Epidemiology, Testing, and Management of Extensively Drug-Resistant Shigellosis

Clinician Outreach and Communication Activity (COCA) Call

Tuesday, February 28, 2023

Free Continuing Education

- Free continuing education is offered for this webinar.
- Instructions on how to earn continuing education will be provided at the end of the call.

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- Content will not include any discussion of the unlabeled use of a product or a product under investigational use with the exception of Dr. Louise Francois Watkins's discussion of treatment options for shigellosis, some of which are considered off-label use for infectious diarrhea.

- CDC did not accept financial or in-kind support from ineligible companies for this continuing education activity.

Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Discuss the clinical characteristics, populations at greatest risk, and evolving epidemiological trends for XDR shigellosis.
2. Describe outbreak investigations of XDR shigellosis in the United States and the United Kingdom.
3. Outline strategies and resources to support the clinical management of XDR shigellosis and educate healthcare professionals about appropriate antibiotic use.
4. Review what CDC is doing to learn more about XDR *Shigella* in the United States and how clinicians and public health officials can help through testing and reporting.

To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Today's Presenters

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Division of Foodborne, Waterborne, and Environmental Diseases
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

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Colorado Department of Public Health and Environment

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UK Health Security Agency

Hannah Charles, MSc, DFPH
Senior Epidemiologist
UK Health Security Agency

What Clinicians Need to Know about Extensively Drug-Resistant (XDR) Shigellosis in the United States

Naeemah Z. Logan, MD

Meseret Birhane, MPH, MAS

Louise Francois Watkins, MD, MPH

National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS) Team

Division of Foodborne, Waterborne, and Environmental Diseases

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COCA Call | February 28, 2023

Outline

- **Background**
  – Transmission and populations at risk
- **Methods**
  – Overview of national surveillance systems
- **CDC Data**
  – Emergence of XDR shigellosis in the United States
- **Treatment Considerations**

Background

Naeemah Logan, MD

Overview of Shigellosis in the United States

- **~450,000 persons are infected annually**
  - ~ 6,380 hospitalizations

Overview of Shigellosis in the United States

- ~450,000 persons are infected annually
- **Most infections caused by *S. sonnei* and *S. flexneri***

Overview of Shigellosis in the United States

- ~450,000 persons are infected annually
- Most infections caused by *S. sonnei* and *S. flexneri*
- **Transmission is fecal-oral**
  - Person-to-person contact
  - Sexual contact
  - Indirectly (contaminated food, water, or fomites)

Overview of Shigellosis in the United States

- ***Shigella* bacteria are easily transmitted**
  - Low infectious dose (10 – 100 organisms)
  - Outbreaks occur in close-contact settings

Overview of Shigellosis in the United States

- **Young children historically at highest risk**

- **Increase in antimicrobial-resistant *Shigella* infections among:**
  - Men who have sex with men (MSM)
  - People experiencing homelessness
  - International travelers
  - Immunocompromised persons
  - People living with HIV

Empiric Antibiotic Options Dwindling for Shigellosis Treatment

- **Antimicrobial treatment is recommended to reduce symptoms and bacterial shedding**

- **Treatment decisions complicated by**
  - Increasing antimicrobial-resistant *Shigella* strains
  - Use of culture-independent diagnostic tests (CIDTs)

Methods

Meseret Birhane, MPH, MAS

Terminology and Definitions

- **Antimicrobial susceptibility testing** (AST; “phenotypic resistance”)
  - Process that determines the concentration of an antimicrobial needed to inhibit the growth of an organism (e.g., *Shigella* bacteria)

Terminology and Definitions

- **Antimicrobial susceptibility testing** (AST; “phenotypic resistance”)

- **Whole genome sequencing** (WGS)
  - Determines the genetic code (DNA) of an entire organism (e.g., *Shigella* bacteria)

Terminology and Definitions

- **Antimicrobial susceptibility testing** (AST; “phenotypic resistance”)
- **Whole genome sequencing** (WGS)
- **Predicted resistance** (“genotypic resistance”)
  - Analysis to screen organism’s genome for the presence of resistance determinants

Terminology and Definitions

- **Antimicrobial susceptibility testing** (AST; “phenotypic resistance”)
- **Whole genome sequencing** (WGS)
- **Predicted resistance** (“genotypic resistance”)
- **Resistance determinants** (“genes and mutations”)
  - Known elements in a bacterium’s genome that confer resistance to a certain antimicrobial or class of antimicrobials

Terminology and Definitions

- **Extensively drug resistance (XDR):**

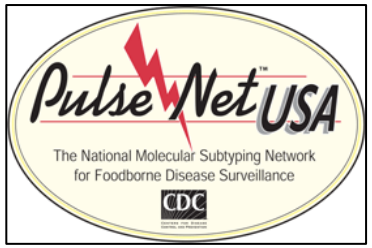
  CDC currently defines XDR *Shigella* as strains resistant to all commonly recommended empiric and alternative antibiotics

  - ampicillin
  - azithromycin
  - ciprofloxacin
  - trimethoprim-sulfamethoxazole
  - ceftriaxone

CDC Surveillance Systems

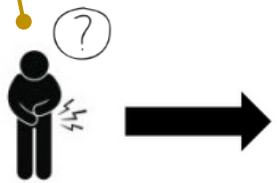
- **NARMS** (phenotypic resistance)
  - National Antimicrobial Resistance Monitoring System
  - Reporting of results may take > 1 year

- **PulseNet** (genotypic resistance)
  - National laboratory network
  - Reporting of results take 2–4 weeks



Isolate Submission and Testing Workflow

Sick Patient



Specimen yields a *Shigella* isolate at the clinical laboratory

Public health laboratory receives isolates for further analysis

Sequencing of some *Shigella* isolates

Every 20th isolate

PulseNet USA
The National Molecular Subtyping Network for Foodborne Disease Surveillance
CDC

Genotypic resistance of sequenced isolates

NARMS
National Antimicrobial Resistance Monitoring System

Phenotypic resistance (antimicrobial susceptibility testing)

Isolate Submission and Testing Workflow

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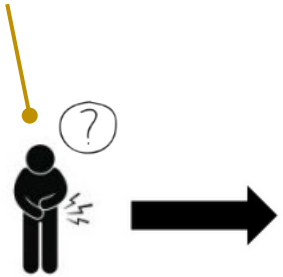

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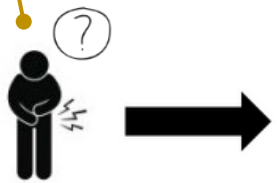

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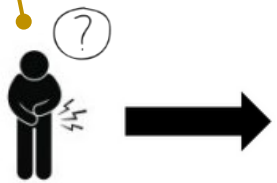

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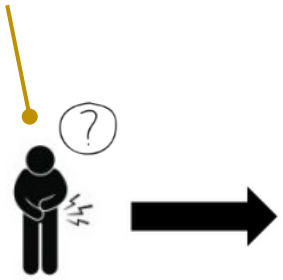

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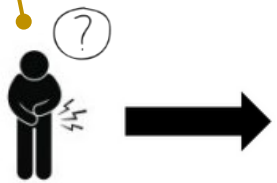

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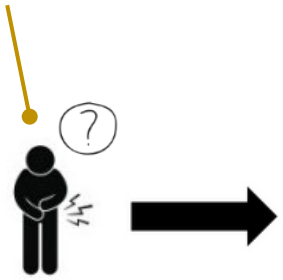

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Phenotypic resistance (antimicrobial susceptibility testing)

Recommendations for Public Health Laboratories

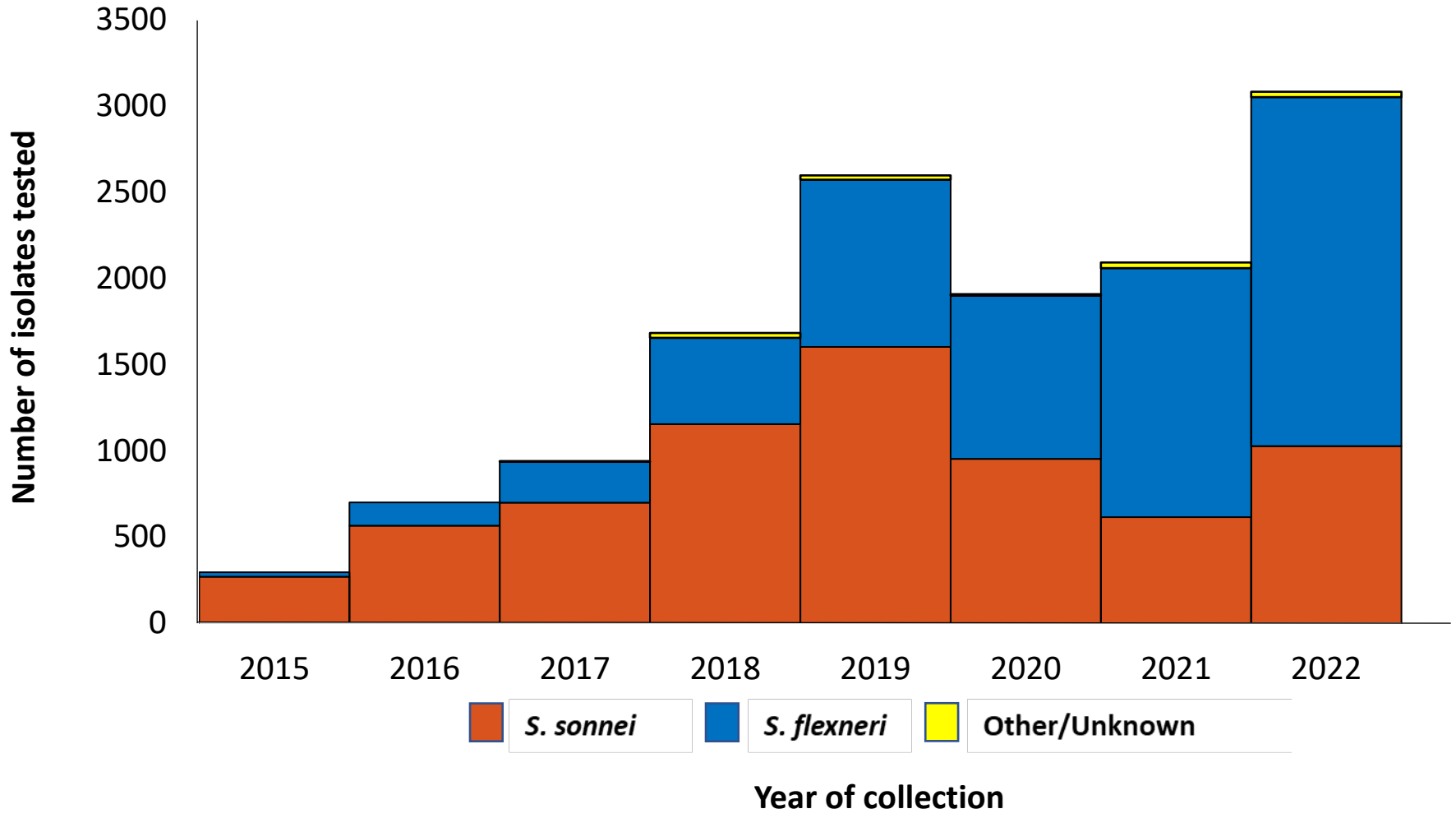
- **Clinical Laboratories**
  - Submit known or suspected XDR *Shigella* isolates to their local or state public health laboratory

- **Public Health Laboratories**
  - Perform whole genome sequencing if possible

Epidemiology and Trends

Naeemah Logan, MD

Total number of *Shigella* spp. isolates (N=13,298) collected by PulseNet in the United States, 2015–2022†



†Among sequenced *Shigella* isolates submitted to CDC's PulseNet Whole Genome Sequencing Database.

Click here to download data

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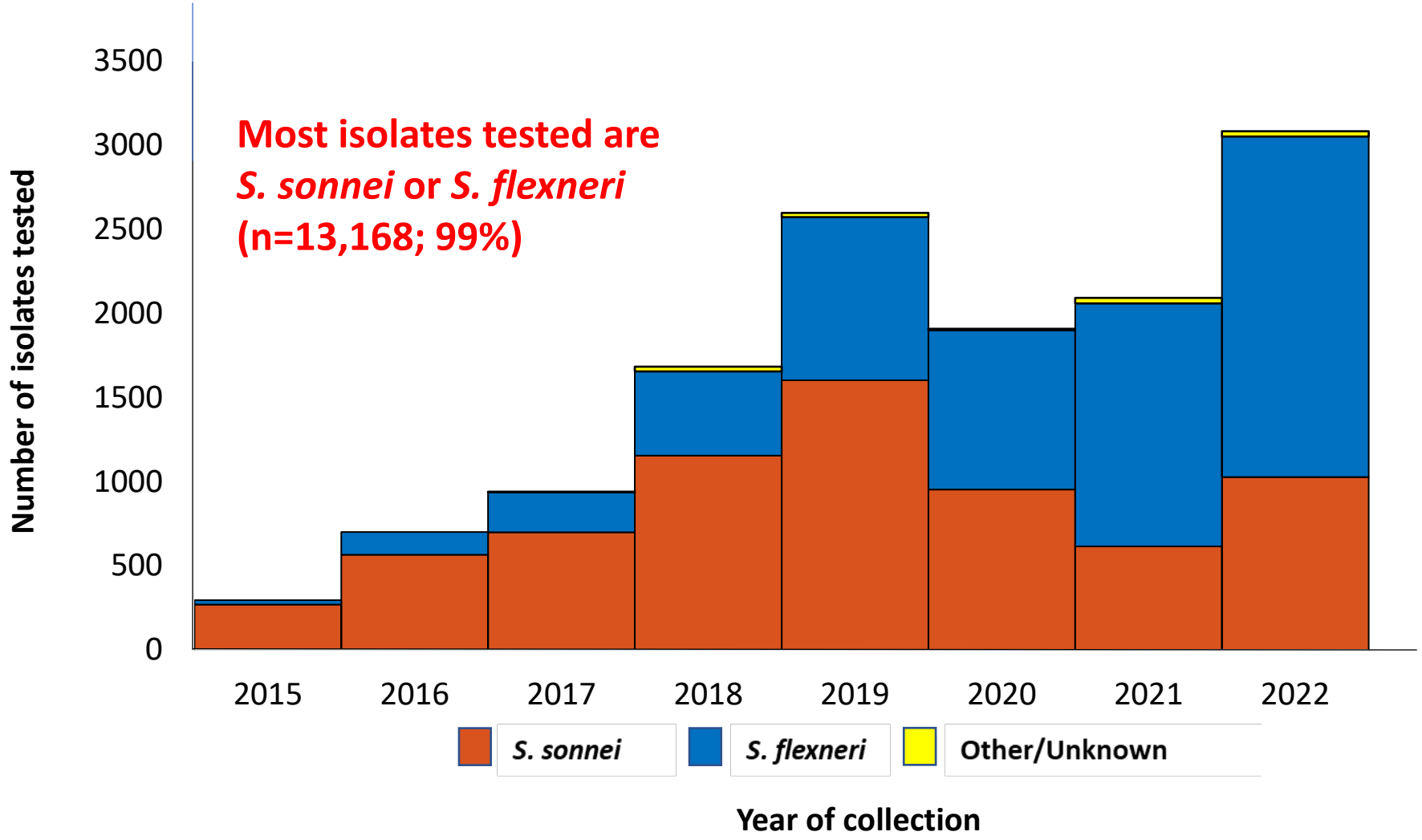

†Among sequenced *Shigella* isolates submitted to CDC's PulseNet Whole Genome Sequencing Database.

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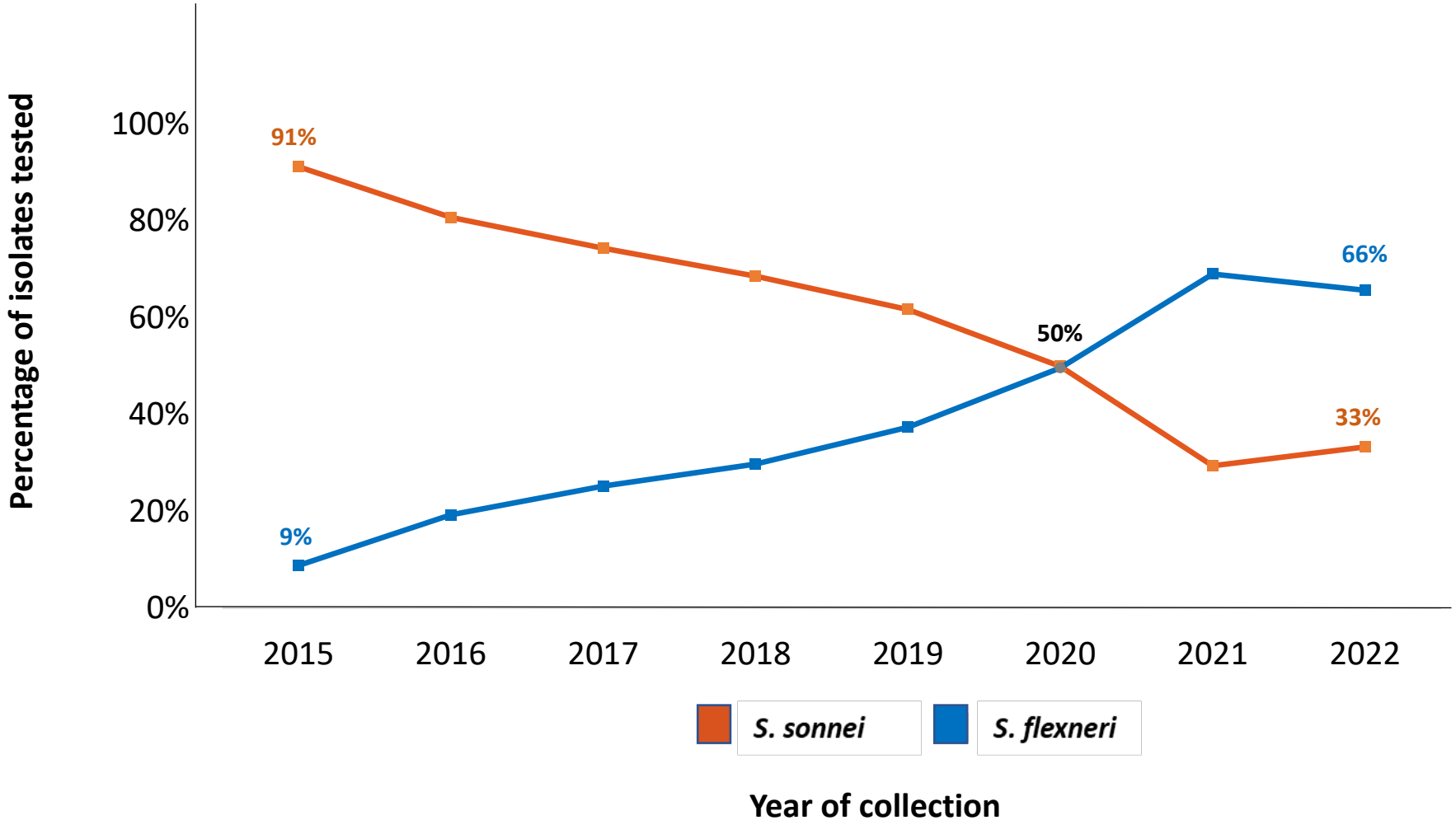
Percentage trends of S. *sonnei* and S. *flexneri* isolates (n=13,168) collected by PulseNet in the United States, 2015–2022†



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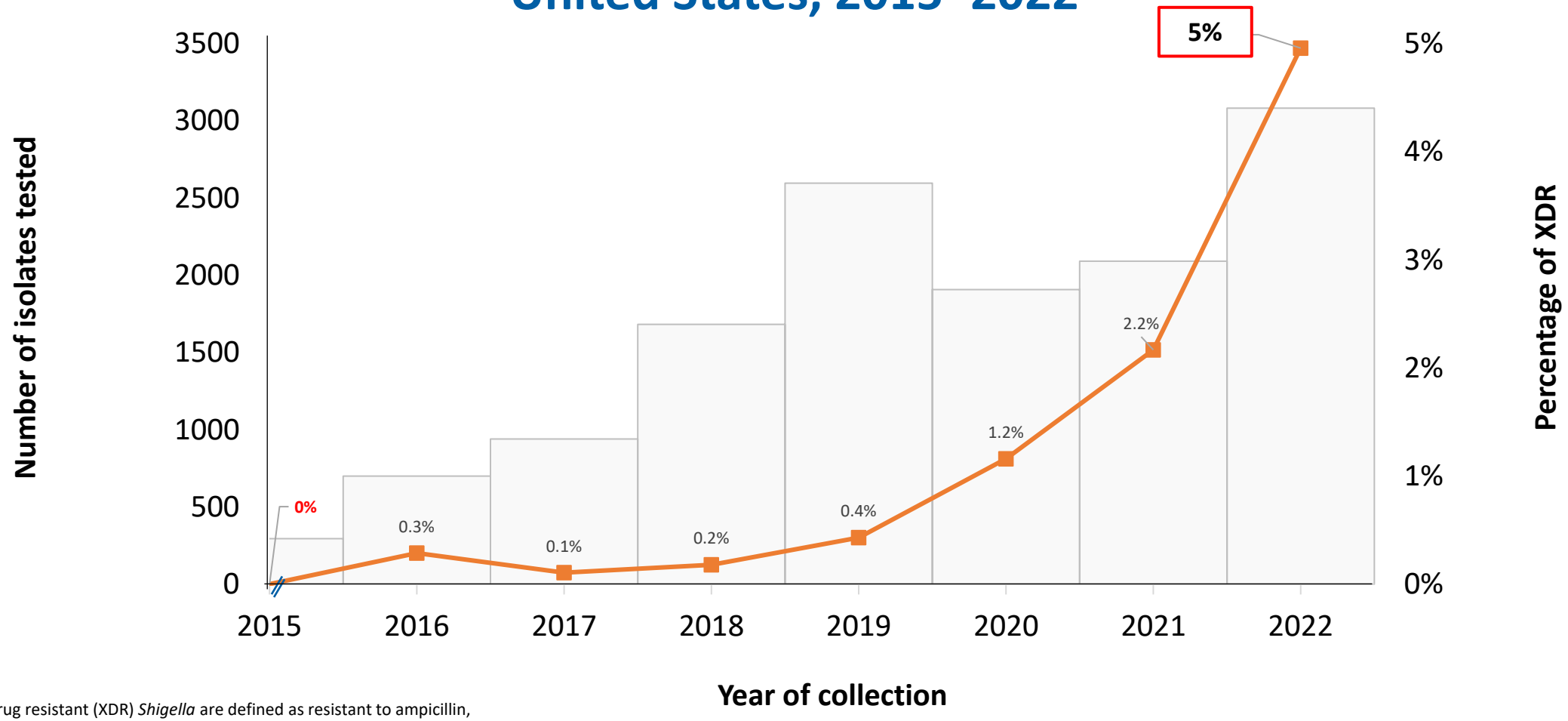
Click here to download data

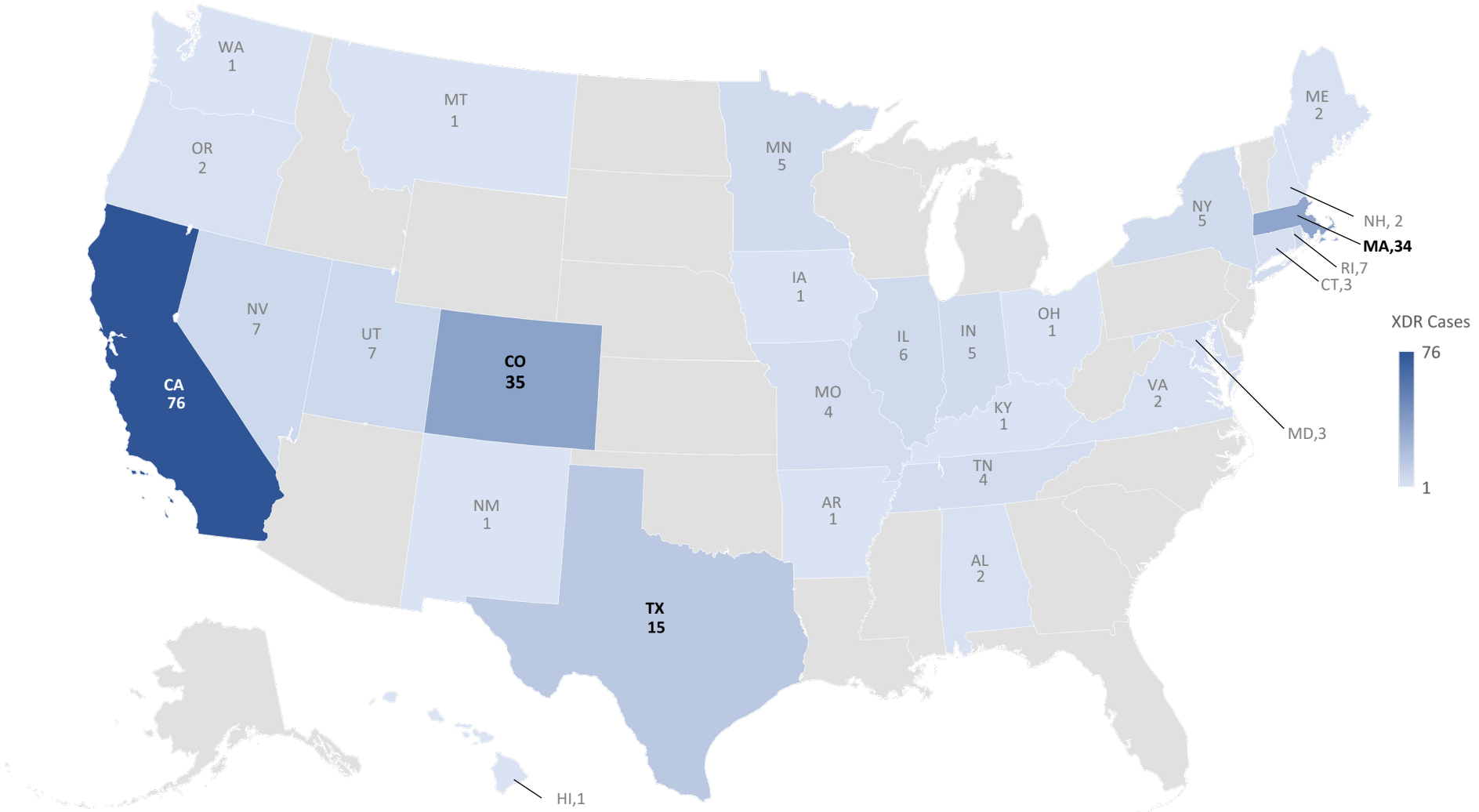
Increase in percentage of *Shigella* isolates that showed an extensively drug-resistant* (n=237) phenotype or genotype United States, 2015–2022†



*Extensively drug resistant (XDR) *Shigella* are defined as resistant to ampicillin, azithromycin, ceftriaxone, ciprofloxacin, and trimethoprim-sulfamethoxazole.
†Among sequenced *Shigella* isolates submitted to CDC's PulseNet Whole Genome Sequencing Database; data are preliminary and based on broth microdilution susceptibility testing and/or presence of resistance genes and mutations found in whole genome sequences of bacterial DNA.

Click here to download data

Cases of extensively drug-resistant* *Shigella* spp. (n=237) in the United States, 2015–2022†



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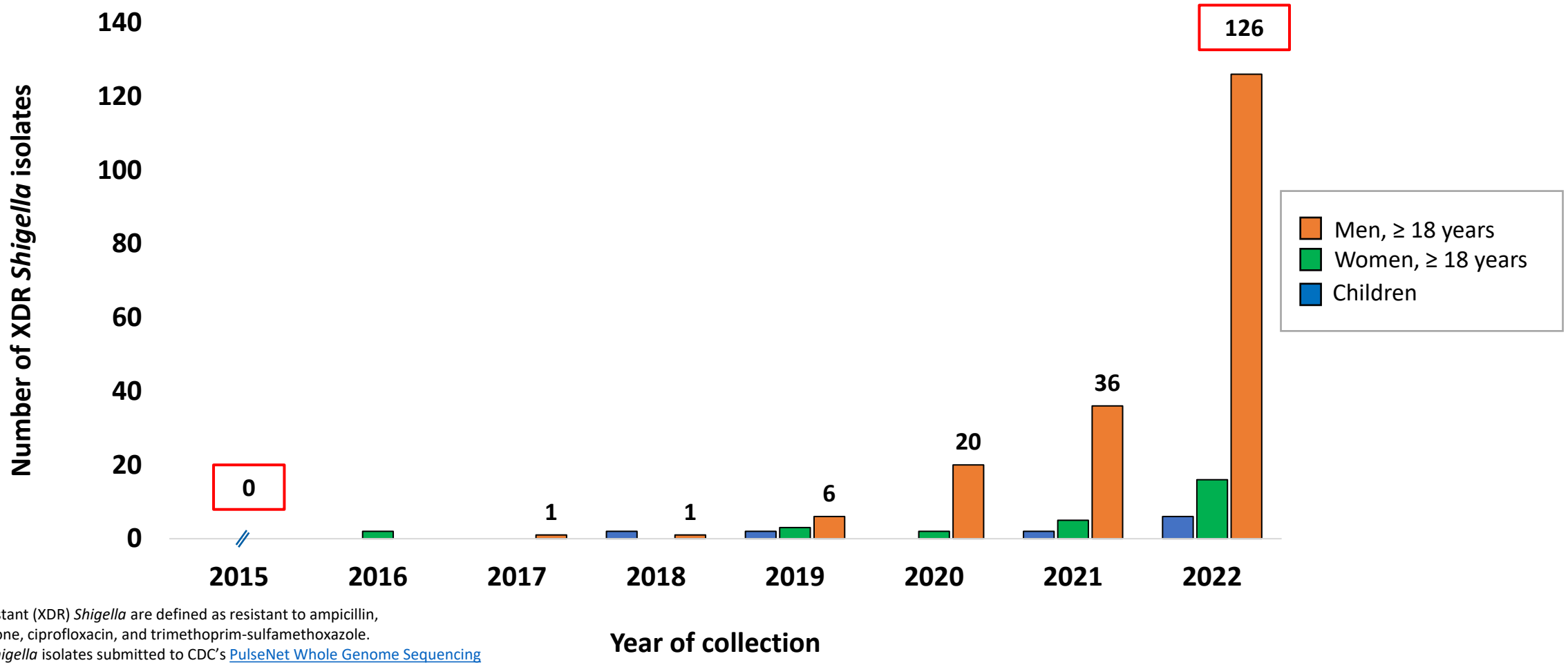
Shigella spp. isolates with extensive drug resistance by demographic group in the United States, 2015–2022†



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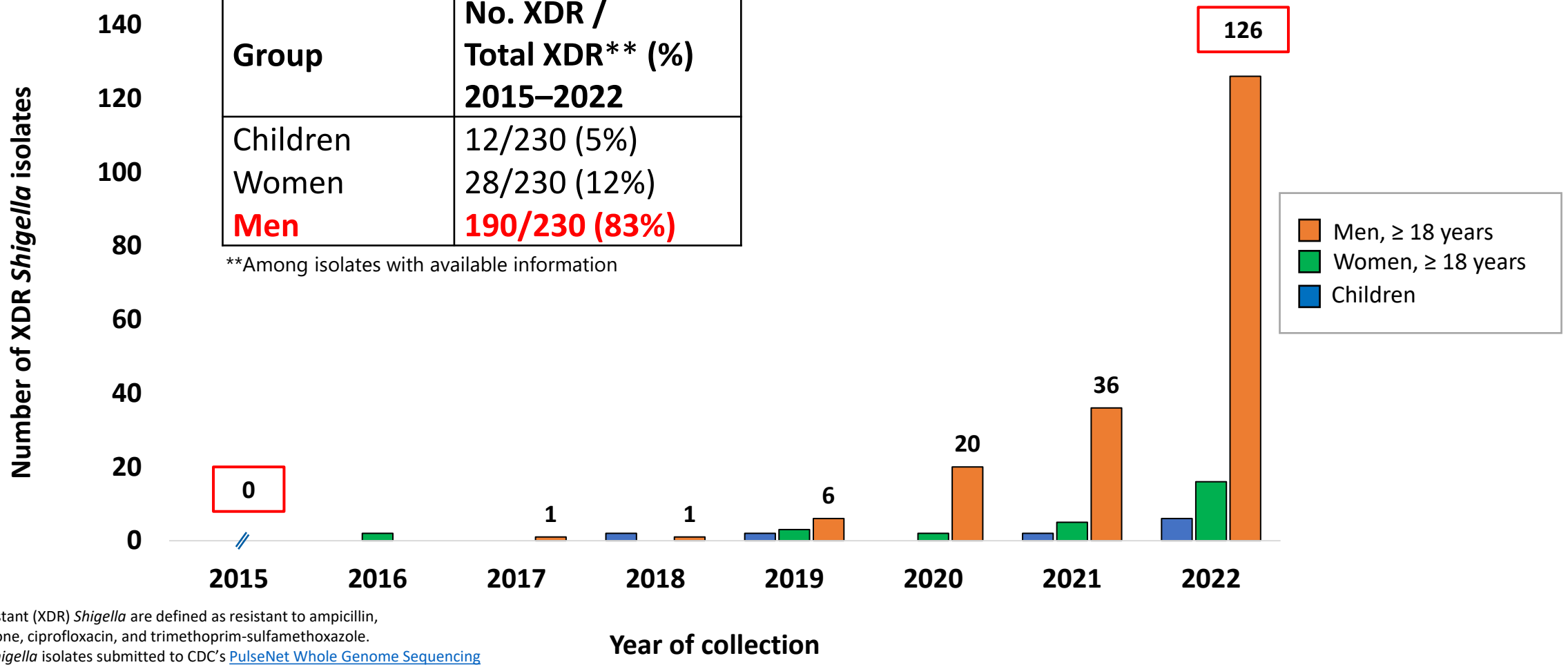
Click here to download data

Shigella spp. isolates with extensive drug resistance by demographic group in the United States, 2015–2022†

Group	No. XDR / Total XDR** (%) 2015–2022
Children	12/230 (5%)
Women	28/230 (12%)
Men	**190/230 (83%)**

**Among isolates with available information



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Click here to download data

Treatment Considerations

Louise Francois Watkins, MD, MPH

Clinical presentation of shigellosis

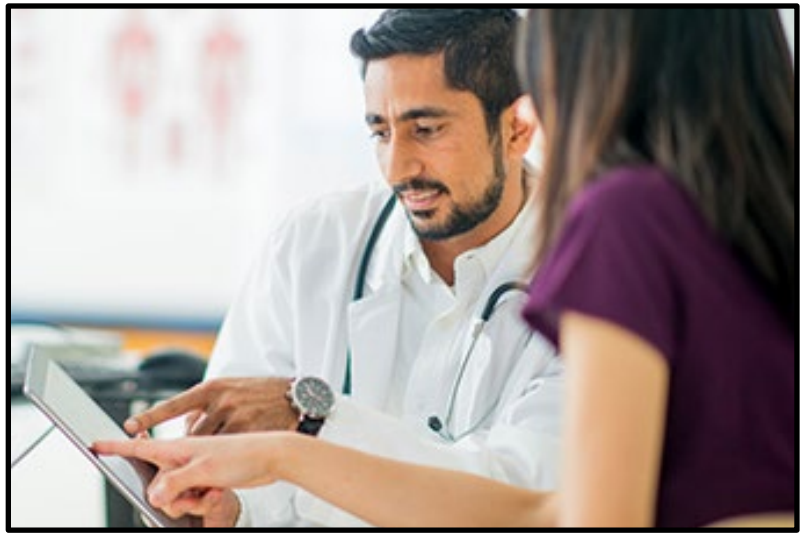
https://www.cdc.gov/shigella/symptoms.html

- Incubation period typically 1–2 days
- The most common symptoms are diarrhea (that can be bloody), fever, abdominal pain, and tenesmus
- Illness is typically self-limited and lasts 5–7 days
  - Symptoms may last longer for those in poor health or with immune compromise
- Complications are rare, but can include
  - Bloodstream infections
  - Reactive arthritis
  - Seizure
  - Hemolytic uremic syndrome

Diagnosis of shigellosis

https://www.cdc.gov/shigella/diagnosistreatment.html

- Consider *Shigella* in the differential diagnosis of patients with acute infectious diarrhea, especially for patients at higher risk for shigellosis
  - Ask about sexual history, travel history, housing status
- Order a stool culture and antimicrobial susceptibility testing (AST)
  - Bacterial isolates are important for outbreak detection and AST
  - If a culture-independent diagnostic test is used, request reflex culture



Management of shigellosis

Supportive care

Antimicrobial treatment

Counseling for infection prevention

Public health reporting

Supportive Care

Management of shigellosis

- Fluid and electrolyte replacement
  - Oral rehydration is often sufficient
- Other supportive nonpharmacologic measures
- Avoid antimotility agents, which may prolong fever, diarrhea, and bacterial shedding

Antimicrobial treatment

Management of shigellosis

- Goals of antimicrobial treatment
  - Reduce duration of illness (1–2 days)
  - Prevent secondary transmission
- Antimicrobial treatment is recommended for patients with severe illness or risk factors for severe illness
  - Patients with mild illness may not require antimicrobial treatment
- Choice of antimicrobial is complicated by availability, efficacy, route of administration, and resistance

Common antimicrobial treatment guidance for shigellosis

Antimicrobial treatment

Source	First-line	Alternative	Comments
Infectious Diseases Society of America (2017)	Azithromycin Ciprofloxacin Ceftriaxone	Trimethoprim-sulfamethoxazole Ampicillin	Alternative treatments recommended only if known to be susceptible
American Academy of Pediatrics (2023)	Fluoroquinolone Azithromycin Ceftriaxone	Trimethoprim-sulfamethoxazole Ampicillin	Alternative treatments recommended only if known to be susceptible
World Health Organization (2005)	Ciprofloxacin	Pivmecillinam* Ceftriaxone Azithromycin (adults)	Ceftriaxone only recommended when local strains known to be resistant to ciprofloxacin

XDR *Shigella* is resistant to ampicillin, azithromycin, ceftriaxone, ciprofloxacin, and trimethoprim-sulfamethoxazole

*Pivmecillinam is not available in the United States

Other potential antimicrobials (and their limitations)

Cells marked "X" indicate the presence of a limitation

Antimicrobial treatment

	Resistance	Poor mucosal penetration	Unavailable in United States	Few clinical trials
1st/2nd gen. cephalosporins	.	X	.	.
Amoxicillin	X	X	.	.
Chloramphenicol	X	.	X	.
Fosfomycin	.	.	.	X
Gentamicin	.	X	.	.
Kanamycin	.	X	.	.
Meropenem	.	.	.	X
Nalidixic acid	X	.	.	.
Nitrofurans	.	X	.	.
Pivmecillinam	.	.	X	.
Tetracycline	X	.	.	.

Fosfomycin or meropenem for shigellosis?

Antimicrobial treatment

	Fosfomycin	Meropenem
Phenotypic resistance present?	Not tested by CDC	No (tested since 2016)
Genotypic resistance present?	Extremely rare	No
CLSI breakpoints available?	No	Yes
Available in oral formulation?	Yes	No
Studied in clinical trials?	Limited	No
On-label use for shigellosis in US?	No	No
International experience?	Yes	Limited

CLSI = Clinical & Laboratory Standards Institute

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Antimicrobial resistance testing results for *Shigella* isolates are available at CDC's NARMS Now: Human Data platform

⟸ QR code https://wwwn.cdc.gov/narmsnow/

NARMS
National Antimicrobial Resistance Monitoring System

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Shigella sequences from U.S. surveillance isolates are uploaded to the National Center for Biotechnology Information's Pathogen Detection Pipeline under BioProject ID PRJNA218110

⟸ QR code https://www.ncbi.nlm.nih.gov/bioproject/218110

NCBI

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CLSI's M100 contains information about clinical breakpoints (select "guest access" to see for free!)

⟸ QR code http://em100.edaptivedocs.net/Login.aspx

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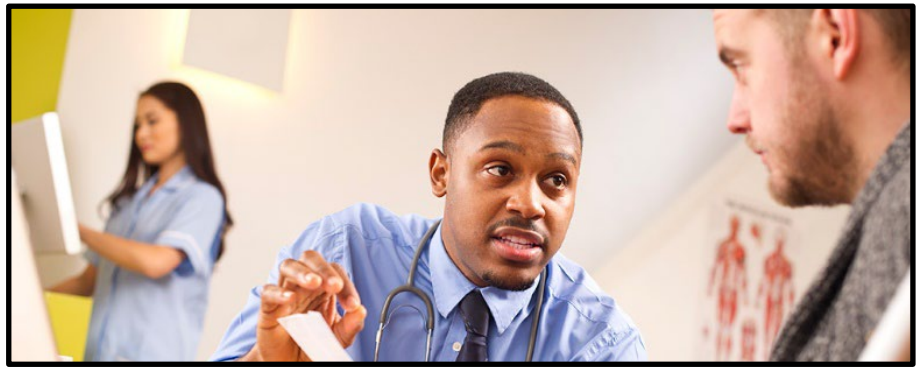
Fosfomycin is the most-prescribed antimicrobial for the treatment of acute infectious diarrhea in Japan overall (37.7%) and among children (44.1%)

⟸ QR code https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06688-2

Counseling for infection prevention

Management of shigellosis

- Stay home from school or high-risk jobs (such as healthcare, food service, and childcare) while sick or until the health department says it's safe to return
- During diarrhea and for 2 weeks after it ends:
  - Abstain from sex (anal, oral, or vaginal)
  - Wash hands often
  - Do not prepare food for others
  - Stay out of recreational water



Public health reporting

Management of shigellosis

- Shigellosis is a nationally notifiable disease
  - Healthcare professionals and clinical laboratories should report all cases to their local or state health department
- Healthcare professionals should consult their local or state health department for guidance on when patients may return to childcare, school, or work
- **To help CDC gather data, report information about treatment response and clinical outcomes of XDR *Shigella* infections to EntericBacteria@cdc.gov**

How should clinicians approach treatment of XDR shigellosis?

- Revisit whether antimicrobial treatment is needed
- Review antimicrobial susceptibility testing (AST) results
- Consult an infectious diseases specialist
- Be aware that there is limited evidence-based guidance for best management of XDR *Shigella* infections
  - CDC does not have official recommendations for antimicrobial management of XDR *Shigella* infections
- Be aware of what we know about resistance of XDR *Shigella* isolates to other antimicrobials
- Be aware of treatment strategies that have been used internationally

More information is available

Contact us:
EntericBacteria@cdc.gov

CDC's *Shigella* HAN	CDC's *Shigella* website	IDSA treatment guidance	AAP treatment guidance

WHO treatment guidance	WHO report: XDR *Shigella*	UK report: XDR *Shigella*	CDC's NARMS Now: Human Data

CDC's *Shigella* Health Alert Network:
https://emergency.cdc.gov/han/2023/han00486.asp
CDC's *Shigella* website:
https://www.cdc.gov/shigella/
IDSA treatment guidance:
https://academic.oup.com/cid/article/65/12/e45/4557073
AAP treatment guidance:
https://publications.aap.org/aapbooks/book/723/chapter/10679299/Shigella-Infections
WHO treatment guidance:
https://www.who.int/publications/i/item/9241592330
WHO report – XDR *Shigella*:
https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON364
UK report – XDR *Shigella*:
https://www.sciencedirect.com/science/article/pii/S147330992200370X?via%3Dihub
CDC's NARMS Now: Human Data:
https://wwwn.cdc.gov/narmsnow/

Knowledge check

- Among sequenced *Shigella* isolates reported to CDC in 2022, what percentage were extensively drug-resistant (XDR)?

  A. 1%

  B. 5%

  C. 10%

  D. 80%

Knowledge check

- Among sequenced *Shigella* isolates reported to CDC in 2022, what percentage were extensively drug-resistant (XDR)?

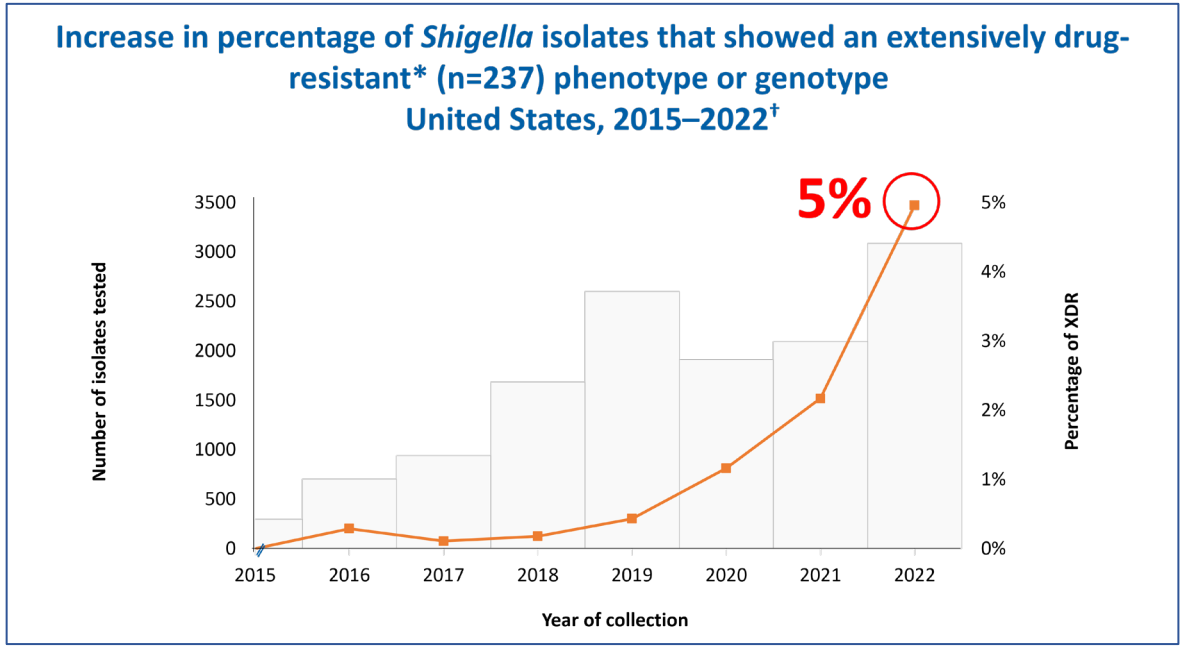
  A. 1%

  B. 5%

  C. 10%

  D. 80%

- Answer: B.
- In 2022, 5% of all *Shigella* isolates uploaded to CDC's PulseNet surveillance system had an XDR resistance pattern.

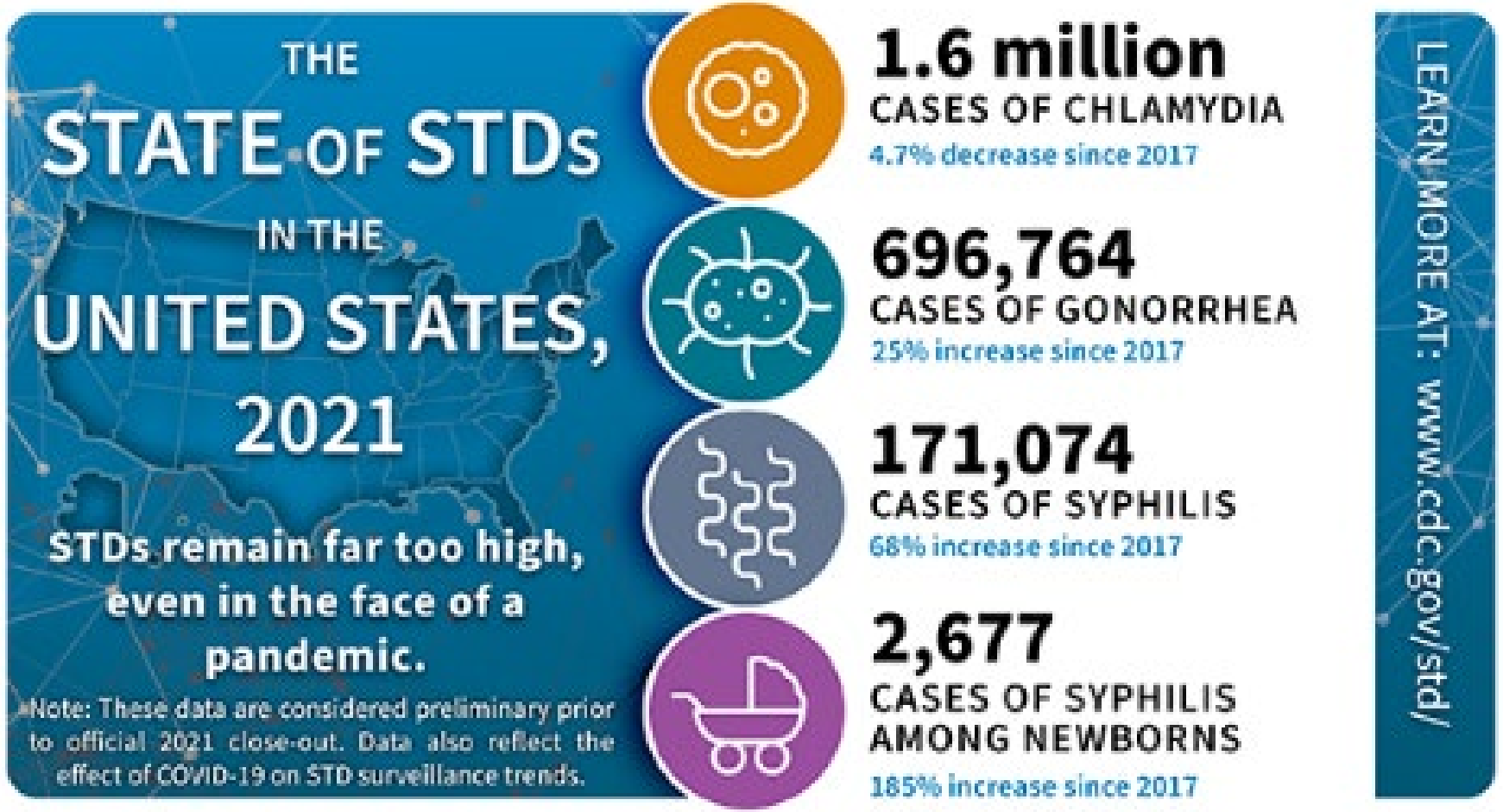


Click here to download data

Shigella as a Sexually Transmitted Infection: An Opportunity for Sexual Health Promotion

Laura Hinkle Bachmann, MD, MPH, FIDSA, FACP
Chief Medical Officer
Division of STD Prevention
National Center for HIV/AIDS, Viral Hepatitis, STD and TB Prevention
Centers for Disease Control and Prevention

February 28, 2023



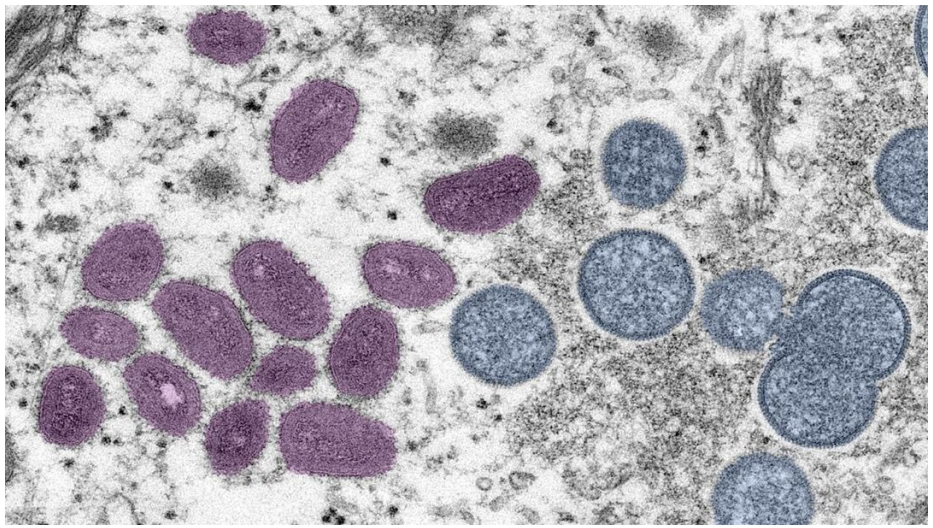
The State of STDs - Infographic (cdc.gov)

New and evolving threats to sexual health

Troubling gonorrhea strain detected in Massachusetts

Chris Dall, MA, January 20, 2023

Topics: Antimicrobial Stewardship , Gonorrhea , Sexually Transmitted Infections



Home / Eurosurveillance / Volume 27, Issue 46, 17/Nov/2022 / Article

Rapid communication

Open Access

Detection of 10 cases of ceftriaxone-resistant *Neisseria gonorrhoeae* in the United Kingdom, December 2021 to June 2022

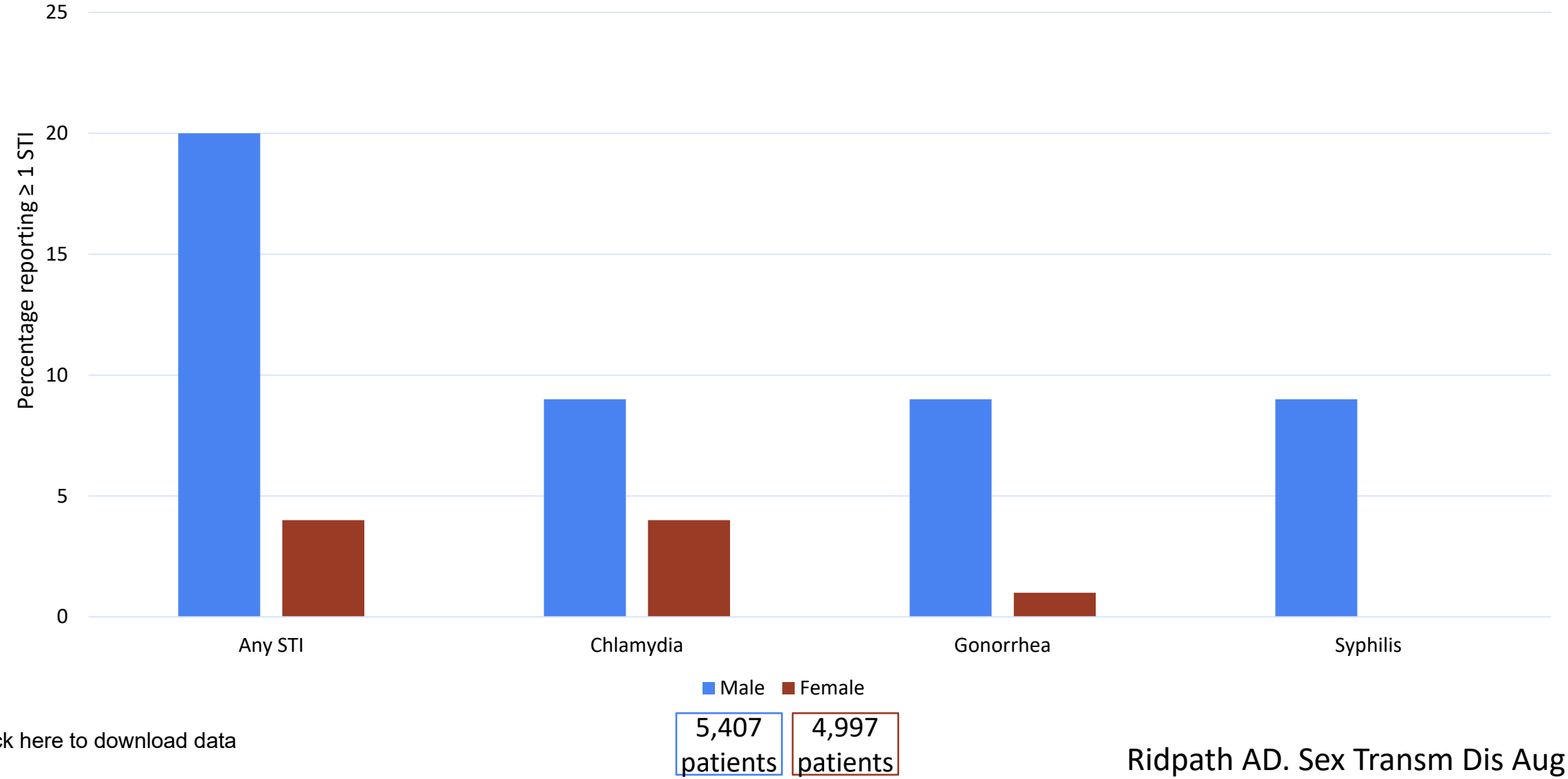
Like 0

Download

Check for updates

Michaela Day[1] , Rachel Pitt[1] , Nisha Mody[1] , John Saunders[1] , Rupa Rai[1] , Achyuta Nori[1] , Hannah Church[1] , Sarah Mensforth[1] , Helen Corkin[1] , Jacqueline Jones[2] , Preneshni Naicker[3] , Wazirzada M Khan[1] , Rebecca Thomson Glover[1] , Kalani Mortimer[1] , Chloe Hylton[1] , Elizabeth Moss[1] , Thomas Joshua Pasvol[1] , Ania Richardson[1] , Suzy Sun[1] , Neil Woodford[1] , Hamish Mohammed[1] , Katy Sinka[1] , Helen Fifer[1]

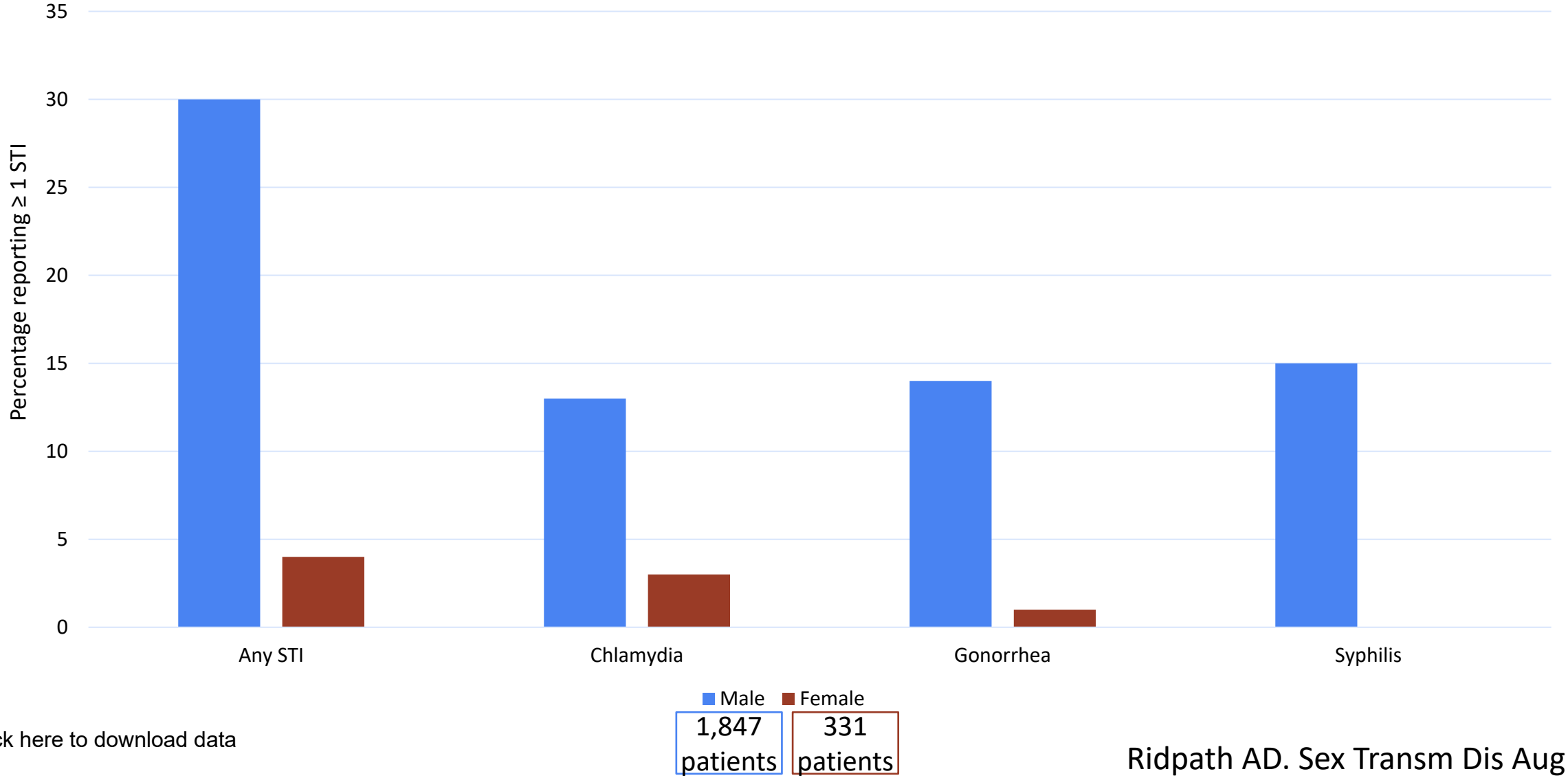
Percentages of reported culture-confirmed *Shigella* cases with at least 1 STI reported within ±12 months by sex in 6 U.S. jurisdictions, 2007–2016



Click here to download data

Ridpath AD. Sex Transm Dis Aug 2022

Percentages of reported culture-confirmed *Shigella flexneri* cases with at least 1 STI reported within ±12 months by sex in 6 U.S. jurisdictions, 2007–2016



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Ridpath AD. Sex Transm Dis Aug 2022

Specific behaviors associated with sexually transmitted enteric infections include:

- Any activity that results in feces from an individual harboring *Shigella*, even microscopic amounts, coming into direct or indirect contact with the partner's mouth
- Specific activities associated with infection with *Shigella* and other enteric pathogens
  - Oral-anal sex
  - Condomless sex
  - Multiple sex partners
  - Attendance at sex parties/venues
  - Using social media to find sex partners

Many of these behaviors associated with STIs, including HIV!

Sexual Health = Health

"When you get into venereal diseases you get into sex and when you get into sex you get into the most fundamental thing in the human race. We can't CURE it" – Philip Mather, ASHA

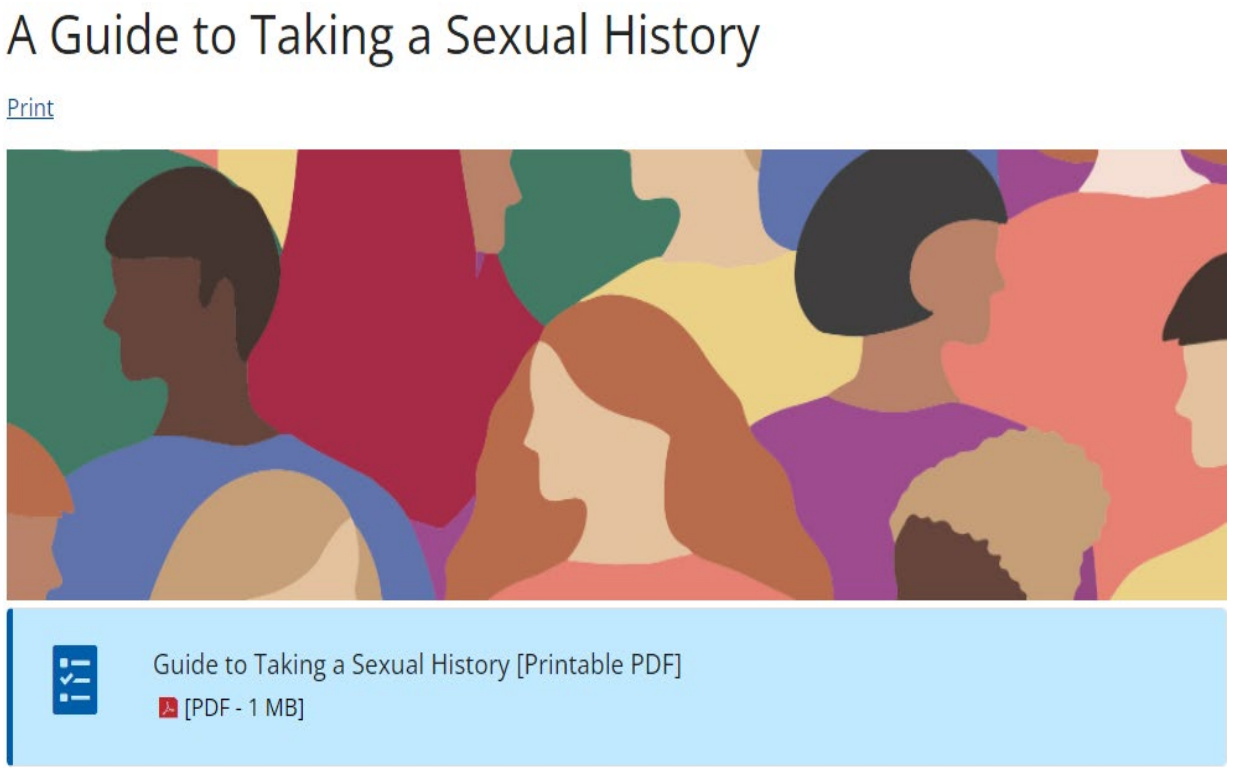
Brandt AM, No Magic Bullet, Oxford University Press, New York, NY, 1987

Integrating sexual health into clinical care

- Provide a welcoming clinical environment
- Incorporate sexual history as routine part of social history
- Screen for STIs including HIV and provide vaccinations per guidelines

Sexual History — an important component of comprehensive care

- Partners
- Practices
- Protection from STIs
- Past History of STIs
- Pregnancy Intention



https://www.cdc.gov/std/treatment/sexualhistory.pdf

STI Screening Recommendations — MSM

- **At least annually**
  - Gonorrhea and chlamydia at anatomic sites of exposure
  - Syphilis
  - HIV
- **Every 3–6 months if at higher risk (multiple partners, anonymous partners, etc.)**
- **Hepatitis A, B, and C screening**
- **Digital anorectal exam**

Workowski KA. STI Treatment Guidelines, 2021. MMWR. July 23, 2021

STI Screening Recommendations — Women

- **Gonorrhea and chlamydia**
  - < 25 years of age annually
  - 25 years and older of age if at risk*
- **Syphilis**
  - High prevalence area or increased risk+
- **Trichomonas**
  - Consider in high prevalence area or at increased risk
- **HIV**
  - All women aged 13–64 years (opt-out)
  - All women who seek evaluation and treatment for STIs
- **Hepatitis B and C screening**

*Sexually active women 25 years or older are at increased risk for chlamydial and gonococcal infections if they have a new partner, more than one sex partner, a sex partner with concurrent partners, or a sex partner who has an STI; practice inconsistent condom use when not in a mutually monogamous relationship; have a previous or coexisting STI; have a history of exchanging sex for money or drugs; or have a history of incarceration.

+history of incarceration or transactional sex work, geography

These recommendations do not apply to pregnant people

Workowski KA. STI Treatment Guidelines, 2021. MMWR. July 23, 2021

STI Screening Recommendations — Transgender and Gender Diverse

- **Consider screening for syphilis at least annually based on reported behaviors and exposure**
- **Offer HIV screening to all transgender persons**
- **Hepatitis B and C screening**
- **Base CT/GC screening on current anatomy and gender of sex partners**
  - Transgender women post vaginoplasty
    - GC/CT (all sites of exposure: oral, anal, genital)
    - Best specimen type based on tissue type used to construct neovagina
  - Transgender men post metoidioplasty
    - If vagina still present and need to screen for STIs, cervical (or vaginal) swab should be used

Workowski KA. STI Treatment Guidelines, 2021. MMWR. July 23, 2021

Prevention — Vaccination

- **Hepatitis A virus (HAV)**
  - MSM
  - Other individuals at increased risk for acquiring HAV or increased risk for severe disease from HAV
- **Hepatitis B virus (HBV)**
  - All unvaccinated adults aged 19-59 years
  - Adults ≥60 years with risk factors for hepatitis B
  - All unvaccinated children and adolescents
- **Human papillomavirus (HPV)**
  - All adolescents at age 11 or 12 years with catch-up vaccination through age 26
  - Shared clinical decision-making for certain adults aged 27–45 years

Prevention basics for sexually-acquired *enteric* infection

- Avoid sexual activity with individuals with diarrhea or who recently recovered from diarrhea
  - Individuals with diarrhea should avoid sexual activity during and for two weeks after their diarrhea ends
- Reduce fecal-oral exposure during sex by washing genitals, anus and hands before and after sex
- Use barriers like condoms and dental dams during oral-genital and oral-anal sex
- Use latex gloves during anal fingering and fisting
- Use latex internal or external condoms during anal and vaginal sex to prevent other STIs

Shigella Infection Among Gay, Bisexual, and Other Men Who Have Sex with Men (MSM) | *Shigella* – Shigellosis | CDC

Self-knowledge check

Which of the following steps can be taken to integrate sexual health into clinical care?

A. Include sexual history as a routine part of care
B. Provide clinical staff with opportunities for cultural competency training
C. Implement a syndemic approach to testing and vaccination strategies
D. All of the above

Self-knowledge check

Which of the following steps can be taken to integrate sexual health into clinical care?

A. Include sexual history as a routine part of care
B. Provide clinical staff with opportunities for cultural competency training
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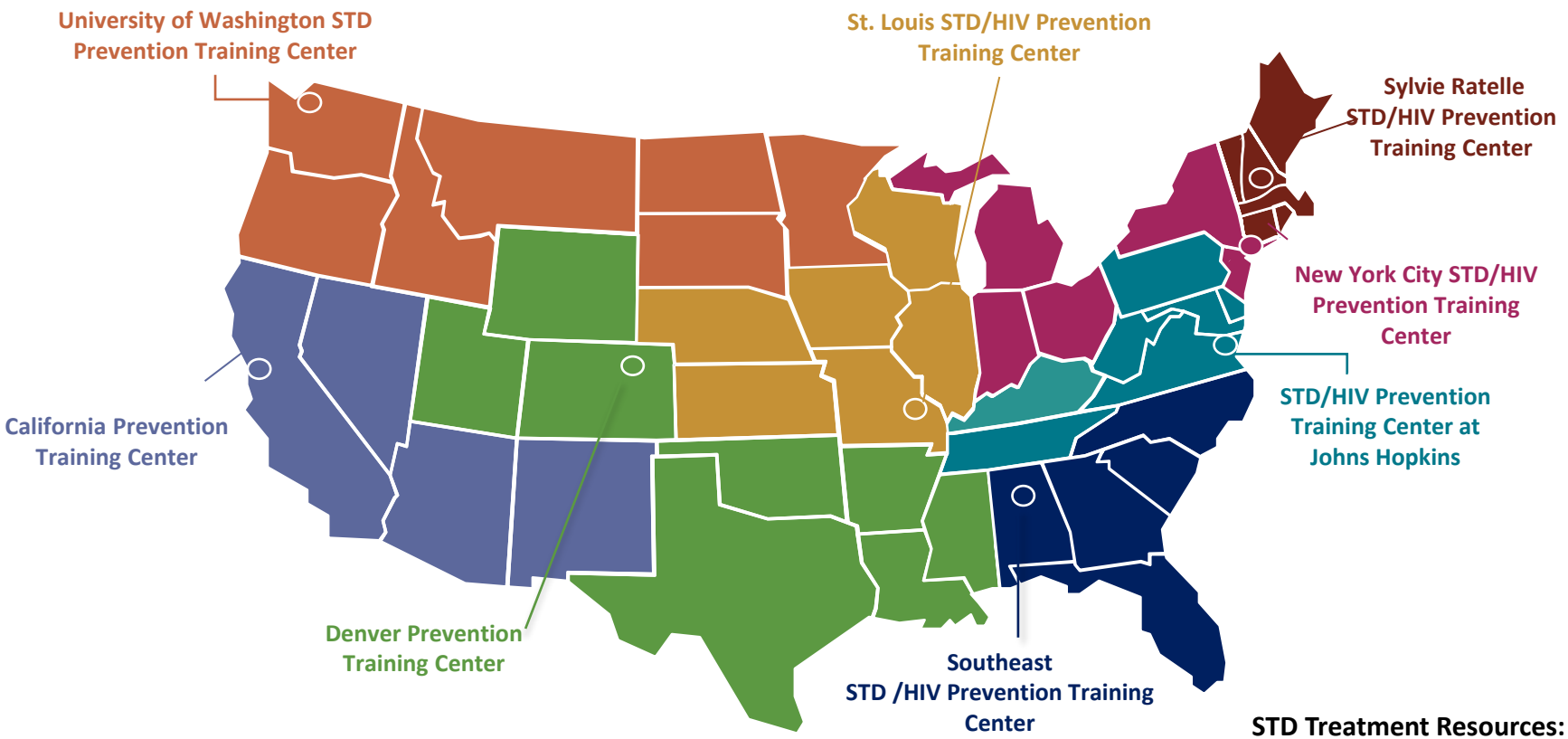
National Network of STD Clinical Prevention Training Centers



STD Treatment Resources:
www.nnptc.org

Clinical Consultations:
www.STDCCN.org

National STD Curriculum

www.std.uw.edu

The *National STD Curriculum* integrates the most recent CDC STD Treatment Guidelines into a free, up-to-date, educational website. The site addresses the epidemiology, pathogenesis, clinical manifestations, diagnosis, management, and prevention of STDs.

- Seven Self-Study Modules
- Twelve Question Bank topics with 100+ interactive board-review style questions
- Modular learning in any order with progress tracker
- Group registration and tracking for staff, students, and health care organizations
- FREE CME and CNE credits

This curriculum was funded by a grant from the U.S. Centers for Disease Control and Prevention (CDC) and developed by the University of Washington STD Prevention Training Center.

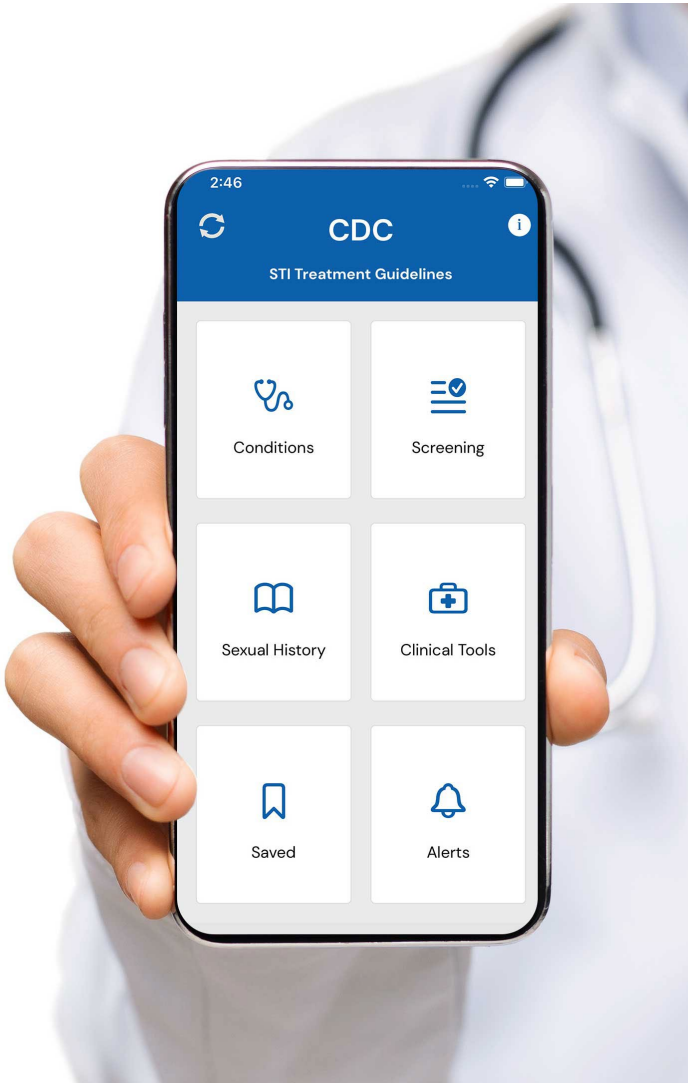
National STD Curriculum

STI Treatment Guide Mobile App

Get treatment regimens *FAST*

Download CDC's free app for iPhone and Android devices

www.cdc.gov/std



Disclaimer

The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

Colorado response to XDR *Shigella*

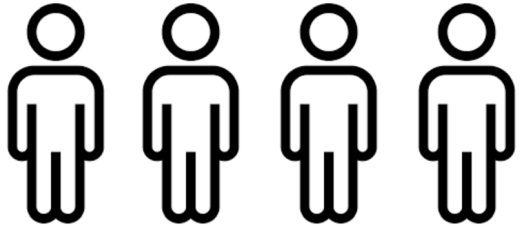
Rachel H. Jervis, MPH
Foodborne, Enteric, Waterborne, + Wastewater Diseases
Program Manager

COCA Call
February 28, 2023

COLORADO
Department of Public Health & Environment

Timeline

Aug. 29, 2022



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Sept. 6, 2022

Sept. 9, 2022

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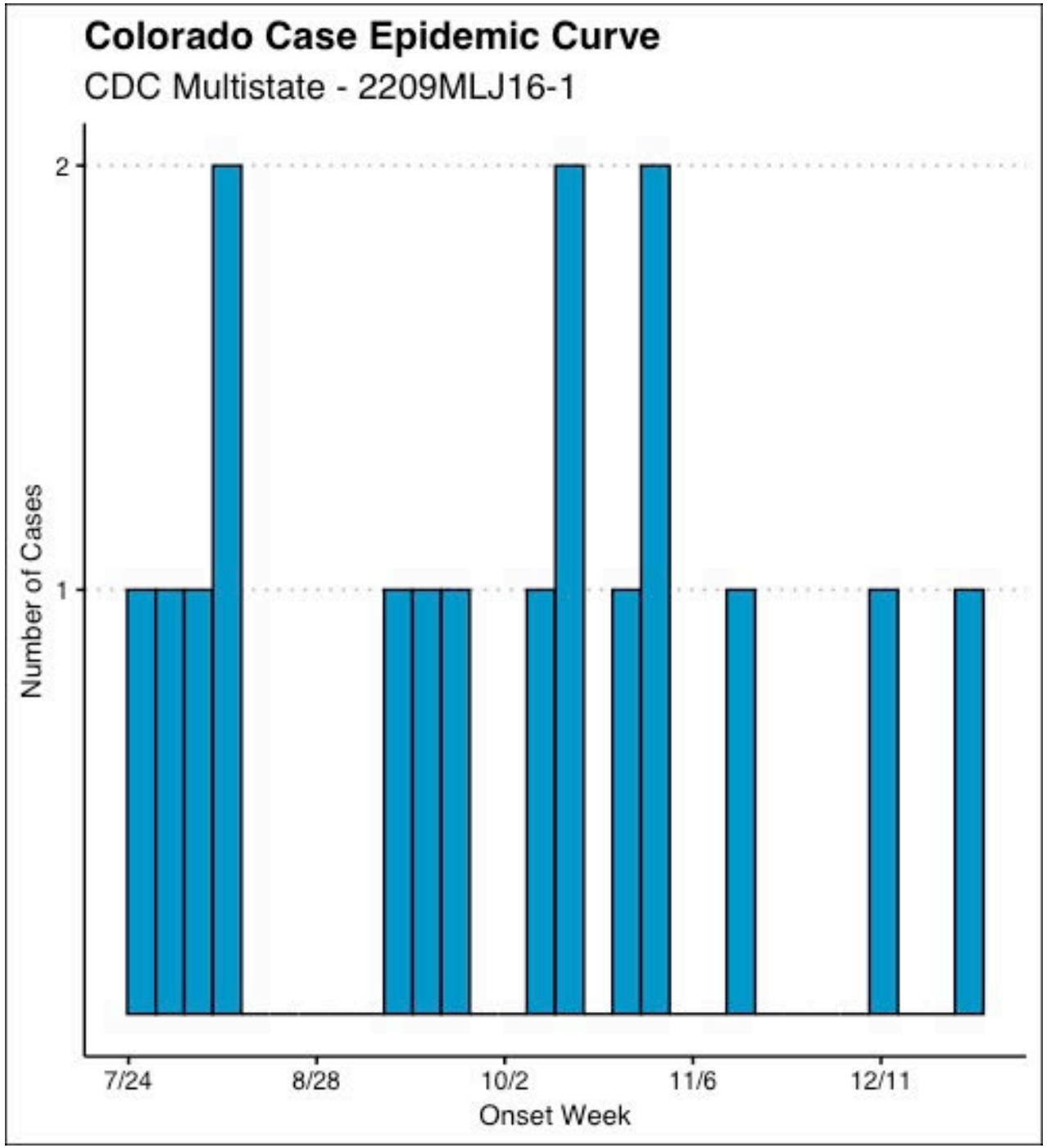
Epidemiology

Click here to download data



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Epidemiology

Click here to download data

	Overall (N=17)
Age - Median (Min, Max)	40 (20, 83)
County	
Adams	2 (11.8%)
Arapahoe	2 (11.8%)
Denver	11 (64.7%)
El Paso	1 (5.9%)
Larimer	1 (5.9%)
Hospitalized	
Yes	8 (47.1%)
Sex	
Male	14 (82.4%)
Female	3 (17.6%)
Men who have sex with men	
Yes	10 (58.8%)
Person Experiencing Homelessness	
Yes	4 (23.5%)
Reports Polysubstance Use	
Yes	5 (29.4%)
Immunocompromised	
Yes	10 (58.8%)

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Health Alert Network

1

2

3

HEALTH ADVISORY | Drug resistant *Shigella* infections | October 17, 2022

Health care providers: Please distribute widely in your office

This information is for the public health and health care community. Do not post this document on a public web or social media site.

Key points

- Multidrug resistant and extensively drug resistant *Shigella* cases continue to be identified in Colorado, including in a cluster impacting men who have sex with men.
  - Multidrug resistant (MDR) *Shigella* is defined as resistance to ampicillin, azithromycin, ciprofloxacin, and cotrimoxazole.
  - Extensively drug resistant (XDR) *Shigella* is defined as resistance to ampicillin, azithromycin, ciprofloxacin, cotrimoxazole, and ceftriaxone.
  - XDR *Shigella* cases have been detected recently in Colorado.
- Clinicians should order stool culture for patients suspected of having *Shigella* and request antimicrobial susceptibility testing to guide treatment decisions when treatment is indicated.
- All culture or PCR positive cases of *Shigella* must be reported to CDPHE and isolate/clinical material must be submitted to the CDPHE laboratory. Additional information below.
- Counsel patients with *Shigella* not to attend child care and/or work in healthcare, food service, or child care until cleared by public health. Counsel patients how to reduce risk of sexual transmission of diarrheal illness. More information: https://cdphe.colorado.gov/play-safe
- Additional information from CDC is forthcoming and CDPHE will distribute to HAN recipients.

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Health Alert Network

Our HAN got some unexpected attention from members of the MSM community.

One video on TikTok spread quickly and received:

- More than 30,000 likes
- More than 1,000 comments
- More than 3,000 shares

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Public education

https://cdphe.colorado.gov/play-safe

Play safe

Diarrhea can spread germs among men who have sex with men.

The facts

- Germs spread easily from any contact with feces (poop).
- It's especially easy to spread germs during oral sex or anal sex play (rimming, fisting, and using anal toys).
- *Shigella*, *Salmonella*, *E. coli*, *Giardia*, and *Cryptosporidium* are some germs spread in feces. These germs can cause diarrhea, stomach cramps, and sometimes fever.
- Illness caused by these germs can be serious, especially if you have HIV.

You can prevent diarrheal illness

- Wash your hands, penis, butt, and sex toys with soap and water before and after sex.
- If you don't have soap and water, use wipes or hand sanitizer (hand gel).
- Avoid sex if you or your partner have diarrhea, or have had it in the last two weeks.
- See your health care provider if you have diarrhea.

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Public education update

https://cdphe.colorado.gov/shigella

Who is most likely to get a *Shigella* infection?

- Young children are the most likely to get a *Shigella* infection, but people of all ages can be affected.
- Travelers to areas with poor sanitation and hygiene systems are more likely to get a *Shigella* infection.
- People who engage in oral-anal or oral sex are more likely to get a *Shigella* infection.
- People who have weakened immune systems due to illness (such as HIV) or medical treatment (such as chemotherapy) can get a more serious illness.

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Self-knowledge Check:

During an XDR *Shigella* outbreak, public health case interviews are used to for all of these EXCEPT:

A. Collect symptom information
B. Collect exposure data
C. Determine antimicrobial resistance of the *Shigella*
D. Provide disease control guidance
E. Detect and solve outbreaks

The correct answer:

During an XDR *Shigella* outbreak, public health case interviews are used to for all of these EXCEPT:

A. Collect symptom information
B. Collect exposure data
C. **Determine antimicrobial resistance of the *Shigella***
D. Provide disease control guidance
E. Detect and solve outbreaks

Rationale: Laboratory testing is necessary to identify antimicrobial resistance.

Thank you!

rachel.jervis@state.co.us

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Department of Public Health & Environment

Disclaimer

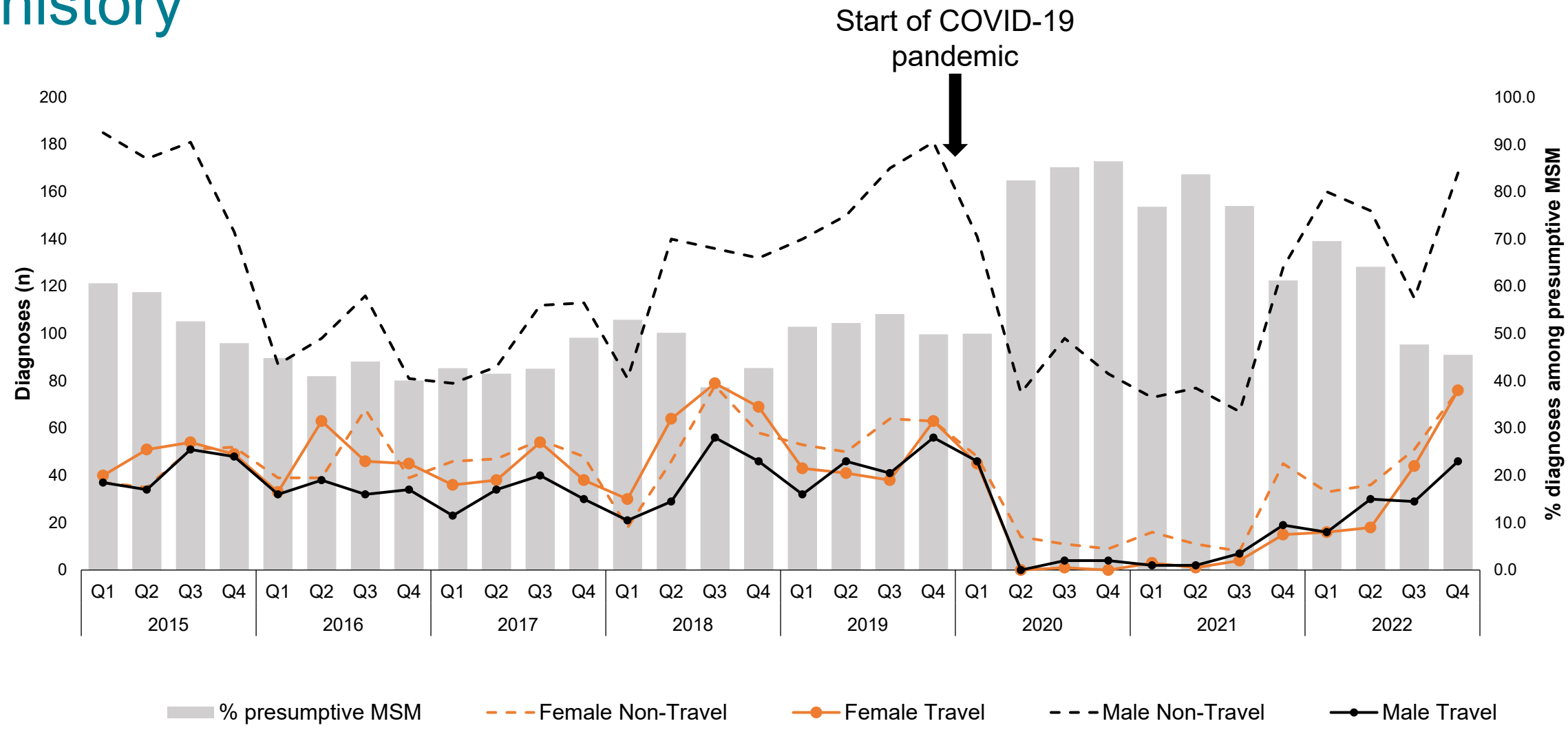
The findings and conclusions in this report are those of the author(s) and do not necessarily represent the official position of the Centers for Disease Control and Prevention (CDC).

UK Health Security Agency

Lessons learnt from an outbreak of sexually transmitted, extensively-drug resistant *Shigella sonnei* in the UK, 2021-22

Dr Gauri Godbole – Consultant Medical Microbiologist
Hannah Charles – Principal Epidemiologist

Shigella spp. trends in England by gender and travel history

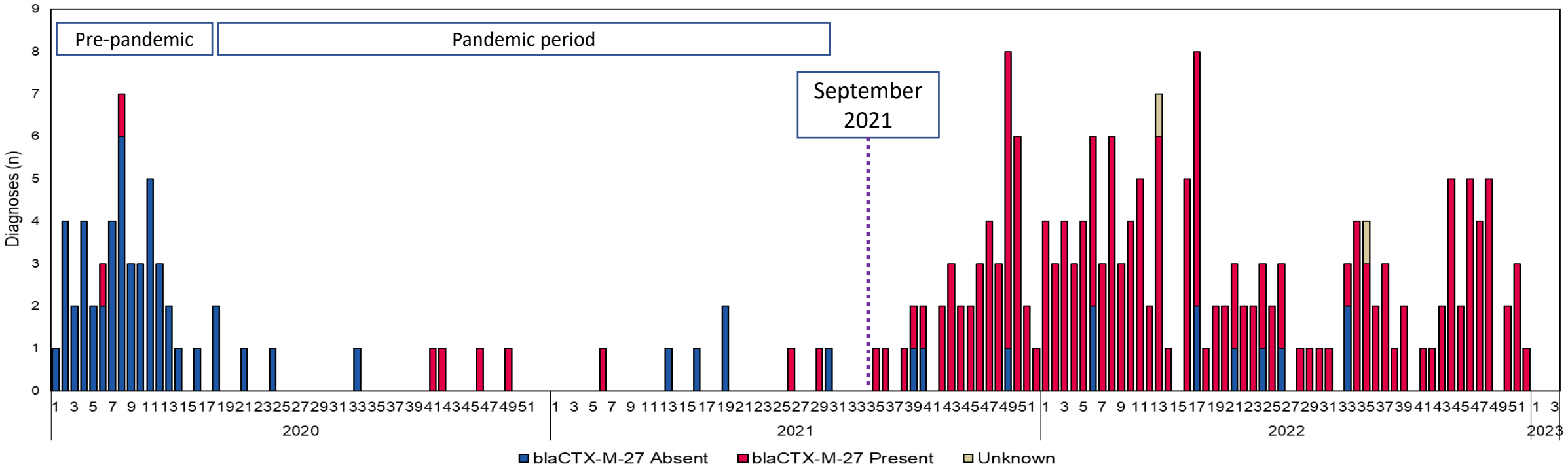


For data requests, please contact Hannah.Charles@ukhsa.gov.uk and Gauri.Godbole@ukhsa.gov.uk

Shigella spp. trends in England by species (among MSM)

For data requests, please contact Hannah.Charles@ukhsa.gov.uk and Gauri.Godbole@ukhsa.gov.uk

Extensively-drug resistant *Shigella sonnei*



- ***S. sonnei* ST152 CC152, 10 SNP cluster also called UK MSM Clade 5**: large MDR cluster endemic in England among gay, bisexual and other men who have sex with men in since 2018, but very low activity between March 2020 and August 2021
- Since **September 2021**, increase in number of *S. sonnei* cases among presumptive MSM + change in AMR profile ($bla_{\text{CTX-M-27}}$) – resulting in XDR profile
- **Risks for health protection**: (i) increased severity due to reduced susceptibility to antimicrobials used to treat sepsis, (ii) transmission outside of sexual networks (spill over to other settings including vulnerable populations), (iii) transfer of AMR determinants to other pathogens

For data requests, please contact Hannah.Charles@ukhsa.gov.uk and Gauri.Godbole@ukhsa.gov.uk

Lessons learnt from an outbreak of sexually transmitted, extensively-drug resistant *Shigella sonnei* in the UK, 2021-22

Situational report to date

- **Case counts:**
  - Confirmed cases: 185 within this outbreak

- **Demographics:**
  - 95% male (175/185);
  - Median age 36 years [IQR: 29-43]
  - Among men, 92% are presumptive MSM (161/175)

- **Clinical severity:**
  - Diarrhoea, abdominal cramps, blood in stools and fever
  - Prolonged symptoms (median 12 days)
  - 49% attended Casualty, 23% hospitalised (median 5 days)
  - 51% needed antibiotic treatment
  - HIV negative on PrEP (73%), living with HIV (n=5)
  - History of another bacterial STI in 2021 (38%)

Data until 21 Jan 2023

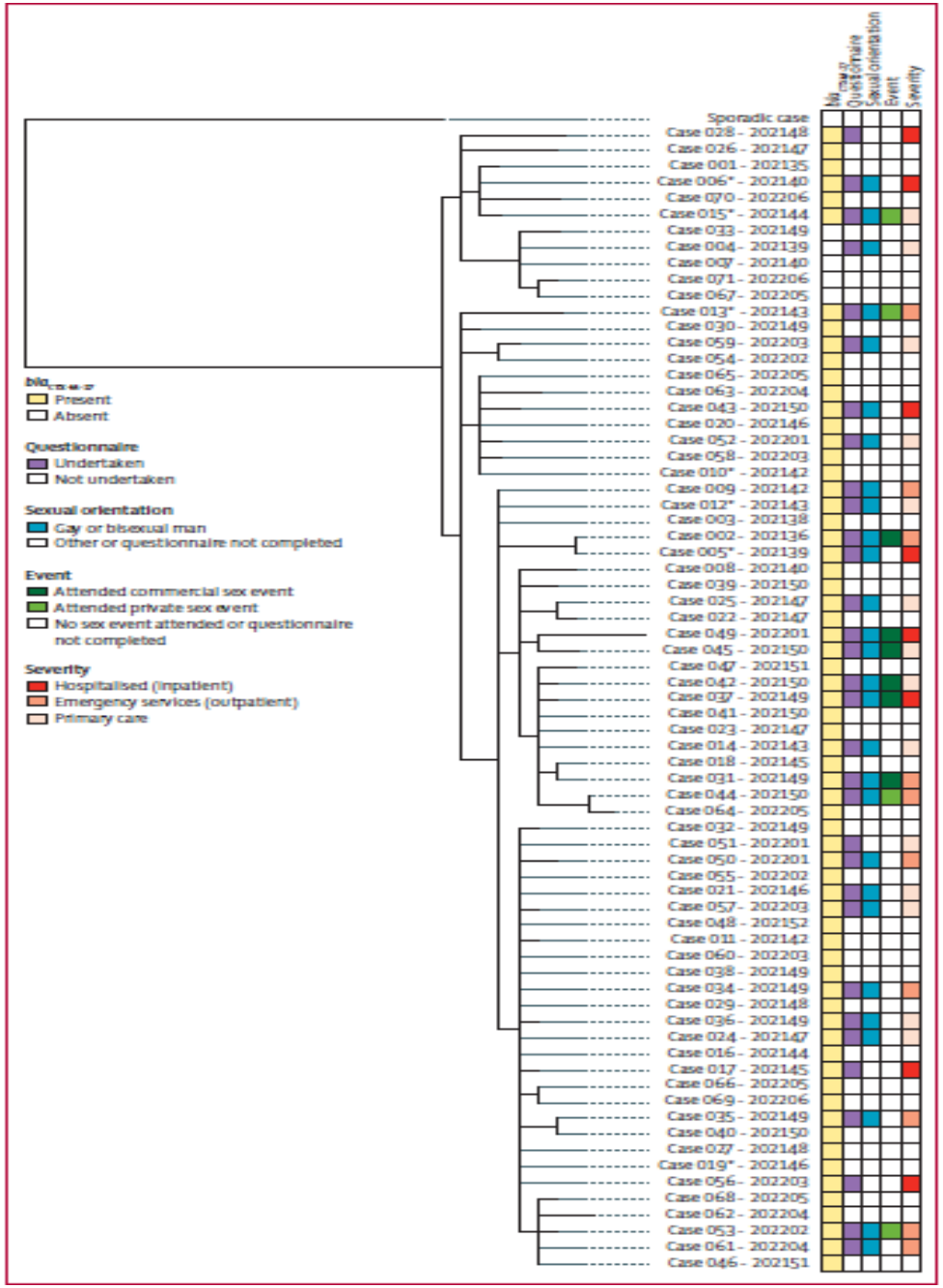
Enhanced surveillance (for initial cases)

- 44% (39/89) of confirmed cases are enhanced, via outbreak questionnaires (n=34) and routine enhanced surveillance questionnaires (n=5)
  - **Gender and sexual orientation:** gay or bisexual men (90%)
  - **Ethnicity:** Any White background (85%)
  - **Contexts of sexual transmission:** most acquired the infection during sex with one or more new partners (n=22) often met via geospatial applications (Grindr, Tinder), in private group sex events (n=4) or in public dark rooms or sex clubs (n=7). Chemsex reported by a minority of cases (n=5).
  - **Suspected route of acquisition:** sex between men (74%), household transmission (n=1), occupational exposure (n=1), unknown (n=8)
  - **Suspected country of acquisition:** England (n=25/39, 64%), Scotland (n=1), Spain (Canary Islands, n=2), France (n=1), Greece (n=1), unknown (n=9)

Data until 2 Apr 2022

S. sonnei ST152, CC152 10SNP 1.1.1.1.377.%.% *bla* $_{CTX\text{-}M\text{-}27}$ located on an IncFII 83 kbp plasmid

Antibiotics (181/185 cases MDR/XDR)	Resistance determinants
Amoxicillin/ ampicillin 3rd gen cephalosporins	*bla*$_{CTX\text{-}M\text{-}27}$
amikacin, gentamicin, tobramycin, streptomycin	*strA:strB; aadA-5*
azithromycin	*mph-A, ermB, mdf(A), sat2A*
fluoroquinolone	*gyrA S83L,D87L; parC S80I; qnrB-19*
trimethoprim	*dfrA-1,dfrA-5,dfrA-17*
sulfamethoxazole	*sul-1, sul-2*
tetracycline	*tetA*
	carbapenems
Susceptible antibiotics	chloramphenicol
	fosfomycin
	temocillin



Guidance on management of cases

- Take a history of recent sexual contact in cases of diarrhoea
- Take a stool sample for enteric PCR and culture and antibiotic susceptibility
- Antibiotics for **severe symptoms** (fever, bloody diarrhoea and/or sepsis), hospital admission, those with prolonged diarrhoea (symptoms beyond 7 days) or who have underlying immunodeficiency
- Start an antibiotic according to local policy and rationalise according to microbiology results
- Oral treatment options for this strain are limited to antibiotics such as chloramphenicol, pivmecillinam, fosfomycin
- Use of either pivmecillinam (800mg TDS PO) or fosfomycin (3g PO day 1,3,5) would be off label or unlicensed, they should only be considered for treating uncomplicated cases such as prolonged diarrhoea. There is no evidence of efficacy in serious infections
- Hospitalised/complications patients: standard sepsis regimen (augmented beta lactam/ 3rd gen cephalosporin+ gentamicin will not work)
- Intravenous agents like ertapenem or meropenem for 3-5 days
- Notify the infection, public health exclusion measures
- **BASHH United Kingdom guideline for the management of sexually transmitted enteric infections 2022**

Advice to patients

- Advice on sexual hygiene and hand washing emphasized
- Avoiding sexual contact for 1 week after complete resolution of symptoms
- https://patient.info/travel-and-vaccinations/travellers-diarrhoea-leaflet/shigella
- Social media campaigns
- Engagement of sexual health clinics

Self-knowledge Check

A 45-year-old previously fit male presents with watery diarrhoea 7-8 times/ day for 3 days. He suspects he has food poisoning from chicken wings he consumed in a local restaurant 3 days prior to onset of symptoms. What additional history would you take?

- A. Recent sexual history
- B. Recent foreign travel
- C. Profession
- D. Severity of illness—continuous fever, severe abdominal cramps, blood in stool, collapse
- E. Recent contact with healthcare / antibiotics
- F. All of the above

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- E. Recent contact with healthcare / antibiotics
- **F. All of the above**

Rationale: Shigellosis is one of the differential diagnoses of gastroenteritis in men who have sex with men and should be suspected in all adult men. A majority of cases of shigellosis in developed countries now occur among MSM. Patients often do not associate illness with a recent sexual encounter. Infection may be acquired via extensive sexual networks at home or abroad, and risk of transmission may be enhanced by use of technology/dating apps. Certain professions have criteria that must be met before returning to work. Most patients recover from shigellosis without antibiotics, but severe cases might require antibiotics and hospital admission. Previous antibiotic use or exposure to healthcare settings may increase selection for resistant pathogens.

Lessons learnt from an outbreak of sexually transmitted, extensively-drug resistant *Shigella sonnei* in the UK, 2021-22

Thank you for listening

Acknowledgements:

- Colleagues from Sexually Transmitted Infection team and Gastrointestinal Bacteria Reference Unit at UKHSA Colindale
- Health Protection Teams
- NHS England
- BASHH

Further information:

- Shigella report published recently by UKHSA: Sexually transmitted Shigella spp. in England: data up to quarter 2, 2022
- https://www.sexwise.org.uk/stis/shigella
- https://www.hperesources.org.uk

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To Ask a Question

- Using the Zoom Webinar System
  - Click on the “Q&A” button
  - Type your question in the “Q&A” box
  - Submit your question

- If you are a patient, please refer your question to your healthcare provider.

- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov

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- All continuing education for COCA Calls is issued online through the CDC Training & Continuing Education Online system at https://tceols.cdc.gov/.

- Those who participate in today's COCA Call and wish to receive continuing education please complete the online evaluation by **Monday, April 3, 2023,** with the course code **WC4520-022823**. The access code is **COCA022823.**

- Those who will participate in the on-demand activity and wish to receive continuing education should complete the online evaluation between **April 4, 2023,** and **April 4, 2025,** and use course code **WD4520-022823.** The access code is **COCA022823.**

- Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CEs obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Today's COCA Call Will Be Available to View On-Demand

- **When:** A few hours after the live call ends*
- **What:** Video recording
- **Where:** On the COCA Call webpage https://emergency.cdc.gov/coca/calls/2023/callinfo_022823.asp

**A transcript and closed-captioned video will be available shortly after the original video recording posts at the above link.*

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- Continue to visit emergency.cdc.gov/coca for more details about upcoming COCA Calls.
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Thank you for joining us today!

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