Global coordinated action against antibiotic resistance
Are we achieving enough?

Otto Cars
Senior Professor, Infectious Diseases
Uppsala university, Sweden

ECCMID, Madrid 22 April 2018
The global policy response to the antibiotic resistance challenge

Too slow
Too weak
Too narrow
The gap between science and policy

No of articles in PubMed

- Antibiotic Resistance
- Antibiotic Policies

© by author
Guadalajara Declaration (2001)
Cuenca Declaration (2008)
Jaipur Declaration (2011)
New Delhi Call to Action (2011)
Barcelona Declaration of WAAMRO (2012)
Chennai Declaration (2012)
U.S. Joint Statement from Health Organizations and CDC (2012)
Statement of the Academies of Science (2013)
G8 Science Ministers (2013)
Antibiotic Resistance Coalition (ARC) Declaration (2014)
Declaration of WAAR (2014)
Declaration of the G7 Health Ministers (2015)
The Copenhagen Recommendations

The Microbial Threat

Communication from the Commission to the European Parliament and the Council

Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) Networks

- European Antimicrobial Resistance Surveillance Network (EARS-Net) (formerly EARSS, integrated in January 2010)
- European Surveillance of Antimicrobial Consumption Network (ESAC-Net) (formerly ESAC, integrated in July 2011)
Five strategic objectives of the Global Action Plan

1. Improve awareness and understanding of antimicrobial resistance
2. Strengthen the knowledge and evidence base through surveillance and research
3. Reduce the incidence of infection
4. Optimize the use of antimicrobial medicines
5. Develop the economic case for sustainable investment and increase investment in new medicines, diagnostics, vaccines
Some causes for the global complacency

- Antibiotic resistance is not a disease
- Inadequate data on health and economic consequences
- The ecological/environmental dimensions ignored
- Not seen as a global development issue
- Blame game
- A slow threat
- Bureaucracy with vertical structures
- Misaligned financial incentives
- Disincentives for collective action
- The global self-deception: There will always be new antibiotics
Resolution adopted by the General Assembly on 5 October 2016

[without reference to a list of conclusions (47)]

71/3. Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance

The General Assembly,

recalling its resolutions 68/403 of 17 December 2013 and 70/287 of 23 July 2016, in which it decided to hold a high-level meeting on antimicrobial resistance on 23 September 2016,

adopts the following political declaration approved by the high-level meeting of the General Assembly on antimicrobial resistance on 23 September 2016.

Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance

We, Heads of State and Government and representatives of States and Governments, meeting at United Nations Headquarters in New York on 23 September 2016, in accordance with General Assembly resolution 68/403 of 17 December 2013, in which the Assembly decided to hold a high-level meeting in 2016 on antimicrobial resistance,

1. Reaffirm that the objective for tackling antimicrobial resistance is the World Health Organization global action plan on antimicrobial resistance and its five overarching strategic objectives developed by the World Health Organization to collaborate with, and subsequently adopted by, the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health.

2. Also reaffirm that the 2005 Agenda for Sustainable Development offers a framework to reverse hazardous and reckless commitments to fight microbial diseases, particularly drug-resistant infections, and recognize that antimicrobial resistance threatens the sustainability and effectiveness of the
The failing machinery....
More that 70 years of antibiotic use
Millions of tons....
The survival of the fittest
• The narrative
• The global microbiome
• The broken innovation model
• Unavailability of old antibiotics
• Access and conservation
• Many new players – leadership and coordination?
• Antibiotic resistance and Agenda 2030
• Global governance- towards a binding legal framework?
Antibiotic resistance has a language problem

A failure to use words clearly undermines the global response to antimicrobials’ waning usefulness. Standardize terminology, urge Marc Mendelson and colleagues.
"A One Health Approach for Tackling Antimicrobial Resistance: Moving from Knowledge to Action"
A Side Event for the 2018 Prince Mahidol Award Conference 2018

**SURVEILLANCE**
- AGISAR at WHO is building capacity to create national surveillance programs to fill knowledge gaps
- GLASS: GLobal One Health Surveillance System
- ATLAS-S: national level surveillance system
- SEDRIC: Global Tricolore Surveillance

**RATIONAL USE OF ANTIBIOTICS**
- **DRIVERS of AMR**: overuse & misuse, expectations of patients to need to use antibiotics
- **CASE Study from Vietnam**: 30% of antibiotics prescribed are inappropriate
- **Rational use of antibiotics**: need for alternative economic incentives
- **Behavior Change**: use of vaccines, incorporation of economics

**GLOBAL POLICY & COORDINATION**
- **Sustainability**: must build institutional capacity across sectors
- **INSTITUTIONAL CAPACITY**: for growth promotion
- **Governance structure**: accountability

**TRI-PARTITE PILLARS**
- Humans + Environment + Agriculture

**NOTE:** A participant of the side event, Tobey Busch, Senior Pharmaceutical Management Advisor from USAID, captured graphic notes of the discussion.
Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050?

Marlieke E. A. de Kraker¹ *, Andrew J. Stewardson², Stephan Harbarth¹
PLOS Medicine | DOI:10.1371/journal.pmed.1002184 November 29, 2016

Estimates of burden of ABR

Europe:
- Population 500m
- 25,000 deaths per year
- 2.5m extra hospital days
- Overall societal costs (€ 900 million, hosp. days)
  - Approx. €1.5 billion per year

Thailand:
- Population 70m
- >38,000 deaths
- >3.2m hospital days
- Overall societal costs
  - US$ 84.6–202.8 mill. direct
  - >US$1.3 billion indirect

United States:
- Population 300m
- >23,000 deaths
- >2.0m illnesses
- Overall societal costs
  - Up to $20 billion direct
  - Up to $35 billion indirect

Source: ECDC 2007
Source: Punsart et al. 2012
Source: US CDC 2013

Global information is insufficient to show complete disease burden impact and costs
Community carriage of ESBLs is common (up to 45%), and nosocomial acquisition occurs at a rate of 20% for every 48 h spent in hospital.

Many common organisms continue to be treated with regimens with reportedly high frequencies of in-vitro non-susceptibility because of insufficient evidence (or local data) to support further changes.

Based on the estimated prevalence of non-susceptibility among positive cultures, empirical treatment guidelines (which rely heavily on commonly available antibiotics such as penicillin and gentamicin) need review.

In practice, tailoring of therapy is usually impossible because of a lack of data about local susceptibility.

Population based sentinel/point prevalence studies of resistance and antibiotic availability and use are needed to:

- provide relevant data for treatment guidelines- what works?
- inform access and stewardship programs
- estimate the burden
- make the economic case for investments
The substantial progress made in the diagnosis and management of HIV, tuberculosis, and malaria has shown that non-expert staff can effectively deliver services that were previously considered too complicated and demanding. With similar concerted international efforts on an international scale, we believe such progress could be achieved for clinical bacteriology.
We seek new approaches that have the potential to transform public health action on a regional or global scale by identifying and filling gaps in knowledge on the burden of resistance to antibacterial agents.

In particular, there is a need to better understand resistance in bacterial infections of newborns and young children.
Creation and use of relevant knowledge

Social movement

Political involvement
Creation and use of relevant knowledge

“Knowledge derived from research must be translated into forms and languages that can empower the public”.

“Politics without knowledge and social movement will not do”.

Social movement

Political involvement
Faecal carriage of ESBL producing isolates

Valverde et al. J Clinical Microbiology 2004; 42:4769-75
Community feecal carriage rates of multi-resistant bacteria (ESBL)
Grouped geographically according to WHO regions

Frequency of fecal carriage of multidrug-resistant *Enterobacteriaceae* in international travellers, February 2012-April 2013

Orphanage in Bamako, Mali
ESBL colonized 100% of the children and 63%, of the adult staff studied.

Vicente Corral Moscoso Hospital, Ecuador
56% of neonates in an Ecuadorian hospital colonized with ESBL producing Enterobacteriaceae
Alarming high rate of CRE colonization in Vietnamese hospitals

Faecal CRE screening of 350 infants admitted to neonatal ICU March-May 2017

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Admission</td>
<td>33% CRE +</td>
</tr>
<tr>
<td>Discharge</td>
<td>83% CRE +</td>
</tr>
</tbody>
</table>

Courtesy of Mattias Larsson1, N. Hong Thi Bich Ngoc2, E. Bornefall3, N. Le Kien Nga2, D. Khu Thi Khanh Duong2, Le Thanh Hai2, D. Tran Minh Dien2, Linus Olson1, Håkan Hanberger3. 1 Karolinska Institutet, Sweden. 2 Vietnam National Children’s Hospital, Hanoi. 3 Linköping University, Sweden.
Alarming high rate of CRE colonization in Vietnamese hospitals

Faecal CRE screening of 350 infants admitted to neonatal ICU March-May 2017

Admission 33% CRE +
Discharge 83% CRE +

Mortality in children with culture verified noscomial infection caused by carbapenem resistant Klebsiella Pneumoniae

CRE 35%
CRE and colistin resistance 55%

Courtesy of Mattias Larsson¹, N. Hong Thi Bich Ngoc², E. Bornefall³, N. Le Kien Nga², D. Khu Thi Khanh Duong², Le Thanh Hai², D. Tran Minh Dien², Linus Olson¹, Håkan Hanberger³.
¹ Karolinska Institutet, Sweden. ² Vietnam National Children’s Hospital, Hanoi. ³ Linköping University, Sweden.
Changing antibiotic resistance: sustainability transformation to a pro-microbial planet

P. Sogaard et al
Current Opinion in Environmental Sustainability 2017, 25:66–76
Penicillin cures gonorrhea in 4 hours!!!!

Each year, an estimated 78 million people are infected with gonorrhoea.

Data from 77 countries show that antibiotic resistance is making gonorrhoea much harder, and sometimes impossible, to treat.

Ongoing gonorrhoea outbreak in England could become untreatable with first-line therapy.

The outbreak is the first time that a high-level, azithromycin-resistant strain of the gonorrhoea bacterium has shown sustained
Lack of access to antibiotics is causing millions of deaths

Lack of access to essential antibiotics
Across developing countries fewer than a third of children with suspected pneumonia receive antibiotics”

The unpleasant truth

• Antibiotic resistance cannot be solved, only managed

• Since decades, the ‘race’ between the evolution of antibiotic resistance and human ingenuity is in favour of the bacteria

• The critical lack of access to effective antibiotics must be seen as an issue of multiple systems failure

• The cost of non-action is enormous but the world’s response is inadequate: political will, collective action and sustainable funding is still insufficient
“The infrastructure of antibiotic discovery both in academia and in industry is at a dangerously low level and needs to be rebuilt”
Lack of New Antibiotics

- 1953: Glycopeptides, Nitroimidazoles, Streptogramins
- 1952: Macrolides
- 1950: Pleuromutilins
- 1948: Cephalosporins
- 1947: Polymyxins, Phenicol
- 1946: Nitrofurans
- 1945: Tetracyclines
- 1943: Aminoglycosides, Bacitracin (topical)
- 1932: Sulfonamides
- 1928: Penicillins

- 1955: Cycloserine, Novobiocin
- 1957: Rifamycins
- 1961: Trimethoprim
- 1962: Quinolones, Lincosamides, Fucidic acid
- 1969: Fosfomycin
- 1971: Mupirocin
- 1976: Carbapenems
- 1978: Oxazolidinones
- 1979: Monobactams
- 1987: Lipopeptides

© ReAct Group 2015

© by author

DISCOVERY VOID
Number of companies that had gained approval for at least one NME for a bacterial disease and which remained active in the field

Kinch et al. Discovery Today Volume 19, Number 9 September 2014
Why is Big Pharma Getting Out of Anti-Infective Drug Discovery?
ICAC3/Sept. 14-17, 2003/Chicago, IL

43rd Annual ICAAC
AMERICAN SOCIETY for MICROBIOLOGY
Drugs for bad bugs: confronting the challenges of antibacterial discovery

- The sequencing of the first complete bacterial genome in 1995 heralded a new era of hope for antibacterial drug discoverers, who now had the tools to search entire genomes for new antibacterial targets.

- Several companies embraced a genomics-derived, target-based approach to screen for new classes of drugs with novel modes of action.
The chemical compound libraries available for screening are not optimal for antibacterial agents.

Must have physicochemical properties required to cross the outer membrane.

Must avoid being pumped out from the periplasm by efflux pumps.

Urgent need to explore new chemical space – natural & synthetic.
Innovative Incentives for Effective Antibacterials

Two conferences in Sweden 2009/10 focusing on the bottlenecks for research and development of new antibiotics

Governments
Academia
Pharmaceutical and biotech industry
Civil society
CALLS UPON THE COMMISSION TO

within 24 months, develop a comprehensive action-plan, with concrete proposals concerning incentives to develop new effective antibiotics, including ways to secure their rational use; and ensure that these proposals take account of the economic impact on the financial sustainability of healthcare systems.
Towards a new model for R&D of antibiotics

• Needs driven - based on analysis of drug pipeline vs global health burden and needs

• Solving the scientific challenges

• Collaboration and knowledge sharing

• Incentives that stimulates R&D of priority antibiotics

• De-linking return of investment from volume sales and price

• Equitable global access and affordability

• Controlled use and distribution
• Priority pathogens list
• Pipeline analysis
• Updated WHO Model List of Essential Medicines

Antibiotics are now grouped to 3 categories:

ACCESS Antibiotics that should be available at all times

WATCH Antibiotics recommended as first- or second-choice treatments for a small number of infections

RESERVE Antibiotics that are last-resort options
<table>
<thead>
<tr>
<th>Reserve group antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam</td>
</tr>
<tr>
<td>4th generation cephalosporins</td>
</tr>
<tr>
<td>e.g. cefepime</td>
</tr>
<tr>
<td>5th generation cephalosporins</td>
</tr>
<tr>
<td>e.g. ceftaroline</td>
</tr>
<tr>
<td>Polymyxins</td>
</tr>
<tr>
<td>e.g. polymyxin B, colistin</td>
</tr>
</tbody>
</table>
Push incentives support and subsidize the overall development cost.

Pull incentives reward successful clinical development, providing guaranteed return on investment (ROI).
Push incentives support and subsidize the overall development cost.

Pull incentives reward successful clinical development, providing guaranteed return on investment (ROI).
The primary aim of the 6th joint call of the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) is to combine the resources, infrastructures, and research strengths of multiple countries in order to address the identification and validation of new targets, the development of new therapies, and new tools for new treatments (including new antibiotics).
Network of major AMR development initiatives

<table>
<thead>
<tr>
<th></th>
<th>CARB-X</th>
<th>GARDP</th>
<th>repair impact fund</th>
<th>ND</th>
<th>BB ENABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Budget</strong></td>
<td>USD 455m (2016-21)</td>
<td>Euro 270m (2017-23)</td>
<td>USD 165m (2018-23)</td>
<td>Euro 85m (2014-20)</td>
<td></td>
</tr>
<tr>
<td><strong>Products</strong></td>
<td>Novel therapeutics, diagnostics, preventatives, devices</td>
<td>Novel therapeutics, Optimize antibiotics, Develop combinations</td>
<td>Novel therapeutics, companion diagnostics</td>
<td>Novel therapeutics</td>
<td></td>
</tr>
<tr>
<td><strong>Pathogens</strong></td>
<td>High priority defined by WHO and CDC, largely Gram-negatives</td>
<td>WHO priority pathogen list, especially Gram-negatives</td>
<td>High priority defined by WHO and CDC</td>
<td><em>E. coli, K. pneumoniae, P. aeruginosa and A. baumannii</em></td>
<td></td>
</tr>
<tr>
<td><strong>Stages of development</strong></td>
<td>Hit-to-lead through end of Phase 1</td>
<td>Any stage of development to patient access</td>
<td>Lead optimization through end of Phase 1</td>
<td>Hit-to-lead through end of Phase 1</td>
<td></td>
</tr>
<tr>
<td><strong>Geography</strong></td>
<td>Global</td>
<td>Global</td>
<td>Europe &amp; U.S.</td>
<td>Europe</td>
<td></td>
</tr>
<tr>
<td><strong>Funding instruments</strong></td>
<td>Non-dilutive funding and expert support</td>
<td>Sponsor role (preclinical studies &amp; clinical trials)</td>
<td>Convertible loans and royalty-based</td>
<td>Financial, in-kind and expertise support</td>
<td></td>
</tr>
<tr>
<td><strong>Funding allotments</strong></td>
<td>Flexible, with milestones; &gt;30% cost share</td>
<td>Direct funding and flexible partnerships</td>
<td>USD 1m to 15m</td>
<td>Flexible</td>
<td></td>
</tr>
<tr>
<td><strong>Conditions</strong></td>
<td>Stewardship and market access requirements</td>
<td>Stewardship and access. Consider in/out licencing</td>
<td>Stewardship and access requirements <em>(in progress)</em></td>
<td>Limited compensation when value generated</td>
<td></td>
</tr>
</tbody>
</table>
Towards a sustainable model of antibiotic research, development and commercialization

http://www.who.int/phi/implementation/2_infobrief_towards_sustainable_model_antibiotic_research_development_commercialization.pdf

“Pharmaceutical and biotech executives have a fiduciary responsibility to their investors”.

“Big pharma’s decision to focus R&D resources in areas of equally high medical need but greater profitability is a translation of that responsibility”.

“To draw private funding away from those more profitable areas and back into antimicrobials, we must develop a model which returns a profit that is competitive with those achieved in other diseases”.

http://www.who.int/phi/implementation/2_infobrief_towards_sustainable_model_antibiotic_research_development_commercialization.pdf
We recommend a partially delinked market entry reward (or a reward that is given in addition to unit sales).

Some members of DRIVE-AB argue that this model leaves in place a strong incentive for the manufacturer to oversell the antibiotic. This is a risk that must be closely monitored.

We recommend that the market entry reward is paid out in equal payments of $200 million per antibiotic over five years after regulatory approval.

Some stakeholders argue for a higher market entry reward amount, and others that a billion dollars is excessive. We have set the parameters to ensure a reasonable return on investment for the developer, but one that is far lower than the profits achieved by the top-selling drugs in recent years.
Entasis Therapeutics and the Global Antibiotic Research & Development Partnership (GARDP) to develop a new treatment for drug-resistant gonorrhea
Antibiotic shortage puts patients at risk, doctors fear

Availability of 36 selected antibiotics in 39 countries (Europe, US, Canada and Australia)

Data collected through an internet-based questionnaire from 28 LMICs on the availability of 24 "forgotten" antibiotics.
Unavailability of old antibiotics threatens effective treatment for common bacterial infections

In addition to the insufficient pipeline of new antibiotics, the unsustainable production and supply of old antibiotics is becoming a serious global problem that limits the treatment options for common bacterial infections. Most infections are still caused by pathogens susceptible to generic antibiotics, which are often pneumonia, was reported unavailable in 2015 in the Netherlands. Ceftibuten, the only recommended oral treatment for febrile urinary tract infections in children in Sweden, was withdrawn from the market in 2016. In 2017, the worldwide shortage of piperacillin-tazobactam, a cornerstone antibiotic and β-lactamase

Thomas Tängdén, Céline Pulcini, Helle Aagard, Manica Balasegaram, Gabriel Levy Hara, Dilip Nathwani, Mike Sharland, Ursula Theuretzbacher, *Otto Cars

www.thelancet.com/infection Vol 18 March 2018
Fundamental systems changes needed

- **Antibiotics**
- Volume sales
- Marketing
- Cultural beliefs, misperceptions
- Misaligned financial incentives
- Irrational use of antibiotics
- Insufficient prevention
Progress in developing multisectoral AMR National Action Plans Feb 2018
Goals  By 2020;
• To launch 1–2 new antibacterial agents and 5–10 new diagnostic techniques.

• To implement the sale of antibiotics only with a prescription in pharmacies across the entire country and in animal husbandry in half of the provinces.

• To optimize surveillance, to establish an evaluation system for antibacterial agent consumption and resistance in both the healthcare and animal husbandry sectors and to set up AMR reference laboratories and bacterial strain banks.

• To implement an antimicrobial stewardship programme in all hospitals.

• To discontinue the use of antibiotics as animal growth promoters.

• To educate medical staff, veterinarians, animal producers, students, and members of the public about AMR, and to set up an annual antibiotic alert week.
Reduce AMR & Increase Access to Effective Antimicrobials in Health Systems

**Data Generation**
- Labs and Lab Capacity for Resistance Surveillance
- Monitoring of Antibiotic Use

**Prevention**
- WASH and Infection Control in all Healthcare Facilities
- Implementation of Vaccination Programs

**Awareness & Behavioral Change**
- Awareness Campaigns
- School Education
- Curricula for Health Care Workers
- Continuous Medical Education

**Access and Conservation**
- Essential Medicines List
- Monitoring Access
- Treatment Guidelines
- Regulation
- Stewardship
- Distribution
CAESAR Network

Network of national surveillance systems for antibiotic resistance in all countries of the WHO European Region that are not part of the European Antimicrobial Resistance Surveillance network (EARS-Net) of the European Centre for Disease Prevention and Control (ECDC).

Provide comparable and validated data on the prevalence and trends of antimicrobial resistance in a core group of invasive bacteria.

CAESAR methodology is fully compatible with EARS-Net of ECDC. Adherence to EUCAST methods is emphasised.

Joint initiative of WHO Europe, ESCMID (ESGARS and EUCAST) and the National Institute for Public Health and the Environment, WHO Collaboration Center on AMR Epidemiology and Surveillance, The Netherlands.
60% of antibiotics prescribed by general practitioners in OECD countries are used for inappropriately
Cecchini M, Lee S. OECD Publishing, forthcoming

Of the estimated 154 million prescriptions for antibiotics written in doctor’s offices and emergency departments in the US each year, 30 percent are unnecessary.
US CDC, 2016

High income countries continue to waste antibiotics
The factors that contribute negatively to the situation seem to be:

- Little sense of urgency about the current AMR situation from most stakeholders and a tendency by many stakeholders to avoid taking charge of the problem
- Lack of institutional support at national, regional and local level
- Lack of professional leadership at each level
- Lack of accountability at each level
- Lack of coordination of the activities between and within levels
“A fundamental issue which will need to be addressed is the current business model for the veterinary profession, whereby veterinary drug wholesalers directly employ a substantial proportion of the veterinarians providing services to the food-producing animal sector, leading to an over-reliance on veterinary drug sales as an income generator for the profession”.
Assessment of 30 pharmaceutical companies

Out of 28 antibiotics in late stages of clinical development, only two have both access and stewardship plans in place.

Eight companies are setting limits on antibiotic wastewater discharge.
No company publishes its environmental audit results, or its discharge levels.

Four companies are taking steps to separate sales agents bonuses from the volume of antibiotics they sell.
“Nobody likes to lose business. We give whatever they ask. Competition, location of shops, license issues...everything has become commercialized.”
- Urban pharmacist

“Even reputed companies offer complimentary. If you prescribe more, they offer air conditioned car or free tickets.... Of late, we are forced to try new antibiotics.”
- Urban doctor
Global increase and geographic convergence in antibiotic consumption between 2000 and 2015

Eili Y. Klein, Thomas P. Van Boeckel, Elena M. Martinez, Suraj Pant, Sumanth Gandra, Simon A. Levin, Herman Goossens, and Ramanan Laxminarayan

A

DDD per 1,000 inhabitants per day

High-income

Upper-middle-income

Low- & lower-middle-income


www.pnas.org/cgi/doi/10.1073/pnas.1717295115
“Antimicrobial teams (including clinical microbiologists, infectious disease specialists, and other appropriate specialists) should be introduced in every hospital. They should have the authority to modify antimicrobial prescriptions of individual clinicians in accordance with locally accepted guidelines, always taking account of the needs of the patient.
Antimicrobial stewardship

We found high-certainty evidence that interventions are effective in increasing compliance with antibiotic policy and reducing duration of antibiotic treatment.

Additional trials comparing antibiotic stewardship with no intervention are unlikely to change our conclusions.

Future research should instead assess different stewardship interventions, and explore the barriers and facilitators to implementation.

Editorial Note

CMI policy on antimicrobial stewardship research
C Pulcini A Huttner
B

DDD's per 1,000 inhabitants per day 2015

High
Upper-middle
Low- & lower-middle
SWEDEN: National prescribing target: 250/1000 inhabitants/year
Antibiotic prescriptions in Swedish outpatients

Different age groups: Prescriptions/1000 inhabitants/year
Transforming our world: the 2030 Agenda for Sustainable Development
The median overall cost to treat a resistant bacterial infection in India: **700 USD**

The time a rural male casual worker in India has to work to earn this amount: **442 days**

Chandy, S: The Journal of Infection in Developing countries. Vol 8, sept 2014
Antibiotics

The cornerstones of basic and modern medicine

Cancer Treatment

Hip Replacement

Organ Transplants

Gonorrhoea

Preterm babies

Complicated deliveries

Wound infections

Urinary tract infections

Pneumonia

Blood infections

Modern medicine

Maternal and child health

Basic health care

Antibiotics
Non-human use of antibiotics
The tension between food safety and food security

- Increasing demand for animal protein
- Projected increase of the consumption of antimicrobials in the food animal sector by 2/3 until 2030

Need for regional and context specific transformation strategies towards sustainable practices and alternatives to antibiotics

Clean water and sanitation

2.4 billion people in the world lack access to toilets and 1.8 billion are using drinking water that is contaminated with feces.

35% of healthcare facilities in LMICs has no access to soap and water.

The costs for antibiotic resistance reach far beyond the health sector

UNGA Adopts Political Declaration on Antimicrobial Resistance, Discusses Links with SDGs

Resolution adopted by the General Assembly on 5 October 2016

[Various reference to a Panel Committee (APLIE.6)]

71/8. Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance

The General Assembly,
Recalling its resolutions 70/183 of 17 December 2015 and 70/297 of 21 July 2016, in which it decided to hold a high-level meeting on antimicrobial resistance on 21 September 2016,
Adopt the following political declaration approved by the high-level meeting of the General Assembly on antimicrobial resistance on 21 September 2016:

Political declaration of the high-level meeting of the General Assembly on antimicrobial resistance

We, Heads of State and Government and representatives of States and Governments, meeting at United Nations Headquarters in New York on 21 September 2016, in accordance with General Assembly resolution 70/183 of 17 December 2015, in which the Assembly decided to hold a high-level meeting in 2016 on antimicrobial resistance,

1. Reaffirm that the blueprint for tackling antimicrobial resistance is the World Health Organization global action plan on antimicrobial resistance and its five overarching strategic objectives developed by the World Health Organization in collaboration with, and subsequently adopted by, the Food and Agriculture Organization of the United Nations and the World Organization for Animal Health;

2. Also reaffirm that the 2030 Agenda for Sustainable Development offers a framework to ensure healthy lives, and recall commitments to fight malaria, HIV/AIDS, tuberculosis, hepatitis, the Ebola virus disease and other communicable diseases and epidemics, including by addressing growing antimicrobial resistance and neglected diseases affecting developing countries in particular, while reiterating that antimicrobial resistance challenges the sustainability and effectiveness of the...
Political declaration on the UN General Assembly High level meeting 21 sept

- Discussed with all UN Member states (national capitals, missions in Geneva and NYC)
- Deals with antimicrobial resistance (AMR) but focus on antibiotics
- Acknowledge the massive social, economic and global health repercussions of AMR
- Commit to work to mobilize predictable and sustained funding
- Strengthening of surveillance, monitoring and regulatory frameworks
- Emphasizes access and affordability
- Acknowledges the importance of de-linking the cost of investments in R&D from the price and volume sales
Political declaration on the UN General Assembly High level meeting  21 sept

**Lacks:**

- Proposals for transparent monitoring of antimicrobial access, use, sales, prescriptions, trade, and resistance patterns
- **Targets** for significantly improved practices of antimicrobial use in human health care and agriculture innovation
- Proposal for **governance** and accountability at the UN level
- Specifics on global **financing** structure.
“......to provide practical guidance for approaches needed to ensure sustained effective global action to address antimicrobial resistance.......”
World Health Organization (WHO) Director General (co-chair)
UN Deputy Secretary General (co-chair)
World Intellectual Property
Food and Agriculture Organization (FAO)
Global Fund to fight AIDS, Tuberculosis and Malaria
Organization for Economic Cooperation and Development (OECD)
World Organisation for Animal Health (OIE)
Joint United Nations Programme on HIV/AIDS (UNAIDS)
United Nations Environment Programme (UNEP)
United Nations Children’s Fund (UNICEF)
World Bank.
World Customs Organization (WCO)
World Intellectual Property Organization (WIPO)
World Trade Organization (WTO)
UNITAID
More and more players engaged

Strategic coordination?
Increasing number of actors

- World Economic Forum
- Fleming Fund
- Antibiotic Resistance Coalition
- Tripartite: WHO FAO OIE
- Wellcome Trust
- UNDP
- OECD
- G20
- Boston Consulting Group
- McKinsey
- WTO
- Consumer Groups in EU and US
- WIPO
- UNICEF
- UNITAID
- ReAct
- GARDP
- Ad-hoc UN Inter-Agency coordination Group
- CDDEP
- Access to Medicines Foundation
- JPIAMR
- UNCTAD
- CARBX
- GLASS
- Medicines Patent Pool
- AMR Industry Alliance
- Investor groups e.g. FAIRR initiative
- World Bank
- UNICEF
- UNITAID
- GARDP
- JPIAMR
- UNCTAD
- CARBX
- GLASS
- Medicines Patent Pool
- AMR Industry Alliance
- Investor groups e.g. FAIRR initiative
- World Bank
- ReAct
Fundamental issues still remain

Transparent surveillance and monitoring

Substantial financing and technical assistance to Low- and middle income countries (LMICs)

Global funding for R&D

No internationally agreed mechanism to ensure access and affordability in LMICs

Capacities to enforce existing regulations are insufficient

No agreements on structural or quantitative targets to optimize use
Are we prepared to accept a 75% compliance with this procedure?
The 5C Framework—
assessment of minimum collaboration needed for a successful policy

Given these global coordination issues, there is a clear role for a binding international legal framework to encompass the issues of access, conservation and innovation.
Towards stronger global governance for AMR

- Intergovernmental agreement
  - Setting global standards and norms
  - Monitoring and accountability
  - Data transparency/audits

- UN coordination

- Funding
  - Research and innovation
  - Infrastructure
  - Capacity building
  - Implementation

- Independent scientific technical advisory panel

- Voluntary

- Legally binding

- Civil society

- Private sector
Montreal Protocol on Substances that Deplete the Ozon layer

Applies the precautionary principle

Quantitative and time-bound targets

Longer time allowed for developing countries to phase out

Transition funds available for developing countries

Development of alternative technologies
ReAct- Action on Antibiotic Resistance

ReAct North America
Baltimore, USA

ReAct Europe
Uppsala, SWE

ReAct LA
Cuenca, ECU

ReAct Africa
Nairobi, KEN

ReAct Asia Pacific
Vellore, IND

www.reactgroup.org
A new initiative led by the Ecuadorian seafood industry is aiming to improve the country’s reputation as a source of safe and sustainable shrimp.

Norwegian Cancer Society

GLOBAL CAMPAIGN: Antimicrobial resistance - the biggest threat to cancer treatment.
A super-wicked problem!

- Time for finding a solution to a policy challenge is running out
- Those seeking to solve the problem are part of the cause
- Central authorities to address the problem are either weak or non-existent
- Policy responses discount the future irrationally.

Super-wicked problems require a shift of policy trajectories, rather than incremental changes to existing policies.
Jasper Littman  Ursula Theuretzbacher
Steven Hoffman Thomas Tängdén
Laura Piddock Dominique Monnet
Christina Greko Anders Karlén
Diarmuid Huges Alexandra Waluszewski
Peter Sogaard  Laura Piddock
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The shadow of antibiotic resistance

A world free from fear of untreatable infections