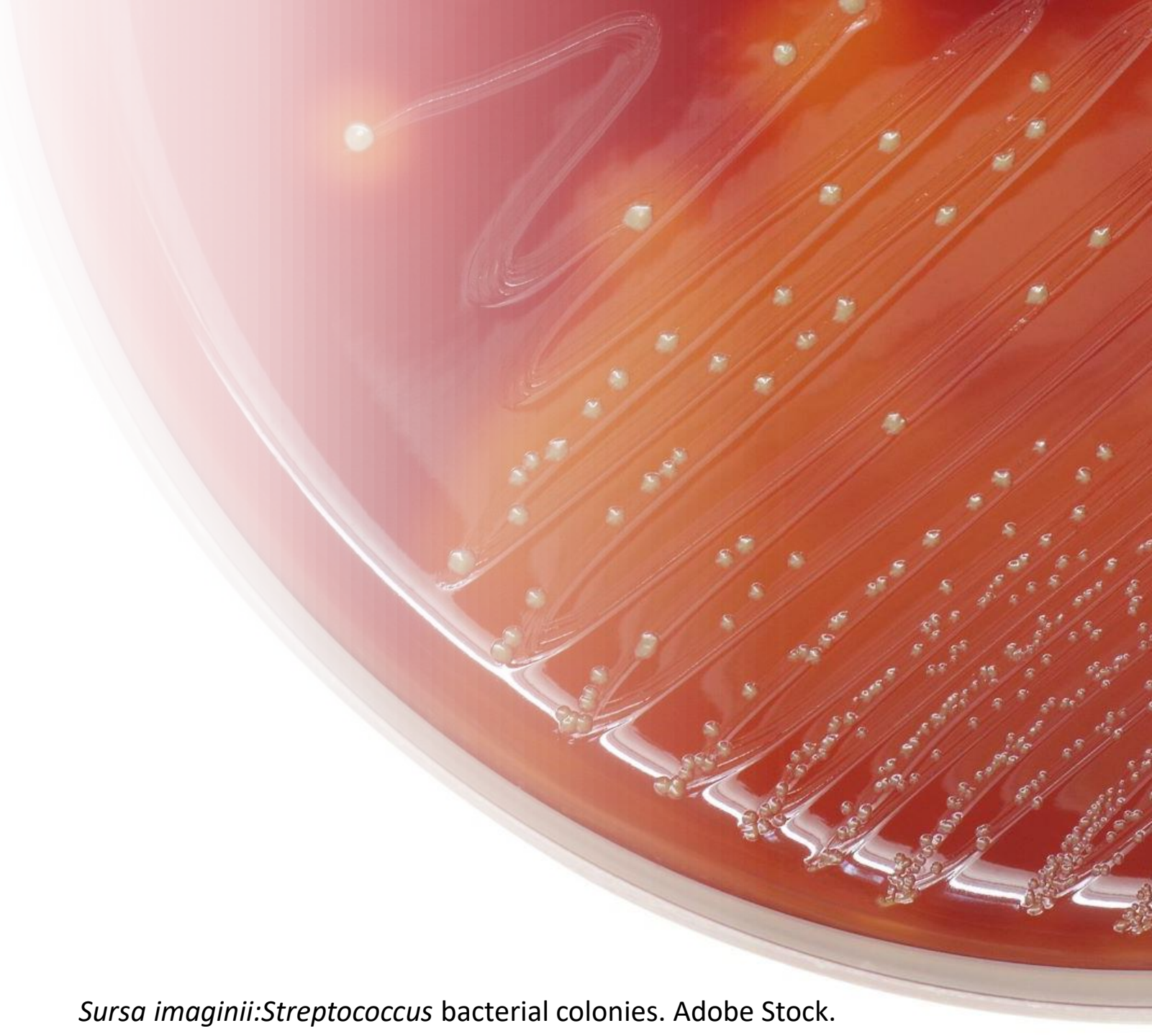




Infecții streptococice (inclusiv invazive): actualități epidemiologice și oportunități de stewardship

Dr. Iacob Diana-Gabriela



Sursa imaginii: Streptococcus bacterial colonies. Adobe Stock.



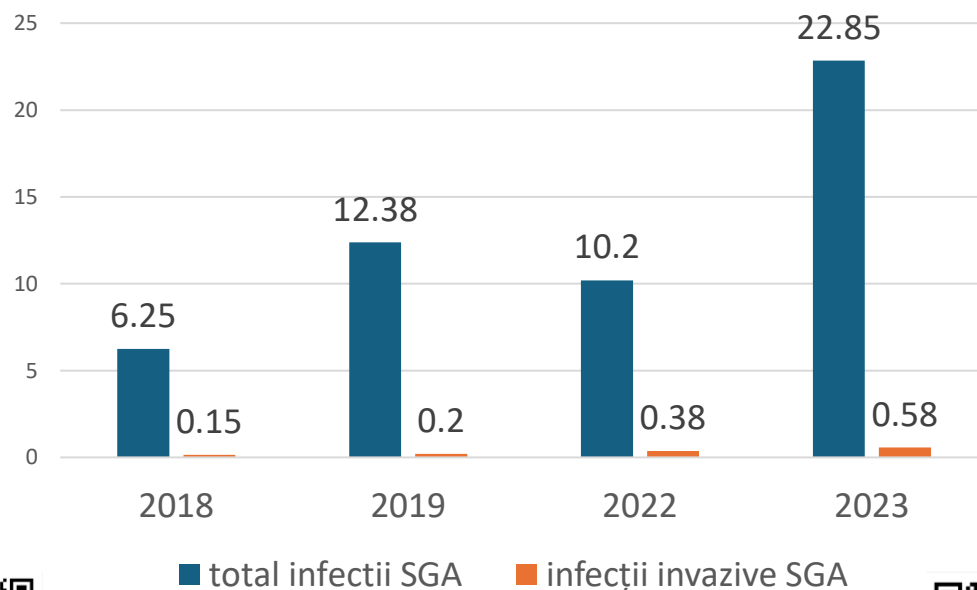
Teme de discuție

- Date epidemiologice
 - Incidența în creștere la nivel internațional și național
 - Experiența SUUB - infecții invazive streptococice
 - Consumul de antibiotice și rezistența asociată infecțiilor streptococice
- Aplicații pentru stewardship antibiotic
 - Decizii în ambulator / spital
 - Intervenții de stewardship
- Perspective de viitor

Date epidemiologice – Streptococ grup A (SGA)

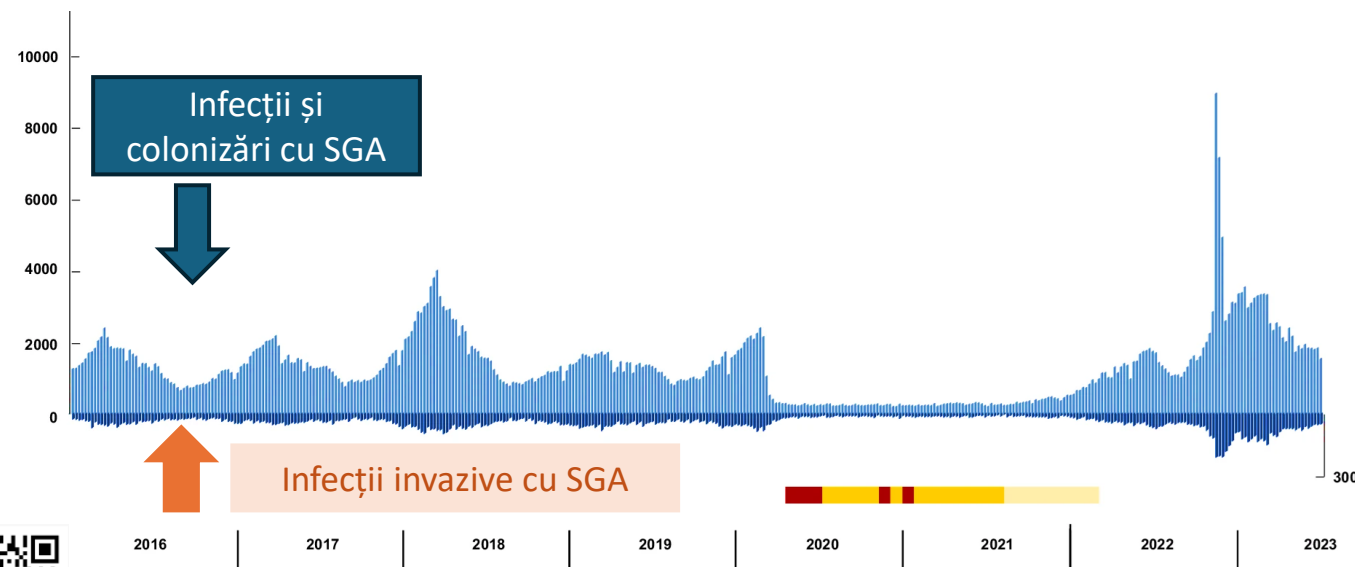
- Cresterea incidenței și severității cazurilor de infecții cu SGA încă din 2008-2019 ^{1,2,3}
- serotipuri invazive frecvent izolate: emm1 – varianta M1 UK, emm12

Incidența infecțiilor cu SGA
la 1000 prezentări în UPU - PedGas-Net (Spania)



Modificat dupa Calvo et al (2024)

Incidența SGA
în Anglia 2016-2023



Modificat dupa Vieira et al (2024)

Date epidemiologice naționale - SGA

- La nivel național:
 - Incidență în creștere în 2022 (2.16/100 000 loc) vs 2020 (1.81/100 000 loc)
 - Apariția de cazuri de scarlatină la grupa de vârstă 15-19 ani (2022)
 - 2023 – raport în curs



Buzău: Varicela, locul I în topul bolilor transmisibile; scarlatina, creștere de 40 de ori în 2023 față de 2022

2024-01-26 09:17:08



Focar de scarlatină într-o școală din Mureș. Copiii bolnavi au fost izolați acasă, dar boala e foarte periculoasă

Vineri 09 Februarie 2024

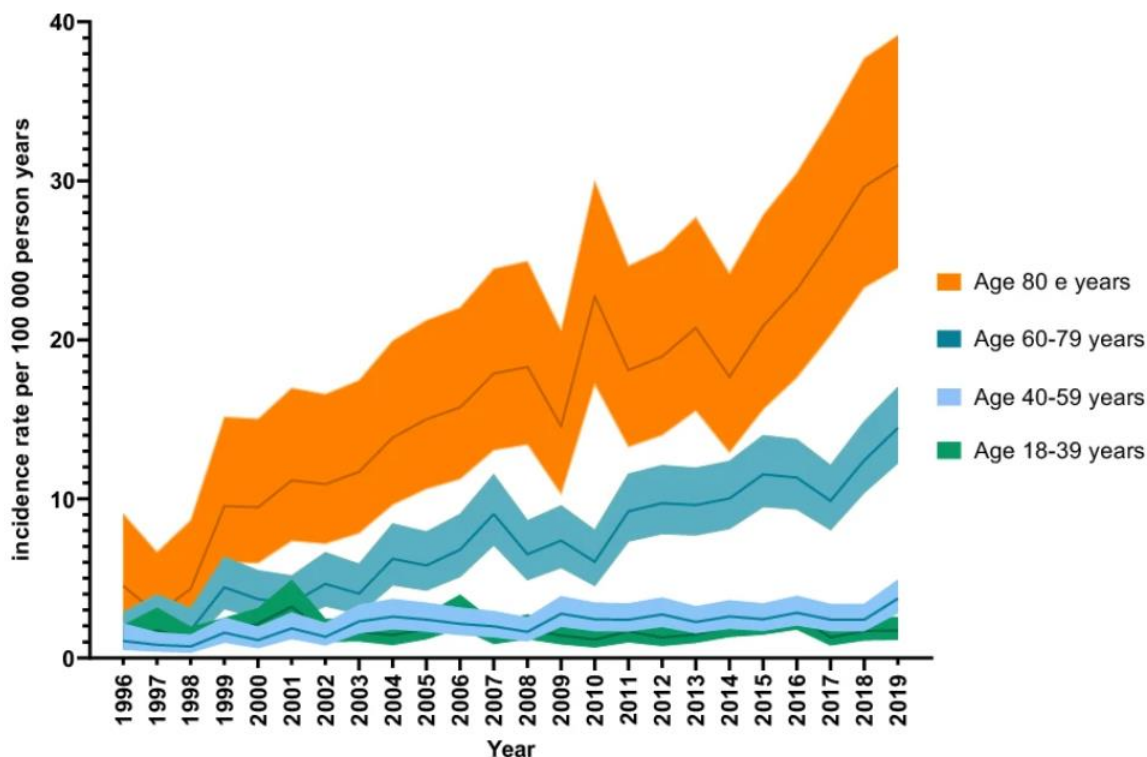
Alertă de scarlatină în Vaslui. Copiii din școli și grădinițe sunt în pericol de infectare

Vineri 14 Octombrie 2022

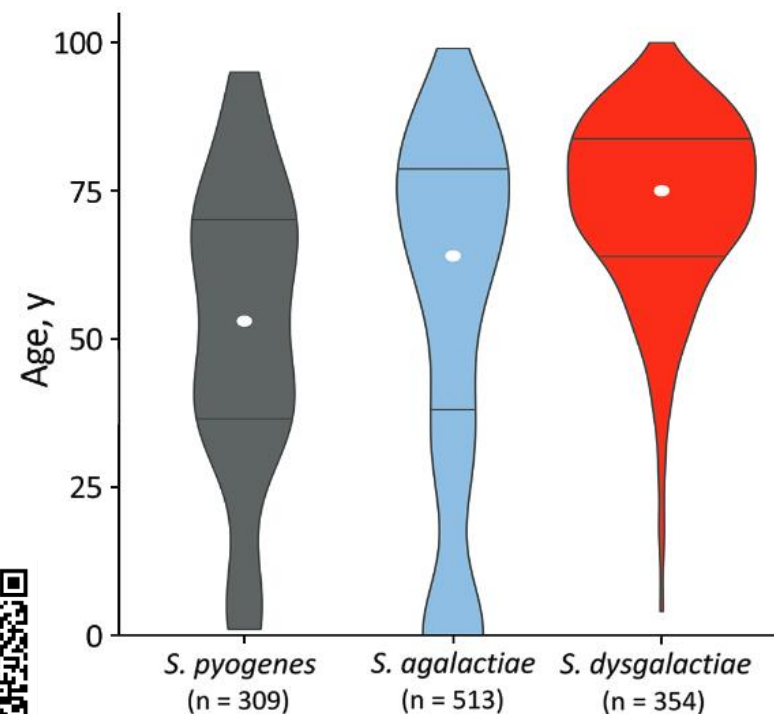
Date epidemiologice – Alte infecții streptococice

- Creșterea incidenței infecțiilor cu Streptococi grup B, predominant la vârstnici ⁴
- creșterea cazurilor de infecții sistemice prin *Streptococcus dysgalactiae* ^{5,6}

Incidența infecțiilor cu Streptococ de grup B pe grupe de vârstă 1996 -2019 (Norvegia)



Distribuția pe grupe de vârstă a infecțiilor sistemice cu Streptococi β hemolitici 1999-2021 (Norvegia)



Situația actuală – consumul de antibiotice

Raport ECDC 2022

Consumul de antibiotice în ambulatoriu

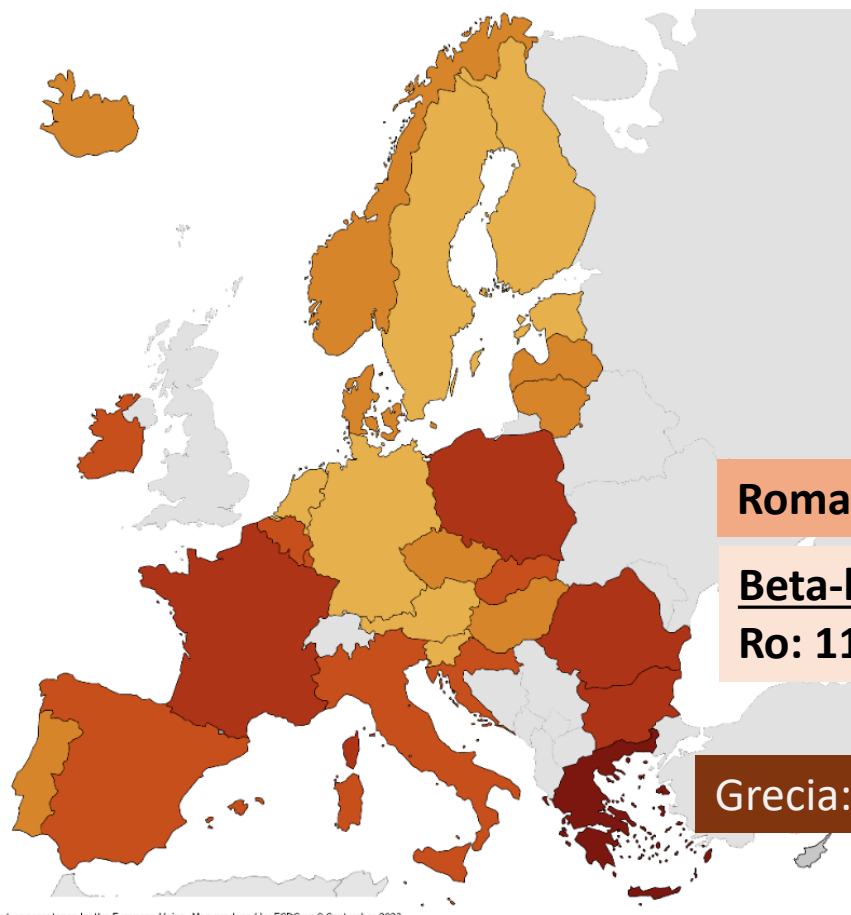


Community

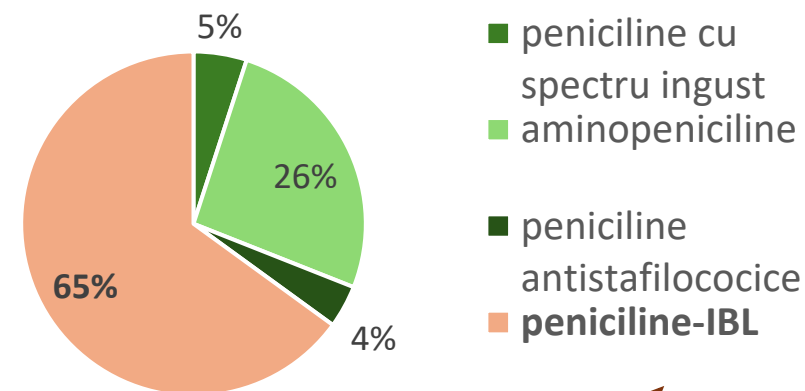
- 8.3 - 12.9
- 13.0 - 17.5
- 17.6 - 22.0
- 22.1 - 26.6
- 26.7 - 31.2
- No data

Non-visible countries

- Liechtenstein
- Luxembourg
- Malta



Raportul CARMIAAM-ROM 2020 Consumul de beta-lactamine

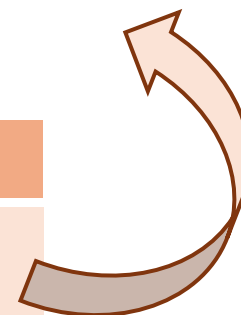


Romania: 26 DDD/1000 locuitori – locul 2

Beta-lactamine în ambulatoriu

Ro: 11.6 DDD/1000 locuitori (locul 3)

Grecia: 31.2 DDD/1000 locuitori – locul 1



Situația actuală – rezistența la antibiotice în infecțiile cu SGA

- Sensibilitate păstrată pentru peniciline
- Rezistența în creștere pentru eritromicină, clindamicină și tetraciclină în proporții variabile între diferite regiuni geografice ^{7,8}

Rezistența raportată CDC	
eritromicină	11.9% (2011) → 24.7% (2019) → 35% (2021)
clindamicină	8.9% (2011) → 23.8% (2019) → 36% (2021)

Distribuția geografică a genelor de rezistență pentru macrolide

(b) <i>Streptococcus pyogenes</i>			<i>erm</i> (B)		<i>erm</i> (TR)		<i>erm</i> (T)		<i>mef</i> (A/E)	
Continent	Period	MR (N)	Mean (%)	Range (%)	Mean (%)	Range (%)	Mean (%)	Range (%)	Mean (%)	Range (%)
Africa	2000–2013	84	19.0	7.6–57.1	26.1	0.0–38.8	-	-	48.8	14.2–57.6
America	1996–2017	1128	25.6	4.1–25.7	30.5	0.0–36.9	25.6	0.0–55.0	13.7	0.0–95.6
Asia	1993–2019	877	54.2	18.6–97.7	3.6	0.0–10.5	-	-	39.7	0.0–80.0
Europe	1995–2016	2873	31.5	5.8–70.9	14.6	0.0–59.0	-	-	40.7	0.0–80.0



- Rezistență raportată și la fluoroquinolone
- Fără date pentru trimetoprim-sulfametoxazol (pentru infecții cutanate)

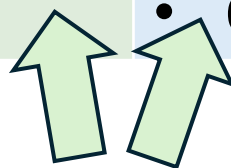
Intervenții de stewardship



Imaginea:
<https://www.orchardsoft.com/blog/antimicrobial-stewardship-its-role-in-veterinary-laboratories/>

Interventii de stewardship aplicabile pentru infecții streptococice

Interventii anterioare prescrierii de AB	Interventii ulterioare prescrierii de AB
• Educarea publicului si a clinicienilor • Crearea unui ghid instituțional • Antibiograme cumulative • Alergia la penicilina – re-evaluare	• Reevaluare trat cu audit+feedback • Conversie iv la po • Optimizarea duratei de tratament • Optimizarea dozelor



Ambulator și intraspitalicesc (infecții invazive):
Penicilina de preferat vs alte beta-lactamine/ alte clase

Decizii în ambulator – Peniciline cu spectru îngust vs alte beta-lactamine

**Peniciline cu
spectru îngust
(Access list –AWARE)**

- **Spectrul îngust**
- **Eficacitate pentru tratament +
prevenirea complicațiilor**
- **Reacții adverse rare**
- **Cost redus**

Microorganism	Regiune geografică	Susceptibilitate față de aminopeniciline (fără beneficiu la clavulanat)
Streptococcus pyogenes	Toate regiunile	100%
Streptococcus agalactiae	Toate regiunile	100%
Streptococcus pneumoniae	Toate regiunile	80-90%

- **Fără beneficiu al
clavulanatului**
- **rezistență la penicilină
raportată⁹**

Modificat după Huttner et al (2019)



Decizii în ambulator – Peniciline cu spectru îngust vs alte beta-lactamine

**Cefalosporine de
generațiile II/III
(WATCH list - AWARE)**

- **Eficacitate păstrată pe**
 - **SGA**
 - **Streptococ grup B**
 - **Streptococcus pneumoniae (rezistență la penicilină în unele regiuni¹⁰)**

Raportul CARMIAAM-ROM 2020

- rezistență la peniciline de ~ 38% (Ro)
 - rezistența la cefalosp gen III –a ~ 19%
- **Spectrul mai larg – Gram negativi**
 - **Risc de reacții adverse**
-

Decizii în ambulator – Peniciline cu spectru îngust vs antibiotice din alte clase

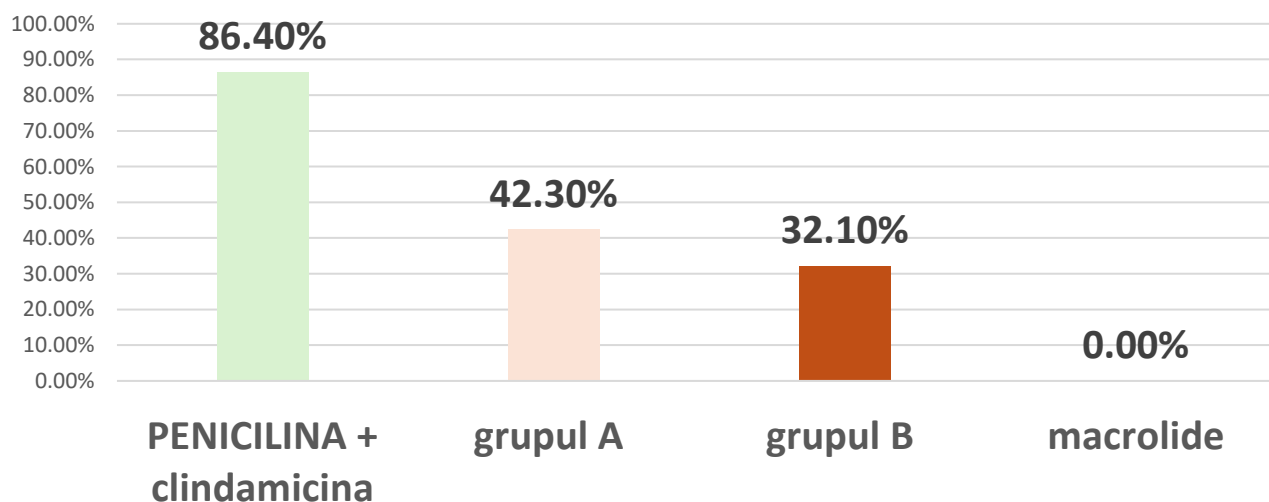
**Macrolide/
Licosamide
(WATCH list - AWARE)**

- **Rezistența în creștere** ^{5,8,10,11}
 - **SGA (~ 20%)**
 - **Streptococ grup B (creștere recentă ~ 15-20%)**
 - **Streptococcus pneumoniae (~ 20-40%)**
 - **Spectrul mai larg**
 - **Risc de reacții adverse**
-

Decizii în spital - Peniciline vs carbapeneme

CARBAPENEME (WATCH list - AWARE)

- Risc de reacții adverse/complicații
- **Eficacitate mai scăzută** în cazurile de **soc toxic streptococic** față de peniciline*



Grupul A – carbapeneme +
glicopeptide/linezolid

Grupul B –
Carbapeneme + glicopeptide +
alte antibiotice cu spectru larg

* Zhang et al, 2023, PloS One, <https://doi.org/10.1371/journal.pone.0292311>

Intervenții de stewardship



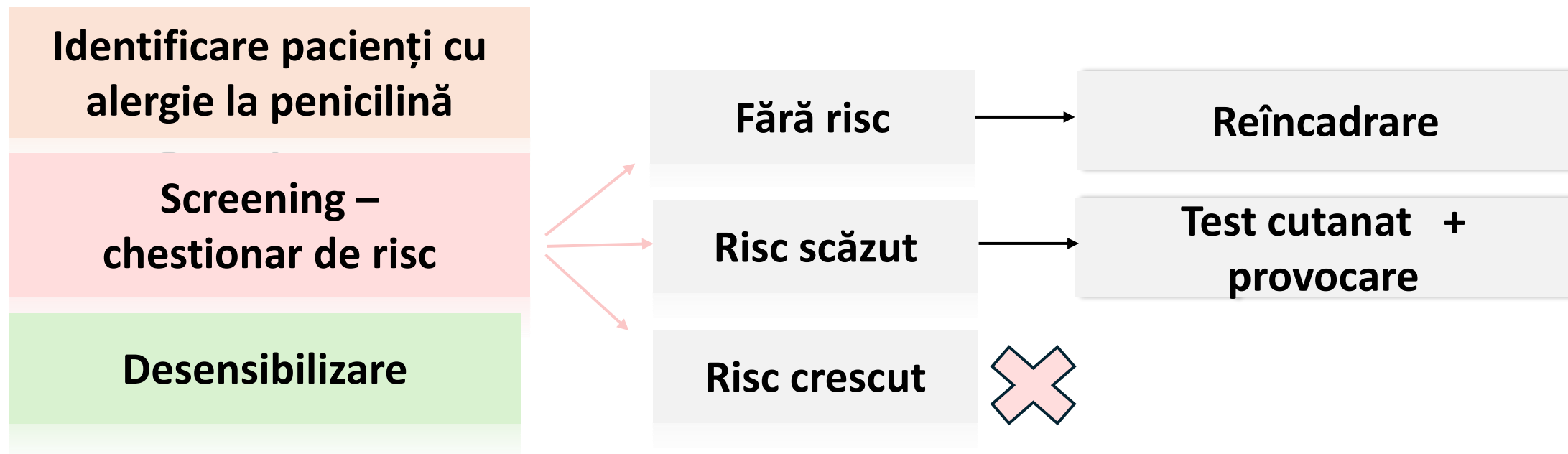
Imaginea:
<https://www.orchardsoft.com/blog/antimicrobial-stewardship-its-role-in-veterinary-laboratories/>

Exemple de intervenții de reevaluare a alergiei la penicilină

- 90-95% din cazuri sunt fals etichetate ca alergii la penicilină ¹²
- Eticheta de alergie la penicilină

Risc de 3x
de reacții adverse

Risc de 23x
de Cl. Difficile



Did you know that

Penicillin is the **most commonly reported drug allergy**

Most patients lose their penicillin allergy after **10 years**



However, **nine out of 10 patients** reporting a penicillin allergy are not truly allergic

Broad-spectrum antibiotics may cause **treatment-resistant superbugs, like MRSA and C-Diff**

When patients are penicillin allergy tested

98%

of hospitalized patients with a history of penicillin allergy would have a negative allergy test result

Healthcare providers can prescribe less expensive, less toxic, and more **appropriate antibiotics**

What is my child's penicillin allergy risk category?

Your child's penicillin allergy risk category was determined by an evidence-based screening questionnaire administered by your nurse during this hospital stay.

For more information, see here: <https://www.cdc.gov/antibiotic-use/clinicians/penicillin-allergy.html>

(Provider Instructions: Please indicate which risk category your patient is by checking box)

No Increased Risk



Check here if applicable

- You do not have a penicillin allergy
- You can safely take penicillins such as: amoxicillin, amoxicillin-clavulanate, ampicillin etc.
- Please inform your Primary Care Provider or Pediatrician that you were screened and found not to have a penicillin allergy

Low Risk



Check here if applicable

- It's unclear if you have a true penicillin allergy
- Avoid penicillins for now (such as: amoxicillin, amoxicillin-clavulanate, ampicillin etc.)
- See an outpatient allergy specialist (see below) to evaluate if you should get tested for penicillin allergy

Moderate Risk



Check here if applicable

- It's unclear if you have a true penicillin allergy
- Avoid penicillins for now (such as: amoxicillin, amoxicillin-clavulanate, ampicillin etc.)
- See an outpatient allergy specialist (see below) to evaluate if you should get tested for penicillin allergy

High Risk



Check here if applicable

- You definitely have a penicillin allergy
- You should always avoid penicillins (such as: amoxicillin, amoxicillin-clavulanate, ampicillin etc.)

Studiu unicentric prospectiv 2021-2023

31/78 (39%) de pacienți cu alergie reclassificați și fără risc la utilizări ulterioare a beta-lactaminelor

+

Educarea pacienților și prescriptorilor



Konold et al, 2023

Do you really have a penicillin allergy?

If not, you may not be getting the best antibiotic for your infection



The facts

While 10% of all people in the US report an allergic reaction to penicillins...

Studies actually show that less than 1% of the population is truly allergic to penicillin.

Why might this be?

- Most people who have a penicillin allergy lose their allergy within 10 years.
- Side effects from a medication might seem like allergic reactions, but they are not the same. Some people may have incorrectly labeled a side effect as an allergic reaction.
- Some people may believe they are allergic to penicillin due to a family member's allergy. People do not need to avoid penicillin if a family member is allergic.

Side effects vs. allergies

A **side effect** is a symptom caused by a medication you took. Side effects are common. They are usually mild and go away quickly. Examples of common side effects include feeling sick to your stomach and having diarrhea.

An **allergic reaction** is caused by the immune system's reaction to a medication. Allergies are rare and usually happen every time you take a particular medication. These occur right away or shortly after taking a medication. Allergic reactions can include itchy rashes, trouble breathing, wheezing, and anaphylaxis.

Why does it matter?

Penicillin and other similar antibiotics often work better for certain infections (i.e., antibiotics given before surgery or dental procedures).

People who report a penicillin allergy often receive other antibiotics that cause more side effects.

If your health care provider discovers that you do not have a true penicillin allergy, they will have more options to treat your bacterial infection.

Make sure you're getting the best antibiotic for your infection. Talk to your health care provider today about your penicillin allergy.

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2. Khan DA, Banerji A, Blumenthal KG, et al. Drug allergy: A 2022 practice parameter update. Journal of Allergy and Clinical Immunology. 2022;150(6):1333-1393. doi: <https://doi.org/10.1016/j.jaci.2022.08.028>
3. AAAAI. Penicillin Allergy FAQ. Updated Sept 2023. <https://www.aaaai.org/tools-for-the-public/conditions-library/allergies/penicillin-allergy-faq>

Facts about Penicillin Allergy Desensitization



Pentru mai multe resurse
(informarea pacienților/ experiența
altor intervenții)

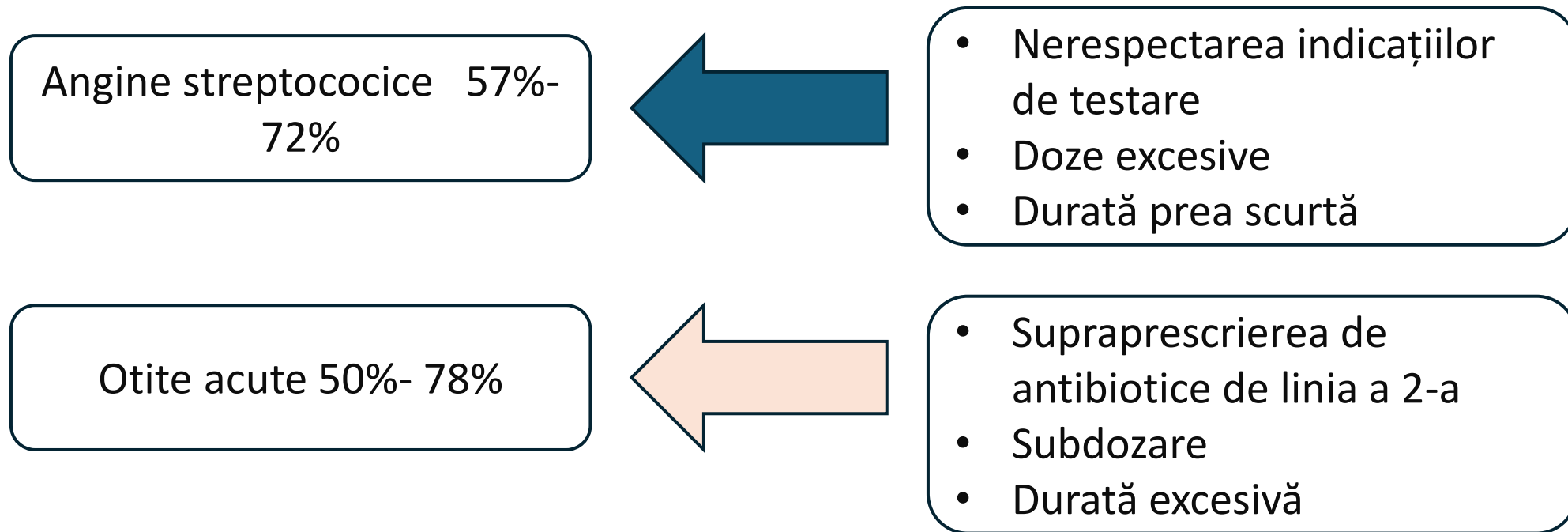


Intervenții anterioare prescrierii – ghidul instituțional



Intervenții anterioare prescrierii – ghidul instituțional (2)

- Complanța față de ghidul de diagnostic si tratament este variabilă ^{13,14,15}



Intervenții anterioare prescrierii – ghidul instituțional (3)

Evaluarea situației actuale (ex: consum de antibiotice)

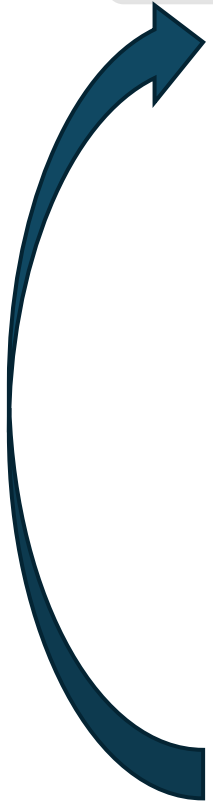
Identificarea recomandărilor de implementat
(dovezi + resurse + beneficiu)

Identificarea revizorilor

Aprobarea prin Comisia de Stewardship și Direcție

Elaborarea unui plan de implementare

Monitorizarea implementării



Intervenții anterioare prescrierii – diagnostic stewardship (ex: teste rapide)

Author; Year, Country; Study Period; Setting	Study Design; Population and Sample Size	Objective	Intervention	Key Findings
Ayanruoh et al., 2009 [12]; USA; September 2005–September 2007; Paediatric ED of inner-city hospital in New York City	Retrospective Cohort; patients aged 3–18 years old, n = 8280	Assess the impact of RDTs on antibiotic prescriptions in children with pharyngitis in the ED	Rapid Streptococcal Test for GAS	Introduction of RDTs was associated with a lower antibiotic prescription rate from 41.38% pre-RDT and 22.45% post-RDT, $p < 0.001$.
Bird et al., 2021 [13]; UK; 2014–2016; Birmingham Children’s Hospital ED	Pragmatic AB single-subject study; children aged 6 months to 16 years presenting to ED with a sore throat, n = 605	Assess efficacy of RDT for GAS combined with established clinical scoring system (McIsaacs Score) in reducing antibiotic prescribing for sore throat	McIsaac clinical score combined with GAS RDT to screen for and treat GAS pharyngitis	Baseline rates of antibiotic prescription rate 79% was reduced to 24% following the implementation of intervention.
Busson et al., 2017 [14]; UK; 2 January–30 March 2015; Saint Pierre’s University Hospital	Cohort study; paediatric patients (<15 years old) presenting to ED with fever of unknown source, suspected influenza, or complicated illness	Evaluate the contribution of the Alere i Influenza A&B test to patient management	Alere i Influenza A&B test	Antibiotics were avoided in 36.2% of patients (20 paediatric patients, 5 adult patients). Antivirals prescribed in 36.2% patients (9 paediatric patients, 16 adult patients).
Cardoso et al., 2013 [15]; Brazil; April–November 2008; University Hospital of Sao Paulo	Cohort study; patients aged between 2 and 15 years with history of sore throat and fever, no signs of viral infection, n = 650	Evaluate the impact of RDTs on the diagnosis and treatment of children with acute pharyngotonsillitis	Clearview Strep A Test (Oxoid), which consists of a rapid immunoassay for the qualitative detection of group A streptococcal antigens (RADT)	Implementation of RDT prevented unnecessary antibiotic prescription in 32.9% of cases.
Crook et al., 2020 [16]; USA; 3 study periods between January 2011 and June 2019; Tertiary-care children’s hospital	Before-and-after intervention study; children aged < 90 days presenting to ED with fever or hypothermia, n = 5317	Assess the impact of clinical guidelines and RDTs on paediatric patient management	BioFire FilmArray Respiratory Panel 2 & mPCR testing with clinical guidelines	Introduction of RDT was associated with a significant reduction in antibiotic prescription in children aged 29–60 days old.
Doan et al., 2009 [17]; Canada; December 2005–April 2006 and November 2006–April 2007; British Columbia Children’s Hospital	RCT; children 3 to 36 months of age with febrile acute respiratory tract infections at a paediatric ED, n = 204	Assess whether early and rapid diagnosis of a viral infection alleviates the need for ancillary testing and antibiotic treatment	Rapid respiratory viral testing program, named VIRAP (for Viral Rapid Program)	No statistically significant difference in ED length of visits, rate of ancillary testing, or antibiotic prescription rate in the ED between the study groups. Significant reduction in antibiotic prescription after ED discharge (in the group who had rapid viral testing RR = 0.36; 95% CI = 0.14, 0.95).

**Este necesară
continuarea
intervenției!**



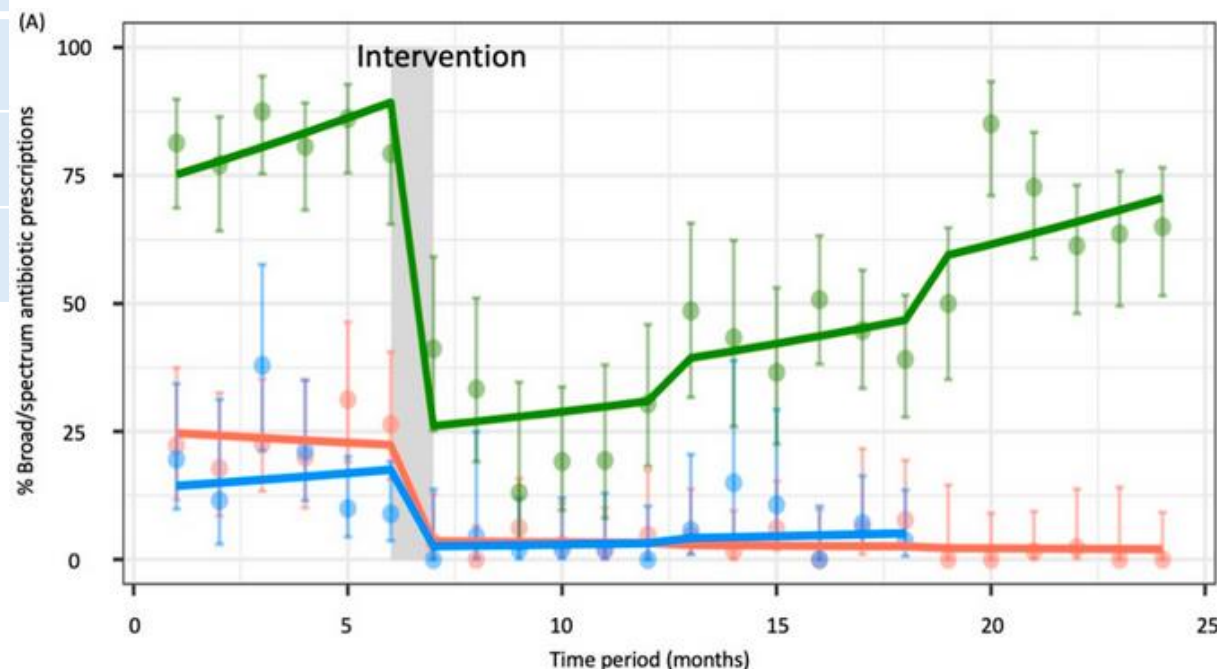
Intervenții ulterioare prescrierii – optimizarea tratamentului antibiotic

- **Reevaluare trat cu audit+feedback**
- Conversie iv la po
- Optimizarea duratei de tratament
- Optimizarea dozelor

Creșterea aderenței față de recomandările de optimizare a prescrierii antibioticelor este mai ridicată prin

asocierea intervențiilor + seminarii/campanii de informare a prescripților

Scăderea consumului de antibiotice cu spectru larg pentru angine în cadrul unei intervenții desfășurate în UPU 2014-2019 (Italia)



Perspective de viitor

- Vaccinare antipneumococică
- Vaccin anti-SGA (studii)



Impact asupra scăderii
rezistenței la
antibiotice

- Campanii de educare și informare



EUROPEAN ANTIBIOTIC AWARENESS DAY



A EUROPEAN
HEALTH INITIATIVE

Keep antibiotics working!

European Antibiotic Awareness Day



Vă mulțumesc pentru atenție!

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