Case Study

Increase of antimicrobial consumption in a medical intensive care unit?

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Objectives

- To learn how to use pharmacy data to measure the level of antibiotic use in a hospital/ward

- To understand the advantages and the limitations of such measurement

Step 1

You are the clinical microbiologist of Hospital A, a 1200-bed teaching hospital. On Thursday March 8, 2001, outside of the hospital self-service restaurant and on your way to the laboratory, you are stopped by Dr. B, one of your colleagues who is Chief of Department of Intensive Care.

Dr. B expressed his concern about the bad prescribing habits of his new residents in the 10-bed adult Medical Intensive Care Unit (MICU). He was the intensivist on duty last Sunday and, when doing the rounds, he noticed that too many of his patients were receiving empiric therapy with imipenem or meropenem. He adds that he found no reason for these prescriptions in the patient charts and decided to stop treatment for several of them. For a long time, he has also been concerned about young doctors' prescribing of third-generation cephalosporins.

Step 1 (continued)

He asks you if you could have a look at antibiotic consumption in the MICU, and possibly compare it to consumption in the other ICU, an 8-bed adult Surgical Intensive Care Unit (SICU).

In the same conversation he mentions his worries that these prescription practices might have an impact on the type of infections that the MICU patients are getting: last week one patient died of bacteremia due to a multi-resistant *Pseudomonas* and presently two patients in the MICU have a ventilator-associated pneumonia due to *Stenotrophomonas maltophilia*. May be you can check this too...

Question 1

- What do you think about this situation? Is this important and does it deserve further investigation?

- If yes, what should be your actions? Whom should you contact?

Step 2

You immediately contact one of the hospital pharmacists, whom you collaborated with on a recent project regarding dose adjustment for aminoglycosides. She says that the pharmacy is keeping track of all orders and deliveries to the different hospital wards.

She also mentions that since 1998, after having been asked by the hospital Drug Committee, the pharmacy produces a yearly report on drug consumption for the whole hospital and by ward. She thinks that she could find these reports. The next day, you receive the following listings (see next pages) with a note saying that she could not find the reports but was able to produce these listings from the pharmacy information system.

Question 2a

- Do you think that there has been an increase in carbapenem use in Hospital A and in the 2 ICUs?
- What about third-generation cephalosporin use?
- What about total antibiotic use?

Product name	Hospital A					
	1998		1999		2000	
	Units	EUROs	Units	EUROs	Units	EUROs
CEFOTAXIME 1G SYRINGE x 1	3723	21542.7	1516	8773.0	0	0.0
CEFOTAXIME 1G VIAL x 1	27391	142036.5	34673	160101.5	37431	158136.4
CEFOTAXIME 2G MINIBAG 50ML	0	0.0	239	1000.8	0	0.0
CEFOTAXIME 2G SYRINGE x 1	470	5402.3	40	460.1	0	0.0
CEFOTAXIME 2G VIAL x 1	14946	154996.5	18552	151968.9	21500	182226.1
CEFOTAXIME 500MG VIAL x 1	3083	7996.7	7402	17147.5	6303	13372.1
CEFOXITIN 1G VIAL x 1	5	39.5	5	39.5	0	0.0
CEFTAZIDIME 1G VIAL x 1	1551	12929.4	1466	10893.1	868	6142.2
CEFTAZIDIME 2G VIAL x 1	6371	108349.1	5916	87977.9	6373	90278.3
CEFTAZIDIME 3G VIAL x 1	1452	32979.7	1486	33126.7	1611	36154.3
CEFTAZIDIME 500MG VIAL x 1	275	1249.0	251	774.7	187	743.1
CEFTRIAXONE 250MG VIAL x 1	4	19.0	24	110.7	26	118.6
CEFTRIAXONE 2G VIAL x 1	-18	-703.5	21	894.8	236	7916.1
CEFTRIAXONE 2G VIAL x 1	17	724.1	31	1206.3	0	0.0
IMIPENEM/CILASTATIN 500MG VIAL x 1	3298	55651.2	4465	75149.7	3513	48614.2
MEROPENEM 1G VIAL x 10	103	52554.0	103	45771.5	175	74305.4
MEROPENEM 500MG VIAL x 10	4	1114.6	0	0.0	3	638.7

Question 2b

- Do you have enough information?
- If not, what information would you like to have?

Step 3

To obtain denominator data, you contacted the hospital administration and obtained the following information on bed occupancy:

	Bed occupancy (%)		
	1998	1999	2000
Hospital A	85.8	85.7	87.2
MICU	78.1	77.0	84.9
SICU	76.0	75.8	81.5

Question 3a

- As an example, calculate the number of occupied bed-days in 2000 for the whole hospital, the MICU and the SICU.

No. occupied bed-days (or no. patient-days)

=

No. beds x Occupancy index x No. days in study period

No. occupied bed-days for Hospital A in 2000

=

1200 x 0.872 x 366

=

382982

No. occupied bed-days for MICU in 2000 =

10 x 0.849 x 366 = **3107**

No. occupied bed-days for MICU in 2000 =

8 x 0.815 x 366 = **2386**

Question 3b

- Do you have enough information to conclude about an increase in carbapenem use?
- If not, what information would you like to have?

Step 4

Again, you phone your colleague pharmacist. She says that data on prescriptions to individual patients are not available. Similarly, she says that neither data on the number of grams, nor on the number of daily doses dispensed to the different hospitalization are available.

She remembers reading that the Defined Daily Doses (DDDs) from WHO are available from the Internet, but she does not know where. You search the Internet and find the following on the WHO Collaborating Centre fro Drug Statistics Methodology (http://www.whocc.no/atcddd/):

WHO Collaborating Centre for Drug Statistics Methodology

Norwegian Institute of Public Health

News
ATC/DDD Index
ATC/DDD methodology
ATC
DDD
ATC/DDD alterations, cumulative lists
ATC/DDD publications
Use of ATC/DDD
Courses
Meetings/open session
Deadlines
Links

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International language for drug utilization research

ATC / DDD

The Anatomical Therapeutic Chemical (ATC) classification system and the Defined Daily Dose (DDD) as a measuring unit have become the gold standard for international drug utilization research.

The ATC/DDD system is a tool for exchanging and comparing data on drug use at international, national or local levels.

Welcome to the WHO Collaborating Centre for Drug Statistics Methodology

Last updated: 2012-01-12

www.whocc.no

News

ATC/DDD course 7-8 June 2012
Read

New ATC/DDDs and alterations from the October 2011 meeting
Read

New ATC/DDD included in the index of 2012
Read

Updates of the list of DDDs for combined products
Read

ATCvet

WHO Collaborating Centre for Drug Statistics Methodology

Norwegian Institute of Public Health

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ATC/DDD Index 2012

www.whocc.no/atc_ddd_index/

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

Search query

ATC code or name Search

containing query

ATC code

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

Name

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

Step 4 (continued)

ATC Code	Name	Adm. route	DDD	U
…	…	…	…	…
J01DA10	Cefotaxime	P	4	g
J01DA11	Ceftazidime	P	4	g
J01DA13	Ceftriaxone	P	2	g
…	…	…	…	…
J01DH02	Meropenem	P	2	g
J01DH51	Imipenem and enzyme inhibitor	P	2	g
…	…	…	…	…

Step 4 (continued)

You phone her again because you are not sure about these DDDs. You know that much higher doses are prescribed in the ICUs and lower doses are prescribed to patients with impaired renal functions.

During your discussion on this issue, she mentions that, if you do not use the DDDs as defined by WHO, you will not be able to compare your results with published data from other hospitals and other ICUs. You finally decide to phone Dr. B and obtain the following:

Name	Dose usually used in MICU and SICU
Cefotaxime	6 g
Ceftazidime	6 g
Ceftriaxone	2 g
Meropenem	4 g
Imipenem/cilastatin	2 g

Question 4

- As an example, calculate the level of carbapenem use in 2000 for Hospital A?

No. grams Antibiotic A =
No. grams per tablet x No. tablets per package x No. packages

or

No. grams Antibiotic A =
No. grams per vial x No. vials per package x No. packages

No. DDDs Antibiotic A =
No. grams Antibiotic A / WHO-defined DDD for Antibiotic A

Use of Antibiotic A =
(No. DDDs Antibiotic A / No. occupied bed-days) x 1000

For Hospital A in 2000:

No. grams Ab A = No. grams per vial x No. vials per package x No. packages

No. grams imipenem = 0.5 g per vial x 1 x 3513 vials = 1756.5 g

No. DDDs Ab A = No. grams Ab A / WHO-defined DDD for Ab A

No. DDDs imipenem = 1756.5 / 2 = 878.25 DDDs

No. grams Ab B = No. grams per vial x No. vials per package x No. packages

No. grams meropenem =

(1 g per vial x 10 vials per package x 175 packages) +

(0.5 g per vial x 10 vials per package x 3 packages) = 1765 g

No. DDDs Ab B = No. grams Ab B / WHO-defined DDD for Ab B

No. DDDs meropenem = 1765 / 2 = 882.5 DDDs

Use of Ab class = (No. DDDs in Ab class / No. occupied bed-days) x 1000

No. DDDs carbapenem = 878.25 + 882.5 = 1760.75 DDDs

Carbapenem use =

(1760.75 DDDs / 382982 occupied bed-days) x 1000 =

4.6 DDD/1000 occupied bed-days = 4.6 DDD/1000 patient-days

No. grams Antibiotic A = No. grams per tablet x No. tablets per package x No. packages

or

No. grams Antibiotic A = No. grams per vial x No. vials per package x No. packages

No. PDDs Antibiotic A =
No. grams Antibiotic A / locally defined PDD for Antibiotic A

Use of Antibiotic A =
(No. PDDs Antibiotic A / No. occupied bed-days) x 1000

Step 5

	Hospital A		
	DDD per 1000 occupied bed-days		
	1998	1999	2000
Cefotaxime	42.2	51.7	54.6
Ceftazidime	12.5	11.9	12.1
Ceftriaxone	0.0	0.1	0.6
Third-generation cephalosporins (ATC group J01DA, Total)	54.7	63.7	67.3
Imipenem	2.2	3.0	2.3
Meropenem	1.4	1.4	2.3
Carbapenems (ATC group J01DH, Total)	3.6	4.3	4.6
…	…	…	…
Antibacterials for systemic use (ATC Group J01, Total)	825.5	915.2	868.4

Step 5

	MICU					
	DDD per 1000 occupied bed-days			PDD per 1000 occupied bed-days		
	1998	1999	2000	1998	1999	2000
Cefotaxime	377.2	361.1	363.0	251.5	240.7	242.0
Ceftazidime	357.4	371.6	375.3	238.2	247.7	250.2
Ceftriaxone	0.0	0.0	0.0	0.0	0.0	0.0
Third-generation cephalosporins (ATC group J01DA, Total)	734.6	732.7	738.3	489.7	488.4	492.2
Imipenem	269.7	367.8	261.4	269.7	367.8	261.4
Meropenem	184.1	165.4	284.0	92.1	82.7	142.0
Carbapenems (ATC group J01DH, Total)	453.9	533.3	545.5	361.8	450.6	403.4
...	...	...	...	...	...	...
Antibacterials for systemic use (ATC Group J01, Total)	1567.9	1605.0	1691.2	n/a	n/a	n/a

	SICU					
	DDD per 1000 occupied bed-days			PDD per 1000 occupied bed-days		
	1998	1999	2000	1998	1999	2000
Cefotaxime	361.5	373.0	371.1	241.0	248.6	247.4
Ceftazidime	305.1	307.7	257.3	203.4	205.2	171.6
Ceftriaxone	0.0	0.0	0.0	0.0	0.0	0.0
Third-generation cephalosporins (ATC group J01DA, Total)	666.6	680.7	628.4	444.4	453.8	418.9
Imipenem	18.8	28.6	15.5	18.8	28.6	15.5
Meropenem	0.0	22.6	0.0	0.0	11.3	0.0
Carbapenems (ATC group J01DH, Total)	18.8	51.2	15.5	18.8	39.9	15.5
...	...	...	...	...	...	...
Antibacterials for systemic use (ATC Group J01, Total)	1982.0	2122.7	2068.1	n/a	n/a	n/a

Question 5a

- What do you think about:
  - the levels and the variations of carbapenem use in Hospital A and in the two ICUs?
  - the levels and the variations of third-generation cephalosporin use in Hospital A and in the two ICUs?
  - the levels and the variations of total antibiotic use in Hospital A and in the two ICUs?

Question 5b

- Do you think that you can confirm the worries of Dr. B about a recent increase in the use of these antibiotics?

- If not, what additional information would you like to have?

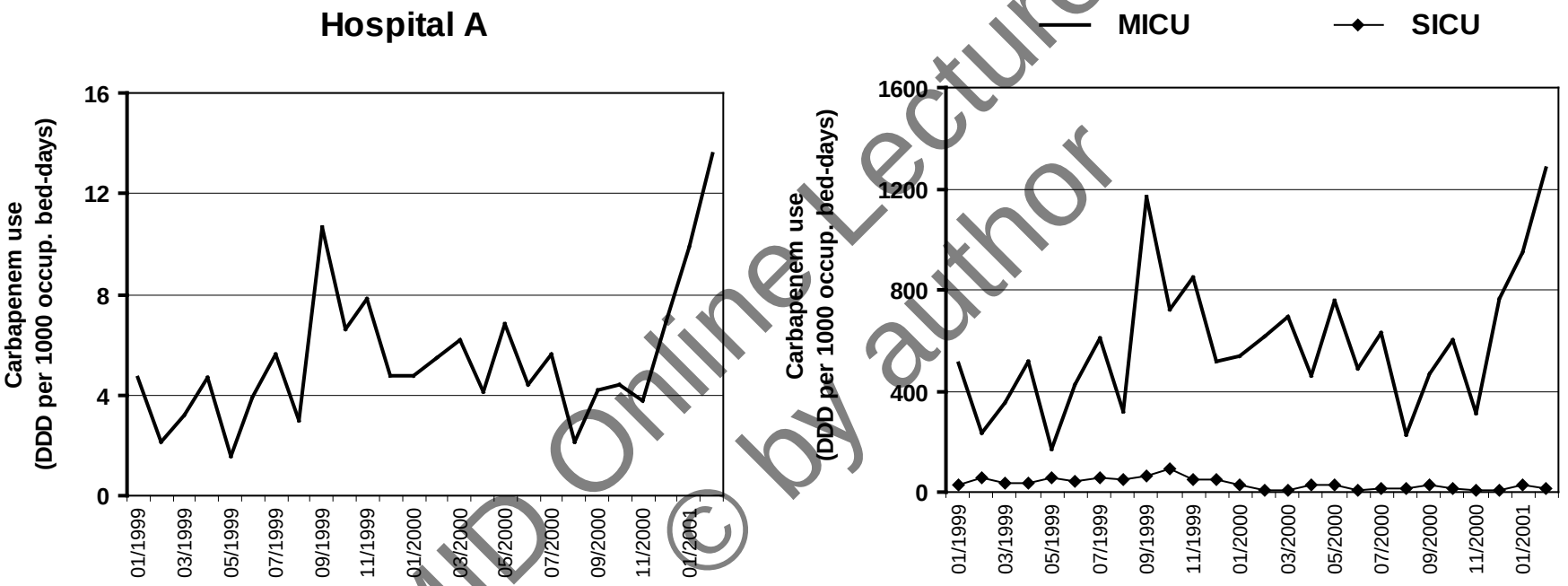
Step 6

You phone the pharmacist and ask for data on carbapenem use in January 2001 and February 2001. You also ask for similar monthly data for 1999 and 2000. She replies that she has no idea about how to obtain data in such format. The solution seems to write a special query to extract them from the pharmacy information system. She will try to have a fellow work on this, but this will take time. Two weeks later, you finally receive the monthly carbapenem use data from the pharmacy. Since, while waiting for these data, you also obtained the number of occupied bed-days each month in Hospital A, in the MICU and in the SICU from January 1999 to February 2001, you are able to produce the following table.

Step 6
(continued)

Month	Carbapenem Use (DDD per 1000 occupied bed-days)		
	Hospital A	MICU	SICU
01/1999	4.7	512.9	27.2
02/1999	2.1	231.5	59.5
03/1999	3.2	351.7	32.6
04/1999	4.7	516.9	37.8
05/1999	1.6	169.7	54.3
06/1999	3.9	425.1	43.2
07/1999	5.6	606.5	59.8
08/1999	3.0	321.8	48.6
09/1999	10.7	1169.2	65.2
10/1999	6.6	719.8	91.9
11/1999	7.8	852.8	48.9
12/1999	4.8	519.2	48.6
01/2000	4.8	539.9	25.1
02/2000	5.5	613.8	10.1
03/2000	6.2	693.6	10.1
04/2000	4.1	461.0	30.2
05/2000	6.8	754.3	25.1
06/2000	4.4	486.6	5.0
07/2000	5.6	627.0	15.1
08/2000	2.1	229.9	15.1
09/2000	4.2	465.3	25.1
10/2000	4.4	602.7	15.1
11/2000	3.8	309.9	10.1
12/2000	6.9	766.7	10.1
01/2001	9.9	946.0	25.3
02/2001	13.6	1283.0	15.5

Step 6
(continued)

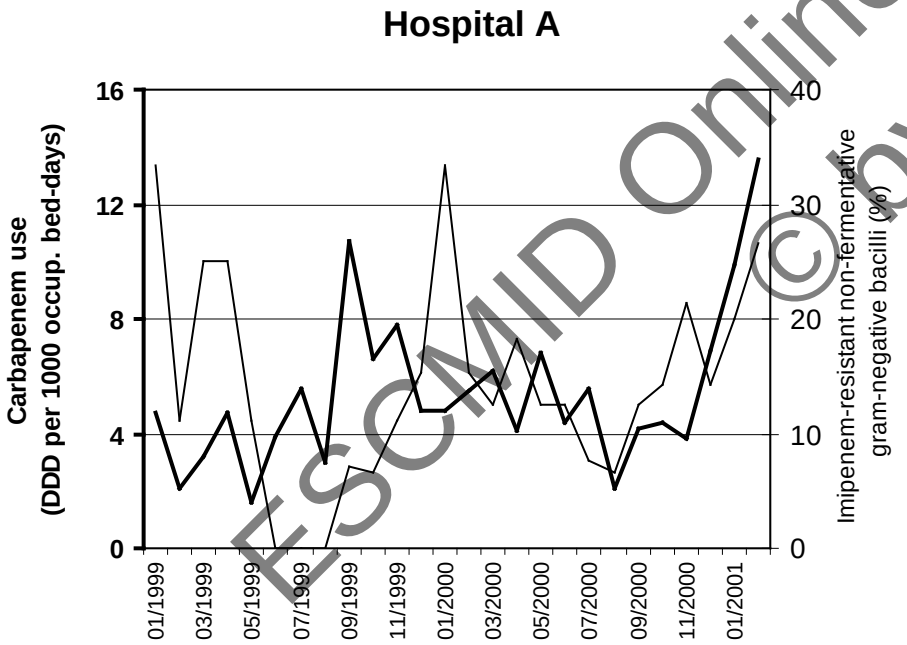


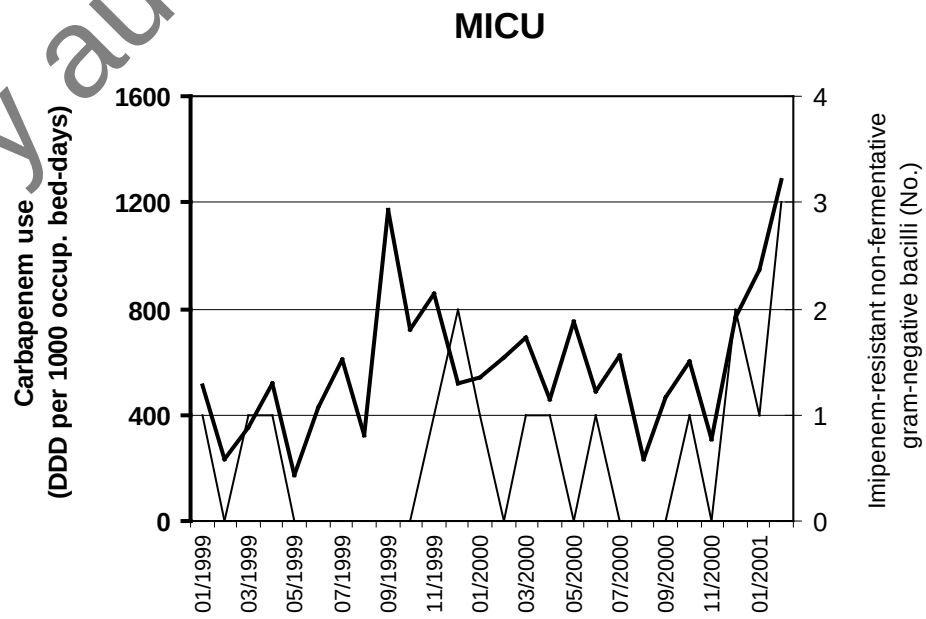
Question 6

- What do you think about these monthly variations of carbapenem use?
- Can you now confirm the worries of Dr. B?
- What would be your next steps?
- What additional information would you like to have?

Conclusion

You decided to search in your own clinical microbiology laboratory database for infections due to carbapenem-resistant non-fermentative gram-negative bacilli (*Pseudomonas aeruginosa* and similar) and produced the following curves on carbapenem use and resistance for the whole hospital and for the MICU (for resistance, only the first isolate of each species per patient has been kept in the database before making the calculations).





Conclusion (continued)

These curves confirmed that carbapenem use recently increased in the MICU and also confirmed Dr. B's worries that this increase already resulted in an increase in the frequency of carbapenem resistance in non-fermentative gram-negative bacilli from this ICU. You immediately contacted Dr. B and both of you agreed to alert the hospital's Infection Control Committee, as well as the Infection Control Department. Your goal was to make sure that all existing and future patients infected with an imipenem-resistant microorganism would be properly isolated to prevent transmission to other patients. Nevertheless, you had no proof that cross-transmission had occurred during the past months. Unfortunately, isolates other than from blood and spinal fluid were not saved in the microbiology laboratory. You decided to prospectively save all carbapenem-resistant gram-negative bacilli isolates and store them in the -80 C freezer for further molecular typing.

Conclusion (continued)

On Thursday March 16, 2001, the Infection Control Committee held a special meeting, where Dr. B and you were invited to present your preliminary results. Possible actions were discussed and the committee emphazised that proper isolation procedures had to be enforced. However, the Infection Control Committtee also agreed with you that excessive carbapenem use was the likely cause for the recent increase in infections due to imipenem-resistant microorganisms.

Following this meeting, you had a short discussion with Dr. B. You agreed that you should contact the hospital's Antibiotic Committee on this issue. On Tuesday March 27, 2001, the Antibiotic Committee held a special meeting where Dr. B and you were invited again to present your results. The Antibiotic Committee decided that the following actions immediately be undertaken:

Conclusion (continued)

- to produce a weekly report on new patients infected by an imipenem-resistant microorganism (by the clinical microbiology laboratory, in collaboration with infection control, to be also reported to the Antibiotic Committee and the Infection Control Committee),
- to examine current hospital guidelines for the treatment of infections,
- to check the processes for delivery of imipenem and meropenem by pharmacy,
- to check the published litterature on possible ways to restrict access to these two antibiotics, so they are only prescribed to the patients who really need them,
- to audit antibiotic prescriptions practices in the hospital, starting with the MICU.

These actions were distributed among the various members of the Antibiotic Committee and everybody agreed to hold another meeting on this issue within the next two weeks.

To be continued…