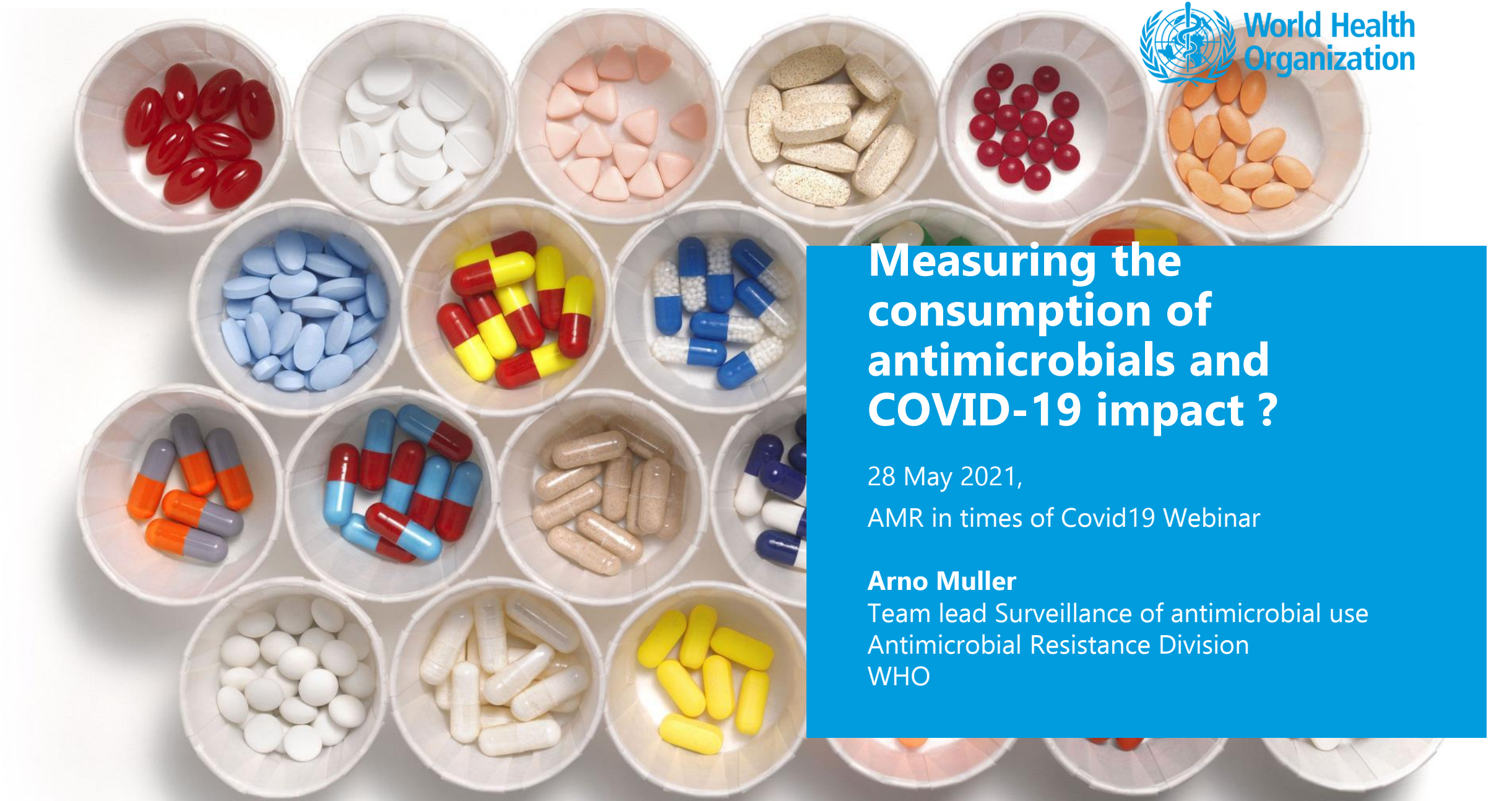


World Health Organization

# Measuring the consumption of antimicrobials and COVID-19 impact ?

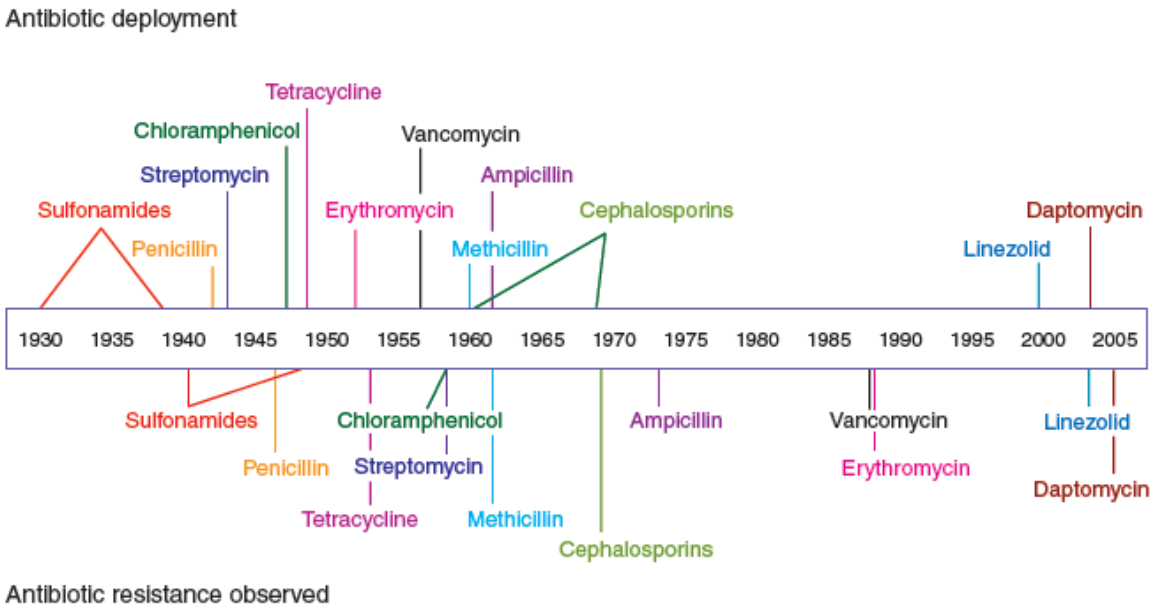
28 May 2021,

AMR in times of Covid19 Webinar

**Arno Muller**
Team lead Surveillance of antimicrobial use
Antimicrobial Resistance Division
WHO

# Introduction

# Antimicrobial Resistance: a Public Health issue

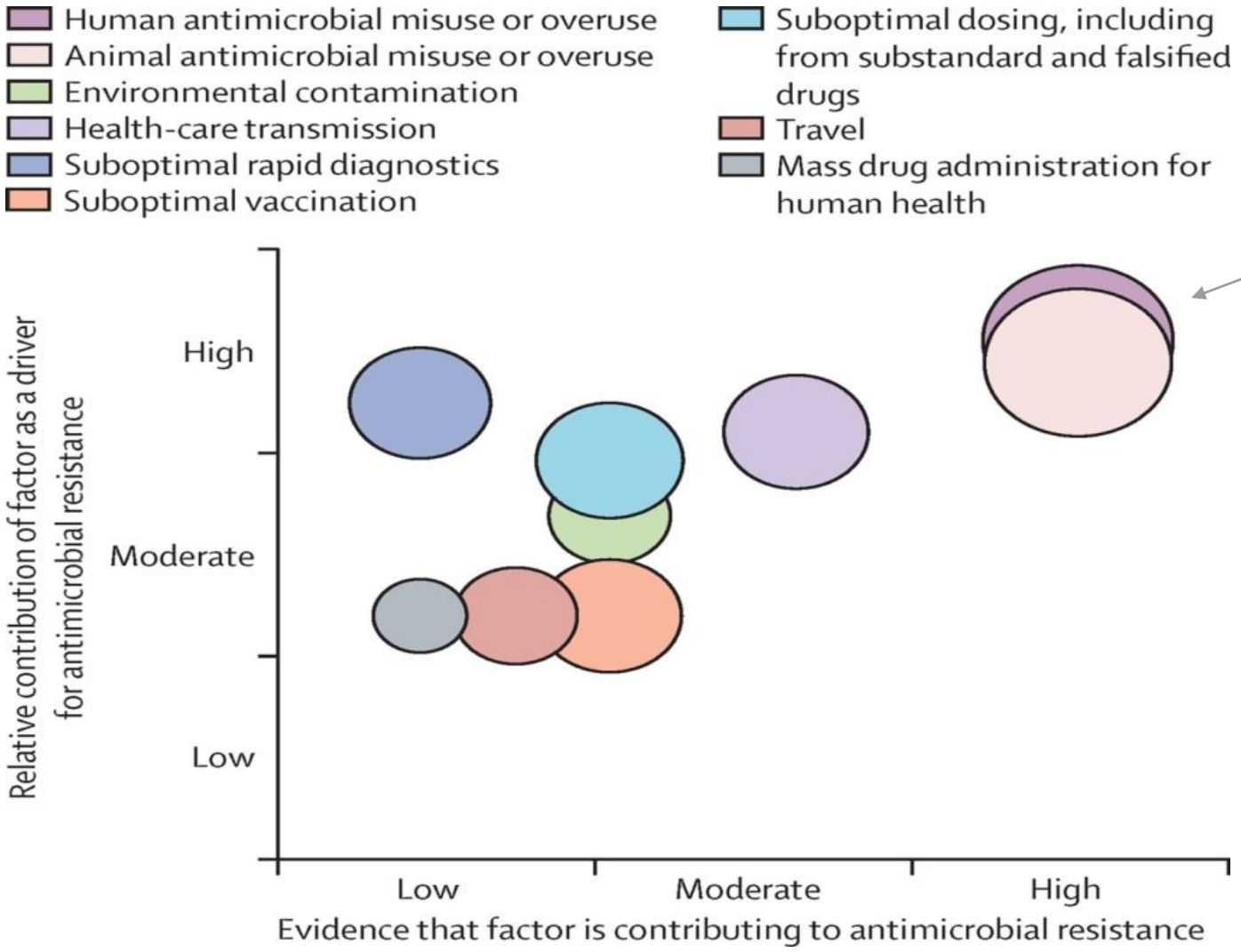



Clatworthyet al. Nature Chemical Biology 2007;3:541-48

- Micro perspective
  - Patient Increased morbidity
    - non-functioning protheses
    - amputations
  - Increased mortality
    - Neonatal infections ICU 9x in LMIC
  - Payer and healthcare provider
    - Longer hospitals stay
    - Longer & expensive treatment (medicines and utilities)
- Macro perspective
  - Health services
    - Procedures are performed less frequently (surgery, cancer…)
  - Socio-economic impact
    - Lost productivity and GDP
    - Health expenditures increased (out of pocket)

Laxminarayan. Lancet ID, 2013.
Blomberg. BMC infect dis, 2007;
O`Neill report, Review on antimicrobial resistance.

# Factors contributing to Antimicrobial Resistance (AMR)




**Biggest drivers:**

- **Misuse or overuse in humans**
- **Misuse or overuse in animals**

*Holmes at al., 2016*

# Global Action Plan on AMR
## - Data for action -

Food and Agriculture Organization of the United Nations

WORLD ORGANISATION FOR ANIMAL HEALTH

World Health Organization

- **Objective 2:** Strengthen the knowledge and evidence base through surveillance research (AMR and AMU)

- **Objective 4:** Optimize the use of antimicrobial medicines

- **Aim:** Ensure continuity of successful treatment & prevention of infectious diseases with effective, safe, quality-assured medicines that are used in a responsible way & accessible to all who need them

- Call for all countries to collect & report data on antimicrobial use

# Measuring the use of antimicrobials

# Data on Antimicrobial Use – What can it tell us?

- Understand volume and pattern of antimicrobial consumption
- Assess prescribing practices and appropriateness of use
- Compare across local, national and international level
- Detect trends over time
- Benchmarking

# WHO strategy for surveillance of use of antimicrobials

Two-pronged approach for measuring the use of antimicrobials in countries

***Antimicrobial consumption***

Routine surveillance

Target: Manufacturers/Importers/Distributors/Health Facilities

**To estimate which antimicrobials are used and how much**

Census data

Metrics: Defined Daily Dose

National ⇨ Facility

***Antimicrobial use***

Surveys

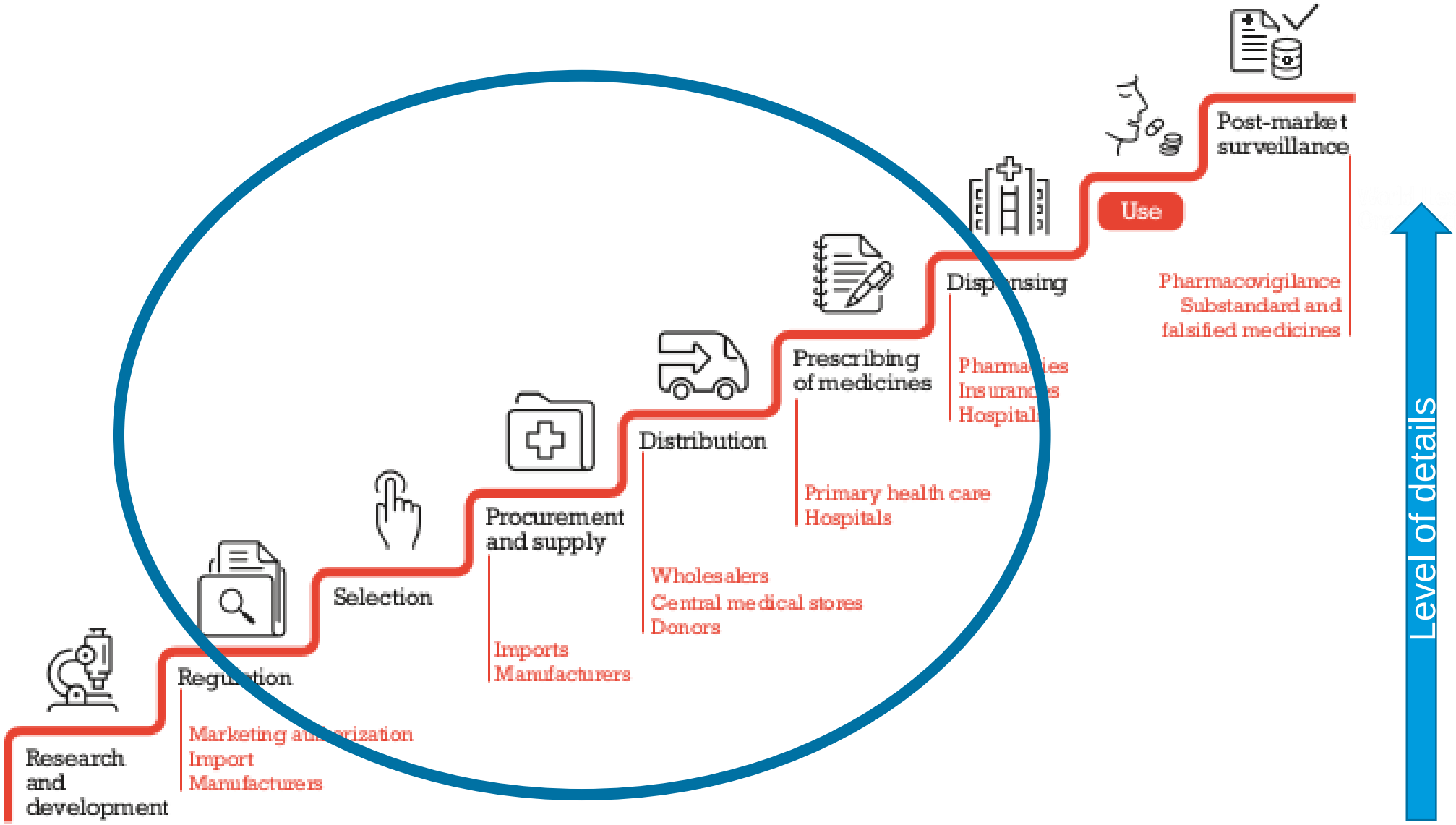
Target: patients, prescribers, dispensers

**To understand how antimicrobials are used**

Sample data

Metrics: Proportion of patients

# Value chain of medicines and antimicrobial consumption



# Monitoring antimicrobial consumption

World Health Organization

## National surveillance

- Provide estimates on types and quantities used at country level
- Targets: national policies, regulations, rational use, supply

## Facility surveillance

- Provide estimates on types and quantities used at facility level
- Targets: national/facility policies, supply, stewardship

## Data providers

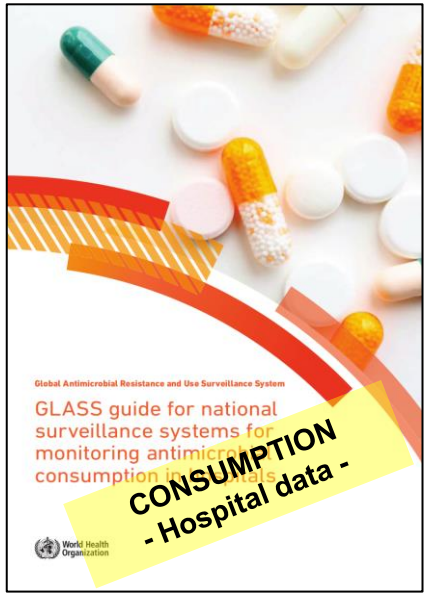

## Data providers

# Methodology for surveillance of antimicrobial consumption

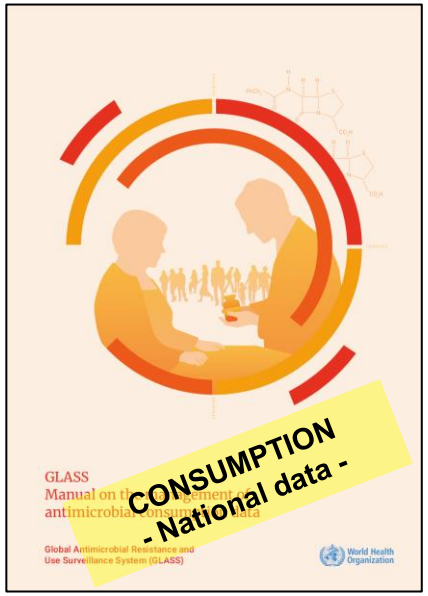
- All antimicrobial classes (antibacterials, antifungals, antivirals, malaria, tuberculosis)
- Using the ATC/DDD system (www.whocc.no)
- At country level
  - Annual data for public and private sectors, for community and hospital healthcare levels
  - Data sources: import, manufacturing, wholesales, distributors, health facilities, health insurance
- At facility level
  - Minimum annual data (quarterly, monthly) for the whole facility, by departments, wards
  - Data sources: hospital pharmacy: procurement, dispensing, e-prescribing systems
- Consumption data
  - List of all authorized antimicrobial medicines including detailed information (ATC code, route, strength, package size) ⇨ content of substance per product
  - Number of packages « consumed » for all authorized antimicrobial medicines
  - Metrics: Defined Daily Dose

# WHO methodologies to measure antimicrobial consumption and use

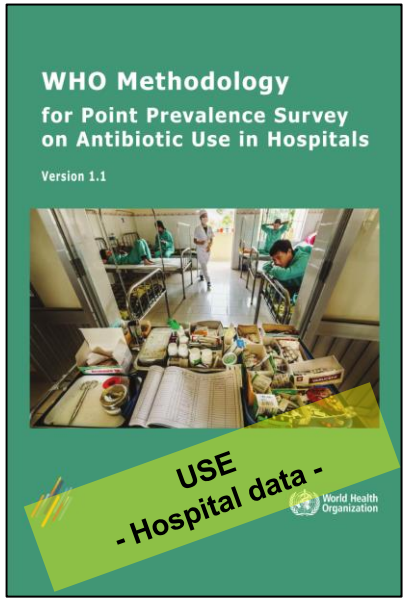

https://apps.who.int/iris/bitstream/handle/10665/336215/9789240012639-eng.pdf



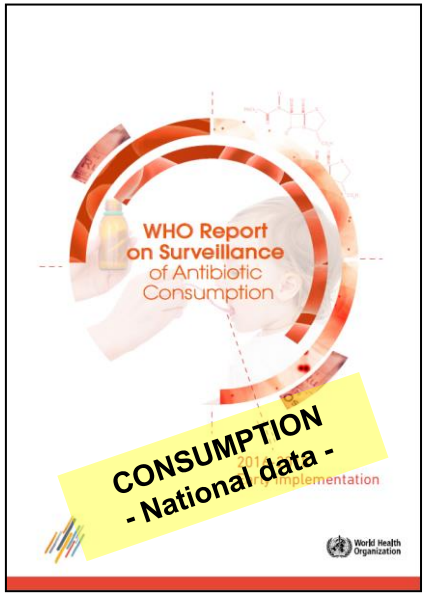

https://apps.who.int/iris/bitstream/handle/10665/336182/9789240000421-eng.pdf




https://apps.who.int/iris/bitstream/handle/10665/336182/9789240000421-eng.pdf




https://www.who.int/medicines/access/antimicrobial_resistance/WHO-EMP-IAU-2018_01/en/

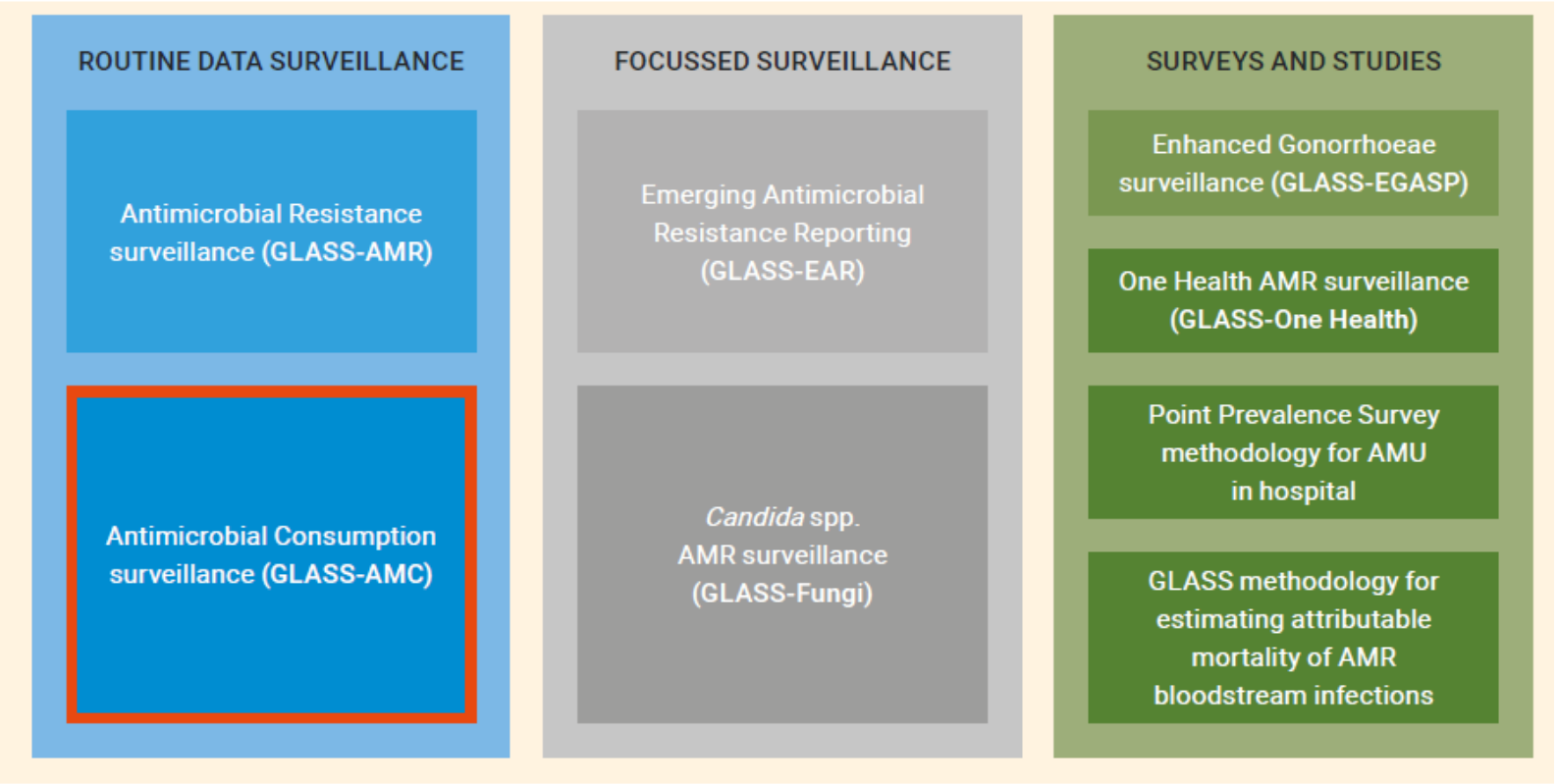



https://www.who.int/medicines/areas/rational_use/oms-amr-amc-report-2016-2018/en/

WHO Methodologies

WHO Report

# WHO GLASS




- First data call on antimicrobial consumption in June 2021
- Roll out of the surveillance of antimicrobial consumption in hospitals
- Point prevalence surveys on antibiotic use in hospitals carried out in Africa, South America and Middle East

# Impact of COVID-19 on antibiotic consumption

# In hospitals

# Increase in antibiotic consumption

| Year | Narrow ß-lactams | Broad Community[a] | Broad Hospital[a] | Anti-MDRO[a] | Anti-MRSA[a] | All Other | Total |
|---|---|---|---|---|---|---|---|
| | | | DOT per 1,000 days present, all eligible facilities | | | | |
| 2015 | 82 | 141 | 155 | 2.0 | 122 | 137 | 638 |
| 2016 | 84 | 136 | 152 | 1.5 | 117 | 136 | 627 |
| 2017 | 87 | 130 | 150 | 1.7 | 113 | 135 | 617 |
| 2018 | 92 | 127 | 146 | 1.8 | 107 | 136 | 609 |
| 2019 | 93 | 120 | 145 | 1.7 | 101 | 141 | 602 |
| **Change/year** | **2.9** | **−5.2** | **−2.4** | **−0.1** | **−5.1** | **0.9** | **−9.1** |
| 2020 | 89 | 129 | 152 | 1.7 | 103 | 153 | 628 |
| **2020 vs 2019** | **−4.5** | **9.1** | **7.5** | **0.1** | **1.6** | **12.2** | **25.9** |

Data from 84 US VA hospitals (Jan-May)
*Dieringer et al, ICHE 2020*

**Table 1**
Main characteristic of patients hospitalized for COVID-19 for ≥48 hours

| Characteristic | No infection ($n = 917$) | Community-acquired co-infection ($n = 31$) | | Hospital-acquired superinfection ($n = 43$) | |
|---|---|---|---|---|---|
| | | Value | p[a] | Value | p[b] |
| Treatment at onset | | | | | |
| Lopinavir/ritonavir | 732 (79.8) | 27 (87.1) | 0.227 | 35 (81.4) | 0.802 |
| Hydroxychloroquine | 799 (87.1) | 29 (93.5) | 0.225 | 40 (93) | 0.186 |
| Azithromycin | 751 (81.9) | 26 (83.9) | 0.779 | 36 (83.7) | 0.761 |
| Remdesivir | 39 (4.3) | 0 (0) | 0.226 | 2 (4.7) | 0.559 |
| Ceftriaxone | 528 (57.6) | 24 (77.4) | 0.028 | 32 (74.4) | 0.029 |
| Ceftaroline | 26 (2.8) | 2 (6.5) | 0.232 | 5 (11.6) | 0.001 |

Data from 889 patients from Barcelona hospitals (Feb-Apr 2020)
*Garcia-Vidal et al, Clin Microbiol Infect 2020*

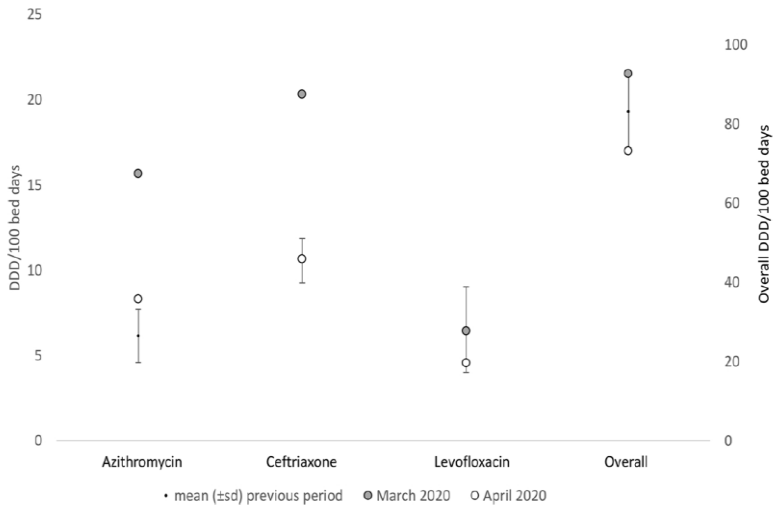
- High prevalence of antibiotic use among COVID-19 patients
- High density of use in the hospitals

# However,

| Year | Antibiotic DOT | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Days Present | Narrow ß-lactams | Broad Community | Broad Hospital | Anti-MDRO | Anti-MRSA | All Other | Total |
| 2015 | 1,291 | 106 | 182 | 200 | 2.6 | 157 | 177 | 824 |
| 2016 | 1,265 | 106 | 173 | 192 | 1.9 | 148 | 172 | 793 |
| 2017 | 1,242 | 109 | 161 | 187 | 2.1 | 140 | 167 | 766 |
| 2018 | 1,230 | 113 | 156 | 179 | 2.2 | 131 | 168 | 749 |
| 2019 | 1,199 | 112 | 144 | 174 | 2.0 | 121 | 169 | 722 |
| **Change per year** | **−23** | **1.5** | **−9.5** | **−6.5** | **−0.1** | **−9.0** | **−2.0** | **−26** |
| 2020 | 1024 | 91 | 132 | 156 | 1.8 | 105 | 171 | 643 |
| **2020 vs 2019** | **−174** | **−21** | **−12** | **−18** | **−0.2** | **−16** | **−12** | **−78** |

Note. MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus areus*.
[a]Days are in thousands.

Data from 84 US VA hospitals (Jan-May)
*Dieringer et al, ICHE 2020*




Data from an Italian hospital
*Giacomelli et al, Pharmacol Res 2021*

- Biphasic behaviour in some hospitals (decrease after initial increase) ⇨ change in patient management
- Overall decrease of level of consumption in hospitals compared to previous year

# In the primary care

# Decrease of consumption

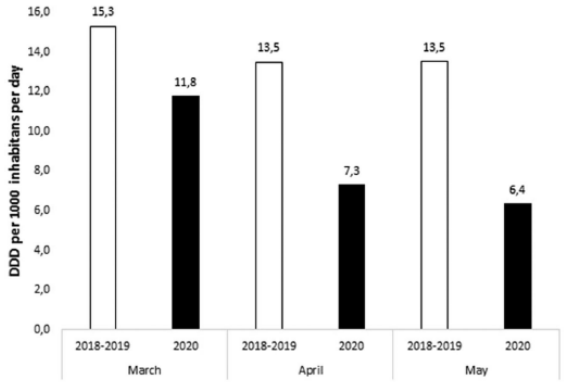



**Figure 1.** Community consumption of systemic antibiotics (J01) in Emilia-Romagna Region: comparison by month and year (period March–May 2018–2019 and 2020).

Data from primary care Italy
*Cagliotti et al, Infectious diseases 2021*

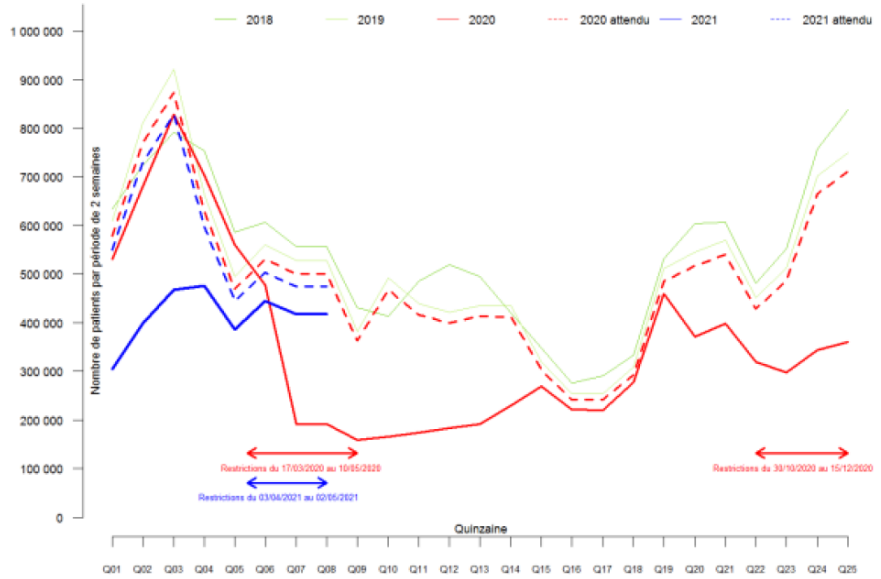
| ATC Level | Antimicrobial Class | National antibiotic use 2019 | National antibiotic use 2020 | Difference |
|---|---|---|---|---|
| | | Total DID | Total DID | |
| J01AA | Tetracyclines | 1.51 | 1.57 | 4% |
| J01CA | Penicillins with extended spectrum | 8.40 | 3.74 | -56% |
| J01CR | Combinations of penicillins, incl. beta-lactamase inhibitors | 4.84 | 4.85 | 0.1% |
| J01DB | First-generation cephalosporins | 1.15 | 0.70 | -39% |
| J01DC | Second-generation cephalosporins | 2.65 | 2.55 | -4% |
| J01DD | Third-generation cephalosporins | 2.02 | 2.27 | 12% |
| J01DH | Carbapenems | 0.04 | 0.06 | 43% |
| J01FA | Macrolides | 3.24 | 4.81 | 49% |
| J01FF | Lincosamides | 0.71 | 1.39 | 95% |
| J01MA | Fluoroquinolones | 2.74 | 3.00 | 9% |
| | Total | 28.39 | 26.82 | -6% |

Data from a Middle East country
*WHO*

- Some countries show decrease of antibiotic consumption in the primary care
- Mainly on first line, cheap antibiotics

# Impact of lock down in France


Whole population




Age group 0-19

- Overall, 29% and 25% decrease in 2020 and 2021
- Bigger decrease among children (0-18y)
- Reason given:
  - isolation of people (including less utilization of the health services)
  - for children: no school, no day care centers
  - Lower circulation of infectious diseases among the population

Weill et al, EPI-PHARE (Groupement d'intérêt scientifique ANSM-Cnam), 27 mai 2021
https://www.epi-phare.fr/rapports-detudes-et-publications/covid-19-usage-des-medicaments-rapport-6

# Impact of COVID-19 on antimicrobial use

- Direct impact
  - COVID-19 patient management
    - Increased use in COVID-19 hospitalized patients
    - Appropriate / Inappropriate use
- Indirect impact
  - Systemic impact of COVID-19 on society
    - Lower access to health services
      - Because of disruption
    - Epidemic aspects
      - Lower circulation of infectious diseases in the population due to lock down

# Conclusion

# Conclusion

- Measuring the use of antimicrobials is very challenging
  - Levels of resources in countries
- Needs for multi-tool approach
- Routine surveillance of antimicrobial consumption allows to detect changes in pattern of use of antimicrobials
- COVID-19 impacted antimicrobial use differently in hospitals and in the community
- Needs longer datasets on use to have better understanding on the changes
- Needs additional work to understand long lasting effects on these changes on the development of antimicrobial resistance

World Health Organization