

## Supplementary Information

For

### Trends in Antibiotic Resistance in Coagulase-Negative Staphylococci, United States, 1999–2012

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**Supplementary Table 1a: *Staphylococcus epidermidis* Resistance, by Drug and Age, Blood Isolates, Inpatients, United States, 1999–2010**

	<b>Ciprofloxacin</b>	<b>Clindamycin</b>	<b>Levofloxacin</b>	<b>Multidrug-resistant†</b>
1999	58.3% (56.8-59.8)	43.4% (42.1-44.8)	57.1% (54.8-59.3)	33.6% (31.3-36.0)
2000	59.8% (58.4-61.2)	47.3% (46.1-48.6)	57.2% (55.8-58.7)	36.2% (34.6-37.9)
2001	60.2% (58.7-61.7)	48.5% (47.2-49.8)	59.7% (58.3-61.2)	35.9% (34.3-37.5)
2002	60.2% (58.8-61.6)	45.2% (44.0-46.4)	60.5% (59.2-61.9)	34.4% (32.9-36.0)
2003	61.8% (60.5-63.1)	45.6% (44.5-46.8)	62.9% (61.6-64.1)	35.6% (34.2-37.0)
2004	62.4% (61.1-63.7)	51.3% (50.2-52.5)	62.6% (61.4-63.8)	39.4% (37.9-40.9)
2005	63.1% (61.6-64.6)	51.7% (50.5-52.8)	78.6% (77.4-79.7)	56.3% (54.4-58.2)
2006	66.6% (65.0-68.1)	51.2% (49.9-52.4)	77.2% (75.9-78.4)	53.4% (51.2-55.5)
2007	65.3% (63.8-66.9)	50.7% (49.4-51.9)	75.0% (73.6-76.3)	53.6% (51.4-55.8)
2008	69.2% (67.3-71.0)	52.9% (51.6-54.2)	76.1% (74.7-77.5)	50.4% (47.9-52.8)
2009	68.8% (66.5-70.9)	55.5% (53.9-57.0)	72.3% (70.6-73.9)	44.5% (42.0-47.1)
2010	66.8% (64.5-69.0)	52.6% (50.7-54.4)	68.9% (66.9-70.9)	40.3% (37.7-42.9)
2011	65.3% (62.6-68.0)	50.4% (48.3-52.5)	66.8% (64.7-68.9)	38.8% (36.0-41.7)
2012	68.4% (64.9-71.6)	48.5% (45.9-51.0)	68.1% (65.1-70.9)	41.1% (37.3-45.0)

† Multidrug-resistant is defined as isolates tested against ciprofloxacin, clindamycin, oxacillin, and levofloxacin in which the isolate was resistant to all four drugs.

**Supplementary Table 1b: *Staphylococcus epidermidis* Resistance, by Drug and Age, Blood Isolates, Inpatients, United States, 1999–2010**

	<b>Ciprofloxacin</b>	<b>Clindamycin</b>	<b>Levofloxacin</b>	<b>Multidrug-resistant†</b>
1999	2448/4196	2306/5311	1092/1913	523/1557
2000	2784/4654	2933/6195	2565/4481	1247/3441
2001	2494/4141	2880/5935	2715/4544	1239/3451
2002	3006/4992	3026/6701	3110/5139	1262/3670
2003	3454/5590	3270/7166	3874/6162	1610/4528
2004	3377/5410	3756/7321	3742/5978	1723/4375
2005	2600/4120	3829/7411	4042/5144	1483/2635
2006	2511/3772	3408/6662	3250/4212	1098/2058
2007	2419/3703	3105/6129	3111/4148	1105/2062
2008	1738/2512	2835/5359	2691/3534	828/1643
2009	1211/1761	2334/4208	2069/2861	647/1453
2010	1140/1706	1491/2837	1476/2141	566/1406
2011	826/1264	1109/2201	1319/1975	446/1149
2012	527/771	754/1556	700/1028	267/649

† Multidrug-resistant is defined as isolates tested against ciprofloxacin, clindamycin, oxacillin, and levofloxacin in which the isolate was resistant to all four drugs. Results are isolates found resistant or intermediately resistant divided by the total number of isolates tested

**Supplementary Table 2a: Multidrug<sup>†</sup> Resistance in Coagulase-Negative Staphylococcal Species**

<b>Drug</b>	<b>All coagulase-negative <i>Staphylococcus</i> species</b>	<b><i>Staphylococcus epidermidis</i></b>	<b><i>Staphylococcus hominis</i></b>
1999	32.8% (31.8-33.8)	34.7% (33.0-36.5)	21.2% (17.0-25.9)
2000	34.9% (34.2-35.6)	38.5% (37.3-39.7)	24.1% (21.5-27.0)
2001	34.1% (33.4-34.7)	36.8% (35.6-38.0)	32.3% (29.4-35.5)
2002	33.1% (32.4-33.7)	36.1% (34.9-37.3)	29.8% (27.0-32.7)
2003	31.4% (30.8-32.0)	36.4% (35.3-37.5)	26.7% (24.2-29.3)
2004	34.0% (33.3-34.6)	40.2% (39.1-41.3)	22.7% (20.4-25.2)
2005	45.3% (44.2-46.3)	54.4% (53.0-55.9)	36.2% (32.6-39.9)
2006	41.4% (40.3-42.6)	53.1% (51.3-54.8)	42.5% (38.2-46.9)
2007	38.9% (37.9-39.9)	51.9% (50.0-53.7)	36.5% (31.9-41.3)
2008	36.2% (35.1-37.3)	46.9% (44.9-49.0)	24.5% (20.6-28.9)
2009	30.2% (29.1-31.3)	40.8% (38.8-43.0)	19.3% (15.6-23.5)
2010	29.4% (28.4-30.5)	35.8% (33.9-37.8)	18.3% (14.7-22.6)
2011	27.7% (26.6-28.8)	35.5% (33.4-37.7)	15.3% (11.6-19.9)
2012	29.6% (28.0-31.3)	36.8% (33.8-39.8)	18.1% (12.9-24.7)

<sup>†</sup> *Multidrug resistant* is defined as proportion of isolates tested against ciprofloxacin, clindamycin, oxacillin, and levofloxacin that were resistant to all four drugs.

**Supplementary Table 2b: Multidrug<sup>†</sup> Resistance in Coagulase-Negative Staphylococcal Species**

<b>Drug</b>	<b>All coagulase-negative <i>Staphylococcus</i> species</b>	<b><i>Staphylococcus epidermidis</i></b>	<b><i>Staphylococcus hominis</i></b>
1999	3056/9317	1018/2931	73/345
2000	5973/17121	2496/6488	230/953
2001	6444/18915	2251/6115	304/940
2002	6317/19112	2238/6201	311/1044
2003	6704/21339	2732/7502	318/1193
2004	6331/18644	3114/7755	266/1171
2005	3873/8553	2423/4450	246/680
2006	2961/7144	1688/3181	218/513
2007	3568/9183	1497/2886	154/422
2008	2644/7300	1073/2286	106/432
2009	1984/6578	866/2120	79/410
2010	1994/6774	842/2351	72/393
2011	1712/6179	704/1982	48/313
2012	910/3070	379/1031	32/177

<sup>†</sup> *Multidrug resistant* is defined as proportion of isolates tested against ciprofloxacin, clindamycin, oxacillin, and levofloxacin that were resistant to all four drugs.

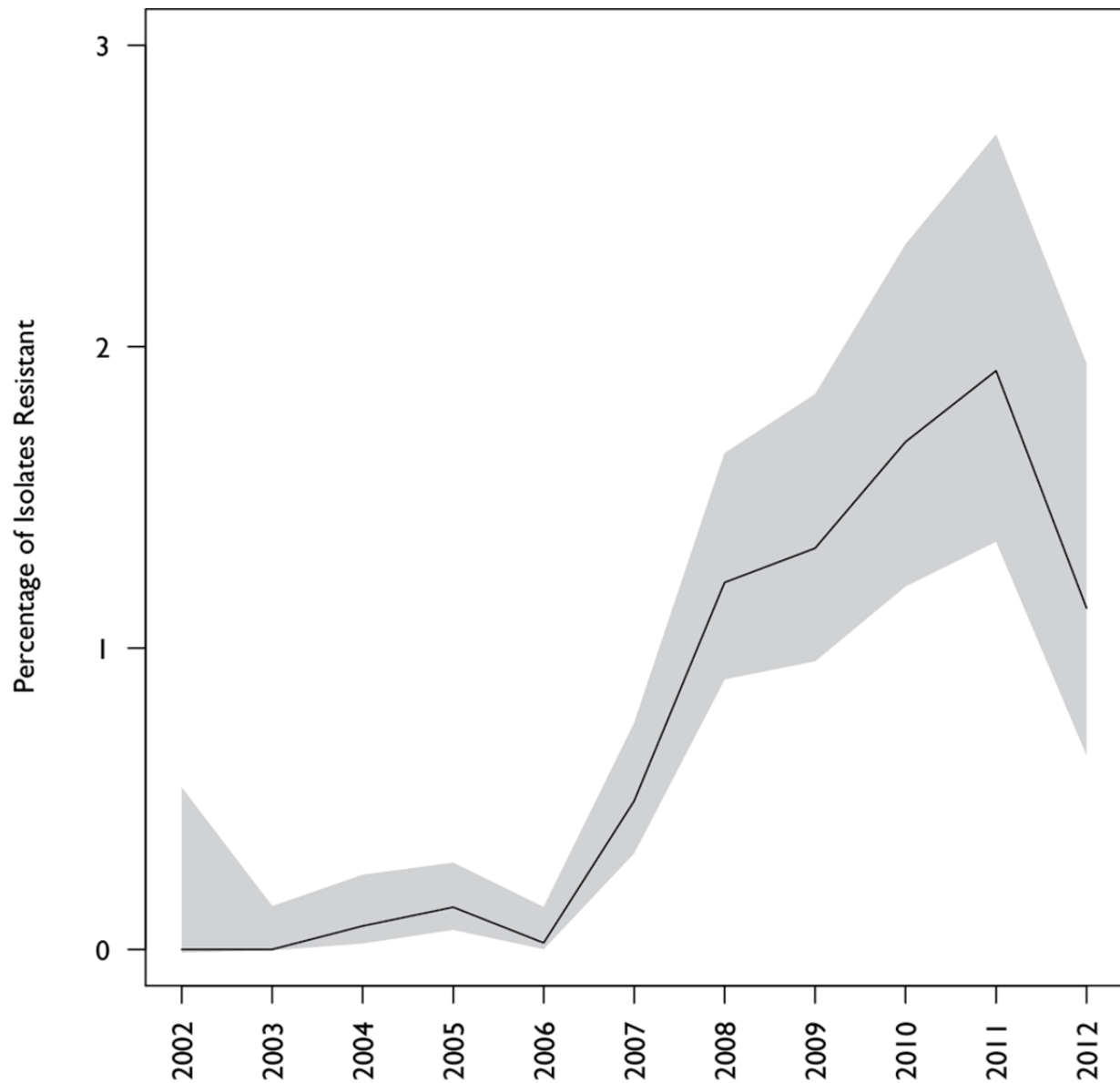
Results are isolates found resistant or intermediately resistant divided by the total number of isolates tested

**Supplementary Table 3: ARIMA Model Parameters and Diagnostic Statistics for Antibiotic Prescription Time Series**

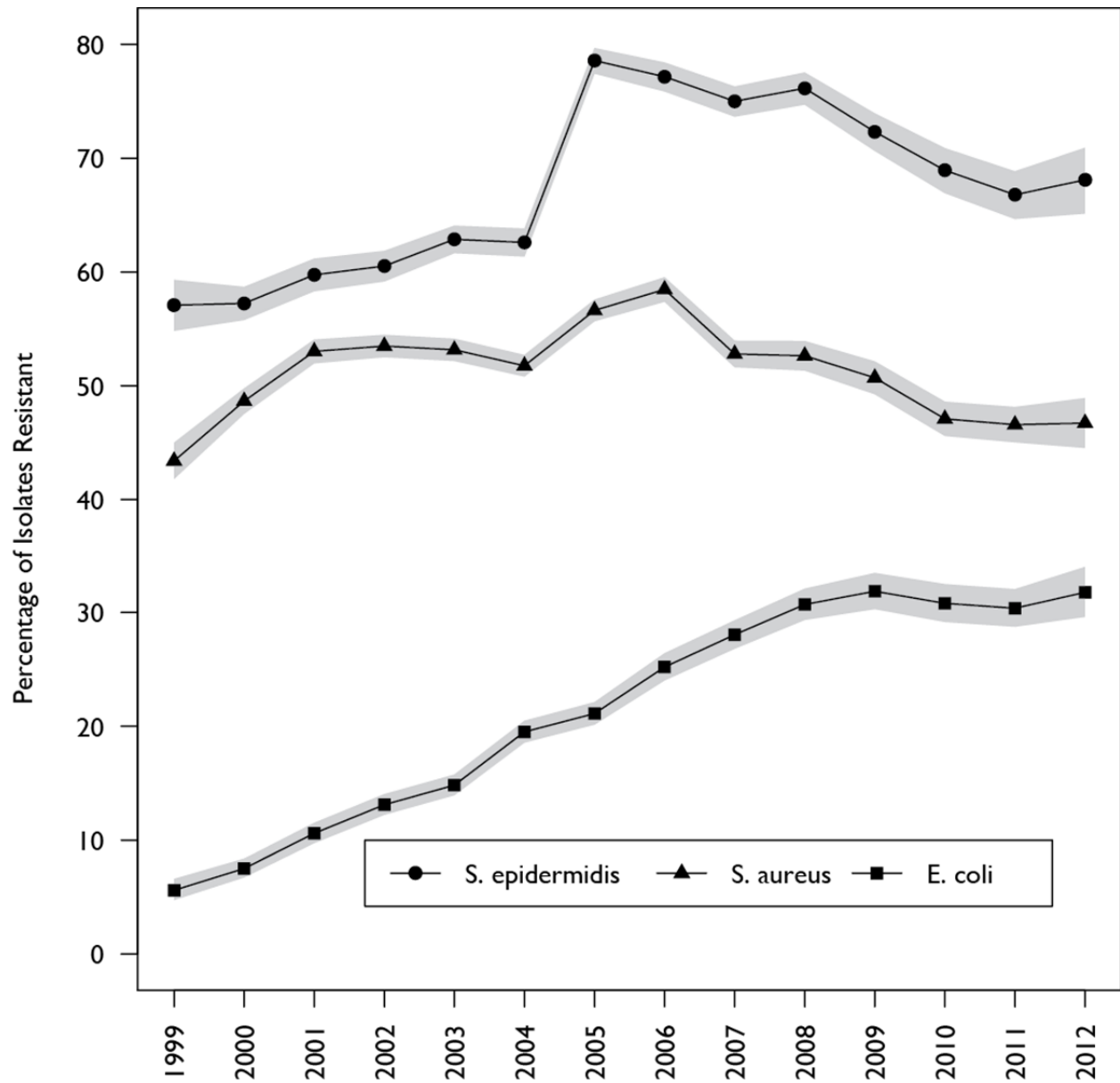
Time Series	ARIMA Parameters	AIC	Q-Statistic*
Levofloxacin prescriptions	arima(2,0,0)	437.76	4.4 p=0.48
Levofloxacin-resistant <i>Staphylococcus epidermidis</i> Blood isolates	arima(1,0,0)	-38.1	0.4 p=0.98
Levofloxacin-resistant <i>Staphylococcus epidermidis</i> all isolates	arima(1,0,0)	-52.8	0.3 p=0.99
Ciprofloxacin prescriptions	arima(0,1,0)	405.3	6.2 p=0.18
Fluoroquinolone Prescriptions	arima(0,2,0)	388.5	2.3 p=0.69
Multidrug-resistant <i>Staphylococcus epidermidis</i> Blood isolates	arima(0,1,0)	-34.7	3.0 p=0.56
Multidrug-resistant <i>Staphylococcus epidermidis</i> all isolates	arima(0,0,1)	-46.4	4.72 p=0.45
Ciprofloxacin-resistant <i>Staphylococcus epidermidis</i> Blood isolates	arima(1,0,0)	-63.6	0.82 p=0.98
Ciprofloxacin-resistant <i>Staphylococcus epidermidis</i> all isolates	arima(1,0,0)	-67.1	2.57 p=0.77

\* In the Box-Ljung white noise test, the null hypothesis is that data are random and uncorrelated; thus a high p-value for the Q-statistic means that we can reject the null hypothesis that the residuals are correlated.

Prescription data source: IMS Xponent®, January, 1999 – December 2010, IMS Health Incorporated. All Rights Reserved. Resistance data source: The Surveillance Network (TSN) Database-USA (managed by Eurofins Medinet, Chantilly, Virginia).

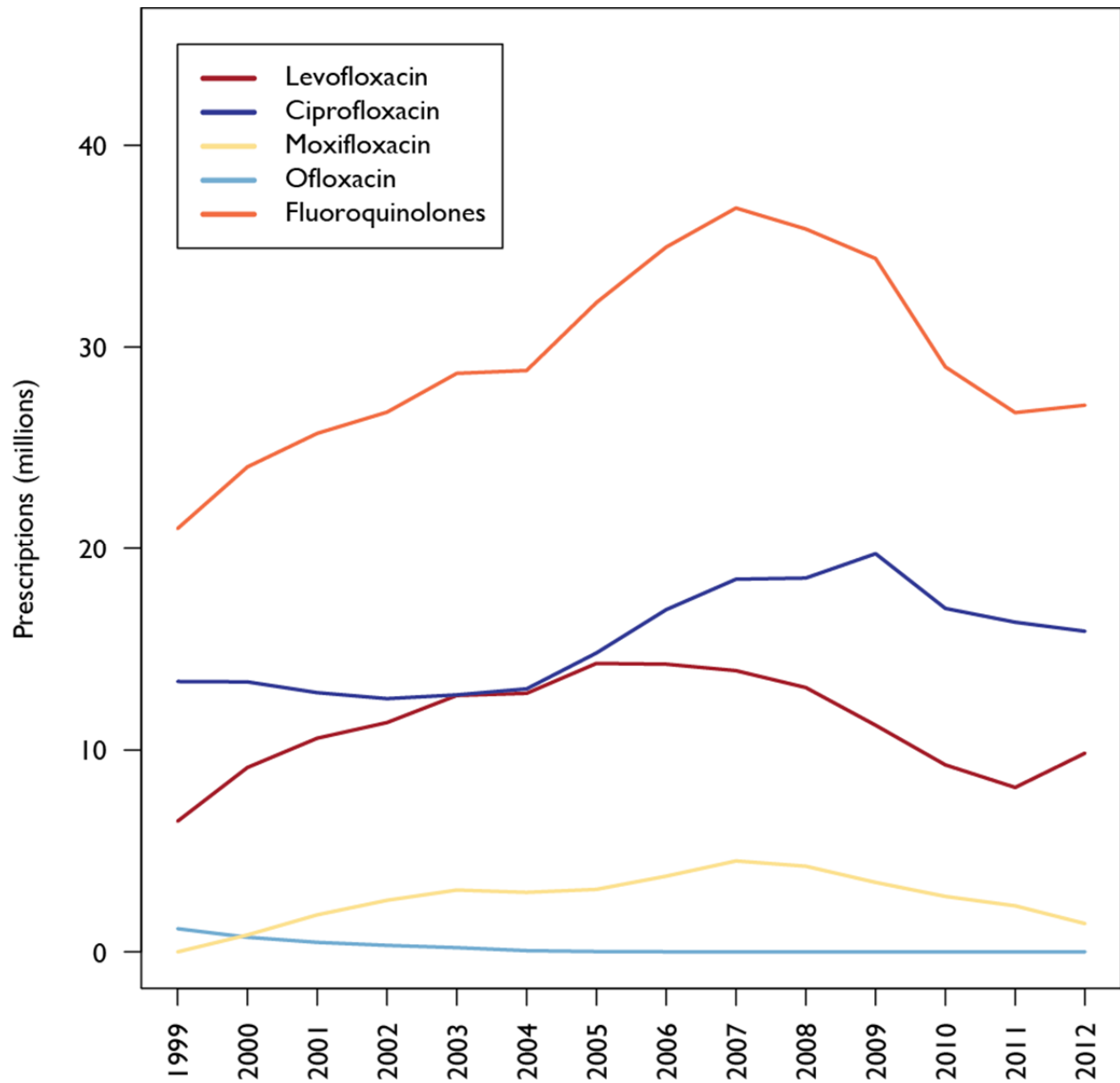


**Supplementary Figure 1: Percentage of *Staphylococcus epidermidis* Inpatient Bloodstream Isolates Resistant to Linezolid, 1999–2012**  
Gray zone represents 95% confidence interval.



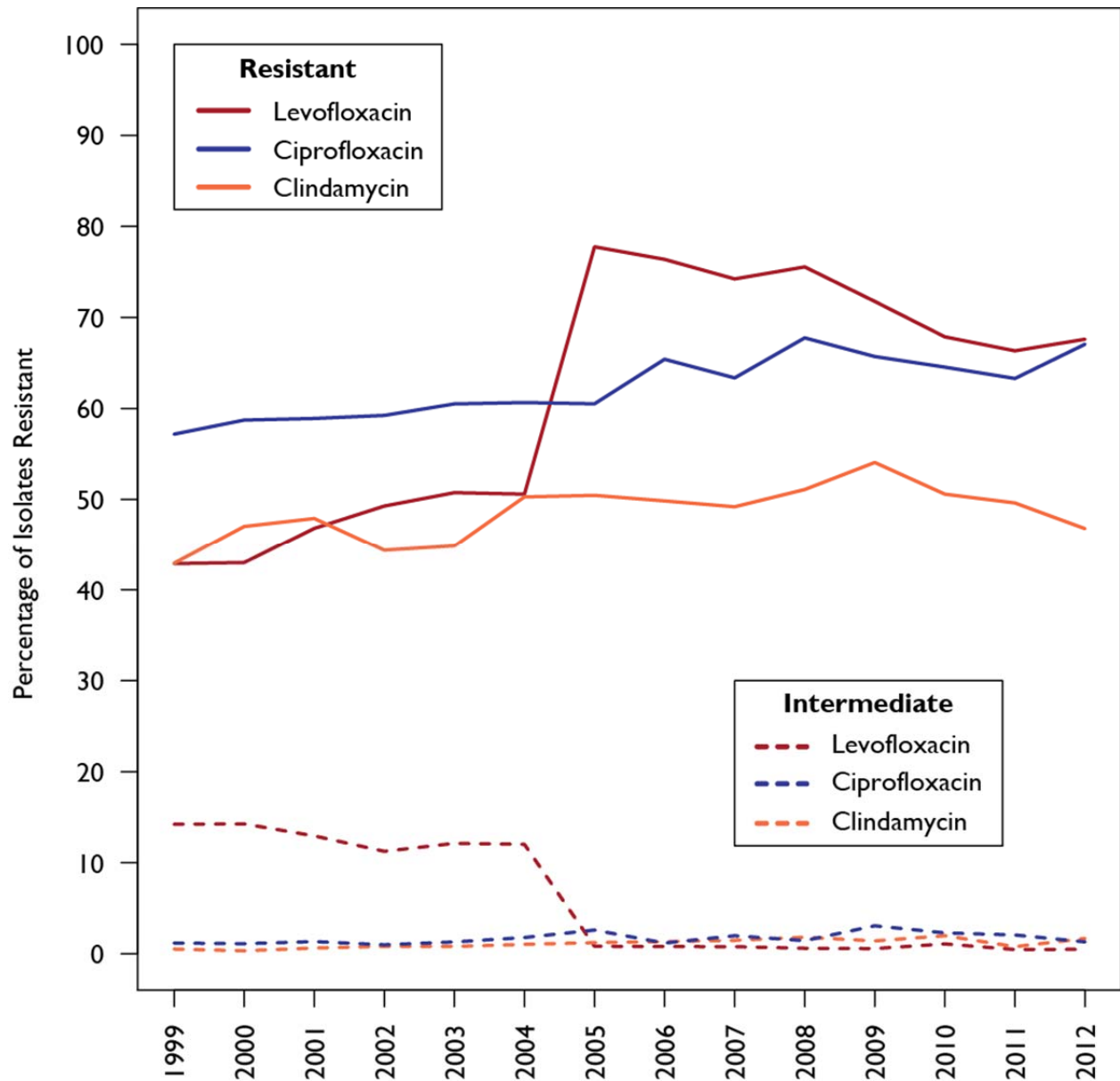
**Supplementary Figure 2: Percentage of *Staphylococcus epidermidis*, *Staphylococcus aureus*, and *Escherichia coli* Inpatient Bloodstream Isolates Resistant to Levofloxacin, 1999–2012**  
 Gray zone represents 95% confidence interval.





**Supplementary Figure 3: Outpatient prescriptions for Fluoroquinolones, 1999–2012**

Source: IMS Xponent®, January, 1999 – December 2010, IMS Health Incorporated. All Rights Reserved.



**Supplementary Figure 4: Percentage of *Staphylococcus epidermidis* Inpatient Bloodstream Isolates Resistant to Levofloxacin, Ciprofloxacin, and Clindamycin 1999–2012**

The solid lines describe isolates classified as resistant, while the dashed lines describe the isolates classified as intermediately resistant. Between 2004 and 2005 the CLSI breakpoints for levofloxacin resistance were changed, the new resistance breakpoints encompassed the intermediate breakpoints from the prior years, so in the analysis in the paper we counted intermediate isolates as resistant. The breakpoints for other drugs did not change over this period.