Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (1 of 8)

Measuring Antimicrobial Use: A Step-by-Step Guide

What is antimicrobial "use"?

The first step in measuring antimicrobial use is determining what you will actually be measuring. Figure 1 displays all of the different steps in the medication use process where one could consider measuring antimicrobial use. Most clinicians would consider "use" of antimicrobials to be administration of a drug to a patient. But it turns out that most studies that report antimicrobial use are actually measuring a different step in the antimicrobial use process, from as far removed as the drug being purchased by the pharmacy, through various steps of ordering and delivering the drug, to steps that occur after the use has actually occurred, such as billing data. It's important to know what step in the process you are measuring, since the data may exist in different places depending on the step, and because comparisons are most valid when performed at the same step.

Table 1: Steps at which antimicrobial use could be measured

Measurement Level	Data Source	Advantage	Disadvantage
Drug purchased by pharmacy	-Pharmacy purchasing data -Wholesaler data	-Easiest to obtain aggregate data	-"Farthest" from actual use -Time trends irregular
Drug prescribed by physician	-Chart orders	-Measures intent	-Impracticable if no computerized prescriber order entry
Drug order entered by pharmacy	-Pharmacy system	-Measures intent	-Can be difficult to query
Drug dispensed by pharmacy	-Pharmacy system	-Approximates administration	-Can be difficult to query
Drug delivered to floor/bedside	-Medication administration record	-Most accurate	-Impracticable if no barcode medication administration scanning
Drug administered to patient	-Hospital billing records -Group data	-Sometimes easier to obtain -Benchmarking	-Over- or under-estimate -Delay
Drug billed to patient	-Pharmacy purchasing -Wholesaler data	-Easiest to obtain aggregate data	-"Farthest" from actual use -Time trends irregular

The level of measurement you choose will likely be determined in part by the healthcare technology used in your institution, particularly whether computerized prescriber order entry and/or barcode medication administration scanning are available.

For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 2 of 8)

OK, I know where I'm getting my data from and what step of the process I'll be measuring. What do I actually want to measure?

This depends, not surprisingly, on what you want to know. If you want to know how often patients are getting any, or particular, antibiotics, you'll be interested in a point (at a particular time, such as at ICU admission) or period (for example, over the course of an admission) prevalence. If you're less interested in the start of antibiotics and more in their finish, you can examine the mean or median duration of antibiotics, for all causes or for a particular infection. Obviously both of these contribute to the total amount of antibiotic use, and so a commonly used metric is the incidence density rate of Defined Daily Doses (DDD) or Days of Therapy (DOT) per 1000 patient-days. Adjusting for patient-days allows comparisons between time periods and across institutions and services with different numbers of patients and different lengths of stay.

Table 2: Measurement metrics

I want to know...	Measurement	Examples
...how often patients are getting antibiotics	Point (period) prevalence	% of CAP patients receiving atypical coverage
...how long people are getting antibiotics for	Mean or median duration	Duration of antibiotic therapy for VAP
...the overall amount of antibiotics received adjusted for patient time at risk	Incidence density rate	Defined daily doses or days of therapy/1000 patient-days

What's a DDD or DOT and how do I measure it?

We mentioned two potential measurements for aggregate antibiotic use – defined daily doses or days of therapy. There are various technical pluses and minuses of the two measures, but both can provide useful information. Defined daily doses (DDD) can be measured on a variety of data sources, and involves summing the total grams of drug used during the period of interest, and dividing by a number set by the World Health Organization as representing an "average", or defined, daily dose. The WHO defined doses for antimicrobials are available here: http://www.whocc.no/atc_ddd_index/

Days of therapy (DOT) involves summing the total number of days that a patient received any number of doses of a drug. Both should be adjusted for some measure of time at risk, such as patient-days, bed-days, admissions, etc. These numbers are typically multiplied by 1000 simply to avoid small fractions. Depending on the drug, the dose given, and the WHO's definition of a daily dose, sometimes the DDDs and DOTs give the same answer. Sometimes they don't. So while either can be a valid measure, they really shouldn't be compared to each other.

For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 3 of 8)

Let's go through some examples. Although we don't typically measure DDD or DOT on individual patients, such an exercise can be useful to show the similarities and differences:

A patient is admitted for a surgical removal of an inflamed appendix. The patient receives cefazolin 1g IV x1 as surgical prophylaxis. After a single post-operative fever spike (white count remains normal), the patient is initiated on vancomycin (1g IV q12h) and ampicillin/sulbactam (3g IV q6h) for 3 days. Three days later the patient is discharged on moxifloxacin 400mg po daily to complete 7 days of antibiotic therapy.

Table 3: Patient-level measurement of DDD and DOT

Drug	Regimen	Total grams	WHO defined daily dose	Defined Daily Doses (DDD)	Days of Therapy (DOT)
cefazolin	1g IV x1	1g	3g	1/3 = 0.33	1
vancomycin	1g IV q12h x3 days	6g	2g	6/2 = 3	3
ampicillin/ sulbactam	3g (2/1g) IV q6h x3 days	24g	2g (of ampicillin)	24/2 = 12	3
moxifloxacin	400mg po qd x4 days	1.6g	0.4g	1.6/0.4 = 4	4
Total				19.33	11

Thus you can see that the number of DDDs and DOTs for a patient can vary depending on factors like the number of doses administered, and the correlation between the actual prescribed dose and the WHO defined daily dose.

More commonly, you would be analyzing large sets of data provided by your IT or pharmacy department of aggregated antimicrobial use. Table 4 on the next page shows an example of the values you might see over several months of antibiotic use in a large healthcare facility, and how DDDs and DOTs might compare.

For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 4 of 8)

Table 4: Aggregate Measurement of DDD and DOT

Drug	Patient Admits	Patient Mean Length of Stay (All Patients)	Patient Days (All Patients)	Number of Patients receiving drug	% Patients receiving drug	Mean duration of therapy for patients receiving drug	Total grams of drug for patients receiving drug	WHO defined daily dose	Defined Daily Doses (DDD)	DDD/1000 patient-days	Days of Therapy (DOT)	DOT/1000 patient-days
Cefazolin	24007	6.04	24007* 6.04= 145002	6481	6481/ 24007= 26.9%	1.8	26489	3g	26489/3 = 8829	(8829/ 145002) * 1000= **60.8**	6481*1.8 = 11665	(11665/ 145002) * 1000= **80.4**
vancomycin	24007	6.04	24007* 6.04= 145002	5715	5715/ 24007= 21.6%	4.8	47992	2g	47992/2 = 23996	(23996/ 145002) * 1000 = **165.2**	5715 * 4.8 = 27432	(27432/ 145002) * 1000 = **168.5**
ampicillin/ sulbactam	24007	6.04	24007* 6.04= 145002	111	111/ 24007= 0.46%	3.3	2974	2g (ampicillin)	2974/2= 1487	(1487/ 145002)*1000 = **10.2**	111 * 3.3 = 366	(366/ 145002) * 1000= **2.5**
moxifloxacin	24007	6.04	24007* 6.04= 145002	723	723/ 24007= 3.0%	6.3	1804	0.4g	1804/0.4= 4510	(4510/ 145002) * 1000 = **31.0**	723 * 6.3 = 4554	(4554/ 145002) * 1000 = **31.4**
Total										**267.2**		**303**

For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 5 of 8)

OK, now what do I do with these numbers?

Once you obtain your data, whatever it is, it's important to put it in context. After all, knowing you use X number of days of therapy of an antibiotic isn't intrinsically meaningful. One level of comparison is to some absolute standard – what should that number be? In a number of quality improvement contexts, we can set an absolute standard goal: no central-line-associated infections, or 100% hand hygiene compliance. Those standards may be high, but they represent a clear goal. However, for some measurements there is not a reasonable absolute standard – we certainly don't want our antibiotic use to be zero, and currently there is no "magic number" that represents the "correct" amount of total antibiotic use! Thus, we are forced to use other standards. One is through comparison to other groups – these might be other hospitals, or other teams or services within an institution. For this comparison challenges can include obtaining data from comparators – some folks don't want to air their possibly dirty laundry – and ensuring that a comparator really represents a good benchmark for your institution. One way to remove the variability with comparators is to use your own institution as a reference standard. When doing so, you'll want to make sure there's adequate data to ensure that you are seeing a real effect, rather than just random variation.

Table 5: Approaches to interpreting DDD/DOT data

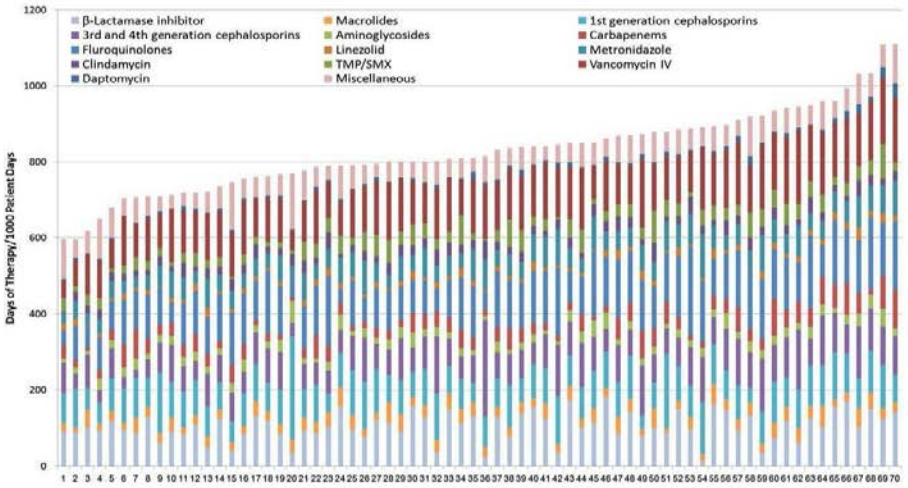
Approach	Pro	Con
Trend institutional data over time	-Allows to see patterns in utilization -Can be statistically tested for significance of trends -Can measure impact of interventions starting at a particular point in time	-Need lots (>1 year) of data points at frequent (month, quarter) intervals -Time-consuming -Doesn't measure appropriateness
Benchmark to external institutions	-Gives comparison to peer institutions -Allows to identify potential areas of excessive use -Understandable to C-suite folks	-Very difficult to obtain data from outside institutions -Risk-adjustment for apples-to-apples comparison

Figure 1 below reports the aggregate antibacterial use in days of therapy per 1000 patient days across 70 university hospitals. Even though these are all academic medical centers, there is nearly a twofold variation in usage from the lowest to highest users. We'd like to be able to isolate what component of the variability comes from potentially improvable practice patterns, and what is a result of different mixes of patients across these institutions.

Figure 1: Aggregate antimicrobial use across university hospitals

For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

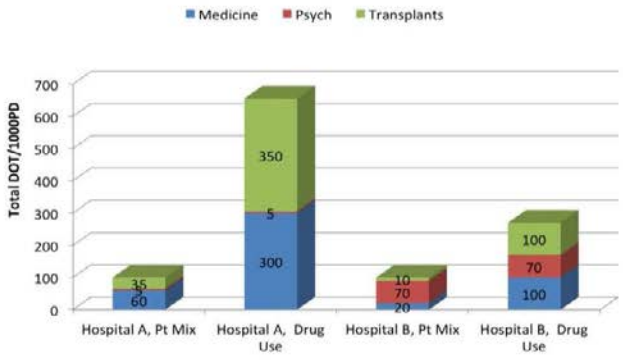
Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 6 of 8)



Polk RE, et al. Clinical Infectious Diseases 2011;53(11):1100–10

Figure 2 illustrates the impact that patient mix can have on utilization. In this hypothetical (and somewhat extreme for illustration purposes) example two hospitals A and B have different percentages of patients on medicine, psychiatry, and transplant services. Although each service has the same utilization rate per patient for each service – 5 days of therapy per 1000 patient days for medicine patients, 1 for psych patients, and 10 for transplant patients – the total utilization at institution A is much higher because of their mix that includes higher-use patients. Thus, these two hospitals have similar "modifiable" antibiotic use rates, but much different overall usage rates.

Figure 2: Effect of patient mix on utilization measures



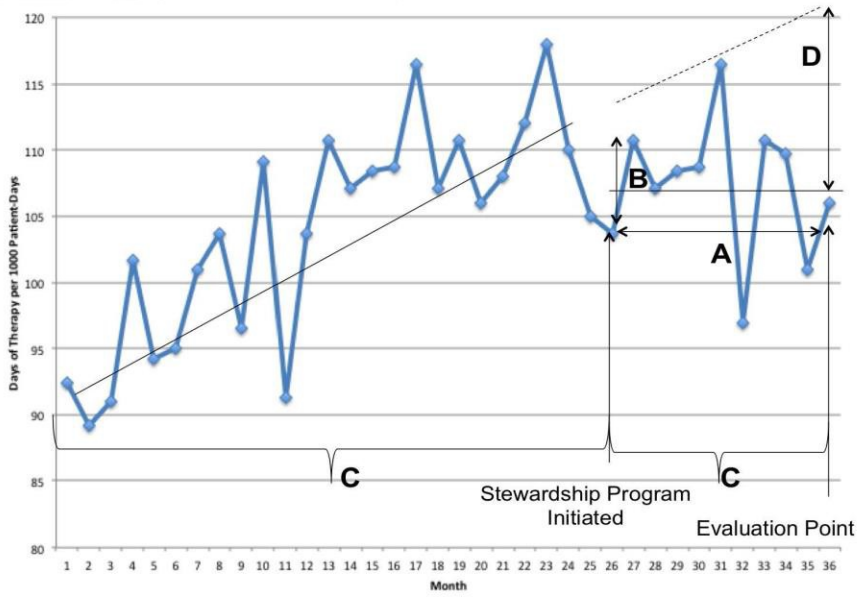
For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

CDPH does not endorse the specific content or recommendations included in these examples. They are for illustrative purposes only.

Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 7 of 8)

To avoid the issues with patient mix, and because data from comparator institutions can be difficult to obtain, institutions often use their own data over a period of time to put their findings in context. Figure 3 is an example of antimicrobial use data over a three-year period at an institution, although the concepts apply to any data that can be measured at repeated intervals over time. First note the general trends imposed onto the large amount of month-to-month variability. Next let's consider this data is being collected to evaluate the impact of an antimicrobial stewardship program, which is given one year to show its effect on utilization. We can ask what the best comparisons to perform on this dataset might be. One might compare the use just before the program was implemented to the utilization at the end of the study period. But in this case it would give a misleading story that there was little effect of the program. Even worse would be comparison of the utilization immediately before to immediately after the initiation of the stewardship program. It's unlikely there would be enough time to see a true effect, and instead the random variation might lead to the conclusion that the program increased utilization. Many studies would report the mean use in the period before the intervention and mean use during the intervention period. But this doesn't account for the trend in utilization, which was clearly increasing before the intervention, and which flattened out afterwards. A more accurate comparison would be to compare the observed trend in antimicrobial use after the intervention to the projected trend in utilization if the intervention had not occurred. Although slightly more complicated statistically, this interrupted time-series approach is recognized as the most valid way to analyze and present such data. Table 6 summarizes analyses at various time points.

Figure 6: Aggregate antimicrobial use plotted over time



For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu

Example 7.1 University of California San Francisco Medical Center Measuring Antimicrobial Use (continued 8 of 8)

Table 6: Analysis points for Figure 3

Comparison	Rationale For?	Rationale Against?
A, the difference between use the first month of the program and the month of evaluation		-Only captures utilization during the program and not prior to program initiation; effect of program not captured
B, the difference between use the month prior to the program and the month after the program started		-Inadequate time to capture effect of intervention
C, the difference between the projected and actual antibiotic use at the month of evaluation	-Captures trend in utilization (usually upwards) prior to intervention -Allows demonstration of cost/utilization avoidance	-Lots of data points required -Statistically analysis somewhat more complex
D, the mean monthly antibiotic use before and after program implementation	-Easily interpretable -Easily to statistically evaluate	-Does not account for pre-existing trends -Can under- or over-estimate impact of program

For more info about this example contact Conan MacDougall, PharmD at macdougallc@pharmacy.ucsf.edu