



**The Lebanese Order of Pharmacists**  
26<sup>th</sup> Annual Congress

**Teaming Up for Excellence in Patient Care**  
**معاً للتميز في رعاية المريض**

# **Diagnosis and treatment of acute uncomplicated urinary tract infections: Cystitis and pyelonephritis**

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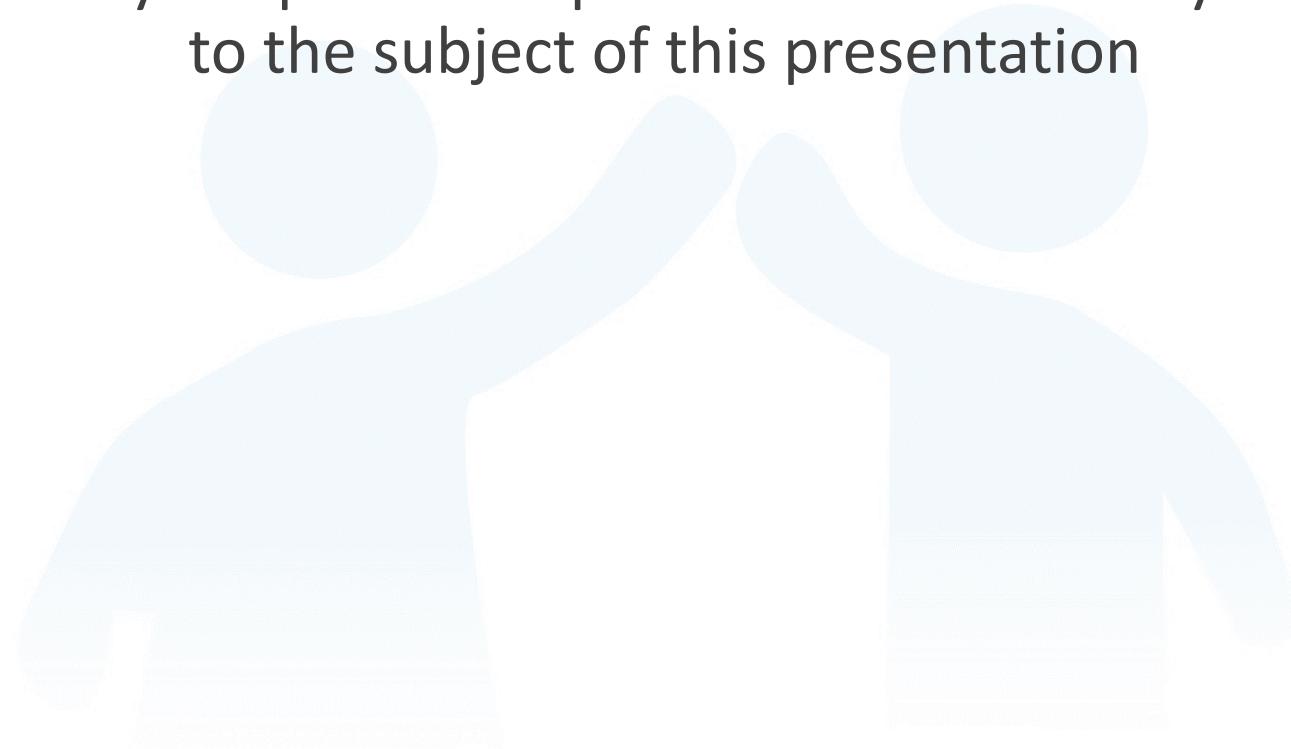
**November 16-18, 2018. Hilton Habtoor Grand. Beirut - Lebanon**



# Disclosure

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“Mira Hleyhel” declare to meeting attendees that there are no financial relationships with any for-profit companies that are directly or indirectly related to the subject of this presentation





# Learning objectives

- **Definition** and **classification** of urinary tract infections (UTIs)
- **Bacteria** that most commonly cause uncomplicated UTIs
- **Predisposing factors** for uncomplicated UTIs
- **Symptoms** and indications for **diagnostic tests** for uncomplicated UTI: cystitis and pyelonephritis
- Choice and duration of **therapy** for uncomplicated cystitis and pyelonephritis
- Level of **adherence to guidelines** for uncomplicated UTI treatment in **Lebanon**



# Introduction

## Urinary tract infections (UTIs)

Among the most common infections

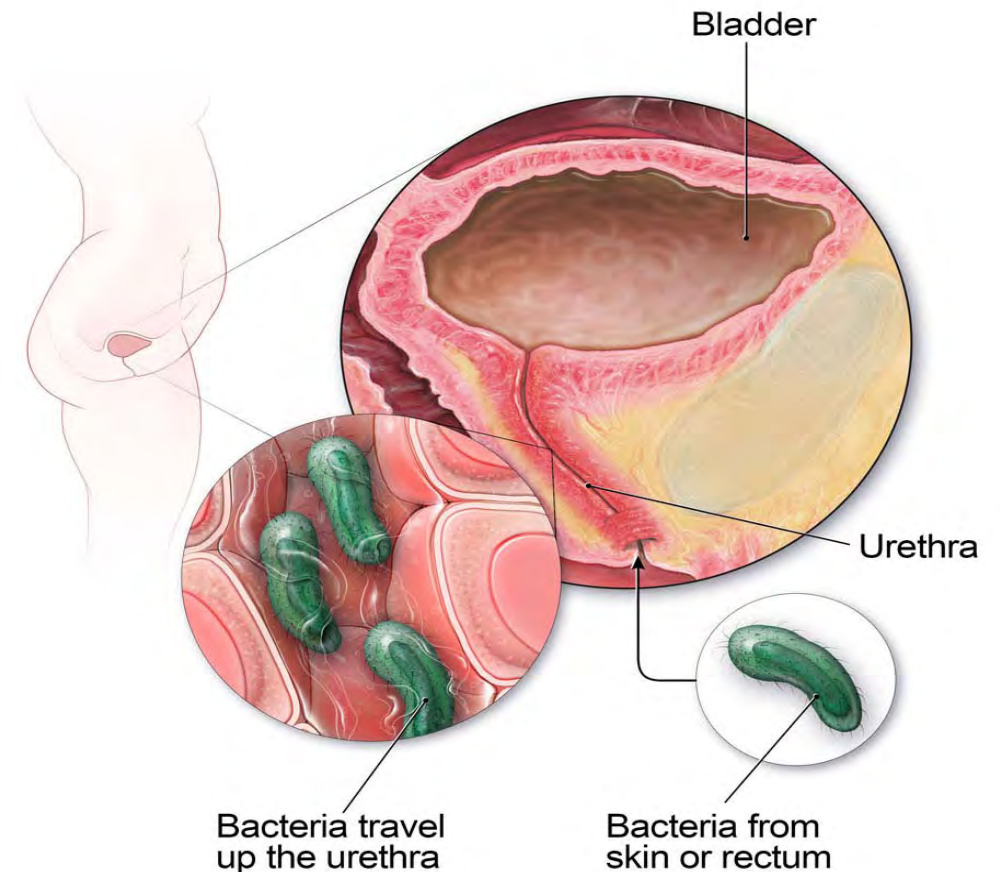
Higher antibiotic resistance due to overuse of fluoroquinolones and excessive duration treatment

Challenge regarding the paucity of available therapeutic options



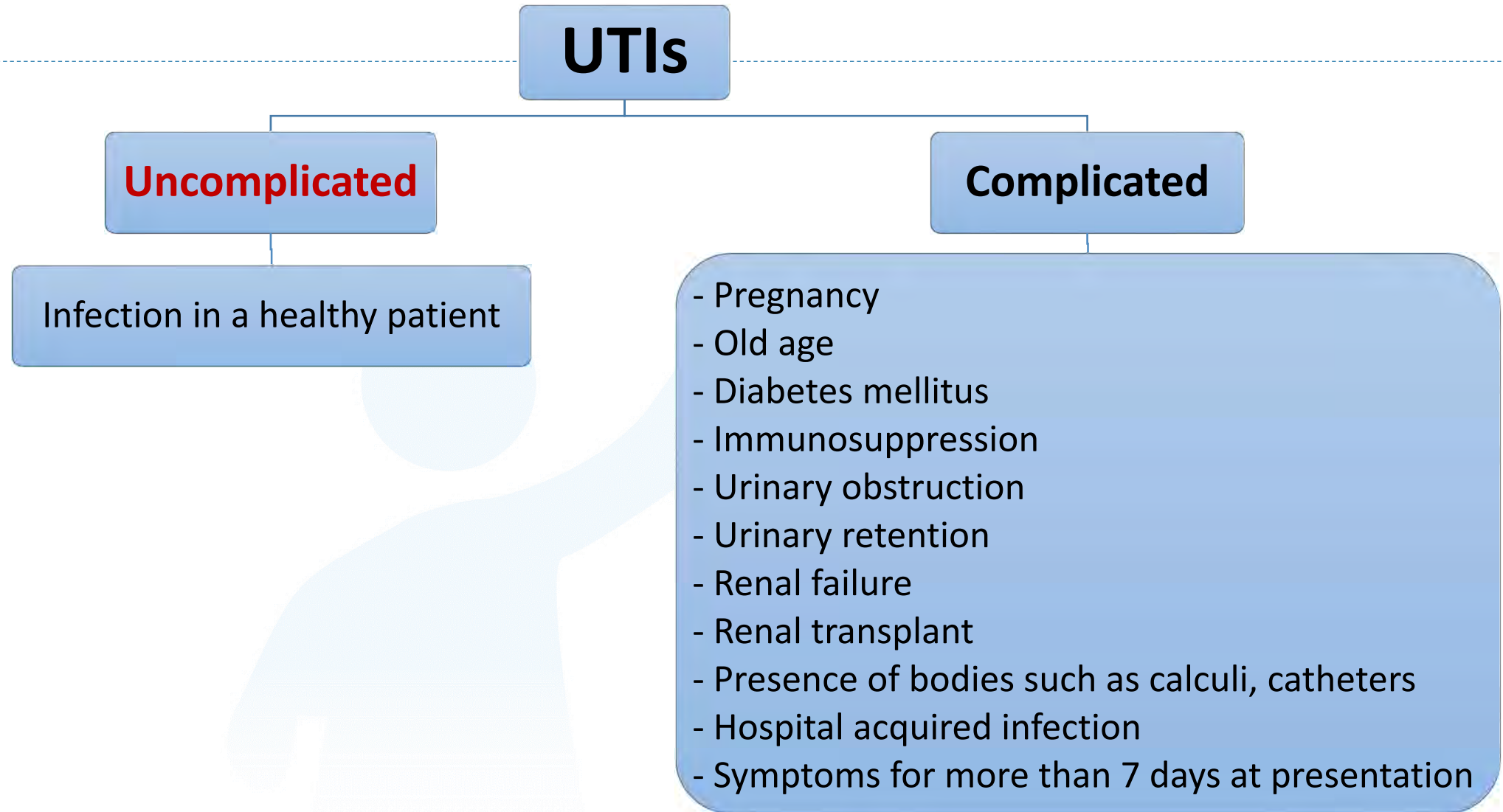
# Definition

- UTI is an inflammation of the urothelium due to an invasion by a pathogen.
- Characterized by the presence of a significant number of bacteria in the urinary tract (i.e.  $\geq 10^5$  organisms/mL)
- **Site of infection:**
  - lower UTIs (urethritis, **cystitis**, and prostatitis)
  - upper UTIs (**pyelonephritis**)





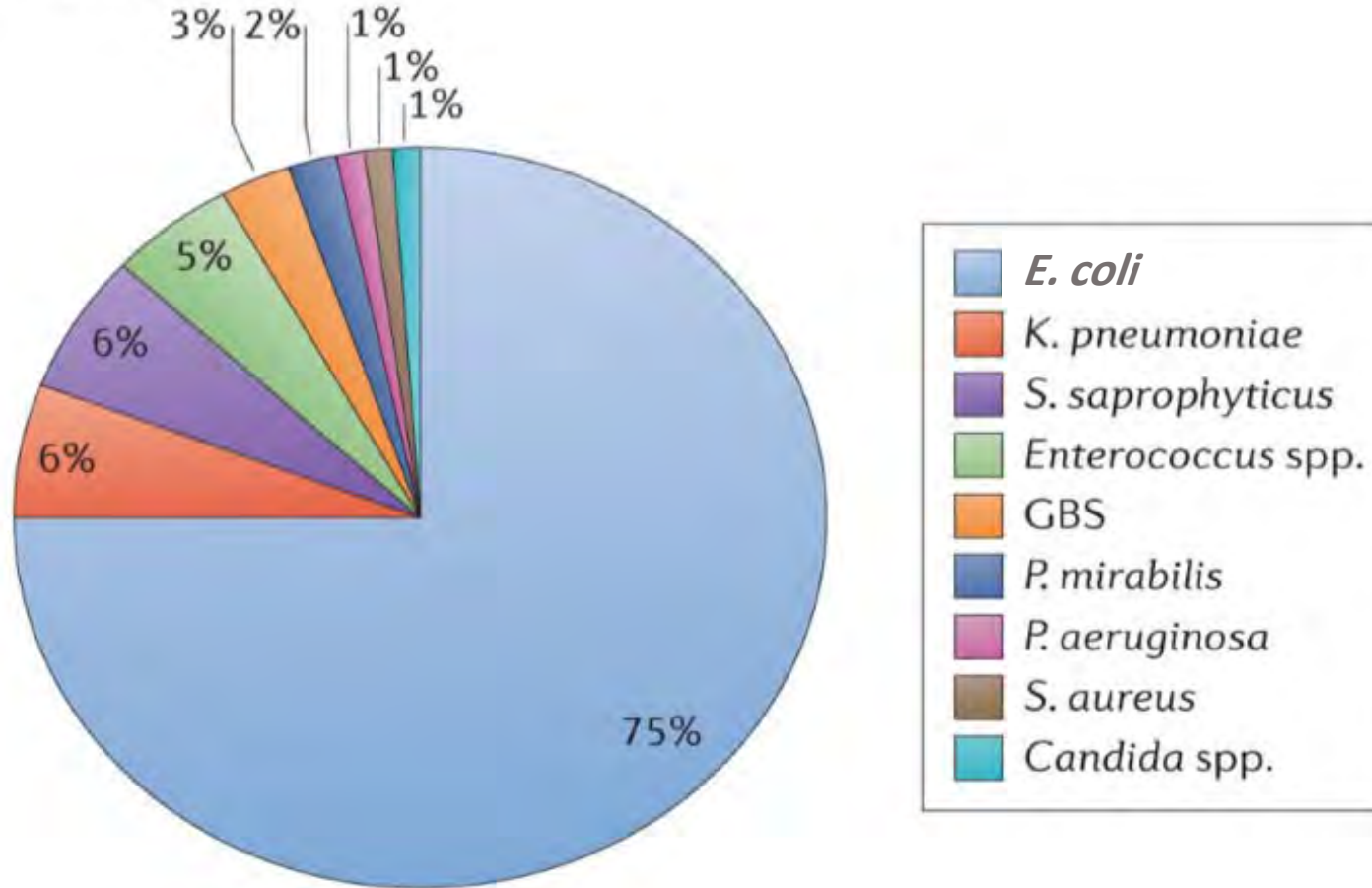
# Classification of UTI





# Etiology

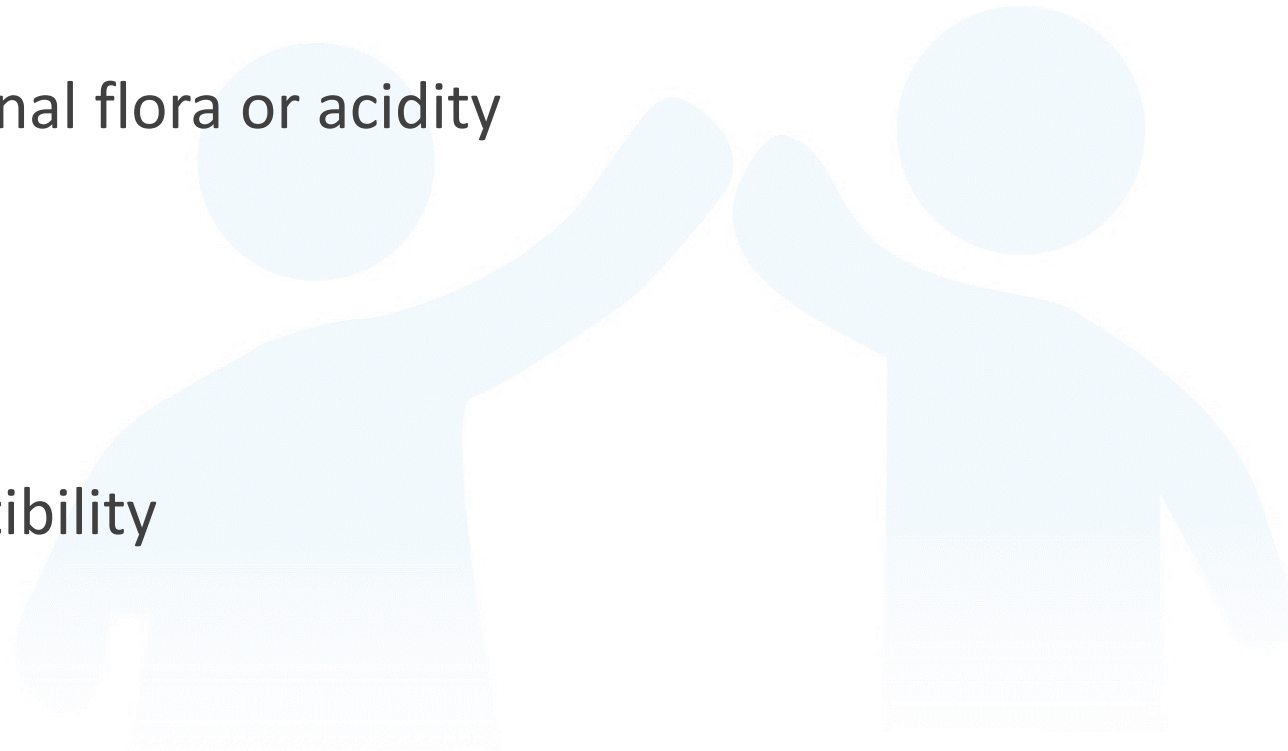
Uncomplicated UTI





# Risk factors

- female gender
- previous UTI
- sexual activity
- changes in vaginal flora or acidity
- pregnancy
- diabetes
- obesity
- genetic susceptibility







# Clinical presentation

## Cystitis

Dysuria

Frequency

Urgency

Occasional suprapubic pain

Low fever ( $<38.3^{\circ}\text{C}$ )

Hematuria

## Pyelonephritis

Chills

High fever ( $>38.3^{\circ}\text{C}$ )

Flank pain

Nausea and vomiting



# Diagnosis

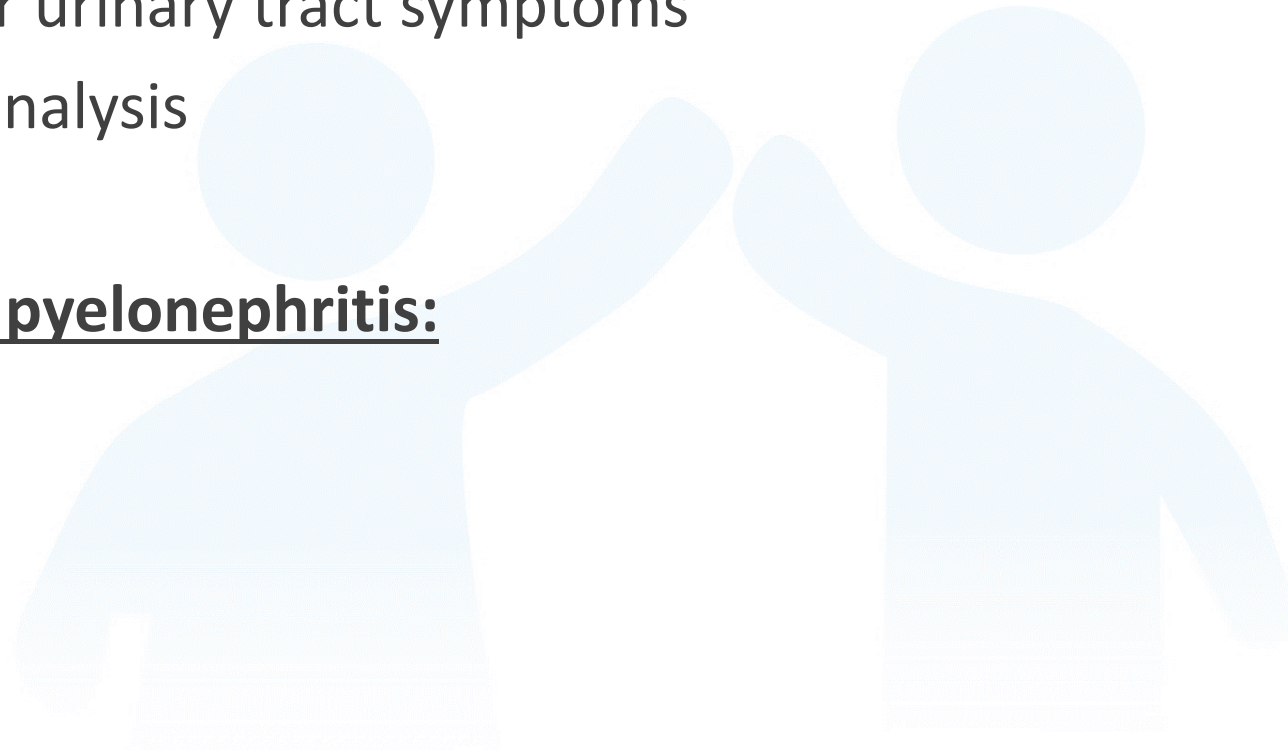
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## Acute uncomplicated cystitis :

- Patients with no risk factors for complicated UTI
- History of lower urinary tract symptoms
- Urine dipstick analysis

## Suspected acute pyelonephritis:

- Urine culture





# Quizz

1) Factors associated with complicated UTI include:

- A. Prior UTI
- B. Pregnancy
- C. Immunosuppression

2) Signs and symptoms of uncomplicated cystitis include:

- A. High fever (>38.5 C)
- B. Flank pain
- C. Frequent and painful urination



# Treatment

## Guidelines:

- The **Lebanese Society of Infectious Diseases and Clinical Microbiology Guidelines for the treatment of urinary tract infections**

*“Husni et al., Lebanese Medical Journal, 2017”*

- Guidelines on treatment of uncomplicated urinary tract infection, published in 2011 by the Infectious Diseases Society of America (IDSA) and the European Society for Microbiology and Infectious Diseases (ESCMID)

*“Gupta et al., Clinical Infectious Diseases, 2011”*



# Recommended antimicrobial regimens for the treatment of acute uncomplicated bacterial cystitis

Antibiotic	Dose	Frequency	Route	Duration
Microcrystalline Nitrofurantoin monohydrate	100 mg	BID	PO	5 days
Fosfomycin trometamol	3g	Once	PO	One single dose
Cefdinir	300 mg	BID	PO	3-7 days
Cefuroxime	500 mg	BID	PO	3-7 days
Cefixime	400 mg	QD	PO	3-7 days
Amoxicillin-clavulanate	1g	BID	PO	3-7 days
Ciprofloxacin	250 mg-500 mg	According to body weight	PO	3-5 days
Ofloxacin	200 mg	BID	PO	3-5 days
Levofloxacin	500 mg	QD	PO	3-5 days
Prulifloxacin	600 mg	QD	PO	3-5 days

**BID:** twice a day    **QD:** daily    **PO:** per os

HUSNI et al., Lebanese guidelines for the treatment of UTIs. Lebanese Medical Journal 2017; 65 (4): 211



# Antibiotic recommendations for acute uncomplicated pyelonephritis

Antibiotic	Dose	Frequency	Route	Duration
Ceftriaxone	2 g	QD	IV/IM	10-14 days*
Aztreonam*	1-2 g	Q8h	IV	10-14 days*
Amoxicillin-clavulanate	1.2 g	Q8h	IV	10-14 days*
Ertapenem	1 g	QD	IV/IM	10-14 days*
Ciprofloxacin	500 mg	BID	IV/PO	7 days**
Prulifloxacin	600 mg	QD	PO	7 days
Ofloxacin	200-400 mg	BID	PO	7 days
Levofloxacin	500-750 mg	QD	PO/IV	7 days

**QD:** daily    **BID:** twice a day    **IV:** intravenous    **IM:** intramuscular    **PO:** per os

\*IV therapy is continued till the patient is stable and can take oral medication (for a total course of 10-14 days)

\*\*Alternative in case of allergy to  $\beta$ -lactams

HUSNI et al., Lebanese guidelines for the treatment of UTIs. Lebanese Medical Journal 2017; 65 (4): 211



# Medication guide

## ■ Nitrofurantoin:

- Contraindicated in pregnancy and breastfeeding
- Should not be consumed with antacids containing magnesium
- Should be taken ideally with food for easy absorption
- Most frequently reported adverse effects: diarrhea, headache, nausea, ...

## ■ Fosfomycin:

- Can be taken with or without food
- Most frequently reported adverse effects: diarrhea, headache, vaginitis, nausea, ...



# Medication guide

## Fluoroquinolones:

- Contraindicated in pregnancy and breastfeeding
- Can be taken with or without food
- Should not be taken with dairy products
- Should be taken either 2 hours before or 6 hours after taking an antacid, multivitamin, or other medicine or supplements that has magnesium, calcium, aluminum, iron, zinc, sucralfate, ...
- Most frequently reported adverse effects:
  - Tendinitis and tendon rupture
  - Peripheral neuropathy and central nervous system effects
  - *Clostridium difficile*-associated diarrhea
  - Photosensitivity/phototoxicity





# Treatment

## Goals of therapy:

- Symptomatic relief
- Clinical response within 24 hours for cystitis and within 48–72 hours for pyelonephritis
- Consideration of **antimicrobial resistance** and **collateral damage**
- **collateral damage** :
  - selection of drug-resistant organisms
  - colonization or infection with multidrug-resistant organisms



# Rational use of medicines

**Overuse and misuse of antibiotics => ↗ antibiotic resistance**

**Rational use of medicines** requires that "patients receive **medications** appropriate to their clinical needs, in **doses** that meet their own individual requirements, for an adequate **period of time**, and at the lowest cost to them and their community".



At least 30% of antibiotics prescribed in the outpatient setting are unnecessary



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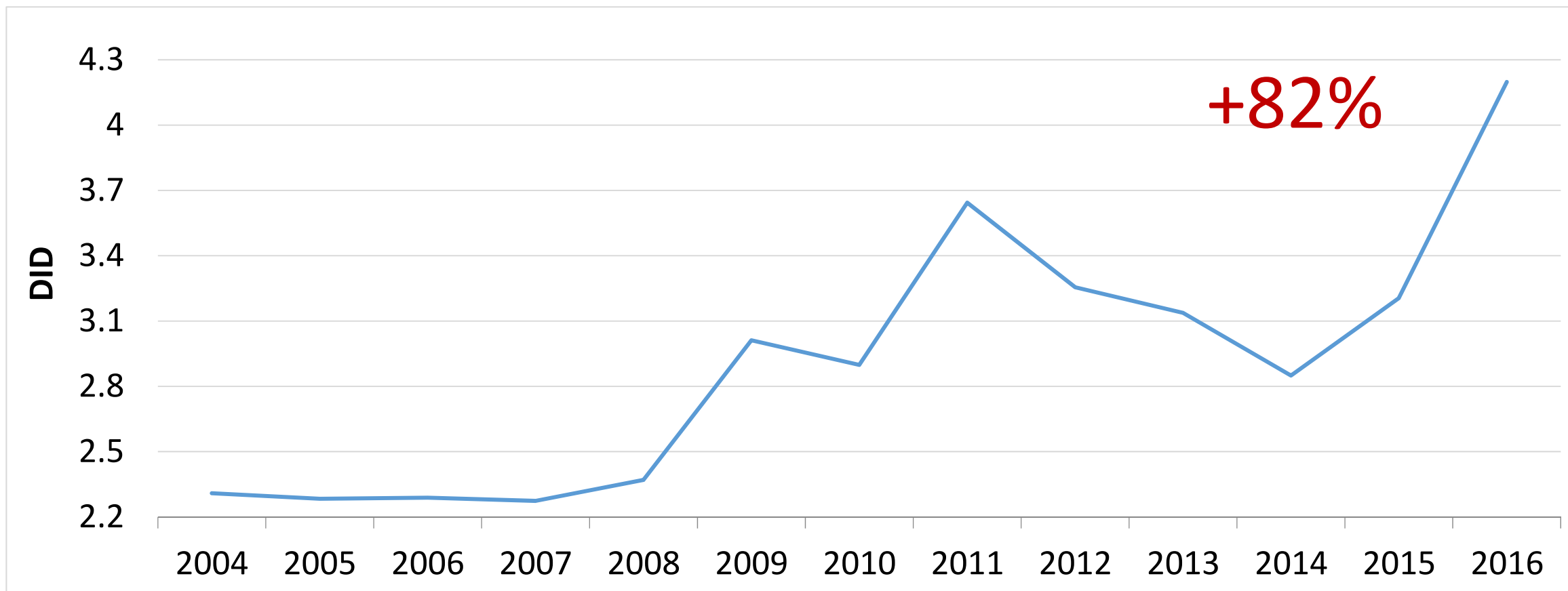


# Antimicrobial resistance

- Associated with use of **broad spectrum cephalosporins** and **fluoroquinolones**
- **Resistance data in Lebanon:** (Araj and Zaatari 2013, 2014, 2015; Moghnieh et al. 2014)
  - Consistent  $\nearrow$  of *Escherichia coli* and *Klebsiella* spp. resistance to fluoroquinolones
  - *E. coli* and *Klebsiella* sp. : 50% resistant to ciprofloxacin, 30% resistant to third generation cephalosporin



# Fluoroquinolones consumption in Lebanon between 2004 and 2016 by Defined Daily Dose/1000 inhabitants/day (DID)



Lahoud et al., unpublished data



# Adherence to guidelines for uncomplicated UTIs treatment in Lebanon

## *1) Adherence to International Guidelines for the Treatment of Uncomplicated Urinary Tract Infections in Lebanon (Kabbara et al., 2018)*

- 376 Patients diagnosed with UTI visiting 15 community pharmacies to purchase antibiotic treatment in 2015-2016:
- Prescribed antibiotics:
  - Fluoroquinolones (39%) of which Ciprofloxacin (19%)
  - Nitrofurantoin (26%)
  - Fosfomycin (5%)
  - Other medications (30%)



# Adherence to guidelines for uncomplicated UTIs treatment in Lebanon

## *1) Adherence to International Guidelines for the Treatment of Uncomplicated Urinary Tract Infections in Lebanon (Kabbara et al., 2018)*

- Appropriateness of treatment

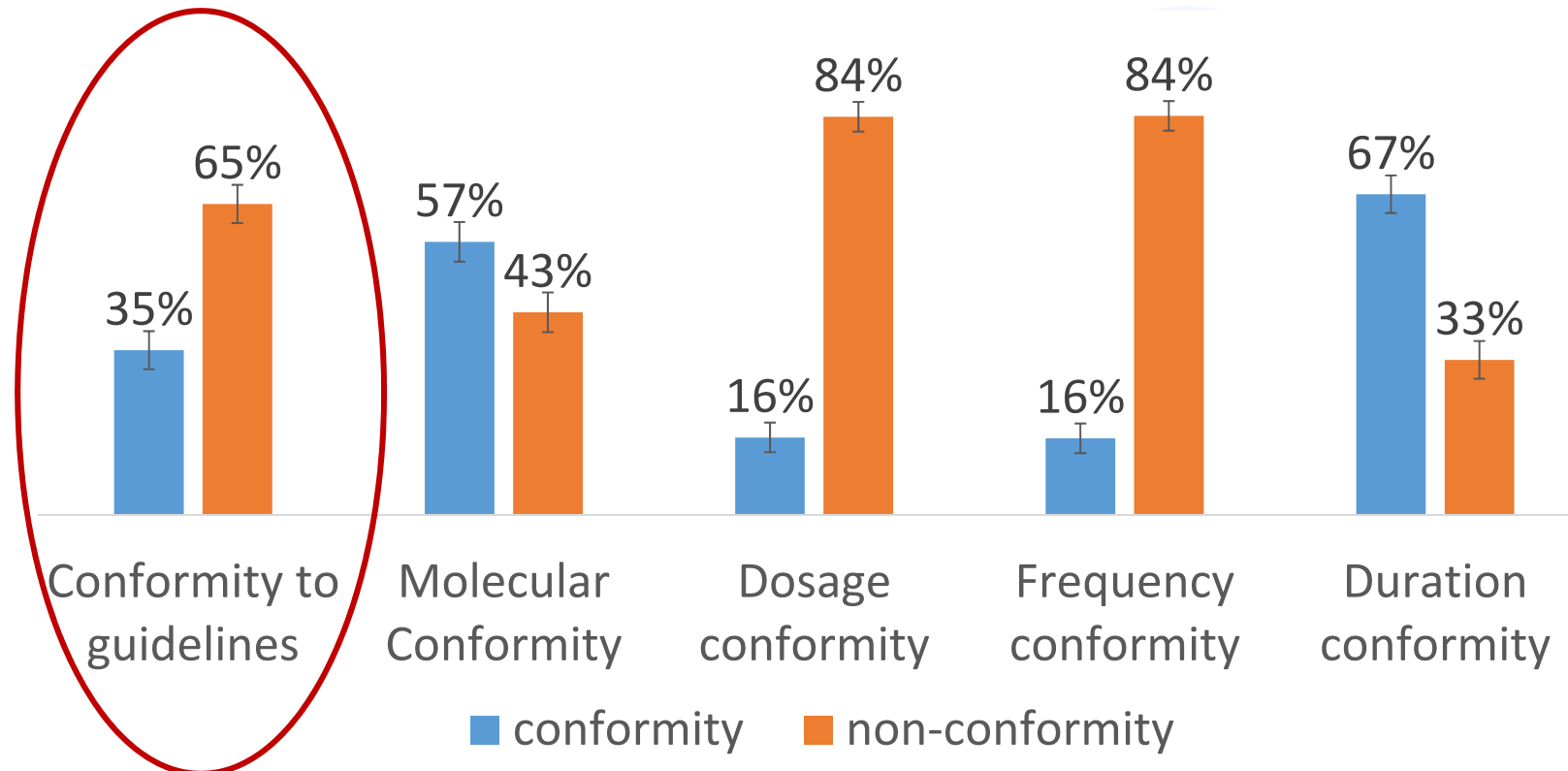
	Appropriate	Nonappropriate
Regimen	80 (21%)	296 (79%)
Drug	131 (35%)	245 (65%)
Dose	276 (73%)	100 (27%)
Duration	219 (58%)	157 (42%)

Kabbara et al., Canadian Journal of Infectious Diseases and Medical Microbiology, 2018



# Adherence to guidelines for uncomplicated UTIs treatment in Lebanon

*2) Unpublished data including 540 prescriptions obtained from 120 physicians (general practitioners, family medicine, infectious, internal medicine, gynecologists, urologists and nephrologists)*





# Quizz

3) The prevalence of inappropriate use of antibiotics for the treatment of outpatient uncomplicated urinary tract infections in Lebanon is :

- A. 20-35%
- B. 25-45%
- C. 40-55%

4) First line therapy for uncomplicated cystitis includes :

- A. Ciprofloxacin
- B. Nitrofurantoin
- C. Beta-lactam





# Key Takeaways

- Most common bacterial cause of uncomplicated UTIs is **E. coli**
- Urine culture **only** for patients with suspected acute pyelonephritis or with risk factors for complicated UTI
- First line therapy for uncomplicated cystitis: **nitrofurantoin** or **fosfomicin**
- For uncomplicated pyelonephritis: immediate case specific empiric treatment followed by definitive therapy after **susceptibility testing**
- High prevalence of **inappropriate use of antibiotics** for the treatment of outpatient uncomplicated urinary tract infections in Lebanon (20-35%)
- Pharmacist's role in **increasing awareness** of treatment duration and the adverse effects of antimicrobial therapy among patients

# THANK YOU

