



Training on GLASS methodology for national surveillance of antimicrobial consumption

Global Antimicrobial Resistance and
Use Surveillance System (GLASS)



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1.3.1Reading-01	1.3.1	AMR fact sheet	https://www.who.int/en/news-room/fact-sheets/detail/antimicrobial-resistance
1.3.2Reading-01	1.3.2	2018 WHO update on clinical pipeline for antibiotics	http://apps.who.int/iris/bitstream/handle/10665/275487/WHO-EMP-IAU-2018.06-eng.pdf?sequence=1&isAllowed=y
1.3.4Exercise-01	1.3.4	WHO South-East Asia Region's antibiotic challenge	https://pubmed.ncbi.nlm.nih.gov/28874338/
1.3.5Reading-01	1.3.5	Global Action Plan follow-up	https://www.who.int/docs/default-source/searo/amr/who-amr--gap-2-years-progress--advocacy.pdf?sfvrsn
1.3.6Reading-01	1.3.6	WHO AWaRe news release	https://www.who.int/publications/i/item/2021-aware-classification

Module 2

REFERENCE	SECTION	DOCUMENT	LINK
2.3.1Reading-01	2.3.1	Introduction to drug classification systems	https://apps.who.int/iris/bitstream/handle/10665/42627/924156234X.pdf?sequence=1&isAllowed=y
2.3.2Reading-01	2.3.2	Introduction to ATC and DDD methodology (Annex 1)	https://www.who.int/publications/i/item/9789240012639
2.3.4Reading-01	2.3.4	List of ATC subgroups under surveillance (Annex 2)	https://www.who.int/publications/i/item/9789240012639
2.4.1Reading-01	2.4.1	Background on the origin of the Defined Daily Dose (DDD)	https://apps.who.int/iris/bitstream/handle/10665/42627/924156234X.pdf?sequence=1&isAllowed=y
2.4.3Reading-02	2.4.3	Basis for assigning a DDD	https://www.whooc.no/ddd/definition_and_general_considera/
2.4.4Reading-01	2.4.4	The concept of the defined daily dose (DDD)	https://apps.who.int/iris/bitstream/handle/10665/42627/924156234X.pdf?sequence=1&isAllowed=y

Module 3

REFERENCE	SECTION	DOCUMENT	LINK
3.4.1Reading-01	3.4.1	Case study Thailand	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5537745/pdf/BLT.16.179648.pdf
3.4.2Reading-01	3.4.2	Case study Sweden	https://pubmed.ncbi.nlm.nih.gov/29147057/

Module 4

REFERENCE	SECTION	DOCUMENT	LINK
4.5.1Reading-01	4.5.1	Background and methods sections of article about surveillance in Vellore	https://apps.who.int/iris/handle/10665/70036
4.5.2Reading-01	4.5.2	Findings section of article about surveillance in Vellore	https://apps.who.int/iris/handle/10665/70036
4.5.3Reading-01	4.5.3	Conclusions from the article about surveillance in Vellore	https://apps.who.int/iris/handle/10665/70036

Abbreviations

ABM	antibacterial medicine
AIDS	acquired immunodeficiency syndrome
AMC	antimicrobial consumption
AMR	antimicrobial resistance
AMS	antimicrobial stewardship
AMU	antimicrobial use
API	active pharmaceutical ingredient
ATC	Anatomical Therapeutic Chemical
AWaRe	Access, Watch and Reserve
CC	Collaborating Centre
DDD	Defined Daily Dose
DID	DDD per 1000 inhabitants per day
DUR	drug utilization research
ESP	extended-spectrum penicillins
GAP-AMR	Global Action Plan on Antimicrobial Resistance
GLASS	Global Antimicrobial Resistance and Use Surveillance System
HIV	human immunodeficiency virus
INBASQ	ingredient base quantity
INN	international nonproprietary name
ISO	International Organization for Standardization
IU	international unit
MU	millions of international units
NGO	nongovernmental organization
OIE	World Organisation for Animal Health
PPS	Point prevalence surveys
UD	unit dose
UN	United Nations
WHO	World Health Organization

Glossary

Access antibiotics

An *AWaRe* (Access, Watch and Reserve) category. WHO recommends that antimicrobials in the Access group be available at all times, as treatments for a wide range of common infections. For example, this group includes amoxicillin, an antimicrobial that is widely used to treat infections such as pneumonia.

Active pharmaceutical ingredient (API)

A substance used in a finished pharmaceutical product and that is intended to furnish pharmacological activity or to otherwise have a direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or to have a direct effect in restoring, correcting or modifying physiological functions in humans.

Anatomical Therapeutic Chemical (ATC) classification system

An international system, controlled by the WHO Collaborating Centre (CC) for Drug Statistics Methodology, that categorizes all medicines into one of 14 anatomical groups, each of which is divided into therapeutic uses and then further subdivided into chemical subgroups.

Antimicrobial

Antimicrobials – including antibiotics, antivirals, antifungals and antiparasitics – are medicines used to prevent and treat infections in humans, animals and plants.

Antimicrobial resistance (AMR)

Antimicrobial Resistance occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death. As a result of drug resistance, antibiotics and other antimicrobial medicines become ineffective and infections become increasingly difficult or impossible to treat.

Antimicrobial stewardship

coherent set of integrated actions which promote the responsible and appropriate use of antimicrobials to help improve patient outcomes across the continuum of care.

Appropriate (optimal) use of antimicrobials

For the purpose of this training course, appropriate prescription or use of antimicrobials means that it is compliant or adherent to treatment guidelines, or that the prescription or use is supported by sensitivity testing. Appropriate use of antimicrobials aims to maximize the therapeutic impact while minimizing toxicity and the development of resistance.

AWaRe classification

Three categories of antibiotics – Access, Watch and Reserve – grouped together based on their treatment profile and potential for development of resistance, with recommendations on when each category should be used. See *Access antibiotics*, *Watch antibiotics* and *Reserve antibiotics*.

Broad-spectrum antibiotics

Antibiotics effective against a wide range of Gram-positive and Gram-negative bacteria. Examples of broad-spectrum antibiotics are aminoglycosides, the second-generation and third-generation cephalosporins, quinolones, carbapenems and some synthetic forms of penicillin.

Combination products

See *Fixed-dose combinations*.

Consumption of antimicrobials

“Consumption data” refers to estimates derived from aggregated data sources (e.g. import or wholesaler data, or aggregated health insurance data), where there is no information available on the patients who are receiving the medicines or why the antimicrobials are being used. These data sources provide a proxy estimate of *use of antimicrobials*.

Defined Daily Dose (DDD)

The assumed average maintenance dose per day for a drug that is being used for its main indication in adults. The DDD is a unit of measurement and does not necessarily reflect the recommended or prescribed daily dose.

Dosage form

The form and configuration of the completed pharmaceutical product (e.g. tablet, capsule, elixir, injection or suppository).

First-line treatment

The initial preferred treatment for any medical condition, recommended on the basis of available evidence. First-line treatments for infections are often narrow-spectrum antibiotics with positive benefit–risk ratios and low resistance potential.

Fixed-dose combinations

A combination of two or more active pharmaceutical ingredients (APIs) in a fixed ratio of doses. This term is used generally to mean a particular combination of APIs, irrespective of the formulation or brand.

Global Antimicrobial Resistance and Use Surveillance System (GLASS)

A system being developed by WHO to promote and support a standardized approach to the collection, analysis and sharing of antimicrobial resistance and use data at a global level. GLASS encourages and facilitates the establishment of national surveillance systems for antimicrobial resistance and use that are capable of monitoring their trends, and producing reliable and comparable data.

International nonproprietary name (INN)

The shortened scientific name based on the active ingredients. WHO is responsible for assigning INNs to pharmaceutical substances.

Microbiological profile

See *Spectrum of activity*.

Minimum inhibitory concentration (MIC)

The lowest concentration of an antimicrobial that inhibits the visible growth of a microorganism after overnight incubation.

“One-Health” approach

A coordinated, collaborative, multidisciplinary and cross-sectoral approach – at local, national and global levels – to attain optimal health for humans, animals and plants, and their shared environment.

Reserve antibiotics

An *AWaRe* (Access, Watch and Reserve) category. The Reserve group includes antibiotics such as colistin and later generations of cephalosporins, which should be considered last-resort options. These antibiotics should be used only in the most severe circumstances, including in specialized settings and specific cases where all other treatments have failed (e.g. for life-threatening infections due to multidrug-resistant bacteria).

Route of administration

The path by which a medicine is taken into the body. Routes of administration are generally classified by the location at which the medicine is applied. Common examples include oral and intravenous administration.

Second-line treatment

Treatment reserved as a second choice for medical conditions, in case of contraindications, failure or adverse effects of the first-line treatment.

Sensitivity test

Laboratory testing used to measure the ability of an antibiotic or other antimicrobial agent to inhibit bacterial growth in vitro.

Spectrum of activity

Range of bacterial species susceptible to a given antimicrobial. These agents are classified as narrow spectrum or broad spectrum. The spectrum of activity of an antimicrobial may change as the bacteria acquire resistance genes.

Strength

Indicates the amount of active ingredient in each dosage.

Use of antimicrobials

“Antimicrobial use data” refers to estimates derived from patient-level data. These data may allow disaggregation of data based on patient characteristics (e.g. gender and age), or indication for which the medicine is being used. This may facilitate assessment of clinical practice against agreed protocols and treatment guidelines. See also *Consumption of antimicrobials*.

Watch antibiotics

An *AWaRe* (Access, Watch and Reserve) category. The Watch group includes antibiotics that are recommended as first-line or second-line treatments for a small number of infections. They have a higher potential for resistance to develop; hence, their use as first-line and second-line treatment should be limited. For example, ciprofloxacin, which is used to treat the urinary tract infection cystitis and upper respiratory tract infections (e.g. bacterial sinusitis and bacterial bronchitis) should be dramatically reduced to avoid further development of resistance.

Introduction

Welcome to this self-paced, online course, which is designed to help you to understand and establish surveillance of the consumption of antimicrobial medicines at country level. The course is based on the World Health Organization (WHO) standardized methodology for global surveillance of antimicrobial consumption (AMC). It is part of WHO's wider efforts to support countries in collecting and using data on AMC, and to facilitate the exchange of data with WHO's Global Antimicrobial Resistance and Use Surveillance System (GLASS).

The development of national surveillance systems is an essential part of national action plans for antimicrobial resistance (AMR). We face a serious threat to global public health from increasing levels of AMR, driven by widespread use of antimicrobials. Yet we lack the valuable data needed to monitor AMC, such data would increase our understanding and help us to develop effective strategies and interventions for optimal use of antimicrobials. The WHO methodology for global AMC surveillance provides a common technical basis for setting up AMC surveillance systems and allows for standardized data collection at the national level.

The main objectives of this course are to:

- introduce the WHO methodology for global AMC surveillance;
- build competencies in key AMC surveillance functions, including data collection and analysis; and
- describe the steps needed to set up structures for AMC surveillance and to generate data.

This course is designed for multidisciplinary professionals in charge of implementing AMC surveillance at national and local level, drug utilization researchers, members of AMR committees, and everyone interested in building competencies in key AMC surveillance functions.

The course comprises five modules. It starts with an overview of the AMR threat and its main drivers, including the use of antimicrobials. The course then moves on to describe the WHO methodology for global AMC surveillance, its data sources and variables, and provides instructions on how to establish national AMC surveillance systems.

You can work through the modules from start to finish, building up your expertise as you complete each module. Alternatively, if you are already familiar with some of the concepts, you can choose to work through a specific module that covers a topic that is new to you. Where a module builds on learnings from an earlier module, this is made clear in the text.

Each module contains text plus a set of different elements, some of which are presented with icons, as shown here:



readings – short texts from publications for you to read as you work through a module;



supplementary readings – longer texts or more detailed information that you can read if you wish to find out more about a particular topic;



videos – short, publicly available videos for you to watch as you work through a module;



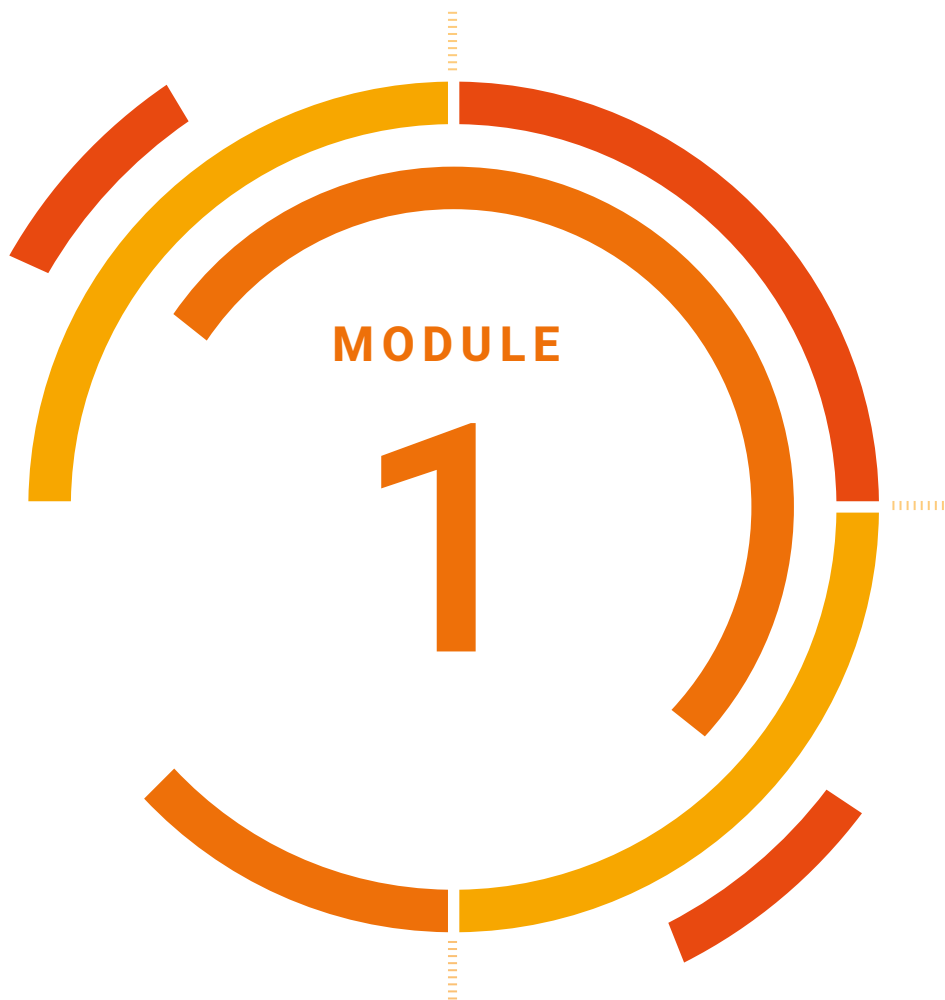
lecture – narrated videos made specifically for this course, with transcripts and given in the notes, for reference;



quizzes and exercises – opportunities for you to test your knowledge, with answers (including feedback on wrong answers) provided at the end of the module; and

- **references** – a list of the references cited in the text, with a URL where the reference is available online.

We hope you will find the course informative and useful. We trust that more countries will join the efforts to measure AMC and help to keep antimicrobials as effective tools in fighting infectious diseases.



Overview of antimicrobial resistance and use

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1.1 Training objectives of Module 1

This introductory module will help you to:

- gain an overview of the issue of resistance to antimicrobials, and of how the (inappropriate) use of antimicrobials leads to resistance;
- understand the differences between sales, prescription, use and consumption of antimicrobials;
- be aware of the international initiatives to monitor antimicrobial consumption (AMC); and
- become familiar with the World Health Organization (WHO) methodology for monitoring AMC.

The antimicrobials are used to treat infections caused by bacteria, parasites, viruses and fungi. This course covers the human use of antimicrobials – it does not discuss antimicrobial use in animals or plants.

1.2 Background

1.2.1 The dawn of the “antimicrobial era”

The discovery of microorganisms as the cause of infectious diseases was a first step in freeing humankind from one of the most important causes of mortality. It was soon understood that hygiene and hand washing were the most effective interventions to reduce transmission of infections in hospitals and health care units, in the home and in public places.

Although hygiene and hand washing can reduce transmission, they cannot cure infections. During the early decades of the 20th century, the first effective antimicrobial products were discovered. As these products were marketed and used in therapy, the antimicrobial era began.

An early type of antimicrobial was the sulfonamides. Domagk, using a systematic screening approach, discovered the antibacterial effects of a red dye, Prontosil. This led to the development and marketing of the first sulfonamides in 1935.

Alexander Fleming observed the antimicrobial activity of the *Penicillium* mould in 1928. He and other chemists then tried to find a method to purify this active ingredient and make it stable. It was not until 1940 that Howard Florey and Ernst Chain found a way to purify enough penicillin to be used in therapeutics. This new antimicrobial helped to save thousands of lives during the Second World War, and Fleming, Chain and Florey were awarded the Nobel Prize in 1945.

Interestingly, in his Nobel Lecture, Fleming explained the importance of the discovery, but also warned about the dangers of penicillin misuse:

“

But I would like to sound one note of warning. Penicillin is to all intents and purposes non-poisonous so there is no need to worry about giving an overdose and poisoning the patient. There may be a danger, though, in underdosage. It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body.

The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant. Here is a hypothetical illustration. Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin the treatment fails. Mrs. X dies. Who is primarily responsible for Mrs. X's death? Why Mr. X whose negligent use of penicillin changed the nature of the microbe. Moral: If you use penicillin, use enough.

– Alexander Fleming. Penicillin.
Nobel Lecture, 11 December 1945 (1).



Exercise 1.1 – a reflection

Note: This reflection exercise invites you to think about antimicrobials. By the end of the course you will have all the information you need to answer the questions that you will find in the reflection exercises.

Since 1945, many agents with antimicrobial activity have been discovered or synthesized.

Take a couple of minutes to think about these questions:

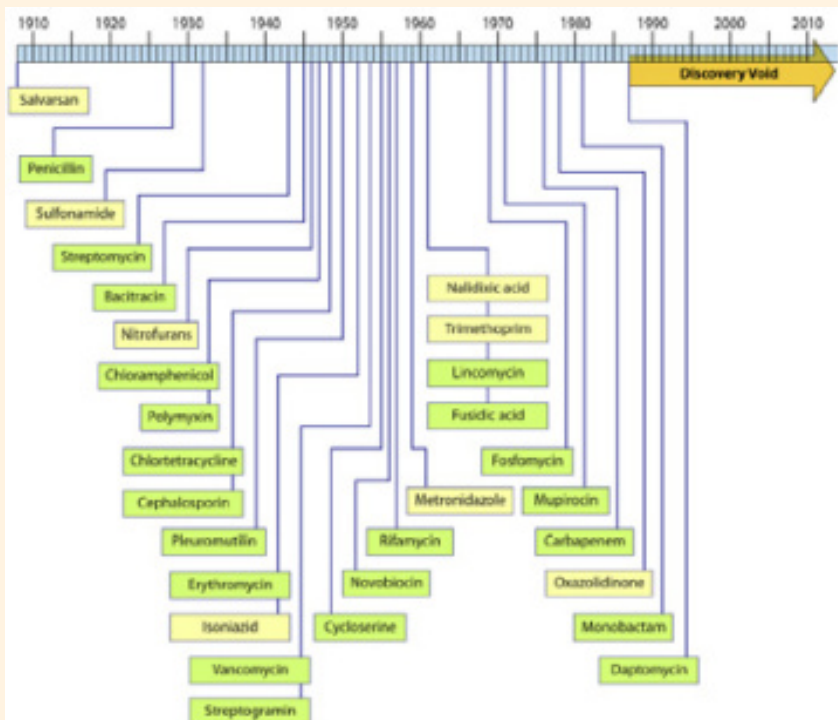
- Can you name four different antimicrobials?
- Even if you are not a medical doctor or you have been away from the clinical practice for a long time, you probably know that different infections require different antimicrobials. Can you name three pairs of “infection – antimicrobial”?

1.2.2 A golden era and the antimicrobial spectrum

After the discovery of penicillin, pharmaceutical companies began a race to discover and identify additional compounds with antimicrobial activity. In those early days, many promising molecules were found in soils, sewage waters, plants and animals all over the world. This was a golden era in the field of antimicrobials.

Fig. 1.1 shows the impressive discovery and commercialization timeline for new families of antimicrobials. Within each family, tens of individual active ingredients with just a few modifications in their chemical structure have been tested and eventually marketed.

Fig. 1.1. Illustration of the “discovery void”. Dates indicated are those of reported initial discovery or patent.



Source: Silver (2011) (2).

Antimicrobials either kill microbes or stop their multiplication. Early in the antimicrobial era, it became clear that not all antimicrobials were effective against all microbes (i.e. the antimicrobial spectrum differs among antimicrobials). The chemical structure of an antimicrobial affects its mechanism of action, and one way to classify antimicrobials is by their chemical structure, as shown in Table 1.1.

Table 1.1. Examples of antimicrobials, classified by chemical structure

SUBGROUP OF ANTIMICROBIALS	RELEVANT EXAMPLES
Tetracyclines	Doxycycline, minocycline, tetracycline
Amphenicols	Chloramphenicol, thiamphenicol
Beta-lactam antimicrobials	Penicillin, amoxicillin, cephalosporins, cloxacillin
Trimethoprim and sulfonamides	Trimethoprim, sulfamethoxazole
Macrolides	Erythromycin, azithromycin
Aminoglycosides	Amikacin, gentamycin
Quinolones	Ciprofloxacin, levofloxacin
Glycopeptides and polymyxins	Vancomycin, colistin

1.3 Antimicrobial resistance

This section explains what antimicrobial resistance (AMR) is, the factors that cause such resistance to develop, the impact of AMR and the rationale for monitoring the use of antimicrobials.

1.3.1 What is AMR?

AMR occurs when microorganisms develop resistance to antimicrobials. Microorganisms that develop resistance can survive exposure to the antimicrobial and continue to multiply, potentially causing more harm and spreading to other animals or people. The development of resistance is part of the evolutionary mechanisms that allow microorganisms to adapt to an adverse environment and thus survive.



Reading 1.1

Read this WHO fact sheet about AMR; it explains:

- what AMR is;
- why AMR is a global concern;
- the factors that accelerate the emergence and spread of AMR;
- the present situation regarding resistance in bacteria in general and in specific diseases (e.g. HIV, influenza malaria and tuberculosis);
- the need for coordinated action on AMR; and
- WHO's response to AMR.

Antimicrobial resistance, WHO (2018) (3) (reference: [1.3.1Reading-01](#))

1.3.2 The need for new antimicrobials

For all of the many different antimicrobials on the market, there is some degree of AMR. Where resistance is high, the antimicrobial can become ineffective; hence, there is an urgent need for researchers and pharmaceutical companies to discover new antimicrobial molecules. A major problem today is that it has become much more difficult to find new antimicrobials. At the same time as antimicrobial resistance is increasing, pharmaceutical companies have no potential new molecules in the pipeline – warning bells are ringing.

Supplementary videos 1.1 and 1.2

If you wish, you can watch these two short videos to understand why it is difficult to find new antibiotics:

Video 1.1: <https://youtu.be/gN-7fFllZY?t=2m1s> (4)

Video 1.2: <https://youtu.be/1wNFcullF8Q> (5)

Even if we succeed in finding new antimicrobials, the question is, will we continue to use them without taking into account the basic principles of their optimal use? The answer is that we probably will overuse any new antimicrobials, and new resistances will soon appear. The inappropriate use of antimicrobials is discussed in Section 1.3.3.

Additional information about how microorganisms acquire resistance to antimicrobials is given in the supplementary reading at the end of this current section, but note that for the purposes of this training, you do not need to be a specialist in AMR. Microbiologists study the mechanisms by which microorganisms acquire resistance, the resistance map of each country and the patterns of antimicrobial susceptibility of different bacterial strains. Thus, microbiologists should be part of an AMR working group, where applicable.

Now take Quiz 1.1 (you will find the solutions at the end of the module).



Quiz 1.1

Quiz 1.1: Part 1

Is the following statement about resistance to antimicrobials true or false?

NO.	QUESTION	TRUE OR FALSE?
1	The main result of resistance to antimicrobials is that medicines become ineffective and infections persist in the body, increasing the risk that infections will spread to others.	

Quiz 1.1: Part 2

The consequences of resistance to antimicrobials depend on the microorganism involved. In the table below, for each microorganism, select the disease most commonly caused by that microorganism, and the antimicrobial to which the organism is most likely to develop resistance.

NO.	WHICH DISEASE DOES IT CAUSE?			TO WHICH ANTIMICROBIAL IS IT INCREASINGLY BECOMING RESISTANT?		
<i>Neisseria gonorrhoeae</i>	Urinary infections	Gonorrhoea	Hospital-acquired pneumonia, sepsis, etc.	Carbapenem	Fluoroquinolones	Third-generation cephalosporin
<i>Klebsiella pneumoniae</i>	Urinary infections	Gonorrhoea	Hospital-acquired pneumonia, sepsis, etc.	Carbapenem	Fluoroquinolones	Third-generation cephalosporin
<i>Escherichia coli</i>	Urinary infections	Gonorrhoea	Hospital-acquired pneumonia, sepsis, etc.	Carbapenem	Fluoroquinolones	Third-generation cephalosporin

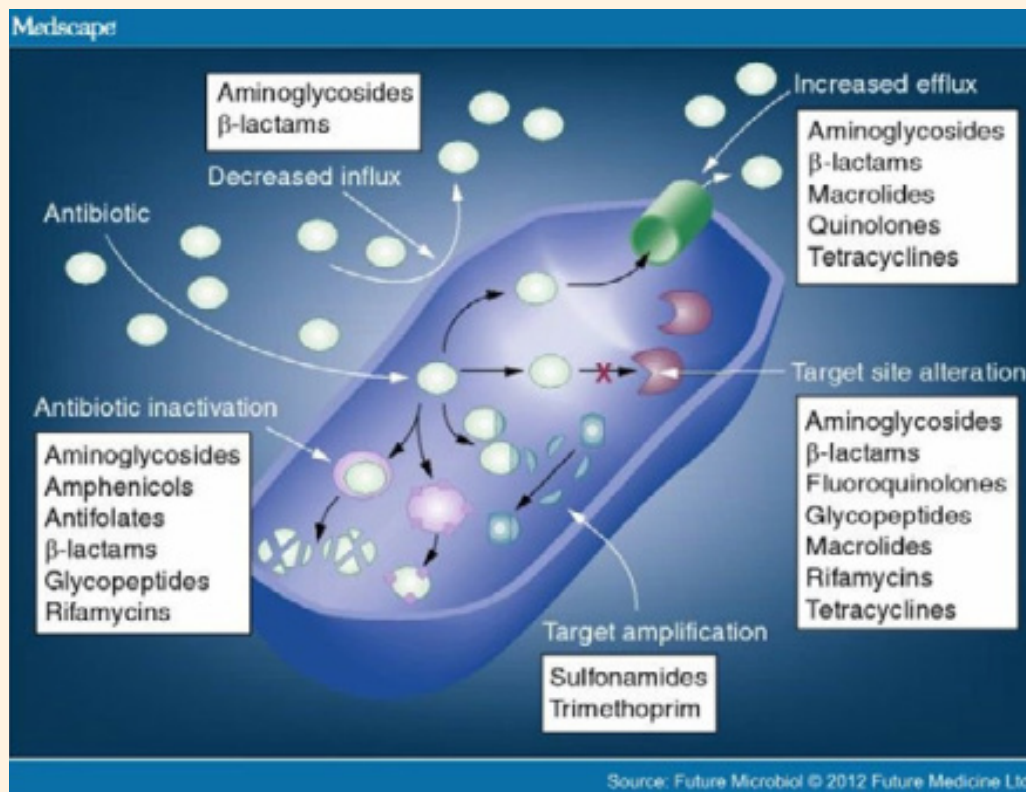
Additional information on how microorganisms acquire resistance to antimicrobials

As illustrated in Fig. 1.2, there are four main mechanisms through which bacteria develop AMR:

- bacteria acquire mechanisms to inactivate or modify the antibacterial agents;
- bacteria “learn” how to alter the target site of the antibacterial agents, reducing its binding capacity;
- bacteria modify some metabolic pathways, so that antibacterial agents are destroyed before they can produce their effect; and
- bacteria decrease permeability or increase active efflux of the antibacterial agents and thus reduce their intracellular accumulation.

These mechanisms arise through mutations of existing genes or through bacteria acquiring new genes from other strains or species.

Fig. 1.2. The main mechanisms through which bacteria develop resistance to particular types of antibacterial agents



Source: Adapted from Schmieder & Edwards (2012) (6).

Supplementary video 1.3

If you wish to, watch this video, which uses animation to explain the main mechanisms by which microorganisms acquire resistance.

Video 1.3: <https://youtu.be/4oukHcpQoXM?t=2m40s> (7)



Supplementary reading 1. 1.

This 2017 publication from WHO discusses antimicrobials that are under development:

Antibacterial agents in clinical development: an analysis of the antibacterial clinical development pipeline, including tuberculosis (8)

This 2018 update of the Executive summary of the 2017 document discusses the antimicrobials that are in the pipeline for two major pathogens. It is based on the outcome of an advisory group meeting in 2018: *Update on antibacterial agents in clinical development (9)*: (reference: [1.3.2Reading-01](#)).

1.3.3 Inappropriate use of antimicrobials

Although microorganisms evolve and can thus spontaneously acquire resistance to antimicrobials, the process is greatly accelerated by various factors in the human, veterinarian and agricultural sectors. Widespread use of antimicrobials is an important cause of AMR due to the exerted selective pressure on microorganisms.

Supplementary video 1.4

If you wish, watch this video, in which the microbiologist Peter Piot explains the consequences of overuse of antimicrobials, particularly for nonmedical use.

Video 1.4: https://youtu.be/2_uB-8RzFYI (10)

Now take Quiz 1.2 (you will find the solutions at the end of the module).



Quiz 1.2

Do the following factors contribute to the development and transmission of resistance to antimicrobials?

FACTOR	YES OR NO?
Overprescription of antimicrobials	
Hand washing before and after being in contact with a patient	
Use of antibacterial products in nonbacterial infections	
Noncompliance by patients	
Weak hospital management practices	
Prescribing antimicrobials after looking at the results of the susceptibility tests	

1.3.4 How antimicrobial use leads to the occurrence and spread of AMR

As we have seen, bacteria and other microorganisms can develop resistance to antimicrobials. In this section, we will consider the consumption and actual use of medicines in general and of antimicrobials in particular. Start by watching Lecture 1.1, which discusses microbiological profile, market offer of medicines, prescription, selling and use of antimicrobials. The publications shown in the slide can be found in the reference list for this module (11-17). The figure showing the life cycle of medicines is adapted from the WHO report on surveillance on antibiotic consumption: 2016 – 2018 (18).

Lecture 1.1.

Microbiological profile, market offer of medicines, prescription, selling and use of antimicrobials

Section 1.3.2 of this module looked at growing concern about antimicrobial resistance at a global scale. Section 1.3.3 then commented on the consequences of the use of antimicrobials without following therapeutic guidelines or not supported by susceptibility testing in the appearance of resistant microorganisms.

Here, we will go into more detail about three aspects:

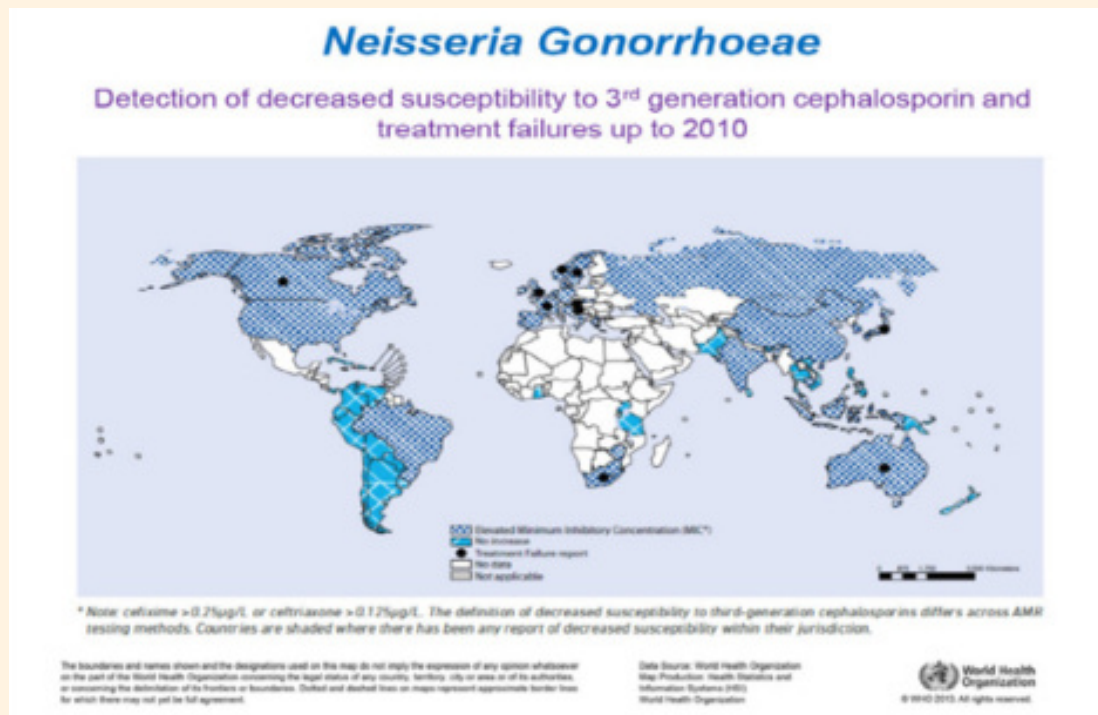
- the differences in the microorganisms that cause diseases in different countries (the so-called microbiological profile);
 - the antimicrobials that are authorized and marketed in a given country; and
 - the prescription and use of those antimicrobials.
- All these concepts will be useful as you proceed with the training.

Selected Bacteria/Resistance Combinations

BACTERIUM	RESISTANCE/ DECREASED SUSCEPTIBILITY TO:
<i>Escherichia coli</i>	3 rd generation cephalosporins, fluoroquinolones
<i>Klebsiella pneumoniae</i>	3 rd generation cephalosporins, carbapenems
<i>Staphylococcus aureus</i>	Methicillin (beta-lactam antibiotics) i.e. MRSA
<i>Streptococcus pneumoniae</i>	Penicillin
<i>Nontyphoidal Salmonella (NTS)</i>	Fluoroquinolones
<i>Shigella species</i>	Fluoroquinolones
<i>Neisseria gonorrhoeae</i>	3 rd generation cephalosporins

There are some specific problems with decreased susceptibility to antimicrobials. As you can see from this table, which was published in the WHO's 2014 global report on surveillance, many *Escherichia coli* strains are already resistant to third-generation cephalosporins. Also, resistance of *E. coli* to the fluoroquinolones is growing.

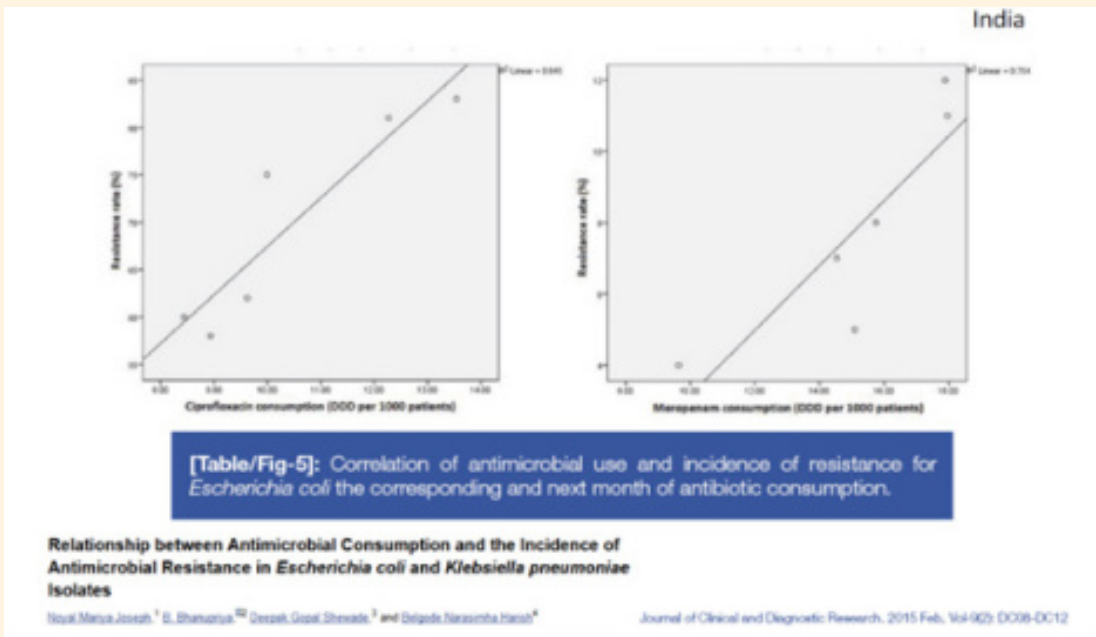
E. coli is one of the agents involved in noncomplicated urinary tract infections, a frequent condition, especially among women. So, resistance to the commonly used fluoroquinolones means that in some cases, to heal patients it is necessary to prescribe other antimicrobials that are not the usual first-line or second-line treatments.



Both the microbiological profile and the distribution of resistant strains are dynamic (that is, they change with time); they also present geographical differences. For example, on the map shown in this slide you can see the country distribution of *N. gonorrhoeae* strains with low susceptibility to third-generation cephalosporins. There are a couple of interesting aspects to this distribution:

First, data are lacking for some countries, and when patients present with gonorrhoea, this lack of information directly affects how prescribers select the most appropriate antimicrobial. So, for those countries, there is an urgent need for actions to improve data collection and the availability of susceptibility tests. Second, the map shows different patterns; these represent differences in the susceptibility of *Neisseria strains* to third-generation cephalosporins.

If a given strain is less susceptible to cephalosporins, this means that greater dosages would be needed to eliminate all bacteria; as a microbiologist would usually say, 'the minimum concentration of cephalosporins needed to inhibit *Neisseria* growth' would be higher. You can see that some areas have declared increased minimum inhibitory concentration levels for third-generation cephalosporins; for example, you can see this in Australia, Brazil, India and the United States of America. Microorganisms do not observe political borders; also, thanks to globalization, with rapid transportation across the globe, it can take just a few hours for a multiresistant strain to move from one continent to another.



Studies in different health care settings from many countries have shown a clear relationship between the use of a specific antimicrobial and resistance to that antimicrobial.

For example, this figure presents the results of a study carried out in Indian hospitals; the graphs show the relationship between antimicrobial consumption and the detection of resistant strains of *E. coli* isolates. You can see that there is a significant correlation between the use of ciprofloxacin (left) and meropenem (right) and the incidence of resistant isolates measured 1 month after the antimicrobial consumption.

Diyarbakir Teaching and Research Hospital is a 672 bed tertiary center with six intensive care units (ICUs), 10 medical units and eight surgical units.

Table 3 Evaluating of treatments according to indications of total usage in 2011 and 2012.

	2011(%)			2012(%)			p
	A	U	I	A	U	I	
ET	54.6	19.1	26.3	63.6	15	21.4	0.023
MEB	79.2	12.5	8.3	84.2	5.3	10.5	
PT	10.3	17.2	72.5	56.3	6.2	37.5	
Total	51	18	31	64.3	12.9	22.8	

A: appropriate; U: unnecessary; I: inappropriate; ET: empirical treatment; MEB: microbiological evidence-based treatment; PT: prophylactic treatment.

Analysis of antimicrobial consumption and cost in a teaching hospital

Fatma Bozkurt^{1,2}, Safak Kaya³, Recep Tekin⁴, Serda Gulsum⁵, Ozcan Devceli⁶, Selim Bayan⁷, Salih Hopyolu⁸

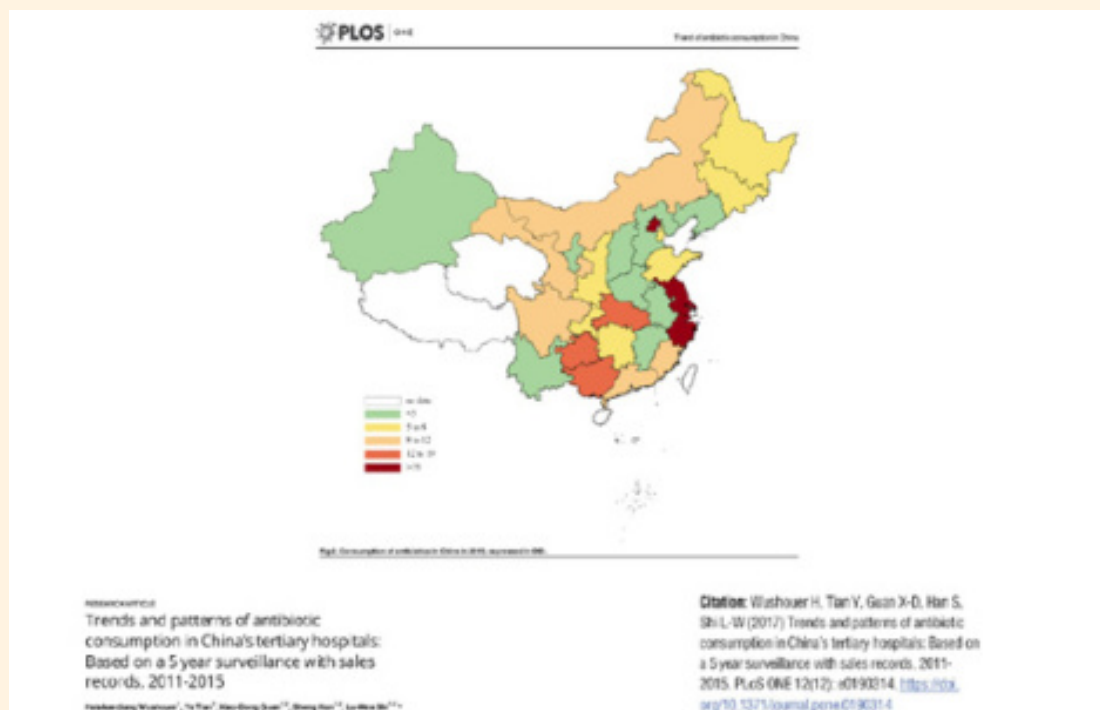
Journal of Infection and Public Health (2014) 7, 161–169

It is interesting to try to understand the characteristics of antimicrobial prescription and use. AMR can develop even when antimicrobials are used appropriately, but if they are used inappropriately, then the resistance that develops is avoidable and unnecessary.

This table comes from a study carried out in a big teaching and research hospital in Turkey. The authors evaluated a number of treatments in 2011 and 2012. They classified treatments as empirical (ET), microbiologically based (MEB) or prophylactic (PT). Antimicrobials can be (and often are) inappropriately prescribed or used; although this happens with other medicines, in the case of antimicrobials, it is extremely important.

In this study, a panel classified the treatments as “appropriate” (A), “unnecessary” (U) or “inappropriate” (I). You can see, for example, that for the treatments based on microbiological evidence (MEB) in 2011 more than three quarters were appropriate (A), whereas for the prophylactic treatments, 72.5% were classified as inappropriate.

In 2011, 18% of the treatments were considered unnecessary. However, the hospital carried out an intervention in that year, which helped to improve the use figures for 2012 – you can see that unnecessary use fell to about 13% in 2012. The results of this study show that well-designed interventions can help to turn the tide on the problem of inappropriate prescription or use.



Of course, there are wide variations in use patterns. Although such variations are seen at a local level (e.g. in different hospital services), they are more important at a country level.

This figure shows the trends and patterns of antimicrobial consumption in China’s tertiary hospitals. In the red area, more than 19 people per 1000 inhabitants were receiving an antimicrobial daily. On the other side of the country, green areas indicate regions where fewer than five people per 1000 inhabitants were exposed to antimicrobials daily. In Module 2 we will explain how it is possible to measure consumption in big populations.

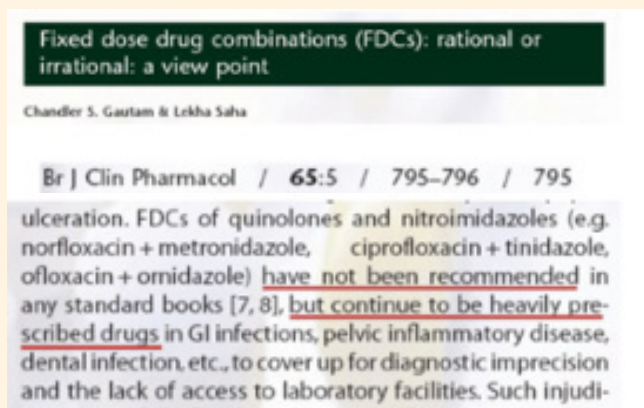
Antibiotics groups/subgroups with ATC codes		Teaching hospital	Non-teaching hospital
		n (%)	n (%)
Total prescribing occasions		30311 (100)	35534 (100)
ANTIBACTERIALS FOR SYSTEMIC USE; J01		25867 (85.3)	35427 (99.7)
Tetracyclines; J01A	Tetracyclines; J01AA	2235 (7.4)	94 (0.2)
Amphenicols; J01B	Amphenicols; J01BA	40 (0.1)	0 (0.0)
β- lactam antibiotics, penicillin; J01C		3100 (10.2)	3268 (9.8)
	Penicillins with extended spectrum; J01CA	778 (2.6)	808 (2.3)
	Beta-lactamase sensitive penicillins; J01CE	3 (0.0)	18 (0.0)
	Beta-lactamase inhibitors; J01CG	5 (0.0)	2 (0.0)
	Combination of penicillin including beta lactamase antibiotics; J01CR	2314 (7.6)	2440 (7.4)
Other beta lactam; J01D		4333 (14.3)	11929 (33.3)
	1st generation Cephalosporins; J01DB	645 (2.1)	135 (0.4)
	2nd generation Cephalosporins; J01DC	2 (0.0)	516 (1.4)
	3rd generation Cephalosporins; J01DD	3686 (12.2)	11174 (31.3)
	Fourth-generation Cephalosporins; J01DE	0 (0.0)	51 (0.1)
	Carbapenems J01DH	0 (0.0)	53 (0.1)
Sulfonamide with Trimethoprim; J01E	Combination of Sulfonamide with Trimethoprim; J01EE	928 (3.1)	6 (0.01)
Macrolides, lincosamides; J01F		842 (2.8)	150 (0.6)
	Macrolides; J01FA	58 (0.2)	78 (0.3)
	Lincosamides; J01FF	784 (2.6)	72 (0.3)
Aminoglycoside; J01G		4068 (13.4)	3484 (10.2)
	Streptomycin; J01GA	212 (0.7)	4 (0.0)
	Other Aminoglycosides; J01GB	3856 (12.7)	3480 (10.2)
Quinolones; J01M	Fluoroquinolones; J01MA	6887 (22.7)	4156 (11.7)
Combination of antibiotics; *J01R	Combination of Antibiotics; *J01RA	1194 (3.9)	9084 (25.1)
Other antibiotics; J01X		2240 (7.4)	3256 (8.8)
	Glycopeptide antibacterials; J01XA	6 (0.0)	16 (0.0)
	Imidazole derivatives; J01XD	2216 (7.3)	3173 (8.6)
	Nitrofurantoin; J01XE	18 (0.1)	5 (0.0)
	Other antibacterials; J01XX	0 (0.0)	62 (0.2)
DRUGS FOR TREATMENT OF TUBERCULOSIS; J04		2257 (7.5)	7 (0.02)
Drugs for treatment of Tuberculosis; J04A			
	Antibiotics; J04AB	574 (1.9)	7 (0.02)
	Hydrazides; J04AC	570 (1.9)	0 (0.0)
	Other drugs for treatment of tuberculosis; J04AK	1113 (3.7)	0 (0.0)
AGENTS AGAINST AMOEBIASIS & OTHER PROTOZOAL DISEASES P01;		2187 (7.2)	100 (0.3)
Agents against amoebiasis & protozoal diseases; P01A			
	Nitroimidazole derivatives; P01AB	2187 (7.2)	95 (0.3)
	Other agents against amoebiasis & other protozoal diseases; P01AX	0 (0.0)	5 (0.01)

n (%): Absolute number of prescribing occasions (percentage of total prescribing occasions).

Sharma, M., Eriksson, B., Marrone, G. et al. Antibiotic prescribing in two private sector hospitals; one teaching and one non-teaching: A cross-sectional study in Ujjain, India. *BMC Infect Dis* 12, 155 (2012)

It is important to monitor consumption patterns in the case of antimicrobials because this is a useful way to identify the reasons behind misuse. For example, the study shown in this slide was carried out to compare teaching and nonteaching hospitals in the same district of India.

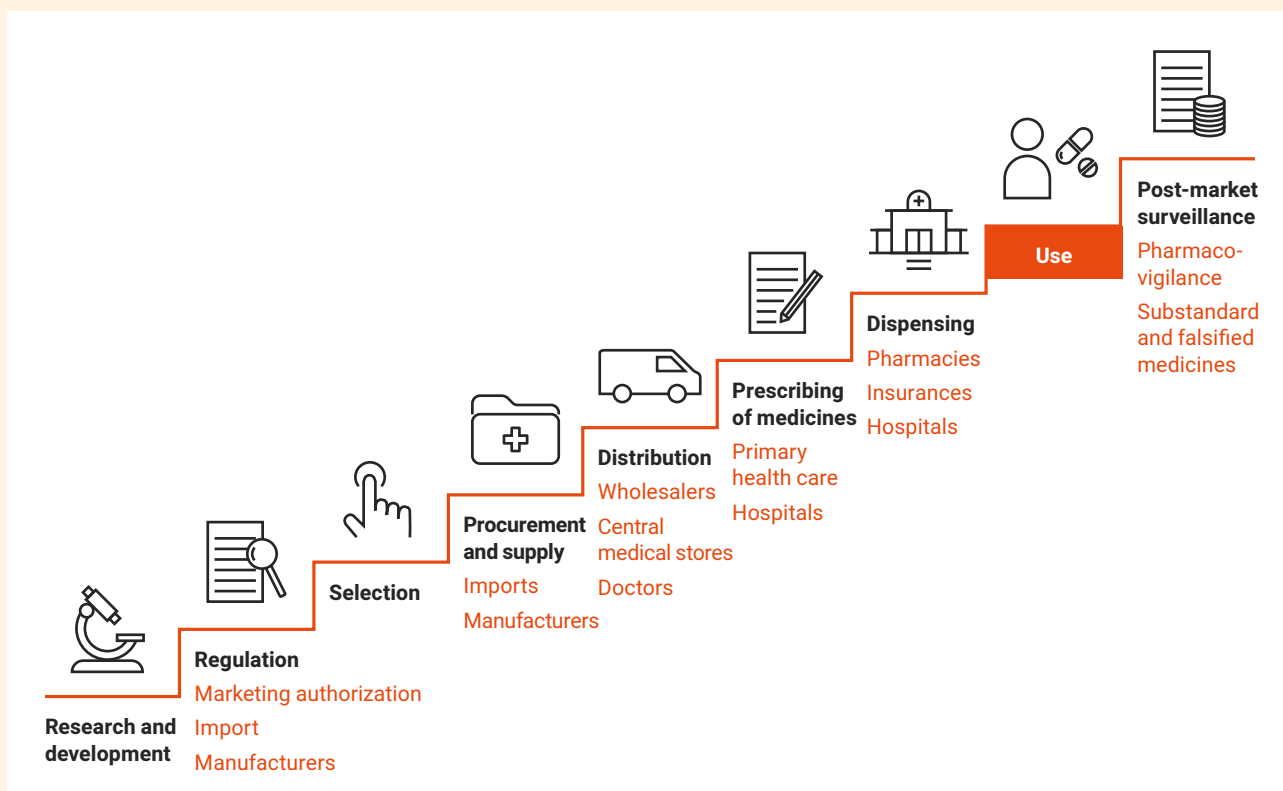
As an example, let’s look at the red line: 25% of the anti-infectives consumed in nonteaching hospitals were products belonging to the “combination of antibiotics”, whereas the consumption in teaching hospitals was just 4%. This is a big difference in consumption.



The point is that the products included under this category are fixed-dose combinations of two antimicrobials (or one antimicrobial plus another active ingredient). These continue to be used and prescribed even though there is poor evidence of efficacy, and they are not in therapeutic guidelines or recommendations.

Probably there are differences in the training, access to information and use of guidelines among different health care settings. Nevertheless, it is worth reflecting on this statement:

A fixed-dose combination that is not recommended can be prescribed or used because it has received marketing authorization.



In other words, the problem of inadequate use of antimicrobials can be explained by failures at different levels of the life cycle of medicines – the actors and processes involved in the use of medicines, from their marketing authorization to final use by the population, not forgetting promotion, prescription and dispensing processes.

These many potential problems mean that it is vital to monitor the consumption of antimicrobials in any country. Monitoring helps to identify overuse or inappropriate use, so that we can design appropriate interventions to improve antimicrobial use, and thus help to reduce resistances.

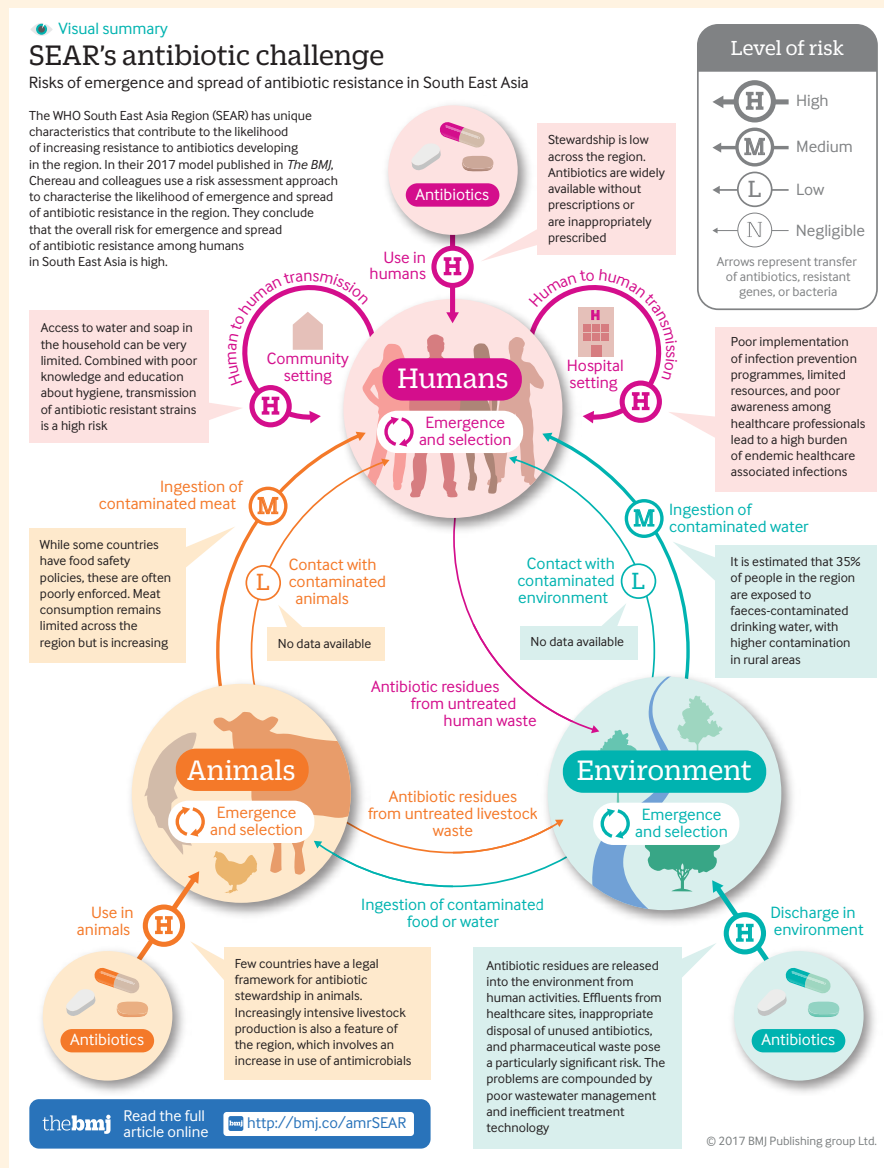
We have looked at how microorganisms develop resistance to antimicrobials, the severe consequences of the growing resistance rates at a global scale, and one of the main causes of this disaster: inappropriate use of antimicrobials. Overuse of antimicrobials happens not just in humans, but also in livestock or agriculture; in addition, antimicrobials can be present in fresh-water sources.

 **Exercise 1.2**

Fig. 1.3 was produced by the WHO South-East Asia Region. It summarizes the complexity of the AMR situation, and highlights the connection between the use and presence of antimicrobials in different sectors, as well as the importance of water and environment as a global connector (19).

You can download the figure at 1.3.4Exercise-01. Study the figure, then take Quiz 1.3.

Fig. 1.3. WHO South-East Asia Region’s antibiotic challenge



Source: Chereau et al. (2017) (19).



Quiz 1.3

Taking into account the messages depicted in Fig. 1.3, please indicate which of the following are considered **high-risk** situations for the emergence and spread of AMR according to current evidence.

NO.	QUESTION	YES OR NO?
1	Contact with contaminated animals	
2	Human-to-human transmission of antimicrobial-resistant strains	
3	Ingestion of contaminated water	
4	Release of antimicrobials into the environment from human activities	
5	Availability of antimicrobials without prescription	

AMR threatens the very core of modern medicine and the sustainability of an effective global public health response to the enduring threat from infectious diseases. Effective antimicrobial drugs are prerequisites for both preventive and curative measures; they protect patients from potentially fatal diseases, and ensure that complex procedures, such as surgery and chemotherapy, can be provided at low risk. Yet systematic misuse and overuse of these medicines in human medicine and food production have put every nation at risk. Unfortunately, few replacement products are in the pipeline. Without harmonized and immediate action on a global scale, experts say that the world is heading towards a post-antimicrobial era in which common infections could once again kill.

1.3.5 The Global Action Plan on AMR

The complexity of the emergence and spread of AMR at a global scale, and the need for urgent action, required collaboration among relevant sectors: human health, animal health and agriculture. Hence, a tripartite collaboration was agreed by the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE) and WHO.

In response, the Global Action Plan (GAP) on AMR was adopted by the World Health Assembly in 2015 (20). It reflected the global consensus that AMR poses a profound threat to human health and included clear objectives and a series of potential measures to attain these objectives. Those measures required actions at different levels: individual Member States, international bodies and the WHO Secretariat.

The five strategic objectives of the GAP-AMR are as follows:

1. Improve awareness and understanding of AMR through effective communication, education and training.
2. Strengthen the knowledge and evidence base through surveillance research.
3. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures.
4. Optimize the use of antimicrobial medicines in human and animal health.
5. Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

In September 2016, global leaders met at the United Nations (UN) General Assembly in New York to commit to fighting AMR together. This was only the fourth time in the history of the UN that a health topic was discussed at the General Assembly (the other topics were HIV, noncommunicable diseases and Ebola). Heads of state and heads of delegations addressed the seriousness and scope of the situation, and agreed on sustainable, multisectoral approaches to face AMR.



Supplementary reading 1.2

If you are interested, you can read:

- the GAP-AMR document that was endorsed by Member States in 2015 (20); and
- the 2-year progress report on the GAP-AMR (21): (reference: 1.3.5Reading-01).



Supplementary video 1.5

If you wish, you can also watch this video, recorded during the 2016 World Health Assembly in Geneva, in which Dr Keiji Fukuda talks about AMR and the AMR-GAP.

Video 1.5: https://youtu.be/PI4e2_HOzcs (22)



1.3.6 Rationale for monitoring antimicrobial use and consumption

The **second strategic objective of the GAP-AMR** is to strengthen the knowledge and evidence base through surveillance research. To meet this objective, it is necessary to design ways to monitor the consumption of antimicrobials. WHO proposed a methodology for AMC surveillance, and this is described in detail in the later modules.

Data on the consumption of antimicrobials can be used to:

- identify and provide early warning of problems relating to changes in exposure and use, and to develop interventions to address the problems identified;
- monitor the outcomes of interventions aimed at changing exposure;
- assess the quality of prescribing against practice guidelines;
- relate exposure to antimicrobials for the development of AMR; and
- raise awareness among health professionals, consumers and policy-makers about the issues of AMR and how inappropriate use of antimicrobials in humans contributes to resistance.

The lecture highlighted the significance of optimal prescribing, dispensing and use habits for antimicrobials as an important way to reduce AMR. However, in many countries there is an opposite challenge to that of overuse of antimicrobials, and that is poor access to essential antimicrobials. This problem occurs where there are limited resources, particularly in some areas (e.g. rural or conflict zones) or population groups.

Thus, to be able to design interventions for optimal use of antimicrobials, we need to know details such as the:

- total or absolute consumption of antimicrobials;
- pattern of consumption of antimicrobials (relative consumption);
- degree of consumption of second-line and reserve or restricted antimicrobials; and
- consumption tendencies of broad-spectrum or parenteral antimicrobials.

In Section 1.2, we briefly described the different antimicrobials according to their mechanism of action and chemical structure. In addition to these classifications, there are some terms that are employed to classify antimicrobials according to their use. These terms, discussed below, are useful for monitoring AMC and interpreting proportional consumption patterns.

First-line and second-line antimicrobials

For any specific infection, there are particular antimicrobials that are recommended for common use based on current microbiological evidence, availability and cost. These are the “**first-line**” antimicrobials and they usually appear as the first option in clinical guidelines. There will be other antimicrobials that are also useful for each specific infection but are not the first to be prescribed – these “**second-line**” antimicrobials are generally recommended in case of therapeutic failure of the first-line options. The general recommendation is to keep these antimicrobials as the second line of defence, just in case of ineffectiveness of the first-line antimicrobials. Each specific infection has its first-line and second-line antimicrobials, and the label of the antimicrobial may differ, depending on which disease it is being used to treat.

Access, Watch and Reserve antibiotics

Another recent categorization for antibiotics takes into account the need to reduce the development of drug-resistant bacteria, and preserve the effectiveness of “last-resort” antibiotics (i.e. those that are used when all others fail). In developing the 2017 Essential Medicines List, WHO experts grouped antimicrobials into three categories – **Access**, **Watch** and **Reserve** (AWaRe). The aim of this categorization was to emphasize the importance of the optimal use of antibiotics, and the potential for AMR. WHO has made recommendations on when each category of antibiotics should be used, to address the diverse challenges of overuse of antibiotics on one hand and poor access to essential antibiotics on the other hand.

WHO recommends that antibiotics in the *Access* group be available at all times, as treatments for a wide range of common infections. For example, this group includes amoxicillin, an antibiotic that is widely used to treat infections such as pneumonia.

The *Watch* group includes antibiotics that are recommended as first-line or second-line treatments for a small number of infections. The aim here is to reduce overuse to avoid further development of resistance. One example of an antibiotic in the Watch group is ciprofloxacin, which is used to treat the urinary tract infection cystitis and upper respiratory tract infections (e.g. bacterial sinusitis and bacterial bronchitis); use of this antibiotic should be dramatically reduced.

The *Reserve* group includes antibiotics such as colistin and some cephalosporins; these antibiotics should be considered last-resort options, and used only in the most severe circumstances when all other treatment options have failed (e.g. for life-threatening infections due to multidrug-resistant bacteria).

Since its inception, the AWaRe classification has been revised and more agents have been classified.



Reading 1.2

The following overview gives more information on the AWaRe classification 2021:

Reading 1: [1.3.6Reading-01](#).

The AWaRe website link is: <https://adoptaware.org>

Section 1.4 introduces the proposed methodology for AMC monitoring by WHO. This methodology was developed to provide information on the use of antimicrobials in all countries.



Exercise 1.3 – a reflection

Note: This is a reflection exercise, not an evaluative one. Please consider it as an invitation to think about antimicrobials and the difficulties of obtaining some of the relevant data. At the end of the present training you will have enough information to answer all the questions that you will find in the reflection exercises.

So far, this module has described different antimicrobials, and highlighted the importance of AMR and the role of AMC in the development of AMR. For this exercise, think about the medicines market in your country – specifically, about those products containing antimicrobials. Perhaps this information is public and accessible in your country; if this is the case, congratulations! Clear, current and easily accessible information on the medicines that are authorized is the first of the many steps for their optimal use.

Which of the following questions regarding your own country could you easily answer?

NO.	QUESTION	COULD YOU EASILY ANSWER THIS QUESTION?	
		YES	NO
1	How many different antibacterial agents are marketed in your country?		
2	How many pharmaceutical products including at least an antibacterial are currently authorized in your country?		
3	How many products including an antimicrobial agent combined with another medicine are currently marketed in your country?		
4	How many people in your country receive an antimicrobial each day?		
5	Which is the antimicrobial most used in your country?		
6	Is the use of “reserve” or restricted antimicrobials increasing in your country?		

1.4 WHO GLASS methodology for surveillance of national antimicrobial consumption

This section gives an overview of the WHO GLASS methodology for monitoring AMC and its objectives; details of the methodology are given in Modules 2–5. Before reading this section, we suggest that you return to the impressions and ideas that you wrote during the reflection in Exercise 1.3. This section will provide some additional questions for you to think about.

As outlined in Section 1.3.5, the second strategic objective of the GAP-AMR proposed surveillance and research on AMC, and the fourth proposed to “optimize the use of antimicrobial medicines in human and animal health”. Hence, the plan asks Member States to provide “stewardship programmes that monitor and promote optimization of antimicrobial use at national and local levels in accordance with international standards in order to ensure the correct choice of medicine at the right dose on the basis of evidence”.

Monitoring AMC is an important element of the GAP-AMR. All countries have some data related to the importation, procurement, distribution or clinical use of antimicrobials in their countries that can be used as the basis of stewardship and monitoring programmes. Many high-income and middle-income countries collect and analyse data on antimicrobial use, and the OIE is developing a database on antimicrobial use in animals. In 2018, WHO published the *WHO report on surveillance of antibiotic consumption*, which included AMC data from 64 countries, as a result of the early implementation of WHO’s surveillance programme on AMC. That programme will help to attain the strategic objectives of the GAP-AMR, especially the second and fourth objectives.

The next two sections briefly describe the objectives of the WHO AMC monitoring programme and explain the difference between antimicrobial use and consumption.

1.4.1 Objectives of WHO surveillance of AMC

The document *WHO GLASS methodology for surveillance of national antimicrobial consumption* forms the basis of this course. In Modules 2–5 we will be working on different aspects of this document, so it will be helpful to understand the background to the described methodology, and its main objectives.

Aims and objectives

Read the text in Box 1.1 to understand the aim and objectives of the WHO GLASS methodology (the text is Section 2.2 of the *GLASS methodology for surveillance of national antimicrobial consumption*) (11), and you can find the full document online: <https://www.who.int/publications/i/item/9789240012639>

Box 1.1

2.2. Aim and objectives of GLASS-AMC

2.2.1. Aim

The aim of the GLASS component on surveillance of national AMC (GLASS-AMC) is to provide a common and standardized methodology for measuring and reporting the consumption of antimicrobial agents at country level. This standardization allows the monitoring of trends over time, facilitates comparisons between countries, and provides a common metric for reporting antimicrobial use at regional and global levels.

The surveillance of AMC is a key to inform strategies to optimize the use of antimicrobials. AMC data can indicate the availability and affordability of antimicrobial agents, and in conjunction with other data, such as AMR data, inform the development of clinical guidelines and protocols, as well as restrictions on use of agents for particular clinical conditions or to nominated prescribers. These steps, which are necessary to ensure optimal use of antimicrobials, are beyond the scope of this document.

2.2.2. Objectives

The specific objectives of the surveillance of national AMC are to provide:

- a methodology that can be integrated in the package of tools to assist the national strategy on optimising the use of antimicrobials (e.g. national action plans on AMR);
- information on quantities and types of consumed antimicrobials for policy-makers and prescribers;
- a common methodology to the countries for collecting, analysing and reporting national antimicrobial consumption data;
- reliable and comparable national consumption data over time and between countries;
- a methodology for collecting global antimicrobial consumption data as part of GLASS;
- comparable consumption data with animal and agricultural consumption data.

A webpage – *Global Antimicrobial Resistance and Use Surveillance System (GLASS)* – provides links to other documents relevant to surveillance: <https://www.who.int/initiatives/glass> (23).

1.4.2 Antimicrobial use versus consumption

Once you know the framework and main objectives of the proposed GLASS methodology for AMC surveillance, establishing a few common definitions will help to ensure the accurate use of the methodology.

Lecture 1.1 (in Section 1.3.4) commented on the differences between prescription, dispensing, consumption, sales and purchase of medicines. See the proposed definitions in Reading.

Definitions

Box 1.2 provides the definitions proposed in the original GLASS document. It is Section 3.1 of the *GLASS methodology for surveillance of national antimicrobial consumption* (11).

Box 1.2

3.1. Definitions

For the purpose of the protocol presented, the following definitions apply:

- **Antimicrobial consumption (AMC) data** refer to estimates derived from aggregated data sources such as import or wholesaler data, or aggregated health insurance data, which provide no information available on the patients who receive the medicines or why the antimicrobials are being used. These data sources provide a proxy estimate of use of antimicrobials. Consumption data may be presented as total consumption for a country or may be disaggregated by health care setting (community or hospital, and public or private sectors).
- **Antimicrobial use data** refer to estimates derived from patient-level data. These data may allow disaggregation based on patient characteristics (e.g. gender and age), or indication for which the medicine is being used. Depending on the source of information, it may be possible to determine the patients' symptoms, physician diagnoses and medications ordered. This will facilitate assessment of clinical practice against agreed protocols and treatment guidelines.

Measuring consumption data is an important starting point for countries with limited experience in data collection. With experience and as data sources become more sophisticated (e.g. e-prescribing records), it is expected that there will be more emphasis on measuring antimicrobial use.

Data on AMC provide information on which antimicrobials are used and in what quantities and allow for the assessment of trends over time. The WHO protocol refers to the surveillance of AMC, which is the subject of interest of these training materials. As mentioned, data on AMC do not provide information on why and how antimicrobials are used; obtaining such information requires data on the prescription, dispensing and use of antimicrobials at the patient level. Thus, WHO has developed tools, such as point prevalence surveys (PPS), to support countries to monitor the use of antimicrobials in hospitals. This methodology is described in the 2019 document *WHO methodology for point prevalence survey on antibiotic use in hospitals. Version 1.1 (24)*.

Having completed the main sections of this module, you should now have a clear understanding of the proposed WHO methodology for monitoring AMC. To complete the module, read the key messages and use the final quiz, Quiz 1.4, to check your understanding of the content of this module.

1.5 Key messages

- AMR threatens the effective prevention and treatment of an ever-increasing range of microbial infections.
- Many antimicrobials are no longer effective to treat common infections, and this seriously compromises the prevention and management of some infections, especially those appearing in patients who are hospitalized or frail.
- Overuse or inappropriate use of antimicrobials is one of the main causes of AMR worldwide.
- The threat of AMR means that it is vital to monitor AMC at all levels (local, national and regional).

1.6 Self-evaluation

Take Quiz 1.4 to check what you have learned in this module.



Quiz 1.4

This quiz has 10 statements and asks you to decide whether they are true or false. Once you have chosen your answers, you will find out your score and, if you chose the wrong answer, you will receive some feedback. At the end, you will have the opportunity to retake the quiz.

NO.	QUESTION	TRUE OR FALSE?
1	Use of antibiotics in nonbacterial infections does not contribute to AMR because the patient does not have any bacteria.	
2	There is much evidence to show that overconsumption of antimicrobials is associated with increasing resistance of microorganisms to those medicines.	
3	One of the objectives of the GAP-AMR is to strengthen knowledge about AMR and the evidence base on AMR through surveillance research.	
4	The most accurate method for determining the exposure of patients to antimicrobials in a given country is to analyse data on the antimicrobial purchases by the country's ministry of health.	
5	The WHO programme on surveillance of AMC is a global programme for the collection and reporting of data on AMC in humans at country, regional and global level.	
6	Unfortunately, data on AMC cannot identify and provide early warning of problems relating to changes in exposure and use.	
7	Data on AMC are useful to monitor the outcomes of interventions aimed at changing exposure.	
8	The aim of the WHO protocol presented here is to provide some ideas that each country can adapt to monitor their AMC for their own use.	
9	The provided methodology can be integrated into the national programme on surveillance of antimicrobial use. The data obtained will be useful for analysing time trends and detecting warnings related to the use of specific antimicrobials.	
10	According to the protocol, "consumption" data are estimates derived from aggregated data sources (e.g. import or wholesaler data, or aggregated health insurance data).	

Congratulations! You have reached the end of the first module of this training, which covered the basics of antimicrobials, AMR and the reasons for monitoring AMC. The remaining modules will allow you to become familiar with and able to use the WHO methodology for surveillance of AMC:

- **Module 2** gives you the opportunity to review and familiarize yourself with the WHO methodology for measuring consumption of antimicrobials, the Anatomical Therapeutic Chemical (ATC) classification system for medicines and the Defined Daily Dose metrics.
- **Module 3** describes a national surveillance system for AMC and how it is possible to set up the surveillance infrastructure.
- **Module 4** describes different data sources for AMC, outlining their strengths and weaknesses.
- **Module 5** describes WHO variables that are used to calculate antimicrobial consumption.

1.7 Exercise solutions and feedback

Answers to Quiz 1.1 (in Section 1.3.2)

The main result of resistance to antimicrobials is that medicines become ineffective and infections persist in the body, increasing the risk that infections will spread to others.

NO.	QUESTION	TRUE OR FALSE?	FEEDBACK
1	The main result of resistance to antimicrobials is that medicines become ineffective and infections persist in the body, increasing the risk that infections will spread to others.	True	Correct. Well done!
		False	Wrong. When bacteria become resistant to a given antimicrobial, this means that antimicrobial is no longer able to kill the bacteria, so the infection persists. Additional antimicrobials should be prescribed. The resistant bacteria can spread to other people.

Resistance to antimicrobials has different consequences, depending on the microorganism involved. Connect the right answers:

MICROORGANISM	WHICH DISEASE DOES IT CAUSE?	TO WHICH ANTIMICROBIAL IS IT INCREASINGLY BECOMING RESISTANT?
<i>Neisseria gonorrhoeae</i>	Gonorrhoea	Third-generation cephalosporin
<i>Klebsiella pneumoniae</i>	Hospital-acquired pneumonia, sepsis, etc.	Carbapenem
<i>Escherichia coli</i>	Urinary infections	Fluoroquinolones

If you made a wrong connection, please read the document again and try to find the right answer in the text.

Answers to Quiz 1.2 (in Section 1.3.3)

Which of the following factors contribute to the development and transmission of resistance to antimicrobials?

FACTOR	ANSWER AND FEEDBACK	
Overprescription of antimicrobials	Correct.	<p>Antimicrobials should be prescribed and used when indicated, in patients with infections sensitive to the prescribed antimicrobial. Empirical use of antimicrobials is possible when the involved agent or its susceptibility is not known, but there are well-defined rules for this approach.</p> <p>Prophylaxis with antimicrobials is also well defined in practice guidelines. It is important to follow those guidelines, to avoid unnecessary exposure to antimicrobials.</p>
Hand washing before and after being in contact with a patient	Incorrect.	<p>Hand washing is a useful practice that reduces the transmission of microorganisms and infections, but it does not contribute to resistance.</p>
Use of antibacterial products in nonbacterial infections	Correct.	<p>Fever and respiratory symptoms are common in some infections produced by viruses, but antibiotics are not useful for killing viruses. Usually, a good clinical diagnosis can identify whether an infection is being produced by a virus or bacteria. In some specific patients, the prophylactic use of antibiotics in viral infections can be useful to avoid secondary bacterial infections, but the systematic prescription of antibiotics in viral infections is unnecessary and increases the chance of resistance developing.</p>
Noncompliance by patients	Correct.	<p>Some patients feel better or present an improvement in symptoms soon after beginning an antimicrobial treatment, but this does not always mean that the infection is completely gone. Stopping a course of treatment early can lead to resistance.</p> <p>Supplementary reading: https://www.who.int/features/qa/stopping-antibiotic-treatment/en/</p>
Weak hospital management practices	Correct.	<p>Appropriate hospital management practices – including hand washing, availability of soap and antiseptics, and isolation practices – help to reduce the risk of in-hospital infections. Additionally, involving microbiologists, infectious disease specialists, pharmacologists and pharmacists help to improve the selection and use of antimicrobials, and thus reduce the emergence of resistance.</p>
Prescribing antimicrobials after looking at the results of the susceptibility tests	Incorrect.	<p>Prescribing antimicrobials after looking at the results of susceptibility tests (when available) is the best way to select the most appropriate antimicrobial for a specific patient.</p>

Answers to Quiz 1.3 (in Section 1.3.4)

Taking into account the messages depicted in Fig. 1.3, please indicate which of the following are considered high-risk situations for the emergence and spread of AMR according to current evidence.

SITUATION OR ACTION	ANSWER AND FEEDBACK	
Contact with contaminated animals	Incorrect.	According to current information, this is a low-risk situation.
Human-to-human transmission of antimicrobial-resistant strains	Correct.	Resistant strains can be transmitted from a patient to another person in community and hospital settings, and in the household. Education about hygiene, access to soap, and antimicrobial stewardship programmes help to reduce this risk.
Ingestion of contaminated water	Incorrect.	The ingestion of contaminated water has a medium risk of transferring bacteria. However, purification of drinking-water is key to avoiding infections due to faecal contamination.
Release of antimicrobials into the environment from human activities	Correct.	Discharge of antimicrobials into the environment due to effluents from health care sites or inappropriate disposal of unused antimicrobials pose a significant risk.
Availability of antibiotics without prescription	Correct.	In many countries, antibiotics can be easily obtained without prescription, despite this practice being banned. This is a high-risk practice that significantly contributes to the increased occurrence of antimicrobial-resistant strains.

Answers to Quiz 1.4 (in Section 1.6)

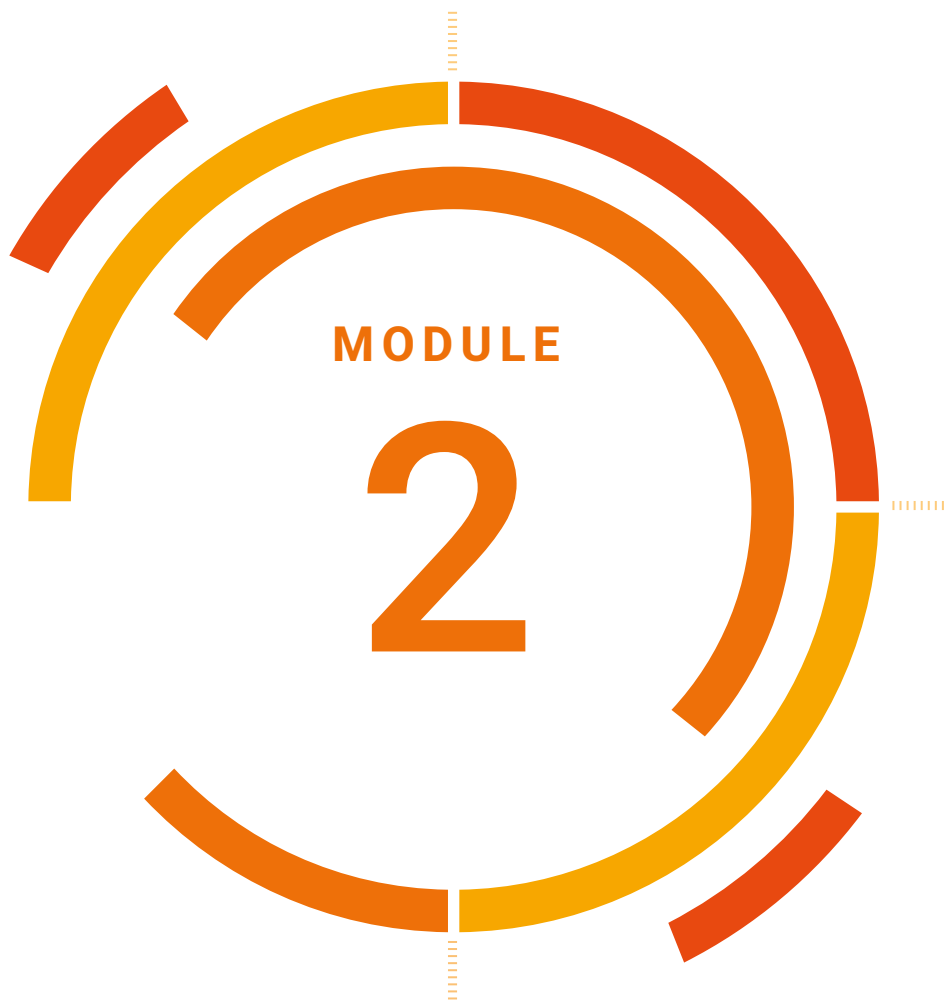
NO.	STATEMENT	TRUE OR FALSE?	FEEDBACK IN CASE OF WRONG ANSWER
1	Use of antibiotics in nonbacterial infections does not contribute to bacterial resistance because the patient does not have any bacteria.	False	Please reconsider your answer. The point is that patients treated with an antibiotic, despite having a viral infection, are actually being exposed to the antibiotic, their intestinal flora is unnecessarily under the effects of those antibiotics, and the active ingredients are metabolized and excreted, thus reaching the environment. So, there are opportunities for developing AMR.
2	There is much evidence to show that overconsumption of antimicrobials is associated with increasing resistance of microorganisms to those medicines.	True	Please reconsider your answer. As explained in Lecture 1.1 and Exercise 1.2, many published studies have shown clear evidence of the connection between AMC and increased resistance.
3	One of the objectives of the GAP-AMR is to strengthen knowledge about AMR and the evidence base on AMR through surveillance research.	True	Please reconsider your answer. It would be useful to revise the five strategic objectives of the GAP-AMR (Section 1.3.5).
4	The most accurate method for determining the exposure of patients to antimicrobials in a given country is to analyse data on the antimicrobial purchases by the country's ministry of health.	False	Please reconsider your answer. Did you notice the word "accurate" in the statement? The most accurate method for determining the exposure to antimicrobials in any population would be to record all patients who have actually ingested a product containing an antimicrobial. This is obviously impossible at large scale, which is why other less accurate but more feasible methods are used to monitor AMC at country level. Such methods include the analysis of bulk purchases by the health ministry or large public health care insurers.

NO.	STATEMENT	TRUE OR FALSE?	FEEDBACK IN CASE OF WRONG ANSWER
5	The WHO programme on surveillance of AMC is a global programme for the collection and reporting of data on AMC in humans at country, regional and global level.	True	Please reconsider your answer. It might be useful to review the information in Box 1.1, in Section 1.4.1.
6	Unfortunately, data on AMC cannot identify and provide early warning of problems relating to changes in exposure and use.	False	Please reconsider your answer. As stated in Section 1.3.6, data on AMC can be used to identify and provide early warning of those problems.
7	Data on AMC are useful to monitor the outcomes of interventions aimed at changing exposure.	True	Please reconsider your answer. Please review the bullet list in Section 1.3.6.
8	The aim of the WHO protocol presented here is to provide some ideas that each country can adapt to monitor their AMC for their own use.	False	Please reconsider your answer. The WHO protocol aims to provide a common methodology for the measurement of AMC that will allow monitoring trends over time, not only at national level, but also at regional and global level.
9	The provided methodology can be integrated into the national programme on surveillance of antimicrobial use. The data obtained will be useful for analysing time trends and detecting warnings related to the use of specific antimicrobials.	True	Please reconsider your answer. It might be useful to review the text in Box 1.1 (in Section 1.4.1).
10	According to the protocol, "consumption" data are estimates derived from aggregated data sources (e.g. import or wholesaler data, or aggregated health insurance data).	True	Please reconsider your answer. You may find it useful to review the definitions of "consumption" and "use" data; for example, consumption data, as defined in Box 1.2 (in Section 1.4.2) are a proxy estimate of the actual use of antimicrobials.

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GLASS methodology for surveillance of antimicrobial consumption

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2.1 Training objectives of Module 2

The objectives of this module are to ensure that you:

- understand the theoretical basis of the Anatomical Therapeutic Chemical and Defined Daily Dose (ATC/DDD) system;
- can use the ATC/DDD system, taking into account different situations; and
- can interpret consumption data expressed as DDD/1000 inhabitants/day.

2.2 Background

In studies of the use of medicines (known as drug utilization research, DUR), a common standard classification system is needed, to ensure that studies carried out in different places take into consideration the same active ingredients. To “measure” medicines consumed, you could count tablets or boxes. But even where you agree to count “boxes” or “packages”, there is a problem because different package sizes can be found in a given country. The same applies for counting tablets or pills, as these come in different sizes; for example, tablets may be 250 mg, 500 mg or 1 g. A common system of classification for medicines, including antimicrobials, is needed, as are standard metrics to facilitate comparisons of antimicrobial consumption (AMC) among health facilities, countries and regions.

This section describes the Anatomic Therapeutic Chemical (ATC) classification system. This system provides a global standard for the classification of medical substances and thus to ensure uniformity in DUR. In order to measure drug use, it is important to have both a classification system and a unit of measurement. This section also describes the most commonly used measure of consumption, a technical unit of measurement called the Defined Daily Dose (DDD). The purpose of the ATC/DDD system is to serve as a tool for drug utilization monitoring and research to improve quality of medicines use. One component of DUR is the presentation and comparison of drug consumption statistics at international and other levels. It is essential that a tool for drug utilization monitoring and research is able to cover most medicines available on the market. An important aim of drug utilization is to monitor rational as well as irrational drug use as an important step in improving the quality of drug use. The classification of a substance in the ATC/DDD system is therefore not a recommendation for use and it does not imply any judgements about efficacy or relative efficacy of drugs and groups of drugs.

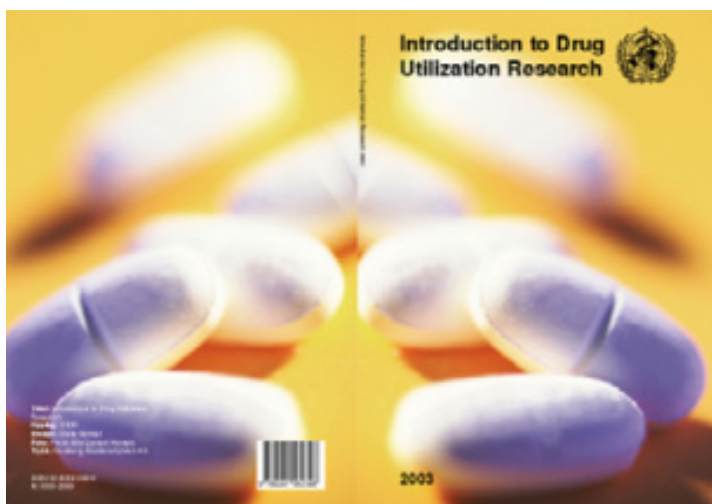
2.3 Measuring AMC – the ATC classification system

The ATC classification and the DDD measuring system are the methodological pillars for the WHO global monitoring of AMC. This module will equip you to make use of the WHO AMC methodology, by explaining these systems and providing practical examples for you to work on.

This section gives a brief historical background on the ATC classification system, uses specific examples to explain the elements of the system, uses a step-by-step example to demonstrate how to determine ATC codes, and identifies the antimicrobials included in the proposed methodology for AMC monitoring.

2.3.1 Historical background

The ATC classification was developed in Norway as a modification and extension of the European Pharmaceutical Market Research Association (EphMRA) classification system. In 1981, the ATC/DDD system was recommended by WHO as the international standard for drug utilization studies. One year later, the *WHO Collaborating Centre for Drug Statistics Methodology* was established in Oslo, Norway, and given the responsibility for coordinating the development and use of the ATC/DDD system. In 1996, the Centre was recognized as a global centre.



Reading 2.1

Chapter 5: Drug classification systems, from the 2013 WHO document *Introduction to drug utilization research* (1) explains how the ATC system came to be in use (reference: [2.3.1Reading-01](#)).



Supplementary reading 2.1

If you would like to know more about the historical background of the ATC classification system, you can also read from the website of the WHO Collaborating Centre (CC) for Drug Statistics Methodology in Oslo, Norway (2).

ATC/DDD toolkit has been recently published by WHO to provide guidance on how to set up and use the international ATC/DDD methodology. This is a comprehensive resource that will be useful if you are interested in undertaking DUR (3).

2.3.2 Understanding the elements of the ATC classification system

Watch Lecture 2.1, which uses specific examples to show how an ATC code is constructed, and what the different elements mean. The references (Section 2.8) include links that you may find it helpful to access during this lecture:

- the WHO CC in Oslo (4);
- the ATC/DDD index published by the WHO CC in Oslo (5); and
- the page from the WHO website that describes the WHO system for international nonproprietary names (INN) (6).

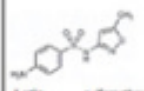
Lecture 2.1.

Measuring consumption of antimicrobial medicines

The ATC Classification System

This presentation describes the Anatomical Therapeutic Chemical classification system for medicines, commonly known as ATC classification.

We will start by defining some terms.

sulfamethoxazole	
	
Latin	sulfamethoxazolium
French	sulfaméthoxazole
Spanish	sulfametoxazol
Russian	сульфаметоксазол
Arabic	سولفاميثوكسازول
Chinese	甲氧苄啶
Phonetic	sulfamethoxazole
Molecular formula	C ₁₂ H ₁₁ N ₂ O ₂ S
ATC Code	J01EC01
Rational commission(s)	Alternate name(s)
EPC	sulphamethoxazole
DCF	sulfamethoxazole
IP	sulphamethoxazole
JAN	acetylsulfamethoxazole
JAN	sulfamethoxazole sodium
Rational commission(s) using same name	
BAI	
DNP	
CSP	
DCF	
FFUM	
JAN	
JP	
Ph. Eur.	

Active ingredient sulfamethoxazole

INN

sulfamethoxazole

The first term is “active ingredient”. An active ingredient is any component that provides pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease, or that affects the structure or any function of the body of humans or animals. An example of an active ingredient is “sulfamethoxazole”. Here, you can see that the British Pharmaceutical Codex (BPC) uses the name “sulphamethoxazole” (with a “ph”) rather than “sulfamethoxazole” (with an “f”). Both spellings designate the same active ingredient.

To avoid confusion, it is important to identify the different active ingredients in a medicine. The international nonproprietary name (or INN) is designated by WHO. Each INN is a unique name that is globally recognized and is public property.

A nonproprietary name is also known as a generic name. In most cases, the name of the active ingredient and the INN are the same; for example, this is the situation with “sulfamethoxazole”, which is both the active ingredient and the INN.

Active ingredient: amoxicillin

INN: amoxicillin

Brand name: Amoxil (example)

Fixed-dose combination: amoxicillin + clavulanic acid (e.g. Augmentin)

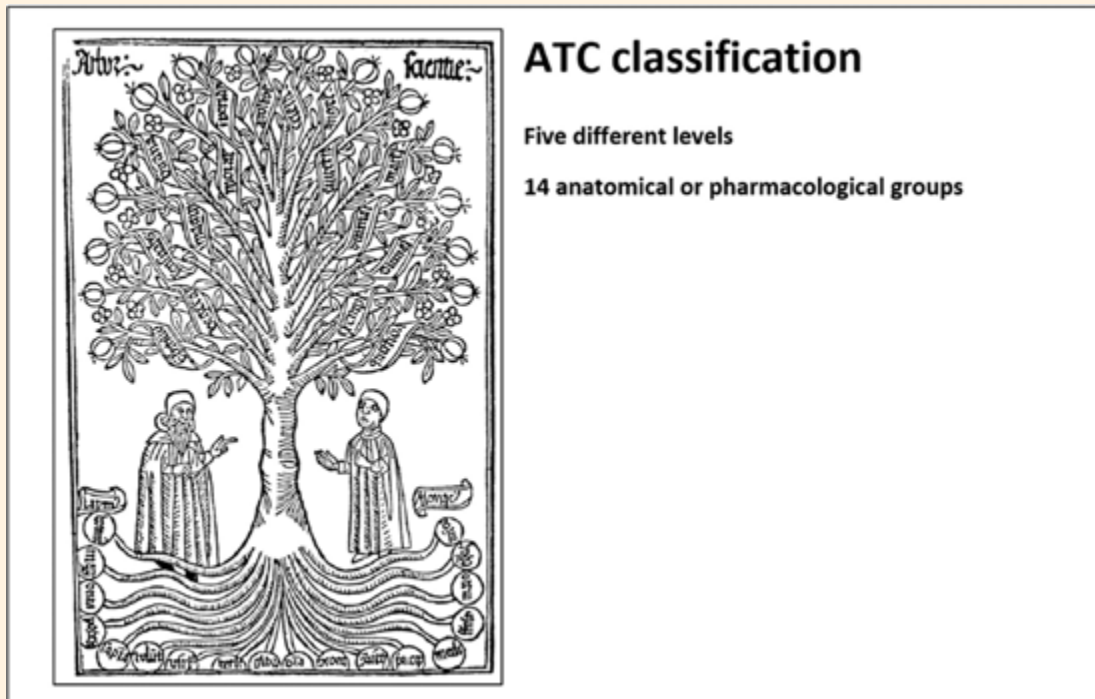
Here we will look at amoxicillin. Again, the name of the active ingredient and the INN are the same. However, we also have a “brand name”. A brand name drug is a medicine that is marketed under a proprietary name that is trademark protected. In the case of amoxicillin, the first and most well-known brand name is Amoxil. Thus, one active ingredient can have different brand names.

Also, a brand name medicine can contain more than one active ingredient. We usually refer to products with more than one active ingredient as “fixed-dose combinations” or, more simply, “combination products”. For example, a product that contains amoxicillin plus another active ingredient, clavulanic acid, is marketed under the brand name Augmentin.

The screenshot shows the website of the WHO Collaborating Centre for Drug Statistics Methodology. The header includes navigation links: Home, ATC/DDD application form, Order ATC Index, WHO Centre, Contact us, Log in, and Search. The main content area features a large orange banner with the text "International language for drug utilization research" and "ATC/DDD". Below this, it states: "The Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD) as a measuring unit have become the gold standard for international drug utilization monitoring and research." It also mentions: "The ATC/DDD system is a tool for exchanging and comparing data on drug use at international, national or local levels." A "Welcome to the WHO Collaborating Centre for Drug Statistics Methodology" message is displayed. A "Public consultation" section highlights "New classification of L01XC Monoclonal antibodies". A "News" sidebar on the right lists several articles with "Read" links, such as "New DDDs for combination products" and "Temporary ATC/DDDs including alterations from the March 2021 meeting". The footer contains contact details for the WHO Collaborating Centre for Drug Statistics Methodology, Norwegian Institute of Public Health, and a copyright notice.

Some medically active substances do not have an ATC code (for example, some old or rarely used substances). The main reason that an active ingredient lacks an ATC code is that no one has applied for a code. However, most active ingredients do have an ATC code, and for any recently marketed molecule, an expert committee of the WHO Collaborating Centre for Drug Statistics Methodology based in Oslo, in Norway, establishes that code and defines the DDD.

So, the WHO CC in Oslo not only maintains the ATC, it also constantly updates the system. The WHO CC website provides definitions of relevant terms, describes the ATC/DDD methodology in detail, and has a search function that you will find useful for identifying ATC codes and DDD values in your research.



The ATC classification system for active ingredients is a tree-like taxonomy. It divides medicines into different groups according to the organ or system on which they act (hence the “anatomical” part of the name). It then divides them according to their therapeutic properties, and finally their chemical and pharmacological properties.

The ATC classification has five different levels and divides all medicines into 14 anatomical or pharmacological groups.

General principles

- Classification is according to the main therapeutic use or pharmacological class.
- Each administration form has only one ATC code (e.g. ciprofloxacin oral and parenteral have the code J01MA02).

BUT

- More than one ATC code can be given in the case of:
 - different therapeutic uses, reflected in different routes of administration (e.g. ciprofloxacin oral has the code J01MA02, drops for conjunctivitis have the code S01AE03); and
 - different strengths.

There are several general principles to be taken into account that underpin the ATC classification and need to be understood when searching for the precise ATC code for an active ingredient.

The two most important principles are that medicines are classified according to their main therapeutic use or pharmacological class, and that each administration route of a medicine has only one ATC code.

- For example, the antimicrobial ciprofloxacin comes in two forms – for oral and parenteral administration – but these different forms have the same code (which is J01MA02).

However, more than one ATC is given in cases where there are clearly different therapeutic uses for an active ingredient, with different routes of administration.

- For example, oral ciprofloxacin has the code J01MA02, but drops of ciprofloxacin for conjunctivitis have a different code – they are classified under the code S01AE03 (where the “S” stands for sensory organs).

The screenshot shows the website interface with the WHO Collaborating Centre for Drug Statistics Methodology logo on the left and the Norwegian Institute of Public Health logo on the right. A navigation menu on the left includes 'News', 'ATC/DDD Index', 'Updates included in the ATC/DDD Index', 'ATC/DDD methodology', 'ATC', 'DDD', 'ATC/DDD alterations, cumulative lists', 'ATC/DDD Index and Guidelines', 'Use of ATC/DDD', 'Courses', 'Meetings/open session', 'Deadlines', and 'Links'. The main content area displays 'Found 3 entries containing 'vancomycin'.' with a 'New search' link. The results list three ATC codes: A07AA09, J01XA01, and S01AA28, each followed by the word 'vancomycin'. Below the list, it states 'Last updated: 2019-12-16'.

The screenshot shows the website interface with the WHO Collaborating Centre for Drug Statistics Methodology logo on the left and the Norwegian Institute of Public Health logo on the right. A navigation menu on the left includes 'News', 'ATC/DDD Index', 'Updates included in the ATC/DDD Index', 'ATC/DDD methodology', 'ATC', 'DDD', 'ATC/DDD alterations, cumulative lists', 'ATC/DDD Index and Guidelines', 'Use of ATC/DDD', 'Courses', 'Meetings/open session', 'Deadlines', and 'Links'. The main content area displays 'Found 17 entries containing 'metronidazole'.' with a 'New search' link. The results list 17 ATC codes and their corresponding drug combinations: A02BD08 (bismuth subcitrate, tetracycline and metronidazole), J01RA03 (cefuroxime and metronidazole), J01RA10 (ciprofloxacin and metronidazole), A02BD03 (lansoprazole, amoxicillin and metronidazole), A02BD02 (lansoprazole, tetracycline and metronidazole), A01AB17 (metronidazole), D06BX01 (metronidazole), G01AF01 (metronidazole), J01XD01 (metronidazole), P01AB01 (metronidazole), P01AB01 (metronidazole), P01AB01 (metronidazole), P01AB51 (metronidazole, combinations), A02BD01 (omeprazole, amoxicillin and metronidazole), A02BD11 (pantoprazole, amoxicillin, clarithromycin and metronidazole), A02BD13 (rebeprazole, amoxicillin and metronidazole), J01RA04 (spiroamycin and metronidazole), and A02BD15 (vonoprazan, amoxicillin and metronidazole). Below the list, it states 'Last updated: 2019-12-16'.

Another example is metronidazole. In the case of parenteral use (e.g. for surgical prophylaxis) it has the code J01XD01, whereas the oral or rectal route, used for trichomoniasis, is classified as P01AB01 (antiparasitic products), and the vaginal gel, used for vaginosis, is classified as G01AF01.

The case of vancomycin is also interesting: this antimicrobial is considered a second-line antibiotic, and it is used parenterally for severe infections. Its ATC code is J01XA01. However, it is also useful for some cases of colitis, where it is administered by mouth and the ATC code for this oral form is A07AA09.

ATC Main Groups	
A	•Alimentary tract and metabolism
B	•Blood and blood forming organs
C	•Cardiovascular
D	•Dermatologicals
G	•Genito-urinary system and sex hormones
H	•Systemic hormonal preparations, excluding sex hormones and insulin
J	•Anti-infectives for systemic use
L	•Antineoplastic and immunomodulating agents
M	•Musculo-skeletal system
N	•Nervous system
P	•Anti-parasitic products, insecticides and repellants
R	•Respiratory system
S	•Sensory organs
V	•Various

The 14 therapeutic groups (first-level or main anatomical groups) are designated by a single capital letter. So, “A” is for medicines acting on the alimentary tract and metabolism, “N” is for medicines acting on the central nervous system, “J” includes anti-infectives for systemic use, and so on.

LEVEL	INDICATES ...	DEFINITION
J	Anti-infectives for systemic use	Main therapeutic group
J01	Antibacterials for systemic use	Therapeutic subgroup
J01M	Quinolone antibacterials	Chemical subgroup
J01MA	Fluoroquinolones	Chemical subgroup
.J01MA02	Ciprofloxacin	Active ingredient

This example shows the rationale of the five-level structure of ATC classification. We saw previously that J01MA02 is the code for ciprofloxacin. Now we can analyse what that code means and why it is used for ciprofloxacin.

The first level is the “J”, which is the main therapeutic group; in this case, it indicates anti-infectives for systemic use.

The second level is the “01” in “J01”. This is the therapeutic subgroup, and the 01 indicates antibacterials for systemic use. This means that **antivirals** for systemic use have a different second-level code (J05, in this case).

The third level is the “M” in “J01M”. This is the chemical subgroup, and the M indicates quinolone antibacterials.

The fourth level is the “A” in “J01MA”. This is a further chemical subgroup, and the A indicates fluoroquinolones.

The final level is the “02” in “J01MA02”. This is the actual active ingredient, and the 02 indicates ciprofloxacin, which is one of the fluoroquinolones. Thus, the ATC code is J01MA02.

Each five-level code is made up of capital letters and numbers, and “0” is always zero, never the letter “O”

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD Index for J01MA02 (ciprofloxacin). The table lists various drugs in the J01MA02 subgroup, including their ATC codes, names, DDD values, and other details.

ATC code	Name	DDD	U	Adm.R.	Note
J01MA01	ofloxacin	0.4	g	O	
J01MA02	ciprofloxacin	1	g	O	
J01MA03	pefloxacin	0.8	g	P	
J01MA04	enoxacin	0.8	g	O	
J01MA05	temafloxacin	0.8	g	O	
J01MA06	norfloxacin	0.8	g	O	
J01MA07	lomefloxacin	0.4	g	O	
J01MA08	floxacin	0.4	g	O	
J01MA09	sparfloxacin	0.2	g	O	
J01MA10	rufloxacin	0.2	g	O	
J01MA11	grepafloxacin	0.4	g	O	
J01MA12	levofloxacin	0.24	g	Inhal.solution	
J01MA13	trovafloxacin	0.2	g	O	
J01MA14	moxifloxacin	0.4	g	P	
J01MA15	gemifloxacin	0.32	g	O	
J01MA16	gatifloxacin	0.4	g	O	
J01MA17	prulifloxacin	0.6	g	O	
J01MA18	pazufloxacin	1	g	P	
J01MA19	garenoxacin	0.4	g	O	
J01MA21	sitafloxacin	0.1	g	O	
J01MA22	tosufloxacin	0.45	g	O	
J01MA23	delafloxacin	0.9	g	O	

Here, we can see all the active ingredients that are currently included under the J01MA chemical subgroup. There are 22 different fluoroquinolones, with each one having a different and consecutive number. Thus, we have ofloxacin (J01MA01) as the first of the active ingredients, followed by ciprofloxacin (J01MA02), pefloxacin (J01CA03), and so on.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD Index for J01C (Beta-lactam antibiotics, penicillins). The page lists various penicillin combinations with their ATC codes, names, DDD, U, Adm.R, and Notes.

ATC code	Name	DDD	U	Adm.R	Note
J01CR01	ampicillin and beta-lactamase inhibitor	6	g	P	Refers to ampicillin
J01CR02	amoxicillin and beta-lactamase inhibitor	1.5	g	O	Refers to amoxicillin
J01CR03	ticarcillin and beta-lactamase inhibitor	3	g	P	Refers to amoxicillin
J01CR04	ticarcillin and beta-lactamase inhibitor	15	g	P	Refers to ticarcillin
J01CR05	pipracillin and beta-lactamase inhibitor	1.5	g	O	Refers to amoxicillin
J01CR50	combinations of penicillins	14	g	P	Refers to piperacillin

The page also includes a sidebar with navigation links such as 'News', 'ATC/DDD Index', 'Updates included in the ATC/DDD Index', 'ATC/DDD methodology', 'ATC', 'DDD', 'Lists of temporary ATC/DDDs and alterations', 'ATC/DDD alterations, cumulative lists', 'ATC/DDD Index and Guidelines', 'Use of ATC/DDD', 'Courses', 'Meetings/open session', 'Deadlines', and 'Links'. The main content area also features a 'List of abbreviations' and a 'Last updated: 2020-12-17' notice.

Certain ATC codes are reserved for special situations. One such situation is that of combination products.

To illustrate this, let's look again at the fixed-dose combination of amoxicillin plus clavulanic acid that we mentioned at the start of this lecture. This is a frequently used combination – the amoxicillin is a penicillin and the clavulanic acid is a beta-lactamase inhibitor.

You can see that the ATC subgroup proposed for combinations of penicillins is J01CR, and that penicillins that combine amoxicillin with a beta-lactamase inhibitor (in this case, clavulanic acid) have the ATC code J01CR02. Not shown here is that when it is used alone, amoxicillin has a different ATC code. It is still "J01", because it is a penicillin, but when used alone it has the third-level code of "CA" rather than "CR". The full ATC code for amoxicillin alone is "J01CA04".

You can also see here that combinations of two or more penicillins – with or without an enzyme inhibitor – are classified at a separate fifth level as J01CR50.

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New search Hide text from Guidelines

J ANTIINFECTIVES FOR SYSTEMIC USE

Anti-infectives are also classified in the following groups:

- A01AB Anti-infectives and antiseptics for local oral treatment
- A02BD Combinations for eradication of *Helicobacter pylori*
- A07A Intestinal anti-infectives
- D01 Antifungals for dermatological use
- D06 Antibiotics and chemotherapeutics for dermatological use
- D07C Corticosteroids, combinations with antibiotics
- D09AA Ointment dressings with anti-infectives
- D10AF Anti-infectives for treatment of acne
- G01 Gynaecological anti-infectives and antiseptics
- P Antiparasitic products, insecticides and repellents
- R02AB Antibiotics
- R05X Other cold preparations
- S01/
- S02/
- S03 Eye and ear preparations with anti-infectives

Even systemically administered antibacterials and antimycotics may be classified in other groups if their target is exclusively local, e.g. the skin - D01 - Antifungals for dermatological use

Inhaled anti-infectives are classified in J.

You can see that anti-infectives and their combinations can act on different pathologies, and that they can be classified in many different ATC groups.

As we saw earlier, one aspect of the ATC classification reflects the main anatomical location where the effect takes place. For example, we can see here that a combination for the eradication of *Helicobacter pylori* is classified under the A02BD subgroup, where the “A” is for “alimentary tract”. One combination for eradication of this microorganism would be amoxicillin + azithromycin + omeprazole.

Another example here is the G01 subgroup, where the “G” is for “gynaecological”. This subgroup combines gynaecological anti-infectives and antiseptics; for example, antibiotics combined with corticosteroids.

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New search Show text from Guidelines

J ANTIINFECTIVES FOR SYSTEMIC USE

J01 ANTBACTERIALS FOR SYSTEMIC USE

- J01A TETRACYCLINES
- J01B AMPHENICOLS
- J01C BETA-LACTAM ANTBACTERIALS, PENICILLINS
- J01D OTHER BETA-LACTAM ANTBACTERIALS
- J01E SULFONAMIDES AND TRIMETHOPRIM
- J01F MACROLIDES, LINCOSAMIDES AND STREPTOGRAMINS
- J01G AMINOGLYCOSIDE ANTBACTERIALS
- J01M QUINOLONE ANTBACTERIALS
- J01R COMBINATIONS OF ANTBACTERIALS
- J01X OTHER ANTBACTERIALS

Last updated: 2020-12-17

Lastly, let's look at another therapeutic subgroup: J01X. New medical substances that do not clearly belong to any existing fourth-level group of related substances will generally be placed in an X group; thus, the "X" denotes "other", and in the case of the J01X subgroup, it is other antibacterials. The antibacterials in this subgroup have various modes of action that do not fall within the chemical subgroups J01A to J01M.

You can see that the fourth levels go from A (the glycopeptide antibacterials) to E (the nitrofurans derivatives). A new fourth level is generally only established when at least two substances with marketing authorisations fit in the group. The J01XX group is used for new and innovative medicinal products for which there is only a single substance.

The screenshot shows the website for the WHO Collaborating Centre for Drug Statistics Methodology, specifically the ATC/DDD Index 2021 page. The page features a navigation menu at the top with links for Home, ATC/DDD application form, Order ATC Index, WHO Centre, Contact us, Log in, and Search. The main content area is titled "ATC/DDD Index 2021" and includes a search query section with input fields for "ATC code" and "name", and a "Search" button. Below the search section, there are sections for "ATC code" and "Name" with bullet points explaining search criteria. The "ATC code" section states that all ATC levels are searchable and that a search will result in showing the exact substance/level and all ATC levels above (up to 1st ATC level). The "Name" section defines "Name" as the name of the substance (normally the INN name) or the name of the ATC level, and notes that trademarks are not searchable. The "DDD" section states that DDDs will be reviewed in 2021 (3 year revision) and are listed here and in the annex I in the printed ATC Index. The page also includes a sidebar with a menu of links and contact information for the WHO Collaborating Centre for Drug Statistics Methodology, Norwegian Institute of Public Health, Oslo, Norway.

In the next section, you will have a chance to try finding ATC codes for proposed active ingredients. For that, you need to use the following link for the WHO CC ATC/DDD index and its search engine: https://www.whocc.no/atc_ddd_index/ (5).



Exercise 2.1

Using what you learned in the lecture about the ATC code structure and how to find the ATC code for any active ingredient in the ATC/DDD index (5), fill in the blanks cells in the table below.

Note that when you are entering a name into the search function of the index, you do not have to write the full name of the substance, you can write just three or four letters.

NO.	SUBSTANCE	ATC CODE
1	Levofloxacin tablets	
2		J01MA04
3	Phenoxymethylpenicillin tablets	
4	Benzathine phenoxymethylpenicillin tablets	
5	Ampicillin + sulbactam, injection	
6	Amoxicillin + esomeprazole + clarithromycin, tablets	

(Note: you will find the solutions at the end of the module.)



Reading 2.2

Now read Annex 1 of the document *GLASS methodology for surveillance of national antimicrobial consumption (7)*. The text summarizes the ATC methodology, and provides some examples and uses (reference: [2.3.2Reading-01](#)).

Having reviewed the principles of the ATC classification system, please take **Quiz 2.1** to test your understanding (you will find the solutions at the end of the module).



Quiz 2.1

This quiz has four statements and asks you to decide whether they are true or false. To do this, you will need to search in the ATC/DDD index (5).

NO.	STATEMENT	TRUE OR FALSE?
1	All antimicrobials are classified under the J therapeutic group.	
2	Medicinal products containing two or more active ingredients are considered combinations in the ATC system, and they have a different ATC code to the single components.	
3	J01R is the subgroup used to classify combinations of a systemic antibacterial with other drugs such as local anaesthetics.	
4	ATC codes are permanent over time. This allows time comparisons of AMC.	

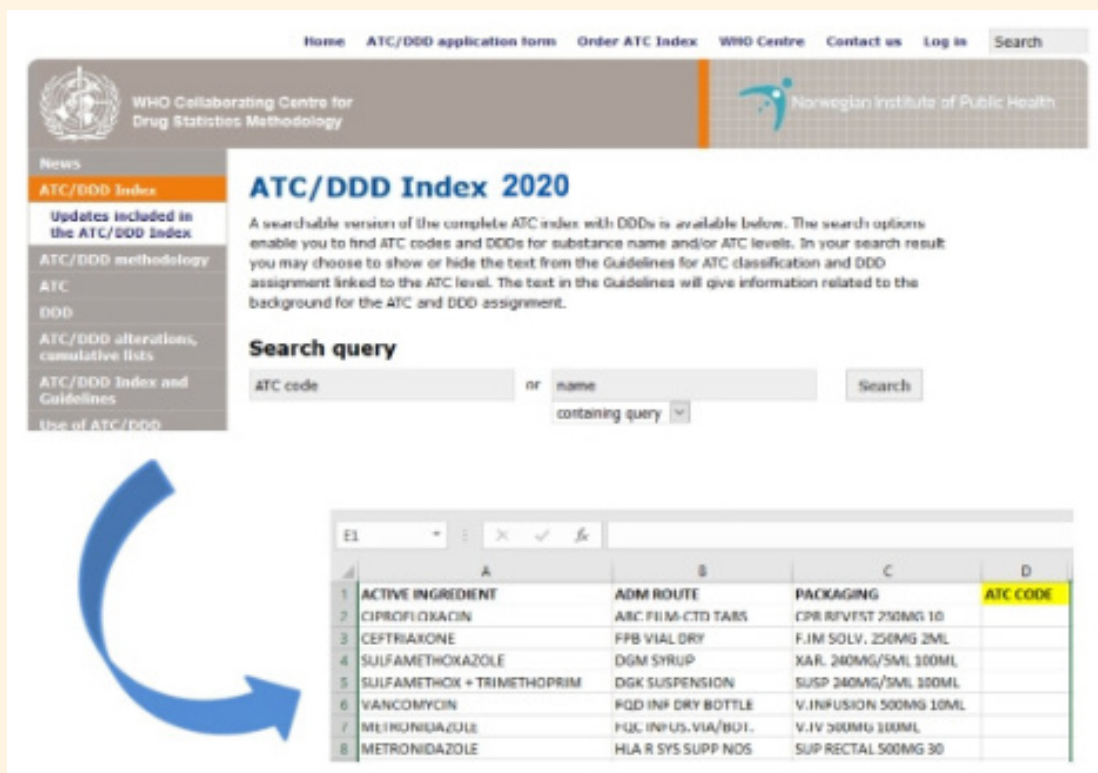
2.3.3 Step-by-step example of determining ATC codes

Next Lecture 2.2 shows how to identify the correct ATC code, and highlights practical issues in using the ATC classification system. This lecture provides practical examples; you can try to do the exercises on paper, using the ATC/DDD index (5).

Assigning an ATC code to each product or active ingredient in a consumption list is generally a straightforward part of AMC monitoring (although it can be hard if the list of medicines to be included is long).

Nevertheless, it is important not to treat this as a mechanical task, because of some of the complexities of the system; for example, the fact that a given active ingredient can appear under different ATC codes. As we will see later in this module, assigning the correct ATC code to each product is the basis for avoiding mistakes in the consumption calculation!

Lecture 2.2.



The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main heading is "ATC/DDD Index 2020". Below the heading, there is a search query form with fields for "ATC code", "name", and "containing query". A blue arrow points from the search form to a sample spreadsheet for recording consumption data.

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-COATED TABLETS	CPR RIFVST 250MG 10	
3	CEFTRIAXONE	FFB VIAL DRY	F.IM SOLV, 250MG 2ML	
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR, 240MG/5ML 100ML	
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	
6	VANCOMYCIN	PQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	
7	METRONIDAZOLE	PQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HIA R SYS SUPP NOS	SUP RECTAL 500MG 30	

In the following series of screenshots, you will have the opportunity to see examples of ATC codification being worked through step by step. The sequence is taken from routine activities that you will do many times while preparing AMC data from your country to be included in a data collection spreadsheet. Here, a sample spreadsheet for recording consumption data is used.

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	
3	CEFTRIAZONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP RECTAL 500MG 30	

First, it is important to become familiar with this screen. This Excel spreadsheet is probably similar to any Excel file containing consumption information that you will handle in the future. You can see four different columns and eight filled rows. The columns are for:

- the active ingredient name (Column A);
- the administration route (B);
- the characteristics of the packaging (C); and
- the ATC code (D).

You can see that Column D (the ATC code) is empty. In this activity, we will fill in the ATC codes for each of the seven active ingredients described in each row.

Let's begin with the first one in Row 2. It's a product containing information for the antimicrobial "ciprofloxacin" – in this case, a preparation of 10 film-coated 250 mg tablets. Column A says that it is "ciprofloxacin", Column B says that the product contains film-coated tablets (which in turn tells you that the product will be for oral use), and Column C says that each package contains 10 of these tablets, each one being 250 mg.

The Excel files containing consumption information can vary, depending on the country and the data source, but you should always identify the variables that we have just described.

Now, we can begin the process of determining the ATC code for each active ingredient.

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Postal address:
 WHO Collaborating Centre for Drug Statistics Methodology
 Norwegian Institute of Public Health
 Postboks 222 Sløyen
 0213 Oslo
 Norway

Visiting/delivery address:
 Sandakerveien 24C
 Bygg C
 0473 Oslo
 Norway

ATC/DDD Index 2021

A searchable version of the complete ATC index with DDDs is available below. The search options enable you to find ATC codes and DDDs for substance name and/or ATC levels. In your search result you may choose to show or hide the text from the Guidelines for ATC classification and DDD assignment linked to the ATC level. The text in the Guidelines will give information related to the background for the ATC and DDD assignment.

Search query

ATC code or Search
 containing query ▾

ATC code

- All ATC levels are searchable.
- A search will result in showing the exact substance/level and all ATC levels above (up to 1st ATC level).

Name

- "Name" is defined as the name of the substance (normally the INN name) or the name of the ATC level. Note that trademarks are not searchable.
- A minimum of three letters must be entered in the name box. Select a query that contain part of or a query that start with the letter entered.
- For ATC combination levels, please note that all active ingredients would normally not be searchable.

DDD

The DDDs, which will be reviewed in 2021 (3 year revision), are listed [here](#) and in the annex I in the printed ATC Index. See also [Guidelines: Part III; D Principles for reviewing and changing DDD and Part V; D Requests for changes to DDDs](#).

Go to the ATC/DDD index that you worked with in previous exercises.

In the Search query, there are fields to write the ATC code or the name of the active ingredient. In this case, type "ciprofloxacin" in the name field, then click the "Search" button. You should see the following screen ...

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New search

Found 8 entries containing 'ciprofloxacin'.

J01MA02 [ciprofloxacin](#)
 J01MA02 [ciprofloxacin](#)
 S01AE03 [ciprofloxacin](#)
 S02AA15 [ciprofloxacin](#)
 S03AA07 [ciprofloxacin](#)
 J01RA10 [ciprofloxacin and metronidazole](#)
 J01RA12 [ciprofloxacin and ornidazole](#)
 J01RA11 [ciprofloxacin and tinidazole](#)

Last updated: 2017-12-20

The screen has eight entries containing “ciprofloxacin”. These eight entries include seven different ATC codes, and it is important to work out which is the right one. To do this, we can use the information from the Excel spreadsheet. That file tells us that the product contains “ciprofloxacin” alone, so we can immediately ignore the last three entries, which are codes for ciprofloxacin combined with other active ingredients.

The file also tells us that the product comes in the form of a tablet. This means that we can also ignore the three ATC codes beginning with “S”, because the therapeutic group “S” is used to classify medicines used for the sensory organs. They include active ingredients administered by the ocular or otological routes (that is, by eye or ear).



Discarding those options leaves only one of the seven ATC codes: J01MA02.

This code appears twice. Click on either of those links to move to the next page in the system.



This page gives the definition of each level for the code, and by scrolling down you can see them all. Thus, the “J” is for anti-infectives for systemic use, the “01” in J01 is for antibacterials for systemic use, the “M” in J01M is for quinolone antibacterials, the “A” in J01MA is for fluoroquinolones and the “02” in the full code, J01MA02, is for ciprofloxacin.

At the bottom of the page, you will see the screen shown here, with two values under the column DDD. We will discuss these in Section 2.4, which focuses on the DDD, the Defined Daily Dose.

J01M QUINOLONE ANTIBACTERIALS
This group comprises quinolone antibacterials, inhibiting the bacterial DNA-gyrase.

J01MA Fluoroquinolones
Flumequine is classified in J01MB.

The DDDs for the fluoroquinolones are mainly based on the treatment of respiratory tract infections. The DDDs for pefloxacin, enoxacin and norfloxacin are based on the treatment of complicated urinary tract infections.

ATC code	Name	DDD	U	Adm.R	Note
J01MA02	ciprofloxacin	1	g	O	
		0.8	g	P	

[List of abbreviations](#)

Last updated: 2019-12-16

For the moment, just notice that there are two different values for the DDD for this ATC code: one of these corresponds to the oral route (the “O” under “Admin. R”) and the other to the parenteral route (the “P” under “Admin. R”). This is why there were two repeats of the ATC code J01MA02 in the search results for ciprofloxacin: one for each route of administration.

We can now complete this Excel spreadsheet for ciprofloxacin, by copying the code J01MA02 and ...

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP RECTAL 500MG 30	

... pasting it into the corresponding cell of the Excel file (i.e. in Row 2, Column D).

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP RECTAL 500MG 30	

Now, we can look at the next active ingredient, ceftriaxone. This time, the product is a vial for intramuscular administration, and it contains 250 mg of ceftriaxone. Using this information, we will repeat the process that we used to find the code for ciprofloxacin.

First, go to the ATC/DDD index or created pdf file and search for “ceftriaxone”

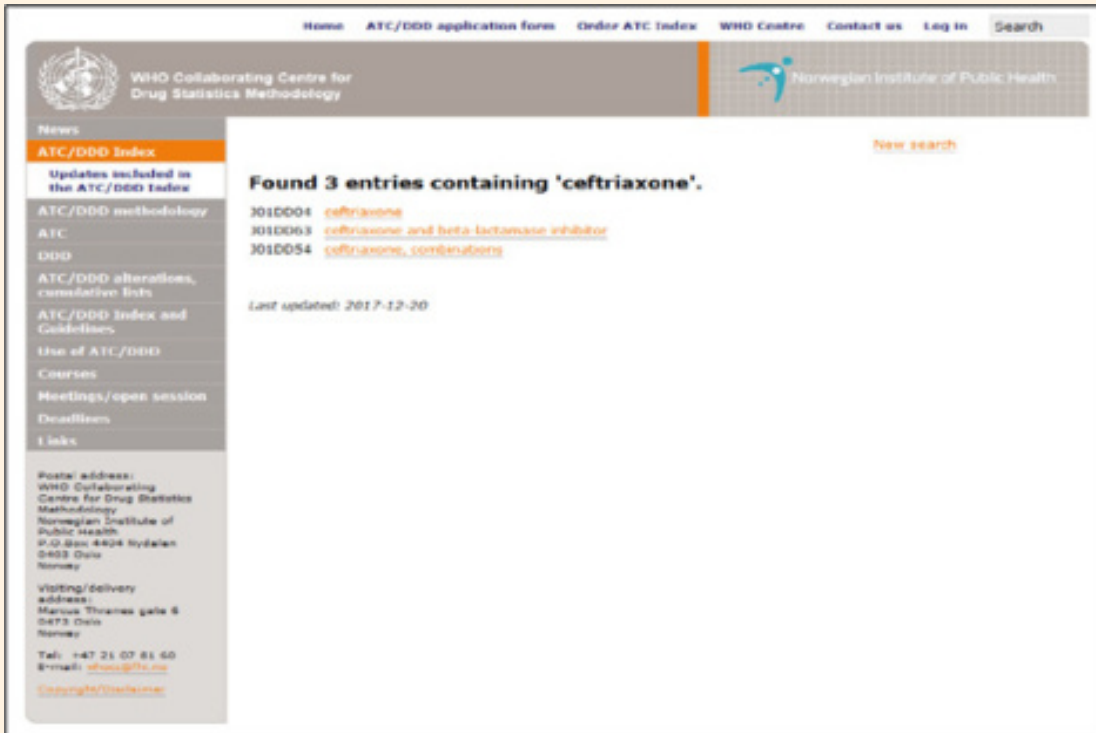
The screenshot shows the website interface for the ATC/DDD Index 2021. At the top, there are navigation links: Home, ATC/DDD application form, Order ATC Index, WHO Centre, Contact us, Log in, and Search. The main header includes the WHO Collaborating Centre for Drug Statistics Methodology logo and the Norwegian Institute of Public Health logo. A sidebar on the left contains a 'News' section and a list of links related to the ATC/DDD Index, such as 'ATC/DDD methodology', 'ATC', 'DDD', and 'Lists of temporary ATC/DDDs and alterations'. The main content area is titled 'ATC/DDD Index 2021' and contains a search form. The search query 'ceftriaxone' is entered in the 'Name' field. Below the search form, there are sections for 'ATC code' and 'Name' with bullet points explaining search criteria. The 'ATC code' section states that all ATC levels are searchable and that a search will result in showing the exact substance/level and all ATC levels above (up to 1st ATC level). The 'Name' section defines 'Name' as the name of the substance (normally the INN name) or the name of the ATC level, and notes that trademarks are not searchable. It also states that a minimum of three letters must be entered in the name box and that for ATC combination levels, all active ingredients would normally not be searchable. The 'DDD' section states that the DDDs, which will be reviewed in 2021 (3 year revision), are listed here and in the annex I in the printed ATC Index. See also [Subdefines: Part III; D Principles for reviewing and changing DDD and Part V; D Requests for changes to DDDs.](#) To express the DDD several abbreviations are used for units and routes of administration.

The screenshot shows the search results for 'ceftriaxone'. The page title is 'Found 3 entries containing 'ceftriaxone''. The results are listed as follows:

- 301DD04 [ceftriaxone](#)
- 301DD63 [ceftriaxone and beta-lactamase inhibitor](#)
- 301DD54 [ceftriaxone, combinations](#)

Below the results, it says 'Last updated: 2017-12-20'. There is a 'New search' link in the top right corner of the results area.

Three different ATC codes will appear on the screen. We know from the Excel spreadsheet that the product is not combined with other active ingredients ...



... hence, we can ignore the last two ATC codes, meaning that the correct ATC code in this case is J01DD04. We copy that ..

	A	B	C	D	F
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	
3	CEFTRIAZONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML		
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML		
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML		
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML		
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP RECTAL 500MG 30		
9					
10					
11					
12					



... and we paste it into the Excel spreadsheet (in Row 4, Column D).

The next product is a syrup containing sulfamethoxazole.

In this case, the ATC/DDD index shows three ATC codes. Most products containing sulfamethoxazole also contain trimethoprim, but checking the Excel spreadsheet, the syrup contains only sulfamethoxazole. So, the correct code is J01EC01, for oral sulfamethoxazole alone.

Clicking on that link and scrolling down, we can see the page shown here.

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP RECTAL 500MG 30	
9				
10				
11				
12				

Again, we can copy the code (in this case, J01EC01) and paste it into Excel (Row 5, Column D).

The next active ingredient is a combination of sulfamethoxazole plus trimethoprim. From our previous search, we know that there is a specific ATC code for this combination.

The DDDs for the sulfonamides are related to the duration of effect, i.e. usually the long-acting sulfonamides will have lower DDDs than the short-acting.

J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives

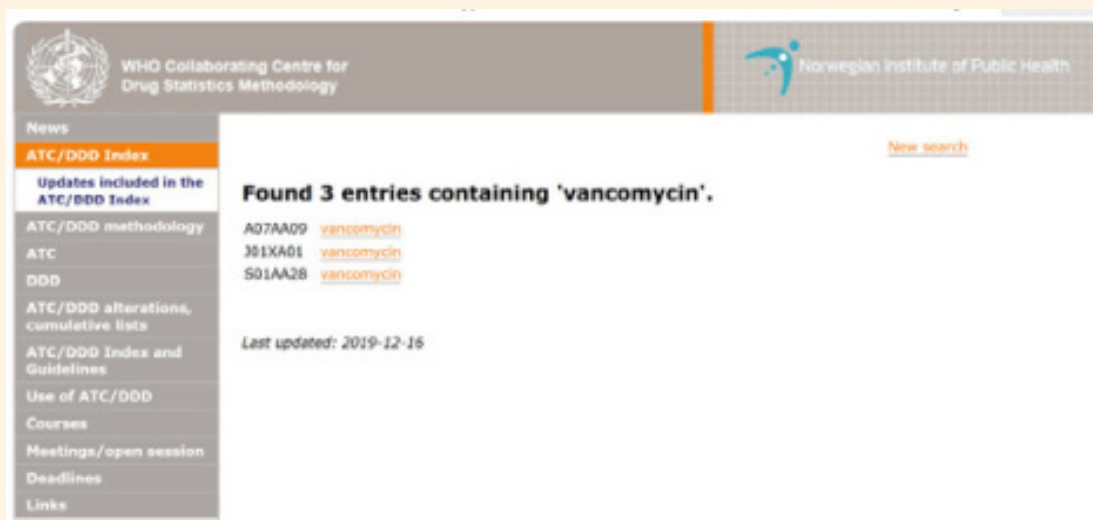
When establishing DDDs for combination products, both components are taken into consideration, see list of DDDs for combination products, www.whocc.no.

ATC code	Name	DDD	U	Adm.R	Note
J01EE01	sulfamethoxazole and trimethoprim				

Click on the link for sulfamethoxazole and trimethoprim, and write down the ATC code J01EE01.

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP RECTAL 500MG 30	

Here, we paste that code into the Excel spreadsheet (Row 6, Column D). The next active ingredient is vancomycin prepared for intravenous infusion.



In this case, the ATC/DDD search engine finds three entries containing “vancomycin” under three different therapeutic groups: “A” for alimentary tract, “J” for anti-infectives for systemic use and “S” for sensory organs. This particular active ingredient is administered orally for specific intestinal infections, where local action is sought; parenterally for systemic infections; and topically for eye infections. In the present example, the product found in the Excel file is prepared for the parenteral route, so the correct ATC code that you should have written down is J01XA01. Here, we copy that code and paste it into the Excel file (Row 6, Column D).

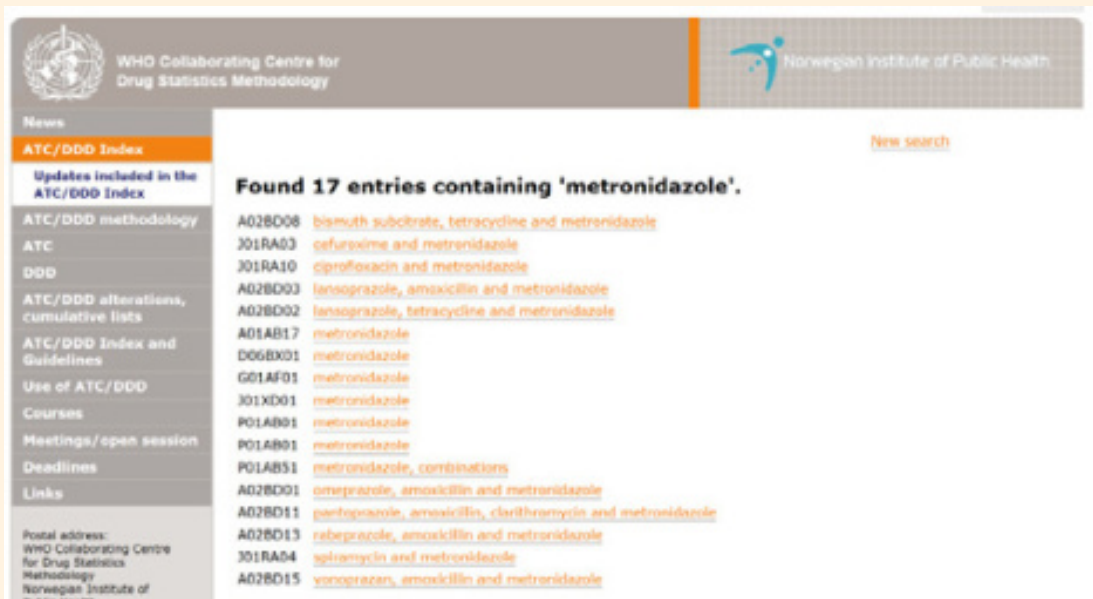
	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	

Now, it is time for the last two products. If you have an Internet connection, try these yourself and write down the results you would put into an Excel spreadsheet,

The next screen shows the results.

	A	B	C	D
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01FC01
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01

This screenshot shows what you should have written down for the last two ATC codes; the next screen shows where these codes were obtained from.



A search for metronidazole finds 17 entries. We know that the first product in the Excel spreadsheet contains metronidazole for intravenous infusion, and that we should therefore look for a J01 group ATC code. The only code with J01 for metronidazole alone is J01XD01, so that is the correct code.

The second product in the spreadsheet contains metronidazole presented as vaginal suppositories; hence, we should look for a G group ATC code (where the G is for genito-urinary system). The only G code in the list is G01AF01, so that is the correct code.

Assigning the correct ATC code to each product is the basis for avoiding mistakes in the consumption calculation. Therefore, we recommend that the person in charge of finding the ATC codes for the different products on any consumption list takes the time to follow the entire process carefully and double checks the assigned codes.

2.3.4 Antimicrobials included in the monitoring on antimicrobial consumption

As described in Section 2.3.3, antimicrobials can be classified into different therapeutic groups within the ATC system. The proposed common WHO AMC surveillance methodology is intended for use by countries in different regions for continuous monitoring, so all participants need to use the same criteria to include products.

In the proposed WHO AMC surveillance methodology:

only systemic antimicrobials are monitored – this means that, for example, no S, D or G groups are included in monitoring, even if active antibacterial ingredients can be found in those and other categories; and

monitoring is undertaken for both antibacterial medicines and other antimicrobials, such as antivirals, anti-tuberculosis (anti-TB) products and antimalarials.

WHO AMC surveillance methodology splits the antimicrobials to be monitored into two groups – a core set and an optional list of antimicrobials.

The **core set of antimicrobials** that all countries should include in their surveillance program the following antimicrobials:

<i>Antibacterials</i>	<i>J01</i>
<i>Antibiotics for alimentary tract</i>	<i>A07AA</i>
<i>Nitroimidazole derivatives for protozoal diseases</i>	<i>P01AB</i>

WHO surveillance program also includes an **optional list of antimicrobials** that countries may include in their surveillance program according to local needs and resources:

<i>Antifungals</i>	<i>J02</i>
<i>Antimycotics</i>	<i>D01BA</i>
<i>Antivirals</i>	<i>J05</i>
<i>Antimycobacterials for treatment of tuberculosis</i>	<i>J04A</i>
<i>Antimalarials</i>	<i>P01B</i>



Reading 2.3

Now read page 4 of the document WHO methodology for a global programme on surveillance of antimicrobial consumption (7). It explains in more detail which antimicrobials are included in monitoring (reference: [2.3.4Reading-01](#)).

2.3.5 Key messages for Section 2.3

The main messages from this section are that:

- the WHO methodology for AMC monitoring focuses on antimicrobials for systemic use – topical antimicrobials are excluded;
- WHO has defined a **core set** of antimicrobials that all countries should include in their surveillance programmes;
- According to the methodology, all active ingredients classified under **J01**, **A07AA** and **P01AB** subgroups should be included in the basic surveillance;
- Countries can also collect data on more than the core set – optional set of antimicrobials, depending on the country’s needs and use of antimicrobials.

Now take Quiz 2.2 to test your understanding (you will find the solutions at the end of the module).



Quiz 2.2

In this quiz, you need to complete the table below by:

- finding the missing ATC codes for each of the five products listed in the table; and
- inserting “Core” or “Optional”, as appropriate, where these designations are missing (if you cannot find the antimicrobial in either the “core” or the “optional” list, you should report it as “Not collected”).

NO.	STATEMENT	TRUE OR FALSE?	STATEMENT
1	Ampicillin + subactam / parenteral	J01CA51	
			Optional
		J01CA01	Not collected
2	Neomycin / cream	A01AB08	Core
		J01GB05	Optional
3	Ciprofloxacin / eye drops	J01MA02	Core
			Optional
		S02AA15	
4	Erythromycin / film-coated tabs	D10AF02	
			Optional
		S01AA17	Not collected
5	Ciprofloxacin + phenazopyridine/ tablets	G04BX06	Core
		J01RA10	Optional

2.4 Measuring AMC – DDD values

Section 2.3 described the internationally accepted ATC classification system for active ingredients, and explained which antimicrobials will be included for the WHO AMC monitoring. This section focuses on the DDD concept, which is generally accepted as being the best technical way to measure the consumption of medicines. It explains how to manage different consumption data and transform them into DDDs, DDD per 1000 inhabitants, and DDD per 1000 inhabitants per day (referred to as DID).




2.4.1 The need for DDD values



Try the following exercise, then watch Lecture 2.3 to see whether your answer was correct.



Exercise 2.2

You receive the following information from five different countries (A, B, C, D and E). Which country is the top consumer of antimicrobials?

COUNTRY	PRODUCT	NO. OF PACKAGES
A		98
B		22
C		2



COUNTRY	PRODUCT	NO. OF PACKAGES
D		700
E		132

 **Lecture 2.3.**

Measuring consumption

DDD rationale



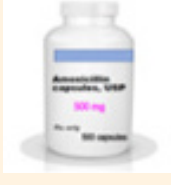
This video explains the correct answer to Exercise 2.2. Have your answer to that exercise at hand when you watch the video, so that you can check it as you watch.

COUNTRY	PRODUCT	NO. OF PACKAGES
A		98
B		22
C		2
D		700
E		132



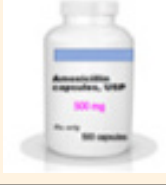


The question that you were asked to answer was:

“You receive the following information from five different countries (A, B, C, D and E). Which country is the top consumer of antimicrobials?”

As depicted here, the table showed the number of packages consumed by each country. There were five different products: four contained amoxicillin and one contained gentamicin.

COUNTRY	PRODUCT	NO. OF PACKAGES	ORDER BY NO. OF PACKAGES
A		98	3
B		22	4
C		2	5
D		700	1
E		132	2

One possible solution would be to order the countries according to the number of packages consumed. Using this method, Country D (with 700 packages) could be considered the highest consumer, and Country C (with only 2 packages), the lowest.

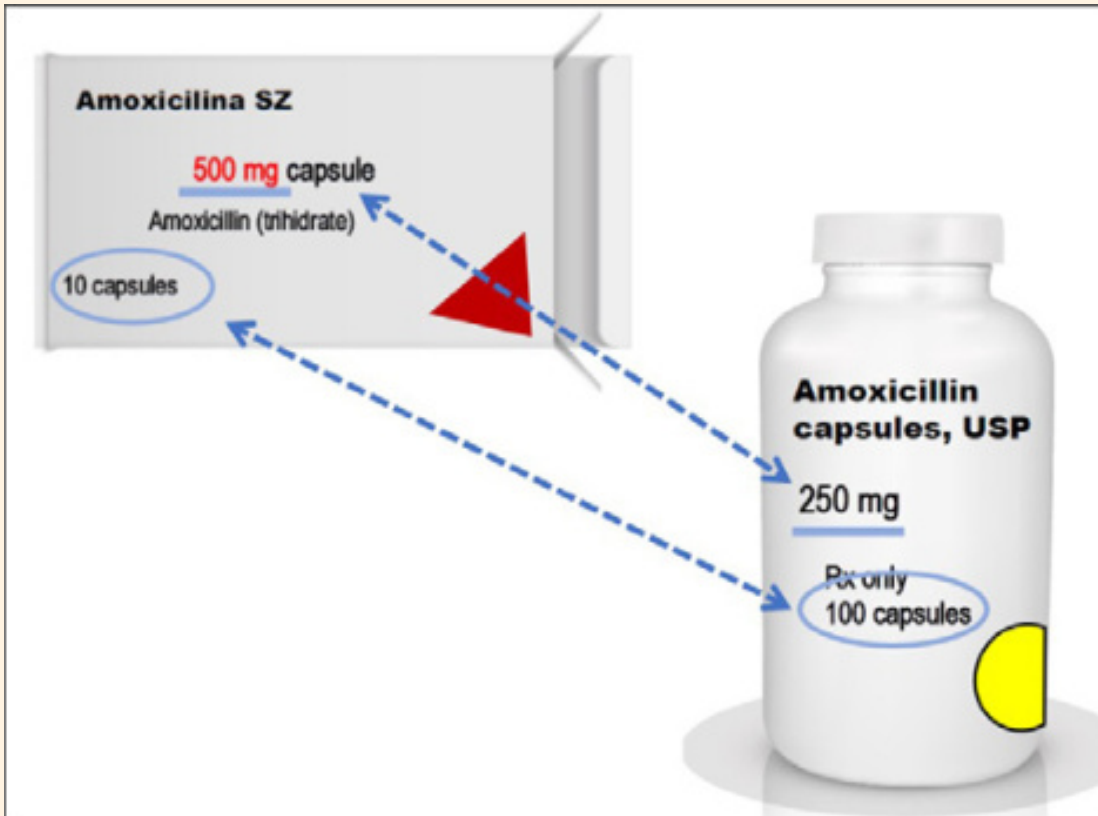
COUNTRY	PRODUCT	NO. OF PACKAGES	ORDER BY NO. OF PACKAGES
A		98	3
B		22	4
C		2	5
D		700	1
E		132	2

But this is not the correct solution to the question of which country is the top consumer. Here, we will explain why that is.

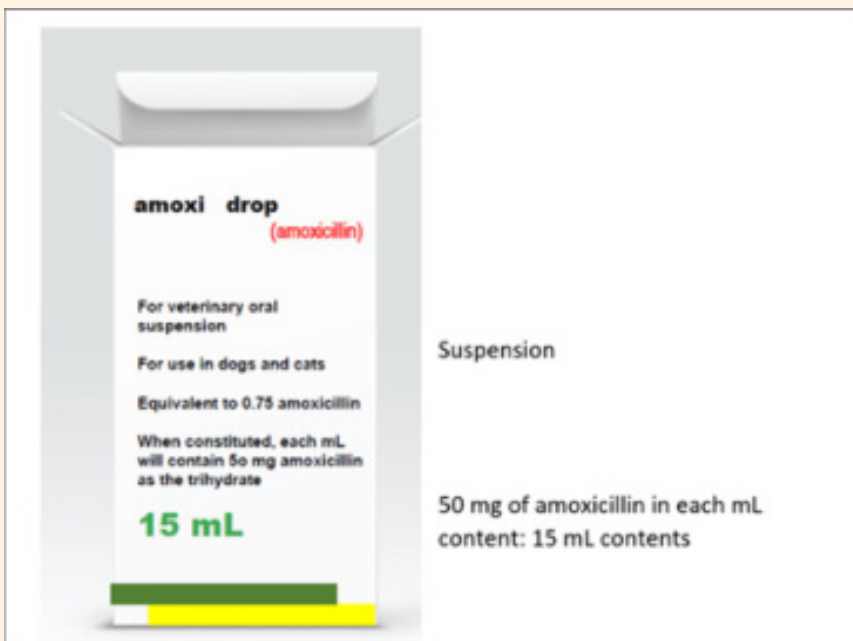
First, it is clear that the packages consumed in each country are different. Second, the active ingredient differs, because four countries consumed amoxicillin and one country consumed gentamicin. Let's have a closer look at the packages.

Countries A and B both consumed amoxicillin. However, Country A consumed Amoxicilina Z, where each package contains 10 capsules of 500 mg of amoxicillin, while Country B consumed Amoxicillin capsules, where each package contains 100 capsules of 250 mg.

Different packages contain different quantities of active ingredient. The number of packages is not a good unit of measure.

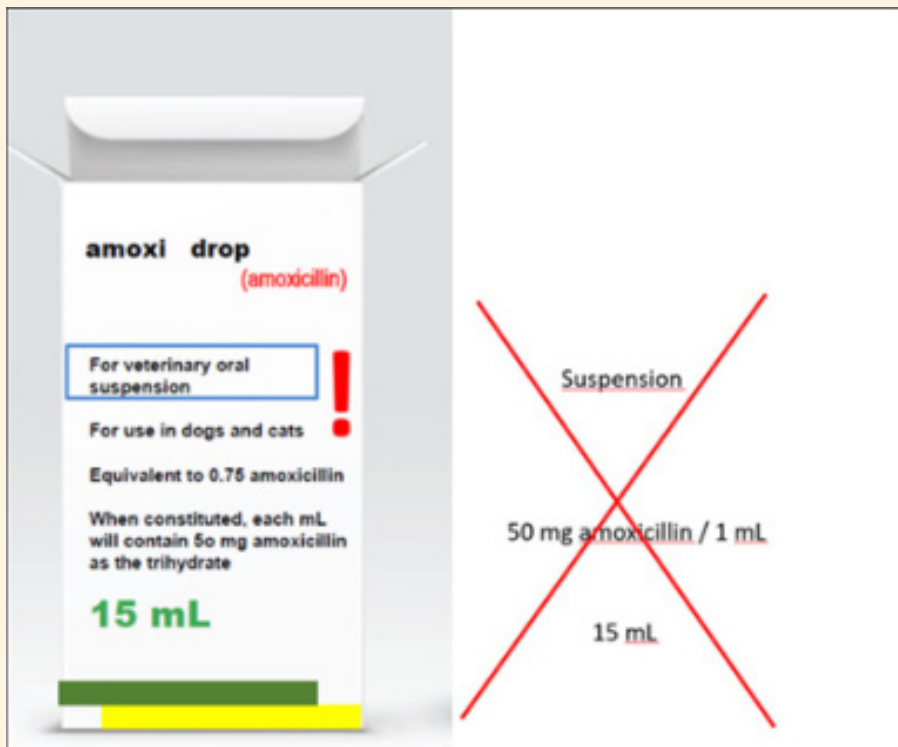


Country C consumed amoxicillin in packages containing 500 capsules of 500 mg of amoxicillin. Clearly, the amount of amoxicillin contained in each package is different. Therefore, it is not possible to simply count the “number of packages” to answer the question of which country was the highest consumer.



Country D is a different case. The package is different, because, according to the information printed on the box, in small letters, Amoxi-Drop is a suspension formulated as follows: each millilitre contains 50 mg of amoxicillin, and the bottle contains 15 millilitres.

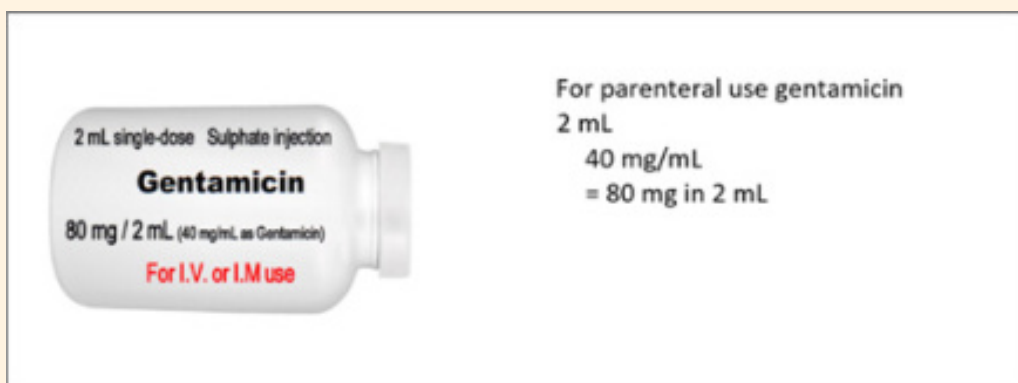
Given this information, can we calculate the total amount of amoxicillin contained in each package?



The answer is: Yes, it is possible to calculate the total amount of amoxicillin. *However, in this case we will not do that!*

As sometimes happens, in this list, there is something wrong – Amoxi-Drop is for veterinary use! Hence, we should not consider this product because we are interested in human consumption of antimicrobials. However, if this product is used by humans (e.g. if a similar ingredient or formulation is not available as a human product), then it should be included.

Each time you receive a list of consumed medicines, you should check what is in the list rather than assuming that it is correct and that all the entries are relevant.



COUNTRY	PRODUCT	TOTAL AMOXICILLIN CONTENT / PACKAGE	NO. OF PACKAGES
A	Amoxicilina 500 mg / capsule 10 capsules	500 mg x 10 caps= 5000 mg	98
B	Amoxicillin capsules 250 mg / capsule 100 capsules	250 mg x 100 caps = 25 000 mg	22
C	Amoxicillin 500 mg / capsule 500 capsules	500 mg x 500 caps = 250 000 mg	2
E	Gentamicin 40 mg / mL 2 mL	40 mg / mL x 2 mL = 80 mg	132

To summarize, at the end we have a list of four countries (not five, because we removed the veterinary product) that have different products containing different amounts of amoxicillin or gentamicin, as shown here. We can then calculate the exact amount of active ingredient in each package. The third column in the table shows the result of multiplying the number of tablets, capsules or millilitres by the strength of each tablet.

We can see, for example, that each package consumed in Country A has 5000 mg of amoxicillin, whereas each package consumed in Country C has 250 000 mg of amoxicillin.

COUNTRY	PRODUCT	TOTAL AMOXICILLIN CONTENT / PACKAGE	NO. OF PACKAGES	TOTAL AMOXICILLIN CONSUMED (MG)
A	Amoxicilina 500 mg / capsule 10 capsules	500 mg x 10 caps= 5000 mg	98	5000 x 98 = 490 000
B	Amoxicillin capsules 250 mg / capsule 100 capsules	250 mg x 100 caps = 25 000 mg	22	25 000 x 22 = 550 000
C	Amoxicillin 500 mg / capsule 500 capsules	500 mg x 500 caps = 250 000 mg	2	250 000 x 2 = 500 000
E	Gentamicin 40 mg / mL 2 mL	40 mg / mL x 2 mL = 80 mg	132	80 x 132 = 10 560

Next, because each country has consumed a different number of packages, we need to add another column to our table, to calculate the total amoxicillin consumed. The final column shows the result of multiplying the amount of amoxicillin in each package by the number of packages.

Country A (with 98 packages) appears to have consumed 490 000 mg of amoxicillin and Country C 500 000 mg (with only 2 packages). This is because the number of capsules differs hugely from one package to another (the packages in Country A contain only 10 capsules, whereas those in Country C contain 500 capsules).

COUNTRY	PRODUCT	TOTAL AMOXICILLIN CONTENT / PACKAGE	NO. OF PACKAGES	TOTAL AMOXICILLIN CONSUMED (MG)
A	Amoxicilina 500 mg / capsule 10 capsules	500 mg x 10 caps = 5000 mg	98	5000 x 98 = 490 000
B	Amoxicillin capsules 250 mg / capsule 100 capsules	250 mg x 100 caps = 25 000 mg	22	25 000 x 22 = 550 000
C	Amoxicillin 500 mg / capsule 500 capsules	500 mg x 500 caps = 250 000 mg	2	250 000 x 2 = 500 000
E	Gentamicin 40 mg / mL 2 mL	40 mg / mL x 2 mL = 80 mg	132	80 x 132 = 10 560

Looking at the table, we now have all the information we need to order the four countries by the total amount of antimicrobial consumed.

The table suggests that Country B (with 550 000 mg) is the top consumer, followed by Country C (with 500 000 mg), Country A (with 490 000 mg) and Country E (with 10 560 mg).

Thus, to the question: *Which country is the top consumer of antimicrobials?* with this analysis of the given data we would answer: Country B!

But...

do these countries have:

- equivalent consumption time?
- similar population?

But... wait a moment! Perhaps we still have some unsolved questions.

For example, do we know if these numbers of packages were consumed over the same time frame for each country? (For example, 1 year?)

It would be helpful to have this information, so that we could review the results for a specific time window.

Also, do the four countries have the same number of inhabitants? Could we standardize the consumption by 1000 inhabitants or by 1 million inhabitants?

This answer is, Yes! We can take these things into account, to have a more accurate way to compare countries.

And also...

Is 1 mg of amoxicillin equal to 1 mg of gentamicin?

There is another issue to consider here.

Three countries reported consumption of *amoxicillin* whereas the fourth country reported the consumption of *gentamicin*.

Is one milligram of amoxicillin the same as one milligram of gentamicin?

The answer is, Absolutely not! These two antimicrobials are used in completely different dosages.

Our situation is like comparing apples and pears. It is not possible to do this unless we use a different method; for example, counting “pieces of fruit” rather than “apples” or “pears”.

In the case of medicines, to compare the consumption of different active ingredients, we need to consider the recommended daily dose of each one. This is where the defined daily dose (or DDD) is needed. The DDD provides a way to overcome this important limitation when measuring the consumption of medicines.

The answer to the proposed exercise is that **more information is needed to compare** the consumption of antimicrobials in those five countries.

In summary, the right answer to the question proposed in this exercise is that we need more information before we can compare the consumption of amoxicillin in these countries.

Many researchers have faced these problems during their analyses of the consumed medicines. And this is why the DDD concept was developed. Section 2.4.2 describes the DDD in detail.



Reading 2.4

To complete this section on the need for DDDs, please read the preface of the 2003 WHO publication *Introduction to drug utilization research (1)*. The preface will give you some background to the origin of the DDD (reference: [2.4.1Reading-01](#)).

2.4.2 DDD metrics

The most commonly used measurement statistic for analysing the consumption of medicines is the DDD value. Thus, we need to understand what a DDD is and, for a given medicine, to be able to differentiate the DDD value from the number of consumed DDD.

Watch Lecture 2.4, which defines the DDD and explains how it can be used as a consumption metric in monitoring AMC. As for previous lectures, you will need to make use of the ATC/DDD index (5) as you work through the exercises in this lecture.

Lecture 2.4.

Measuring consumption

DDD definition and metrics



To avoid differences and mistakes in studies that measure or monitor the consumption of medicines, it was decided to establish a standard dose for each active ingredient.

In the previous section, we saw that there are many differences in the size of packages, and in the strength of the tablets, vials or suspensions contained in those packages. We could see that the number of packages is not a useful, uniform and repeatable measure

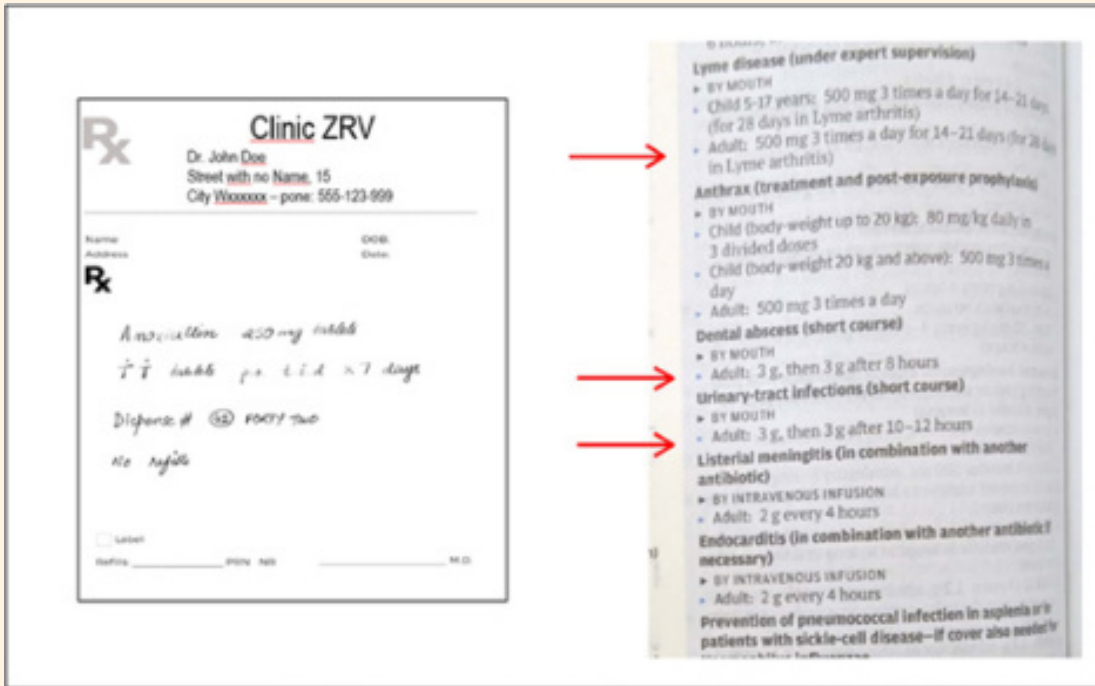
Rx Clinic ZRV
Dr. John Doe
Street with no Name, 15
City Wxxxxxx - phone: 555-123-999

Name _____ DOB: _____
Address _____ Date: _____

Rx
Amoxicillin 250mg tablets
1 1 tablet po. t.i.d x 7 days
Dispense # **42** FORTY TWO
No refills

Label
Refills: _____ PRN NR _____ M.D.

The ideal situation would be to identify a standard value for each medicine; for example, a recommended dosage for each medicine. In reality, this is not easy to do. Here, we will use the example of amoxicillin to see that the amount of this antimicrobial prescribed to a given patient depends largely on the infection site.



This excerpt from the British National Formulary, giving the recommendations for amoxicillin, clearly shows that the daily dosages and the treatment duration differ, depending on whether the patient presents with Lyme disease, a dental abscess or a urinary tract infection.

However, we could reach an agreement about the main indication of use of any medicine.

The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults.

The basis of the DDD concept is that the DDD represents the assumed average maintenance dose per day for a medicine used for its main indication in adults.

This definition has several key elements:

1. The DDD is “defined” or assumed. It is a **technical unit (fixed unit of measurement)** and does not necessarily correspond to the recommended or prescribed daily dose (PDD).
2. It is based on the main indication for that medicine.
3. It is measured as the total dosage in 24 hours.
4. It takes into account the maintenance dosage, rather than the initial dosage. The initial dosage is normally not considered, because in some medicines the initial dosage can be higher or lower than the maintenance dosage. If the initial dosage is the basis for the DDD, this is mentioned in the ATC/DDD guidelines.
5. It is based on the dosage recommended in adults.

The screenshot shows the website of the WHO Collaborating Centre for Drug Statistics Methodology. The main heading is "Definition and general considerations" for the Defined Daily Dose (DDD). The page includes a navigation menu at the top with links like Home, ATC/DDD application form, Order ATC Index, WHO Centre, Contact us, Log in, and Search. A sidebar on the left lists various resources such as News, ATC/DDD Index, and application forms. The main content area is divided into sections: "Definition and introduction" explaining the basic definition of DDD, "Application for DDD" detailing the criteria for assignment, and "Use of ATC/DDD" discussing the limitations of DDD data. A "Contents" box on the right provides a quick overview of the page structure.

The WHO CC for Drug Statistics Methodology in Oslo (Norway) is responsible for assigning the value of the DDD for any medicine included in the ATC classification system.

The value of the DDD for any active ingredient is set (and is then revised, if necessary) at the request of users, following a standard process that is clearly described on the website of the Oslo CC.

This screenshot provides detailed information for the ATC code J01CA04, amoxicillin. It includes a description of the drug group (beta-lactam antibiotics), its mechanism of action, and specific DDD values for different routes of administration. A table lists the ATC code, name, DDD, unit, and administration route. The DDD is 1.5 g for oral (O) administration and 3 g for parenteral (P) administration. The page also includes a list of abbreviations and a last updated date of 2019-12-16.

ATC code	Name	DDD	U	Adm.R	Note
J01CA04	amoxicillin	1.5	g	O	
		3	g	P	

Continuing with the example of amoxicillin, if we look this up in the ATC/DDD index, we can see that the value of the DDD for amoxicillin is 1.5 g for the oral route and 3 g for the parenteral route.

However, there are things to consider about the DDD:

- As we mentioned, it is only a *measuring unit* of use; it does not necessarily reflect the recommended or average *prescribed* dose.
- Because the unit is “daily dosage”, the DDD does not take into account the total duration of treatment (i.e. the number of days).
- For antimicrobials, DDDs are based on use in infections of moderate severity.
- The DDD depends on the administration route; for example, the parenteral and oral formulation of the same substance may have different DDDs if the recommended dose differs.

J01C BETA-LACTAM ANTIBIOTICS, PENICILLINS
This group comprises penicillin beta-lactam antibacterials, inhibiting the bacterial cell wall synthesis. Combinations of penicillins from different 4th levels, including beta-lactamase inhibitors, are classified in J01CR.

J01CA Penicillins with extended spectrum
This group comprises penicillins with enhanced activity against gram-negative rods, e.g. ampicillin and similar antibiotics.

The esters, for instance pivampicillin and pivmecillinam, have a higher bioavailability and thus a lower DDD than the corresponding non-ester compounds.
The DDDs for some of the compounds, for instance carbenicillin, piperacillin, ticarcillin and sulbactam, are based on the dosages used for narrow indications, i.e. life-threatening infections.

ATC code	Name	DDD	U	Adm.R	Note
J01CA04	amoxicillin	1.5	g	O	
		3	g	P	

[List of abbreviations](#)

Last updated: 2018-12-16

AMOXICILLIN ZZ 1000

Composition: 1000 mg Amoxicillin
Film Tablet
for bacterial infection
10 film tablets

Using the standard DDD value for the route of administration, it is possible to make certain calculations. For example, it is possible to estimate the number of DDD contained in the package shown in this slide – a product containing 10 tablets of 1000 mg of amoxicillin each.

J01C BETA-LACTAM ANTIBACTERIALS, PENICILLINS
 This group comprises penicillin beta-lactam antibacterials, inhibiting the bacterial cell wall synthesis. Combinations of penicillins from different 4th levels, including beta-lactamase inhibitors, are classified in J01CR.

J01CA Penicillins with extended spectrum
 This group comprises penicillins with enhanced activity against gram negative rods, e.g. ampicillin and similar antibiotics.

The esters, for instance pivampicillin and pivmecillinam, have a higher bioavailability and thus a lower DDD than the corresponding non-ester compounds.
 The DDDs for some of the compounds, for instance carbenicillin, piperacillin, ticarcillin and sulbenicillin, are based on the dosages used for narrow indications, i.e. life threatening infections.

ATC code	Name	DDD	U	Adm.R.	Note
J01CA04	amoxicillin	1.5	g	0	
			3	0	P

DDD value (oral) = 1.5 g
1.5 g = 1500 mg
Each tablet contains 1000 mg




Given that 1.5 grams is equivalent to 1500 mg, the DDD value for amoxicillin is 1500 mg.

When using a DDD value, it is important to take into account the units.

To avoid mistakes, always convert values so that you are working with a single unit (in this case, mg).

Number of DDD per package

DDD value = 1.5 g
 1.5 g = 1500 mg



Each tablet contains 1,000 mg

Each tablet = 0.67 DDD of amoxicillin

Each package contains 10 tablets


The number of DDD of amoxicillin per package is 6.7

To calculate how many DDD of amoxicillin each package of “Amoxicillin AL 1000” contains, we proceed as follows:

- The value of the DDD for amoxicillin is 1500 mg.
- Each tablet contains 1000 mg; therefore, one tablet contains 0.67 DDD.
- Each package contains 10 tablets; therefore, the number of DDD of amoxicillin per package is 6.7.

Number of DDD per package

DDD value = 1.5 g
1.5 g \equiv 1500 mg



Each capsule contains 500 mg

Each capsule = 0.3 DDD of amoxicillin

Each package contains 10 capsules


The number of DDD of amoxicillin per package is 3

Let's try to do this with another package: Amoxicilina SZ. How many DDD of amoxicillin does this package contain?

- The value of the DDD for oral amoxicillin is the same: 1500 mg.
- Each capsule contains 500 mg; therefore, one tablet contains 0.3 DDD (that is, 500 mg divided by 1500 mg = 0.3).
- Each package contains 10 capsules; therefore, the number of DDD of amoxicillin per package is 3.

Number of DDD per package

DDD value = 1.5 g
1.5 g \equiv 1500 mg



Each capsule contains 500 mg

Each capsule = 0.3 DDD of amoxicillin

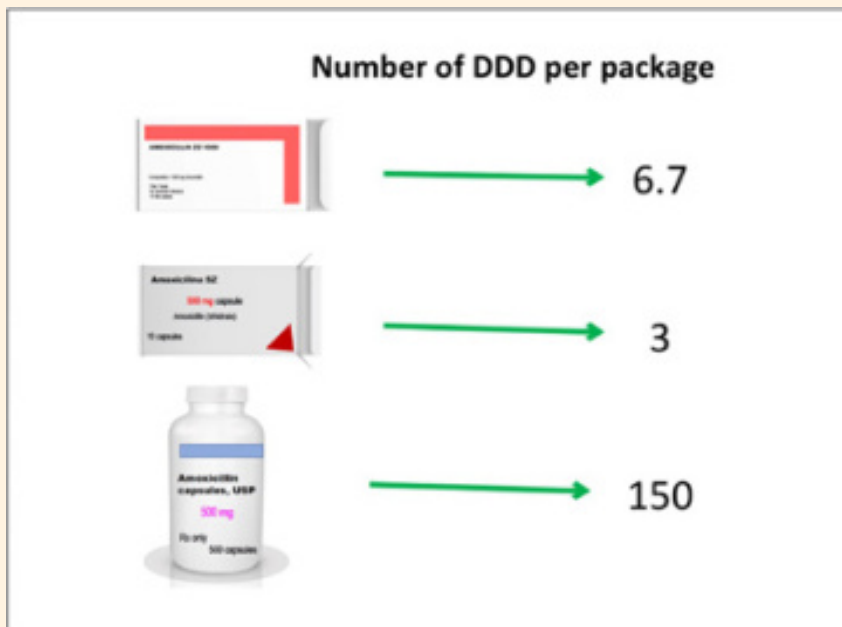
Each package contains 500 capsules

The number of DDD of amoxicillin per package is 150

Here is another example before you have a go at calculating the DDD yourself.

This amoxicillin comes packaged as 500 capsules containing 500 mg of amoxicillin each:

- As in the previous calculation, the value of the DDD for oral amoxicillin is 1500 mg.
- As in the previous calculation, each capsule contains 500 mg, so each tablet contains 0.3 DDD.
- For Ranbaxy, each package contains 500 capsules; therefore, the number of DDD of amoxicillin per package is 150 (that is, 500 capsules x 0.3 DDD each = 150).



Now, we can clearly see the differences in the number of DDD of amoxicillin contained in each package: they range from 3 to 150. In some cases, the difference is minor (for example, between Amoxicillin AL 1000 at 6.7 and Amoxicilina Sandoz at 3), but in other cases it is major (for example, between Ranbaxy at 150 and the other packages – this major difference is due to Ranbaxy having 500 pills in just one box).

No. of DDD per package	No. of treatment days
6.7	6.7
3	3
150	150

Finally, if we have assumed that the DDD is the **average** daily dose, when we use the DDD value as a metric for consumption, we can assume that it is equivalent to the number of “treatment days”.

If one package contains 3 DDD, this means that one package contains amoxicillin to treat one patient for 3 days, or to treat three patients for a single day.

Of course, when making these assumptions it is important to remember what the DDD value means. It is a technical unit that is obtained after taking into account the average maintenance daily dosage, not the actual dose prescribed to a given patient.

However, using the DDD values allows us to share a common methodology for calculating the amount of medicines consumed in different places over a particular time.

2.4.3 Theoretical aspects of DDD

Later in this section, you will have the chance to try calculating the number of DDD and learn how to take into account two additional elements: the time frame and the population. But first, let’s consider some aspects of the DDD definition. The text of this section, up to Reading 2.5, has been adapted from the website of the WHO CC for Drug Statistics Methodology in Oslo (4).

Definition and assignment of DDD

The WHO CC defines the DDD as follows:

“The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.”

The words “average maintenance dose”, “main indication” and “adults” in that definition help us to understand why the value of some DDD can be different from the usually prescribed dose. As mentioned previously, the DDD is a unit of measurement; it does not necessarily reflect the recommended or prescribed daily dose (PDD).

Thus, drug consumption data presented in a DDD gives only a rough estimate of consumption, not an exact picture of actual use. However, the DDD does provide a fixed unit of measurement that is independent of price and dosage form (e.g. tablet strength), allowing researchers to assess trends in drug consumption and to compare population groups.

A DDD is only assigned for drugs that already have an ATC code, but the reverse is not true; thus, some medicines with an ATC code do not have a defined DDD. For example, DDDs are not established for topical products (e.g. dermatologicals), sera, vaccines, antineoplastic agents, allergen extracts, general and local anaesthetics, and contrast media.

The basic principle is to assign only one DDD per route of administration within an ATC code. DDDs for plain substances are normally based on monotherapy.

A DDD is assigned based on the following aspects:

- The average adult dose used for the main indication, as reflected by the ATC code.
- When the recommended dose refers to body weight, an adult is considered to be a person of 70 kg.
- Even special pharmaceutical forms mainly intended for children (e.g. mixtures and suppositories) are assigned the DDD used for adults – some exceptions are made for some products only used by children (e.g. growth hormones and fluoride tablets).
- The maintenance dose (long-term therapeutic dose) is usually preferred when establishing the DDD. The initial dose may differ, but this is not reflected in the DDD.
- A DDD is usually established according to the declared content (strength) of the product. Where a substance has various salts, these are usually given the same DDD. Exceptions are described in the guidelines for the different ATC groups; for example, the DDDs for antimalarials are expressed as the base.
- Prodrugs, which have not been given a separate ATC code, are normally not given a separate DDD.
- The DDD is often identical for various dosage forms of the same drug. Different DDDs may be established when the bioavailability is substantially different for various routes of administration (e.g. oral and parenteral administration of morphine), or if the dosage forms are used for different indications.

DDDs for combination products

In the case of combination products, DDDs are based on the main principle of counting the combination as one daily dose, regardless of the number of active ingredients included in the combination.

If a treatment schedule for a patient includes, for example, two separate single-ingredient products, then the consumption will be measured by counting the DDDs of each single-ingredient product separately.

However, if a treatment schedule includes a combination product containing two active ingredients, then the calculated consumption measured in DDDs will normally be lower, because the DDD for the *combination* will be counted.

Examples of calculating a DDD for a combination product

- Product A contains a fixed combination of 800 mg of sulfamethoxazole and 160 mg of trimethoprim. The DDD of this combination product is assigned 2 unit doses (UD) = 1 tablet. The dosing schedule of 1 tablet of product A daily will be calculated as 1 DDD (even though it will be equivalent to 1.5 DDD of the active single-ingredient products).
- Product B contains a fixed combination of 875 mg of amoxicillin and 125 mg of clavulanic acid. The DDD value of this combination is 1 g (using the DDD assigned for this combination given by the oral route; that is, DDD = 1 g).

The Oslo WHO CC website lists the DDDs of all combined products, including antimicrobials

https://www.whocc.no/ddd/list_of_ddd_combined_products/. (8).

The WHO methodology for AMC surveillance recommends that at least the core set of antimicrobial classes are monitored by all national surveillance programmes. The Oslo WHO CC list of DDDs for combinations that belong to the core antimicrobials is shown in Table 2.1.

IMPORTANT: For your work, you will need to use the file on ATC/DDD index for combinations with antimicrobials, which was created by WHO. In this file, WHO has assigned codes for each of the combination with antimicrobials defined by the Oslo WHO CC by adding an underscore and a number (e.g. J01CA20_1. J01CA20_2). These codes are not assigned by the Oslo WHO CC. This WHO file on ATC/DDD index for combinations is not included in the training material. To obtain this file, please write to GLASS AMC Team in WHO: glass-amc@who.int.

Table 2.1. List of DDDs of combined products within the core classes of antimicrobials

ATC CODE	DOSAGE FORM	ACTIVE INGREDIENTS PER UNIT DOSE (UD)	DDD COMBINATION
J01AA20	tab	tetracycline 115.4 mg/ chlortetracycline 115.4 mg/ demeclocycline 69.2 mg	2 UD (=2 tab)
J01CA20	tab	pivampicillin 0.25 g/ pivmecillinam 0.2 g	3 UD (=3 tab)
J01CA20	tab	pivampicillin 0.125 g/ pivmecillinam 0.1 g	6 UD (=6 tab)
J01CE30	powder for inj	Combination of benzylpenicillin/procain-benzylpenicillin/ benzathine benzylpenicillin	3.6 g expressed as benzylpenicillin
J01CR50	tab	ampicillin 0.25 g/ cloxacillin 0.25 g	4 UD (=4 tab)
J01CR50	powder for inj	ampicillin 0.66 g/ oxacillin 0.33 g	2 UD (=2 g)
J01CR50	caps	ampicillin 0.125g/ oxacillin 0.125 g	8 UD (=8 caps)
J01CR50	tab	ampicillin 0.25 g/ flucloxacillin 0.25 g	4 UD (=4 tab)
J01CR50	powder for inj	ampicillin 250 mg/ cloxacillin 250 mg	2 UD (=2 grams of powder for injection)
J01CR50	powder for inj	ampicillin 500 mg/ cloxacillin 500 mg	2 UD (=2 grams of powder for injection)
J01CR50	tab	ampicillin 125 mg/ cloxacillin 125 mg	8 UD (=8 tab)
J01EC20	tab	sulfacarbamide 0.167 g/ sulfadiazine 0.167 g/ sulfadimidine 0.167 g	4 UD (=4 tab)
J01EE01	inf conc	sulfamethoxazole 80 mg/ trimethoprim 16 mg	20 UD (=20 mL)
J01EE01	mixt	sulfamethoxazole 0.2 g/ trimethoprim 40 mg	8 UD (=40 mL)
J01EE01	tab	sulfamethoxazole 0.4 g/ trimethoprim 80 mg	4 UD (=4 tab)
J01EE02	mixt	sulfadiazine 0.205 g/ trimethoprim 45 mg	4 UD (=20 mL)
J01EE02	tab	sulfadiazine 0.41 g/ trimethoprim 90 mg	2 UD (=2 tab)
J01EE03	tab	sulfametrole 0.8 g/ trimethoprim 0.16 g	2 UD (=2 tab)
J01EE03	powder for inj	sulfametrole 0.8 g/ trimethoprim 0.16 g per vial	2 UD (defined as 2 vials)
J01EE06	tab	sulfadiazin 0.25 g/ tetroxoprim 0.1 g	2 UD (=2 tab)
J01EE07	tab	sulfamerazin 0.12 g/ trimethoprim 80 mg	4 UD (=4 tab)
J01RA04	tab	spiramycin 1.5 MU/ metronidazole 250 mg	3 UD (=3 tab)
J01RA04	tab	spiramycin 0.75 MU/ metronidazole 125 mg	6 UD (=6 tab)
J01RA05	tab	levofloxacin 250 mg/ ornidazole 500 mg	2 UD (=2 tab)
J01RA07	tab	azithromycin 1000 mg (1 tab)/ fluconazole 150 mg (1 tab)/ secnidazole 1000 mg (2 tab) (combination package)	4 UD (=4 tab)
J01RA09	tab	ofloxacin 200 mg/ ornidazole 500 mg	2 UD (=2 tab)
J01RA10	tab	ciprofloxacin 500 mg/ metronidazole 200 mg	2 UD (=2 tab)
J01RA11	tab	ciprofloxacin 500 mg/ tinidazole 600 mg	2 UD (=2 tab)
J01RA11	tab	ciprofloxacin 250 mg/ tinidazole 300 mg	4 UD (=4 tab)
J01RA12	tab	ciprofloxacin 500 mg/ ornidazole 500 mg	2 UD (=2 tab)
J01RA13	tab	norfloxacin 400 mg/ tinidazole 600 mg	2 UD (=2 tab)

In some cases, the strength of a product is expressed in “international units” (IU) or “millions of international units” (MU). Table 2.2 includes a conversion factor list. Please keep it for future consultation:

Table 2.2. Conversion factors for active ingredients given by different routes of administration

ATC5	ACTIVE INGREDIENT	ADMINISTRATION ROUTE	FROM	TO	FACTOR
J01CE01	benzylpenicillin	P	MU	g	0.6
J01CE02	phenoxymethylpenicillin	O	MU	g	0.625
J01FA02	spiramycin	O	MU	g	0.3125
J01CE08	benzathine benzylpenicillin	P	MU	g	0.6
J01CE09	procaine benzylpenicillin	P	MU	g	1

MU: million international units; O: oral; P: parenteral.

Example

The DDD value for procaine benzylpenicillin (J01CE09) is 0.6 g.

ATC CODE	NAME	DDD	U	ADM.R	NOTE
J01CE09	procaine benzylpenicillin	0.6	g	P	

Product A contains 2 mL of procaine benzylpenicillin per bottle (strength: 800 000 units/mL). This means that one bottle of Product A contains 1 600 000 units, or 1.6 MU (million international units).

To convert the amount to grams, apply the conversion factor: 1.6 MU x 1 = 1.6 g

1 DDD of procaine benzylpenicillin = 0.6 g; therefore, 1.6 g of procaine benzylpenicillin = 2.66 DDD.

In some cases, the DDD value changes according to the formulation. A particular case is erythromycin, where there is a specific DDD for one salt – erythromycin ethylsuccinate.

Table 2.3 lists some relevant examples.

Table 2.3. Examples of DDD values that differ according to the formulation

ATC CODE	NAME	DDD	UNIT OF DDD	ADMINISTRATION ROUTE
J01CR02	amoxicillin and enzyme inhibitor	1.5	g	O
		3	g	P
J01FA01	erythromycin ethylsuccinate	2	g	O
	erythromycin	1	g	O
J01MA02	ciprofloxacin	1	g	P
		0.8	g	P
J01GB01	tobramycin	0.112	g	Inhalation powder
		0.3	g	Inhalation solution
		0.24	g	P

ATC CODE	NAME	DDD	UNIT OF DDD	ADMINISTRATION ROUTE
P01AB01	metronidazole	2	g	O
P01AB01	metronidazole	2	g	R
J01XD01	metronidazole	1.5	g	P

Now take Quiz 2.3 to test your understanding of this section. You will find the solutions at the end of this module.



Quiz 2.3

Are the following statements about the concept and uses of DDD true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	The DDD value of any medicine is the average number of doses per day for that medicine.	
2	When you present consumption figures as number of DDD, this means the number of treatment days if each patient had consumed a dose equal to the value of the DDD for that medicine.	
3	Even special pharmaceutical forms mainly intended for children (e.g. mixtures and suppositories) are assigned the DDD used for adults.	



Reading 2.5

Sometimes, you will not find a defined DDD for a specific product marketed in your country. In such cases, a product may still be of interest from the point of view of antimicrobial resistance (e.g. because it contains an irrational fixed-dose combination that includes an antimicrobial of special interest). Therefore, you need to know how to report its consumption. Read the Oslo WHO CC website about the basis for assigning a DDD.

Basis for assigning a DDD (reference: [2.4.3Reading-02](#))

2.4.4 Using DDDs

As described in previous sections, a DDD value provides a measure of extent of use. However, for comparative purposes, these data are usually adjusted for population size or population group, depending on the medicines of interest and the level of data disaggregation that is possible.

For most antimicrobials, the DDDs/1000 inhabitants/day (DID) will be calculated for the total population, including all age and gender groups.

It may also be possible to stratify the national estimates by age group, gender and sectors (community and hospital, public and private). Where there is stratification, it is important to carefully consider the appropriate estimate for the denominator; for example, DDDs/1000 children aged under 5 years/day, or DDDs/1000 women/day.



Reading 2.6

First, read pages 38–39 of the 2003 WHO publication Introduction to drug utilization research (reference: [2.4.4Reading-01](#)).

Now move on to Exercise 2.3, to try calculating DDDs adjusted for population size or population group.



Exercise 2.3

Step 1. Imagine that colleagues from two different countries have sent you data detailing the consumption of three antimicrobials in their country, expressed as number of DDD.

ANTIMICROBIAL	COUNTRY A (NO. OF DDD)	COUNTRY B (NO. OF DDD)
Amoxicillin	4 380 000	648 000
Ciprofloxacin	5 840 000	1 080 000
Azithromycin	2 920 000	540 000

Based on the data in the table, please answer the following questions:

- Which country has consumed more ciprofloxacin – Country A or Country B?
- Which country has consumed less azithromycin – Country A or Country B?

Once you have answered, even if you are not confident of your answer, carry on to Step 2 of the exercise.

Step 2. Now, imagine that you have also been able to call the colleagues from both countries and ask them for additional information. Things you would ask your colleagues for are the reference population, and the measurement time window. From this, imagine that you have been able to expand on the table in Step 1, as follows:

ANTIMICROBIAL	COUNTRY A 2 000 000 INHABITANTS 1 YEAR (365 DAYS)	COUNTRY B 1 200 000 INHABITANTS 3 MONTHS (90 DAYS)
	NO. OF DDD	NO. OF DDD
Amoxicillin	4 380 000	648 000
Ciprofloxacin	5 840 000	1 080 000
Azithromycin	2 920 000	540 000

Armed with this additional information, would you change your answer to the questions in Step 1?

Note that the total population is different in both countries: Country B is smaller than Country A. Also, the time frame for the consumption is different: In Country A it covers 1 year whereas in Country B that volume of DDD was consumed in just 90 days.

With this additional information in mind, return to your answers to Step 1 and think about whether you would like to change your answers to the questions:

- Which country has consumed more ciprofloxacin – Country A or Country B?
- Which country has consumed less azithromycin – Country A or Country B?

Once you have decided on your answers, or have decided that you cannot find a satisfactory answer, move on to Step 3 of this exercise.

Step 3. Medicines utilization figures should ideally be presented as numbers of DDD per 1000 inhabitants per day. Therefore, let us start with the initial data, to transform raw consumed DDD in the standard form of DDD/1000 inhabitants/day or DID.

ANTIMICROBIAL	COUNTRY A 2 000 000 INHABITANTS 1 YEAR (365 DAYS)		
	NO. OF DDD	NO. OF DDD/INHABITANTS/YEAR	NO. OF DDD/1000 INHABITANTS/DAY
Amoxicillin	4 380 000	2.19	6
Ciprofloxacin	5 840 000	2.92	8
Azithromycin	2 920 000	1.46	4

The table shows the different calculations step by step. We have the number of DDD (e.g. 4 380 000 DDD for amoxicillin). However, the total population of the country is 2 000 000 inhabitants; hence, we should divide the amoxicillin consumption by 2 000 000 for the number of inhabitants, to obtain the consumption per inhabitant per year, which will be 2.19.

You can repeat these operations with ciprofloxacin and azithromycin, to obtain, respectively, 2.92 and 1.46 DDD/inhabitants/year.

Next, for amoxicillin we can transform this figure to obtain the number of DDD/1000 inhabitants/year. To do this, we multiply 2.19 by 1000, to obtain 2190.

But this consumption refers to a year (365 days). So, we need to divide the previous numbers by 365 to obtain the *daily* consumption expressed in the final column: 6, 8 and 4 DDD/1000 inhabitants/day, for amoxicillin, ciprofloxacin and azithromycin, respectively.

Try following these calculations to obtain the figures for Country B, then move on to Step 4. The table shows the information regarding the consumption of three antimicrobials in Country A and Country B, standardized to be fully comparable.

ANTIMICROBIAL	COUNTRY A 2 000 000 INHABITANTS 1 YEAR (365 DAYS)		COUNTRY B 1 200 000 INHABITANTS 3 MONTHS (90 DAYS)	
	NO. OF DDD	NO. OF DDD/1000 INHABITANTS/DAY	NO. OF DDD	NO. OF DDD/1000 INHABITANTS/DAY
Amoxicillin	4 380 000	6	648 000	6
Ciprofloxacin	5 840 000	8	1 080 000	10
Azithromycin	2 920 000	4	540 000	5

Taking these steps into account may change the answers you gave in Step 1 and Step 2. The correct answers are as follows:

- Which country has consumed more ciprofloxacin – Country A or Country B?

The answer is *Country B*, with 10 DDD/1000 inhabitants/day, in contrast to 8 DDD/1000 inhabitants/day consumed in Country A. So, 10 patients per 1000 inhabitants are exposed to ciprofloxacin in Country B per day, whereas in Country A, the exposure is 8 patients per 1000 inhabitants per day.

- Which country has consumed less azithromycin – Country A or Country B?

The answer is *Country A*, with 4 DDD/1000 inhabitants/day, because the consumption in Country B is higher, at 5 DDD/1000 inhabitants/day.

Now that you have the essentials to operate with DDD metrics, it is important to take into account some of the peculiarities and exceptions presented in Section 2.4.3 regarding the measurements with DDD and the conversion from packages to DDD when the package is not a capsule or a tablet. You can return to that point if you have some doubts.

Now take Quiz 2.4 to test your understanding of this section. You will find the solutions at the end of this module.



Quiz 2.4

Are the following statements about DDDs true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	For liquid preparations for oral use of a combination product, 1 unit dose (1 UD) means 1 spoon.	
2	AMC presented in DDD does not give an exact picture of actual use; it is just an estimate of consumption.	
3	For topical products containing an antimicrobial, it is possible to use the DDD established for oral preparations with the same active ingredient.	

2.4.5 Step-by-step exercise in consumption of antimicrobials

Section 2.3 described the ATC classification system, while Section 2.4 so far has described the concept of establishing a DDD value for a given active ingredient and explained how to express AMC data as “number of consumed DDD”. Various examples showed how to work with DDD and transform raw “number of DDD” values into DDD/1000 inhabitants/day (DID), to give a context to the raw data and to compare values within countries or across time.

Lecture 2.5 gives practical step-by-step examples of how to identify the DDD values for different products, and work with these DDD to express consumption as DID. This lecture has worked examples, so you can try to do the exercises with the ATC/DDD index (5). You will need paper, a pen and a calculator at hand to practice with these calculations. You will have another opportunity to practice in Module 5.

 Lecture 2.5.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DiD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592				
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808				
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01RC01	33272				
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022				
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302				
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707				
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22				
12									
13									

In this exercise, we will calculate the consumption of a series of antimicrobials in DiD. Our starting point is this Excel file that we saw in Section 2.3.3.

The spreadsheet shows the number of packs of 10 products containing antimicrobials consumed during the first trimester of 2017 (that is, 90 days) in a large country (its estimated population data for 2017 was 198 000 000 inhabitants). When you receive a file containing data on consumption of medicines, it will be similar to this one.

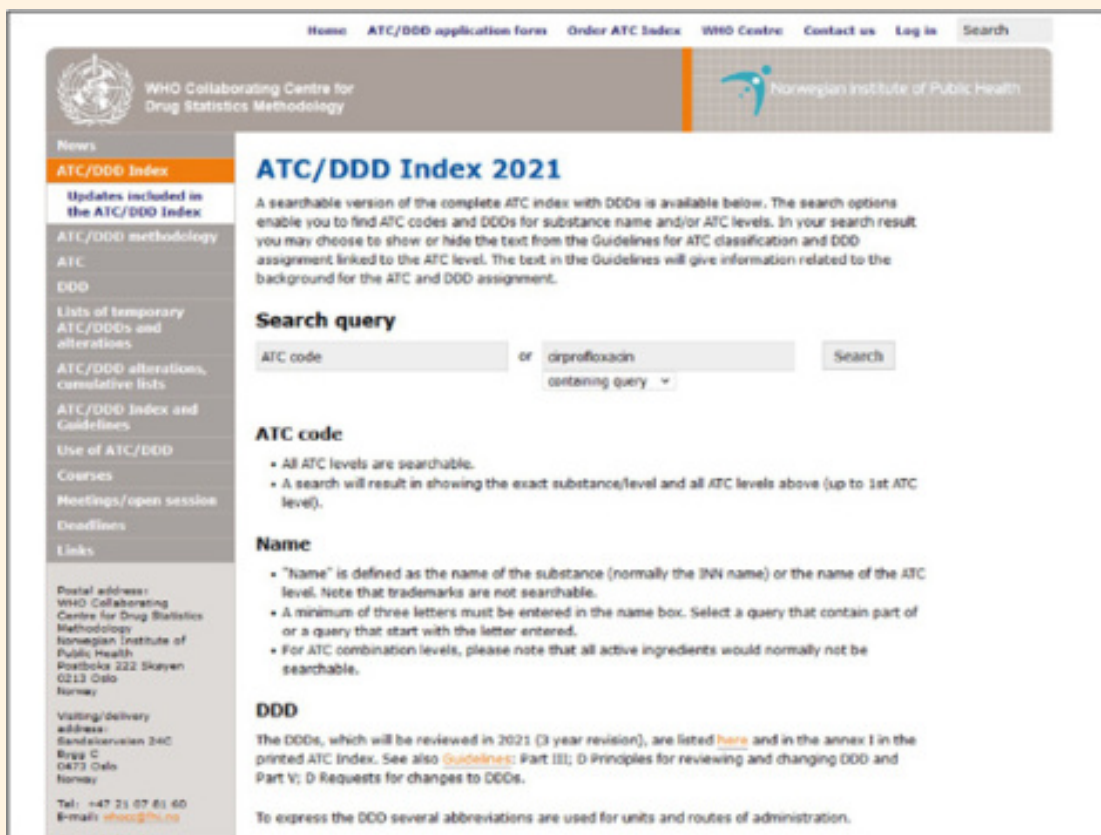
In this exercise, we will be writing down the information that you would put in the different columns in order to easily transform the raw number of packages consumed into DiD.

First, you have another chance to practise with ATC codes. In Section 2.3.3, you identified the ATC codes for the first seven rows. Now three additional rows have been added. If you wish, you can use the ATC/DDD index to find the correct ATC codes for the blank cells.

Once you have finished, move on to the next screen to check the solution.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DiD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592				
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808				
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01RC01	33272				
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022				
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10		38302				
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML		9707				
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML		22				

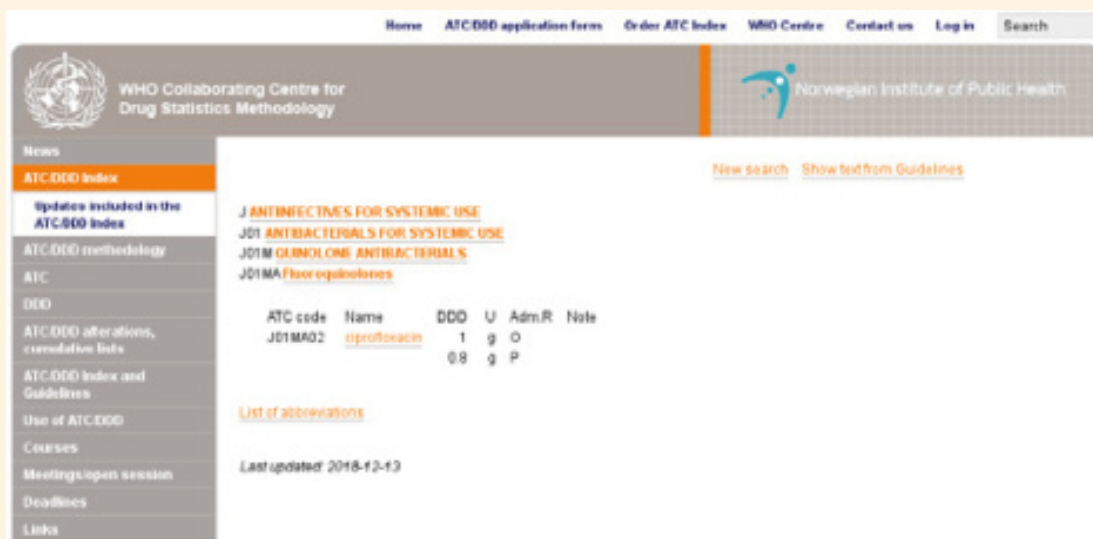
This screenshot shows the correct ATC codes for the suggested products. This is the first step in the process of determining the DDD value and the DID.



To find the DDD value for each active ingredient, go to the ATC/DDD index or created pdf file. We will start with “ciprofloxacin” – type this into the “Name” box in the search function.



Now, we need to select the appropriate entry. In this case, we know that it is the first option in the list – ciprofloxacin for systemic use formulated as a single component, with the ATC code J01MA02 – so select that option.



Now scroll to the bottom of that screen, where you will see both the ATC code and the DDD value, defined for oral ciprofloxacin and for parenteral ciprofloxacin. For some active ingredients, the DDD values for different modes of administration are the same, but in other cases they differ. Here, for ciprofloxacin, we can see that the values are different. We know that the form referred to in the Excel spreadsheet is tablets, so the correct choice here is oral ciprofloxacin, and the correct DDD is thus 1 g.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3582	1000 MG			
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808				
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272				
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022				
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYLPENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE05	38302				
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707				
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22				
12									

Now, write down the figure that you would include in the Excel spreadsheet. Given that we will be dealing with different products with different DDD values, it is best to use a single unit for the DDD values, and we will choose milligrams. So, the value to write down, that you would include in the Excel spreadsheet, is “1000 MG” (i.e. 1 g = 1000 mg).

Now we can proceed to the next product: ceftriaxone.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD index for ceftriaxone. The ATC code is J01DD04, the name is ceftriaxone, and the DDD value is 2 g. The website also includes a navigation menu, a search bar, and a sidebar with various links and news items.

Find this product in the ATC/DDD index. You will see that the DDD value is 2 g (i.e. 2000 mg).

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DID
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPB REVEST 250MG 10	J01MA02		3592 1000 MG			
3	CEFTRIAZONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04		26808 2000 MG			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01		35272			
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01		87115			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01		153			
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01		2022			
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01		2325			
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 6.8 MU/ML 2ML 10	J01CE09		38302			
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09		9707			
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57.70ML	J01CR02		22			
12									

The next product is sulfamethoxazole.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD index for sulfamethoxazole. The ATC code is J01EC01, the name is sulfamethoxazole, and the DDD value is 2 g. The website also includes a navigation menu, a search bar, and a sidebar with various links and news items.

You can see from the Excel spreadsheet that we need the DDD value of the preparation containing oral sulfamethoxazole alone, with the ATC code J01EC01. The DDD is 2 g (i.e. 2000 mg).

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	1000 MG			
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG			
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022				
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYLPENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302				
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707				
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22				
12									

The next product also contains sulfamethoxazole, but in this case, it is combined with trimethoprim in the same tablet. This is an important example, because consumption of this product is high in many countries.

The product is a fixed combination. As explained in Section 2.4.3, this means that we need to know the specific content of each of the active ingredients (sulfamethoxazole and trimethoprim). We will now see how to find that information. Start by searching for sulfamethoxazole in the ATC/DDD index, and clicking on the product with the ATC code J01EE01.

The DDDs for the sulfonamides are related to the duration of effect, i.e. usually the long-acting sulfonamides will have lower DDDs than the short-acting.

J01EE Combinations of sulfonamides and trimethoprim, incl. derivatives

When establishing DDDs for combination products, both components are taken into consideration, see list of DDDs for combination products, www.whooc.no.

ATC code	Name	DDD	U	Adm.R.	Note
J01EE01	sulfamethoxazole and trimethoprim				

If you scroll down to the bottom of the page for “J01EE01 sulfamethoxazole and trimethoprim”, you will see that no DDD is given.

J01 ANTIBACTERIALS FOR SYSTEMIC USE

This group comprises antibacterials for systemic use, except antimycobacterials, which are classified in J04. The antibacterials are classified according to their mode of action and chemistry.

Combinations of two or more systemic antibacterials from different third levels are classified in J01R, except combinations of sulfonamides and trimethoprim, which are classified at a separate 4th level, J01EE.

Combinations of antibacterials and tuberculostatics are classified in J04AM.

Combinations of antibacterials with other drugs, including local anesthetics or vitamins, are classified at separate 5th levels in the respective antibacterial group by using the 50-series. Common cold preparations containing minimal amounts of antibacterials are classified in R05X.

Inhaled antiinfectives are classified here based on the fact that preparations for inhalation can not be separated from preparations for injection.

J01E SULFONAMIDES AND TRIMETHOPRIM

This group comprises systemic sulfonamide and trimethoprim preparations. Combinations of sulfonamide and trimethoprim are classified in J01EE. Preparations containing two or more sulfonamides are classified within the different 4th levels, using the 5th level code 20.

In such combinations, the half-life of the most long-acting sulfonamide determines the classification. Sulfonamides in combinations with other antibacterials (excl. trimethoprim) are classified in J01R. Dapsone is classified in J04 - Antimycobacterials. See also A07A - Intestinal antiinfectives.

Preparations, which in addition contain a urine acidifier, such as vitamin C, calcium- or ammonium chloride, are classified at the plain 5th levels.

The DDDs for the sulfonamides are related to the duration of effect, i.e. usually the long-acting sulfonamides will have lower DDDs than the short-acting.

The ATC/DDD index has particular specifications for DDD values for products that combine two or more active ingredients in a single product. Thus, if you scroll up in the page for "J01EE01 sulfamethoxazole and trimethoprim", you will see that combinations of sulfonamide and trimethoprim are classified under J01E, whereas sulfonamides in combinations with other antibacterials (excluding trimethoprim) are classified under J01R.

WHO Collaborating Centre for Drug Statistics Methodology

Norwegian Institute of Public Health

List of DDDs combined products

The principles for assignment of DDDs for combination products are given in the [Guidelines for ATC classification and DDD assignment](#). See also the main [principles for assignment of DDDs for combined products](#).

For combination products where the DDDs deviate from the main principles the DDDs are included in a separate list (see below). The DDDs in the list are expressed in unit dose (UD).

DDD's decided in October 2018 are included in the list. See new products included [here](#).

ATC Code	Brand name	Dosage form	Active ingredients per unit dose (UD)	DDD comb.
A02BD08	Pylera	caps	bismuth subcitrate 0.14 g/ tetracycline 0.125 g/ metronidazole 0.125 g	12 UD (=12 caps)
A03AX58	Meteospasmyl	caps	alverine 60 mg/ simethicone 0.3 g	2 UD (=2 caps)
A04AA55	Akynzeo	caps	palonosetron 0.5 mg/ netupitant 300 mg	1 UD (=1 caps)

To find the DDD for this product, go to the side bar of the ATC/DDD index site and click on “DDD”, then on “List of DDDs combined products”, as shown in this screenshot.

The list gives the DDD values for a range of combinations. Now, scroll down within the list to find the J01EE codes.

J01CR50	Vicillin-S	Powder for inj	ampicillin 250 mg/ cloxacillin 250 mg	2 UD (=2 grams of powder for injection)
J01CR50	Vicillin-S	Powder for inj	ampicillin 500 mg/ cloxacillin 500 mg	2 UD (=2 grams of powder for injection)
J01CR50	Vicillin-S	tab	ampicillin 125 mg/ cloxacillin 125 mg	8 UD (=8 tab)
J01EC20	Trisulfamid	Tab	sulfacarbamide 0.167 g/ sulfadiazine 0.167 g/ sulfadimidine 0.167 g	4 UD (=4 tab)
J01EE01	Bactrim, Eusaprim, Trimetoprim-sulfa	Inf conc	sulfamethoxazole 80 mg/ trimethoprim 16 mg	20 UD (=20 ml)
J01EE01	Bactrim, Eusaprim, Trimetoprim-sulfa	Mixt	sulfamethoxazole 0.2 g/ trimethoprim 40 mg	8 UD (= 40 ml)
J01EE01	Bactrim, Eusaprim Trimetoprim-sulfa	Tab	sulfamethoxazole 0.4 g/ trimethoprim 80 mg	4 UD (=4 tab)
J01EE02	Triglobe, Trimin Sulfa	Mixt	sulfadiazine 0.205 g/ trimethoprim 45 mg	4 UD (=20 ml)
J01EE02	Triglobe, Trimin Sulfa	Tab	sulfadiazine 0.41 g/ trimethoprim 90 mg	2 UD (=2 tab)
J01EE03	Lidaprim	Tab	sulfametrole 0.8 g/ trimethoprim 0.16 g	2 UD (=2 tab)
J01EE03	Lidaprim	Powder for inj	sulfametrole 0.8 g/ trimethoprim 0.16 g per vial	2 UD (defined as 2 vials)
J01EE06	Sterinor	Tab	sulfadiazin 0.25 g/ tetroxoprim 0.1 g	2 UD (=2 tab)
J01EE07	Berlocombin	Tab	sulfamerazin 0.12 g/ trimethoprim 80 mg	4 UD (=4 tab)
J01RA05	Duobact	tab	levofloxacin 250 mg/ amoxicillin 500 mg	2 UD (=2 tab)

These are the J01EE products listed.

J01CR50	Ampiclox	Tab	benzathine benzylpenicillin ampicillin 0.25 g/ cloxacillin 0.25 g	benzylpenicillin 4 UD (=4 tab)
J01CR50	Amposium	Powder for inj	ampicillin 0.66 g/ oxacillin 0.33 g	2 UD (= 2 g)
J01CR50	Amposium	Caps	ampicillin 0.125g/ oxacillin 0.125 g	8 UD (= 8 caps)
J01CR50	Co-fluampicil	Tab	ampicillin 0.25 g/ flucloxacillin 0.25 g	4 UD (=4 tab)
J01CR50	Vicillin-S	Powder for inj	ampicillin 250 mg/ cloxacillin 250 mg	2 UD (=2 grams of powder for injection)
J01CR50	Vicillin-S	Powder for inj	ampicillin 500 mg/ cloxacillin 500 mg	2 UD (=2 grams of powder for injection)
J01CR50	Vicillin-S	tab	ampicillin 125 mg/ cloxacillin 125 mg	8 UD (=8 tab)
J01EC20	Trisulfamid	Tab	sulfacarbamide 0.167 g/ sulfadiazine 0.167 g/ sulfadimidine 0.167 g	4 UD (=4 tab)
J01EE01	Bactrim, Eusaprim, Trimetoprim-sulfa	Inf conc	sulfamethoxazole 80 mg/ trimethoprim 40 mg	20 UD (=20 ml)
J01EE01	Bactrim, Eusaprim, Trimetoprim-sulfa	Mixt	sulfamethoxazole 0.2 g/ trimethoprim 40 mg	8 UD (= 40 ml)
J01EE01	Bactrim, Eusaprim Trimetoprim-sulfa	Tab	sulfamethoxazole 0.4 g/ trimethoprim 80 mg	4 UD (=4 tab)
J01EE02	Triglobe, Trimin Sulfa	Mixt	sulfadiazine 0.205 g/ trimethoprim 45 mg	4 UD (=20 ml)
J01EE02	Triglobe, Trimin Sulfa	Tab	sulfadiazine 0.41 g/ trimethoprim 90 mg	2 UD (=2 tab)
J01EE03	Lidaprim	Tab	sulfametrole 0.8 g/ trimethoprim 0.16 g	2 UD (=2 tab)
J01EE03	Lidaprim	Powder for inj	sulfametrole 0.8 g/ trimethoprim 0.16 g per vial	2 UD (defined as 2 vials)
J01EE06	Sterinor	Tab	sulfadiazin 0.25 g/ tetroxoprim 0.1 g	2 UD (=2 tab)
J01EE07	Berlocombin	Tab	sulfamerazin 0.12 g/ trimethoprim 80 mg	4 UD (=4 tab)
J01RA05	Duobact	tab	levofloxacin 250 mg/ amoxicillin 500 mg	2 UD (=2 tab)

Now we need to find the combination that we are working with. That combination – a suspension containing sulfamethoxazole (200 mg) and trimethoprim (40 mg) – appears as the second item in the J01EE01 entries. The DDD is given on the left, and the value appears as: 8 UD (= 40 mL)

Thus, the DDD for this product is 8 UD, which is equivalent to 40 mL.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPB REVEST 250MG 10	J01MA02	3592	1000 MG			
3	CEFTRIAZONE	FPB VIAL DRY	F.IM SOL.V. 250MG 2ML	J01DD04	26808	2000 MG			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG			
5	SULFAMETHOX + TRIMETHOPRIM	DGM SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022				
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302				
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707				
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/37 70ML	J01CR02	22				
12									

So, the value that you should write down, which would be needed to complete that row in the Excel spreadsheet, is "8 UD (=40 mL)".

The next item in the list is parenteral vancomycin. As usual, go to the ATC/DDD index website or created pdf file, search for "vancomycin", then find the page for ATC code J01XA01.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD index for J01XA01 (vancomycin). The table below is a reproduction of the data shown on the website:

ATC code	Name	DDD	U	Adm.R	Note
J01XA01	vancomycin	2	g	P	

This is the parenteral form of vancomycin, and it has a DDD value of 2 g. So, the value that you should have written down is 2000 mg.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPB REVEST 250MG 10	J01MA02	3592	1000 MG			
3	CEFTRIAZONE	FPB VIAL DRY	F.IM SOL.V. 250MG 2ML	J01DD04	26808	2000 MG			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG			
5	SULFAMETHOX + TRIMETHOPRIM	DGM SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153	2000 MG			
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022				
8	METRONIDAZOLE	HLA R SYS SUPP NOS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302				
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707				
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/37 70ML	J01CR02	22				
12									

The next product is metronidazole, and the spreadsheet lists two presentations: a parenteral one (ATC group J01) and a vaginal one (ATC group G). Metronidazole for gynaecological use is not included in either the core group or the optional one, according to the WHO methodology, so we will not report its consumption, and will simply leave the remaining cells for that product blank for now.

However, we will look for the DDD value assigned to parenteral metronidazole. Follow the usual steps to find the DDD of this product on the ATC/DDD index website or on the created pdf file.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD Index for J01XD01 (metronidazole). The DDD value is listed as 1.5 g. The website also includes a search bar and a list of abbreviations.

ATC code	Name	DDD	U	Adm.R	Note
J01XD01	metronidazole	1.5	g	P	

You will see that the DDD value for parenteral metronidazole is 1.5 g. So, the correct value that you should write down, that would be included in the Excel spreadsheet, is 1500 mg.

	A	B	C	D	E	F	G	H	I
	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
1	OPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 30	J01MA02	3592	1000 MG			
2	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG			
3	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG			
4	SULFAMETHOX + TRIMETHOPRIM	DGE SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 LID (=80 ml)			
5	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 30ML	J01XA01	153	2000 MG			
6	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022	1500 MG			
7	METRONIDAZOLE	H.L.A.R SYS SU/PP NOS	SU/PP VAG 500MG 30	G01AF01	2325				
8	PROCAINE BENZYLPENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707				
10	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22				
11									
12									

The next product is procaine benzylpenicillin. With the name and the ATC code, you can easily find the DDD value.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD index for procaine benzylpenicillin. The ATC code is J01CE09, the name is procaine benzylpenicillin, and the DDD value is 0.6 g. The website also includes a navigation menu on the left and a search bar at the top.

ATC code	Name	DDD	U	Adm.R	Note
J01CE09	procaine benzylpenicillin	0.6	g	P	

In this case, the value is 0.6 g. Thus, the value that you should have written down in 600 mg.

The screenshot shows an Excel spreadsheet with columns for drug name, route, packaging, ATC code, number of packs, DDD value, number of DDD, and DDD/1000 inh. The row for procaine benzylpenicillin is highlighted in red, showing a DDD value of 0.6 g.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3392	1000 MG			
3	CEFTRIAZONE	FPB VIAL DRY	F, IM SOL V, 250MG 2ML	J01DD04	26808	2000 MG			
4	SULFAMETHOXAZOLE	DGM SYRUP	KAR, 240MG/5ML 100ML	J01EC01		33272 2000 MG			
5	SULFAMETHOX + TRIMETHOPRIM	DGE SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01		87115 8 UD (x40 ml)			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V, INFUSION 500MG 10ML	J01XA01		153 2000 MG			
7	METRONIDAZOLE	FQC INFUS. VIA/BOT.	V, IV 500MG 100ML	J01XD01		2022 1500 MG			
8	METRONIDAZOLE	HLA 8 SYS SUPP NOS	SUP VAG 500MG 30	G03AF04		2325			
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F, IM SOL 0.8 MU/ML 2ML 10	J01CE09		38102 600 MG			
10	CLARITHROMYCIN	DGI DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09		9707			
11	AMOXICILLIN + SUBACTAM	DGI DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02		22			
12									

The next product is oral clarithromycin. Again, find the DDD value from the website.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays the ATC/DDD index for clarithromycin. The ATC code is J01FA09, the name is clarithromycin, and the DDD value is 0.5 g. The website also includes a navigation menu on the left and a search bar at the top.

ATC code	Name	DDD	U	Adm.R	Note
J01FA09	clarithromycin	0.5	g	O	
		1	g	P	

The DDD for the oral route is 0.5 g. Thus, the value that you should have written down is 500 mg.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD	DDD/1000 inh	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	2500 MG			
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG			
5	SULFAMETHOX + TRIMETHOPRIM	DGE SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153	2000 MG			
7	METRONIDAZOLE	FQC INFUS.VIA/BOF.	V.IV 500MG 100ML	J01XD01	2022	1500 MG			
8	METRONIDAZOLE	HLA B SYS SUDD NDS	SUP VAG 500MG 30	G01AF01	2325				
9	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG			
10	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707	500 mg			
11	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22				
12									

The final product is a fixed-dose combination of amoxicillin plus sulbactam, a beta-lactamase inhibitor. The ATC code is J01CR02. Find the relevant page on the ATC/DDD index website.

J01CR Combinations of penicillins, incl. beta-lactamase inhibitors
 This group comprises combinations of penicillins and/or beta-lactamase inhibitors. Combinations containing one penicillin and enzyme inhibitor are classified at different 5th levels according to the penicillin.
 Combinations of two or more penicillins with or without enzyme inhibitor are classified at a separate 5th level, J01CR50. Sultamicillin, a prodrug for sulbactam and ampicillin, is given a separate 5th level code: J01CR04.

The DDD for sultamicillin, a prodrug for sulbactam and ampicillin, is lower than the corresponding DDD for the ordinary combination due to higher bioavailability.

ATC code	Name	DDD	U	Adm.R	Note
J01CR02	amoxicillin and beta-lactamase inhibitor	1.5	g	O	Refers to amoxicillin
		3	g	P	Refers to amoxicillin

A DDD value has been defined for this product, with a value of 1.5 g for the oral route and 3 g for the parenteral route. The product is a syrup, so the route we are interested in is the oral one; thus, the DDD value is 1.5 g. Thus, the value that you should have written down is 500 mg.

	A	B	C	D	E	F	G	H	I	J
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/pack	Consumed DDD	DDD	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	2500 MG				
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG				
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG				
5	SULFAMETHOX + TRIMETHOPRIM	DGE SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153	2000 MG				
7	METRONIDAZOLE	FQC INFUS.VIA/BOF.	V.IV 500MG 100ML	J01XD01	2022	1500 MG				
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707	500 MG				
10	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22	1500 MG				
11										
12										

Now, we have all the DDD values for the antimicrobials included on our consumption list (at this stage, we can remove the gynaecological formulation of metronidazole).

The next step is to calculate the number of DDD of each active ingredient included in one single pack.

	A	B	C	D	E	F	G	H	I	J
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/pack	Consumed DDD	DDD	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVISIT 250MG 10	J01MA02	3592	3000 MG				
3	CEFTRIAXONE	FFB VIAL DRY	F,IM SOLV, 250MG 2ML	J01DD04	26808	2000 MG				
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR, 240MG/5ML 100ML	J01EC01	33272	2000 MG				
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V,INFUSION 500MG 10ML	J01XA01	153	2000 MG				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V,IV 500MG 100ML	J01XD01	2022	1500 MG				
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F, IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707	500 MG				
10	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22	3000 MG				
11										

- Each tablet contains 250 mg
- 1 DDD = 1000 mg
- Each tablet = 250 mg / 1000 mg = 0.25 DDD
- Each package contains 10 tablets
- Each package = 0.25 DDD x 10 tablets = 2.5 DDD

To calculate the number of DDD per pack, we will take into account the information that appears in the Packaging column, as well as the information that was just added to the DDD value column.

Let's start with the first product: ciprofloxacin.

The Packaging column tells us that each tablet contains 250 mg, and the DDD value column that 1 DDD of ciprofloxacin is 1000 mg. So, a single tablet contains 0.25 DDD. This value is obtained by dividing the content of each tablet by the DDD value (that is, 250 mg divided by 1000 mg).

Now, we also know that each package contains 10 tablets. So, to know the number of DDD contained in one package, we multiply the DDD content of each single tablet by 10, for the 10 tablets. The result is that one package contains 2.5 DDD.

	A	B	C	D	E	F	G	H	I	J
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/pack	Consumed DDD	DDD	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVISIT 250MG 10	J01MA02	3592	3000 MG	2.5			
3	CEFTRIAXONE	FFB VIAL DRY	F,IM SOLV, 250MG 2ML	J01DD04	26808	2000 MG				
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR, 240MG/5ML 100ML	J01EC01	33272	2000 MG				
5	SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V,INFUSION 500MG 10ML	J01XA01	153	2000 MG				
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V,IV 500MG 100ML	J01XD01	2022	1500 MG				
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F, IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707	500 MG				
10	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22	3000 MG				
11										

- Each tablet contains 250 mg
- 1 DDD = 1000 mg
- Each tablet = 250 mg / 1000 mg = 0.25 DDD
- Each package contains 10 tablets
- Each package = 0.25 DDD x 10 tablets = 2.5 DDD

Now, we can add this value to the correct cell in the Excel spreadsheet (i.e. in the "Nr DDD x PACK" column). The operation is quite simple, but it is important to understand its mechanics. We will now look at another example.

A	B	C	D	E	F	G	H	I
ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD x PACK	Consumed DDD	DDD
1 CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	1000 MG		2.5	
3 CEFTRIAXONE	FBV VIAL DRY	F IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG			
4 SULFAMETHOXAZOLE	DGM SYRUP	KAR. 240MG/5ML 100ML	J01EC01	31272	2000 MG			
5 SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)			
6 VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153	2000 MG			
7 METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022	1500 MG			
8 PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL. 6.8 MU/ML 2ML 10	J01CE09	38302	600 MG			
9 CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	3707	500 MG			
10 AMOXICILIN + SULBACTAM	DGI DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22	1500 MG			

- Each 2 mL vial contains 250 mg
- 1 DDD = 2000 mg
- Each vial = 250 mg / 2000 mg = 0.125 DDD
- Each package contains 1 vial
- Each package = 0.125 DDD x 1 vial = 0.125 DDD

The next product is ceftriaxone. In this case, it appears as a 2 mL vial for intramuscular injection.

The Packaging column tells us that each vial contains 250 mg of ceftriaxone, and the DDD value column that 1 DDD for parenteral ceftriaxone is 2000 mg.

So, each 250 mg vial is equivalent to 0.125 DDD of ceftriaxone – a value obtained by dividing 250 mg by 2000 mg.

This package has only one vial, so each package contains 0.125 DDD. Thus, the value that you should have written down is 0.125 DDD.

A	B	C	D	E	F	G	H	I
ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/ pack	Consumed DDD	DDD
1 CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	1000 MG		2.5	
3 CEFTRIAXONE	FBV VIAL DRY	F IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG		3.125	
4 SULFAMETHOXAZOLE	DGM SYRUP	KAR. 240MG/5ML 100ML	J01EC01	31272	2000 MG			
5 SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (=40 ml)			
6 VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153	2000 MG			
7 METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022	1500 MG			
8 PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL. 6.8 MU/ML 2ML 10	J01CE09	38302	600 MG			
9 CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	3707	500 MG			
10 AMOXICILIN + SULBACTAM	DGI DRY SYRUP/DROP	PO P/SUSP 400MG/57 70ML	J01CR02	22	1500 MG			

- Each 5 mL of syrup contains 240 mg
- 1 DDD = 2000 mg
- Each 5 mL = 240 mg / 2000 mg = 0.12 DDD
- Each mL = 0.12 DDD / 5 mL = 0.024 DDD
- Each bottle contains 100 mL
- Each bottle = 0.024 DDD x 100 mL = 2.4 DDD

The next product is sulfamethoxazole, and it appears as a syrup. The original Excel spreadsheet says that each 5 mL of syrup contains 240 mg of antimicrobial. And we can see from the spreadsheet that 1 DDD of sulfamethoxazole is 2000 mg.

The 240 mg contained in 5 mL represent 0.12 DDD (that is, 240 mg divided by 2000 mg). Hence, a single millilitre contains 0.024 DDD (that is, 0.12 divided by 5).

Now, because each bottle contains 100 mL, each bottle is equivalent to 2.4 DDD (that is, 0.024 DDD multiplied by 100). Thus, the value that you should have written down is 2.4 DDD.

	A	B	C	D	E	F	G	H	I	J
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/pack	Consumed DDD	DDD	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA32	3192	1000 MG	2.5			
3	CEFTRIAXONE	FPB VIAL DRY	F,IM SOLV, 250MG 2ML	J01DD04	26808	2000 MG	0.125			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR, 240MG/3ML 100ML	J01EC01	33272	2000 MG	2.4			
5	SULFAMETHOX + TRIMETHOPRIM	DKX SUSPENSION	SUSP 240MG/3ML 100ML	J01EE01	87115	8 UD (=40 ml)				
6	VANCOMYCIN	FQD INF DRY BOTTLE	V,INFUSION 500MG 10ML	J01XAC1	153	2000 MG				
7	METRONIDAZOLE	FOC INFUS.VIA/BOT.	V,IV 500MG 100ML	J01XD01	2022	1500 MG				
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F, IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/3ML 60ML	J01FA09	9707	500 MG				
10	AMOXICILLIN + SUBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/37 70ML	J01CR02	22	1000 MG				

- 40 mL of 200 mg + 40 mg / 5 mL = 8 UD = 1 DDD
- Each bottle contains 100 mL
- 100 mL / 40 mL = 2.5 DDD per bottle

The next product is the fixed-dose combination of sulfamethoxazole and trimethoprim. The DDD value that we found for this product is expressed as unit dose (UD).

For this product, we already know that 40 mL of suspension equates to 8 UD, and 8 UD equates to 1 DDD. So, because each bottle contains 100 mL, each bottle is equivalent to 2.5 DDD (that is, 100 mL divided by 40 mL).

	A	B	C	D	E	F	G	H	I	J
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/pack	Consumed DDD	DDD	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA32	3192	1000 MG	2.5			
3	CEFTRIAXONE	FPB VIAL DRY	F,IM SOLV, 250MG 2ML	J01DD04	26808	2000 MG	0.125			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR, 240MG/3ML 100ML	J01EC01	33272	2000 MG	2.4			
5	SULFAMETHOX + TRIMETHOPRIM	DKX SUSPENSION	SUSP 240MG/3ML 100ML	J01EE01	87115	8 UD (=40 ml)	2.5			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V,INFUSION 500MG 10ML	J01XAC1	153	2000 MG	?			
7	METRONIDAZOLE	FOC INFUS.VIA/BOT.	V,IV 500MG 100ML	J01XD01	2022	1500 MG	?			
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F, IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/3ML 60ML	J01FA09	9707	500 MG	?			
10	AMOXICILLIN + SUBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/37 70ML	J01CR02	22	1000 MG	?			

Now it is time for you to practise. Focus on the four products marked with a question mark (?).

Pause the video, and use paper, pen and calculator to determine the values, then move on to the next screen to check your results.

	A	B	C	D	E	F	G	H	I	J
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD/pack	Consumed DDD	DDD	
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA32	3192	1000 MG	2.5			
3	CEFTRIAXONE	FPB VIAL DRY	F,IM SOLV, 250MG 2ML	J01DD04	26808	2000 MG	0.125			
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR, 240MG/3ML 100ML	J01EC01	33272	2000 MG	2.4			
5	SULFAMETHOX + TRIMETHOPRIM	DKX SUSPENSION	SUSP 240MG/3ML 100ML	J01EE01	87115	8 UD (=40 ml)	2.5			
6	VANCOMYCIN	FQD INF DRY BOTTLE	V,INFUSION 500MG 10ML	J01XAC1	153	2000 MG	0.25			
7	METRONIDAZOLE	FOC INFUS.VIA/BOT.	V,IV 500MG 100ML	J01XD01	2022	1500 MG	0.33			
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F, IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG				
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/3ML 60ML	J01FA09	9707	500 MG	3.0			
10	AMOXICILLIN + SUBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/37 70ML	J01CR02	22	1000 MG	5.6			

You can check your results with those that appear in column "G".

If you got them right, well done! If you made a mistake, you can retry your calculations.

The next screen shows the calculations in detail. Once you have mastered them, you can move on to calculating the final value.

<p>Vancomycin: 10 mL for infusion containing 500 mg (because no additional information is given, we would assume that the total content of vancomycin is 500 mg)</p> <ul style="list-style-type: none"> 500 mg / 2000 mg = 0.25 DDD per bottle 	<p>Metronidazole: 100 mL for infusion containing 500 mg (because no additional information is given, we would assume that the total content of metronidazole is 500 mg)</p> <ul style="list-style-type: none"> 500 mg / 1500 mg = 0.33 DDD per bottle
<p>Clarithromycin: 60 mL bottle</p> <ul style="list-style-type: none"> 5 mL contain 125 mg; 60 mL / 5 mL = 12 12 x 125 mg = 1500 mg per bottle 1500 mg / 500 mg (DDD value) = 3.0 DDD per bottle 	<p>Amoxicillin+sulbactam: 70 mL bottle</p> <ul style="list-style-type: none"> 5 mL contain 400 mg amoxicillin (+ 57 mg sulbactam); only amoxicillin is taken into account 70 mL / 5 mL = 14 14 x 400 mg = 5600 mg per bottle 5600 mg / 1000 mg (DDD value) = 5.6 DDD per bottle

This table shows how the values were calculated.

The screenshot shows a spreadsheet with columns for Active Ingredient, ADM ROUTE, PACKAGING, ATC CODE, Nv. PACKS, DDD value, Nv. DDD x PACK, Consumed DDD, and DDD. Row 7 highlights Procaine Benzylpenicillin with a packaging of 2 IM SOL 0.8 MU/VL 2ML D. Below the spreadsheet is 'Annex 4: Conversion factor List' with a table and a list of calculations.

ATC	Administration Route	From	To	Factor
J03CE01	P	MU	G	0.8
J03CE02	O	MU	G	0.625
J03FA02	O	MU	G	0.3125
J03CE08	P	MU	G	0.8
J03CE09	P	MU	G	1

- 2 mL of procaine benzylpenicillin, each mL contains 0.8 MU
- 1 MU = 1 g; so 0.8 MU = 0.8 g = 800 mg
- 800 mg x 2 (mL) = 1600 mg
- 1600 mg / 600 mg (DDD) = 2.67 DDD per bottle

Now, we will look at procaine benzylpenicillin. This antimicrobial is a special case, because the strength is expressed in millions of international units (MU). So, we need to know the conversion factor, which is shown in the conversion factor list.

We can see that the product contains 2 mL of procaine benzylpenicillin, and that each millilitre contains 0.8 MU; 1 MU equals 1 g, so 0.8 MU equals 0.8 g or 800 mg.

Because the product contains 2 mL, we multiply the 800 mg by 2, to give 1600 mg.

The DDD value column tells us that the DDD is 600 mg, so we divide 1600 mg by 600 mg to arrive at 2.67 DDD per bottle.

A	B	C	D	E	F	G	H	I
ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD x PACK	Consumed DDD	DDD
1 CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	1000 MG	2.5		
3 CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG	0.125		
4 SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG	2.4		
5 SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (+40 ml)	2.5		
6 VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01KA01	153	2000 MG	0.25		
7 METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022	1500 MG	0.33		
8 PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG	2.67		
9 CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707	500 MG	3.0		
10 AMOXICILLIN + SUBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/5ML 70ML	J01CR02	22	1500 MG	3.7		

- Basal information: No. of packs consumed during 90 days
Reference population: 198 000 000 inhabitants
- No. DDD consumed during 90 days:
No. packs x No. DDD x pack
 $3592 \times 2.5 = 8980 \text{ DDD}$

Now we move on to "Consumed DDD". That is, we will calculate the number of DDD consumed during the period for which we have information. We already know that the number of packs that appear in the Excel spreadsheet were consumed during one trimester; that is, during 90 days.

This step is easy – we simply multiply the number of packs consumed by the number of DDD per pack.

Let us do this for the first product, ciprofloxacin. We have 3592 packs with 2.5 DDD per pack, giving a figure of 8980 DDD consumed.

Pause the video here and try these simple calculations to complete this column by yourself. Once you have finished, you can continue to the next screenshot to check your results.

A	B	C	D	E	F	G	H	I
ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD x PACK	Consumed DDD	DDD
1 CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	1000 MG	2.5	8980	
3 CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26808	2000 MG	0.125	3351	
4 SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG	2.4	79852	
5 SULFAMETHOX + TRIMETHOPRIM	DGK SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (+40 ml)	2.5	217787	
6 VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01KA01	153	2000 MG	0.25	38.25	
7 METRONIDAZOLE	FQC INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	2022	1500 MG	0.33	667	
8 PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 0.8 MU/ML 2ML 10	J01CE09	38302	600 MG	2.67	102286	
9 CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9707	500 MG	3.0	29121	
10 AMOXICILLIN + SUBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/5ML 70ML	J01CR02	22	1500 MG	3.7	81.4	

- Basal information: No. of packs consumed during 90 days
Reference population: 198 000 000 inhabitants
- No. DDD / 1000 inhabitants consumed during 90 days:
 $\text{Consumed DDD} \times (1000 \text{ inhabitants} / 198\,000\,000 \text{ inhabitants}) = \text{Consumed DDD} / 198\,000$
- $\text{DDD} = \text{Consumed DDD} / 1000 \text{ inhabitants} / 90 \text{ days}$
 $8980 / 198\,000 = 0.045 \text{ DDD} / 1000 \text{ inhabitants}$ $0.045 / 90 \text{ days} = 0.0005 \text{ DDD}$

This screen shows the number of DDD consumed during these 90 days for the nine products.

The final step is to take into account the reference population (that is, the population of the area or the country where these data come from) and the time period.

Our reference population was high: 198 000 000 inhabitants. Looking at the first row, ciprofloxacin, the 8989 DDD were consumed among 198 000 000 inhabitants. First, to calculate the consumption per capita, we divide the 8989 DDD by 198 000 000, then multiply this value by 1000 to obtain the result per 1000 inhabitants, which is 0.045 DDD of ciprofloxacin per 1000 inhabitants.

But... this is the consumption during a 90-day period. And it is difficult to manage the idea of “90 days”, as we are more used to “days”, “months” or “years”.

To unify this, the last step is to adjust the time window to obtain the DDD per 1000 inhabitants per day (DID). This metric can be roughly interpreted as the number of individuals per 1000 inhabitants on antimicrobial treatment per day. DID is an easy calculation too. As we have data for about 90 days, to obtain the daily consumption, we can simply divide the DDD per 1000 inhabitants by 90.

The result will be a small number, because the consumption refers only to 90 days and the country population is high. Nevertheless, this is the mechanics of the process, and the fact that there are a lot of decimal figures means that you have to be very accurate with the calculations and also the transcriptions to the spreadsheet that you use to record consumption. For ciprofloxacin, the result is 0.0005 DID.

Try the remaining calculations yourself, then check your results in the next screenshot.

	A	B	C	D	E	F	G	H	I
	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD x PACK	Consumed DDD	DID
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 30	J01MA02	3592	1000 MG	2.5	8980	0.0005
3	CEFTRIAXONE	FPB VIAL DRY	F.IM SOLV. 250MG 2ML	J01DD04	26908	2000 MG	0.125	3331	0.0002
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 340MG/SAL. 100ML	J01EC01	33272	2000 MG	2.4	7982	0.0045
5	SULFAMETHOX + TRIMETHOPRIM	DGM SUSPENSION	SUSP 240MG/SAL. 100ML	J01EE01	87115	8 UD (-40 mg)	2.5	21787	0.0122
6	VANCOMYCIN	FQD INF DRY BOTTLE	V.INFUSION 500MG 10ML	J01XA01	153	2000 MG	0.25	38.25	0.000002
7	METRONIDAZOLE	FQD INFUS.VIA/BOT.	V.IV 500MG 100ML	J01XD01	3023	1500 MG	0.33	667	0.00004
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 6.8 MU/ML 2ML 30	J01CE09	38302	600 MG	2.67	10286	0.0057
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/SAL. 60ML	J01FA09	9007	300 MG	3.0	29121	0.0016
10	AMOXICILIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/SAL. 70ML	J01CR02	22	1500 MG	3.7	81.4	0.000005

Did you get the right answers? If so, very good!

This is the end of the conversion exercise. As you have seen, once you have clearly identified the exceptions that need to be removed or given special treatment, the task is fairly mechanical.

With the information in this Excel file, you can begin your report. We will discuss this in depth in Modules 4 and 5.

	A	B	C	D	E	F	G	H	I
1	ACTIVE INGREDIENT	ADM ROUTE	PACKAGING	ATC CODE	Nr. PACKS	DDD value	Nr. DDD x PACK	Consumed DDD	DDD
2	CIPROFLOXACIN	ABC FILM-CTD TABS	CPR REVEST 250MG 10	J01MA02	3592	1000 MG	2.5	8980	0.0005
3	CEFTRIAKONE	FFB VIAL DRY	F IM SOLV. 250MG 2ML	J01DD04	26908	2000 MG	0.125	3361	0.0002
4	SULFAMETHOXAZOLE	DGM SYRUP	XAR. 240MG/5ML 100ML	J01EC01	33272	2000 MG	2.4	79852	0.0045
5	SULFAMETHOX + TRIMETHOPRIM	DGX SUSPENSION	SUSP 240MG/5ML 100ML	J01EE01	87115	8 UD (-40 ml)	2.5	217787	0.0122
6	VANCOMYCIN	FQD INF DRY BOTTLE	V. INFUSION 500MG 10ML	J01KA01	153	2000 MG	0.25	38.25	0.000002
7	METRONIDAZOLE	FQC INFUS.VIA/BOT.	V. IV 500MG 100ML	J01KD01	2023	1500 MG	0.33	667	0.00004
8	PROCAINE BENZYL PENICILLIN	FPV VIAL	F. IM SOL 6.8 MU/ML 2ML 10	J01CB01	38302	600 MG	2.67	102286	0.0057
9	CLARITHROMYCIN	DGJ DRY SYRUP/DROP	SUSP 125MG/5ML 60ML	J01FA09	9307	300 MG	3.0	29123	0.0016
10	AMOXICILLIN + SULBACTAM	DGJ DRY SYRUP/DROP	PO P/SUSP 400MG/5ML 70ML	J01CR01	22	1500 MG	3.7	81.4	0.000005
11									

J01C DID: 0.0057 + 0.000005 = 0.005705 DID

Before we complete this module, let us see a small sample of what can be done with these data.

Once you have the consumption expressed in DID, you can add the results to find other information.

For example, the therapeutic subgroup J01C includes all beta lactam antibiotics of the penicillin family. So, to know how many DID in this family have been consumed by our population in this period, we can add all DID belonging to the J01C subgroups.

Excellent! We are now at the end of this process. The first time you complete one of these spreadsheets, it may seem like a laborious task. However, as you gain practice, you will find it gets faster.

It is important to know the mathematical logic behind the calculations, so that you can clearly understand and master the operations involving DDD and interpret the results.

2.5 Keeping the ATC/DDD index up to date

It is recommended to always use the newest version of the ATC/DDD index. The WHO CC for Drug Statistics Methodology in Oslo updates the ATC/DDD system continuously to: account either for new pharmaceutical substances or existing substances that are not yet captured by the system; and alter the ATC codes or DDD values for substances that have already been captured, when that is justified. The list of new ATC codes, DDDs and alterations decided at the meetings of the WHO International Working Group for Drug Statistics Methodology are published on their website. Because of the continuous revisions, it is essential that everyone reports the version of the ATC/DDD used to calculate the consumption. This is important when comparisons are to be made over time and between countries, because such comparisons can only be done if based on the same ATC/DDD version.

As mentioned, the ATC classification is updated annually and does not cover all substances and combinations available globally. Thus, some substances or combinations that exist in your country may be missing from the current ATC classification. If you find that a substance or combination is missing, please send this information to WHO GLASS AMC team (glass-amc@who.int) or WHO CC for Drug Statistics Methodology in Oslo, Norway (whocc@fhi.no), so that an ATC code and a DDD value can be assigned.

To correctly classify the missing substance or combination, the CC needs the information shown in Table 2.4.

Table 2.4. Information needed by the WHO Collaborating Centre for Drug Statistics Methodology, for establishing ATC codes and DDD values

INFORMATION NEEDED FOR ATC	INFORMATION NEEDED FOR DDD
<ul style="list-style-type: none"> • Product name • All active ingredients (including non-antimicrobials) • Formulation (e.g. tablet, syrup, injection) • Indications • Target population, if mentioned (e.g. paediatric products) • Mechanisms of action 	<ul style="list-style-type: none"> • Strength of the product • Dose recommendation according to indication • Frequency of dosing • Route of administration • For combination products, specify whether it is a combination pack with different tablets (e.g. kits for <i>Helicobacter pylori</i>).

Congratulations! You have completed Module 2. In Modules 3 and 4, you will learn about aspects of the national surveillance system, and will gain practical skills that will help you to gather information on AMC, for calculation of the consumed DDD.

2.6 Key messages

The ATC classification and the DDD measuring system are the methodological pillars for the WHO global monitoring of AMC.

In the ATC classification system, the active substances are classified in a hierarchy with five different levels.

Medicines are classified according to their main therapeutic use or pharmacological class, and each administration route of a medicine has only one ATC code.

A given active ingredient can have different ATC codes if it is available in two or more strengths or routes of administration with clearly different therapeutic uses.

WHO methodology uses the number of DDD to measure the consumption of antimicrobials.

To adjust for population size, the consumption is usually presented as DID.

Initially, to identify the different active ingredients in a medicine, the INN is designated by WHO, and in most cases, the name of the active ingredient and the INN are the same.

A single active ingredient can have different brand names, and a brand name can contain more than one active ingredient.

Products that contain two or more active ingredients are referred to as “fixed-dose combinations” or “combination products”.

Combination products are given different ATC codes from plain products containing a single active ingredient.

The ATC/DDD index has particular specifications for DDD values for combination products.

It is recommended to always use the newest version of the ATC/DDD index.

Because of the continuous revisions, everyone should report the version of the ATC/DDD used to calculate the consumption.

The WHO global programme on AMC surveillance monitors antimicrobials for systemic use.

Antimicrobials that are administered topically or for other localized use are excluded from the surveillance programme.

The WHO global programme on AMC surveillance includes a core set of antimicrobial classes (J01, P01AB and A07AA) to be monitored in all national surveillance programmes.

2.7 Exercise solutions and feedback

Answers to Exercise 2.1 (in Section 2.3.2)

NO.	SUBSTANCE	ATC CODE	FEEDBACK
1	Levofloxacin tablets	J01MA12	This is a direct ATC. If you got it wrong, please check that the name you have written in the search field is spelt correctly.
2	Enoxacin	J01MA04	This is a direct search. If you got it wrong or could not find the code, it may be that you have written the capital letter "O" instead of the number "0" in the code.
3	Phenoxymethylpenicillin tablets	J01CE02	This is a direct ATC. If you got it wrong, please check that the name you have written in the search field is spelt correctly.
4	Benzathine phenoxymethylpenicillin tablets	J01CE10	This is a direct ATC. If you got it wrong, please check that the name you have written in the search field is spelt correctly. Also, take care, because some salts and prodrugs have a different ATC than the original molecule.
5	Ampicillin + sulbactam, injection	J01CR01	Some combinations have a specific ATC. This is the case here, where ampicillin with a beta-lactamase inhibitor is classified under J01CR01. Note that ampicillin combined with an analgesic would be classified as J01CA51.
6	Amoxicillin + esomeprazole + clarithromycin, tablets	A02BD06	Again, this combination has a specific ATC. As noted in the lecture, in this case, the expected effect of amoxicillin is local (in the stomach, against <i>H. pylori</i>); thus, the combination is classified under group A (medicines acting on the alimentary tract and metabolism).

Answers to Quiz 2.1 (in Section 2.3.2)

Here are the answers to the quiz. If you chose the wrong answer, check the feedback for an explanation, and revisit Section 2.3.2.

NO.	STATEMENT	ANSWER	FEEDBACK FOR WRONG ANSWERS
1	All antimicrobials are classified under the J therapeutic group.	False	Remember that group J is defined as "anti-infectives for systemic use". So, although most products are classified under the J group, some of them are included in different therapeutic groups.
2	Medicinal products containing two or more active ingredients are considered combinations in the ATC system, and have a different ATC code to the single components.	True	To identify the correct ATC code, it is essential to ensure that data collection is homogeneous. A given active ingredient can have different ATC codes and it is important to accurately identify the appropriate one.
3	J01R is the subgroup used to classify combinations of a systemic antibacterial with other drugs such as local anaesthetics.	False	J01R includes combinations of two or more antibacterials, except for combinations of sulfonamides and trimethoprim, which are under the code J01EE.
4	ATC codes are permanent over time. This allows time comparisons of AMC.	False	ATC codes can change over time, and the list is frequently updated to add newly discovered and marketed products. All changes can be found in the ATC/DDD index website. Deleted ATC codes are never used again for new substances.

Answers to Quiz 2.2 (in Section 2.3.2)

Here are the answers to the quiz, with the answers given in the shaded cells. If you chose the wrong answer, check the feedback for an explanation, and revisit Section 2.3.2.

PRODUCTS	COMPOSITION / PACKAGING	ATC CODE	CORE OR OPTIONAL (ACCORDING TO THE WHO METHODOLOGY FOR AMC MONITORING)	FEEDBACK (FOR INCORRECT ANSWERS)
1	Ampicillin + sulbactam / parenteral	J01CA51	Core	Sulbactam is an inhibitor of beta-lactamase, and a specific ATC has been defined for this combination.
		J01CR01	Optional	
		J01CA01	Not collected	
2	Neomycin / cream	A01AB08	Core	The ATC classification takes into account the therapeutic uses of a given medicine. Thus, the administration route gives information that helps to identify the right ATC code. In this case, the product is formulated as a cream.
		J01GB05	Optional	
		D06AX04	Not collected	
3	Ciprofloxacin / eye drops	J01MA02	Core	The ATC classification has defined different ATC codes for the same active ingredient, according to its potential therapeutic use. In this case, "eye drops" suggests an ophthalmological use rather than an otological or oral use.
		S01AE03	Optional	
		S02AA15	Not collected	
4	Erythromycin / film-coated tabs	D10AF02	Core	It is important to take into account the information about the packaging of the antimicrobial, because this will help you to select the precise ATC for the product.
		J01AF01	Optional	
		S01AA17	Not collected	
5	Ciprofloxacin + phenazopyridine/ tablets	G04BX06	Core	This product includes a combination of the antibacterial ciprofloxacin (J01M) group and the analgesic phenazopyridine (G04BX06). However, the combination of these active ingredients has no specific ATC defined.
		J01RA10	Optional	
		Not defined	Not collected	

Answers to Quiz 2.3 (in Section 2.4.3)

Here are the answers to the quiz. If you chose the wrong answer, check the feedback for an explanation, and revisit Section 2.4.3.

NO.	STATEMENT	ANSWER	FEEDBACK FOR WRONG ANSWERS
1	The DDD value of any medicine is the average number of doses per day for that medicine.	False	Please, pay attention to the precise meaning of the DDD and how is it defined. You will find this information in Reading 2.1 and Reading 2.2.
2	When you present consumption figures as number of DDD, this means the number of treatment days if each patient had consumed a dose equal to the value of the DDD for that medicine.	True	Please, take into account the difference between the DDD value for a given medicine and the number of DDD consumed for a given medicine. You can revisit the narrated video presented in this section, and specifically the last slide.
3	Even special pharmaceutical forms mainly intended for children (e.g. mixtures and suppositories) are assigned the DDD used for adults.	True	Be careful! Usually there are no separate DDD for children. So, the DDD estimates for paediatric formulations are more difficult to interpret.

Answers to Quiz 2.4 (in Section 2.4.4)

Here are the answers to the quiz. If you chose the wrong answer, check the feedback for an explanation, and revisit Section 2.4.4.

NO.	STATEMENT	ANSWER	FEEDBACK FOR WRONG ANSWERS
1	For liquid preparations for oral use of a combination product, 1 unit dose (1 UD) means 1 spoon.	False	Please review the definition of "unit dose", and the cases in which it is used.
2	AMC presented in DDD does not give an exact picture of actual use; it is just an estimate of consumption.	True	Consumption data presented as DDD are an <i>estimate</i> of consumption. This is a useful approach for AMC monitoring at a country scale, but it is important to be aware of the limitations of this method.
3	For topical products containing an antimicrobial, it is possible to use the DDD established for oral preparations with the same active ingredient	False	Revise the definition and general considerations for the use of DDD, as well as the limitations of this method for conducting consumption analyses without biases.

2.8 References

1. World Health Organization, International Working Group for Drug Statistics Methodology, WHO Collaborating Centre for Drug Statistics Methodology, WHO Collaborating Centre for Drug Utilization Research and Clinical Pharmacological Service; 2003 (<https://apps.who.int/iris/bitstream/handle/10665/42627/924156234X.pdf?sequence=1&isAllowed=y>, accessed 26 March 2020).
2. History. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology; (https://www.who.no/atc_ddd_methodology/history/, accessed 2 April 2020).
3. ATC/DDD toolkit. Geneva: World Health Organization; (<https://www.who.int/medicines/regulation/medicines-safety/toolkit/en/>, accessed 26 March 2020).
4. Home page. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology; (<https://www.who.no/>, accessed 2 April 2020).
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7. WHO. GLASS methodology for surveillance of national antimicrobial consumption. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/9789240012639>, accessed 23 August 2021).
8. List of DDDs combined products. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology; (https://www.who.no/ddd/list_of_ddd_combined_products/, accessed 2 April 2020).



National surveillance
systems for antimicrobial
consumption

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3.1 Training objectives of Module 3

The objectives of this short module are to:

help you to identify the key elements and steps on how to establish a national team for antimicrobial consumption (AMC) and a surveillance structure; and share successful experiences from two countries (Thailand and Sweden) of creating national systems for antimicrobial surveillance.

3.2 Background

In Module 1 we saw the importance of monitoring AMC to identify potential problems that could contribute to the increase of antimicrobial resistance (AMR). In Module 2 you had the chance to gain experience in the use of the Anatomical Therapeutic Chemical (ATC) classification and Defined Daily Dose (DDD) and DDD/1000 inhabitants/day (DID) as standard metrics for consumption of antimicrobials in the World Health Organization (WHO) methodology.

Here we underline the importance of setting up national AMC surveillance programmes for improving the use of antimicrobials and informing antimicrobial stewardship. As the surveillance enables measuring the AMC patterns, it highlights the areas of antibiotic use with room for improvement, which can then be targeted by stewardship interventions. WHO defines stewardship as “the careful and responsible management of something entrusted to one’s care” (1). In the case of antibiotics and other antimicrobials, this means appropriate use to improve human, animal or plant health outcomes, while minimizing the development and spread of AMR, and ensuring food safety and security.

The term “antimicrobial stewardship” is encountered in many different and diverse contexts, ranging from antimicrobial stewardship programmes in hospitals and the community, to veterinary antimicrobial stewardship. It involves “the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance” (2). Three goals have been defined for antimicrobial stewardship:

to work with health care practitioners to help each patient receive the most appropriate antimicrobial with the correct dose and duration; to prevent antimicrobial overuse, misuse and abuse in both hospital and outpatient settings; and to minimize the development of AMR.

To reach these goals, multifaceted actions need to be taken at local, country, regional and global levels. AMC surveillance is an important part of the effort to contain increases in AMR. The success of the global AMC surveillance programme that WHO coordinates depends on the active involvement of as many countries as possible.

The pilot phase of the WHO global programme on AMC surveillance took place from 2016 to 2018. A report describing the early implementation of the programme was published in November 2018 (3). The report presents data on the consumption of systemic antimicrobials from 65 countries and areas, contributing to our understanding of how antimicrobials are used in these countries.

To ensure the use of a common methodology for the surveillance of AMC, it is recommended that each country set up a team responsible for establishing and running the national surveillance programme. This module describes the different levels of the AMC surveillance system, and explains how to set up a national surveillance system. It also shares some country experiences that illustrate some of the practicalities of organizing a national system for the surveillance of AMC.

3.3 Setting up a national surveillance system

This section discusses the responsibilities of the AMC national team and who should be included in that team. It also explains the various steps involved in setting up the national surveillance system.

3.3.1 Responsibilities and composition of the AMC national team

To set up a useful and well-structured national team for the surveillance of AMC, it is important to know:

the responsibilities of the national team, within the framework of the WHO global antimicrobial surveillance programme; and the recommendations on the composition of the national team.

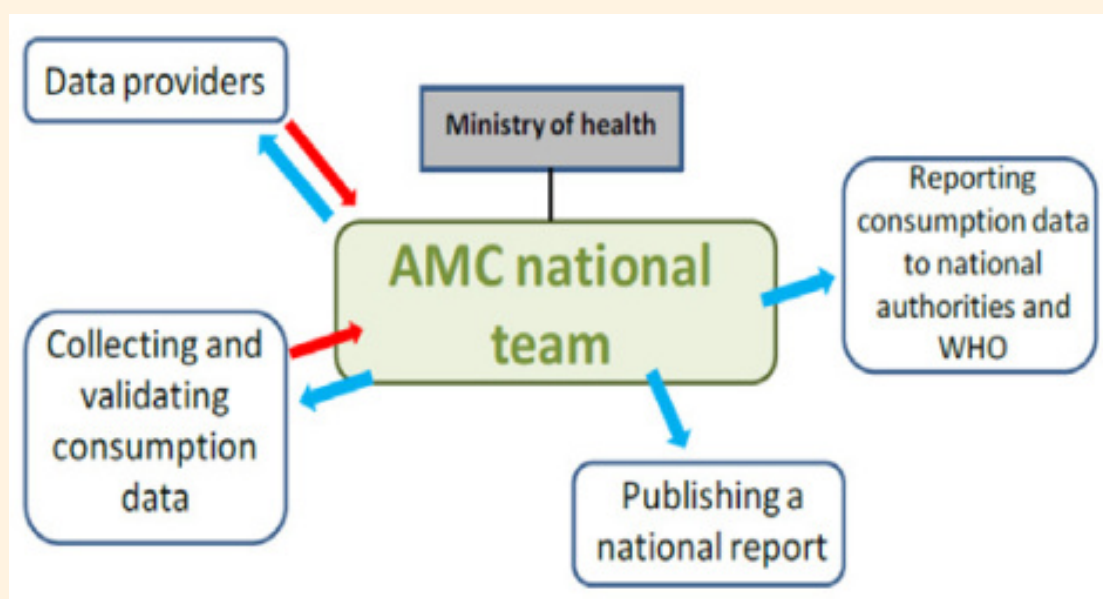
Both topics are described in Lecture 3.1.

Lecture 3.1.

The AMC national team

Although the antimicrobial resistance is a global threat, much of the ground work needed to address the problem must be done at local, national and regional levels. Accordingly, the WHO programme on surveillance of AMC involves activities at three levels: national, regional and global. For example, the figure shows the communication on AMC data between one national team in Africa and WHO headquarters in Geneva, and the support of national AMC activities provided by the WHO Regional Office for Africa.

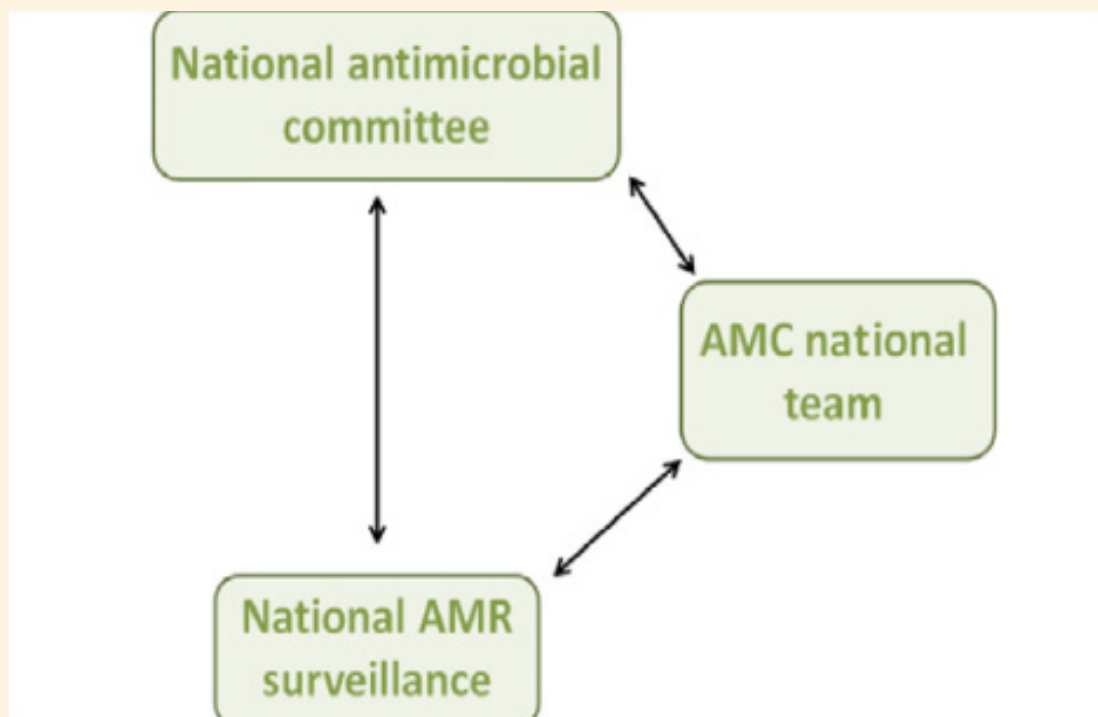
All Member States are invited to contribute at a global level by participating in the Global Antimicrobial Resistance and Use Surveillance System (GLASS), which is hosted by WHO. Participation involves enrolling in the WHO global programme on surveillance of AMC, nominating a national focal point and setting up an AMC national team – that team is the focus of this lecture.



At national level, the AMC national team has the important role of establishing and coordinating the country's surveillance of AMC. Its tasks include collecting and validating the consumption data that comes from data providers identified by the team.

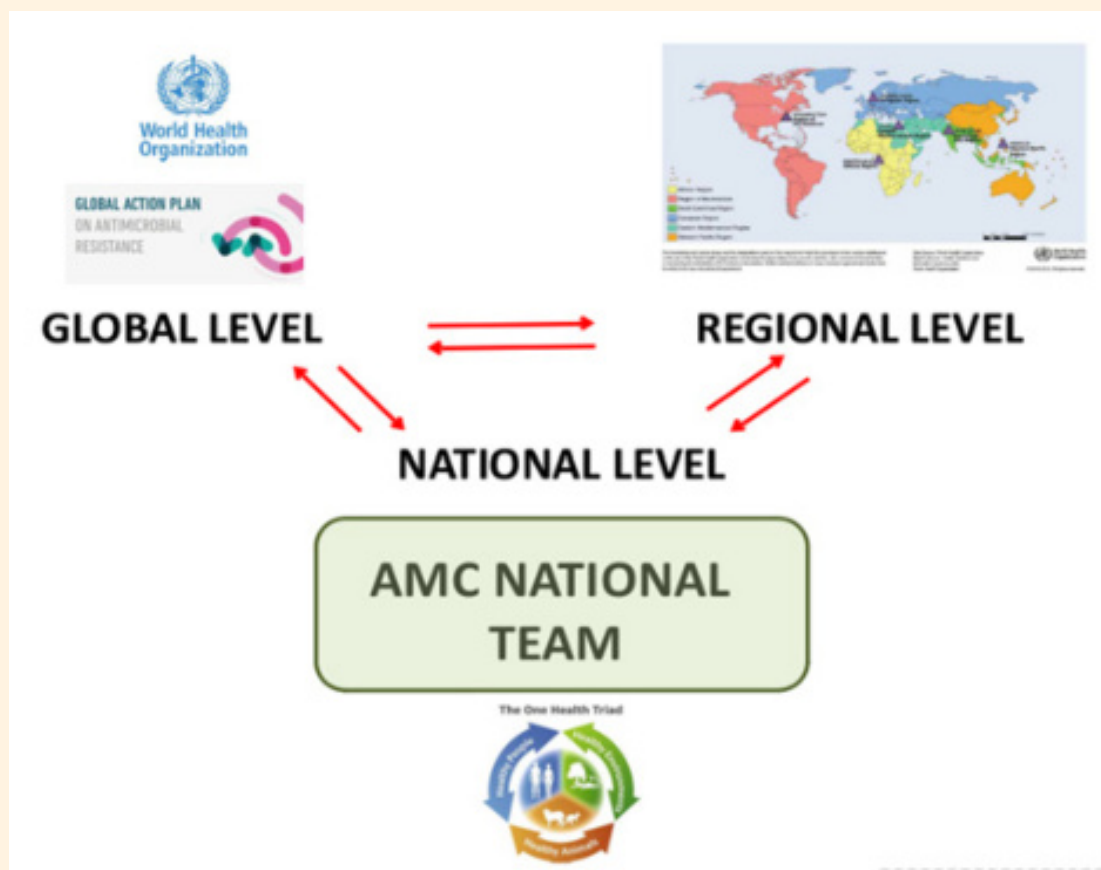
Another vital function of the team is to report AMC data. The AMC national team reports the data at a national level, and makes the results available to relevant stakeholders in the country on a regular basis (for example, by publishing a national report). The team should also report at a global level, to WHO, by uploading the data to the GLASS platform.

To ensure that the AMC national team has support from the national authorities, it should be placed under the authority of the country's ministry of health. Also, there should be regular communication between the AMC national team and data providers, to ensure that the information gathered and reported is accurate and up to date.



To promote good integration of the surveillance of AMC with other relevant national activities, the AMC national team should have links with the national bodies overseeing antimicrobials and antimicrobial resistance (e.g. national antimicrobial committee or equivalent, and the program in charge of the surveillance of antimicrobial resistance).

It should be taken into account that antimicrobial consumption is only one element of a national program on antimicrobial use. Activities such as the development of clinical guidelines and protocols, the availability and affordability of antimicrobial agents, restrictions on use of agents for particular clinical conditions or to nominated prescribers and other activities related to the responsible use of antimicrobials are beyond the scope of the main task of the AMC national team. As these activities are related to the consumption of antimicrobials, it is important that they are coordinated.

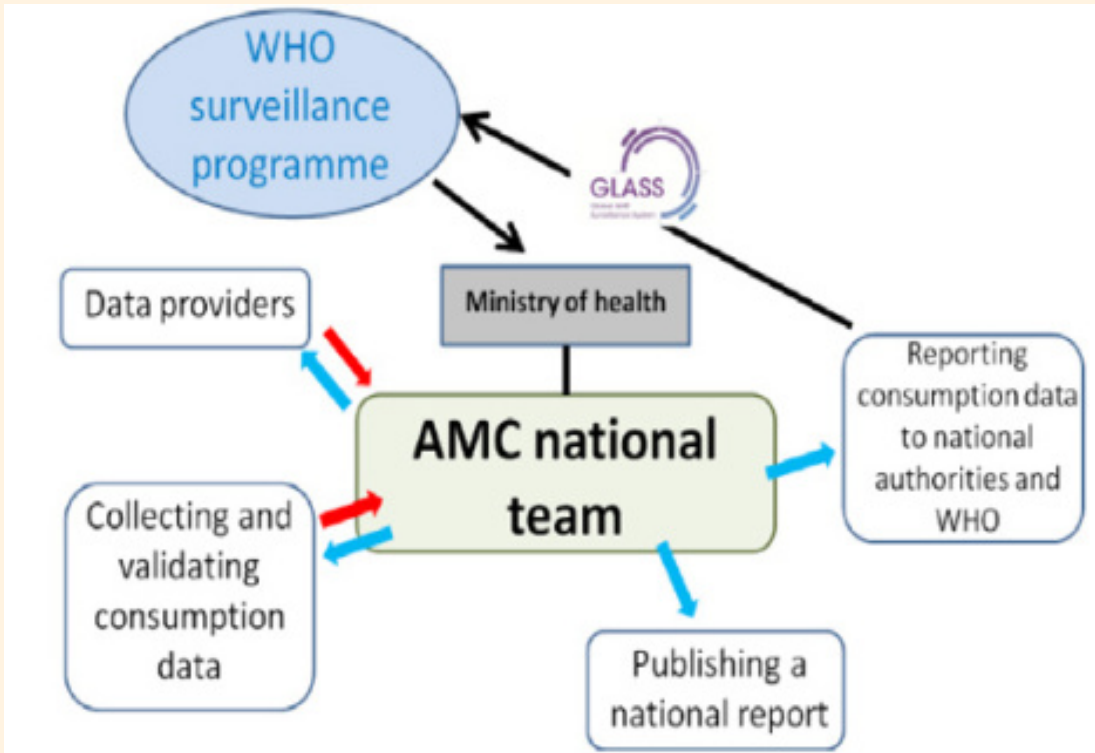


As mentioned previously, there are three levels of surveillance:

- At the *national* level, the AMC national team implements a national surveillance programme on AMC and reports national data at global level., with support from the WHO country and regional offices.
- At the *regional* level, the relevant WHO regional office is responsible for coordinating the WHO’s AMC surveillance programme.
- At a *global* level, WHO is responsible for supporting regional offices and countries for AMC surveillance. In addition, WHO is responsible for coordinating its own surveillance programme on AMC – that programme includes collating and reporting AMC data at the global level.

Understanding how the three levels interact regarding the consumption of antimicrobials helps to highlight the importance of ensuring accurate data collection and analysis at the national level. Effective and well-structured national teams are vital if WHO is to produce accurate information on global AMC that is appropriately interpreted. The teams act as a focal point for collaboration with WHO.

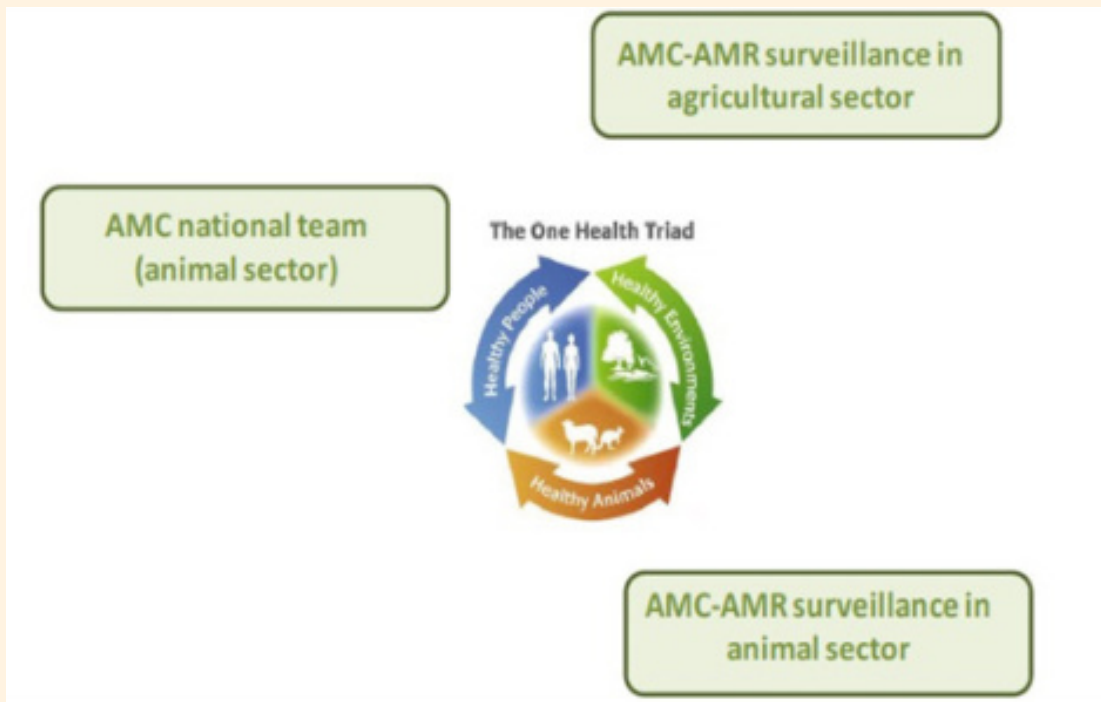
The next lecture in this module describes the steps involved in setting up a national programme to monitor AMC.



WHO gathers data from the WHO regions; it also provides advice and policies to the regions and the countries. Thus, information flows in both directions.

As mentioned at the start of this lecture, WHO global surveillance of AMC is part of the Global Antimicrobial Resistance and Use Surveillance System (GLASS).

WHO has developed GLASS to help to standardize surveillance of AMR and AMC across the world. GLASS collects and reports data on AMR and AMC rates, aggregated at the national level. The GLASS system makes it possible to collect comparable and validated data on AMR and AMC, and then to analyse those data, and share them with countries and partners. The data can be used to inform decision-making; drive local, national and regional action; and provide the evidence for interventions and advocacy. The AMC national team should appoint a national focal point to report AMC monitoring to GLASS.



As part of the “One Health” approach, the AMC national team should have links with the programmes in charge of the surveillance of antimicrobial use and resistance in the animal and agricultural sectors.

3.3.2 Steps in setting up the national AMC programme

Watch Lecture 3.2, which describes the steps in setting up a national programme on surveillance of AMC.

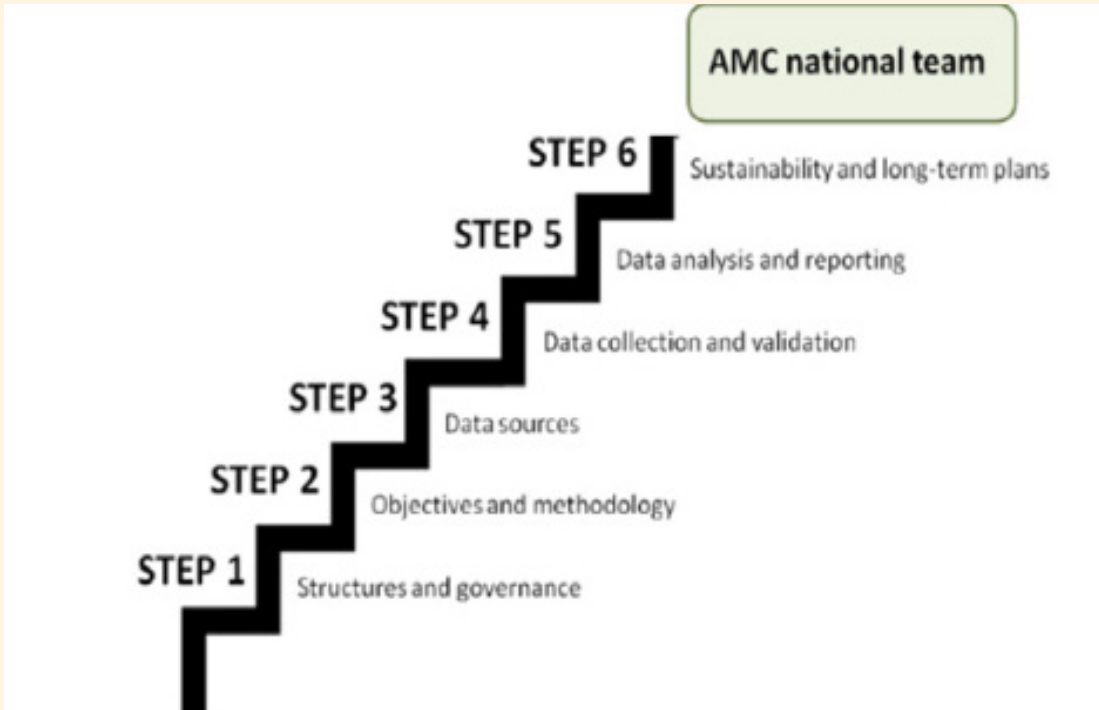
Lecture 3.2.

Steps in setting up the national AMC programme

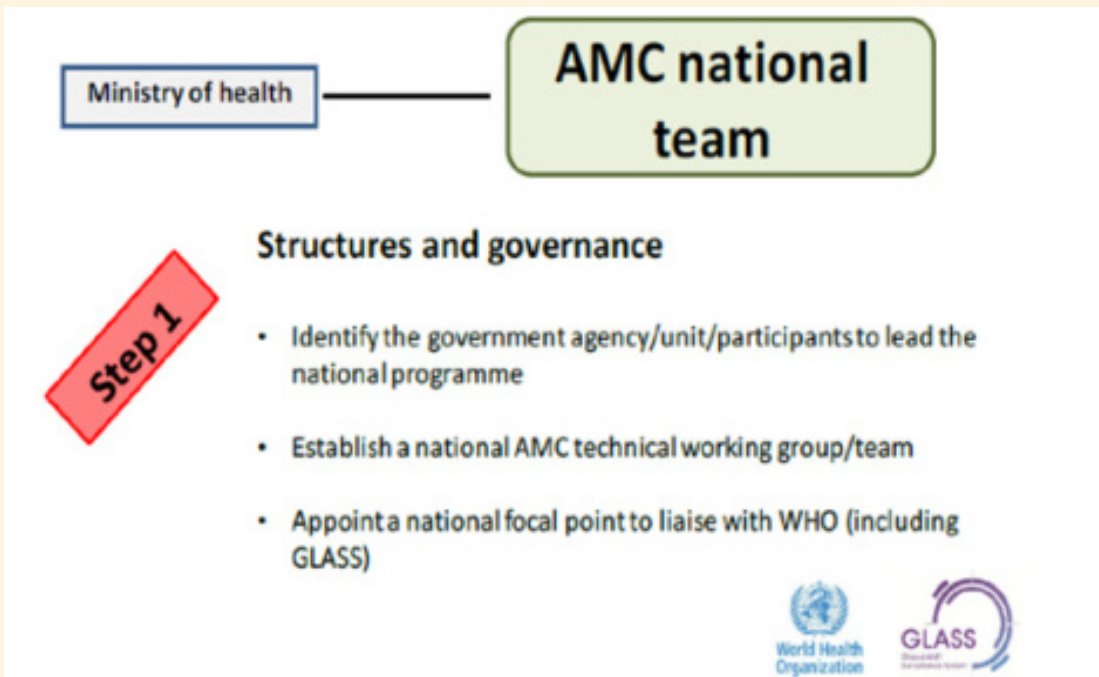


Lecture 3.1 described the main objectives of the AMC national team, and how that relates to the regional and global levels.

The lecture also mentioned that the team should be under the ministry of health, and should have links with other sectors, such as the agricultural and animal sectors.



This lecture describes the six steps in setting up a national programme on surveillance of AMC and discusses the composition of the team.



As already mentioned, the first step is to define the structures and governance of the AMC national team. This starts with identifying the government agency, unit or participants to lead the national programme within the ministry of health. For coordination purposes, the team needs to be linked or to report to the national AMR steering committee.

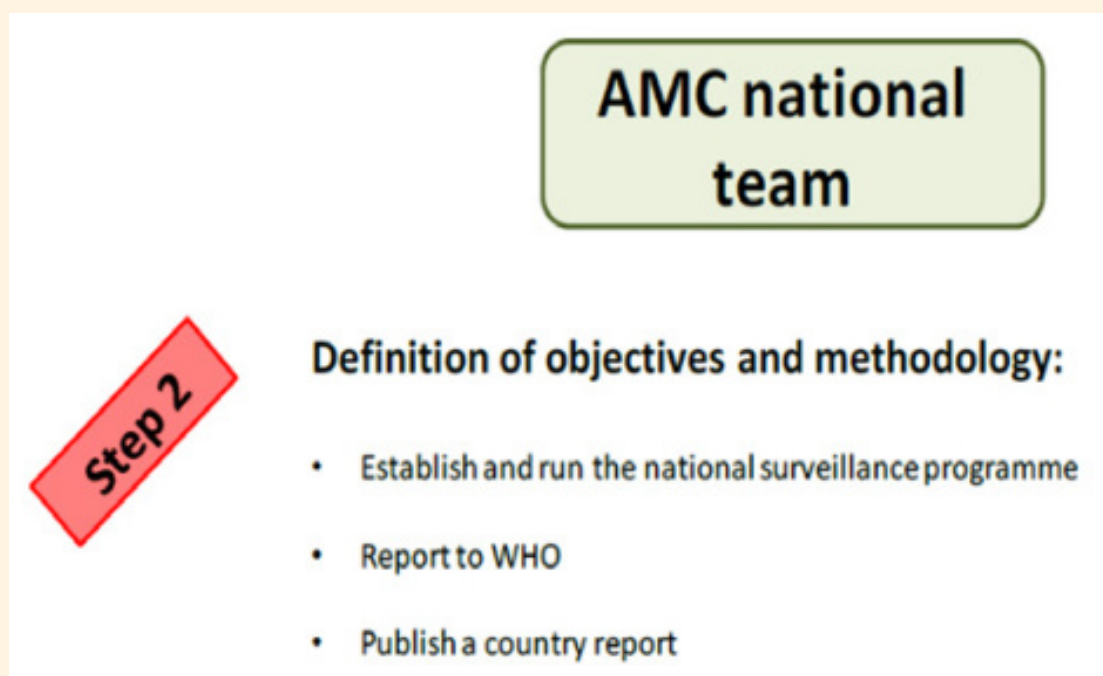
This national AMC technical working group or team needs to be established with clear terms of reference, covering skills in pharmaceutical supply chain systems and data management. The ministry of health also needs to appoint a national focal point for AMC surveillance to liaise with WHO (including GLASS).

The composition of the AMC national team is important, partly to ensure its continuity over time, and partly to ensure the accuracy of its main activity, which is AMC surveillance:

- Given that the team will deal with antimicrobials, at least some members should have a healthcare background in pharmaceuticals (for example, a pharmacist or a clinical pharmacologist).
- Knowledge of data management will also be useful, because the team will aggregate information from different sources.
- At least one member should have knowledge of other areas; for example, a microbiologist (with knowledge of antimicrobial resistance in the country), and a clinician or a physician with experience in clinical practice.
- Also essential are members with knowledge of the national procurement and supply systems, and regulation of medicines.

The AMC national team operates both as a collaborative group and also through working groups. For example, in some settings it may be appropriate to establish a technical working group to coordinate the data collection. If there are multiple data providers, including from the private sector, it may be necessary to establish contracts, to facilitate the release of data.

Finally, in this step, someone from the AMC national team should be nominated as the WHO focal point for AMC surveillance in that country. This person will be responsible for the uploading of AMC data into GLASS, communicating with WHO and ensuring that information received from WHO is shared with the team.



The second step entails defining the objectives of the country's surveillance programme for AMC and ensuring that the team is familiar with the WHO methodology on AMC monitoring, including the ATC/DDD index.

As summarized in Lecture 3.1, the main responsibility of the AMC national team is to establish and run the national surveillance programme on AMC. The next steps in the process cover the activities that this entails, particularly data collection, validation and analysis.

The national team should report to WHO through GLASS. Also, it should ensure that national AMC data are made broadly available on a regular basis; for example, by publishing a country report and making it publicly available.

To meet these objectives, it is important to identify available data resources, and ensure that sufficient human and financial resources are allocated to the national AMC surveillance programme.

AMC national team

Step 3

Data sources

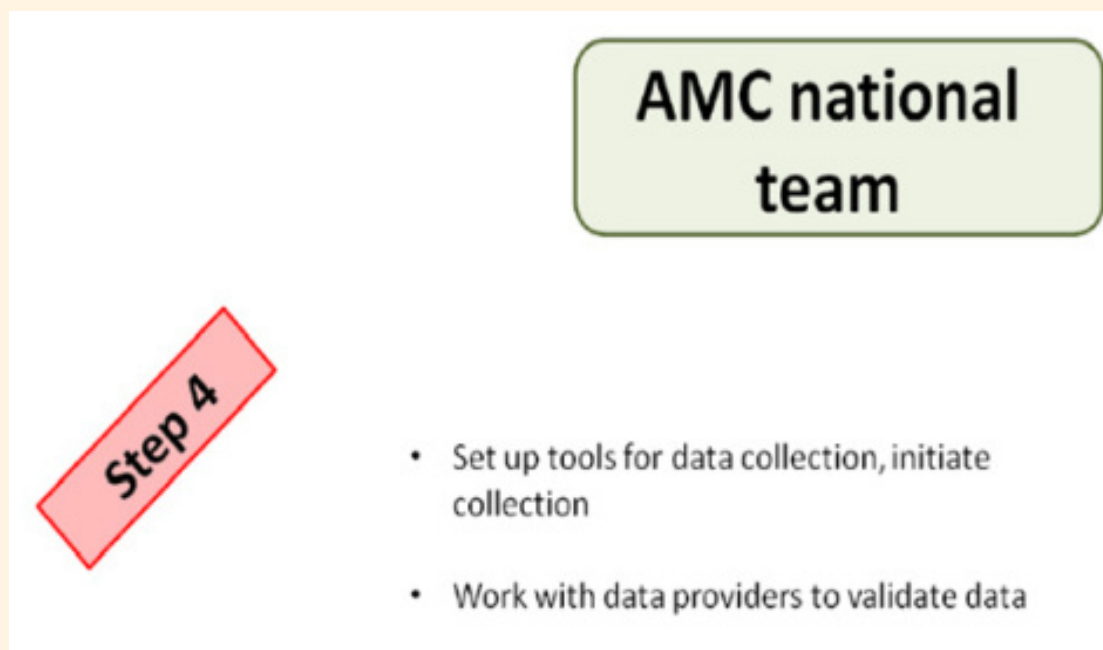
- Identify possible data sources for monitoring AMC – select the most suitable
- Meet data providers – explain purpose of programme and how data will be used
- With data providers, agree on data submission process and legal considerations

In running the national AMC surveillance programme, it is recommended that countries follow the WHO methodology, which is described in Module 2 of this training. Using a common methodology means that AMC results can more easily be compared across countries and over time and can be used to build global and regional consumption maps.

One of the bases of the surveillance is identifying possible data sources for monitoring AMC, and selecting the most suitable data sources, given the objectives and resources available. Use of these data is described in Module 4.

It can be difficult to obtain certain consumption data that originate from different places; for example, sometimes obtaining data requires the collaboration of different ministries. Hence, where necessary, this step includes meeting with the data providers to explain the purpose of the surveillance programme and how the requested data will be used. It may also be helpful to organize a methodology workshop for the data providers.

The final part of this third step is to work with the data providers to agree on the process for data submission, and on any legal considerations related to data ownership, sharing and dissemination. It is important to coordinate data collection from the different providers, ensure that deadlines are met and support data providers (for example, through a help desk).



The fourth step is data collection and validation, which starts with collecting the requested data from the data providers (Step 3). In this step, the AMC national team will first set up tools for data collection (starting with simple tools), and initiate data collection.

Once data have been collected, it is important to validate the data, to ensure that the results of data analysis are reliable. Validation is a two-step process. The first step is to check that the data are complete (for example, that all the information is provided in the correct format, and that there are not a lot of missing data). The second step is to check that the data make sense (for example, are the values for a specific product within the expected range?).

Validation is a key role of the team, because using data that are inaccurate or incomplete, or making errors in data entry (for example, misplacing a decimal point) could change consumption figures. Thus, information that is not validated could produce misleading or imprecise messages for the country, and at regional or global level.

The slide features a light green rounded rectangle at the top right containing the text 'AMC national team'. On the left side, there is a red diamond-shaped label with the text 'Step 5' written inside. To the right of this label, the title 'Data analysis and reporting' is displayed in bold. Below the title is a bulleted list of four tasks.

AMC national team

Step 5

Data analysis and reporting

- Develop a data analysis plan
- Clean and analyse data
- Report and publish results
- Submit national data to WHO

Step 5 is data analysis and reporting.

The first activity is to develop a data analysis plan that outlines the results to be generated, according to the objectives of the plan and the target audience. The next task is to clean and analyse the AMC data, as set out in the data analysis plan. The results of the analyses are then reported and published, and used to inform national strategies to optimize antimicrobial use and combat antimicrobial resistance.

Not all countries will have the capacity for full data analysis and reporting. In such cases, information on drug utilization research may be useful. The text at the end of this Lecture 3.2 has links to various publications on this topic.

The last activity in Step 5 is to submit national data to WHO; this is done through the GLASS platform on an annual basis. Reporting accurate national data at a global level helps to identify perhaps less frequent country or local specific consumption profiles and tendencies that may nevertheless be important. These data are the basis for regional and global campaigns, and policies that, in turn, contribute to improved local consumption.

The diagram features a light green rounded rectangle at the top right containing the text "AMC national team". Below it, a red diamond-shaped box on the left contains the text "Step 6". To the right of the diamond is the title "Sustainability and long-term plans" in bold black text. Below the title is a bulleted list of three items.

AMC national team

Step 6

Sustainability and long-term plans

- Develop IT tools for data collection
- How do we ensure sustainability of the programme?
- How can you collaborate with other relevant programmes?

The sixth and final step is sustainability and long-term plans. A first task in this step is to develop IT tools for data collection; for example, setting up electronic support systems to facilitate data extraction. Automating data collection as much as possible reduces manual work; this decreases the risk of data errors and promotes sustainability.

Another task for the AMC national team is to think about how representative the data are, and how data quality and coverage could be improved. Initially, it may not be possible to obtain complete coverage; in such cases, the team can start small, validate the data quality and then scale up over time.

Ensuring the sustainability of the AMC surveillance programme requires, for example, funding, capacity-building and governance structures.

Finally, it is important to explore possible collaborations between the AMC national team and other relevant surveillance programmes, such as those for antimicrobial resistance and for AMC in other sectors, such as agriculture and animal health.

Information on drug utilization research

As mentioned in Lecture 3.2, some countries will not have the capacity for full data analysis and reporting. In such cases, information on drug utilization research may be useful; for example, the 2003 publication *Introduction to drug utilization research* (4) (which we looked at in Module 2) and information from the Advisory Group on Integrated Surveillance of Antimicrobial Resistance (ASIGAR) (5). Other materials from WHO that may be of interest are the ATC/DDD toolkit (6) and the publication *Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation* (7).

3.4 Successful experiences

The initial sections of this module outlined the theoretical basis for establishing a national team for monitoring AMC at country level, within the framework of the national plan to reduce AMR. This section provides two examples of national surveillance systems – one from Thailand, the other from Sweden – that illustrate the practicalities of establishing the AMC national team and setting up the surveillance infrastructure.

3.4.1 Country 1 – Thailand

Thailand developed a national strategic plan on AMR; one of the pillars of the plan was monitoring of AMC. Reading 3.1 describes the situation that prompted the action, the challenges found, and the lessons learned.



Reading 3.1

Tangcharoensathien et al. (2017) Antimicrobial resistance: from global agenda to national strategic plan, Thailand. (8) (reference: 3.4.1Reading-01).

Read this article about Thailand's experience of setting up a national strategic plan – this will take about 15 minutes. We recommend that you read the full article, but if you are short of time, the parts that are most important are:

- the abstract (provided in Box 3.1);
- the sections titled “Relevant changes” and “Conclusion”; and
- Boxes 1 and 2 in the article.

Box 3.1**Antimicrobial resistance: from global agenda to national strategic plan, Thailand****Abstract**

Problem: In Thailand, antimicrobial resistance has formed a small component of national drug policies and strategies on emerging infectious diseases. However, poor coordination and a lack of national goals and monitoring and evaluation platforms have reduced the effectiveness of the corresponding national actions.

Approach: On the basis of local evidence and with the strong participation of relevant stakeholders, the first national strategic plan on antimicrobial resistance has been developed in Thailand.

Local setting: Before the development of the plan, ineffective coordination meant that antimicrobial resistance profiles produced at sentinel hospitals were not used effectively for clinical decision-making. There was no integrated system for the surveillance of antimicrobial resistance, no system for monitoring consumption of antimicrobial drugs by humans, livestock and pets and little public awareness of antimicrobial resistance.

Relevant changes: In August 2016, the Thai government endorsed a national strategic plan on antimicrobial resistance that comprised six strategic actions and five targets. A national steering committee guides the plan's implementation and a module to assess the prevalence of household antimicrobial use and antimicrobial resistance awareness has been embedded into the biennial national health survey. A national system for the surveillance of antimicrobial consumption has also been initiated.

Lessons learnt: Strong political commitment, national ownership and adequate multisectoral institutional capacities will be essential for the effective implementation of the national plan. A robust monitoring and evaluation platform now contributes to evidence-based interventions. An integrated system for the surveillance of antimicrobial resistance still needs to be established.

Once you have read about Thailand's experience in more detail, please take Quiz 3.1 to test your understanding (you will find the solutions at the end of the module).

**Quiz 3.1**

Are the following statements about the article in Reading 3.1 true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	In Thailand, antimicrobial use in pets is being monitored because people often use antimicrobials created for human consumption to treat their pets.	
2	The development of the strategic plan in Thailand was only possible because the country followed the WHO recommendations.	
3	The examination of key data sets on antimicrobial sales in Thailand indicated that it might be feasible to apply similar approaches to those used in Europe.	

3.4.2 Country 2 – Sweden

Sweden has long had a national strategic programme against AMR. Reading 3.2 is an article that describes the many lessons learned during the 20 years that the programme has been running, providing a unique view based on long-term expertise.



Reading 3.2

Mölstad et al. (2017). Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance. (9) (reference: [3.4.2Reading-01](#)).

Read this article about Sweden's experience with its national strategic programme against AMR – this will take about 15 minutes. We recommend that you read the full article, but if you are short of time, the parts that are most important are:

- the abstract (provided in Box 3.2);
- the sections titled “Next steps”, “Lessons learnt” and “Relevant changes”; and
- Boxes 1, 2 and 6 of the article.

Box 3.2

Lessons learnt during 20 years of the Swedish strategic programme against antimicrobial resistance

Abstract

Increasing use of antimicrobials and rising levels of bacterial resistance to antimicrobials are a challenge to global health and development. Successful initiatives for containing the problem need to be communicated and disseminated. In Sweden, a rapid spread of resistant pneumococci in the southern part of the country triggered the formation of the Swedish strategic programme against antimicrobial resistance, also known as Strama, in 1995. The creation of the programme was an important starting point for long-term coordinated efforts to tackle antimicrobial resistance in the country.

This paper describes the main strategies of the programme: committed work at the local and national levels; monitoring of antimicrobial use for informed decision-making; a national target for antimicrobial prescriptions; surveillance of antimicrobial resistance for local, national and global action; tracking resistance trends; infection control to limit spread of resistance; and communication to raise awareness for action and behavioural change. A key element for achieving long-term changes has been the bottom-up approach, including working closely with prescribers at the local level. The work described here and the lessons learnt could inform countries implementing their own national action plans against antimicrobial resistance.

Once you have read about Sweden’s experience in more detail, please take Quiz 3.2 to test your understanding (you will find the solutions at the end of the module).



Quiz 3.2

Are the following statements about the article in Reading 3.2 true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	Statistics on prescriptions and sales of antimicrobials from all pharmacies in Sweden are made available monthly.	
2	Because the Swedish strategic programme is well developed and has long experience (20 years), it is no longer necessary to engage new stakeholders and include the issue of antimicrobial resistance at all educative levels.	
3	AMC in Sweden can be considered low, compared with other countries. In 2016, the number of DID was 12.5.	

3.5 Key messages

Reaching the goals for antimicrobial stewardship requires multifaceted actions to be conducted at local, national, regional and global levels.

AMC surveillance is an important part of the effort to contain increases in AMR.

Member States participating in GLASS should enrol in the WHO global programme on surveillance of AMC, nominate a national focal point and set up an AMC national team, to take charge of the surveillance of AMC.

As part of the “One Health” approach, the AMC national team should have links with the programmes in charge of the surveillance of antimicrobial use and resistance in the animal and agricultural sectors.

There are six steps to setting up an AMC national team, from structures and governance (Step 1) to sustainability and long-term plans (Step 6).

Congratulations! You have finished Module 3. Now you can proceed to Module 4, which describes different data sources for analysing AMC.

3.6 Exercise solutions and feedback

Answers to Quiz 3.1 (in Section 3.4.1)

Here are the answers to the quiz (the correct answer is given in bold in each case). If you chose the wrong answer, check the feedback for an explanation, and revisit Section 3.4.1.

NO.	STATEMENT	ANSWER	FEEDBACK FOR WRONG ANSWERS
1	In Thailand, antimicrobial use in pets is being monitored because people often use antimicrobials created for human consumption to treat their pets.	True	Correct.
		False	Please revisit the "Relevant changes" section of the paper.
2	The development of the strategic plan in Thailand was only possible because the country followed the WHO recommendations.	True	Please revisit the "Lessons learnt" sections of the paper. Although it is recommended to follow the WHO recommendations, other factors may be more important in a particular country.
		False	Correct. Other factors can be essential to the development of the strategic plan, such as strong political commitment or increased institutional capacities.
3	The examination of key data sets on antimicrobial sales in Thailand indicated that it might be feasible to apply similar approaches to those used in Europe.	True	Correct. It is important to examine the available consumption data sets in order to know what can be done with these data, and the accuracy and weaknesses of the information.
		False	Please revisit the "Relevant changes" section of the paper.

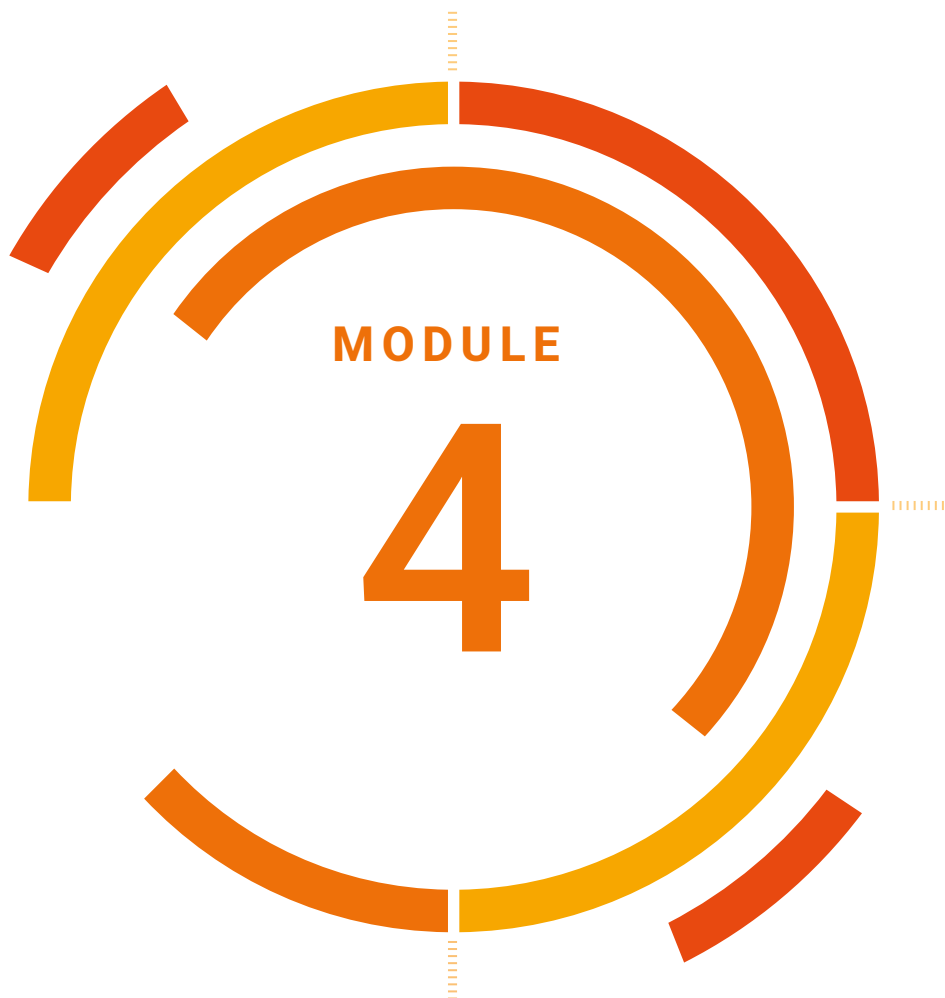
Answers to Quiz 3.2 (in Section 3.4.2)

Here are the answers to the quiz (the correct answer is given in bold in each case). If you chose the wrong answer, check the feedback for an explanation, and revisit Section 3.4.2.

NO.	STATEMENT	ANSWER	FEEDBACK FOR WRONG ANSWERS
1	Statistics on prescriptions and sales of antimicrobials from all pharmacies in Sweden are made available monthly.	True	Correct. Although this provides high-quality estimates, it is not possible in all countries.
		False	Please revisit the paper (try searching for "monthly" in the text, to find the relevant section).
2	Because the Swedish strategic programme is well developed and has long experience (20 years), it is no longer necessary to engage new stakeholders and include the issue of antimicrobial resistance at all educative levels.	True	Please revisit Box 6 in the paper.
		False	Correct. Despite the long experience in the programme, it is always necessary to engage new stakeholders and include the AMR concepts at all levels in order to avoid a rebound effect.
3	AMC in Sweden can be considered low, compared with other countries. In 2016, the number of DID was 12.5.	True	Correct.
		False	Please revisit the paper (try searching for "1.25" in the text, to find the relevant section).

3.7 References

1. Antimicrobial stewardship programmes in health-care facilities in low-and middle-income countries: a WHO practical toolkit. Geneva: World Health Organization; 2019 (<https://apps.who.int/iris/bitstream/handle/10665/329404/9789241515481-eng.pdf>, accessed 27 April 2020).
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3. WHO Report on Surveillance of Antibiotic Consumption 2016 - 2018 Early implementation World Health Organization; 2018 (<https://www.who.int/publications/i/item/who-report-on-surveillance-of-antibiotic-consumption>, accessed 26 March 2020).
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5. Advisory Group on Integrated Surveillance of Antimicrobial Resistance. Geneva: World Health Organization; (<https://apps.who.int/iris/handle/10665/255747>, accessed 26 March 2020).
6. ATC/DDD toolkit. Geneva: World Health Organization; (<https://www.who.int/medicines/regulation/medicines-safety/toolkit/en/>, accessed 26 March 2020).
7. Methods to analyse medicine utilization and expenditure to support pharmaceutical policy implementation. Geneva: World Health Organization; 2018 (<https://apps.who.int/iris/handle/10665/274282>, accessed 26 March 2020).
8. Tangcharoensathien V, Sattayawutthipong W, Kanjanapimai S, Kanpravidh W, Brown R, Sommanustweechai A. Antimicrobial resistance: from global agenda to national strategic plan, Thailand. *Bull World Health Organ.* 2017;95(8):599 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5537745/pdf/BLT.16.179648.pdf>, accessed 26 March 2020).
9. Mölsted S, Löfmark S, Carlin K, Erntell M, Aspevall O, Blad L et al. Lessons learnt during 20 years of the Swedish strategic programme against antibiotic resistance. *Bull World Health Organ.* 2017;95(11):764 (<https://www.ncbi.nlm.nih.gov/pubmed/29147057>, accessed 26 March 2020).



Data sources for the
surveillance of antimicrobial
consumption

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4.1 Training objectives of Module 4

The objectives of this module are to ensure that you:

- are aware of the different sources of antimicrobial consumption (AMC) data;
- know the strengths and limitations of each data source; and
- can identify the different AMC data sources available in your country.

4.2 Background

Previous modules explained the importance of monitoring AMC as part of the objectives of the Global Action Plan on Antimicrobial Resistance (GAP-AMR) (Module 1), how to measure consumption (Module 2) and the importance of establishing an AMC national team (Module 3). The present module describes potential sources of AMC data at country level. This module:

- reviews different sources of AMC data, their description and coverage;
- describes the different health sectors to be monitored and their characteristics;
- discusses appropriate data sources for AMC estimates; and
- provides an example, with commentary, of how to select data sources for AMC purposes.

4.3 Sources of AMC data

This section discusses potential sources of data, the strengths and weaknesses of those different sources, and how to put the data into context.

4.3.1 Data sources for consumption and use

Lecture 4.1 describes how certain words – for example, “use”, “prescription” and “consumption” – are used within the framework of surveillance of the use of medicines. It also describes different information sources for AMC data.

Lecture 4.1.

Data sources for monitoring antimicrobial use and consumption

In previous sections of this course, we have commented on the need to combat antimicrobial resistance, and design measures to stop the present tendency towards increasing resistance. One of those measures is having accurate and up-to-date information on antimicrobial consumption.

What does “consumption” mean
in relation to antimicrobials?

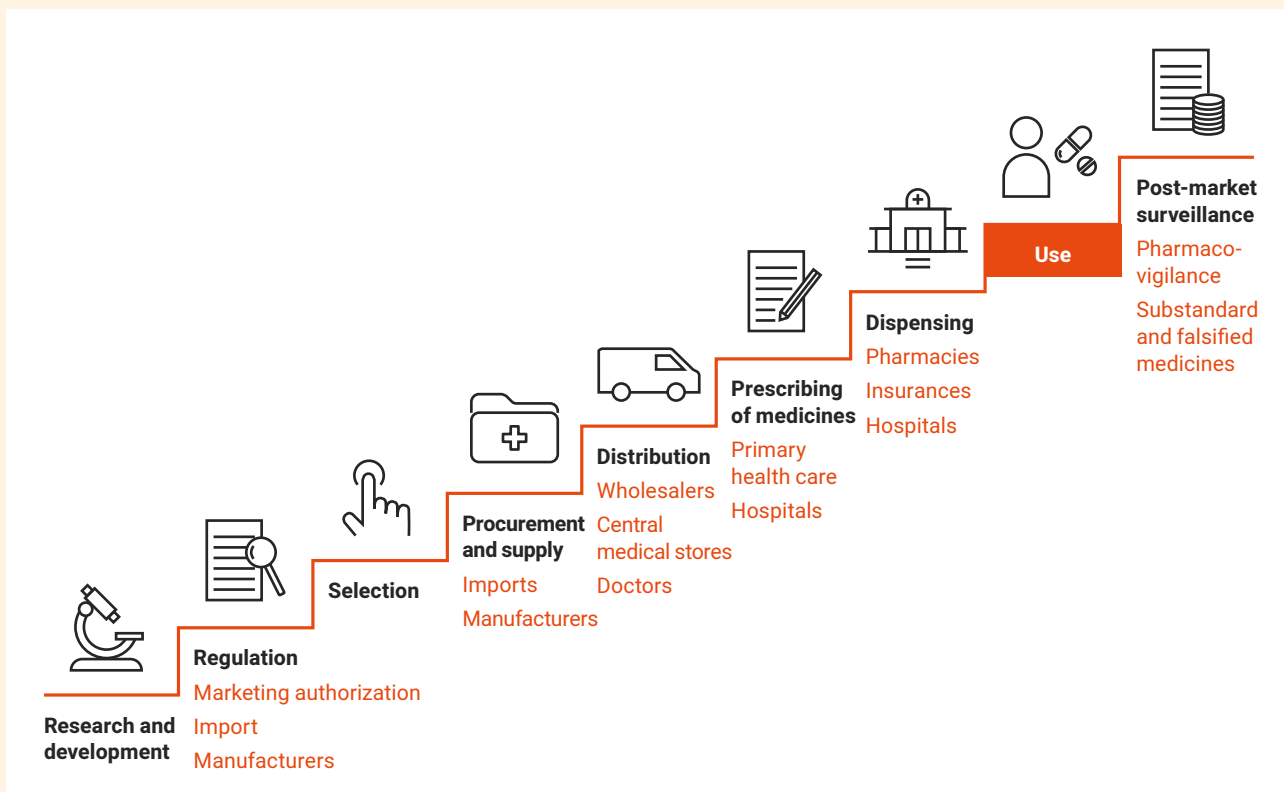


Module 1 discussed the difference between the terms *use* and *consumption* when talking about antimicrobials. That module defined those terms (using the definitions from the WHO methodology document), so you already know that the two words are not synonymous.

As a quick reminder, antimicrobial *consumption* data refer to estimates derived from aggregated data sources; for example, from import, wholesalers or health insurance companies. These data sources generally provide no information on the patients who are receiving the medicines, or why they are receiving them; also, they give no information on how the antimicrobials are being used. Thus, consumption data provide a proxy estimate of antimicrobial use, in terms of which antimicrobials are used and in what quantities.

On the other hand, antimicrobial *use* data refer to estimates derived from patient-level data, such as data on the prescribing, dispensing or use of antimicrobials.

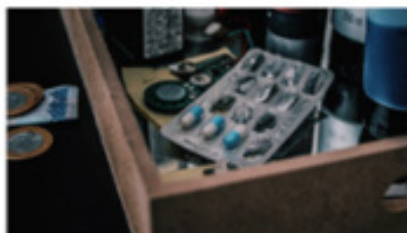
In this training course, we are interested in the surveillance of antimicrobial *consumption* rather than antimicrobial *use*. Before describing the different data sources, let's think about what it means to take a medicine and how we could actually measure that.



This picture shows the value chain of pharmaceuticals and health products; that is, the different links and roles involved in the use of medicines.

This complex value chain ensures that patients receive the medicine they need. It has several major components: research into the medicine, regulatory marketing approval and selection of medicines, procurement and distribution to the dispensing point, prescribing and dispensing to the end users, optimal use of the medicines by patients and, finally, post-market surveillance.

Information on the use of a given medicine can be obtained from four levels of the value chain. These levels are procurement and supply, distribution, prescribing and dispensing. However, the information obtained from each of these levels differs because different data sources have different strengths and limitations. Now, we will look at some examples.



**“Stored”
antimicrobials, in
drawers or
medicine chests**

The closer the data source is to the end user, the more accurate is the estimate but the more laborious it may be to achieve complete national coverage.

Ideally, we would be interested in monitoring all patients who have actually taken an antimicrobial. But, obviously, in practice, this is difficult or impossible, because it would require a team of observers to monitor all potential patients, to confirm that they have actually ingested an antimicrobial. This has been done – for example, where medicines have been administered by nurses to a small group of patients – but it is only feasible on a small scale. Instead, antimicrobial *use* data refers to estimates that are derived from patient-level data. These data can sometimes be broken down based on patient demographic characteristics (such as gender and age) or the indication for which the medicine is being used. Depending on the source of the information, it may also be possible to determine the patients’ symptoms, the physician diagnoses and the medications ordered. Such information can be used to assess clinical practice against agreed protocols and treatment guidelines. At the end of this section, there is information about one WHO tool for assessing the use of antimicrobials in hospitals with point prevalence surveys (1).

When talking about the use of medicines at the patient level, there are some other factors to take into account. First, not all the tablets that are prescribed and dispensed are actually taken by patients. For example, if a package includes more tablets than are needed to complete a treatment, people usually keep the remaining pills in a drawer or medicine cabinet at home.

On the other hand, the patient or another member of the household may then take the tablets remaining in a package that was sold weeks or even months before.

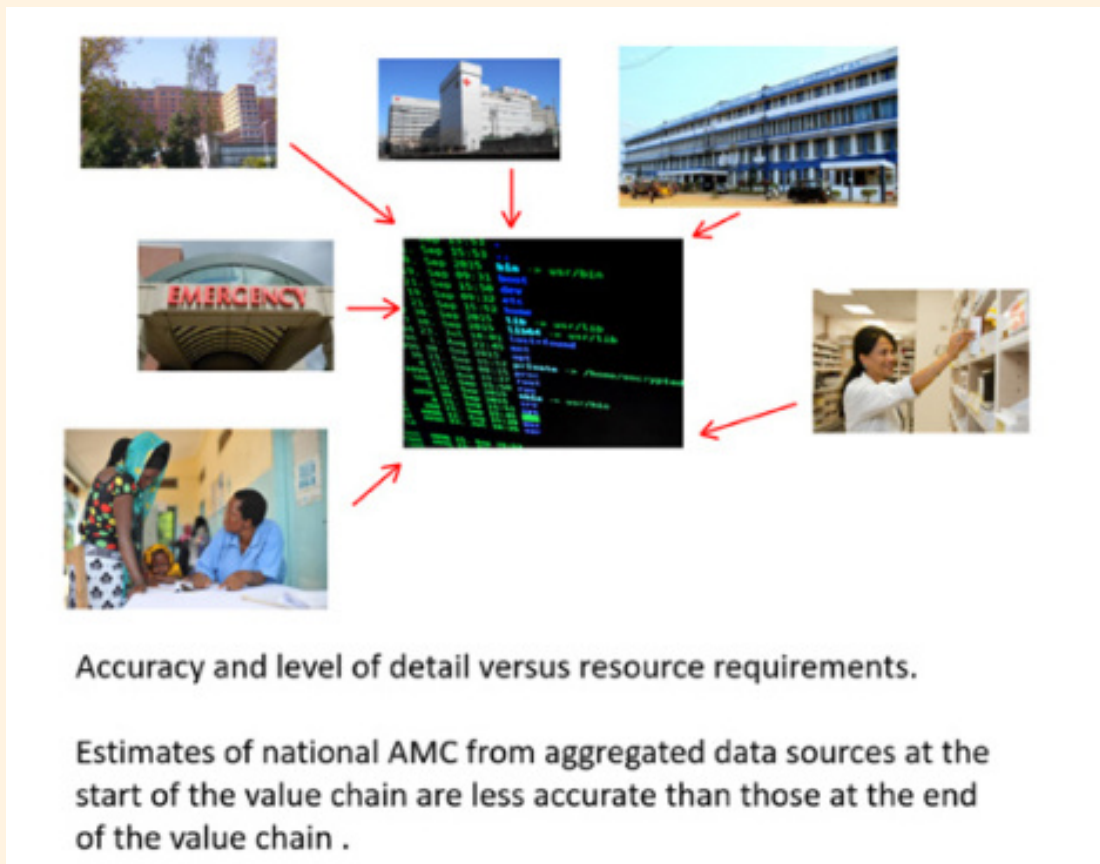
It is difficult for data sources to reflect this situation. Clearly, monitoring medicine cabinets to look for antimicrobials can only be done in small studies – it is not realistic at a large scale.

Consumption data are from official channels (e.g. from manufacturers and distributors up to health care providers)



As mentioned previously, this training focuses on the collection of *consumption* data rather than *use* data. Consumption data provide information on the quantity and types of consumed antimicrobials, without any patient-level details. Consumption data are the data that are used in the WHO methodology for national surveillance of AMC (2). Remember that the term “consumption data” refers to estimates derived from aggregated data sources, such as importers, wholesalers or health insurance companies. According to WHO methodology, data are collected from official channels only, so no data explicitly capturing antimicrobials circulating on the informal market are to be obtained. To monitor the *consumption* of antimicrobials at a country or regional level, the realistic approach (although not the most accurate) is to gather information from different sources about bulk acquisition of medicines – for example, import agencies, manufacturers and distributors, health ministries, medicines agencies and procurement entities. In doing this, it is important to avoid an overlap between data sources, which would result in double counting.

Some of these sources only include data taken from the public health sector, whereas others include data from both the public and the private sector.



These aggregated centralized data at the start of the value chain are often collected for administrative purposes, which makes them more accessible and less laborious, and helpful for routine surveillance in the early stages of the collection process. However, the issue of excess stock is also more significant in data sources nearer to the start of the value chain of pharmaceuticals (that is, further away from the end user; for example, import, production and central procurement records) compared with data from sources closer to the end of the value chain, such as prescribing and dispensing records. In terms of data coverage, these aggregated national data sources at the start of the value chain represent, by definition, the consumption by the whole population more accurately than the more scattered health care providers' records. On the other hand, because of the stock issue and other imprecisions, using these data sources increases the bias when estimating antimicrobial consumption, and provides no patient-level detail. However, collecting information from data sources closer to the end user often requires more resources.

It is up to the country to work out a compromise between accuracy and level of detail versus resource requirements. Despite these issues, aggregated data are considered a good proxy for antimicrobial use, and they enable countries with limited resources to use pre-existing data sources to build sustainable programmes for AMC surveillance.

When reporting data on antimicrobial consumption, it is essential to specify the data sources used, and comment on the completeness of the data.

4.3.2 Data sources: strengths and weaknesses

As explained in Lecture 4.1, the aggregated data on AMC from different sources provide a proxy estimate of the use of antimicrobials (i.e. an approximation of the actual use of these medicines). Another aspect of this type of data is coverage, which refers to the proportion of all antimicrobials used that is estimated to be covered by the data sources. For example, data sources may cover only the public sector, or may have wider coverage, encompassing both the public and private sector.

Before selecting data sources for AMC monitoring, it is important to understand the strengths, limitations and biases of the data sources chosen. Lecture 4.2 describes different data sources, and discusses the strengths and weaknesses of each source.



Lecture 4.2.

Data sources: strengths and limitations


1. Community, household survey data

Strengths:

- data reflect actual use

Limitations:

- can be time consuming and difficult
- recall bias



Community or household survey data can provide data at the patient level that closely reflect actual use. However, carrying out such surveys is time consuming and difficult, especially in rural and remote areas. Another limitation of survey data is recall bias (that is, participants may not remember events accurately or may forget to mention events), and this should be taken into account when analysing data from community or household surveys.

Data sources: strengths and limitations

2. Prescribed antimicrobials

Strengths:

- contains significant patient information
- may include diagnosis and co-prescriptions

Limitations:

- patients not obtaining and taking antimicrobials
- antimicrobials being available without prescription



Antimicrobials are medicines that require a prescription, and that prescription contains a lot of significant information. For example, a prescription should include the name of the antimicrobial, and the dosage and duration of treatment. These data should also be included in the patient's clinical chart. Some health professionals maintain databases that also include the diagnosis and any co-prescribed medicines. Thus, it seems that prescriptions could be valuable in monitoring actual antimicrobial use. However, there are two main limitations to the use of prescriptions as an information source.

One issue is that patients can receive a prescription, but they do not necessarily go to the pharmacy, obtain the medicine and take it as prescribed. Another issue is that, in some settings, it is easy to purchase antimicrobials without a prescription. Thus, although "prescription" is another proxy for antimicrobial use, and analysis of prescription data can be useful, the limitations of this approach should be taken into account.

Gathering information on prescriptions requires a health care system that is prepared to collect and retrieve this information.

Another way to gather patient-level consumption data is through health insurance data. Such sources often include complete and detailed patient-level information, but it may not contain information from the private sector; sometimes, the information provided only covers reimbursement of antimicrobials. In addition, the data may not be representative of the whole population, because in many settings only selected populations are covered by health insurance.

Data sources: strengths and limitations

3. Dispensed antimicrobials

Strength:

- data reflect actual use

Limitations:

- may need to pay for data
- may have legal restraints
- information may differ among countries
- does not include concomitant treatments



Dispensing records in pharmacies are another source of information on antimicrobial consumption. Sales from pharmacies and drug stores provide information that is closer to the actual use of antimicrobials by patients, but collecting such data can be difficult, labour intensive and time consuming if the only records available are manual ones (not all countries have electronic databases).

Some well-known and reliable initiatives, such as the company IQVIA (formerly Quintiles and IMS Health), provide sales data in many countries, but this information source also has some limitations. Market research companies of this type are private entities, so the information often needs to be purchased, and it may come with legal restraints on use and sharing of the data.

Another limitation of dispensing records is that the information collected is not the same in all countries. For example, if Country A does not include hospitals in the consumption data, the data provided are useful for time comparisons within Country A, but may not be suitable for comparison with other countries. Also, in some countries, dispensing records may not be available from the public sector.

Finally, a dispensing record does not take into account concomitant treatments.

Data sources: strengths and limitations

4. Donations



Strength:

- significant proportion of antimicrobials

Limitation:

- may be difficult to differentiate populations

In some countries, donations may account for a significant proportion of antimicrobials dispensed for specific clinical programmes such as malaria, tuberculosis and HIV/AIDS (including antibiotics for opportunistic infections).

Again, there are limitations on this data source; for example, it may be difficult to differentiate between the local population and special populations (such as migrants or refugees).

Data sources: strengths and limitations

5. Wholesalers



Strengths:

- data on purchase and supply
- may be disaggregated

Limitations:

- other importers
- difficulty of obtaining from private sector
- possible duplication and overestimation

Wholesalers are a good source of consumption data. In most countries, wholesalers are the main legal entity able to import medicines for distribution, and to provide data on purchase and supply. In some cases, the data may be disaggregated by region, sector or type of facility.

Distribution and supply data are likely to be closer to actual consumption than purchase data. However, as with other sources, there are limitations. For example, in some countries, wholesalers are not the only institutions that can import medicines; other importers can include medical, dental and veterinary practitioners, pharmacists and health care institutions.

It may be difficult to obtain data from the private sector. Also, in some countries, a large number of wholesalers supply smaller wholesalers, increasing the risk of duplication and overestimation of data.

Data sources: strengths and limitations

6. Procurement



Strengths:

- data on purchases, disaggregated

Limitations:

- may not reflect total public consumption
- may include stock not supplied

Another important data source is public sector procurement. The public sector is likely to have reasonable documentation of purchases, with the data probably disaggregated and broken down according to facility types (for example, hospital and community) or geographical location.

However, this only provides data for public sector acquisitions, so it may not reflect total public sector consumption, if other procurement is undertaken directly by hospitals and health facilities. Therefore, the AMC national team should map and analyse the particular characteristics of the country's value chain of pharmaceuticals.

Additionally, it is possible that data include stock that was procured but never supplied to health facilities.

Data sources: strengths and limitations

7. Domestic manufacturers



Strengths:

- easy to identify producers

Limitations:

- private companies may be unwilling to provide data
- reflects production not consumption
- may include antimicrobials for export

The production of antimicrobials by domestic manufacturers is another data source. It should be easy to identify local licensed producers, and there is likely to be a good register of the product volumes for local use and for export.

Nevertheless, private companies may be unwilling to provide data and, once again, volumes reflect production rather than consumption patterns. Also, some of the domestic manufacturing may be directed for export. If so, these quantities need to be documented in order to obtain more accurate consumption figures.

Data sources: strengths and limitations

8. Import data



Strengths:

- centralized records
- realistic data on consumption

Limitations:

- incomplete documentation
- parallel trade stock movements
- match import cycles not consumption
- misses re-export

Import permits are another source of data. Governments issue such permits for the importation of medicines purchased from international manufacturers. Usually, records of import permits are centralized, and they are often standardized for customs declaration forms, which include information such as product type (branded or generic), volume, port of origin, country of manufacture, batch number and expiry date. Over-the-counter products are also included in these registries, providing more realistic data on the actual consumption of antimicrobials.

Again, this source has some limitations. For example, documentation may be incomplete, it may include parallel trade stock movements (that is, companies buy drugs from countries where the prices are low and resell them in countries where the prices are high), and volumes may match import cycles rather than consumption patterns. Also, import reports do not capture the re-export of medicines.

Another potential source of information on importation is records from the main nongovernmental organizations (NGOs). For example, NGOs may distribute medicines for specific programmes (such as tuberculosis), or manage donations of medicines. Although the records from NGOs provide only partial information on importation, they can still be useful.

Now that you have finished the lecture, please read the text in Boxes 4.1 and 4.2.

Procurement and supply at country level

Box 4.1 explains what procurement and supply of antimicrobial agents at the country level involves, and summarizes potential sources of information on AMC. The text is from pages 14–15 of the *WHO methodology for a global programme on surveillance of antimicrobial consumption (2)*.

Box 4.1

Procurement and supply at country level

Procurement and supply of antimicrobial agents at the country level may be complex.

In its simplest and 'idealised' form, for a country without domestic manufacturing capacity, antimicrobials are imported (licensed imports with customs records), are supplied and distributed by licensed wholesalers and distributors to:

- Public and private hospitals
- Community health facilities and community pharmacies.

Then, are provided to patients based on prescriptions written by appropriately registered health care professionals. In some countries, these medicines will be reimbursed by health insurance programs, with or without the imposition of patient co-payments.

The reality in many countries is quite different. Antimicrobials may be sourced from both international and domestic producers.

- Imports may be subject to re-export to other countries
- Domestic producers may export part of their production.
- Orders may be placed with wholesalers or directly with manufacturers.
- Imported products may be used in the veterinary and agriculture sectors as well as for human use.

- Healthcare professionals and patients may be able to import products directly.
- Antimicrobials may be purchased over-the-counter as well as with prescription.
- Borders may be 'porous' with illegal imports and exports.
- Patients may buy products in neighbouring countries where products are cheaper.

POTENTIAL SOURCES OF INFORMATION ON ANTIMICROBIAL CONSUMPTION

There are a number of potential sources of information on consumption of antimicrobials:

- import data (using data from customs records and declaration forms)
- production records of domestic manufacturers (exclude any exports of products)
- wholesaler/distributor data – this could be data on procurement by wholesalers or records of sales by the wholesalers to healthcare facilities and pharmacies
- public sector procurement records – these exist where there is both centralised and decentralised purchasing of medicines for the public sector
- donations – this may relate to particular programs such as HIV, TB, malaria or for special populations such as migrants and refugees
- records from community and hospital pharmacies and licensed drug stores
- data from health insurance programs
- prescribing records of doctors and dispensing records of pharmacists
- information on antimicrobial use from patients themselves.

Summary of different data sources

Box 4.2 provides a table that summarizes different data sources for consumption estimates, and outlines the general strengths and limitations of the data obtained from the different levels of the value chain. The table is Annex 2 of the 2018 publication *WHO report on surveillance of antibiotic consumption Early implementation 2016–2018 (3)*.

Box 4.2

Summary of different data sources

Common data sources containing aggregated information on antimicrobial consumption and their respective strengths and limitations

Data source	Strengths	Limitations
Import data	<ul style="list-style-type: none"> - Import permits issued by Government - Centralized records - Standardised reporting for customs declaration forms including product type (generic, branded), volume, port of origin, country of manufacture, batch number, expiry date) - Includes OTC medicines 	<ul style="list-style-type: none"> - Documentation may be incomplete - May include parallel trade stock movements - Not account for smuggled goods or illegal entry of products - Volumes match import cycles not consumption patterns - Are administrative records and not formatted for research and analysis
Domestic manufacturers	<ul style="list-style-type: none"> - Local licensed producers should be easily identified - Can separate product volumes for local use and for export - Can request data in format suitable for analysis 	<ul style="list-style-type: none"> - Private companies may be unwilling to provide data - Volumes reflect production not consumption patterns
Public sector procurement	<ul style="list-style-type: none"> - Likely to have reasonable documentation of purchases - Disaggregation of distribution data to facility types (community and hospital) and geographical location is possible - May be single (or limited number) of procurement agencies 	<ul style="list-style-type: none"> - Only provides data for public sector - May not reflect total public sector consumption if other procurement is undertaken by hospitals, health facilities - May include stock procured but never supplied
Wholesalers	<ul style="list-style-type: none"> - Only legal entity able to import medicines for distribution - Can provide purchase and supply data - Supply data may be disaggregated (community/hospital; by regions, facility type) - Data collection easier where limited numbers of wholesalers - Distribution/supply data likely to be closer to actual consumption than purchase data 	<ul style="list-style-type: none"> - Some countries medical, dental, veterinary practitioners and pharmacists can also import medicines - May be difficult to get data from private sector - Large number of wholesalers in some settings - May supply other smaller wholesalers not 'end-users' - Wholesalers may provide agriculture and veterinary sectors as well as for human use
Donations/Programs	<ul style="list-style-type: none"> - May be significant proportion of antimicrobials dispensed for specific clinical programs or specific populations 	<ul style="list-style-type: none"> - May be difficult to differentiate donations for local population and special populations (migrants, refugees)
Community and hospital pharmacies, drug stores Dispensing data	<ul style="list-style-type: none"> - Sales from pharmacies or drug stores is closer to the actual use of antimicrobials by the patients - Can separate community and hospital sectors - Potentially can separate to public and private sectors - May include some OTC medicines 	<ul style="list-style-type: none"> - Large number of facilities makes data collection resource intensive - May be difficult to collect data where only manual records exist - May be difficult to get information from private sector - Does not take account of compliance with therapy
Health insurance data	<ul style="list-style-type: none"> - Patient-level consumption data - May be disaggregated by patient demographic characteristics - Geographic data may be available - Disaggregation to community and hospital sectors possible - Often limited number of data providers - Data more accessible if public sector agencies 	<ul style="list-style-type: none"> - May be difficult to get information from private sector - Only reimbursed antimicrobials reported - Selected populations covered by health insurance; may not be representative of whole population - Administrative records may not include all the variables of interest
Prescribing records of (health professionals or databases)	<ul style="list-style-type: none"> - May have patient characteristics, diagnosis, dose, duration, co-prescribed medicines 	<ul style="list-style-type: none"> - Prescribed medicines may not be dispensed - Samples of prescribers may not be representative and therefore not reflect national data
Community, household survey data	<ul style="list-style-type: none"> - Patient-level data will be available - Most closely reflects actual consumption - Repeat surveys can provide longitudinal data 	<ul style="list-style-type: none"> - Time-consuming and labour intensive to collect the data - Issues of representativeness of the data collected
Commercial data sources (e.g. IQVIA – previously IMS Health)	<ul style="list-style-type: none"> - Standardised data collection - Capacity to combine data from multiple sources including manufacturer records, hospital and pharmacy data 	<ul style="list-style-type: none"> - Data must be purchased - May be limited data collection in some countries - May not be able to examine data at regional, local, facility or prescriber level - Use of EphMRA/PBIRG classification rather than ATC codes so may be limited information at the pharmacological or chemical subgroup level

Now take Quiz 4.1 to test your understanding of this section. You will find the solutions at the end of this module.



Quiz 4.1

Are the following statements about data sources for monitoring AMC true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	Imported products may also be used in the veterinary and agricultural sectors.	
2	Prescriptions are a highly reliable source for monitoring AMC because antimicrobials cannot be purchased without prescription.	
3	Customs records are a good tool for knowing the importation of antimicrobials.	
4	Medical records from health insurance companies are useful tools for estimating AMC in the private sector.	

4.3.3 Putting data into context

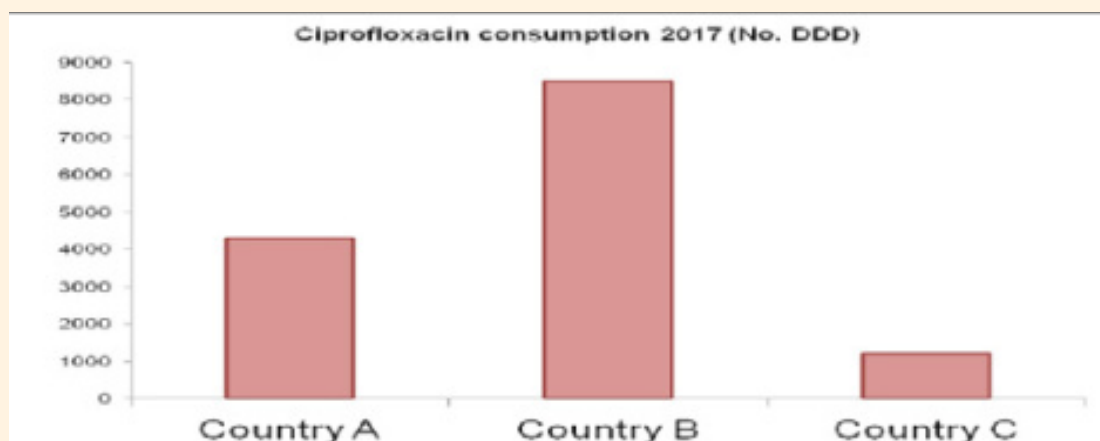
To understand the meaning of any consumption data, it is essential to take into account the context of those data. Lecture 4.3 describes this idea.



Lecture 4.3.

Putting data into context

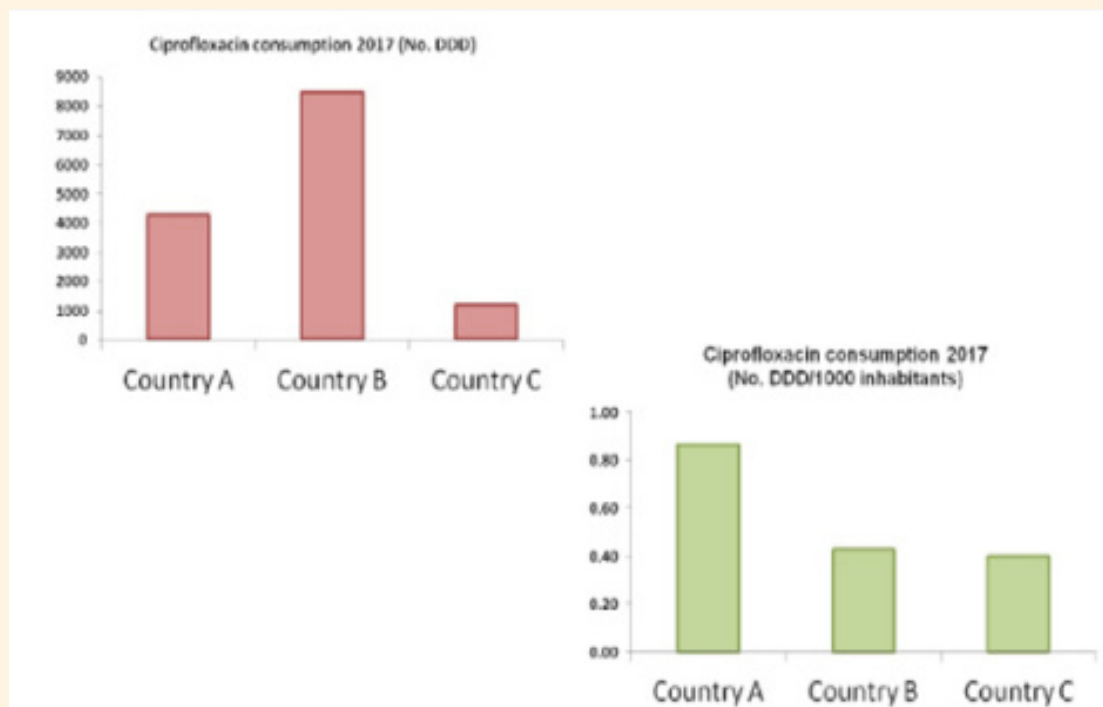
Collecting consumption data is important, but it is also important to have some additional information that puts these data into context.



This figure represents the 2017 consumption of ciprofloxacin in three different countries, expressed in Defined Daily Doses (DDD). You can easily see that Country B consumed the highest number of DDD of ciprofloxacin, and that Country C consumed the lowest.

If we look at just the absolute volume, this finding is true. But for the analysis of antimicrobial consumption data, we are interested in the population exposed to antimicrobials. So, we need to take into account the population of the three countries.

Country A has 5 million inhabitants, Country B has 20 million inhabitants and Country C has 3 million inhabitants. The next slide shows the graph when the population is taken into account.



This figure represents the 2017 consumption of ciprofloxacin in three different countries, expressed in Defined Daily Doses (DDD). You can easily see that Country B consumed the highest number of DDD of ciprofloxacin, and that Country C consumed the lowest.

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Country A has 5 million inhabitants, Country B has 20 million inhabitants and Country C has 3 million inhabitants. The next slide shows the graph when the population is taken into account.



Another point to be considered is how representative and valid the data from different sources are. In the case of antimicrobials, some sources may be able to provide high-quality data but only for a limited population. This is the case for health insurance data, especially those from private companies; such data will probably include a lot of detailed information, such as age, diagnosis and concomitant treatments, but they cover only a selected population.

Other data sources may cover the entire population (for example, import and manufacturing data), but the information will be of lower quality.

Thus, before choosing data sources, it is important to consider how representative they are at the country level, and what sectors they cover.

Despite their limitations, data sources with small coverage should not automatically be discarded. They can be of interest if you are studying the particular population or sector that the source covers.

The next section provides a couple of exercises that give you the opportunity to think about available data sources of antimicrobial consumption, and about the strengths and weaknesses of each source.

4.3.4 Exercises

When researchers use any set of data, it is important to know what the data set includes and what it excludes, and its potential biases. You can then take this information into account when analysing the data.

Now complete Exercises 4.1 and 4.2. You will find the solutions at the end of this module.



Exercise 4.1

Based on what you have learned in Sections 4.3.1–4.3.3, fill the six blank cells in the table below with the items labelled A–F in the box that follows the table. Each of the items in the list labelled A–F fits in only one empty cell.

NO.	DATA SOURCE	STRENGTHS	LIMITATIONS
1	Domestic manufacturers	Can separate product volumes for local use and for export	
2	Prescriber records		Samples of prescribers may not be representative and therefore may not reflect national data Cumbersome data collection if no (electronic) system is in place to capture the information
3		Standardized data collection	Data must be purchased
4		Disaggregation of distribution data to facility types and geographical location is possible	Only provides data for public sector
5	Wholesalers	Supply data may be disaggregated	
6		May be a significant proportion of antimicrobials dispensed for specific clinical programmes	May be difficult to differentiate those medicines used for the local population and special populations

Information to be inserted:

- A. Donations
- B. Commercial data sources (e.g. IQVIA)
- C. Volumes reflect production not consumption patterns
- D. May have patient characteristics, diagnosis, duration and co-prescribed medicines
- E. Public sector procurement
- F. May be few or many wholesalers
In some countries, health facilities and practitioners may be allowed to import medicines r



Exercise 4.2

This exercise is designed to help you to think about possible sources of AMC data in your country, and about the characteristics and scope of those sources. Try filling out the table below using information for your country. The first row of the table has been filled in as an example, based on:

- the source being hospital pharmacies in the public sector, providing consumption data on a yearly basis;
- the data being prepared by the medicines unit of the ministry of health; and
- the communication channel being an agreement between the medicines unit and the AMC national team.

This is just a first approach to data sources – you will have the opportunity to fill in the gaps and revise the table later on in this module.

DATA SOURCE NAME	INCLUDED SECTORS	FREQUENCY OF UPDATES	STRENGTHS	LIMITATIONS AND WEAKNESSES	DATA OWNER	COMMUNICATION CHANNEL
Hospital pharmacies	Public	Yearly	Data on hospital-use medicines	Only public sector. Not all hospitals have pharmacy units	Medicines unit,	

4.4 Health care sectors to be monitored

Now that we have discussed data sources and their characteristics, the next step is to identify the health care sectors that can be monitored. This section provides definitions of the terms used for the various health care sectors, and explains how those sectors differ in the medicines that are prescribed.

4.4.1 Definitions of health care sectors

In monitoring AMC, different types of health care sector need to be taken into account. These sectors include community hospital, public and private. The text in Box 4.3 gives definitions of the various health care sectors to be monitored.

Definitions

Read the text in Box 4.3, which provides definitions of the various health care sectors. The text is taken from *GLASS methodology for surveillance of national antimicrobial consumption (2)*.

Box 4.3

Definitions

Different types of healthcare sectors may be considered in monitoring of antimicrobial consumption including:

1. Community and hospital sectors.
2. Public and private sectors.

In many countries that are starting data collection, it will not be possible to disaggregate data by sector and only total consumption data will be able to be reported.

The community sector

The community sector corresponds to primary care and may also include out-patient hospital care; it is sometimes referred to as ambulatory care. Primary care corresponds to care provided by general practitioners, family doctors, nurses, physician assistants, pharmacists or clinical officers.

Residential care (e.g. nursing homes, day care centres) is also typically considered to belong to the community sector.

As an example, in many countries, antimicrobials reported in the community sector are usually prescribed by general practitioners and dispensed or supplied to the patients in pharmacies or licensed drug stores.

The hospital sector

The hospital sector corresponds to care provided to in-patients (admitted patients) in healthcare facilities. These can include general and district hospitals as well as secondary and tertiary care hospitals and other specialist health clinics.

As an example, in many countries, antimicrobials reported in the hospital sector are usually prescribed by hospital doctors and administered to the patients directly by the healthcare professionals in those facilities.

Public and private sectors

Countries may also be able to collect data separately for public and private sectors. This can provide important information about differences between prescribing practices between the two sectors.

4.4.2 Sectors differ in the medicines prescribed

Each of the different health care sectors has specific characteristics, and takes care of patients with different diseases and severity. Thus, the medicines prescribed in each health care sector also differ. This means that when you are considering AMC, the health care sector that the data cover will affect the findings, even when looking at information from a single country and a particular period, as illustrated by these examples.

Infections treated in hospitals and primary care centres are not the same. This is because the causal agents are different, and the possibility of finding more resistant microbes is higher in some hospital wards. For example, the proportions of narrow-spectrum antimicrobials are expected to be higher in primary care than in hospitals. Conversely, because of the expected higher prevalence of resistant microbes – such as methicillin-resistant *Staphylococcus aureus* (MRSA) – in hospital settings, the higher use of broad-spectrum antimicrobials in hospitals might be justified.

In some hospitals, the antimicrobials that can be prescribed are limited to those included in hospital formularies. Among these antimicrobials, there are last-resort active ingredients (e.g. most “reserve” active ingredients, such as aztreonam).

The antimicrobials consumed in public health care centres (both hospitals and ambulatory) are sometimes limited by a reference list of products (e.g. the reimbursement list of the national formulary). On the other hand, in private practice, practitioners and specialists can prescribe any antimicrobial approved in the country, and patients usually pay for these medicines themselves. For example, carbapenems may not be available in public hospitals or may not be reimbursable by health insurance companies. Also, in some countries, public sector hospitals may only use medicines from the national essential medicines list that is available in the hospital formularies.

These and other factors can explain differences in consumption profiles found in a single country. Knowing in advance the characteristics of each data source, including its limitations and weaknesses, will help to avoid misinterpretations and mistakes.

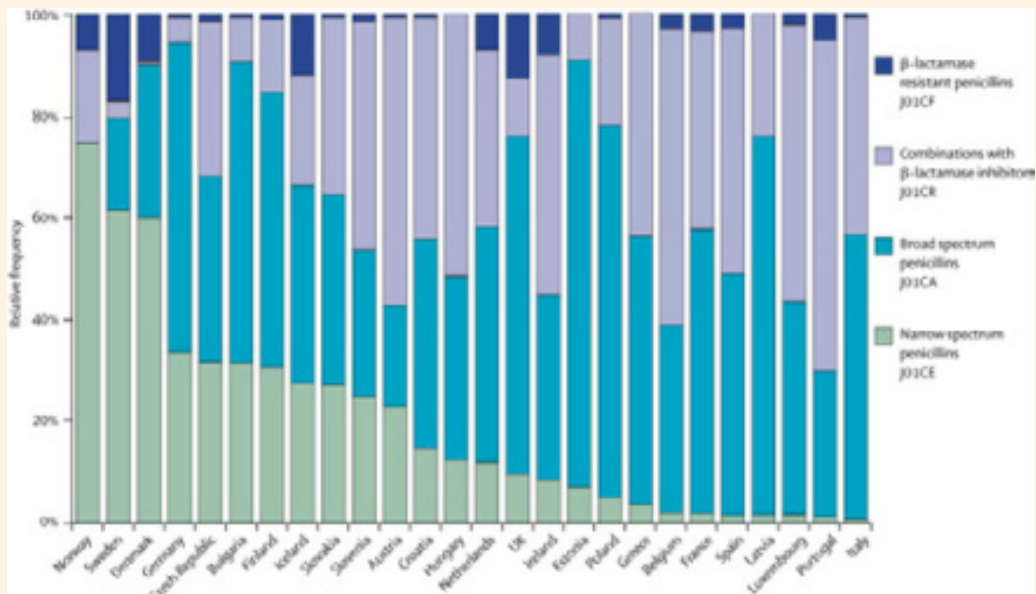
Now, revisit Exercise 4.2 and see whether you can add any additional sources or fill in any additional cells in the table. Then take Quiz 4.2. Solutions to the quiz are given at the end of this module.



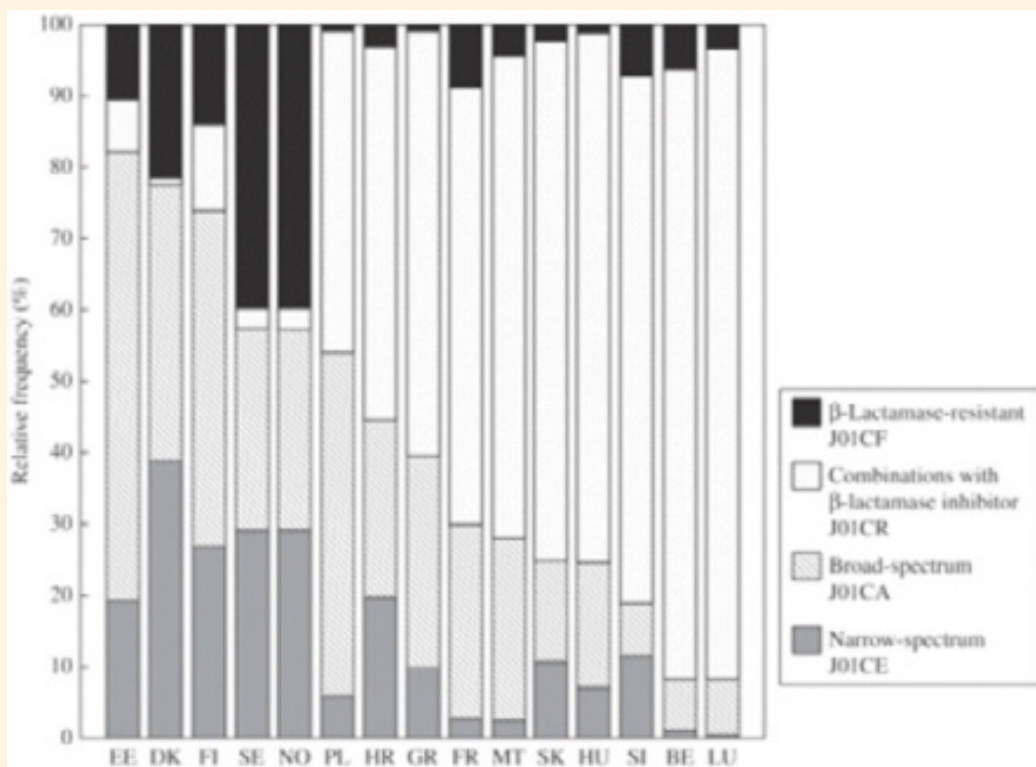
Quiz 4.2

Opposite are two figures from complementary studies on AMC in Europe. Fig. A shows outpatient use of penicillins (Anatomical Therapeutic Chemical [ATC] subgroup J01C) and Fig. B shows the use of penicillins for hospital care; both studies refer to 2002 data. Look at the two figures, focusing on the consumption figures for Norway (NO) and Denmark (DK), then decide whether the statements about the comparison between the figures are true or false.

Fig. A. Outpatient use of penicillins (J01C) in 26 European countries in 2002 in descending order of narrow-spectrum penicillins



Source: Goossens et al. (2005) (4).



Source: Vander Stichele et al. (2006) (5).

Are the following statements about the comparison between Fig. A and Fig. B true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	Between 30% and 40% of the penicillins consumed in hospitals in Denmark and Norway were narrow spectrum (J01CE).	
2	In Norway, 40% of the penicillins consumed in hospitals were beta-lactamase resistant penicillins (J01CF), whereas outpatient consumption of J01CF penicillins was about 10%.	
3	In Denmark, the proportion of broad-spectrum penicillins (J01CA) consumed in hospital care and in ambulatory care is similar.	

4.5 Practical experience of selecting data sources for AMC

In this section we will examine one country-specific experience that illustrates some of the practicalities of selecting data sources for AMC.

This example is based on a study published by WHO, describing the implementation of five pilot projects for community-based surveillance of antibacterial medicine (ABM) use and antimicrobial resistance (AMR) in five resource-constrained settings (6). The report was published in 2009, but the AMC analysis from different data sources is still valid and useful.

Here, we will go step by step through the experience of Vellore, a town in India. The report describes surveillance of both AMR and AMC; however, this training is focused on AMC, so this section considers only the parts of the report that deal with AMC.

4.5.1 Background and methods

Start with Reading 4.1, then take Quiz 4.3 (the solutions to the quiz are given at the end of this module).



Reading 4.1

First, read the background and the methods sections of the text (Sections 3.1 and 3.2) about Vellore, to understand the location where the surveillance was conducted, and the description of the AMC data sources (6) (reference: 4.5.1Reading-01).



Quiz 4.3

Are the following statements about the data collection methodology described in the report true or false?

NO.	STATEMENT	TRUE OR FALSE?
1	In the study, purchase data could be obtained from all pharmacies and hospitals.	
2	In the private sector pharmacies, data were extracted from purchase bills or from dispensing records.	
3	The available source of data used in each facility varied throughout the study.	

4.5.2 Findings

This section focuses on the findings of the study of Vellore, focusing particularly on two figures taken from the findings section of the report. There is no quiz for this section, just a reading.



Reading 4.2

This reading is part of the *Findings* sections of the text (Section 3.3) about Vellore (6): (reference: 4.5.2Reading-01).

We will focus on the following figures:

- Fig. A (taken from Fig. 3.4, on page 36 of the report) represents the annual use of antimicrobials by facility type, measured as percentage of prescription containing a specific antimicrobial; and
- Fig. B (taken from Fig. 3.8, on page 39 of the report) represents the annual use of antimicrobials by facility type, measured as the number of DDD of specific antimicrobials per 100 patients.

Fig. A. Annual use of ABMs by facility type measured as percentage of prescriptions containing a specific ABM

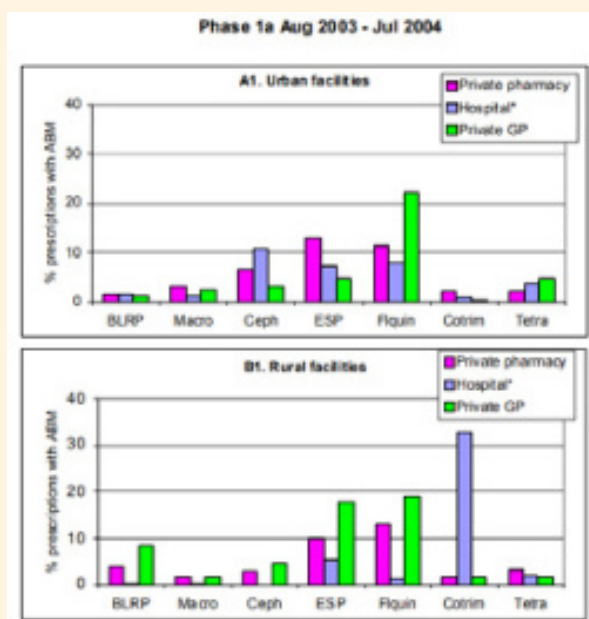
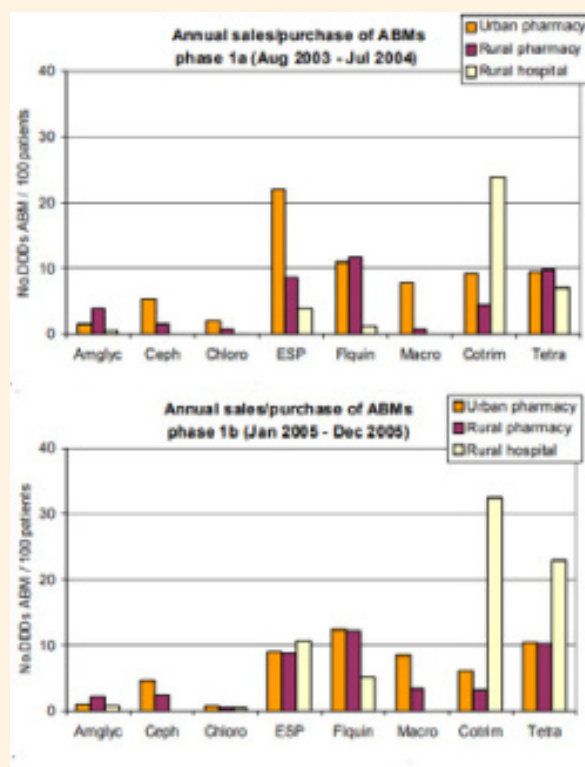


Fig. B. Annual sales/purchase of ABMs by facility expressed as number of DDDs of specific ABM prescribed per 100 patients during phases 1a and 1b (2003–2005)



As the authors suggest in the report, in Fig. A, we can focus on extended-spectrum penicillins (ESP) and private pharmacies (fuchsia-coloured bar). Where the consumption data for Phase 1a are measured as a percentage of prescriptions containing an antimicrobial, it can be seen that the percentage was comparable (at ~10%) in urban facilities (on the left of the figure) and rural facilities (on the right). However, in Fig. B, where the consumption data for Phase 1a (on the left of the figure) are measured as number of DDD per 100 patients receiving antimicrobials, you can see a clear difference between urban and rural use of this antimicrobial.

Looking again at Fig. B, in Phase 1a, the highest annual sales or purchases of antimicrobial in urban pharmacies was ESP (at 22 DDD/100 patients), while in rural hospitals the highest consumption was of cotrimoxazole (at 25 DDD/100 patients). However, 18 months later, in Phase 1b (on the right of the figure), annual sales or purchases of ESP in urban pharmacies had reduced by half (to <10 DDD/100 patients), whereas the consumption of cotrimoxazole and tetracyclines in rural hospitals had clearly increased.

The authors suggest being cautious when interpreting these data, because “the sources used varied in type and potential accuracy”. As mentioned above, it is important to be careful with potential biases of the data used in any AMC analysis, in order to avoid misinterpreting an increase or a decrease in AMC.

4.5.3 Lessons learned

This section focuses on the lessons learned from the study of Vellore. Reading published studies about AMC is the best way to prepare for your own practice. Other researchers and groups working with medicines consumption can provide interesting and new examples of data collection, data analyses and interventions that they have designed, to improve how medicines are prescribed and used, based on their results. The case study conducted in India includes some final reflections that may be relevant for your data analyses; these are presented in Reading 4.3.



Reading 4.3

For the final part of this section, read the lessons learned about antibiotic use, in Section 3.4.2 of the report (6) (reference: [4.5.3Reading-01](#)).

The author’s interesting self-criticism, summarized in Box 4.4, provides some useful conclusions.

Box 4.4.

Conclusions from the findings on ABM use



“There was also no way of differentiating from purchase records which stock was used for in-patient care and which for out-patient care.”

“There is also sometimes reluctance on the part of private pharmacists to share such information.”

“... medicines purchased in a particular period (especially if as short as a month) may not be dispensed or sold in the same period.”

“Bulk purchase/sales data also present particular challenges in the choice of a suitable denominator.” [When calculating DDD per 100 patients]

In these cases, population size for the entire catchment area is 100 000. Note that this is less of an issue for national monitoring of AMC, but should be considered for regional or facility-based monitoring.

4.6 Key messages

The relevance of a given consumption data set depends on how it is measured and expressed.

DDDs are an internationally accepted reference measure.

For comparison purposes, the metric DDDs/1000 inhabitants/day (DID) is used to adjust the data for population size or population group. It is important to know the context of the data to be used (i.e. reference population and period).

Usually, different data sources will be necessary in order to gain a complete picture of AMC.

When using and combining different data sources, it is important to identify potential overlaps and repetitions.

In time comparisons, it is important to use the same data sources throughout the analysed period, to avoid biases.

The relevance of a given consumption data set depends on how it is measured and expressed.

Congratulations on finishing Module 4. You are now ready to move on to Module 5, which provides more detail on calculating AMC.

4.7 Exercise solutions and feedback

Answers to Quiz 4.1 (in Section 4.3.2)

Here are the answers to the quiz. If you chose the wrong answer, check the feedback for an explanation, and revisit Section 4.3.2.

STATEMENT	TRUE OR FALSE?	FEEDBACK IN CASE OF WRONG ANSWER
Imported products may also be used in the veterinary and agricultural sectors.	True	Part of the production or importation may be consumed in other sectors, in addition to human use – these alternative uses should be quantified and taken into account.
Prescriptions are a highly reliable source for monitoring AMC because antimicrobials cannot be purchased without prescription.	False	Although many countries require a prescription to dispense antimicrobials, illegal over-the-counter purchase of antimicrobials happens frequently. So, prescriptions have some limitations as an information source.
Customs records are a good tool for knowing the importation of antimicrobials.	True	Customs records are a good tool for knowing the importation of antimicrobials and other medicines, although this information source has some biases. Also, this information can sometimes be difficult to obtain, because customs are not under the responsibility of the health ministry.
Medical records from health insurance companies are useful tools for estimating AMC in the private sector.	True	Medical records or prescription records from private health insurance companies can be useful consumption information tools, but it is not always easy to access such records. In addition, it is hard to analyse medical records, so prescription records may be more useful.

Answers to Exercise 4.1 (in Section 4.3.4)

Here is the completed table for the exercise. If you put any of the text into the wrong cells, please revisit the text of Box 4.2, where you will find the complete table that lists the different potential data sources, and gives their strengths and limitations.

DATA SOURCE	STRENGTHS	LIMITATIONS
Domestic manufacturers	Can separate product volumes for local use and for export	Volumes reflect production not consumption patterns
Prescriber records	May have patient characteristics, diagnosis, duration, co-prescribed medicines	Samples of prescribers may not be representative and therefore may not reflect national data Cumbersome data collection if no (electronic) system is in place to capture the information
Commercial data sources (e.g. IQVIA)	Standardized data collection	Data must be purchased
Public sector procurement	Disaggregation of distribution data to facility types and geographical location is possible	Only provides data for public sector
Wholesalers	Supply data may be disaggregated	May be few or many wholesalers. In some countries, health facilities and practitioners may be allowed to import medicines
Donations	May be a significant proportion of antimicrobials dispensed for specific clinical programmes	May be difficult to differentiate those medicines used for the local population and special populations

Answers to Quiz 4.2 (in Section 4.4.2)

STATEMENT	TRUE OR FALSE	FEEDBACK IN CASE OF WRONG ANSWER
Between 30% and 40% of the penicillins consumed in hospitals in Denmark and Norway were narrow spectrum (J01CE).	True	Look at the column for Denmark and Norway in Figure B. The lower portion of the column refers to narrow-spectrum penicillins, and represents 40%.
In Norway, 40% of the penicillins consumed in hospitals were beta-lactamase resistant penicillins (J01CF), whereas outpatient consumption of J01CF penicillins was about 10%.	True	Check that you have selected the correct column in both graphs.
In Denmark, the proportion of broad-spectrum penicillins (J01CA) consumed in hospital care and in ambulatory care is similar.	False	If you looked at the same column in both graphs (Denmark, DK), you will find that broad-spectrum penicillins represent about 40% of the hospital-consumed penicillins and about 30% of the outpatient consumption.

Answers to Quiz 4.3 (in Section 4.5.1)

STATEMENT	TRUE OR FALSE	FEEDBACK FOR WRONG ANSWERS
In the study, purchase data could be obtained from all pharmacies and hospitals.	True	Wrong. In this study, bulk sales and purchase data could not be collected from private general practitioners and private hospitals. Available information included all pharmacies and some public hospitals.
	False	Correct. Available information in this study included all pharmacies, but only some public hospitals.
In the private sector pharmacies, data were extracted from purchase bills or from dispensing records.	True	Correct. This source of information is different to that available for hospitals and public clinics.
	False	Wrong. You will find the right answer in the methods section of the text in Reading 4.1.
The available source of data used in each facility varied throughout the study.	True	Wrong. Have another look at the methods section. In this study, there were different data sources according to the different facilities, but the researchers used the same source of data in each facility throughout the study. This consistency made temporal comparisons possible in the different phases of the study.
	False	Correct. Although there were different data sources according to the facility type, the researchers used the same source of data in both study phases. This allowed comparisons between both phases.

4.8 References

1. WHO methodology for point prevalence survey on antibiotic use in hospitals. Geneva: World Health Organization; 2018 (<https://www.who.int/publications/i/item/WHO-EMP-IAU-2018.01>, accessed 28 March 2020).
2. GLASS methodology for surveillance of national antimicrobial consumption. Geneva: World Health Organization; 2020. (<https://www.who.int/publications/i/item/9789240012639>, accessed 23 August 2021).
3. WHO report on surveillance of antibiotic consumption Early implementation 2016–2018. Geneva: World Health Organization; 2018 (<https://www.who.int/publications/i/item/who-report-on-surveillance-of-antibiotic-consumption>, accessed 29 March 2020).
4. Goossens H, Ferech M, Vander Stichele R, Elseviers M, Group EP. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet*. 2005;365(9459):579–87 (<https://www.ncbi.nlm.nih.gov/pubmed/15708101>, accessed 29 March 2020).
5. Vander Stichele R, Elseviers M, Ferech M, Blot S, Goossens H, Group ESoACP. Hospital consumption of antibiotics in 15 European countries: results of the ESAC Retrospective Data Collection (1997–2002). *J Antimicro Chemoth*. 2006;58(1):159–67 (<https://academic.oup.com/jac/article/58/1/159/727102>, accessed 29 March 2020).
6. Community-based surveillance of antimicrobial use and resistance in resource-constrained settings: report on five pilot projects. Geneva: World Health Organization; 2009 (<https://apps.who.int/iris/handle/10665/70036>, accessed 29 March 2020).



Variables for the GLASS
methodology for surveillance of
antimicrobial consumption

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5.1 Training objectives of Module 5

The objectives of this module are to ensure that you:

- know the different variables that are used to calculate antimicrobial consumption (AMC) and to put AMC information into context;
- understand the various elements of data collection from WHO methodology for AMC surveillance;
- are aware of the importance of the denominator and AMC data contextual information; and
- can calculate the Defined Daily Dose (DDD) and DDD/1000 inhabitants/day (DID).

5.2 Background

Welcome to Module 5 of this training course. At this point, you have already had the opportunity to:

- update your knowledge of antimicrobials and antimicrobial resistance (AMR), and the link between the use of antimicrobials and the antimicrobial resistance (Module 1);
- understand the principles of the WHO methodology for AMC surveillance, including the use of ATC/DDD Index (Module 2);
- learn the role of the AMC national team and how to set up a national AMC surveillance system (Module 3); and
- understand the different AMC data sources (Module 4).

Now, it is time to put all this information together and look in depth at variables for data collection. This module provides a template for collecting national AMC data, analysing that data at country level, and submitting AMC information to WHO for consolidation at regional and global level.

The first step is to become familiar with the information that needs to be collected, and to understand why this information is necessary for generating quantitative estimates of AMC. Later sections of this module give practical step-by-step examples to illustrate how to calculate the DDD and DID from the variables collected at the product level.

5.3 AMC data collection

The main objective of this section is for you to become familiar with the required information on AMC data, and on the denominator data and contextual information that are essential for understanding how antimicrobials have been consumed in your country.

We will start with a general overview of data collection. Read the text in Box 5.1, which covers elements of data collection, and is taken from the document *GLASS methodology for a global programme on surveillance of antimicrobial consumption (1)*. Then take Quiz 5.1 to test your understanding.

Box 5.1

Data collection

Collection of data on antimicrobial consumption, population and questionnaires is the responsibility of the country and its AMC national team for the surveillance programme.

At country level, protocols, forms and related documents provided by WHO might be translated into national language. If necessary, extra documents such as training materials may be produced by countries to facilitate the national data collection. The national data providers may need some training on which data to collect and how to report them to the AMC national team.

The data collection process at national level can be split into different tasks according the following points:

1. Every year, the national team sends a call for data to the data providers.
2. The data providers deliver the requested information to the national team in the agreed format.
3. The national team checks and validates the data delivered by the data provider. If there are issues with the data or clarifications are needed, the national team will contact the data providers.
4. When the data are validated, the national team prepares the data for submission to WHO.

Data collection for antimicrobial consumption

Antimicrobial consumption (AMC) is defined as quantities of antimicrobials used in a specific setting (total, community, hospital) during a specific period of time (e.g. days, months, and year).

For global reporting, national estimates of consumption are reported for the calendar year (January to December). The ATC/DDD methodology is used to standardize the data collection and reporting of antimicrobial consumption.

Elements of data collection

There are three elements to the data collection, namely antimicrobial consumption data, denominator data and descriptive or contextual information that is relevant for interpreting the consumption estimates calculated.



Quiz 5.1

Are the following statements about data collection true or false? (The solutions to the quiz are at the end of the module.)

NO.	STATEMENT	TRUE OR FALSE?
1	As hospitals use very specific last-resort or restrictive antimicrobials, hospital settings are excluded from the AMC calculations.	
2	The denominator data (population) is optional and of secondary importance. What is really important is antimicrobial consumption data (numerator).	
3	Contextual information includes information on data sources, antimicrobials included in the surveillance and specific exclusions of health sector facilities.	

5.4 Principles for AMC data collection

5.4.1 Collecting data at product level

The WHO methodology (1) requires AMC data to be collected at product level for both proprietary and generic products. The calculation of the AMC consumption is done at substance level.

AMC consumption at substance level (e.g. the total amount of oral amoxicillin consumed) is calculated by adding or aggregating the consumption of all products containing that substance (in this case, amoxicillin). This is product-level data, and it takes into account product-level information such as the administration route, package size and strength.

Read Box 5.2, which provides text on AMC data from page 17 of the document *GLASS methodology for surveillance of national antimicrobial consumption (1)*.

Box 5.2

Antimicrobial consumption data

Product level data

The first step requires identification of all the products for the antimicrobial agents registered (i.e., with marketing authorization) in the country – a valid national exhaustive register of products. In some cases, this will not already exist and this list of products will need to be developed. **For each antimicrobial substance, this means a list of all products by formulation, strength and pack size.** For commonly used products with multiple manufacturers this could mean 50 or more product lines for a single INN like amoxicillin or ceftriaxone. The register file will need to be updated each year as new products receive marketing authorization.

Package level data

Consumption is expressed as the total numbers of packages for each product in the register of antimicrobial products that are consumed during the defined period of time. **Mostly these will be annual (yearly) data.** However, data may be available for different time periods such as quarterly.

Substance level data

Consumption at substance level can be summarized as aggregated DDDs. As noted earlier, the numbers of DDDs is calculated as follows:

Number of DDDs = Total grams used / DDD value in grams

Where the total grams of the medicine used is determined by adding the amounts of active ingredients across the various formulations (different strengths of tablets or capsules, syrup formulations) and pack sizes. The DDD value is assigned by the WHO Collaborating Centre (http://www.whocc.no/atc_ddd_index/).

5.4.2 Putting data collection into practice



A first step in the WHO methodology is that the AMC national team should prepare the list of all antimicrobial-containing products in the country that have marketing authorization, and select those products to be included in the monitoring.

This register of products is the basis for AMC monitoring. The register should contain enough information to be able to identify the product, the substance and the content of substances in the package. Once prepared, the register should be updated each year, before starting the annual analysis. The data collected on the antimicrobials will allow you to identify each package, classify it according to the ATC system and calculate the number of DDDs per package.

Module 2 discussed the antimicrobials to be included in the monitoring and outlined those that are mandatory and those that are optional. In summary, the antimicrobials for which data are to be collected are as follows:

- *Mandatory* collection of systemic antibiotics (J01, A07AA, P01AB):
 - J01 – Antibacterials for systemic use (e.g. tetracyclines, beta-lactams, sulfonamides, quinolones, aminoglycosides and amphenicols);
 - A07AA – Intestinal antibiotics: *vancomycin and colistin for oral therapy* (inj./iv form in J01); and
 - P01AB – Nitroimidazole derivatives for amoebiasis, trichomoniasis and giardiasis: oral metronidazole.
- *Optional* collection of antimycotics and antifungals for systemic use (D01BA, J02), antimycobacterials for TB (J04), antimalarials (P01B), and antivirals for systemic use (J05).

Section 5.7 gives a detailed description of each variable that needs to be collected according to the WHO methodology for AMC monitoring. For now, it is sufficient to understand that the following information will be required for each product:

- An **official code (product ID)** to identify the package, which must be unique for each package. Many countries do not have this code; in such cases, countries could create such a code in the first year of the data collection process, and then use that code every year (to make it easier to review the collected data).
- The **package label**; that is, a free text variable containing the brand name, package size, strength and formulation. This will be complemented by the name of the ingredients and the level 5 ATC code.
- Specific information on the **package size**.
- Specific information on the **strength** of each item (e.g. tablets and vials). This information, together with the package size, is needed to calculate the number of DDD per package.

5.5 Calculating DDD values at substance level

In Module 2 (Section 2.4.5) you went through a step-by-step exercise for calculating DDD at product level. You also saw how to easily transform DDD into DID, by adding a denominator of reference population and time.

The GLASS methodology for a global programme on surveillance of AMC is based on these calculations. Lecture 5.1 takes you step by step through the process of calculating total DDD for a particular substance. As mentioned in Section 5.4.1, AMC consumption at substance level (e.g. the total amount of a substance) is calculated by adding or aggregating the consumption of all products containing that substance.

This lecture has worked examples, so you will need pen, paper and calculator, and the online ATC/DDD index that you have used previously (2).

Lecture 5.1.

	A	B	C	D	E
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682
2	LABEL	Forfilin -250	Forfilin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab
3	PACK SIZE	10	10	15	7
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab
8	CONSUMED PACKAGES	3488	5978	2642	4326
9					
10					
11					

	F	G	H	I
1809AA6683	1812AA7010	1812AA6773	1809AA6745	
Gen-Levo IV 100 ml	Lamivudin IV 100ml	Levodol eye drops	Levomac 750	
1	5	10 ml	12	
single-use container	single-use container	eye drops	film coated tab	
IV	IV	ocular	oral	
500 MG / 100 ML	5 MG/ML	5 MG/ML	750 MG	
levofloxacin 500 MG/100 ML	levofloxacin 5 MG/1 ML	levofloxacin 5 MG/ML	levofloxacin 750 MG/tab	
568	173	122	1250	

This lecture shows a common situation in AMC monitoring; that is, receiving a list of packages of the antimicrobials consumed. Such lists are the basis for calculating consumption by active ingredient, and also the total consumption of the antimicrobials being monitored.

In the example shown here, the researcher has received the 2017 list of the consumed packages for eight products containing levofloxacin, which is a “Watch” antimicrobial (you may remember that we discussed the Access, Watch and Reserve – AWaRe – categorization in Module 1).

The question for this exercise is: *How many DDD of levofloxacin were consumed in the country in 2017?*

The first step is to identify the meaning of each variable in the list.

	A	B	
1	PRODUCT_ID	2002AA8584	Forflin – 250 contains:
2	LABEL	Forflin -250	
3	PACK SIZE	10	10 tablets per package
4	FORM	film coated tab	
5	ROUTE OF ADMIN	oral	
6	STRENGTH	250 MG	with 250 mg of levofloxacin per tablet.
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	
8	CONSUMED PACKAGES	3486	3,486 packages were consumed
9			
10			

Here, you can see the description of each cell for the first product, Forflin-250.

The number appearing in the ‘PRODUCT_ID’ row is the country’s specific identifier for that product. The spreadsheet also tells you that there are 10 tablets per package, that each tablet contains 250 mg of levofloxacin, and that 3486 packages were consumed.

With the information given, you can calculate the number of DDD contained in the 3486 consumed packages. If you remember how to do this based on previous modules, pause the lecture and have a go before moving on to the next screen.

Home ATC/DDD application form Order ATC Index WI

WHO Collaborating Centre for Drug Statistics Methodology

News

ATC/DDD Index

Updates included in the ATC/DDD Index

ATC/DDD methodology

ATC

DDD

ATC/DDD alterations, cumulative lists

ATC/DDD Index and Guidelines

Use of ATC/DDD

Courses

Found 5 entries containing 'levofloxacin'.

A02BD10 [lansoprazole, amoxicillin and levofloxacin](#)

J01MA12 [levofloxacin](#)

J01MA12 [levofloxacin](#)

S01AE05 [levofloxacin](#)

J01RA05 [levofloxacin and ornidazole](#)

Last updated: 2017-12-20

J ANTIINFECTIVES FOR SYSTEMIC USE

J01 ANTIBACTERIALS FOR SYSTEMIC USE

J01M QUINOLONE ANTIBACTERIALS

J01MA Fluoroquinolones

ATC code	Name	DDD	U	Adm.R	Note
J01MA12	levofloxacin	0.5	g	O	
		0.5	g	P	

The first step is to find the DDD value of levofloxacin.

You can do this through the ATC/DDD index, which you used in Module 2.

Search the ATC/DDD index for levofloxacin. You will find that the DDD value for oral administration of levofloxacin is 0.5 g, which is 500 mg.

	A	B
1	PRODUCT_ID	2002AA8584
2	LABEL	Forflin -250
3	PACK SIZE	10
4	FORM	film coated tab
5	ROUTE OF ADMIN	oral
6	STRENGTH	250 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab
8	CONSUMED PACKAGES	3486
9		
10		

Forflin-250 (levofloxacin)

0.5 g = 500 mg = 1 DDD

↓

1 tablet(250 mg) = 0.5 DDD

↓

10 tablets per pack = $10 \times 0.5 \text{ DDD} = 5 \text{ DDD / pack}$

↓

3486 packs consumed = $5 \times 3486 = 17\,430 \text{ DDD consumed}$

With the DDD at hand, the calculation is easy. The proposed product (Forflin) contains 10 tablets, and each tablet contains 250 mg of levofloxacin. So, each 250 mg tablet contains half a DDD (because 250 mg is half of 500 mg).

Thus, if one tablet contains 0.5 DDD, one pack of 10 tablets contains $10 \times 0.5 \text{ DDD}$; that is, 5 DDD.

Thus, the 3486 packs consumed during the period in question represents $5 \text{ DDD} \times 3486 \text{ packs}$, which gives a total of 17 430 DDD of levofloxacin consumed.

	A	B
1	PRODUCT_ID	2002AA8584
2	LABEL	Forlin -250
3	PACK SIZE	10
4	FORM	film coated tab
5	ROUTE OF ADMIN	oral
6	STRENGTH	250 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab
8	CONSUMED PACKAGES	3486
9		
10		

Forlin-250 (levofloxacin)

$$0.5 \text{ g} = 500 \text{ mg} = 1 \text{ DDD}$$

$$1 \text{ tablet} = 250 \text{ mg}$$

$$10 \text{ tablets per pack} = 2500 \text{ mg}$$

$$3486 \text{ packs consumed} = 2500 \text{ mg} \times 3486 = 8\,715\,000 \text{ mg}$$

$$8\,715\,000 \text{ mg} / 500 \text{ mg} = 17\,430 \text{ DDD consumed}$$

Another way to calculate this result is to calculate the number of grams of levofloxacin per pack, then transform this result into DDD.

Each tablet contains 250 mg of levofloxacin, and there are 10 tablets per pack, giving 2500 mg per pack. So, we can calculate the number of milligrams in the 3486 packs consumed during the period in question, and divide that by 500 (because 500 mg is 1 DDD). This gives the same result; that is, 17 430 DDD consumed.

Both ways yield the same result, so you can choose which one to use.

	A	B	C	D	E
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682
2	LABEL	Forlin -250	Forlin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab
3	PACK SIZE	10	10	15	7
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab
8	CONSUMED PACKAGES	3486	5978	2642	4326
9	DDD	17 430			
10					
11					

Now we can include the value for that product in the table that we are building, adding it to Row 9 (the DDD row).

Now, pause the lecture and try calculating the number of DDD consumed for the next three products: Forflin-500, Gen-Levo 250 and Gen-Levo 500.

Once you have your results, please carry on to the next screen, where you can check your results.

	A	B	C	D	E	F
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682	1809AA6683
2	LABEL	Forflin -250	Forflin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 100 ml
3	PACK SIZE	10	10	15	7	1
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab	single-use container
5	ROUTE OF ADMIN	oral	oral	oral	oral	IV
6	STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML 5ml
8	CONSUMED PACKAGES	3486	5978	2642	4326	
9	DDD		17 430	59 780	19 815	43 260
10						
11						
12						

Look at the answers in the table. If you calculated the values correctly, congratulations, you can fast forward to Screenshot 11.

If any of your results do not match with the results presented in this table, then go through Screenshots 8–10, which explain the solutions step by step.

	A	B	C	D	E
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682
2	LABEL	Forflin -250	Forflin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab
3	PACK SIZE	10	10	15	7
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab
8	CONSUMED PACKAGES	3486	5978	2642	4326
9	DDD		17 430		
10					
11					

Forflin-500 (levofloxacin)

$$0.5 \text{ g} = 500 \text{ mg} = 1 \text{ DDD}$$

$$1 \text{ tablet (500 mg)} = 1 \text{ DDD}$$

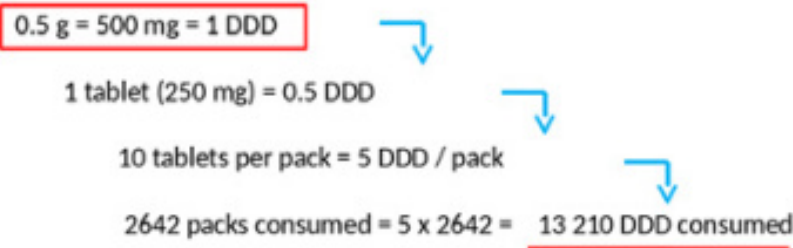
$$10 \text{ tablets per pack} = 10 \text{ DDD / pack}$$

$$5978 \text{ packs consumed} = 10 \times 5978 = \underline{59\,780 \text{ DDD consumed}}$$

This is the calculation for Forflin-500. In this case, each tablet contains 1 DDD of levofloxacin (500 mg).

	A	B	C	D	E
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682
2	LABEL	Forflin -250	Forflin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab
3	PACK SIZE	10	10	15	7
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab
8	CONSUMED PACKAGES	3486	5978	2642	4326
9	DDD	17 430			
10					
11					

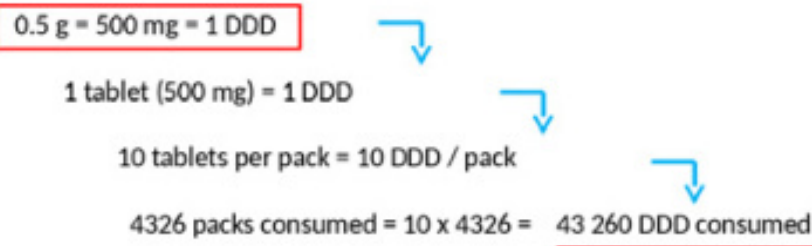
Gen-Levo 250 (levofloxacin)



The calculation for Gen-Levo 250 is similar to the first example for levofloxacin.

	A	B	C	D	E
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682
2	LABEL	Forflin -250	Forflin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab
3	PACK SIZE	10	10	15	7
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab
8	CONSUMED PACKAGES	3486	5978	2642	4326
9	DDD	17 430			
10					
11					

Gen-Levo 500 (levofloxacin)



The calculation for Gen-Levo 500 is similar to that for Forflin-500.

The main objective of this exercise is to give you confidence in carrying out these important calculations.

	A	B	C	D	E	F
1	PRODUCT_ID	2003AA5564	2003AA5590	1809AA6681	1809AA6682	1809AA6683
2	LABEL	Forflin -250	Forflin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 300 ml
3	PACK_SIZE	30	30	15	7	1
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab	single-use container
5	ROUTE OF ADMIN	oral	oral	oral	oral	IV
6	STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 300 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML lev
8	CONSUMED PACKAGES	3486	5978	2642	4326	568
9	DDD		17 430	59 780	19815	43 260
10						
11						
12						

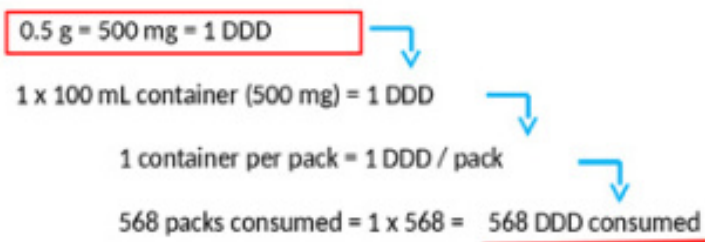
Now, you can go to the next product, which is Gen-Levo IV. This product is a single-use container for intravenous perfusion.

The screenshot shows the WHO Collaborating Centre for Drug Statistics Methodology website. The main content area displays search results for 'levofloxacin', stating 'Found 5 entries containing 'levofloxacin''. The results list ATC codes and names: A02BD10 (lansoprazole, amoxicillin and levofloxacin), J01MA12 (levofloxacin), J01AE05 (levofloxacin), and J01RA05 (levofloxacin and eridazole). Below the results, there is a table with columns for ATC code, Name, DDD, U, Adm.R, and Note. The table shows two entries for J01MA12: one with DDD 0.5 g O and another with DDD 0.5 g P. A red arrow points to the second entry (0.5 g P).

Because this is an intravenous product, starting by checking the DDD value for parenteral levofloxacin. You will see that it is the same as for oral levofloxacin; that is, 0.5 g, which is 500 mg.

	A	B	C	D	E	F
1 PRODUCT_ID	2002AAE584	2002AAE590	1809AA6681	1809AA6682	1809AA6683	
2 LABEL	Forfilin - 250	Forfilin - 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 500 ml	
3 PACK SIZE	30	10	15	7	1	
4 FORM	film coated tab	film coated tab	film coated tab	film coated tab	single-use container	
5 ROUTE OF ADMIN	oral	oral	oral	oral	IV	
6 STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML	
7 BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	
8 CONSUMED PACKAGES	3486	5978	2642	4326	568	
9 DDD		17430	59780	13210	43260	
10						
11						
12						

Gen-Levo IV 100 mL (levofloxacin)



Each container holds 100 mL, with 500 mg of levofloxacin, which is the DDD for this antimicrobial. Thus, one container holds 1 DDD, and there is one container per pack, so the 568 packs consumed represent 568 DDD consumed.

	A	B	C	D	E	F	G	H	I
1 PRODUCT_ID	2002AAE584	2002AAE590	1809AA6681	1809AA6682	1809AA6683	1809AA6684	1809AA6685	1809AA6686	1809AA6687
2 LABEL	Forfilin - 250	Forfilin - 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 500 ml	Lamivudin 100mg	Lamivudin 150mg	Lamivudin 200mg	Lamivudin 250mg
3 PACK SIZE	30	10	15	7	1	3	3	3	3
4 FORM	film coated tab	film coated tab	film coated tab	film coated tab	single-use container	single-use container	single-use container	single-use container	single-use container
5 ROUTE OF ADMIN	oral	oral	oral	oral	IV	IV	IV	IV	IV
6 STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML	5 MG/ML	5 MG/ML	5 MG/ML	5 MG/ML
7 BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/ML	levofloxacin 5 MG/ML	levofloxacin 5 MG/ML	levofloxacin 5 MG/ML
8 CONSUMED PACKAGES	3486	5978	2642	4326	568	120	120	120	120
9 DDD		17430	59780	13210	43260	600	600	600	600

	A	B	C	D	E	F	G	H	I
1 PRODUCT_ID	2002AAE584	2002AAE590	1809AA6681	1809AA6682	1809AA6683	1809AA6684	1809AA6685	1809AA6686	1809AA6687
2 LABEL	Forfilin - 250	Forfilin - 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 500 ml	Lamivudin 100mg	Lamivudin 150mg	Lamivudin 200mg	Lamivudin 250mg
3 PACK SIZE	30	10	15	7	1	3	3	3	3
4 FORM	film coated tab	film coated tab	film coated tab	film coated tab	single-use container	single-use container	single-use container	single-use container	single-use container
5 ROUTE OF ADMIN	oral	oral	oral	oral	IV	IV	IV	IV	IV
6 STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML	5 MG/ML	5 MG/ML	5 MG/ML	5 MG/ML
7 BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/ML	levofloxacin 5 MG/ML	levofloxacin 5 MG/ML	levofloxacin 5 MG/ML
8 CONSUMED PACKAGES	3486	5978	2642	4326	568	120	120	120	120
9 DDD		17430	59780	13210	43260	600	600	600	600

By now, you should be confident with your calculations. Try calculating the DDD result for the three remaining products in the table (Lamivudin IV 100 mL, Levocin eye drops and Levomac 750).

	A	F	G	H	I	
1	PRODUCT_ID	1809AA6683	1812AA7010	1812AA6773	1809AA6745	
2	LABEL	Gen-Levo IV 100 ml	Lamiwin IV 100ml	Levoflox eye drops	Levomac 750	
3	PACK SIZE	1	5	10 ml	12	
4	FORM	single-use container	single-use container	eye drops	film coated tab	
5	ROUTE OF ADMIN	IV	IV	ocular	oral	
6	STRENGTH	500 MG / 100 ML	5 MG/ML	5 MG/ML	750 MG	
7	BASIC INGREDIENT QTY.	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/1 ML	levofloxacin 5 MG/ML	levofloxacin 750 MG/tab	
8	CONSUMED PACKAGES	568	173	322	1250	
9	DDD		568	865	xxx	22 500

	A	B	C	D	E	
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682	
2	LABEL	Forfilin -250	Forfilin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	
3	PACK SIZE	10	10	15	7	
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab	
5	ROUTE OF ADMIN	oral	oral	oral	oral	
6	STRENGTH	250 MG	500 MG	250 MG	500 MG	
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	
8	CONSUMED PACKAGES	3486	5978	2642	4326	
9	DDD		17 430	59 780	19815	43 260

This table shows the results. If you calculated the values correctly, congratulations, you can fast forward to Screenshot 19.

If any of your results do not match those shown in the table, then check Screenshots 16–18, which take you through the solutions step by step.

	A	B	C	D	E	F	G	H	I
1	PRODUCT_ID	2002AA8584	2002AA8590	1809AA6681	1809AA6682	1809AA6683	1812AA7010	1812AA6773	1809AA6745
2	LABEL	Forfilin -250	Forfilin -500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 100 ml	Lamiwin IV 100ml	Levoflox eye drops	Levomac 750
3	PACK SIZE	10	10	15	7	1	5	10 ml	12
4	FORM	film coated tab	film coated tab	film coated tab	film coated tab	single-use container	single-use container	eye drops	film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral	IV	IV	ocular	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML	5 MG/ML	5 MG/ML	750 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/1 ML	levofloxacin 5 MG/ML	levofloxacin 750 MG/tab
8	CONSUMED PACKAGES	3486	5978	2642	4326	568	173	322	1250
9	DDD		17 430	59 780	43 260	865	xxx	22 500	43 260

Lamiwin IV 100 mL (levofloxacin)

0.5 g = 500 mg = 1 DDD

1 x 100 mL container (5 mg/mL = 500 mg/100 mL) = 1 DDD

5 containers per pack = 5 DDD / pack

173 packs consumed = 5 x 173 = 865 consumed DDD

The case of Lamiwin IV 100 mL is similar to that of Gen-Levo IV 100 mL in column F (Screenshot 13). Here, the product strength is given as “5 mg of levofloxacin / mL”; however, the single-use container has a volume of 100 mL, so the whole 100 mL container has 500 mg of levofloxacin, which equates to 5 mg of levofloxacin per mL.

PRODUCT_ID	2020AAT04	2020AAT03	2020AAT02	2020AAT01	2020AAT00	2020AAT00	2020AAT00	2020AAT00	2020AAT00
LABEL	Fortio 250	Fortio 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo 500 Tab	Gen-Levo IV 500/ml	Levoflo IV 500ml	Levoflo eye drops	Levoflox P08
PACK SIZE	30	30	30	7	7	3	3	30 ml	30
FORM	film-coated tab	film-coated tab	film-coated tab	film-coated tab	film-coated tab	single-use container	single-use container	eye drops	film-coated tab
ROUTE OF ADMIN	oral	oral	oral	oral	oral	iv	iv	ocular	oral
STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG	500 MG / 100 ML	500 MG	5 mg/ml	750 MG
ANAL INVENTORY KEY	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/ml	levofloxacin 750 MG/tab
CLASSIFIED PHARMACOLOGICAL	Q08A	Q08A	Q08A	Q08A	Q08A	Q08A	Q08A	Q08A	Q08A
DD		17.430	35.790	29833	41.240	368	379	30	1.094

3.4. Antimicrobials included in monitoring

The WHO surveillance program focuses only on antimicrobials for systemic use. Topical antimicrobials are excluded.

WHO has defined a core set of antimicrobials that all countries should include in their surveillance program:

Antibacterials	J01
Antibiotics for alimentary tract	A07AA
Nitroimidazole derivatives for protozoal diseases	P01AB

In addition, the WHO surveillance program includes an optional list of antimicrobials that countries may include in their surveillance program according to local needs and resources:

Antifungals	J02
Antimycotics	CO1BA
Antivirals	J05
Antimycobacterials for treatment of tuberculosis	J04A
Antiparasitics	P01B

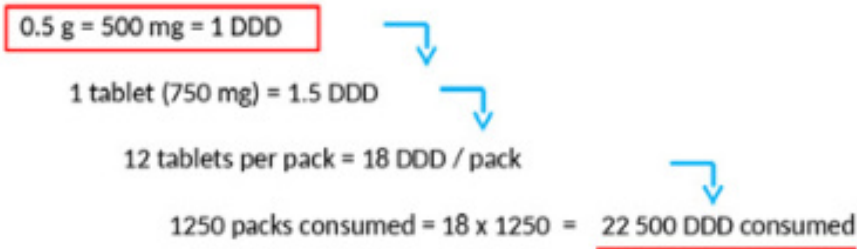


Levoflo eye drops are a special case because they are not for systemic use; instead, they are for topical use, with the ATC code S01AX19.

According to the ATC/DDD webpage, no DDD value has been defined for ocular use of levofloxacin. Also, according to the GLASS methodology, antimicrobials of the ATC “S” group are not included in the monitoring.

	A	B	C	D	E	F	G	H	I
1	PRODUCT_ID	1809AA6684	1809AA6700	1809AA6680	1809AA6682	1809AA6683	1809AA7010	1812AA6773	1809AA6745
2	LABEL	Gen-Levo 250	Gen-Levo 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 100 ml	Lamivudin IV 100ml	Levofloxacin eye drops	Levomac 750
3	PACK SIZE	12	12	12	12	1	5	10 ml	12
4	FORM	Film coated tab	Film coated tab	Film coated tab	Film coated tab	single-use container	single-use container	eye drops	Film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral	IV	IV	ocular	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML	5 MG/ML	5 MG/ML	750 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/1 ML	levofloxacin 5 MG/ML	levofloxacin 750 MG/tab
8	CONSUMED PACKAGES	548	576	3647	4134	503	322	322	1250
9	DDD		17 400	58 760	11 700	41 360			

Levomac 750 (levofloxacin)



The final example is similar to the other oral products we have already calculated. In this case, each tablet includes 750 mg of levofloxacin; thus, each tablet contains 1.5 DDD of levofloxacin.

	A	F	G	H	I
1	PRODUCT_ID	1809AA6683	1812AA7010	1812AA6773	1809AA6745
2	LABEL	Gen-Levo IV 100 ml	Lamivudin IV 100ml	Levofloxacin eye drops	Levomac 750
3	PACK SIZE	1	5	10 ml	12
4	FORM	single-use container	single-use container	eye drops	film coated tab
5	ROUTE OF ADMIN	IV	IV	ocular	oral
6	STRENGTH	500 MG / 100 ML	5 MG/ML	5 MG/ML	750 MG
7	BASIC INGREDIENT QTY.	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/1 ML	levofloxacin 5 MG/ML	levofloxacin 750 MG/tab
8	CONSUMED PACKAGES	568	173	322	1250
9	DDD		568	865	300
10					22 500

	A	B	C	D	E	F	G	H	I
1	PRODUCT_ID	1809AA6684	1809AA6700	1809AA6680	1809AA6682	1809AA6683	1809AA7010	1812AA6773	1809AA6745
2	LABEL	Gen-Levo 250	Gen-Levo 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo IV 100 ml	Lamivudin IV 100ml	Levofloxacin eye drops	Levomac 750
3	PACK SIZE	12	12	12	12	1	5	10 ml	12
4	FORM	Film coated tab	Film coated tab	Film coated tab	Film coated tab	single-use container	single-use container	eye drops	Film coated tab
5	ROUTE OF ADMIN	oral	oral	oral	oral	IV	IV	ocular	oral
6	STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG / 100 ML	5 MG/ML	5 MG/ML	750 MG
7	BASIC INGREDIENT QTY.	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 250 MG/tab	levofloxacin 500 MG/tab	levofloxacin 500 MG/100 ML	levofloxacin 5 MG/1 ML	levofloxacin 5 MG/ML	levofloxacin 750 MG/tab
8	CONSUMED PACKAGES	548	576	3647	4134	503	322	322	1250
9	DDD		17 400	58 760	11 700	41 360		300	

We have now calculated the number of DDD in the consumed packages for the different products. The next step is to sum all of the levofloxacin-containing products in order to estimate the number of consumed DDD of levofloxacin.

Can you work out the answer?

PRODUCT ID	2022A0204	2022A0205	2022A0202	2022A0202	2022A0202	2022A0202	2022A0202	2022A0202	2022A0202
LABEL	Popflor 250	Korflo 500	Gen-Levo 250 Tab	Gen-Levo 500 Tab	Gen-Levo 500 Tab	Gen-Levo 500 Tab	Gen-Levo 500 Tab	Gen-Levo 500 Tab	Gen-Levo 500 Tab
PACK SIZE	20	20	20	20	20	20	20	20	20
FORM	Film-coated tab	Film-coated tab	Film-coated tab	Film-coated tab	Film-coated tab	Film-coated tab	Film-coated tab	Film-coated tab	Film-coated tab
ROUTE OF ADMIN	oral	oral	oral	oral	oral	oral	oral	oral	oral
STRENGTH	250 MG	500 MG	250 MG	500 MG	500 MG	500 MG	500 MG	500 MG	500 MG
BASIC INCREMENT QTY	levofloxacin 250 MG/Tab	levofloxacin 500 MG/Tab	levofloxacin 250 MG/Tab	levofloxacin 500 MG/Tab	levofloxacin 500 MG/Tab	levofloxacin 500 MG/Tab	levofloxacin 500 MG/Tab	levofloxacin 500 MG/Tab	levofloxacin 500 MG/Tab
CONTAINED PACKAGES	1405	3070	2642	4028	540	170	322	1220	22 500
Sum	17 430	59 780	13 210	43 260	568	865	22 500		

Total consumed DDD:	
17 430	
59 780	
13 210	
43 260	
568	
865	
+ 22 500	
157 613 DDD of levofloxacin	

If you got this right, well done. The studied country consumed a total of 164 218 DDD of levofloxacin during 2017.

At the end of the process outlined in Lecture 5.1, you have all the products measured in the same unit (DDD). This means that you can add the consumption of different antimicrobials of the same therapeutic or chemical group (e.g. all fluoroquinolones). Also, you can add the consumption of the different therapeutic subgroups, to find the total consumption of antimicrobials.

These results are useful for knowing the proportion of the different antimicrobials consumed, and also for making temporal comparisons.

Although the consumption expressed in DDD is useful in itself, the data can be even more useful if they are refined using the denominator and the contextual information. We will look at this in Section 5.6.

5.6 Denominator data and contextual information

In this section we will look at the requirements for the denominator and the contextual information, which are needed to help to understand the meaning of the calculated amount of DDDs consumed.

In Module 4, we saw that data sources may differ in terms of the population (i.e. denominator) and the health sector covered (e.g. hospital or community sector, and public or private health care).

Read the text in Box 5.3, which is from *GLASS methodology for surveillance of national antimicrobial consumption* (1), to understand what is meant by the terms “denominator data” and “contextual information”.

Box 5.3**Denominator data and contextual information****Denominator data**

The total numbers of DDDs derived as consumption estimates should be adjusted for the population to which the data apply.

For national estimates of consumption, the appropriate population will be the total national population (all age and gender groups combined). WHO may not use the same population used in national reporting systems for all Member States so, use the UN World Population Prospects database to estimate the denominator. However, this population denominator may differ from the population estimates provided by the national authorities. For example, some countries have a large migrant population that may not be counted into the World Population Prospects, but is included in the population estimates by the national authorities.

Reporting metrics

The standard reporting metric for national estimates is **DDDs/1000inhabitants/day (DID)**. Other metrics can be also used, such as DDD/inhabitant/day or DDD/100 beds/day (for hospitals).

The data collection template requires entry of numbers of packages for each product included in the register. These packages may be added to give a total number of packages consumed. This will provide a crude estimate of the number of courses of treatment with antimicrobials used per year and is based on the assumption that one package = one course of treatment. This measure needs to be interpreted carefully. In some settings, a package of oral medicine will represent a course of treatment. In other settings, patients may buy small numbers of tablets or capsules or dispensing is from large containers of the medicine, in which case a package will have very little meaning. A package is not likely to be a good guide to a course of treatment with an injectable antimicrobial.

Contextual information relating to data collection

It is important to report the sources of data used, the sectors being reported, the antimicrobial agents included in the surveillance and to identify if there are any sectors or facility types that have been excluded from the calculations, e.g. public vs private sector, hospitals vs. primary care.

This may be supplemented by questionnaires or other surveys.

5.7 Variables in the WHO GLASS methodology for surveillance

Read the text of Box 5.4 of national antimicrobial consumption, then watch Lecture 5.2, which discusses the complete list of variables that need to be collected according to the GLASS methodology for AMC monitoring. For each variable, the lecture explains the meaning and its usefulness in monitoring AMC.

The following information is a summary taken from the document *GLASS methodology for surveillance of national antimicrobial consumption (1)*. It provides an overview of variables in relation to the:

- antimicrobial medicines register,
- consumption packages,
- population estimates and population-adjusted estimates, and
- contextual information.

Box 5.4 Variables

Variables for the register on antimicrobials

Some countries will already have an electronic database of all antimicrobial products that have marketing authorization (= registered products). Where such a database exists, the relevant data can be copied into the cells of the spreadsheet.

Where there is no existing list of products, this will need to be created.

This is a significant task in Year 1. For subsequent years, the data register file can be edited and new products added. The descriptions for products could be maintained (with zero consumption) and this will provide a 'historical' file of products and consumption over the years.

The initial product-level variables included in the register are shown in Table 5.1. A description of the variables, data type, variable type, information and data rules and response options are provided in Annex 3 of the GLASS methodology document. Some additional variables were added later, such as the year of authorization/registration and end date of authorization/registration. This information allows you to know if the product is still on the market.

Table 5.1: Product level data variables for the antimicrobial register

Variable name	Content
COUNTRY	Based on ISO 3166 alpha-3 country codes
PRODUCT_ID	Unique identifier of the medicinal product package (MPP).
LABEL	Medicinal product package label
PACKSIZE	Size of the package
PACKSIZE_UNIT	Pack size unit of measurement
PAEDIATRICS_PRODUCT*	Is it a paediatric medicine product
FORM*	Pharmaceutical formulation type
ROUTE_ADMIN	Route of administration
STRENGTH	Quantity of the main ingredient of each item
STRENGTH_UNIT	Unit measurement of strength
INBASQ	Basic ingredient quantity
INBASQ_UNIT	Unit measurement of the basic ingredient quantity
ATC5	WHO ATC code at substance level (ATC5-level)
SALT*	Salt of the active substance (hexamine, erythromycin only)
COMBINATION	The WHO CC has defined DDD for combined products
PRODUCT_NAME*	Medicinal product name
INGREDIENTS*	Ingredient name: e.g. amoxicillin and enzyme inhibitor.
PRODUCT_ORIGIN*	The product can be import, donation or locally produced.
MANUFACTURING_COUNTRY	The country of the manufacturer of the product.
MARKET_AUTHORIZATION_HOLDER*	The name of marketing authorization holder
GENERIC*	Is the product a generic?
CONV_FACTOR (macro)	Transform strength expressed in IU into G.
WHO_DDD (macro)	The DDD defined by the WHO CC for the ATC code
WHO_DDD_UNIT (macro)	Unit measurement of the WHO DDD (MG, G, IU, MU, UD)
DPP (macro)	DDD Per Package

Source: WHO antimicrobial medicines collection protocol year 2016

*optional variables for dataset; macro = calculated automatically by Excel macro

Variables for consumption estimates (packages and DDDs)

The numbers of packages of each product imported/sold/dispensed are recorded. The numbers of packages can be aggregated by the desired level of ATC code and reported as total number of packages. The number of packages of each product is also multiplied by the number of DDDs per package to calculate the total numbers of DDDs for each product. The numbers of DDD are aggregated by at the desired ATC code level to give total number of DDDs.

Consumption data may also be reported by sector – total consumption data disaggregated to hospital and community (ambulatory care) data, or to public and private sector. The consumption variables included in the spreadsheet are shown in Table 5.2. A full description of the variables, data type, variable type, information and data rules and response options are provided in Annex 3.

Table 5.2 : Consumption data variables

Variable name	Content
Consumption by packages	
TOTAL PACKAGES	Total number of packages consumed during the year
COMMUNITY PACKAGES	Total number of packages consumed in community during the year
HOSPITAL PACKAGES	Total number of packages consumed in hospital sector during the year

Source: GLASS methodology for surveillance of national antimicrobial consumption

DDD = Defined Daily Doses

Variables for population estimates

In terms of national AMC surveillance, national statistics for population denominators may be used. For WHO and GLASS reports, WHO will use its standardized population denominators.

Variables for population-adjusted estimates

The total numbers of packages and DDDs are divided by population estimates and the estimates adjusted to express consumption as numbers of packages/inhabitants/year (PIY) or numbers of DDDs/1000 inhabitants/day (DID).

Contextual information

Additional information obtained by questionnaire or survey may help with interpretation of the consumption estimates.

Lecture 5.2.

Data to be collected

- The description of the products from the national register of antimicrobial products according to the defined variables (Table 5.1 in Box 5.4)
- The number of packages consumed

The data to be collected include variables used in registering the products containing antimicrobials and variables used to show the number of packages consumed.

The collected information will form the basis for calculating AMC by aggregating data from the product level to the therapeutic group level.

The register

The register includes mandatory and optional fields

- **Mandatory variables**
 - Allow identification of package
 - Allow calculation of DDD / package
 - Identify ATC code and route of administration
- **Optional variables**
 - Additional information (e.g. generics, marketing authorization holder and country of origin)

We will start with the register of antimicrobials. This register includes **mandatory variables** that allow the identification of the package and calculation of the number of DDD per package (as we saw in Section 5.5), and that identify the ATC code and route of administration.

In addition, a few **optional variables** provide information that is not necessary for calculating consumed DDD, but may be useful in terms of understanding the pharmaceutical market. This includes information on things such as generics, the holder of the marketing authorization and the country of origin of the antimicrobials.

MANDATORY VARIABLES

COUNTRY

- ISO three-letter code
 - e.g. France: FRA
 - e.g. Burkina Faso: BFA

YEAR

- Year of the period under surveillance

The first mandatory variable is the description of the *country*. The country is described using a three-letter country code that is based on the ISO3166 codes that are listed on the International Organization for Standardization (ISO) site (there is a reference for this list in the transcript) (3).

To be able to compare the results with those obtained in other countries, you also need to know the *year* under surveillance.

The slide is titled "Product_ID" and is part of a section on "MANDATORY VARIABLES". It lists the following points:

- Medicinal Package Product Code
 - Unique identifier of the package
 - Official code (authorization number)
 - Other number (e.g. 1, 2, 3, 4)
- Must be unique
- Links package with consumption data
- Important for validation

One important variable is the *product ID*, which is the unique identifier of the package, and comprises an official code plus another number.

This product ID is unique, links the package listed in the register with consumption data, and is important for validation.

Because the product code is unique, it must not change over time. Hence, when a particular medicinal product is no longer available on the market or is no longer registered, this code should not be attributed to another product.

Where a medicinal product does not have a code, then the country should provide or create one (ensuring that it is unique).

The slide is titled "Label" and is part of a section on "MANDATORY VARIABLES". It lists the following points:

- Label of the package
- Free text
- Must include complete information
 - Good example: Augmentin 500 mg x 10 tabl.
 - Bad example: Augmentin

The *label* is a free text variable, which should fully describe the characteristics of the product, such as the name, package size, strength and pharmaceutical formulation.

The information needs to be as complete as possible, to allow for validation of the product through cross-checking of that information by an external reviewer.

The screenshot shows a good example of a label (Augmentin 500 mg, 10 tablets), and a bad example, which just gives the name of the product (Augmentin).

MANDATORY VARIABLES

PackSize + PackSize_Unit

- **PackSize**
 - No. of items in the package
 - For tablets, vials etc.: e.g. 10 vials 1 g each = **10**
 - For syrups, mL of the final product (+INBASQ): e.g. 100ml 75mg/5ml: **100**
- **PackSize_Unit**
 - Unit of measurement for the package size
 - For tablets, vials etc.: no. of pieces (**pcs**)
 - For syrups: **mL**

The *pack size* includes information on the number of items (for example, tablets, pills or vials) contained in one package. This information is essential for calculating the number of DDD contained in each package.

In terms of *units*, for most pharmaceutical forms, the pack size must be reported as the *number of pieces*. For instance, if a package contains 10 vials, the package size would be 10 (that is, the number of vials in the package, and not the volume of reconstituted product).

For products that are administered as liquid form (for example, in a syrup), the pack size unit should be reported as millilitres of final reconstituted product. For instance, if a package contains 100 mL of syrup, with the product at 75 mg / 5 mL, the unit is 100 (that is, the number of millilitres of the product).

MANDATORY VARIABLES

Strength + Strength_Unit

- Strength – quantity of main ingredient (e.g. per tablet or per dose); for example:
 - 10 tablets 1g =1
 - 100 mL 75 mg / 5 mL = 75
- Strength_Unit – unit of measurement (e.g. g, mg, IU, MU, UD)

The information about the package size combined with information about the strength together form the basis for calculating the quantity of active ingredient in the package. The strength refers to the quantity of the main ingredient in one unit; for example, per tablet or per dose in the case of a syrup. Thus, if a package contains 10 tablets, each of which contains 1 g, the strength is recorded as "1". Similarly, if a package contains 100 mL of syrup, in which a dose is 5 mL and contains 75 mg, the strength is 75.

The measurement units can be expressed in different ways; for example, "grams", "milligrams", "international units", "millions of international units", "unit doses", "pieces" or "millilitres".

Unit doses are used in the case of combination products. For some substances used in combination with others, the WHO Collaborating Centre in Oslo has defined rules, such as taking into account only the antimicrobial substance and not the combined substance – that is the case, for example, for amoxicillin plus clavulanic acid.

For products that contain multiple antimicrobial substances, the WHO Collaborating Centre has defined a DDD for the combined products. Where this is the case, the strength should be reported in the same units as the DDD for the corresponding combined product.

MANDATORY VARIABLES

INBASQ + INBASQ_UNIT

- Ingredient base quantity
 - Only for syrups
 - Denominator part of the strength
 - E.g. : 100 ml 75mg/5ml : 5
- INBASQ_UNIT
 - Unit of measurement : always ml
- In all other cases (including perfusion fluids or ampules), the INBASQ should be set to 1.

INBASQ stands for *ingredient base quantity*. The variables INBASQ and INBASQ_UNIT are used only for syrups and solutions. They describe the quantity of the *ingredient base* and its units.

These variables are used for describing concentration of fluids (e.g. 200 mg / 10 mL). In syrups and solutions, INBASQ describes the denominator part of the strength. In all other cases (including perfusion fluids or ampules), the INBASQ cell should be set to 1 or left empty.

MANDATORY VARIABLES

PACKCONTENT + PACKCONTENT_UNIT

- Quantity of active substance per package –
For tablets, vials, etc.
- PACKSIZE multiplied by STRENGTH
 $10 \times 1 = 10 \text{ g}$
- For syrups
 - PACKSIZE multiplied by STRENGTH divided by INBASQ
 $(100 \times 75) / 5 = 1250 \text{ mg} = 1.25 \text{ g}$

The quantity of active substance per package is described with two variables: *packcontent* and *packcontent_unit*.

Both variables can be calculated automatically, by multiplying the package size by the strength, and dividing by the INBASQ value.

MANDATORY VARIABLES

ROUTE_ADMIN

- Route of administration
 - Unique choice
 - O : Oral
 - P : Parenteral
 - R : Rectal
 - IP : Inhalation powder
 - IS : Inhalation solution

The *route of administration* is a code that describes how the product is administered – oral, parenteral, rectal, inhalation powder or inhalation solution.

This information is used to attribute the ATC code and the DDD value.

MANDATORY VARIABLES

ATC5

- ATC substance code (level 5)
 - ATC code of the package
 - Takes into account the active substances and route of administration
 - If there is no ATC code, report this to WHO, to pass the information to the WHO CC in Oslo, who may then assign a code.

Module 2 described the ATC classification system and explained how to find the right ATC code for a given product. This variable is also mandatory – it is needed so that the content of all products with the same active ingredient can be added together.

MANDATORY VARIABLES

COMBINATION

- **Combination code**
 - WHO CC Oslo has a specific list for some combinations (e.g. bactrim and HIV products). In this case, insert combination code.

Combination products are a special case. Module 2 described the rules for assigning an ATC code and a DDD value for combinations, and explained that the website for the WHO CC in Oslo lists combined products (4) https://www.whocc.no/ddd/definition_and_general_considera/#ddd2

For all combination products where the DDD assigned deviates from the general principles, a list of DDDs are available on the WHO CC in Oslo: https://www.whocc.no/ddd/list_of_ddd_combi-ned_products/

The WHO methodology for AMC surveillance recommends that at least the core set of antimicrobial classes are monitored by all national surveillance programmes. The list of DDDs for combinations that belong to the core antimicrobial classes that are subject to mandatory surveillance is shown in Table 2.1. (Module 2 - 2.4.3).

IMPORTANT: For your work, you will need to use the file on ATC/DDD index for combinations with antimicrobials, which was created by WHO. In this file, WHO has assigned codes for each of the combination with antimicrobials defined by the Oslo WHO CC by adding an underscore and a number (e.g. J01CA20_1. J01CA20_2). These codes are not assigned by the Oslo WHO CC. This WHO file on ATC/DDD index for combinations with antimicrobials is not included in this training material. To obtain the file, please write to GLASS AMC team in WHO Geneva: glass-amc@who.int.

MANDATORY VARIABLES

SALT

- Associated salt used only for:
 - erythromycin: only ethylsuccinate
 - methenamine: hippurate or mandelate
- For these two substances, provide value for associated salt
- For all other substances, do not provide any salt

The variable *salt* is used only for the salts associated with erythromycin (where there is only one salt, ethylsuccinate) and methenamine (where there are two salts, hippurate and mandelate). For these two substances, WHO has defined a DDD value for the associated salt, which is different from the DDD value for the substance alone.

For all other substances, no salt is specified.

MANDATORY VARIABLES

CONV_FACTOR

- Conversion factor from IU to g
- For some products (peni V and G), *strength* is expressed in IU but DDD in g

ATCS	Administration Route	From	To	Factor
J01CE01	P	MU	G	0.6
J01CE02	O	MU	G	0.625
J01FA02	O	MU	G	0.3125
J01CE08	P	MU	G	0.6
J01CE09	P	MU	G	1

The *conversion factor* is a variable that transforms strength expressed in international units (IU) into strength expressed in grams.

This variable is automatically completed in the WHO template for estimating antimicrobial consumption.

If there is no need to convert from international units to grams, this factor must be set to 1.

The table shows the list of current conversion factors.

If strength is expressed in international units and DDD in grams, and there is no applicable conversion factor, then no DDD per medical product will be calculated, and no consumption for this product will be reported.

MANDATORY VARIABLES

WHO_DDD + WHO_DDD_UNIT

- The DDD defined by the WHO CC in Oslo for the corresponding combination code, if relevant
 - The unit of measurement of the DDD (g, mg, IU or UD)

Other important variables are the DDD value and its unit. As explained in Module 2, the DDD value is defined by the WHO Collaborating Centre in Oslo, with corresponding codes if the antimicrobial is part of a combination.

DDD values are given in grams, milligrams, international units (IU) or unit doses (UD).

OPTIONAL VARIABLES

FORM

- Free text
- The form of the package
 - tablet, film or dispersible tablet, solution for infusion...
- Useful for validation

Now we will look at the optional variables for the register of antimicrobial products. The first of these is a free text variable that contains information on the *form* of the package; that is, whether it is a tablet, a film or dispersible tablet, a solution for infusion and so on. Information on the form of the antimicrobial is useful for validation purposes.

OPTIONAL VARIABLES

PAEDIATRIC_PRODUCT

- If this is a paediatric package
- YES or NO
- This is important, because, children <8 years almost only use paediatric forms
- Thus paediatric form is a good proxy for estimating consumption in young children < 8-10 years

The next optional variable is to know whether a product is designated for *paediatric use*. This information is useful because paediatric forms are almost always used in children aged under 8 years; thus, paediatric forms are a good proxy for estimating antimicrobial consumption in young children (aged under about 8 to 10 years), who have probably received a paediatric formulation.

OPTIONAL VARIABLES

PRODUCT ORIGIN

- What is the source of the product?
- Coded value: import, donation, locally produced product

Products with antimicrobials can have different sources and origin. So, the optional variable Product origin is to know whether the product is imported, locally produced, or a donation. Donated products often have a different procurement and supply chain arrangements compared to the rest of the medicines that are procured by the state actors. So, the quantities of donated products may be documented by non-state entities and in a different manner.

OPTIONAL VARIABLES

PRODUCT_NAME

- Name of the product
 - e.g.: Augmentin 1g x 10 tabl: Augmentin

MARKET_AUTH HOLDER

- Name of the marketing authorisation holder

MANUFACTURING_COUNTRY

- Country of manufacturing

Additional optional variables are the name of the product, the name of the marketing authorization holder and the country of manufacturing.

OPTIONAL VARIABLES

YEAR AUTHORIZATION

- Year when the marketing authorization was granted

YEAR WITHDRAWAL

- Year when the marketing authorization was withdrawn

The other two related optional variables about the year when the marketing authorization of a drug was 1) granted and 2) withdrawn allow you to know if the product is still on the market.

OPTIONAL VARIABLES

INGREDIENTS

- List of active substances in the package
- Useful for validation

GENERICS

- Is the product a generic
- YES or NO

Finally, the last two optional variables in the register are the active *ingredients* included in the package and also whether or not the product is a generic one.

CONSUMPTION DATA

COUNTRY

- ISO three-letter codeholder
 - e.g. France: FRA
 - e.g. Burkina Faso: BFA

YEAR

- Year of the period under surveillance

Other inclusions in the register are consumption data and population data. For consumption data, four different variables are taken into account; the first two of these are the *country* and *year* under surveillance.

COUNTRY

CONSUMPTION DATA

Health care level in which data have been collected

- T: Total
- C: Community
- H: Hospital

SECTOR

Health care sector in which data have been collected

- G: Global
- PUB: Public
- PRV: Private

PACKAGES

The number of packages consumed for the country, year, product and health care level and sector

The other two variables in consumption data are the *level* in which data have been collected (that is, whether they are total, community or hospital), the *sector* in which data have been collected (that is, whether they are global, public or private) and information on the *packages* (that is, the number of packages consumed for the country, year, product and sector).

POPULATION DATA

- COUNTRY
- YEAR
- SECTOR
- AM_CLASS
- POPULATION

Finally, in terms of population data, the variables in the register are country, year, sector, antimicrobial class and the reference population for the consumption information.

The population estimate reported needs to correspond to the population to which the consumption of antimicrobials applies.

5.8 Monitoring variables

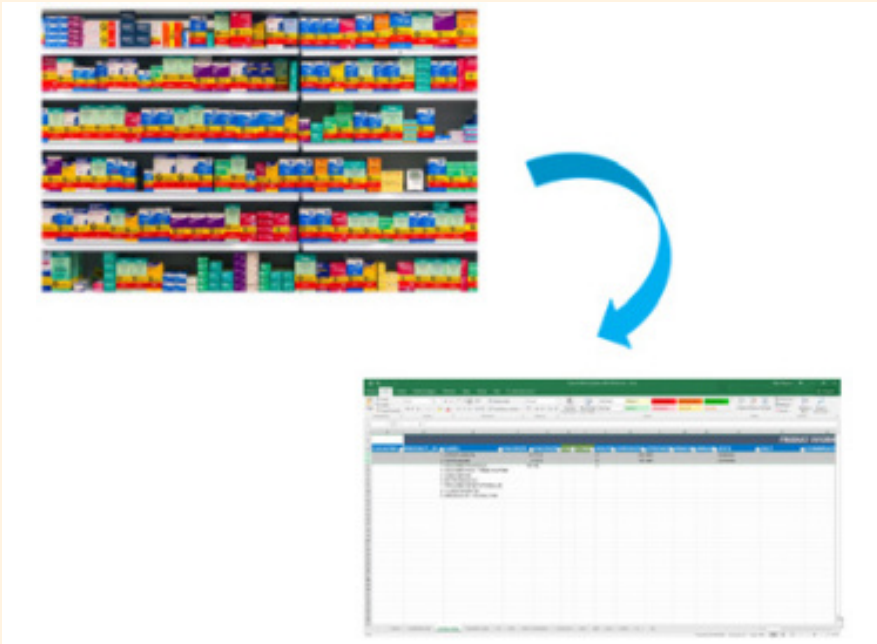
This section illustrates the practicalities of the variables and calculations that you will find in the WHO AMC methodology. Lecture 5.3 gives you the opportunity to practise some of the concepts covered in Module 2 (i.e. ATC/DDD classification) and earlier in this current module (variables and consumption calculations).

This lecture has worked examples, so you will need a paper, pen and calculator, and the ATC/DDD index that you have used previously (2,4).

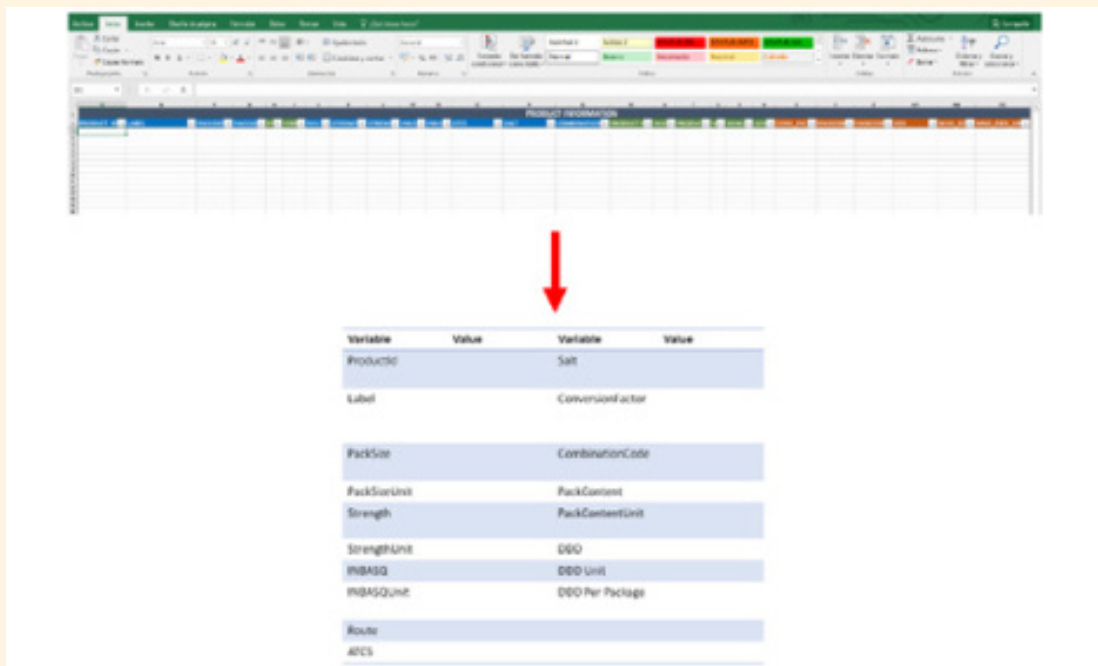
So, get your materials ready and watch Lecture 5.3!



Lecture 5.3.

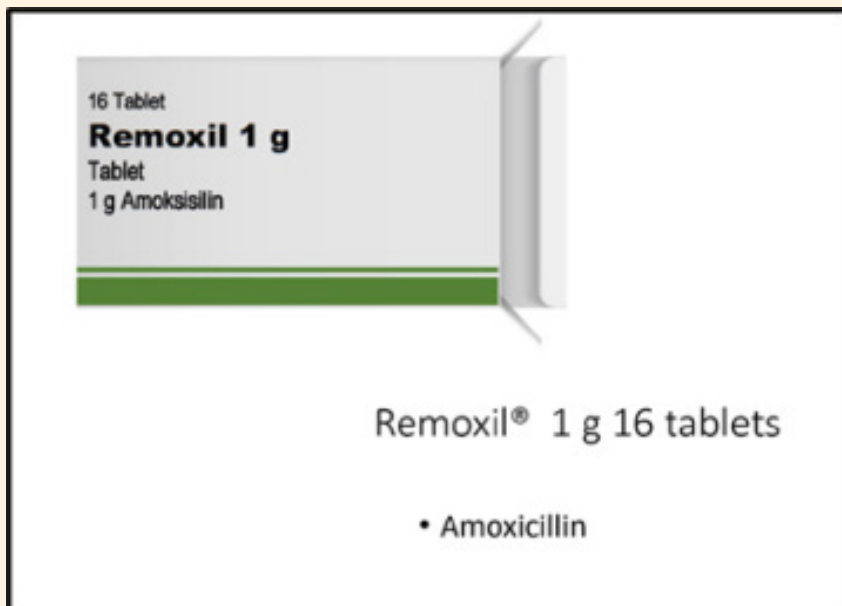


This lecture gives you some tasks to do that will help you to become more familiar with the different variables of the WHO methodology for antimicrobial consumption, and the need to prepare an accurate register of the antimicrobials for the data analysis.



When you are creating your AMC register, you will need to identify the variables to be collected from each antimicrobial that has been approved for the market in your country. Lecture 5.2 took you through the many variables – the ones that we are interested in here are those included in the present table.

For this task, we will try to complete this table for various products. You can use the ATC/DDD index online for this, or the summary list of the ATC codes for antimicrobials and their DDD values that was provided for this exercise.

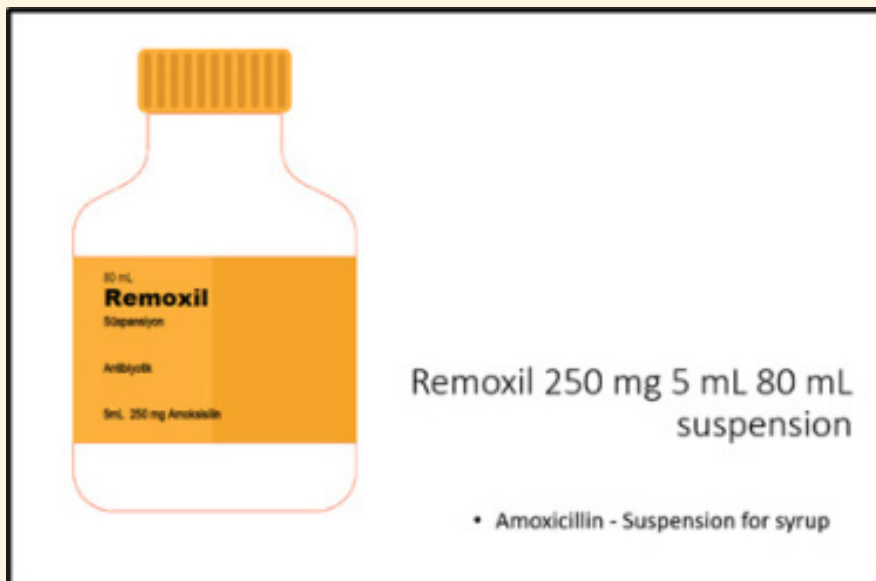


Let's begin with a product containing 16 amoxicillin tablets, each containing 1 gram of amoxicillin. Pause the lecture and try filling in the table yourself, then move on to the next screen to find the solution.

Variable	Value	Variable	Value
ProductID	1	Salt	
Label	Remoxil 1 g 16 tablets	ConversionFactor	
PackSize	16	CombinationCode	
PackSizeUnit	PCS	PackContent	16
Strength	1	PackContentUnit	G
StrengthUnit	G	DDD	1
INBASQ		DDD Unit	G
INBASQUnit		DDD Per Package	16
Route	O		
ATCS	J01CA04		

This slide shows the completed table for the Remoxil product. If you have forgotten what any of these variables relate to, just go back to Lecture 5.2 in Section 5.7. You will become familiar with the different variables once you start to use them routinely.

Now, let's try with another product.



In this example, we have the same brand name, Remoxil, but the formulation is a suspension for syrup. The bottle contains 80 mL, and each 5 mL dose contains 250 mg of amoxicillin.

Again, try to complete the rows for this product in the table, then move on to the next screen to find the solution.

Variable	Value	Variable	Value
ProductID	2	Salt	
Label	Remoxil 250 mg 5 mL 80 mL suspension	ConversionFactor	
PackSize	80	CombinationCode	
PackSizeUnit	ML	PackContent	4
Strength	250	PackContentUnit	G
StrengthUnit	MG	DDD	1
INBASQ	5	DDD Unit	G
INBASQUnit	ML	DDD Per Package	4
Route	O		
ATC5	J01CA04		

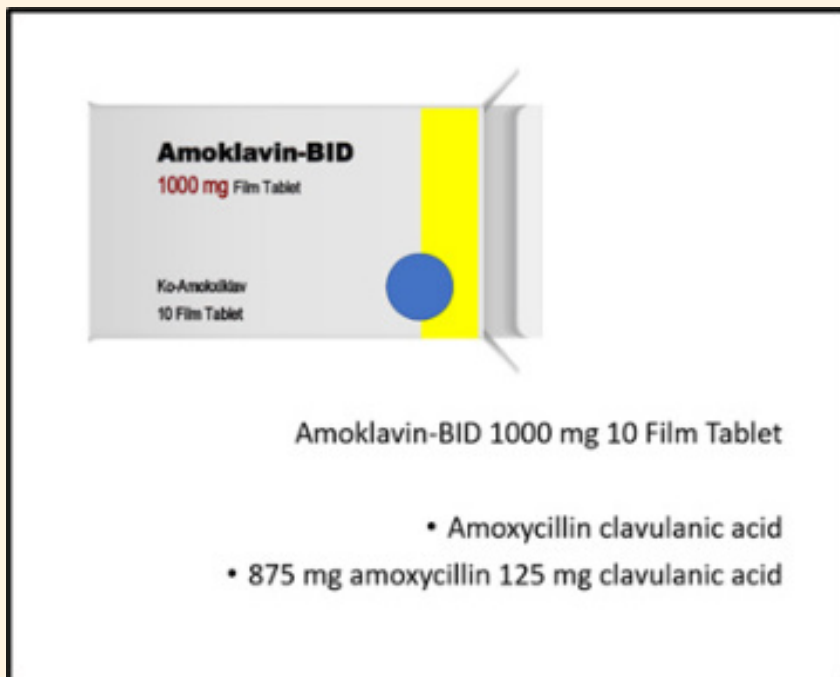
In this case, the completed table is a little different, because here we can fill in the variables INBASQ and INBASQ_UNIT.

In Lecture 5.2 we saw that INBASQ (ingredient base quantity) is only used for syrups, and it represents the denominator of the dose. Here, the bottle contains 80 mL, and each 5 mL contains 250 mg of amoxicillin (250 mg / 5 mL). In all other cases (including perfusion fluids and ampules) the INBASQ is simply set to 1.

Here, the INBASQ is "5" (i.e. the denominator of the dose), and the INBASQ_UNIT is "mL".

We can use this information to calculate the PACKCONTENT and PACKCONTENT_UNIT, as follows:

- For syrups, PACKCONTENT = (PACKSIZE multiplied by STRENGTH) divided by INBASQ.
- In the present example: $(80 \text{ mL} \times 250 \text{ mg}) / 5 \text{ mL} = 4000 \text{ mg} = 4 \text{ g}$.



In this example, we have a product containing amoxicillin and clavulanic acid to enter into the AMC database.

Again, try to complete the rows for this product in the table, then move on to the next screen to find the solution.

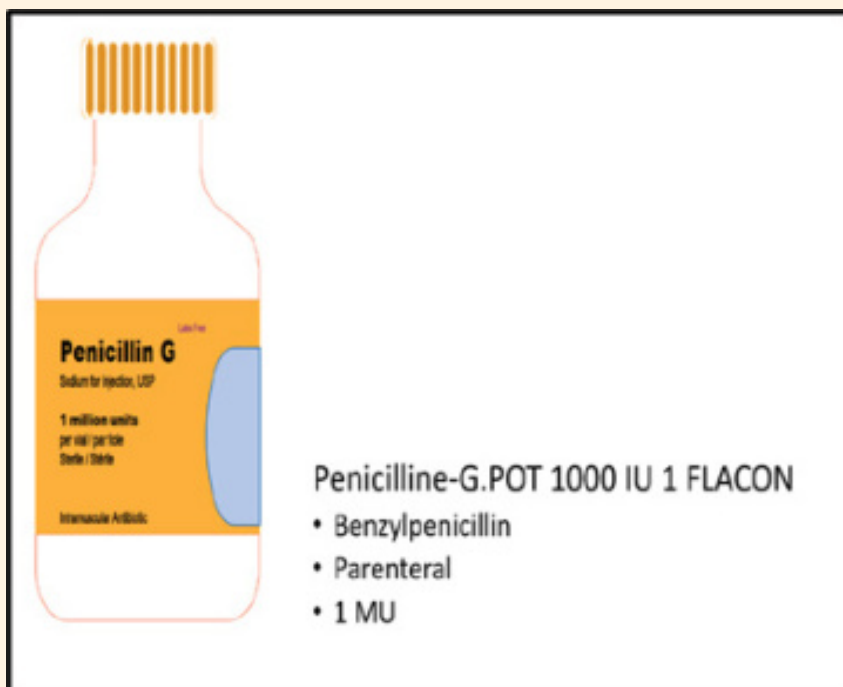
Variable	Value	Variable	Value
ProductID	3	Salt	
Label	Amoklavin-BID 1000 mg 10 Film Tablet	ConversionFactor	
PackSize	10	CombinationCode	
PackSizeUnit	PCS	PackContent	8.75
Strength	875	PackContentUnit	G
StrengthUnit	MG	DDD	1
INBASQ		DDD Unit	G
INBASQUnit		DDD Per Package	8.75
Route	O		
ATC5	J01CR02		

According to the ATC/DDD classification guidelines, the DDD value for amoxicillin + clavulanic acid (a beta-lactamase inhibitor) refers to the *amoxicillin* content and it is 1.5 g for the oral route.

Each tablet of Amoklavin-BID contains 875 mg of amoxicillin and 125 mg of clavulanic acid. Given that the DDD value is based only on the amoxicillin content, each package of 10 tablets contains $875 \text{ mg} \times 10 \text{ tablets}$, which equates to 8750 mg of amoxicillin.

The DDD value is 1.5 g, which is 1500 mg. Thus, each package contains $8750 \text{ mg} / 1500 \text{ mg}$, which is 5.8 DDD.

Now, let's look at a parenteral antimicrobial.



Here, we need to find the different variables and codes for this parenteral product that contains penicillin G.

You will see that, in this case, the strength is expressed in millions of international units (MU). Again, try to complete the rows for this product in the table, then move on to the next screen to find the solution.

Variable	Value	Variable	Value
ProductID	5	Salt	
Label	Penicilline-G.POT 1000 IU 1 Flacon	ConversionFactor	0.6
PackSize	1	CombinationCode	
PackSizeUnit	PCS	PackContent	0.6
Strength	1	PackContentUnit	G
StrengthUnit	MU	DDD	3.6
INBASQ		DDD Unit	G
INBASQUnit		DDD Per Package	0.16
Route	P		
ATCS	J01CE01		

Here is the result for that particular penicillin G product. In this example, we need to use the conversion factor variable (discussed in Section 5.7), because the strength units here are millions of international units (MU), so the MU value needs to be converted into grams or milligrams.

As described in Section 5.7, the conversion factor from MU to grams is 0.6 for the ATC code J01CE01.

Thus:

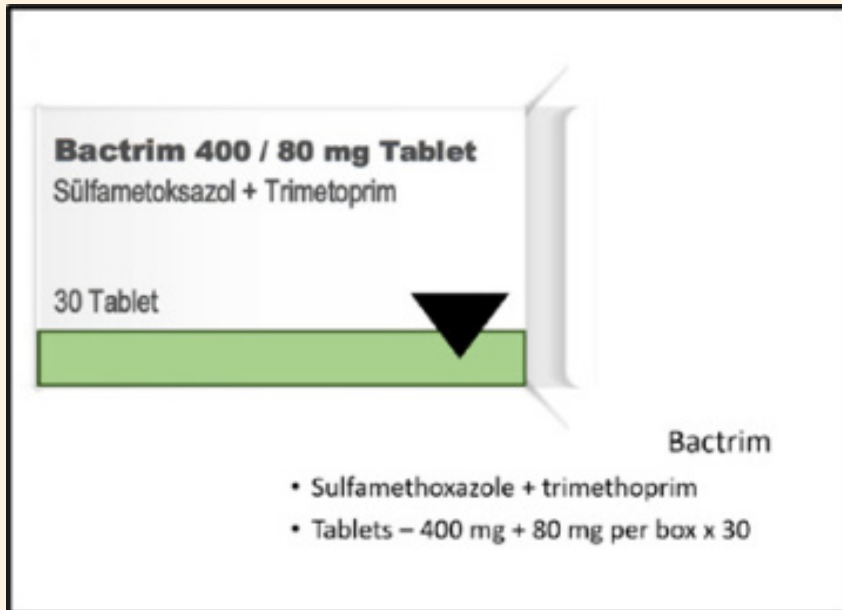
- $1 \text{ MU (strength)} \times 0.6 \text{ (conversion factor)} = 0.6 \text{ g (pack content)}$.
- Because the value of 1 DDD is 3.6 g, the DDD per package is $0.6 / 3.6 = 0.17 \text{ DDD}$.



In this example, the product contains 20 capsules, each of which contains 250 mg of vancomycin. Again, try to complete the rows for this product in the table, then move on to the next screen to find the solution.

Variable	Value	Variable	Value
ProductID	8	Salt	
Label	Vancocin 250 mg 20 capsules	ConversionFactor	
PackSize	20	CombinationCode	
PackSizeUnit	PCS	PackContent	5
Strength	250	PackContentUnit	G
StrengthUnit	MG	DDD	2
INBASQ		DDD Unit	G
INBASQUnit		DDD Per Package	2.5
Route	O		
ATC5	A07AA09		

Here is the solution, which takes into account that oral vancomycin is classified under the ATC code A07AA09.



It is important to remember the exceptions and particularities of the ATC classification system. Revisit Module 2 if you are unsure about this.

Again, try to complete the rows for this product in the table, then move on to the next screen to find the solution.

Variable	Value	Variable	Value
ProductID	9	Salt	
Label	Bactrim Tablets 400 mg + 80 mg perbox x 30	ConversionFactor	
PackSize	30	CombinationCode	J01EE01_3
PackSizeUnit	PCS	PackContent	30
Strength	1	PackContentUnit	UD
StrengthUnit	UD	DDD	4
INBASQ		DDD Unit	UD
INBASQUnit		DDD Per Package	7.5
Route	O		
ATCS	J01EE01		

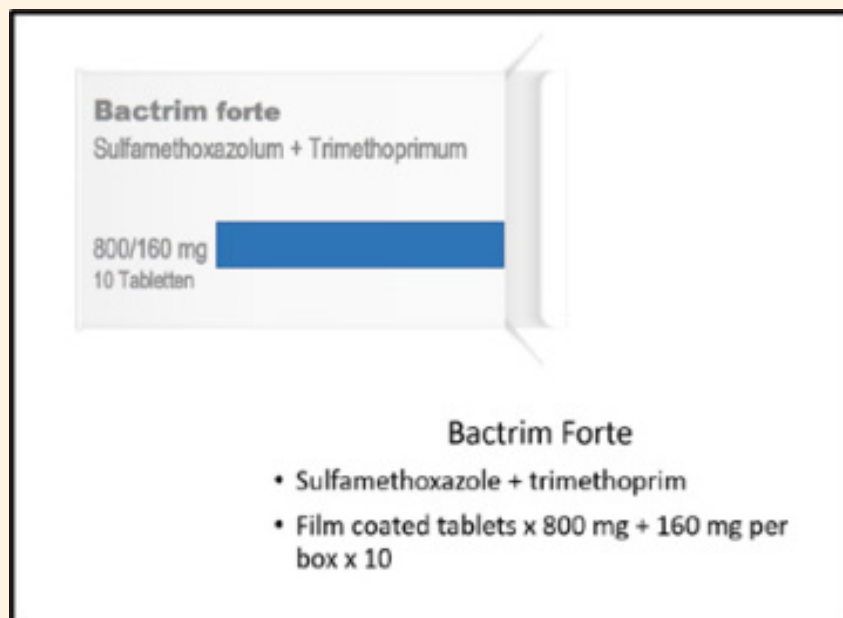
Here is the solution. It is important to remember that the fixed combination of sulfamethoxazole and trimethoprim has the ATC code J01EE01.

Now, each tablet contains 400 mg / 80 mg (that is, 400 mg of sulfamethoxazole and 80 mg of trimethoprim). The list of DDDs of combined products provides a DDD for an oral combination of 400 mg / 80 mg; that value is 4 unit doses.

If each tablet is 1 unit dose, then four tablets (with 4 unit doses) would equal 1 DDD.

The package contains 30 tablets; thus, the DDD per package is:

$30 \text{ tablets} / 4 \text{ UD per DDD} = 7.5 \text{ DDD per package.}$



Sometimes, the particular combination of sulfamethoxazole and trimethoprim cannot be found on the ATC/DDD webpage.

Again, try to complete the rows for this product in the table, then move on to the next screen to find the solution.

Variable	Value	Variable	Value
ProductID	10	Salt	
Label	Bactrim Forte Film coated tablets x 800 mg + 160 mg per box x 10	ConversionFactor	
PackSize	10	CombinationCode	J01EE01_3
PackSizeUnit	PCS	PackContent	20
Strength	2	PackContentUnit	UD
StrengthUnit	UD	DDD	4
INBASQ		DDD Unit	UD
INBASQUnit		DDD Per Package	5
Route	O		
ATC5	J01EE01		

In the present example, the content per tablet is 800 mg of sulfamethoxazole and 160 mg of trimethoprim. You will find that this combination is not provided in the list of DDDs for combined products. However, we previously found a DDD value for a product with 400 mg of sulfamethoxazole and 80 mg of trimethoprim. The 800 mg / 160 mg product is equal to two times 400 mg / 80 mg:

- $800 \text{ mg} / 160 \text{ mg} = 2 \times (400 \text{ mg} / 80 \text{ mg})$.

Thus, the STRENGTH variable in this case is "2".

PACK_CONTENT is PACKSIZE multiplied by STRENGTH; that is, 10×2 , which equals 20.

Finally, the assigned DDD value is 4 unit doses.

So, $20 \text{ (PackContent)} / 4 \text{ UD (DDD value)} = 5 \text{ DDD per pack}$.

Now that you have finished Lecture 5.3, take Quiz 5.2 to test your understanding (the solutions to the quiz are at the end of the module).



Quiz 5.2

Please complete the table below for each of the three specific products containing antimicrobials listed here:

1. Ery 500 comp. film. 500 mg N10 (active ingredient: erythromycin ethylsuccinate)
2. Vancomycin Vial Dry Inf 1 g
3. Gentamicin 80 mg × 10 tablets

PRODUCTID			
Label		Salt	
PackSize		ConversionFactor	
PackSizeUnit		CombinationCode	
Strength		PackContent	
StrengthUnit		PackContentUnit	
INBASQ		DDD	
INBASQUnit		DDDUnit	
Route		DDD per package	
ATC			

5.9 Exercise solutions and feedback

Answers to Quiz 5.1 (in Section 5.3)

Here are the answers to the quiz. If you chose the wrong answer, check the feedback for an explanation, and revisit Section 5.3.

STATEMENT	TRUE OR FALSE	FEEDBACK IN CASE OF WRONG ANSWER
As hospitals use very specific last-resort or restrictive antimicrobials, hospital settings are excluded from the AMC calculations.	False	The WHO protocol defines AMC as quantities of antimicrobials used in a specific setting (total, community, hospital) during a specific period of time (e.g. days, months and years).
The denominator data (population) is optional and of secondary importance. What is really important is antimicrobial consumption data (numerator).	False	The WHO methodology uses DID as a common measurement of AMC. Thus, reference time (days, months) and population are also necessary.
Contextual information includes information on data sources, antimicrobials included in the surveillance and specific exclusions of health sector facilities.	True	Revisit the sections of the WHO protocol given in Box 5.1.

Answers to Quiz 5.2 (in Section 5.8)**Product 1: Ery 500 comp. film. 500 mg N10 (active ingredient: erythromycin ethylsuccinate)**

PRODUCTID	1		
Label	Ery 500 comp. film. 500 mg N10	Salt	Erythromycin ethylsuccinate
PackSize	10	ConversionFactor	
PackSizeUnit	PCS	CombinationCode	
Strength	500	PackContent	5
StrengthUnit	MG	PackContentUnit	G
INBASQ		DDD	1
INBASQUnit		DDDUnit	G
Route	0	DDD per package	5
ATC	J01FA01		

Product 2: Vancomycin Vial Dry Inf 1 g

PRODUCTID	2		
Label	Vancomycin Vial Dry Inf 1g	Salt	
PackSize	1	ConversionFactor	
PackSizeUnit	PCS	CombinationCode	
Strength	1	PackContent	1
StrengthUnit	G	PackContentUnit	G
INBASQ		DDD	2
INBASQUnit		DDDUnit	G
Route	P	DDD per package	0.5
ATC	J01XA01		

Product 3: Gentamicin 80 mg × 10 tablets

Check whether there has been an error. There is no product that contains oral gentamicin. If this route of administration has been marketed in your country, please contact WHO for assignment of a DDD.

5.10 References

1. GLASS methodology for a global programme on surveillance of antimicrobial consumption.. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/9789240012639>, accessed 26 August 2021).
2. ATC/DDD Index 2020. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology; (https://www.whooc.no/atc_ddd_index/, accessed 2 April 2020 2020).
3. ISO 3166 Country codes. Geneva: International Organization for Standardization; (<https://www.iso.org/iso-3166-country-codes.html>, accessed 1 April 2020).
4. List of DDDs combined products. Oslo, Norway: WHO Collaborating Centre for Drug Statistics Methodology; (https://www.whooc.no/ddd/list_of_ddd_combined_products/, accessed 2 April 2020).



World Health Organization
20 avenue Appia
1211 Geneva 27 - Switzerland

<https://www.who.int/health-topics/antimicrobial-resistance>

