

Supplementary Online Content

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

eTable 1: Distribution of Positive *Escherichia coli* Culture Combinations by First Episode

First positive culture combination (n, %)	Overall	EOS	LOS
Blood culture	358 (49.7)	212 (96.4)	146 (29.1)
CSF culture	6 (0.8)	3 (1.4)	3 (0.6)
Urine culture	322 (44.7)	2 (0.9)	320 (63.9)
Blood + CSF cultures	10 (1.4)	3 (1.4)	7 (1.4)
Blood + urine cultures	24 (3.3)	0 (0)	24 (4.8)
Blood + CSF + urine cultures	1 (0.1)	0 (0)	1 (0.2)
Total	721	220	501

Footnotes: Not all infants had all three culture types performed. Decimals may not add up to 100 due to rounding. CSF (cerebrospinal fluid); EOS (early onset sepsis); LOS (late onset sepsis).

eTable 2. Nonsusceptibility Counts and Rates Over Time by Patient Category and Antibiotic Category

Patient category	Drug category	2009	2010	2011	2012	2013	2014	2015	2016	2017
Overall	Ampicillin	35/51 (68.6)	47/69 (68.1)	66/99 (66.7)	58/89 (65.2)	68/102 (66.7)	56/84 (66.7)	59/88 (67.0)	50/79 (63.3)	40/59 (67.8)
	Aminoglycosides	9/51 (17.6)	16/69 (23.2)	21/99 (21.1)	17/89 (19.1)	13/102 (12.8)	9/84 (10.7)	12/88 (13.6)	10/78 (12.8)	12/59 (20.2)
	ESBL	3/50 (6.0)	0/67 (0)	4/96 (4.2)	1/86 (1.2)	11/99 (11.1)	4/84 (4.8)	2/84 (2.4)	4/78 (5.1)	5/51 (9.8)
	Carbapenems	0/48 (0)	0/65 (0)	0/89 (0)	0/77 (0)	0/95 (0)	0/83 (0)	0/79 (0)	0/76 (0)	0/50 (0)
Blood and CSF	Ampicillin	23/34 (67.7)	26/37 (70.3)	31/43 (72.1)	37/57 (64.9)	38/55 (69.1)	30/36 (83.3)	37/50 (74)	31/49 (63.3)	29/37 (78.4)
	Aminoglycosides	7/34 (20.6)	7/37 (18.9)	10/43 (23.3)	10/57 (17.5)	9/55 (16.4)	4/36 (11.1)	8/50 (16)	4/48 (8.3)	8/37 (21.6)
	ESBL	2/34 (5.9)	0/36 (0)	3/43 (7.0)	1/54 (11.3)	6/53 (11.3)	0/36 (0)	1/49 (2)	3/49 (6.1)	3/31 (9.7)
	Carbapenems	0/33 (0)	0/35 (0)	0/40 (0)	0/50 (0)	0/51 (0)	0/35 (0)	0/47 (0)	0/46 (0)	0/32 (0)
Urine	Ampicillin	12/18 (66.7)	22/34 (64.7)	39/61 (63.9)	25/38 (65.8)	31/48 (64.6)	29/51 (56.9)	24/40 (60)	23/34 (67.7)	12/23 (52.2)
	Aminoglycosides	2/18 (11.1)	9/34 (26.5)	14/61 (23.0)	9/38 (23.7)	4/48 (8.3)	5/51 (9.8)	5/40 (12.5)	7/34 (20.6)	5/23 (21.7)
	ESBL	1/17 (5.9)	0/33 (0)	1/58 (1.7)	0/38 (0)	5/47 (10.6)	4/52 (7.7)	1/36 (2.8)	2/33 (6.1)	2/21 (9.5)
	Carbapenems	0/16 (0)	0/32 (0)	0/54 (0)	0/32 (0)	0/45 (0)	0/52 (0)	0/34 (0)	0/34 (0)	0/19 (0)
BW <1,500 g	Ampicillin	21/30 (70)	32/47 (68.1)	41/64 (64.1)	35/52 (67.3)	44/63 (69.8)	32/50 (64)	37/53 (69.8)	29/44 (65.9)	24/34 (70.6)
	Aminoglycosides	8/30 (26.7)	12/47 (25.5)	17/64 (26.6)	12/52 (23.1)	11/63 (17.5)	9/50 (18)	10/53 (18.9)	8/43 (18.6)	6/34 (17.7)
	ESBL	3/29 (10.3)	0/46 (0)	2/63 (3.2)	0/49 (0)	10/62 (16.1)	3/50 (6)	1/50 (2)	1/43 (2.3)	4/30 (13.3)
	Carbapenems	0/28 (0)	0/44 (0)	0/57 (0)	0/46 (0)	0/58 (0)	0/50 (0)	0/48 (0)	0/41 (0)	0/29 (0)
BW ≥1,500 g	Ampicillin	14/21 (66.7)	15/22 (68.2)	25/35 (71.4)	24/37 (64.9)	24/39 (61.5)	24/34 (70.6)	22/35 (62.9)	21/35 (60)	16/25 (64)
	Aminoglycosides	1/21 (4.8)	4/22 (18.2)	4/35 (11.4)	5/37 (13.5)	2/39 (5.1)	0/34 (0)	2/35 (5.7)	2/35 (5.7)	6/25 (24)
	ESBL	0/21 (0)	0/21 (0)	2/33 (6.1)	1/37 (2.7)	1/37 (2.7)	1/34 (2.9)	1/34 (2.9)	3/35 (8.6)	1/21 (4.8)
	Carbapenems	0/20 (0)	0/21 (0)	0/32 (0)	0/31 (0)	0/37 (0)	0/33 (0)	0/31 (0)	0/35 (0)	0/21 (0)
EOS	Ampicillin	12/20 (71.4)	10/14 (71.4)	12/19 (63.2)	19/28 (67.9)	17/32 (53.1)	19/21 (90.5)	27/34 (79.4)	14/25 (56)	20/26 (76.9)
	Aminoglycosides	1/20 (5)	1/14 (7.14)	1/19 (5.3)	3/28 (10.7)	3/32 (9.4)	2/21 (9.5)	4/34 (11.8)	3/25 (12)	5/26 (19.2)
	ESBL	0/20 (0)	0/13 (0)	1/19 (5.3)	0/26 (0)	3/31 (9.7)	0/21 (0)	1/35 (2.9)	1/25 (4)	1/21 (4.8)
	Carbapenems	0/20 (0)	0/12 (0)	0/18 (0)	0/24 (0)	0/30 (0)	0/21 (0)	0/32 (0)	0/23 (0)	0/23 (0)
	Ampicillin and gentamicin	1/20 (5)	1/14 (7.1)	1/19 (5.3)	3/28 (10.7)	3/32 (9.4)	2/21 (9.5)	4/35 (11.4)	3/25 (12)	4/26 (15.4)

LOS	Ampicillin	14/21 (66.7)	15/22 (68.2)	25/35 (71.4)	24/37 (64.9)	24/39 (61.5)	24/34 (70.6)	22/35 (62.9)	21/35 (60)	16/25 (64)
	Aminoglycosides	1/21 (4.8)	4/22 (18.2)	4/35 (11.4)	5/37 (13.5)	2/39 (5.1)	0/34 (0)	2/35 (5.7)	2/35 (5.7)	6/25 (24)
	ESBL	0/21 (0)	0/21 (0)	2/33 (6.1)	1/37 (2.7)	1/37 (2.7)	1/34 (2.9)	1/34 (2.9)	3/35 (8.6)	1/21 (4.8)
	Carbapenems	0/20 (0)	0/21 (0)	0/32 (0)	0/31 (0)	0/37 (0)	0/33 (0)	0/31 (0)	0/35 (0)	0/21 (0)

Footnotes: Nonsusceptibility counts and rates by year, antibiotic category, and by patient category (specimen source, grouping infants as either blood/CSF culture positive or urine culture positive; birth weight status, grouping infants as either <1,500 grams or ≥1,500 grams and by timing of infection, grouping infants as either EOS or LOS). Numerator includes nonsusceptible isolates, denominator includes isolates tested to the drug category, and rates are in parentheses. BW (birth weight); CSF (cerebrospinal fluid); EOS (early onset sepsis); ESBL (extended-spectrum β-lactamase); g (grams); LOS (late onset sepsis).

eTable 3. Estimated Yearly Change in Nonsusceptibility by Patient Category and Antibiotic Category

Category	Antibiotic(s)	Yearly change (%)	Lower confidence limit (%)	Upper confidence limit (%)
Overall	Ampicillin	-0.28	-1.75	1.18
	Aminoglycoside	-0.85	-1.93	0.23
	ESBL	0.46	-0.18	1.11
	Carbapenem	0	--	--
Blood and CSF	Ampicillin	0.63	-1.2	2.46
	Aminoglycoside	-0.85	-2.29	0.6
	ESBL	0.28	-0.57	1.13
	Carbapenem	0	--	--
Urine	Ampicillin	-0.98	-3.24	1.27
	Aminoglycoside	-0.72	-2.36	0.91
	ESBL	0.79	-0.02	1.6
	Carbapenem	0	--	--
BW <1,500g	Ampicillin	0.23	-1.65	2.11
	Aminoglycoside	-1.44	-3.04	0.15
	ESBL	0.23	-0.7	1.17
	Carbapenem	0	--	--
BW ≥1,500g	Ampicillin	-0.76	-3.08	1.56
	Aminoglycoside	0.01	-1.24	1.26
	ESBL	0.78	-0.34	1.89
	Carbapenem	0	--	--
EOS	Ampicillin	1.44	-1.05	3.93
	Aminoglycoside	1.33	-0.15	2.81
	ESBL	0.62	-0.67	1.91
	Carbapenem	0	--	--
	Ampicillin + Gentamicin	1.11	-0.4	2.62
LOS	Ampicillin	-1.1	-2.89	0.69
	Aminoglycoside	-1.53	-2.88	-0.18
	ESBL	0.5	-0.29	1.3
	Carbapenem	0	--	--

Footnotes: Yearly change estimates by antibiotic category and patient category (overall; specimen source, grouping infants as either blood/CSF culture positive or urine culture positive; birth weight status, grouping infants as either <1,500 grams or ≥1,500 grams and by timing of infection, grouping infants as either EOS or LOS). To estimate the average absolute change per year in the proportion of nonsusceptibility in each category and its confidence interval, generalized linear models were used to model nonsusceptibility (yes/no) as a function of year. BW (birth weight); CI (confidence interval); CSF (cerebrospinal fluid); EOS (early onset sepsis); ESBL (extended-spectrum β -lactamase); g (grams); LOS (late onset sepsis).

eTable 4. Multivariable Regression of Isolate Antibiotic Susceptibility Profile and In-Hospital Mortality

Comparison	aOR	95% CI
Group 1 vs 2	0.98	0.33, 2.91
Group 1 vs 3	0.55	0.13, 2.37
Group 2 vs 3	0.56	0.15, 2.13
Group 1 vs 2+3	0.87	0.31, 2.47
Group 1+2 vs 3	0.56	0.15, 1.99

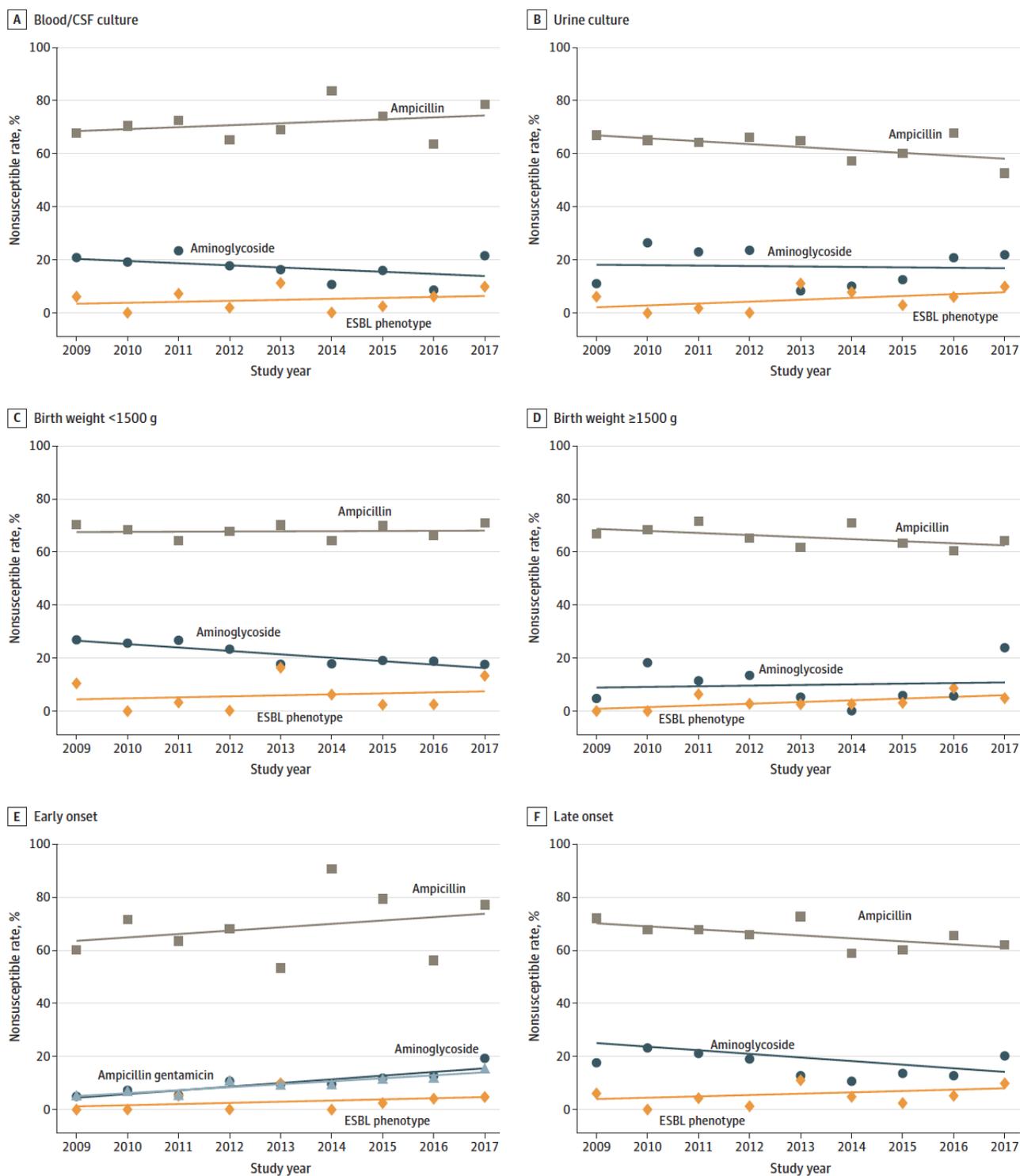
Footnotes: All analyses adjusted for birth weight, sex and teaching hospital status. There were no isolates susceptible to ampicillin and nonsusceptible to gentamicin. aOR (adjusted odds ratio); CI (confidence interval).

Group 1: Ampicillin and gentamicin susceptible (n=69)

Group 2: Ampicillin nonsusceptible and gentamicin susceptible (n=127)

Group 3: Ampicillin and gentamicin nonsusceptible (n=22)

eFigure. Neonatal *Escherichia coli* Nonsusceptibility Trends Over Time by Specimen Source, Birth Weight Category, and Timing of Infection



The eFigure shows the nonsusceptibility trends by specimen source, grouping infants as either (a) blood/CSF culture positive or (b) urine culture positive; birth weight status, grouping infants as either (c) <1500 g or (d) \geq 1500 g and by timing of infection, grouping infants as either (e) early onset sepsis or (f) late onset sepsis. Nonsusceptibility counts and rates for each patient group and antibiotic category by year are shown in eTable 2 in the Supplement. CSF (cerebrospinal fluid); ESBL (extended-spectrum β -lactamase).