Preventive measures for AMR COVID-19 lessons and the role of research

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2018-2023

- Horizon 2020
- Innovative Medicine Initiative
- Joint Programming Initiatives on Antimicrobial Resistance
- AIFA
- WHO
- ESCMID
- German Center for Infectious Diseases Research
- GARDP
Lesson learned before COVID-19 pandemic

Lessons learned after COVID-19 pandemic

Research role and inputs

Urgent actions

Preparedness plans

Not covering:
- LMIC
- One Health aspect
In the field of prevention of antibiotic resistant infections a global mea culpa is absolutely necessary.

Let him who is without sin cast the first stone
Gospel according to John 8:7
1. AMR is widespread in the WHO European Region although burden **IS EXTREMELY HETEROGENOUS**

The difference in resistance rates must be considered a **threat** for EU public health and the **rights** of citizens for equal healthcare standard.

*Cephalosporins-resistant K. pneumoniae, National voluntary surveillance, %R 2017-2021*  
[www.epi.net-eu](http://www.epi.net-eu)
2. Substantial underestimation of infection control role

Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis

Panel: WHO priority list for research and development of new antibiotics for antibiotic-resistant bacteria

**Multidrug-resistant and extensively-resistant Mycobacterium tuberculosis**

**Other priority bacteria**

Priority 1: critical
- *Acinetobacter baumannii*, carbapenem resistant
- *Pseudomonas aeruginosa*, carbapenem resistant
- *Enterobacteriaceae*, carbapenem resistant, third-generation cephalosporin resistant

Priority 2: high
- *Enterococcus faecium*, vancomycin resistant
- *Staphylococcus aureus*, methicillin resistant, vancomycin resistant
- *Helicobacter pylori*, clarithromycin resistant
- *Campylobacter spp.*, fluoroquinolone resistant
- *Salmonella spp.* fluoroquinolone resistant
- *Neisseria gonorrhoeae*, third-generation cephalosporin resistant, fluoroquinolone resistant

Priority 3: medium
- *Streptococcus pneumoniae*, penicillin non-susceptible
- *Haemophilus influenzae*, ampicillin resistant
- *Shigella spp.*, fluoroquinolone resistant
3. Lack of knowledge on the effect of linking infection prevention to antibiotic prescription

The highest effect of AMS in reducing resistance rates was observed when programmes were when implemented with infection control measures in particular with hand-hygiene interventions (reduction of 66%) compared to when implemented alone.
Why linking IPC and AMS plans is essential?

- Effective implementation of IPC reduces hospital transmission and therefore infections.
- Local AMR surveillance systems inform policies on empiric therapy and support appropriate antibiotic usage and surgical prophylaxis.
- Effective IPC interventions limit the usage of urinary catheters and reduce risk of catheter-related infections.
AMS and IC in high endemic setting of MDR-GN: the SAVE programme

- Educational AS and IPC intervention with a stepped-wedge implementation since June 2018
- 9-month maintenance phase /random audits
- 2 REFERENCE PHYSICIANS PER WARD ARE CERTIFIED FOR ANTIBIOTIC PRESCRIPTION AND IPC

A significant change in level of overall antibiotic consumption and resistance rates was measured both in terms of DOTs/1000 PDs and DDDs/1000 PDs

The effect was consistent during COVID-19 pandemic

Carrara & Tacconelli, Int J Antim Agents 2022
Lesson (not) learned before COVID-19 pandemic

- IPC interventions must be linked with AMS policy plans
- Insufficient awareness of importance of IPC in hospitals, and long term-facilities and nursing homes
- Insufficient political commitments
- Severe underinvestment of research
- Limited evidence in vulnerable population
- Insufficient educational activities and programme of audit and feedback in healthcare settings
- Underpowered IPC personnel
- Insufficient consideration of conflict of interests of prescribers
- Limited attention to IPC in scientific publications
COVID-19 has brought into sharp focus the failure of not preventing and preparing for pandemic
Beyond COVID-19
A paradigm shift in infection management?

▪ The population at risk of severe COVID-19 largely overlaps with the population at risk of resistant infections. Will societies continue to accept substantial numbers of avoidable deaths caused by AMR while risking an unprecedented economical and societal crisis to protect the same risk group from COVID-19?

▪ The necessary efforts to fight AMR is marginal compared with the current activities against COVID-19.

Vehreschild, Tacconelli, Giske, Peschel Lancet Infect Dis 2020
Impact of COVID-19 on antibiotic usage in HIC

157 patients with bacterial infections
88% healthcare acquisition
Antibiotic resistance rates
+++ Gram-negatives

Ghosh, J Infection Pub Health 2021

Floridia, ARIC 2022
COVID-19 showed the bleak landscape of non-existent or difficult-to-change guidelines for IPC and antibiotic policy in several countries.

We need mechanisms for rapid development of evidence based guidelines tailored on local epidemiology and availability of diagnostics and antibiotics, which can differ widely from one country to another.
Guidance document on empiric therapy for MDR-GNB infections calibrated on local epidemiology, availability of diagnostics and drugs following antimicrobial stewardship principles.

GRADE-Adolopment methodology was used to adopt, adapt, and update existing guidelines to country-specific settings and stewardship principles.

COVID-19 showed (also) the need to link research resources to a fast and effective deliver of new cutting edge evidence.
The importance of cohorts in producing new clinical evidence

26 Partners from 10 European and 5 not European countries
7 linked and international Parties

~ 1,300,000 Individual patients’ data
44 prospective cohorts
21 retrospective cohorts

8 cohorts (EU/non-EU) >900,000 individuals
7 cohorts (EU/non-EU) ~65,000 individuals

5 cohorts (EU) >250,000 individuals

WP11 Ethics requirement
WP1 Coordination
WP2 COVID-19 cohorts and long term sequela
WP3 Population-based cohorts
WP4 Fragile population cohorts
WP5 Healthcare workers cohorts
WP6 Biobanking genomics, viral-host interaction.
WP7 Data management
WP8 Statistical/cost analysis and modelling
Analysis
WP9 Global COVID-19 guidance
WP10 Dissemination
COVID-19 research brings to light severe limitations in data sharing

Inconsistency in application of GDPR across Member States
Stringent local legal and ethical requirements impeding rapid collection of data and analysis
Lack of common standards on data use, and data interoperability
Lack of agreement on the use of metadata standards
Lack of standardised reporting on harmonisation procedures
Multiple community-developed standards for interoperability

Poor digital literacy and data science skills of staff of data owners (hospitals etc.)
Standard funding frameworks do not always adapt well to projects formulated to address a pandemic
Barriers of sharing individual patient data for EHR and for some retrospective cohort data

- GDPR application
- Common standard
- Interoperability
- Digital literacy

ORCHESTRA, ReCoDID, UNCOVER, ECRAID, SYNCHROS, EU-Response

Tacconelli, Lancet Reg Health – Europe 2022
Rinaldi, Nature Digital Medicine 2022
Lesson learnt from cohorts studies

- Cohorts represent **the most feasible design** to explore risk factors, genome associations, public health interventions, burden, and long term sequelae of infectious diseases with pandemic potential
- Provide **early information** to design randomised clinical trial (RCT)
- Essential role in **data harmonisation** and dictionary
- Opportunity to select **vulnerable populations**
- The model could be a core component of preparedness plan and be applied to other infectious diseases emerging (MPX,...) or at highest burden in Europe as AMR
Lessons learnt for COVID:
New coordination mechanisms
Urgent actions
National plan to contrast AMR
Urgent to be done: at country level (providing sufficient resources)

1. **Active real-time monitoring** of HAI and AMR
2. **Active real-time surveillance** of antibiotic consumption in the hospital and community
3. **Mandatory audit and feedbacks** for IPC and AMS to be connected with accreditation of a facility
4. **Compulsory educational programs** in IPC and AMS in medical schools and in specialties
5. **Calibrated evidence based national recommendations** in the field of IPC and antibiotic therapy (including new antibiotics)
National pandemic preparedness plan
Wake-up call: addressing IPC and AMS through pandemic preparedness (1)

- IPC and AMS as unique core capabilities
- Need to establish automated surveillance for HAI, resistance and antibiotic consumption
- Demand for re-assessment of data sharing and systems interoperability procedures and of management of privacy vs public health needs (e.g. federated learning)
Wake-up call: addressing IPC and AMS through pandemic preparedness (2)

- Multidisciplinary scientific and political leadership clearly defining IPC and AMS targets to be mandatorily implemented at country level and requiring allocation of adequate resources
- Powerful and contextualized awareness campaigns
- Mechanism to rapid update of guidance documents
- Knowledge of ATB and IPC team role in pandemic scenario
- Maintaining mechanisms of perpetual infectious diseases cohorts
Wake-up call for research

INSUFFICIENT RESEARCH IN:

- Effective IPC in vulnerable population: elderly and Nursing homes / pregnant women / children
- Mechanisms for rapid IPC /AMS guidelines development calibrated at local level
- Implementation science for IPC and antibiotic policy
- Need to establish perpetual cohorts in AMR and IPC to be included in a coordination mechanism of trial as in ECRAID where the networks enable the conduct of perpetual strategic cohorts with the in-built agility to pivot to emerging diseases when an epidemic strikes.