

Shigella Infections with Decreased Susceptibility to
Azithromycin and Association with Bacterial
Sexually Transmitted Infections in New York City,
2014–2016

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Shigellosis

- Infection with *Shigella* species (*flexneri*, *sonnei*, *dysenteriae*, *boydii*)
- Third most common cause of bacterial enteric infections in the United States
- Transmitted person-to-person, via fecal oral route
 - Very low infectious dose
 - Exposure occurs by direct contact with an infected person's feces, ingestion of contaminated food or water, or via fomites
 - Humans and primates are only known reservoir
- Most common symptoms include diarrhea, abdominal pain and fever

Shigellosis

- Risk factors
 - Travel to endemic countries
 - Overcrowding
 - Poverty
 - Childcare attendance
 - Sexual contact with infected person
- Outbreaks have been observed among observant Jewish communities^{1,2}, in day cares³, and among men who have sex with men (MSM)⁴

¹Garrett V, Bornschlegel K, Lange D, Reddy V, Kornstein L, Kornblum J, et al. A recurring outbreak of *Shigella sonnei* among traditionally observant Jewish children in New York City: the risks of daycare and household transmission. *Epidemiology and Infection*. 2006 Dec;134(6):1231-6

²Sobel J, Cameron D, Ismail J, Strockbine N, Williams M, Diaz P, et al. A prolonged outbreak of *Shigella sonnei* infections in traditionally observant Jewish communities in North America caused by a molecularly distinct bacterial subtype. *Journal of Infectious Diseases*. 1998;177:1405-9

³Totaro J, Tan C, Reddy V, Dail K, Davies M, Jenkins P, et al. Day care related outbreaks of Rhamnose negative *Shigella sonnei* – Six states, June 2001-March 2003. *Morbidity and Mortality Weekly Report*. 2004 Jan;53(03):60-63.

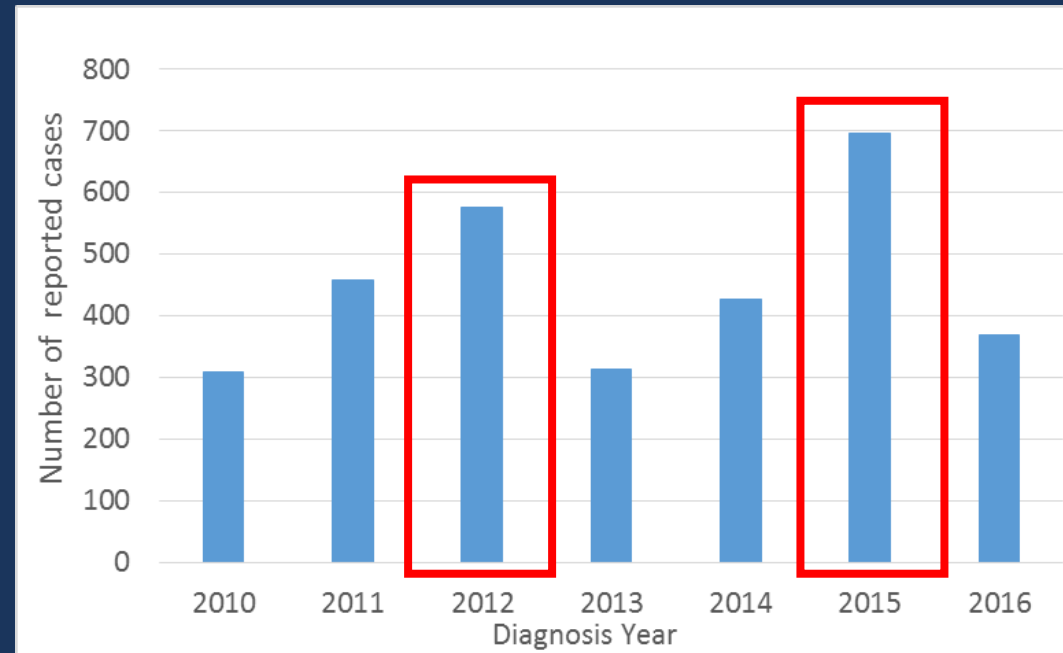
⁴Aragon TJ, Vugia DJ, Shallow S, Samuel MC, Reingold A, Angulo FJ, et al. Case-control study of shigellosis in San Francisco: The Role of Sexual Transmission and HIV Infection. *CID*. 2007;44:327-34.

Treatment

- Treatment not usually recommended unless immunocompromised or for severe infections⁵
- Antibiotics may be prescribed to shorten disease duration and decrease severity of illness
- High rates of resistance to ampicillin and trimethoprim-sulfamethoxazole have been observed
- As a result, azithromycin and ciprofloxacin are often prescribed
 - Increasing rates of resistance to ciprofloxacin and decreased susceptibility to azithromycin have been reported

Shigellosis in NYC

- Reportable disease
- Large cyclical outbreaks observed among children in observant Jewish population; most recent October 2014-March 2015



Shigellosis in NYC

- Isolates forwarded to Public Health Laboratory (PHL) for serogrouping and antibiotic susceptibility testing (AST) against multiple antibiotics, including azithromycin and ciprofloxacin
 - Decreased susceptibility to azithromycin (DSA) defined as minimum inhibitory concentration (MIC) $\geq 16 \mu\text{g/mL}$ for *S. flexneri* and MIC $\geq 32 \mu\text{g/mL}$ for *S. sonnei*
- Cases investigated if reported to be associated with high risk setting (foodhandler, day care attendee, healthcare worker, nosocomial) or if isolate is resistant to ciprofloxacin and/or DSA

Enhanced Surveillance, March 2013-May 2015

- Overlapped with 2014/2015 outbreak; only sporadic cases included in analysis
- Of 683 cases:
 - 19% DSA
 - 4% ciprofloxacin resistant
 - 1% both DSA and ciprofloxacin resistant
- Case comparison
 - DSA or ciprofloxacin resistant cases older and more likely to be male than those susceptible to both antibiotics
 - 85% of DSA or ciprofloxacin resistant cases who were interviewed identified as MSM
 - DSA cases were more likely to have an HIV infection when compared to susceptible and ciprofloxacin resistant cases

May 2015-Present

- DSA and ciprofloxacin resistance continues to increase

| Antibiotic | Year | | | | | |
|---------------|--------------|---------|--------------|---------|--------------|---------|
| | 2014 (n=377) | | 2015 (n=618) | | 2016 (n=307) | |
| | Count | Percent | Count | Percent | Count | Percent |
| Azithromycin | 51 | 14 | 104 | 17 | 122 | 40 |
| Ciprofloxacin | 8 | 2 | 19 | 3 | 28 | 9 |

- Questions remain about risk factors
 - Prior antibiotic use
 - Sexual behaviors and networks
 - Sexually transmitted infection (STI)

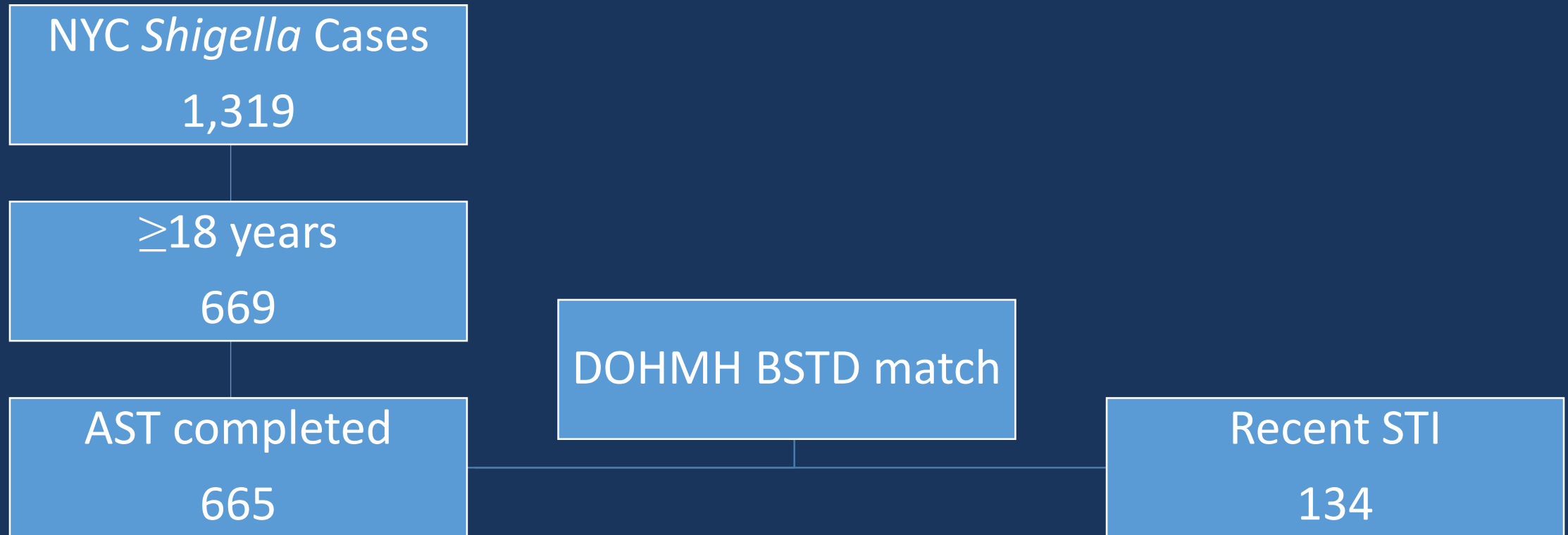
Study Question

- Azithromycin common treatment for other bacterial STIs
 - *Chlamydia trachomatis*
 - *Neisseria gonorrhoeae*
- Sought to examine the relationship between DSA-shigellosis and recent history of bacterial STI
- Sought to examine recent proportions of DSA-shigellosis patients who identify as MSM

Case Match

- Shigellosis data:
 - DOHMH Bureau of Communicable Diseases (BCD) registry
 - NYC residents ≥ 18 years-old
 - Diagnosed with shigellosis 2014-2016
 - AST completed by PHL
- Bacterial STI data
 - DOHMH Bureau of Sexually Transmitted Diseases Control (BSTD) registry
 - NYC residents
 - Diagnosed with *C. trachomatis* or *N. gonorrhoeae*
- Selected for individuals with an STI diagnosis date within the 12 months prior to shigellosis diagnosis

Match Results

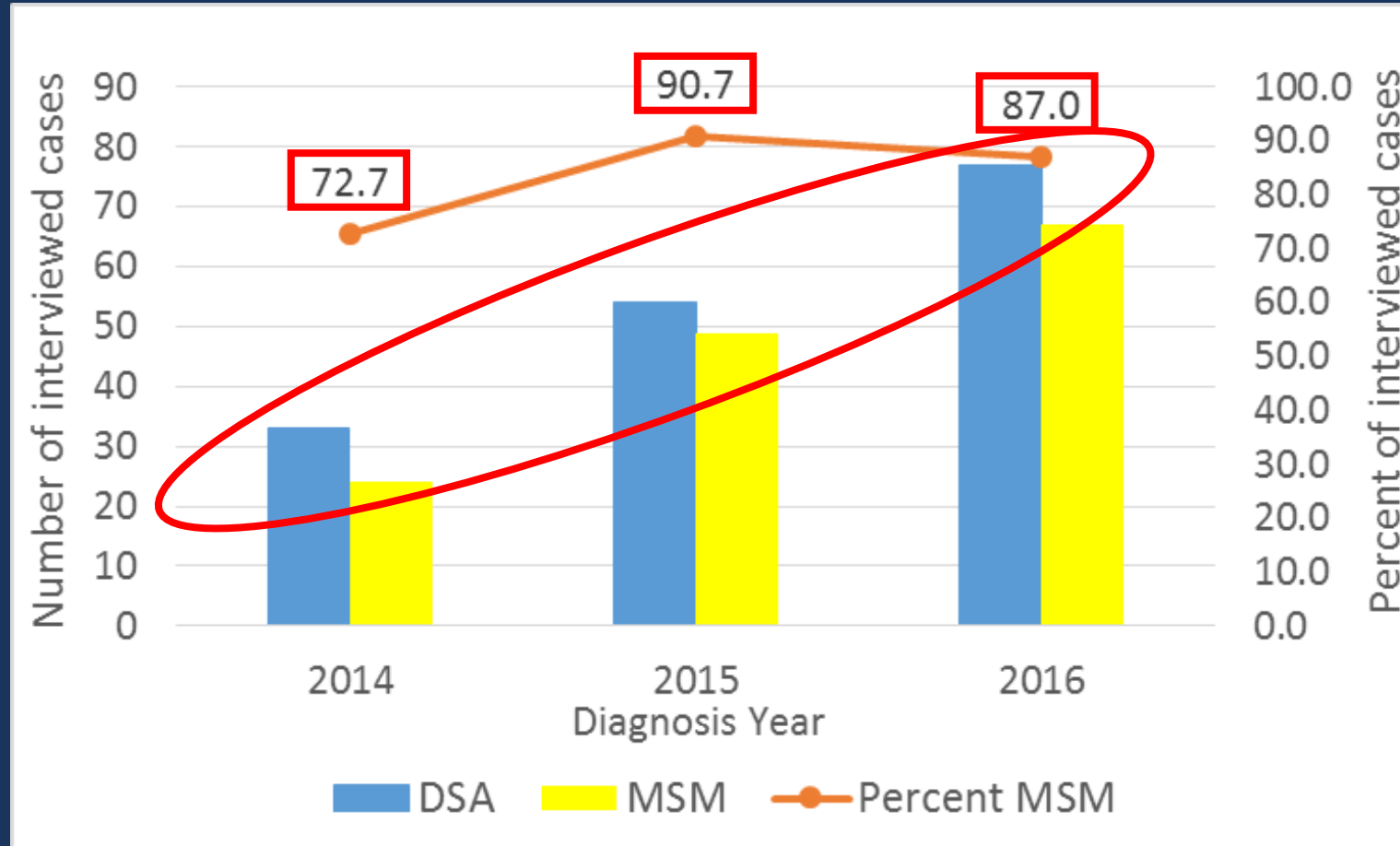


Bacterial STI and DSA-Shigellosis

| | DSA | | No DSA | | Total |
|--------|-------|---------|--------|---------|-------|
| | Count | Percent | Count | Percent | |
| STI | 80 | 29% | 54 | 14% | 134 |
| No STI | 193 | 71% | 339 | 86% | 532 |
| Total | 273 | n/a | 393 | n/a | 665 |

RR = 2.13, 95% CI: 1.57-2.90

MSM Identification among DSA-Shigellosis Cases



Limitations

- Interview data only available for cases with DSA or ciprofloxacin resistance; unable to assess potential confounding
 - MSM
 - Previous antibiotic use
- Potential for non-differential misclassification – cases who did not reside in NYC at time of *C. trachomatis* or *N. gonorrhoeae* diagnosis

Conclusions

- *Shigella* infections exhibiting DSA in NYC continue to occur disproportionately among MSM
- Risk of DSA-shigellosis significantly high among those with a prior infection of *C. trachomatis* or *N. gonorrhoeae*
- AST results and recent STI history should be used to guide shigellosis treatment when indicated

Next Steps

- Project to interview all shigellosis cases (August 1, 2017)
 - Added questions regarding recent STI infection, HIV pre-exposure prophylaxis (PrEP), sexual behaviors and sexual networks
 - Interviewing providers about previous antibiotic use
 - Allow for comparison of resistant cases to non-resistant; aim to better identify risk factors for patients with shigellosis resistant to ciprofloxacin and/or DSA

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Thank you!

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