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a:care

**A:CARE CONGRESS**

# Principles of Anti-Microbial Resistance (AMR) stewardship and impact of adherence

**Prof. Evangelos J. Giamarellos-Bourboulis, MD, PhD, FISAC**

Professor of Internal Medicine; Director: MsC program of Infectious Diseases;  
National and Kapodistrian University of Athens

President: European Shock Society

Chairman: European Sepsis Alliance

Greece

# CONFLICT OF INTEREST DISCLOSURE



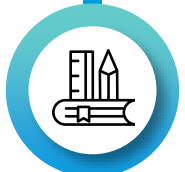
Honoraria (paid to the University of Athens) from Abbott CH, Brahms ThermoFisher GmbH Germany, GSK and Sobi



Consultant for Fab'nTech, InflaRx GmbH, UCB and Xbiotech Inc



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# Question 1

**WHY, IN YOUR OPINION, DOES  
ANTIMICROBIAL STEWARDSHIP MATTER?**

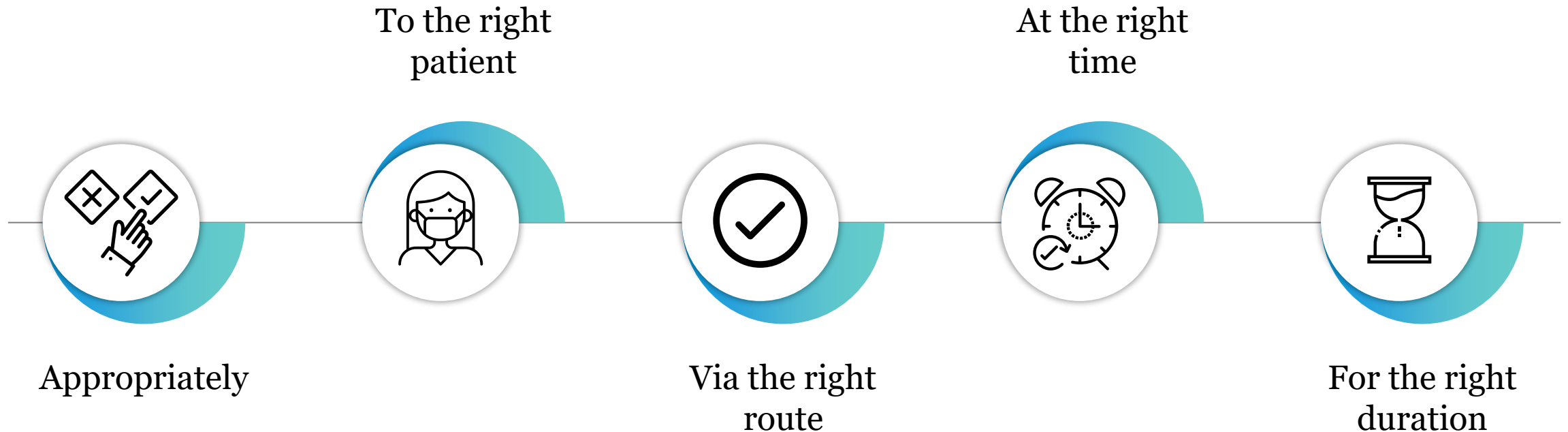
- Prevents mortality of the elderly
- Prevents infections by difficult-to-treat microorganisms
- Prevents adverse effects from the use of antimicrobials
- All the above

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# ANTIMICROBIAL STEWARDSHIP DEFINITION

A SYSTEMATIC APPROACH TO PROMOTING AND MONITORING JUDICIOUS USE OF ANTIMICROBIALS TO PRESERVE THEIR FUTURE EFFECTIVENESS BY ADMINISTERING ANTIMICROBIALS





Education programs

Encourage and maintain good adherence to rationally prescribed antimicrobial



**KEEP ANTIMICROBIALS ALIVE**



Audits in the general ward

Stop antimicrobials when given for too long



# Question 2

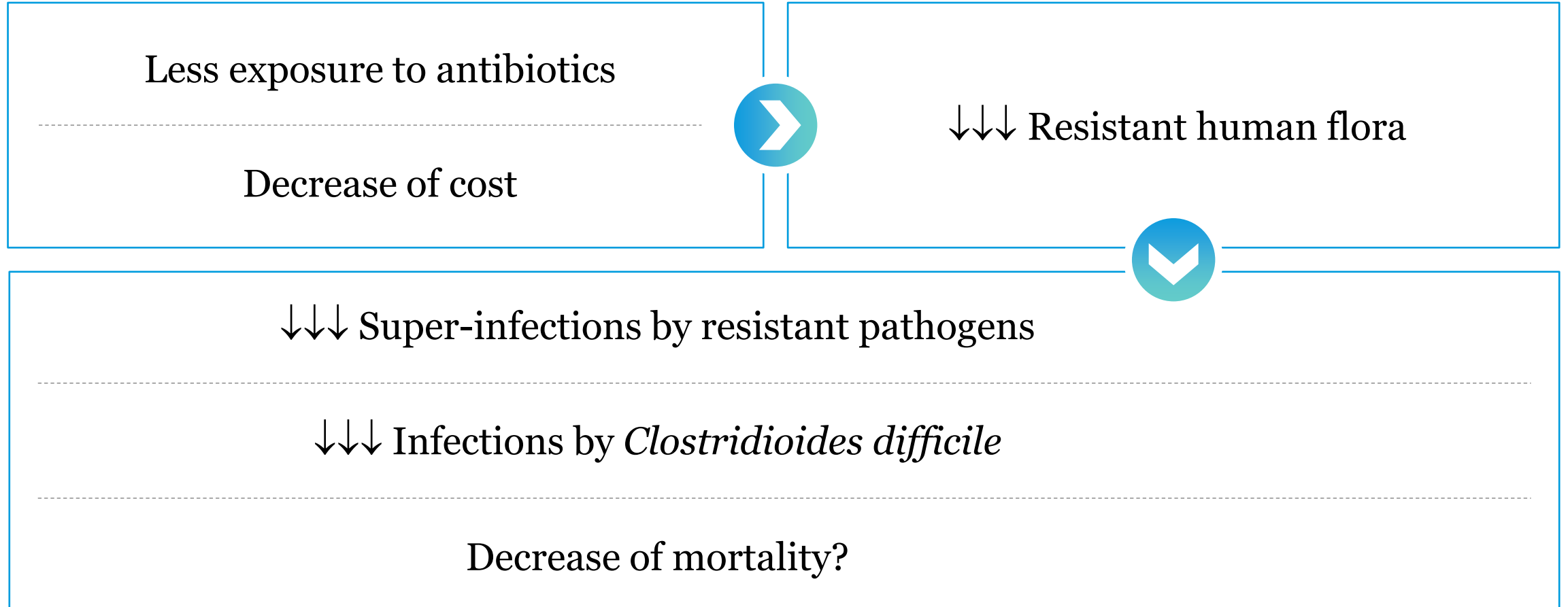
CASE 1: A MAN OF 75 YEARS IS HOSPITALIZED FOR PNEUMONIA FOR WHICH HE RECEIVES PIPERACILLIN/TAZOBACTAM FOR 25 DAYS. HE IS DISCHARGED ON DAY 26 AND AFTER 25 DAYS HE IS ADMITTED WITH FEVER, HYPOTENSION AND DIARRHEA. THE PATIENT IS STARTED ON MEROPENEM WITH NO RESPONSE. THE PATIENT DIES AFTER 72 HOURS. WHAT WENT WRONG?

- 1 The prolonged duration of treatment led to side-effects
- 2 He developed infection by carbapenem-resistant micro-organism
- 3 He developed infection by *C.difficile*
- 4 2 and 3 are the most likely explanations
- 5 All the above may have happened

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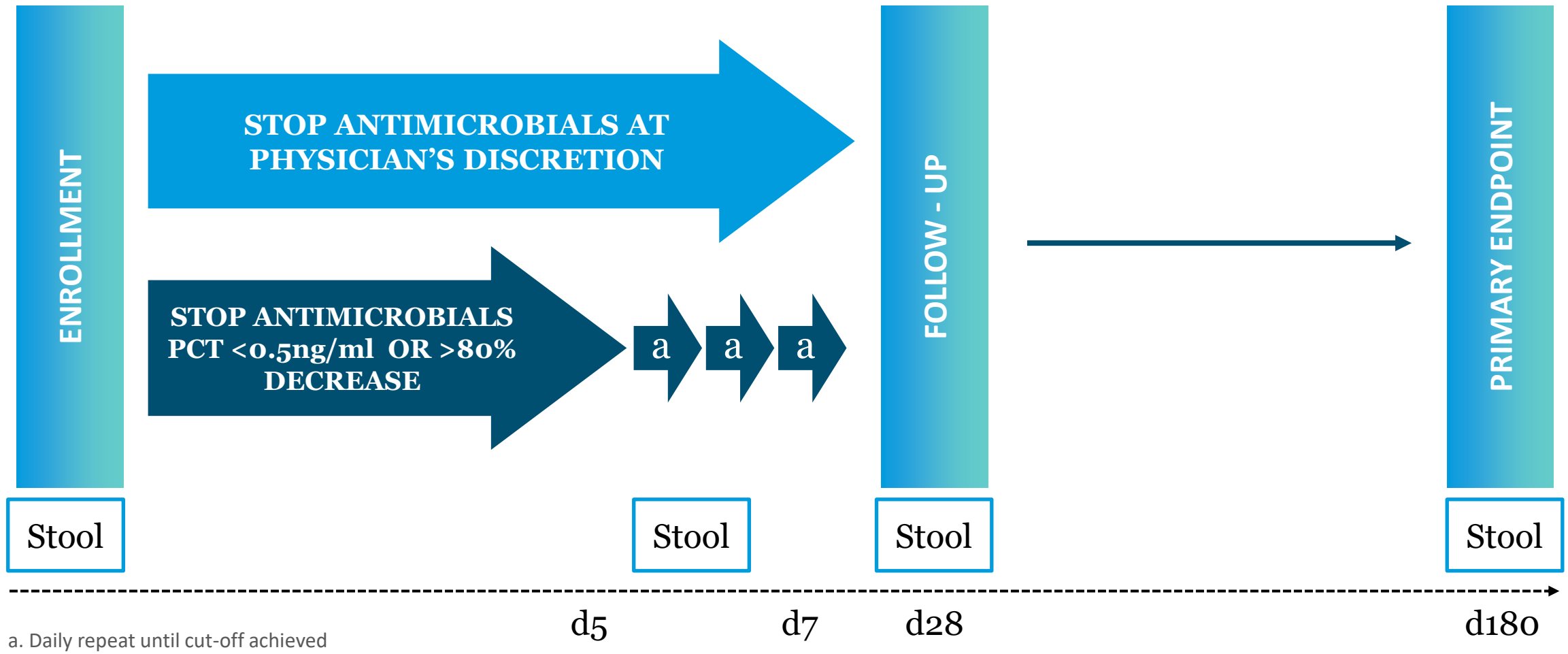


# WHY TO USE BIOMARKERS TO GUIDE EARLY STOP OF ANTIBIOTICS?





# PROGRESS TRIAL: A MAJOR PARADIGM



Kyriazopoulou E, et al. Procalcitonin to Reduce Long-Term Infection-associated Adverse Events in Sepsis. A Randomized Trial. *Am J Respir Crit Care Med*. 2021;203(2):202-210.

# PROGRESS\*: PRIMARY STUDY ENDPOINT

The rate of INFECTION-ASSOCIATED ADVERSE EVENTS at 6 months Composite by ANY of:



*C. difficile* Infection and/or

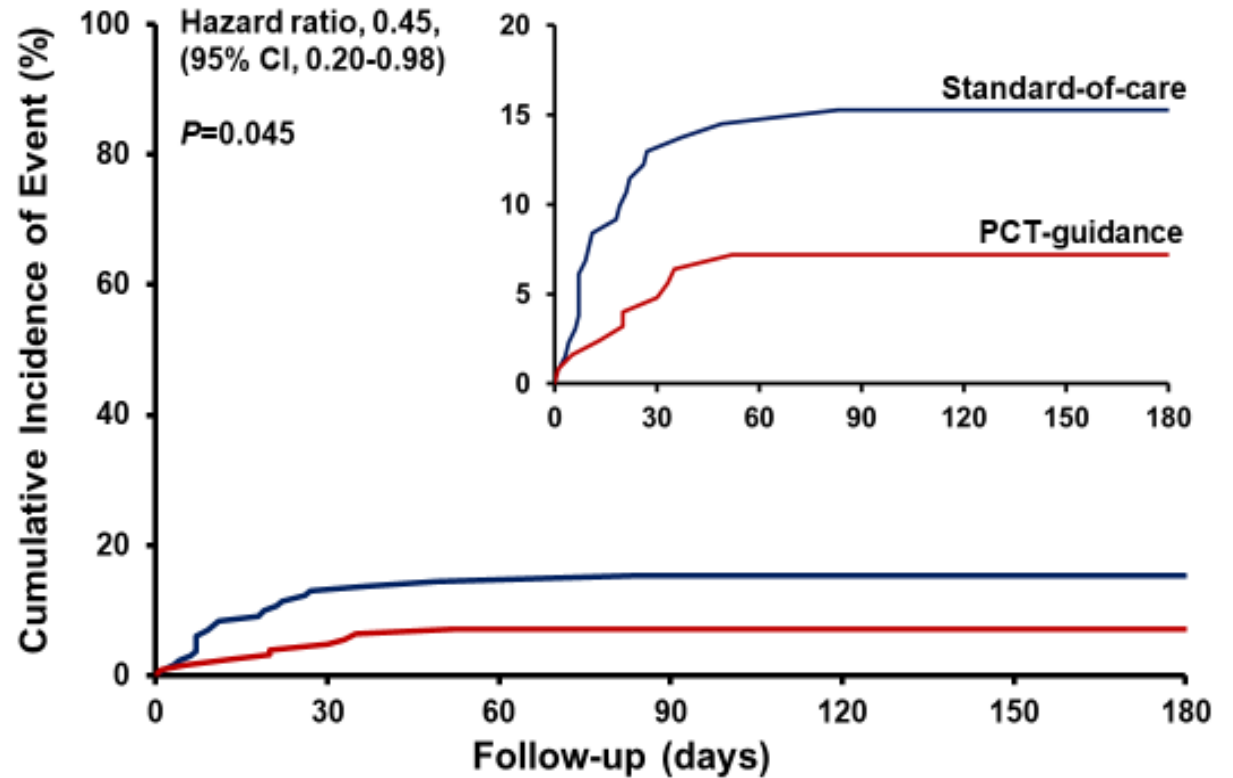


MDRO Infection and/or



*C. difficile* or MDRO infection-associated death

\* PROcalcitonin-Guided antimicrobial therapy to REduce long-term Sequelae of infections



## NO. AT RISK

Standard-of-care	131	87	81	78	77	76	76
PCT-guidance	125	102	87	85	84	84	83

# Question 3

**CASE 2: A WOMAN OF 30 YEARS IS SUFFERING FROM RELAPSING EPISODES OF CYSTITIS. SHE IS ADVISED TO RECEIVE ONE PILL OF NITROFURANTOIN DAILY BEFORE NIGHT SLEEP FOR ONE YEAR. SUDDENLY THE PATIENT HAS FEVER OF 40°C AND RIGOR. WHAT WENT WRONG?**

- She forgot to get her pill because of overwhelming activities
- She feels well and she self-neglects to continue treatment
- Nitrofurantoin gives her nausea and she stopped it without asking her physician
- All the above may have happened

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# ANTIMICROBIALS FOR RELAPSING CYSTITIS

<b>Chemoprophylaxis &lt;6 months (n= 59)</b>	<b>Success rate</b>	
<b>Trimethoprim/sulfamethoxazole 80/400 mg qd</b>	20.0%	
<b>Norfloxacin 100 mg qd</b>	42.9%	p: 0.060
<b>Nitrofurantoin 50 mg qd</b>	59.1%	

<b>Chemoprophylaxis ≥6 months (n= 122)</b>	<b>Success rate</b>	
<b>Trimethoprim/sulfamethoxazole 80/400 mg qd</b>	82.8%	
<b>Norfloxacin 100 mg qd</b>	72.3%	p: 0.046
<b>Nitrofurantoin 50 mg qd</b>	96.8%	

mg: milligram      qd: once daily

Alexiou Z, Mouktaroudi M, Koratzanis G, et al. The significance of compliance for the success of antimicrobial prophylaxis in recurrent lower urinary tract infections: the Greek experience. *Int J Antimicrob Agents*. 2007;30(1):40-43. doi:10.1016/j.ijantimicag.2007.02.017

# ANTIMICROBIAL STEWARDSHIP: PATIENT-RELATED FACTORS OF ADHERENCE

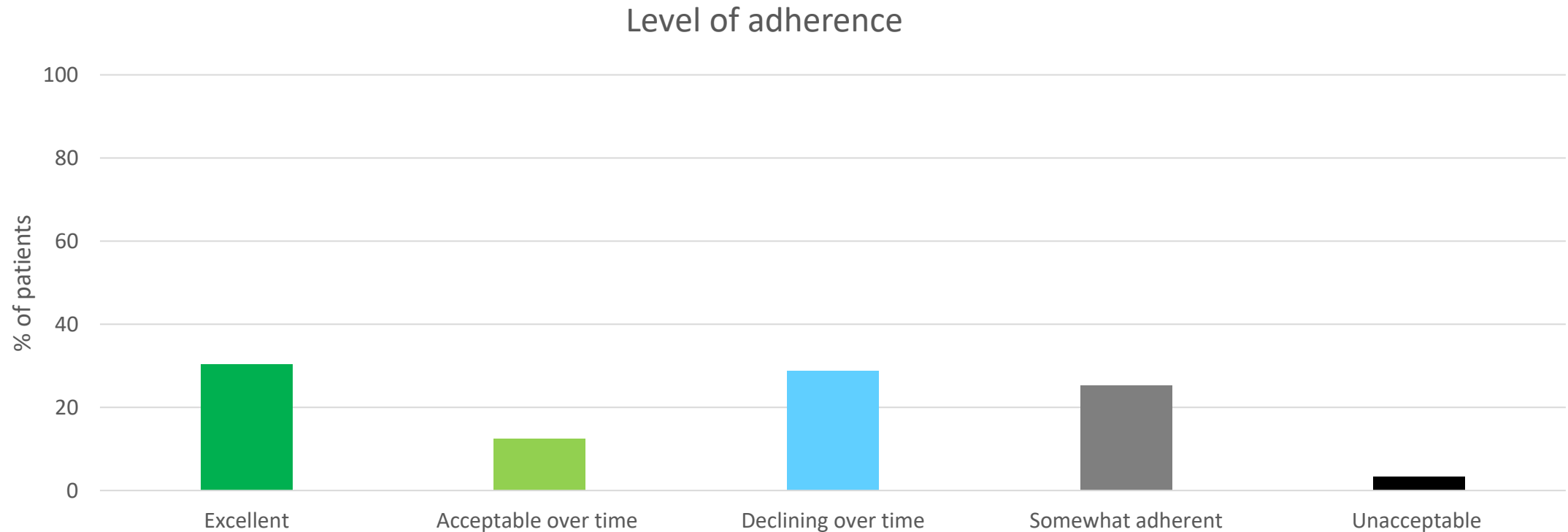
SYSTEMATIC REVIEW (87 STUDIES FROM 33 COUNTRIES) OF PATIENT-RELATED DETERMINANTS OF ANTIBIOTIC USE:

- 1 Demographic and socio-economic characteristics
- 2 Patient–doctor interactions
- 3 Treatment characteristics (e.g. administration frequency)
- 4 Attitudes (e.g. expecting antibiotics)
- 5 Access to treatment (e.g. patients’ direct costs)
- 6 Characteristics of the condition in question (e.g. duration of symptoms)
- 7 Level of knowledge about antibiotics

**‘Barriers’ to responsible antibiotic use and adherence**

# ANTIMICROBIAL STEWARDSHIP: PATIENT ADHERENCE IN PHARYNGITIS

Medication Event Monitoring System from the Pharmacy (n= 481 patients)



# THE IMPORTANCE OF ADHERENCE



Non-adherence often affects the outcome of treatment<sup>1</sup>



Exposing microbes to sub-therapeutic doses of medication drives resistance<sup>2</sup>

## MOST COMMON RISK FACTORS FOR NON-ADHERENCE<sup>3</sup>

- 1 Younger age
- 2 Low income
- 3 Low educational level
- 4 Male gender (worse than female)
- 5 Living alone

## INFECTIONS WITH FREQUENT NON-ADHERENCE<sup>1</sup>

- 1 HIV infection
- 2 Tuberculosis
- 3 Chronic osteomyelitis
- 4 Diabetic foot infections

1. WHO 2003 Adherence to long-term therapies <http://whqlibdoc.who.int/publications/2003/9241545992.pdf> 2. Davidson RJ. In vitro activity and pharmacodynamic/pharmacokinetic parameters of clarithromycin and azithromycin: why they matter in the treatment of respiratory tract infections. *Infect Drug Resist.* 2019;12:585-596. Published 2019 Mar 8. 3. Zanichelli V, et al. Patient-related determinants of antibiotic use: a systematic review. *Clin Microbiol Infect.* 2019 Jan;25(1):48-53.

# THE IMPORTANCE OF THE DIALOG

## PATIENT-DOCTOR INTERACTIONS THAT HAD AN IMPACT ON ADHERENCE INCLUDE:



Clearly understanding the advice provided by the doctor (including receiving written as well as verbal instructions)

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Not feeling ignored by the doctor

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Feeling a sense of control over one's own treatment

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Being ready to return for a follow-up visit



# ANTIMICROBIAL STEWARDSHIP: MAIN CONCLUSIONS



- Molecular diagnosis
- Use of biomarkers (initiate treatment, stop treatment)
- **CONTINUOUSLY EDUCATE**
- Support (with diligence)
- Consultation and pharmacy



- Feedback to the physician
- Calm the fear for need of antimicrobials for flu
- **EXPLAIN** why adherence is needed
- **DISCUSS** with treating physicians