

Appendix 1. Indications for Antibiotics and Corresponding ICD-9-CM Codes

Cesarean delivery

ICD-9-CM procedure code 74.x or diagnosis code 669.7x

Preterm premature rupture of membranes (requires two codes)

ICD-9-CM diagnosis code 644.20 or 644.21 **and**

ICD-9-CM diagnosis code 658.10, 658.11, 658.13, 658.20, 658.21, or 658.23

Chorioamnionitis

ICD-9-CM diagnosis 658.40, 658.41, or 658.43

Endometritis

ICD-9-CM diagnosis 670.0x, 670.1x, or 670.2x

Group B streptococcus colonization

ICD-9-CM diagnosis code V02.51

Infection

ICD9 diagnosis codes for pyelonephritis, pneumonia, systemic inflammatory response syndrome, sepsis, acute appendicitis, urinary tract infection, cholecystitis, or diverticulitis

3rd and 4th degree vaginal lacerations

ICD-9-CM diagnosis code 664.2x or 664.3x

Uterine tamponade

ICD-9-CM procedure code 75.8

Manual placenta extraction

ICD-9-CM procedure code 75.4

ICD-9-CM International Classification of Diseases, 9th Revision, Clinical Modification

Appendix 2. Antibiotics Included in Analysis

Penicillins

Amoxicillin
Amoxicillin/clavulanic acid
Ampicillin
Ampicillin/sulbactam
Benzylpenicillin (Penicillin G)
Carbenicillin
Cloxacillin
Dicloxacillin
Methicillin
Nafcillin
Oxacillin
Penicillin
Phenoxymethylpenicillin (Penicillin V)
Piperacillin/tazobactam
Ticaricillin/clavulanic acid

Cephalosporins

First generation

Cephalothin
Cephapirin
Cephradine
Cephalexin
Cefazolin
Cefadroxil

Second generation

Cefamandole
Cefaclor
Cefotetan
Cefoxitin
Cefuroxime
Cefmetazole
Cefonicid
Cefprozil
Loracarbef

Third generation

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Ceftriaxone
Ceftazidime
Cefotaxime
Ceftizoxime
Ceftibuten
Cefixime
Cefperazone
Cefpodoxime
Cefdinir

Fourth generation

Cefepime

Aminoglycosides

Amikacin
Gentamicin
Tobramycin

Carbapenems

Doripenem
Ertapenem
Imipenem/cilastatin
Meropenem

Macrolides

Azithromycin
Clarithromycin
Clindamycin
Erythromycin
Fidaxomicin
Spiramycin

Fluoroquinolones

Ciprofloxacin
Levofloxacin
Moxifloxacin
Ofloxacin

Tetracyclines

Doxycycline
Tetracycline

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Others

Metronidazole

Vancomycin

Aztreonam

Linezolid

Daptomycin

Chloramphenicol

Sulfamethoxazole/trimethoprim

Nitrofurantoin

Actinomycin

Rifampin

The antibiotics in the table were queried in the Perspective database for this analysis along with common trade names.

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Appendix 3. Use of Individual Antibiotics Among Women by Type of Delivery

Antibiotics	Number of patients	Percent of women (%)
Cesarean delivery		
Cefazolin	1,307,914	68.86
Erythromycin	283,788	14.94
Ampicillin	175,933	9.26
Clindamycin	167,661	8.8
Cefoxitin	124,195	6.5
Gentamicin	91,234	4.8
Penicillin	89,248	4.7
Cefotetan	32,427	1.7
Azithromycin	28,661	1.5
Cephalexin	22,516	1.2
Metronidazole	21,898	1.2
Vaginal delivery (with indication for antibiotics)		
Penicillin	267,698	35.0
Ampicillin	246,630	32.2
Erythromycin	133,419	17.4
Clindamycin	52,803	6.9
Gentamicin	40,686	5.3
Cefazolin	35,354	4.6
Vancomycin	14,837	1.9
Azithromycin	14,078	1.8
Amoxicillin	9,711	1.3
Vaginal delivery with no indication for antibiotics		
Erythromycin	467,585	16.3
Ampicillin	222,834	7.8
Penicillin	143,587	5.0
Cefazolin	69,549	2.4
Clindamycin	42,375	1.5
Gentamicin	30,877	1.1

47 additional antibiotics were administered to <1% of women undergoing cesarean, 46 to women undergoing vaginal delivery with an indication for antibiotics, and 49 to vaginal delivery with no indication for antibiotics. Evidence-based diagnoses for administration of antibiotics includes preterm premature rupture of membranes, endometritis, chorioamnionitis, GBS colonization, and other infectious complications.

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Appendix 4. Adjusted and Unadjusted Models for Antibiotic Administration During Vaginal Delivery Hospitalizations With an Indication for Antibiotics

	Unadjusted model risk ratio (95% CI)	Adjusted model adjusted risk ratio (95% CI)
Year		
2006	Referent	Referent
2007	0.99 (0.98, 0.99)**	0.99 (0.98, 0.99)**
2008	0.97 (0.96, 0.97)**	0.97 (0.97, 0.98)**
2009	0.97 (0.97, 0.98)**	0.97 (0.97, 0.98)**
2010	0.96 (0.95, 0.96)**	0.96 (0.96, 0.96)**
2011	0.96 (0.95, 0.96)**	0.97 (0.96, 0.97)**
2012	0.95 (0.95, 0.96)**	0.96 (0.96, 0.97)**
2013	0.95 (0.95, 0.95)**	0.96 (0.95, 0.96)**
2014	0.92 (0.92, 0.92)**	0.92 (0.92, 0.93)**
2015 1 st quarter	0.91 (0.90, 0.92)**	0.92 (0.91, 0.92)**
Age in years		
18-24	Referent	Referent
25-34	0.97 (0.97, 0.97)**	0.98 (0.98, 0.99)**
35-39	0.95 (0.95, 0.96)**	0.97 (0.97, 0.98)**
≥ 40	0.95 (0.95, 0.96)**	0.98 (0.97, 0.98)**
Marital Status		
Married	Referent	Referent
Single	1.03 (1.03, 1.03)**	1.03 (1.02, 1.03)**
Other/Unknown	1.01 (1.01, 1.01)**	1.00 (1.00, 1.01)
Race		
White	Referent	Referent
Black	1.01 (1.01, 1.02)**	1.00 (1.00, 1.00)
Other	0.99 (0.98, 0.99)**	0.99 (0.99, 0.99)**
Unknown	0.95 (0.90, 1.00)*	0.96 (0.91, 1.01)
Payer		
Medicare	1.02 (1.00, 1.03)*	1.03 (1.01, 1.04)**
Medicaid	1.02 (1.01, 1.02)**	1.00 (1.00, 1.00)
Commercial	Referent	Referent
Uninsured	0.97 (0.96, 0.98)**	0.97 (0.96, 0.98)**
Unknown	0.98 (0.97, 0.99)**	0.99 (0.98, 1.00)*
Rurality		
Urban	1.06 (1.05, 1.06)**	1.10 (1.10, 1.11)**

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Rural	Referent	Referent
Hospital Teaching		
No	Referent	Referent
Yes	0.92 (0.92, 0.92)**	0.91 (0.90, 0.91)**
Hospital Bed Size		
<400	Referent	Referent
400-600	0.99 (0.99, 1.00)**	1.01 (1.01, 1.01)**
>600	0.95 (0.95, 0.95)**	1.01 (1.01, 1.02)**
Region of Hospital		
Northeastern	Referent	Referent
Midwest	1.24 (1.23, 1.24)**	1.21 (1.21, 1.22)**
South	1.12 (1.12, 1.13)**	1.08 (1.08, 1.09)**
West	1.12 (1.12, 1.13)**	1.07 (1.07, 1.08)**
Postpartum hemorrhage	1.05 (1.04, 1.05)**	1.05 (1.04, 1.05)**
Preeclampsia	1.03 (1.02, 1.03)**	1.03 (1.02, 1.03)**
Gestational diabetes	1.00 (1.00, 1.01)	1.02 (1.01, 1.02)**
Pregestational diabetes	1.03 (1.02, 1.04)**	1.04 (1.03, 1.06)**
Multiple gestation	1.01 (1.00, 1.02)	1.02 (1.01, 1.03)*

Adjusted model includes all of the factors in the table as well as adjustment for hospital-level clustering. *CI*, confidence interval. * $p < 0.05$; ** $p < 0.01$. Evidence-based diagnoses for administration of antibiotics includes preterm premature rupture of membranes, endometritis, chorioamnionitis, GBS colonization, and other infectious complications.

Appendix 5. Adjusted and Unadjusted Models for Antibiotic Administration During Cesarean Delivery Hospitalizations

	Unadjusted model risk ratio (95% CI)	Adjusted model adjusted risk ratio (95% CI)
Year		
2006	Referent	Referent
2007	1.00 (0.99, 1.00)*	1.00 (0.99, 1.00)*
2008	0.99 (0.99, 0.99)**	0.99 (0.99, 1.00)**
2009	1.00 (1.00, 1.01)*	1.01 (1.00, 1.01)**
2010	1.03 (1.02, 1.03)**	1.03 (1.02, 1.03)**
2011	1.03 (1.03, 1.03)**	1.03 (1.03, 1.04)**
2012	1.04 (1.03, 1.04)**	1.04 (1.04, 1.04)**
2013	1.04 (1.03, 1.04)**	1.03 (1.03, 1.04)**
2014	1.03 (1.03, 1.03)**	1.02 (1.02, 1.03)**
2015 1 st quarter	1.03 (1.02, 1.03)**	1.02 (1.02, 1.03)**
Age in years		
18-24	Referent	Referent
25-34	0.97 (0.97, 0.97)**	0.99 (0.99, 0.99)**
35-39	0.95 (0.95, 0.95)**	0.98 (0.98, 0.99)**
≥ 40	0.94 (0.94, 0.94)**	0.98 (0.98, 0.98)**
Marital Status		
Married	Referent	Referent
Single	1.02 (1.02, 1.02)**	1.01 (1.01, 1.01)**
Other/Unknown	0.98 (0.98, 0.98)**	0.98 (0.98, 0.98)**
Race		
White	Referent	Referent
Black	1.01 (1.01, 1.01)**	1.00 (1.00, 1.00)*
Other	0.96 (0.96, 0.96)**	0.98 (0.98, 0.98)**
Unknown	1.04 (1.02, 1.06)**	1.01 (1.00, 1.03)
Payer		
Medicare	1.02 (1.02, 1.03)**	1.03 (1.03, 1.04)**
Medicaid	1.04 (1.03, 1.04)**	1.01 (1.01, 1.01)**
Commercial	Referent	Referent
Uninsured	1.03 (1.02, 1.03)**	1.01 (1.01, 1.01)**
Unknown	1.01 (1.01, 1.02)**	1.00 (1.00, 1.00)
Rurality		
Urban	0.97 (0.97, 0.97)**	1.02 (1.02, 1.02)**

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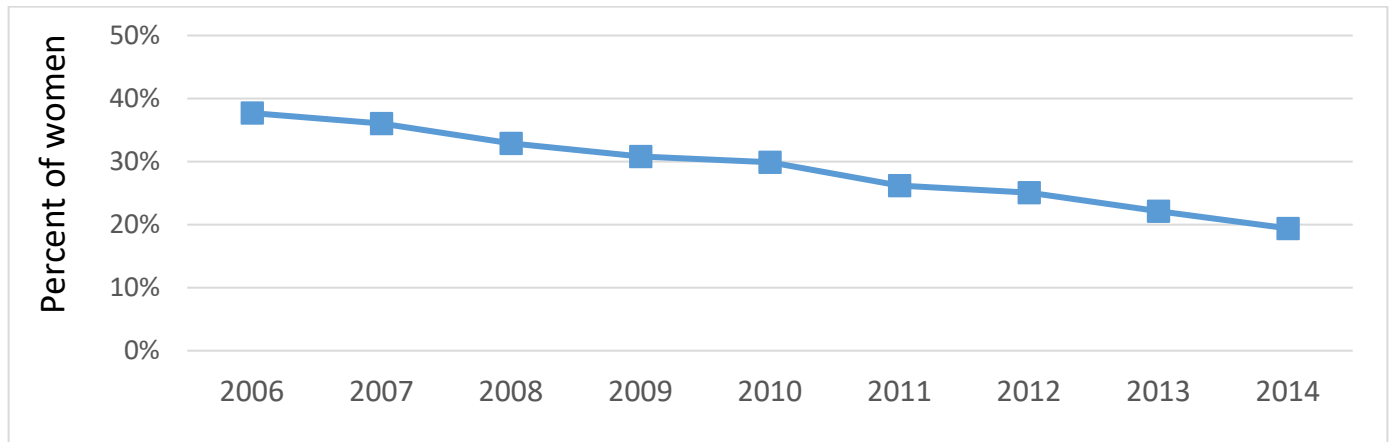
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Rural	Referent	Referent
Hospital Teaching		
No	Referent	Referent
Yes	0.92 (0.92, 0.92)**	0.97 (0.97, 0.97)**
Hospital Bed Size		
<400	Referent	Referent
400-600	0.95 (0.95, 0.96)**	0.97 (0.97, 0.97)**
>600	0.93 (0.93, 0.94)**	0.98 (0.97, 0.98)**
Region of Hospital		
Northeastern	Referent	Referent
Midwest	1.29 (1.29, 1.30)**	1.27 (1.27, 1.28)**
South	1.30 (1.29, 1.30)**	1.27 (1.27, 1.27)**
West	1.23 (1.23, 1.24)**	1.20 (1.20, 1.21)**
Postpartum hemorrhage	1.02 (1.02, 1.03)**	1.03 (1.03, 1.03)**
Preeclampsia	1.01 (1.00, 1.01)**	1.00 (1.00, 1.00)
Gestational diabetes	1.00 (0.99, 1.00)*	1.00 (1.00, 1.01)*
Pregestational diabetes	1.02 (1.01, 1.02)**	1.01 (1.01, 1.02)**
Multiple gestation	0.99 (0.99, 0.99)**	0.99 (0.99, 1.00)*

Adjusted model includes all of the factors in the table as well as adjustment for hospital-level clustering. *CI*, confidence interval. * $p < 0.05$; ** $p < 0.01$. Evidence-based diagnoses for administration of antibiotics includes preterm premature rupture of membranes, endometritis, chorioamnionitis, GBS colonization, and other infectious complications.

Appendixes 6–8 demonstrate the proportion of women each year receiving antibiotics based on vaginal versus cesarean delivery, and if vaginal delivery occurred whether there was an evidence-based diagnosis for administering antibiotics including preterm premature rupture of membranes, endometritis, chorioamnionitis, GBS colonization, and other infectious complications. Only hospitals that contributed data over the entire study period are included in this analysis.

Appendix 6. Proportion of women by year receiving antibiotics with vaginal delivery (no indication for antibiotics).

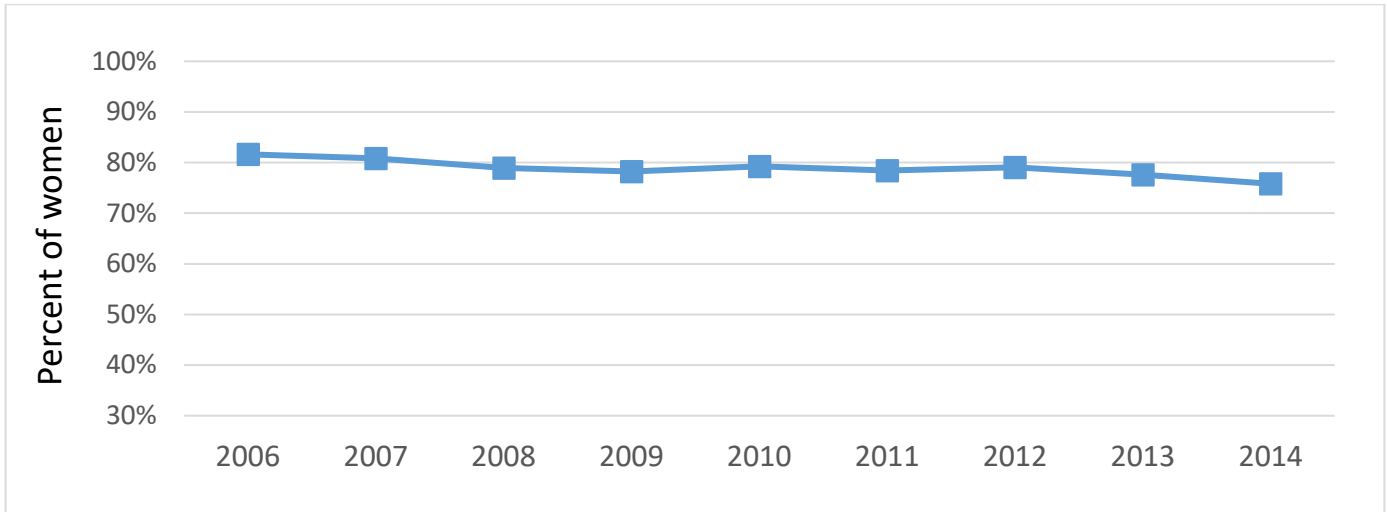


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Appendix 7. Proportion of women by year receiving antibiotics with vaginal delivery (indication for antibiotics).

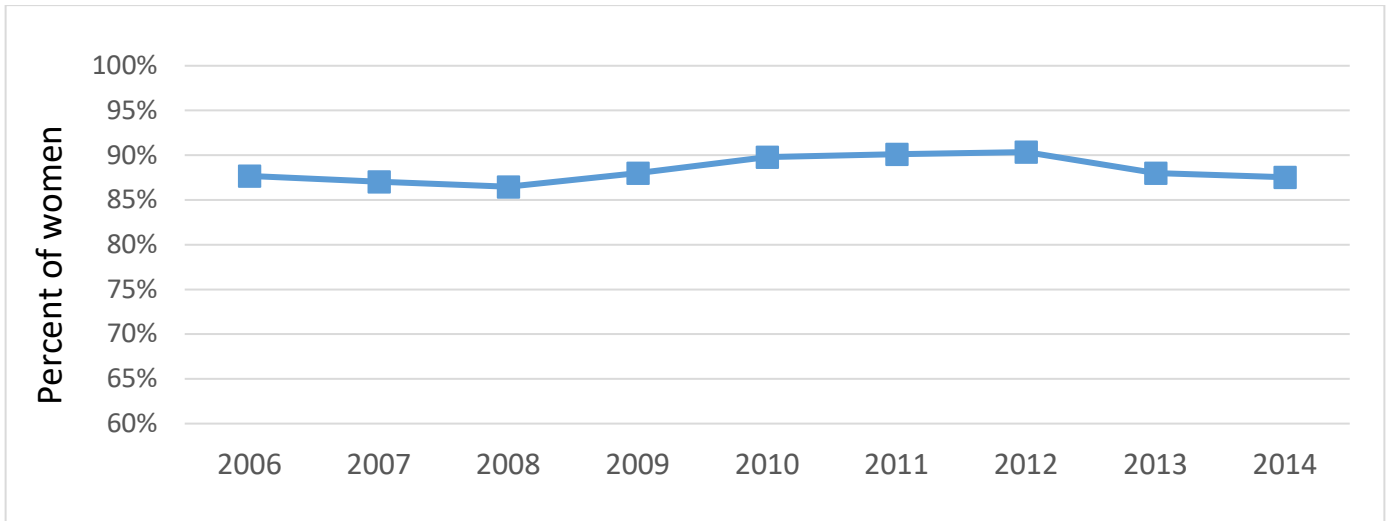


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Appendix 8. Proportion of women by year receiving antibiotics with cesarean delivery.

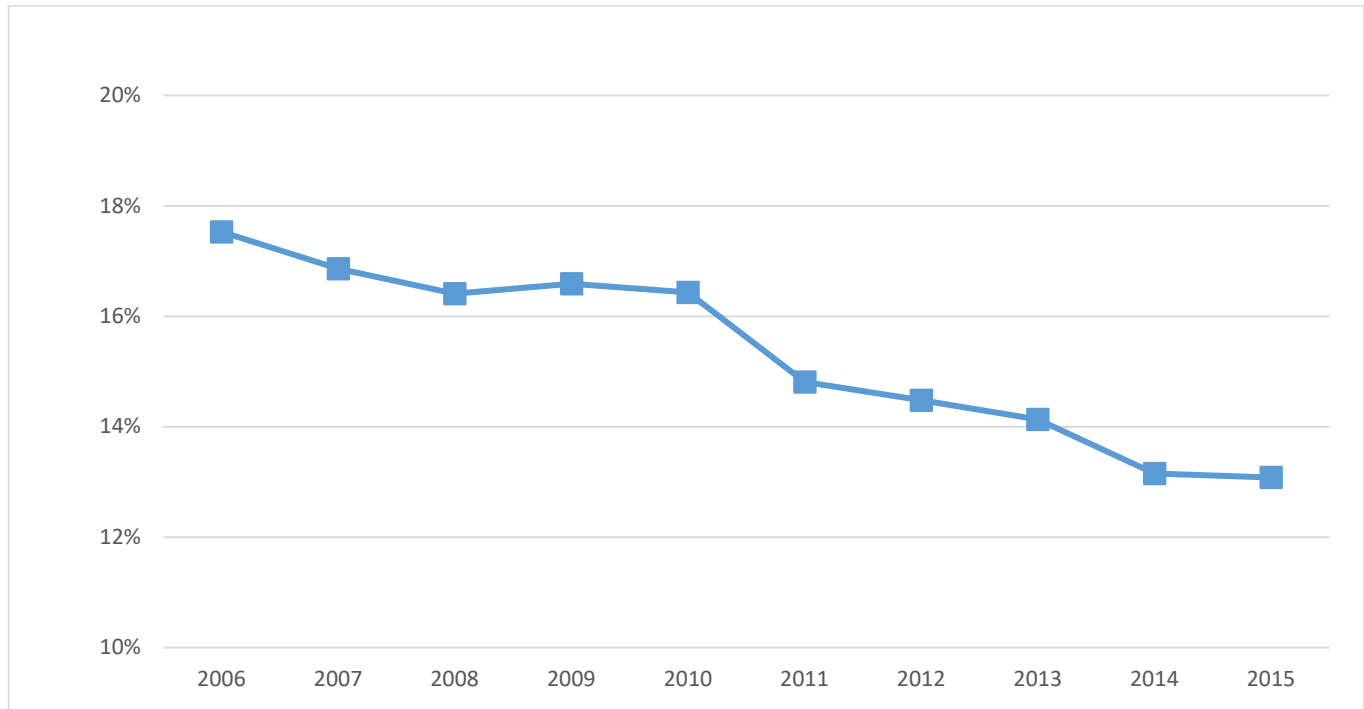


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Appendix 9. Proportion of women by year receiving antibiotics excluding erythromycin with vaginal delivery (without an indication for antibiotics) with additional exclusions. This figure demonstrates the proportion of women each year receiving antibiotics excluding erythromycin who underwent vaginal delivery without an evidence-based diagnosis for administering antibiotics. Women with penicillin allergy are excluded from this sensitivity analysis. Women with premature rupture of membranes, preterm delivery, preterm labor, and delayed or prolonged labor were additionally excluded.



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