

ENASPOC

the European Network for Antibiotic Stewardship at the Point-of-Care

**AMR and ENASPOC:
Support for antibiotic prescribing
decisions is available, let's get started**

112. October | 2023

ENASPOC

European Network
for Antibiotic Stewardship
at the Point of Care



Lars Bjerrum,
Professor
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The Expert group:

Support on point of care testing to guide antibiotic prescriptions for respiratory illness



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The Expert Group: Some Achievements...

- Define **‘European guidance’** on the use of CRP POCT and complementary strategies to promote optimal use of antibiotics and to mature antibiotic stewardship
- Agreement on important **Consensus Statements**
- **Symposium** at ECCMID Congress, Copenhagen 2023
- **Papers** on Antibiotic Stewardship, for general practitioners, pediatricians, and policy makers
- More info at the Homepage: www.enaspoc.com



www.enaspoc.com

ENASPOC – the European Network for Antibiotic Stewardship at the Point-of-Care

Background

Antimicrobial resistance (AMR) is broadly recognized as a global threat that needs to be addressed urgently. Over-prescribing of antibiotics in primary care is a significant contributor to rising AMR, and respiratory tract infections (RTIs) are a major source of inappropriate prescriptions.

C-reactive Protein point of care testing (CRP POCT), and complementary strategies, are tried, tested, and proven to be very effective at reducing antibiotic prescribing without compromising patient safety or satisfaction when properly implemented. Yet mature adoption of CRP POCT in primary care is observed in relatively few European countries, with the Nordics, the Netherlands, and Switzerland leading the way.

AMR increases the risks for us all and society as a whole would benefit from rapid and broad implementation of proven, available solutions like CRP POCT, rather than waiting for innovation in new antibiotics or diagnostics.

ENASPOC is a new initiative to improve antibiotic stewardship in primary care and rapidly close the gap between available evidence and implementation.

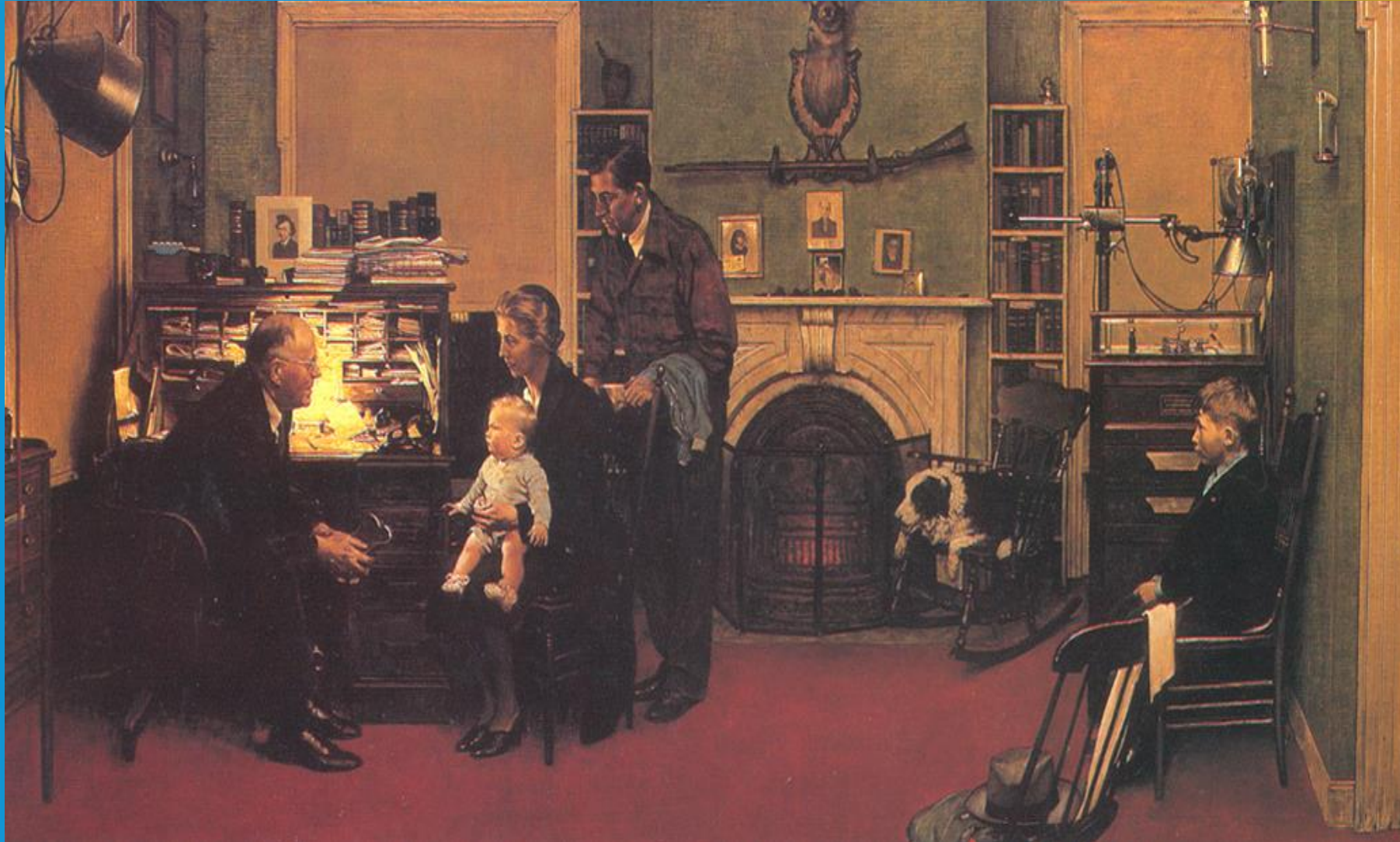


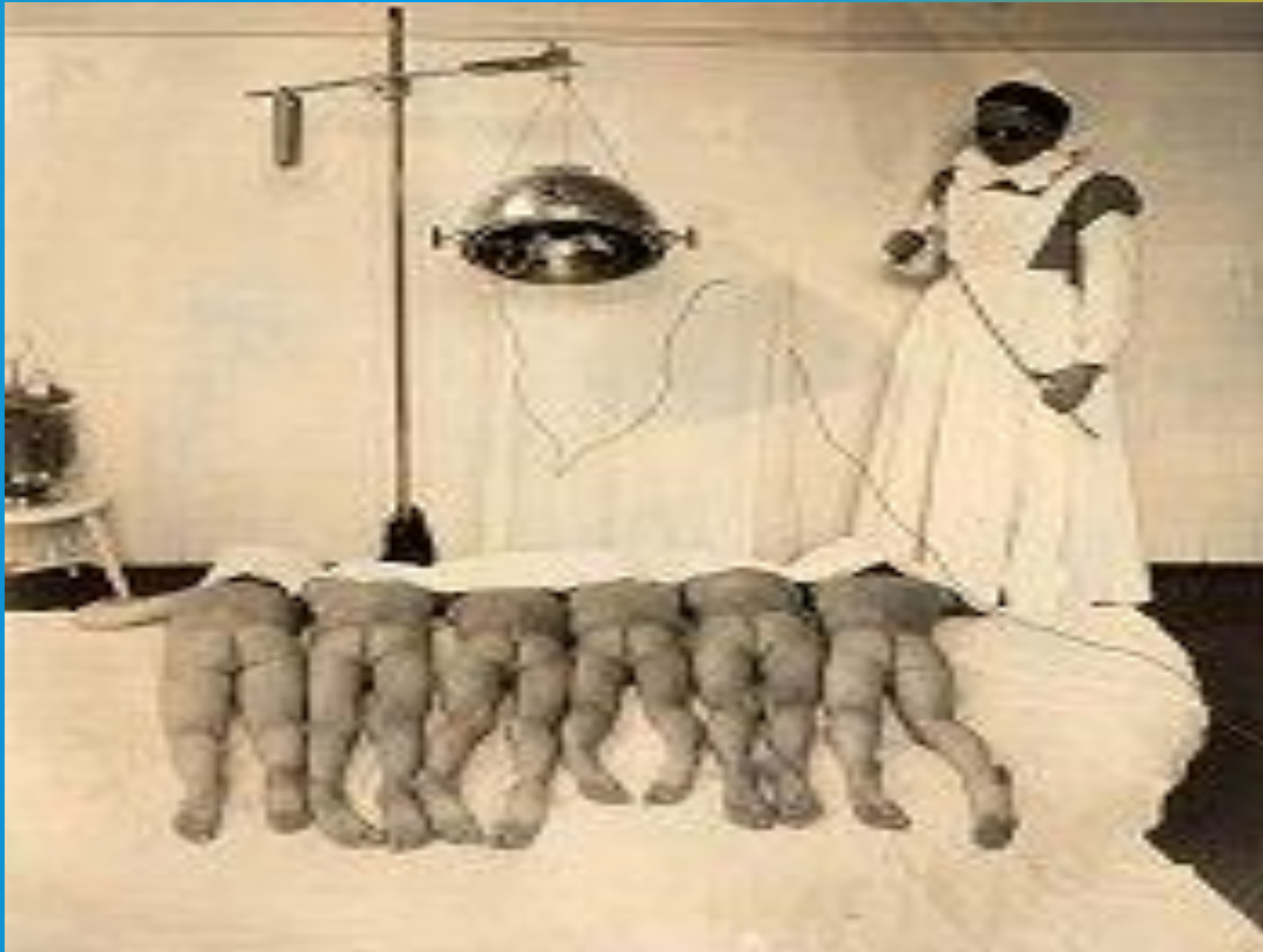
CONSENSUS STATEMENT #1: AMR IS A GLOBAL THREAD



WHO: Antimicrobial resistance is a global threat that must urgently be addressed

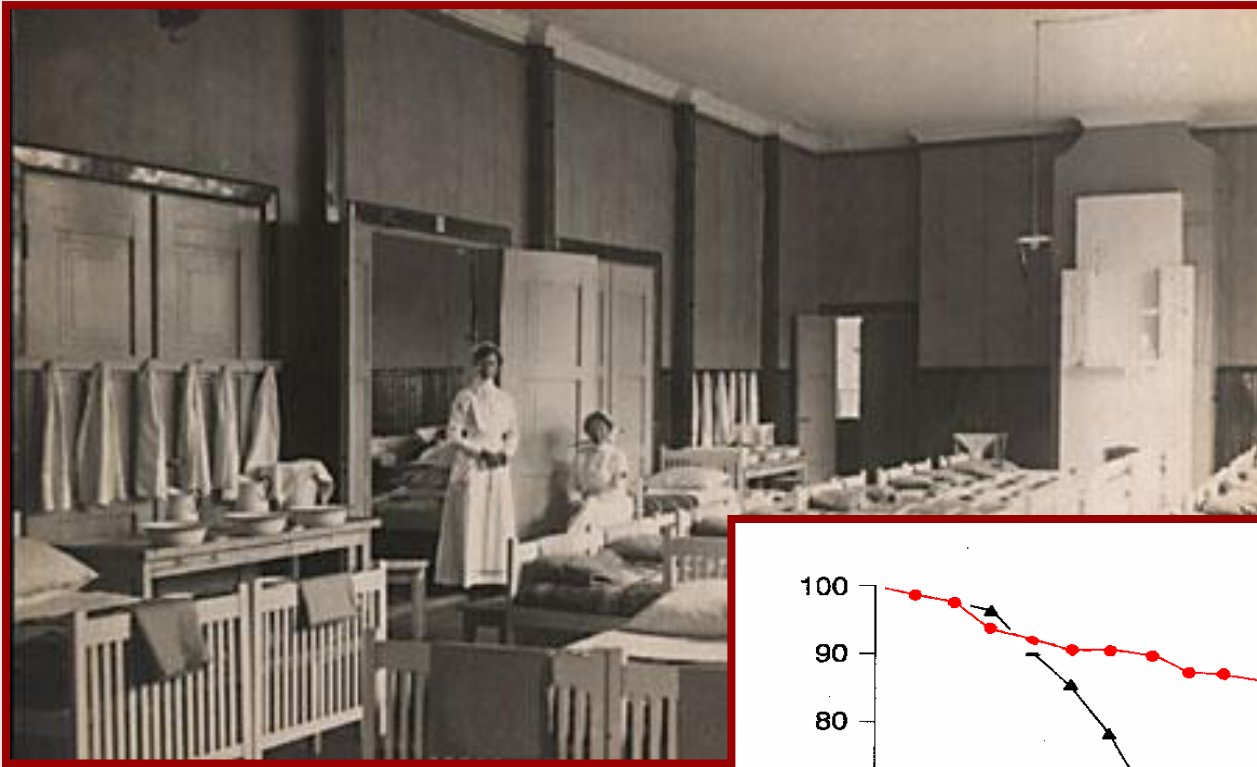
General Practice Year 1900







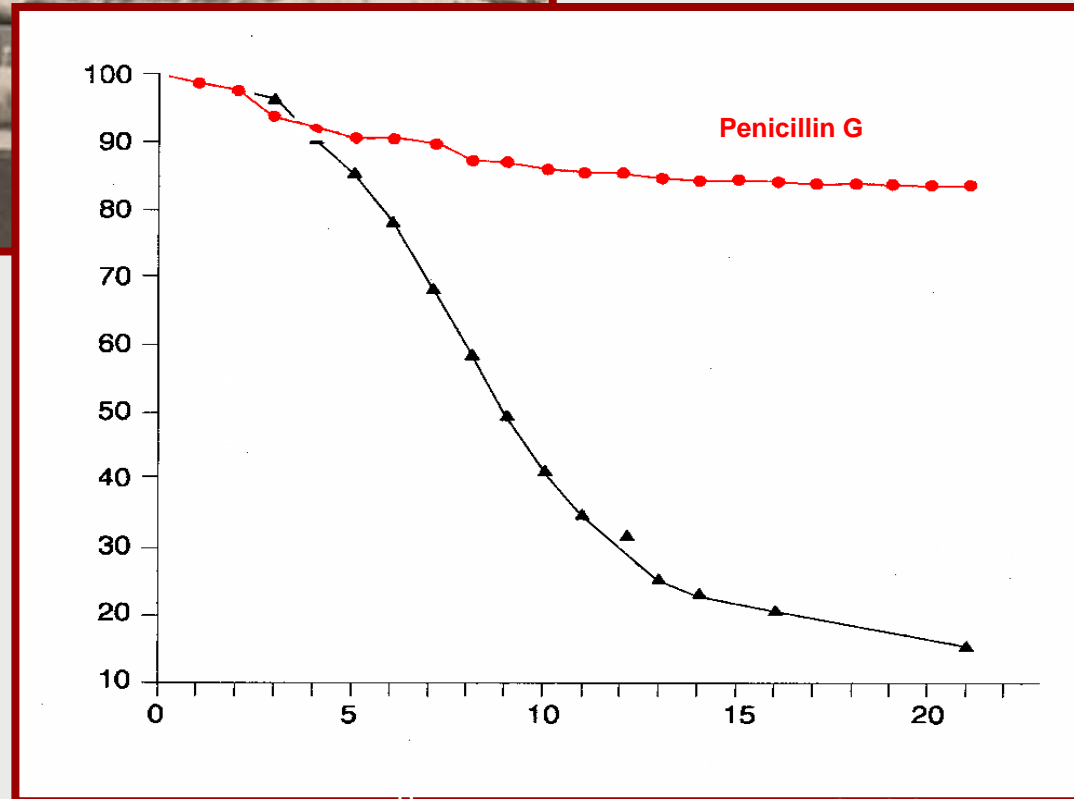
THE DOCTOR, BY SIR LUKE FILDES (1891)



Patients with pneumonia and bacteria in the blood

Penicillin increased the chance of survival from 10% to 90%

Adapted from Austrian *et al.*
Ann. Int. Med 1964; 60, 759



From discovery of penicillin (1928) to industrial production (1945)

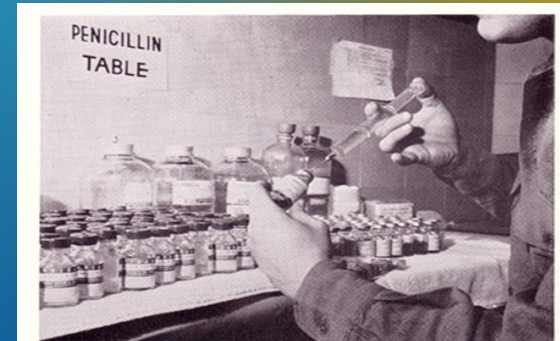
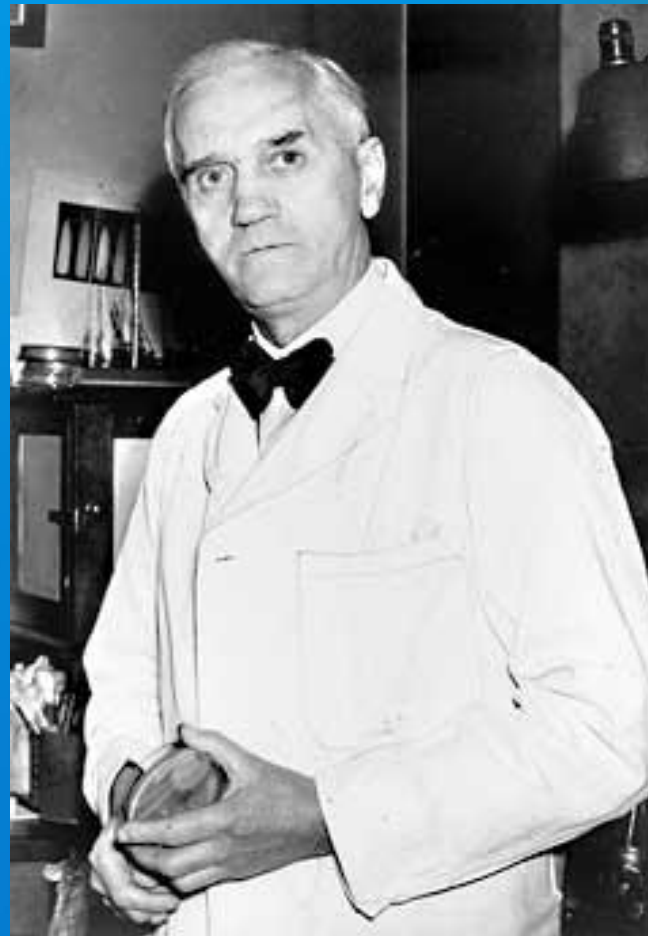
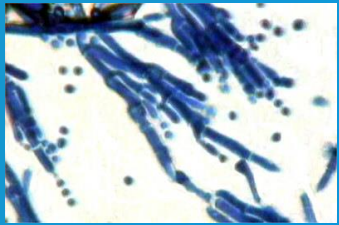
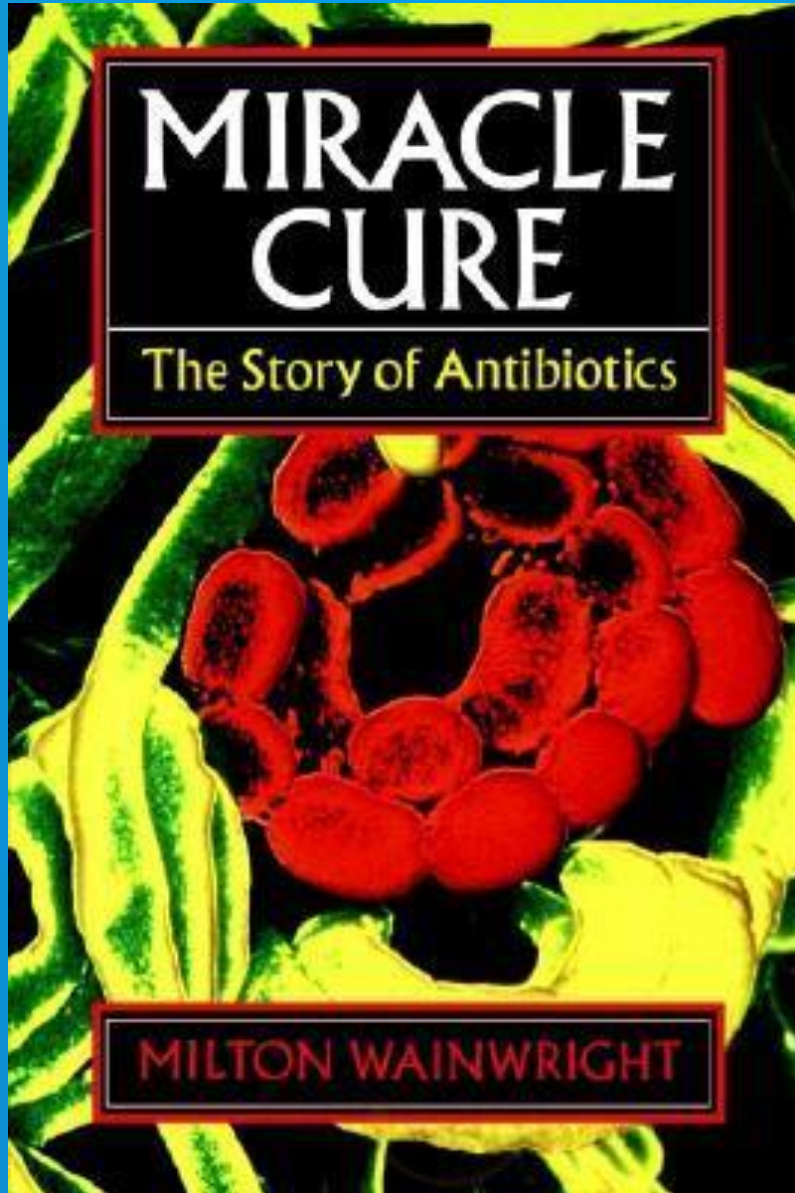


FIGURE 112.—Standard preparation of penicillin for use. Distilled water, 10 cc., is added to sealed vials containing 100,000 Oxford units of sodium penicillin.





The Mold in Dr. Florey's Coat

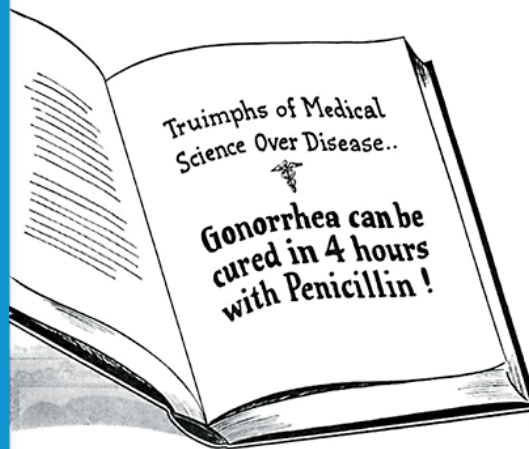
The Story
of the
Penicillin
Miracle



"Admirable, superbly researched... perhaps the most exciting tale of science since the apple dropped on Newton's head."
—Simon Winchester,
The New York Times

ERIC LAX

Another chapter added
to medical history...



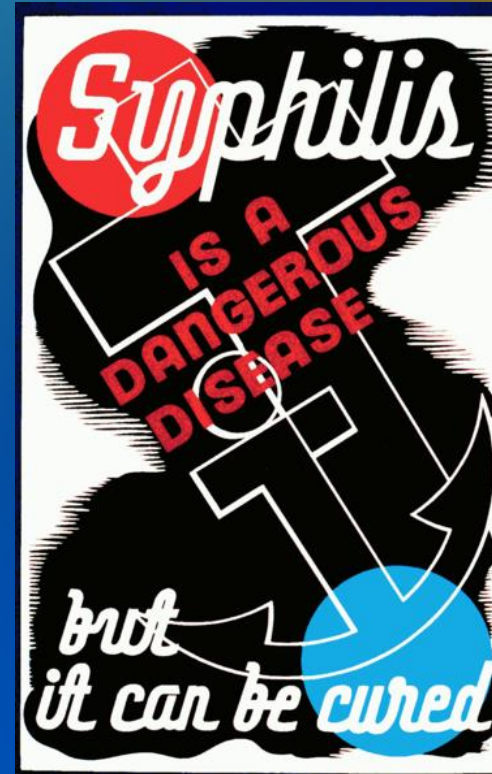
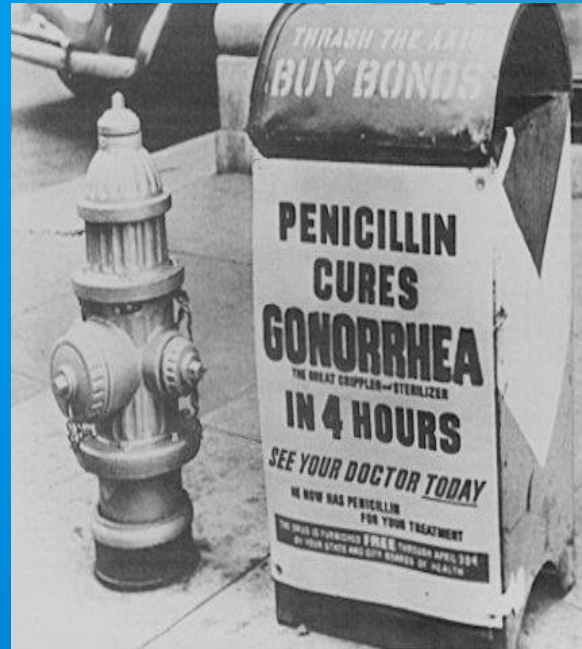
Smallpox, yellow fever, tetanus, diphtheria, typhoid, whooping cough, pneumonia—and now gonorrhea! One by one medical science is finding sure and lasting cures for some of the dread diseases, which for so long have preyed upon mankind.

The latest success is with gonorrhea—that great crippler and sterilizer—which can be cured in four hours with penicillin!

For those afflicted, penicillin has been provided FREE. They have only to see their doctors and arrange for treatment. The drug is provided FREE through April 30th by your...

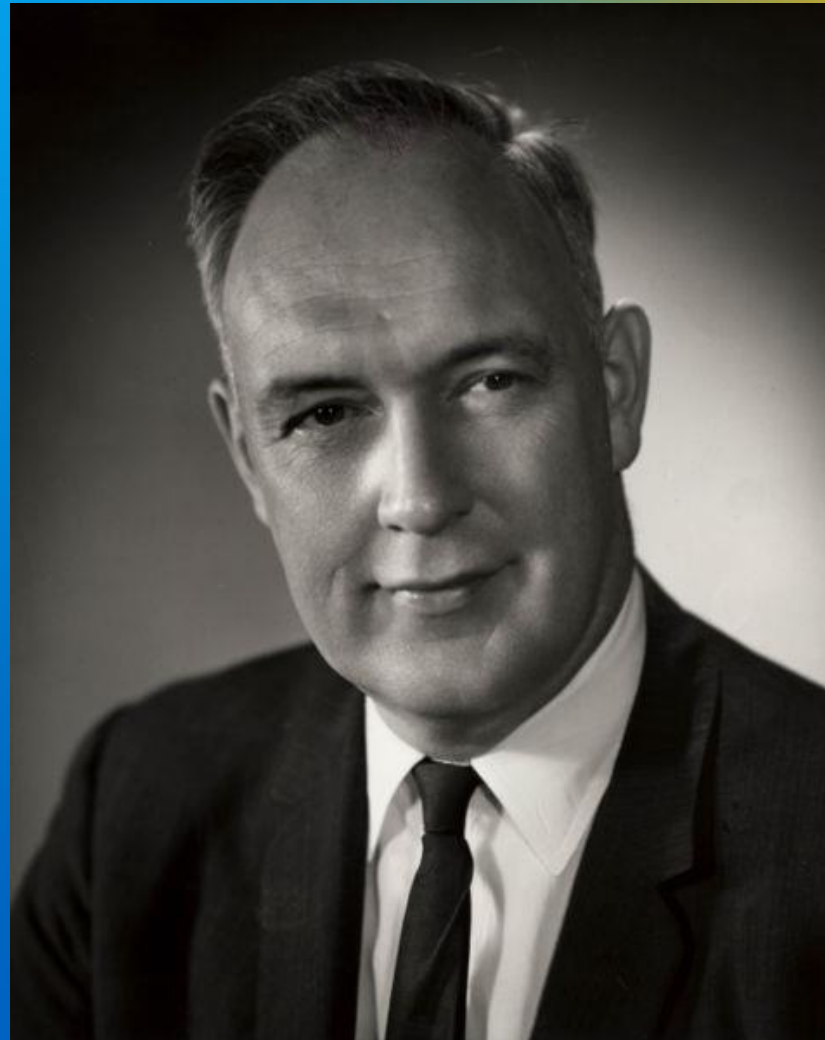
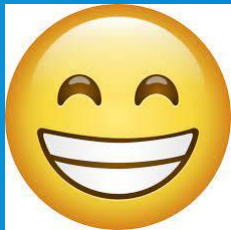
STATE AND CITY HEALTH DEPARTMENTS

For Use in Greater New Orleans



World Microbiological Congress 1969

“We have come to the
moment where we can
close the book about
infectious diseases...”



William H. Stewart
Surgeon General of United States
1965-69

The miracle came to an end by the discovery of bacteria that were resistant to antibiotics



AMR: the “silent” epidemic

- Cause of 1 of 3 hospital deaths due to untreatable secondary bacterial infections
- Cause 1,27 million deaths globally directly attributable to bacterial AMR
- Cause 4.95 million deaths associated with bacterial AMR (Lancet 2022)

An effective stewardship of antibiotics can help ensure that antibiotics remains effective for future generations

15

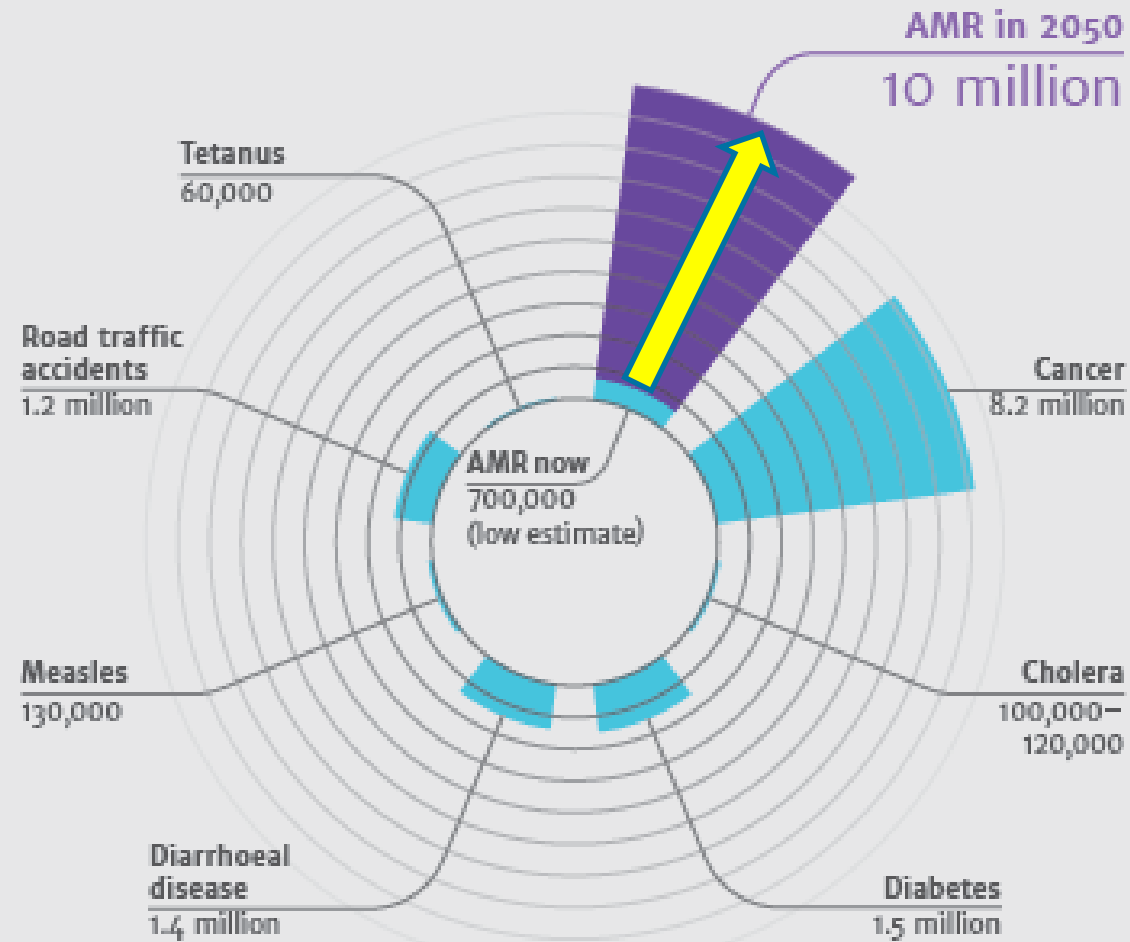




Review on Antimicrobial Resistance
Tackling drug-resistant infections globally

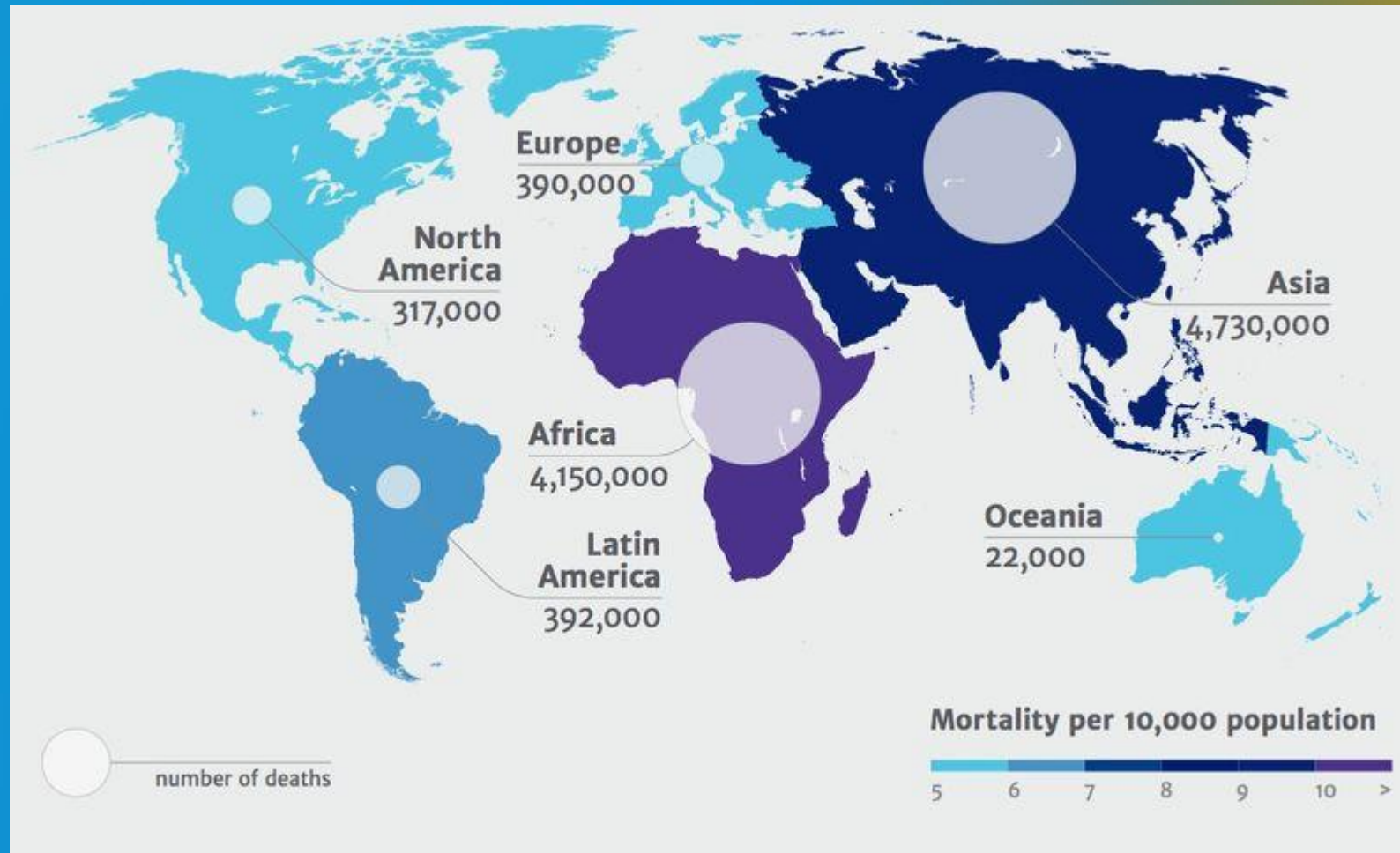
UK dec. 2014

Deaths attributable to AMR every year compared to other major causes of death

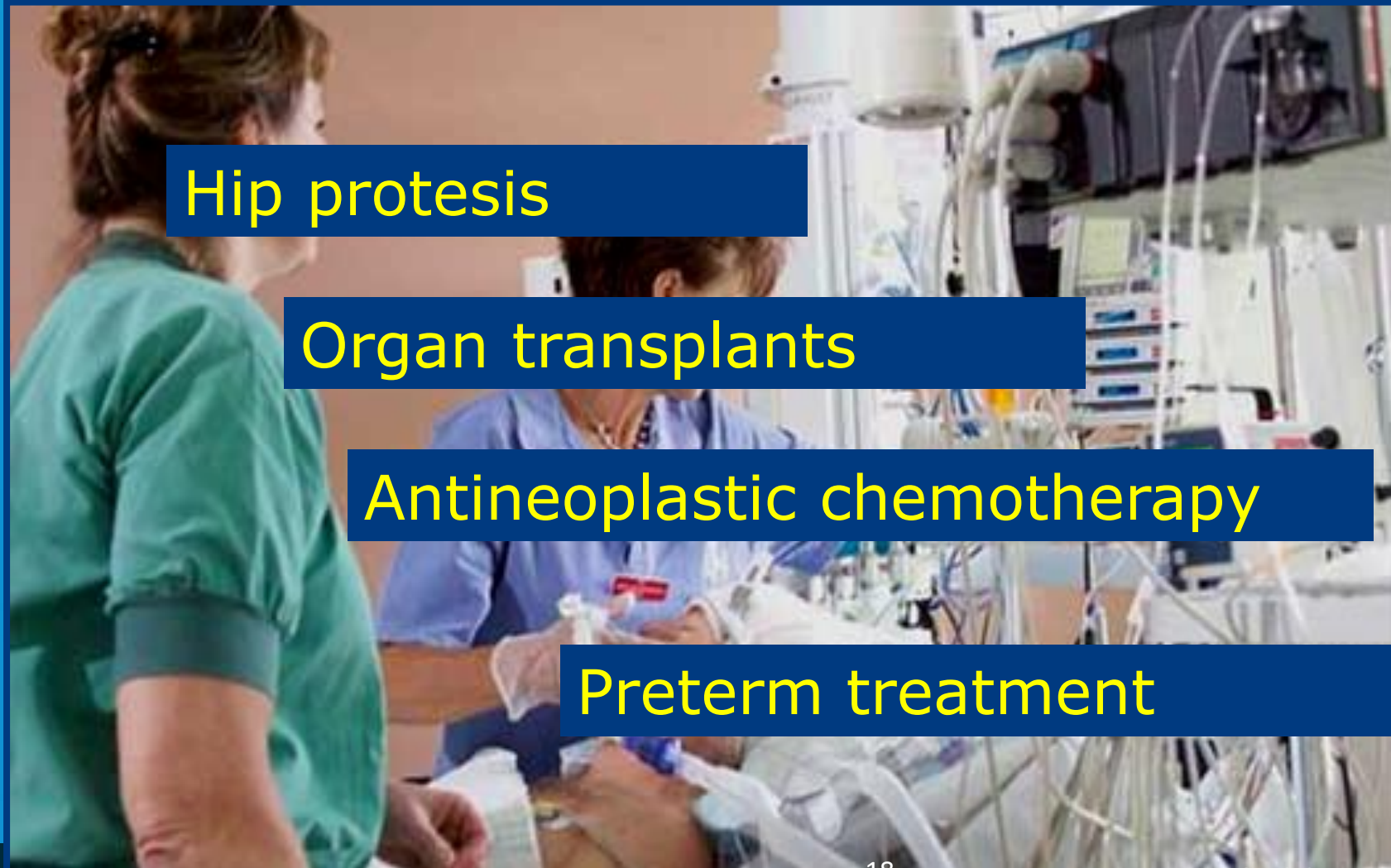


Estimated number of deaths due to antibiotic resistance in 2050

17



Without effective antibiotics advanced interventions will be too dangerous...



Hip protesís

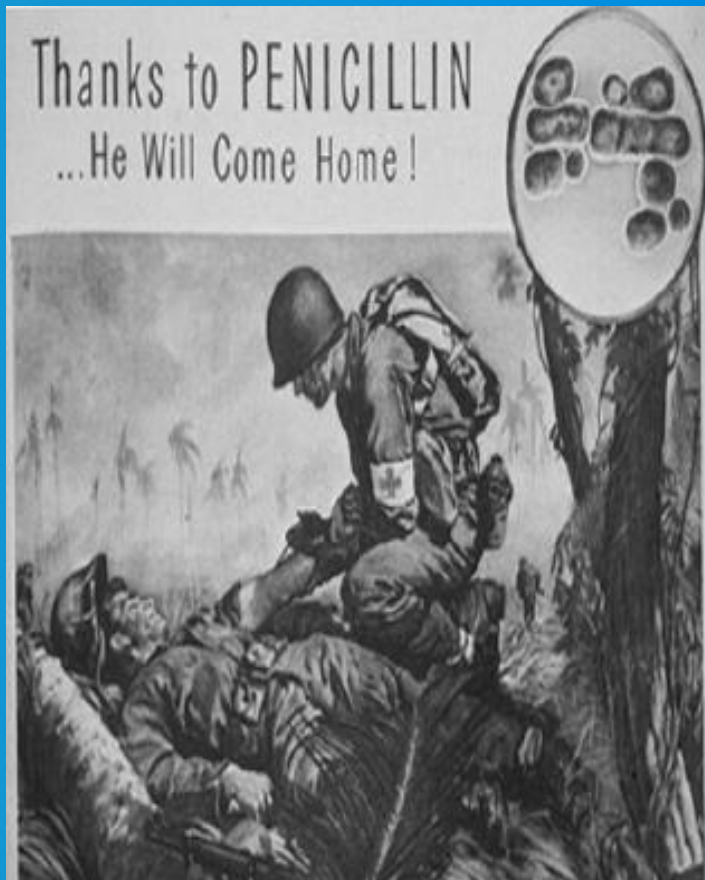
Organ transplants

Antineoplastic chemotherapy

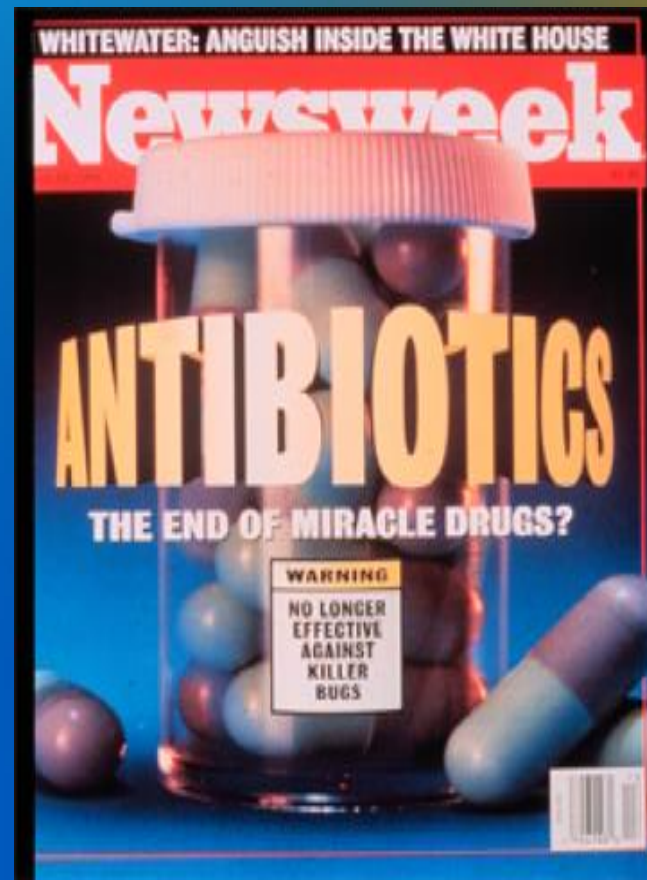
Preterm treatment

Are we at the end of the antibiotic era?

20 century: Start of the antibiotic era



21 century: End of the antibiotic era?





Children in Denmark treated for
TB 1932



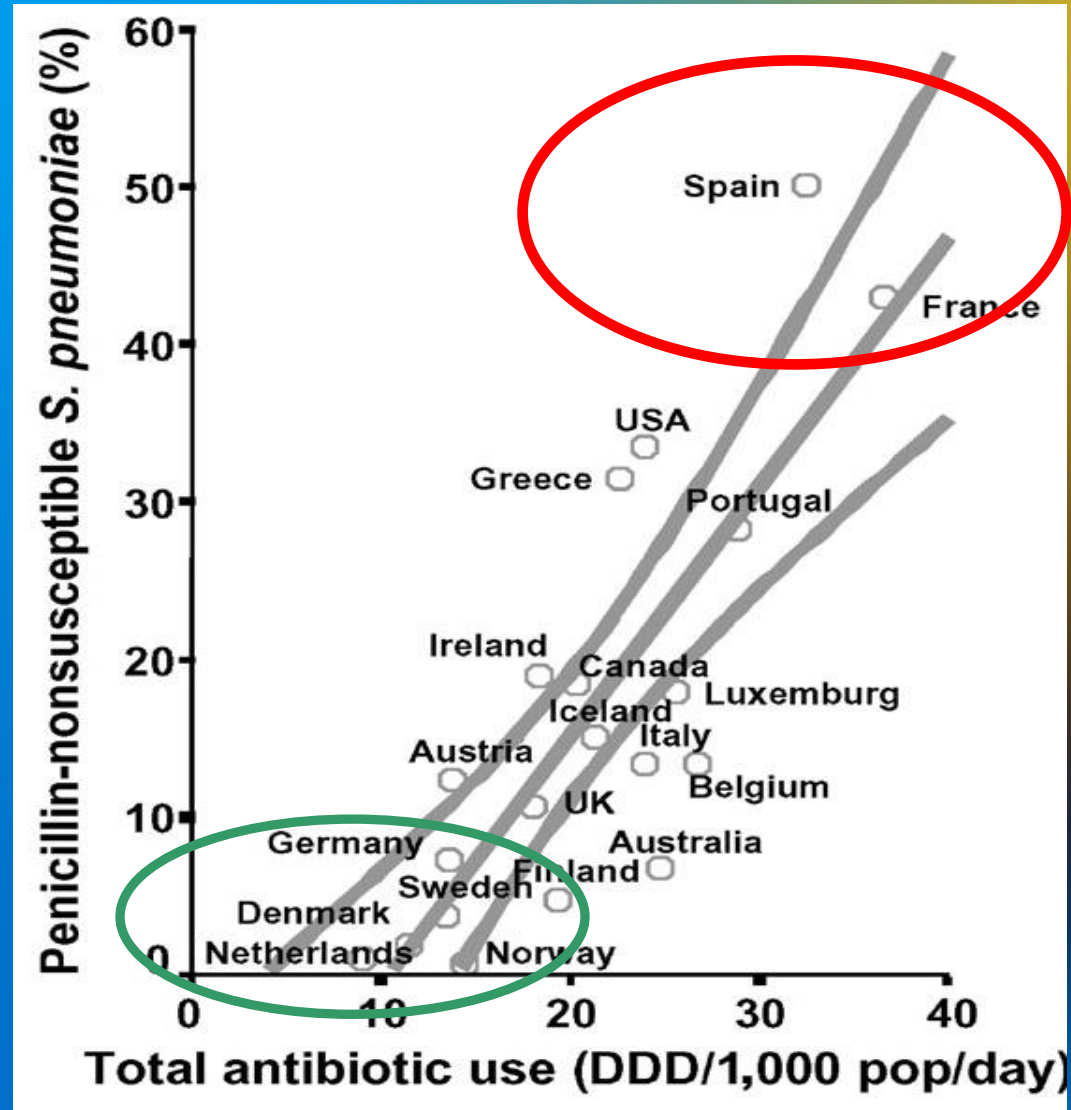
22 Century: Back to the pre-antibiotic era?

Antibiotic stewardship: Primary Care has a key role to reduce AMR



Penicillin-resistance in pneumococci

Linear correlation between
use of antibiotics and
antibiotic resistance

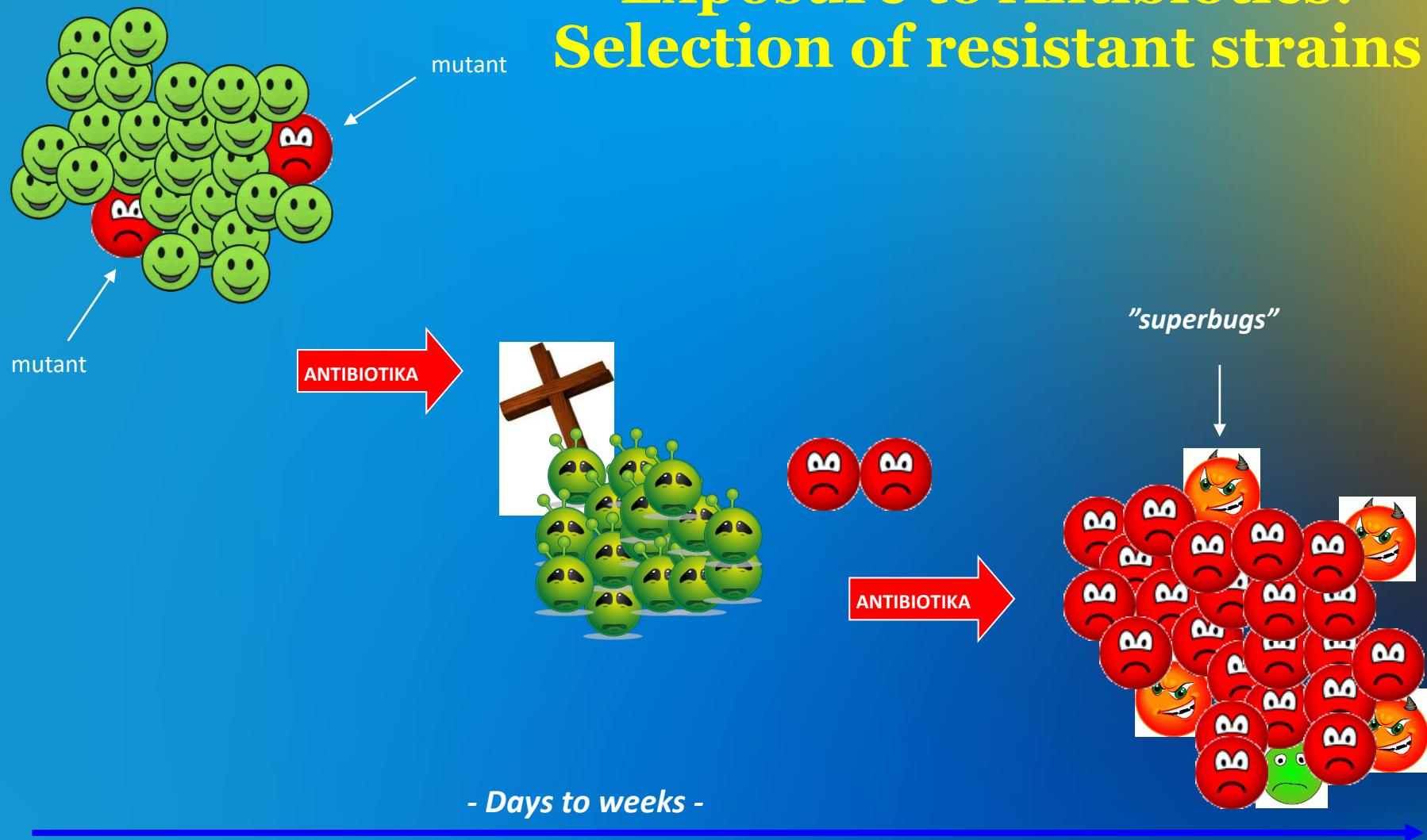


From: Emerging Infectious Diseases 2004;19(3):514

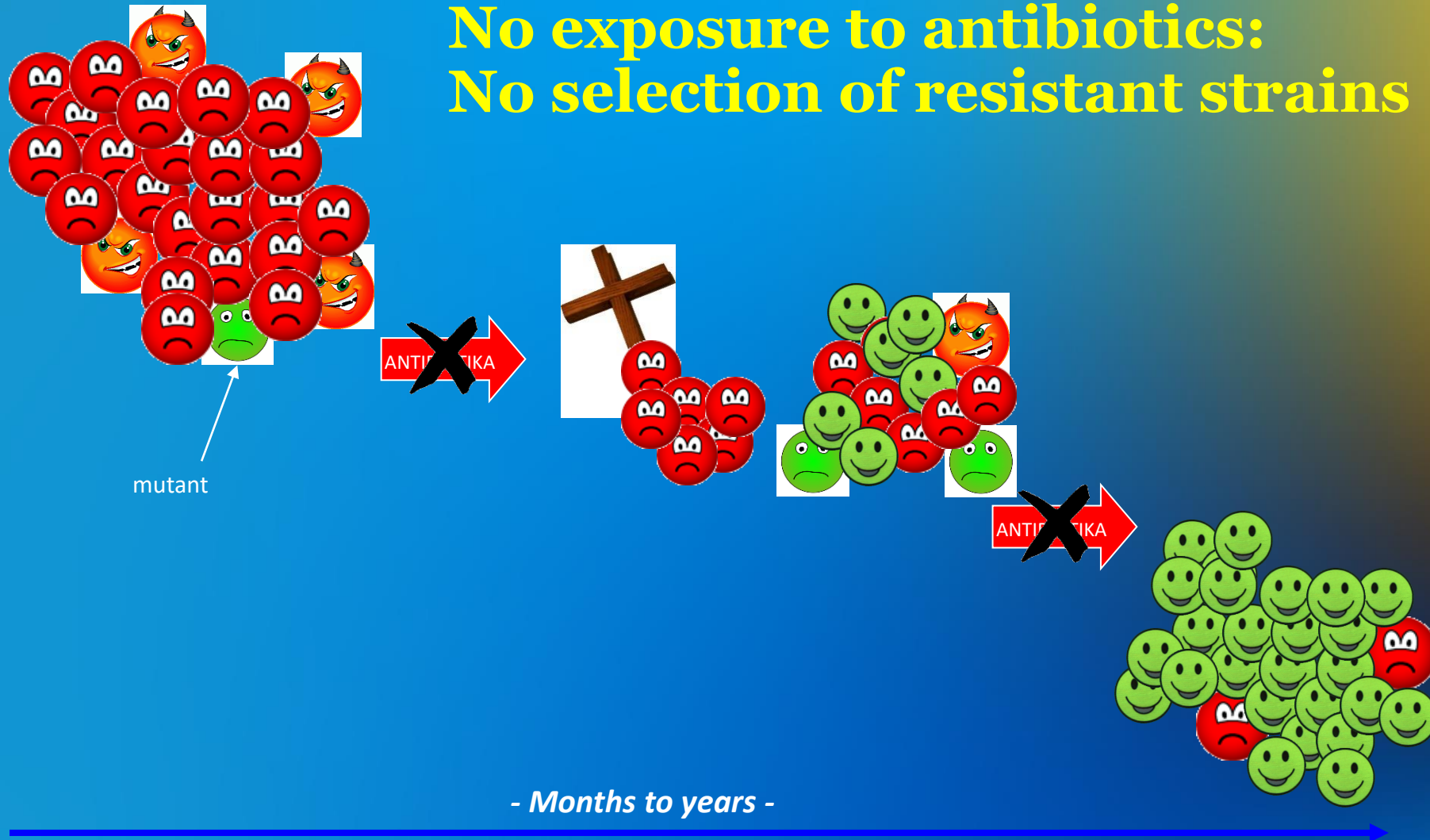
High use of antibiotics is the most important driver for selection of Resistant strains



Exposure to Antibiotics: Selection of resistant strains



No exposure to antibiotics: No selection of resistant strains



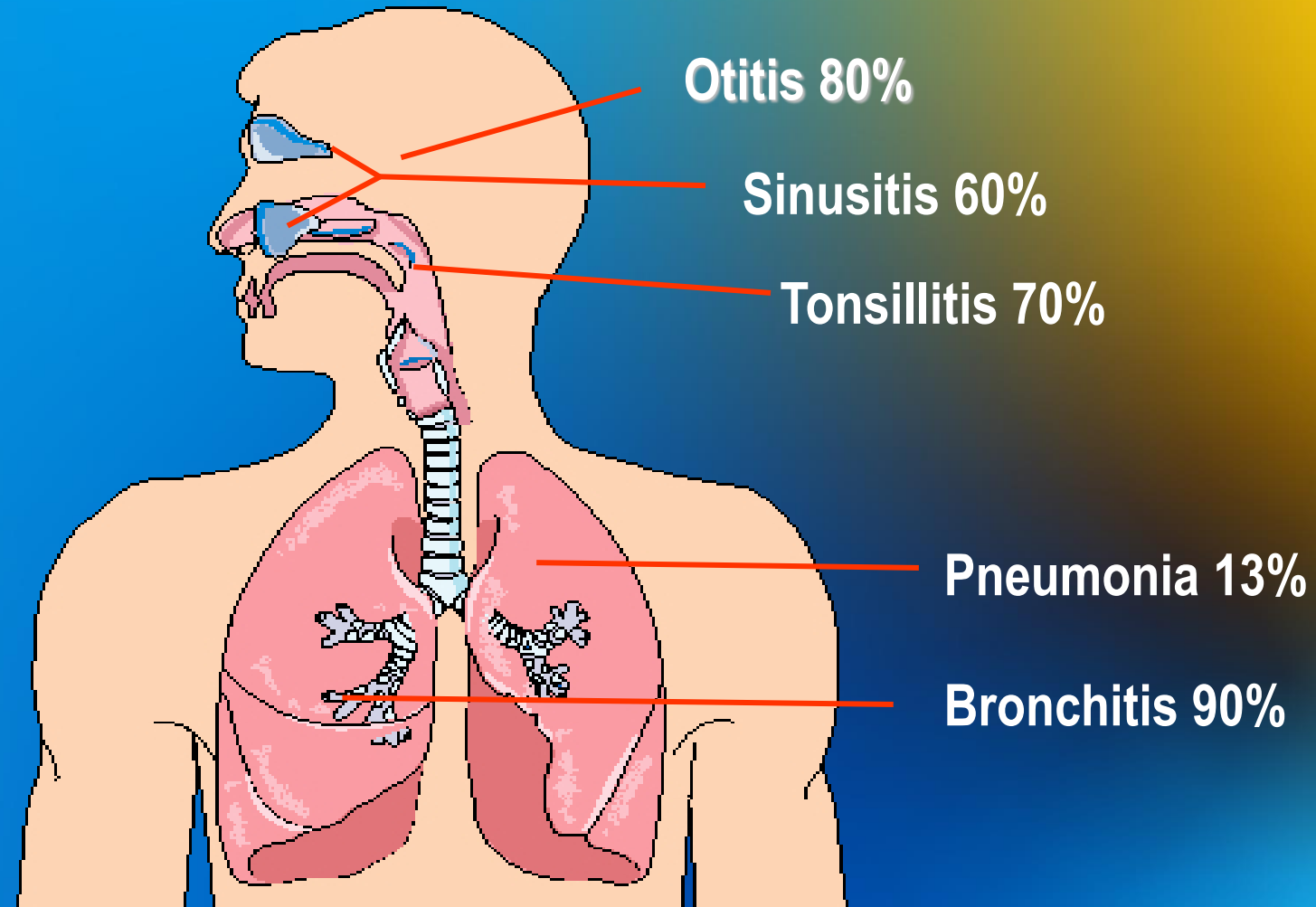
**CONSENSUS STATEMENT #2:
ANTIBIOTIC OVERPRESCRIBING LEADS TO AMR**



Antibiotic overprescribing for respiratory tract infections in primary care is a significant contributor to rising antimicrobial resistance

Upper and lower RTIs

% due to virus





Er...? sniff sniff
cough cough
rasp rasp...

You're asking
the wrong man!

**Antibiotics
DON'T WORK
ON COLDS
OR MOST COUGHS & SORE THROATS**

- The best thing for them is lots of water, and plenty of rest, and possibly a cold & flu remedy from your local pharmacy.
- Because antibiotics are designed to cure bacterial illnesses like pneumonia, taking antibiotics when you don't need them will also kill some of the good bacteria that help to keep your body healthy.
- Of course, when you really do need antibiotics, don't worry, your doctor will prescribe them.

NHS

The majority of respiratory tract infections are viral





The majority of antibiotic prescriptions for respiratory tract infections are inappropriate

Assesment of clinical signs and symptoms is not sufficient to distinguish between serious infections and self-limiting conditions



Point of Care testing improve the quality of the clinical decision on treatment

**CONSENSUS STATEMENT #3:
CRP TESTING CAN REDUCE ANTIBIOTIC OVERPRESCRIBING**



CRP point of care testing (CRP POCT) is an established tool that is proven to effectively and safely reduce overprescribing of antibiotics for lower resp. tract infections in adults presenting at primary care.

AIM:

To improve antibiotic stewardship in primary care and close the gap between evidence based knowledge and performance.

Strategy:

One of the main strategies is a broad implementation of CRP POCT testing in primary care

Until now, only few countries have implemented CRP POCT in primary care: Nordic countries, Netherlands and Switzerland

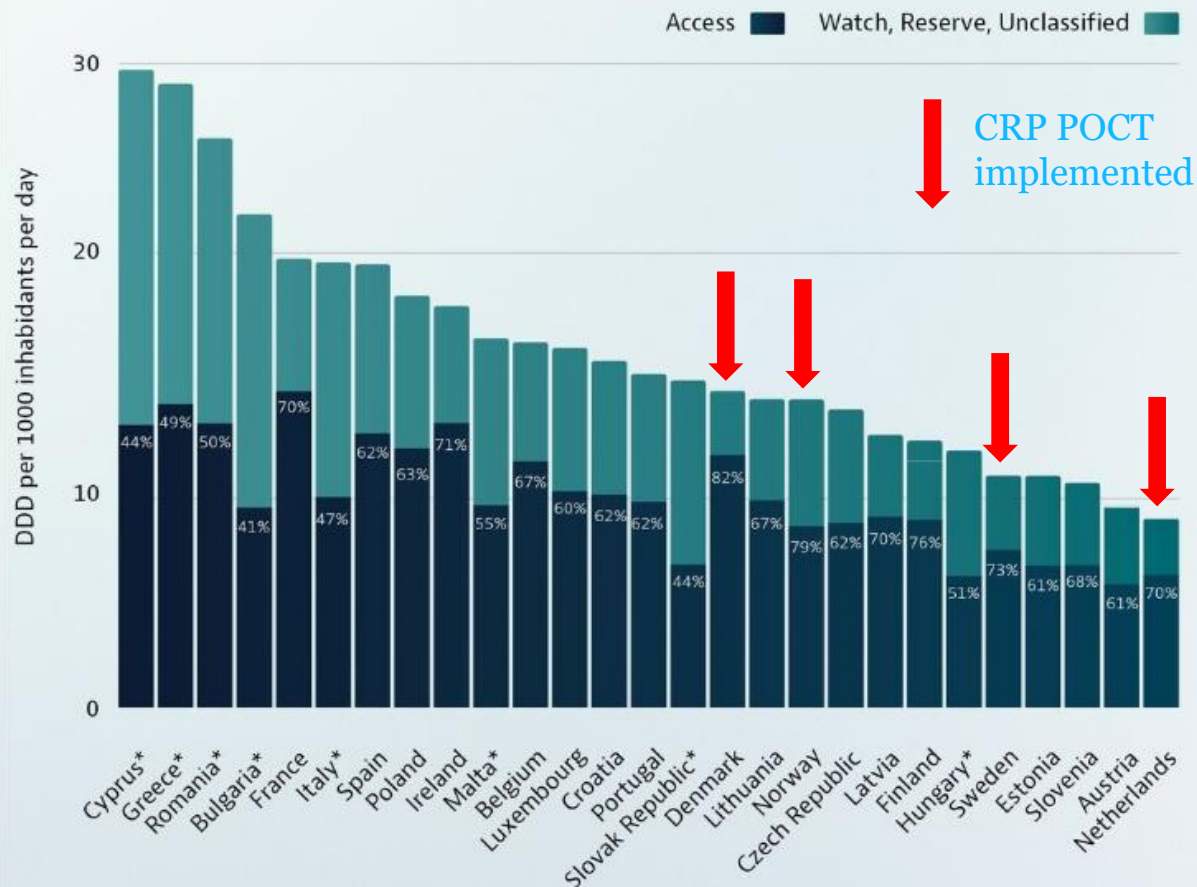
Report (2022):

Antimicrobial Resistance in the EU/EEA - A One Health response



Total antibiotic consumption in humans according to the 'Access, Watch, Reserve' classification, 2020

The WHO has set a national-level target that at least 60% of all antibiotic consumption be for 'Access' antibiotics by 2023. Consumption of 'Access' antibiotics relative to all categories shown in the bars.



WHO AwaRe classification

'Access' group: antibiotics with high therapeutic value and low selection for AMR (>60%)

'Reserve' group: last resort antibiotics, saved for infections with multidrug-resistant organisms

Antimicrobial Resistance in the EU/EEA

A One Health Response

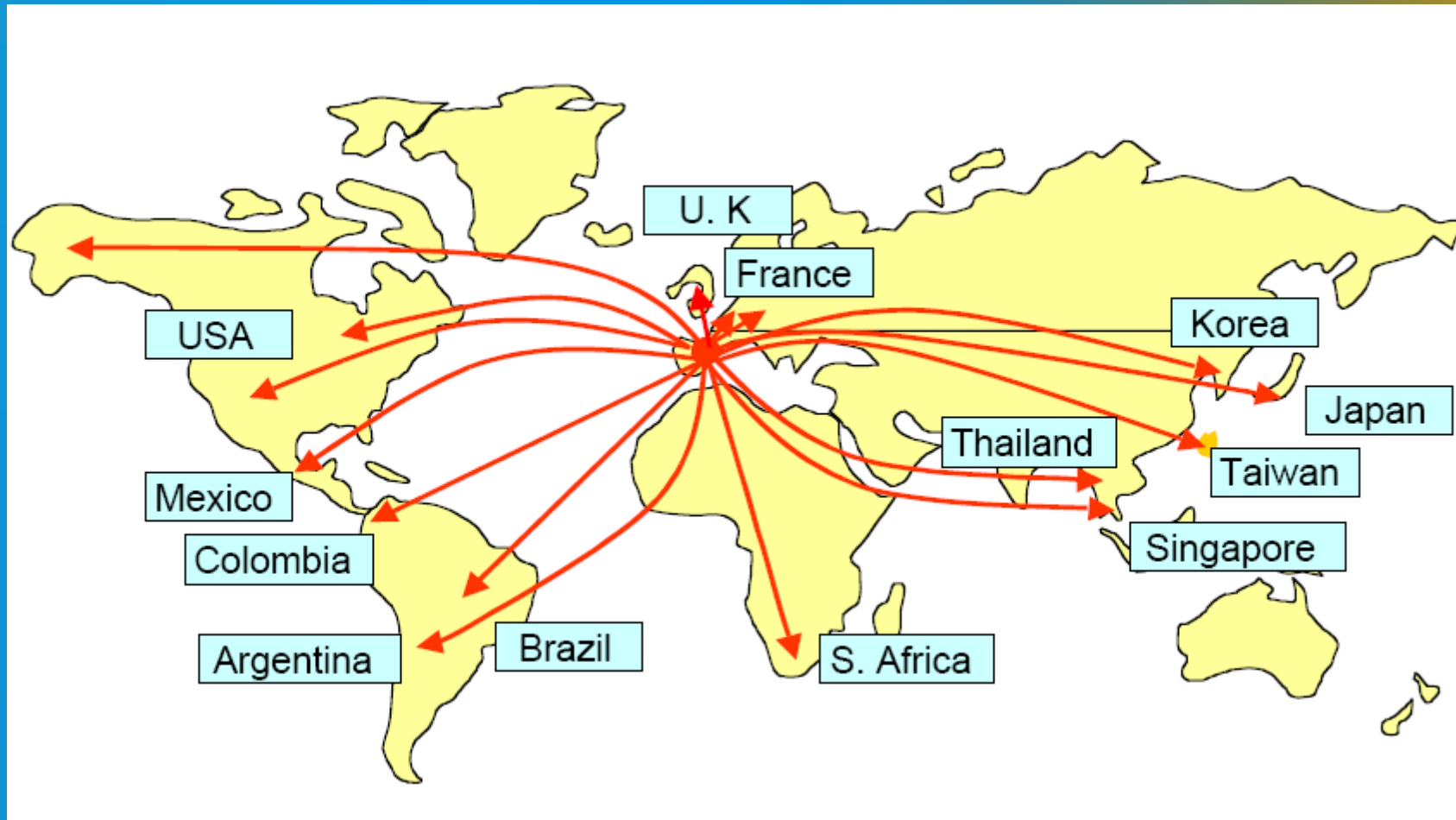


Some Key messages:

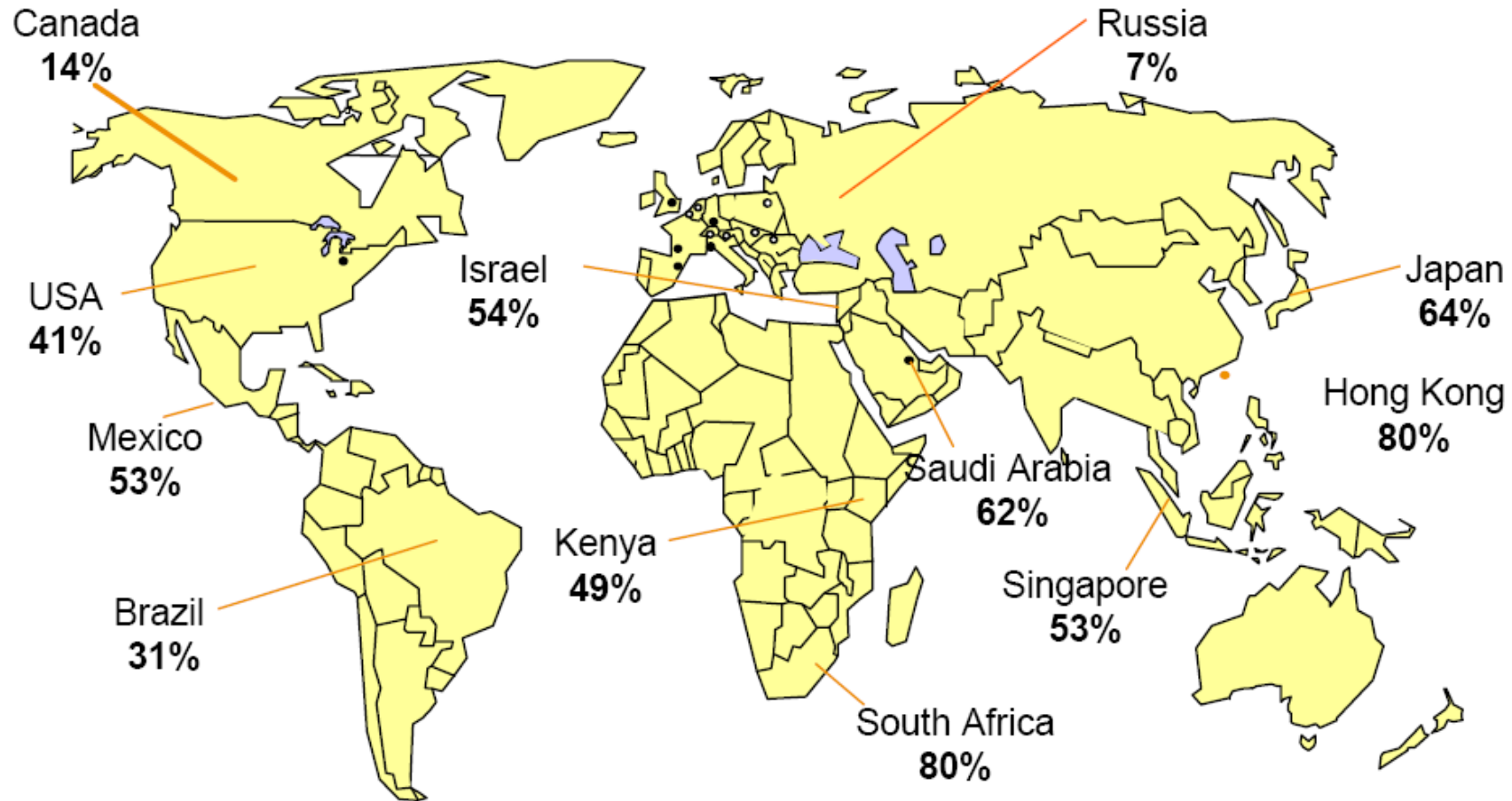
AMR cannot be contained within borders or regions, underlining the need for concerted action throughout the EU/EEA.

It is important to establish a system to share and promote the implementation of best practices to tackle AMR.

Global spread of pc-resistant pneumococci



Worldwide Distribution of Penicillin Resistant Pneumococci



CONSENSUS STATEMENT #4:

BROAD GLOBAL APPLICATION OF CRP POCT IS NEEDED



To safely reduce antibiotic prescribing in primary care for patients presenting with respiratory illness, a broader application of CRP POCT globally is recommended

CONSENSUS STATEMENT #5:

CRP POCT SHOULD BE COMBINED WITH COMPLEMENTARY STRATEGIES



An effective implementation, combining CRP POCT together with evidence-based complementary strategies, can increase the contribution to more appropriate antibiotic prescribing

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PUBLICATIONS BASED ON GOOD SCIENTIFIC EVIDENCE

Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care (Review)

Aabenhus R, Jensen JUS, Jørgensen KJ, Hróbjartsson A, Bjerrum L



2014

Authors' conclusions

A point-of-care biomarker (e.g. C-reactive protein) to guide antibiotic treatment of ARIs in primary care can reduce antibiotic use

Cochrane Library Trusted evidence. Informed decisions. Better health.

Cochrane Reviews ▾ Trials ▾ Clinical Answers ▾ About ▾ Help ▾

Cochrane Database of Systematic Reviews | Review - Intervention

Biomarkers as point-of-care tests to guide prescription of antibiotics in people with acute respiratory infections in primary care

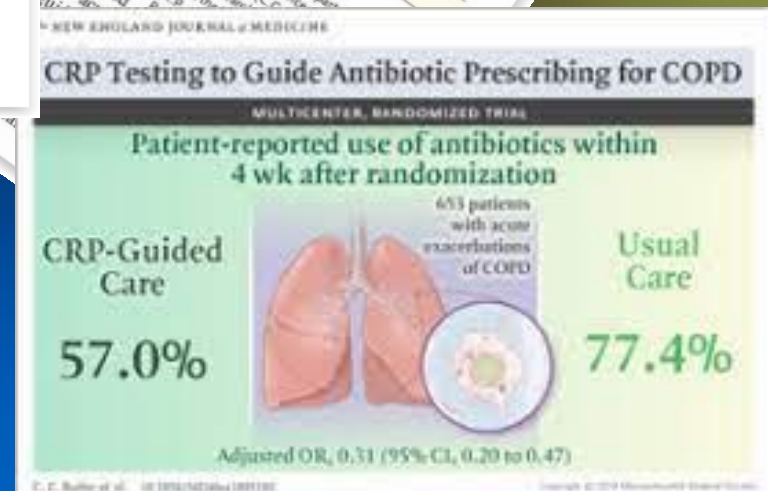
✉ Siri Aas Smedemark, Rune Aabenhus, Carl Llor, Anders Fournaise, Ole Olsen, Karsten Juhl Jørgensen
Authors' declarations of interest

Version published: 17 October 2022 | Version history

<https://doi.org/10.1002/14651858.CD010130.pub3>

Authors' conclusions:

- Use of CRP test as an adjunct to standard care reduces the number of antibiotic prescriptions in primary care patients with symptoms of acute RTI.
- CRP testing does not affect recovery rates.



Data collection from GPs winter 2017-2018

- 143 GPs
- 7813 Patients with RTI

4617 Patients (59%) had a CRP test

- CRP >20: >25% got antibiotics
- CRP >40: >50% got antibiotics
- CRP >50: >75% got antibiotics

(BJGP 2021)



RESEARCH



C-reactive protein cut-offs used for acute respiratory infections in Danish general practice

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Abstract

Background: GPs can use the C-reactive protein (CRP) point-of-care test (POCT) to assist when deciding whether to prescribe antibiotics for patients with acute respiratory tract infections (RTIs).

Aim: To estimate the CRP cut-off levels that Danish GPs use to guide antibiotic prescribing for patients presenting with different signs and symptoms of RTIs.

Design & setting: A cross-sectional study conducted in general practice in Denmark.

Method: During the winters of 2017 and 2018, 143 GPs and their staff registered consecutive patients with symptoms of an RTI according to the Audit Project Odense (APO) method. CRP cut-offs were estimated as the lowest level at which half of the patients were prescribed an antibiotic.

Results: In total, 7813 patients were diagnosed with an RTI, of whom 4617 (59%) had a CRP test performed. At least 25% of the patients were prescribed an antibiotic when the CRP level was >20 mg/L, at least 50% when CRP was >40 mg/L, and at least 75% when CRP was >50 mg/L. Lower thresholds were identified for patients aged ≥65 years and those presenting with a fever, poor general appearance, dyspnoea, abnormal lung auscultation, or ear/facial pain, and if the duration of symptoms was either short (≤1 day) or long (>14 days).

Conclusion: More than half of patients presenting to Danish general practice with symptoms of an RTI have a CRP test performed. At CRP levels >40 mg/L, the majority of patients have an antibiotic prescribed.

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Competing interest: The authors declare that no competing interests exist.

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CRP levels and antibiotic prescribing in Danish General Practice

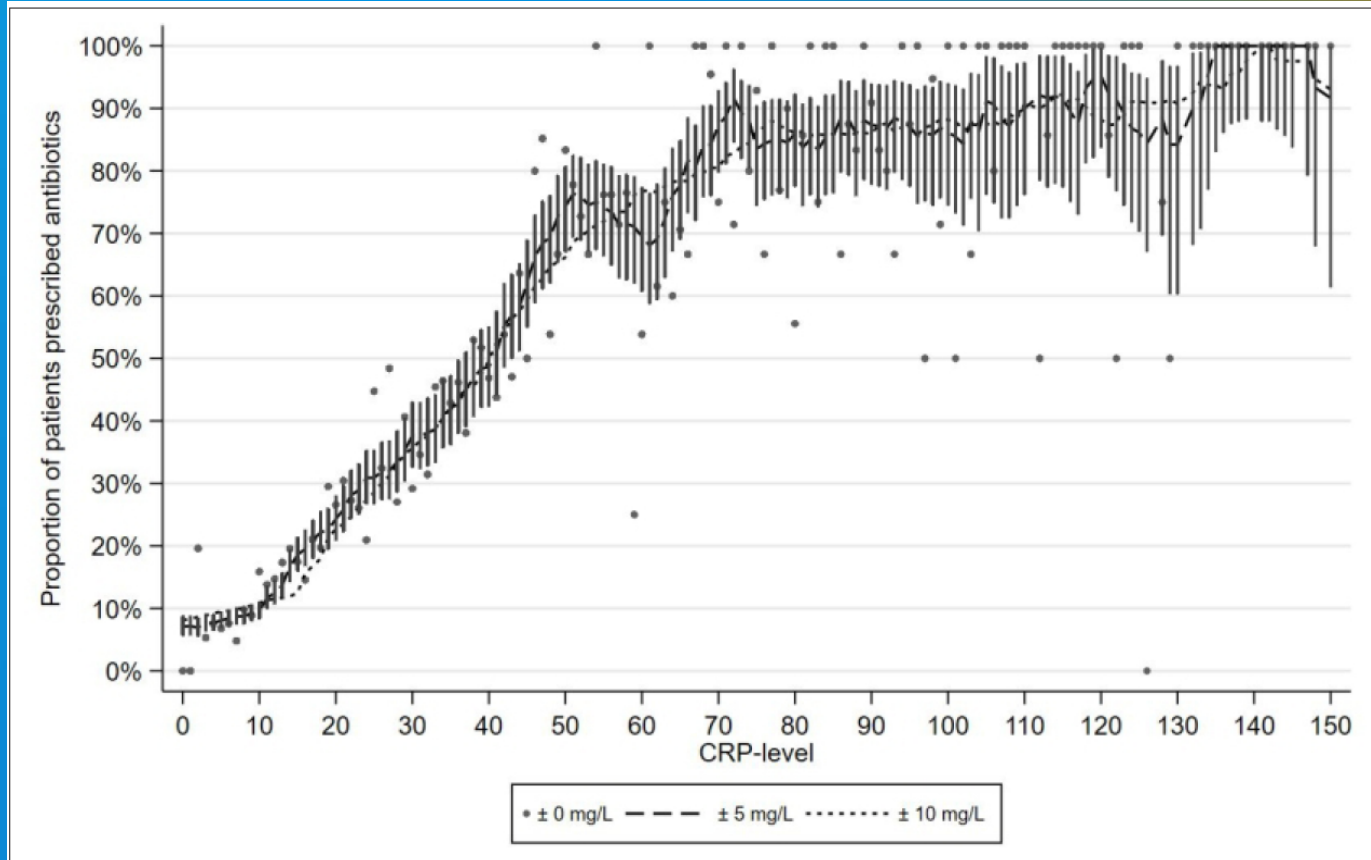


Figure 1 C-reactive protein (CRP) levels and the proportion of patients prescribed an antibiotic. Legends indicate the width of the interval around the index CRP level used to calculate the proportion of patients who were prescribed antibiotics, respectively 0, 5, and 10mg/L above and below. Bars indicate 95% confidence intervals. CRP levels 150–300mg/L not shown.



**PAPER
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Article

The Role of CRP POC Testing in the Fight against Antibiotic Overuse in European Primary Care: Recommendations from a European Expert Panel

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† These authors contributed equally to this work.

Abstract Tackling antibiotic resistance represents one of the major challenges in modern medicine, and limiting antibiotics' overuse represents the first step in this fight. Most antibiotics are prescribed in primary care settings, and lower respiratory tract infections (LRTIs) are one of the most common indications for their prescription. An expert panel conducted an extensive report on C-reactive protein point-of-care (CRP POC) testing in the evaluation of LRTIs and its usefulness to limit antibiotic prescriptions. The expert panel stated that CRP POC testing is a potentially useful tool to limit antibiotic prescriptions for LRTI in a community setting. CRP POC must be used in conjunction with other strategies such as improved communication skills and the use of other molecular POC testing. Potential barriers to the adoption of CRP POC testing are financial and logistical issues. Moreover, the efficacy in limiting antibiotic prescriptions could be hampered by the fact that, in some countries, patients may gain access to antibiotics even without a prescription. Through the realization of a better reimbursement structure, the inclusion in standardized procedures in local guidelines, and better patient education, CRP point-of-care testing can represent a cornerstone in the fight against antimicrobial resistance.

Keywords: C-reactive protein; antimicrobial resistance; primary care



Citation: Gentile I, Schiano Moriello N, Hopstaken R, Llor C, Melbye H, Senn O. The Role of CRP POC Testing in the Fight against Antibiotic Overuse in European Primary Care: Recommendations from a European Expert Panel. *Diagnostics* 2023, 13, 320. <https://doi.org/10.3390/diagnostics13030320>

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Guidance on C-reactive protein point-of-care testing and complementary strategies to improve antibiotic prescribing for adults with lower respiratory tract infections in primary care

Oliver Van Hecke^{1,2,†}, Lars Bjerrum^{3†}, Ivan Gentile^{4†}, Rogier Hopstaken^{5†}, Hasse Melbye^{6†}, Andreas Plate^{7†}, Jan Y. Verbakel^{8,7,†}, Carl Llor^{9†} and Annamaria Staiano^{10†}

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The world faces the threat of increasing antimicrobial resistance, and there is growing consensus that swift action must be taken to improve the rational use of antibiotics and increase the stewardship of antibiotics to safeguard this key resource in modern healthcare. This paper provides the perspective of an international group of experts on the role of C-reactive protein point-of-care testing (CRP POCT) and other complementary strategies to improve antibiotic stewardship in primary care, with regards to the diagnosis and treatment of adult patients presenting symptoms of lower respiratory tract infections (LRTIs). It provides guidance regarding the clinical assessment of symptoms in combination with C-reactive protein (CRP) results, at the point of care, to support the management decision, and discusses enhanced patient communication and delayed prescribing as complementary strategies to decrease the inappropriate use of antibiotics. Recommendation: CRP POCT should be promoted to improve the identification of adults presenting with symptoms of LRTIs in primary care who might gain additional benefit from antibiotic treatment. Appropriateness of antibiotic use can be maximized when CRP POCT is used together with complementary strategies such as enhanced communication skills training and delayed prescribing in addition to routine safety netting.



C-reactive Protein Point-of-care Testing and Complementary Strategies to improve Antibiotic Stewardship in Ambulatory Care of Children

Annamaria Staiano^{1,†}, Lars Bjerrum^{2,†}, Carl Llor^{3,†}, Hasse Melbye^{4,†}, Rogier Hopstaken^{5,†}, Jan Y Verbakel^{6,7,†}, Ivan Gentile^{8,†}, Andreas Plate^{9,†}, Oliver van Hecke^{7,10,†}

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†These authors have contributed equally to this work and share first authorship./

‡These authors have contributed to and reviewed this work.

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**CONSENSUS STATEMENT #6:
CRP POCT USEFUL IN CHILDREN WITH RTI**



In the ambulatory care of febrile children presenting with symptoms of respiratory illness, CRP POCT can be useful to guide decisions regarding antibiotic prescribing and hospital referrals.

**CONSENSUS STATEMENT #7:
CRP POCT IS ECONOMICALLY VIABLE**



The use of CRP POCT for the management of patients presenting symptoms of LRTIs in primary care can be economically viable in several contexts



UK



France



Belgium



Italy



Germany



Spain



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at the Point of Care



CONSENSUS Reached on initiatives in primary care to combat AMR based on good scientific evidence: CRP-testing has a key Role