Integrated Activity and Tools for Antimicrobial Stewardship, Infection Prevention & diagnostic Stewardship

Introduction to Measuring Success

Learning Objectives

1. To understand the need to measure outcomes, process measures, impact and surveillance of antibiotic consumption and tracking use

2. To understand the common methods and tools used in measure of process, outcomes, impact and surveillance of antibiotic consumption and tracking use

3. To understand key performance indicators, using data to inform prescribing practices

Background

- A large number of medicines and brands in market
  -Including fixed dose combinations variability in local context
  -High level of antibiotic consumption
- Inappropriate use of antibiotics
- Consequences of high and inappropriate use – AMR
- Strategies are needed to contain AMR
- Strategies are needed to improve antibiotic use
- Antimicrobial Stewardship (AMS) could be employed for this purpose.

The Need for Surveillance

There is a need for measure and surveillance of process measures, outcomes, antibiotic consumption and monitoring as part of AMS:

- Know the level of antibiotic consumption in countries, regions, healthcare facilities and departments within facilities.
- Recognize, understand and measure inappropriate use at the patient and hospital level
- Develop strategies by identifying areas of overuse/inappropriate use, use this information for intervention measures
- Evaluate the success of AMS by measuring change in level of antibiotic use and inappropriate use

Global Antibiotic Consumption

- WHO supported 57 countries in technical capacity building for monitoring AMC beginning 2016

  - Launched in November 2018 (WAAW)
  - **https://www.who.int/medicines/areas/rational_use/oms-amr-amc-report-2016-2018/en/**

Many local regional national and international surveillance programmes exist; PAHO, EU, US-CDC

eurosurv-23-46-4.pdf; NHSN | CDC; Latin American countries advance in the surveillance of antimicrobial consumption - PAHO/WHO | Pan American Health Organization

Eurosurveillance

CDC

PAHO Pan American Health Organization World Health Organization Americas Region

5. Assessing AMS programmes

- **Baseline:** Measure the **quantity** and **quality** of **antibiotic prescribing and use,** to identify priority areas for AMS interventions
- **Goal:** to **compare** results within a hospital, department or ward **over time; AB prescribing and use, patient outcomes etc**

- ✓ ***Structure measures*:** core elements
- ✓ ***Outcome measures*:** ABX use, patient outcomes
- ✓ ***Process measures*:** proportions e.g. of pneumonia patients receiving appropriate antibiotic treatment

What to Measure: Patient Outcomes

- **In-hospital mortality:**
  -No deaths / Total no of hospitalizations
  -Assessed by chart review and administrative data, can be in hospital or at a specific time point after admission (e.g. 30 days).
- **Infection-specific mortality (eg CAP mortality):**
  -It is difficult to assess whether a specific death is related to underlying disease, or infection or by AMR. The numerator and denominator must be clearly defined.
- **Length of stay**:
  -Days of hospitalization by type of infection / Total no of patients with that infection. Requires chart review and administrative data
- **Readmission:** within 30 days after discharge
- **Other:** C difficile, MDRO, resistance trends

What to Measure: process measures

- Documented indication for antibiotic use
- Compliance with current clinical treatment guidelines
- Stop/review date
- Length of therapy by indication
- 48-hour review De-escalation
- IV-to-oral switch
- Surgical prophylaxis (antibiotics) Surgical prophylaxis right agent and right time

Indicator Construction

- **Indication/ guideline compliance**: No of patients with a written indication for antibiotic treatment / Total no of patients treated with antibiotic(s)
  - No of patients with an indication receiving empirical treatment with antibiotic(s) according to clinical guidelines / Total number of patients with this indication
- **Stop order**: Number of patients with a written stop/review date for antibiotic treatment / Total number of patients treated with antibiotic(s)
- **Days of Therapy:** Total no of days of antibiotic treatment for a specific indication / Total no of patients treated with antibiotic(s) for that indication
- **48 Hour review**: No of patients where a 48-hour review is performed / Total no of patients treated with antibiotic(s) hospitalized >48 hours. No of patients where a de-escalation from the initial therapy is performed / Total no of indicated empirical treatments
- **IV to Oral**: No of regimens switched to oral route / Total no of regimens that can be switched to oral route based on predefined criteria
- **Surgical Prophylaxis**: No of patients receiving surgical antibiotic prophylaxis according to guidelines / Total no of surgical patients receiving antibiotic prophylaxis (timing 60 min before surgery and stop at 24 hours)

What to Measure: Antibiotic consumption

Antibiotics prescribed when not needed, e.g. fever without evidence of infection, asymptomatic colonization, viral infections, malaria.

Overly broad spectrum More broad-spectrum antibiotics (WATCH and RESERVE antibiotics) are prescribed than necessary (e.g. surgical prophylaxis).

Unnecessary combination therapy, including certain fixed dose combinations Multiple antibiotics are used, particularly with overlapping spectra and in combinations not shown to improve clinical outcomes.

Wrong antibiotic choice; Wrong antibiotic(s) are prescribed for particular indications/infections.

Wrong dose, interval, route or duration: Antibiotics are prescribed with the wrong dose (over- or underdosing), interval (eg too much time between doses), wrong route (eg IV instead of oral), duration (eg surgical prophylaxis)

Delayed administration Administration of the antibiotic(s) is delayed from the time of prescription. Repeat doses are not administered in a timely way,

Measuring Consumption: Surveillance Definitions

- Grams of Antimicrobials
- Antimicrobial expenditures
- DDD – Defined Daily Dose
- DOT – Days of Therapy
- Antimicrobial free days
- PPS – Point Prevalence Survey

Defined Daily Doses

- Defined Daily Doses (DDD) is a measure of prescribing/dispensing volume/flow

- DDD represents assumed average maintenance dose per day for a medicine used for its main indication in adults.

- The DDD is not a recommended dose but an analytical unit to compare prescribing/dispensing activity.

- The DDD is used as a metric of medicine consumption

GLASS methodology for surveillance of national antimicrobial consumption

Context & Purpose of DDD

- Measuring just the volume of prescribed/dispensed medicines may not be enough
- Main problem - a single medicine item can be for any quantity or duration
- There is a need for a system which more reliably measures medicine volume
- The system of DDDs helps to overcome these issues.
- In the DDD system - each medicine given a value within its recognized dosage range
- DDD is a unit of measurement – it's not a recommended dose & may not be a real dose
- The amount of an individual medicine can be expressed in DDDs

DDD in practice

- DDD is calculated by converting aggregate quantities available from pharmacy inventory records or sales.

- DDD approximately indicates how many potential treatment days of a medicine have been procured, distributed or consumed.

- It is expressed as:

  - number of DDD per 1000 inhabitant per day for total drug consumption.

  - Number of DDDs per 100 beds per day (100 bed days) for hospital use.

DDD Calculation

The DDD of a specific antibiotic encountered among 100 patients:

1. Total dose of the specific antibiotic in grams per patient

   = Unit strength x no. of units per day x no. of days.

2. Number of DDD of specific antibiotic per patient

   = Total dose of specific antibiotic (in grams) per patient

   divided by the DDD for that specific antibiotic.

3. DDD of the specific antibiotic encountered per 100 patients per period

   = Sum of DDDs per patient per period x 100

   divided by total number of patient encounters during the period.

Calculation Examples

Rx: levofloxacin DDD = 0.5 g Rx: Levofloxacin 500mg po od x 7 days DDD = (0.5g dose / 0.5g DDD) x 7d = 1 DDD x 7d = 7 DDD Rx: Levofloxacin 750mg po od x 7 days DDD = (0.75g dose / 0.5g DDD) x 7d = 1.5 DDD x 7d = 10.5 DDD

Rx: Levofloxacin 750mg po q48h x 7 days DDD = (0.75g/0.5g DDD) x 4 (# days on which patient received a dose) = 6 DDD

In 2011, hospital XYZ dispensed 13,000 grams of meropenem; WHO DDD for meropenem: 2 g = 6500 DDD (13,000 / 2) If 391,116 occupied bed days in 2011, then 6500 DDD / 391,116 X 1000 = 16.6 DDD / 1000 patient days

Example of DDD Calculation

Estimation in hospital: DDD/100 bed days

Question:

Calculate the DDD per 100 bed days for a 200 bed healthcare facility in your country

Steps

Step 1 - Calculation of total units of amoxicillin use in hospital:

- Amoxicillin used as: tablets (250mg, 500mg)
  : injection/infusion as co-amoxiclav (amoxicillin = 1000 mg)

- Total consumption of all three preparations during one year:
  2000 units of 250 mg amoxicillin (oral)
  8000 units of 500 mg amoxicillin (oral)
  3000 units of 1000 mg amoxicillin (parenteral)

Step 2 - Calculation of total quantity in grams:

- Quantity of oral amoxicillin used in 1 year multiplied by strength of the product
  = (2,000 × 0.25 gm) + (8,000 × 0.5 gm) = 4500 gm

- Quantity of parenteral amoxicillin used in 1 year multiplied by strength of the product = (3,000 × 1.0 gm) = 3000 gm

Steps

Step 3 - Calculation of total DDD:

- DDD of oral amoxicillin is 1500 mg = 1.5 gm
- DDD of parenteral amoxicillin is 3000 mg = 3 gm

- Divide total quantity of oral amoxicillin by assigned DDD

  = 4,500 gm / 1.5 gm = 3000 DDDs
- Divide total quantity of parenteral amoxicillin by assigned DDD

  = 3,000 gm / 3.0 gm = 1000 DDDs

- Total DDDs (Oral + Parenteral amoxicillin) = 3000 + 1000 = 4000 DDDs

Steps

Step 4 - Calculation of number (No.) of bed days

- No. of bed-days = No. of beds X occupancy index X No. of days
- If No. of beds = 200, Occupancy Index = 0.80, No. of days = 365 (one year period)

  No. of Bed-days = 200 X 0.80 X 365 = 58,400

Step 5 – Calculation of DDD / 100 bed days

- **DDD / bed days** = Total DDDs ÷ No of bed-days
  = 4000 ÷ 58,400 = 0.068 DDDs per occupied bed-days
- **DDD / 100 bed days** = 0.068 x 100 = 6.8 DDDs per 100 bed days

DDD advantages

- Can benchmark between institutions.
- Can be captured in absence of computerized data using purchasing information.
- Can be used to compare consumption of different medicines within same therapeutic group.
- Medicine utilization can be compared over a time for monitoring purposes.
- The extent of use of medicines can be monitored regularly.
- Changing trends can be brought to notice of Antibiotic Policy Committee.

DDD disadvantages

- Caution when comparing different services or case mix.
- Inaccurate in certain populations (eg pediatric, renal failure.
- When comparing different institutions, need to compare different formularies and dosing recommendations.
- More difficult to calculate needs denominators.
- Potential for confusion with historical data.
- Skin preparations such as ointments or creams whose daily use is heavily influenced by the patients.
- Vaccinations and other kinds of 'one-off' treatments.
- Medicines that are combined preparations, mixtures and compounds.

Days of Therapy (DOT)

- Days of Therapy (DOT) is also known as ‘antimicrobial days’
- DOT: ‘the aggregate sum of days for which any amount of a specific antimicrobial agent is administered to individual patients as documented’.
- In simple terms: it is the total number of days patient is on antibiotic, irrespective of the dose.
- Any dose of an antibiotic received during a 24-hour period represents 1 DOT.
- For patients on multiple antibiotics, total DOT is sum of DOTs for each antibiotic.

DOT calculation

Rx: Levofloxacin 500mg po od x 7 days DOT = 1 DOT x 7d = 7 DOT

Rx: Levofloxacin 750mg po od x 7 days DOT = 1 DOT x 7d = 7 DOT

Rx: Levofloxacin 750mg po q48h x 7days = 4 DOT

Rx: Cefazolin 2 g q8h iv X 1 day = 1 DOT

Rx: Cefazolin 1 g iv X 1 dose = 1 DOT

Rx: Levofloxacin 750mg po od x 7 days + Vancomycin 1g iv q12h x 7 days: DOT Levofloxacin = 1 DOT x 7d = 7 DOT DOT Vancomycin = 1 DOT x 7d = 7 DOT Total DOT = 14 DOT

DOT calculation

Consider the following situations where patient is administered:

1.Amoxicillin 250mg orally, thrice daily x 5 days = 5 DOT

1.Amoxicillin 875mg orally, twice daily x 5 days = 5 DOT

3. Levofloxacin 750mg orally, once daily x 7 days
   + Vancomycin 1g intravenously, twice daily x 7 days

DOT Levofloxacin = 1 DOT x 7 days = 7 DOT

DOT Vancomycin =   1 DOT x 7 days = 7 DOT

Total DOT =   DOT Levofloxacin + DOT Vancomycin = 14 DOT

DOT advantages and disadvantages

- **Advantages**
  -Can be used to benchmark between institutions if normalized to patient days
  -Allows for multiple patient populations to be compared
  -Not affected by change in dosing
  -Is preferred method by many
- **Disadvantages**
  -The denominator of patient days is required to standardize for benchmarking between institutions
  -Requires computerized pharmacy records to obtain data (manual counting isnt practical)
  -Favors mono therapy, eg patient on meropenem ves ceftriaxone metronidazole, unless patient days is by each agent
  -Overestimates one time doses

DOT as a metric

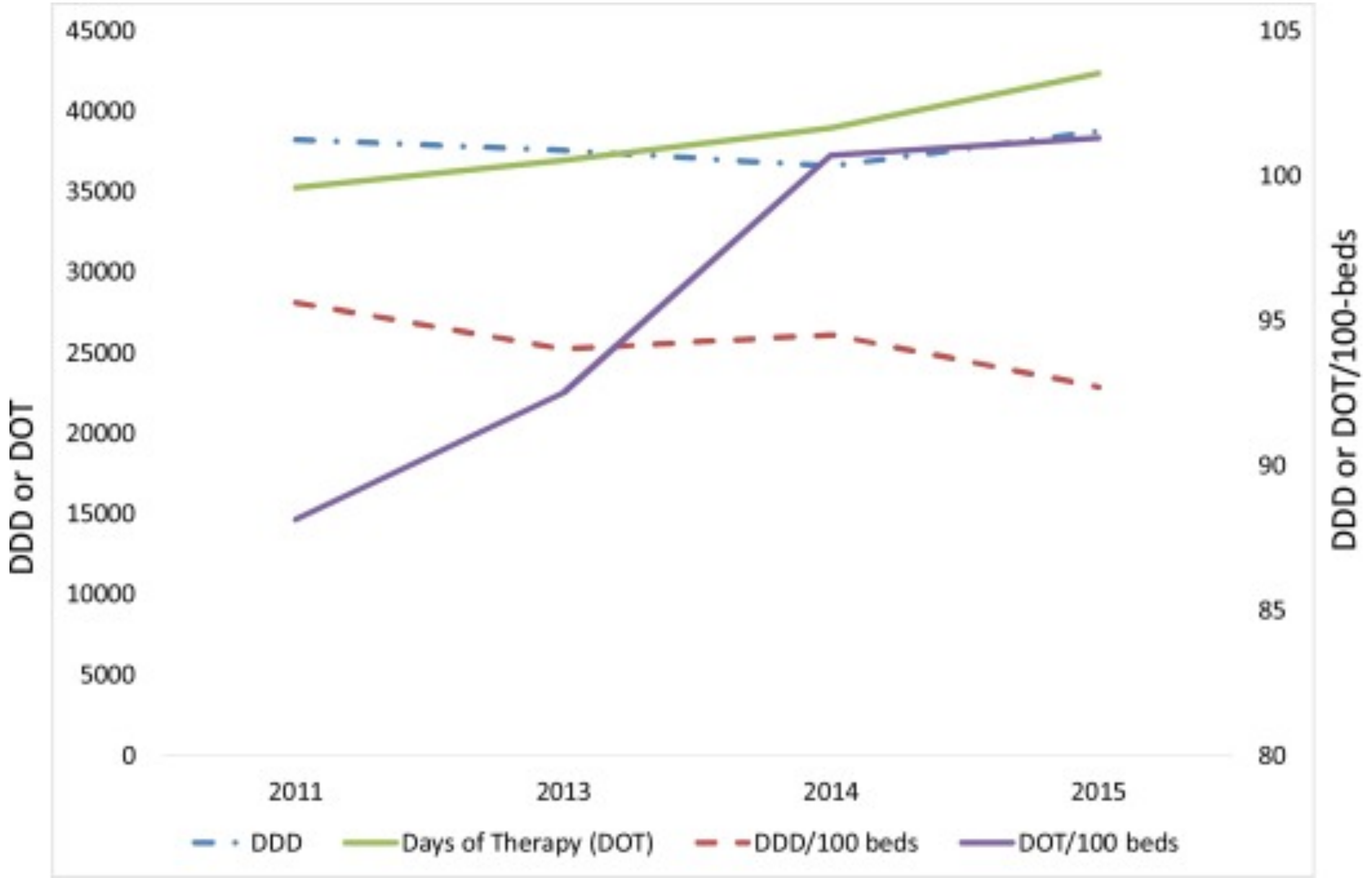
Advantages:

- Easy to compute. It could be used to benchmark (DOT/patient days) within and between institutions.
- Allows multiple patient populations to be compared accurately.
- Is not affected by change in dosing or formulation

Disadvantages:

- Does not distinguish between Single dose vs Multiple dose
- The DOT for patients who receive a dosing interval >24 hours (e.g. renal failure) does not reflect patient exposure; it only reflects antibiotic administration
- Over-estimation with one time doses (e.g. surgical prophylaxis) - one dose of a multi-dose regimen is counted the same as multiple doses received in a day.

DDD DOT example



[Benchmarking of antibiotic usage: An adjustment to reflect antibiotic stewardship program outcome in a hospital in Saudi Arabia - ScienceDirect]

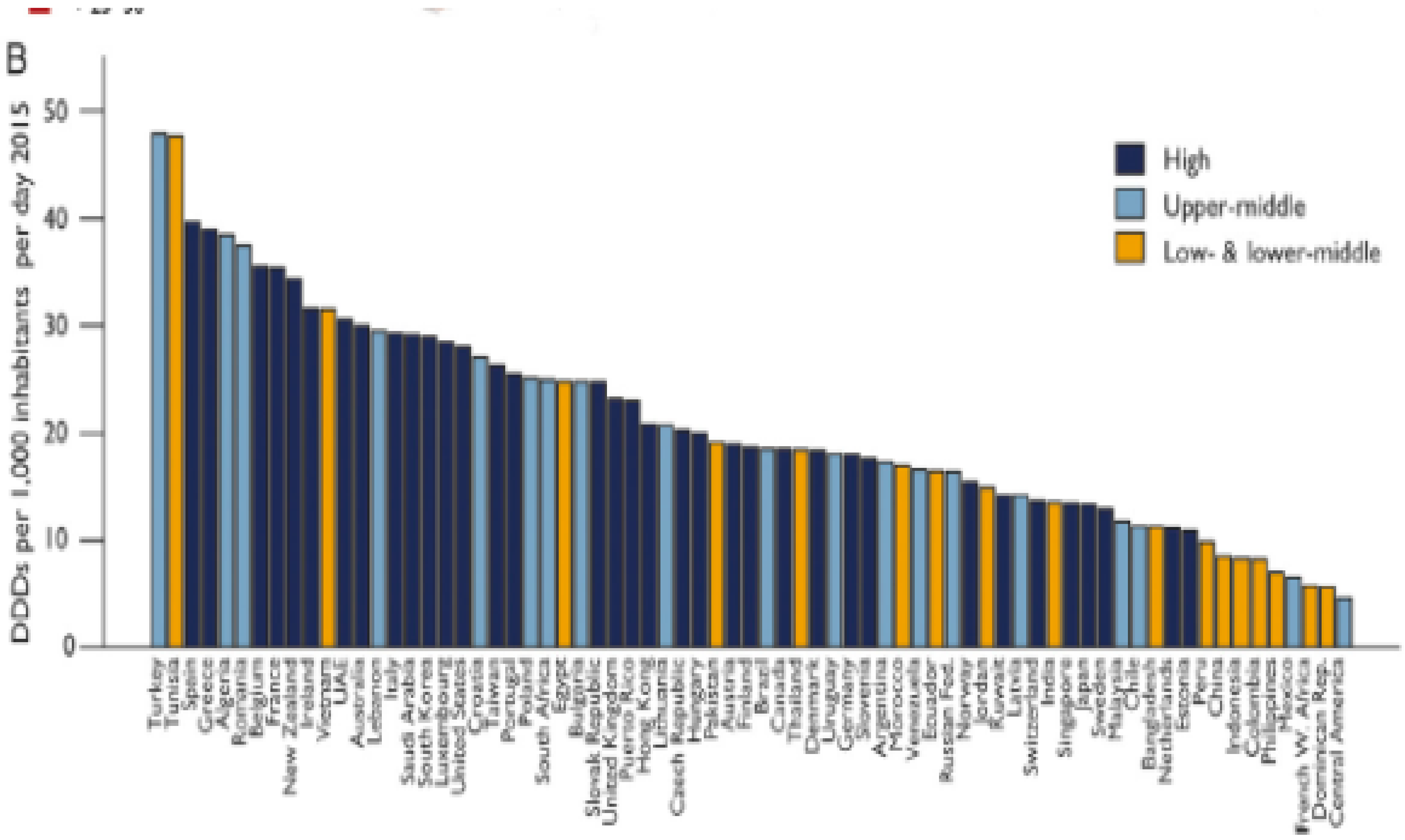
Point Prevalence Survey (PPS)

- PPS is a systematic and structured way of collecting data on antibiotic use.
- PPS will measure the number of people taking antibiotics at a given point in time
- PPS can assist in the following ways:

1. monitor rates of antibiotic prescribing between different departments/ hospitals/ regions/ countries in hospitalized patients.
2. determine variation in antibiotics, dose and indication across centers.
3. understand the quality of antibiotic use & identify targets for improvement
4. plan on interventions to promote stewardship
5. assess the effectiveness of interventions through repeated surveys.

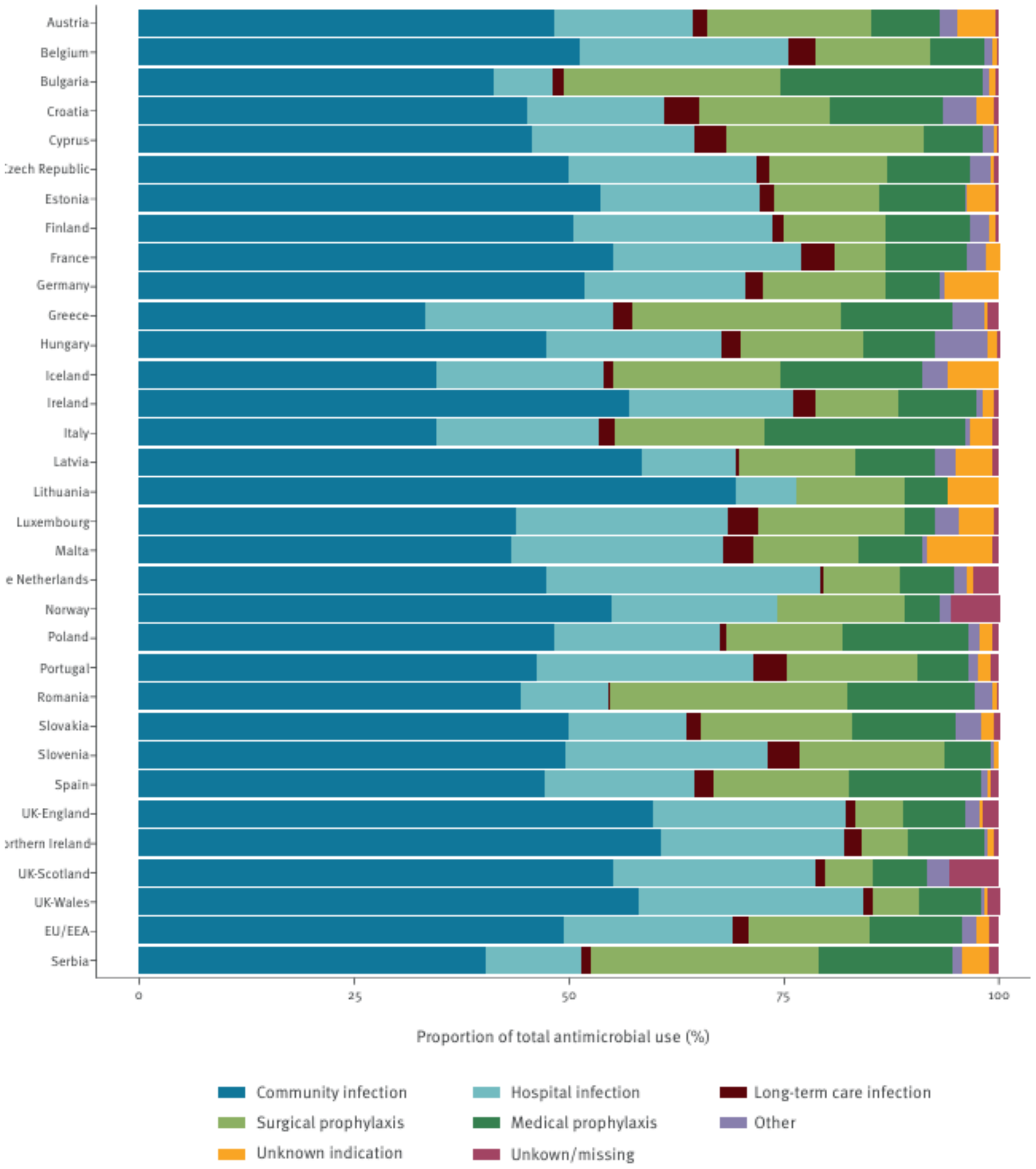
WHO-EMP-IAU-2018.01-eng.pdf

Global Antibiotic Consumption



Klein EY et al PNAS February 2018 : DDD/1000 1000 inhabitants/day 2000-15

PPS Example



eurosurv-23-46-4.pdf

Questions within PPS

What is the quantity and quality of antibiotic use?

- Geographical distribution and ranges
- Broad versus narrow spectrum antibiotic use
- Adults - children - neonates
- Dose
- Indications for therapy: treatment vs prophylaxis; medical vs surgical, community vs hospital associated infections

Questions within PPS

What are the determinants of inappropriate antibiotic use ?

- Patient: age, diagnosis, indication
- Institution : hospital type, ward type, national/local policy, existing guidelines
- Geographical factors: region, country, cultural, availability of antibiotics on the market, prescriber related (training)
- Reason for prescription
- Stop or review date written in notes
- Treatment decision supported by microbiology data and/or biomarker

Using Data to Inform Prescribing Practices: Evaluation of the AMS Program

- Interventions:
  -Count the number of interventions made, orders reviewed and acceptance rate
- Potential interventions include
  -Dose optimization
  -Guideline compliance
  -Escalation of therapy
  -De-escalation of therapy
  -Discontinuation of therapy
  -Route change (eg IV to PO)
- Cost savings
- Outcomes
- The future: mobile apps, EMR, AI, Machine learning

WHO Methods: Online Resources

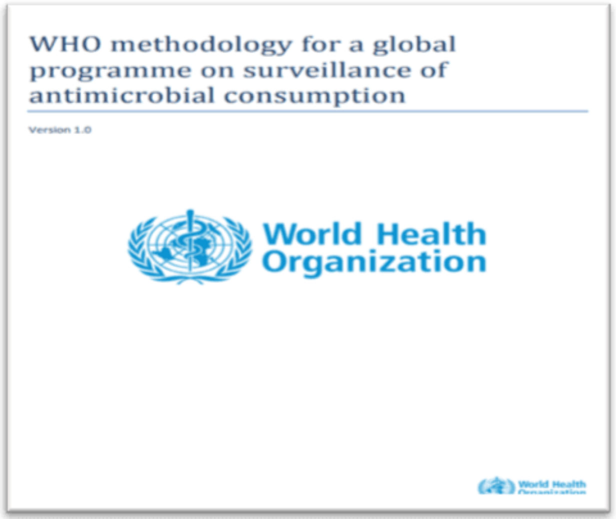
Antimicrobial Consumption (AMC) Surveillance

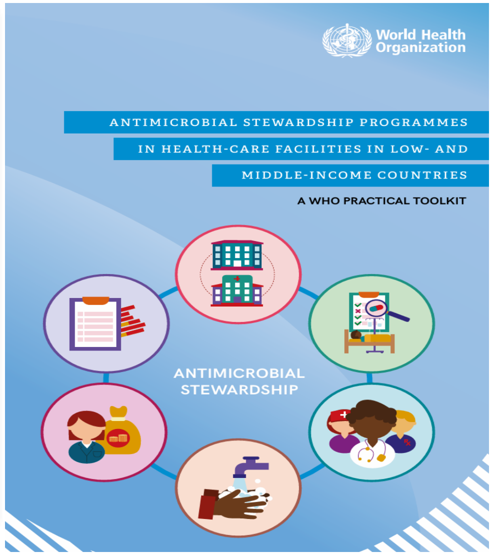
- National level protocol: https://www.who.int/medicines/areas/rational_use/WHO_AMCsurveillance_1.0.pdf

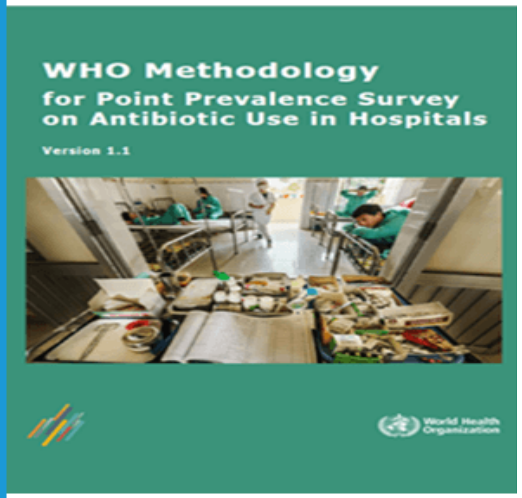
Antimicrobial Use (AMU) Monitoring

- Facility level protocols:

https://www.who.int/publications/i/item/9789241515481; https://www.who.int/publications/i/item/9789240025530; https://www.who.int/medicines/access/antimicrobial_resistance/WHO-EMP-IAU-2018_01/en/







References