Measuring Antibiotic Consumption

Khalid Eljaaly, PharmD, MS, BCPS, BCIDP

- Assistant Professor of Infectious Disease Pharmacotherapy, Faculty of Pharmacy, King Abdulaziz University
- Head of Health Interprofessional Research Branch in University Vice-Presidency for Development & Head of Research Unit in Health Promotion Center, KAU, Jeddah, Saudi Arabia
- Honorary Research Fellow, University of Arizona, Tucson, AZ, USA
- @khalideljaaly @khalid_eljaaly2
- Antibiotics in Saudi Arabia (Group)

Objectives

- Discuss the advantages and disadvantages of key measures of antibiotic consumption
- Calculate the defined daily doses and days of therapy

Q: What measures can be used for antibiotic consumption?

Q: Which measures are used in your institution?

Q: Did you collect/calculate them yourselves?

Numerators for Measuring Antimicrobial Consumption

Preferred

- Defined daily doses (DDD)
- Days of therapy (DOT)
- Standardized measures and useful for interfacility comparisons

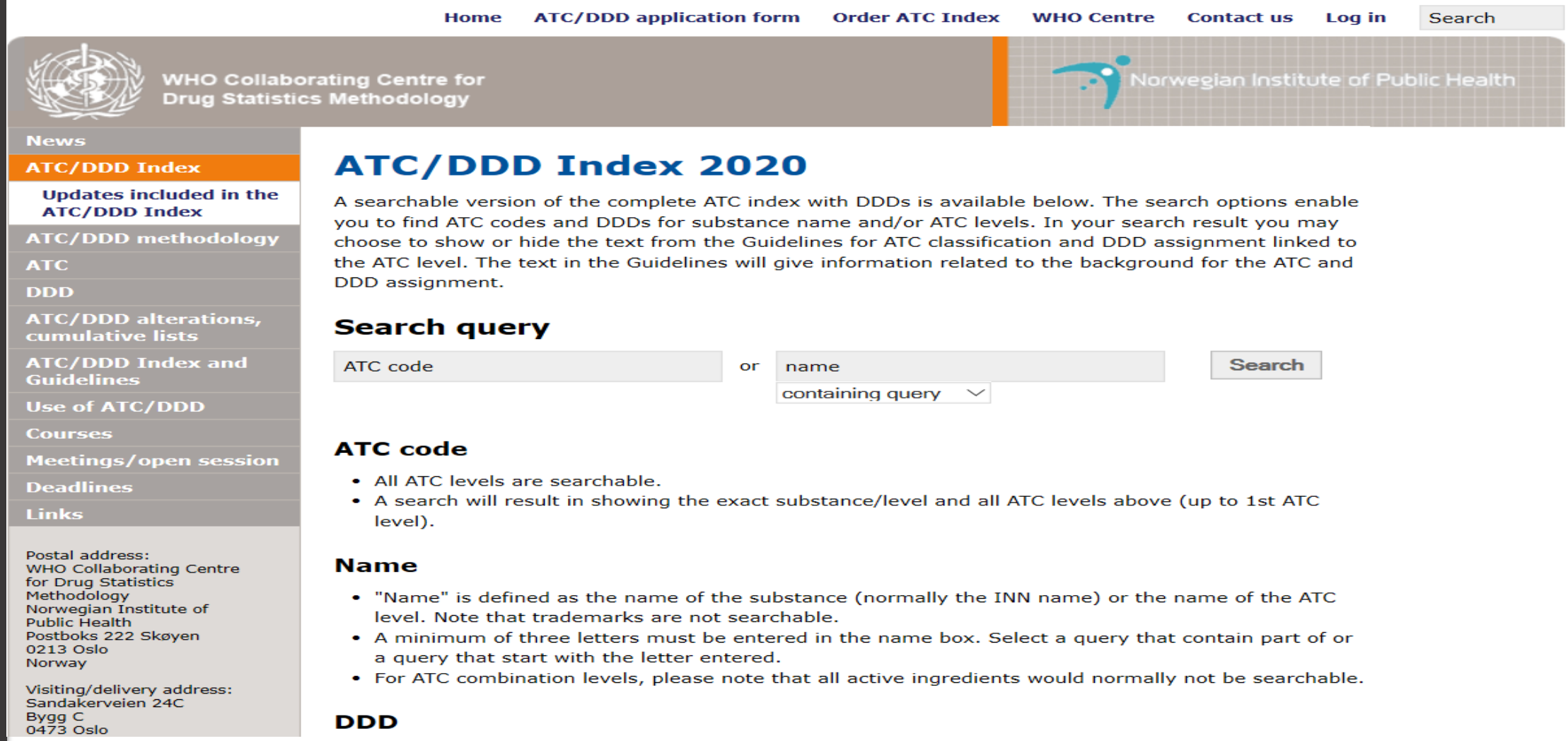
Others

- Length/duration of therapy (LOT)
- Prescribed daily dose
- Number of grams
- Number of tablets
- Number of prescriptions

Defined Daily Doses (DDD)

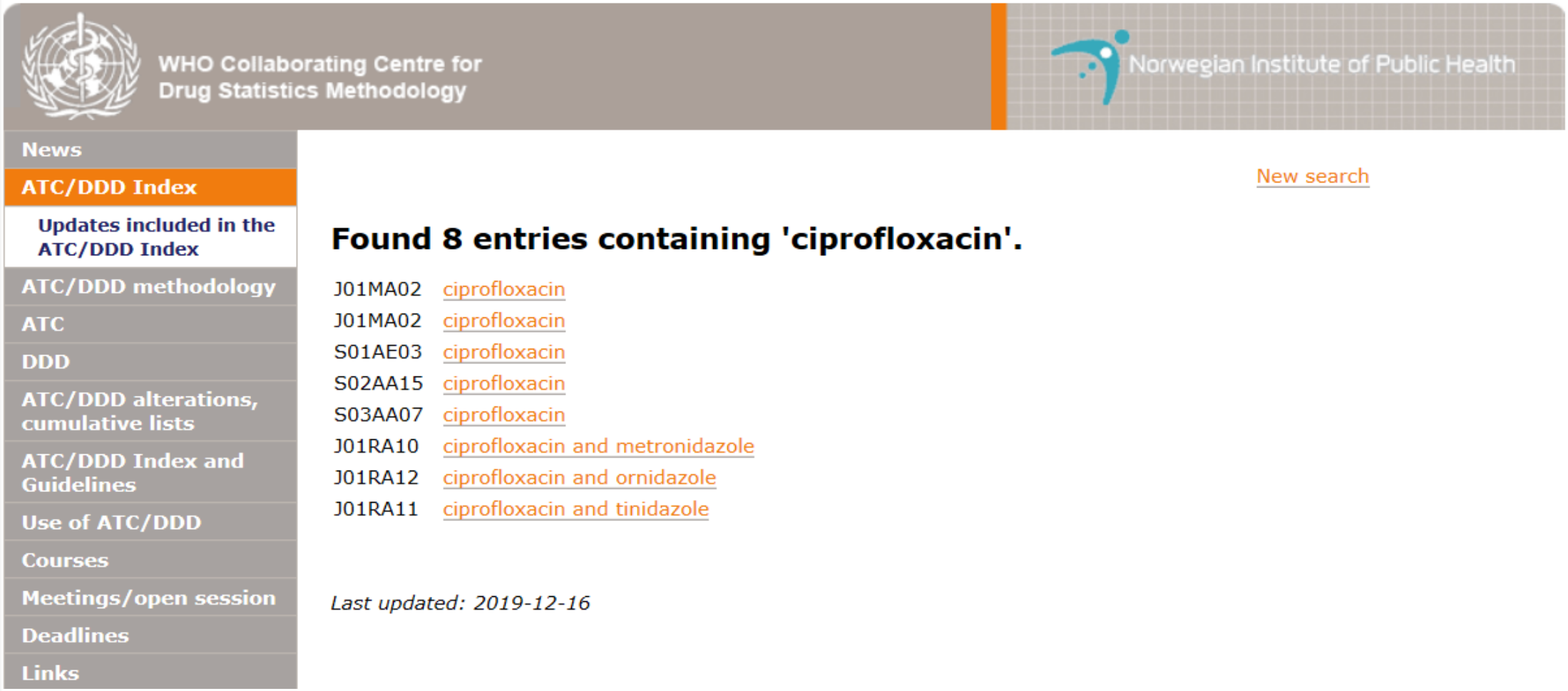
- **Drug DDD=** Number of grams dispensed / WHO DDD
- **WHO DDD:** The assumed average maintenance dose per day for a drug used in its main indication in adults

How to Get the DDD for a Specific Antibiotic/Formulation



World Health Organization Collaborating Centre for Drug Statistics Methodology. ATC Index with DDDs. Available from: http://www.whocc.no/atc_ddd_index

How to Get the DDD for a Specific Antibiotic/Formulation



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How to Get the DDD for a Specific Antibiotic/Formulation

J01 ANTIBACTERIALS FOR SYSTEMIC USE

This group comprises antibacterials for systemic use, except antimycobacterials, which are classified in J04. The antibacterials are classified according to their mode of action and chemistry.
Combinations of two or more systemic antibacterials from different third levels are classified in J01R, except combinations of sulfonamides and trimethoprim, which are classified at a separate 4th level, J01EE.
Combinations of antibacterials and tuberculostatics are classified in J04AM.
Combinations of antibacterials with other drugs, including local anesthetics or vitamins, are classified at separate 5th levels in the respective antibacterial group by using the 50-series.
Inhaled antiinfectives are classified here based on the fact that preparations for inhalation can not be separated from preparations for injection.

J01M QUINOLONE ANTIBACTERIALS

This group comprises quinolone antibacterials, inhibiting the bacterial DNA-gyrase.

J01MA Fluoroquinolones

Flumequine is classified in J01MB.

The DDDs for the fluoroquinolones are mainly based on the treatment of respiratory tract infections. The DDDs for pefloxacin, enoxacin and norfloxacin are based on the treatment of complicated urinary tract infections.

ATC code	Name	DDD	U	Adm.R	Note
J01MA02	ciprofloxacin	1	g	O	
		0.8	g	P	

List of abbreviations

Last updated: 2019-12-16

World Health Organization Collaborating Centre for Drug Statistics Methodology. ATC Index with DDDs. Available from: http://www.whocc.no/atc_ddd_index

Ciprofloxacin DDD Calculation

Form	Strength	# Dispensed	Total # mg	Total # grams	WHO DDD	Cipro DDD
Tab	250 mg	10	?	?	1	?
Tab	500 mg	30	?	?	1	?
IV	2 mg/ml Vial = 100 ml	20	?	?	0.8	?
Total				Total per tab: ? Total per IV: ?		?

Ciprofloxacin DDD Calculation

Form	Strength	# Dispensed	Total # mg	Total # grams	WHO DDD	Cipro DDD
Tab	250 mg	10	2500 mg	2.5 gm	1	2.5 DDD
Tab	500 mg	30	15000 mg	15 gm	1	15 DDD
IV	2 mg/ml Vial = 100 ml	20	4000 mg	4 gm	0.8	5 DDD
Total				Total/tab: 17.5 gm Total/IV: 4 gm		22.5 DDD

Levofloxacin DDD Calculation

- **Levofloxacin DDD = 0.5 g**
  - Levofloxacin 750mg PO q24h X7days
    - **Total DDD for course = ? DDD**
  - Levofloxacin 750mg PO q48h X7days
    - **Total DDD for course = ? DDD**

Levofloxacin DDD Calculation

- **Levofloxacin DDD = 0.5 g**
  - Levofloxacin 750mg PO q24h X7days
    - **Total DDD for course = (0.75g/0.5g) X7d = 10.5 DDD**
  - Levofloxacin 750mg PO q48h X7days
    - **Total DDD for course = (0.75g/0.5g) X4d = 6 DDD**

Piperacillin/Tazobactam DDD

- Piperacillin/tazobactam 4.5 g q6h X7days

ATC code	Name	DDD	U	Adm.R	Note
J01CR05	piperacillin and beta-lactamase inhibitor	14	g	P	Refers to piperacillin

- **Total DDD for course = ? DDD**

Piperacillin/Tazobactam DDD

Piperacillin/tazobactam 4.5 g q6h X7days

ATC code	Name	DDD	U	Adm.R	Note
J01CR05	piperacillin and beta-lactamase inhibitor	14	g	P	Refers to piperacillin

If:

pip/tazo 4.5g → 4g pip

Total pip/tazo 18g → ?g Total pip

?g Total pip = 18 X 4/4.5 = 16g

- **Total DDD for course = (16g/14g) X7d = 8 DDD**

Colistin DDD

- Colistin 4.5 MU IV q12h with 2 MU inh q8h both X7days

ATC code	Name	DDD	U	Adm.R	Note
J01XB01	colistin	3	MU	Inhal.powder	
		3	MU	Inhal.solution	
		9	MU	P	

- **Total DDD for course = [(9MU/9MU) + (6MU/3MU)] X7d = 21 DDD**

Q: What are some advantages and disadvantages of DDD as a consumption measure?

DDD Advantages

- Published by WHO and well known internationally
- Updated annually
- Does not require patient-level data
- Ease of having antibiotic use information for ward/unit/hospital

DDD Disadvantages

- DDD might change
- Based on a standardized dose, not prescribed dose
- Debatable DDD correction factor (e.g., ceftriaxone: 1 g vs 2 g)
- Loading doses
- Need to consider changes in dosing recommendations
- Inappropriate for children

DDD Disadvantages – Cont'd

- Underestimation of use in renally impaired patients
- Overestimation of use in indications required higher doses or longer durations
- PO vs IV (amoxicillin: 3g for IV and 1.5g for PO)
- Piperacillin and enzyme inhibitor (WHO DDD refers to piperacillin)
- Combination therapy of narrow spectrum agents contributes more to DDD than monotherapy of broad spectrum agents

Days of Therapy (DOT) vs. Length of Therapy (LOT)

- **DOT:** number of days a **single** antimicrobial is administered regardless of the number of doses administered or dosage strength
- **LOT:** number of days a patient receives any antimicrobial

DOT and LOT Calculation

	Day 1	Day 2	DOT	LOT
Cefepime	**X**	**X**	**?**	
Vancomycin	**X**	**X**	**?**	
Total			**?**	**?**

DOT and LOT Calculation

	Day 1	Day 2	DOT	LOT
Cefepime	**X**	**X**	**2**	
Vancomycin	**X**	**X**	**2**	
Total			**4**	**2**

DOT and LOT Calculation

	Day 1	Day 2	Day 3	Day 4	Day 5	DOT	LOT
Vancomycin	X	X				?	
Cloxacillin		X	X	X	X	?	
Total						?	?

DOT and LOT Calculation

	Day 1	Day 2	Day 3	Day 4	Day 5	DOT	LOT
Vancomycin	**X**	**X**				**2**	
Cloxacillin		**X**	**X**	**X**	**X**	**4**	
Total						**6**	**5**

DOT and LOT Calculation

	Day 1	Day 2	DOT	LOT
Cefepime	X	X	2	
Vancomycin	X	X	2	
Total			4	2

	Day 1	Day 2	Day 3	Day 4	Day 5	DOT	LOT
Vancomycin	X	X				2	
Cloxacillin		X	X	X	X	4	
Total						6	5

Q: What are some advantages and disadvantages of DOT as a consumption measure?

DOT Advantages

- Recommended in U.S by CDC National Healthcare Safety Network (NHSN) and guidelines by Infectious Disease Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA)
- Not affected by different dosing recommendations or percent of renally impaired patients
- Can be used in paediatrics

DOT Disadvantages

- Combination therapy of narrow spectrum agents contributes more DOT than monotherapy of broad spectrum agents
- More difficult to measure (particularly without computerized records)
- Need for patient level information
- May miss DOT in patients receiving every other day dosing

DDD vs. DOT

Table 1. Comparison of aggregate drug use by defined daily dose (DDDs) per 1000 patient-days and days of therapy (DOTs) per 1000 patient-days for 10 common antibacterial drugs.

Parenteral antibiotic	No. of hospitals	Mean DDDs per 1000 patient-days ± SD	Mean DOTs per 1000 patient-days ± SD	*P*	Mean difference between DDD and DOT, %	Importance of the mean difference[a]	DDD, g/day[b]	Mean administered daily dose, g/day
Cefazolin	130	80.3 ± 35.4	94.3 ± 27.7	<.0001	−17.4	Moderate	3	2.46
Levofloxacin	123	75.6 ± 57.5	74.9 ± 55.8	.3	0.7	Minor	0.5	0.51
Gatifloxacin	53	56.5 ± 67.9	52.1 ± 48.6	.4	7.9	Moderate	0.4	0.42
Ceftriaxone	130	44.9 ± 28.2	62.9 ± 35.9	<.0001	−28.6	Major	2	1.46
Vancomycin	130	46.1 ± 39.0	52.7 ± 26.6	.013	−6.6	Moderate	2	1.63
Piperacillin-tazobactam	127	30.3 ± 20.3	42.7 ± 28.5	<.0001	−40.9	Major	14	10.1
Metronidazole	126	28.1 ± 14.3	32.8 ± 15.4	<.0001	−7.0	Moderate	1.5	1.32
Azithromycin	130	20.8 ± 17.1	18.0 ± 14.8	<.0001	13.4	Moderate	0.5	0.55
Ciprofloxacin	123	18.0 ± 22.1	13.5 ± 16.3	<.0001	24.9	Moderate	0.5	0.72
Clindamycin	129	21.7 ± 12.5	22.3 ± 10.8	.23	−2.8	Minor	1.8	1.79

Polk RE. Clin Infect Dis 2007;44:664-70

Denominator

- Includes all patients, not just those who received antimicrobials
- Enable the measurement of use over time and between hospitals
- Account for fluctuations in hospital activity such as the number of patients in hospital and their length of stay

Denominator

- Examples:
  - Number of patient days: Number of admissions during a designated time X average LOS
  - Occupied bed days
  - Admissions
  - Days present
- Can you access these hospital activity data for your hospital?

Squeezing the Balloon

- Consider measuring and combining similar antimicrobials:
  - All antipseudomonal drugs
  - All anti-MRSA drugs

ANTIMICROBIAL STEWARDSHIP

FROM PRINCIPLES TO PRACTICE

BSAC BRITISH SOCIETY FOR ANTIMICROBIAL CHEMOTHERAPY

CHAPTER 15

AUTHORS: DEBBIE GOFF, CELINE PULCINI, MUSHIRA ABDULAZIZ ENANI, KHALID ELJAALY, KIRSTY BUISING & ARJUN RAJKHOWA

STEWARDSHIP IN DEVELOPED COUNTRIES

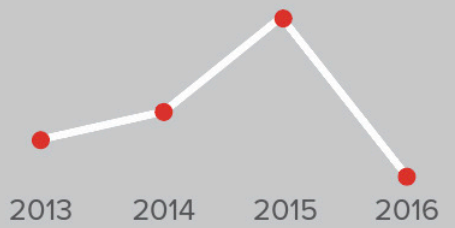
COLISTIN USE

1368 → 554

60%

REDUCTION

ACINETOBACTER RESISTANCE TO COLISTIN



28%REDUCTION

TIGECYCLINE

458 → 246

46%

REDUCTION

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Impact of requiring re-authorization of restricted antibiotics on day 3 of therapy

Khalid Eljaaly[1–4]*, Salwa Elarabi[2], Samah Alshehri[1–4] and David E. Nix[4,5]

[1]Department of Clinical Pharmacy, King Abdulaziz University, Jeddah, Saudi Arabia; [2]Department of Pharmacy Services, St. Elizabeth's Medical Center, Brighton, MA, USA; [3]Department of Pharmacy Practice, Massachusetts College of Pharmacy and Health Sciences University, Boston, MA, USA; [4]Department of Pharmacy Practice and Science, University of Arizona, Tucson, AZ, USA; [5]Department of Medicine, Division of Infectious Diseases, University of Arizona, Tucson, AZ, USA

- Significant reduction in median (IQR) days of therapy for:
  - broad-spectrum Gram-negative agents: 5 (3–6) to 3 (3–5) days (P<0.001)
  - PO vancomycin: 6.5 (6–7) to 3 (3–4.5) days

Proportion of subjects receiving restricted agents for >4days: 57.8% to 30.1% (P<0.001)

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- Honorary Research Fellow, University of Arizona, Tucson, AZ, USA
- @khalideljaaly @khalid_eljaaly2
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