Campylobacteriosis in the United States

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Campylobacter and campylobacteriosis

- Low infectious dose (~500 organisms)
- Incubation period of 2-5 days
- Acute gastroenteritis
- Sepsis, deep tissue infections are rare

- 1950's - described as a rare case of bacteremia in immunocompromised persons
- 1970's - new culture methods: common cause of diarrheal illness
- Almost all diagnosed illness due to thermophilic *C. jejuni/coli*

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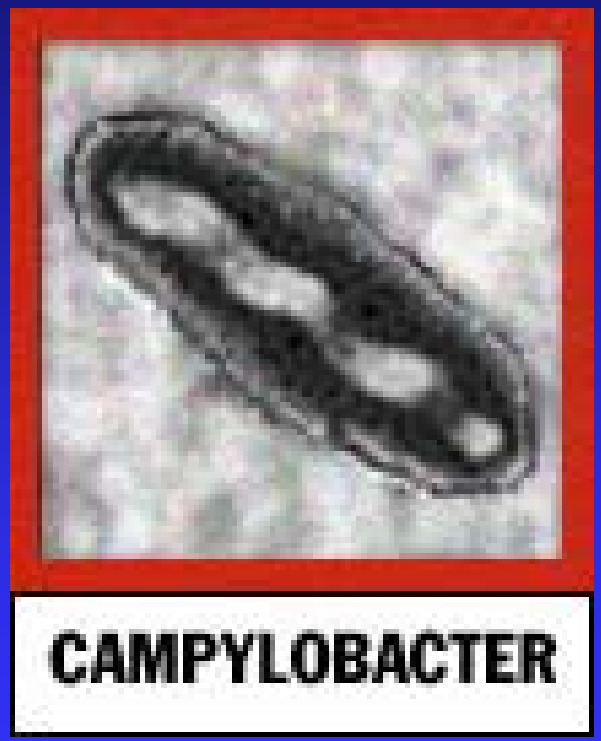
The *Campylobacter* genus of organisms

- **Most (~95%) human illness is caused by *Campylobacter jejuni***

- **Some other species:**
  - ***C. coli***
  - ***C. fetus (C. fetus subsp fetus)***
  - ***C. upsaliensis***
  - ***C. hyointestinalis***
  - ***C. lari***



Reservoir in animals: *Campylobacter jejuni*

- Birds (poultry): colonizes intestinal tract, and causes no symptoms
- Cattle: lives in gut, usually causing no symptoms, and can colonize the mammary glands
- In young dogs and cats: can cause diarrheal illness

Diagnosis of campylobacteriosis

- **Isolated from stool, occasionally blood**
- **Selective media**
  - **CCDA** (charcoal cefoperazone deoxychocolate agar)
- **Special atmosphere and temperature**
  - **Micro-aerobic atmosphere (5% O2, 15% CO2, 85% N2)**
  - **Increased isolation of *C. jejuni* and *C. coli* at 42 degrees C**

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Treatment of campylobacteriosis

- Cramps can be severe and diarrhea can be prolonged
- Fluid rehydration (IV or oral)
- Antimicrobial therapy can decrease duration of symptoms if given very early in illness
- Erythromycin, fluoroquinolones
- Increasing resistance to fluoroquinolones

Public health burden of campylobacteriosis:

- **Acute illness**
  - **~15% of diagnosed cases are hospitalized***
  - **~0.2% of diagnosed cases are fatal***
- **Post-infectious sequelae**
- **Guillain Barre syndrome:**
  - **Profound, reversible ascending paralysis**
  - **Follows 1 in 1000 cases after 3- 6 weeks**
- **Reactive arthropathy:**
  - **Cases described**
  - **Rate of this complication is unclear**

* 2003 FoodNet Annual Report: www.cdc.gov/foodnet

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Measuring the public health burden of campylobacteriosis

- *Campylobacter* is the most common bacterial cause of enteric infections in many developed nations
- In 1982 in the U.S. passive national surveillance began: 3 per 100,000 infections were reported each year
- In 1996, FoodNet began active surveillance/sentinel sites
- Reported incidence was 24 per 100,000
  - 95% *Campylobacter jejuni*
  - 5% *Campylobacter coli*
  - <1% other *Campylobacters*

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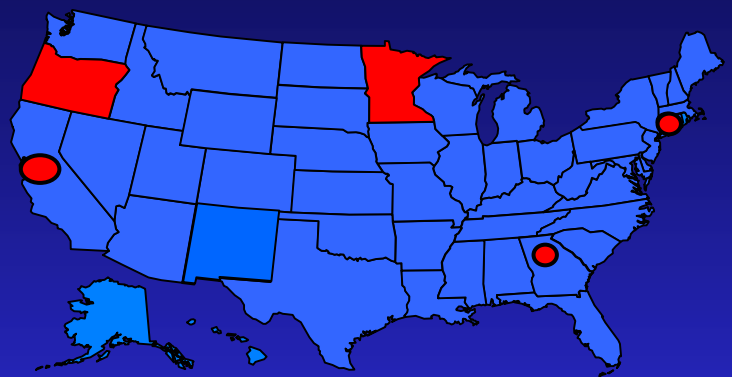
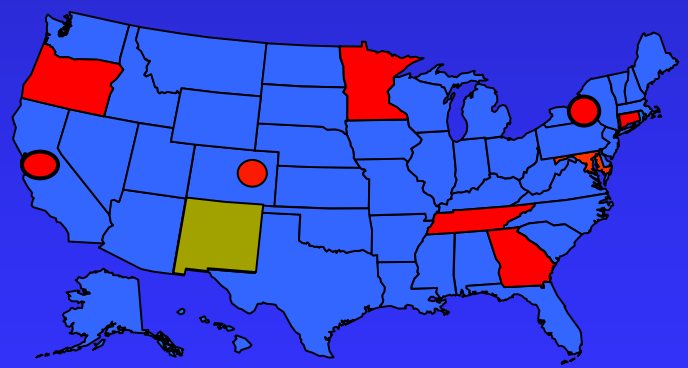
FoodNet sentinel sites have expanded



1996 – 5% of U.S. population



2003 - 14% of U.S. population

Year	Population in millions
1996	14.3
1997	16.1
1998	20.7
1999	25.9
2000	30.5
2001	34.1
2002	38.0
2003	41.5

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FoodNet incidence, all sites, 2004 (Isolates per 100,000 population)

Pathogen	2004
Campylobacter	12.9
Salmonella	14.7
E. coli O157:H7	0.9
L. monocytogenes	0.27

MMWR 2005; 54:352-356 (April 15, 2005)

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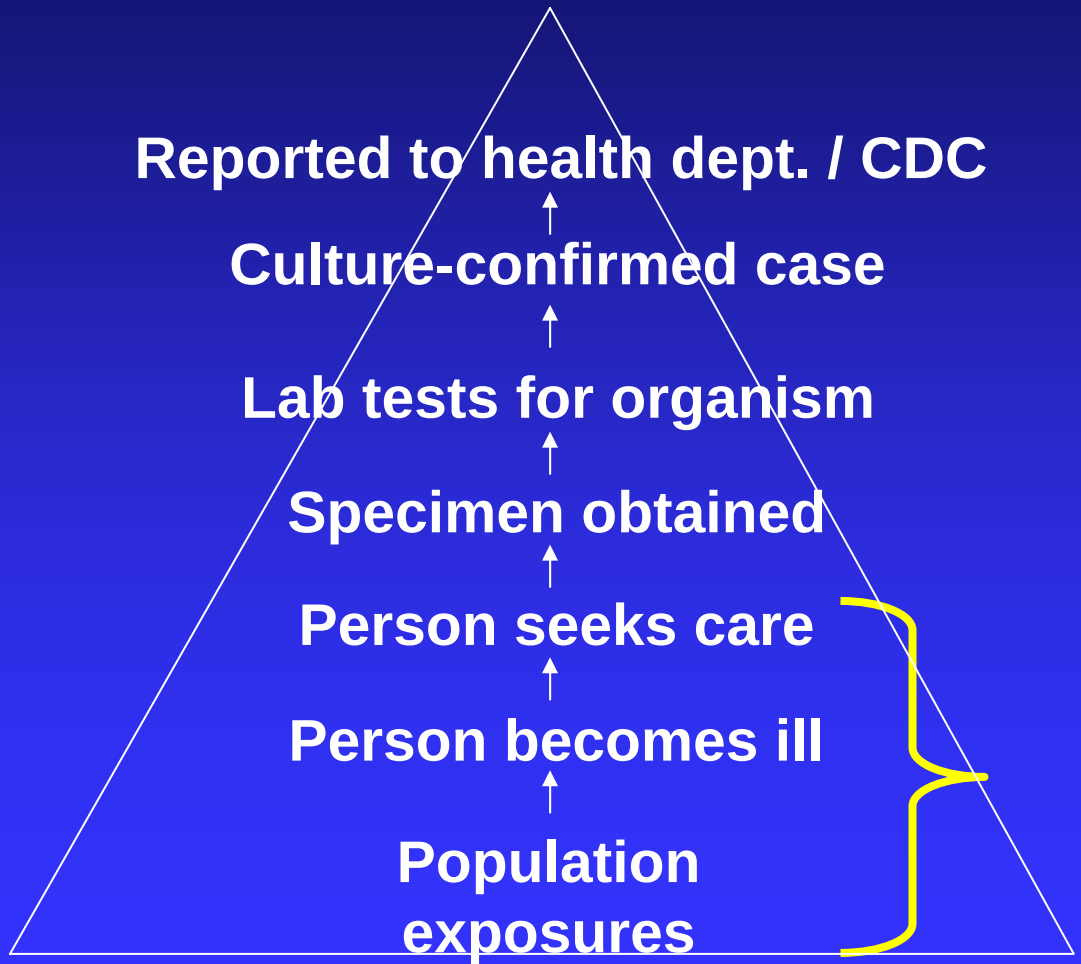
Diagnosed cases are a small fraction of the total number of infections



FoodNet

← Active surveillance

← Laboratory surveys

← (Physician surveys)

← Population surveys

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Public health burden of campylobacteriosis

- **Samuels: estimated 34 cases of illness for every one reported (1.4 million in 1999)***
- **2004: FoodNet illness rate was 12.9 per 100,000**
- **Could estimate 480 per 100,000 actual illnesses, or 1.2 million cases in 2004**

Samuel et al. CID 2004:38 (Suppl 3) S165-171

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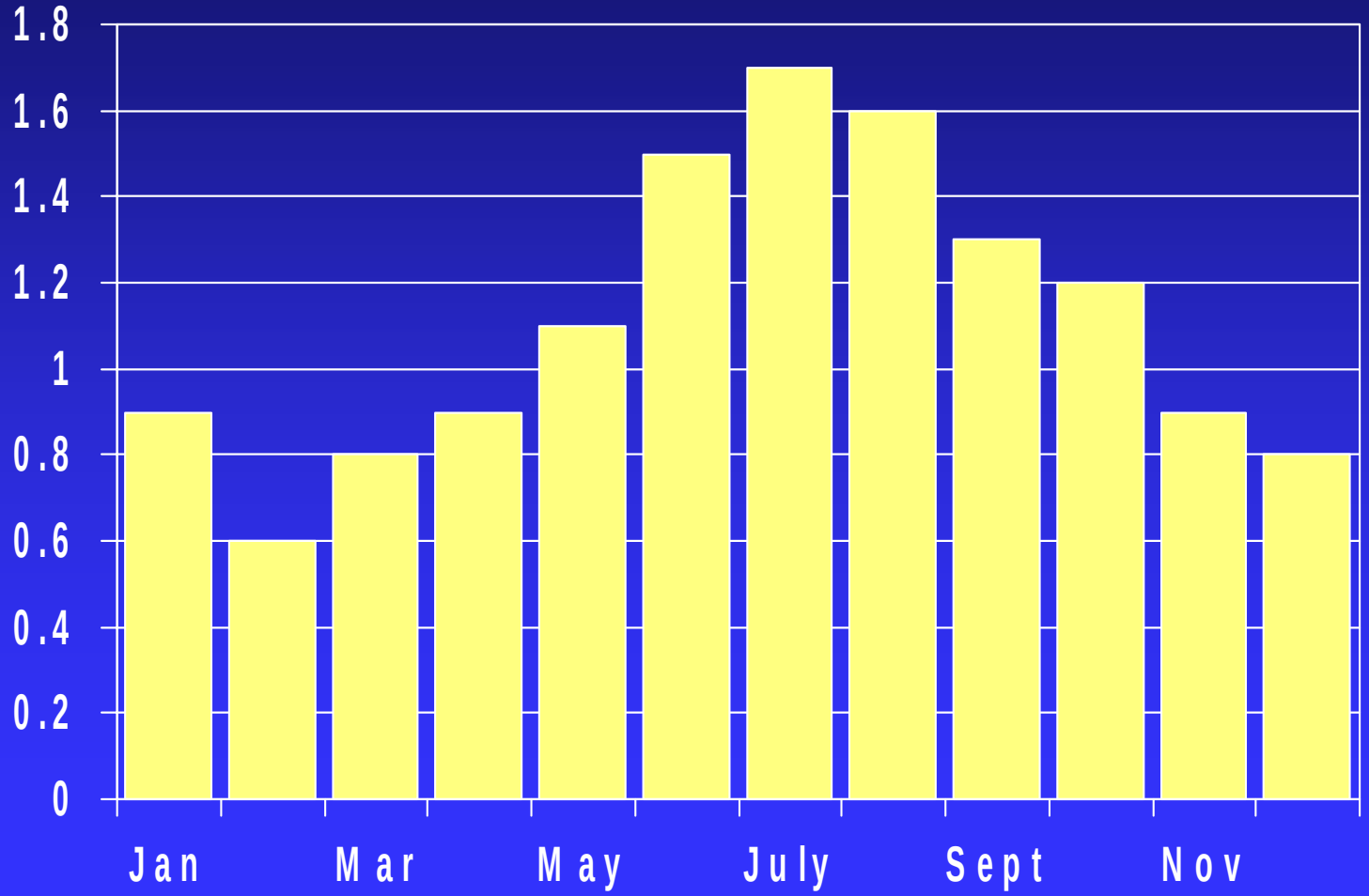
Incidence of diagnosed *Campylobacter* infection by month, FoodNet, 2002

(infections/month per 100,000 population)



FoodNet annual report 2002

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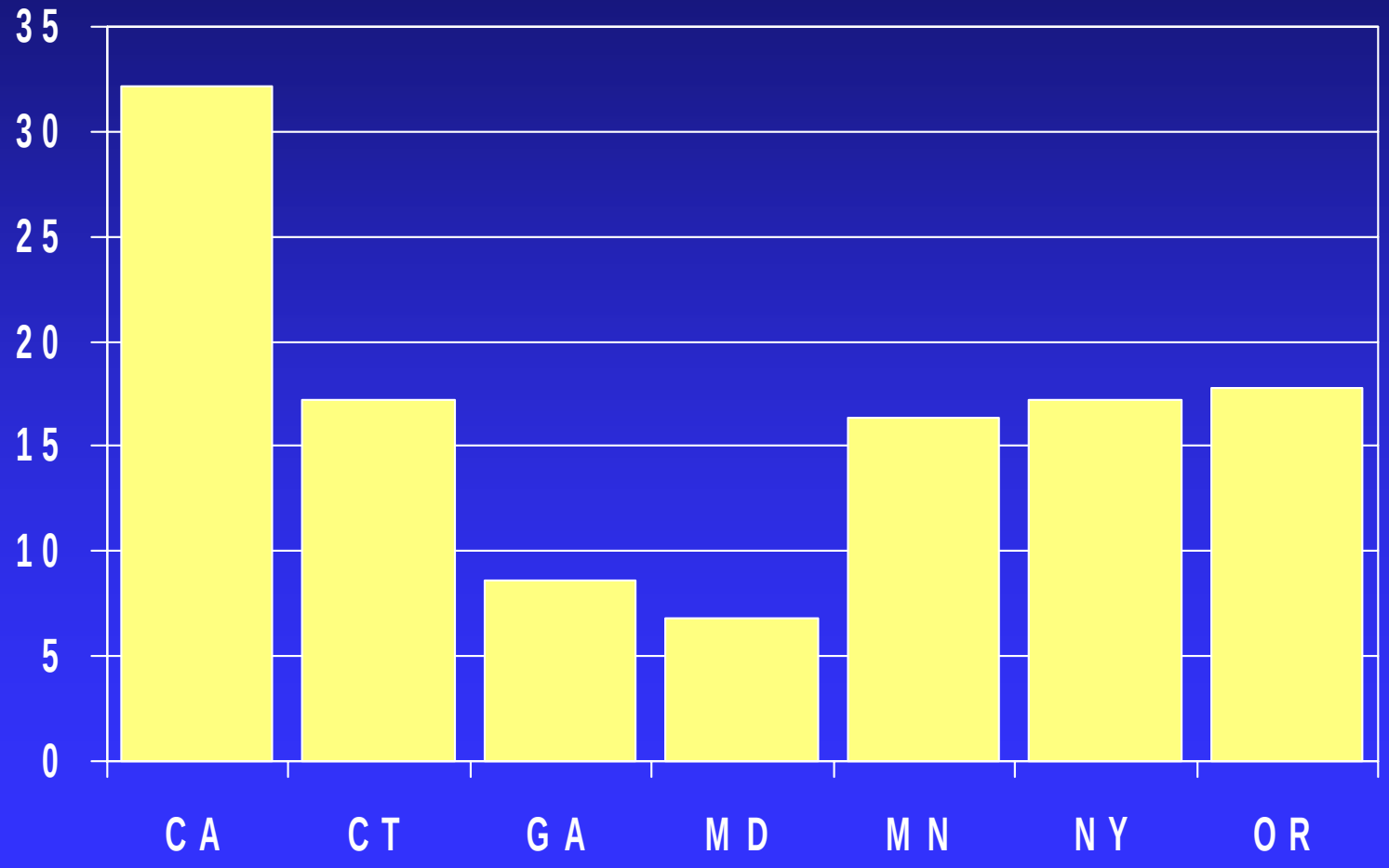
Incidence of diagnosed *Campylobacter* infection by site, FoodNet, 1999
(per 100,000 population)



Samuel et al. CID 2004:38 (Suppl 3) S165-171

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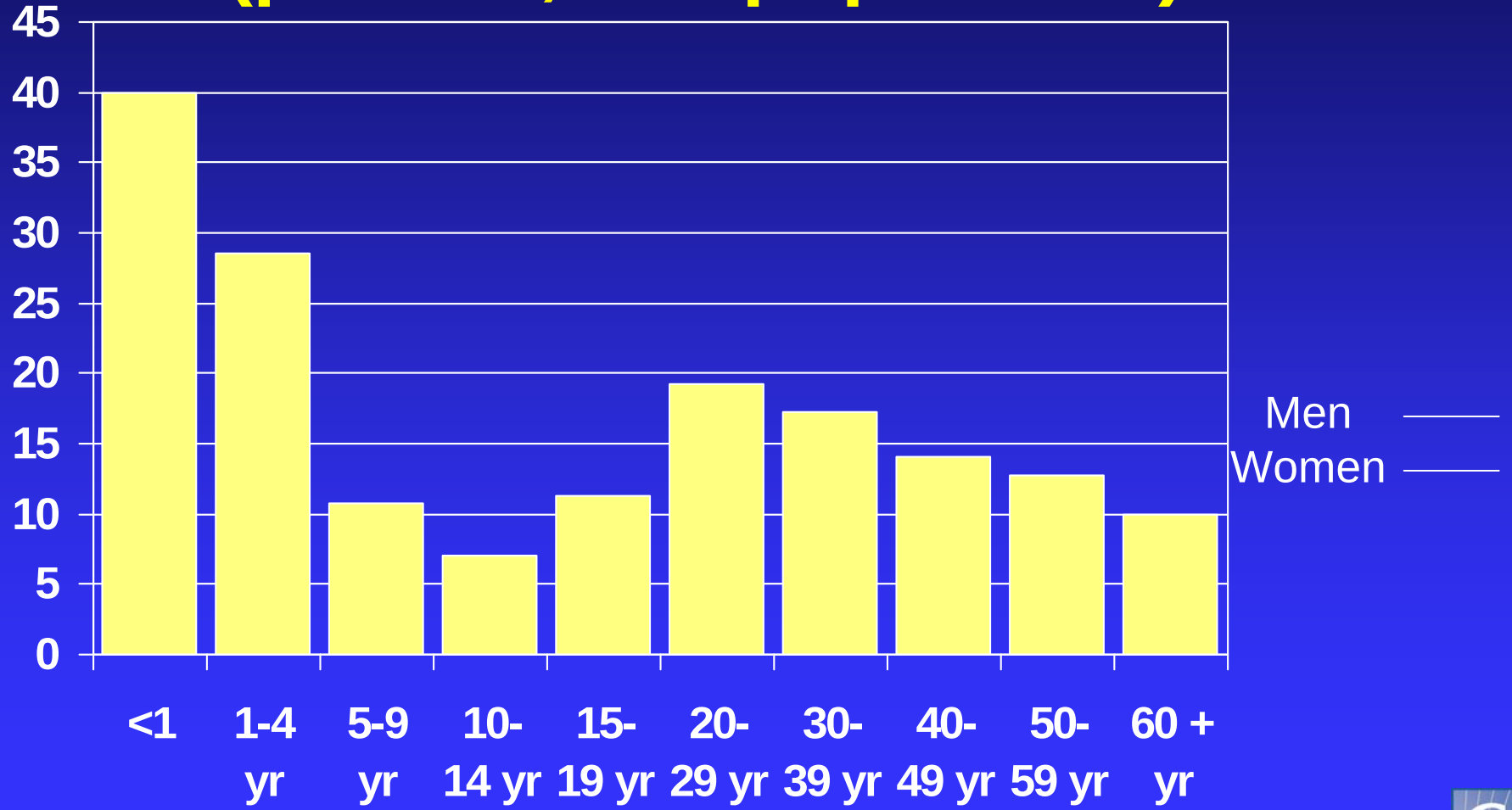
Incidence of diagnosed *Campylobacter* infection by age, FoodNet, 1999 (per 100, 000 population)



Samuel et al. CID 2004:38 (Suppl 3) S165-171

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General observations on *Campylobacter* outbreaks

- Outbreaks are rare: 3 per year in the United States.
- Seasonality different from sporadic cases
- Raw milk is the most common food associated with outbreaks
  - Tend to occur in spring and fall, unlike sporadic cases
  - Can occur with well-managed “certified” herds
- Cross contamination of a variety of foods may be the most common scenario: “multiple foods”, “undetermined foods”

- Waterborne outbreaks account for the most cases
  - Also occur in the spring
  - Before the increase in sporadic cases

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Case-control studies of sporadic cases

- People with infection are enrolled as cases
- Comparable healthy people enrolled as controls
- Both are interviewed about a period of interest
- Better if broad population included, and whole year
- Expensive and intensive effort

- Dependent on human memory
- Can only examine those things people have observed
- Often find multiple associations, need multivariable analyses
- Provide relative measures of importance, rather than precise allocation of cases across different sources.

FoodNet case-control study: Methods

- Study period: January 1, 1998 - March 1, 1999
- Study design: population based case-control study
- Study location: 7 FoodNet sites in CA, CT, GA, MD, MN, NY, and OR
- Cases: 1316 patients with symptomatic culture-confirmed *Campylobacter* infections not part of an outbreak
- Controls: 1 per patient, matched by age-group and telephone exchange

Friedman et al., CID 2004:38 (Suppl 3) S285-296

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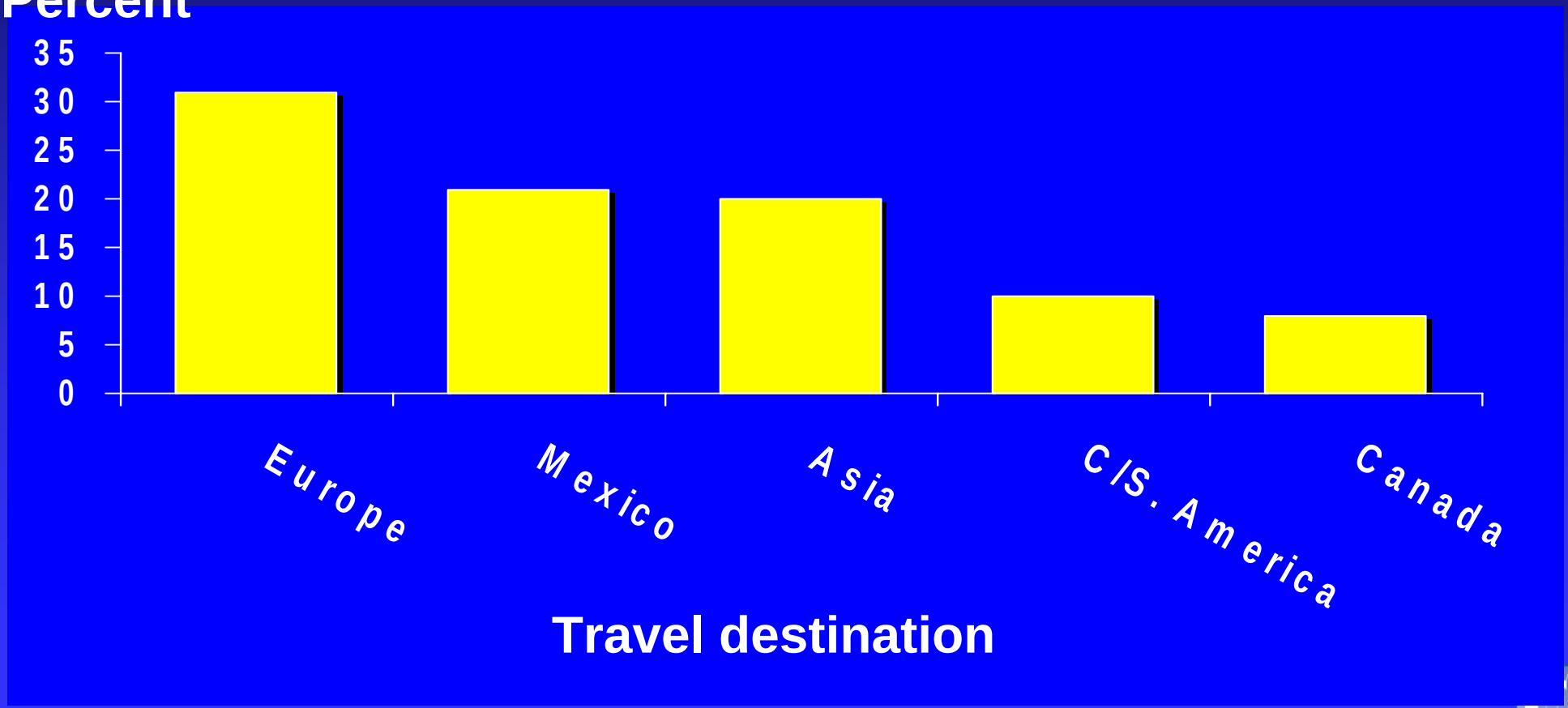
FoodNet case-control study: Foreign travel

- Foreign travel: 13% of cases, 1.5% of controls
  matched odds ratio= 10.0, p <0.01



FoodNet case-control study – independent risk factors on multivariable analysis (non-travelers)

Risk Factor	% attributable	mOR	(95%CI)
Chicken at restaurant	24%	2.2	(1.7, 2.9)
Non-poultry meat at restaurant	21%	1.7	(1.3, 2.2)
Turkey at restaurant	4%	2.5	(1.3, 4.7)
Undercooked chicken	3%	2.1	(1.2, 3.4)
Raw seafood	3%	1.9	(1.1, 3.4)
Raw milk	1%	4.3	(1.3, 14.2)
Untreated surface water	3%	3.3	(1.5, 7.5)
Contact w/ puppy	5%	3.4	(1.8, 6.5)
Contact w/ farm animals	4%	2.0	(1.2, 3.6)
Contact with animal stool	6%	1.4	(1.02, 1.9)

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FoodNet case-control study Conclusions

- Foreign travel was an important risk factor
- Eating poultry (chicken and turkey) at commercial establishments was significant risk factor
- Eating other meats at commercial food establishments also a significant risk factor
- Most chicken not memorably undercooked. This may indicate that poor food handling practices in restaurants play a role
- Contact with animals was a risk factor, especially for children
- Raw milk, untreated water accounted for a small proportion of cases
- No association with illness in family

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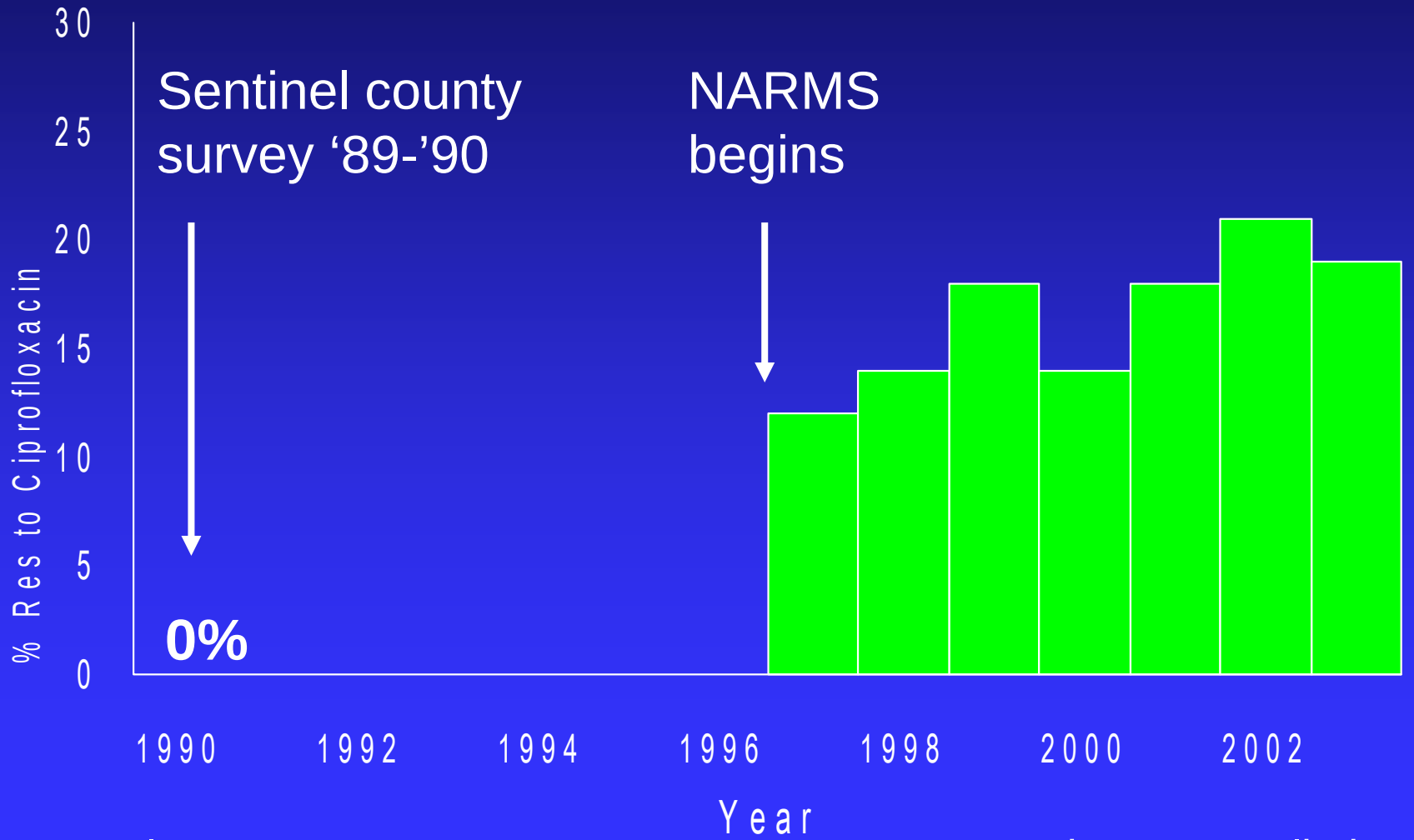
FoodNet studies: Fluoroquinolone-resistant infections

- Three sites measured resistance of 858 Campys in the study
- 11% FQ-resistant, so could compare those vs susceptible
- 2 separate and significant risk factors identified:
  - Foreign travel: 42% of FQ R vs 9% of FQ S
  - Chicken or turkey at restaurant:
    55% of FQ R vs 21% of healthy controls

- Diarrheal illness caused by FQ R strains was longer than that caused by FQ- S strains

Kassenborg et al. CID 2004:38 (Suppl 3) S279-284
Nelson et al. JID 2004; 190:1150-1157

Ciprofloxacin resistance in *Campylobacter jejuni*, 1990 – 2003*



Gupta et al. EID 2004; 10: 1102-1109

*2003 NARMS data are preliminary

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Regulation of fluoroquinolone resistance in *Campylobacter*

- 1995 Center for Veterinary Medicine/FDA approved use of fluoroquinolones in poultry
- Approved to treat *E. coli* pneumonitis in chickens
- 1999: Increasing FQ resistance in *Campylobacter*
- 2000: CVM proposed withdrawal
  - Abbott – pulled from market
  - Bayer – contested the withdrawal
- 2002-4:
  - Tyson, Perdue, others would no longer use
  - McDonalds, Wendy's, others would no longer buy
- July 28, 2005: FDA Commissioner withdrew approval for FQ
- Sept 12, 2005: Bayer announced they will not contest further

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Campylobacter in infants – FoodNet case-control study

- 24 months 2002-2004 data intake
- 123 cases and 928 controls

- Preliminary results
-
- If < 6 months old
  - Breast feeding protective
  - Riding in shopping cart with fresh meat or poultry

- If > 6 months old
  - Visiting a farm
  - Having pets with diarrhea

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Survey of retail packages of poultry

- **New Zealand: 300 packages purchased at 17 stores**
- **Examined and rinsed the outside of the packaging,**
  - **24% of the external samples yielded *Campy***
    - **Offal packs: 52%**
    - **Whole chicken: 34%**
    - **Parts: 14%**
  - **Only 0.3% yielded *Salmonella***
- **United Kingdom: 895 packages of raw chicken**
  - **3% of external samples yielded Campylobacter**
  - **0.2% yielded Salmonella**
- **(cross contamination begins in the grocery cart)**

Whyte, et al. Poster P126, IAFP 2003, New Orleans

Burgess, J Food Protect 2005; 68:469-475

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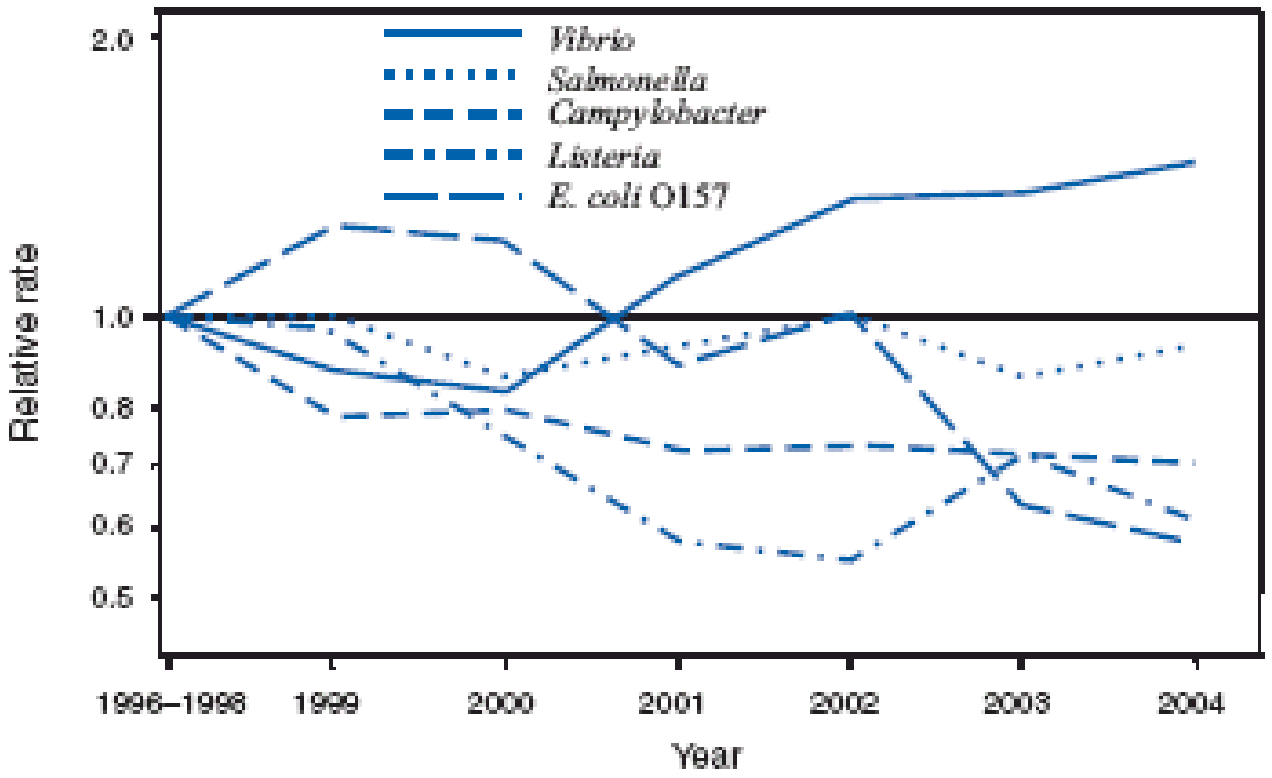
FoodNet trends 1996-2004

FIGURE 1. Relative rates compared with 1996–1998 baseline period of laboratory-diagnosed cases of infection with *Campylobacter*, *Escherichia coli* O157, *Listeria*, *Salmonella*, and *Vibrio*, by year — Foodborne Diseases Active Surveillance Network, United States, 1996–2004



MMWR 2005; 54:352-356 (April 15, 2005)

Since 1996-98, significant decreases in Infections with:

***Salmonella* - 8%**
***Campylobacter* - 31%**
***Listeria* - 40%**
***E. coli O157* - 42%**

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Why are *Campylobacter* infections decreasing in the United States?

- Decreased participation in reporting?
  - Active surveillance corrects for that
- Decreased culturing for *Campylobacter* in laboratories?
  - FoodNet surveys: >99% of labs culture for *Campylobacter*, no change in methods used
- Decreased likelihood that a culture will be ordered?
  - No change observed in FoodNet surveys
- Decreased chance ill patient visits physician?
  - No change observed in FoodNet surveys
- Real decrease in infection rate?
  - Most likely explanation
- What has changed in poultry processing?

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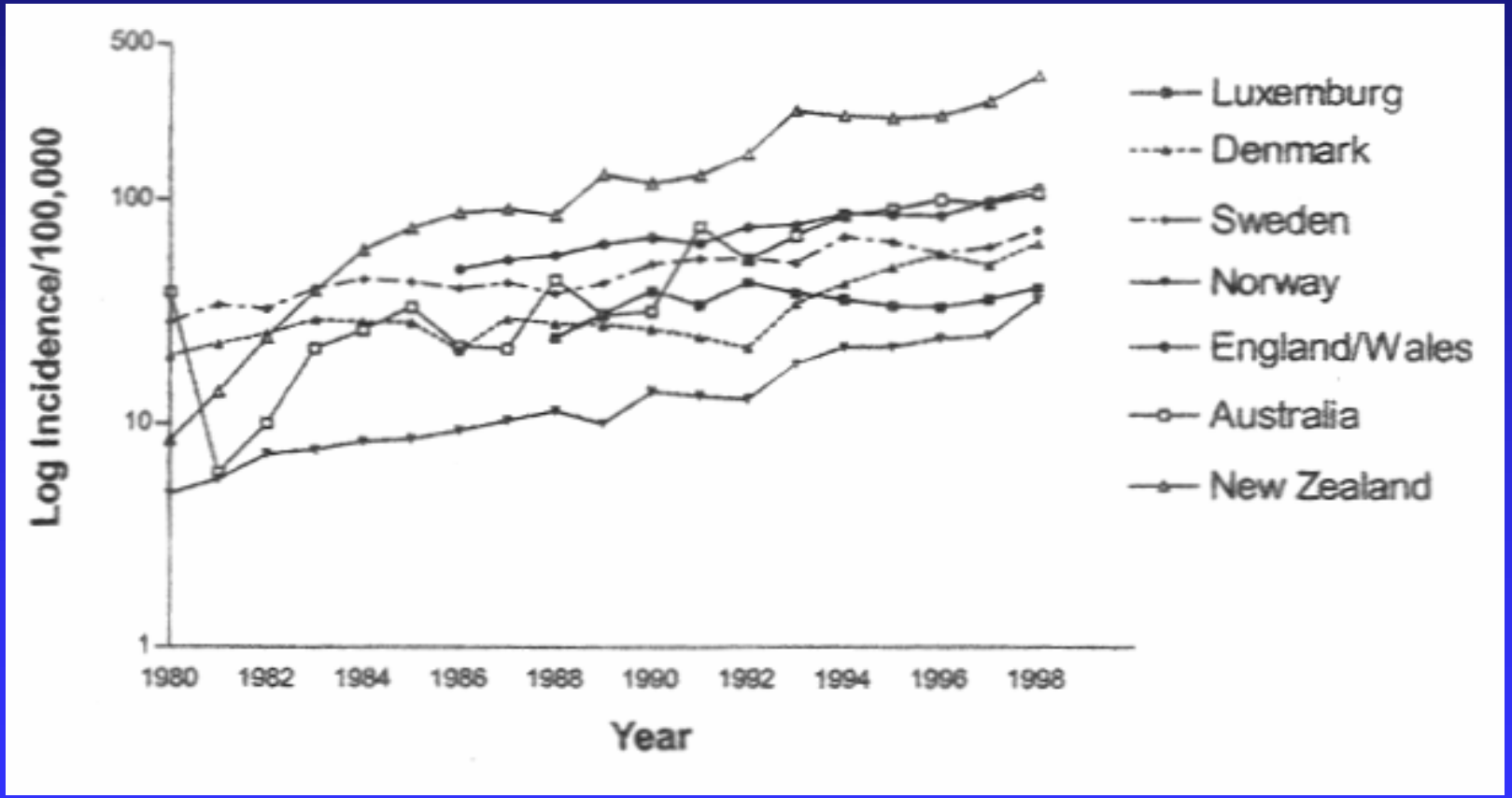
Recent major changes in poultry production and processing in the United States

- Major pathogen reduction efforts linked to switch to Hazard Analysis-Critical Control Point inspection at slaughter
- Progressive implementation:
  - largest plants in 1997
  - smallest in 2000

- Increased water flow in scald tanks and chiller baths
- High pressure chlorinated water sprays after evisceration
- 60% increase in volume of water used in processing
- Hyper-chlorination of water in chill tanks to 50 ppm, using continuous injection manifolds the length of the tanks
- *Salmonella* positivity per carcass decreased from 20% to 9%

Trends in annual incidence of reported *Campylobacter* infections in some developed nations



European Intervention Trials

- 1999: Belgian “intervention”: the dioxin event
- 2000: Icelandic interventions
  - Freezing meat from positive flocks
  - 70% drop in domestic cases
- 2002: Norwegian intervention
  - Similar to Icelandic intervention
- Danish interventions
  - 2001: Freezing negative flocks, marketing as “Campy-free”
  - 2003: Switched, and began freezing positive flocks

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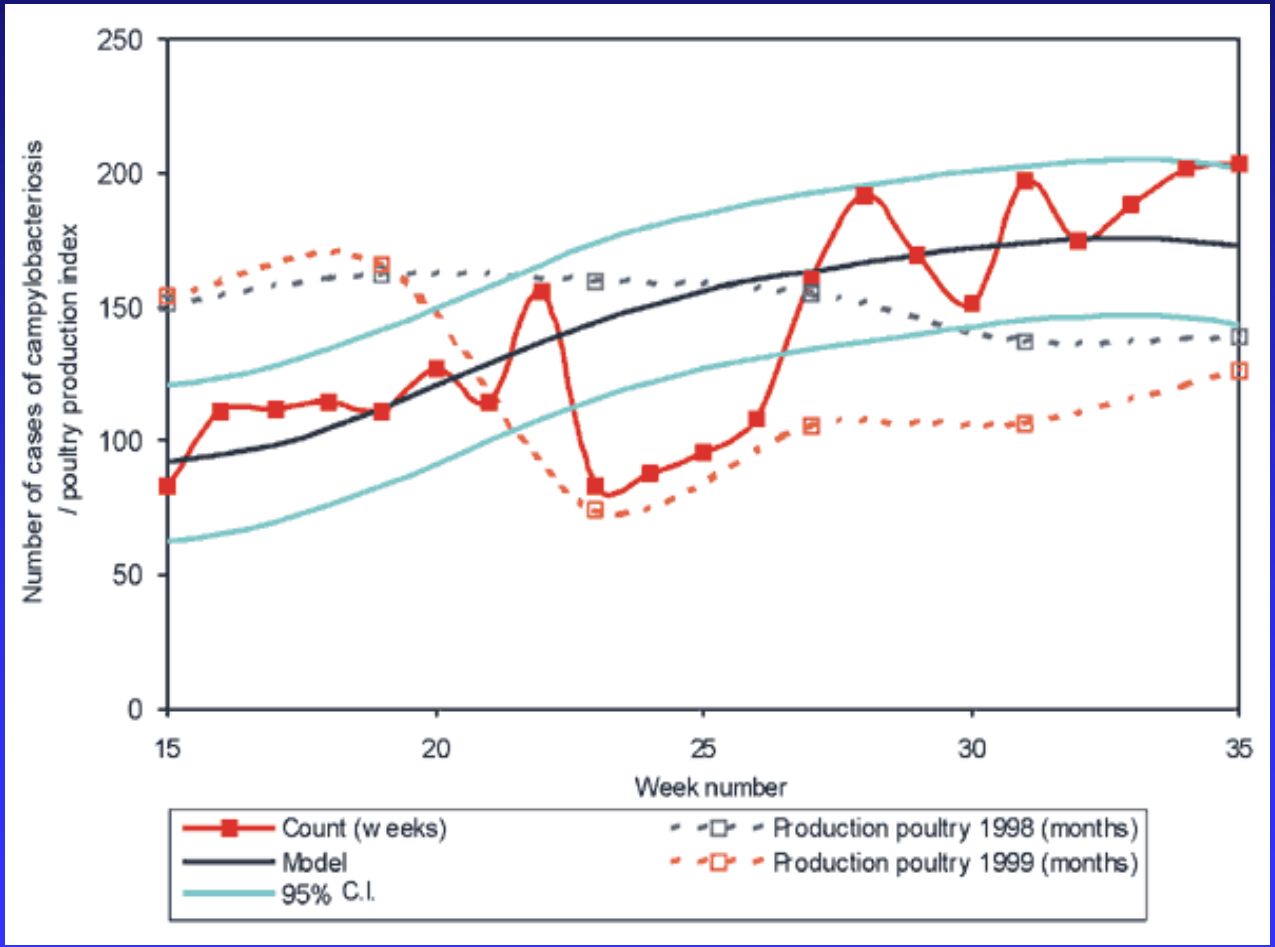
Belgian Dioxin Experience: Actual vs expected reported cases per week, 1999



Campylobacter **cases dropped >30% when local chicken and other meats taken off the market because of dioxin in the chicken feed**

Vellinga et al: Emerging Infectious Diseases Journal 8: 19-22, 2002

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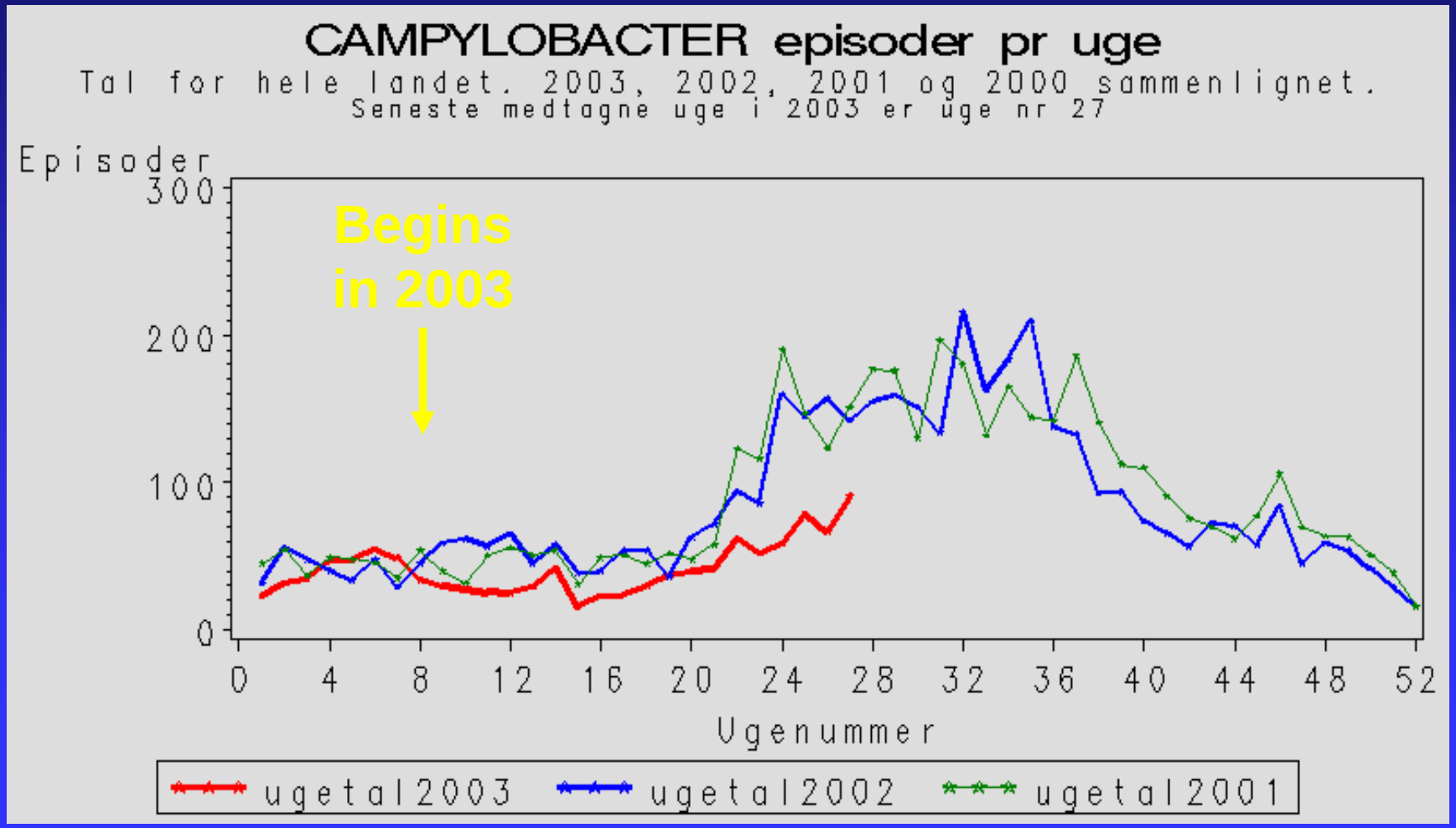
Danish intervention trial
Reported cases per week, 2001-2003



http://www.ssi.dk/graphics/html/Udbrudmonitor/OPDATER1/ugegraf-camp.htm

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An epidemiological puzzle
Transmission that does not occur

- Experimental infectious dose for humans is low
- Very little transmission from person-to-person
  - Secondary transmission rates in families are very low.
  - Little evidence of person-to-person transmission in child-care centers
  - Little evidence of transmission among men who have sex with men
  - No outbreaks in psychiatric institutions

- Conclude *Campylobacter* in human feces is largely non-infectious

Recurrent *Campylobacter jejuni* Infections at a Correctional Facility—Washington, March-December, 2002

Michael Lynch, MD, MPH
Foodborne and Diarrheal Diseases Branch
Centers for Disease Control and Prevention

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March-December, 2002

- WA Department of Health identified multiple outbreaks of *C. jejuni* infections
- Inmates and staff at state correctional facility
- Indistiguishable PFGE pattern

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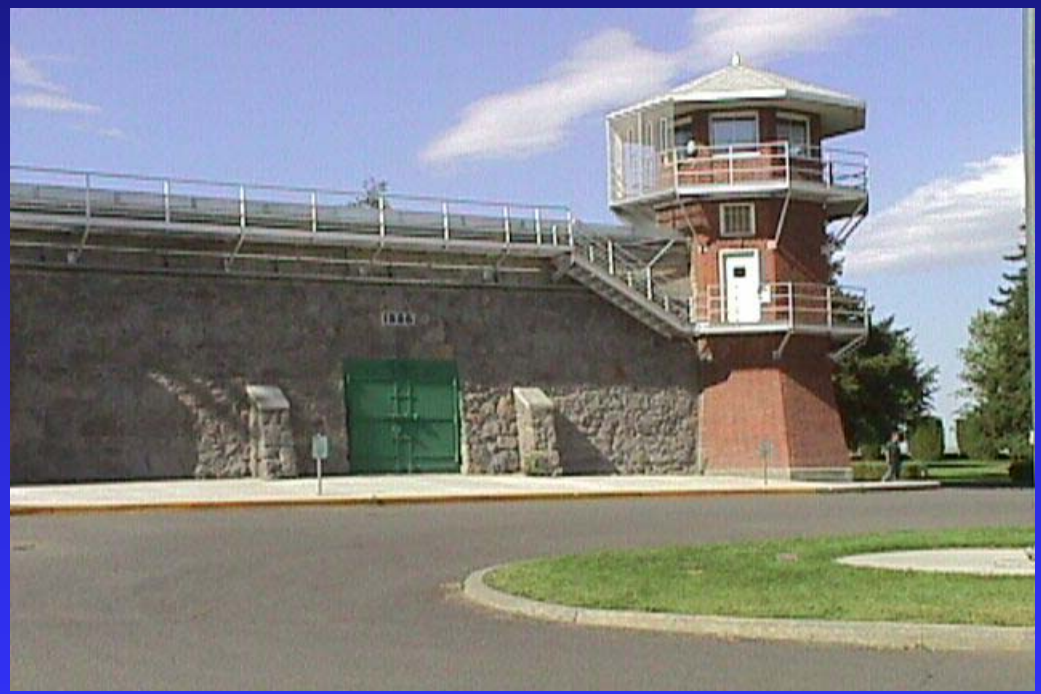
Correctional Facility A

- Oldest facility in WA prison system
- Cases confined to one area
- All patients ate food from same kitchen



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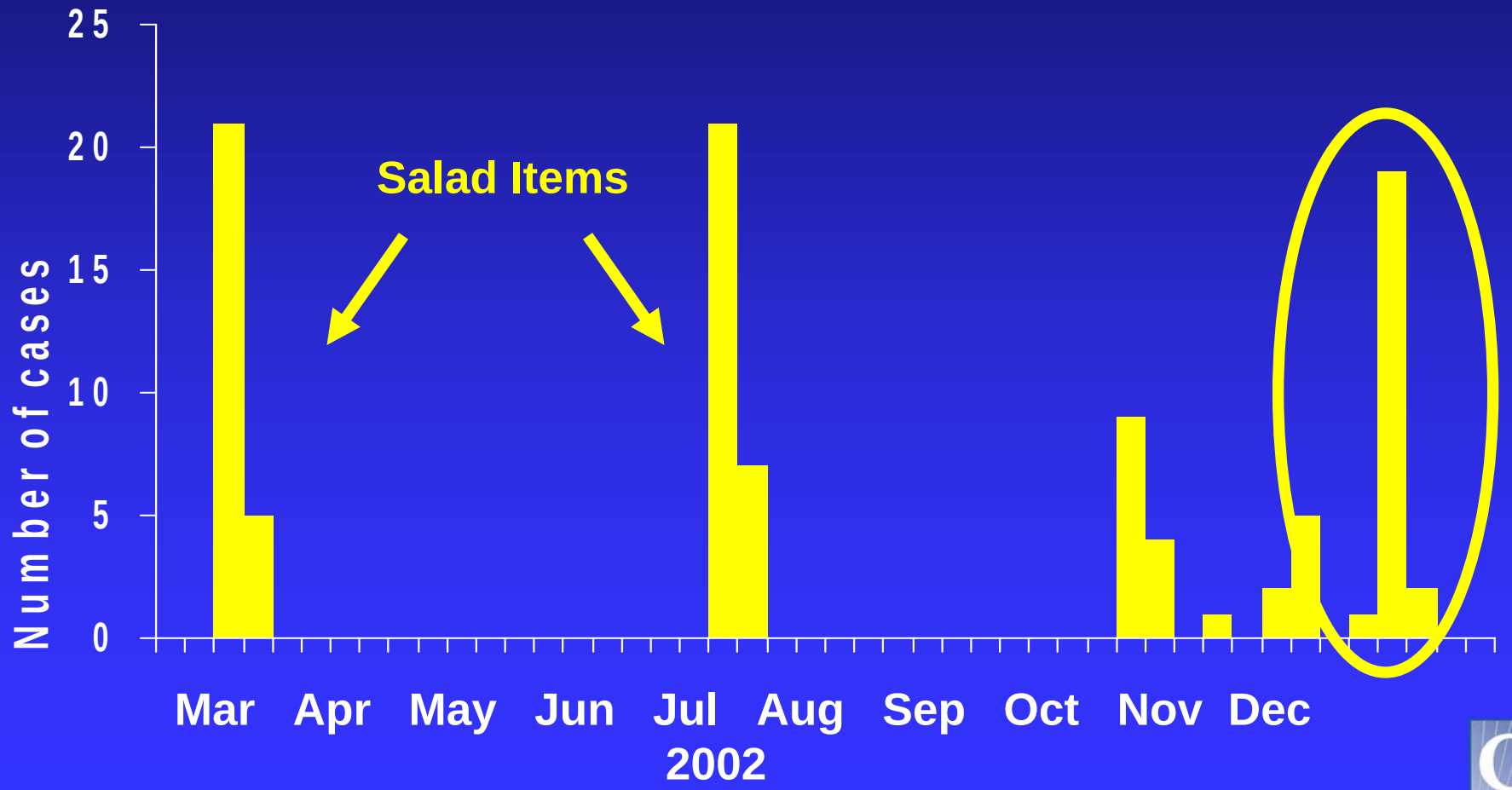
Culture-Confirmed Cases of *C. Jejuni* by Week of Onset, Correctional Facility A March-December, 2002 (n=97)



Case-Control Study

- **Case definition (n = 18)**
  - Culture confirmed *C. jejuni*
  - Inmate
  - Onset December 19-24, 2002
- **Controls (n = 39)**
  - Well inmates
  - Frequency-matched by housing unit
- **Questioned regarding food and water**

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Univariate Results

Exposure	Cases n=18	Controls n=39	OR_{MH}*	95% CI
Tuna Salad	88%	54%	6.4	1.4-29.0
Pasta Salad	72%	41%	4.5	1.2-16.2
Vegetable Soup	72%	35%	3.6	1.1-11.7
Mixed Vegetables	67%	39%	4.9	1.3-19.2
Salad Dressing	61%	30%	4.4	1.2-15.6

*controlled for housing unit

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Multivariate Results

Exposure	OR*	95% CI
Tuna Salad	9.8	1.5-62.1
Pasta Salad	5.0	1.1-23.4

*also controlled for housing unit

Cold salad items implicated in earlier outbreaks

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Environmental Investigation

- No ingredient from common source
-
- Salad items prepared in same room
- Equipment and surface samples negative

Salad Preparation Room

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Confirming Connection from Equipment Room to Kitchen

Roof Equipment Room Drain Flow

Pigeon droppings

Cooling Towers

Pigeon droppings

Drain

Open Pipe

Food Cart

Conclusions

- Molecular subtyping of *Campylobacter* isolates linked several outbreaks at one facility
- Salad items source of illness
- Probably contaminated from pipe
- Open pipe was capped

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Campylobacter: Some eternal mysteries

- 1) What is the pathogenesis of the infection?
- 2) Why are there large geographic differences in incidence?
- 3) Why are most strains non-clonal? Why are some clonal?
- 4) Mechanism of seasonality?
- 5) Why are virtually all vehicles fluid and cold?
- 6) Why is secondary transmission rare, given low dose?
- 7) Where are all the non-jejuni infections?

Summary

- *Campylobacter* sporadic infections are typically associated with poultry.
- Important cause of traveler's diarrhea
- Control measures targeted at poultry are probably having a real effect in decreasing the burden of disease
- Fluoroquinolone use a textbook example of why clinical medicine is affected by agriculture practice
- Other routes of transmission indicate that multi-pronged prevention is needed

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A Massive International Outbreak of Gastroenteritis with Multiple Etiologies Among Resort Island Visitors and Residents – Ohio, 2004

Ciara O'Reilly, PhD
Foodborne and Diarrheal Disease Branch
Centers for Disease Control and Prevention

Background

- **August 16, 2004: Ohio Department of Health reported to CDC 70 cases of gastroenteritis**
  - **All patients had traveled to South Bass Island, Ohio**
- **August 19, CDC Epi-Aid Team arrived in Ohio**

South Bass Island, Lake Erie, Ohio

Case Finding Results (N=1450)

Demographics

- **98% visitors**
  - **26 states and 2 foreign countries**
- **61% female**
- **Median age 40 (7 months – 83 years)**

Clinical Information (N=1450)

Symptom	% of Cases
Diarrhea	83%
Cramps	80%
Nausea	77%
Vomiting	50%
Fever	45%
Bloody diarrhea	5%
Median duration of illness	4 days (1- 52)

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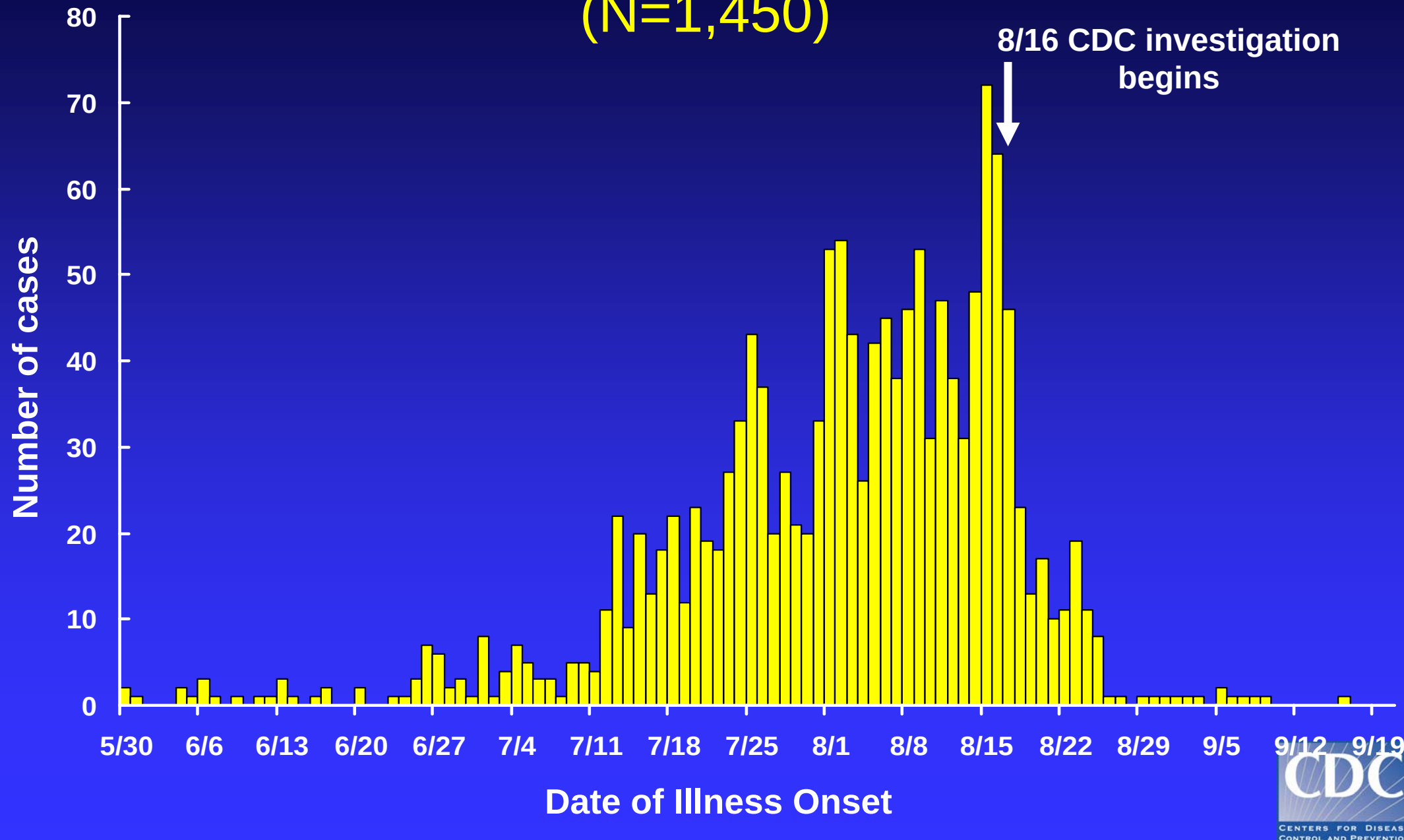
Case Finding Laboratory Results (N=1450)

- **155 (11%) persons reported submitting stool specimens**

- **29 laboratory confirmed cases**
  - **16 *Campylobacter jejuni***
  - **9 Norovirus**
  - **3 *Giardia***
  - **1 *Salmonella* Typhimurium**

Cases of Gastroenteritis by Date of Onset and Etiology, South Bass Island, Ohio, May – September, 2004 (N=1,450)



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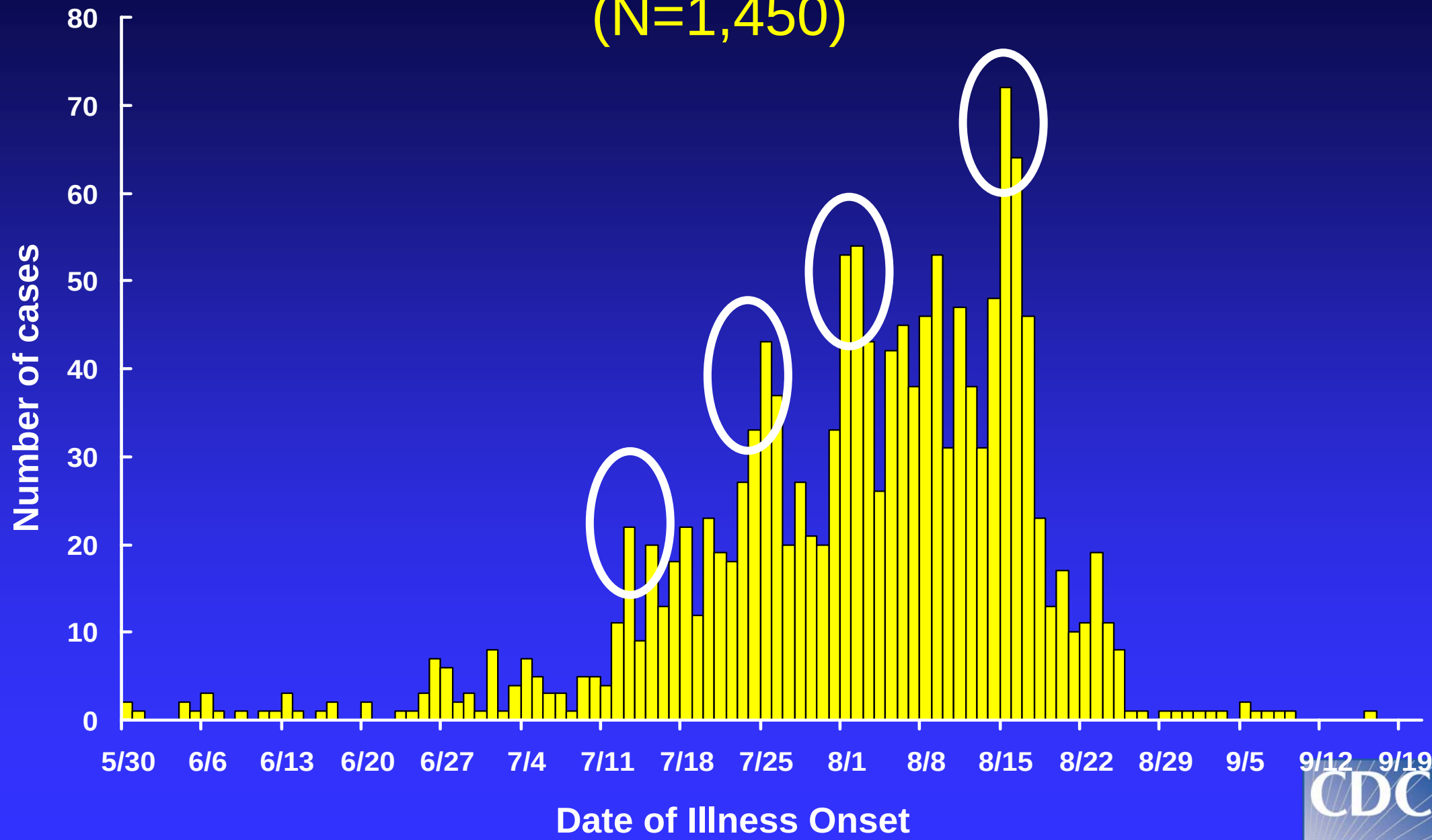

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Case-Control Study, August 30 - September 7

- **Hypothesis: contaminated water**
- **Case Definition**
  - **Case: diarrhea in a visitor with a history of travel to South Bass Island for a single visit during May – Sept 2004**
  - **Control: well traveling companions of cases**
- **Questionnaire focused on water**

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Case-Control Study Bivariate Analysis Water Exposure on the Island

Type of Drink	Cases (%) n=100	Controls (%) n=117	Matched Odds Ratio	95%CI
Bottled water	37 (37)	43 (37)	1.0	0.5-2.3
Tap water	68 (68)	41 (35)	4.3	2.2-9.3
Filled water bottle	19 (19)	7 (6)	6.0	1.6-30.0
Drink with ice	72 (73)	62 (53)	7.1	2.2-25.5

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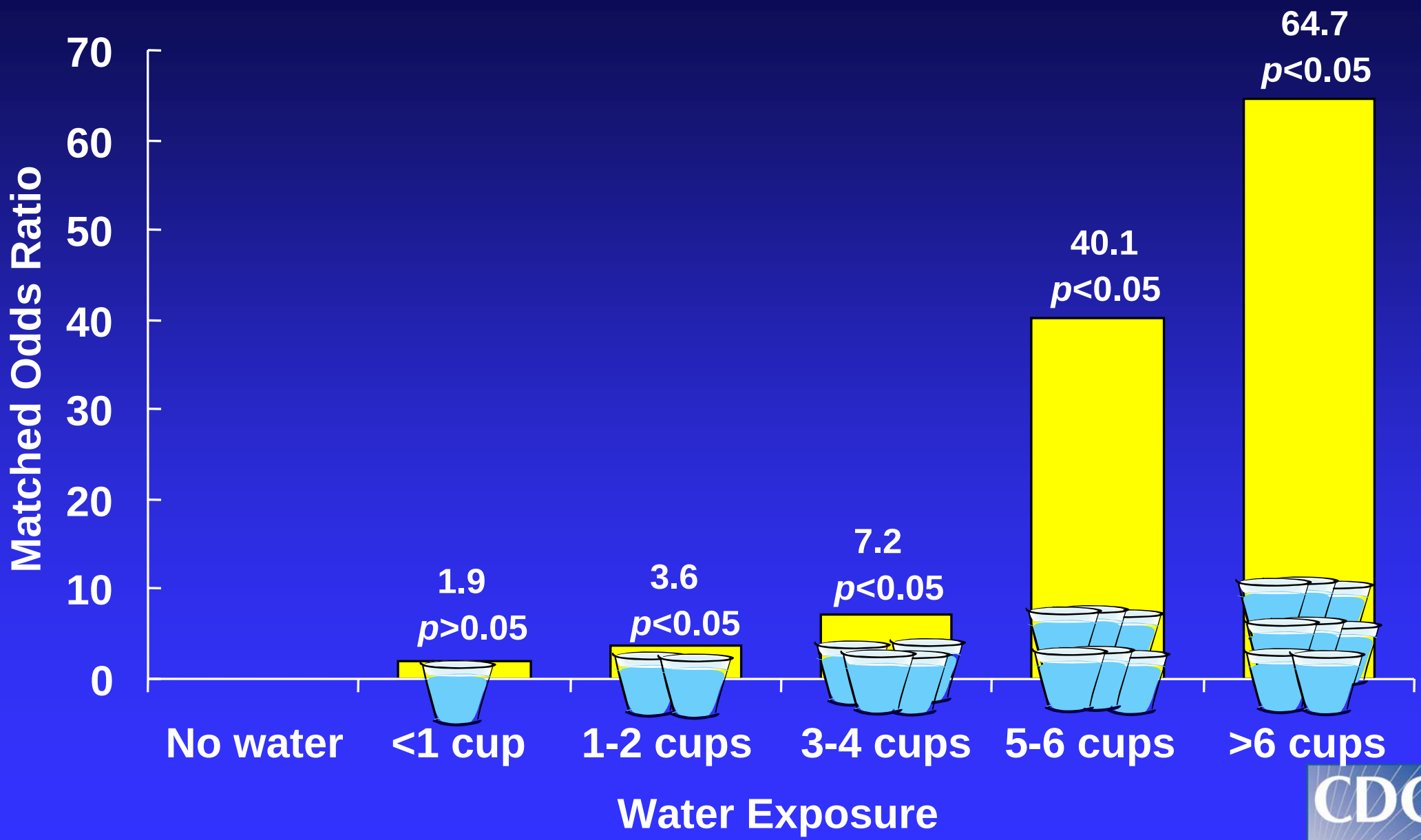
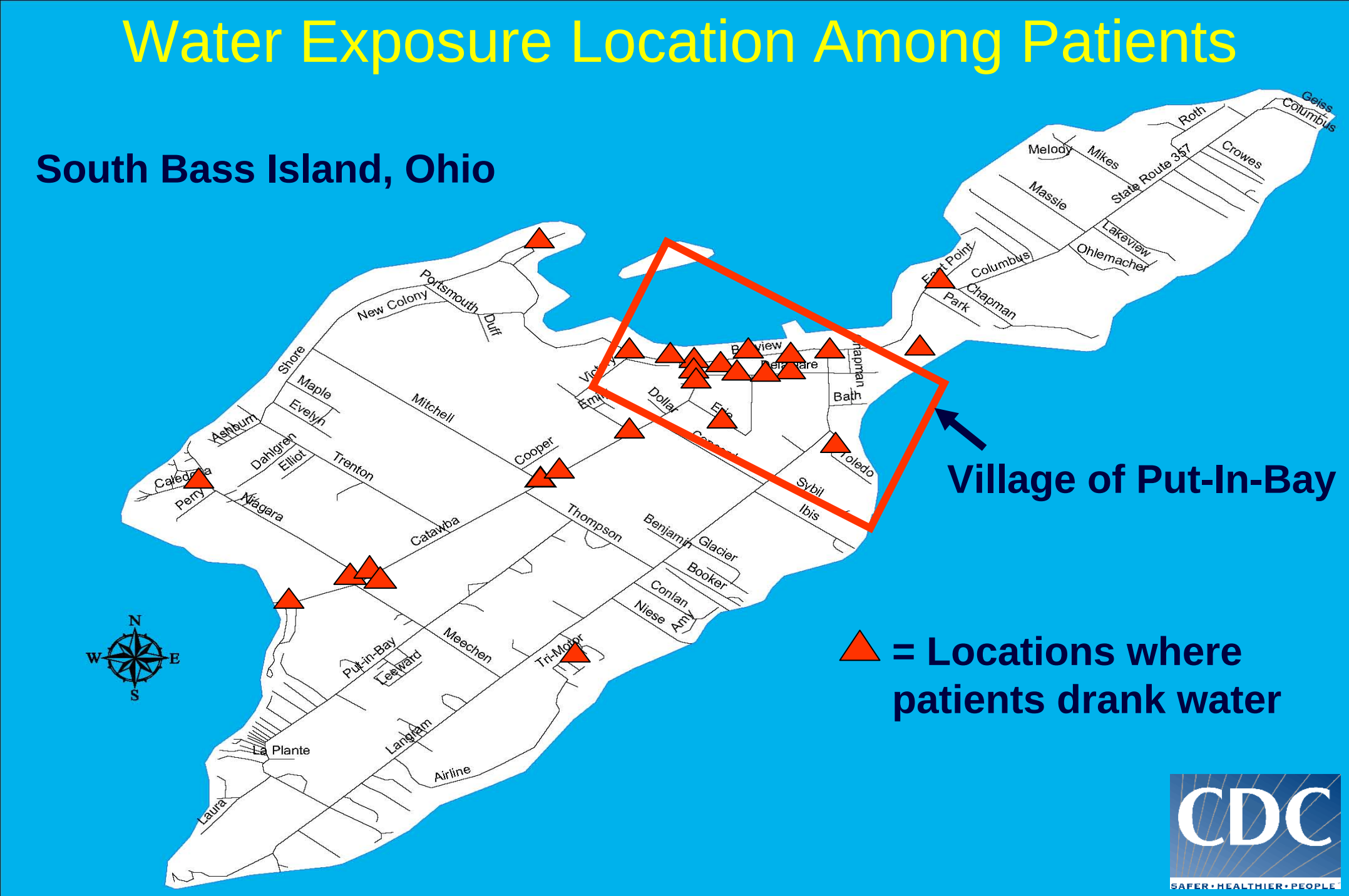
Case-Control Study Dose-Response Effect



Water Sources on the Island

- **Chlorinated municipal supply**
- **Public and private ground water wells**
- **Auxiliary ground water wells**

Water Exposure Location Among Patients

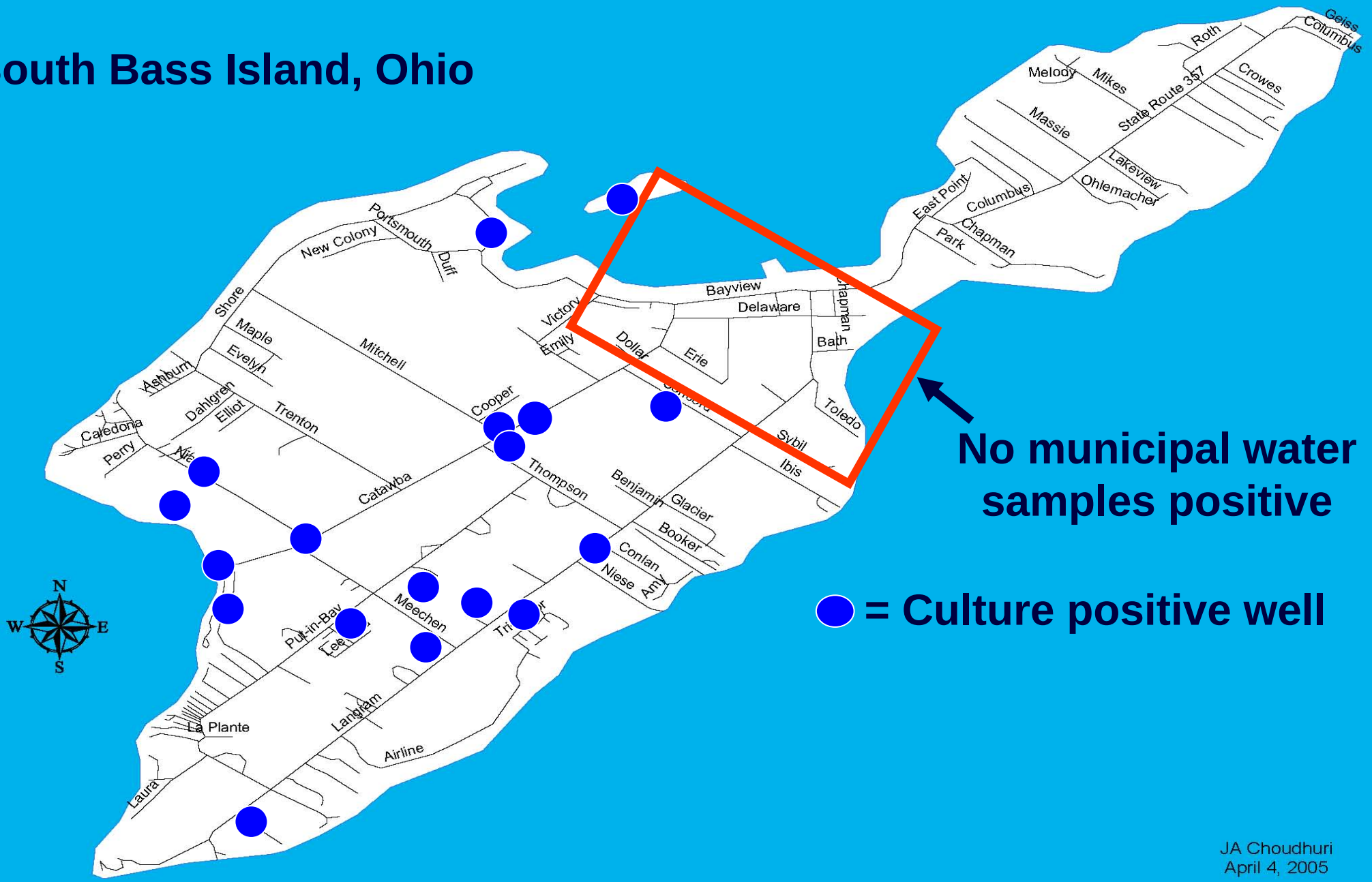


Environmental Investigation

- **Multiple agencies**
  - **Local health department**
  - **4 state agencies**
  - **CDC: NCEH, DPD, FDDB**
- **Water sampling**
  - **300 water samples**
  - **90 locations**
- **Large volume water samples**

Water Sampling Results

South Bass Island, Ohio



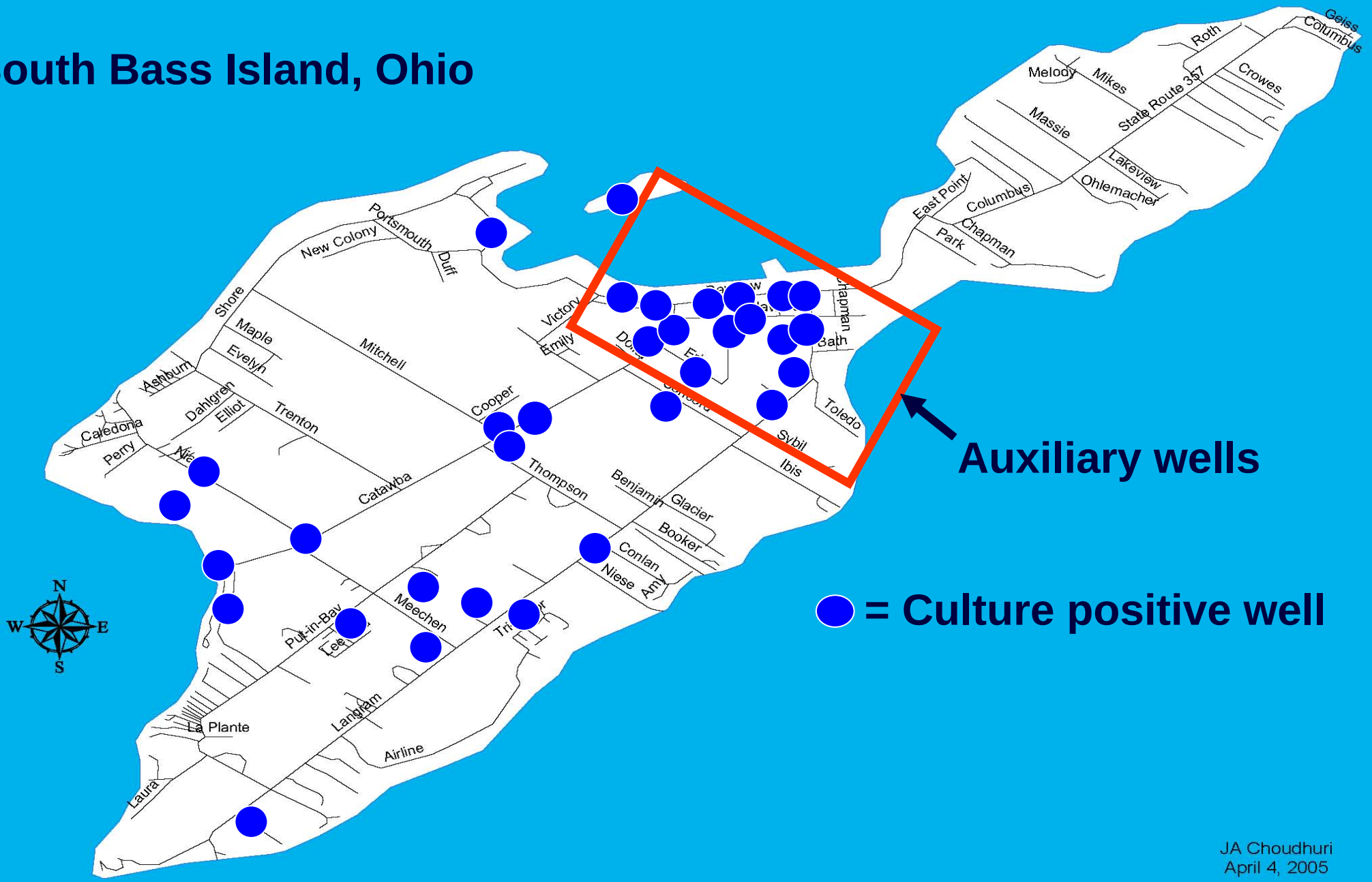
No municipal water samples positive

● = Culture positive well

JA Choudhuri
April 4, 2005

Water Sampling Results

South Bass Island, Ohio



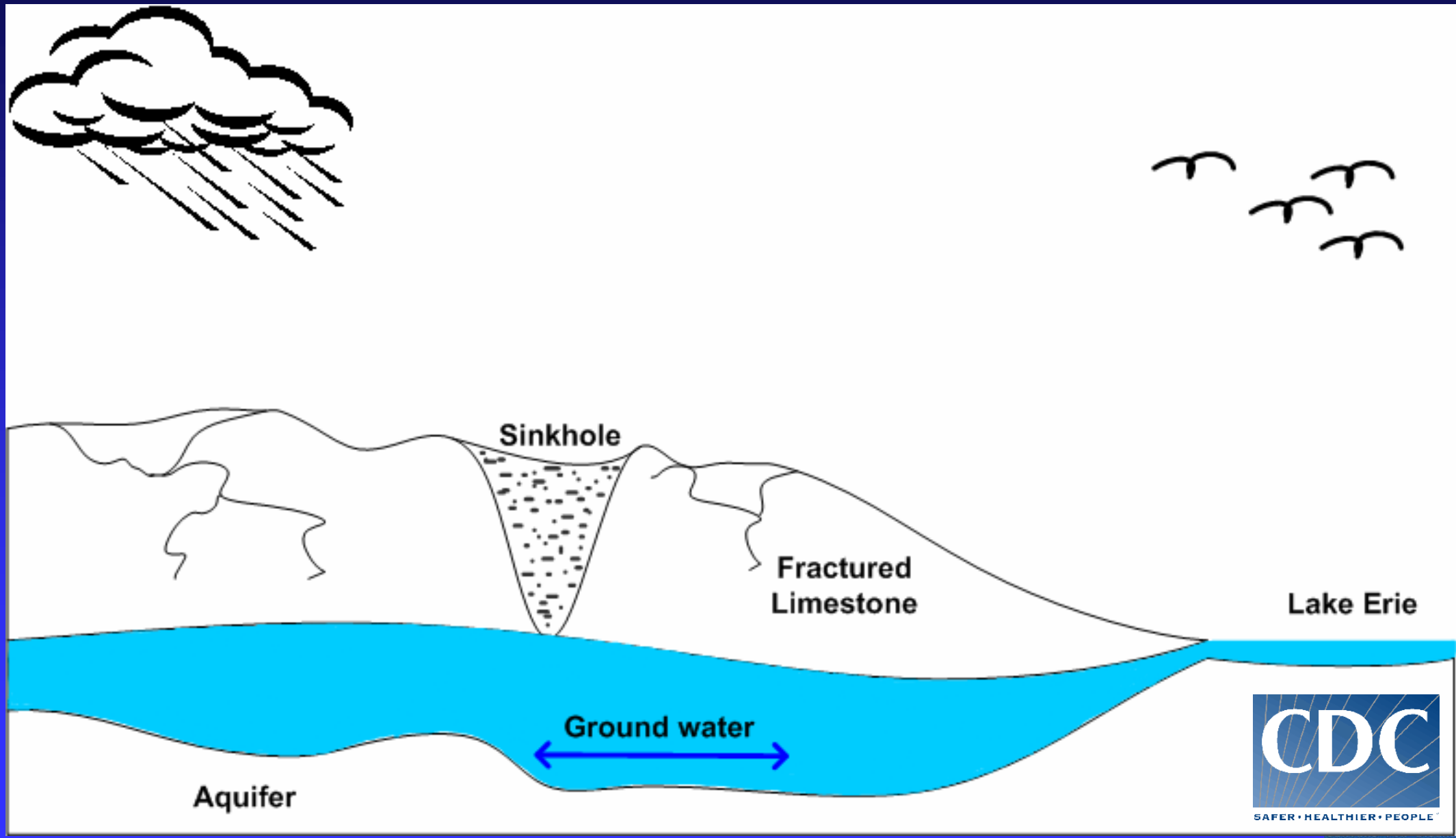
JA Choudhuri
April 4, 2005

Environmental Laboratory Results

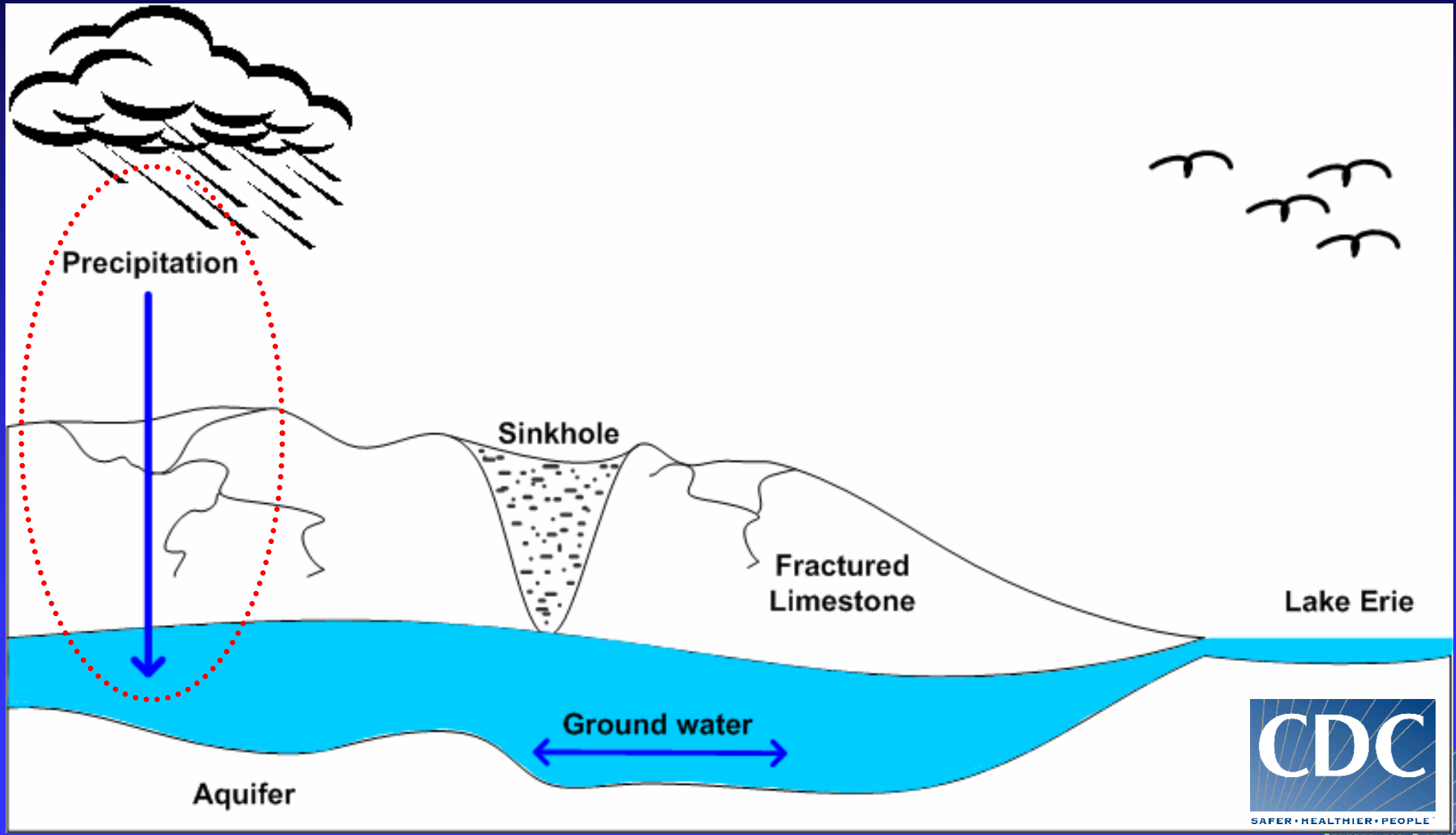
- **Culture methods**
  - **Many wells positive for Total Coliforms and *E. coli***
  - ***C. jejuni* was cultured from one well water sample**

- **Molecular methods: Large volume water sampling indicated contamination with multiple fecal microbes**
  - ***E. coli***
  - ***C. jejuni***
  - ***Salmonella* spp**
  - ***Giardia* spp**

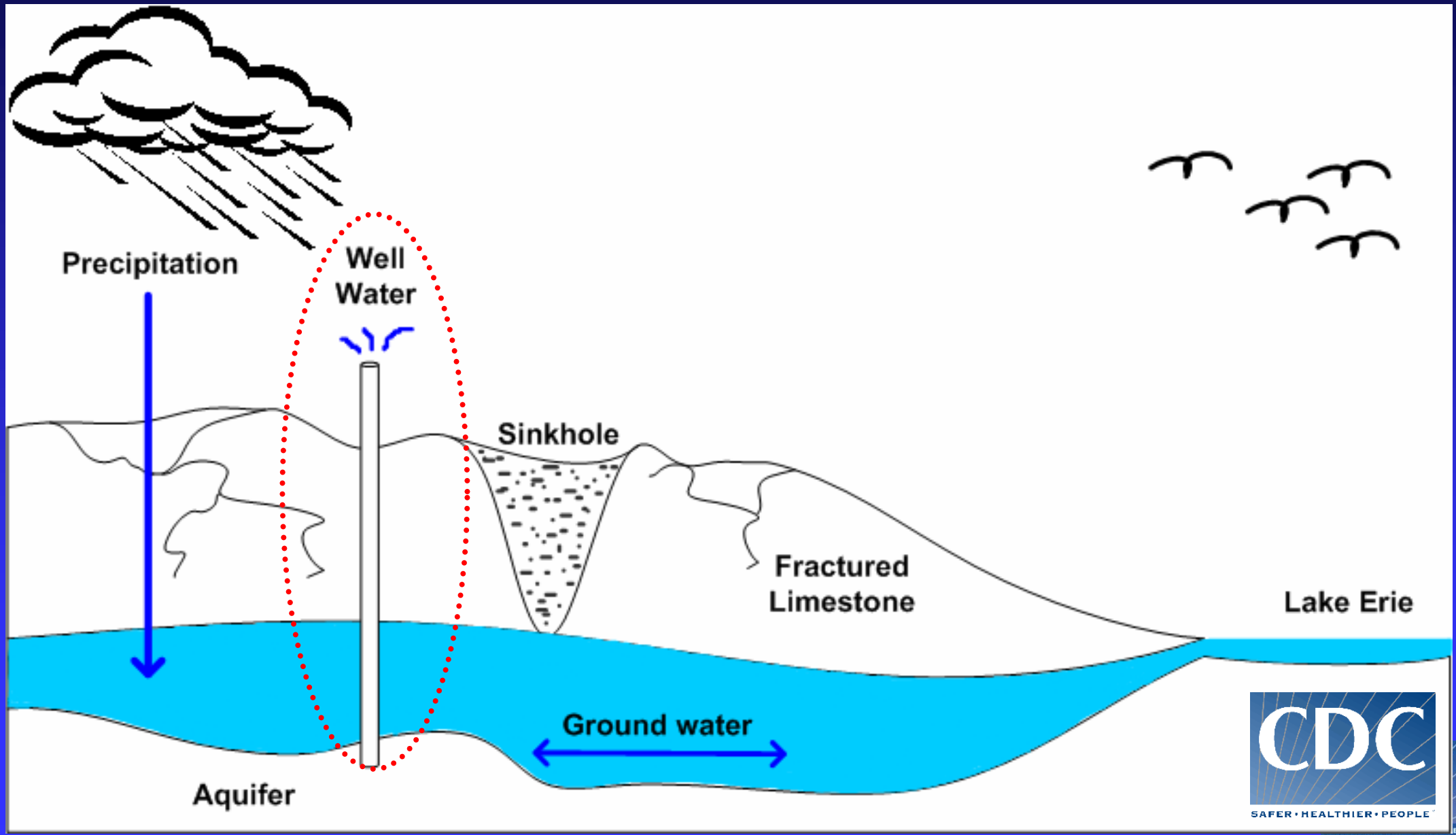
Karst Hydro-Geology on South Bass Island



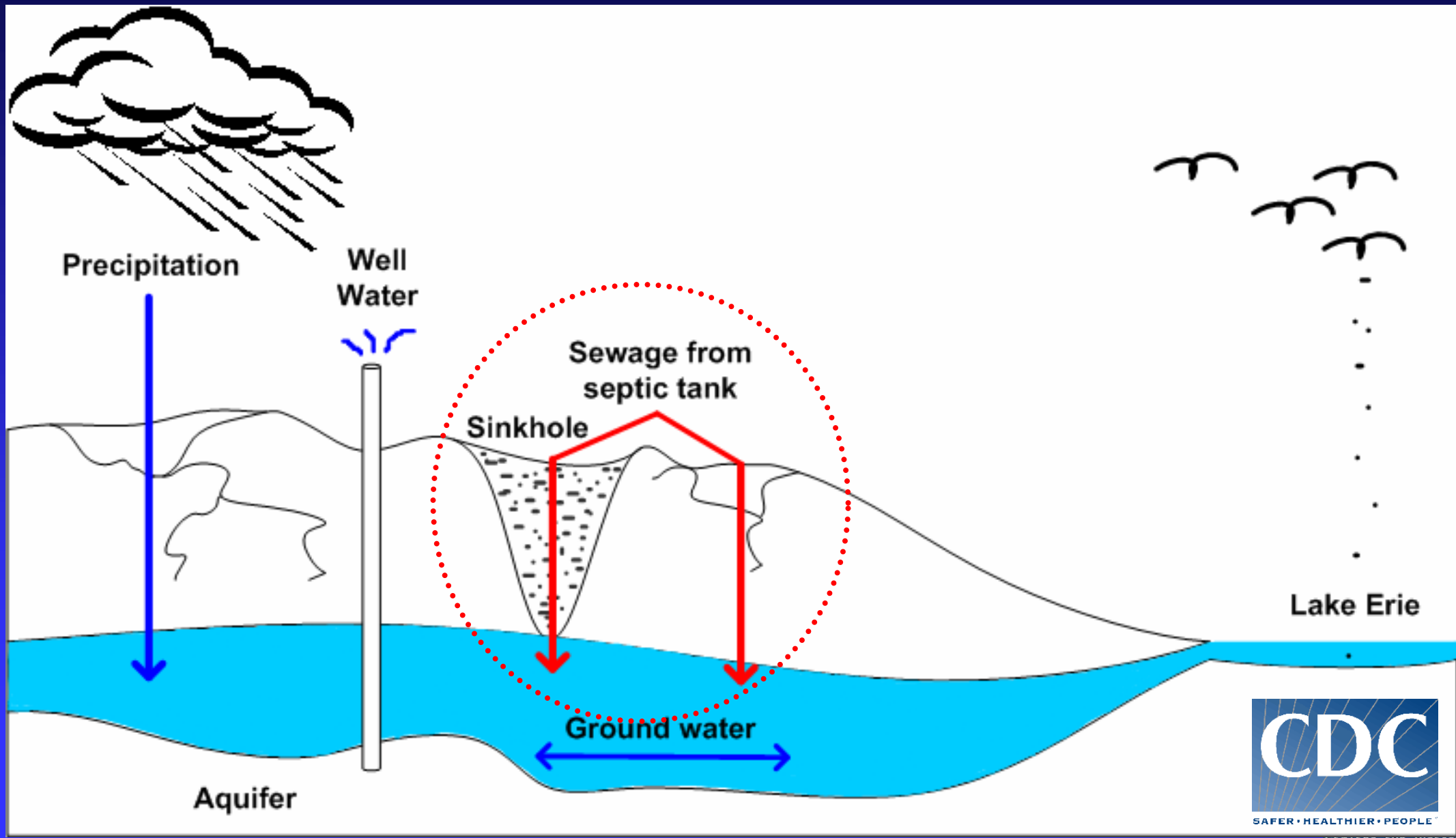
Karst Hydro-Geology on South Bass Island



Karst Hydro-Geology on South Bass Island



Karst Hydro-Geology on South Bass Island



CDC
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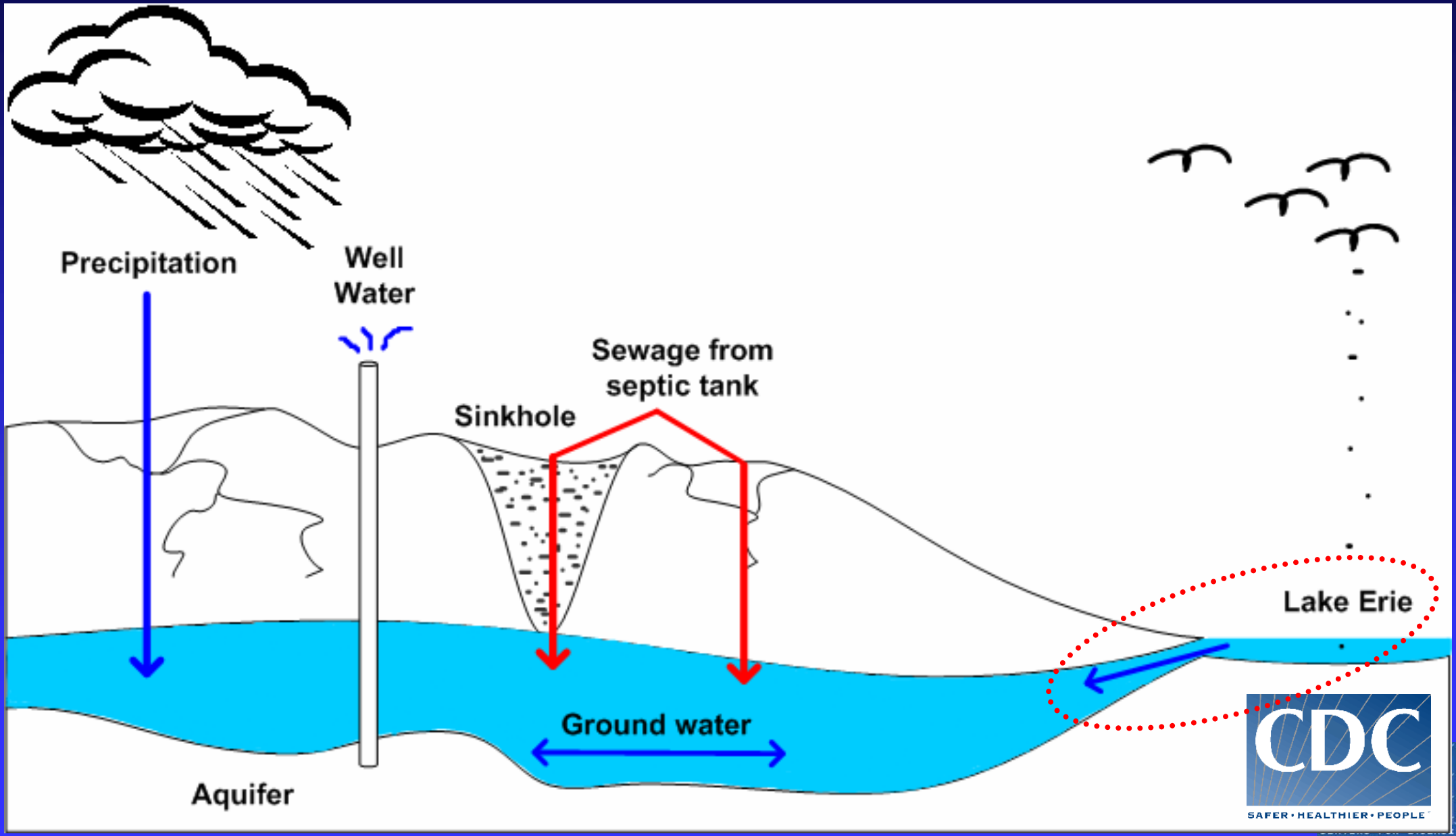
Karst Hydro-Geology on South Bass Island



Conclusions

- **Strong statistically significant association between drinking tap water on the island and illness**
- **Sewage-contamination of the aquifer supplying ground water wells was the likely source of this large outbreak**
- **Underlying geology on the island was a contributing factor**

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION