Journal of Antimicrobial Chemotherapy Advance Access published February 1, 2014

J Antimicrob Chemother
doi:10.1093/jac/dku003

Journal of Antimicrobial Chemotherapy

Measuring antimicrobial use in hospitalized patients: a systematic review of available measures applicable to paediatrics

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Received 16 August 2013; returned 6 November 2013; revised 1 December 2013; accepted 27 December 2013

Objectives: The optimal measure to use for surveillance of antimicrobial usage in hospital settings, especially when including paediatric populations, is unknown. This systematic review of literature aims to list, define and compare existing measures of antimicrobial use that have been applied in settings that included paediatric inpatients, to complement surveillance of resistance.

Methods: We identified cohort studies and repeated point-prevalence studies presenting data on antimicrobial use in populations of inpatients or validations/comparisons of antimicrobial measures through a systematic search of literature using MEDLINE, EMBASE, CINAHL and LILACS (1975–2011) and citation tracking. Study populations needed to include hospitalized paediatric patients. Two reviewers independently extracted data on study characteristics and results.

Results: Overall, 3878 records were screened and 79 studies met selection criteria. Twenty-six distinct measures were found, the most frequently used being defined daily doses (DDD)/patient-days and exposed patients/patients. Only two studies compared different measures quantitatively, showing (i) a positive correlation between proportion of exposed patients and antimicrobial-days/patient-days and (ii) a strong correlation between doses/patient-days and agent-days/patient-days ($r=0.98$), with doses/patient-days correlating more with resistance rates ($r=0.80$ versus 0.55).

Conclusions: The measure of antimicrobial use that best predicts antimicrobial resistance prevalence and rates, for surveillance purposes, has still not been identified; additional evidence on this topic is a necessity.

Keywords: surveillance, antimicrobial resistance, correlation, daily doses, days of therapy

Introduction

The increasing prevalence of antibiotic-resistant microorganisms, including strains resistant to multiple agents, is of concern.[1–5] Resistant microorganisms are transmitted from patient to patient and are further selected following antimicrobial exposure.[6] Controlling antimicrobial use, through antimicrobial stewardship programmes, is thus an important intervention for the control of resistance in the inpatient microbiome.[2] Qualitative work aims to ensure an appropriate use of antimicrobial agents, while quantitative surveillance of antibiotic use at the population level allows benchmarking and monitoring of temporal trends. Integrating surveillance of antimicrobial use with surveillance of bacterial resistance rates can direct efforts to control resistance.[7,8]

Measures quantifying antimicrobial use in hospitalized populations have been described previously.[8–12] The numerators used quantify the volume or duration of exposure to antibiotics while the denominators describe the population at risk of exposure to antimicrobials (person or person-time). However, none of these measures completely captures the complete picture of antimicrobial consumption and thus the selection of the optimal measures to be recommended for use in surveillance studies is not obvious. Moreover, if surveillance is to include paediatric populations (e.g. paediatric and neonatal intensive care units or paediatric hospitals), an additional challenge arises, as prescriptions for neonates and paediatric patients are based on patient weight, which is often not the case in adult populations. Many measures that quantify the volume of antimicrobials used depend on doses administered, but do not take into account prescriptions based on body weight. This is why, for instance, the WHO does not recommend the use of defined daily doses (DDD) for paediatric patients,[9] which in turns explains why paediatric patients are often excluded from

studies employing or evaluating antimicrobial use measures,[11–15] although these populations are exposed to antibiotics and may thus become colonized or infected with antibiotic-resistant microorganisms, much as in adult populations.[16–19]

We are currently considering the implementation of quantitative surveillance of antibiotic use in Québec hospitals, which would complement surveillance of antimicrobial resistance, but aiming to include paediatric populations. We aimed to describe existing measures of antimicrobial use in cohort and repeated point-prevalence studies including paediatric inpatient populations, to understand how well these measures correlated and to assess their ability to predict future antimicrobial resistance prevalence and rates.

Methods

Search strategy

We developed a review protocol and MEDLINE (OvidSP interface), EMBASE (OvidSP interface), CINAHL and LILACS were screened for eligible studies published between 1975 and September 2011, to include the final steps of the development of the ATC/DDD system, adopted by the WHO in 1981.[9] Lists of search terms (see Table S1, available as Supplementary data at *JAC* Online) were built around the following concepts: (i) children or infants; (ii) utilization; (iii) anti-infective; and (iv) surveillance or measurement. To address potentially biased reporting of research results, we hand-searched all abstracts published in 2011 in two proceedings (Infection Diseases Society of America, Society for Healthcare Epidemiology of America).[20] Reference lists of selected articles were screened manually. Finally, for eligible studies comparing measures of antimicrobial use only, we used Google Scholar to identify studies citing them.

Study eligibility

Selected designs included cohort studies and repeated point-prevalence studies, studies presenting data on antimicrobial use in a population, validations of antimicrobial use measures or comparisons of antimicrobial measures. Only repeated point-prevalence studies (versus single point-prevalence studies) were included because of the longitudinal aspect provided by the repetition of the study. Study populations were required to include paediatric hospitalized patients. Only publications in English, French or Spanish were included. Publications were excluded when the purpose was to measure antimicrobial use and outcomes in individuals rather than in a population. Studies that described antimicrobial expenses solely for budget purposes or total drug use in a hospital or that studied allergic reactions were excluded. Editorials, reviews and commentaries were also excluded from the final analyses, but references were screened for eligible studies.

Study selection

Two reviewers (E. F. and P. S. F.) independently screened the titles and abstracts of the records retrieved by the electronic search. Subsequently, the same two reviewers independently reviewed the full text of all potentially eligible studies. For each step, results obtained were compared after screening of the first records. Discrepancies between reviewers were resolved through discussion.

Data extraction

Two reviewers (E. F. and P. S. F.) independently extracted relevant information (in duplicate). The first 10 studies were used as a pilot to clarify any ambiguity. Data to be extracted were divided into three sections:

(i) Identification and description of studies: design, type and number of geographical units (hospital or ward), population characteristics (e.g. age range, intensive care units or teaching hospitals), cohort size, period covered by the data, number and width of time intervals, and purpose of the measurement (antimicrobial resistance, various, unknown).
(ii) Description of measures: units, antimicrobials selected, details on the computation, granularity of the data (individual or group), and strengths and limitations (according to authors and reviewers).
(iii) Comparison of measures: when antimicrobial use measures were compared with at least one other measure (other antimicrobial use or antimicrobial resistance), information was noted on how measures were compared (qualitatively or quantitatively), how they agreed and whether time lags were considered.

Analysis of selected studies

Frequency distributions of studies and identified measures were produced, and a narrative synthesis of results was performed. The potential influences of study design (i.e. type and number of geographical units and time intervals; population characteristics), purpose of measurement and selected antimicrobials were explored by stratifying or restricting the analyses on these characteristics. Study power was qualitatively assessed based on the number of observations (cohort size and timepoints), especially for studies comparing measures.

In studies where measures were not compared, we focused on the measures chosen rather than on the results, so power and biases were not relevant. For studies on the correlation between different measures, selection bias was not an issue because these studies simply described the strength of the relation between two measures of the same concept (antimicrobial use) in the same population. However, choices in the computation of measures could lead to different correlation coefficients and so details on computation were extracted. In studies comparing the ability of different measures to predict resistance, results could be influenced by biases.[21,22] Therefore, the potential biases that we considered included: (i) inclusion of unused doses in the calculation of antimicrobial use measures; (ii) consideration of potential time lags between antimicrobial use density and resistance rates; (iii) occurrence of interventions targeting either antimicrobial use or transmission of resistant microorganisms between patients during the study period; (iv) definition of resistance; and (v) choices of geographical unit, time intervals, antimicrobial classes and resistances.

Results

Selected studies

A flow chart of eligible study selection is presented in Figure 1.[23] The reviewers screened 3878 records, of which 79 studies met the selection criteria. Study designs could differ substantially, as shown in Table 1. Selected studies included 19 surveillance cohorts, 56 other cohort studies and four repeated point-prevalence studies. Twenty-six studies (33%) used more than one measure; although 79 studies were selected, information was extracted on 119 measures. In eight studies (10%), results obtained with different measures were compared, and quantitative methods (correlation coefficients) were used in two of these studies,[12,24–30] one of which also compared the correlation of each measure with antimicrobial resistance.[26]

Measures of antimicrobial use

Thirteen different numerators and five different denominators were used and are detailed in Tables 2 and 3. They were combined to produce 26 distinct measures (Table 4). Several measures

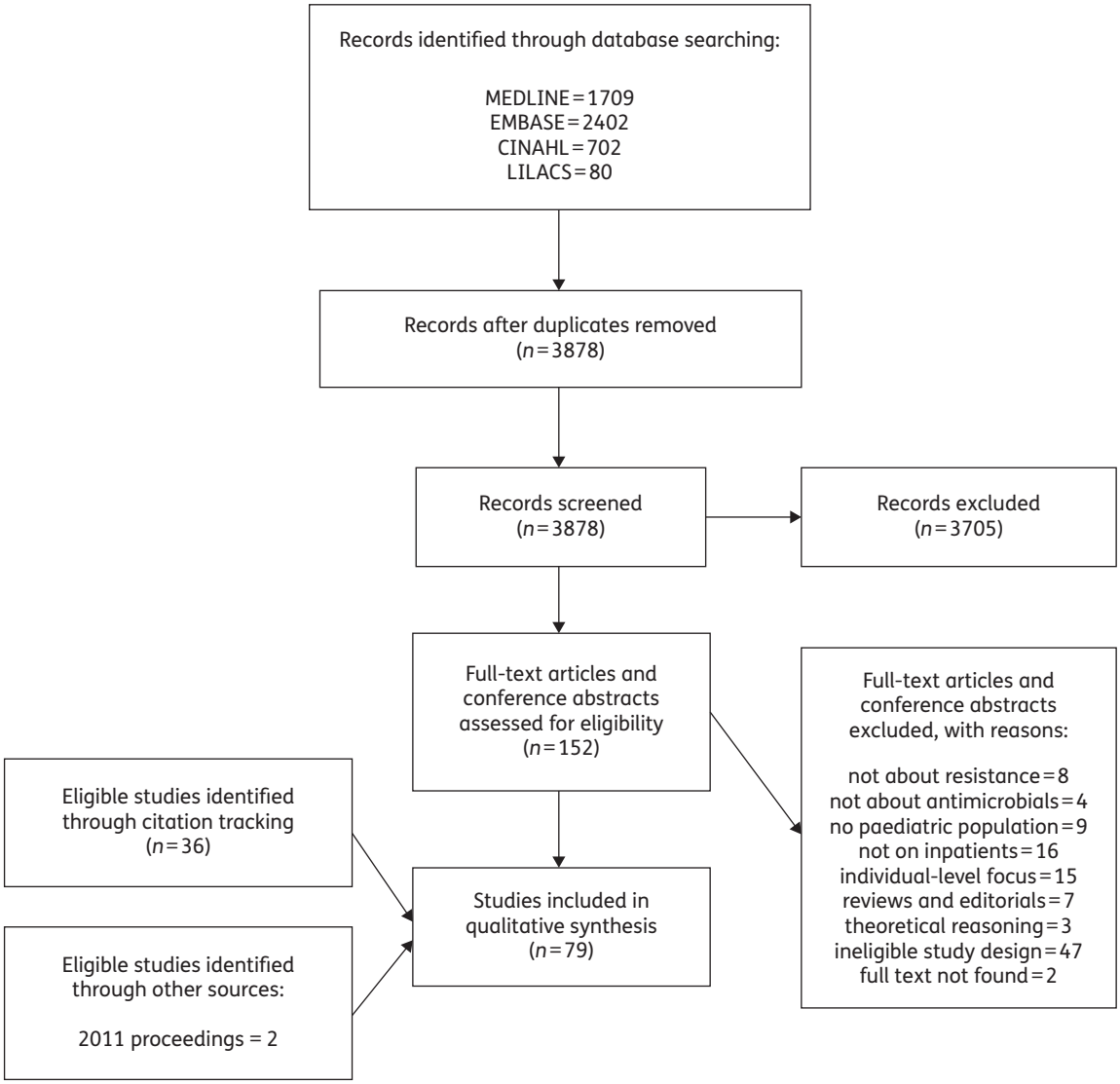

Figure 1. Flow diagram of the selection of studies.

referred to similar concepts. Measures using DDD, recommended daily doses (RDD), RDD in mg/kg, prescribed daily doses (PDD) and undefined doses combine information on quantities prescribed and duration of therapy, using different values in their definition of what is a standard daily dose. Grams and costs also estimate quantities and duration of therapy. Agent-days and antimicrobial-days measure the duration of treatments. Other measures reported exposure to antimicrobials: any exposure (proportion of patients exposed) and number of treatment periods, courses or agents.

Associations and correlations between measures

Table 5 summarizes the eight studies that compared different measures.[12,24–30] Three studies commented on the quantitative results obtained using different measures. Antachopoulos *et al.*[24] demonstrated an underestimation of the number of doses prescribed to paediatric and neonatal populations when using DDD/patient-days; Berrington[12] mentioned that DDD were closer to agent-days than to antimicrobial-days; Valcourt *et al.*[30] obtained identical values for PDD and agent-days. Although a few authors have mentioned the limited interpretation of DDD measures in paediatric populations,[10,24–33] Berild *et al.*[25] noted that DDD were still easier to interpret than costs, since costs could also reflect changes in preferred agents used and in prices. Four studies used sets of measures and underlined the relationships between the proportion of exposed patients, the duration of treatment and the quantity of antimicrobials prescribed;[27–30] they showed how, for example, a stable proportion of exposed patients combined with a decrease in the duration of treatment led to a reduction in total quantities prescribed to patients.[29] Valcourt *et al.*[30] also pointed out that the average duration of treatment was related to the average length of stay (potential exposure time).

Di Pentima *et al.*[26] showed that quinolone RDD in mg/kg/patient-days and quinolone-days/patient-days were highly

Table 1. Description of selected studies

Study characteristics	Studies	
	n	%
Design		
repeated point-prevalence study	4	5
surveillance cohort	19	24
other cohort study	56	71
Purpose of measurement		
antimicrobial resistance	68	86
not specified	11	14
Measures		
1	53	67
2	21	27
3	2	3
4	2	3
10	1	1
Measured antimicrobials		
all	60	76
specific agents	19	24
Unused doses		
not specified	64	81
included	5	6
excluded	9	11
excluded doses returned to pharmacy	1	1
Age groups included		
children and neonates only	47	59
adults also included	32	41
Type of geographical unit		
hospital	17	22
department	6	8
ward	56	71
Geographical units (range)	1–75	—
Time intervals (range)	1 day–6.5 years	—
Timepoints (range)	1–61	—
Comparison of measures		
no	71	90
yes	8	10
qualitative	6	75
quantitative (correlation)	2	25
Correlation with resistance		
no	78	99
yes	1	1

correlated ($r=0.98$) in one hospital during the 8 year follow-up. When analyses were restricted to either levofloxacin or ciprofloxacin, the correlation (r) was 0.85 and 0.96, respectively. The study of Gerber *et al.*,[27] with data from 40 hospitals, reported a positive correlation (r not provided) between the proportion of exposed patients and antimicrobial-days/patient-days; correlation was computed for total antimicrobial use and was then restricted to broad-spectrum antimicrobials. These authors mentioned that hospitals where a greater proportion of patients received antimicrobials also prescribed treatments for longer durations, a correlation that could have been different in another population.

Prediction of antimicrobial resistance

Only one study calculated the correlation of two different measures with rates of resistance.[26] Di Pentima *et al.*[26] reported that quinolone RDD in mg/kg/patient-days were more positively correlated to rates of resistance in Gram-negative bacilli than quinolone-days ($r=0.803$ versus $r=0.553$).

Discussion

To our knowledge, this is the first systematic review of available measures of antimicrobial use in inpatient populations that also include paediatric patients. Although many measures were found, few were compared quantitatively, and only one study calculated the correlation between antimicrobial use measures and resistance.

Measures of antimicrobial use

Twenty-six different measures were found in the literature, the most frequently used being DDD/patient-days and exposed patients/patients. The limitations of the DDD/patient-days method in paediatrics have been mentioned, but this well-known and clearly defined measure can still be used in specific situations, such as to follow antimicrobial use density in a population where patients' average weight is constant. Other authors preferred to develop new measures, such as RDD in mg/kg and RDD numerators or the kg-days denominator. Confronted with such a variety of measures, it is important to understand how these measures compare with one another in order to choose the most appropriate measure that could be used in the surveillance of resistance rates.

An important limitation of many of our eligible studies was the use of ill-defined measures. Whenever possible, numerators were renamed according to definitions provided by Berrington[12] and de With *et al.*[14] Measures using DDD were usually well documented because this method is well known and easy to reference.[9] On the other hand, standard doses were not always provided for PDD, RDD and RDD in mg/kg measures and not all publications explained how these standard daily doses were defined. In some publications, it was not always possible to distinguish agent-days from antimicrobial-days or courses from treatment periods. Authors also only seldom specified if they had included prescribed but unused doses in their measures, which is particularly important if one is measuring antimicrobial use to determine its association with resistance. Regarding denominators, it was not always clear if the day of discharge was excluded or not in values of patient-days/bed-days, even though potentially important variations in rates of healthcare-associated infections can be observed when using different denominator definitions.[34,35]

Associations and correlations between measures

Of the 26 measures identified, 17 were compared with at least one other measure, but only four measures were compared

Table 2. Frequency distribution and description of numerators found in selected studies

Category/units	Description[a]	Studies[b] *n*	Studies[b] %
Exposures			
exposed	patients prescribed/administered antimicrobials, regardless of quantity or duration	39	49.4
treatment periods	number of distinct periods of consecutive days when a patient is prescribed/administered at least one antimicrobial; a treatment combining different antimicrobials is counted as 1 treatment period	5	6.3
courses	number of distinct periods of consecutive days when a patient is prescribed/administered a specific antimicrobial; therefore, the sum of courses will not equal treatment periods	4	5.1
agents	number of different antimicrobials to which a patient was exposed	3	3.8
Quantity			
DDD	defined daily dose, as defined by the ATC/DDD system; 1 DDD is the average quantity (in grams) given to a 70 kg adult for 1 day; these values are identical worldwide	33	41.8
currency	costs of prescribed/administered antimicrobials	6	7.6
grams	grams of prescribed/administered antimicrobials	4	5.1
RDD in mg/kg	standard daily dose varies according to the weight of the patient; this measure was developed for paediatric populations; this measure is usually named DDD in mg/kg, but because these standards are not defined by the ATC/DDD system, RDD in mg/kg seems to be a more appropriate name	4	5.1
doses	these doses were not defined in the studies	2	2.5
RDD	recommended daily dose; similar to DDD, but the standard daily dose is defined by local guidelines	1	1.3
PDD	prescribed daily dose; similar to DDD, but the doses actually prescribed/administered are considered to be the standard	1	1.3
Duration			
agent-days	patient-days when a specific antimicrobial was prescribed/administered.	12	15.2
antimicrobial-days	patient-days when any antimicrobial was prescribed/administered (alone or in combination); therefore, the sum of agent-days will not equal antimicrobial-days	5	6.3

[a]Terminology in this table may not match that used in studies. Numerators extracted were sometimes renamed depending on the description provided by the authors.
[b]Some studies used more than one measure; although 79 studies were selected, information was extracted on 119 measures and percentages do not add up to 100%.

Table 3. Frequency distribution and description of denominators found in selected studies

Category/units	Description[a]	Studies[b] *n*	Studies[b] %
Person-time			
patient-days	sum of days spent in hospitals or wards by all patients; no distinction is made between patient-days and bed-days	62	78.5
kg-days	sum of [expected weight (in kg) of patients at a certain age×the number of patient-days of that age]	1	1.3
Person			
patients	patients included in the study	32	40.5
admissions	admissions to wards or hospitals	22	27.8
Other			
currency	costs of all prescribed/administered drugs	2	2.5

[a]Terminology in this table may not match that used in studies. Denominators extracted were sometimes renamed depending on the description provided by the authors.
[b]Some studies used more than one measure; although 79 studies were selected, information was extracted on 119 measures and percentages do not add up to 100%.

Table 4. Frequency distribution of measures of antimicrobial use found in selected studies

	Studies[b]		
Category/measure[a]	*n*	%	references[c]
Exposure/person-time			
treatment periods/patient-days	2	2.5	12,39
exposed patients/patient-days	1	1.3	39
courses/patient-days	1	1.3	12
Quantity/person-time			
DDD/patient-days	31	39.2	10,12,16,24,25,30,32,33,40–62
grams/patient-days	4	5.1	28,63–65
currency/patient-days	3	3.8	17,25,40
RDD in mg/kg/patient-days	3	3.8	24,26,66
doses/patient-days	2	2.5	67,68
RDD in mg/kg/kg-days	1	1.3	69
RDD/patient-days	1	1.3	70
PDD/patient-days	1	1.3	30
Duration/person-time			
agent-days/patient-days	9	11.4	12,26,30,71–76
antimicrobial-days/patient-days	4	5.1	12,27,67,77
Exposure/person			
exposed patients/patients	27	34.2	16–19,25,27,28,30,44,47,71,76,78–92
exposed patients/admissions	11	13.9	29,59,70,75,77,93–98
treatment periods/admissions	2	2.5	12,99
courses/admissions	2	2.5	12,100
agents/patients	2	2.5	71,87
treatment periods/patients	1	1.3	80
courses/patients	1	1.3	79
agents/admissions	1	1.3	96
Quantity/person			
DDD/admissions	2	2.5	12,31
currency for antimicrobials/patients	1	1.3	43
Duration/person			
agent-days/admissions	3	3.8	12,29,101
antimicrobial-days/admissions	1	1.3	12
Quantity/other			
currency for antimicrobials/currency for all drugs	2	2.5	43,71

[a]Terminology in this table may not match that used in studies. Measures extracted were sometimes renamed depending on the description provided by the authors.
[b]Some studies used more than one measure, so although 79 studies were selected, information was extracted on 119 measures and percentages do not sum to 100%.
[c]References 39–101 are available as Supplementary data at *JAC* Online.

quantitatively. According to these results, RDD in mg/kg/patient-days and agent-days/patient-days were strongly correlated, and so were the measures exposed patients/patients and antimicrobial-days/patient-days. When RDD in mg/kg is a good representation of daily doses actually prescribed to paediatric patients, it approximates agent-days; it was therefore not a surprise to find that this measure was highly correlated with days of therapy. The magnitude of the correlations between two measures varied, as analyses were restricted to certain classes of agents. Obviously, as all identified measures aim to quantify antimicrobial use in a population, a relatively high level of correlation is expected between them.[36] Indeed, expected similarities and differences between measures can be used in sets of measures to better understand changes occurring in antimicrobial use in a population,[37] as was done in the four studies analysing how the proportion of exposed patients, the duration of treatment and the quantity given can all have an impact on a population's global antimicrobial use.

Table 5. Studies comparing different measures of antimicrobial use

Reference	Comparison method	Measures compared	Geographical unit	Time intervals (n×interval)	Agents	Summary of results
12	descriptive	DDD/PD DDD/admissions agent-days/PD agent-days/admissions AM-days/PD AM-days/admissions courses/PD courses/admissions tx periods/PD tx periods/admissions	13 departments (1 paediatric)	1×1 year	all	• correlation analyses were done, but data from the paediatric department were excluded from these analyses; patient-days give lower measure estimate than admissions • DDD are closer to agent-days than to antimicrobial-days • measures accounting for combinations are lower than the others
24	descriptive	DDD/PD RDD in mg/kg/PD	3 wards (adult, paediatric, neonatal)	1×1 year	ceftriaxone	• the adjusted doses gave higher values, especially in neonatology
25	descriptive	DDD/PD currency/PD	1 department (1 NICU and 1 paediatric ward)	7×1 year	all	• costs and DDD show the same trends, but while the interpretation of DDD appears straightforward, costs are influenced by changes in prescribed antimicrobials and in deals with drug companies
28	descriptive	grams/PD exposed/patients	1 NICU	4×6 months	all	• the proportion of exposed patients, the number of admissions and the average weight of treated patients have not changed, so the authors explain the observed decrease in grams/patient-days by the shorter duration of treatment
29	descriptive	exposed/admissions agent-days/admissions	1 NICU	10×1 year	all	• even though the proportion of exposed patients remained stable, the mean duration of treatment decreased, which resulted in a decrease in antimicrobial use
30	descriptive	DDD/PD PDD/PD agent-days/PD exposed/patients	3 wards (PICU, NICU, CICU)	1×1 year 2×1 year (PICU)	vancomycin linezolid	• in critically ill children, drug use density of vancomycin is significantly less when measured with DDD compared with PDD, a more appropriate method in children. • the simplest and most accurate method of assessing drug use density is agent-days, which allows comparison of drug use density between different paediatric facilities or clinical units; PDD and agent-days are identical at the group level • the proportion of patients who are exposed is similar in the 3 ICUs, but agent-days vary because of different average lengths of stay in each ICU
26[a]	correlation	RDD in mg/kg/PD agent-days/PD	1 hospital	8×1 year	ciprofloxacin levofloxacin	• quinolone doses/1000 patient-days and days of therapy/1000 patient-days are strongly correlated (r=0.9777 for quinolones, r=0.848 for levofloxacin only and r=0.955 for ciprofloxacin only).
27[a]	correlation	exposed/patients AM-days/PD	40 hospitals	1×1 year	all broad-spectrum	• the authors conclude that the two measures are correlated because hospitals who expose more patients also prescribe for longer durations of treatment; however, correlation coefficients are not provided, only P values

AM, antimicrobial; CICU, cardiac intensive care unit; exposed, exposed patients; NICU, neonatal intensive care unit; PD, patient-days; PICU, paediatric intensive care unit; tx, treatment.
[a]Measures were compared using correlation coefficients; other studies made a qualitative description.

Prediction of antimicrobial resistance

In the single study comparing the correlation of two measures of antimicrobial use with resistance rates, in children, RDD in mg/kg was more strongly correlated with resistance than agent-days.[26] RDD in mg/kg/patient-days might be a more precise measure; on a particular day and for a particular patient, agent-days can be equal to either 0 or 1, while the number of standard doses can take any value $\geq$0. The same type of reasoning could apply to patient-days, which combine information on the number of admissions and patients' length of stay, thus offering a wider range of possible values. On the other hand, in a situation where exposure could be highly misclassified (including e.g. unused doses or days, or doses and days prescribed by the hospital but administered to discharged patients), it is possible that a simple measure of exposure (yes or no) would better reflect reality.

Future work

The results of this systematic literature review would require confirmation by other studies comparing more measures, a wider range of agents, microorganisms and resistance definitions, using analytical methods such as regression models and considering potential time lags. These factors could all have an influence on the various measures' ability to predict resistance. In our case, because of our particular interest in healthcare-associated resistance, prediction of the incidence of resistant healthcare-associated infections, as well as prediction of the prevalence and acquisition of resistance in inpatients' microbiome (2008 HICPAC recommendations[38]) would be especially relevant. However, such a study would probably not have to compare all measures identified in this review. For instance, DDD and RDD include the information provided by grams and costs, but in a more standardized manner, which simplifies comparisons between agents and prevents the introduction of temporal bias due to market fluctuations. Market fluctuations also limit the use of costs as a denominator. Moreover, as PDD and agent-days are equivalent, only one of these measures can be kept. Finally, as patients' weights are not always known (especially in adults), RDD and RDD in mg/kg could be combined into a single measure.

Limitations

There are limitations to this review. First, it only includes studies that were published or presented at conferences; some research teams could have studied this topic without communicating their results. Inability to demonstrate a difference between measures, even though interesting, could have led to publication bias. Moreover, studies where antimicrobial use was only one factor among many others could have been missed, but antimicrobial exposure is such an important determinant of resistance that this seems improbable. We have screened abstracts from two conferences held in the USA to minimize publication bias, but screening additional abstracts, from other conferences held elsewhere in the world, could have reduced this bias even further. Second, due to insufficient measure definitions and to the use of a variable nomenclature for equivalent measures, we might have misclassified identified measures. For an easier interpretation of published results, we encourage our colleagues to carefully define their measures. Third, some of the studies only presented paediatric or neonatal data; we, however, hypothesize that measures meaningful for paediatric populations can also be generalized to adult populations, while the reverse is not necessarily true. Fourth, a large variety of designs had to be considered. Studies compared different measures and their data came from different settings varying in time interval and number of geographical units. This heterogeneity can be important because in some settings two measures provide similar information (e.g. admissions and patients are more similar if the time interval is longer). Agents and microorganisms under study can also vary: the study that compared measures with resistance rates focused on quinolones and Gram-negative bacilli. Results could be different for other agents and microorganisms. Finally, because of our particular interest in long-term surveillance, we excluded single point-prevalence studies while keeping repeated point-prevalence studies, although one could object that both types of studies use similar metrics.

Because so little quantitative data were found, vague definitions of measure and design heterogeneity have probably not influenced our conclusions. Adding single point-prevalence studies would probably make exposed patients/patients the most frequent measure, but would probably not bring additional comparisons of measures' ability to predict resistance because of the limited number of measures applicable in point-prevalence studies. Our conclusions might be likely to differ substantively if a large number of studies were missed due to the search strategy or in the case of substantial publication bias.

Conclusions

The choice of a measure of antimicrobial use depends on the purpose of the measurement. It is hypothesized frequently that the regulation of antimicrobial use could lead to better control of resistant microorganisms. In this context, surveillance systems were developed not only to monitor resistant microorganisms, but also to monitor antimicrobial use. However, little information is available to guide policy makers in the choice of the ideal measure for a surveillance system, particularly when including paediatric populations. Our results showed that the measure of antimicrobial use that is the most appropriate is still unclear. Along with a certain degree of standardization, additional evidence on this topic is required.

Acknowledgements

A summary of this review has been presented at the CACMID—AMMI Canada 2013 Annual Conference, Québec City, Canada (Abstract SP-22).

We would like to thank Ms Lorie Kloda and Ms Lindsay Sikora for their methodological advice on selection of studies, Ms Denise Dumas and Mr Jean-Baptiste Anumu Kpetsu for their help in the comparison of the two data extractions, and Dr Jesse Papenburg for his comments on the presentation of results.

Funding

This study was supported by internal funding.

Transparency declarations

None to declare.

Supplementary data

Table S1 and references 39-101 are available as Supplementary data at *JAC* Online (http://jac.oxfordjournals.org/).

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