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# Pertussis Epidemiology in the Acellular Vaccine Era

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Vaccines and Related Biological Products Advisory Committee

September 20, 2024

# Outline

- Pertussis overview
- Types of pertussis vaccines
- Pertussis in the United States
  - Vaccine recommendations and vaccination coverage
  - Disease burden and epidemiologic trends up to the COVID-19 pandemic
  - Transition from whole cell to acellular vaccines in context of disease resurgence
  - Waning immunity from acellular vaccines
  - Epidemiologic trends post-pandemic

# Pertussis (whooping cough)

- Acute respiratory infection caused by *Bordetella pertussis*
- Highly contagious
  - Transmitted via respiratory droplets
  - Humans are the only natural reservoir
- Symptoms can affect all ages
  - Range from prolonged cough illness to mild and asymptomatic infection
  - Severity of symptoms differs by age and vaccination status
  - Infants at highest risk of morbidity and mortality
- Transmission dynamics not well understood
  - Asymptomatic infection thought to play a role

# Pertussis Epidemiology

- Poorly controlled despite high vaccination coverage
- Endemic disease
- Cyclical pattern with peaks every 3-5 years
- True population burden underestimated
  - Under-diagnosed
    - Early symptoms non-specific, mimic other respiratory infections
    - Diagnostic tests not as reliable later in infection
  - Under-reported
    - Milder cases may not meet case definition for reporting

# Pertussis Vaccines

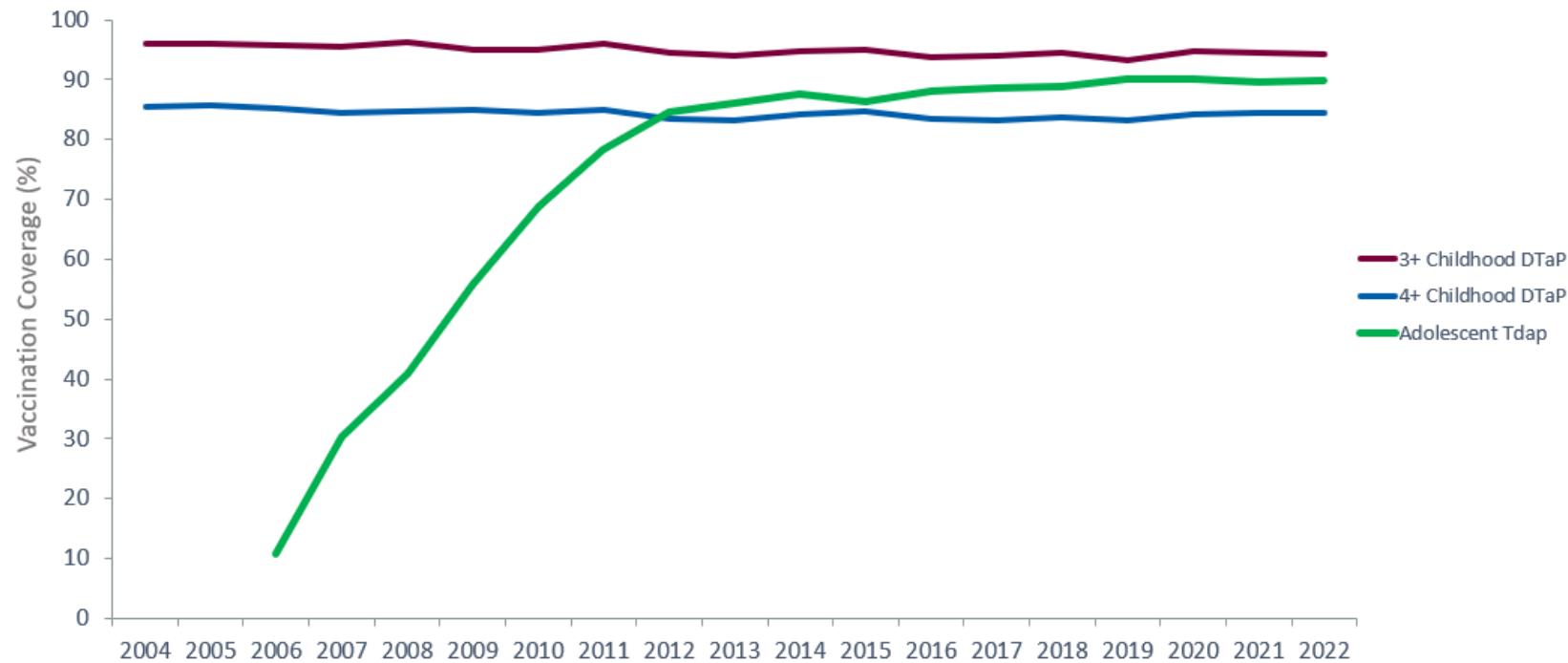
- **Whole cell vaccines (1940s)**
  - Safe and effective but reactogenic
  - Injection site reactions, fever, febrile seizures
  - Increased public concern and declines in vaccination
  - Led to global effort to develop vaccines with less adverse effects
- **Acellular vaccines (1990s)**
  - Recombinant vaccines containing 1-5 pertussis antigens
  - Safe, less reactogenic
  - High efficacy similar to whole cell vaccines
  - Replaced whole cell vaccines in most developed countries
  - Two formulations licensed in the U.S. (pediatric DTaP and adolescent/adult Tdap)
    - Combined with tetanus and diphtheria toxoids

# United States Pertussis Vaccination Schedule

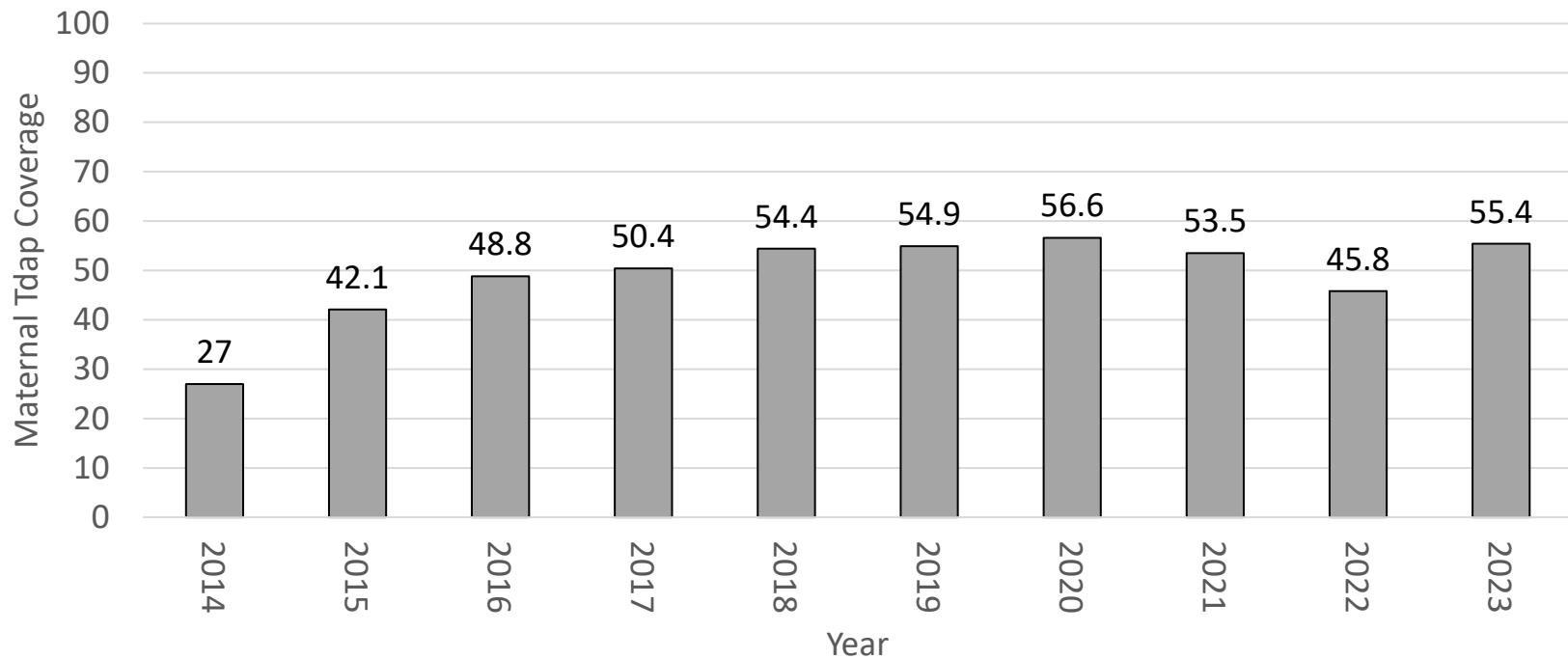


DTaP for young children	Tdap for preteens	Tdap for pregnant women	Tdap for adults
✓ 2, 4, and 6 months ✓ 15 through 18 months ✓ 4 through 6 years	✓ 11 through 12 years	✓ During the 27-36th week of each pregnancy	✓ Anytime for those who have never received it

# Childhood and Adolescent Pertussis Vaccination Coverage, United States, 2004-2022

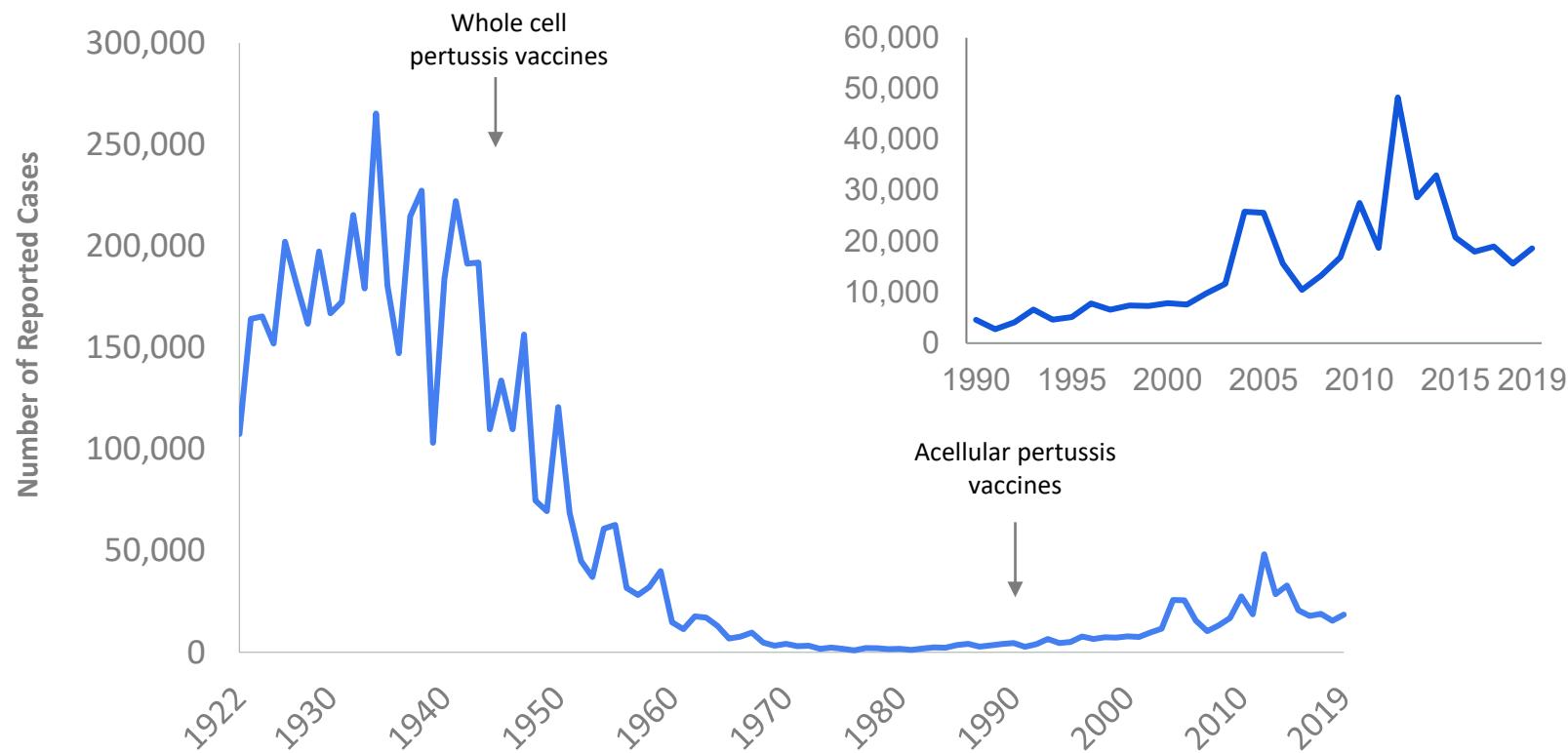


# Maternal Tdap Coverage, United States, 2014-2023

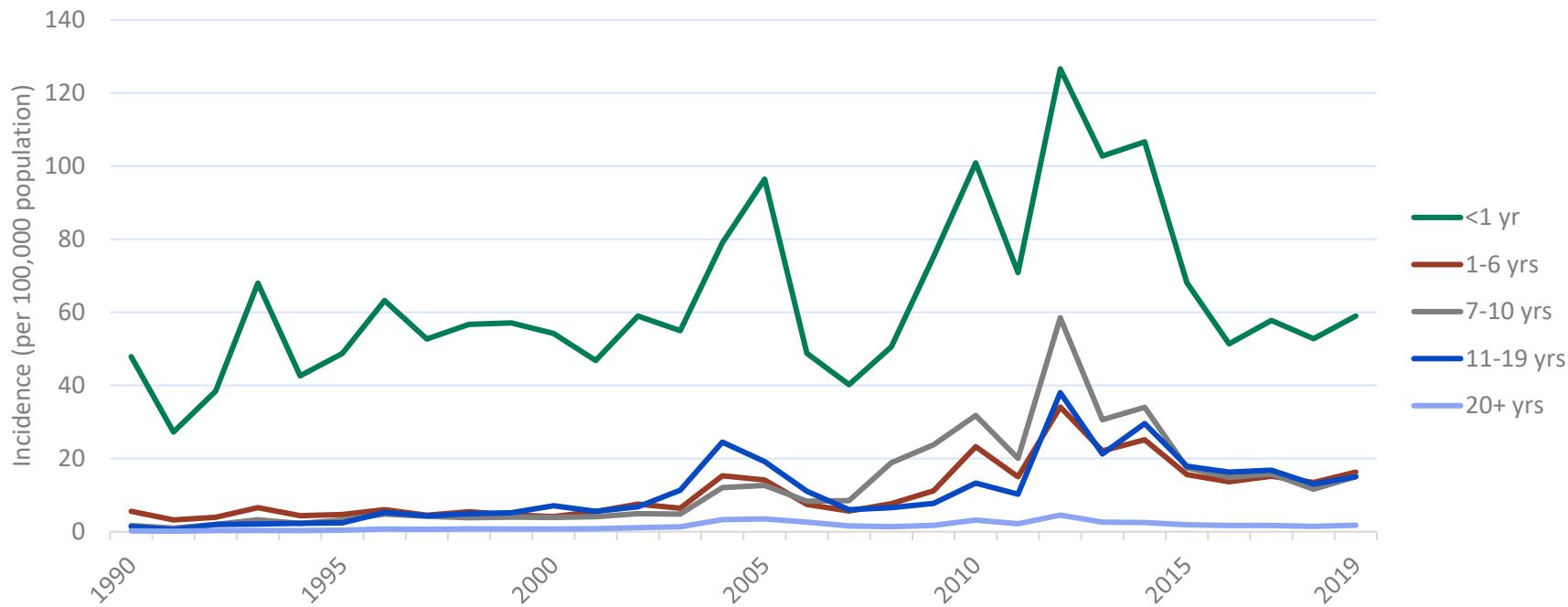


# Historical trends in reported pertussis cases, United States

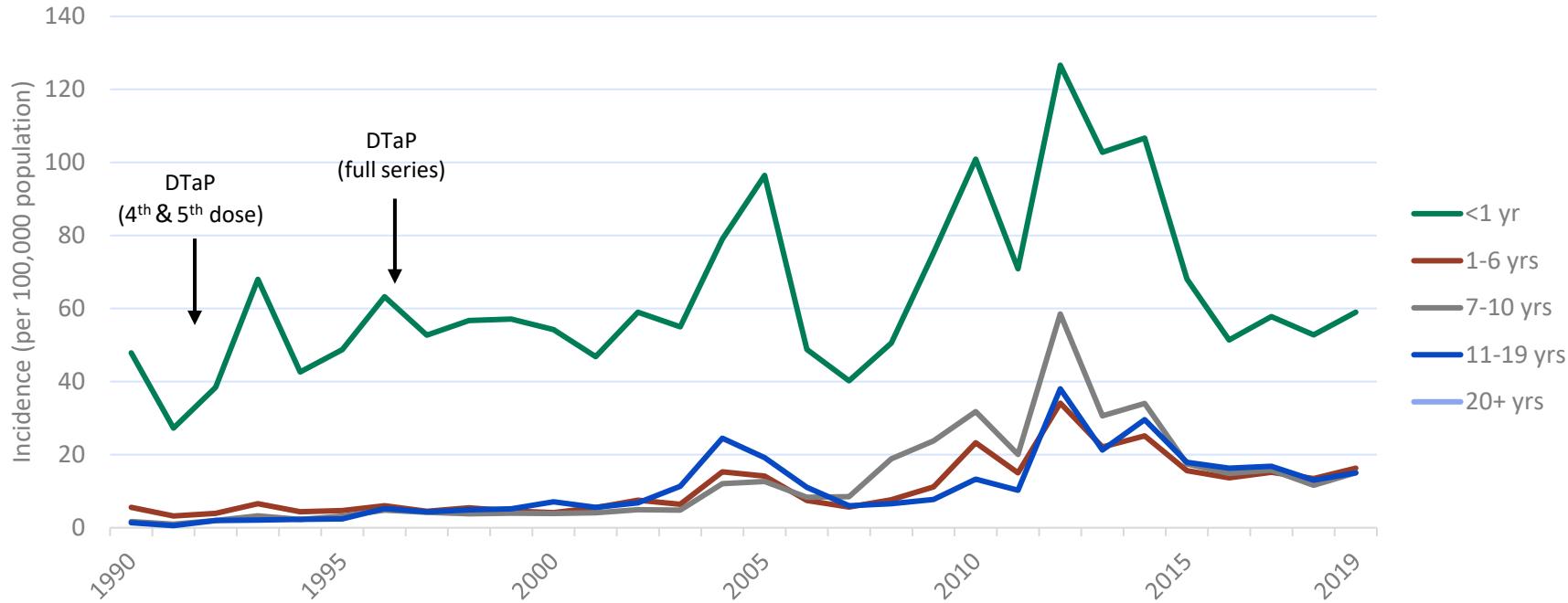
# Reported Pertussis Cases, United States, 1922-2019



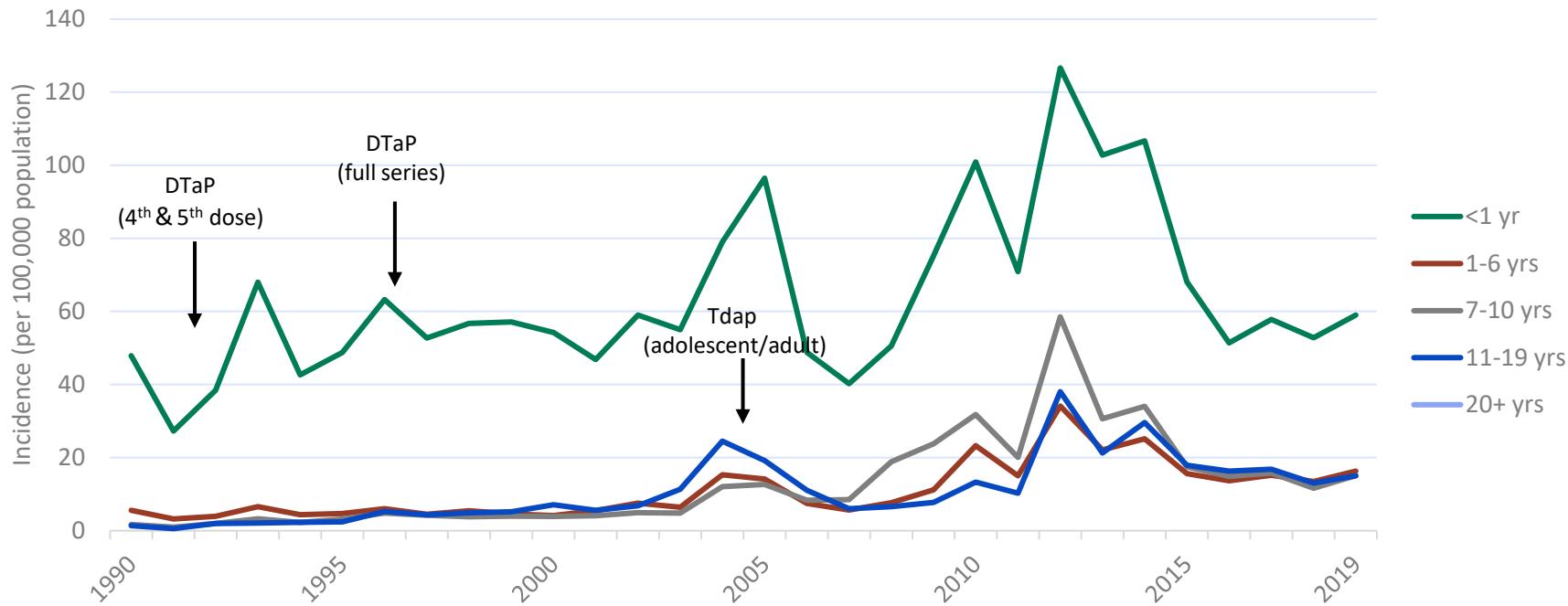
# Pertussis Incidence by Age Group, United States, 1990-2019



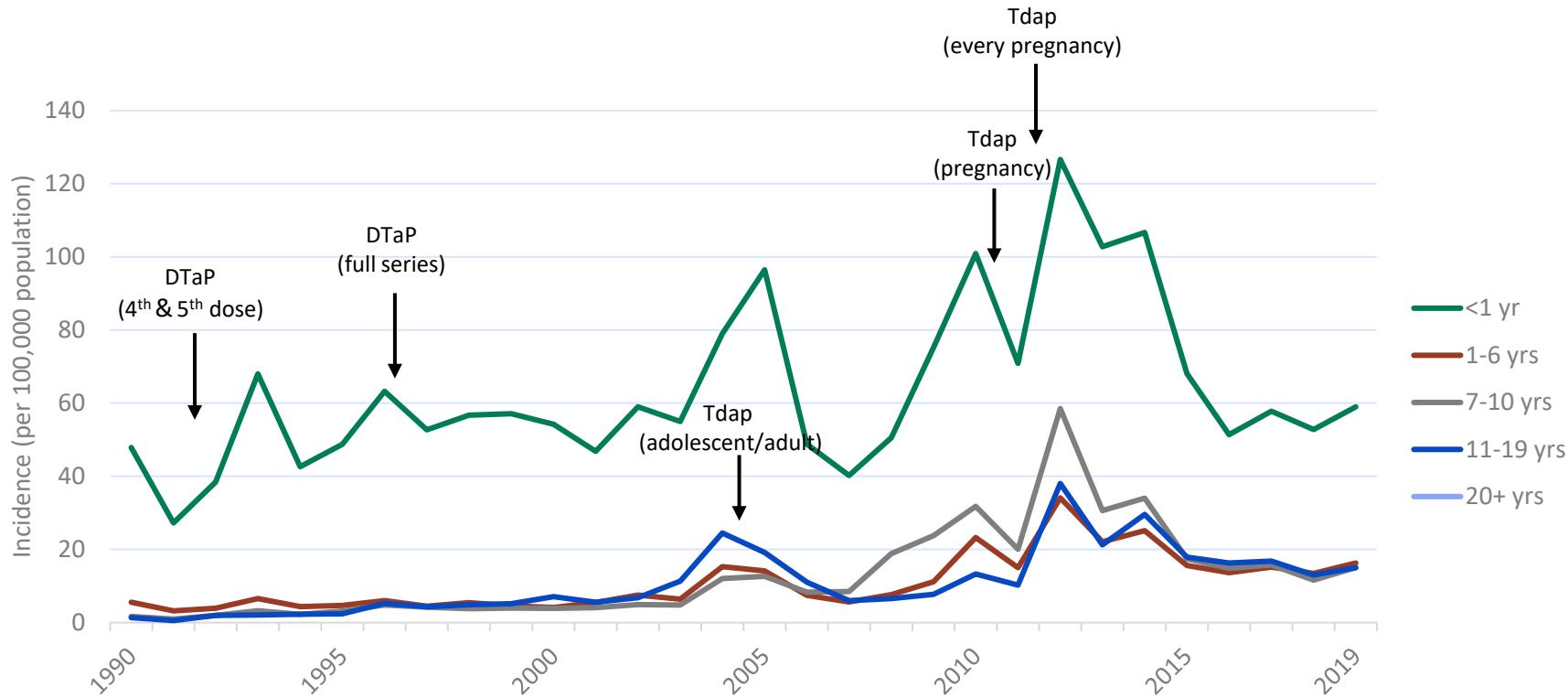
# Pertussis Incidence by Age Group, United States, 1990-2019



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# Possible Reasons for Pertussis Resurgence

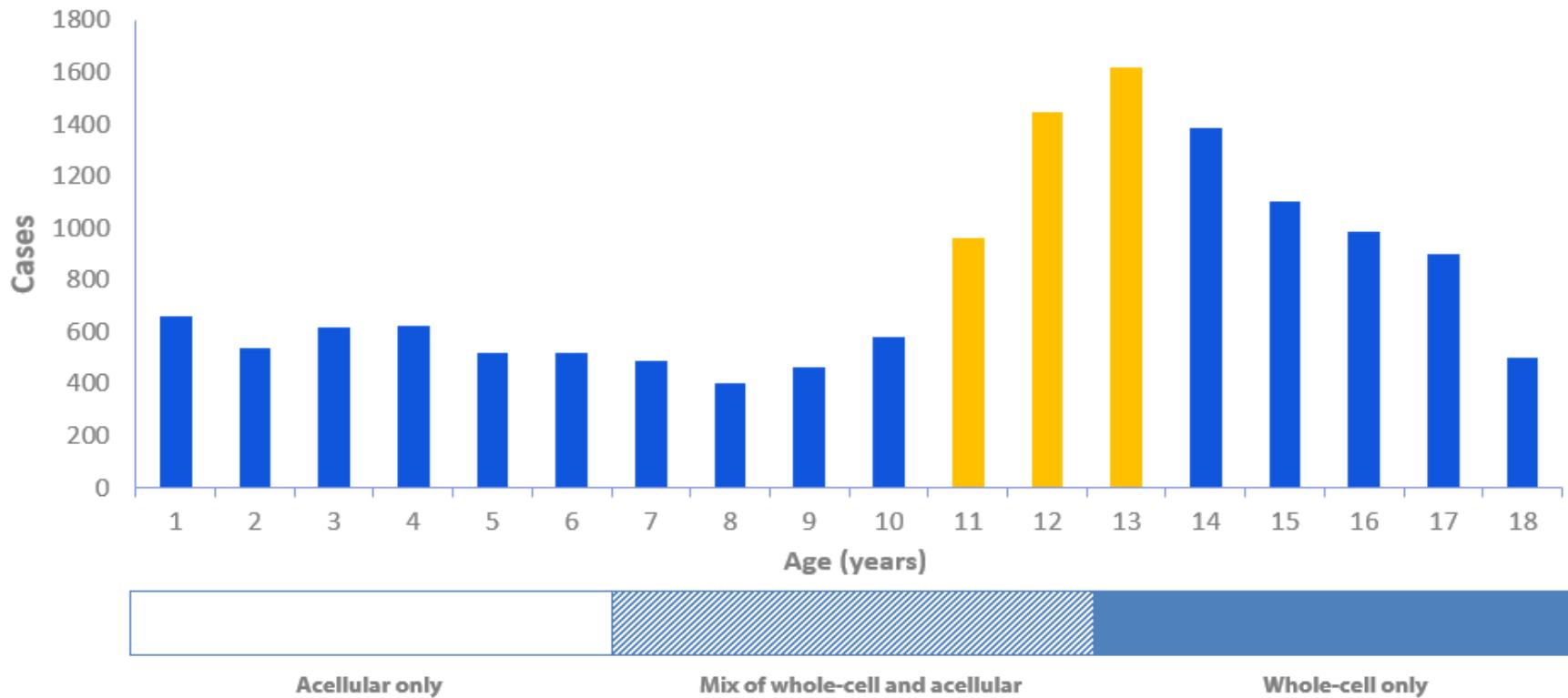
- Improved, more sensitive diagnostic tests
- Strain adaptation to vaccine pressure
- Increased awareness and testing

# Possible Reasons for Pertussis Resurgence

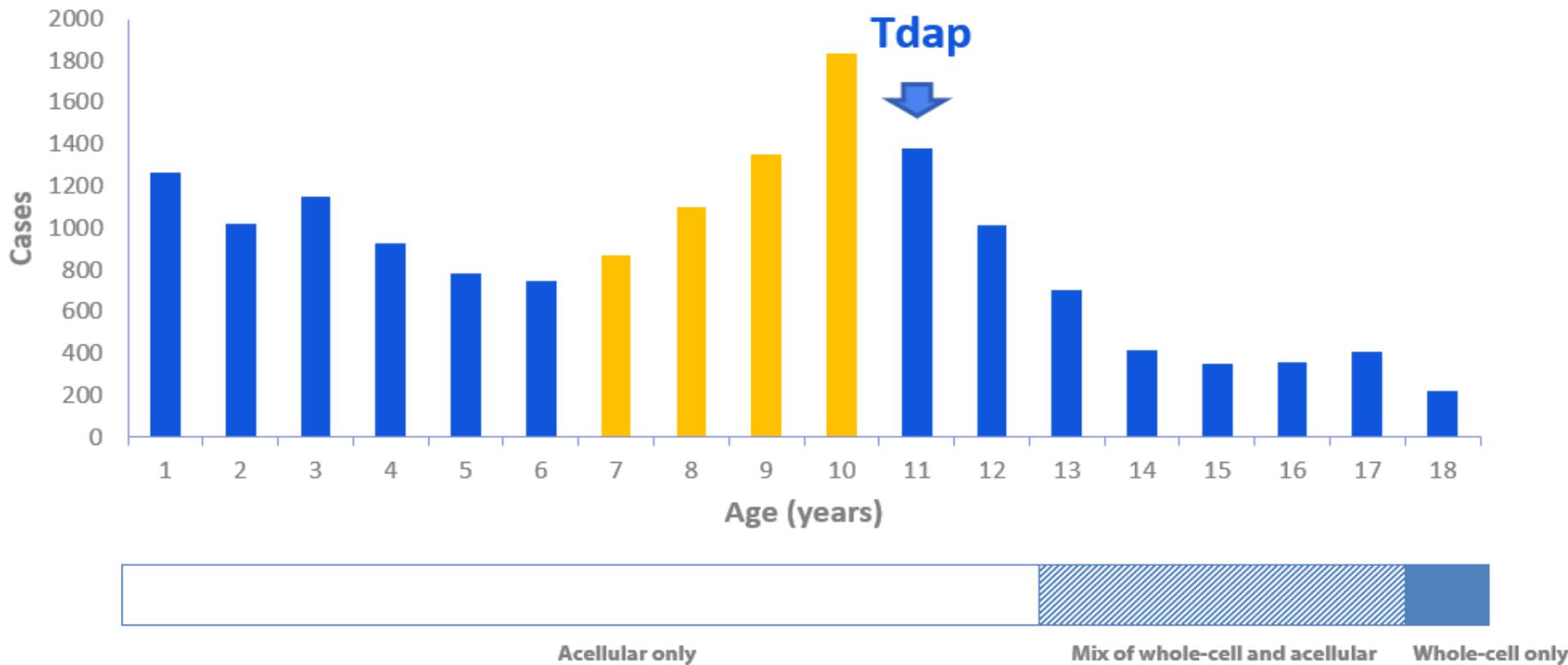
- Improved, more sensitive diagnostic tests
- Strain adaptation to vaccine pressure
- Increased awareness and testing
- **Flawed acellular vaccines**
  - Less protection against transmission
  - Faster waning of immunity

# Age-related shifts during epidemic peak years in the United States

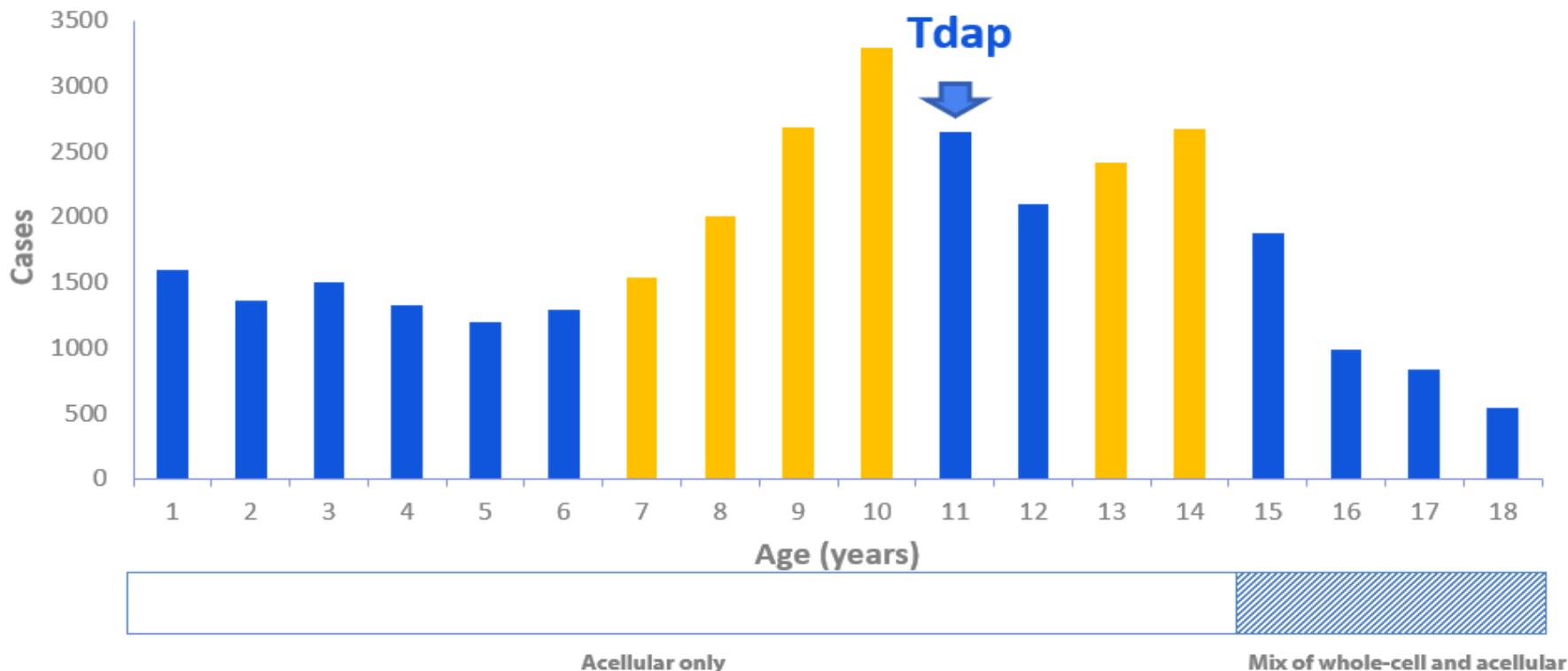
# Reported Pertussis Cases by Age, United States 2004 (N=25,827)



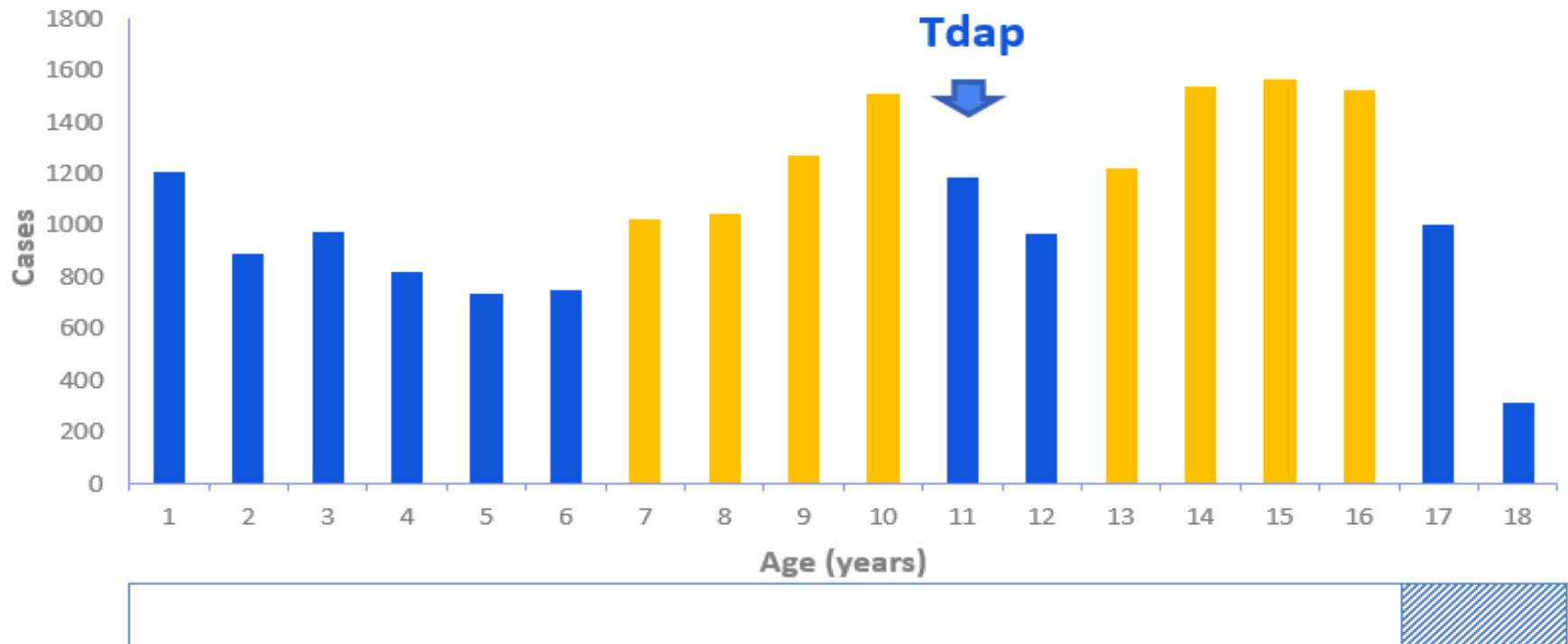
# Reported Pertussis Cases by Age, United States 2010 (N=27.550)



# Reported Pertussis Cases by Age, United States 2012 (N=48.277)



# Reported Pertussis Cases by Age, United States 2014 (N=32,971)



Acellular only

Mix of whole-cell and acellular

**Vaccine effectiveness studies evaluate duration of protection**

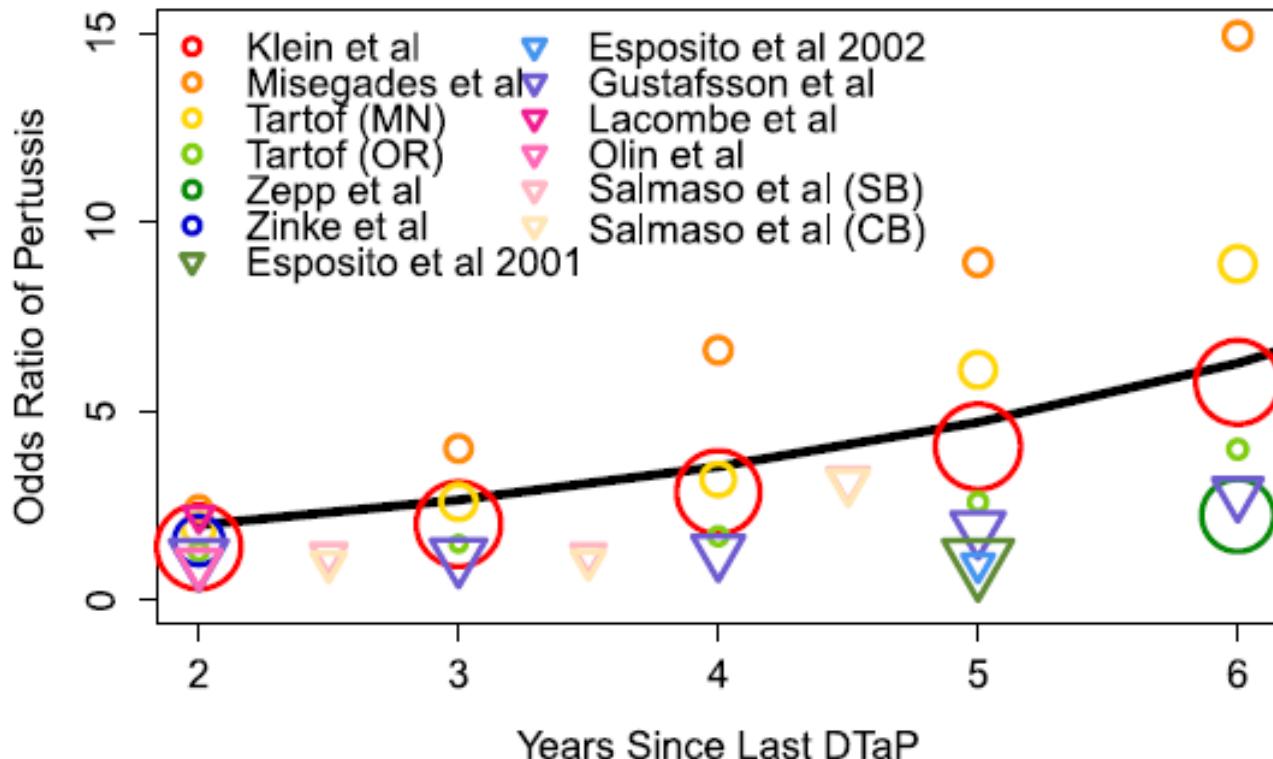
# DTaP Vaccine Effectiveness (VE)– California, 2010

	Case (n)	Control (n)	VE, %	95% CI
<b>Overall VE, all ages (4-10 years)</b>				
0 dose	53	19	Ref	--
5 doses	629	1,997	88.7	79.4 – 93.8

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0 dose	53	19	Ref	--
5 doses	629	1,997	88.7	79.4 – 93.8
<b>Time since 5<sup>th</sup> dose</b>				
0 doses	53	19	Ref	--
< 12 months	19	354	98.1	96.1 – 99.1
12 – 23 months	51	391	95.3	91.2 – 97.5
24 – 35 months	79	366	92.3	86.6 – 95.5
36 – 47 months	108	304	87.3	76.2 – 93.2
48 – 59 months	141	294	82.8	68.7 – 90.6
60+ months	231	288	71.2	45.8 – 84.8

# DTaP Duration of Protection



# Tdap VE– Washington, 2012

	Case (n)	Control (n)	VE, %	95% CI
<b>Overall VE, all ages</b>				
No Tdap dose	109	154	Ref	---
Tdap dose	342	1092	63.9	49.7 – 74.1

# Tdap VE– Washington, 2012

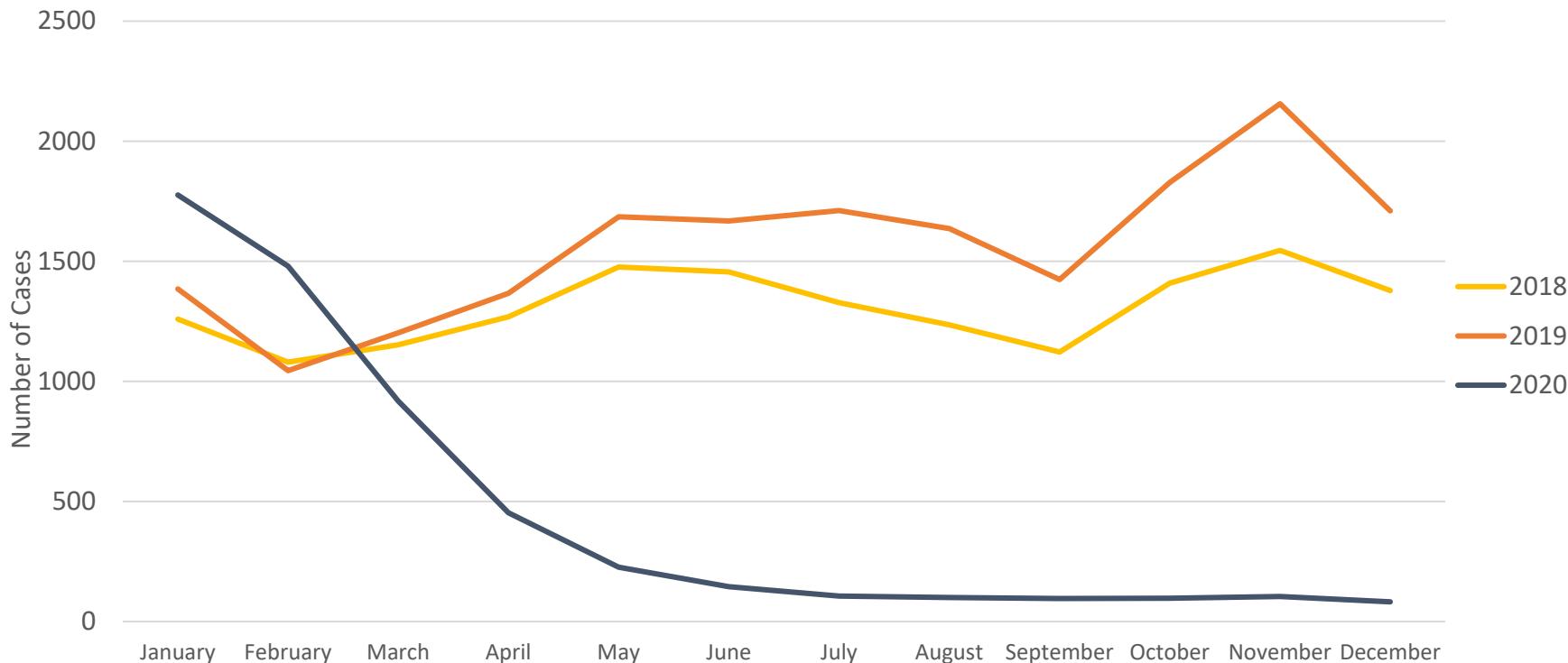
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Tdap dose	342	1092	63.9	49.7 – 74.1
<b>Time since Tdap</b>				
No Tdap dose	109	154	Ref	---
< 1 year	69	332	73.1	60.3-81.8
1 - < 2 years	124	389	54.9	32.4-70.0
2 - < 4 years	148	371	34.2	-0.03-58.0

# Tdap Duration of Protection

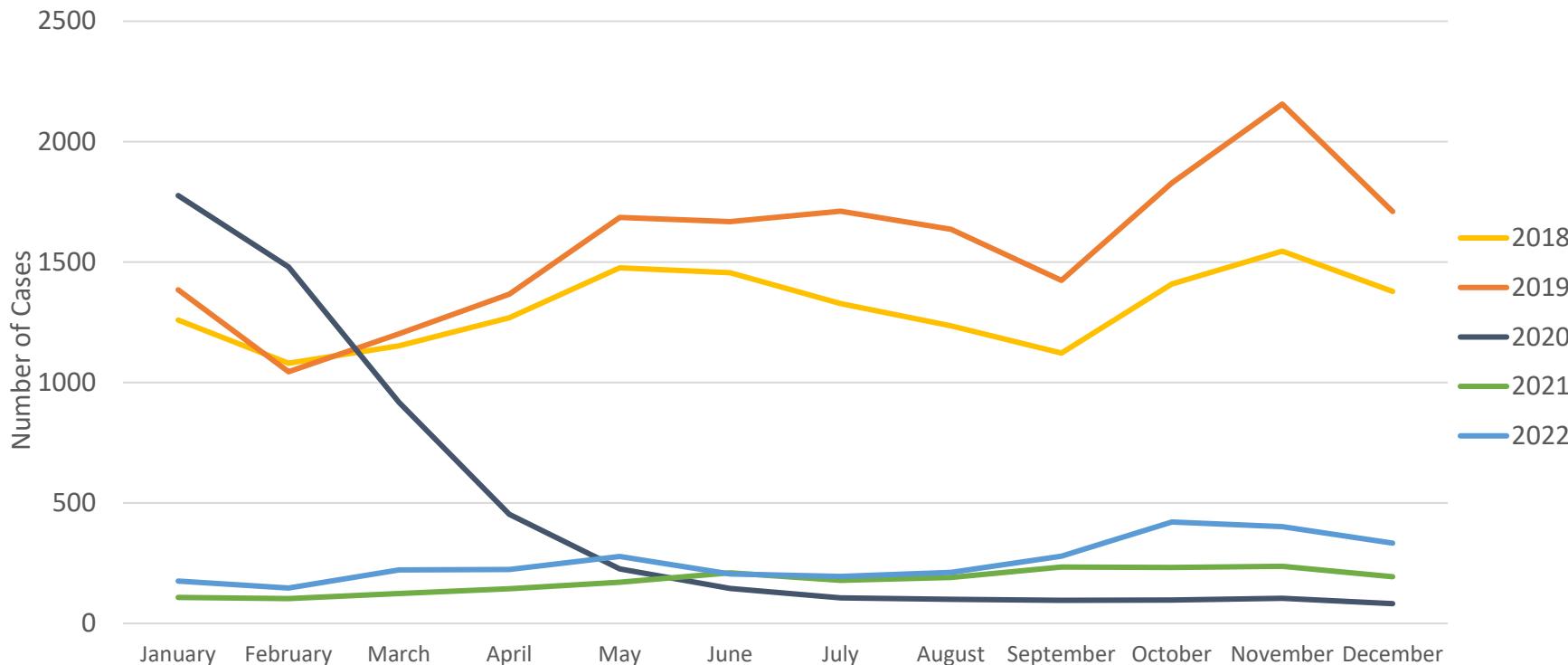
<i>Time since Tdap</i>	Koepke, 2014	Acosta, 2015	Klein, 2016	Breakwell, 2016	Briere, 2018
Vaccine effectiveness (%)					
<1 year	75	73	68	76	62
1- <2 years	68	54	56	63	
2- <4	34	32	25	56	21

# Post-pandemic pertussis epidemiology

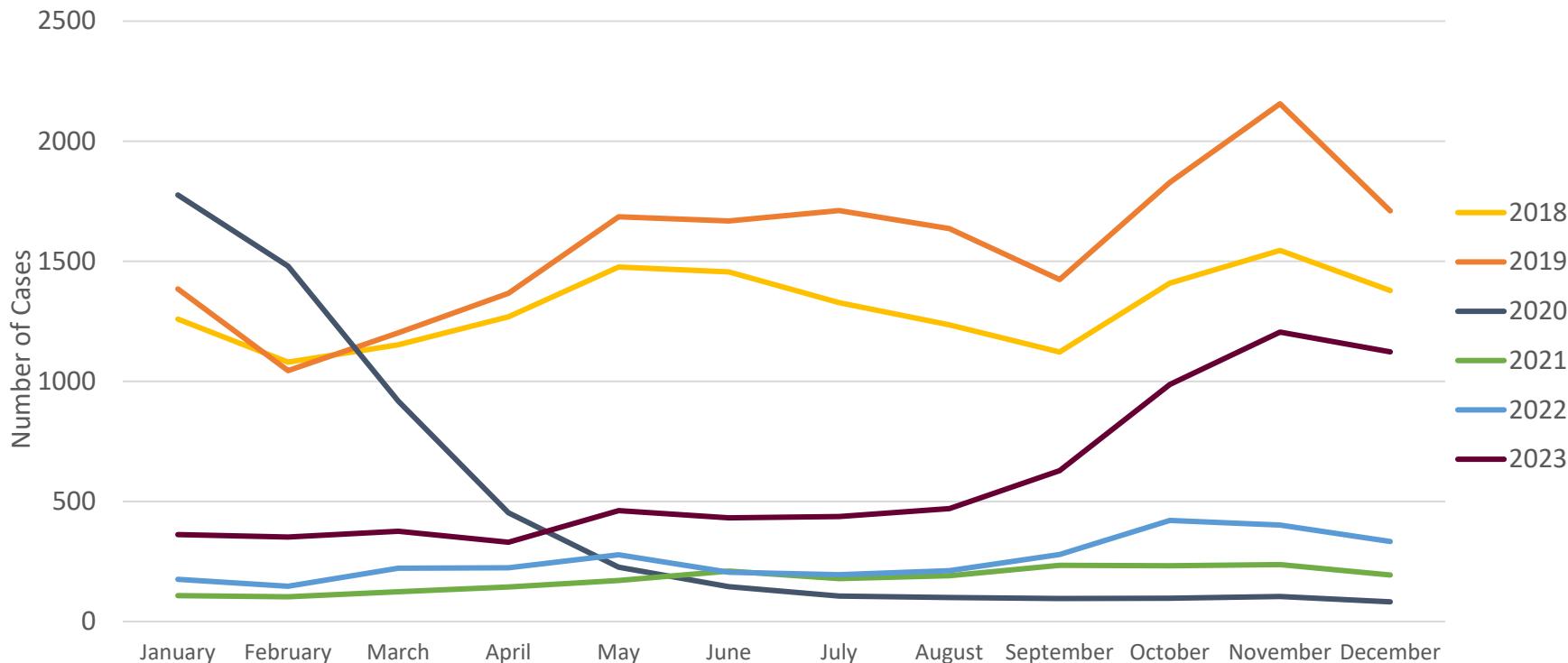
# Reported Pertussis Cases, United States, 2018-2020



# Reported Pertussis Cases, United States, 2018-2022



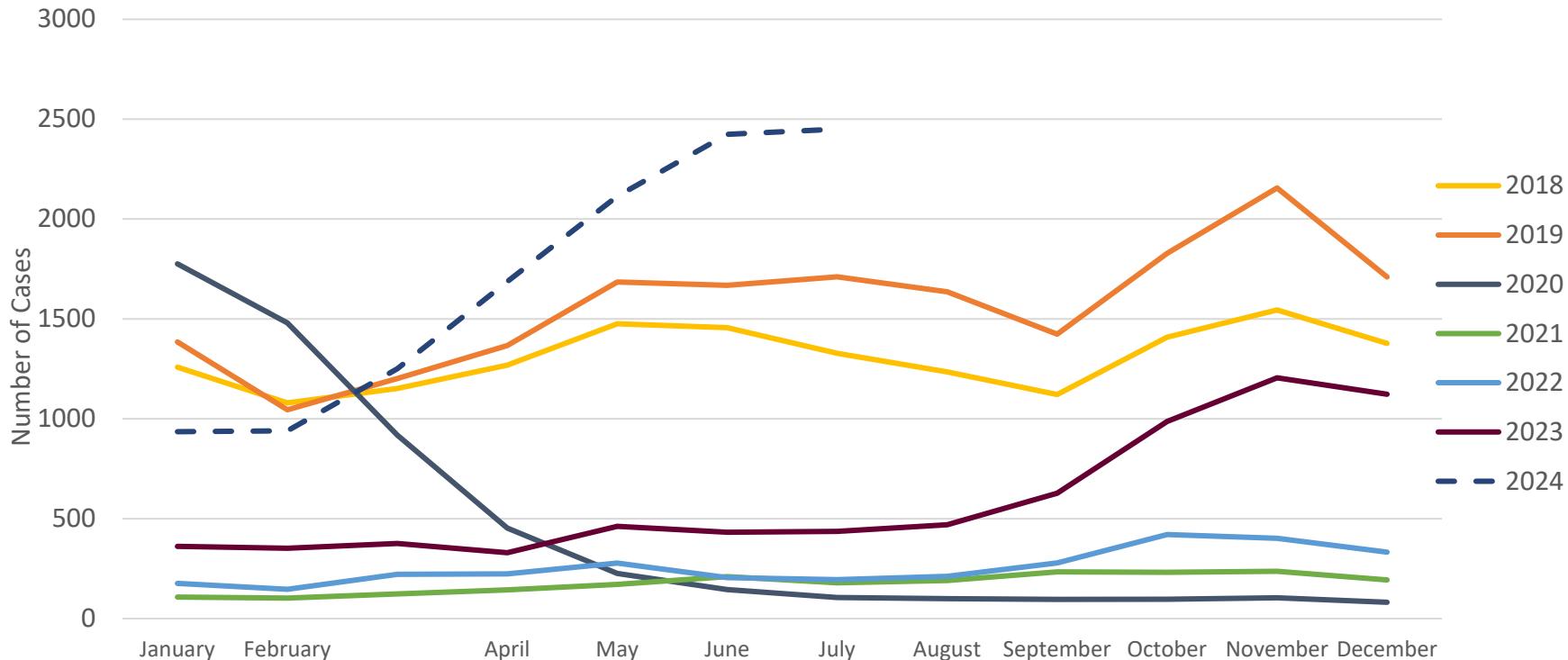
# Reported Pertussis Cases, United States, 2018-2023\*



\*2023 and 2024 data are provisional

CDC, National Notifiable Diseases Surveillance System, Updated September 6<sup>th</sup> 2024

# Reported Pertussis Cases, United States, January 2018-July 2024\*

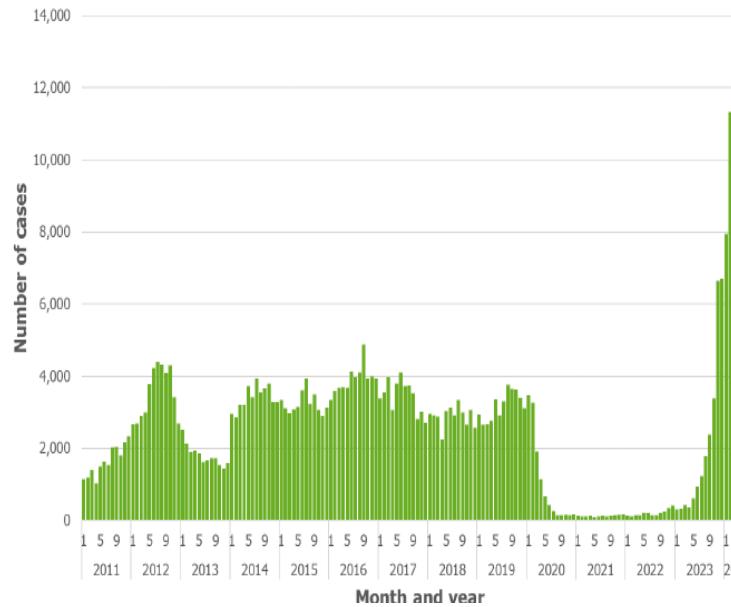


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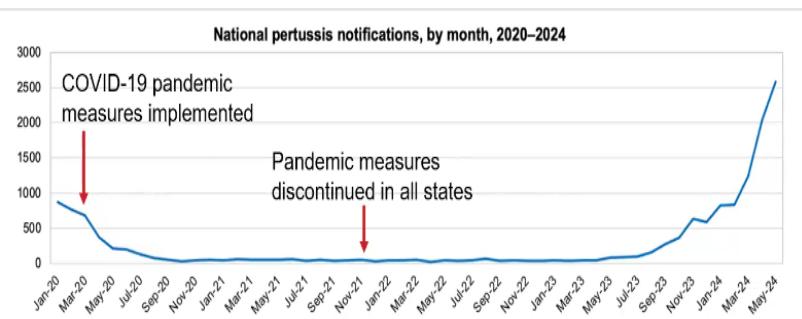
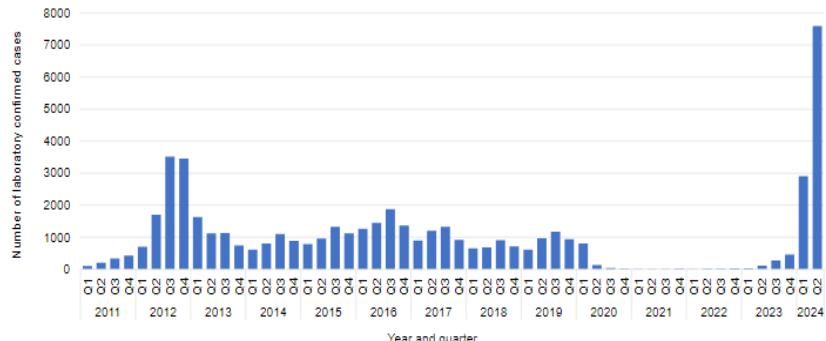
SOURCE: CDC, National Notifiable Diseases Surveillance System, Updated September 6<sup>th</sup> 2024

# Post-pandemic Rebound in Other Countries

**Figure 1.** Number of pertussis cases reported to ECDC, by month and year, 1 January 2011 to 31 March 2024<sup>4</sup>, EU/EEA<sup>3</sup>



**Figure 3. Laboratory confirmed cases of pertussis by quarter in England: 2011 to June 2024 (note 1)**

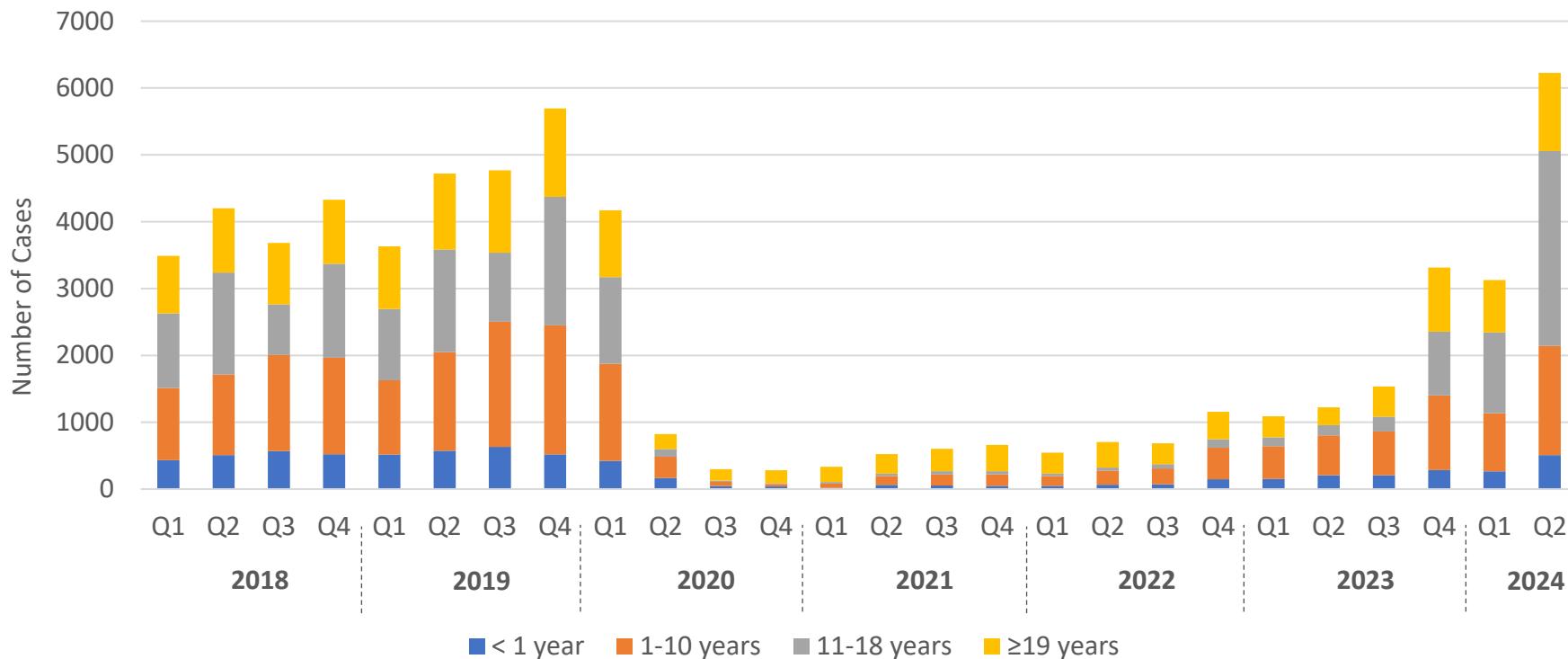


[Increase of pertussis cases in the EU/EEA \(europa.eu\)](https://ecdc.europa.eu/en/increase-pertussis-cases-eu-eea)

[Confirmed cases of pertussis in England by month - GOV.UK \(www.gov.uk\)](https://www.gov.uk/government/statistics/confirmed-cases-of-pertussis-in-england-by-month)

Presentation at 14<sup>th</sup> International Bordetella Symposium

# Reported Pertussis Cases by Year, Quarter, and Age, 2018–Q2 2024\*



\*2023 and 2024 data are provisional

CDC, National Notifiable Diseases Surveillance System, Updated September 6<sup>th</sup> 2024

# Outbreaks Reported Across the Country

**HEALTH** Whooping cough [Add Topic +](#)

**New York health officials sound alarm on whooping cough outbreak in schools**

Emilee Coblenz, USA TODAY  
Published 8:00 p.m. ET Jan. 3, 2024 | Updated 8:00 p.m. ET Jan. 3, 2024

**The Mirror US on MSN** · 3d

**Schools across US seeing outbreaks of whooping cough as cases soar**

The Register-Guard · [San Francisco Chronicle](https://www.sfgate.com) · <https://www.sfgate.com> · [Bay Area whooping cough outbreak](#) · WEB Mar 27, 2024 · Whooping cough, also known as the highly contagious illness impacting Wisconsin

Whooping cough cases reported in Lane County as Oregon case counts continue to spike

Lane County Public Health has declared a "community-wide outbreak" of pertussis, commonly called whooping cough. On [mlive](https://www.mlive.com/public-interest/2023) · <https://www.mlive.com/public-interest/2023> · [Whooping cough outbreak reported](#) · WEB Oct 18, 2023 · Six cases of pertussis illness, also known as whooping cough, were reported in Northern Michigan -

**Wausau-Rhinelander WSAW-TV** · [Marathon Co. health officials caution everyone amid whooping cough outbreak](#) · [7 Wausau-Rhinelander WSAW-TV](#) · [Follow](#)

**High outbreak reported in North Carolina**

WSPA - A whooping cough outbreak has been reported in North Carolina. The North Carolina Department of Health and Senior Services (DHSS) said 27 cases of whooping cough, known as pertussis, have been reported in the state so far this year. The cases are scattered across the state, with the highest number of cases reported in the western part of the state. The whooping cough outbreak is believed to have started in late December and has continued through January. The whooping cough outbreak is believed to have started in late December and has continued through January. The whooping cough outbreak is believed to have started in late December and has continued through January.

**Whooping cough cases on the rise, nearly 3 times as high as last year: CDC**

There have been at least 4,864 whooping cough cases reported this year so far.

By [Mary Kekatos](#) and [Dr. Michelle March](#)  
May 31, 2024, 2:22 PM

**abc NEWS**

**At least 4,864 cases have been reported so far this year, which is much higher than the 1,746 cases reported at the same time last year.**

**PERTUSSIS (WHOOPING COUGH) OUTBREAK in Lexington**

# Summary

- Pertussis morbidity and mortality significantly lower than pre-vaccine era but remains significant public health burden
- Pertussis resurgence associated with introduction of acellular vaccines
  - Waning immunity from current vaccines well documented
- Need for improved vaccines with longer duration of protection
  - Development impeded by longstanding knowledge gaps and lack of accepted correlate of protection
  - No clear pathway to licensure
    - Infant vaccine efficacy studies with unvaccinated controls unethical
    - Booster vaccine efficacy studies long, expensive, and won't address duration of protection

# Thank you

Susan Hariri, PhD

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