Q&A

GLASS guide for national surveillance systems for monitoring antimicrobial consumption in hospitals

National AMC Monitoring

- What is the difference between antimicrobial use (AMU) and antimicrobial consumption (AMC)?
- Why should we monitor AMC?
- What is the One Health approach?
- What is the difference between antimicrobials and antibiotics?
- There exists a large informal market with substandard or falsified medicines. Should data be obtained from the informal market?
- What do I do if data/reports do not disaggregate by non-human use (e.g., animal or agricultural use)?
- Commercial AMC data for my country is available from IQVIA. How can I obtain this data? Is it freely available?
- There are a number of data sources available in my country. Some sources may have better data quality but poorer coverage whereas other sources have more complete coverage. Which should I choose?
- After having collected and calculated AMC in my country, the consumption estimates and patterns of antimicrobial use differ greatly from a neighboring country. How should I interpret this?
- I have searched in the ATC/DDD index for penicillin G and penicillin V, but the index returns the message, “No match found. Please try again.” Are these antibiotics not included in the index?
- In my data, there are several combinations of drugs that do not have ATC codes. Should I include these in my analysis?
- If my dataset has combinations made of two or more drugs with different ATC codes, which code should I use?
- In my data, there are both oral and parenteral formulations of one drug, but the ATC/DDD index only has one DDD listed for oral formulations. What should I do about the parenteral formulations?
- How can I submit a request to add a new ATC code?
- I am looking for erythromycine in the search engine of the ATC/DDD index but cannot find it. Why?

- When I search for metronidazole, I get at least 7 different ATC codes to choose from. Which one should I use?
- What is the difference between DDD and prescribed daily dose (PDD)?
- Why is it important to report which version or year of the ATC/DDD index I have used to calculate AMC?
- How do I assign ATC codes for combination products?
- When searching for the DDD value for amoxicillin and clavulanic acid in the ATC/DDD index, there is a note saying “refers to amoxicillin” after the ATC code for amoxicillin and beta-lactamase inhibitor. What does this mean?
- How can I find the DDD value for combination products?
- Do I need to account for the strengths of the active ingredients in the combination product if it differs from the strengths specified in the list of combination products on the WHOCC webpage?

Hospital AMC Monitoring

- Which data sources may be used for monitoring AMC in hospitals and what are their strengths and limitations?
- Why is it useful to monitor antimicrobial consumption at different hospital levels?
- What should be considered, if data are collected at the hospital unit level?
- How are mixed wards handled?

National AMC Monitoring

1. **What is the difference between antimicrobial use (AMU) and antimicrobial consumption (AMC)?**

Antimicrobial use data generally refer to individual patients' use of antimicrobials. These data are collected at the patient level and often include information on indication, treatment, and patient characteristics. While use data are especially helpful in tracking potential sources of antimicrobial resistance because it provides information on prescribing behavior, collection of antimicrobial use data requires a huge amount of resources and is generally not feasible at the national level, especially in the absence of electronic patient records.
Antimicrobial consumption generally refers to estimates of aggregated data, often obtained from import, manufacturer, or reimbursement records. Such records are kept by a variety of private and governmental agencies and are frequently used as a proxy for antimicrobial use data.

2. **Why should we monitor AMC?**

While antimicrobials are essential in treating infectious diseases, they are often prescribed inappropriately. This overconsumption and inappropriate use is a major driver of antimicrobial resistance, which is an urgent threat to global health.

3. **What is the One Health approach?**

"'One Health' is an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes.
The areas of work in which a One Health approach is particularly relevant include food safety, the control of zoonoses (diseases that can spread between animals and humans, such as flu, rabies and Rift Valley Fever), and combatting antimicrobial resistance (when bacteria change after being exposed to antimicrobials and become more difficult to treat)."
Cited from the WHO website: https://www.who.int/features/qa/one-health/en/.

4. **What is the difference between antimicrobials and antibiotics?**

Antimicrobials are drugs treating infection caused by microorganisms and can be grouped according to the microorganism that is the primary target of the drug. These includes bacteria, fungus, viruses, and protozoa. Antibiotics are a subgroup of antimicrobials and refer to drugs that are used to treat bacterial infections.

5. **There exists a large informal market with substandard or falsified medicines. Should data be obtained from the informal market?**

According to WHO protocol, AMC data should be collected from official channels only (e.g., national regulatory authorities); data circulating in the informal market should not be included in country consumption estimates, even though this may lead to an underestimation of AMC. Typically, complete data from the informal market are difficult to obtain (if at all possible) and the data sources may be more prone to variations and errors. This complicates comparisons of consumption estimates across time. To better interpret the data obtained from official channels and get a sense of the potential underestimation of AMC, it is useful to understand the market share of the informal market.

6. **What do I do if data/reports do not disaggregate by non-human use (e.g., animal or agricultural use)?**

If non-human use data cannot be disaggregated from human-use data, report the data still and cite this as a limitation in the report. Data may evolve over time, and tracking these changes is important.

7. **Commercial AMC data for my country is available from IQVIA. How can I obtain this data? Is it freely available?**

IQVIA data must be purchased from IQVIA.

8. **There are a number of data sources available in my country. Some sources may have better data quality but poorer coverage whereas other sources have more complete coverage. Which should I choose?**

For national surveillance of AMC, coverage is generally of priority and countries are therefore usually recommended to use data sources with the most complete coverage. However, this decision should take data quality into consideration. For example, if the majority of antimicrobials are prescribed by the public sector and the private sector is limited it could be reasonable to assume that the public procurement data is close to nationally complete. In this case, public procurement data might be more suitable than import and manufacturing data even if the latter sources has a somewhat higher coverage. In other words, there is no simple rule for selection of data sources but each country needs to take a number of factors into consideration including coverage, data quality and manpower required to collect the data. Data

sources for surveillance of AMC can and are expected to evolve and change with time. Take note whenever changes to data sources occur.

9. **After having collected and calculated AMC in my country, the consumption estimates and patterns of antimicrobial use differ greatly from a neighboring country. How should I interpret this?**

The differences may derive from factors related to the data sources, errors in data management and analyses, or an actual difference in consumption. Some questions to ask include:

a. Are the data sources and coverage comparable?
b. Are the same classes of antimicrobials included?
c. Are there any errors in the dataset?
d. Are there any errors or differences in the analyses? For example, is the denominator correct? Did you use the same ATC/DDD version?
e. Is there a difference in the burden and panorama of infectious diseases between the countries? Is there a difference in population demographics?

10. **I have searched in the ATC/DDD index for penicillin G and penicillin V, but the index returns the message, "No match found. Please try again." Are these antibiotics not included in the index?**

Some antibiotics are referred to by more than one name. In this example, the ATC codes are assigned to benzylpenicillin and phenoxymethylpenicillin instead of penicillin G and penicillin V. Make sure to check all possible names before concluding that a drug is not listed in the ATC/DDD index.

11. **In my data, there are several combinations of drugs that do not have ATC codes. Should I include these in my analysis?**

If antibiotics in your data do not have ATC codes assigned, make note of the quantities of those products and the indications for which they are generally used in the country context. Include these in your report but not in the calculation of overall DDDs and DIDs. If this is a commonly used combination product in your country, inform the WHO Collaborating Centre for Drug Statistics Methodology (WHOCC).

12. **If my dataset has combinations made of two or more drugs with different ATC codes, which code should I use?**

Make note of these combinations. Include these in your report but not in the calculation of overall DDDs and DIDs. If they are common, inform the WHOCC.

13. In my data, there are both oral and parenteral formulations of one drug, but the ATC/DDD index only has one DDD listed for oral formulations. What should I do about the parenteral formulations?

Make note of the quantities of those products and the indications for which they are generally used in the country context. Include these in your report but not in the calculation of overall DDDs and DIDs. Inform the WHOCC on strength, recommended dosing and indication.

14. How can I submit a request to add a new ATC code?

Requests for ATC classification of a medicinal substance should be addressed to the WHO Collaborating Centre for Drug Statistics Methodology in Oslo, Norway.

15. I am looking for erythromycine in the search engine of the ATC/DDD index but cannot find it. Why?

The search engine is sensitive to spelling. Thus, the substance name should be spelled according to International Nonproprietary Names (INN). For example, according to INN the correct spelling is “erythromycin.” Thus, you will not get a hit if it is spelled as e.g. “erythromycine” or “erythromycin.” In case you are not sure of the spelling, you can type in the first letters e.g. “ery” and get a full list of all substances starting with ery.
Link to the published INN lists: https://www.who.int/medicines/services/inn/en/.

16. When I search for metronidazole, I get at least 7 different ATC codes to choose from. Which one should I use?

Substances are classified in the ATC index according to their main therapeutic area. Thus, one substance may have several ATC codes if different formulations have different therapeutic indications. However, note that only *one* ATC code can be assigned per substance and route of administration. For national AMC surveillance, only systemic antimicrobials are included. In this case, only the oral/rectal and parenteral formulation of Metronidazole are of interest. In the case of Metronidazole, these two routes of administration have different ATC codes. Assign the ATC code according to the route of administration of the product.

17. What is the difference between DDD and prescribed daily dose (PDD)?

Defined daily dose (DDD) is the "assumed average maintenance dose per day for a drug used for its main indication in adults" and can be seen as an international compromise or average between recommended or prescribed daily doses in various countries. Thus if the prescribed daily dose in your country is on average higher than the assigned DDD, then DDD/1000 inhabitants/day will be an overestimation of the number of individuals on treatment with that specific antimicrobial on a given day. The benefit of DDDs is that it is standardized and facilitates comparisons across countries and over time.

18. Why is it important to report which version or year of the ATC/DDD index I have used to calculate AMC?

WHOCC updates the ATC/DDD index on an annual basis. Although the aim is to keep the ATC and DDD constant across years, an update of the DDD may be necessary at times to better reflect the actual recommended or prescribed dose. For example, a review of DDD for antibiotics were undertaken in 2019 and the DDD value increased for several antibiotics. Thus, using the same dataset, the ATC/DDD 2019 version would result in lower AMC estimates than the 2018 version. Note that updates of existing ATC and DDD are rare and is mostly not a problem. It is possible to convert calculated consumption estimates using different ATC/DDD versions if you know which version was used.

19. How do I assign ATC codes for combination products?

The WHOCC uses several strategies to assign ATC codes to combination products. If you have a combination product, you can follow the steps below to identify the correct ATC code:

f. Search the ATC/DDD index for any of the active ingredients in the combination product in the search engine. Do you find the exact combination of active ingredients in the results?
g. Search individually for each active ingredient in your combination product. Does any of them show up with an option "X, combinations" where X is the name of the active ingredient?
h. If the active ingredients in the combination product belong to the same subclass (4th level ATC), some subclasses have the option "combinations of X" where X is the name of the subclass.
i. For some antimicrobials, there are separate classes (3rd level ATC) dedicated for combination products, e.g. J01R for antibiotics.
j. In some cases, you may not find a suitable ATC code for the combination products. Take note and inform the WHO Collaborating Center.

20. When searching for the DDD value for amoxicillin and clavulanic acid in the ATC/DDD index, there is a note saying "refers to amoxicillin" after the ATC code for amoxicillin and beta-lactamase inhibitor. What does this mean?

This means that you should only consider the strength of amoxicillin when calculating consumption of amoxicillin and clavulanic acid. For example, if the strength of a tablet of amoxicillin/clavulanic acid is 500 mg/125 mg, then you should only count 500 mg.

21. How can I find the DDD value for combination products?

With the exception of some antivirals and antibiotics, you will notice that DDD for most combination products cannot be found in the search engine for the ATC/DDD index. All combination products with DDD assigned in unit dose (UD) can be found in a separate list under the headline "DDD" in the menu field on the WHOCC webpage. Similarly to the search engine, this list is updated annually. Thus, combination products that previously lacked DDD values may have a DDD assigned in the new version of the ATC/DDD index.
Link to the list of DDD for combined products:
https://www.whocc.no/ddd/list_of_ddds_combined_products/

22. Do I need to account for the strengths of the active ingredients in the combination product if it differs from the strengths specified in the list of combination products on the WHOCC webpage?

Yes, you do. For example, if you have a product with tablets containing 800 mg/160 mg of sulfamethoxazole/trimethoprim than you need to multiply UD by 2 as the strength in the WHOCC list of combination products is 400 mg/80 mg. The challenge is when you have combination products where the strengths of the individual active ingredients vary differently from the strengths in the WHOCC list. Then you cannot directly multiply or divide the UD. In these cases, you may include the product in your report but not in the calculation of overall DDDs and DIDs.

Hospital AMC Monitoring

23. Which data sources may be used for monitoring AMC in hospitals and what are their strengths and limitations?

For monitoring antimicrobial consumption different data sources may be used. The choice of the data source depends on the availability of the data, the ease of data retrieval, the quality and completeness of the data records and their suitability to achieve the surveillance objectives of the individual hospital. Different data sources have different strengths and limitations, which should be considered.

a. Purchase data

Procurement data of the hospital administration or hospital pharmacy

Advantages:

- Data on the purchase of medicinal products are ordinarily available in most of the hospital administrations and/or hospital pharmacies.
- They can easily be retrieved on a regular basis and are therefore suitable for routine AMC-surveillance.

Limitations:

- Purchase records may not fully cover the amount of antimicrobials used in the hospital for several reasons:
  - □ Medicinal products retrieved from other hospitals/pharmacies
  - □ Donations
  - □ Medicinal products distributed and provided by public health institutions
  - □ Medicinal products purchased by the individual patient outside of the hospital (outpatient pharmacy, licensed drug stores)
- Disaggregation of the data according to the hospital setting (ambulatory care/ inpatients) and different organisational levels and units (e.g. medical specialties, ICU/ general wards) may not be possible.
- No exact information about the time period during which the antimicrobials have been consumed. Analyses of the data may be limited to yearly time intervals.
- No Information about the administration of the medicinal products to the individual patient and the modalities of prescribing (e. g. indication, dose...)

b. Unit-based dispensing data of the pharmacy

Data on the dispensing of antimicrobials to wards or departments by the pharmacy

Advantages:

- Data on the dispensing of medicinal products are ordinarily available in most hospital pharmacies.
- Data can easily be retrieved on a regular basis and are therefore suitable for routine AMC-surveillance.

- Data may be disaggregated with respect to different hospital settings and units allowing for stratified data analyses.
- Date of dispensing is ordinarily recorded allowing for analysis of different time intervals and aggregation levels (yearly, quarterly, monthly).

Limitations:

- Dispensing records may not fully cover the amount of antimicrobials used in the hospital for several reasons:
  - □ Medicinal products retrieved from other hospitals/pharmacies
  - □ Donations
  - □ Medicinal products distributed and provided by public health institutions
  - □ Medicinal products purchased by the individual patient outside of the hospital (outpatient pharmacy, drug store)
- No Information about the administration of the medicinal products to the individual patient and the modalities of prescribing (e. g. indication, dose…)
- If data are only available in paper-based form, aggregation and analysis of the data at the hospital unit-level and for shorter than yearly time intervals may be cumbersome.
- If the medicinal products are dispensed to central stocks serving several wards/departments, an allocation of antimicrobial consumption to certain hospital units may be compromised.

c. Patient-based dispensing data of the pharmacy or billing data

Advantages:

- Records on the dispensing or sold of medicinal products to the individual patient are ordinarily available in pharmacies of hospitals with patient-based distribution of medicinal products.
- Further information about the prescription modalities at the patient-level might be available allowing for more detailed analyses.
- In the case information about the affiliation of the patient (hospital unit) is recorded, data may be aggregated and analyzed at the hospital unit-level (e.g. ward, medical specialty).
- The date of dispensing is ordinarily recorded allowing for analysis of different time intervals and aggregation levels (yearly, quarterly, monthly).

Limitations:

- Dispensing and billing records may not fully cover the amount of antimicrobials used in the hospital for several reasons:
- Medicinal products retrieved from other hospitals/ pharmacies
- Donations (e.g. provided directly to the respective hospital department)
- Medicinal products distributed and provided by public health institutions
- Medicinal products purchased by the individual patient outside of the hospital (outpatient pharmacy, drug store).
- If data are only available in paper-based form, aggregation and analysis of the data may be cumbersome. From a practical point of view, the availability of electronic records is required.
- No information is available about the factual administration of the medicinal products to the individual patient.
- If there is no additional information recorded about the location (hospital unit) of the patient, aggregation and analysis of the data according to hospital setting (ambulatory care/inpatient) and hospital unit (department, ward) won´t be possible.

d. Prescription/administration data

Data on the prescription (e.g. patient records, electronic health records) and/or the administration of antimicrobials (e.g. bar-coded patient administration

Advantages:

- Besides the name of the medicinal product further information about the prescription modalities at the patient-level might be available allowing for more detailed analyses.
- In the case information about the patients location (hospital unit/department) is recorded, data may be aggregated and analyzed accordingly.
- The availability of the prescription date allows analysis of different time intervals and aggregation levels (yearly, quarterly, monthly).
- If the data are electronically available, monitoring of antimicrobial consumption is possible on a regular basis.

Limitations:

- Prescription records only, do not provide information whether the medicinal product has been administered to the patient.
- If data are only available in paper-based form, extraction, aggregation and analysis of the data may be too cumbersome. From a practical point of view, the availability of electronic records is indispensable.
- Medicinal products obtained by the patient without any prescription are not included (e.g. medicinal product sold in a drug store) in the data set.

- If there is no additional information recorded/available about the location (ward/department) of the patient, aggregation and analysis of the data according to hospital setting (ambulatory care/inpatient) and hospital unit (department, ward) is not possible.

General remarks
The different data sources and the extent of the documentation determine possibilities and detail of analyses. As with respect to the data sources the type of the collected data varies, analyses results of AMC may provide deviating results. This should be considered, if data sources have changed overtime in order to interpret longitudinal data correctly.

24. Why is it useful to monitor antimicrobial consumption at different hospital levels?

Depending on the available data sources collection and analysis of the data can be performed at different organizational levels:

- whole hospital
- medical specialty/department
- ward and ward type
- patient

Data collected and analyzed at the level of the whole hospital, for example of all inpatients irrespective of their affiliation to a certain ward or type of medical department, provides important insights into the amount and profile of antimicrobial consumption and the spectrum of antimicrobials used in the hospital. These data are essential in order to obtain a thorough picture of the actual situation, which forms the basis e.g. for the work of the pharmacy and therapeutics committee and antimicrobial stewardship teams.
Indeed, for antimicrobial stewardship purposes it would be useful to additionally have an estimate about the antimicrobial consumption estimates at hospital unit-level. So, ward-level data may reflect the amount and type of antimicrobial treatments of the patients, which have been cared for on the specific ward, more precisely. The responsible physicians mostly are informed about the type of patients/infections treated and therefore may interpret the data within this context.
In addition, the different medical specialties or departments may serve as a surrogate marker for patient characteristics with respect to type of disease and treatment (patient mix). Thus, data collected and analyzed at the specialty/department-level may inform more precisely about specific treatment practices and may support reasonable planning and focusing of antimicrobial stewardship activities.
In general, the finer the granularity of the collected data, the more detailed analyses may be performed and the closer to the patient is the information which can be extracted from the data. In addition to the hospital level data, unit-level data provide a more comprehensive picture allowing to finetune and tailor antimicrobial stewardship activities more properly.

25. What should be considered, if data are collected at the hospital unit level?

It is important to ensure that antimicrobial consumption data and hospital activity data are congruent with respect to the specific hospital unit and the envisaged time period. For example, if antimicrobial consumption should be monitored at the ward-level in quarterly time intervals antimicrobial consumption data AND hospital activity data need to be collected accordingly in order to provide meaningful calculation results. If there is a discrepancy, for example if consumption data are available at ward level but hospital activity are only available at the level of overarching departments or the whole hospital, analysis at the ward-level is not possible. Reasonable calculation results can only be obtained for these hospital units for which both groups of data do exactly correspond. This should be kept in mind especially before the background that consumption and hospital activity data mostly stem from different data sources (hospital pharmacy and administration, respectively).

26. How are mixed wards handled?

Most of the hospitals have at least one single ward, which cannot be assigned to one medical or surgical specialty/department as it cares for patients with mixed disease entities. Some hospitals even follow a policy of flexible bed allocation throughout the whole hospital. In these cases, using aggregated data at hospital unit-level (e.g. ward-level dispensing data) does not allow to assign antimicrobial consumption to specific service lines, which for mixed wards would only possible, if patient-level data were available. Nevertheless, it remains meaningful to collect and analyze the data at hospital unit-level (e.g. ward-level). Even if the interpretation of the data is more difficult, especially when the patient mix changes significantly over time, the attending physicians may know which type of patients they have cared for and are able to put the data into the right context.

In this context, it should be considered that it is useful to establish and maintain a hospital register for documentation of the hospital structure. It should contain information about the allocation of single wards to the different service lines and the overarching departments and thereby should provide a basis for meaningful collection, analysis and interpretation of the data. It should be updated regularly and changes in ward allocation should be documented in order to allow for meaningful longitudinal analyses. A standardized approach of ward allocation may facilitate comparisons between different wards of the same hospital or with similar wards of other hospitals. Even if unit-level data are not available a hospital register may provide useful background for the interpretation of facility-wide data.

In such a hospital register, mixed wards may formally be assigned to an overarching "Mixed Adult Ward". If the ward harbours mainly conservative (e.g. internal medicine and neurology) or surgical patients (e.g. general surgery and urology), the ward may be assigned to an overarching medical or surgical ward (see "GLASS guide for national surveillance systems for monitoring antimicrobial consumption in hospitals", Annex 5). Thus, even if data of mixed wards cannot be analyzed at the specialty-level (e.g. traumatology, internal medicine), the possibility to perform an analysis at the overarching department-level remains unchanged. In addition, stratified analyses according to ward type (e.g. general wards versus intensive care units) are possible.

Example of a hospital registry for the documentation of hospital structure and the allocation of mixed wards.

Example	Ward name	Ward type	Specialities*	Overarching department
Example 1	A	General ward	Internal/general medicine	Adult medical ward
Example 2	B	General ward	Internal medicine and neurology	Adult medical ward
Example 3	C	General ward	General surgery and traumatology and urology	Adult surgical ward
Example 4	D	General ward	General surgery and general medicine	Mixed adult ward
Example 4	E	General ward	Traumatology	Adult surgical ward
Example 6	F	Intensive Care Unit	Mixed pediatric Intensive Care Unit	Pediatric Intensive Care Unit

* The different specialties represented in one single ward