Statistical tests of resistance trend

The description of NARMS data in the reports highlights general changes in resistance from previous years. In order to understand the significance of these changes, and whether they point to real trends, appropriate statistical analyses were applied to each data source. Separate analyses were done for human and retail meat data to answer separate questions. FDA is answering the question of whether there is any significant monotonic trend across all years of retail meat testing, while CDC is answering the question of whether there is any significant change between a baseline/moving average (which consists of a 3 year average) and the current year. The two analyses should be examined independently.

Statistical analysis of resistance trends in human isolates

To understand changes in the prevalence of antimicrobial resistance among *Salmonella* and *Campylobacter* from humans, we used logistic regression to model annual data from 2004–2014. Since 2003, all 50 states have participated in *Salmonella* surveillance and all 10 states in the Foodborne Diseases Active Surveillance Network (FoodNet) have participated in *Campylobacter* surveillance. We compared the prevalence of selected resistance patterns among bacteria isolated in 2014 with the average prevalence of resistance from two reference periods: 2004–2008 and 2009–2013.

We defined the prevalence of resistance as the percentage of resistant isolates among all isolates tested. Changes in the percentage of isolates that are resistant may not reflect changes in the incidence of resistant infections because of fluctuations in the incidence of illness caused by the pathogen or serotype from year to year. The incidence and relative changes in the incidence of *Salmonella* and *Campylobacter* infections are reported annually from surveillance in FoodNet sites (CDC, 2014).

2014 vs. 2004–2008

The differences between the prevalence of resistance in 2014 and the average prevalence of resistance in 2004–2008 (Figure 1) were statistically significant for the following pathogen-resistance combinations:

Among nontyphoidal *Salmonella*

- Decreased susceptibility to ciprofloxacin was higher (4.3% vs. 2.4%; odds ratio [OR]=2.0, 95% confidence interval [CI] 1.5–2.5)

Among *Salmonella* of particular serotypes

- ACSSuT resistance in ser. Typhimurium was lower (14.5% vs. 22.3%; OR=0.6, 95% CI 0.4–0.9)
- ACSSuTAuCx resistance in ser. Newport was lower (3.0% vs. 11.7%; OR=0.3, 95% CI 0.1–0.6)

Among *Campylobacter jejuni*

- Resistance to ciprofloxacin was higher (26.7% vs. 21.6%; OR=1.4, 95% CI 1.2–1.6)

The differences between the prevalence of resistance in 2014 and the average prevalence of resistance in 2004–2008 (Figure 1) were *not* statistically significant for the following pathogen-resistance combinations:

Among nontyphoidal *Salmonella*

- Ceftriaxone resistance (2.4% vs. 3.2%; OR=0.8, 95% CI 0.6–1.1)
- Resistance to one or more classes (17.7% vs. 18.7%; OR=1.0, 95% CI 0.9–1.1)
- Resistance to three or more classes (9.3% vs. 11.1%; OR=0.9, 95% CI 0.7–1.0)

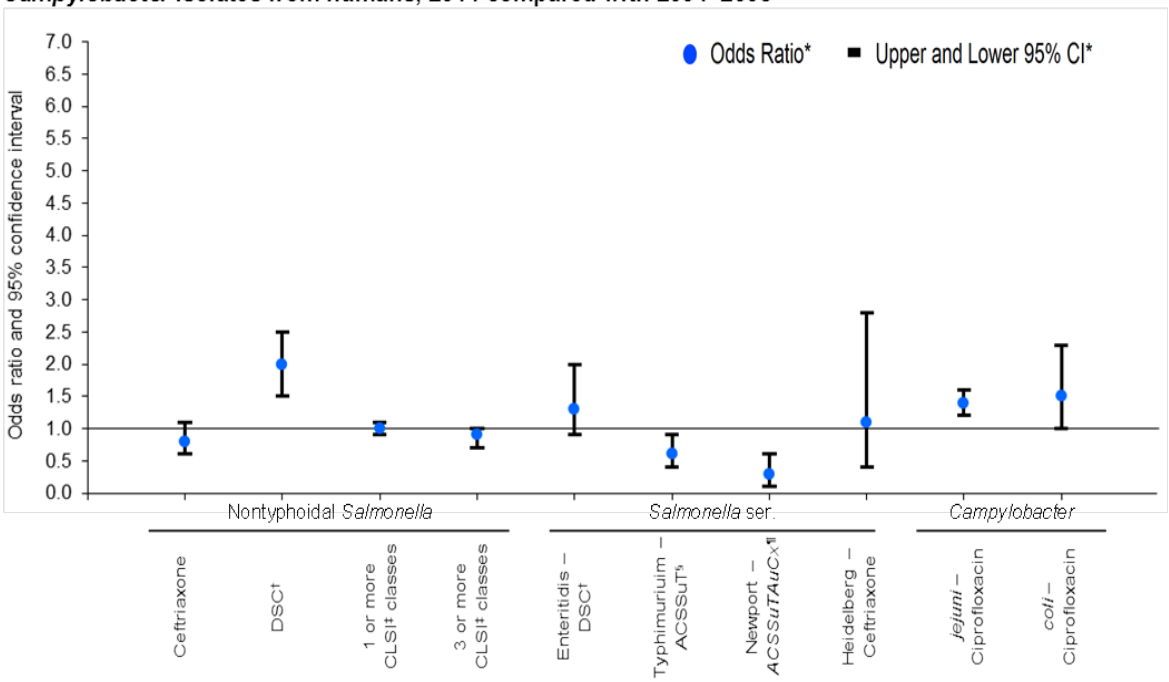
Among *Salmonella* of particular serotypes

- Decreased susceptibility to ciprofloxacin in ser. Enteritidis (8.0% vs. 6.2%; OR=1.3, 95% CI 0.9–2.0)
- Ceftriaxone resistance in ser. Heidelberg (8.5% vs. 8.5%; OR=1.1, 95% CI 0.4–2.8)

Among *Campylobacter coli*

- Ciprofloxacin resistance (35.6% vs. 27.6%; OR=1.5, 95% CI 1.0–2.3)

Figure 1. Changes in prevalence of selected resistance profiles among *Salmonella* and *Campylobacter* isolates from humans, 2014 compared with 2004–2008*



2014 vs. 2009–2013

The differences between the prevalence of resistance in 2014 and the average prevalence of resistance in 2009–2013 (Figure 2) were statistically significant for the following selected pathogen-resistance combinations:

Among nontyphoidal *Salmonella*

- Decreased susceptibility to ciprofloxacin was higher (4.3% vs. 3.0%; OR=1.5, 95% CI 1.2–1.9)

The differences between the prevalence of resistance in 2014 and the average prevalence of resistance in 2009–2013 (Figure 2) were *not* statistically significant for the following selected pathogen-resistance combinations:

Among nontyphoidal *Salmonella*

- Ceftriaxone resistance (2.4% vs. 2.8%; OR=0.9, 95% CI 0.6–1.2)
- Resistance to one or more classes (17.7% vs. 16.3%; OR=1.1, 95% CI 1.0–1.3)
- Resistance to three or more classes (9.3% vs. 9.3%; OR=1.0, 95% CI 0.9–1.2)

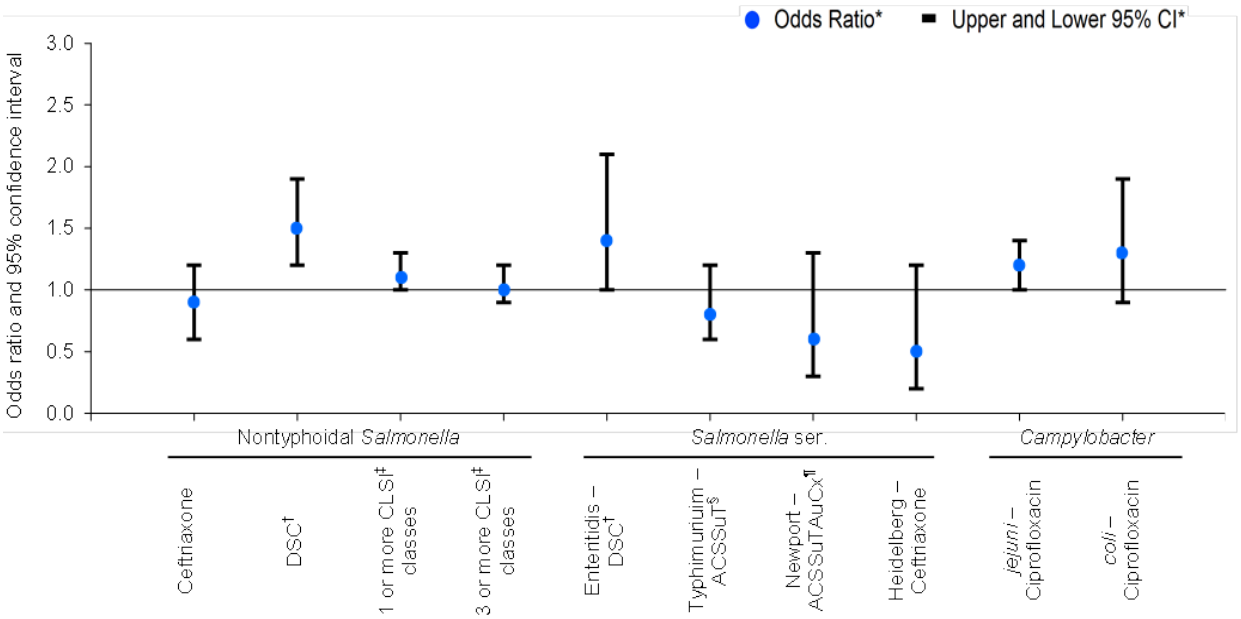
Among *Salmonella* of particular serotypes

- Decreased susceptibility to ciprofloxacin in ser. Enteritidis (8.0% vs. 5.9%; OR=1.4, 95% CI 1.0–2.1)
- ACSSuT resistance in ser. Typhimurium (14.5% vs. 17.4%; OR=0.8, 95% CI 0.6–1.2)
- ACSSuTAuCx resistance in ser. Newport (3.0% vs. 5.4%; OR=0.6, 95% CI 0.3–1.3)
- Ceftriaxone resistance in ser. Heidelberg (8.5% vs. 18.1%; OR=0.5, 95% CI 0.2–1.2)

Among *Campylobacter jejuni* and *C. coli*

- Ciprofloxacin resistance in *C. jejuni* (26.7% vs. 23.3%; OR=1.2, 95% CI 1.0–1.4)
- Ciprofloxacin resistance in *C. coli* (35.6% vs. 31.8%; OR=1.3, 95% CI 0.9–1.9)

Figure 2. Changes in prevalence of selected resistance profiles among *Salmonella* and *Campylobacter* isolates from humans, 2014 compared with 2009–2013*



* The prevalence of resistance in 2014 was compared with the average prevalence from two reference periods, 2004–2008 and 2009–2013. Logistic regression models adjusted for site using a 9-level categorical variable (9 US census divisions) for *Salmonella* and 10-level categorical variable (10 FoodNet states) for *Campylobacter*. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using unconditional maximum likelihood estimation. ORs that do not include 1.0 in the 95% CIs are reported as statistically significant.

† DSC: Decreased susceptibility to ciprofloxacin (MIC ≥0.12 µg/mL for *Salmonella*)

‡ Antimicrobial classes of agents are those defined by the Clinical and Laboratory Standards Institute (CLSI)

§ ACSSuT: resistance to at least ampicillin, chloramphenicol, streptomycin, sulfonamide, and tetracycline

¶ ACSSuTAuCx: resistance to at least ACSSuT, amoxicillin-clavulanic acid, and ceftriaxone

References:

CDC. Foodborne Diseases Active Surveillance Network (FoodNet): FoodNet Surveillance Report for 2014 (Final Report). Atlanta, Georgia: U.S. Department of Health and Human Services, CDC. 2014.

Statistical analysis of resistance trends in retail meat isolates

We applied the Mann and Kendall methods to NARMS retail meat isolates collected from 2002 through 2014. Mann and Kendall methods are designated to statistically assess the significance of a monotonic trend of the variable of interest over time. Mann and Kendall methods are non-parametric rank based methods.

The Mann and Kendall trend test requires a minimum of 3 time points of data, therefore the results are available from 2004-2014, even though the testing started in 2002. However, the trend test uses all of the data gathered from 2002 to the specific year indicated in the table to showthe overall direction of the trend from the time sampling began until 2014, the years the trend became significant, and the relative rate that the trend is increasing or decreasing compared to previous years.

The results are comprised of the p-value (testing the significance of the trend), score (an indication of the direction of the trend), and rate (the magnitude of the change in resistance). Highlighted numbers indicate statistically significant p-values (at alpha=0.05).

We applied the test considering the following antimicrobial/bacterium combinations:

Salmonella: ceftriaxone, gentamicin, ACSSuT (ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline)**,** and the combination of at least three classes (MDR >=3)**.**

Campylobacter: erythromycin, ciprofloxacin, and gentamicin.

E. coli: Ceftriaxone, ciprofloxacin, azithromycin, gentamicin, and the combination of at least three classes (MDR >=3).

Enterococcus: linezolid, daptomycin, gentamicin, vancomycin, and penicillin

Significant trends in retail meat surveillance

The tables contain only those antimicrobial and bacterium combinations of medical importance for which there was at least one source with significant findings. Tables also contain the isolate source, years the data were collected, the corresponding resistance percentage, and the results of the Mann and Kendall trend test.

Salmonella (Table 1)

1. In 2011, there was a significant increasing trend in resistance to at least 3 classes of drugs (MDR>=3) among retail chicken meat isolates. The rate of increase was slower (0.919 percent increase) in 2014 compared to 2013.

2. Among ground turkey meat isolates, there was a significant increasing trend in resistance to at least 3 classes of drugs between 2008 and 2014. The rate of increase was slower (2 percent resistance) in 2014 compared to 2013.

3. Among ground turkey meat isolates, there has been a significant increasing trend in resistance to ACSSuT between 2011 and 2014. In 2014, the yearly rate of increase was slower (0.252 percent resistance) compare to 2013.

Table 1. Antimicrobial resistance trends among *Salmonella* from retail meat

Drug	Isolate source	Year / metrics	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
MDR >=3	Retail Chicken	% resistance	10	28.9	28.7	24.8	21.7	23.2	33.8	47.4	40.9	44.3	33.2	25	20.3
		p-value	N/A	N/A	1	0.625	0.816	0.720	0.772	0.276	0.120	**0.046**	0.061	0.149	0.502
		Score	N/A	N/A	1	0	-2	-3	3	10	16	23	25	22	12
		Rate	N/A	N/A	9.350	2.367	-1.125	-0.800	1.275	2.962	3.041	3.22	2.32	1.815	0.919
	Ground Turkey	% resistance	14.9	18.4	25.4	26.8	24.5	40.5	50.8	25.9	32.7	50	39.6	39.6	36
		p-value	N/A	N/A	0.285	0.084	0.234	0.056	**0.010**	**0.031**	**0.024**	**0.009**	**0.012**	**0.013**	**0.020**
		Score	N/A	N/A	3	6	6	11	17	18	22	29	33	37	39
		Rate	N/A	N/A	5.25	4.083	2.95	4.2	5.25	4.083	2.312	3.51	2.47	2.272	2.038
ACSSuT	Ground Turkey	% resistance	0	0	2.8	0.5	0.6	1.6	1.6	.5	2.5	3.1	3.3	2.8	2.3
		p-value	N/A	N/A	0.540	0.470	0.312	0.180	0.124	0.310	0.137	**0.037**	**0.009**	**0.006**	**0.011**
		Score	N/A	N/A	2	3	5	8	11	9	15	24	34	40	42
		Rate	N/A	N/A	1.4	0.208	0.158	0.2	0.25	0.125	0.225	0.312	0.33	0.306	0.252
	Ground Beef	% resistance	0	0	14.3	12.5	5.3	0	12.5	14.3	28.6	0	23.1	20	30.8
		p-value	N/A	N/A	0.540	0.470	0.613	1	0.750	0.300	0.085	0.349	0.147	0.078	**0.021**
		Score	N/A	N/A	2	3	3	0	3	9	17	11	19	26	38
		Rate	N/A	N/A	7.15	5.208	1.545	0	0	1.545	2.233	1.325	1.8	1.783	2.038

Campylobacter (Table 2)

1. There was a significant increasing resistance trend to erythromycin among chicken isolates in 2008 and 2009 and in 2013. The rate of increase (0.05 percent resistance) in 2014 was at its lowest since testing began.

Table 2. Antimicrobial resistance trends among *Campylobacter* from retail poultry meat°

Drug	Isolate source	Year / metrics	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Erythromycin	Retail Chicken	% resistance	0.0	0.0	0.8	0.5	0.9	0.6	1.2	1.0	0.6	0.6	0.7	1.6	0.3
		p-value	N/A	N/A	0.540	0.470	0.129	0.180	**0.048**	**0.024**	0.073	0.144	0.155	**0.044**	0.196
		Score	N/A	N/A	2	3	7	8	14	19	18	17	19	30	22
		Rate	N/A	N/A	0.4	0.208	0.237	0.15	0.166	0.15	0.11	0.066	0.051	0.076	0.050

° Isolates were collected from poultry only. Ground turkey did not yield enough isolates to test for trends.

E.coli (Table 3)

1. There has been an overall increase in resistance to ceftriaxone among turkey isolates since the testing began in 2002. We found a significant increasing trend between 2007 and 2014. Resistance to ceftriaxone resistance increased at a slower rate (0.19 percent resistance) compared to 2013 (0.958).

2. Ceftriaxone resistance also increased from 0.5% in 2002 to 6.8% in 2008. A significantly increasing trend was found in 2008. In 2014, the rate of increase in resistance was slightly faster (0.1 percent resistances) compared to 2013.

3. Overall, there has been an increase in resistance to at least three classes (MDR>=3) among ground turkey isolates since the testing began in 2002. We observed a significant increasing trend since 2009. MDR>=3 in turkey increased at a slower rate (0.75 percent resistance) compared to 2013.

4. In 2014 we saw a significant decreasing trend in resistance to at least three classes in pork chop. 2014 saw a faster decreasing rate (0.54 percent resistance) compared to 2013.

5. Among turkey isolates, there was a significant increasing trend in resistance to ACSSuT between 2011 and 2014. In 2014, ACSSuT resistance increased at a slightly slower rate (0.232 percent resistance) compared to 2013.

Table 3. Antimicrobial resistance trends among *E. coli* from retail meat

Drug	Source of isolates	Year / metrics	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Ceftriaxone	Ground Turkey	% resistance	1.3	0.3	1.3	2.3	3.1	6.0	3.7	6.9	8.9	10.1	9.7	6.7	4.3
		p-value	N/A	N/A	1	0.470	0.129	**0.035**	**0.022**	**0.006**	**0.001**	**0.0002**	**0.0002**	**0.0005**	**0.002**
		Score	N/A	N/A	0	3	7	12	16	23	31	40	48	51	51
		Rate	N/A	N/A	0	0.667	0.85	0.94	0.8	0.913	0.983	1.025	1.025	0.958	0.190
	Pork Chop	% resistance	0.5	0.9	0.4	0.5	0.6	0.7	3.4	6.8	0.0	0.0	1.2	1.4	2.9
		p-value	N/A	N/A	1	1	1	0.566	0.171	**0.046**	0.401	1	0.638	0.370	0.198
		Score	N/A	N/A	-1	-1	1	4	10	17	9	1	7	14	22
		Rate	N/A	N/A	-0.05	-0.025	0.012	0.04	0.1	0.25	0.1	0	0.04	0.090	0.1
MDR >=3	Ground Turkey	% resistance	53.3	52.6	51.6	52.0	53.9	56.5	63.3	65.0	55.0	63.9	67.8	58.8	53.7
		p-value	N/A	N/A	0.334	0.334	0.592	0.47	0.136	**0.031**	**0.044**	**0.016**	**0.005**	**0.007**	**0.032**
		Score	N/A	N/A	-3	-4	0	5	11	18	20	27	37	40	36
		Rate	N/A	N/A	-0.85	-0.566	-0.075	0.433	1.15	1.685	1.062	1.412	1.667	1.163	0.75
	Pork Chop	% resistance	15.8	15.1	21.1	15.6	15.9	14.5	17.8	14.3	16.4	8.9	11.2	13.0	9.8
		p-value	N/A	N/A	1	0.625	0.816	0.72	1	0.548	0.92	0.38	0.161	0.086	**0.032**
		Score	N/A	N/A	1	0	2	-3	1	-6	-2	-11	-19	-26	-36
		Rate	N/A	N/A	2.65	0.091	0.137	-0.15	0.025	-0.141	-0.083	-0.26	-0.533	-0.423	-0.541
ACSSuT	Ground Turkey	% resistance	0.0	2.7	0.5	1.8	0.8	1.9	2.0	2.3	2.2	3.0	5.1	3.2	2.0
		p-value	N/A	N/A	1	0.75	0.816	0.47	0.238	0.108	0.076	**0.016**	**0.005**	**0.002**	**0.007**
		Score	N/A	N/A	1	2	2	5	9	14	18	27	37	46	45
		Rate	N/A	N/A	0.25	0.425	0.175	0.2	0.2	0.225	0.2	0.275	0.328	0.287	0.232

Enterococcus (Table 4)

1. 2014 saw a significant increasing resistance trend to gentamicin among chicken isolates. The rate of increase in resistance was (0.75 percent resistance) faster compared to 2013. However, there is a significant decreasing resistance trend to gentamicin in turkey isolates from 2010 to 2014. The rate of decrease in resistance was slower (0.14 percent resistance) compared to the year before.

Table 4. Antimicrobial resistance trends among *Enterococcus* from retail meat

Drug	Isolate source	Year / metrics	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Gentamicin	Retail Chicken	% resistance	22.4	20.2	19.3	18.1	23.0	19.5	19.4	25.4	31.8	26.9	29.4	24.3	26.8
		p-value	N/A	N/A	0.334	0.084	0.816	0.72	0.562	0.904	0.358	0.156	0.061	0.064	**0.044**
		Score	N/A	N/A	-3	-6	-2	-3	-5	2	10	17	25	28	34
		Rate	N/A	N/A	-1.55	-1.316	-0.975	-0.58	-0.175	0.045	0.566	0.78	0.866	0.777	0.75
	Ground Beef	% resistance	2.4	1.8	1.0	1.8	0.9	0.5	2.0	0.9	0.4	0.0	0.0	0.7	0.7
		p-value	N/A	N/A	0.334	0.470	0.129	0.035	0.287	0.166	**0.045**	**0.011**	**0.003**	**0.005**	**0.008**
		Score	N/A	N/A	-3	-3	-7	-12	-8	-12	-20	-29	-38	-41	-44
		Rate	N/A	N/A	-0.7	-0.4	-0.337	-0.375	-0.2	-0.183	-0.2	-0.214	-0.2	-0.173	-0.142