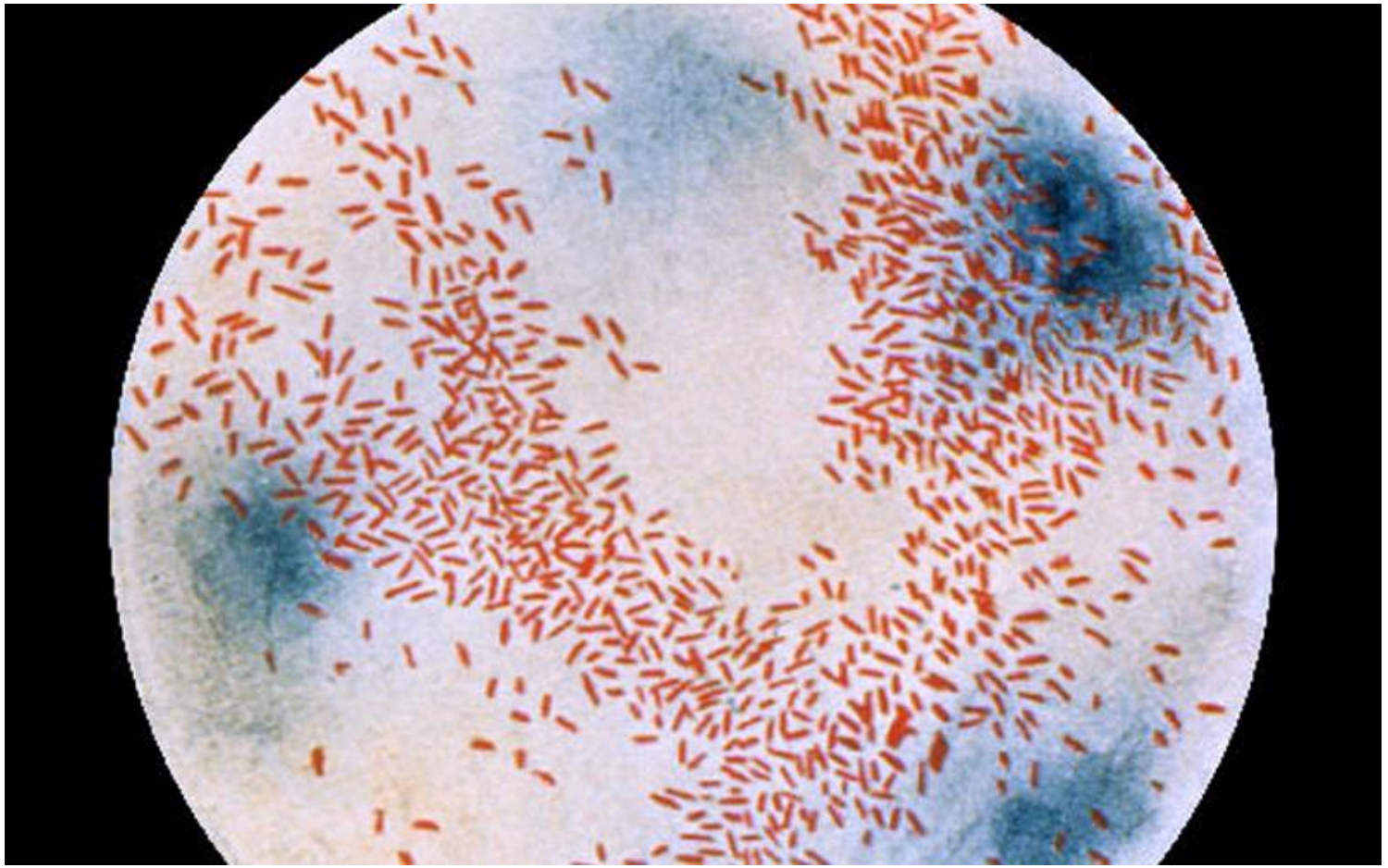
Times they are changing': Shifts in the epidemiology of *Haemophilus influenzae*



Colorado Children's' Immunization Coalition Provider Education
December 14, 2017

COLORADO

Emily Spence Davizon,
Colorado Department of Public Health and Environment

Today's talk:

Background- what we do as epidemiologists at CDPHE

Epidemiology of *Haemophilus influenzae* in the US and CO

Results of a "time to serotype" analysis

Learning objectives:

Be familiar with the role of the state public health department

Describe changes in epidemiology of H flu pre vs. post vaccine era

Know where serotyping is performed

Vaccine-preventable disease unit

Part of the Communicable Disease Branch at CDPHE

We do:

Surveillance- counting sick people, mostly

Technical assistance- helping generalist epidemiologists, health care providers, members of the public

Surge capacity and coordination

"This is a second opinion. At first, I thought you had something else."

Nomenclature and numbers

Haemophilus influenzae is a cause of **bacterial infections** that are often severe, particularly among infants

First described in 1892 during an outbreak of influenza

Given the name *Haemophilus* by Winslow, et al. in 1920

Not until 1933 that was established that influenza was caused by a virus and that *H. influenzae* was a cause of secondary infection

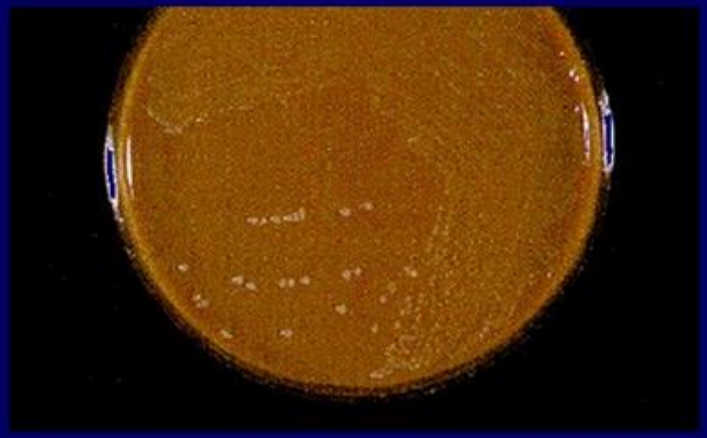
Nomenclature and numbers

H flu may be encapsulated (typeable) or unencapsulated (nontypeable)

-6 capsular antigens (a-f)
-unencapsulated lacks expression of capsular antigens

H. influenzae (Hi) Serotypes

- Encapsulated
  - Type b (Hib)
  - Type non - b (a, c, d, e, f)
- Unencapsulated
  - Nontypeable (NT)



CDC
Centers for Disease Control and Prevention

Nomenclature and numbers

Not all H flu is Hib!

- 91 cases of invasive H flu in 2015, only 2 were Hib
- No cases of Hib in 2016 or 2017 YTD

Type b, Hib, the most well-known and feared type of H flu

Only Hib may require disease control intervention

Nomenclature and numbers

Invasive disease

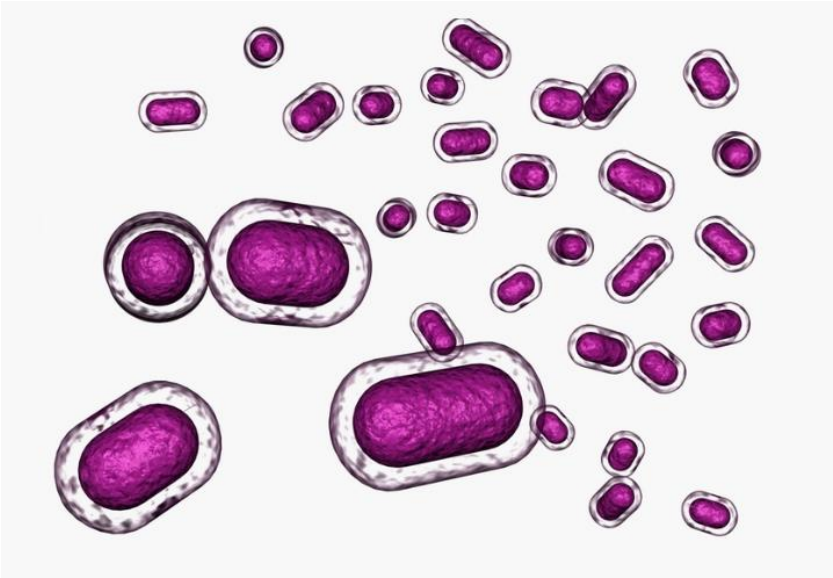
Determined by a + culture or PCR from a normally sterile site -blood, spinal fluid, etc.

Non-invasive disease

Localized infection in a non-sterile site that is “open” to the environment- skin, lung, etc.

Invasive Hi is reportable in Colorado

Epidemiology



Gram-negative coccobaccilus

Reservoir: upper respiratory tract

Transmission: person-to-person, respiratory droplets or contact with discharges from the nose/throat of infected person;

in neonates- aspiration of amniotic fluid or contact with genital tract secretions containing the organism

H flu disease

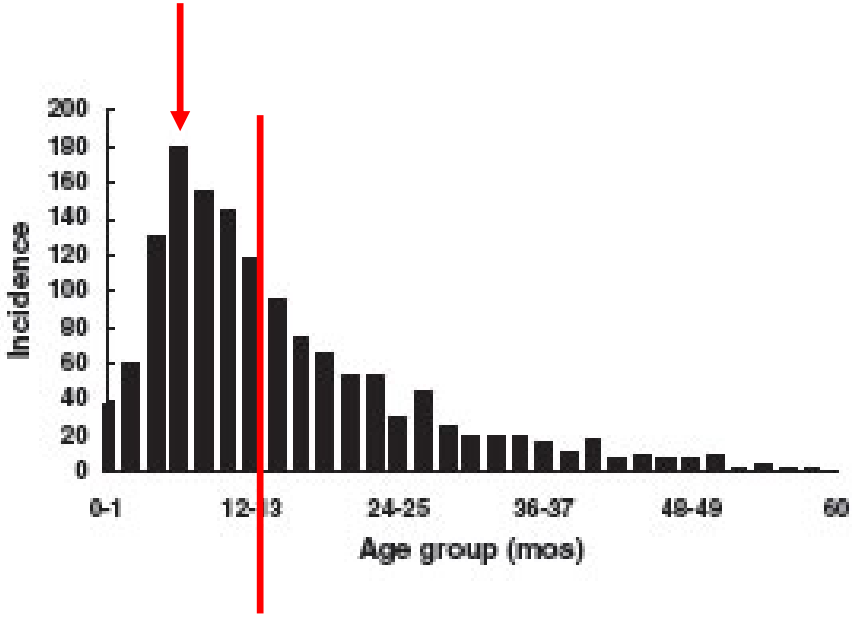
In the pre-vaccine era:

- Type b responsible for 95% of invasive disease
- Nontypeable strains are a common cause of ear infections in children and bronchitis in adults

Post-vaccine era:

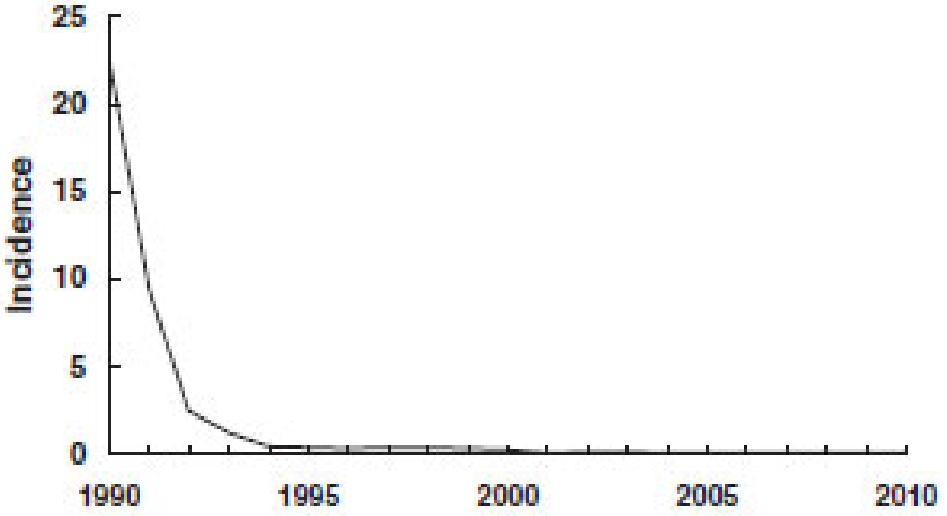
- Nontypeable strains a common cause of invasive Hi disease; generally thought to be less virulent

Haemophilus influenzae type b 1986 Incidence* by Age Group



*Rate per 100,000 population, prevaccine era

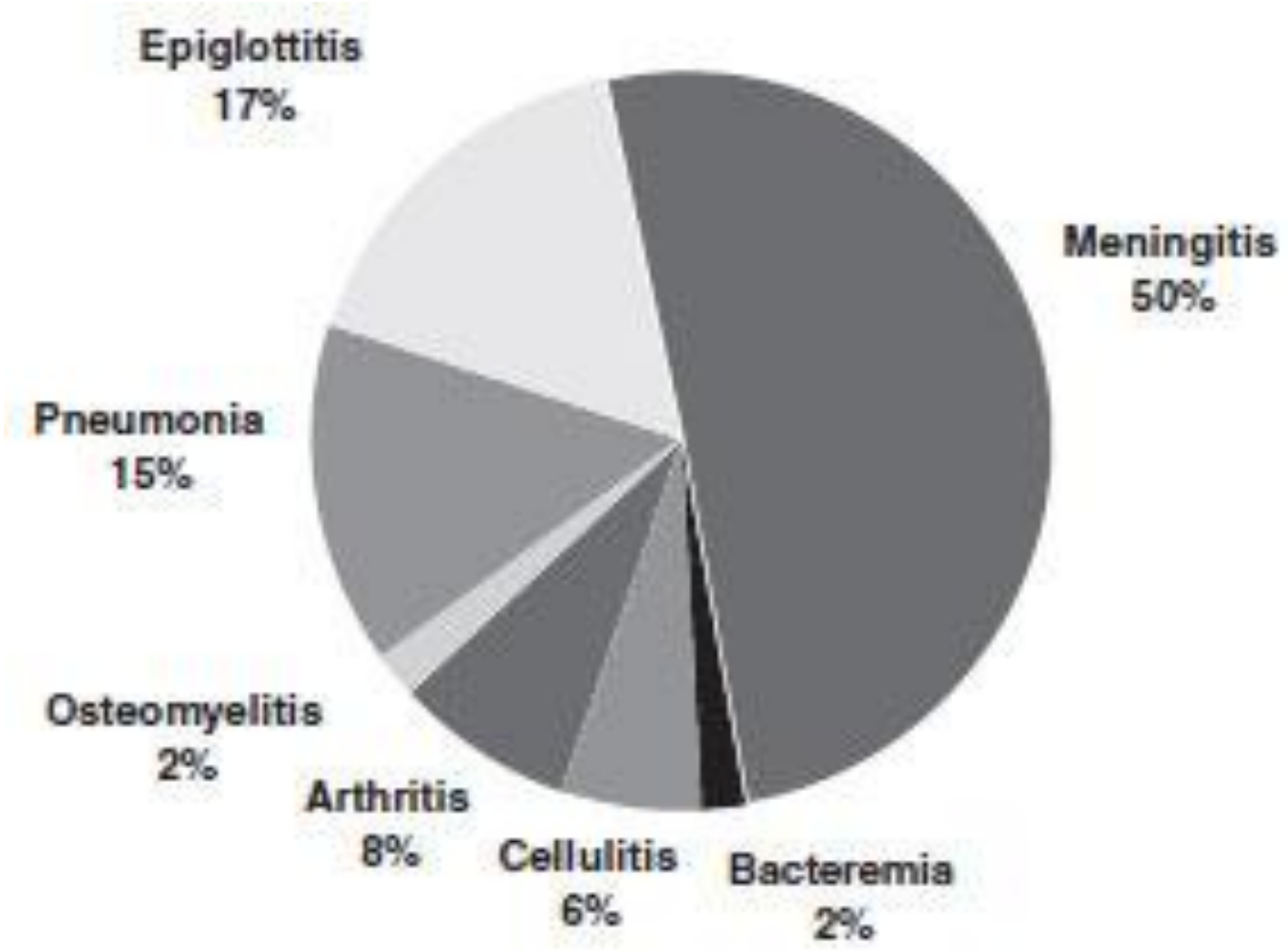
Incidence* of Invasive Hib Disease, 1990-2010



*rate per 100,000 children <5 years of age

Source: CDC, Epidemiology and Prevention of Vaccine-Preventable Diseases, "The Pink Book," 12th Edition, 2011

Haemophilus influenzae type b clinical features, pre-vaccine



Source: CDC Pinkbook

Hib Vaccines

Polysaccharide

- Available 1985-1988
- Age-dependent immune response; not effective <18 months of age
- No booster response

Polysaccharide conjugate

- Stimulates T-dependent immunity
- Enhanced Ab production, esp. in young children
- Booster response with repeat doses

Hib vaccines

Hib Conjugate Vaccines

PRP-T: ActHIB, Pentacel, Hiberix (booster dose only) MenHibrix

PRP-OMP: PedvaxHIB, COMVAX

Currently no vaccines for non-b H flu

Hib vaccines

Immunogenicity and efficacy

- 95%+ infants develop protective Ab levels after primary series
- Clinical efficacy estimates at 95-100%
- Effective in those at increased risk for invasive disease*

Surveillance data sources

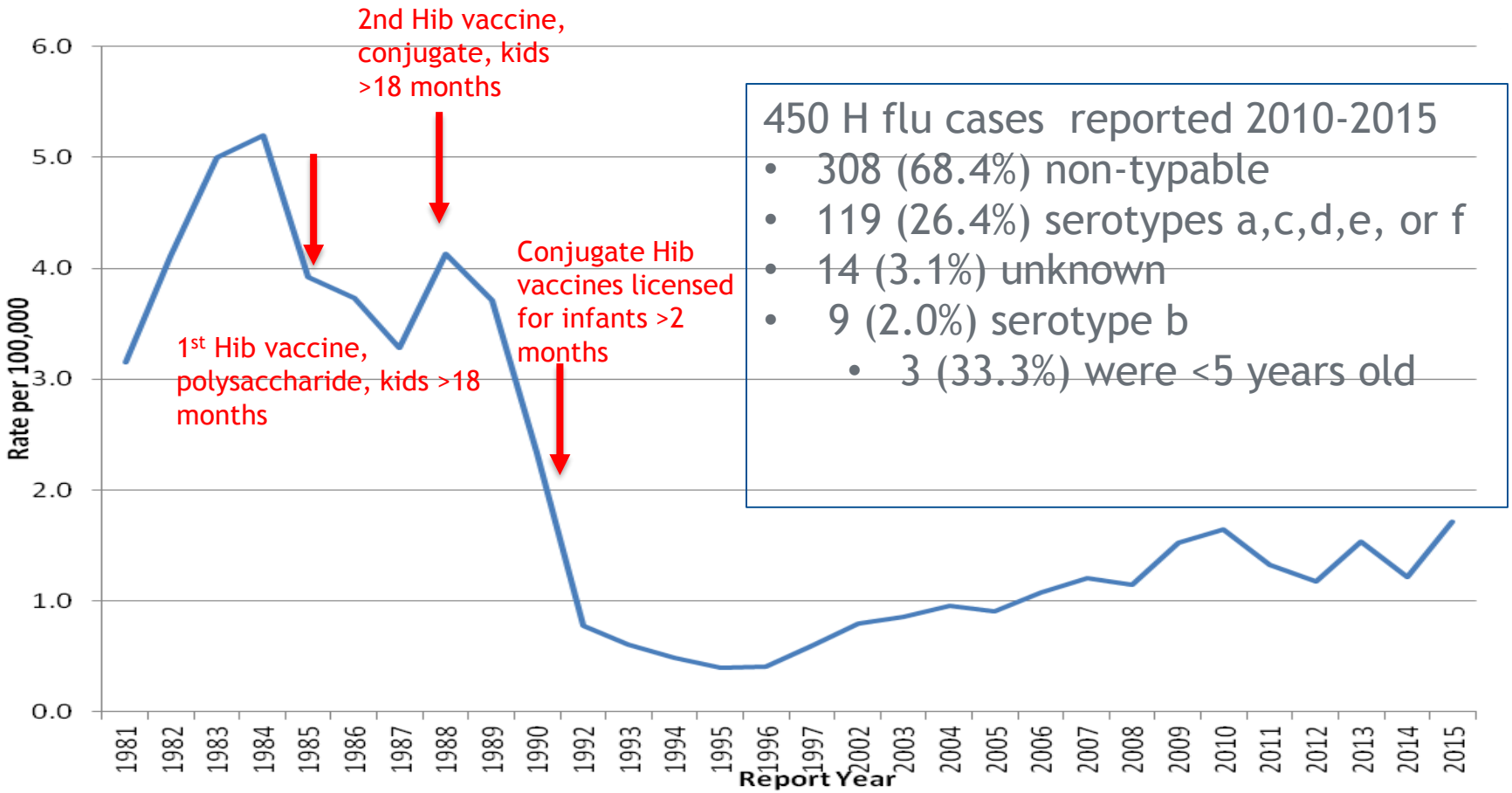
Reportable conditions in Colorado- routine surveillance/investigation

CDC funded Emerging Infections Program (EIP) Active Bacterial Core Surveillance

-enhanced surveillance in 5 county metro area; 10 sites nationally

-lab and epi data matched

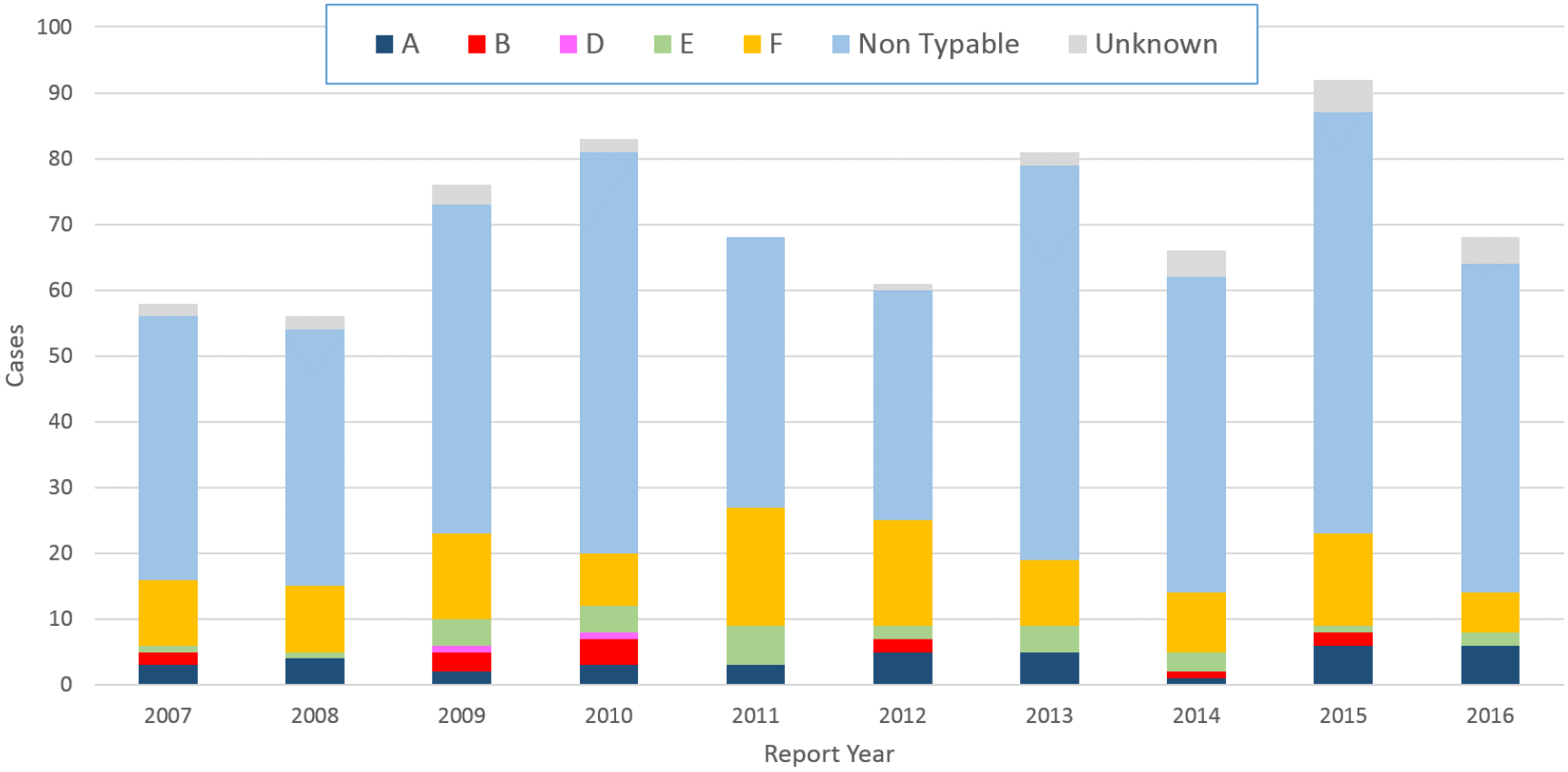
Rates of Invasive H. influenzae by Report Year, Colorado, 1981-2015



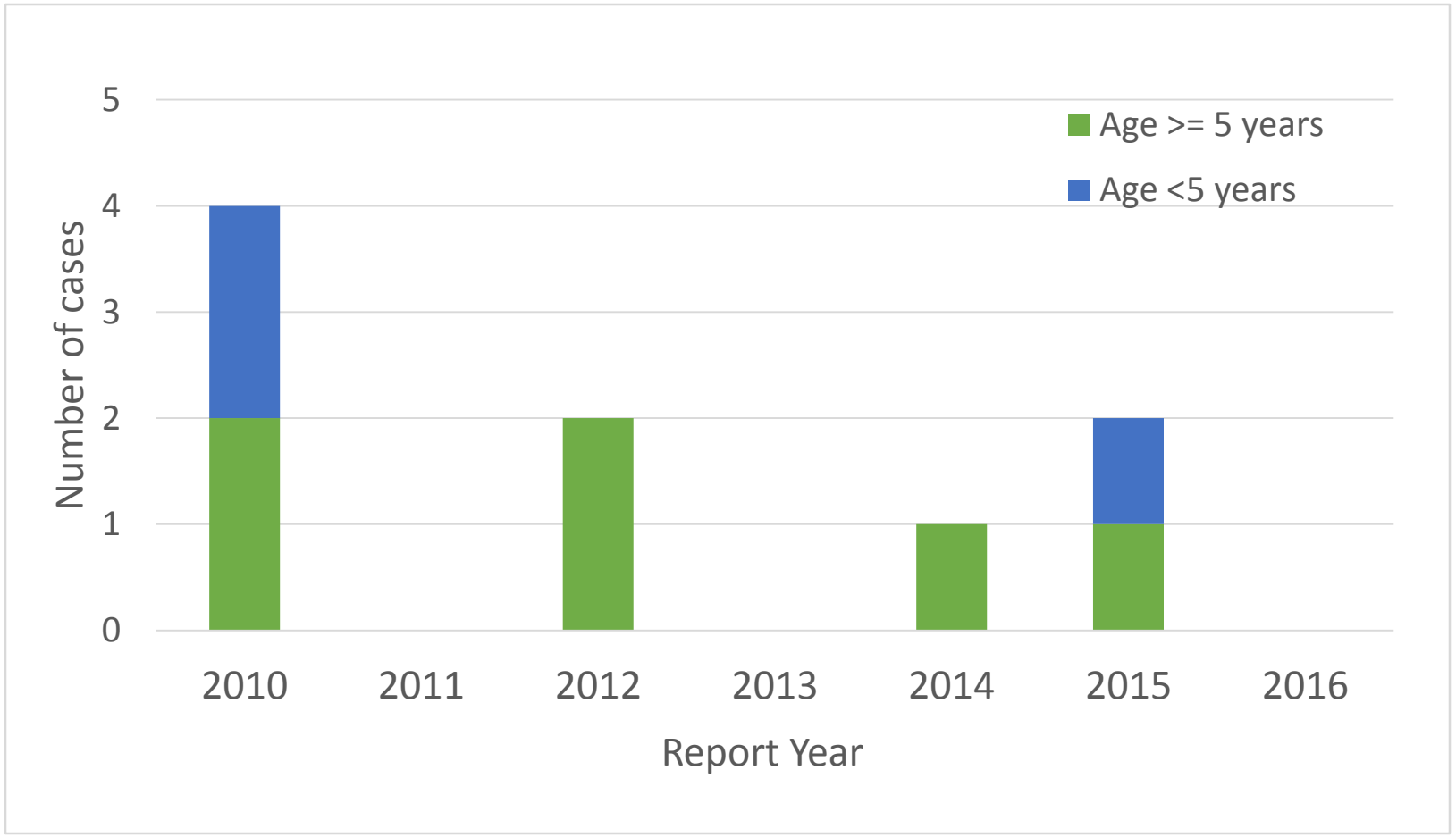
450 H flu cases reported 2010-2015

- 308 (68.4%) non-typable
- 119 (26.4%) serotypes a,c,d,e, or f
- 14 (3.1%) unknown
- 9 (2.0%) serotype b
  - 3 (33.3%) were <5 years old

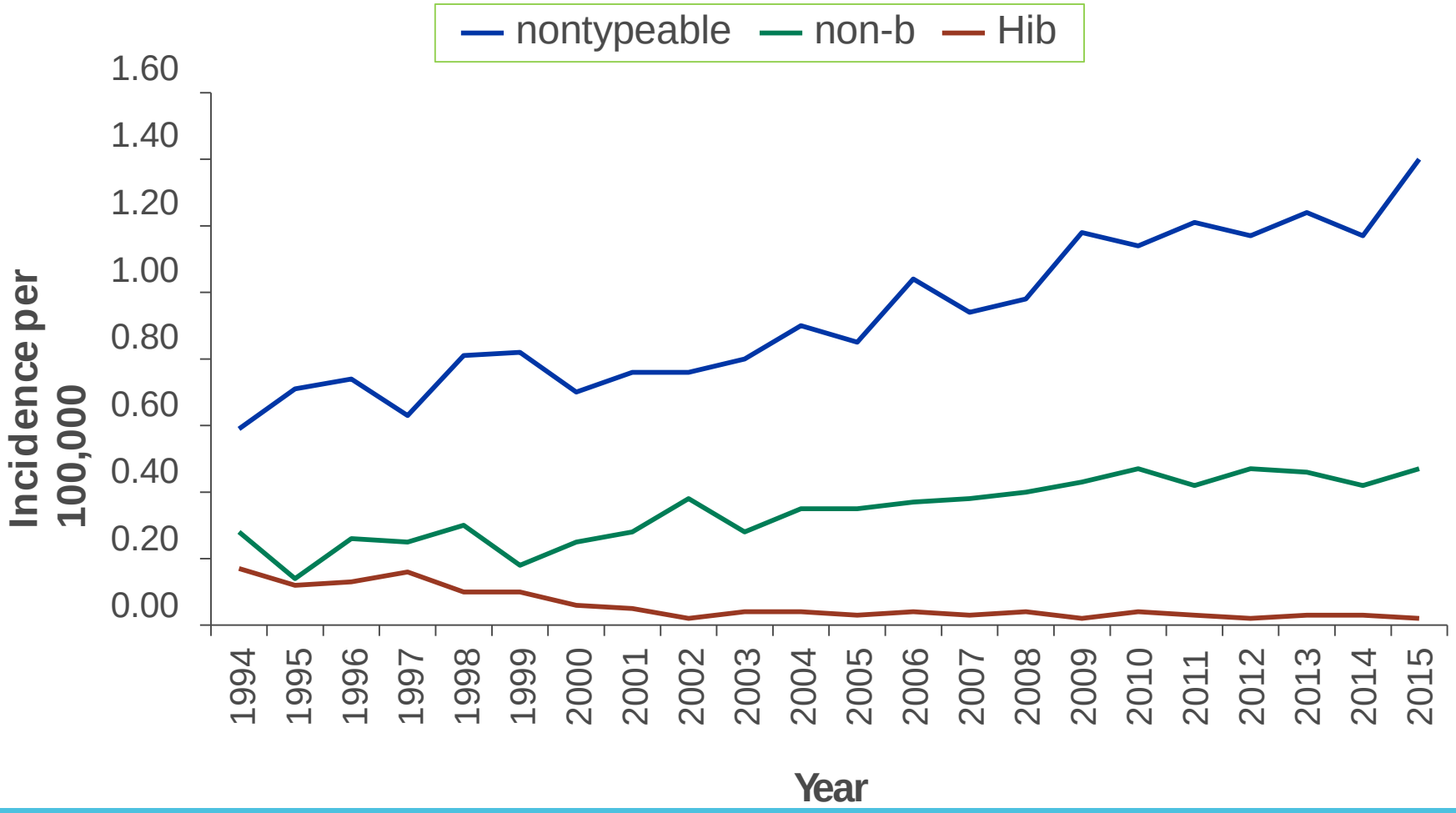
Reported Cases of Invasive *Haemophilus influenzae* by serotype, Colorado, 2007 - 2016



Cases of Invasive H. influenzae Serotype b (Hib) by Age Group and Report Year, Colorado, 2010-2016

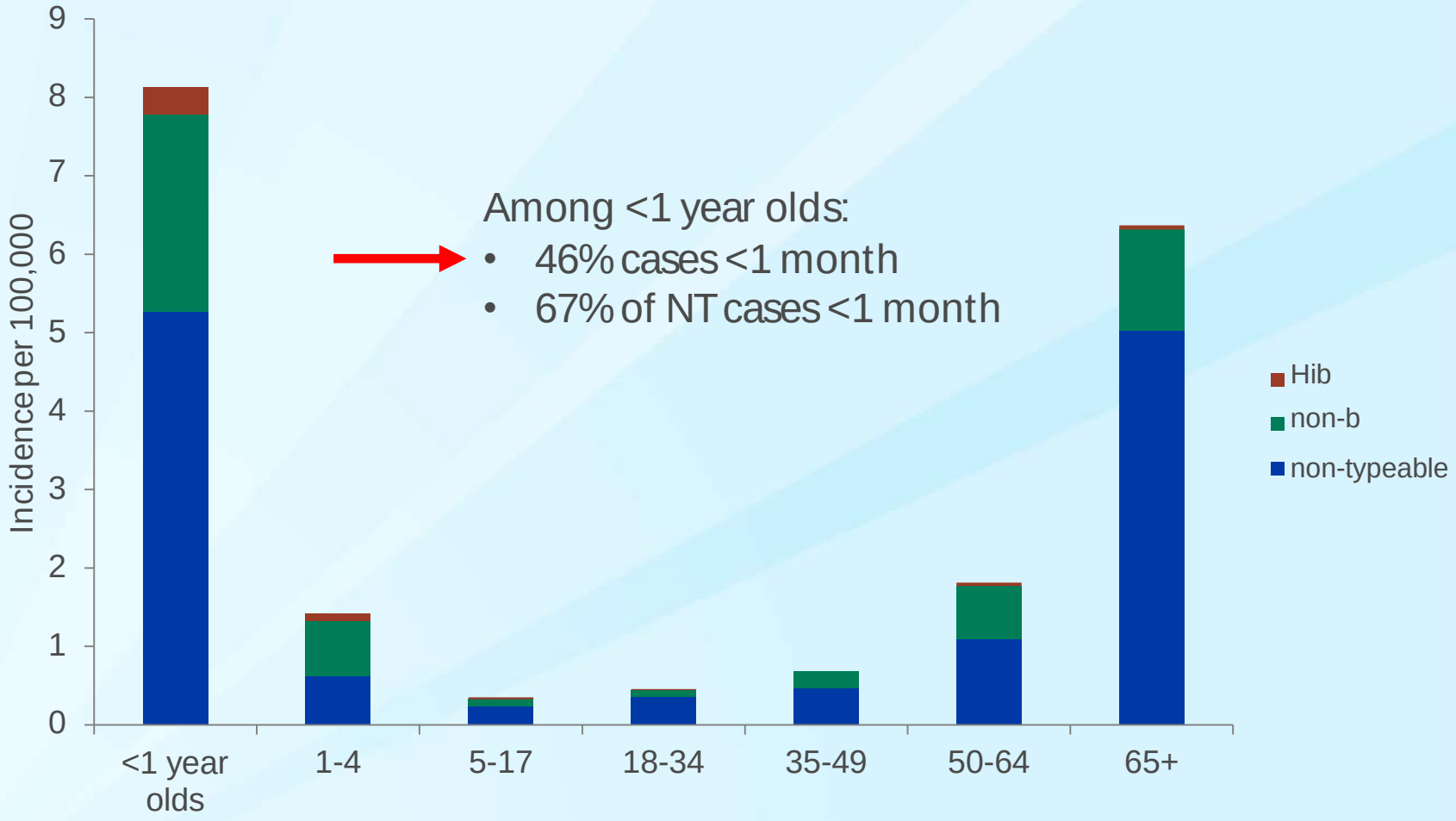


Incidence of *H. influenzae*, United States, 1994-2015



ABCs cases from 1999-2015 and estimated to the U.S. population

Estimated U.S. incidence of *H. influenzae* by age group and serotype, 2010-2015



Change in incidence of *H. influenzae* serotypes, United States, 2003-2008 vs. 2009-2014

Serotype	2003-2008 Incidence*	2009-2014 Incidence*	Percent change in incidence
Hib	0.04	0.03	-25%
Non-b	0.41	0.45	10%
a	0.04	0.09	109%
c	0.004	0	-100%
d	0.004	0.0001	-98%
e	0.09	0.07	-19%
f	0.27	0.28	3%
Nontypeable	1.04	1.19	14%
Total	1.48	1.67	13%

*Average annual incidence for the time period

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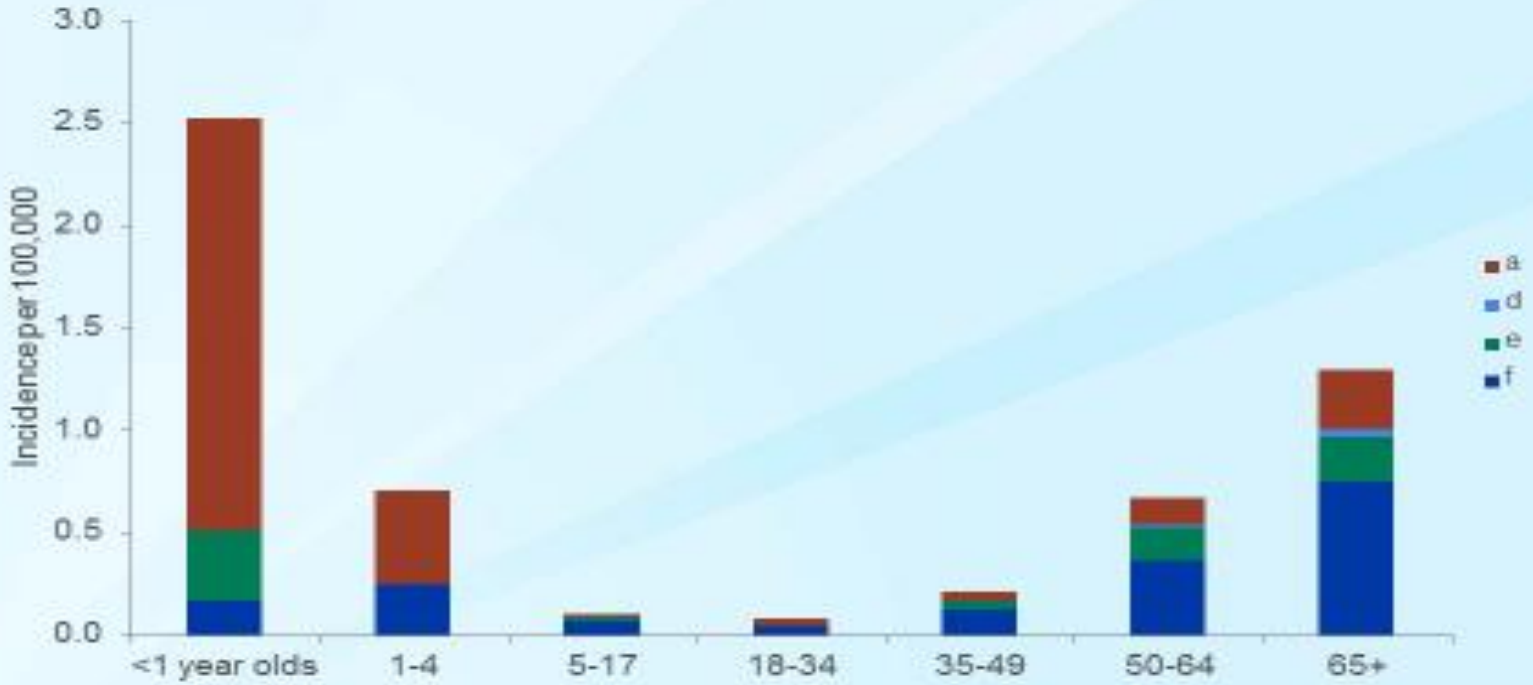
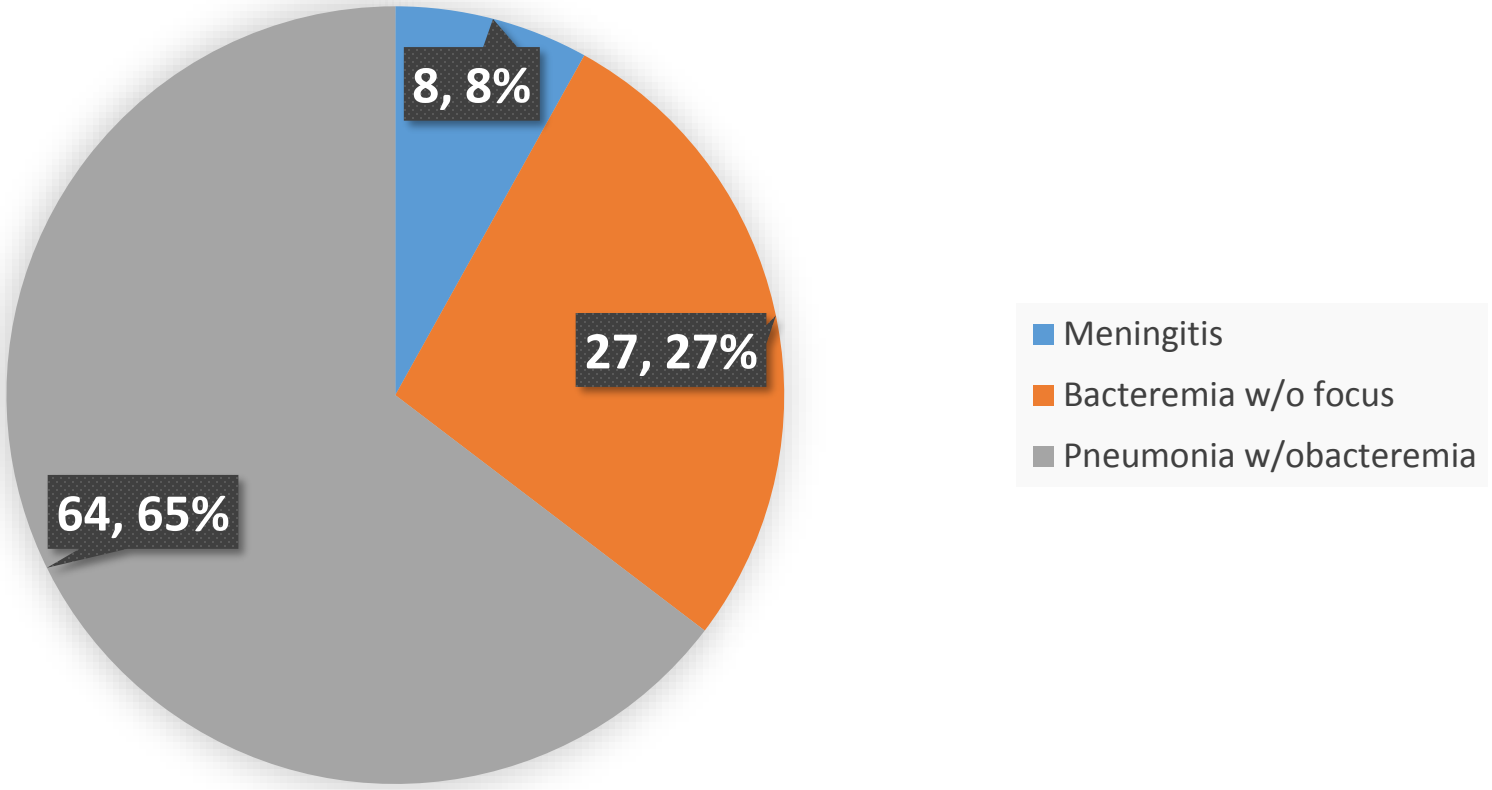
Total	1.48	1.67	13%

*MacNeil et al CID 2011;**Average annual incidence for the time period

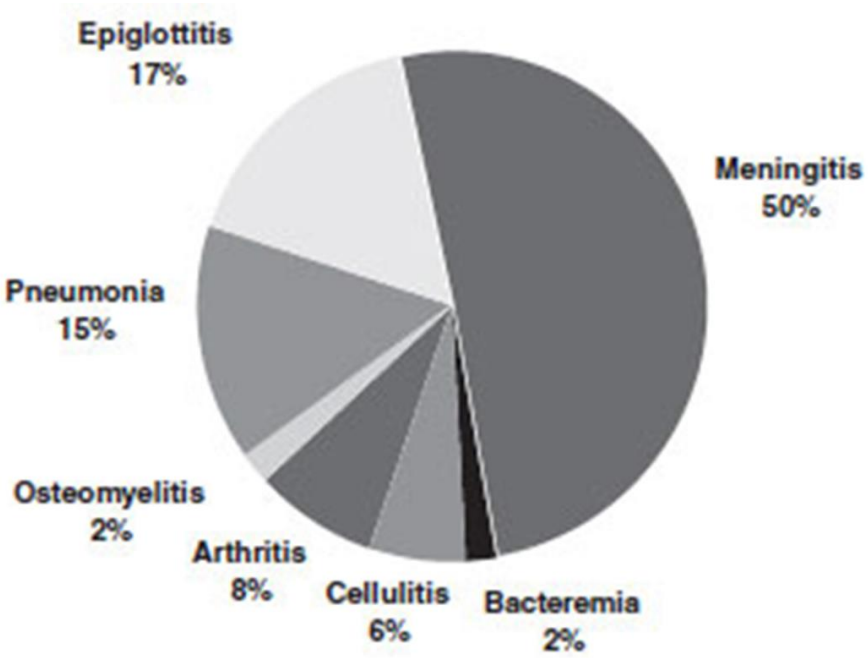
Estimated U.S. incidence of non-b *H. influenzae* by age group and serotype, 2010-2015

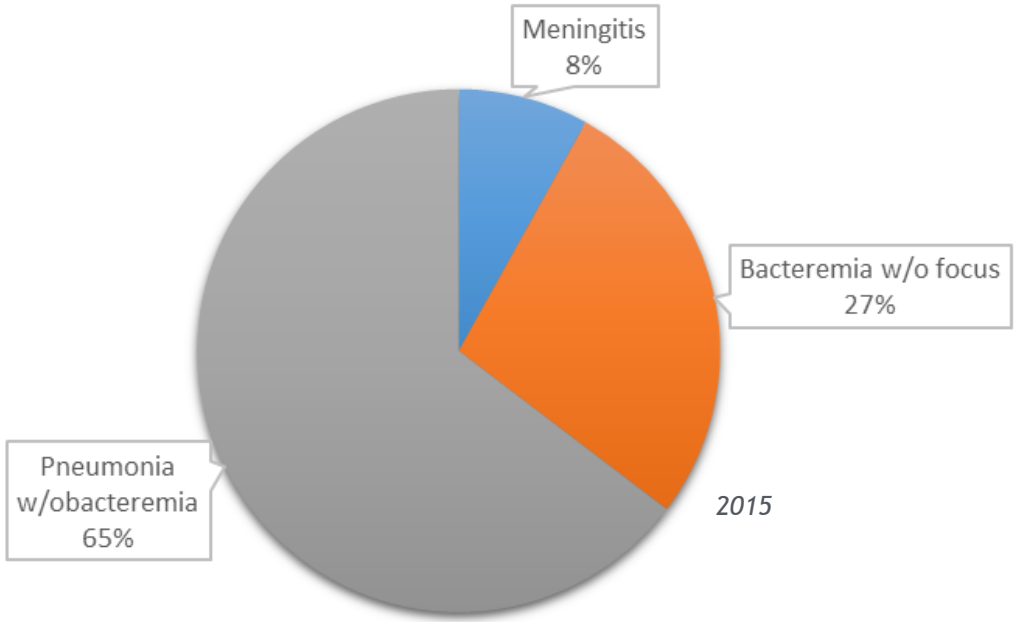


Haemophilus influenzae clinical syndromes, 2015, Active Bacterial Core Surveillance

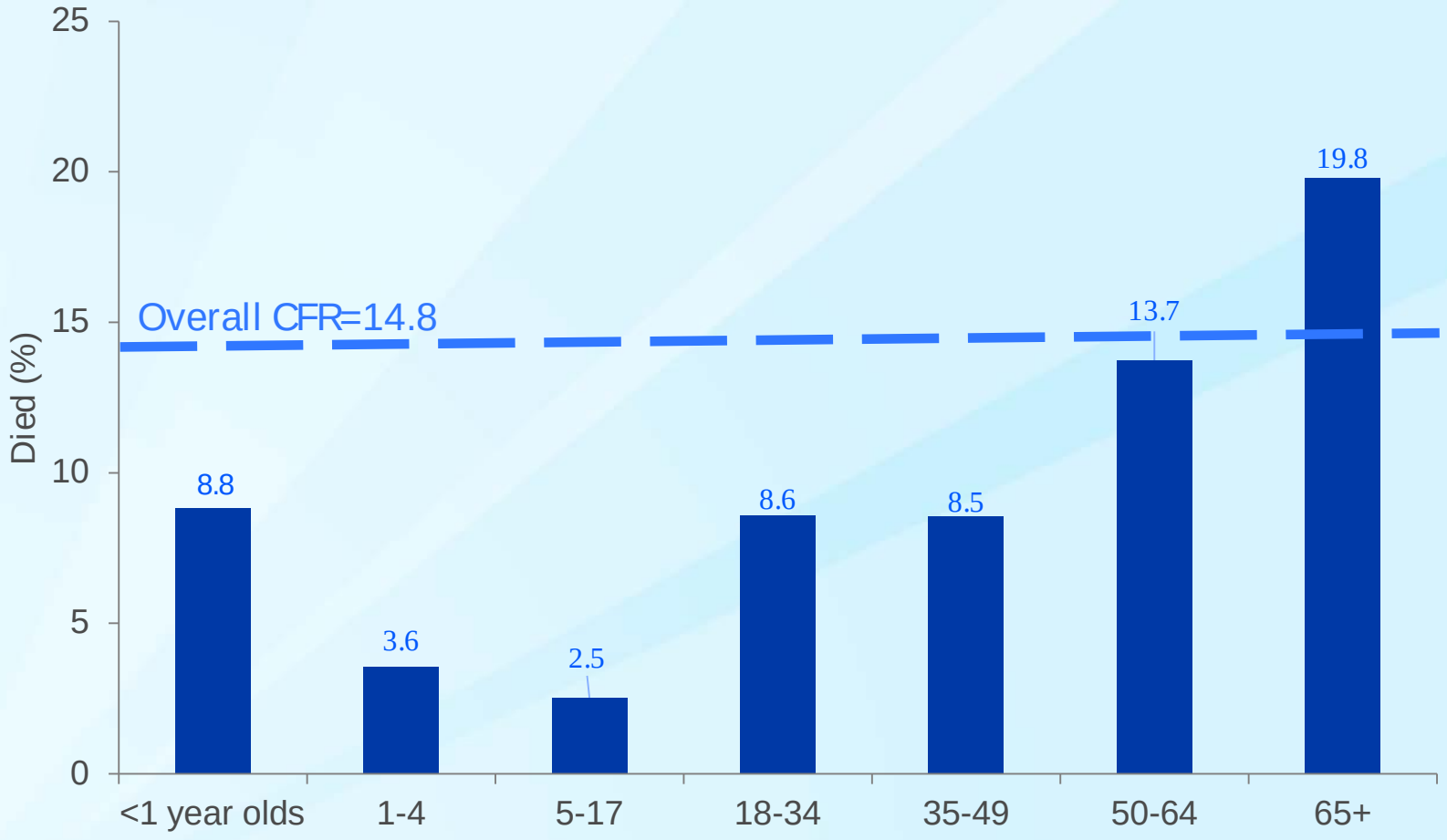


Pre- vaccine era vs. post

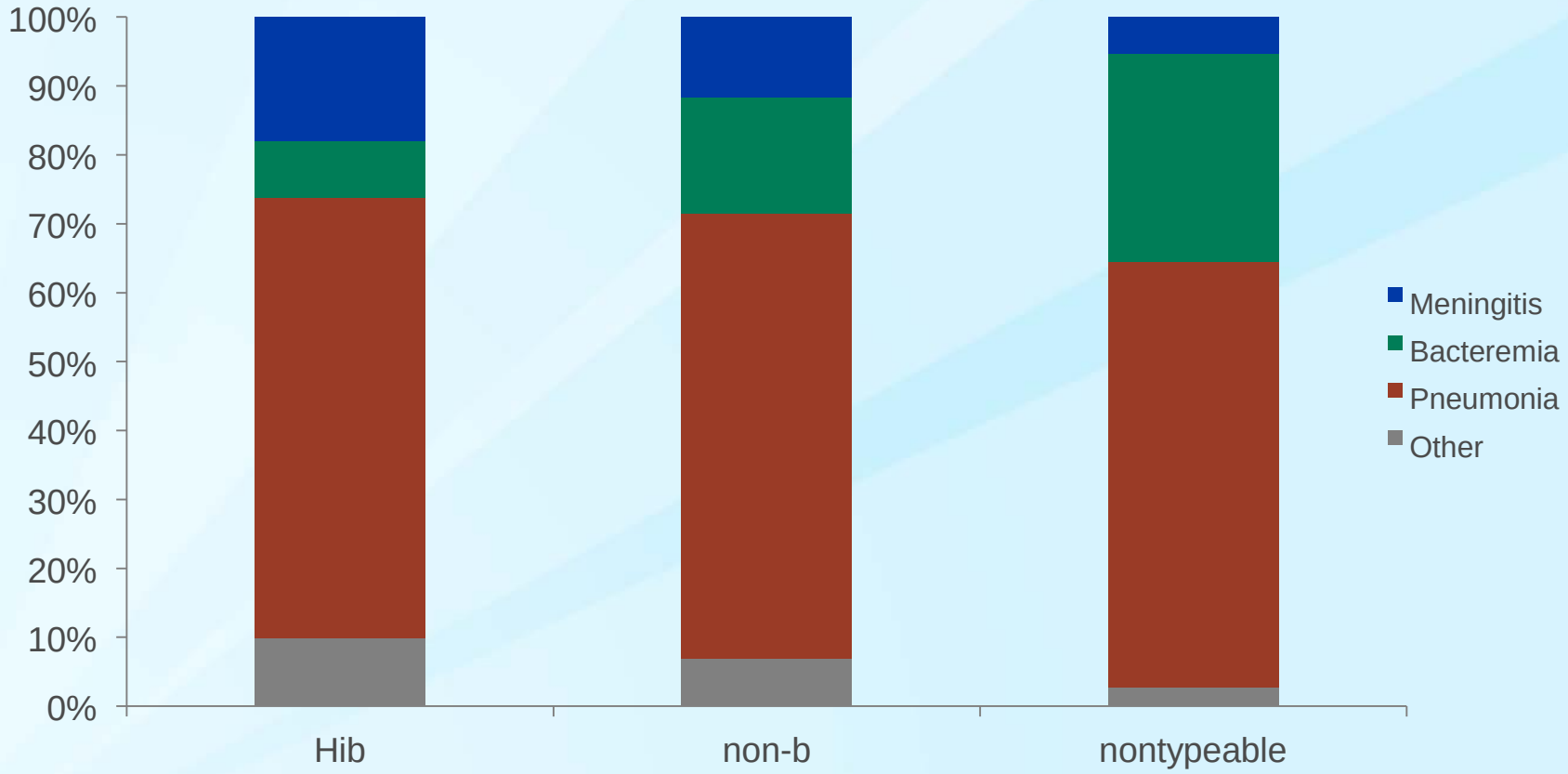




Total *H. influenzae* case fatality by age group, 2010-2015



Clinical syndromes of *H. influenzae* by serotype, 2009-2014



Risk factors for Hib

Exposure factors

- Household crowding/large household size
- Child care attendance
- Low SES, low parental education levels
- School-aged sibling

Host factors

- Race/ethnicity (Hispanic and AI/AN- may be confounded by SES)
- Chronic disease
- Gender (possibly)- risk higher for males

Protective factors

For infants less than 6 months of age:

- Breastfeeding
- Passive acquisition of maternal Ab

How serotype is determined

Isolates forwarded from clinical or commercial labs to CDPHE lab

CDPHE lab :

- PCR to confirm species
- PCR to determine serotype
- Confirm serotype with anti-sera agglutination (and morphology)

Time to serotype

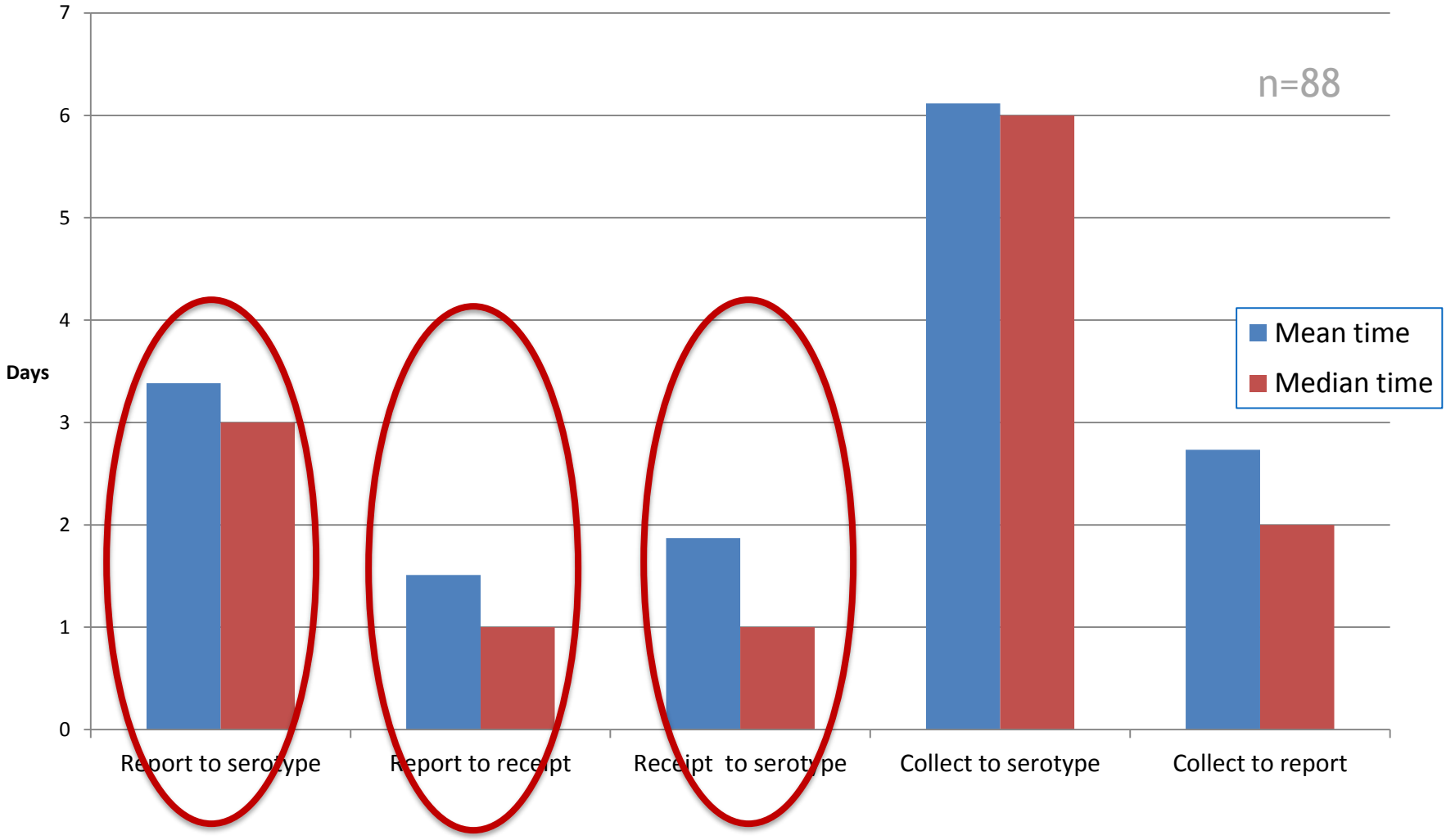
Serotyping of H flu isolates **only** available at state public health laboratory

Requested data on all specimens serotyped in 2015

Matched to CEDRS cases (disease surveillance database)

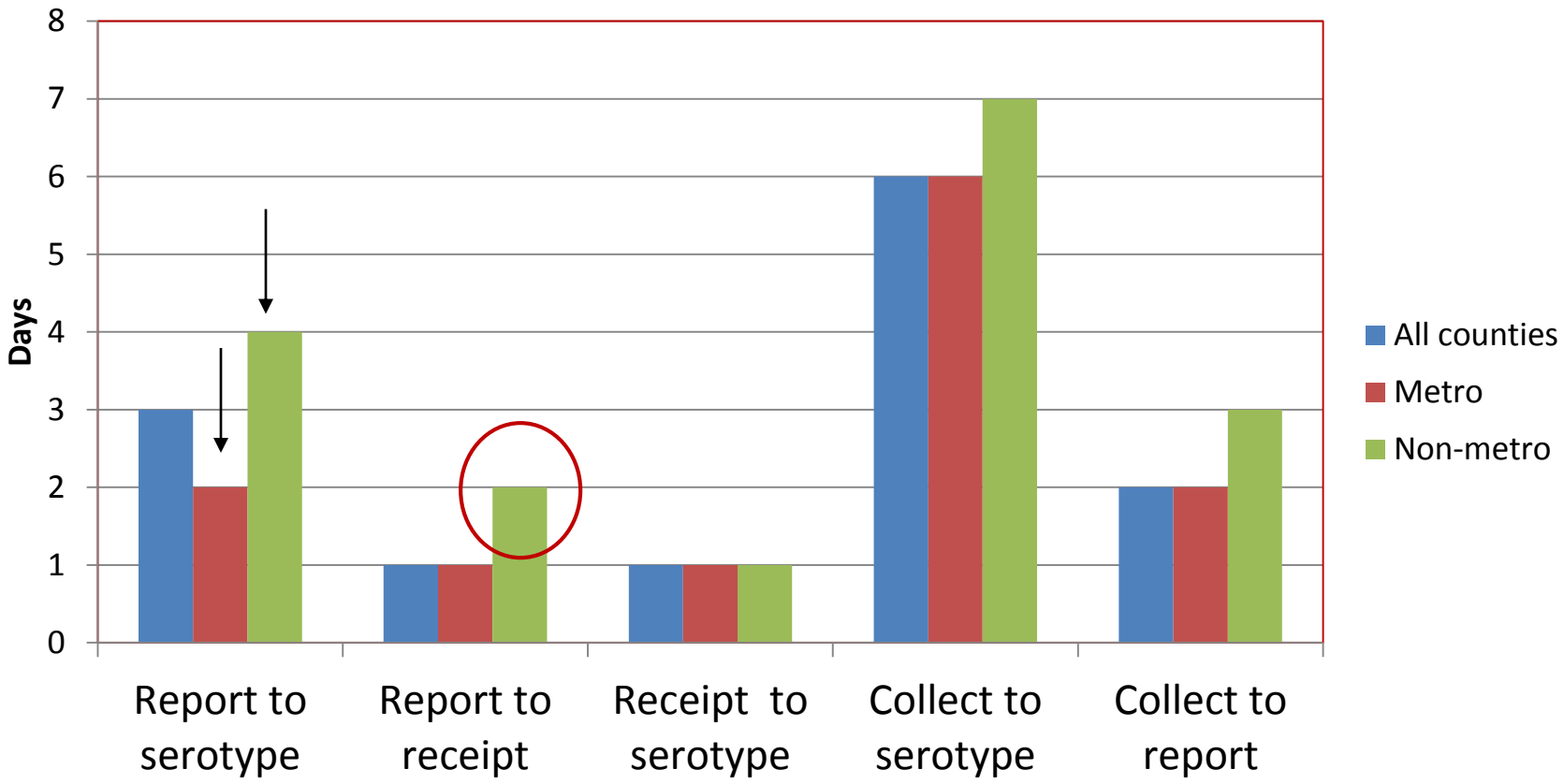
Looked at all reports and metro vs. non-metro (Adams, Arapaho, Denver, Douglas, Jefferson) reports

Time-to-serotype for *Haemophilus influenzae* specimens, Colorado (all counties), 2015

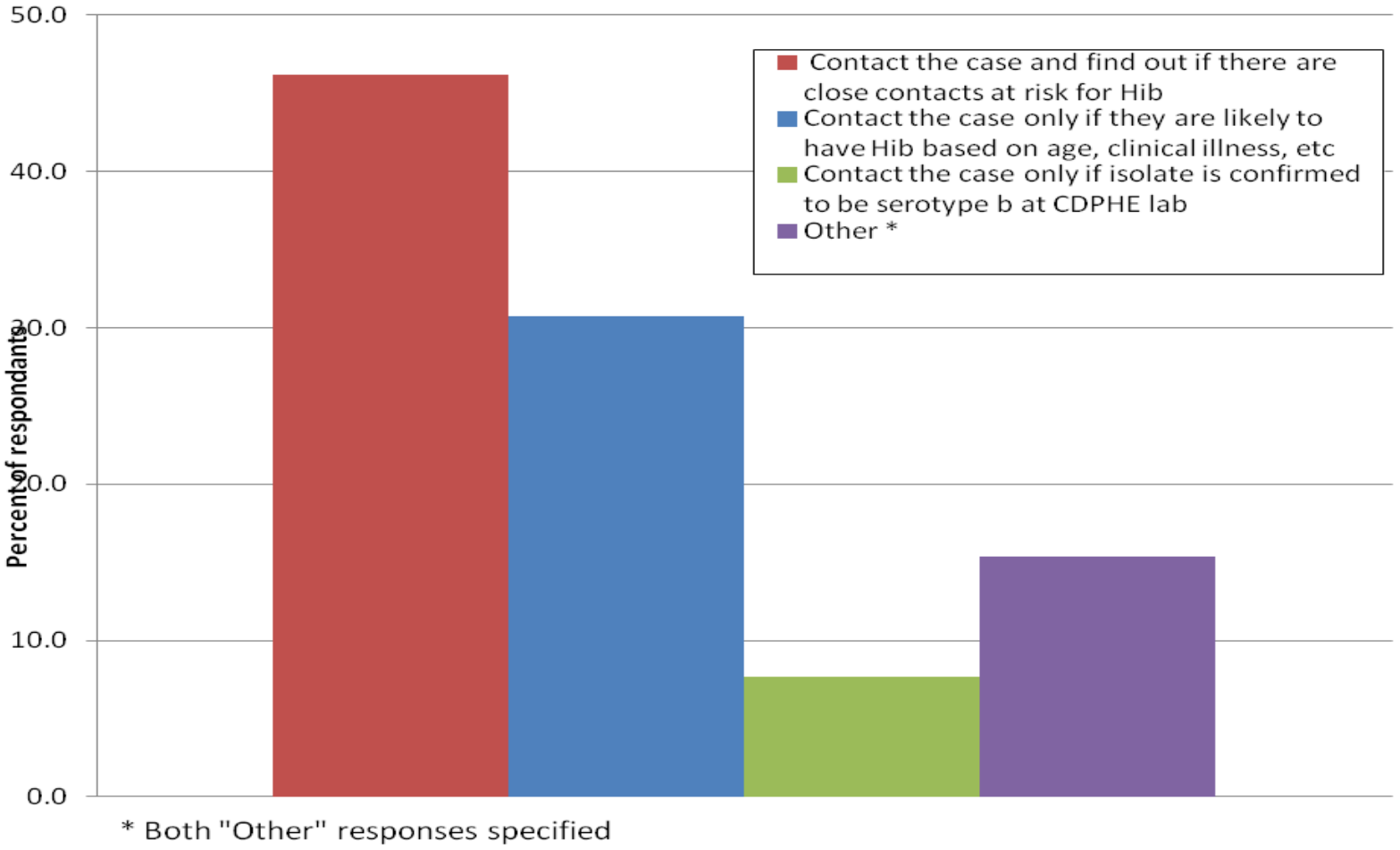


Metro vs. non-metro

Median time-to-serotype for *Haemophilus influenzae* specimens, Colorado (2015)



When you are notified of a case of Hi, do you:



Take home messages

Hib is rare and not clinically distinct from other invasive H flu in the post-vaccine era

Non-typeable H flu has increased, causes most invasive infections

Hia is emerging as a cause of severe Hi invasive disease

National guidelines don’t specify an approach to the time between reporting and serotype

Surveillance tracks clinical and epidemiological changes of H flu in post-vaccination era

Thank you! And Thanks to:

Our LPHA and lab partners

Lisa Miller

Meghan Barnes

Emily Travanty

Amanda Reiff

Karen Edge

Questions?

Resources

American Academy of Pediatrics. Red Book 2015: Report of the Committee on Infectious Diseases, 30th Edition. Illinois, American Academy of Pediatrics, 2015.

CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases. Atkinson W, Hamborsky J, Kroger A L, Wolfe S, eds. 13th ed. Washington DC: Public Health Foundation, 2015 or http://www.cdc.gov/vaccines/pubs/pinkbook/index.html

CDC. Manual for the Surveillance of Vaccine-Preventable Diseases. Roush S, Baldy L, eds.. Atlanta, GA, 2015. https://www.cdc.gov/vaccines/pubs/surv-manual/index.html

Prophylaxis criteria

If **any** household contact (4 hrs day for prev 7 days) meets any of below criteria, prophylaxis recommended for **all** household contacts of Hib case, except pregnant women:

<12 months of age and has not completed the Hib primary vaccine series

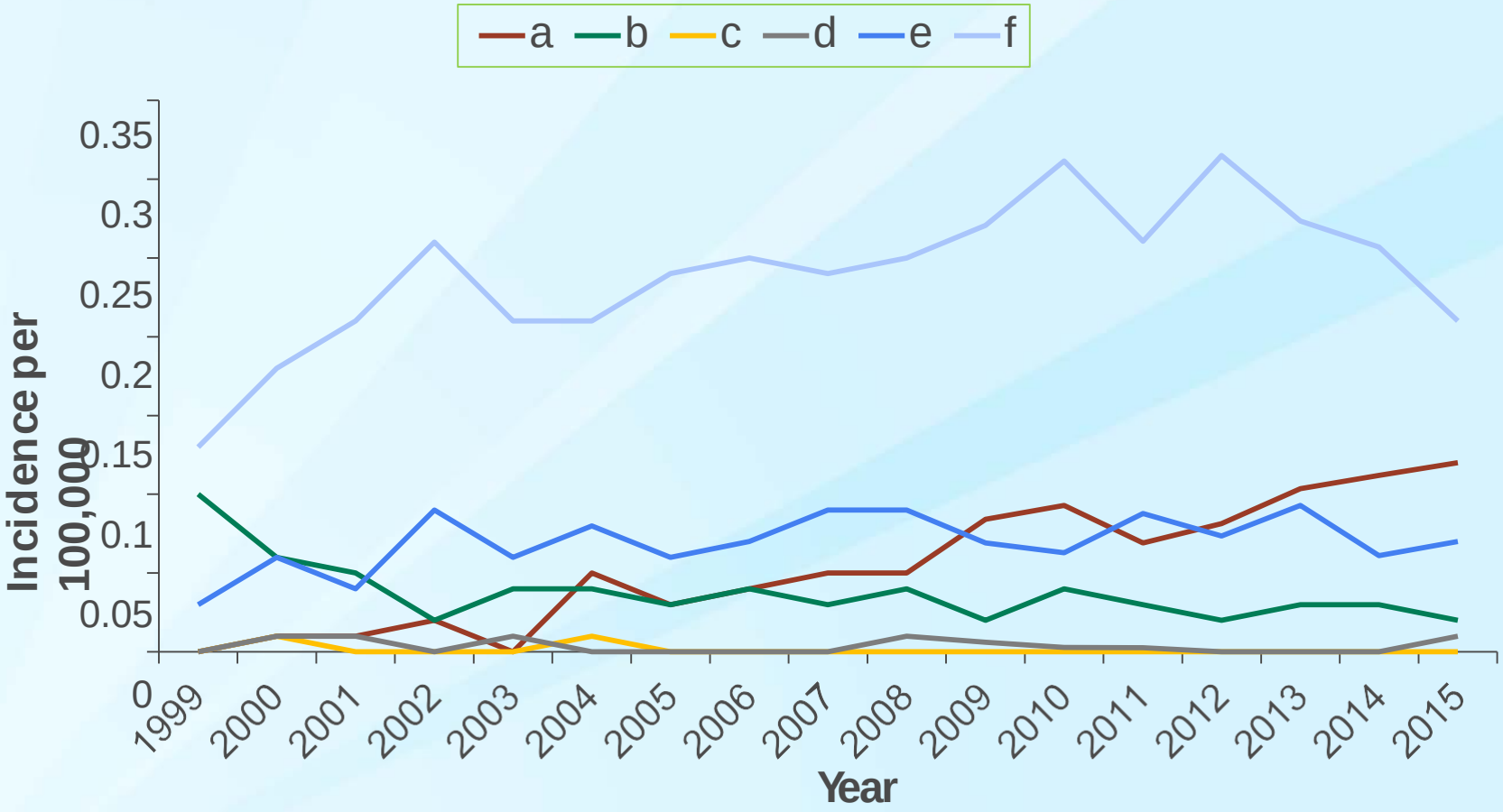
OR

immunocompromised child, regardless of Hib immunization status

OR

contact is <4 years of age and unimmunized or incompletely immunized for Hib.

Incidence of *H. influenzae* serotypes, United States, 1999-2015



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