European Science Foundation
Standing Committee for the European Medical Research Councils (EMRC)

ESF EMRC EXPLORATORY WORKSHOP

Antibiotic Prescribing Quality Indicators

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Scientific Report

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Annex 1: General format of the indicators

All indicators are described in a way that allows them to be read and scored on their own. Nevertheless no single indicator can provide a complete picture of the quality of antibiotic use in ambulatory care. The final set will be based on the result of your scoring.

Indicator number: Title [Label]
All indicators are numbered, given an informative title and a label. For this occasion the number and the label allow you to link this document with the scoring sheet. After selection and approval of the final set of ESAC indicators the number and label will allow linking this set with a table showing indicator values for individual countries.

Definition
Provides a basic description of the indicator.

Public health objective
Describes the justification for the selection of the particular indicator, i.e. its relevance to reducing antimicrobial resistance, clinical relevance to the patient health benefit and relevance to cost-effectiveness. These can be in general affected both by the volume of prescribed antibiotics and the choice of antibiotics.

Calculation formula:
Describes how the indicator value is calculated, either as a formula or as a description in words. Any suggestions to optimise the calculation/construction of the indicators or its description are welcome.

Benchmark and recommended action
Aims to provide the framework for the development of a benchmark, the interpretation of the indicator and the recommended action at the national level, based on the epidemiology of infectious diseases and national guidelines. In general one benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence indicators. A range of acceptable indicator values should be defined rather than one threshold value. For any action planned explicit targets should be set.

Limitations
Enumerates specific limitations of the indicator, which should be taken into consideration regarding its interpretation. Since most proposed indicators are based on ATC/DDD methodology, recommended by WHO, they share the common limitations of this methodology[1]. Not all antibacterials are classified within ATC J01 class, which also represents the denominator for the calculation of all proportional indicators. Moreover, "Defined Daily Dose" (DDD) only represents the assumed average maintenance dose per day for a drug used for its main indication in adults. For a deeper understanding of antibiotic use, in general we suggest to use additional outcome measures, such as the number of prescriptions or packs.

ESAC boxplot
Summarises the indicator values from all countries able to provide data required for the calculations. The median, quartiles and extreme values are shown.

[1] Vander Stichele RH, Elseviers M, Ferech et al. European surveillance of antimicrobial consumption: data collection performance and methodological approach. Br J Clin Pharmacol 2004; 58: 419-428.

Annex 2: List of proposed indicators

Indicator **1**: Consumption of antibacterials for systemic use (J01) expressed in DDD per 1000 inhabitants per day (DID) **[J01_DID]**

Indicator **2**: Consumption of tetracyclines (J01A) expressed in DDD per 1000 inhabitants per day (DID) **[J01A_DID]**

Indicator **3**: Consumption of penicillins (J01C) expressed in DDD per 1000 inhabitants per day (DID) **[J01C_DID]**

Indicator **4**: Consumption of cephalosporins (J01D) expressed in DDD per 1000 inhabitants per day (DID) **[J01D_DID]**

Indicator **5**: Consumption of sulfonamides and trimethoprim (J01E) expressed in DDD per 1000 inhabitants per day (DID) **[J01E_DID]**

Indicator **6**: Consumption of MLS, i.e. macrolides, lincosamides and streptogramins (J01F) expressed in DDD per 1000 inhabitants per day (DID) **[J01F_DID]**

Indicator **7**: Consumption of quinolones (J01M) expressed in DDD per 1000 inhabitants per day (DID) **[J01M_DID]**

Indicator **8**: Consumption of tetracycline (J01A) expressed as percentage of the total antibiotic consumption (J01) **[J01A_%]**

Indicator **9**: Consumption of penicillins (J01C) expressed as percentage of the total antibiotic consumption (J01) **[J01C_%]**

Indicator **10**: Consumption of cephalosporins (J01D) expressed as percentage of the total antibiotic consumption (J01) **[J01D_%]**

Indicator **11**: Consumption of sulfonamides and trimethoprim (J01E) expressed as percentage of the total antibiotic consumption (J01) **[J01E_%]**

Indicator **12**: Consumption of MLS, i.e. macrolides, lincosamides and streptogramins(J01F) expressed as percentage of the total antibiotic consumption (J01) **[J01F_%]**

Indicator **13**: Consumption of quinolones (J01M) expressed as percentage of the total antibiotic consumption (J01) **[J01M_%]**

Indicator **14**: Consumption of β-lactamase sensitive penicillins (J01CE) expressed as percentage of the total antibiotic consumption (J01) **[J01CE_%]**

Indicator **15**: Consumption of combinations of penicillins, including β-lactamase inhibitor (J01CR) expressed as percentage of the total antibiotic consumption (J01) **[J01CR_%]**

Indicator **16**: Consumption of 3rd and 4th generation of cephalosporins {J01(DD+DE)} expressed as percentage of the total antibiotic consumption (J01) **[J01DD+DE_%]**

Indicator **17**: Ratio of the consumption of narrow spectrum {J01(CE+DB+FA01)} to the consumption of broad spectrum penicillins, cephalosporins and macrolides {J01(CR+DC+DD+(F-FA01))} **[J01_N/B]**

Indicator **18**: Consumption of fluoroquinolones (J01MA) expressed as percentage of the total antibiotic consumption (J01) **[J01MA_%]**

Indicator **19**: Seasonal variation of the total antibiotic consumption (J01) **[J01_SV]**

Indicator **20**: Seasonal variation of quinolone consumption (J01M) **[J01M_SV]**

Indicator **21**: Index of seasonal variation of quinolone consumption (J01M) taking into account their use in DDD per 1000 inhabitants per day (DID) **[J01M_SVDID]**

Indicator **22**: Index of longitudinal trends of antibiotic consumption **[J01_TT]**

Structural indicators

Indicator **23**: Diversity of the therapeutic arsenal of antibacterials for systemic use (J01) **[J01_DU99]**

Indicator **24**: Number of items recorded in the national register of available antibacterials for systemic use (J01) **[J01_NR]**

ESAC European Surveillance of Antimicrobial Consumption

Indicator 1: Consumption of antibacterials for systemic use (J01) expressed in DDD per 1000 inhabitants per day (DID) [J01_DID]

Definition

Consumption of antibacterials for systemic use (J01) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Antibiotics allow treatment of serious bacterial infections. The largest volume of antibiotics is prescribed in ambulatory care. This use is increasingly recognized as the major selective pressure driving resistance, which in turn makes them ineffective. Therefore antibiotics should be used appropriately, i.e. (no) antibiotics for those who will (not) benefit from the treatment. In addition, unnecessary use of antibiotics requires more resources, motivates patients to reconsult and exposes them to the additional risk of side effects, whereas underprescribing could be associated with higher risk of complications of untreated infections.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01)} \times 1000}{\text{Denominator: Population at risk} \times \text{Days in data collection period}}$$

Benchmark and recommended action

One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

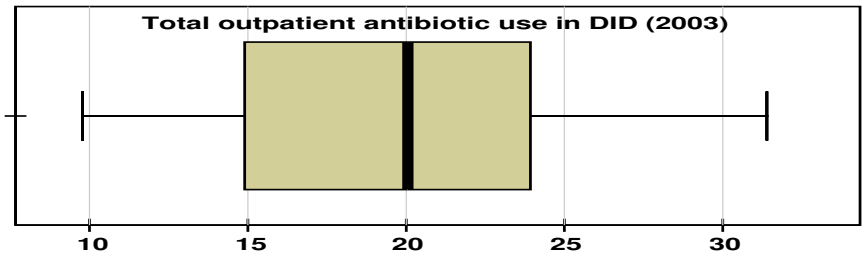
Limitations

DDDs, currently representing the best measure to quantify exposure to antibiotics use on a national level, have some general limitations and ideally should be complemented by alternative measures, if available.

Because of different coverage of different data sources, the population at risk varies between countries.

Some antimicrobial drugs, for example combinations for *Helicobacter pylori* eradication, are classified outside J01.

ESAC boxplot



Indicator 2: Consumption of tetracyclines (J01A) expressed in DDD per 1000 inhabitants per day (DID) [J01A_DID]

Definition

Consumption of tetracyclines (J01A) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Tetracyclines represent long-established and inexpensive antibiotics with a broad range of indications in ambulatory care. However, in most cases they are not the first line therapy. In addition, their use is associated with resistance and side effects.

Therefore they should be used only for those who will benefit from the treatment, taking into account the availability of alternative narrow spectrum antibiotics.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01A)} \times 1000}{\text{Population at risk} \times \text{Days in data collection period}} \quad \text{Denominator:}$$

Benchmark and recommended action

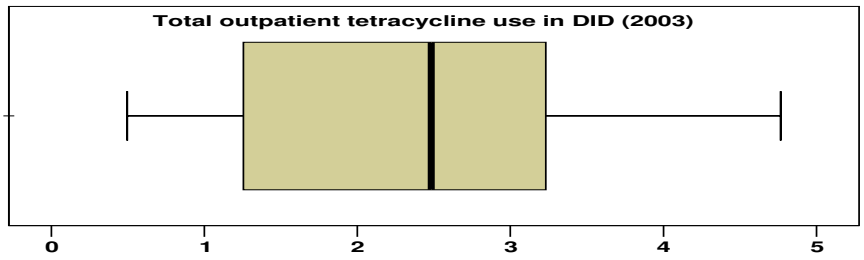
One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Limitations

DDD, currently representing the best measure to quantify exposure to antibiotics use on a national level, also have some limitations (see GENERAL).

This indicator can be considered to be rather a quantitative than a qualitative indicator, and should be interpreted in connection with use of other antibiotic classes.

ESAC boxplot



Indicator 3: Consumption of penicillins (J01C) expressed in DDD per 1000 inhabitants per day (DID) [J01C_DID]

Definition

Consumption of penicillins (J01C) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Penicillins represent the most frequently prescribed antibiotic class in all European countries and their use is associated with development of resistance. Nevertheless, they are the first line therapy for many indications in ambulatory care, and their use can limit the use of other antibiotic classes. As for total antibiotic use, inappropriate use of penicillins requires more resources, motivates patients to reconsult, exposes them to the additional risk of side effects or could be associated with higher risk of complications of untreated infections.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01C) x 1000}}{\text{Population at risk x Days in data collection period}} \text{ :Denominator}$$

Benchmark and recommended action

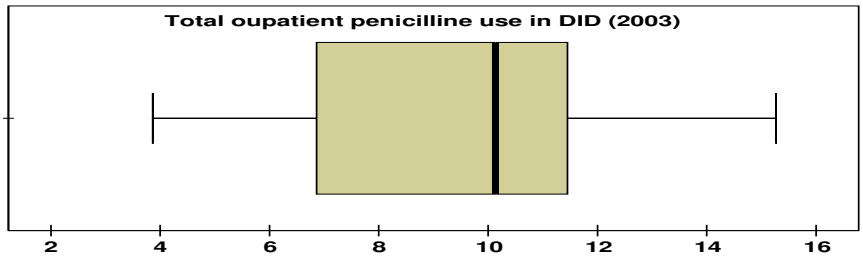
One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

DDD, currently representing the best measure to quantify exposure to antibiotics use on a national level, also have some limitations (see GENERAL).

J01C class consists of five subclasses with different characteristics. Therefore, this indicator should be considered to be rather a quantitative than a qualitative indicator, and interpreted in connection with relevant proportional indicators (J01C_%, J01CE_% and J01CR_%).

ESAC boxplot



Indicator 4: Consumption of cephalosporins (J01D) expressed in DDD per 1000 inhabitants per day (DID) [J01D_DID]

Definition

Consumption of cephalosporins (J01C) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Cephalosporins represent the first line therapy in a limited amount of indications in ambulatory care. Excessive use of cephalosporins is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01D)} \times 1000}{\text{Population at risk} \times \text{Days in data collection period}} \quad \text{Denominator:}$$

Benchmark and recommended action

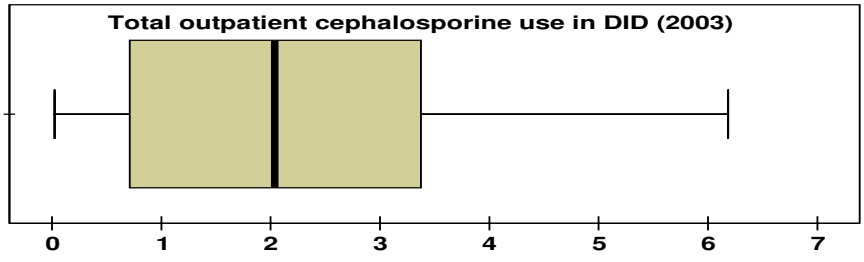
Individual countries should define their own range of acceptable use considering the limited indications of cephalosporins. One benchmark on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. If the use is above the upper limit of the adequate range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

DDD, currently representing the best measure to quantify exposure to antibiotics use on a national level, also have some limitations (see GENERAL).

J01D class consists of four generations with different characteristics, and should be interpreted in connection with relevant proportional indicators (J01DD+DE_%).

ESAC boxplot



Indicator 5: Consumption of sulfonamides and trimethoprim (J01E) expressed in DDD per 1000 inhabitants per day (DID) [J01E_DID]

Definition

Consumption of sulfonamides and trimethoprim (J01E) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Sulfonamides and trimethoprim represent long-established and inexpensive antibacterial agents. They represent the first line therapy for some indications, but their use is associated with resistance and side effects.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01E) x 1000}}{\text{Population at risk x Days in data collection period}} \text{ :Denominator}$$

Benchmark and recommended action

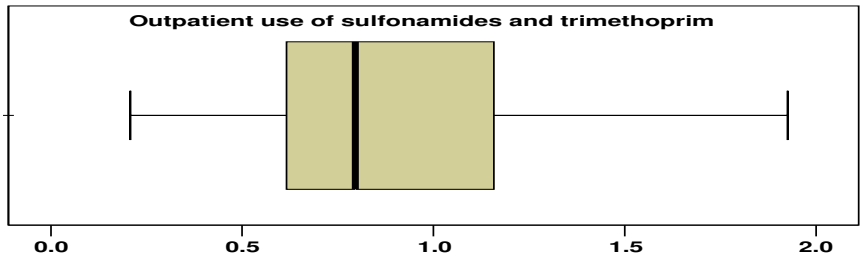
One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Limitations

DDD, currently representing the best measure to quantify exposure to antibiotics use on a national level, also have some limitations (see GENERAL).

This indicator can be considered to be rather a quantitative than a qualitative indicator, and should be interpreted in connection with use of other antibiotic classes.

ESAC boxplot



Indicator 6: Consumption of MLS, i.e. macrolides, lincosamides and streptogramins (J01F) expressed in DDD per 1000 inhabitants per day (DID) [J01F_DID]

Definition

Consumption of MLS (J01F) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Generally MLS are not recommended as first choice antibiotic therapy in ambulatory care, but provide a valuable alternative for penicillins in case of IgE mediated penicillin allergy. In addition, in many European countries alarming levels of macrolide resistance in *Streptococcus pneumoniae* have been observed. Therefore the newer macrolides should be reserved as second line antibiotics. Use of erythromycin could indicate conservative and cost conscious use, but comparing to alternative narrow spectrum antibiotics erythromycin has more side effects.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01F)} \times 1000}{\text{Denominator: Population at risk} \times \text{Days in data collection period}}$$

Benchmark and recommended action

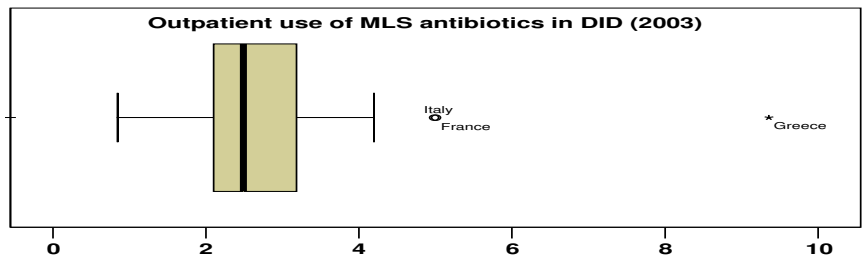
Individual countries should define their own range of acceptable use considering the limited indications of MLS. One benchmark on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. If the use is above the upper limit of the adequate range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

DDD, currently representing the best measure to quantify exposure to antibiotics use on a national level, also have some limitations (see GENERAL).

J01F class consists of three different antibiotic classes from which predominantly macrolides are used in ambulatory care. Macrolides themselves could be further subdivided according to their chemical or clinical characteristics, but this is not reflected in the ATC classification.

ESAC boxplot



Indicator 7: Consumption of quinolones (J01M) expressed in DDD per 1000 inhabitants per day (DID) [J01M_DID]

Definition

Consumption of quinolones (J01M) expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Quinolones do not represent the first line therapy for most indications in ambulatory care, particularly not for respiratory tract infections. As quinolone use should be restricted and mainly reserved for well-defined indications, considerable use can indicate non-adherence to recommended drug choice. Excessive use of quinolones is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01M)} \times 1000}{\text{Population at risk} \times \text{Days in data collection period}} \quad \text{Denominator:}$$

Benchmark and recommended action

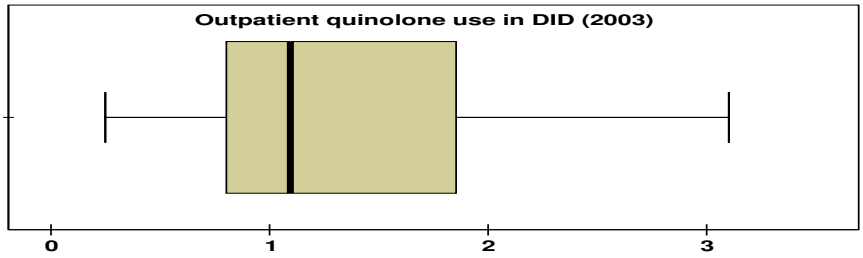
Individual countries should define their own range of acceptable use considering the limited indications of quinolones. One benchmark on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. If the use is above the upper limit of the adequate range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

DDD, currently representing the best measure to quantify exposure to antibiotics use on a national level, also have some limitations (see GENERAL).

J01M class consists of older quinolones and fluoroquinolones, which have different characteristics. Fluoroquinolones themselves could be further subdivided according to their spectrum of activity against *Streptococcus pneumoniae*, what is not reflected in the ATC classification.

ESAC boxplot



Indicator 8: Consumption of tetracycline (J01A) expressed as percentage of the total antibiotic consumption (J01) [J01A_%]

Definition

Consumption of tetracyclines (J01A) in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of tetracyclines on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Tetracyclines represent long-established and inexpensive antibiotics with a broad range of indications in ambulatory care. However, in most cases they are not the first line therapy. In addition, their use is associated with resistance and side effects.
Therefore they should be used only for those who will benefit from the treatment, taking into account of the availability of alternative narrow spectrum antibiotics.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01A)} \times 100}{\text{DDD (J01)}} \text{ \%}$$

Denominator:

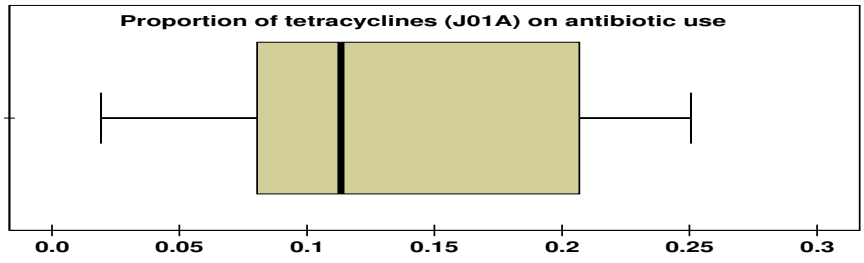
Benchmark and recommended action

One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID and use of other antibiotic classes.

ESAC boxplot



Indicator 9: Consumption of penicillins (J01C) expressed as percentage of the total antibiotic consumption (J01) [J01C_%]

Definition

Consumption of penicillins (J01C) in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of penicillins on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Penicillins represent the most frequently prescribed antibiotic class in all European countries and their use is associated with development of resistance. Nevertheless, they are the first line therapy for many indications in ambulatory care, and their use can limit the use of other antibiotic classes. As for total antibiotic use, inappropriate use of penicillins requires more resources, motivates patients to reconsult, exposes them to the additional risk of side effects or could be associated with higher risk of complications of untreated infections.

Calculation formula:

$$\text{Numerator: } \frac{\text{DDD (J01C)} \times 100}{\text{DDD (J01)}} \text{ \%}$$

Denominator:

Benchmark and recommended action

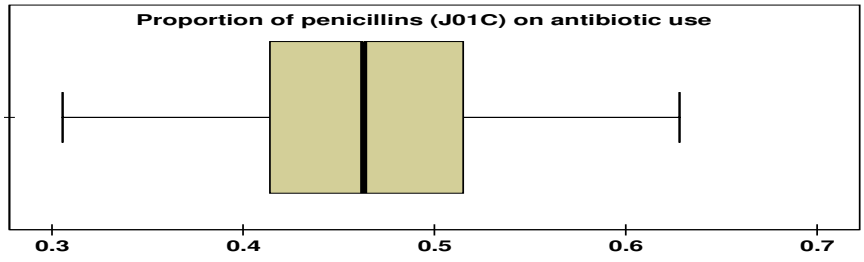
One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID.

J01C class consists of five subclasses with different characteristics. Therefore, this indicator should be considered together with more specific proportional indicators (J01CE& and J01CR%).

ESAC boxplot



Indicator 10: Consumption of cephalosporins (J01D) expressed as percentage of the total antibiotic consumption (J01) [J01D_%]

Definition

Consumption of cephalosporins (J01D) in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of cephalosporins on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Cephalosporins represent the first line therapy in a limited amount of indications in ambulatory care. Excessive use of cephalosporins is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects.

Calculation formula:

$$\frac{\text{DDD (J01D)} \times 100}{\text{DDD (J01)}} \quad \%$$

Benchmark and recommended action

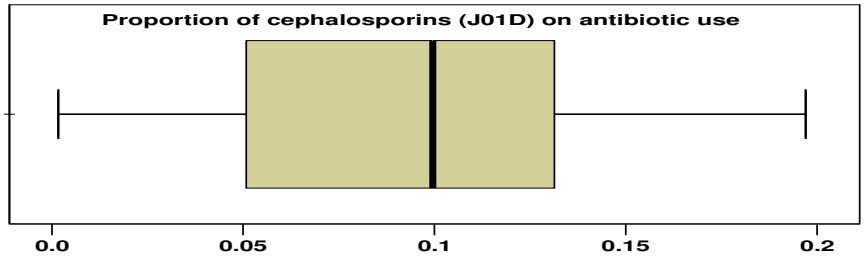
Individual countries should define their own range of acceptable use considering the limited indications of cephalosporins. One benchmark on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. If the use is above the upper limit of the adequate range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID.

J01D class consists of four generations with different characteristics and should be interpreted in connection with more specific proportional indicators (J01DD+DE_%).

ESAC boxplot



Indicator 11: Consumption of sulfonamides and trimethoprim (J01E) expressed as percentage of the total antibiotic consumption (J01) [J01E_%]

Definition

Consumption of sulfonamides and trimethoprim (J01E) consumption in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of sulfonamides and trimethoprim on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Sulfonamides and trimethoprim represent long-established and inexpensive antibacterial agents. They represent the first line therapy for some indications, but their use is associated with resistance and side effects.

Calculation formula:

$$\frac{\text{DDD (J01E)} \times 100}{\text{DDD (J01)}} \quad \%$$

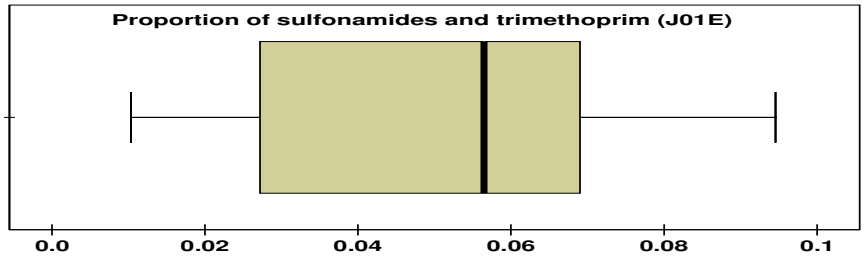
Benchmark and recommended action

One benchmark value on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. We suggest individual countries to position themselves and to define their own benchmark, based on the epidemiology of infectious diseases and national guidelines. A range of acceptable use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID and use of other antibiotic classes.

ESAC boxplot



Indicator 12: Consumption of MLS, i.e. macrolides, lincosamides and streptogramins(J01F) expressed as percentage of the total antibiotic consumption (J01) [J01F_%]

Definition

Consumption of MLS (J01F) in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of penicillins on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Generally MLS are not recommended as first choice antibiotic therapy in ambulatory care, but provide a valuable alternative for penicillins in case of IgE mediated penicillin allergy. In addition, in many European countries alarming levels of macrolide resistance in *Streptococcus pneumoniae* have been observed. Therefore the newer macrolides should be reserved as second line antibiotics. Use of erythromycin could indicate conservative and cost conscious use, but comparing to alternative narrow spectrum antibiotics erythromycin has more side effects.

Calculation formula:

$$\frac{\text{DDD (J01F)} \times 100}{\text{DDD (J01)}} \quad \%$$

Benchmark and recommended action

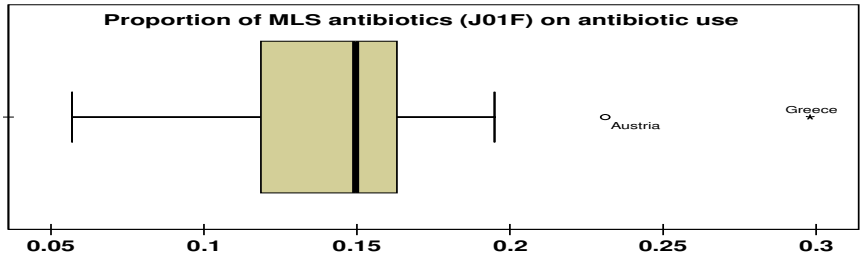
Individual countries should define their own range of acceptable use considering the limited indications of MLS. One benchmark on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. If the use is above the upper limit of the adequate range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID.

J01F class consists of three different antibiotic classes from which predominantly macrolides are used in ambulatory care. Macrolides themselves could be further subdivided according to their chemical or clinical characteristics, but this is not reflected in the ATC classification.

ESAC boxplot



Indicator 13: Consumption of quinolones (J01M) expressed as percentage of the total antibiotic consumption (J01) [J01M_%]

Definition

Consumption of quinolones (J01M) in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of quinolones on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Quinolones do not represent the first line therapy for most indications in ambulatory care, particularly not for respiratory tract infections. As quinolone use should be restricted and mainly reserved for well-defined indications, considerable use can indicate non-adherence to recommended drug choice. Excessive use of quinolones is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects.

Calculation formula:

$$\frac{\text{DDD (J01M)} \times 100}{\text{DDD (J01)}} \quad \%$$

Benchmark and recommended action

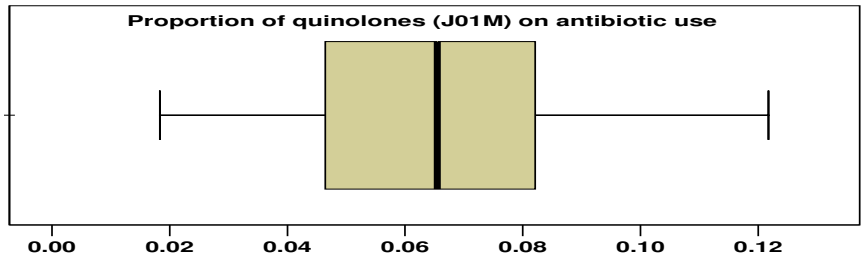
Individual countries should define their own range of acceptable use considering the limited indications of quinolones. One benchmark on European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. If the use is above the upper limit of the adequate range, more detailed assessment of the use pattern is recommended in order to define the action required and the proper target.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID.

J01M class consists of older quinolones and fluoroquinolones, which have different characteristics. Fluoroquinolones themselves could be further subdivided according to their spectrum of activity against *Streptococcus pneumoniae*, what is not reflected in the ATC classification.

ESAC boxplot



Indicator 14: Consumption of β-lactamase sensitive penicillins (J01CE) expressed as percentage of the total antibiotic consumption (J01) [J01CE_%]

Definition

Consumption of β-lactamase sensitive penicillins (J01CE), i.e. narrow spectrum penicillins in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of narrow spectrum penicillins on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Penicillins represent the first line therapy for many indications in ambulatory care, and their use can limit the use of other antibiotic classes. The use of narrow spectrum penicillins allows treatment of infections caused by susceptible bacterial strains without excessive elimination of normal flora and thus lowers the selection pressure for resistance. Available literature suggests that high use of narrow spectrum penicillins is correlated with low levels of *Streptococcus pneumoniae* resistance.

Inexpensive narrow spectrum penicillins are also associated with less side effects and considered more cost effective than broad spectrum penicillins. In addition, the consumption level of these traditional antibiotics reflects the conservativeness of the national antibiotic policy.

Calculation formula:

$$\frac{\text{DDD (J01CE)} \times 100}{\text{DDD (J01)}} \quad \%$$

Benchmark and recommended action

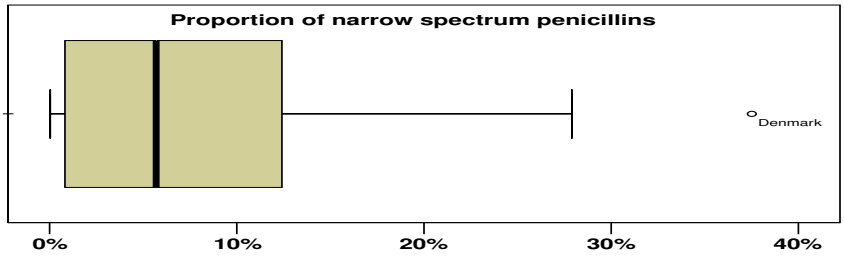
Considering the favorable characteristics of narrow spectrum penicillins, their use is expected to be high. Individual countries should define their own range of acceptable use based on evidence-based national guidelines, demographical characteristics and epidemiological data, including resistance patterns. If the use is below the lower limit of the adequate range, actions to increase use of narrow spectrum penicillins should be considered and a proper target defined.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic (J01) and penicillin (J01C) use expressed in DID.

In some countries the use of narrow spectrum penicillins can be limited by their availability and existing resistance level.

ESAC boxplot



Indicator 15: Consumption of combinations of penicillins, including β-lactamase inhibitor (J01CR) expressed as percentage of the total antibiotic consumption (J01)

[J01CR_%]

Definition

Consumption of combinations of penicillins, including β-lactamase inhibitor (J01CR), i.e. combinations of penicillins with β-lactamase inhibitor in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of combinations of penicillins, including β-lactamase inhibitor on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Unlike broad spectrum penicillins, their combinations with β-lactamase inhibitor are effective in the treatment of infections caused by β-lactamase producing strains. This therapeutic advantage is counterbalanced by the increased risk of side effects and the higher cost. Therefore, they represent the first line therapy in only a limited amount of indications in ambulatory care. In addition excessive use of combinations of penicillins with β-lactamase inhibitor is associated with development of resistance.

Calculation formula:

$$\frac{\text{DDD (J01CR)} \times 100}{\text{DDD (J01)}} \quad \%$$

Numerator: DDD (J01CR) x 100

Denominator: DDD (J01)

Benchmark and recommended action

Individual countries should define their own range of acceptable use considering the limited number of indications where combinations of penicillins with β-lactamase inhibitor represent the first line antibiotic. Individual countries should define their own range of acceptable use based on evidence-based national guidelines, demographical characteristics and epidemiological data, including resistance patterns.

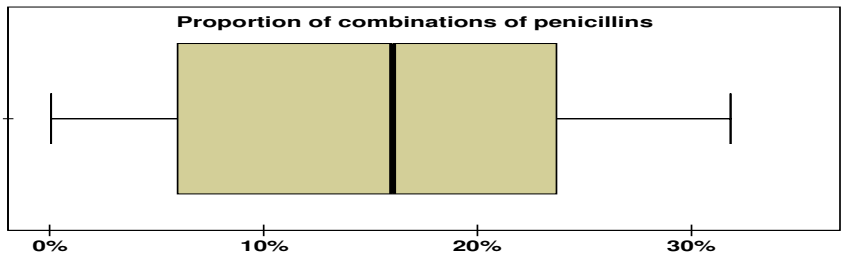
If the use is above the upper limit of the adequate range, actions to decrease use of combinations of penicillins with β-lactamase inhibitor should be considered and a proper target defined.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic (J01) and penicillin (J01C) use expressed in DID.

As dosage varies between countries, additional outcome measures to DDD should be considered to interpret this indicator.

ESAC boxplot



Indicator 16: Consumption of 3rd and 4th generation of cephalosporins {J01(DD+DE)} expressed as percentage of the total antibiotic consumption (J01)

[J01DD+DE_%]

Definition

Consumption of the 3rd and 4th generation of cephalosporins {J01(DD+J01DE)} in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of these cephalosporins on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Cephalosporins represent the first line therapy in a limited amount of indications in ambulatory care. Excessive use of cephalosporins is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects.

Unlike the 1st and the 2nd generation of cephalosporins, the 3rd and 4th generation of cephalosporins are considered to be primarily hospital antibiotics, which should normally not be used in ambulatory care. The use of the 3rd and 4th generation of cephalosporins should be reserved for justified hospital use, as their use in ambulatory care is associated with foreseeable emergence of resistance.

Calculation formula:

$$\frac{\text{DDD } \{J01(DD+DE)\} \times 100}{\text{DDD } (J01)} \quad \%$$

Benchmark and recommended action

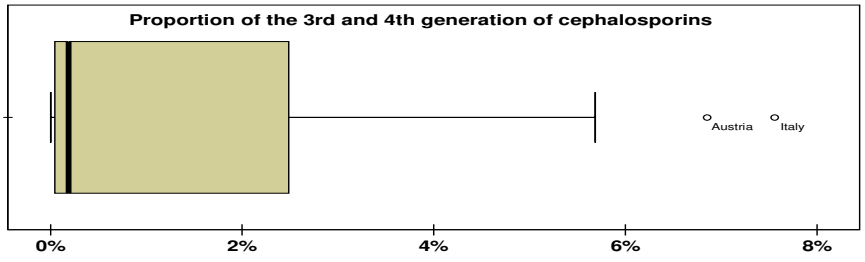
Since the 3rd and 4th generation of cephalosporins should be reserved for hospital use, their use in ambulatory care is expected to be negligible.

Actions to restrict the use of 3rd and 4th generation of cephalosporins should be considered, if it is substantial.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic (J01) and cephalosporin (J01D) use expressed in DID.

ESAC boxplot



Indicator 17: Ratio of the consumption of broad spectrum penicillins, cephalosporins and macrolides {J01(CR+DC+DD+(F-FA01))} to the consumption of narrow spectrum {J01(CE+DB+FA01)} [J01_B/N]

Definition

The ratio of the consumption of broad spectrum penicillins, cephalosporins and macrolides {J01(CR+DC+DD+(F-FA01))} to the consumption of narrow spectrum {J01(CE+DB+FA01)} gives an estimate of the balance between the use of broad spectrum versus narrow spectrum antibiotics. This ratio allows comparing patterns of antibiotic use between different areas and time periods.

Public health objective

β-lactamase sensitive penicillins, first generation cephalosporins and erythromycine represent commonly used narrow spectrum antibiotics. In contrast to combinations of penicillins with β-lactamase inhibitor, second and third generation cephalosporins and newer macrolides, their use allows treatment of infections caused by susceptible bacterial strains without excessive elimination of normal flora and thus lowers the selection pressure for resistance. Furthermore the latter antibiotics represent the first line therapy in only a limited amount of indications in ambulatory care.

Calculation formula:

$$\frac{\text{DDD } \{J01(CR+DC+DD+(F\text{-}FA01))\}}{\text{DDD } \{J01(CE+DB+FA01)\}}$$

Benchmark and recommended action

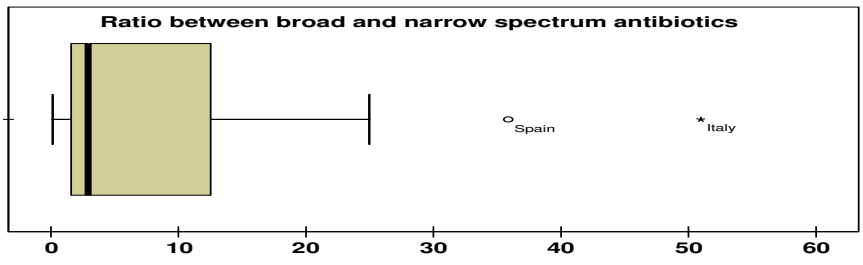
Individual countries should define their own range of acceptable ratios between broad and narrow spectrum antibiotics considering the limited number of indications where combinations of penicillins with β-lactamase inhibitor, second and third generation cephalosporins and newer macrolides represent the first line antibiotic.

If the indicator value is above the upper limit of the adequate range, actions to optimise the balance between narrow and broad spectrum antibiotics should be considered and a proper target defined.

Limitations

This indicator should be interpreted in connection with total antibiotic (J01) and the use of the respective antibiotic classes. Since this indicators based on a ratio, their use both in the numerator and the denominator should be assessed.

ESAC boxplot



Indicator 18: Consumption of fluoroquinolones (J01MA) expressed as percentage of the total antibiotic consumption (J01) [J01MA_%]

Definition

Consumption of fluoroquinolones (J01MA) in DDD per 1000 inhabitants per day (DID) expressed as percentage of the total antibiotic use (J01) in DID gives an estimate of the proportion of fluoroquinolones on total antibiotic use, which allows to compare patterns of antibiotic use between different areas and time periods.

Public health objective

Compared to the other quinolones, fluoroquinolones have an enhanced spectrum of activity allowing their use against respiratory pathogens. Nevertheless, they do not represent the first line therapy for respiratory tract infections in ambulatory care. Furthermore, as fluoroquinolone use should be restricted and mainly reserved for well-defined indications, considerable use can indicate non-adherence to recommended drug choice. Excessive use of fluoroquinolones is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects.

Calculation formula:

$$\frac{\text{DDD (J01MA)} \times 100}{\text{DDD (J01)}} \ \%$$

Benchmark and recommended action

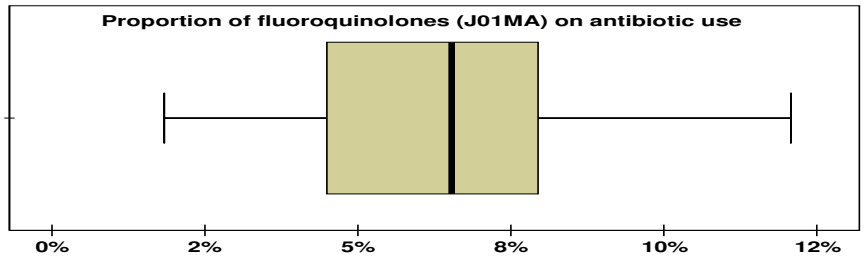
Individual countries should define their own range of acceptable use considering the limited number of indications where fluoroquinolones represent the first line antibiotic. Individual countries should define their own range of acceptable use based on evidence-based national guidelines, demographical characteristics and epidemiological data, including resistance patterns. If the use is above the upper limit of the adequate range, actions to decrease use of fluoroquinolones should be considered and a proper target defined.

Limitations

This proportional indicator should be interpreted in connection with total antibiotic use expressed in DID.

Fluoroquinolones could be further subdivided according to their spectrum of activity against *Streptococcus pneumoniae*, what is not reflected in the ATC classification.

ESAC boxplot



Indicator 19: Seasonal variation of the total antibiotic consumption (J01) [J01_SV]

Definition

Seasonal variation of the total antibiotic consumption (J01) is described by the increase in antibiotic use during the two winter quarters (i.e. October-March) relative to the use during the two summer quarters (i.e. April-September) expressed as a percentage (see calculation formula).

Public health objective

Winter months are characterized by an increased incidence of respiratory tract infections, which is resulting in higher prescriptions rates for antibiotics during this period. Nevertheless, as the vast majority of respiratory tract infections is of viral origin and self-limiting, the increase of antibiotic consumption in winter months should be finite. Excessive winter consumption of antibiotics suggests their inappropriate prescribing for respiratory tract infections, such as the common cold, flu and bronchitis.

Calculation formula:

$$\left(\frac{\text{DDD (J01 in October-March)}}{\text{DDD (J01 in April-September)}} - 1 \right) \times 100 \quad \%$$

The quarters covering 2 winter seasons are used for calculation of the indicator value (see diagram 1).

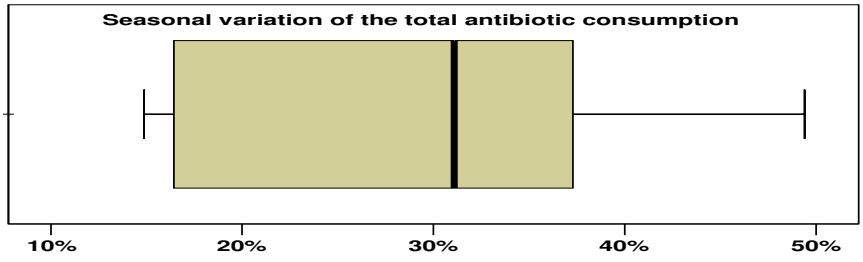
Benchmark and recommended action

Individual countries should define their own range for acceptable seasonal variation based on evidence-based national guidelines, demographical characteristics and epidemiological data. If the seasonal variation is above the upper limit of the adequate range, actions to decrease seasonal variation should be considered and a proper target defined.

Limitations

Calculation of this indicator is limited by the availability of quarterly data on antibiotic use.
This indicator should be interpreted in connection with total antibiotic use expressed in DID. Since seasonal variation is influenced both by antibiotic use during the two winter quarters and the use during the two summer quarters, the latter use should also be taken into account for the interpretation of this indicator.

ESAC boxplot



Definition

Seasonal variation of quinolone consumption (J01M) is described by the increase in quinolone use during the two winter quarters (i.e. October-March) relative to the use during the two summer quarters (i.e. April-September) expressed as a percentage (see calculation formula).

Public health objective

Winter months are characterized by an increased incidence of respiratory tract infections, which is reflected in higher prescriptions rates for antibiotics. Since quinolones are not the antibiotics of choice for the treatment of respiratory tract infections in ambulatory care, the increase of antibiotic consumption in winter months should not be observed.

As excessive quinolone use for treatment of respiratory tract infections is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects, this use should be restricted for well-defined indications and mainly reserved for hospital use.

Calculation formula:

$$\left(\frac{\text{DDD (J01M in October-March)}}{\text{DDD (J01M in April-September)}} - 1 \right) \times 100 \quad \%$$

The quarters covering 2 winter seasons are used for calculation of the indicator value (see diagram 1).

Benchmark and recommended action

Since quinolones are not the antibiotics of choice for the treatment of respiratory tract infections in ambulatory care, seasonal variation of quinolones should not be observed.

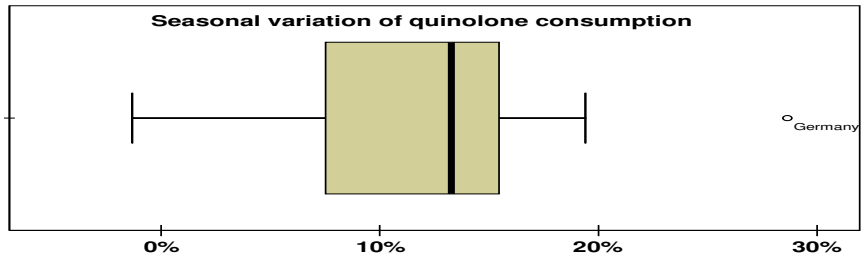
Actions to restrict seasonal variation of quinolones should be considered, if it is substantial.

Limitations

Calculation of this indicator is limited by the availability of quarterly data on antibiotic use. This indicator can reveal negative values as well, specifically in countries with summer peaks of use.

This indicator should be interpreted in connection with total antibiotic use expressed in DID, as in countries with very low levels of quinolone use the calculation can be biased.

ESAC boxplot



Indicator 21: Index of seasonal variation of quinolone consumption (J01M) taking into account their use in DDD per 1000 inhabitants per day (DID) [J01M_SVDID]

Definition

The index of seasonal variation of consumption of quinolones (J01M) taking into account their use in DDD per 1000 inhabitants per day (DID) describes the pattern of quinolone use in a complex way (see calculation formula). This allows to adjust for the level of quinolone use in the country, limiting the interpretation of the indicator of "Seasonal variation of quinolone consumption (J01M)".

Seasonal variation of quinolone consumption (J01M) is described by the increase in quinolone use during the two winter quarters (i.e. October-March) relative to the use during the two summer quarters (i.e. April-September) expressed as a percentage. Consumption of quinolones (J01M) is expressed in DDD per 1000 inhabitants per day (DID) gives an estimate of their utilisation in a given area and period, which allows to compare antibiotic use between areas with different number of population.

Public health objective

Winter months are characterized by an increased incidence of respiratory tract infections, which is reflected in higher prescriptions rates for antibiotics. Since quinolones are not the antibiotics of choice for the treatment of respiratory tract infections in ambulatory care, the increase of antibiotic consumption in winter months should not be observed.

As excessive quinolone use for treatment of respiratory tract infections is associated with development of resistance, requires more resources and exposes patients to the additional risk of side effects, this use should be restricted for well-defined indications and mainly reserved for hospital use.

Calculation formula:

$$\text{Numerator: DDD (J01M in October-March)} \quad \left(\frac{\text{DDD (J01M in October-March)}}{\text{DDD (J01M in April-September)}} - 1\right) \times \left(\frac{\text{DDD J01M} \times 1000}{\text{Population at risk} \times \text{days in data collection period}}\right) \times 100$$

Denominator: DDD (J01M in April-September) Population at risk x days in data collection period

The quarters covering 2 preceding winter seasons are used for calculation of the indicator value (see diagram 1).

Benchmark and recommended action

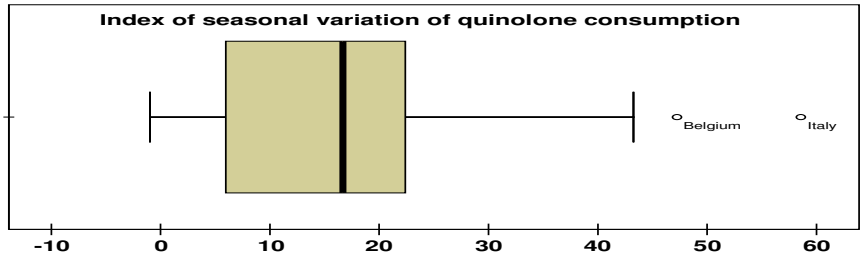
Since quinolones are not the antibiotics of choice for the treatment of respiratory tract infections in ambulatory care, seasonal variation of quinolones should not be observed. Therefore the first factor of the formula should be close to zero and consequently the index value should be close to zero too. Actions to restrict seasonal variation of quinolones should be considered, if this is not the case (see boxplot).

Limitations

Calculation of this indicator is limited by the availability of quarterly data on antibiotic use. This indicator can reveal negative values as well, specifically in countries with the summer peaks of use.

This index' value has no concrete meaning, but allows ranking countries based on their seasonal variation of quinolones consumption taking into account their total use.

ESAC boxplot



Indicator 22: Index of longitudinal trends of antibiotic consumption [J01_TT]

Definition

The index of longitudinal trends of antibiotic consumption describes the evolution of national antibiotic consumption in a defined period (see calculation formula). Antibiotic consumption is expressed in DDD per 1000 inhabitants per day.

Public health objective

The median level of antibiotic consumption in Europe remains relatively stable, but consumption in individual countries can show particular trends. These are in nature determined by changes in incidence of infectious diseases, but introduction of new medicines, dosage adjustments, national campaigns, threshold to consult and other structural factors can influence evolution of antibiotic consumption at national level.

This indicator allows one to identify significant increases or decreases of consumption, for which consequently the relevance needs to be assessed taking into account the epidemiological trends.

Calculation formula:

The index for a certain year is given by the coefficient for the slope of the linear regression analysis (95% CI) of 9 data points, representing the average use of each set of four consecutive quarters within the last 3 years (equivalent to the use in the last 12 months - see diagram 1). Quarterly use data are standardised by the average use over the same period.

Benchmark and recommended action

If statistically significant increase or decrease of national antibiotic consumption is identified and cannot be explained by observed epidemiological trends, more detailed analysis, comprising the assessment of the whole indicator set over the last 3 years, should be initiated to spot the origin of this evolution. For indicators accountable for the detected trend relevant recommendations for the respective antibiotic classes should be followed.

Limitations

Calculation of this indicator is limited by the availability of quarterly data on antibiotic use. To assess trend over time, countries not able to provide quarterly data should plot their consumption data for all available years, not just compare any two years, since these can be biased by occasional epidemics of infectious diseases. For countries able to provide quarterly data, seasonality is smoothened by using moving average of use in 4 consecutive quarters to calculate each individual point for the linear regression. As a consequence these points are highly correlated.

As trends of antibiotic use are not necessarily linear over longer period, the observation periods of 3 consecutive years is suggested. In addition this enhances sensitivity of the indicator to spot the most recent trend.

If the index is not statistically significant, still increase or decrease of antibiotic consumption of subclasses is possible. Therefore, we recommend that a more detailed analysis of the whole indicator set should be performed prior to any interpretation of this indicator. In any case this index should be interpreted together with the absolute level of antibiotic consumption in the country and trends in preceding years.

ESAC boxplot

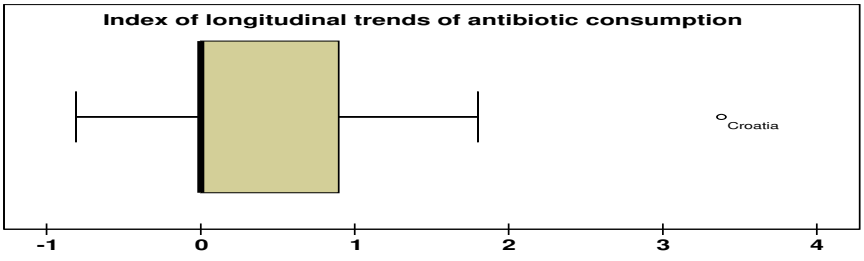
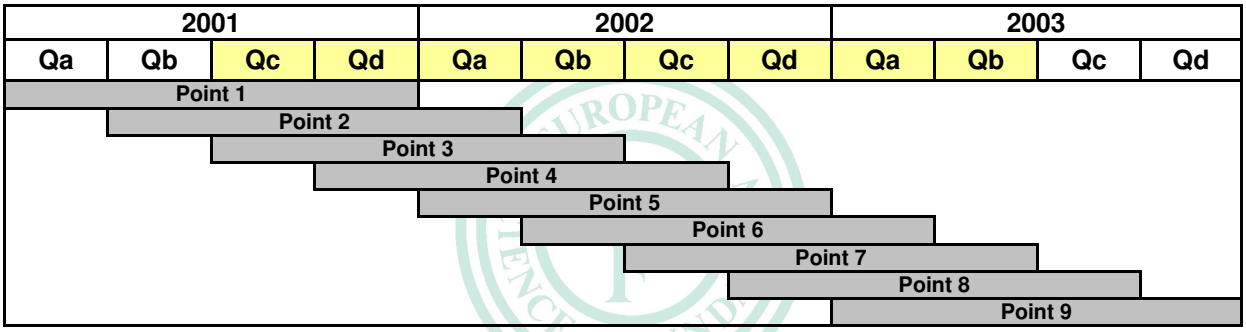


Diagram 1 supporting interpretation of the calculation formula for indicators 19-22

Indicators 19-21 on seasonal variation of the antibiotic consumption are calculated from the 2 preceding winter seasons, if available (these quarters used are marked in yellow) If not, we accepted quarterly data covering the latest 2 available calendar years to calculate the indicator value for 2003

Indicator 22 on longitudinal trends of antibiotic consumption is calculated from quarterly data covering 3 consecutive years. For calculation of the indicator value for 2003, 9 data points (marked in grey) were used. They represent the average use of each set of four consecutive quarters within the last 3 years.



Structural indicators

Indicator 23: Diversity of the therapeutic arsenal of antibacterials for systemic use (J01) [J01_DU99]

Definition

The diversity of the therapeutic arsenal of antibacterials for systemic use (J01) gives the number of different antibiotic substances routinely used in the country.

Public health objective

As only a limited number of antibiotics can be considered as the first line therapy for common infectious diseases, majority of the national antibiotic consumption should result from the use of a relatively narrow range of substances. This indicator may give a rough estimate of the adherence to guidelines in a straightforward way using administrative data.

Calculation formula:

Antibiotic substances are ranked by their consumption expressed in defined daily doses (DDD) and the number of drugs accounting for the cumulative percentage of 99% of the total consumption is determined.

Benchmark and recommended action

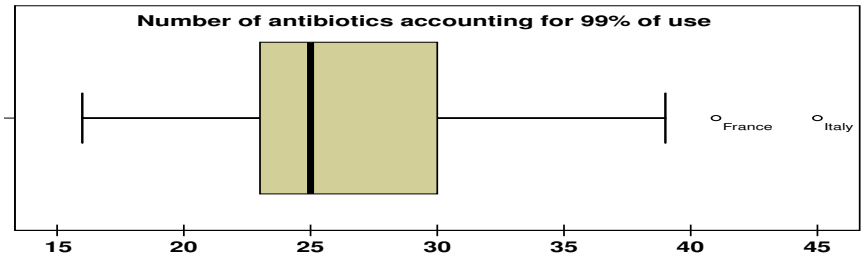
This indicator should be considered as a structural indicator rather than a prescribing indicator. One benchmark value on European level cannot be given. We suggest individual countries to position themselves and to define their own benchmark, based on the national guidelines. If the number of substances is outside the acceptable the range, more detailed assessment of the pattern of antibiotic consumption is recommended in order to define the action required.

Limitations

The threshold level of 99% has been chosen arbitrarily as a compromise between 90%, often referred in the literature as "Drug Utilisation 90%" method, and the total number of substances for which any is observed in the country.

This indicator does not differentiate between use of different substances within one (appropriate) antibiotic class ("me-too") or use of different substances from different antibiotic classes and strongly depends on the pharmaceutical market characteristics. Therefore this indicator should be interpreted together with other indicators and national registers of available antibiotics.

ESAC boxplot



Indicator 24: Number of items recorded in the national register of available antibacterials for systemic use (J01) [J01_NR]

Definition

The number of items recorded in the national register of available antibacterials for systemic use (J01) gives the number of medicinal product presentations registered in the country.

Public health objective

This indicator may give a rough estimate of the availability of antibiotics at the national market, which is a conditio sine qua non for their prescription in ambulatory care.

Calculation formula:

The number of items recorded in the national register of available antibacterials for systemic use at the start of the respective year.

Benchmark and recommended action

This indicator should be considered as a structural indicator rather than a prescribing indicator. One benchmark value on European level cannot be given, since this strongly depends on the pharmaceutical market characteristics and cannot be influenced by the national antibiotic policy. We suggest individual countries to position themselves and to define their action targeting the market structure, e.g. to restrict the availability of antibiotics for ambulatory care or their reimbursement.

Limitations

This structural indicator can be interpreted only together with other indicators.
This indicator strongly depends on the penetration of "me-too" and generic products.

ESAC boxplot