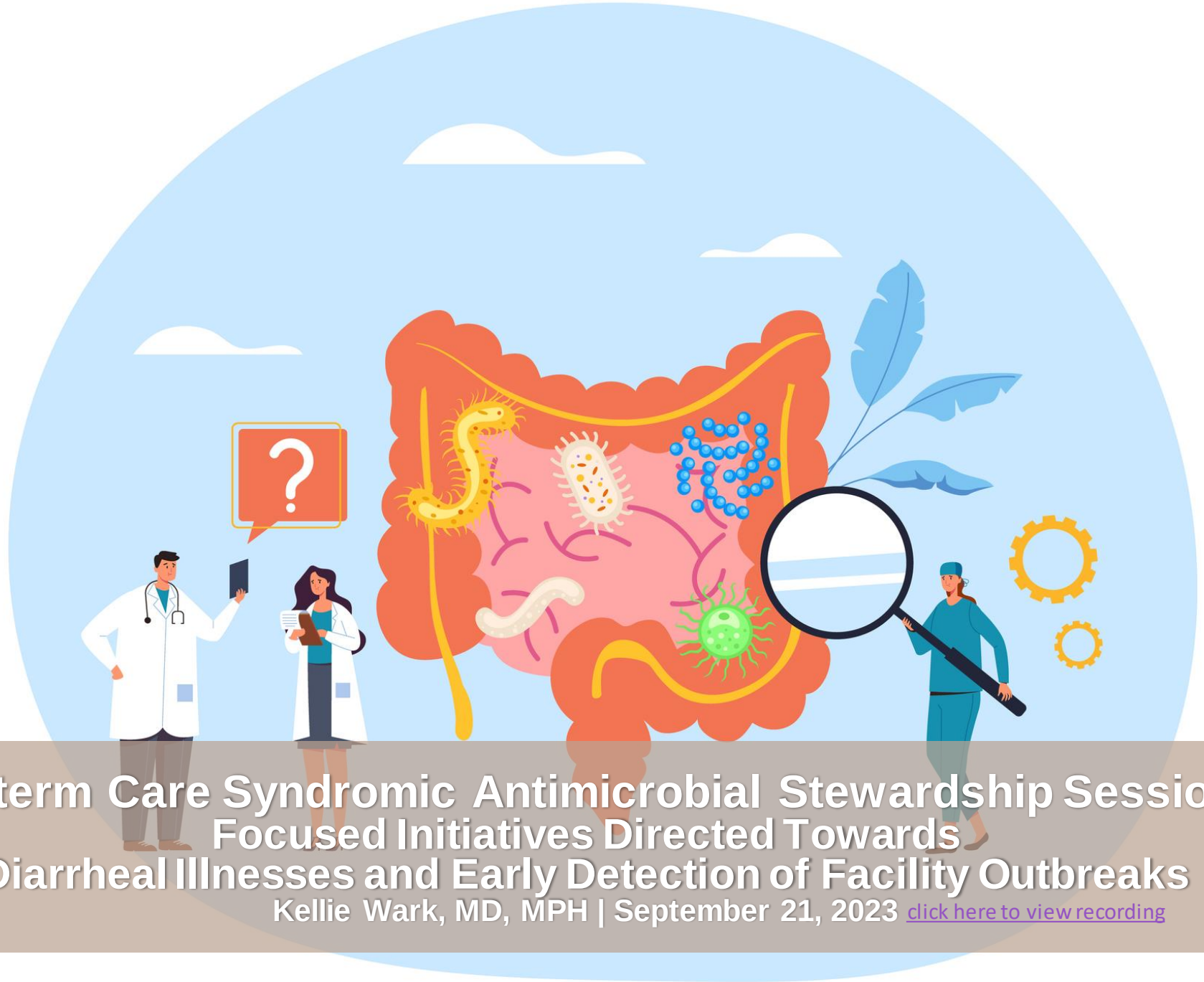


Long-term Care Syndromic Antimicrobial Stewardship Session #4
Focused Initiatives Directed Towards Diarrheal Illnesses and Early Detection of Facility Outbreaks

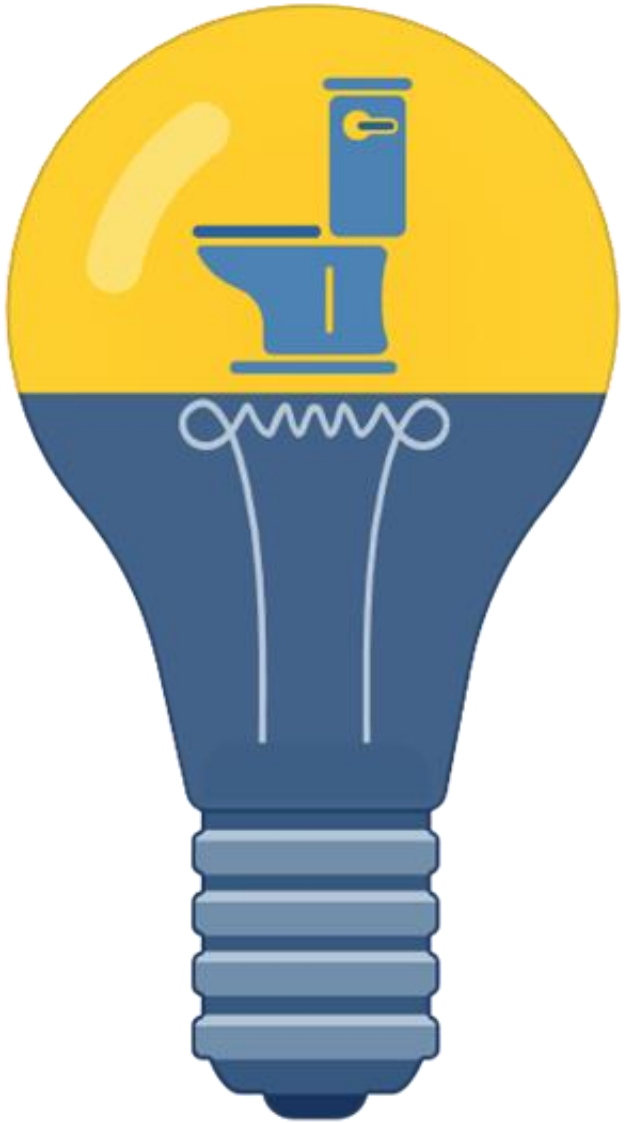
Kellie Wark, MD, MPH | September 21, 2023 click here to view recording

Kansas Department of Health and Environment
Division of Public Health

Presenter

Kellie Wark, MD, MPH
Antimicrobial Stewardship Lead
Kansas Department of Health and Environment
Kellie.Wark@ks.gov

Asst. Professor of Infectious Disease
The University of Kansas Health Systems
kwark@kumc.edu



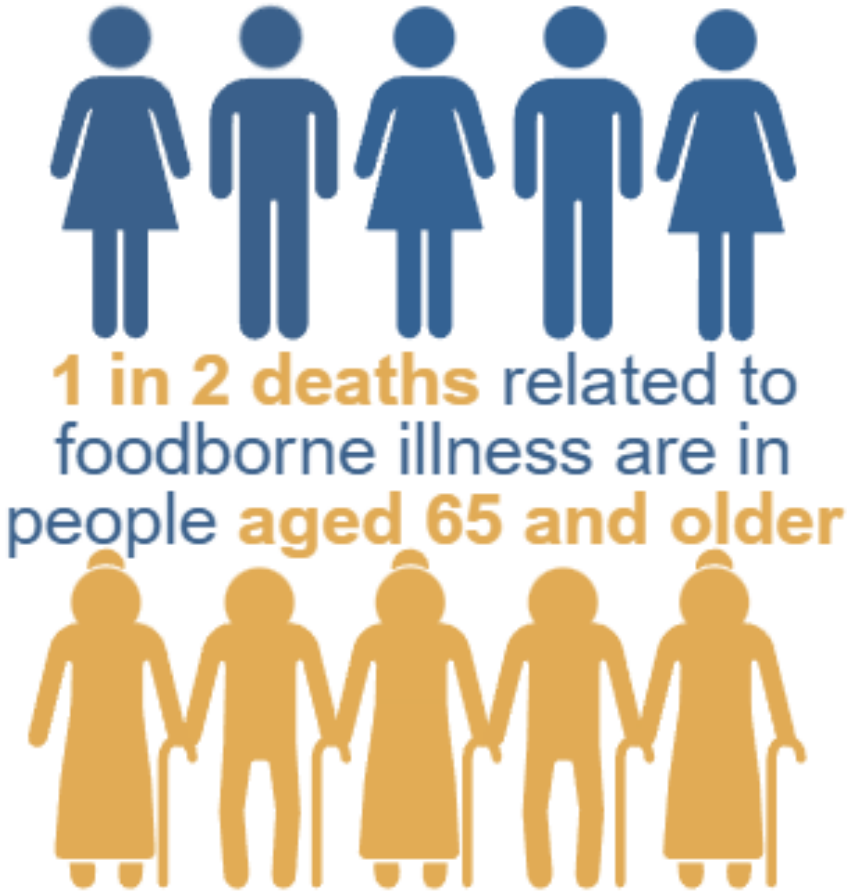
Objectives

- Discuss the regional and national epidemiology of *C. diff*, norovirus and rotavirus trends
- Identify and implement infection control strategies to limit spread of enteric pathogens in healthcare facilities
- Contrast *C. diff* prevention strategies
- Discuss diagnostic limitations of molecular testing (e.g., GI PCR panel)
- Compare regional hepatitis A trends and identify vaccination opportunities for hepatitis A

Epidemiology - Foodborne Diseases

Contaminated food related cases:

- **148 million illnesses**
- **128,000 hospitalizations** (foodborne-related) to **228,000** (total enteric pathogen-related)
- **1,350 deaths** (from US foods) to **2,600 deaths** (total enteric-related)



Sources: Delahoy M., et al. MMWR 2023;72(26);701-706.
Scallan E. et al. EID 2011;17:7-15.

Factors placing senior citizens at higher risk for foodborne illness

- Immune function decreases with age
- Chronic diseases (malnutrition, immobility) associated with greater vulnerability to diarrheal illnesses
- Digestive system changes and reduced stomach acid production, the major defense against enteric pathogens
- Slower digestion, giving pathogens extended amount of time to colonize and infect
- Older people may be more likely to experience sequelae
  - Reactive arthritis, Guillain-Barre syndrome, irritable bowel disorder

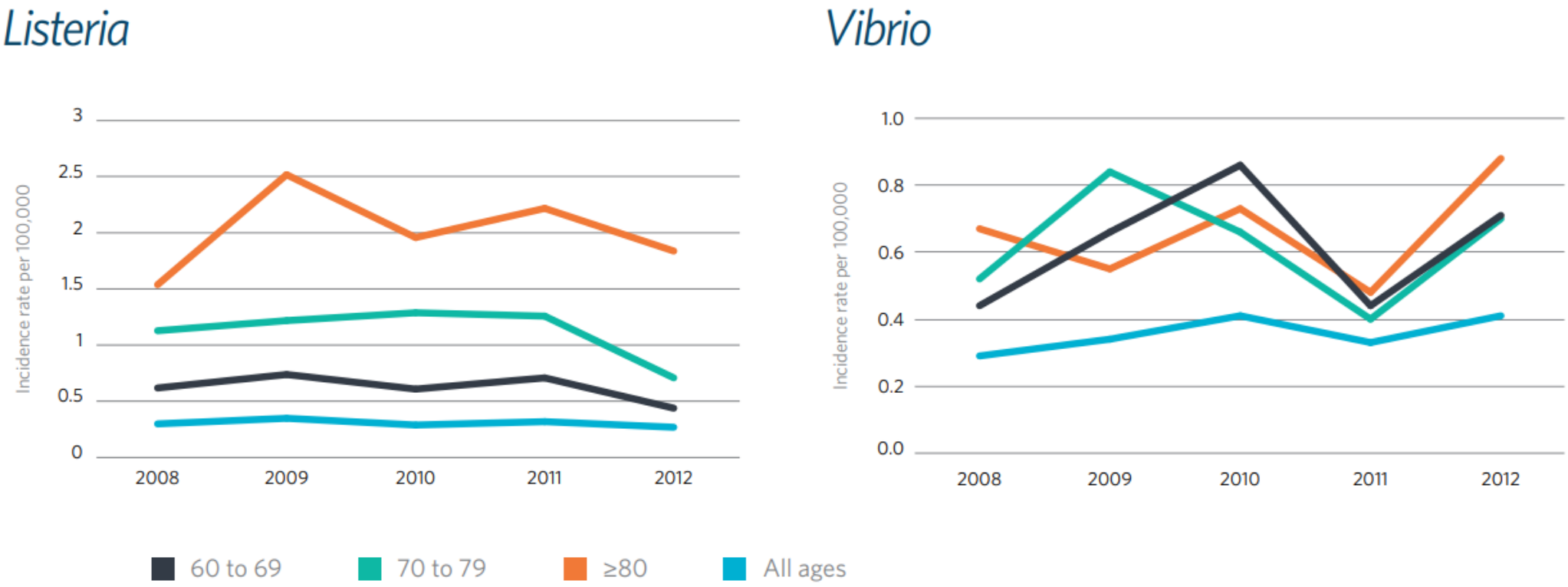
Sources: Kendall P., et al. CID 2006; 42(9):1298-304. Lew J., et al. JAMA 1991;265; 3280-84.

Seniors and Foodborne Diseases

Seniors are disproportionately affected by *Listeria*, *Salmonella*, *E.coli* 0157:H7, *Vibrio*

People Age 60 and Up Are Especially Vulnerable to *Listeria* and *Vibrio* Infections

Incidence of *Listeria* and *Vibrio* illnesses per 100,000 people, 2008-12



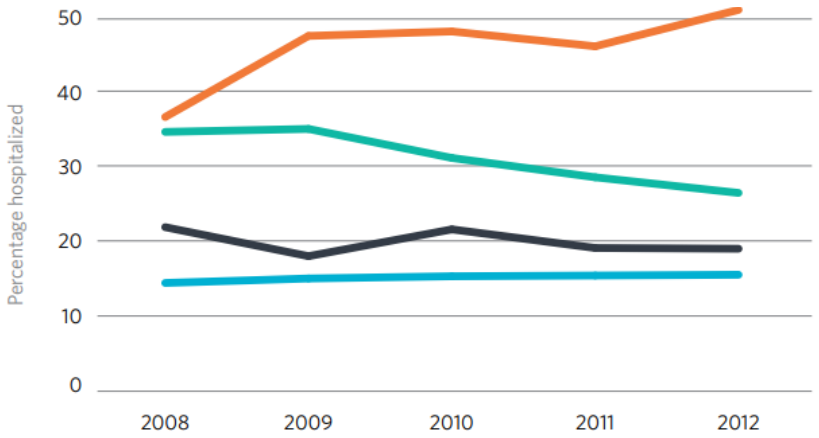
Sources: FoodNet Annual Reports-final data, cdc.gov/foodnet/data/reports.html.

Foodborne Illnesses Often Lead to Hospital Stays for People Age 60 and Up

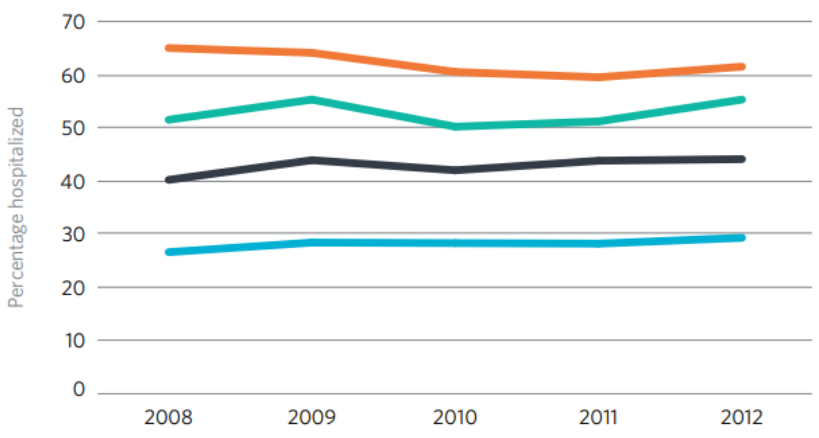
Proportion of people hospitalized for *Campylobacter*, *Salmonella*, *E. coli* 0157:H7, and *Vibrio* illnesses, 2008-2012

All ages
≥80
70 to 79
60 to 69

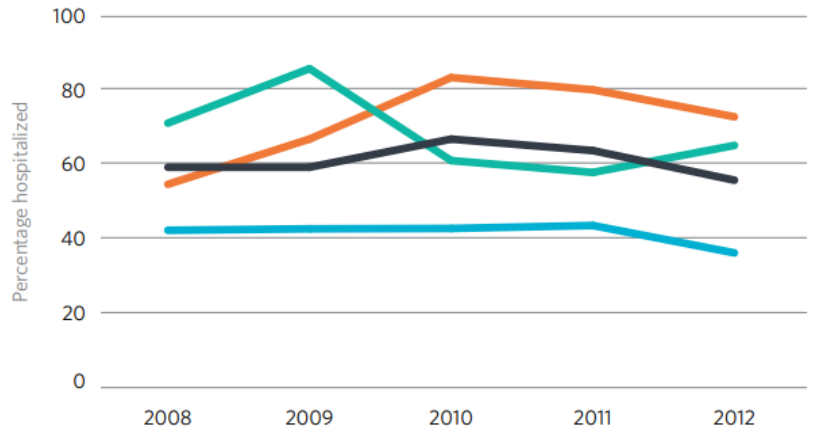
Campylobacter



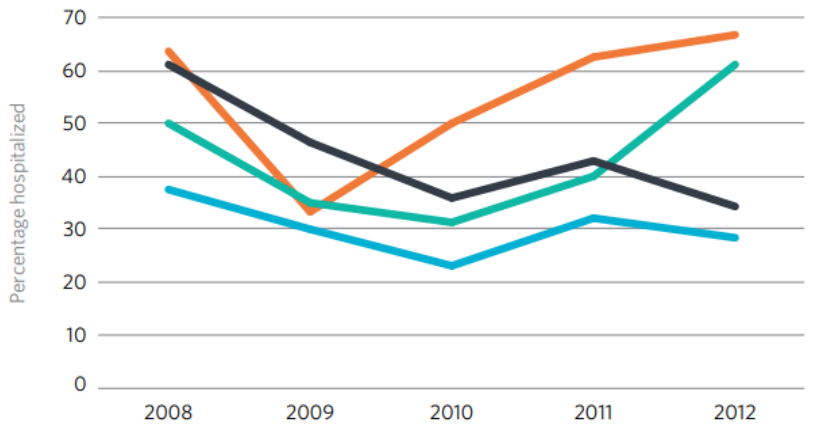
Salmonella



E. coli 0157:H7



Vibrio



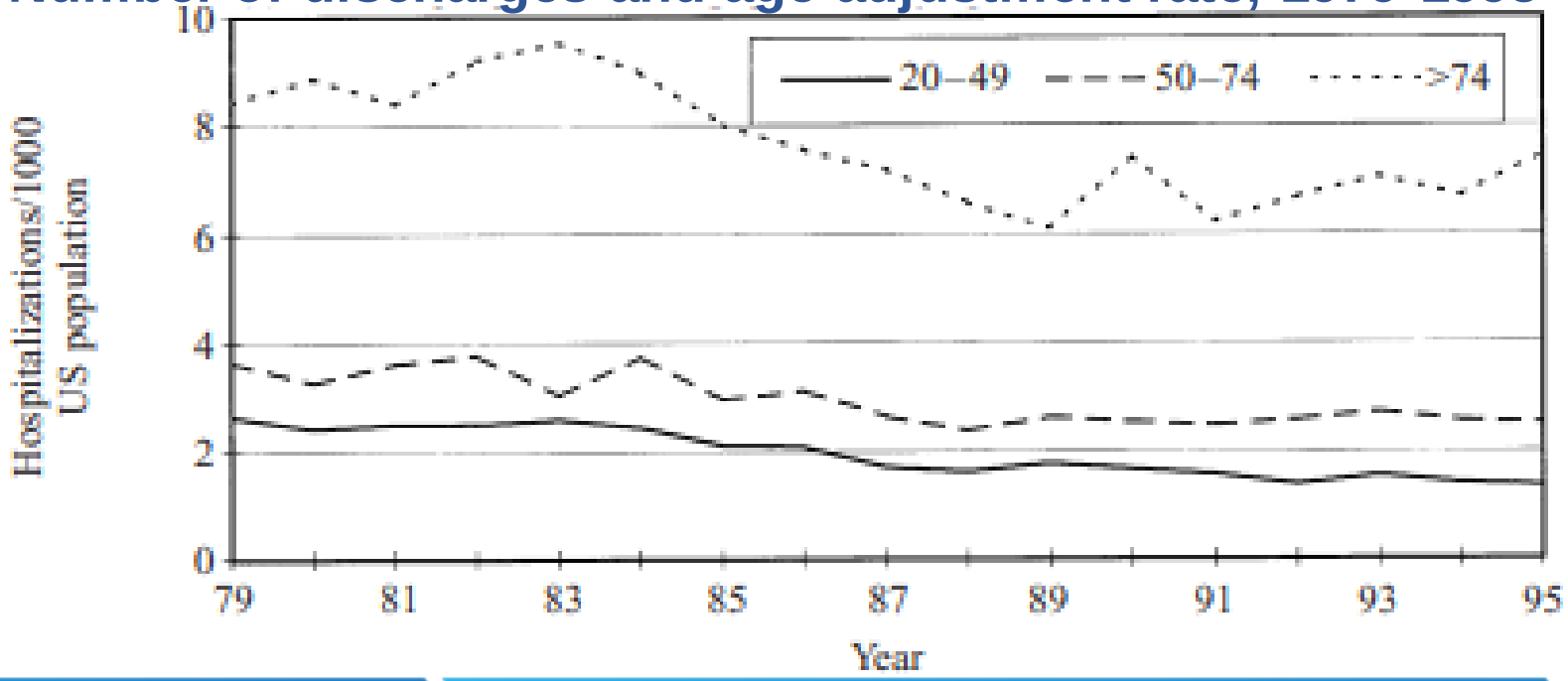
Sources: FoodNet Annual Reports-final data, cdc.gov/foodnet/data/reports.html.

Hospitalizations by Foodborne Diseases

Foodborne-related hospitalizations were highest among seniors

- Gastroenteritis accounted for 1.5% of all adult-related hospitalizations
- Highest in oldest, for >75 years 7.6 hospitalizations per 1000 persons

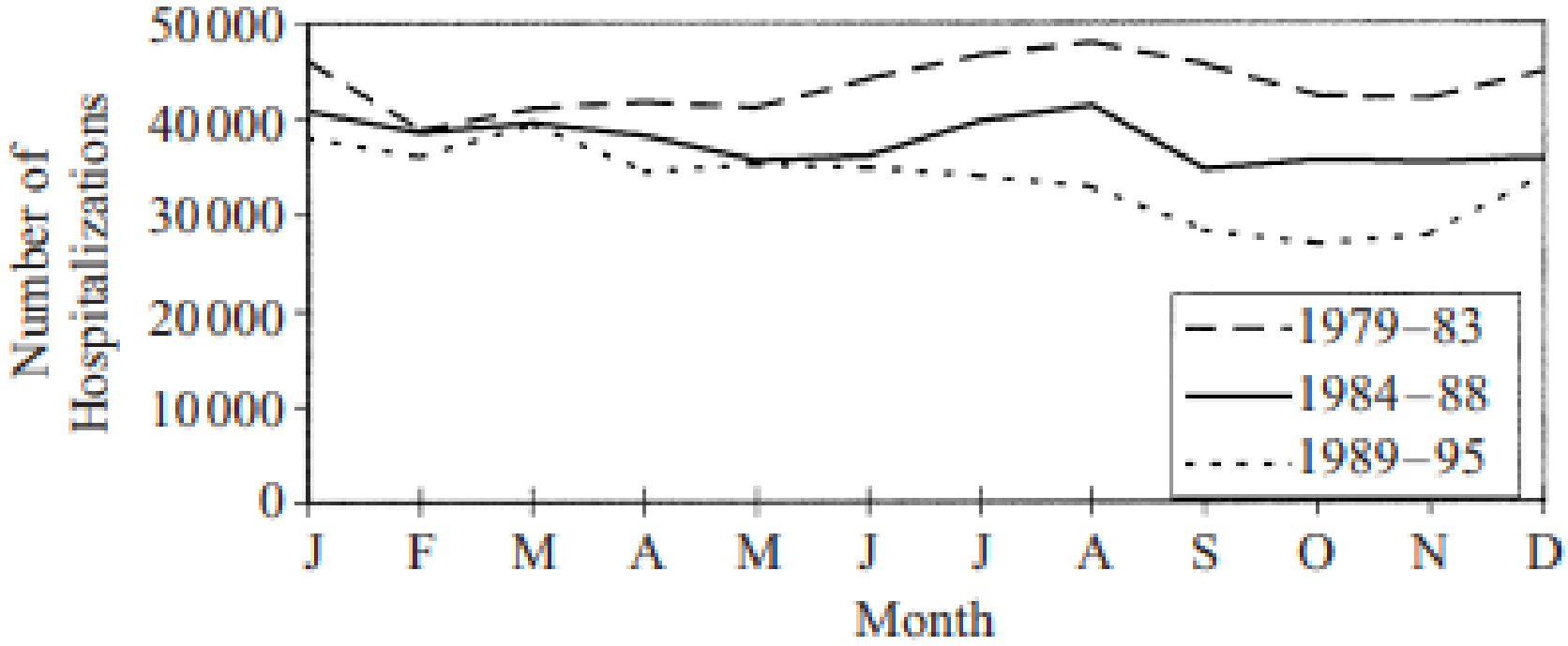
Number of discharges and age adjustment rate, 1979-1995



Sources: Mounts A., et al. Epidemiol Infect 1999;123(1):1-8.

Hospitalizations by Foodborne Diseases

Gastroenteritis Hospitalizations by Month, 1979-1995



Sources: Mounts A., et al. Epidemiol Infect 1999;123(1):1-8.

Healthy People 2030 - Foodborne Illnesses

Foodborne Illness		
Goal	**Target** (infections per 100,000 population)	**Status**
Reduce *Salmonella* infections	Baseline: 15.3 (2016-18) Target: 11.5 Status: 13.3 (2021)	Improving
Reduce *Campylobacter* infections	Baseline: 16.2 (2016-18) Target: 10.9 Status: 17.2 (2021)	Unchanged to worsening
Reduce Shiga-toxin producing *E.coli* infections	Baseline: 4.6 (2016-18) Target: 3.7 Status: 4.6 (2021)	Unchanged
Reduce *Listeria* infections	Baseline: 0.27 (2016-18) Target: 0.22 Status: 0.31 (2021)	Worsening

Source: https://health.gov/healthypeople/objectives-and-data/browse-objectives/foodborne-illness

2022 Food Safety Report

Measuring progress toward foodborne illness prevention

Pathogen	Change from baseline (2016–2018)	Rate in 2022 per 100,000 people	Target rate based on Healthy People 2030 goals
Campylobacter	↑ 7%	17.4	10.9
Cyclospora	↑ 430%	0.6	None
Listeria	↔ No change	0.26	0.22
Salmonella	↔ No change	14.5	11.5
Shigella	↔ No change	3.9	None
STEC Shiga toxin-producing *E. coli*	↔ No change	4.6	3.7
Vibrio	↑ 54%	0.9	None
Yersinia	↑ 144%	1.9	None

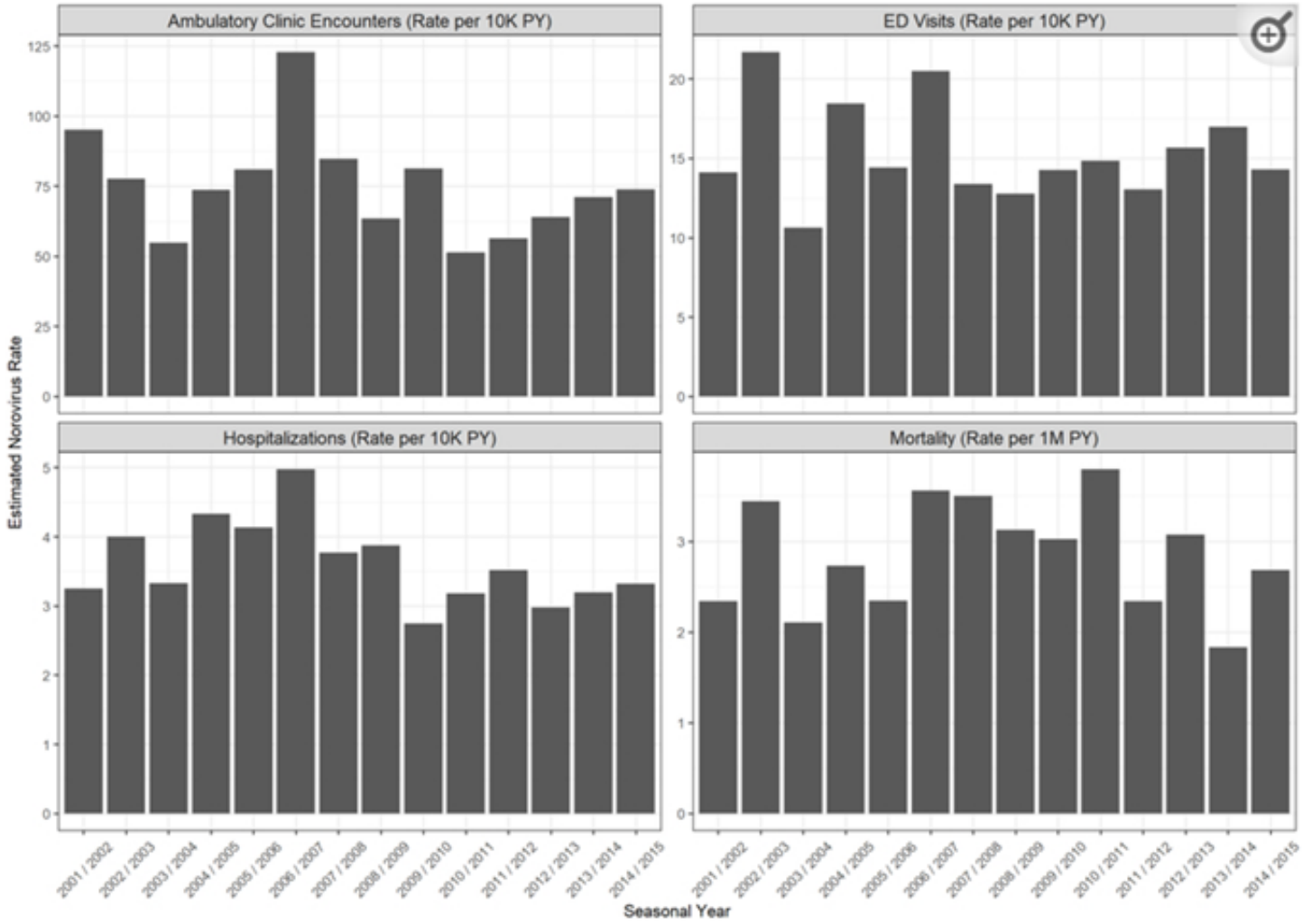
Rates & targets are numbers of infections per 100,000 people per year. They include only domestically acquired infections. Targets based on Healthy People 2030 goals, which were set using average annual incidences during 2016–2018. No change indicates that the 95% credible interval of the percentage change included zero. For more information, visit cdc.gov/FoodNet.

Source: https://www.cdc.gov/foodnet/reports/preliminary-data.html

Hospitalizations by Norovirus

Norovirus associated clinic & ED visits are disproportionately high for those aged 85+

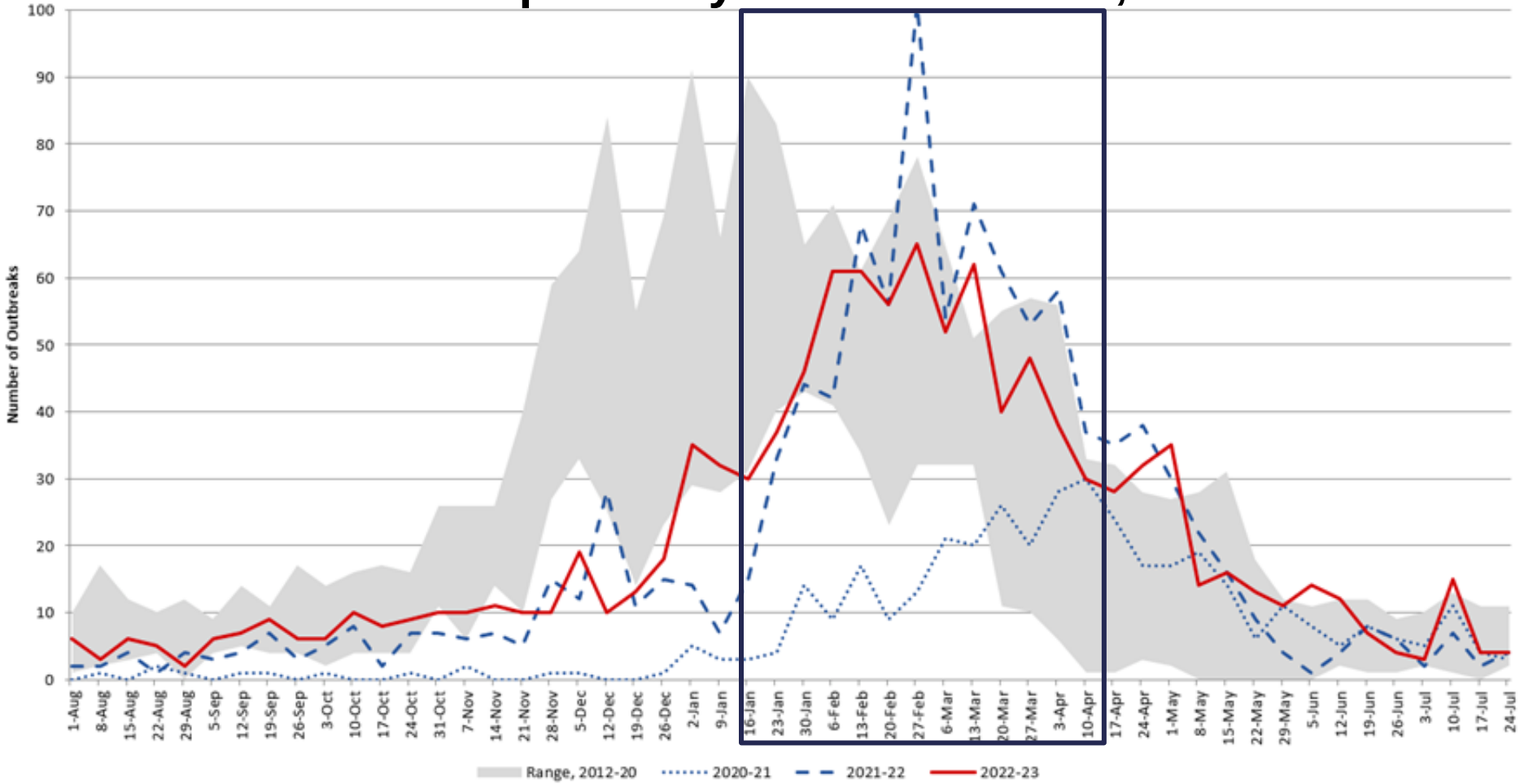
- Clinic visits:
  - Aged 85+: **151**/10k person-years (PY)
  - All ages: 75/10k PY
  - 2.3 million clinic visits/year
- ED visits:
  - Aged 85+: **32**/10k PY
  - All ages: 15/10k PY
  - 2.3 million ED visits/year



Sources: Burke R., et al. CID 2021;73(1):e1-8

Seasonality of Norovirus

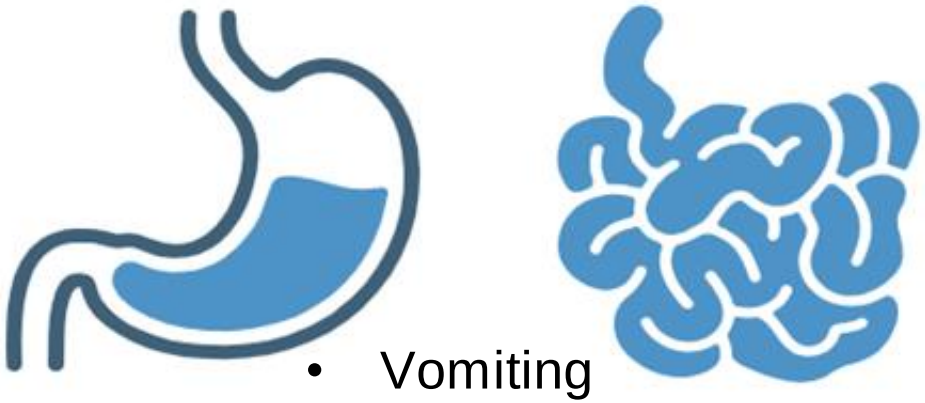
Norovirus Outbreaks Reported by NoroSTAT Sites, 2012-2023



Source: https://www.cdc.gov/norovirus/reporting/norostat/data.html

Terminology and Common Pathogens

Gastroenteritis



- Vomiting
- Nausea
- Fever, chills
- Abdominal pain
- "Stomach flu"

- Norovirus
- Rotavirus
- Sapovirus
- *S. aureus* (foodborne)
- Toxoplasma
- Hepatitis A
- *B. cereus*

Colitis

- Diarrhea
- Nausea
- Abdominal pain

- Campylobacter
- Salmonella
- *E. coli* (ETEC, STEC)
- Shigella
- Listeria
- Cryptosporidium
- Cyclospora
- Giardia
- Yersinia

Common Sources

Contribution of Different Food Commodities (Categories) to Estimated Domestically-Acquired Illnesses and Deaths, 1998-2008

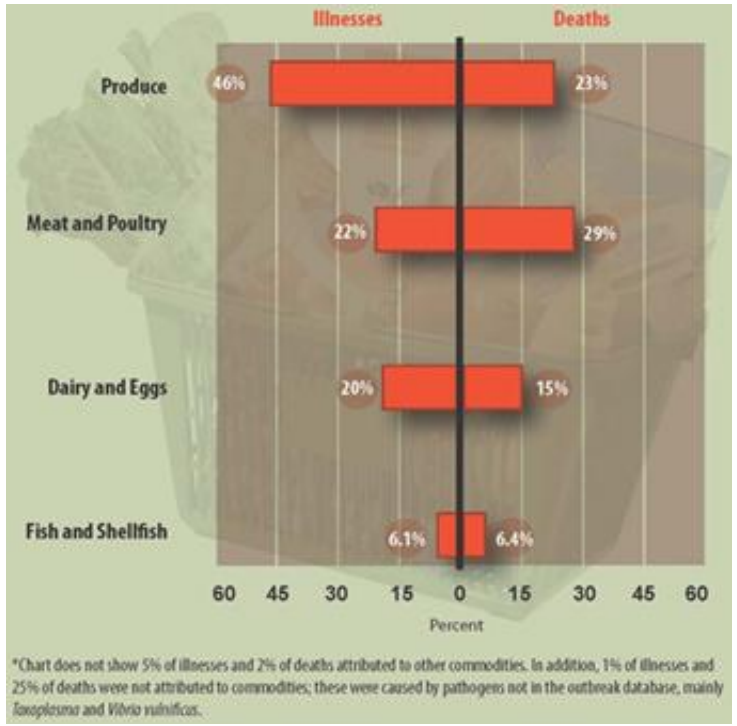


Table 1. Estimates of annual domestically acquired foodborne illnesses attributed to specific food commodities and commodity groups, by pathogen type, United States, 1998–2008*

Commodity or commodity group	No. (%) illnesses				
	All agents	Bacterial	Chemical	Parasitic	Viral
Aquatic animals†	589,310 (6.1)	142,415 (3.9)	153,488 (61.6)	77,795 (33.3)	215,613 (3.9)
Fish	258,314 (2.7)	15,362 (0.4)	148,958 (59.8)	955 (0.4)	93,040 (1.7)
Shellfish†	330,997 (3.4)	127,053 (3.5)	4,531 (1.8)	76,840 (32.9)	122,573 (2.2)
Crustaceans	46,528 (0.5)	32,626 (0.9)	1,247 (0.5)		12,654 (0.2)
Mollusks	284,469 (3.0)	94,427 (2.6)	3,283 (1.3)	76,840 (32.9)	109,919 (2.0)
Land animals†	4,021,839 (41.7)	2,334,000 (64.0)	33,031 (13.3)	156 (0.1)	1,654,651 (30.0)
Dairy	1,330,098 (13.8)	656,951 (18.0)	3,773 (1.5)		669,374 (12.1)
Eggs	574,298 (6.0)	179,421 (4.9)	6,995 (2.8)		387,882 (7.0)
Meat-poultry†	2,117,442 (22.0)	1,497,628 (41.1)	22,263 (8.9)	156 (0.1)	597,394 (10.8)
Meat†	1,174,257 (12.2)	844,006 (23.2)	2,437 (1.0)	156 (0.1)	327,658 (5.9)
Beef	639,640 (6.6)	482,199 (13.2)	661 (0.3)		156,780 (2.8)
Game	9,934 (0.1)	5,111 (0.1)	1,568 (0.6)	156 (0.1)	3,100 (0.1)
Pork	524,684 (5.4)	356,697 (9.8)	209 (0.1)		167,778 (3.0)
Poultry	943,185 (9.8)	653,622 (17.9)	19,826 (8.0)		269,737 (4.9)
Plants†	4,924,877 (51.1)	1,169,202 (32.1)	62,753 (25.2)	69,023 (29.5)	3,623,899 (65.8)
Grains-beans	435,936 (4.5)	183,394 (5.0)	12,995 (5.2)		239,547 (4.3)
Oils-sugars	65,631 (0.7)		2,344 (0.9)		63,287 (1.1)
Produce†	4,423,310 (45.9)	985,807 (27.0)	47,414 (19.0)	69,023 (29.5)	3,321,066 (60.3)
Fruits-nuts	1,123,808 (11.7)	230,636 (6.3)	29,483 (11.8)	60,573 (25.9)	803,116 (14.6)
Vegetables†	3,299,501 (34.2)	755,171 (20.7)	17,931 (7.2)	8,450 (3.6)	2,517,949 (45.7)
Fungi	4,542 (0.0)	686 (0.0)	3,857 (1.5)		
Leafy	2,152,652 (22.3)	188,327 (5.2)	9,113 (3.7)	7,256 (3.1)	1,947,955 (35.4)
Root	349,715 (3.6)	96,910 (2.7)	1,240 (0.5)		251,566 (4.6)
Sprout	32,703 (0.3)	32,703 (0.9)			
Vine-stalk	759,889 (7.9)	436,546 (12.0)	3,721 (1.5)	1,194 (0.5)	318,428 (5.8)
Undetermined	102,275 (1.1)	156 (0.0)		86,686 (37.1)	15,433 (0.3)
Total	9,638,301 (100.0)	3,645,773 (100.0)	249,273 (100.0)	233,660 (100.0)	5,509,596 (100.0)

*Most estimates from (*1*); some were made as described in Methods. Numbers of illnesses are the most probable estimate, as described in Methods. Estimates are rounded; some row and column sums may differ from their totals. Blank cells indicate no data.
†Indicates commodity group.

Source: Painter J., et al. Emerg Infect Dis 2013; 19(3):407-15.

Common Sources

Point Prevalence Sampling of Retail Chickens:

Salmonella

- Retail raw chicken: 12% (meat) to 44% (skinned parts such as chicken breasts, thighs)
- Breaded Not-ready-to-eat: 27%

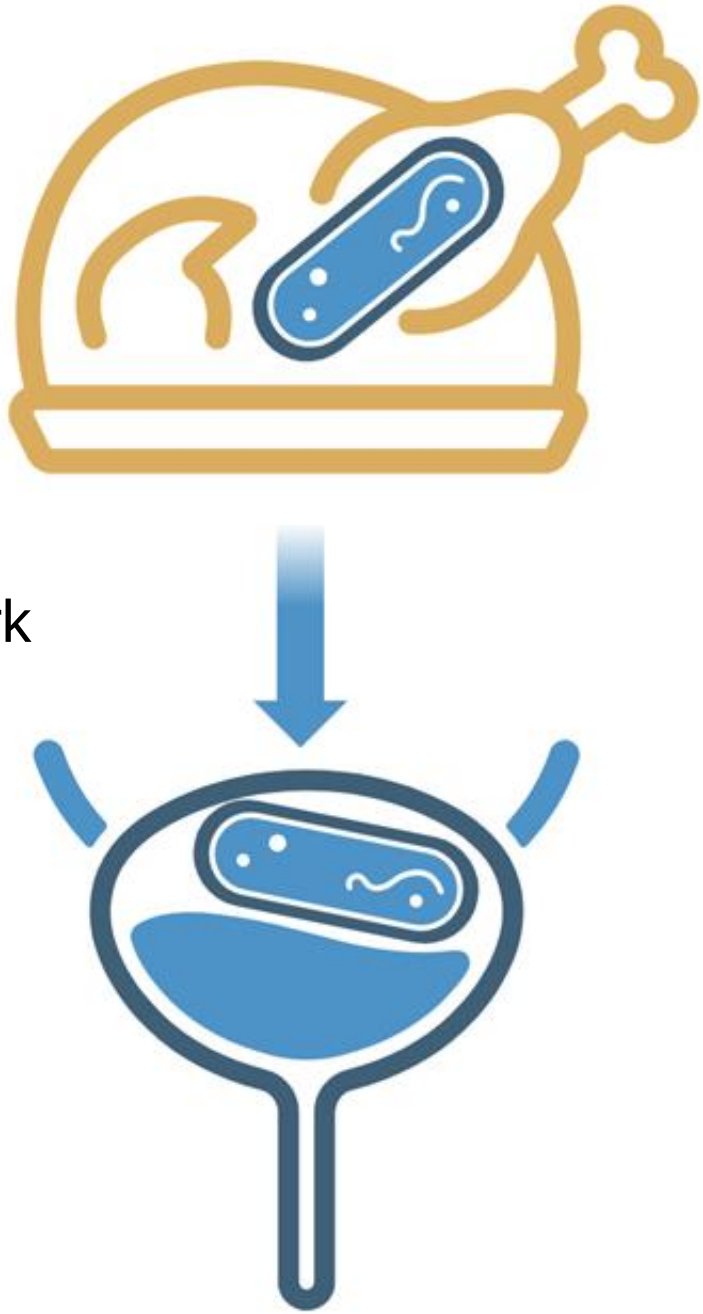
Campylobacter

- Retail raw chicken: 36%
- Farm chicken: 19%

Photo: chicken.ca/

Sources: Guran S et al., Food Control 2017; 73(B): 462-67.
FDA Chicken Survey, 2023.
Poudel et al, Am Soc Micro 2022;10(3).

Extra-intestinal Infections



California: young healthy female *E. coli* UTIs (2001)

- 49% *E. coli* Bactrim-resistant UTIs same *E. coli* O11/O77/O17/O73:K52:H18-ST69 clonal group
- Spread to drug-resistant UTIs and pyelonephritis in Michigan, Minnesota, Colorado

Arizona: point prevalence study identifies same chicken and pork *E. coli* with community *E. coli* UTIs (2018)

- Over 12 months, samples from chicken and pork concurrent human urine cultures, whole genome sequencing identified common sequence (ST131) in 15% of human isolates (182/1888) and 13th most common sample from meats (1.3%, 25/1923) with 84% poultry meat sharing same ST131-H22 plasmid
- 1/3 of the human *E.coli* isolates were resistant to > 3 antibiotic classes

Case-control study MDR *E. coli* UTIs

- Greater chicken intake associated 3.7 greater odds (OR 3.7, 95% CI 1.1-12.4) of MDR UTI, 4-fold greater odds of ESBL *E. coli* UTI with excess pork intake (OR 4, 95% CI 1-15.5)

Source: Manges A., et al NEJM; 2001;345:1007-13. Vincent C., et al. Emerg Infect Dis 2010;16(1):88-95. Liu C., Am Soc Micro mBio; 2018;9(4).

Diagnosis: Culture Independent Diagnostic Tests (CIDTs)

Detection of gene or antigens of specific pathogens

- Multiplex PCR panels or “syndromic panels”
- Luminex GPP (first FDA approved panel in 2013)
- BioFire FilmArray GI Panel (FDA approved 2014)
- Verigene EP nucleic acid test (FDA approved 2014)

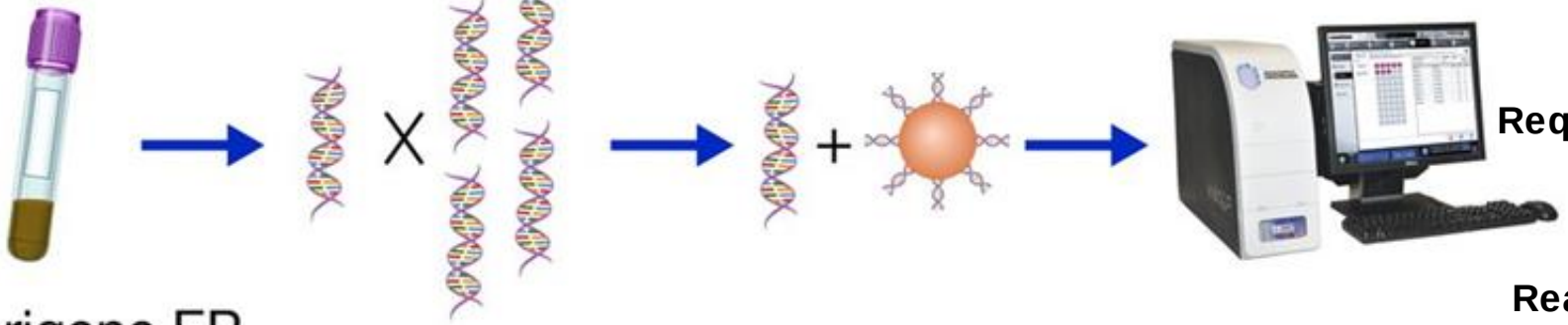
Targets Included on Commercial, FDA-cleared GI Multiplex Assays

	Multiplex panel[b]		
Target[a]	Verigene EP	FilmArray GI	xTAG GPP
Aeromonas		IUO[c]	
Campylobacter	✓	✓	✓
Clostridium difficile (toxin A/B)		✓	✓
Plesiomonas shigelloides		✓	
Salmonella	✓	✓	✓
Yersinia enterocolitica	✓	✓	RUO[d]
Vibrio spp.	✓	✓	✓
EAEC		✓	
EPEC		✓	
ETEC		✓	✓
STEC (*stx*$_1$ and *stx*$_2$)	✓[e]	✓	✓
E. coli 0157		✓	✓
EIEC[f]/*Shigella*	✓	✓	✓
Cryptosporidium		✓	✓
Cyclospora cayetanensis		✓	
Entamoeba histolytica		✓	✓
Giardia lamblia		✓	✓
Adenovirus 40/41		✓	✓
Norovirus GI/GII	✓	✓	✓
Rotavirus A	✓	✓	✓
Sapovirus		✓	
Astrovirus		✓	

Source: Binnicker M. J Clin Micro 2015;53(12).

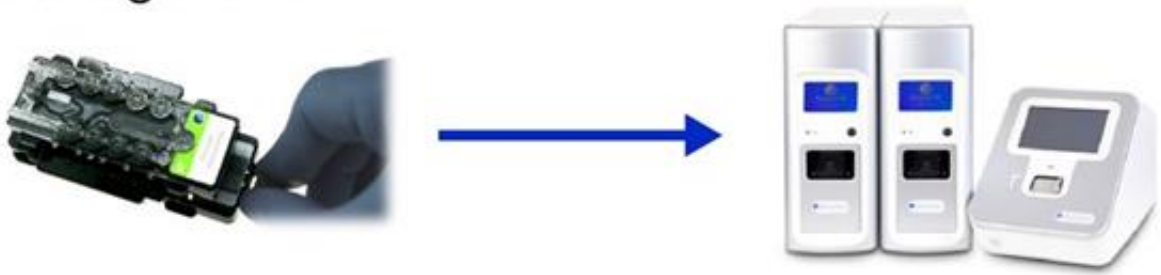
Throughput

A. xTAG GPP



Targets: 14
Process Time: 45 min
Time/run: ~5 hr
Requires separate extraction (~45 min)
Footprint: moderate
Price: $37k (2015 USD)
Reagent price/specimen: $80-90

B. Verigene EP



Targets: 9
Process Time: <5 min
Time/run: ~2 hr
No separate extraction
Footprint: small-moderate
Price: $40k (2015 USD)
Reagent price/specimen: $80

C. FilmArray GI

Targets: 22
Process Time: 2 min
Time/run: ~1 hr
No separate extraction
Footprint: small
Price: $39k (2015 USD)
Reagent price/specimen: $155

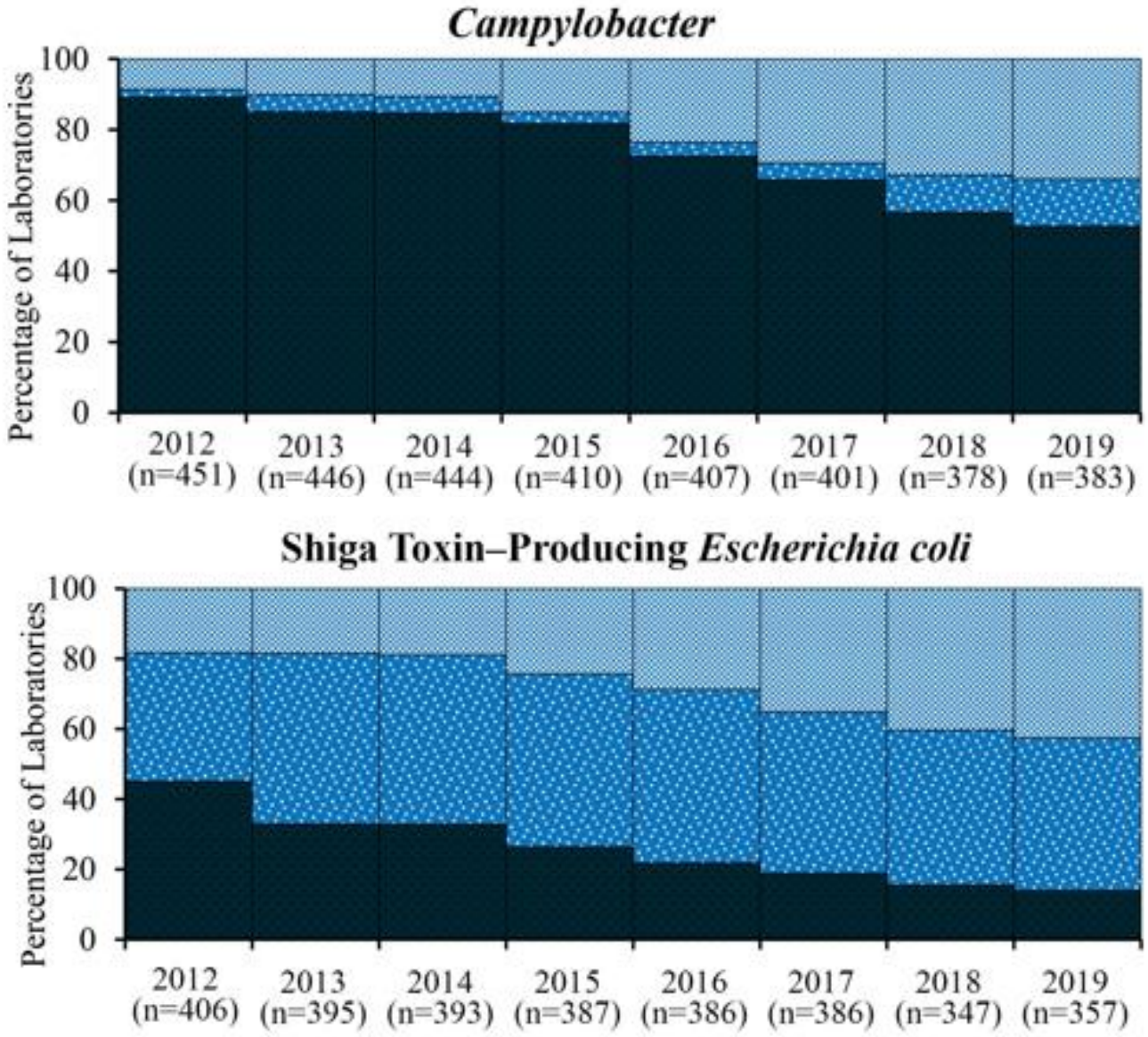
Turnaround Time

Source: Binnicker M. J Clin Micro 2015;53(12).

Culture Independent Diagnostic Tests (CIDTs)

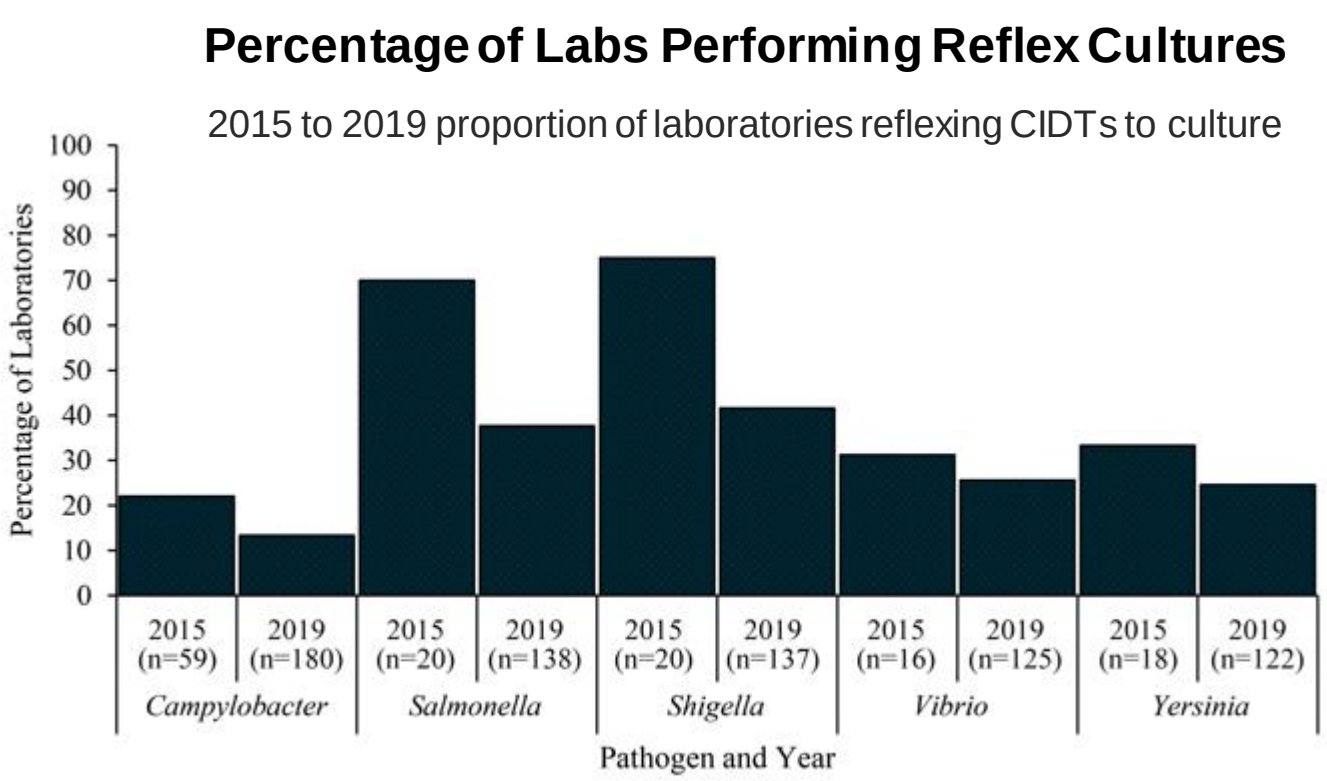
From 2012 onwards, labs using molecular GI tests has increased significantly, corresponding to decreases in conventional cultures

Percentage of Labs Performing CIDT (blue)



Source: Ray L., et al. OFID 2022;9(8): afac344, https://doi.org/10.1093/ofid/ofac344
Published by Oxford University Press on behalf of Infectious Diseases Society of America 2022.

Diagnostic Stewardship



Pros

- Rapid
- Detect pathogens directly from stool
- Easier than traditional lab-based tests
- Batching of samples
- Detects multiple pathogens same specimen
- Greater sensitivity
- Cheaper (sometimes)

Cons

- No data on antibiotic susceptibilities
- No data on strain types
- Unable to link to outbreaks (whole-genome sequencing, need the isolate)
- Over-sensitivity → over-diagnosis
- Doesn't distinguish viable pathogen (only DNA or RNA)

Source: Ray L., et al. OFID 2022;9(8): afac344, https://doi.org/10.1093/ofid/ofac344
Published by Oxford University Press on behalf of Infectious Diseases Society of America 2022. This work is written by (a) US Government employee(s) and is in the public domain in the US.

Diagnostic Stewardship

Implications of multiplex PCR panels

- Because unable to distinguish viable from non-viable pathogens, shedding or positive results for long periods following resolution of disease (especially problematic for norovirus, rotavirus, Salmonella)
- Increases GI positive results by 2 to 4-fold compared to conventional methods
  - Clinicians faced with dilemmas of interpreting presence of organisms that have not been routinely tested for in the past (e.g., sapovirus, EPEC)
  - Co-infection rates increase - insufficient data available to guide laboratorians and clinicians on how to interpret
- Routine cultures will still be needed to determine appropriate treatment
- Increased C.diff detection in colonized, with potential impacts on isolation and treatment decisions (PCR only, not a 2-step test)

Norovirus Outbreak Response and Control

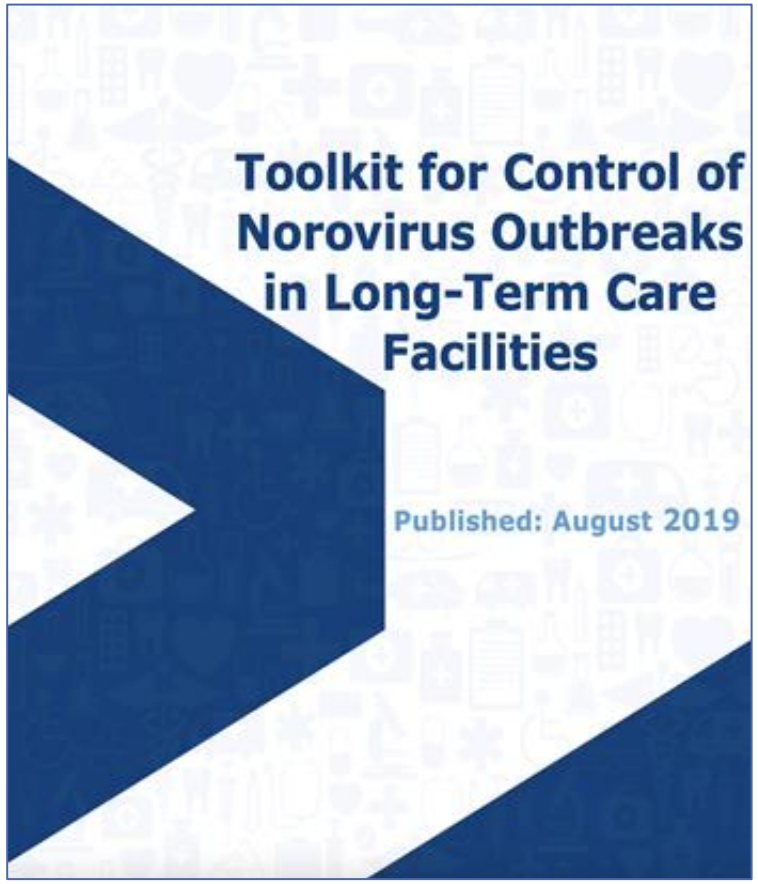
Steps	Control Interventions
Report	❑ Report suspected outbreak to KDHE, work with public health staff ❑ Information to collect: Date of earliest illness? When did other illnesses occur? How many residents in facility? How many have been ill? How many staff and how many have been ill? Have infected residents been in 1 unit or wing, or spread across facility? Have any dietary or food staff been ill? ❑ Complete line listing of infected residents
Test	❑ Submit stool specimens, KDHE staff can assist in KHEL submissions
Survey	❑ Implement active daily surveillance for gastroenteritis among residents and staff
Infection Control	❑ Place patients with suspected norovirus gastroenteritis on contact precautions until symptom-free for at least 48 hours ❑ For the duration of the outbreak, increase frequency of hand hygiene audits on affected units, provide written and verbal staff feedback
Cohort	❑ Cohort residents to single unit or area if possible (symptomatic, asymptomatic exposed or asymptomatic unexposed patient groups) ❑ Symptomatic patients remain in room (social distancing)

Download: health.pa.gov/topics/Documents/Programs/HAIP-AS/Norovirus%20Toolkit.pdf

Norovirus Outbreak Response and Control

Steps	Control Interventions
Hand Hygiene	❑ Promote adherence to hand hygiene among healthcare workers, patients, visitors ❑ Use soap and water during outbreaks
PPE	❑ Use PPE (gowns and gloves) when entering affected patient care areas and remove carefully to avoid contaminating clothing
Transfers & Admissions	❑ When transferring ill patients, notify receiving facility to ensure continuation of contact precautions ❑ When transferring well patients, notify receiving facility of presence of a suspected gastrointestinal outbreak
Cleaning & Disinfection	❑ Commercial disinfection products registered with EPA for use in healthcare facilities; follow manufacturer instructions for method of application, amount, dilution and contact time ❑ EPA's Registered Antimicrobial Products Effective Against Norovirus (not all commercial cleaning products act dually as a disinfecting agent) ❑ Routine cleaning, disinfection of high-touch environmental surfaces (commodes, toilets, faucets, telephones, door handles, computer equipment, kitchen preparation surfaces)
Staff	❑ Exclude ill workers from work for minimum of 48 hours after symptom resolution, upon return to work reinforce hand hygiene ❑ Cohort staff on each ward if possible ensure staff don't move between patient cohorts ❑ Limit visitation and exclude ill persons from visiting the facility via posted notices

Resources

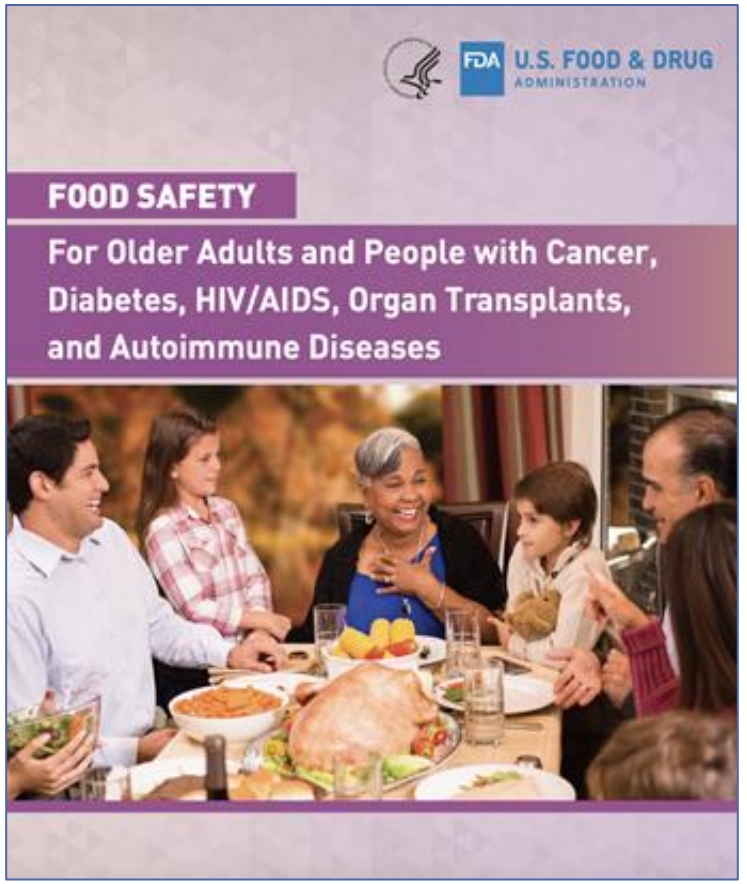


Outbreak and Control Response Checklists

health.pa.gov/topics/Documents/Programs/HAIP-AS/Norovirus%20Toolkit.pdf

Tools, line-list spreadsheet downloads, educational handouts, posters

foodsafety.uw.edu/sites/foodsafety.uw.edu/files/documents/norovirus/WA-IFS-CoE-Norovirus-Toolkit.pdf



Background (specific foods-pathogens), senior stories

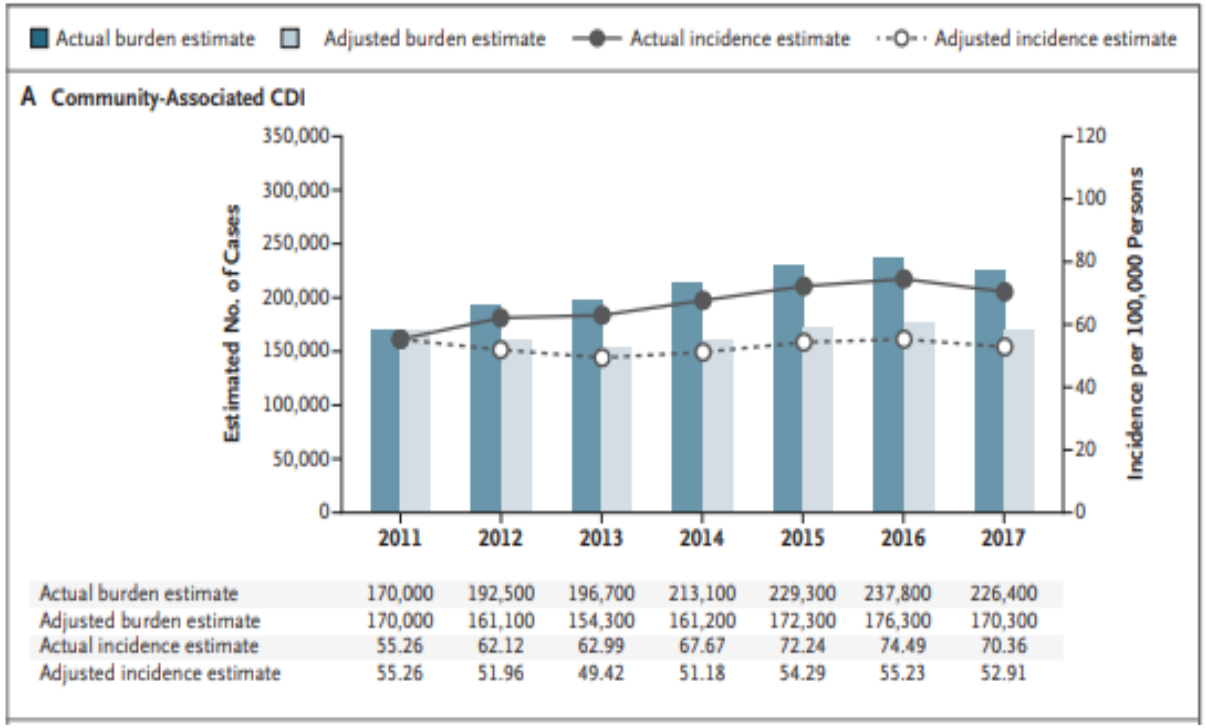
fda.gov/media/83744/download?attachment

Epidemiology - *C. diff*

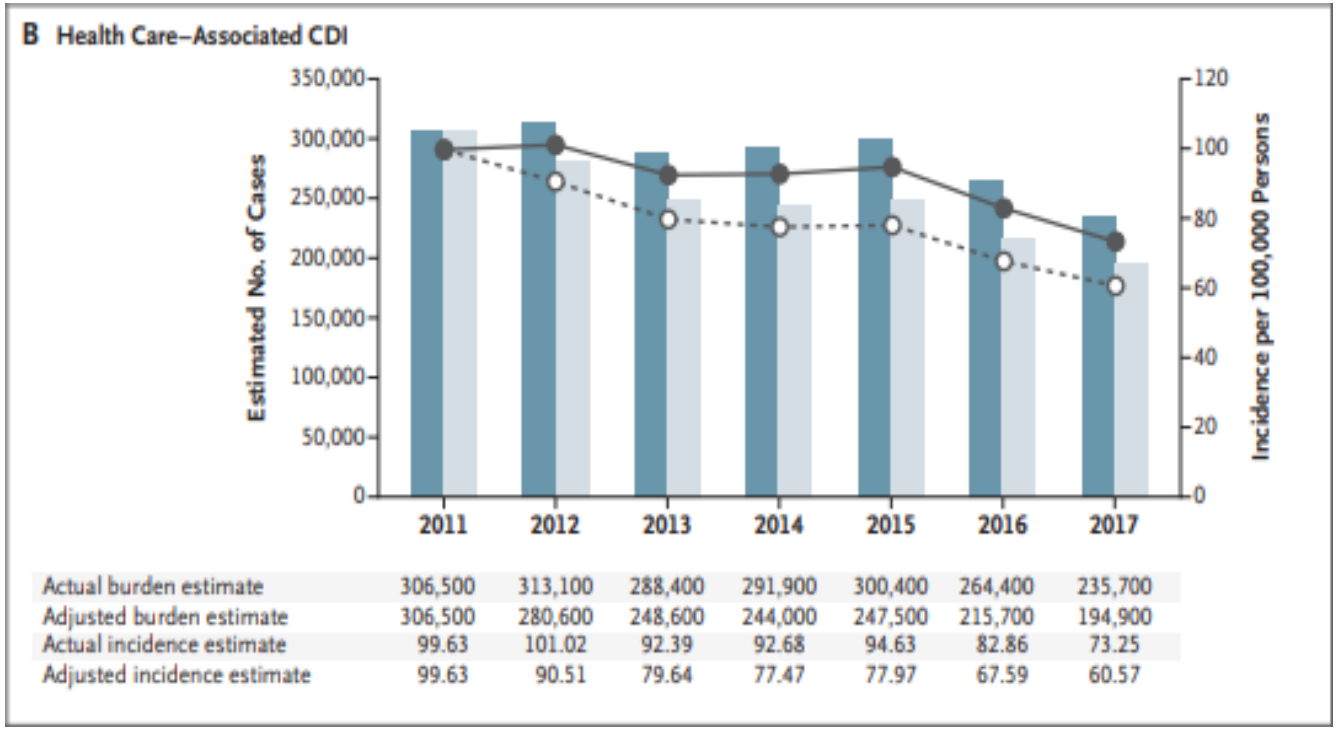
- Leading cause of antibiotic- and healthcare-associated infectious diarrhea in the US
- CDC “Urgent Threat”
- Decreasing incidence of healthcare-associated CDI and increasing incidence of community-associated CDI

Sources: 2019 Antibiotics Resistance Threats Report. CDC. 2019.
Guh AY, et al. N Engl J Med 2020;1320-30.

Epidemiology - *C. diff*



	2011	2012	2013	2014	2015	2016	2017
Actual burden estimate	170,000	192,500	196,700	213,100	229,300	237,800	226,400
Adjusted burden estimate	170,000	161,100	154,300	161,200	172,300	176,300	170,300
Actual incidence estimate	55.26	62.12	62.99	67.67	72.24	74.49	70.36
Adjusted incidence estimate	55.26	51.96	49.42	51.18	54.29	55.23	52.91



	2011	2012	2013	2014	2015	2016	2017
Actual burden estimate	306,500	313,100	288,400	291,900	300,400	264,400	235,700
Adjusted burden estimate	306,500	280,600	248,600	244,000	247,500	215,700	194,900
Actual incidence estimate	99.63	101.02	92.39	92.68	94.63	82.86	73.25
Adjusted incidence estimate	99.63	90.51	79.64	77.47	77.97	67.59	60.57

Source: Guh AY, et al. N Engl J Med 2020;1320-30.

C. diff Diagnostic Tests

Test	About the Test
PCR Detects toxin genes	Highly sensitive for organism detection **Cannot** distinguish disease from colonization
Stool toxin EIA Detects *C. diff* toxins A & B	Analytical limit of detection ~1 ng/mL for each toxin Less sensitive than PCR Good specificity (96%-98%) vs culture
EIA for *C. diff* glutamate dehydrogenase	Good sensitivity Specificity is poor; cannot distinguish b/w toxigenic and nontoxigenic strains

Sources: Crobach M., et al. Clin Microbiol Infect 2009; 15: 1053
Eastwood et al. J Cin Microbiol 2009;47:3211
Crobach M., et al. Adv Exp Med Biol 2018;1050-27

Dilemmas and Challenges in C.diff Diagnosis

Unable to differentiate colonization vs infection with PCR testing

- May result in:
  - Overdiagnosis
  - Overtreatment
- Especially in low pretest probability

Results in

- Treatment of colonization
- Increasing development MDROs
- Recurrent *C.diff* diagnosis
- Increased healthcare costs

- There is no “gold standard” test

Clinical assessment for C. diff is critical to appropriately interpreting lab findings

Source: Lee et al. Infect Dis Ther. 2021; 10:687
Erb et al. Clin Microbiol. 2015; 21:998:e9

Diagnostic Algorithm: IDSA Recommendations

Use toxin stool test as PART of:

Multi-step algorithm (e.g., toxin + PCR) rather than PCR alone

- Patients with unexplained and new onset of >3 unformed stools in 24h
- No role for repeat testing (within 7 days) during same episode of diarrhea
- Do not test from asymptomatic patients

Source: McDonald et al. CID 2018;66:e1

Post-Infectious GI symptoms

Observational cohort of *C. diff* cases vs matched non-*C. diff* controls (n=41)

6 months post-*C. diff* infection (CDI), 1 in 4 with CDI met definition for new-onset irritable bowel syndrome (IBS) &/or functional GI disorders

Condition, n (%)	CDI Cases	Non-CDI Controls	*P* Value
Irritable bowel syndrome or functional GI disorders	**22%** (9/41)	0 (0)	.0024
Irritable bowel syndrome	**12.2%** (5/41)	0 (0)	NS
Persistent (functional) diarrhea	**14.6%** (6/41)	0 (0)	.023
Abdominal bloating	**9.7%** (4/41)	0 (0)	NS

NS = not significant

Source: Sethi S., et al. J Hosp Infect 2011;77:172

Post-Infectious GI symptoms

Observational case-control 1998-2007 *C. diff* (n=891)

14.1% cases post-6 months CDI developed IBS, dyspepsia, GERD, or functional diarrhea

Condition	Rate Ratio (CDI cases vs Non-CDI controls)	95% Confidence Interval
Irritable bowel syndrome	**6.1**	2.9-12.9
GERD	1.9	1.4-2.6
Dyspepsia	3.3	1.4-7.7

Source: Guiterrez R., et al. Gastroenterology 2015; 149(6):1408-14

C. diff Treatment Guidelines

Diagnosis	Recommended Treatment	Alternative Treatment	Adjunctive
Initial episode	Fidaxomicin 200 mg BID x 10 days	PO Vancomycin 125 mg QID x 10 days If no other available agents: metronidazole 500 mg TID x 10 days	Bezlotoxumab may be considered during first episode if risks for *C. diff* recurrence are present
First recurrence	Fidaxomicin 200 mg BID x 10 days **OR** Fidaxomicin 200 mg BID x 5 days or QOD x 10 days (#20)	PO vancomycin tapered/pulsed regimen: 125 mg QID x 10-14 days 125 mg BID x 7 days 125 mg QD x 7 days 125 mg q2-3d x 2-8 wks **OR** PO Vanc 125 mg QID x 10 days	Bezlotoxumab
Second recurrence (i.e., 3 *C. diff* episodes) or **more**	Same	Same	Bezlotoxumab **OR** Fecal transplant (expert panel suggestion that have had recurrence at 3rd *C. diff* episode with appropriate antibiotics)

Source: Johnson S., et al. CID; 2021; 73(5): e1029-44.

Updated 2021 IDSA/SHEA *C. diff* Guidelines

In patients w/ recurrent *C. diff*, should **fidaxomicin** be used over vancomycin?

Outcomes (Follow-up)	Participants (Studies)	RR (95% CI)	Anticipated Absolute Effects	
			Risk With Vancomycin	Risk Difference With Fidaxomicin (95% CI)
Sustained CDI resolution (30 days after Tx)	253 (3 RCTs)	**1.27** (1.05-1.54)	558 per 1000	**151 more per 1000** (34 more to 269 more)
Sustained CDI response (90 days after Tx)	75 (1 RCT)	**1.56** (0.99-1.14)	410 per 1000	**229 more per 1000** (9 more to 449 more)
CDI initial clinical cure (2 days after Tx)	253 (3 RCTs)	**1.03** (0.94-1.14)	853 per 1000	**26 more per 1000** (58 fewer to 110 more)
Serious adverse events (follow-up 90 days)	75 (1 RCT)	**0.68** (0.35-1.29)	410 per 1000	**132 fewer per 1000** (345 fewer to 80 more)
All-cause mortality (follow-up 90 days)	75 (1 RCT)	**0.81** (0.20-3.38)	103 per 1000	**19 fewer per 1000** (150 fewer to 112 more)

Tx = treatment

Source: Johnson S., et al. CID; 2021; 73(5): e1029-44.

Fidaxomicin Logistical Issues

- Challenges with cost/coverage and availability
- Prescribing best practices
  - Evaluate insurance coverage
    - Private: Variable coverage → **check eligibility for patient assistance program (PAP)**
    - Government (Medicare/Medicaid): Variable coverage; typically not eligible for PAP
    - None (self-pay): **Check eligibility for PAP**
  - Be prepared to issue back-up prescription for PO vancomycin

Fidaxomicin Merck PAP

- Provides fidaxomicin at **no cost** to eligible patients
  - Approval process takes ~20 minutes once receive paperwork
  - Can expedite shipping so patients receive product the next day
  - Max 90-day supply at a time, up to 3 refills; valid for 12 months
- Eligibility (note, some patients have received exemptions beyond these criteria)
  - US resident with prescription
  - Do not have prescription insurance
  - Cannot afford medication (income-based)

To access, use the following links:

Tablets: merckhelps.com/DIFICID%20Tablets

Enrollment Form: merckhelps.com/MPAP/MPAP_Enrollment_Form_US-NON-06566_English.pdf

Oral suspension: Merck Programs to Help Those in Need - Product (merckhelps.com)

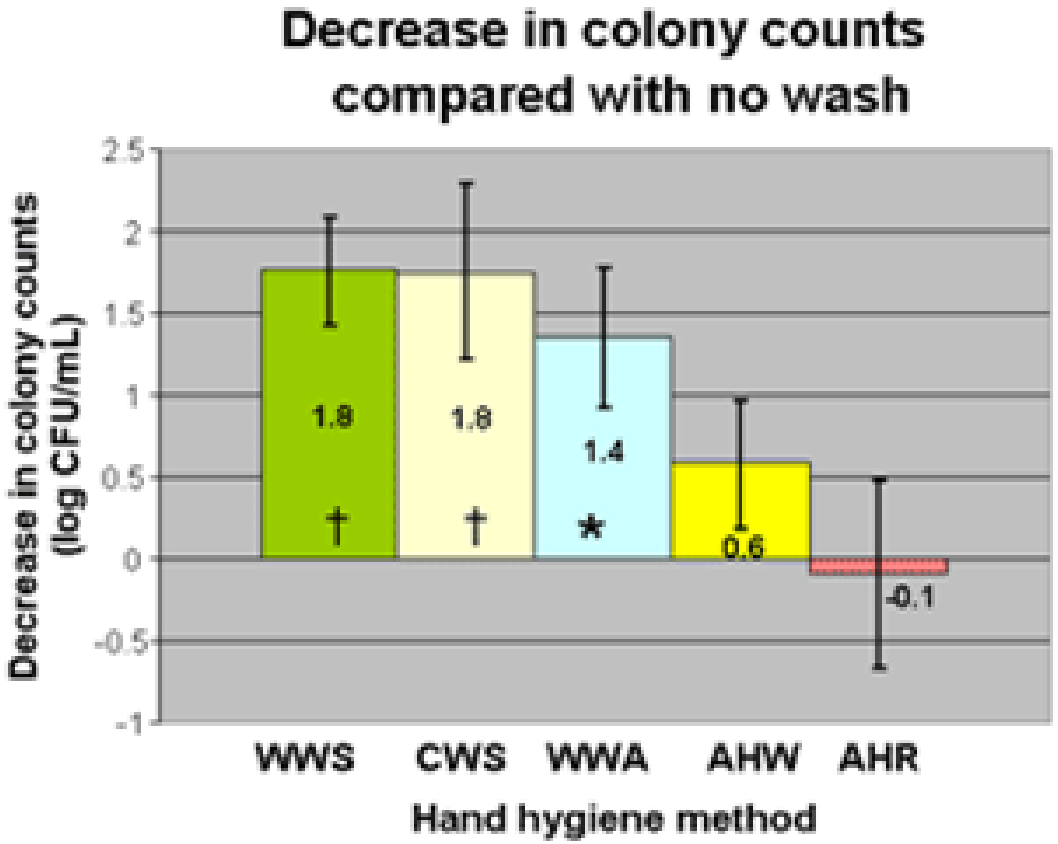
CDI Outbreak Response and Control

Steps	Control Interventions
Report	❑ Report suspected outbreak to KDHE, work with public health staff ❑ Information to collect: Date of earliest illness? When did other illnesses occur? How many residents in facility? How many have been ill? How many staff and how many have been ill? Have infected residents been in 1 unit or wing, or spread across facility? Have any dietary or food staff been ill? ❑ Complete line listing of infected residents
Test	❑ Submit stool specimens, KDHE staff can assist in KHEL submissions
Survey	❑ Implement active daily surveillance for diarrhea among residents and staff
Infection Control	❑ Place in contact precautions until 48 hours after diarrhea is resolved (for outbreak settings) ❑ For the duration of the outbreak, increase frequency of hand hygiene audits on affected units, provide written & verbal staff feedback ❑ Private patient room preferable, especially for incontinent residents - if not available, cohort with dedicated commodes ❑ Use dedicated equipment for each patient ❑ Use single-use, disposable thermometer
Hand Hygiene	❑ Promote adherence to hand hygiene among healthcare workers, patients, visitors ❑ Use soap and water during outbreaks

Norovirus Outbreak Response and Control

Steps	Control Interventions
PPE	❑ Use PPE (i.e., gowns and gloves) when entering affected patient care areas and remove carefully to avoid contaminating clothing ❑ Change gloves immediately if soiled ❑ Change gown & gloves in between patients if cohorting
Transfers & Admissions	❑ When transferring ill patients, notify receiving facility to ensure continuation of contact precautions ❑ When transferring well patients, notify receiving facility of presence of a suspected gastrointestinal outbreak
Cleaning & Disinfection	❑ Commercial disinfection products registered with EPA for use in healthcare facilities; follow manufacturer instructions for method of application, amount, dilution and contact time ❑ EPA's Registered Antimicrobial Products Effective Against C.diff (not all commercial cleaning products act dually as a disinfecting agent) ❑ Routine cleaning, disinfection of high-touch environmental surfaces (e.g., commodes, toilets, faucets, telephones, door handles, computer equipment, kitchen preparation surfaces)
Antimicrobial Stewardship	❑ Establish multidisciplinary (i.e., medical staff, nursing, pharmacy) efforts to monitor and improve antibiotic use ❑ Evaluate antimicrobial use among CDI patients and share with your medical staff and facility leadership

Efficacy Hand Hygiene Methods for Removing *C. diff* Contamination from Hands



WWS = warm water and soap

CWS = cold water and soap

WWA = warm water and antibacterial

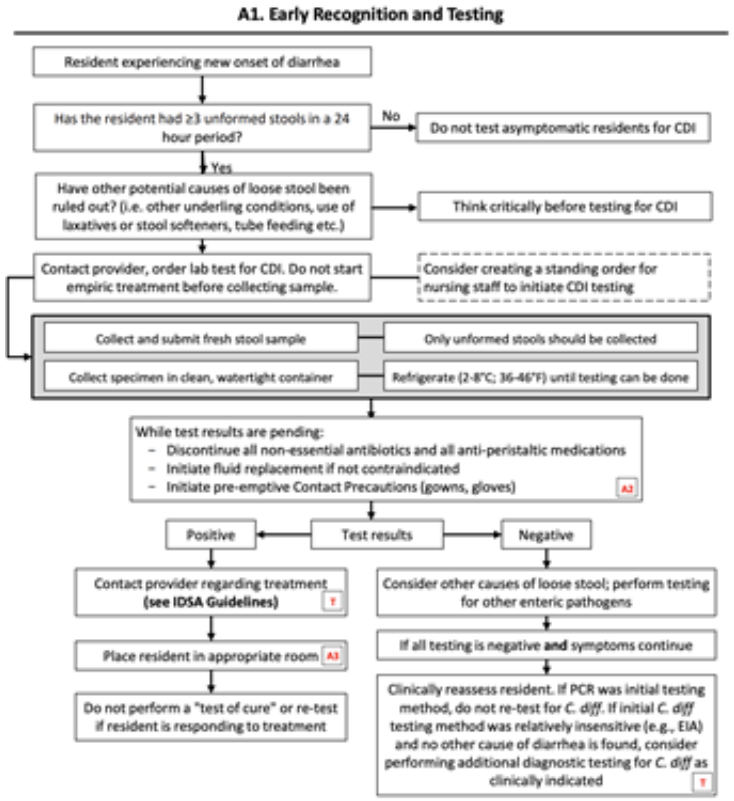
AHW = alcohol hand wipe

AHR = alcohol hand rub

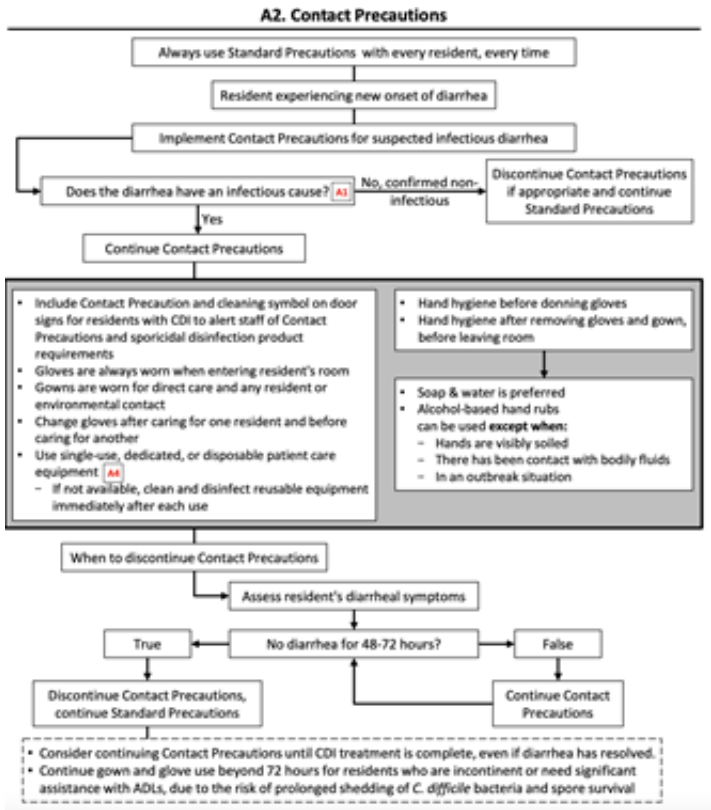
CFU = colony forming units.
* Different from AHR ($P<0.05$).
† Different from AHR and

Source: Oughton M., et al. 47th Annual ICAAC Meeting; 2007; Sept 17-20

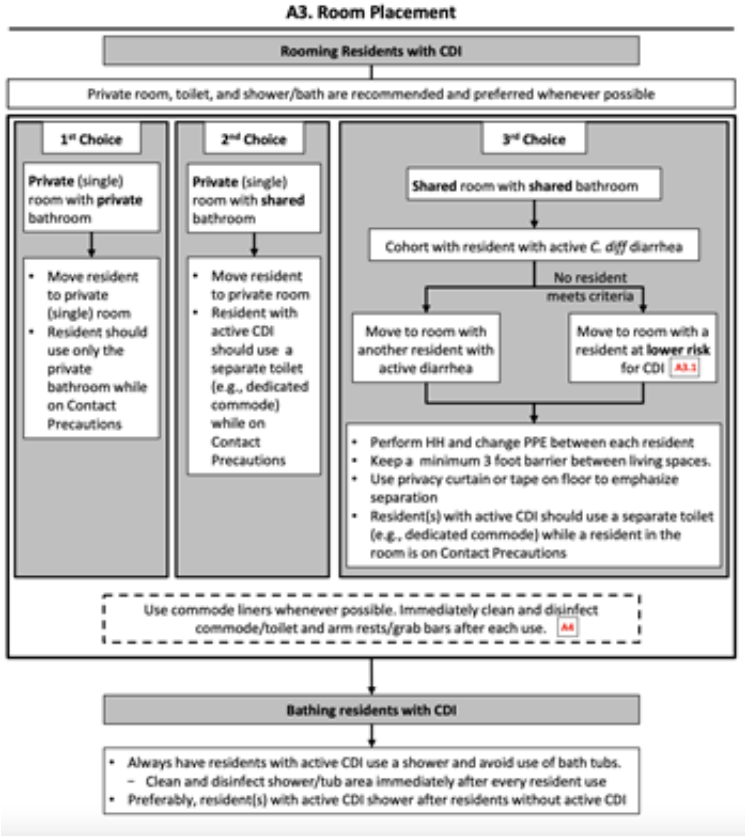
Resources



Early Recognition & Testing Algorithm



Contact Precautions Algorithm



Room placement Algorithm

Download: health.state.mn.us/diseases/cdiff/hcp/ltcalgorithms.pdf

Resources

Example CDI Prevention and Control Policy

Policy: *Clostridium difficile* Infection (CDI) Prevention and Control and Treatment of Residents

Purpose: The purpose of this policy is to reduce the acquisition and transmission of *C. difficile* in this facility, and to provide guidelines for the care of residents with CDI.

Facility Name:
Effective date:
Review date:
Approvals: *[Medical director, or other approving authority]*
Responsibility: *[nursing staff, environmental services/housekeeping, etc.]*

Background Information

- *Clostridium difficile* is an anaerobic, Gram-positive, spore-forming bacteria
  - *C. difficile* spores can remain in the environment for months if contaminated surfaces and/or items are not properly cleaned and disinfected
- The bacteria are found in feces, and transmitted via the fecal-oral route. Health care workers can spread the bacteria to other residents or contaminate surfaces through hand contact.
- Risk factors for CDI are:
  - Recent antibiotic use
  - Age >65 years
  - Other serious illnesses
- Signs and symptoms of CDI:
  - Watery, liquid diarrhea lasting for 3 or more days
  - Fever
  - Loss of appetite
  - Abdominal pain/cramps
  - Nausea

Procedure

I. Early Recognition of CDI and laboratory testing

1. Consider CDI in a resident who has ≥3 unformed stools in a 24-hour period with no other

C. diff IPC Policy
health.state.mn.us/diseases/cdiff/hcp/ltctoolkit/expolicy.docx

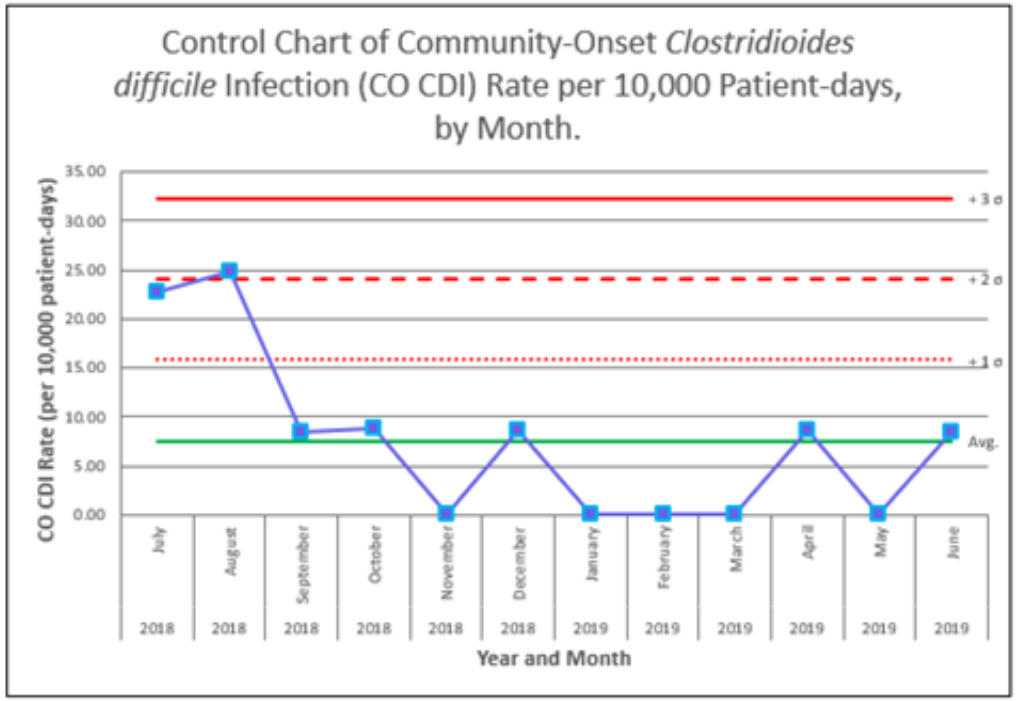
Community-Onset *Clostridioides difficile* Infection (CO CDI) Control Chart

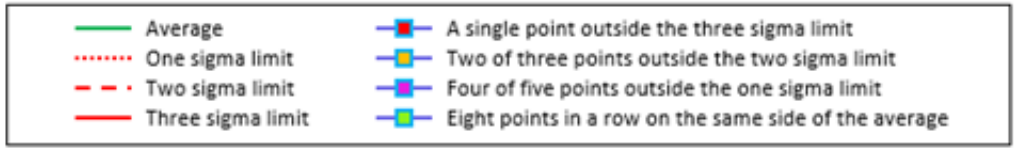
Instructions

- For current standardized surveillance definitions for this measure, see the CDC's NHSN protocol: MDRO and CDI Module Protocol
- **Option 1 (preferred)**: For facility-wide surveillance, collect the count of infections (numerators) and the count of patient days (denominators) for the whole facility's inpatient population, by month, for a one year period.
- **Option 2**: For inpatient unit surveillance, collect the count of infections (numerators) and the count of patient days (denominators) for the unit, by month, for a one year period. In the chart title, add the name of the unit (e.g. ..."Patient-days in Add Unit Name, by Month.")
- **Option 3**: For outpatient unit surveillance, specifically emergency departments or 24-hour observation units, collect the count of infections (numerators) and the count of admissions (denominators) for the unit, by month, for a one year period. In the chart title, change the name of the denominator "Patient-days" to "Admissions", and add the name of the unit (e.g. ...per 10,000 Admissions in Add Unit Name, by Month."). Change the y-axis label to reflect the denominator is "...per 10,000 admissions", rather than "per 10,000 patient-days.

- Select the month you want to begin with: July
- Enter year of the month you want to begin with: 2018
- Enter the count of infections and patient days, or admissions, to the corresponding month. Only edit the purple cells.

Year	Month	Infections	Days or Admission	Rate
2018	July	3	1318	22.76
2018	August	3	1212	24.75





Surveillance HAI Spreadsheet
kdheks.gov/epi/hai/CAH_Toolkit/Spreadsheet_2_Interactive_HAI_Tracking_Tools.xlsx

Hepatitis A Virus (HAV) Outbreaks

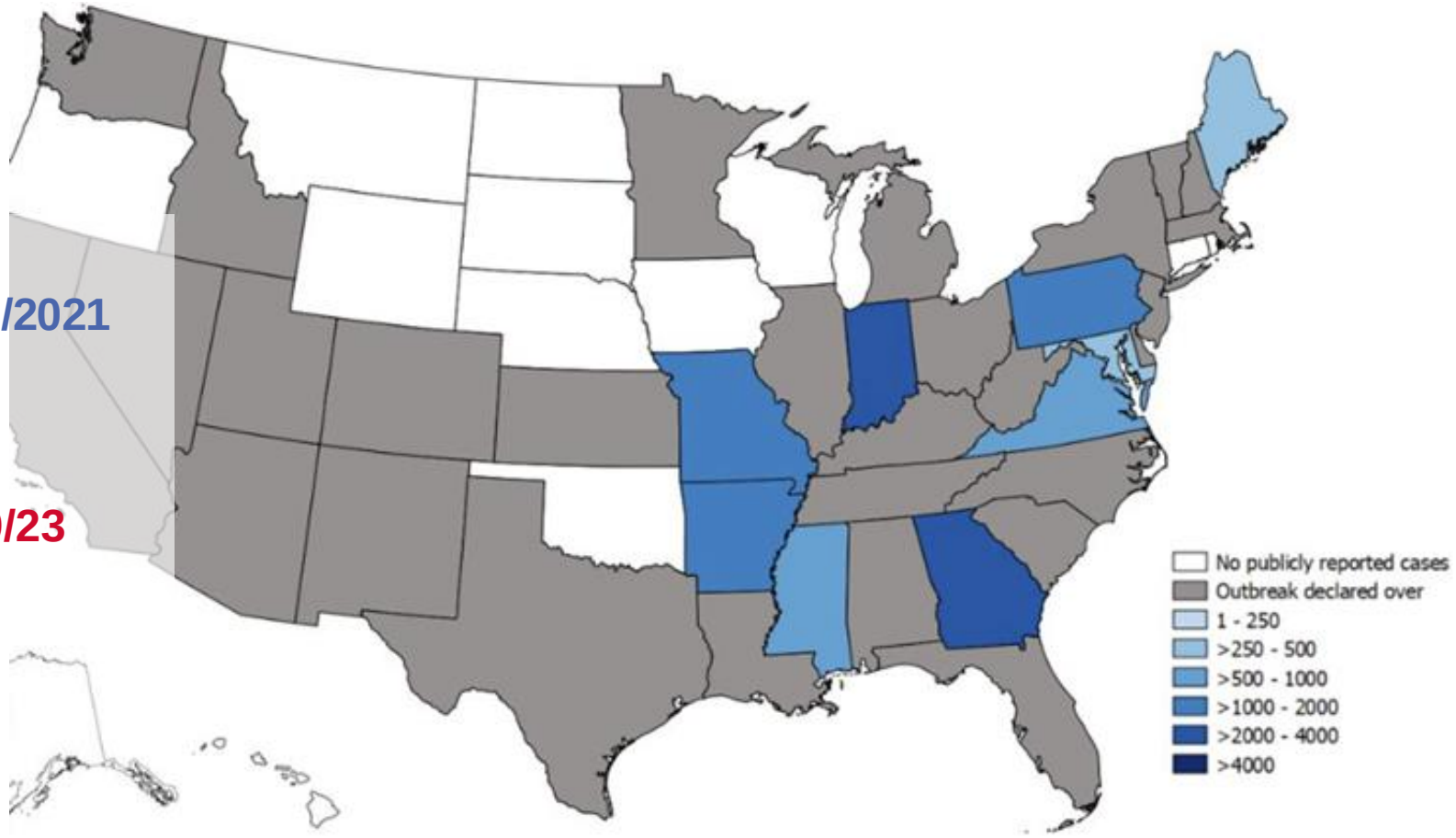
Source: cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm

HAV Outbreaks

State-Reported HAV Outbreak Cases as of Sept 1, 2023

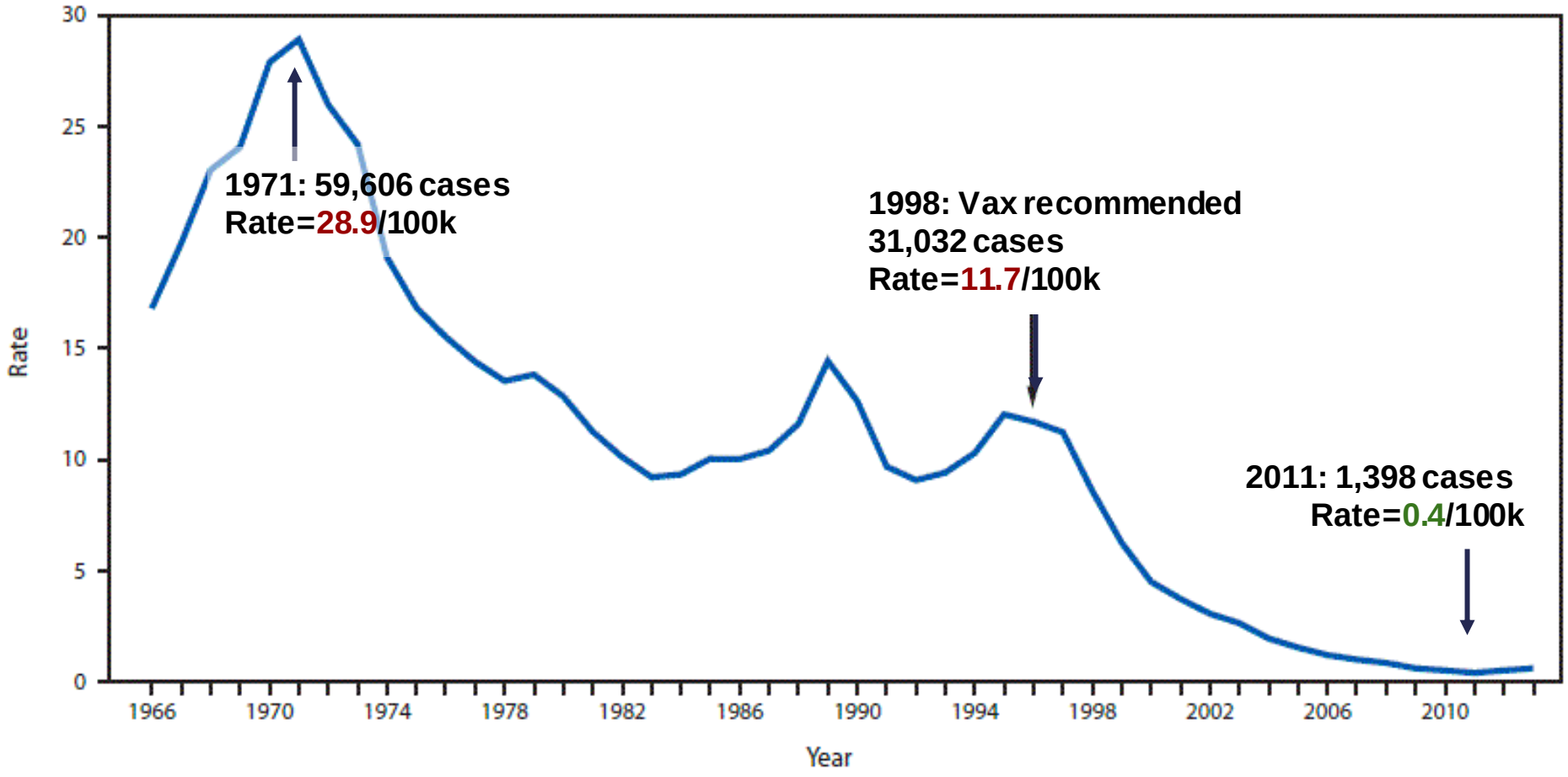
Kansas: 425 cases
(330/78% hospitalized) 5/2020-12/2021
5 deaths

Missouri: 1,129 cases
(660/58% hospitalized) as of 8/9/23
5 deaths



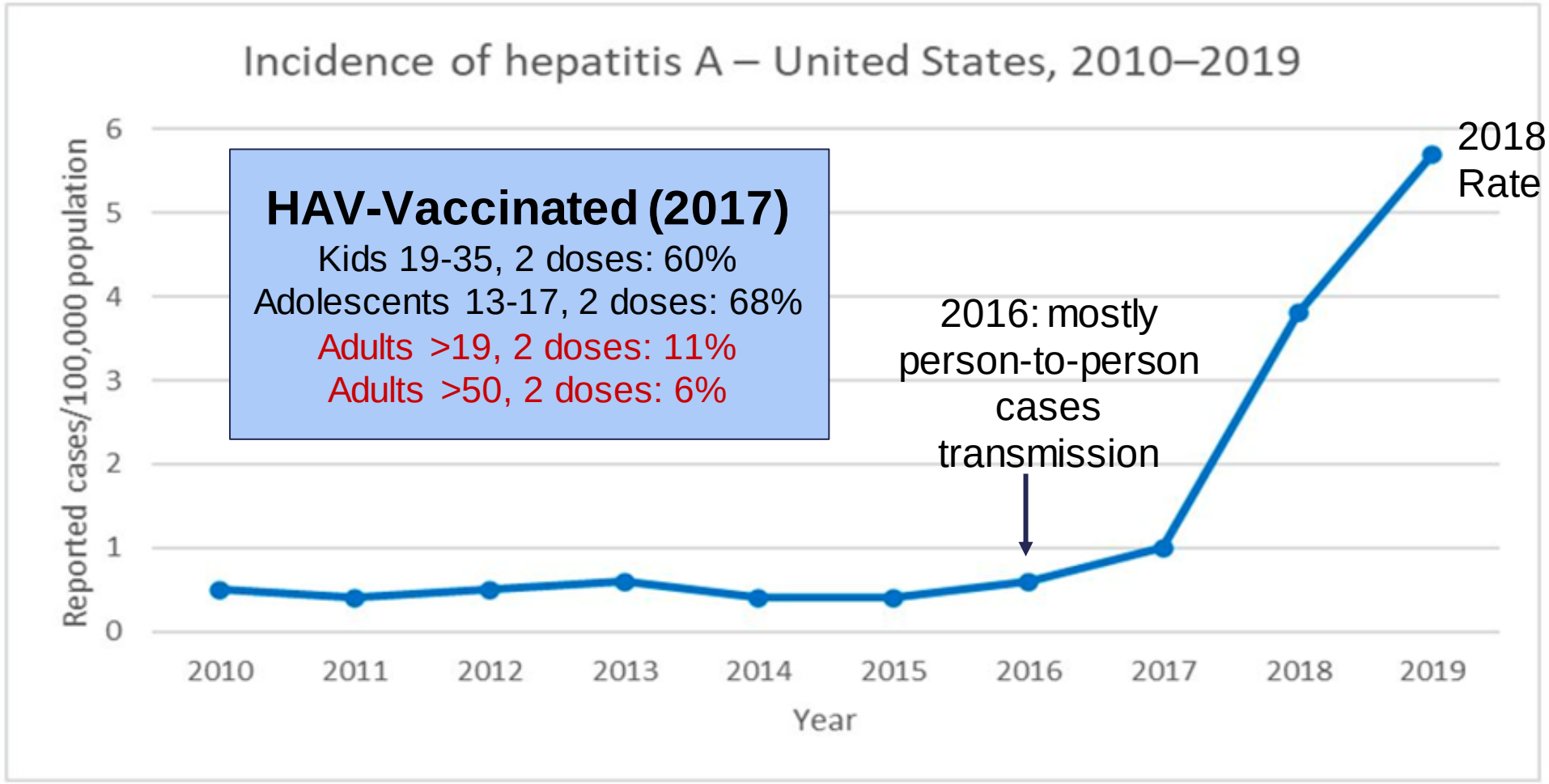
Source: Widespread outbreaks of hepatitis A across the U.S. | CDC
cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm

National HAV Epidemiology



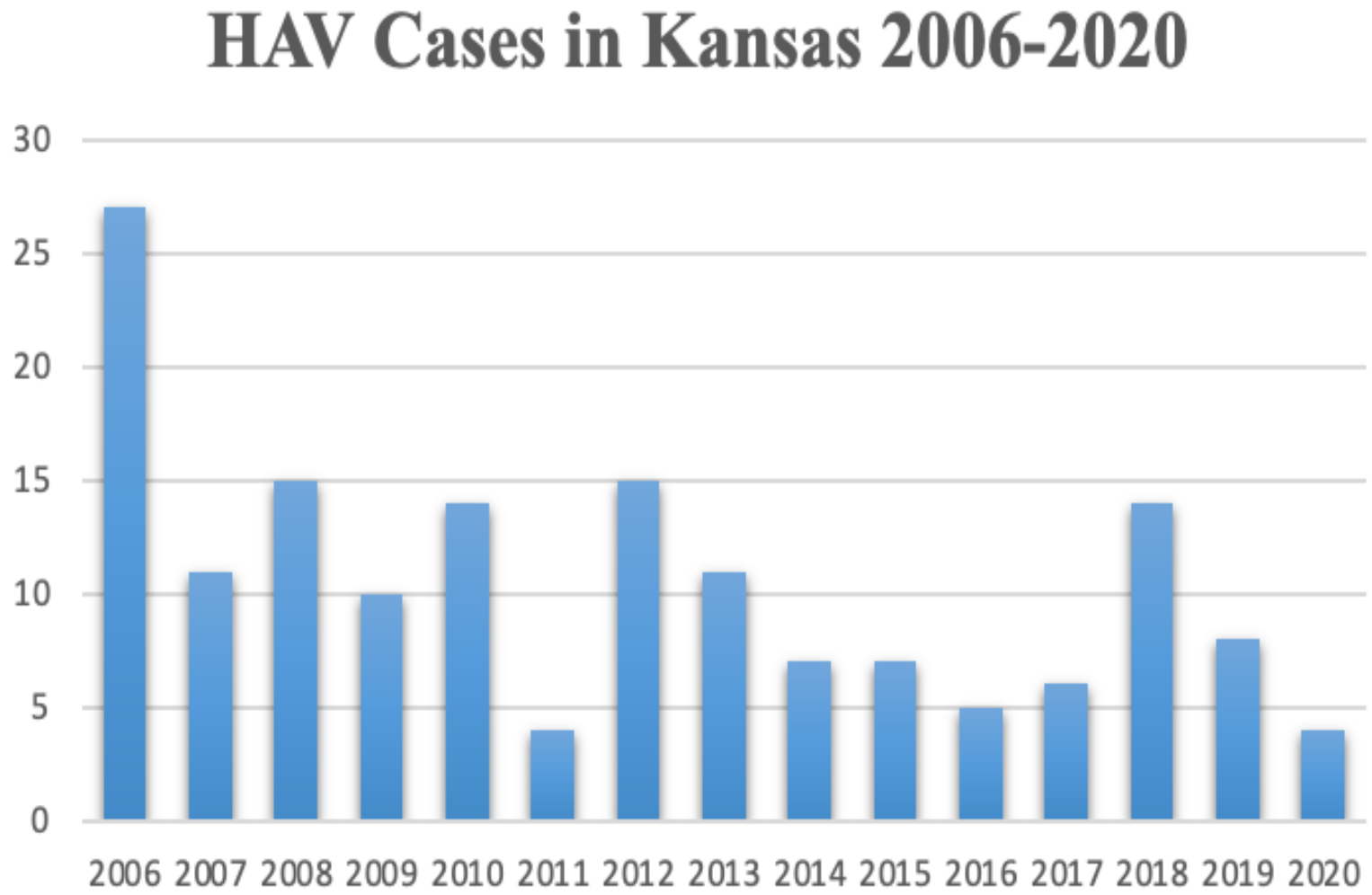
Source: MMWR 2018;66:1171-77

National HAV Epidemiology



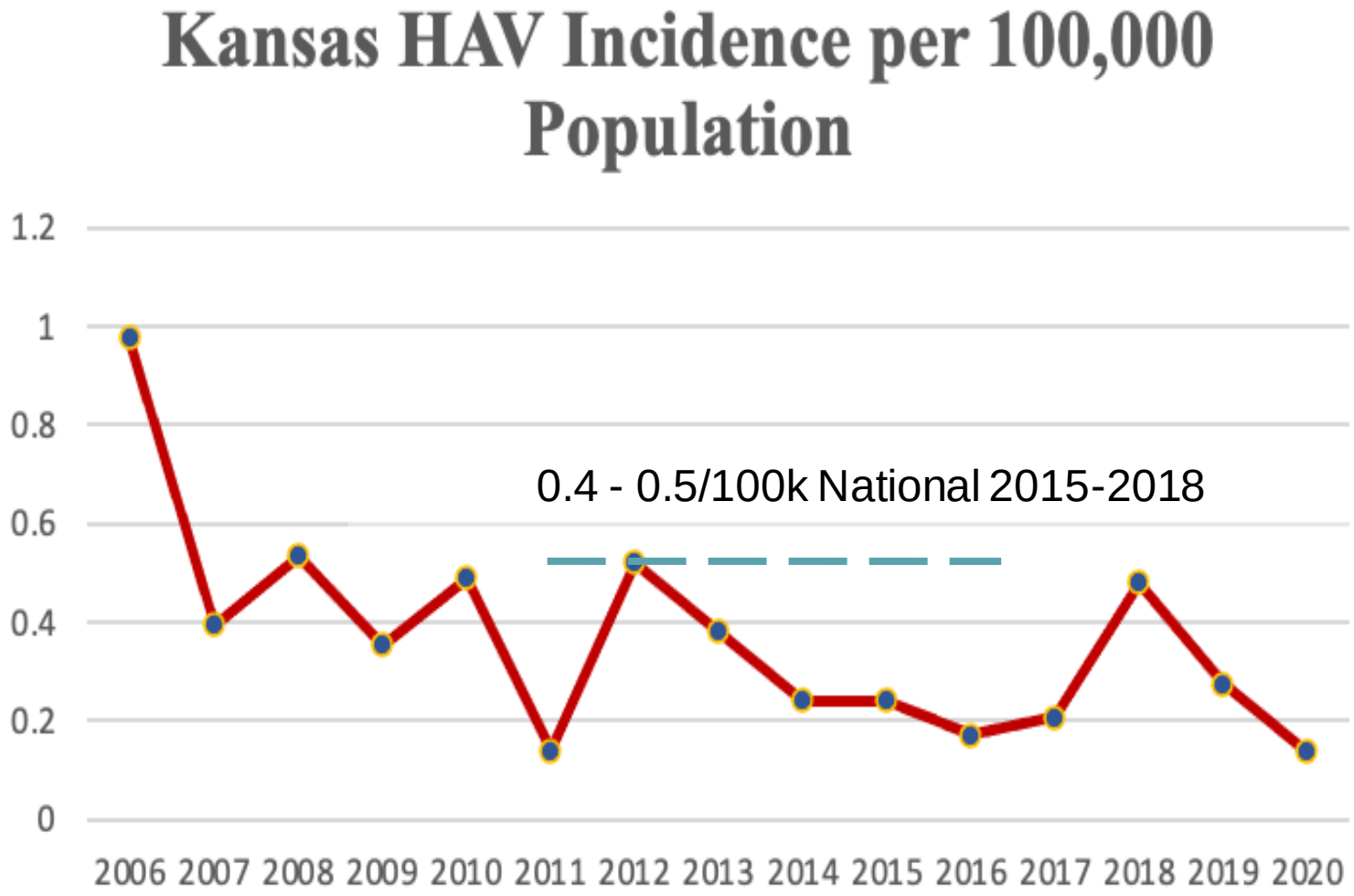
Source: MMWR 2018;66:1171-77

Kansas HAV Epidemiology



Source: kdhe.ks.gov/Archive.aspx

Kansas HAV Epidemiology



Source: kdhe.ks.gov/Archive.aspx

HAV Vaccine

Combination inactivated HAV + HBV vaccine

- 3 dose (0, 1, & 6 months)
- >18 years

Tradename: Twinrix

Inactivated antigenic HAV vaccines

- 2 doses (0 & 6-12 months apart)
- Lifelong immunity
- >1 year

Tradename: Havrix

Vaccine Efficacy

HAV Havrix

- Seroconversion following primary series ~100% (healthy adults)
- Ab persistence 20+ years in >95% healthy adults
- Since HAV vaccination available in ‘95, HAV prevalence decreased 95%

Yet… ¾ of Americans remain susceptible

Highest Risk

- Homeless
- Drug abuse/IVDU
- Cirrhosis
- HIV
- MSM
- Healthcare workers / work with high-risk people
- Endemic regional travels

Sources: Barker L, et al CID 2020;71(10):e571-e579
Heins N et al. Vaccine 2014(32)13:1807-13

Strategies to improve patient and worker vaccinations

Facility-Based

- Standing orders (e.g., on admit or discharge) rather than requiring physician's signature
- High-risk patients by diagnoses and age (identified by EHR or physician, nurse, pharmacist or IPaC)
- Leadership support (visibly vaccinate institutional leaders)

Provider-Based

- Practice-based tracking systems to identify high-risk adults and remind during visit
- Preventative checklists
- Meta-analysis of 41 studies: reminders improved vaccination rates 80%

Quality of Care Metric

- IDSA issued Executive Summary on Immunization Coverage, citing need to care and other organization promote immunization as indicator of healthcare quality in managed s

Occupational Health Partnership

- Offer flexible worksite vaccine delivery (e.g., multiple locations and times, via mobile carts)
- Offer free access w/o out of pocket expense to HCWs
- Monitor and report rates (ID areas/sectors with low coverage for targeted intervention)

Sources: Szilagyi P., JAMA 2000; 284(14):1820; IDSA Executive Summary. CID. 2007;44(12):1529-31

Thank You!

Kellie Wark, MD, MPH
AS Lead
Kellie.Wark@ks.gov

Bryna Stacey, MPH, BSN, RN, CIC
HAI/AR Section Director
Bryna.Stacey@ks.gov

Loretta Fitzgerald, RN, BSN
Quality Improvement Consultant – Infection Control
lfitzgerald@kfmc.org