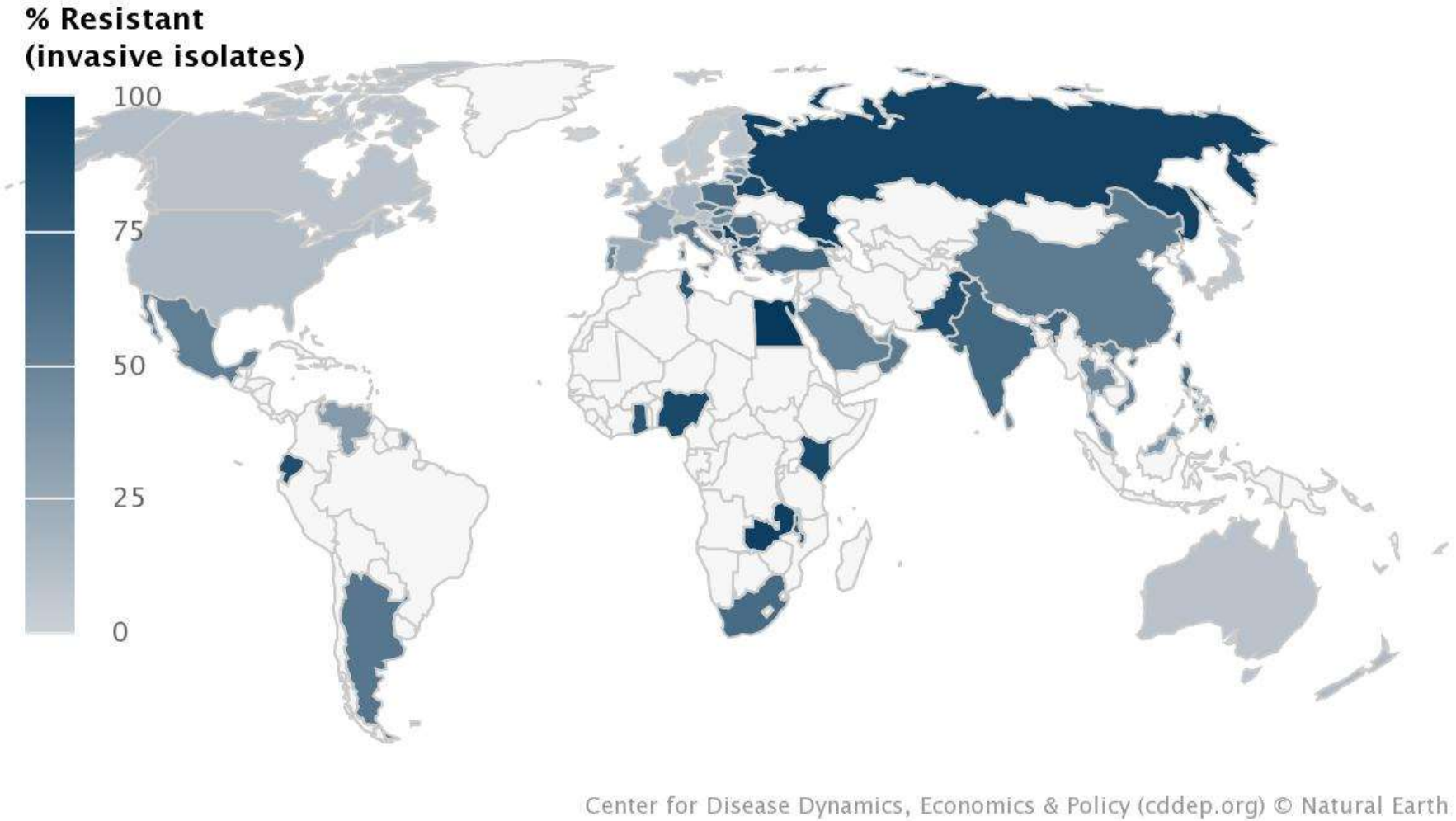
Resistance of *Klebsiella pneumoniae* to Aminoglycosides



Center for Disease Dynamics, Economics & Policy (cddep.org) © Natural Earth

ResistanceMap.org

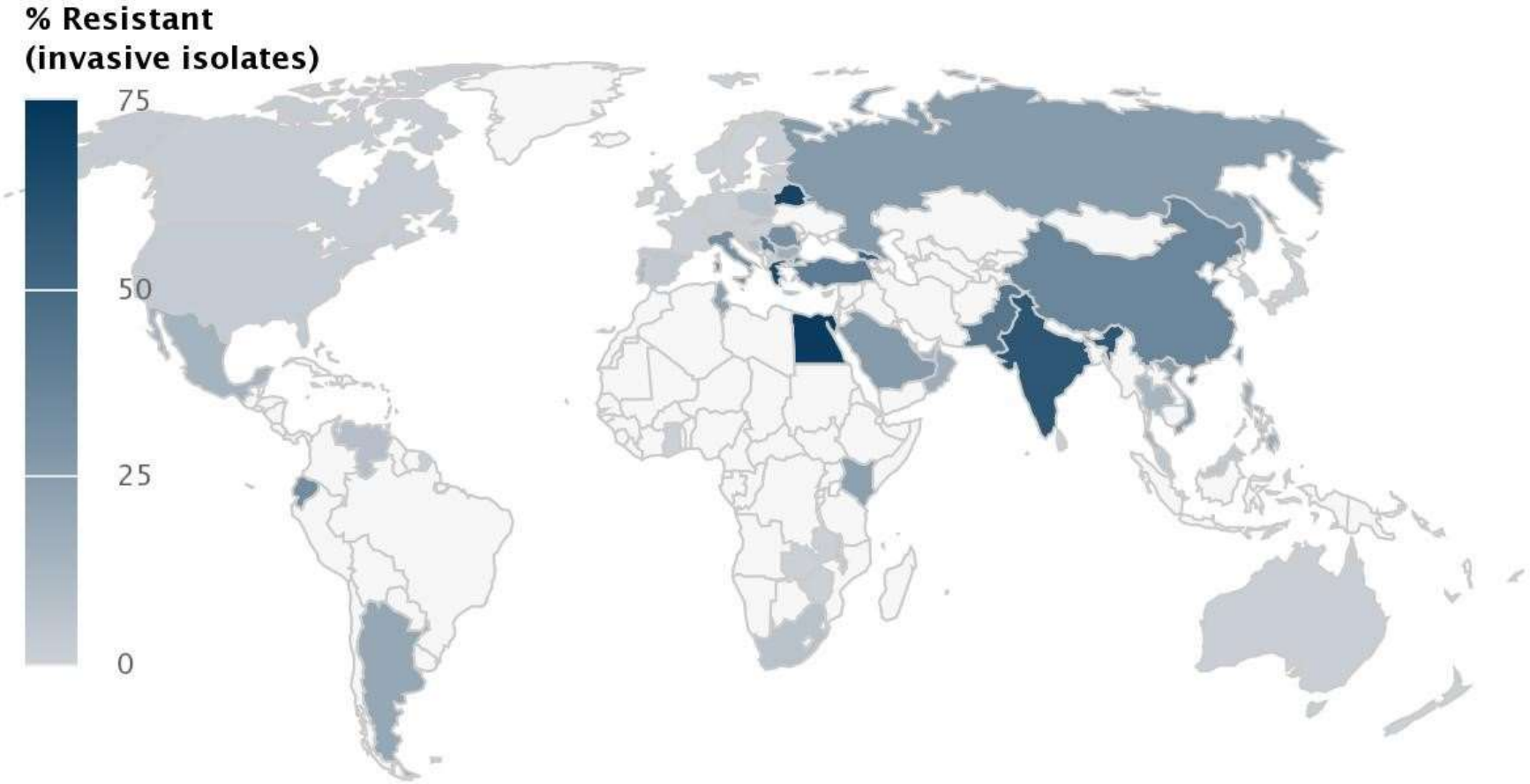
Resistance of *Klebsiella pneumoniae* to Cephalosporins (3rd gen)



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

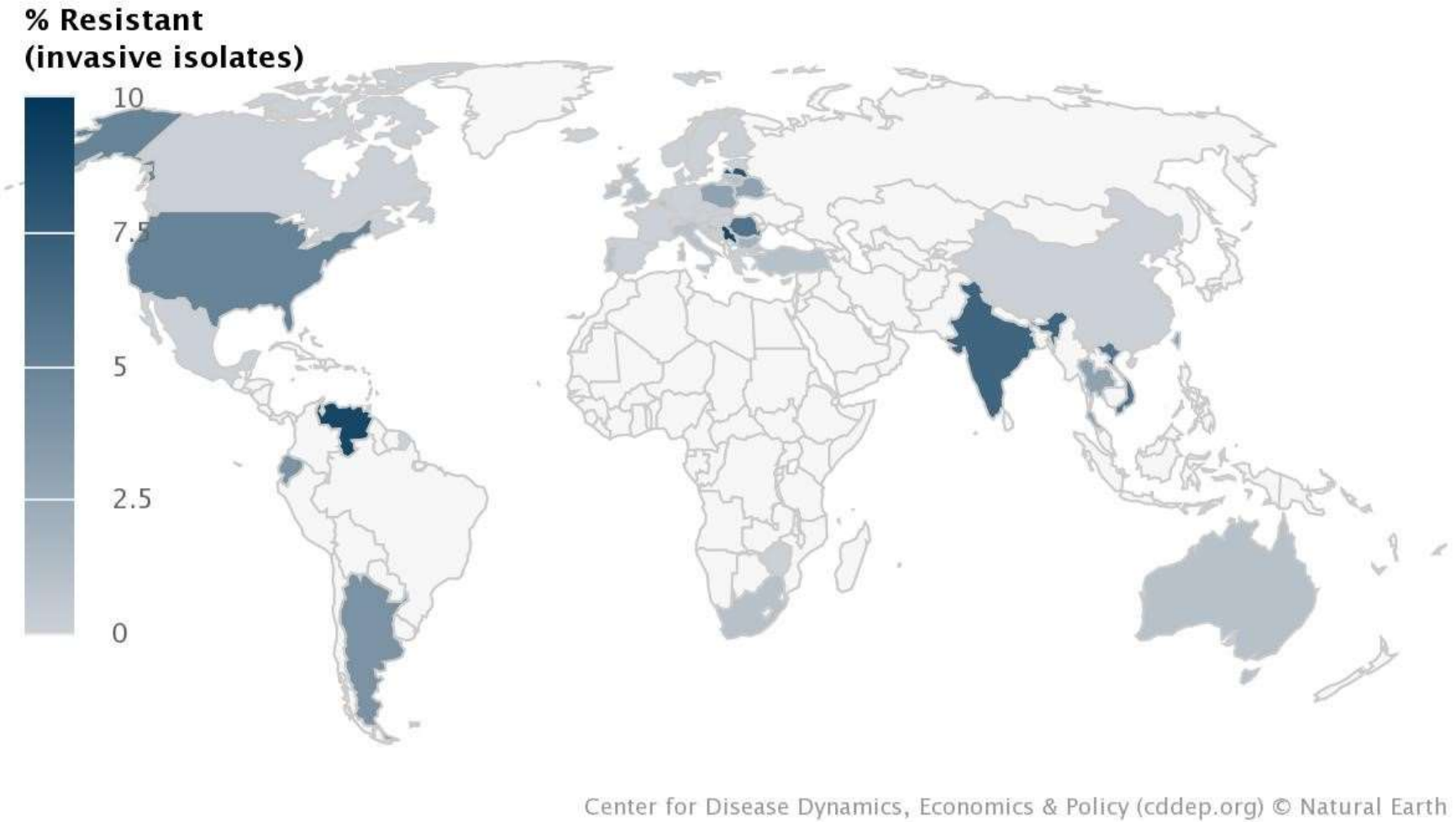
Resistance of *Klebsiella pneumoniae* to Carbapenems



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

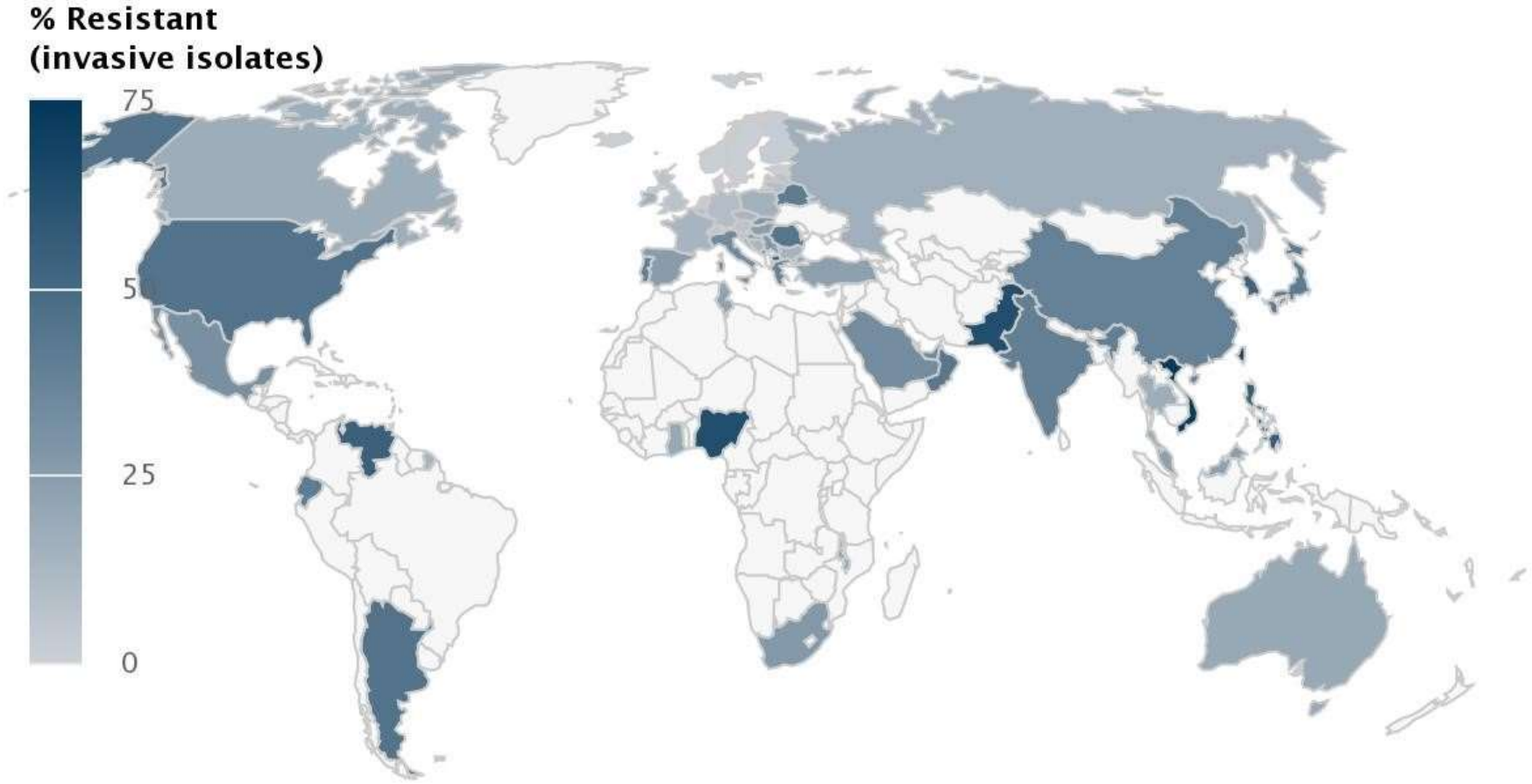
Resistance of *Enterococcus faecalis* to Vancomycin



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

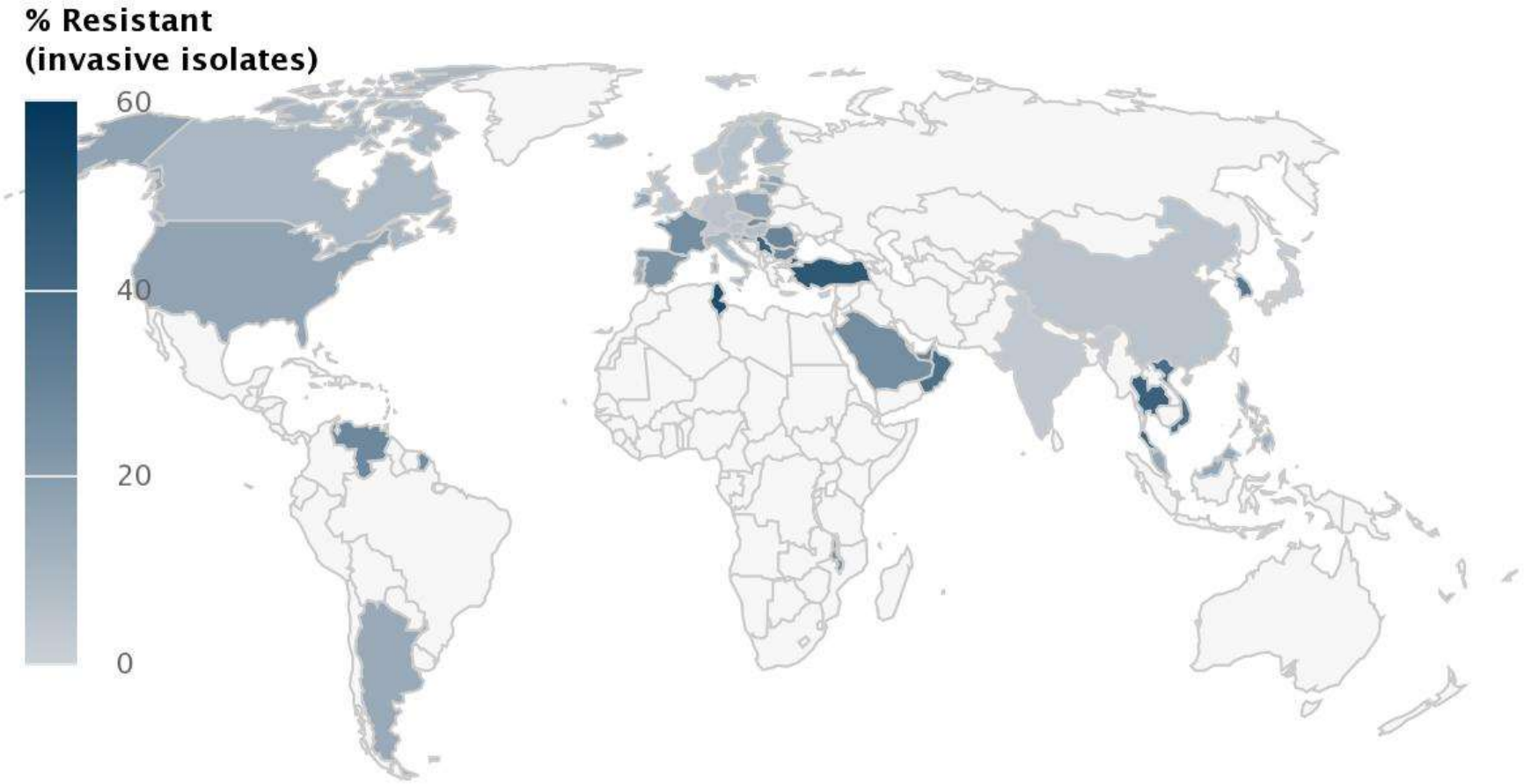
Resistance of *Staphylococcus aureus* to Oxacillin (MRSA)



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

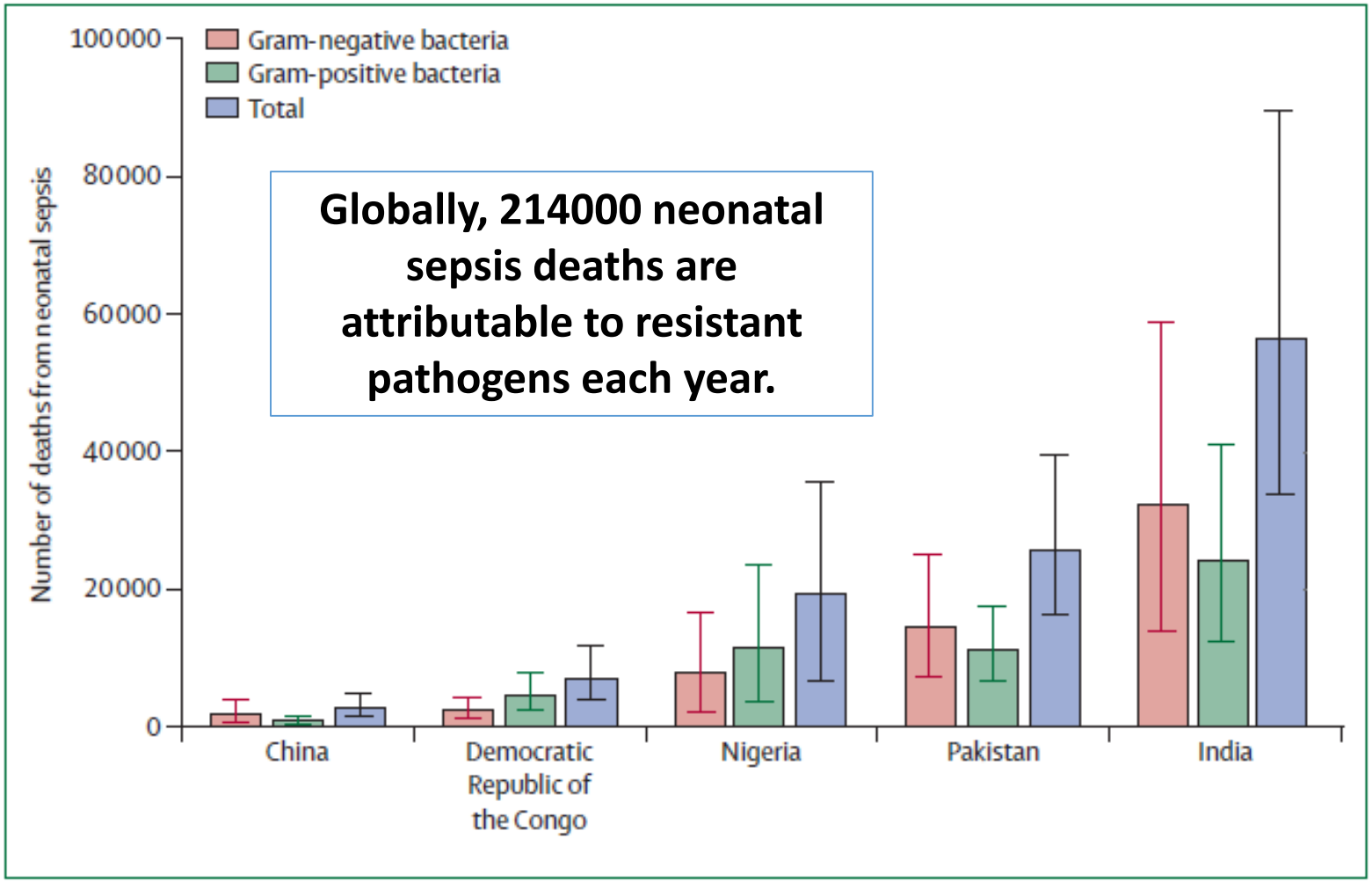
Resistance of *Streptococcus pneumoniae* to Penicillins



ResistanceMap.org

In cammino per il mondo: neonatologia senza confini

Estimated neonatal sepsis deaths/year caused by bacteria resistant to first-line antibiotics in five high-burden countries



Antimicrobials: access and sustainable effectiveness. The Lancet 2016

High prevalence of colonisation with carbapenem-resistant Enterobacteriaceae among patients admitted to Vietnamese hospitals: Risk factors and burden of disease

Journal of Infection 2019

In LMICs antibiotic resistance is a serious problem, due to limitations of resources for surveillance of resistances and for infection prevention and control.

CRE colonisation according to level of care and type of department.

Patient type	Variable	ICU	Ward	Emergency	Total
Neonatal	N Total	247			247
	N CRE+	161			161
	%CRE+	**65**			**65**
	N KP	99			99
	N EC	89			89
Paediatric	N Total	391	772	56	1219
	N CRE+	270	376	9	655
	%CRE+	**69**	**49**	**16**	**54**
	N KP	171	342	4	517
	N EC	117	347	7	471

Klebsiella pneumoniae was 55% carbapenem resistant and the most common cause of infection in pediatric ICUs.

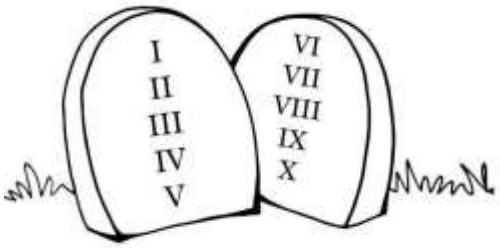
At an 80-bed NICU mortality was singnificantly associated (OR 5.5) with CRE colonisation and hospital-acquired infection.

Risk factors for CRE colonisation: long hospitalization, HAI, treatment with a carbapenem.

Against killer superbugs WHO recommends:

1. Infection prevention and control strategies
2. Hand hygiene
3. Surveillance of CRE infections and colonizations
4. Contact precautions
5. Patient isolation/cohort care
6. Environmental cleaning
7. Surveillance cultures of the environment
8. Monitoring, auditing and feedback (appropriate ATB use)

«Ten commandments» for the appropriate use of antibiotics



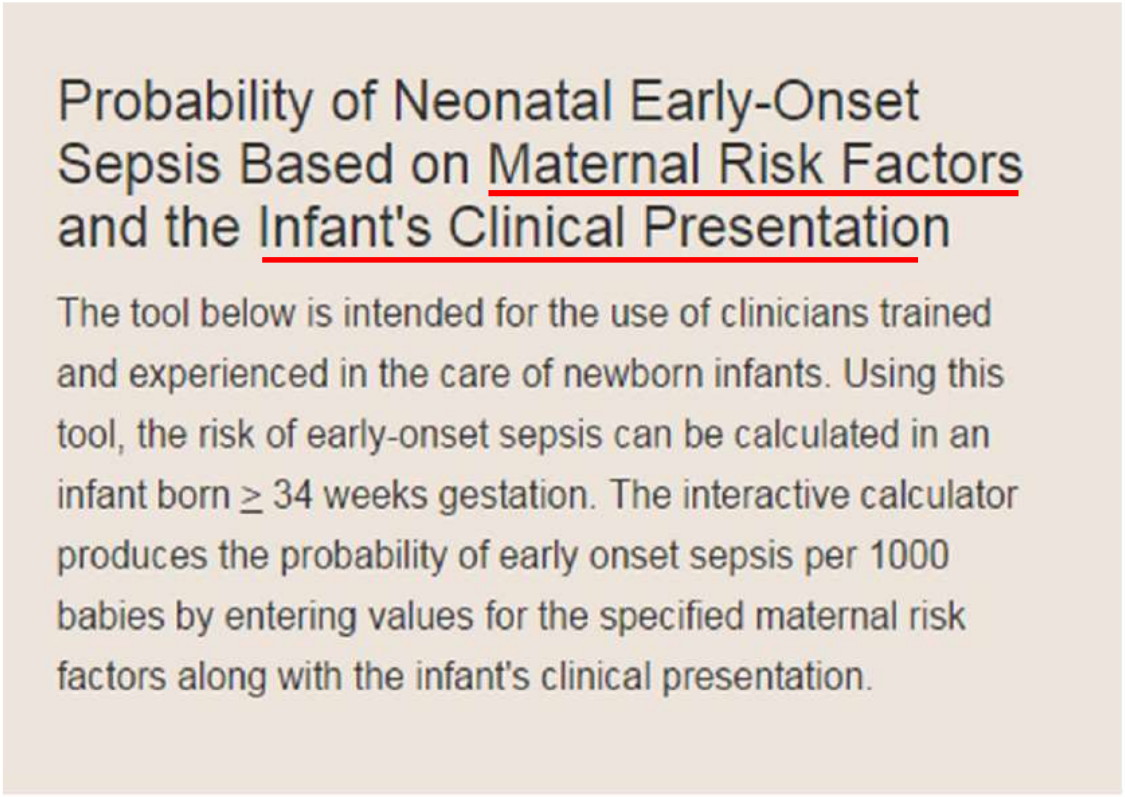
1. Use antibiotic **ONLY WHEN NEEDED**
2. Prescribe **ATB EMPIRICALLY but INTELLIGENTLY:** know local epidemiology and susceptibility trends
3. Rely upon the clinical **MICROBIOLOGY LABORATORY**
4. Select the **ADEQUATE** ANTIBIOTIC
5. Consider **PHARMACOKINETICS and PHARMACODYNAMICS**
6. Use **THE SHORTEST ATB COURSE** that has proven clinical efficacy
7. Use **ATB COMBINATION ONLY IN SPECIFIC SITUATIONS**
8. Follow **ONLY EVIDENCE-BASED GUIDELINES**
9. Avoid low quality and sub-standard drugs
10. Prevent self-prescription and prescription changes

Frontiers in Microbiology, 2011

1. Use antibiotic **ONLY WHEN NEEDED**

Neonatal Early-Onset Sepsis Calculator

- https://neonatalsepsiscalculator.kaiserpermanente.org/



Available on a website and/or mobile phone

Puopolo et al.

Neonatal Early-Onset Sepsis Calculator

Please enter details below.

Predictor	Scenario
Incidence of Early-Onset Sepsis	0.5/1000 live births (CDC nationa
Gestational age	35 weeks 4 days
Highest maternal antepartum temperature	98.8 Fahrenheit
ROM (Hours)	7.8
Maternal GBS status	◉ Negative ○ Positive ○ Unknown
Type of intrapartum antibiotics	○ Broad spectrum antibiotics > 4 hrs prior to birth ○ Broad spectrum antibiotics 2-3.9 hrs prior to birth ○ GBS specific antibiotics > 2 hrs prior to birth ◉ No antibiotics or any antibiotics < 2 hrs prior to birth

Calculate » Clear

Risk per 1000/births	
EOS Risk @ Birth	0.58

EOS Risk after Clinical Exam	Risk per 1000/births	Clinical Recommendation	Vitals
Well Appearing	0.24	No culture, no antibiotics	Routine Vitals
Equivocal	2.89	Blood culture	Vitals every 4 hours for 24 hours
Clinical Illness	12.13	Empiric antibiotics	Vitals per NICU

Classification of Infant's Clinical Presentation Clinical Illness Equivocal Well Appearing

Neonatal Early-Onset Sepsis Calculator

Classification of Infant's Clinical Presentation

Clinical Exam	Description
Clinical Illness	1. Persistent need for NCPAP / HFNC / mechanical ventilation (outside of the delivery room) 2. Hemodynamic instability requiring vasoactive drugs 3. Neonatal encephalopathy /Perinatal depression ▪ Seizure ▪ Apgar Score @ 5 minutes < 5 4. Need for supplemental O_2 ≥ 2 hours to maintain oxygen saturations > 90% (outside of the delivery room)
Equivocal	1. Persistent physiologic abnormality ≥ 4 hrs ▪ Tachycardia (HR ≥ 160) ▪ Tachypnea (RR ≥ 60) ▪ Temperature instability (≥ 100.4°F or < 97.5°F) ▪ Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O_2 2. Two or more physiologic abnormalities lasting for ≥ 2 hrs ▪ Tachycardia (HR ≥ 160) ▪ Tachypnea (RR ≥ 60) ▪ Temperature instability (≥ 100.4°F or < 97.5°F) ▪ Respiratory distress (grunting, flaring, or retracting) not requiring supplemental O_2 Note: abnormality can be intermittent
Well Appearing	No persistent physiologic abnormalities

Association of Use of the Neonatal Early Onset Sepsis Calculator with Reduction in Antibiotic Therapy and Safety: A Systematic Review and Meta-analysis.

JAMA 2019

13 studies analyzing a total of 175,752 newborns were included.

Meta-analysis revealed a **relative risk of antibiotic use of 56% (95% CI, 53%-59%) in before-after studies including newborns** regardless of exposure to chorioamnionitis.
Proportions of missed cases of EOS were comparable between management guided by the EOS calculator (5 of 18 [28%]) and conventional management strategies (8 of 28 [29%]) (pooled odds ratio, 0.96; 95% CI, 0.26-3.52; P = .95).

CONCLUSIONS AND RELEVANCE:
Use of the neonatal EOS calculator is associated with a **substantial reduction in the use of empirical antibiotics** for suspected EOS, with no increase in missed cases of sepsis.

Sepsis calculator to support antibiotic stewardship in early-onset neonatal sepsis: a meta-analysis

Paediatrica Indonesiana 2018

From five studies, the use of sepsis calculator reduced:

- Inappropriate use of antibiotics (RR 0.46)
- Blood culture sampling (RR 0.46)
- Higher level neonatal care admissions (RR 0.68)

This calculator could be implemented at no extra cost

CATEGORICAL RISK ASSESSMENT

Obstetric Specific Risk Factors:

Major

- Maternal fever (>38°C)
- Membrane rupture >18 hours
- Foul-smelling amniotic fluid
- Vaginal or urinary infection
- Chorioamnionitis
- Membrane rupture < 37 wks GA
- Preterm delivery (< 35 wks GA)

Minor

- Membrane rupture >12 <18 hours
- Preterm delivery 35-37 wks GA
- Stained amniotic fluid
- Alterations in fetal heart rate or unexplained birth asphyxia

Suspected sepsis if
1 major or 2 minor

Clinical signs of possible neonatal sepsis (PSBI):

- ✓ Respiratory distress
- ✓ Cariovascular instability
- ✓ Neurological signs
- ✓ Gastrointestinal signs
- ✓ Skin and Umbilical signs
- ✓ Musculoskeletal signs
- ✓ Temperature < 35.5 or > 37.7 °C

Protocol used in Benin hospitals, by N. Rouvinez

EOS E. coli GBS K. Pneumonia N. gonorrhoeae	Penicillin + gentamicin
	- if *Listeria monocytogenes*: amoxicillin + gentamicin
	- if *S.aureus*: flucloxacillin + gentamicin
LOS	*First line*: flucloxacillin + gentamicin
Gram-negative Stap. aureus Strept. Pneum.	*Second line:*
	- vancomycin + gentamicin (with caution)
	- vancomycin + piperacillin/tazobactam (to extend Gram-negative cover)
	Third line: meropenem, ciprofloxacin
Meningitis	*First line*: cefotaxime with amoxicillin ± gentamicin
	Second line: meropenem
Gram positive multiresistant bacteria	Currently: glycopeptide antibiotics are the mainstay of therapy, especially vancomycin; if necessary linezolid, clindamycin, rifampicin and daptomycin could be alternative regimens
	In the future: novel cephalosporins like ceftaroline and ceftobiprole; novel lipoglycopeptide antibiotics are oritavacin and dalbavancin; telavacin has been approved in the USA in adults
Gram negative multiresistant bacteria	Currently: aminoglycosides and cephalosporins are the antibiotics of choice; carbapenems, colistin, co-trimoxazole, ticarcillin-clavulanic acid could be the an alternative; fluoroquinolone, ciprofloxacin, tigecycline and tetraciclins could only be justified in extreme cases.
	In the future: treatment options are extremely limited

2. Prescribe ATB **empirically but intelligently**: KNOW LOCAL EPIDEMIOLOGY and SUSCEPTIBILITY TRENDS

<u>Barriers in LMICs</u>:

lack of culture laboratory tests and antibiograms
and
scarce microbiological surveillance data

Arch Dis Fet Neon Ed 2012
Early Hum Dev 2012

3. Rely upon the clinical **MICROBIOLOGY LABORATORY**

4. Select the **ADEQUATE ANTIBIOTIC**

In LMICs most hospitals often lack:

- ✓ Basic laboratory investigations, such as C-reactive protein and full blood count
- ✓ Microbiological facilities to detect invasive infections (blood and cerebrospinal fluid cultures)
- ✓ Reliable surveillance programs

Epidemiological surveillance of infections and antibiotic use and resistance in LMICs is imperative.

Managing severe infection in infancy in resource poor settings, Early Hum Dev 2012

5. Consider **PHARMACOKINETICS and PHARMACODYNAMICS**

To designing rational dosing schemes, we need to consider:

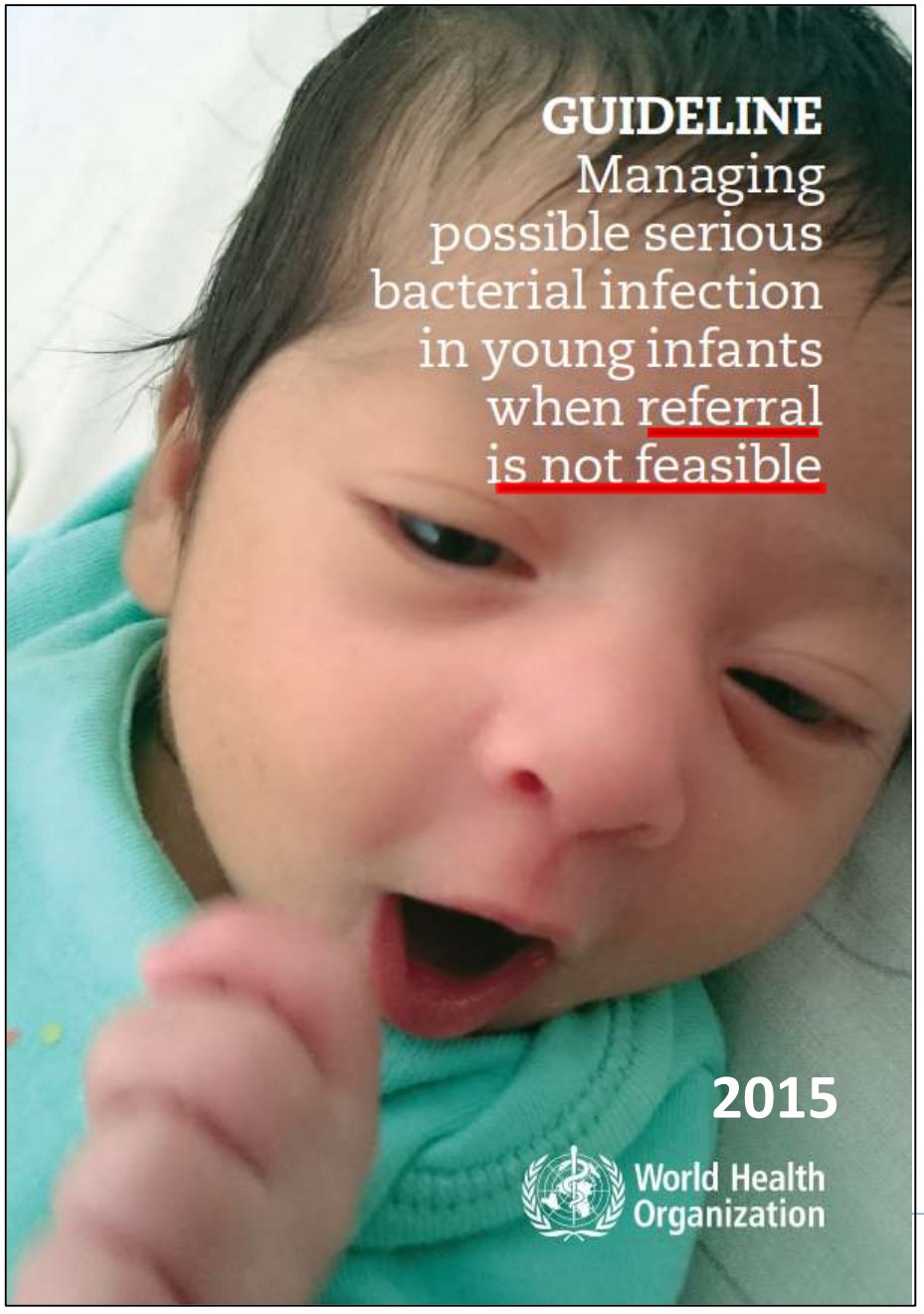
1. ATB can be classified as:

Concentration-dependent: aminoglycosides, fluoroquinolones, colistin, metronidazole

Time-dependent: beta-lactams and most macrolides

2. ATB **dosing must be adjusted** for current weight, gestational age, chronological age, renal function, to avoid prescribing too little or too much.

3. Use the **intravenous or**, if not possible, the **intramuscular route**.
Avoid oral administration.



ATB management in community-based neonatal sepsis

Recommendation 4: Young infants (0–59 days) identified with clinical severe infection whose families do not accept or cannot access hospital care should be managed in outpatient settings by an appropriately trained health worker with one of the two following regimens:

Option 1: Intramuscular gentamicin 5–7.5 mg/kg *(4)* (for low-birth-weight infants gentamicin 3–4 mg/kg) once daily for seven days and twice daily oral amoxicillin, 50 mg/kg per dose for seven days. Close follow-up is essential.

Strong recommendation based on moderate quality evidence

Option 2: Intramuscular gentamicin 5–7.5 mg/kg *(4)* (for low-birth-weight infants gentamicin 3–4 mg/kg per day once daily) once daily for two days and twice daily oral amoxicillin, 50 mg/kg per dose for seven days. Close follow-up is essential. A careful assessment of the child on day 4 is mandatory for this option in order to determine if the child is improving.

Strong recommendation based on low quality evidence

SATTs & AFRINEST RCT trials

In cammino per il mondo: neonatologia senza confini

6. Use **THE SHORTEST ATB COURSE** that has proven clinical efficacy

SHORTER IS BETTER

- 10 days for bacteraemia
- 14 days for GBS uncomplicated meningitis
- 21 days minimum for Gram-negative meningitis and Lysteria monocytogenes
- 4-6 weeks for complicated infections

- 7-10 days in neonates > 1500 g BW, who become asymptomatic with 5 days of therapy, if cultures are sterile in a well-appearing child

In neonates with negative cultures at 48 hours:

- STOP antibiotics at 48 hours, if asymptomatic
- Continue treatment for 7 days, if clinical signs of sepsis persist over 24 hours

Neonatal sepsis, The Lancet 2017
Choice and duration of antimicrobial therapy for neonatal sepsis, Int J Ped 2011

Prophylactic antibiotics in neonates at risk:

WHO recommendations

WHO 2013

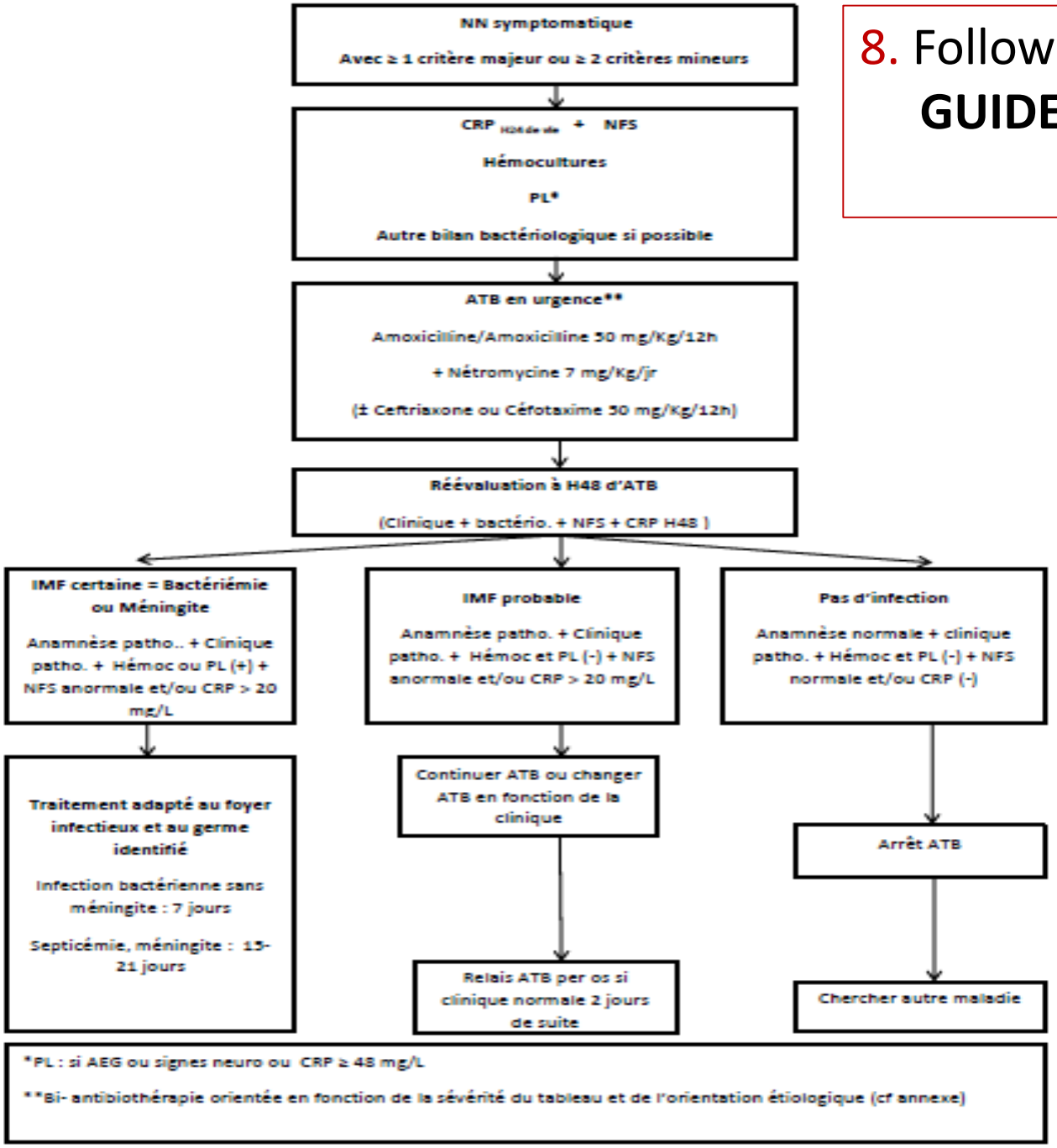
- Give prophylactic antibiotics to neonates with documented risk factors for infection:

  - Membranes ruptured > 18 h before delivery.
  - Mother had fever > 38° C before delivery or during labour.
  - Amniotic fluid was foul-smelling or purulent.

- Give IM or IV ampicillin and gentamicin for at least **2 days and reassess**
- **Continue treatment only if there are signs of sepsis (or a positive blood culture)**.

7. Use **ATB COMBINATIONS ONLY IN SPECIFIC SITUATIONS**

- Consider a third-generation cephalosporin to add to ampicillin plus aminoglycoside only for meningitis.
- Avoid therapy with overlapping activity: eg. meropenem with metronidazole to treat necrotizing enterocolitis.
- Tailor therapy to pathogen and discontinue the therapy if pathogen not isolated, or based on suceptibility test.

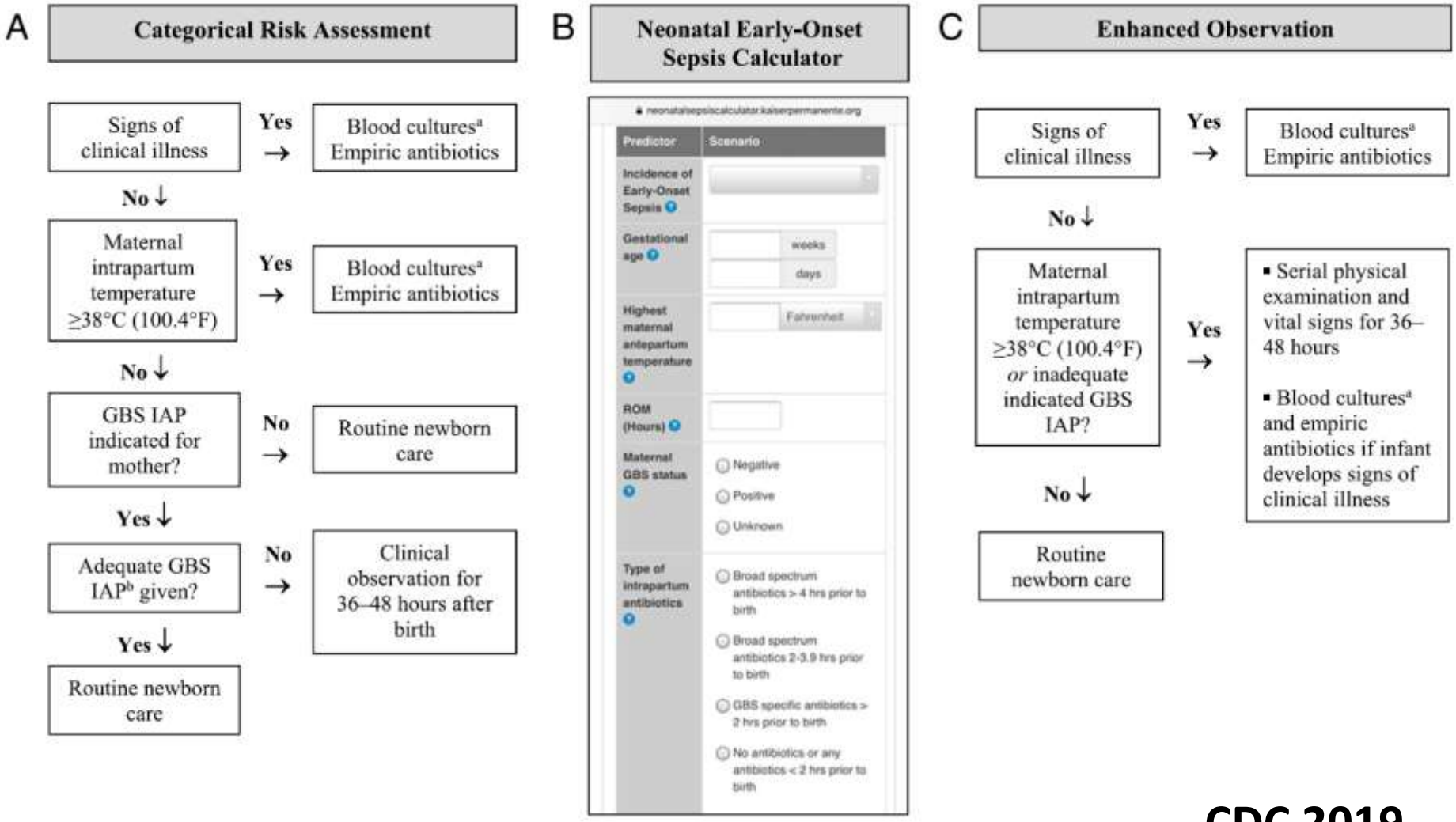


8. Follow only evidence-based **GUIDELINES**

- CHUMEL, Cotonou, Benin
- Hospital Saint-Jean De Dieu, Tanguieta, Benin
- L'abbraccio Hopital des Enfants, Sokponta, Benin

By Nicole Rouvinez

Prophylactic antibiotics in neonates at risk: CDC recommendations



CDC 2019

Table 1. Current WHO recommendation for antibiotic therapy in infants aged 0–59 days with signs of possible serious bacterial infection or for prophylaxis.

Reference	Conditions	Antibiotics	Dosing regimen
Pocket Book of Hospital Care for Children, 2013	Prophylaxis in neonates with documented risk factors	IM or IV ampicillin and gentamicin for at least 2 days	*Gentamicin* (IM/IV): First week of life Low-birthweight infants: 3 mg/kg once a day; normal birthweight: 5 mg/kg per dose once a day Weeks 2–4 of life: 7.5 mg/kg once a day *Ampicillin* (IM/IV): First week of life: 50 mg/kg every 12 h Weeks 2–4 of life: 50 mg/kg every 8 h *Benzylpenicillin (penicillin G)* (IM): First week of life: 50,000 U/kg every 12 h; weeks 2–4 and older: 50,000 U/kg every 6 h *Procaine benzylpenicillin* (IM): 50,000 U/kg once a day *Cloxacillin* (IV): First week of life: 25–50 mg/kg every 12 h Weeks 2–4 of life: 25–50 mg/kg every 8 h
	Case definition PSBI	IM or IV gentamicin and benzylpenicillin or ampicillin for at least 7–10 days	
	Greater risk of staphylococcus infection	IV cloxacillin and gentamicin for at least 7–10 days	
Managing possible serious bacterial infection in young infants when referral is not possible, 2015	Referral to hospital for young infants with PSBI is not possible	Option 1: IM gentamicin once daily for 7 days and oral amoxicillin twice daily for 7 days Option 2: IM gentamicin once daily for 2 days and oral amoxicillin twice daily for 7 days	*Gentamicin*: IM 5–7.5 mg/kg (for low-birthweight infants gentamicin 3–4 mg/kg) once daily *Amoxicillin*: Oral 50 mg/kg twice daily

PAEDIATRICS AND INTERNATIONAL CHILD HEALTH, 2018

9. Avoid low quality and sub-standard drugs
10. Prevent self-prescription and prescription changes

Generic drugs that don't meet the requirements of bioequivalence shoud not be used.
Unfortunately, national health authorities of many country don't consider those requirements.

Lack of quality control, **corruption**, **counterfeit drugs**, **deficient control at drugstores** aggravate the problem.

Antibiotic availability **without prescription** and **unregulated use** are major drivers of resistance.

Atb resistance in India: drivers and opportunity for action, PlosMed 2016

A medicine shop at Dantokpa market, Cotonou, Benin

Audit of Antibiotic Prescribing Practices for Neonatal Sepsis and Measurement of Outcome in New Born Unit at Kenyatta National Hospital

93% of the neonates admitted received ATB for presumed EOS
7% for presumed LOS

- Documentation of clinical features and perinatal risk factors was very poor.
- Blood cultures were done only in 4% of the neonates
- Lumbar puncture was not done in any of the neonates
- Complete blood count in 70%, C-reactive protein in 60%

According to Kenyan guidelines, appropriate ATB (penicillin+gentamicin) were prescribed in 98% of neonates.

Against guidelines, empiric ATB were almost never stopped after 48-72 hours if the neonates remained well, because of inability to confirm infection.

International J Pediatrics 2019

Implementation and Impact of an Antimicrobial Stewardship Program at a Tertiary Care Center in South India

Open Forum Infectious Disease 2018

Stakeholders including the Indian government have recognized antibiotic resistance as a major problem.

From 2017 to 2021 India is implementing the **National Action Plan to improve antibiotic use.**

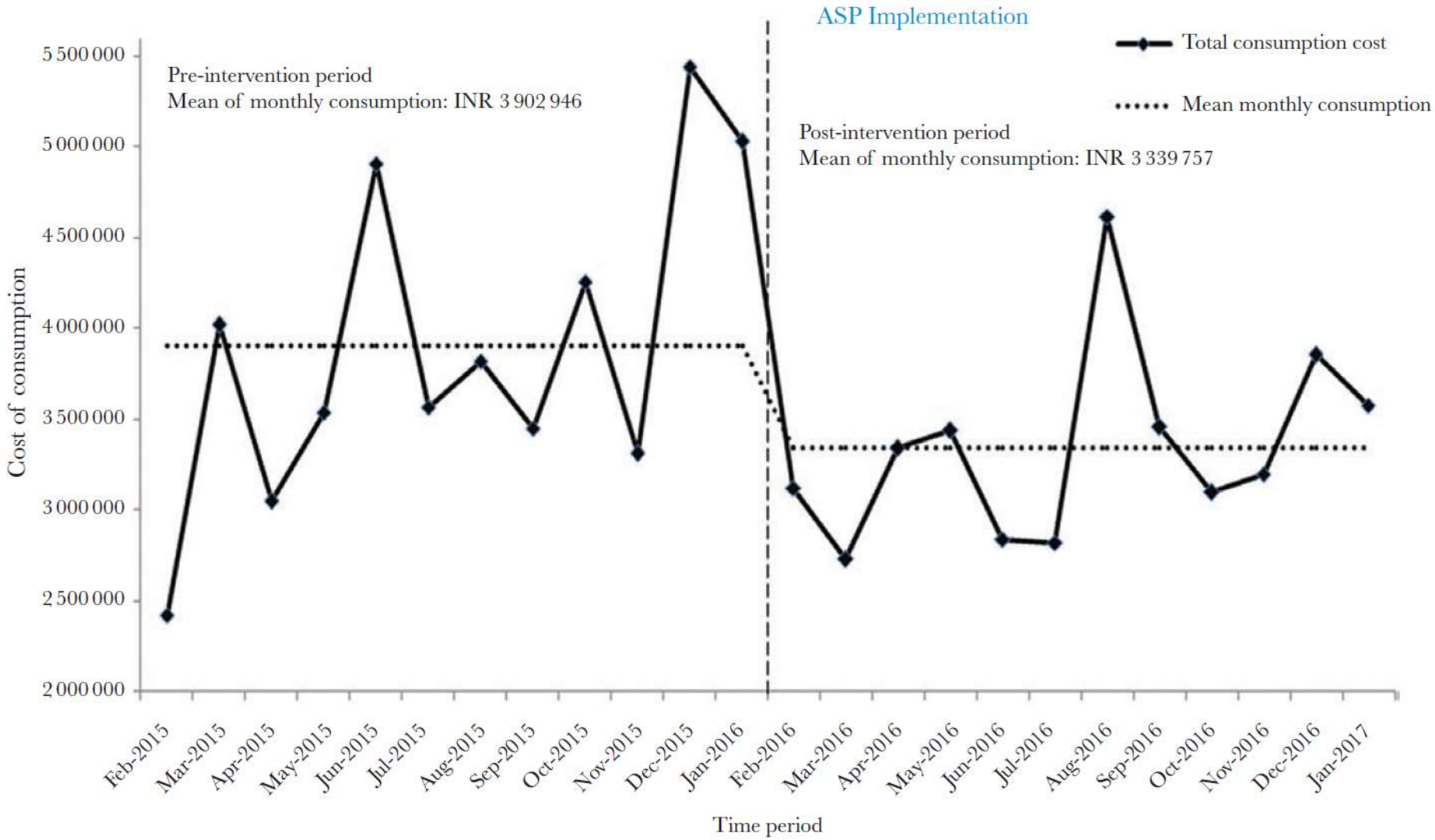
In the tertiary care center in the state of Kerala a formal **Antimicrobial Stewardship Program** was developed, a **dedicated multidisciplinary team (with clinical pharmacists included)** was created, and a **list of «restricted antimicrobials»** was generated.

Postprescriptive auditing and feedback were performed.

Parameter	Definition
Right indication [18]	When the prescribed antimicrobial is the most appropriate selection in terms of the pathogen, if known, and the site of infection (eg, prescribing polymyxin B instead of colistin for multidrug-resistant *Klebsiella pneumoniae* urinary tract infection is considered inappropriate because polymyxin B does not achieve optimal concentrations in the urine)
Right drug [10]	When the antimicrobial is the narrowest and the most effective option (eg, prescribing meropenem instead of ceftriaxone for pan-sensitive *Escherichia coli* in blood is considered inappropriate in a hemodynamically stable patient)
Right dose	When the loading dose and maintenance dose of the prescribed antimicrobial is appropriate and accurate for the patient's diagnosis as per standard recommendations [19] (antimicrobials that required a loading dose for this study included colistin, tigecycline, polymyxin B, and caspofungin)
Right frequency [38]	When the frequency of the prescribed antimicrobial dose is appropriate for the patient's diagnosis as per standard recommendations
Right duration	When the prescribed antimicrobial has been administered for the correct duration based on the patient's diagnosis as per standard recommendations [19–21]

Open Forum Infectious Disease 2018

The Antimicrobial Stewardship Program team defined **appropriateness** using the **«5 Rs»**


ASP Implementation
Total consumption cost
Mean monthly consumption
Pre-intervention period
Mean of monthly consumption: INR 3 902 946
Post-intervention period
Mean of monthly consumption: INR 3 339 757
Cost of consumption
5 500 000
5 000 000
4 500 000
4 000 000
3 500 000
3 000 000
2 500 000
2 000 000
Feb-2015
Mar-2015
Apr-2015
May-2015
Jun-2015
Jul-2015
Aug-2015
Sep-2015
Oct-2015
Nov-2015
Dec-2015
Jan-2016
Feb-2016
Mar-2016
Apr-2016
May-2016
Jun-2016
Jul-2016
Aug-2016
Sep-2016
Oct-2016
Nov-2016
Dec-2016
Jan-2017
Time period

Antibiotics are limited, non-renewable resources, that we all need during our life.

«Every antibiotic expected by a patient, every unnecessary prescription written by a doctor, every uncompleted course of antibiotics, and every inappropriate or unnecessary use in animals or agriculture is potentially signing a death warrant for a future patient». *Dryden 2009*

We should not wait for governments to implement measures that regulate drug usage.
Change must start with us all.

Global Action Plan on Antimicrobial Resistance, WHO 2015

PREVENTION FIRST ! WHO 2015

Preventing bacterial diseases is the best way to avoid the use of antibiotics and all of its consequences. It can be cost-effective and implemented in all settings.

Vaccines, along with **hygiene measures**, are **key elements** of infection prevention to reduce antibiotic use.

Consider **maternal immunization programmes** (such as maternal tetanus or pertussis) for preventing neonatal infections.

Potential vaccine candidates for neonatal sepsis include Group B Streptococcus and E. coli.

Developing vaccines in the era of genomics, Cl Micr Inf 2012

THANK YOU