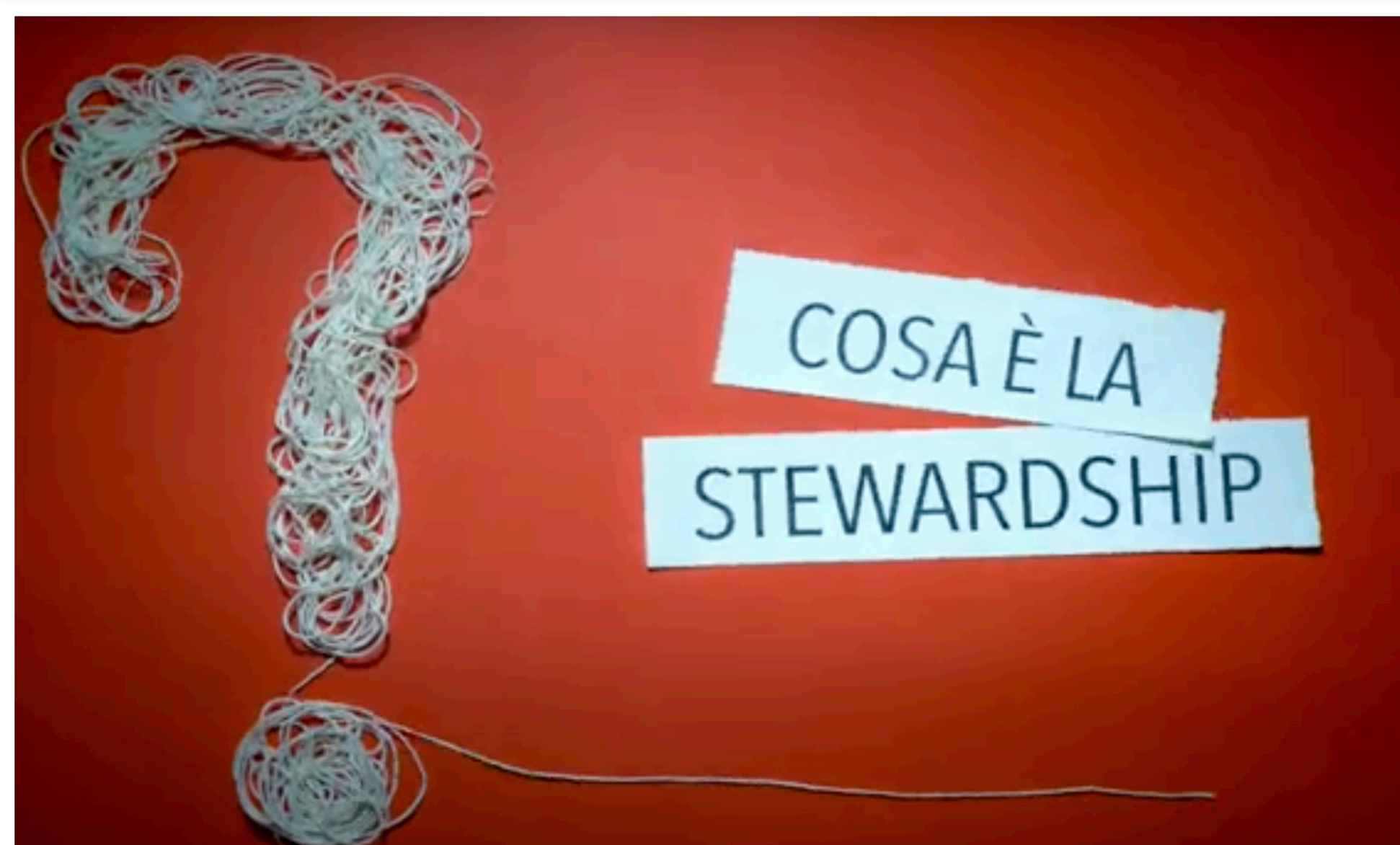


LA STEWARDSHIP ANTIBIOTICA

IL RUOLO DEL MEDICO

Laura Bernini
UOC Malattie Infettive
Ospedale San Donato, Arezzo

STEWARDSHIP

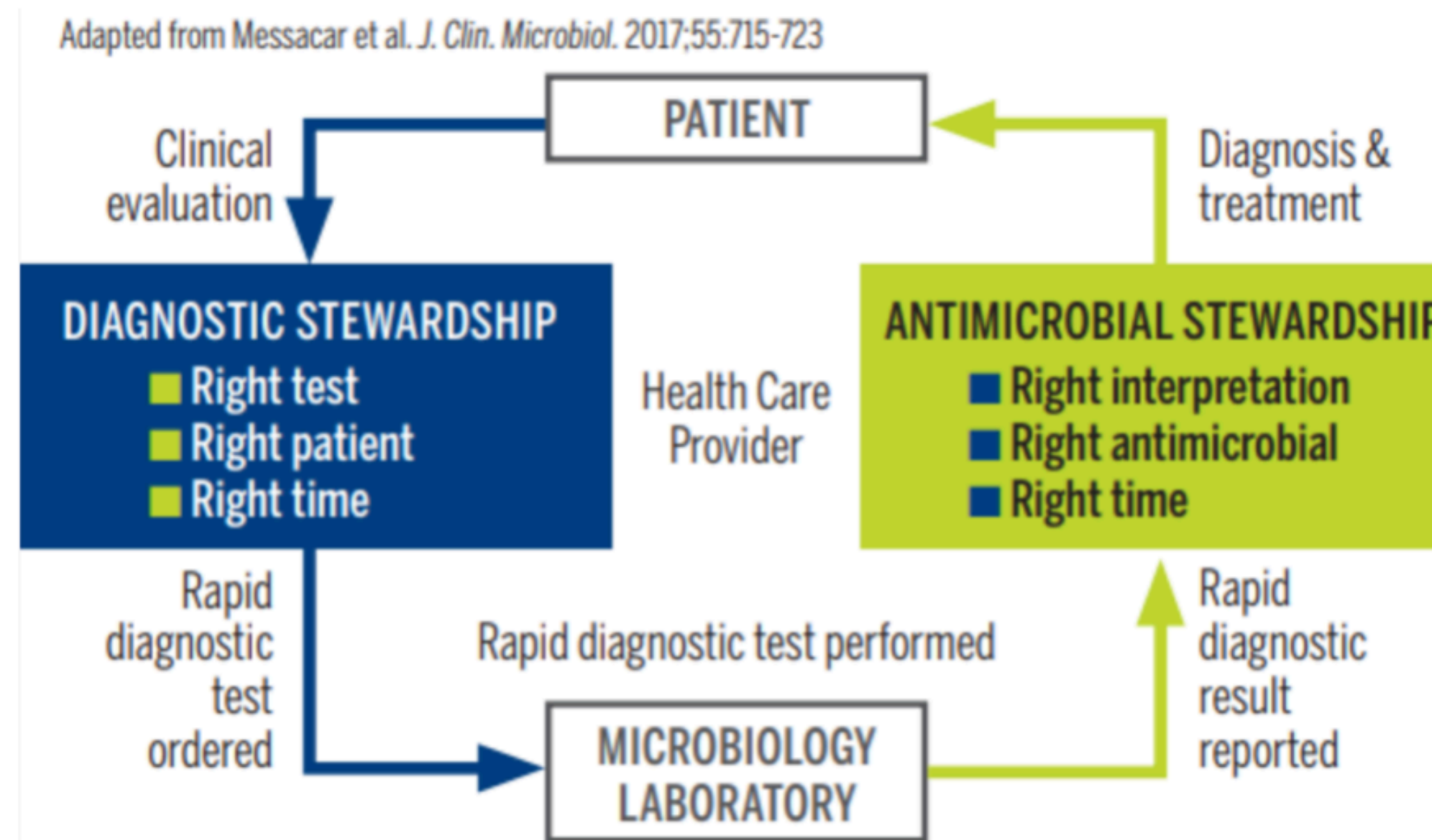


Stewardship, una parola, tante applicazioni.
Il termine anglosassone “stewardship” non è traducibile con un corrispettivo italiano, ma letteralmente significa: “gestione etica (responsabile) delle risorse”



STEWARDSHIP ANTIMICROBICA

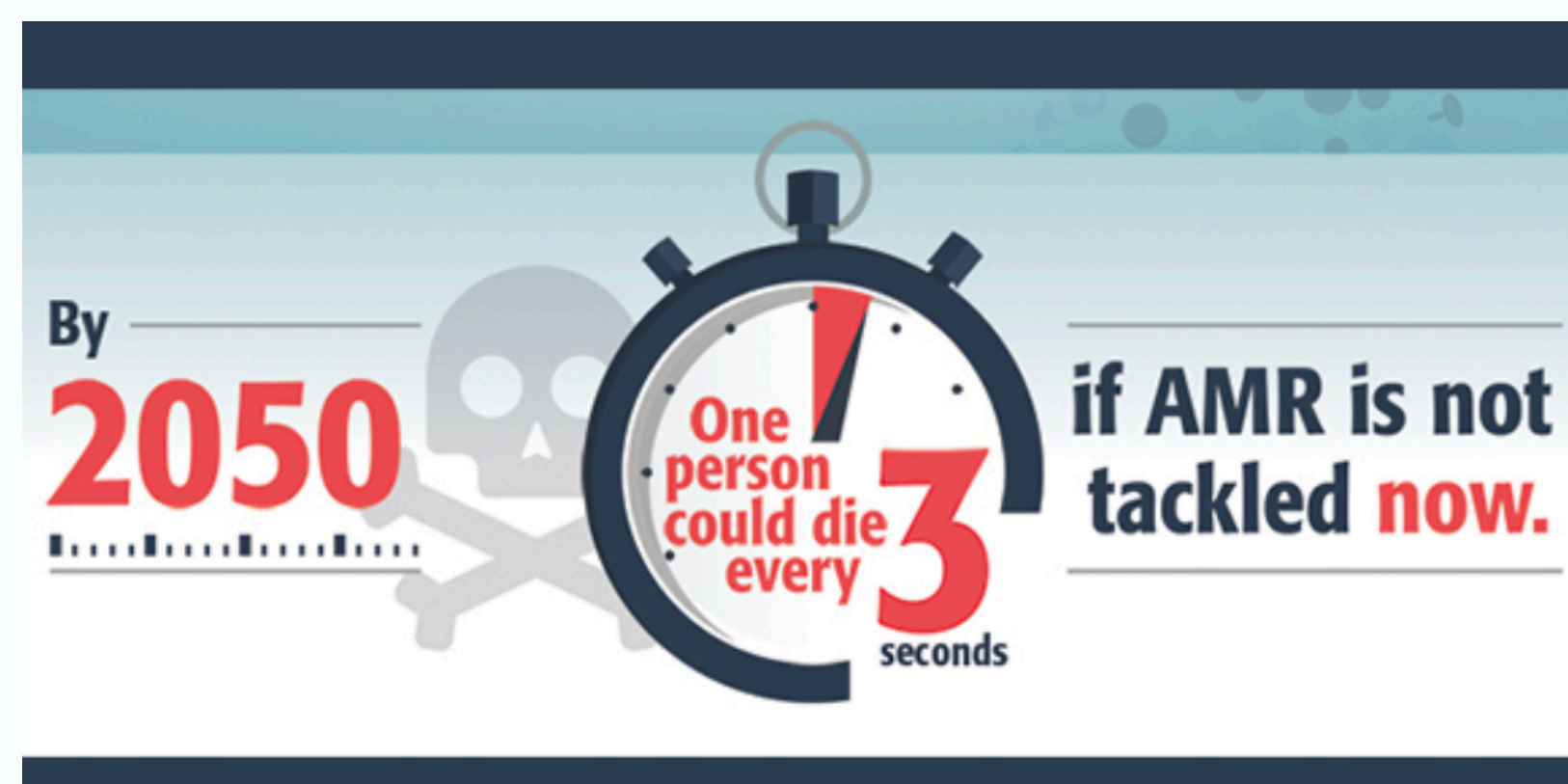
Antimicrobial Stewardship significa sostanzialmente promuovere programmi di buon uso degli antibiotici per contrastare il fenomeno dell'antibiotico-resistenza.



STEWARDSHIP ANTIBIOTICA

Multidrug resistance (MDR), defined as resistance to at least one agent in three or more antimicrobial classes, exacerbates the challenge by narrowing therapeutic options and increasing treatment failures, costs, and mortality

While surveillance systems increasingly monitor AMR trends by bacterial species and drug class, few studies have examined resistance trends through a gender lens, especially in LMIC settings.



AMR NUMERI E PIANI D'AZIONE

Antimicrobial resistance (AMR) is a growing public health threat.

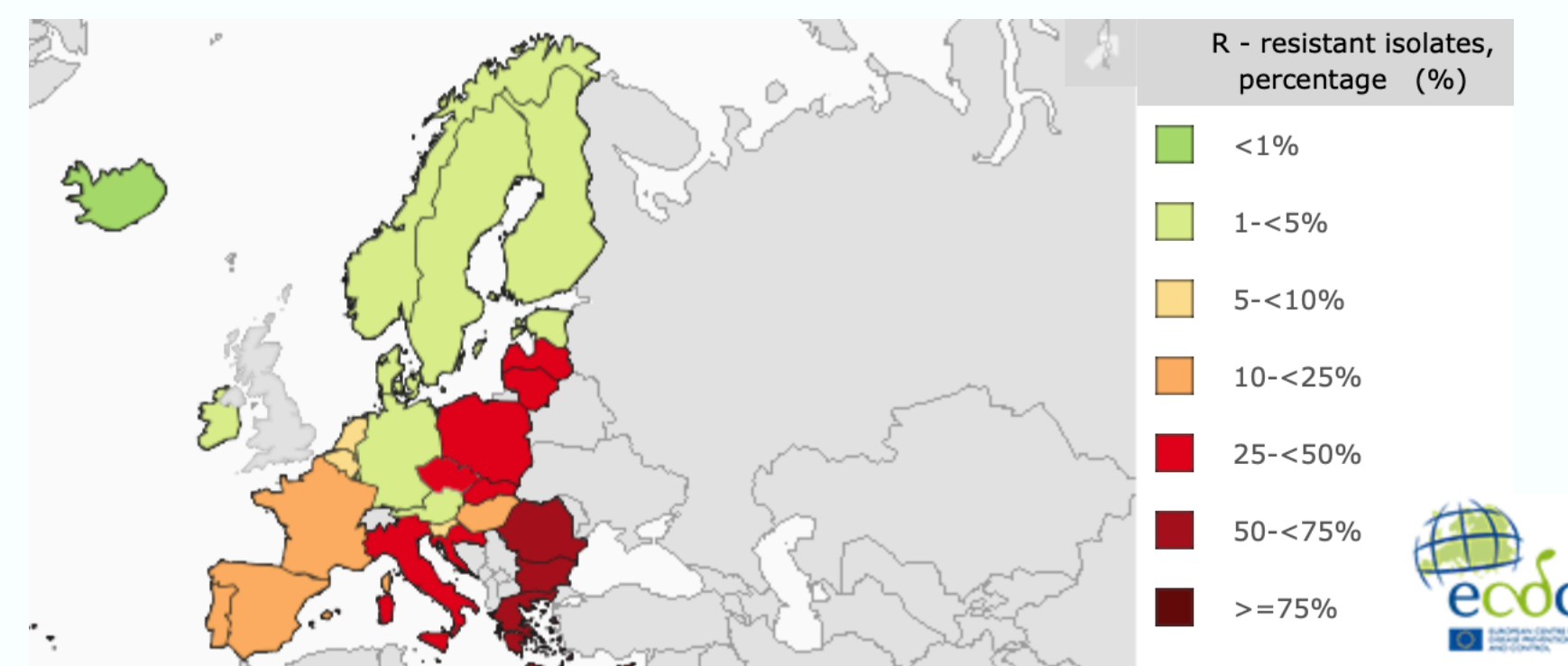
An estimated 1.27 million deaths were directly attributed to drug-resistant bacterial infections in 2019.

In 2015, Member States of the World Health Organization (WHO) endorsed the Global Action Plan on Antimicrobial Resistance and committed to developing and implementing national action plans (NAPs) on AMR.

Klebsiella pneumoniae ▼

Combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycoside) ▼

R - resistant isolates, percentage ▼ | ▶ ◀▶▶ 2024 ▼ ▶▶▶

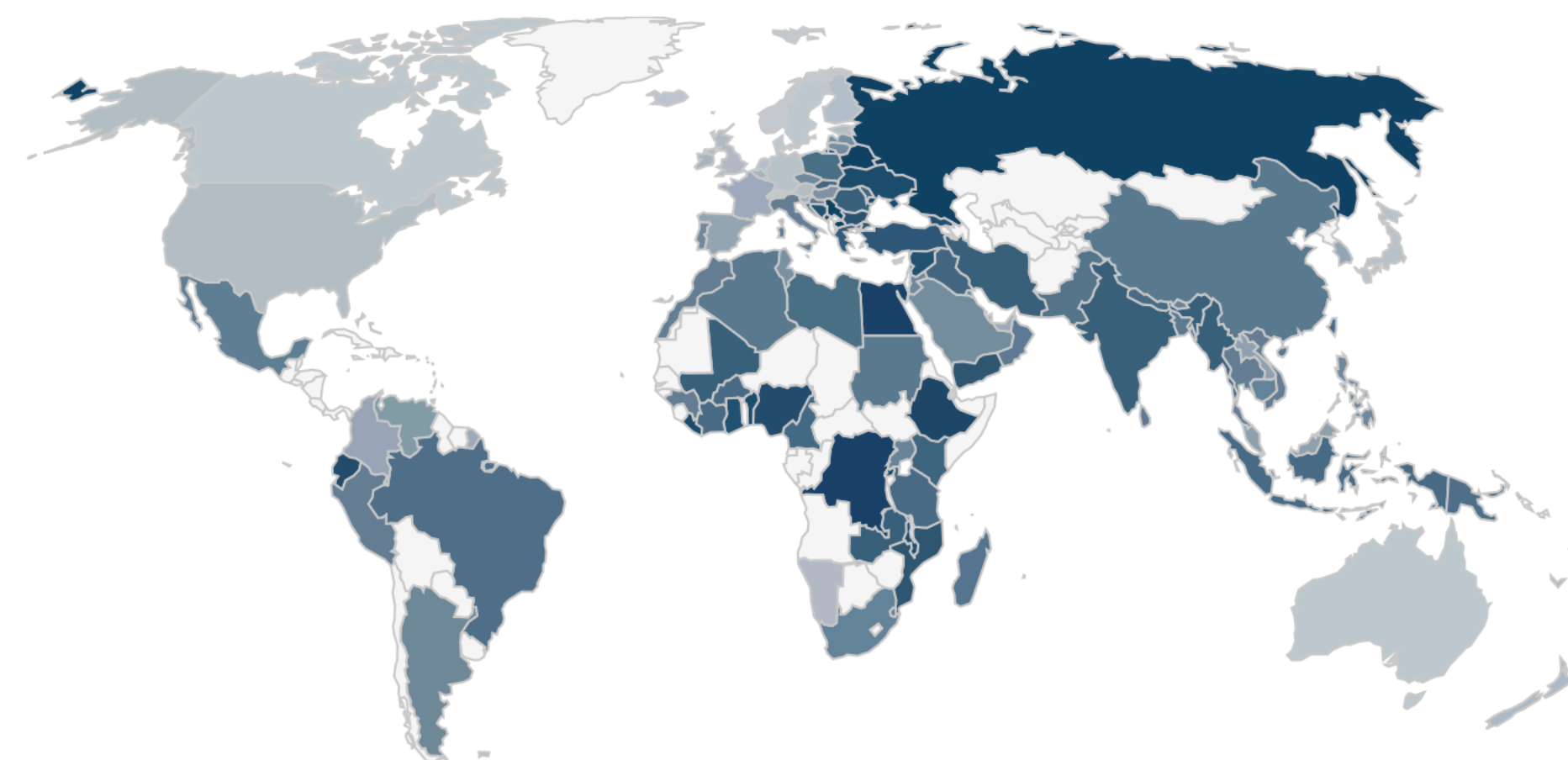


Resistance of *Klebsiella pneumoniae* to Cephalosporins (3rd gen)

- +

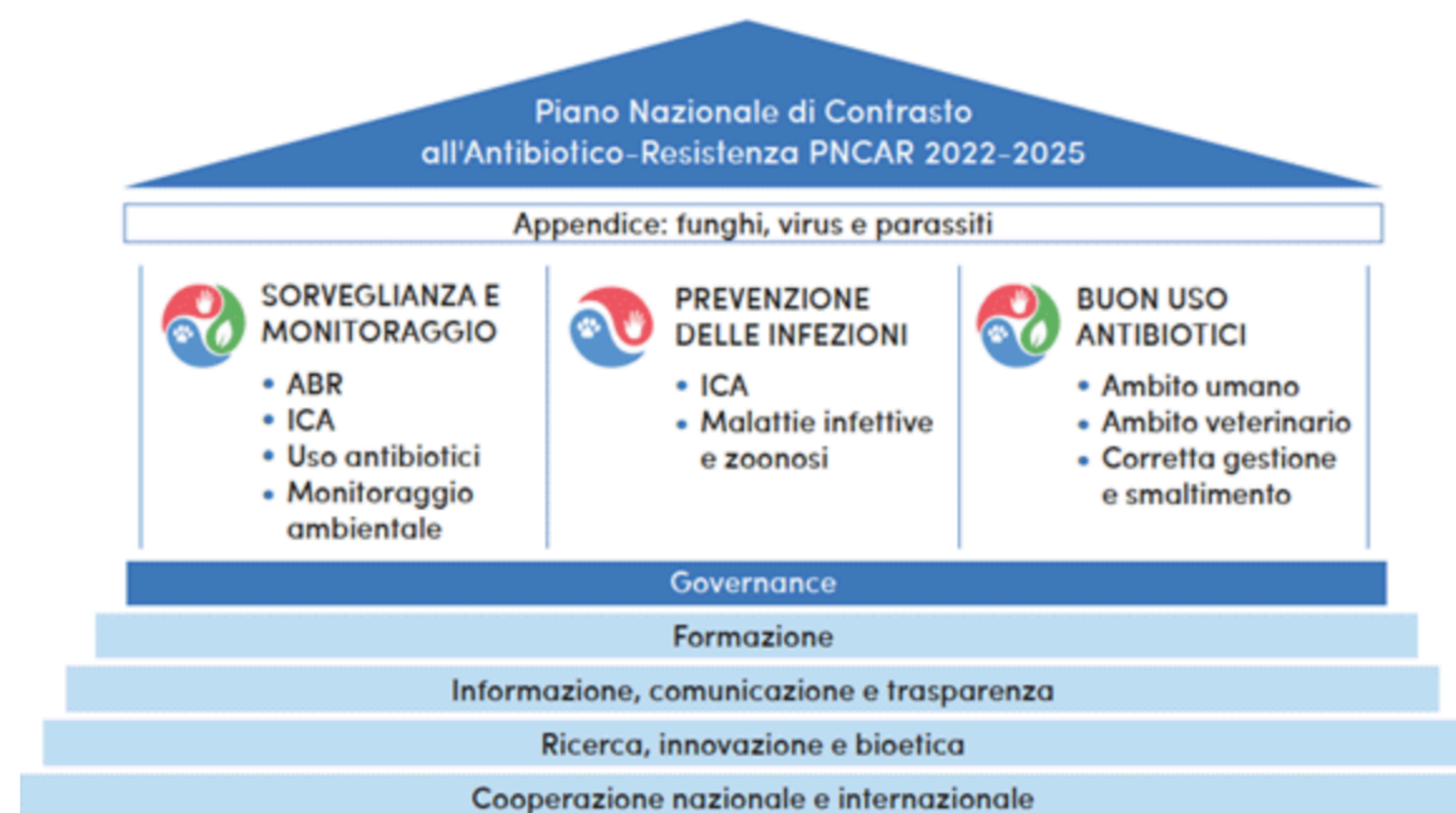
% Resistant
(invasive isolates)

100
75
50
25
0



125 out of 145 publicly available NAPs did not mention sex or gender

Immagine 1: Struttura del PNCAR 2022-2025



Fonte: Piano Nazionale di Contrasto all'Antibiotico-Resistenza (PNCAR) 2022-2025

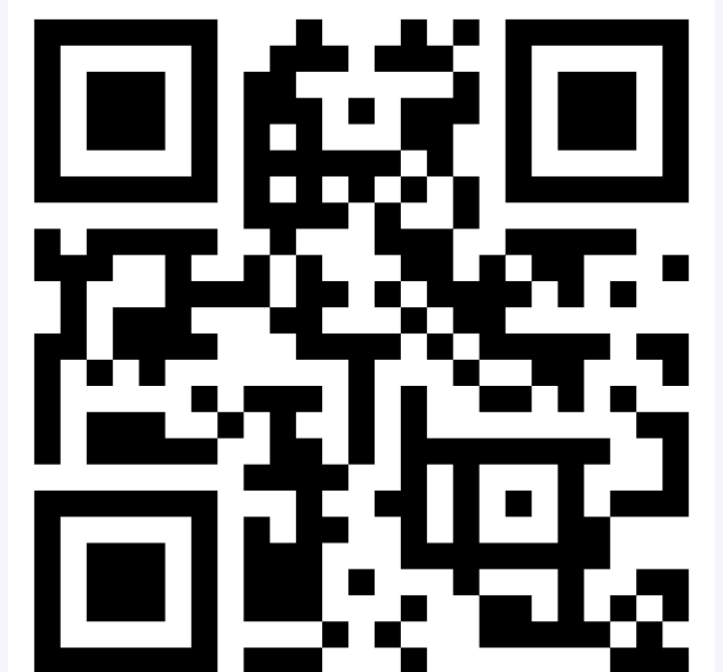
Addressing gender inequalities in national action plans on antimicrobial resistance

Guidance to complement the people-centred approach



Despite this lack of attention to gender, research indicates that exposure and susceptibility to infection, health-seeking behaviours, as well as patterns of antimicrobial prescribing and use are all influenced by gender considerations (14–19).

Gender may also affect who has the resources and decision-making power to access appropriate care and treatment for (drug-resistant) infections, which contributes to differences in the quality of care received and patient outcomes



STEWARDSHIP ANTIBIOTICA

Biological, behavioral, and structural factors contribute to sex-based differences in infection risk and antibiotic exposure.

Women, for instance, experience more frequent urinary tract infections and are more likely to receive empiric antibiotic treatment for reproductive or urogenital symptoms, potentially leading to greater antimicrobial exposure and resistance development

Addressing gender inequalities
in national action plans on
antimicrobial resistance

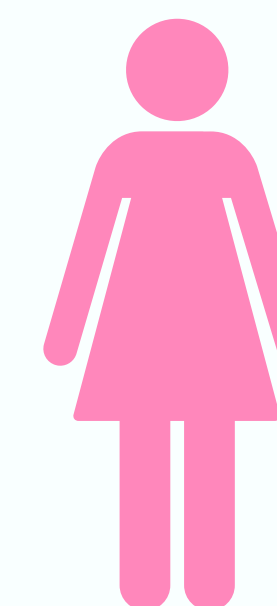
Guidance to complement the people-centred approach



World Health
Organization

PUNTI CHIAVE

- Mancanza di acqua pulita e servizi igienici “sicuri” pone le donne a maggior rischio di esposizione alle infezioni (esigenze di igiene mestruale)
- Donne responsabili di fornitura di acqua ad uso domestico nel 70% dei casi
- Ritardo diagnostico o automedicazione dovute a limitata autonomia finanziaria o decisionale
- Percezione della mascolinità
- Difficoltà culturali/religiose



Addressing gender inequalities
in national action plans on
antimicrobial resistance

Guidance to complement the people-centred approach



World Health
Organization

PUNTI CHIAVE

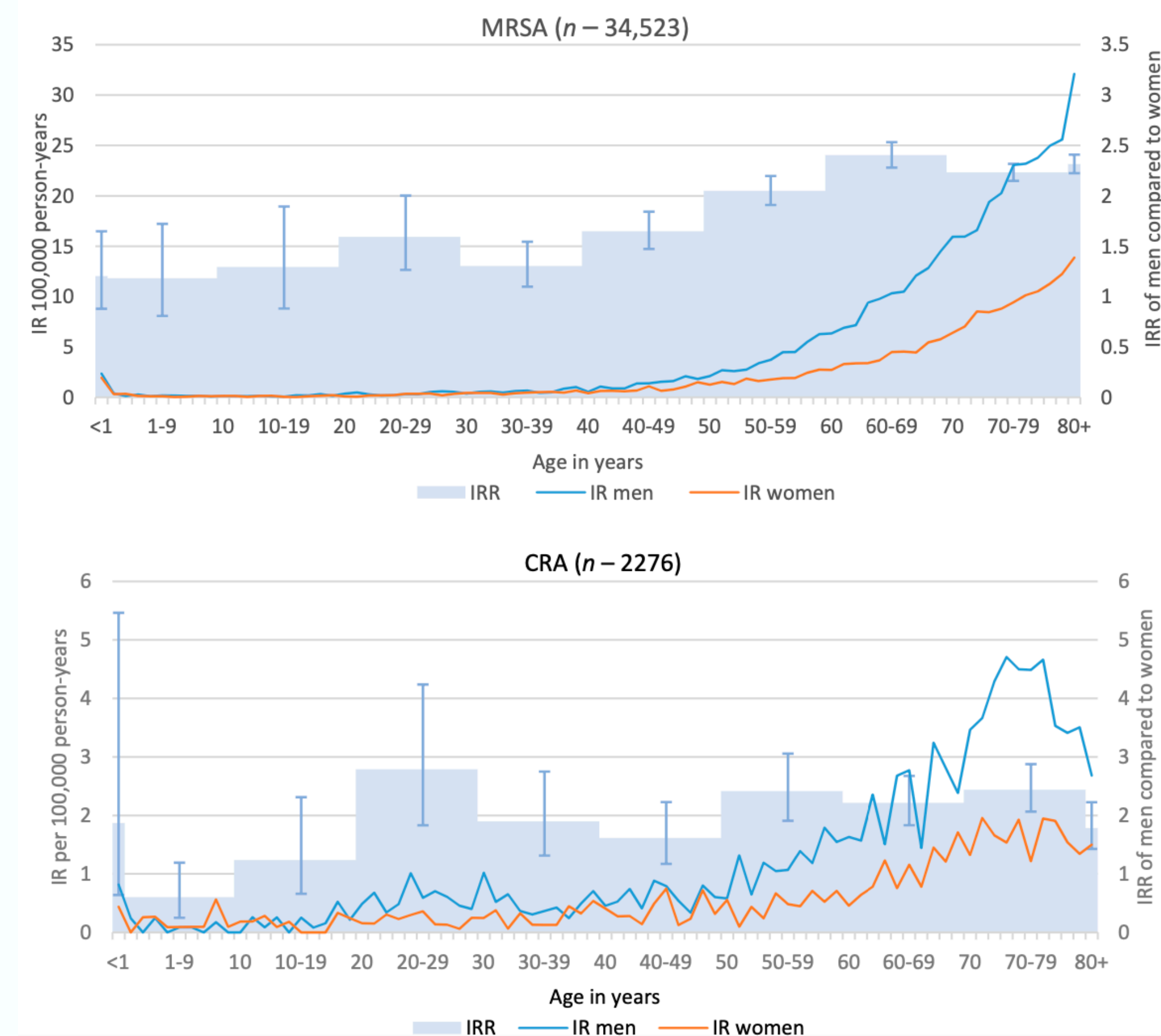
- Sesso maschile più rappresentato in allevamenti animali, agricoltura industriale, macelli aumenta in rischio di alcune infezioni MDR nel sesso maschile
- Percezione della mascolinità (soprattutto per MSM)
- Uomo culturalmente visto come percettore del reddito primario, accesso ritardato alle cure ad esempio TBC



Article

Bugs That Can Resist Antibiotics but Not Men: Gender-Specific Differences in Notified Infections and Colonisations in Germany, 2010–2019

Michael Brandl ^{1,2,*} , Alexandra Hoffmann ³, Niklas Willrich ³, Annicka Reuss ³, Felix Reichert ^{1,2} , Jan Walter ¹, Tim Eckmanns ³ and Sebastian Haller ³





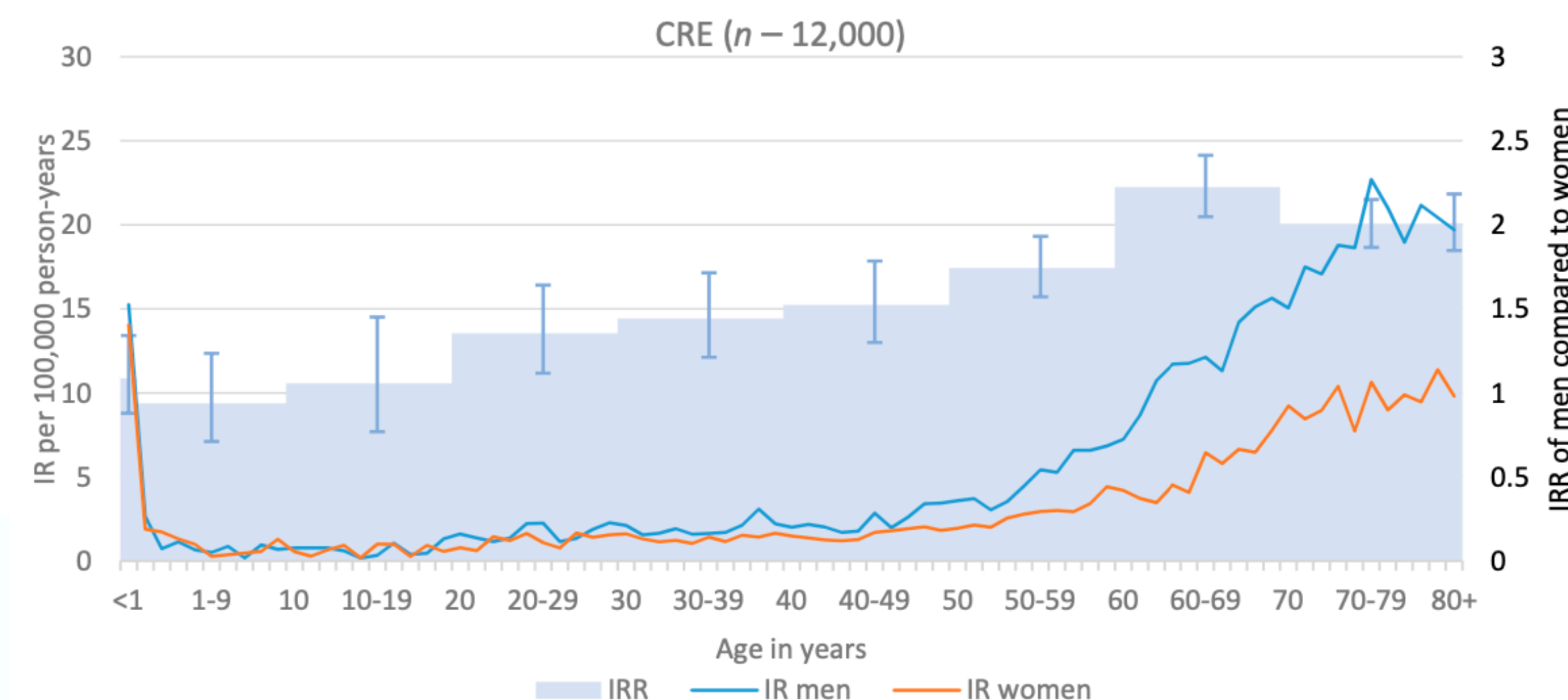
microorganisms



Article

Bugs That Can Resist Antibiotics but Not Men: Gender-Specific Differences in Notified Infections and Colonisations in Germany, 2010–2019

Michael Brandl ^{1,2,*} , Alexandra Hoffmann ³, Niklas Willrich ³, Annicka Reuss ³, Felix Reichert ^{1,2} , Jan Walter ¹, Tim Eckmanns ³ and Sebastian Haller ³



PUNTI CHIAVE

Addressing gender inequalities
in national action plans on
antimicrobial resistance

Guidance to complement the people-centred approach



- Overall, women are 27% more likely to receive antibiotics throughout their lifetime than men.
- Female doctors tend to adopt a more conservative wait-and-see approach to prescribing antibiotics compared to their male counterparts.
- Antimicrobial stewardship recommendations made by male pharmacists are more likely to be accepted than those made by their female colleagues.

Box 1. Examples of sex as a risk factor for (drug-resistant) infections

- **Anatomical differences between the sexes.**
These can drive differences in susceptibility to infection. For example, women are more susceptible to urinary tract infections, due to a shorter urethra, proximity of the urethra to the rectum and vagina, and vaginal dysbiosis (17). Females have a 10% prevalence of bacteriuria compared with 0.1% in males (27). Urinary tract infections can lead to major complications, such as organ damage and kidney infections.



Gravidanza fisiologica

PRIMA PARTE

Sezione 1 - Informazioni alle donne in gravidanza
Sezione 2 - Screening delle infezioni in gravidanza

Sezione 2. Screening delle infezioni in gravidanza

2.1. Batteriuria asintomatica (*Asymptomatic Bacteriuria, ASB*)

QUESITI

- Alle donne in gravidanza dovrebbe essere offerto lo screening per batteriuria asintomatica?
- Nelle donne in gravidanza asintomatiche lo screening della batteriuria dovrebbe essere eseguito tramite urinocoltura oppure tramite esame delle urine standard?
- Nelle donne in gravidanza lo screening della batteriuria asintomatica tramite urinocoltura dovrebbe essere eseguito su un solo campione oppure su due campioni successivi?
- Nelle donne in gravidanza lo screening della batteriuria asintomatica dovrebbe essere offerto soltanto alla prima visita oppure ripetuto anche nei trimestri successivi?



Gravidanza fisiologica

PRIMA PARTE

Sezione 1 - Informazioni alle donne in gravidanza

Sezione 2 - Screening delle infezioni in gravidanza

Raccomandazione

1. Lo screening della batteriuria asintomatica non dovrebbe essere offerto a tutte le donne in gravidanza

raccomandazione condizionata, qualità delle prove bassa o molto bassa

La Raccomandazione 1 si fonda sulle prove di qualità molto bassa degli studi inclusi su screening di batteriuria asintomatica (ASB) in gravidanza. Gli eventi sono pochi, le stime degli effetti sono molto imprecise e il rapporto beneficio/danno dello screening risulta incerto. Le prove che indicano che il trattamento antibiotico in donne in gravidanza con diagnosi di ASB allo screening riduce modestamente l'incidenza di pielonefrite e il numero di neonati di basso peso alla nascita sono di bassa qualità e sono state prodotte prevalentemente oltre 30 anni fa, in setting con pratiche diagnostico-assistenziali verosimilmente molto diverse da quelle attuali.

Questa raccomandazione considera i benefici derivanti dal contenimento dell'utilizzo inappropriato di antibiotici che rappresenta l'intervento principale per prevenire l'insorgere e la diffusione della resistenza.

- **Immune response differences.** Men are generally more susceptible to infectious diseases than women. However, women often experience a heightened immune response to pathogens, with more severe disease symptoms (24). Because of their stronger antibody response and local and systemic reaction, in general, women have stronger acquired immunity from bacterial and viral vaccines than men (24).

A questo proposito, è necessario ricordare che il sistema immunitario presenta differenze sesso-specifiche determinate soprattutto da fattori genetici ed ormonali che agiscono dall'età pre-natale a quella adulta.

Estrogeni tendono a stimolare la risposta immunitaria umorale e cellulo-mediata, promuovendo la produzione di anticorpi (anche in risposta a vaccini), ma ponendo le donne a maggior rischio di malattie autoimmuni.

Androgeni possono inibire le cellule natural killer, i linfociti T CD8+, e la produzione di citochine ed anticorpi.

Complessivamente tali differenze determinano un certo vantaggio immunologico nelle donne rispetto agli uomini in età giovane-adulta. Non è ancora ben definito se tale vantaggio persista anche in età avanzata, grazie a una "riserva immunologica" determinata dalla pregressa esposizione estrogenica.

- **Physiological changes.** Over the life course, there are also important age-dependent differences between the sexes. In populations older than 65 years, the risk and prevalence of urinary tract infections in female and male populations are more balanced (27). Pregnant or postnatal women are at a higher risk of infection including sepsis compared with the general population (28). Such infections can lead to premature birth and neonatal infections.

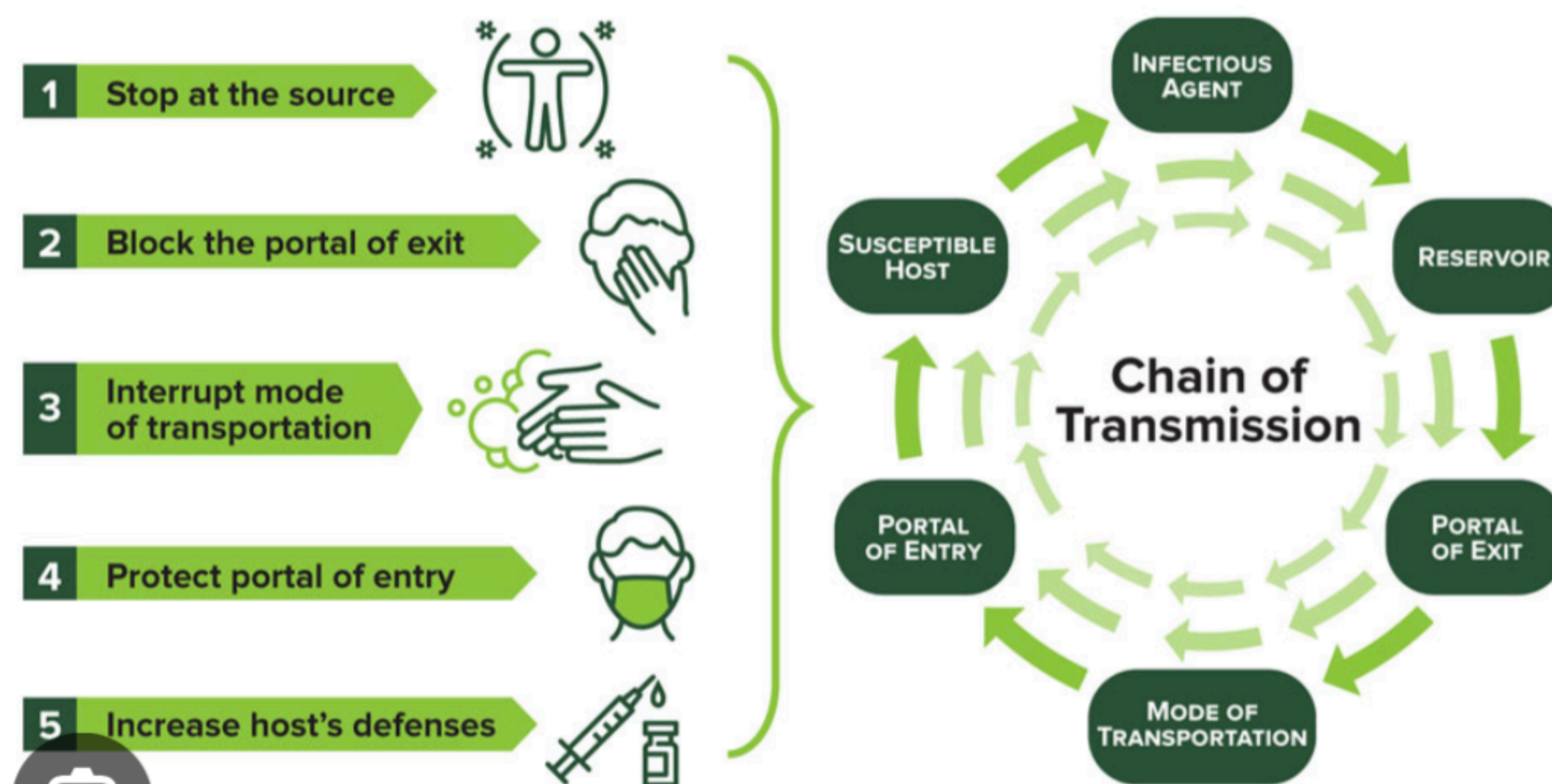
QUINDI IL MEDICO COME PUO' INTERVENIRE?

- Considerare il paziente che si presenta davanti a noi (es. sesso, area geografica di provenienza) ed interfacciarsi con il/la paziente considerando anche fattori socio-culturali
- Saper riconoscere i fattori di rischio per colonizzazione ed infezione per destinare il trattamento antibiotico solo a casi selezionati
- Prevenzione della trasmissione delle infezioni (INFECTION CONTROL)
- Corretto approccio diagnostico (microbiologico) privilegiando terapie antibiotiche mirate

QUINDI IL MEDICO (ANZI, IL SANITARIO!) COME PUO' INTERVENIRE?

INFECTION CONTROL

Break the Chain | 5 steps of infection prevention



THE UNIVERSITY OF
ALABAMA AT BIRMINGHAM

QUINDI IL MEDICO COME PUO' INTERVENIRE?

- Scegliere l'antibiotico con più ristretto spettro d'azione
- Dosaggio antibiotico adeguato (MAI SOTTODOSARE) rispettando anche la farmacocinetica
- Considerare anche il distretto da trattare per scegliere l'antibiotico con miglior penetrazione
- Short therapy

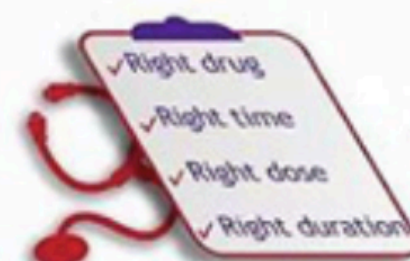


BEFORE USING ANTIBIOTICS

THINK TWICE



FIRST
Is it necessary?



SECOND
Is it appropriate?

ANTIBIOTIC RESISTANCE can lead to increased DEATHS.
Step into change: THINK TWICE.

Check the name on the order and the patient.
Use 2 identifiers.
Ask patient to identify himself/herself.
When available, use technology (eg, bar-code system).



PERSON

Check the medication label.
Check the order.
CHECK for ALLERGIES.



MEDICATION

Check the order.
Confirm appropriateness of the dose using a current drug reference.
If necessary, calculate the dose and have another nurse calculate the dose as well.



DOSE

Right:



TIME

Again, check the order and appropriateness of the route ordered.
Confirm that the patient can take or receive the medication by the ordered route.



ROUTE

Document administration AFTER giving the ordered medication.
Chart the time, route, and any other specific information as necessary. Eg: the site of an injection or any laboratory value or vital sign that needed to be checked before giving the drug.



DOCUMENTATION

Confirm the rationale for the ordered medication. What is the patient's history? Why is he/she taking this medication?
Do not forget they have the RIGHT to REFUSE.



REASON

Make sure that the drug led to the desired effect.
Be sure to document your monitoring of the patient and any other nursing interventions that are applicable.



RESPONSE

When giving medications
THINK

SHORT THERAPY

- Shorter course antimicrobial therapy has demonstrated non-inferior outcomes compared to longer courses certain common infections and in specific patient groups;
- The risk of selective pressure on both antimicrobial-resistant strains and *C. difficile* infections escalates with each additional day of antimicrobial treatment;
- Applicability of the evidence to specific patient sub-groups, such as critically ill and immunocompromised patients, is limited, and the safety of shorter courses in these populations is uncertain;
- A patient-tailored approach, considering individual patient factors and treatment response, is preferred over a 'one size fits all' approach.
- Implementation of patient-tailored approaches in clinical practice presents challenges, including the need for novel decision support tools and biomarkers;
- Overall, shorter course antimicrobial therapy shows promise in reducing treatment duration while maintaining clinical efficacy. Further research and implementation strategies are needed to optimise the use of shorter courses and tailor treatment durations to individual patients.

Advantages and disadvantages of shorter antimicrobial courses

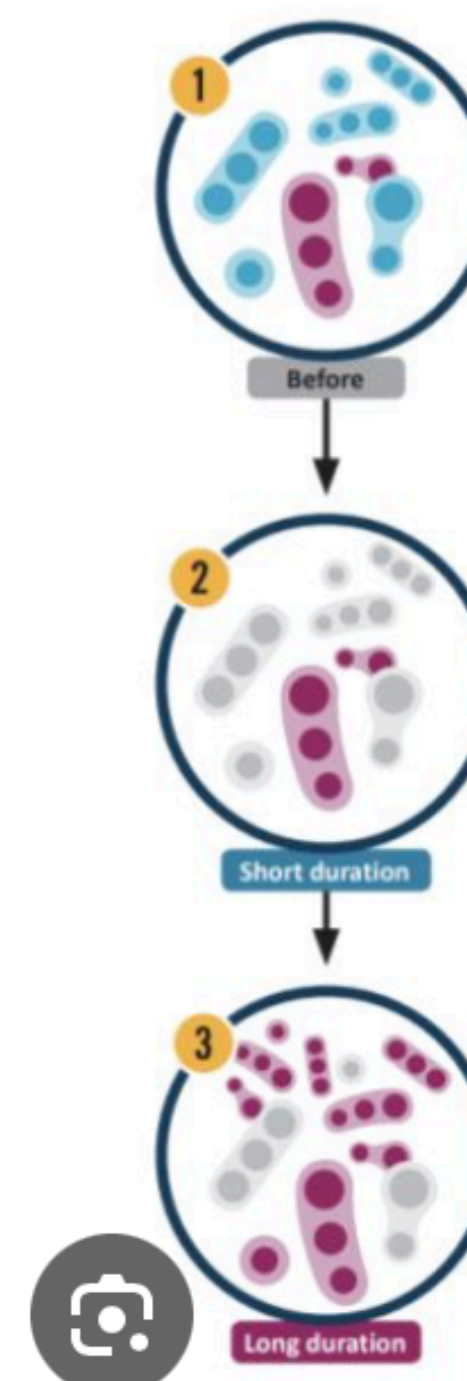
SHORTER IS SMARTER

Prescribers/Clinicians:
Reducing duration of antibiotic therapy in long-term care

Public Health Ontario | Santé publique Ontario

Antibiotic use drives selective pressure

Selective pressure kills **susceptible bacteria** and allows **resistant organisms** to thrive and multiply.



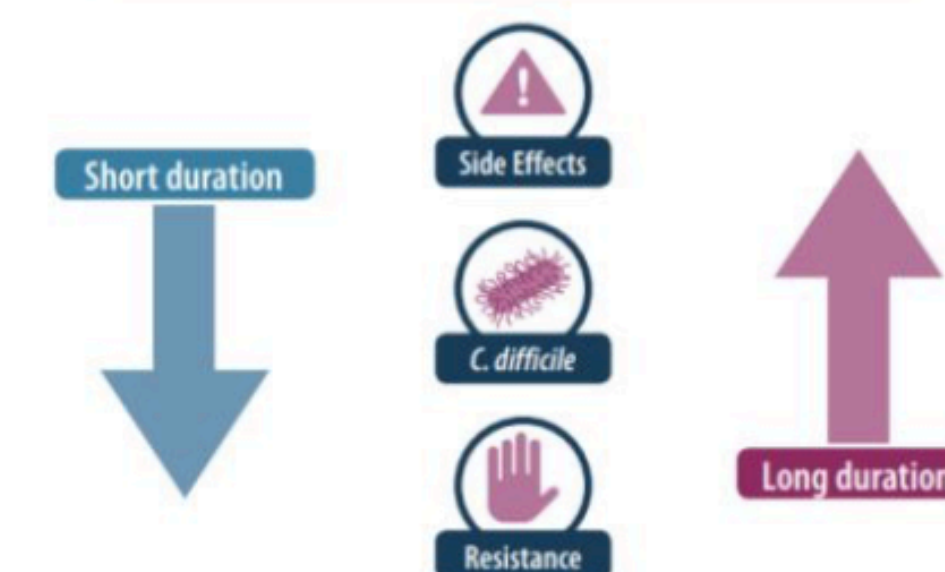
Shorter courses are as effective as longer courses

Uncomplicated cystitis		Pneumonia	
Short 3-6 days	Long 7-14 days	Short 5 days	Long 7-10 days

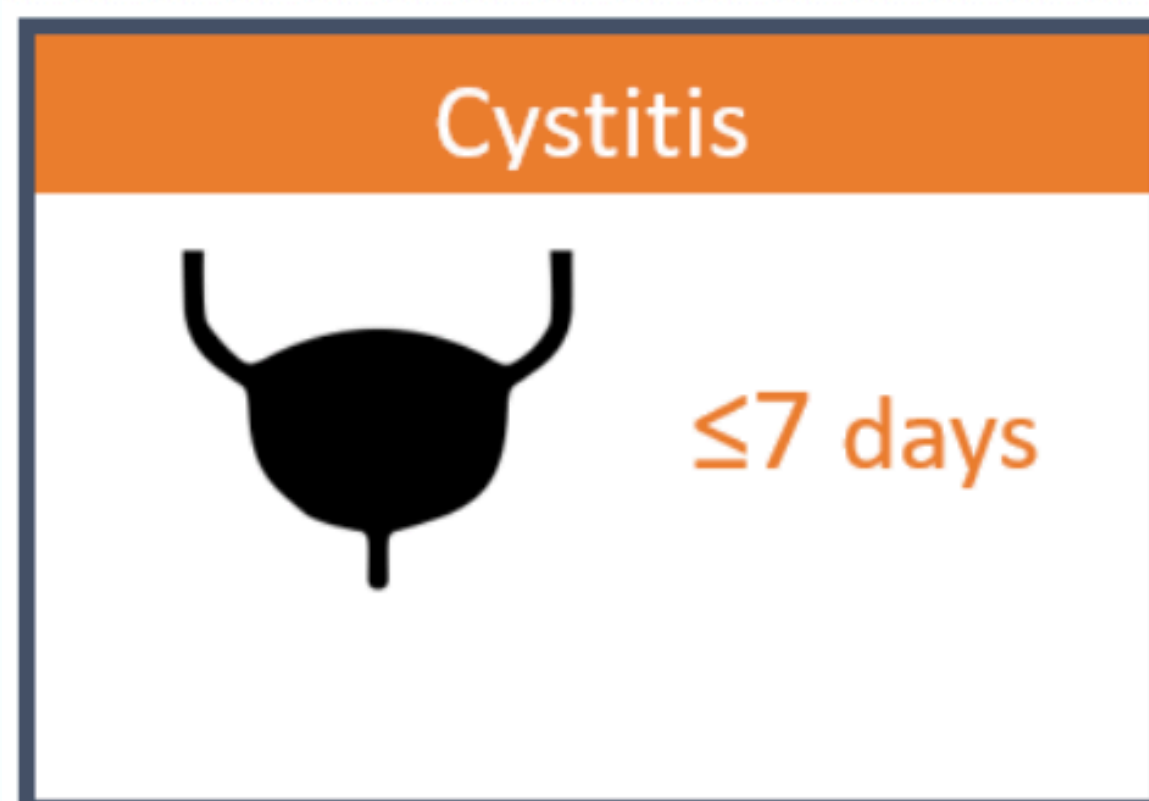
Cellulitis	
Short 5 days	Long 10 days

Based on studies in hospitalized and ambulatory patients for common infections seen in long-term care.

Shorter courses have a lower risk of harm



SHORT THERAPY



Key Points¹¹⁻¹⁴: For uncomplicated cystitis, evidence supports 3 days of TMP-SMX (Bactrim) or 5 days of nitrofurantoin. Alternate options include 3 days of fluoroquinolones or 5 days of a beta-lactam (e.g., amoxicillin-clavulanate, cephalexin, cefuroxime). For complicated cystitis (including catheterized patients and those with urologic abnormalities), evidence supports 7 days of treatment. For pyelonephritis, longer courses of 7 days (fluoroquinolone) to 10-14 (TMP/SMX, beta-lactams) days are appropriate. Bacteria in the urine without any urinary symptoms is considered asymptomatic bacteriuria and should NOT be treated (exceptions: pregnancy, impending urologic surgery).

SHORT THERAPY

Cellulitis/Skin & Soft
Tissue Infection



5-7 days

Community Acquired
Pneumonia



3-5 days

Uncomplicated Gram-
negative Bacteremia



=7 days

TAKE HOME MESSAGES

- Importanza dell'AMR in ambito internazionale
- Differenze di genere ancora poco considerate e “contabilizzate” nei piani di azione
- Differenze di genere tra pazienti ma anche tra operatori sanitari
- Buon uso degli antibiotici e infection control come chiave dell'AMS

GRAZIE PER L'ATTENZIONE