Antibiotic Stewardship Conference: FROM EXPERT CONSENSUS TO EUROPE-WIDE ACTION AT THE POINT OF CARE

BRUSSELS

29 NOVEMBER | 2022





ANTIBIOTIC STEWARDSHIP CONFERENCE:

FROM EXPERT CONSENSUS TO EUROPE-WIDE ACTION AT THE POINT OF CARE

WELCOME

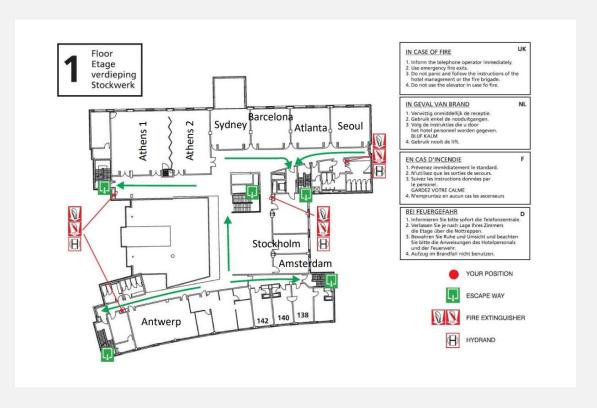
DR. O. VAN HECKE
UNIVERSITY OF OXFORD
GENERAL PRACTITIONER



Outline

- Welcome Dr Oliver Van Hecke
- Safety and facilities
- Rationale
- Introductions
 - Expert working group
 - Diagnostic representatives Abbott
 - Facilitators (MindGap)
- The ENASPOC Network
- Conference objectives
- Agenda overview

Safety and facilities



WELCOME AND INTRODUCTION

Rationale - in a nutshell

IN THEORY: CONSENSUS

- Antibiotic resistance is a major global threat
- Inappropriate prescribing => resistance
- A significant portion of antibiotic prescriptions in primary for respiratory tract infections are not appropriate
- CRP POCT and complementary strategies can help, when used properly

IN PRACTICE: LACK OF ACTION

- More than enough research on the subject
- Not enough practical action => opportunity to improve antibiotic stewardship
- New medicines will not help without behavior change, as resistance will be rebuilt

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The Expert group on CRP point of care testing to guide antibiotic prescriptions for respiratory illness

Lars Bjerrum Denmark	Andreas Plate Switzerland
Ivan Gentile Italy	Annamaria Staiano Italy
Rogier Hopstaken The Netherlands	Oliver Van Hecke The UK
Carl Llor Spain	Jan Verbakel Belgium
Hasse Melbye Norway	

WELCOME AND INTRODUCTION

The Expert Group

- Define 'European guidance' on the use of CRP POCT and complementary strategies to promote optimal use of antibiotics and to mature antibiotic stewardship
- Current output: Consensus Statements shared
- In progress: several **papers for publication** on the subject, for general practitioners, pediatricians, and policy makers

WELCOME AND INTRODUCTION

Welcome from the organizing team



FELICIA LONGOBARDI
Abbott Rapid Diagnostics

Marketing Director



Abbott Rapid Diagnostics Ass. Medical Director



CHRISTIAN MONTAG

MindGap - Healthcare Market Research
Partner - Senior Business Consultant

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WELCOME AND INTRODUCTION

What is ENASPOC?

- International, multi-disciplinary network
- Advance proven technologies e.g. CRP POCT to optimise treatment for respiratory tract infections in primary care.
- Focus on effective implementation strategies
- Membership
- Invitation to join



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Conference Aim

HOW WE WILL ACHIEVE THE OBJECTIVE

Share **'European guidance' to enable improved practice** with the relevant stakeholders

Co-create regional implementation plans with key stakeholders to enable the approach to the European guidance

Support the execution of country-level action plans, that will positively **affect the desired behavioral change**

WELCOME AND INTRODUCTION

CONSENSUS STATEMENTS

CONSENSUS STATEMENT 1:

Antimicrobial resistance is a global threat that must urgently be addressed.

CONSENSUS STATEMENT 2:

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

CONSENSUS STATEMENT 3:

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

CONSENSUS STATEMENT 4:

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:

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

CONSENSUS STATEMENT 6:

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:

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



WELCOME AND INTRODUCTION

Agenda Overview

MORNING PROGRAM: PRESENTATION OF THE 'EUROPEAN GUIDANCE'

- Share the expert group's consensus on the use of CRP POCT and complementary strategies
- Understand how to address overprescription for respiratory illness in primary care

AFTERNOON PROGRAM: ACTION PLAN CO-CREATION WORKSHOPS

- Split into break-out groups per country for co-creation of action plans
- Draft a national action plan per country

ANTIBIOTIC STEWARDSHIP CONFERENCE:

FROM EXPERT CONSENSUS TO EUROPE-WIDE ACTION AT THE POINT OF CARE

The Importance of Antibiotic Stewardship in Primary Care

PROF I. GENTILE
UNIVERSITY OF NAPLES
FEDERICO II



DISCLOSURES

Prof. Ivan Gentile has acted as a consultant for Abbvie, MSD, Gilead, Pfizer, Nordic/Infectopharm, Angelini, Correvio, Abbott, SOBI, Basilea, GSK

AGENDA

Definition and Impact of Antimicrobial Resistance

Causes of Antimicrobial Resistance

Antimicrobial Stewardship Program as a solution

AGENDA

Definition and Impact of Antimicrobial Resistance

Causes of Antimicrobial Resistance

Antimicrobial Stewardship Program as a solution

What is Antimicrobial Resistance?

- Antimicrobial Resistance (AMR) occurs when bacteria, viruses, fungi and parasites do not respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death.
- WHO has declared that AMR is one of the top 10 global public health threats facing humanity

Impact of Antimicrobial Resistance

Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis

Alessandro Cassini, Liselatte Diaz Högberg, Diamantis Plachouras, Annalisa Quattrocchi, Ana Hoxha, Gunnar Skov Simonsen, Mélanie Colomb-Cotinat, Miljam E Kretzschmar, Brecht Devlessschauwer, Michele Cecchini, Driss Ait Duakrim, Tiago Cravo Oliveira, Marc J Struelens, Carl Suetens, Dominique L Monnet, and the Burden of AMR Collaborative Group*

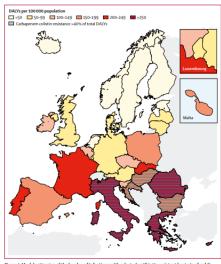


Figure 4: Model estimates of the burden of infections with selected antibiotic-resistant bacteria of public health importance in DALYs per 100 000 population, EU and European Economic Area, 2015 Greece did not report data on 5 pneumonios isolates to the European Antimicrobial Resistance Surveillance Network in 2015, DALYs-disability-adjusted life-years.

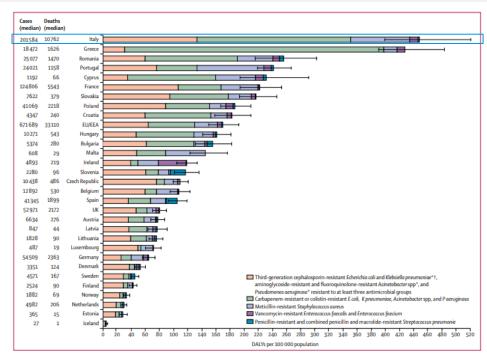
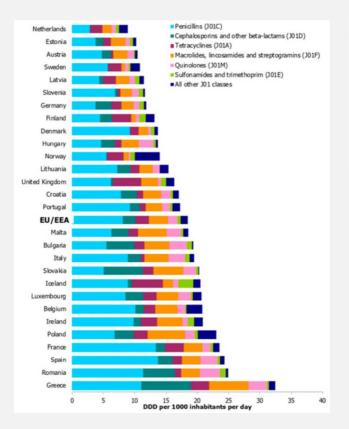
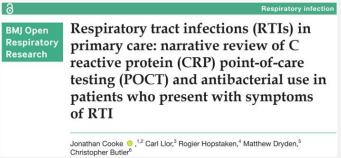


Figure 3: Burden of infections with antibiotic-resistant bacteria in DALYs, EU and European Economic Area, 2015

Error bars are 95% uncertainty intervals. Greece did not report data on 5 pneumonioe isolates to the European Antimicrobial Resistance Surveillance Network in 2015. DALY rates are age-standardised to limit the effect of demographic differences across countries; numbers of cases and deaths are not age-standardised. DALYs-disability-adjusted life-years. "Excludes those resistant to carbapenem or colistin." The 2015, most of the third-generation cephalosporin-resistant E coli (88-6%) and K pneumoniae (85-3%) isolates reported to the European Antimicrobial Resistance Surveillance Network produced an extended-spectrum B-lactamase."

Use of antibiotics across Europe





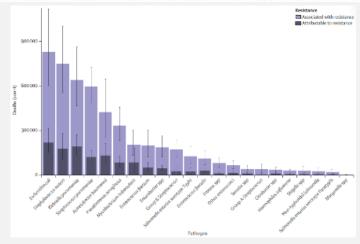
The influence of biomarkers on antimicrobial prescribing rates in patients presenting in primary care with symptoms of RTI

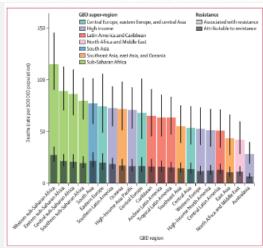
A 2015 survey of countries that employed CRP POCT as a diagnostic and/or prognostic tool in general practice showed those countries that used CRP POCT to some or a wide extent were: Finland, Netherlands, Denmark, Norway, Sweden, Germany, Czech Republic, Hungary, Austria, Slovenia, Latvia and Estonia. 33 34 Interestingly, these countries are the lowest 12 prescribers of antibacterials in the latest ESAC survey (figure 1). 35 We have sought to review the evidence for the use of point-of-care (POC) biomarkers in reducing antimicrobial prescribing in primary care by prescribers who see patients presenting with symptoms of RTI. We felt that an update of our 2016

Impact of Antimicrobial Resistance

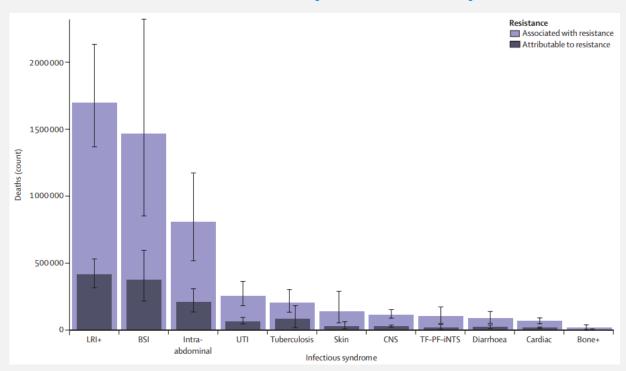


Findings On the basis of our predictive statistical models, there were an estimated 4.95 million (3.62-6.57) deaths associated with bacterial AMR in 2019, including 1.27 million (95% UI 0.911-1.71) deaths attributable to bacterial AMR. At the regional level, we estimated the all-age death rate attributable to resistance to be highest in western sub-



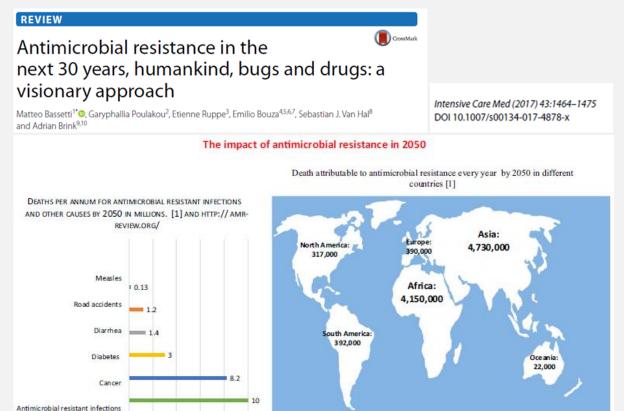


Global deaths (counts) attributable to and associated with bacterial antimicrobial resistance by infectious syndrome, 2019



Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022 Feb 12;399(10325):629-655.

Impact of Antimicrobial Resistance



Final Report

DRUG-RESISTANT INFECTIONS

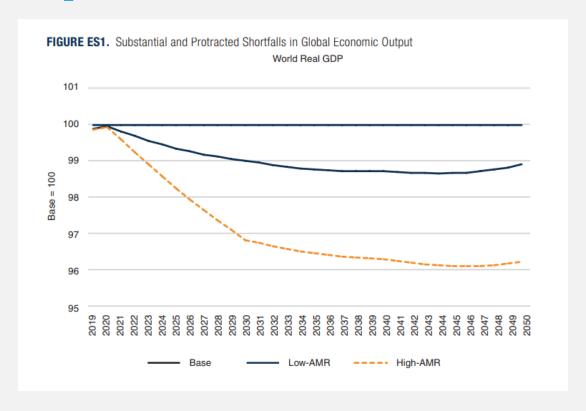
A Threat to Our Economic Future

March 2017

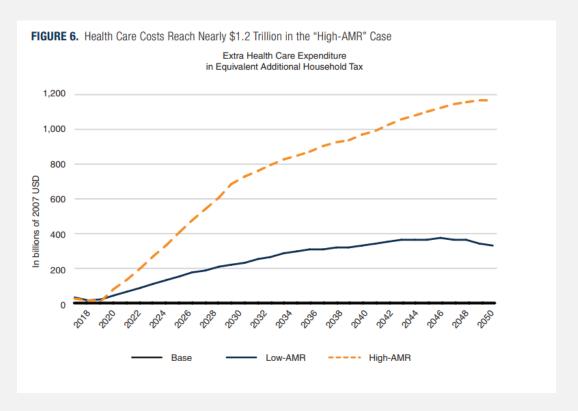




Economic impact of Antimicrobial Resistance



Economic impact of Antimicrobial Resistance



CONSENSUS STATEMENT #1

Antimicrobial resistance is a global threat that must urgently be addressed

AGENDA

Definition and Impact of Antimicrobial Resistance

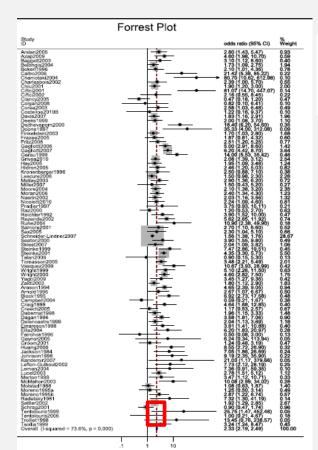
Causes of Antimicrobial Resistance

Antimicrobial Stewardship Program as a solution

Causes of Antimicrobial Resistance



Causes of Antimicrobial Resistance



A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance

Brian G Bell^{1*}, Francois Schellevis^{2,3}, Ellen Stobberingh⁴, Herman Goossens⁵ and Mike Pringle¹

Bell et al. BMC Infectious Diseases 2014, 14:13 http://www.biomedcentral.com/1471-2334/14/13



Using a large set of studies we found that antibiotic consumption is associated with the development of antibiotic resistance.

A subsequent meta-analysis, with a subsample of the studies, generated several significant predictors. Countries in southern Europe produced a stronger link between consumption and resistance than other regions so efforts at reducing antibiotic consumption may need to be strengthened in this area. Increased consumption of antibiotics may not only produce greater resistance at the individual patient level but may also produce greater resistance at the community, country, and regional levels, which can harm individual patients.

Causes of Antimicrobial Resistance

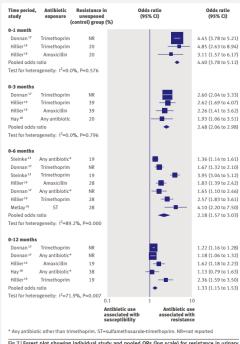


Fig 2 | Forest plot showing individual study and pooled ORs (log scale) for resistance in urinary tract bacteria (E coli) and antibiotic exposure. Studies grouped according to time period during which exposure was measured and ordered within each time period by increasing standard error

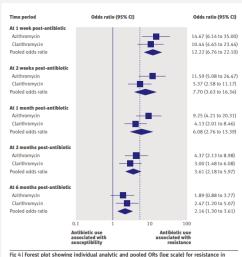


Fig 4 | Forest plot showing individual analytic and pooled ORs (log scale) for resistance in respiratory tract streptococci of healthy volunteers from the Malhotra-Kumar study 35 and previous antibiotic prescribing



Cite this as: *BMJ* 2010;340:c2096 doi:10.1136/bmi.c2096

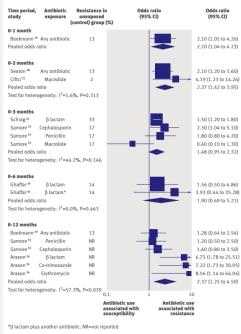
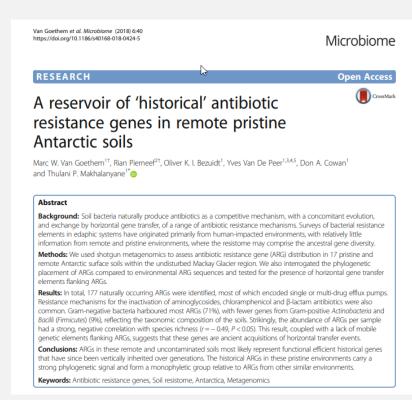
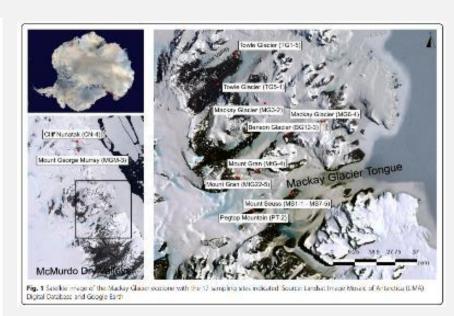


Fig 3 | Forest plot showing individual study and pooled ORs (log scale) for resistance in

rig 3 | rotest plot showing individual study and plotted one (ug scale) for reststance in respiratory tract bacteria and previous antibiotic prescribing. Studies grouped according to time period during which exposure was measured and ordered within each time period by increasing standard error

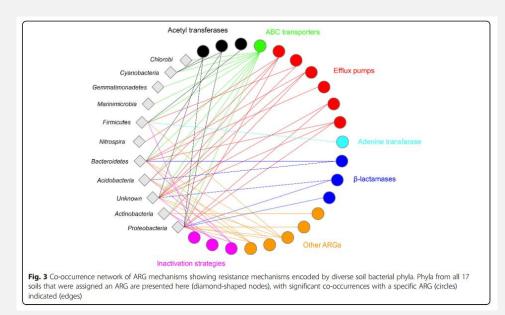
Causes of Antimicrobial Resistance





Antibiotic resistance is often already present in nature, selective pressure with overuse of antibiotics greatly augment the diffusion

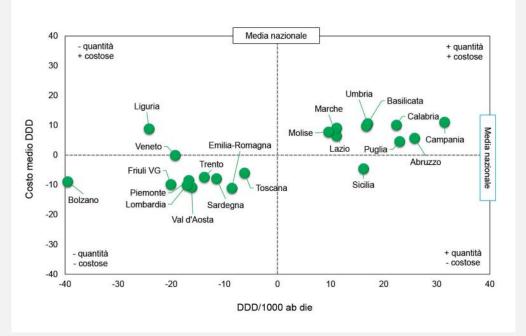
Table 2 ARG families found exclusively in a single community Sample site ARG family description MS4-1 Multidrug efflux pump MGM-3 Dihydrofolate reductase, which cannot be inhibited by trimethoprim Tet35 is a tetracycline efflux pump found MS1-1 in the Gram-negative Vibrio and Stenotrophomonas. Unrelated to other tet resistance genes TG5-1 Aminoglycoside 6-N-acetyltransferase, which modifies aminoglycosides by acetylation CN-4 Adenine transferase/methyltransferase, conferring resistance to erythromycin/ kasugamycin Mutation frequency decline (Mfd) protein



Van Goethem, et al. Microbiome 2018

My personal experience in the hospital setting

Figura 1.1 Variabilità regionale del consumo (DDD/1000 ab *die*) di antibiotici sistemici (J01) per quantità e costo medio di giornata di terapia nel 2019 (convenzionata e acquisti strutture sanitarie pubbliche)

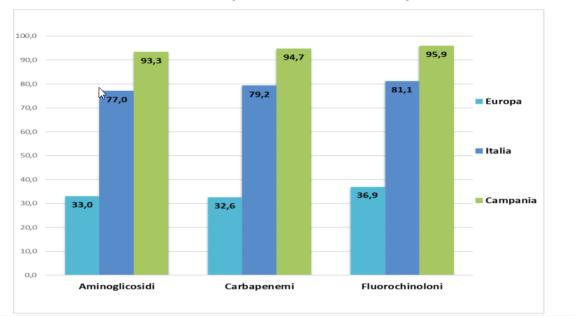


Campania region has the highest antibiotic consumption pro capita in all Italy, antibiotics resistance is also significantly higher than the rest of the country

Source: Italian Medicines Agency (AIFA)

My personal experience in the hospital setting

Figura 10. Confronto tra le % di resistenza a Aminoglicosidi, Carbapenemi e Fluorochinoloni degli isolati invasivi di *A. baumannii complex* rilevate in Italia e Campania nel 2019



Source: Regione Campania

Causes of Antimicrobial Resistance

UK Health Security Agency

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR)

Report 2021 to 2022

Over the past 5 years, the majority of antibiotics in England were prescribed within general practice, with this trend continuing in 2021 (72.1% of overall prescribing, 11.5 DID). The

J Antimicrob Chemother 2018; 73 Suppl 2: ii2-ii10 doi:10.1093/jac/dkx504

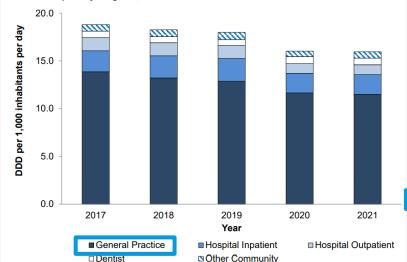
Journal of Antimicrobial Chemotherapy

Antibiotics in primary care in England: which antibiotics are prescribed and for which conditions?

F. Christiaan K. Dolk^{1,2}†, Koen B. Pouwels¹⁻³†, David R. M. Smith¹, Julie V. Robotham¹‡ and Timo Smieszek^{1,3}*‡

*Modelling and Economics Unit, National Infection Service, Public Health England, London, UK: ²PharmacoTherapy, -Epidemiology & -Economics, Department of Pharmacy, University of Graningen, Graningen, The Netherlands; *NAC Centre for Outbreek Analysis and Modelling, Department of Infectious Disease Epidemiology, Imperial College School of Public Health, Landon, UR

Figure 3.1 Total antibiotic consumption by setting, expressed as DDDs per 1,000 inhabitants per day, England, 2017 to 2021



Objectives: To analyse antibiotic prescribing behaviour in English primary care with particular regard to which antibiotics are prescribed and for which conditions.

Methods: Primary care data from 2013–15 recorded in The Health Improvement Network (THIN) database were analysed. Records with a prescription for systemic antibiotics were extracted and linked to co-occurring diagnostic codes, which were used to attribute prescriptions to clinical conditions. We further assessed which antibiotic classes were prescribed and which conditions resulted in the greatest share of prescribing.

Results: The prescribing rate varied considerably among participating practices, with a median of 626 prescriptions/1000 patients (IQR 543–699). In total, 69% of antibiotic prescriptions (n = 3156507) could be linked to a body system and/or clinical condition. Of these prescriptions, 46% were linked to conditions of the respiratory tract, including ear, nose and throat (RT/ENT); leading conditions within this group were cough symptoms (22.7%), lower respiratory tract infection (RTI) (17.9%), sore throat (16.7%) and upper RTI (14.5%). After RT/ENT infections, infections of the urogenital tract (22.7% of prescriptions linked to a condition) and skin/wounds (16.4%) accounted for the greatest share of prescribing. Penicillins accounted for 50% of all prescriptions, followed by macrolides (13%), tetracyclines (12%) and trimethorim (11%).

Conclusions: The majority of antibiotic prescriptions in English primary care were for infections of the respiratory and urinary tracts. However, in almost one-third of all prescriptions no clinical justification was documented. Antibiotic prescribing rates varied substantially between practices, suggesting that there is potential to reduce prescribing in at least some practices.

Causes of Antimicrobial Resistance

J Antimicrob Chemother 2018; **73** Suppl 2: ii19-ii26 doi:10.1093/iac/dkx502

Journal of Antimicrobial Chemotherapy

Actual versus 'ideal' antibiotic prescribing for common conditions in English primary care

Koen B. Pouwels¹⁻³†, F. Christiaan K. Dolk^{1,2}†, David R. M. Smith¹, Julie V. Robotham¹‡ and Timo Smieszek^{1,3}*‡

Actual versus 'ideal' antibiotic prescribing

JAC

Table 1. Actual and 'ideal' antibiotic prescribing proportions among patients without comorbidities consulting at a general practice

Condition	Consultations (n)	Proportion of consultations with a systemic antibiotic prescription (95% CI)	Ideal proportion of consultations resulting in systemic antibiotic prescriptions (IQR) ¹⁶
Acne	60959	0.43 (0.43-0.44)	0.21 (0.10-0.35)
Acute bronchitis	17084	0.82 (0.82-0.82)	0.13 (0.06-0.22)
Acute cough	573827	0.41 (0.41-0.41)	0.10 (0.06-0.16)
Acute otitis media (age 0–1 year)	14886	0.92 (0.91-0.92)	0.19 (0.09-0.33)
Acute otitis media (age 2–18 years)	39513	0.88 (0.88-0.89)	0.17 (0.08-0.30)
Acute rhinosinusitis	74359	0.88 (0.88-0.88)	0.11 (0.05-0.18)
Acute sore throat	386971	0.59 (0.58-0.59)	0.13 (0.07-0.22)
Asthma exacerbation	23292	0.47 (0.46-0.47)	_c
COPD exacerbation	13840	0.73 (0.72-0.74)	0.54 (0.31-0.78)
Gastroenteritis (age >2 years)	114290	0.05 (0.05-0.05)	0.09 (0.04-0.16)
Impetigo	29809	0.53 (0.52-0.53)	0.12 (0.06-0.53)
Influenza-like illness	23787	0.18 (0.18-0.19)	_c
Lower respiratory tract infection ^a	161065	0.87 (0.87-0.88)	_c
Upper respiratory tract infection ^b	383847	0.25 (0.25-0.25)	_c
Urinary tract infection age (>14 years)	128566	0.92 (0.91-0.92)	0.75 (0.61-0.86)
-			

CONSENSUS STATEMENT #2

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

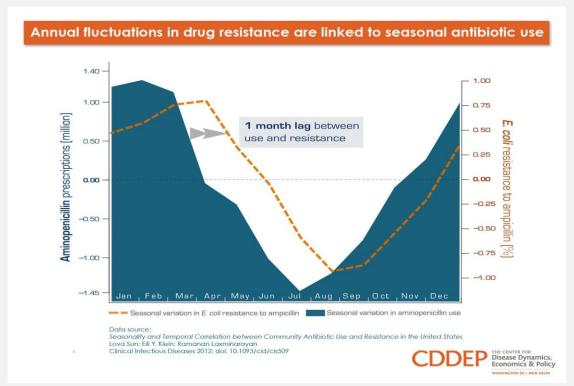
AGENDA

Definition and Impact of Antimicrobial Resistance

Causes of Antimicrobial Resistance

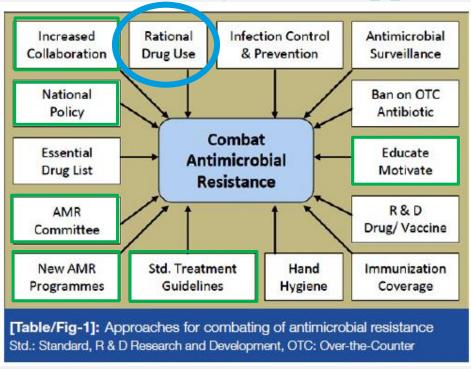
Antimicrobial Stewardship Program as a solution

Potentially reversible damage



Seasonal fluctuations in aminopenicillin prescribing in the community together with the rates of E. coli resistance to ampicillin in hospitalized patients. Prescriptions for aminopenicillins peaked in February, at the height of the flu season. There was a onemonth lag between use and E. coli resistance rates to the same drug class. The study included over a decade (1999-2010) of US nationally-representative data and advanced statistical techniques that allow for the inference of causality.

Fighting against AMR – a systemic approach



RAJESH R UCHIL¹, GURDEEP SINGH KOHLI², VIJAY M KATEKHAYE³, ONKAR C SWAMI⁴

Antimicrobial Stewardship

The Search for Good Antimicrobial Stewardship

Dale N. Gerding, MD

Copyright 2001

JOURNAL ON QUALITY IMPROVEMENT

SYMPOSIUM ON ANTIMICROBIAL THERAPY

Antimicrobial Stewardship

SHIRA DORON, MD, AND LISA E. DAVIDSON, MD

Mayo Clin Proc. 2011;86(11):1113-1123

The goal of antimicrobial stewardship is **3-fold**.

The first goal is to work with health care practitioners to help each patient receive the most appropriate antimicrobial with the correct dose and duration.

The second goal is to prevent antimicrobial overuse, misuse, and abuse.

The third goal is to minimize the development of resistance.



A coherent set of actions which promote using antimicrobials responsibly.

"Treat infected patients at the dose and the duration likely to minimize the risk of resistance with low risk of failure and toxicity at a reasonable cost"

Safely reducing the use of antimicrobials

COMMUNITY LEVEL

Aims

- 1) Reducing inappropriate prescriptions
- 2) Optimizing dose and duration of treatment

Key Role

- 1) Primary care physician
- 2) Patient
- 3) Community pharmacist

HOSPITAL LEVEL

Aims

- 1) Optimizing dose and **duration** of treatment
- 2) Reducing **inappropriate** prescriptions

Key Role

- 1) Hospital physician
- 2) Microbiologist
- 3) Hospital pharmacist

The role of Rapid Diagnostics in tackling AMR

RAPID DIAGNOSTICS WOULD REDUCE UNNECESSARY PRESCRIPTION

Out of 40m people who are given antibiotics for respiratory issues, annually in the US:

27m

13m

get antibiotics unnecessarily

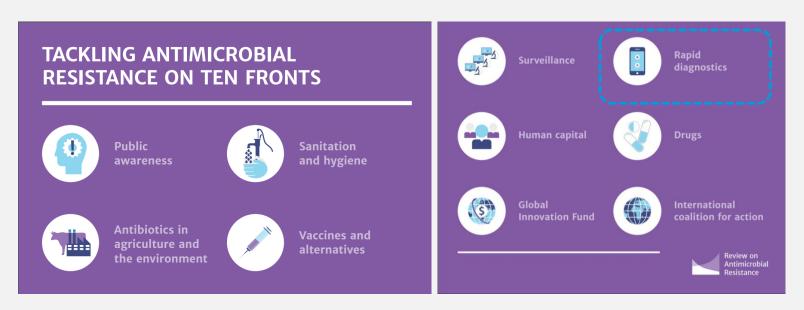
who need antibiotics get then

Data extracted from: Shapiro D J, Hicks L A, Pavia A T, Hersh A L. Antibiotic prescribing for adults in ambulatory care in the USA, 2007–09. Journal of Antimicrobial Chemotherapy 2013,

JIM O'NEILL. THE REVIEW ON ANTIMICROBIAL RESISTANCE 2016

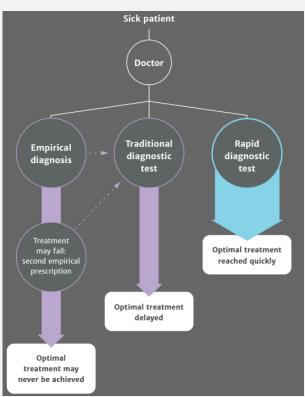


The role of Rapid Diagnostics in tackling AMR

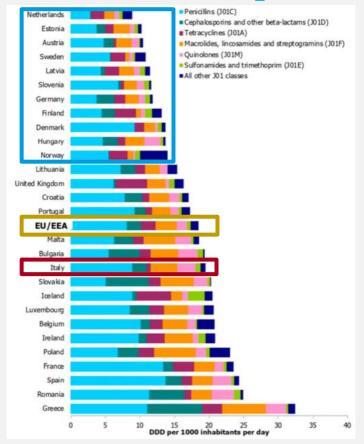


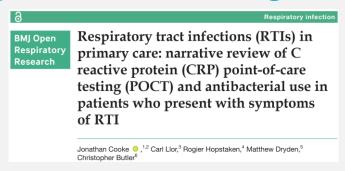
JIM O'NEILL, THE REVIEW ON ANTIMICROBIAL RESISTANCE 2016

Rapid diagnostics would optimize treatment



The role of Rapid Diagnostics in tackling AMR





The influence of biomarkers on antimicrobial prescribing rates in patients presenting in primary care with symptoms of RTI

A 2015 survey of countries that employed CRP POCT as a diagnostic and/or prognostic tool in general practice showed those countries that used CRP POCT to some or a wide extent were: Finland, Netherlands, Denmark, Norway, Sweden, Germany, Czech Republic, Hungary, Austria, Slovenia, Latvia and Estonia. ³³ ³⁴ Interestingly, these countries are the lowest 12 prescribers of antibacterials in the latest ESAC survey (figure 1). ³⁵ We have sought to review the evidence for the use of point-of-care (POC) biomarkers in reducing antimicrobial prescribing in primary care by prescribers who see patients presenting with symptoms of RTI. We felt that an update of our 2016

Conclusions

- Antibiotic resistance (AMR) is one of the greatest threats to global health and it is accelerated mainly by the misuse and abuse of antibiotics.
- The phenomenon of AMR is at-least partially reversible with a wise use of antibiotics.
- An integrated strategy can reduce the rate of inappropriate prescribing of antibiotics.
- Among the different approaches, the use of rapid test is one of the most promising.

Antibiotic Stewardship Conference: FROM EXPERT CONSENSUS TO EUROPE-WIDE ACTION AT THE POINT OF CARE

The Importance of Antibiotic Stewardship in Primary Care

DR. O. VAN HECKE
UNIVERSITY OF OXFORD & GENERAL PRACTITIONER

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