

Supplementary Online Content

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eMethods: Eligible antimicrobial drugs

eTable 1: Demographic and clinical characteristics of surveyed patients

eTable 2: Antimicrobial drug groups administered to surveyed patients

eTable 3: Rationales for antimicrobial drug use

eTable 4: Antimicrobial drugs given for non-infection-related reasons

eTable 5: Antimicrobial drugs where no rationale for use was documented

eTable 6: Common antimicrobial drugs administered to patients to treat infections at selected sites

eTable 7: Common antimicrobial drugs given for treatment of community-onset lower respiratory infections, without other infection sites, in non-neonatal critical care and non-critical care locations

eReferences

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods. Eligible Antimicrobial Drugs

Eligible antimicrobial drugs included those in the following World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) 2nd-level classifications,^{1,2} administered enterally (excluding rectal), parenterally (intravenous or intramuscular) or via inhalation: J01 (antibacterials for systemic use), J02 (antimycotics for systemic use), and selected J04 agents (antimycobacterials). Penicillins reported as “penicillin,” “penicillin G,” or “penicillin G potassium” were considered to be benzylpenicillin and coded as J01CE01. Penicillins reported as “penicillin G benzathine” were considered to be benzathine benzylpenicillin and coded as J01CE08. Penicillins reported as “penicillin V” were considered to be phenoxymethylpenicillin and coded as J01CE02. Selected agents within the following ATC 4th-level classifications were also eligible: J05AB (nucleoside and nucleotide antivirals, excluding drugs used to treat HIV or viral hepatitis), J05AH (neuraminidase inhibitor antivirals), A07AA (intestinal anti-infectives), D01BA (oral/enteral griseofulvin and terbinafine), and P01AB (oral/enteral metronidazole and tinidazole). Additional eligible antimicrobial drugs included rimantidine (J05AC02), amantadine (N04BB01), pentamidine isethionate (P01CX01), and clotrimazole (A01AB18) when the administration route was listed as oral/enteral.

eTable 1. Demographic and clinical characteristics of patients receiving antimicrobial drugs as compared to patients not receiving antimicrobial drugs.

Characteristic	Patients receiving antimicrobial drugs, N=5635	Patients not receiving antimicrobial drugs, N=5647	<i>P</i> value ^a
Sex – no. (%)			<0.001
Male	2648 (47.0)	2386 (42.3)	
Female	2981 (52.9)	3255 (57.6)	
Missing	6 (0.1)	6 (0.1)	
Age category – no. (%)			<0.001
<1 yr	239 (4.2)	912 (16.2)	
1-17 yr	261 (4.6)	218 (3.9)	
18-24 yr	180 (3.2)	282 (5.0)	
25-44 yr	764 (13.6)	922 (16.3)	
45-64 yr	1680 (29.8)	1380 (24.4)	
65-84 yr	1944 (34.5)	1485 (26.3)	
≥85 yr	567 (10.1)	447 (7.9)	
Missing	0	1 (0.02)	
Race – no. (%)			<0.001
American Indian or Alaska Native	66 (1.2)	53 (0.9)	
Asian	123 (2.2)	131 (2.3)	
Black or African-American	896 (15.9)	1009 (17.9)	
Multiple races or other unspecified race	122 (2.2)	132 (2.3)	
Native Hawaiian or other Pacific Islander	7 (0.1)	13 (0.2)	
White	3906 (69.3)	3631 (64.3)	
Unknown or Missing	515 (9.1)	678 (12.0)	
Ethnicity – no. (%)			0.001
Hispanic or Latino	382 (6.8)	464 (8.2)	
Not Hispanic or Latino	1908 (33.9)	1807 (32.0)	
Unknown	3146 (55.8)	3127 (55.4)	
Missing	199 (3.5)	249 (4.4)	
Hospital size category – no. (%)			<0.001

Characteristic	Patients receiving antimicrobial drugs, N=5635	Patients not receiving antimicrobial drugs, N=5647	P value ^a
Small (<150 beds)	2150 (38.2)	1923 (34.1)	
Medium (150-399 beds)	2428 (43.1)	2567 (45.5)	
Large (≥400 beds)	1057 (18.8)	1157 (20.5)	
Hospital location ^b on the survey date – no. (%)			<0.001
Critical care unit	985 (17.5)	722 (12.8)	
Mixed acuity	65 (1.2)	54 (1.0)	
Newborn/special care nursery	29 (0.5)	456 (8.1)	
Specialty care area	268 (4.8)	201 (3.6)	
Step-down unit	239 (4.2)	227 (4.0)	
Ward (not nursery)	4049 (71.9)	3987 (70.6)	
Central line in place on survey date – no. (%)			<0.001
Yes	1483 (26.3)	638 (11.3)	
No	4143 (73.5)	4997 (88.5)	
Missing	9 (0.2)	12 (0.2)	
Urinary catheter in place on survey date – no. (%)			<0.0001
Yes	1787 (31.7)	872 (15.4)	
No	3834 (68.0)	4760 (84.3)	
Missing	14 (0.2)	15 (0.3)	
Ventilator in place on survey date – no. (%)			<0.0001
Yes	392 (7.0)	135 (2.4)	
No	5240 (93.0)	5508 (97.5)	
Missing	3 (0.05)	4 (0.07)	
Median days from admission to survey (IQR)	3 (1-7)	2 (1-5)	<0.0001 [†]
Outcome at hospital discharge – no. (%)			
Died	240 (4.3)	-- ^g	
Survived	5282 (93.7)		
Unknown or missing	113 (2.0)		

Percentages may not add up to 100 due to rounding.

^aChi-square test, except where indicated.

^bLocations as defined in the National Healthcare Safety Network. Critical care units include level II/III and level III neonatal intensive care units.

^cMedian test.

[†]Patient outcome at the time of hospital discharge was assessed for patients on antimicrobial drugs; among those not on antimicrobial drugs, outcome data were available for just 4% of patients; therefore, data are not shown.

eTable 2. Antimicrobial drug groups (World Health Organization Anatomical Therapeutic Chemical 4th level classifications) representing >1% of antimicrobial drugs administered to surveyed patients.

Antimicrobial drug group	Antimicrobial drugs, N=9865
Fluoroquinolones – no. (% of all antimicrobial drugs)	1388 (14.1)
Levofloxacin – no. (% of all drugs in group)	768 (55.3)
Ciprofloxacin – no. (% of all drugs in group)	450 (32.4)
Moxifloxacin – no. (% of all drugs in group)	169 (12.2)
Norfloxacin – no. (% of all drugs in group)	1 (0.1)
Glycopeptides (parenteral) – no. (% of all antimicrobial drugs)	1213 (12.3)
Vancomycin – no. (% of all drugs in group)	1212 (99.9)
Telavancin – no. (% of all drugs in group)	1 (0.1)
Penicillin combinations – no. (% of all antimicrobial drugs)	1081 (11.0)
Piperacillin/tazobactam – no. (% of all drugs in group)	829 (76.7)
Ampicillin/sulbactam – no. (% of all drugs in group)	174 (16.1)
Amoxicillin/clavulanate – no. (% of all drugs in group)	73 (6.8)
Ticarcillin/clavulanate – no. (% of all drugs in group)	5 (0.5)
Third-generation cephalosporins – no. (% of all antimicrobial drugs)	1037 (10.5)
Ceftriaxone – no. (% of all drugs in group)	864 (83.3)
Ceftazidime – no. (% of all drugs in group)	72 (6.9)
Cefotaxime – no. (% of all drugs in group)	69 (6.7)
Cefpodoxime – no. (% of all drugs in group)	21 (2.0)
Cefdinir – no. (% of all drugs in group)	6 (0.6)
Ceftizoxime – no. (% of all drugs in group)	4 (0.4)
Cefixime – no. (% of all drugs in group)	1 (0.1)
First-generation cephalosporins – no. (% of all antimicrobial drugs)	983 (10.0)
Cefazolin – no. (% of all drugs in group)	913 (92.9)
Cephalexin – no. (% of all drugs in group)	67 (6.8)
Cefadroxil – no. (% of all drugs in group)	3 (0.3)
Macrolides – no. (% of all antimicrobial drugs)	485 (4.9)
Azithromycin – no. (% of all drugs in group)	444 (91.5)
Erythromycin – no. (% of all drugs in group)	28 (5.8)
Clarithromycin – no. (% of all drugs in group)	13 (2.7)
Imidazole derivatives (parenteral) – no. (% of all antimicrobial drugs)	420 (4.3)
Metronidazole	420 (100)
Triazole antifungals – no. (% of all antimicrobial drugs)	364 (3.7)
Fluconazole – no. (% of all drugs in group)	305 (83.8)
Voriconazole – no. (% of all drugs in group)	49 (13.5)
Posaconazole – no. (% of all drugs in group)	7 (1.9)
Itraconazole – no. (% of all drugs in group)	3 (0.8)
Carbapenems – no. (% of all antimicrobial drugs)	313 (3.2)
Meropenem – no. (% of all drugs in group)	105 (33.6)
Ertapenem – no. (% of all drugs in group)	92 (29.4)
Doripenem – no. (% of all drugs in group)	58 (18.5)
Imipenem – no. (% of all drugs in group)	58 (18.5)
Lincosamides – no. (% of all antimicrobial drugs)	289 (2.9)
Clindamycin – no. (% of all drugs in group)	289 (100)

Antimicrobial drug group	Antimicrobial drugs, N=9865
Intestinal anti-infectives – no. (% of all antimicrobial drugs) Vancomycin (oral/enteral) – no. (% of all drugs in group) Nystatin – no. (% of all drugs in group) Rifaximin – no. (% of all drugs in group) Neomycin – no. (% of all drugs in group)	281 (2.9) 123 (43.8) 117 (41.6) 39 (13.9) 2 (0.7)
Aminoglycosides other than streptomycin – no. (% of all antimicrobial drugs) Gentamicin – no. (% of all drugs in group) Tobramycin – no. (% of all drugs in group) Amikacin – no. (% of all drugs in group)	247 (2.5) 165 (66.8) 72 (29.2) 10 (4.1)
Extended-spectrum penicillins – no. (% of all antimicrobial drugs) Ampicillin – no. (% of all drugs in group) Amoxicillin – no. (% of all drugs in group) Piperacillin – no. (% of all drugs in group)	237 (2.4) 161 (67.9) 58 (24.5) 18 (7.6)
Nucleoside and nucleotide antivirals (excluding reverse transcriptase inhibitors) – no. (% of all antimicrobial drugs) Acyclovir – no. (% of all drugs in group) Valgancyclovir – no. (% of all drugs in group) Valacyclovir – no. (% of all drugs in group) Ganciclovir – no. (% of all drugs in group) Famciclovir – no. (% of all drugs in group) Cidofovir – no. (% of all drugs in group)	204 (2.1) 135 (66.2) 30 (14.7) 23 (11.3) 13 (6.4) 2 (1.0) 1 (0.5)
Fourth-generation cephalosporins – no. (% of all antimicrobial drugs) Cefepime – no. (% of all drugs in group)	193 (2.0) 193 (100)
Sulfonamide and trimethoprim combinations – no. (% of all antimicrobial drugs) Trimethoprim/sulfamethoxazole – no. (% of all drugs in group)	179 (1.8) 179 (100)
Nitroimidazole derivatives (oral/enteral) – no. (% of all antimicrobial drugs) Metronidazole – no. (% of all drugs in group)	179 (1.8) 179 (100)
Other antibacterials Linezolid – no. (% of all drugs in group) Daptomycin – no. (% of all drugs in group)	171 (1.7) 110 (64.3) 61 (35.7)
Tetracyclines – no. (% of all antimicrobial drugs) Doxycycline – no. (% of all drugs in group) Tigecycline – no. (% of all drugs in group) Minocycline – no. (% of all drugs in group) Tetracycline – no. (% of all drugs in group)	129 (1.3) 86 (66.7) 29 (22.5) 11 (8.5) 3 (2.3)
Second-generation cephalosporins – no. (% of all antimicrobial drugs) Cefoxitin – no. (% of all drugs in group) Cefuroxime – no. (% of all drugs in group) Cefotetan – no. (% of all drugs in group)	127 (1.3) 67 (52.8) 39 (30.7) 21 (16.5)

Percentages may not add up to 100 due to rounding.

eTable 3. Rationale for use within antimicrobial drug groups defined in accordance with the World Health Organization Anatomical Therapeutic Chemical Classification 4th level. Drug groups representing >1% of antimicrobial drugs given to surveyed patients are shown.

Antimicrobial drug group	Rationale ^a					
	Infection treatment only, No. (%)	Medical prophylaxis only, No. (%)	Surgical prophylaxis only, No. (%)	Non-infection related rationale only, No. (%)	Multiple rationales, No. (%)	No documented rationale, No. (%)
Fluoroquinolones (N=1388)	1222 (88.0)	48 (3.5)	38 (2.7)	0	7 (0.5)	73 (5.3)
Glycopeptides (N=1213)	1098 (90.5)	4 (0.3)	86 (7.1)	0	6 (0.5)	19 (1.6)
Penicillin combinations (N=1081)	986 (91.2)	9 (0.8)	44 (4.1)	0	14 (1.3)	28 (2.6)
Cephalosporins, 3 rd generation (N=1037)	982 (94.7)	12 (1.2)	17 (1.6)	0	1 (0.1)	25 (2.4)
Cephalosporins, 1 st generation (N=983)	202 (20.6)	24 (2.4)	710 (72.2)	0	8 (0.8)	39 (4.0)
Macrolides (N=485)	410 (84.5)	35 (7.2)	1 (0.2)	16 (3.3)	1 (0.2)	22 (4.5)
Imidazole derivatives (parenteral) (N=420)	344 (81.9)	5 (1.2)	41 (9.8)	1 (0.2)	3 (0.7)	26 (6.2)
Triazole antifungals (N=364)	247 (67.9)	78 (21.4)	2 (0.6)	0	1 (0.3)	36 (9.9)
Carbapenems (N=313)	287 (91.7)	1 (0.3)	19 (6.1)	0	2 (0.6)	4 (1.3)
Lincosamides (N=289)	198 (68.5)	5 (1.7)	75 (26.0)	0	2 (0.7)	9 (3.1)
Intestinal anti-infectives (N=281)	181 (64.4)	23 (8.2)	0	19 (6.8)	1 (0.4)	57 (20.3)
Aminoglycosides other than streptomycin (N=247)	197 (79.8)	11 (4.5)	27 (10.9)	0	0	12 (4.9)
Extended-spectrum penicillins (N=237)	175 (73.8)	40 (16.9)	12 (5.1)	0	1 (0.4)	9 (3.8)
Nucleoside and nucleotide antivirals (excluding reverse transcriptase inhibitors) (N=204)	79 (38.7)	99 (48.5)	1 (0.5)	0	2 (1.0)	23 (11.3)
Cephalosporins, 4 th generation (N=193)	185 (95.9)	2 (1.0)	0	0	0	6 (3.1)
Sulfonamide and trimethoprim combinations (N=179)	96 (53.6)	66 (36.9)	0	0	1 (0.6)	16 (8.9)
Nitroimidazole derivatives (oral/enteral) (N=179)	166 (92.7)	6 (3.4)	0	1 (0.6)	0	6 (3.4)
Other antibacterials (N=171)	167 (97.7)	0	1 (0.6)	0	0	3 (1.8)

Antimicrobial drug group	Rationale ^a					
	Infection treatment only, No. (%)	Medical prophylaxis only, No. (%)	Surgical prophylaxis only, No. (%)	Non-infection related rationale only, No. (%)	Multiple rationales, No. (%)	No documented rationale, No. (%)
Tetracyclines (N=129)	111 (86.1)	2 (1.6)	1 (0.8)	1 (0.8)	1 (0.8)	13 (10.1)
Cephalosporins, 2 nd generation (N=127)	46 (36.2)	3 (2.4)	72 (56.7)	0	2 (1.6)	4 (3.2)
<i>All antimicrobial drugs (N=9865)</i>	7590 (76.9)	570 (5.8)	1156 (11.7)	40 (0.4)	54 (0.5)^b	455 (4.6)

Percentages may not add up to 100 due to rounding.

^aRationale categories as shown in the table are mutually exclusive.

^bAntimicrobial drugs with multiple rationales listed include: 41 drugs given for both infection treatment and surgical prophylaxis; 10 drugs given for both infection treatment and medical prophylaxis; 2 drugs given for both surgical and medical prophylaxis; and 1 drug given for medical prophylaxis and for a non-infection-related reason.

eTable 4: Antimicrobial drugs given for non-infection-related reasons (N=41).

Antimicrobial drug	No. (%)
Rifaximin	17 (41.5)
Erythromycin	12 (29.3)
Azithromycin	4 (9.8)
Neomycin, oral/enteral	2 (4.9)
Amantadine	1 (2.4)
Clotrimazole	1 (2.4)
Doxycycline	1 (2.4)
Metronidazole, parenteral	1 (2.4)
Metronidazole, oral/enteral	1 (2.4)
Nystatin	1 (2.4)

Percentages may not add up to 100 due to rounding.

eTable 5. Antimicrobial drugs for which no rationale for use was documented (N=455). Drug groups are defined in accordance with the World Health Organization Anatomical Therapeutic Chemical Classification 4th level. Drug groups representing >1% of antimicrobial drugs with no documented rationale for use are shown.

Antimicrobial drug group	No. (%)
Fluoroquinolones	73 (16.0)
Intestinal anti-infectives	57 (12.5)
Cephalosporins, 1 st generation	39 (8.6)
Triazole antifungals	36 (7.9)
Penicillin combinations	28 (6.2)
Imidazole derivatives (parenteral)	26 (5.7)
Cephalosporins, 3 rd generation	25 (5.5)
Nucleoside and nucleotide antivirals, excluding reverse transcriptase inhibitors	23 (5.1)
Macrolides	22 (4.8)
Glycopeptides	19 (4.2)
Sulfonamide and trimethoprim combinations	16 (3.5)
Tetracyclines	13 (2.9)
Aminoglycosides other than streptomycin	12 (2.6)
Extended-spectrum penicillins	9 (2.0)
Lincosamides	9 (2.0)
Cephalosporins, 4 th generation	6 (1.3)
Nitroimidazole derivatives (oral/enteral)	6 (1.3)

eTable 6. Common antimicrobial drugs administered to patients to treat infections at selected sites, overall and by site of infection. Each column of the table includes antimicrobial drugs given for the specified infection site with or without other infection sites.

Rank	Patients given antimicrobial drugs for any infection (No., %), N=4278	Patients given antimicrobial drugs for LRI (No., %), N=1480	Patients given antimicrobial drugs for UTI (No., %), N=955	Patients given antimicrobial drugs for SSTI (No., %), N=688	Patients given antimicrobial drugs for GTI (No., %), N=537	Patients given antimicrobial drugs for BSI (No., %), N=401	Patients given antimicrobial drugs for UND (No., %), N=364
1	Vancomycin ^a (1103, 25.8)	Levofloxacin (377, 25.5)	Ceftriaxone (297, 31.1)	Vancomycin ^a (331, 48.1)	Metronidazole ^a (199, 37.1)	Vancomycin ^a (163, 40.6)	Vancomycin ^a (130, 35.7)
2	Ceftriaxone (825, 19.3)	Azithromycin (353, 23.9)	Ciprofloxacin (179, 18.7)	Pip/tazo (134, 19.5)	Metronidazole ^b (127, 23.6)	Pip/tazo (74, 18.5)	Pip/taz (80, 22.0)
3	Pip/tazo (788, 18.4)	Ceftriaxone (339, 22.9)	Levofloxacin (153, 16.0)	Clindamycin (85, 12.4)	Vancomycin ^b (108, 20.1)	Ceftriaxone (57, 14.2)	Ampicillin (57, 15.7)
4	Levofloxacin (694, 16.2)	Pip/tazo (323, 21.8)	Pip/tazo (107, 11.2)	Cefazolin (78, 11.3)	Pip/taz (73, 13.6)	Levofloxacin (34, 8.5)	Gentamicin (49, 13.5)
5	Azithromycin (390, 9.1)	Vancomycin ^a (304, 20.5)	Vancomycin ^a (106, 11.1)	Ceftriaxone (59, 8.6)	Ciprofloxacin (63, 11.7)	Ampicillin (28, 7.0)	Levofloxacin (48, 13.2)
6	Ciprofloxacin (385, 9.0)	Moxifloxacin (129, 8.7)	Fluconazole (53, 5.5)	Levofloxacin (47, 6.8)	Levofloxacin (57, 10.6)	Cefazolin (24, 6.0)	Cefepime (39, 10.7)
7	Metronidazole ^a (347, 8.1)	Cefepime (73, 4.9)	TMZ (41, 4.3)	Amp/sulb (41, 6.0) Ciprofloxacin (41, 6.0)	Vancomycin ^a (38, 7.1)	Ciprofloxacin (23, 5.7)	Ceftriaxone (37, 10.2)
8	Fluconazole (219, 5.1)	Clindamycin (57, 3.9)	Cefazolin (33, 3.5)	Fluconazole (29, 4.2)	Ceftriaxone (25, 4.7)	Cefepime (19, 4.7)	Metronidazole ^a (23, 6.3)
9	Clindamycin (199, 4.7)	Ciprofloxacin (51, 3.4)	Cefepime (31, 3.2)	Cefepime (27, 3.9)	Fluconazole (19, 3.5)	Daptomycin (18, 4.5)	Cefotaxime (22, 6.0)
10	Cefepime (185, 4.3)	Fluconazole (47, 3.2) Linezolid (47, 3.2)	Gentamicin (22, 2.3)	Linezolid (26, 3.8)	Amp/sulb (15, 2.8)	Gentamicin (15, 3.7)	Meropenem (20, 5.5)

LRI=lower respiratory infection. UTI=urinary tract infection. SST=skin and soft tissue infection. GTI=gastrointestinal tract infection. UND=undetermined infection site, including empiric therapy. BSI=bloodstream infection. Pip/tazo=piperacillin/tazobactam. Amp/sulb=ampicillin/sulbactam. TMZ=trimethoprim/sulfamethoxazole.

^aIndicates parenteral form of the antimicrobial drug.

^bIndicates oral/enteral form of the antimicrobial drug.

eTable 7. Common antimicrobial drugs given for treatment of community-onset lower respiratory tract infections, without other infection sites,^a in non-neonatal critical care and non-critical care locations

^aDrugs shown are those used to treat lower respiratory tract infections only, without other infection sites.

^bExcludes antimicrobial drugs given to patients in level III and level II/III neonatal intensive care units.

^cExcludes antimicrobial drugs given to patients in neonatal step-down units and well-baby nurseries

^dParenteral formulation of the drug.

Rank	No. of Drugs (%)	
	Non-neonatal critical care, ^b N=366	Non-neonatal non-critical care, ^c N=1248
1	Levofloxacin 54 (14.8)	Azithromycin 246 (19.7)
2	Vancomycin ^d 53 (14.5)	Ceftriaxone 217 (17.4)
3	Piperacillin/tazobactam 48 (13.1)	Levofloxacin 205 (16.4)
4	Azithromycin 45 (12.3) Ceftriaxone 45 (12.3)	Vancomycin ^d 99 (7.9)
5	Moxifloxacin 11 (3.0)	Piperacillin/tazobactam 92 (7.4)

eReferences

- 1) World Health Organization Collaborating Centre for Drug Statistics Methodology. Anatomic Therapeutic Classification structure and principles. http://www.whocc.no/atc/structure_and_principles/. Accessed December 11, 2013.
- 2) World Health Organization Collaborating Centre for Drug Statistics Methodology. Anatomic Therapeutic Classification index. http://www.whocc.no/atc_ddd_index/. Accessed July 9, 2013.