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Pertussis Epidemiology in the Acellular Vaccine Era

Susan Hariri, PhD

Division of Bacterial Diseases

National Center for Immunization and Respiratory Diseases

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

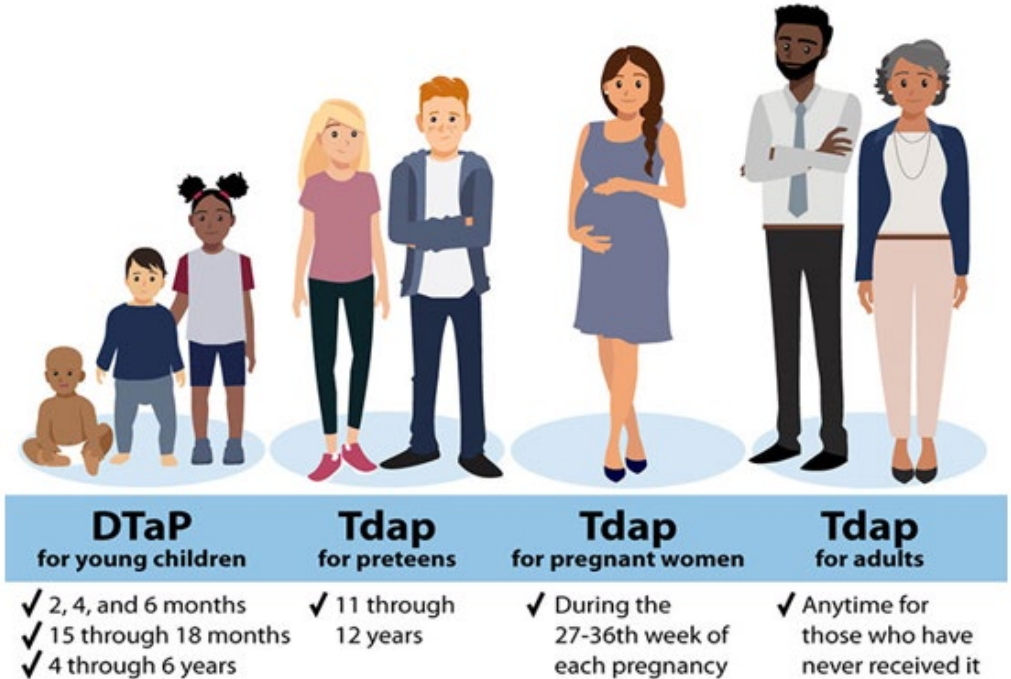
Pertussis Epidemiology

- **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

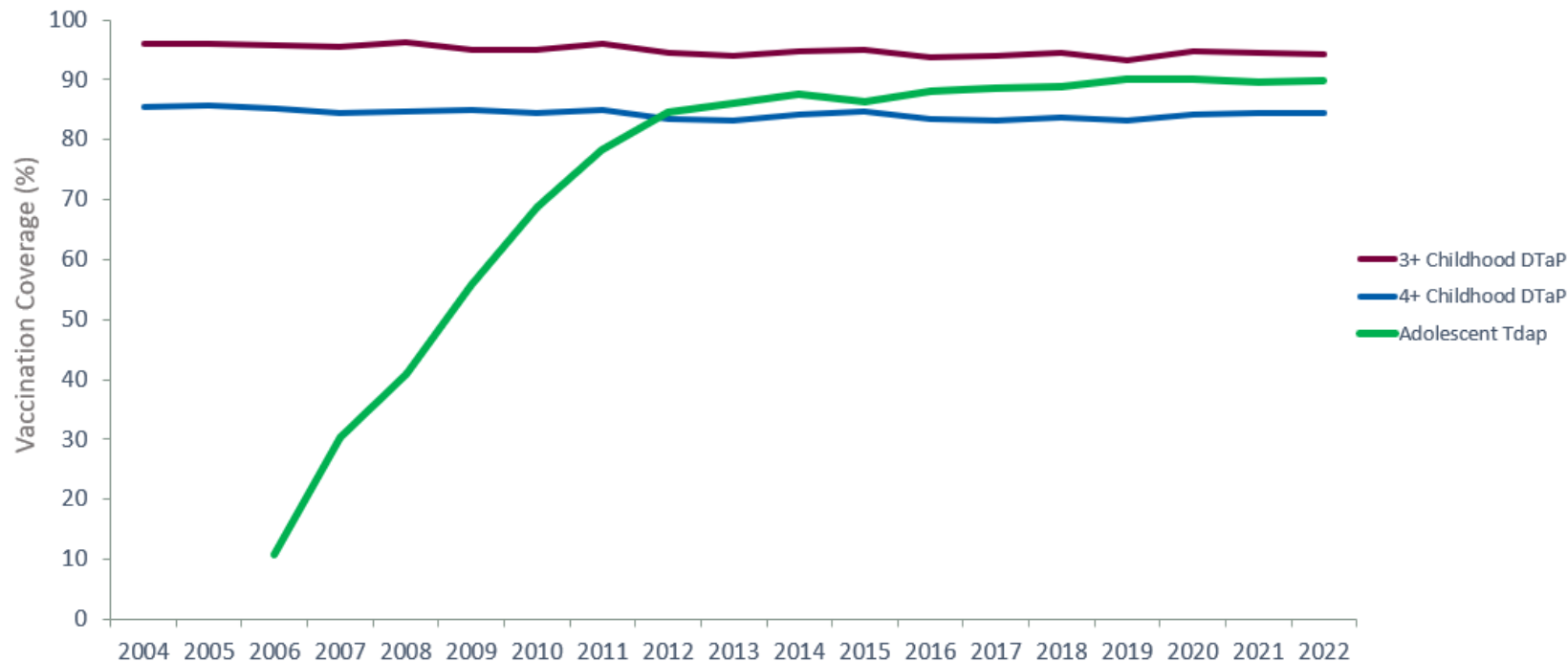
Pertussis Vaccines

- **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

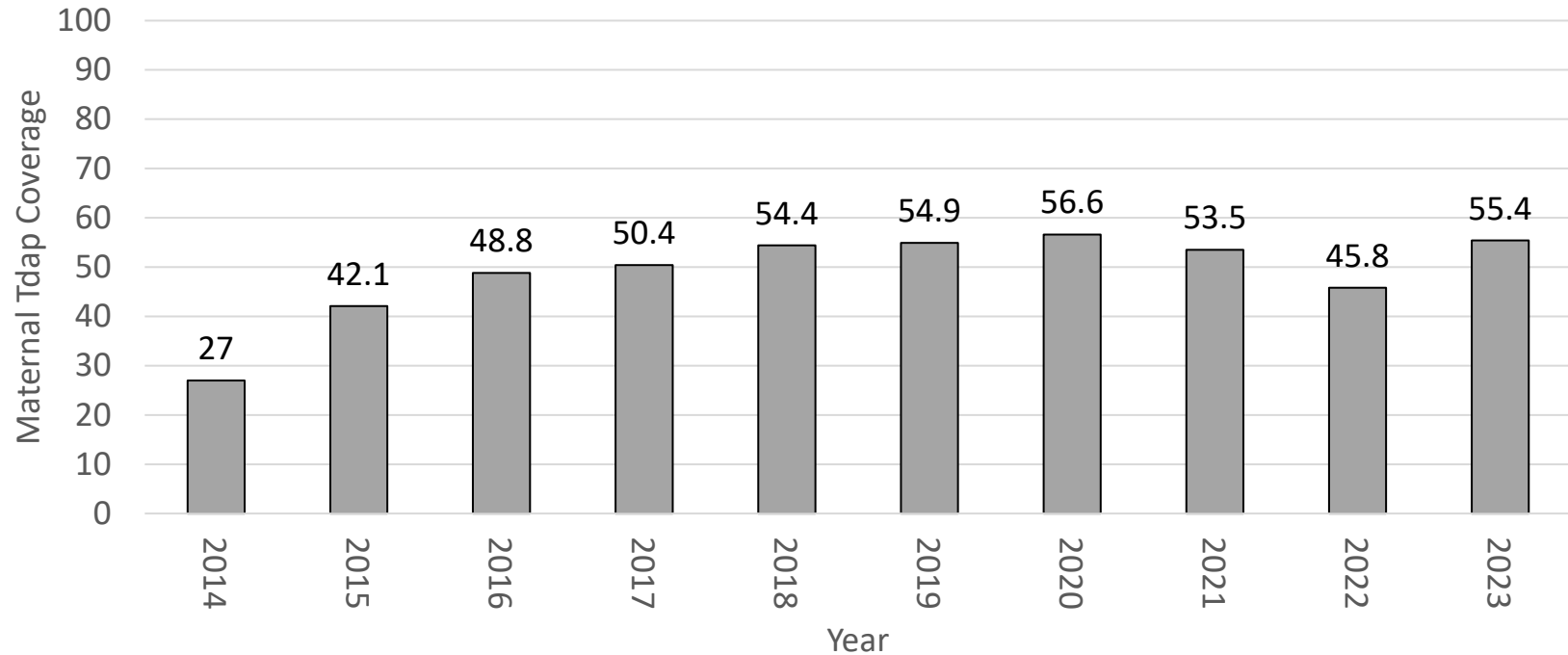
United States Pertussis Vaccination Schedule



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

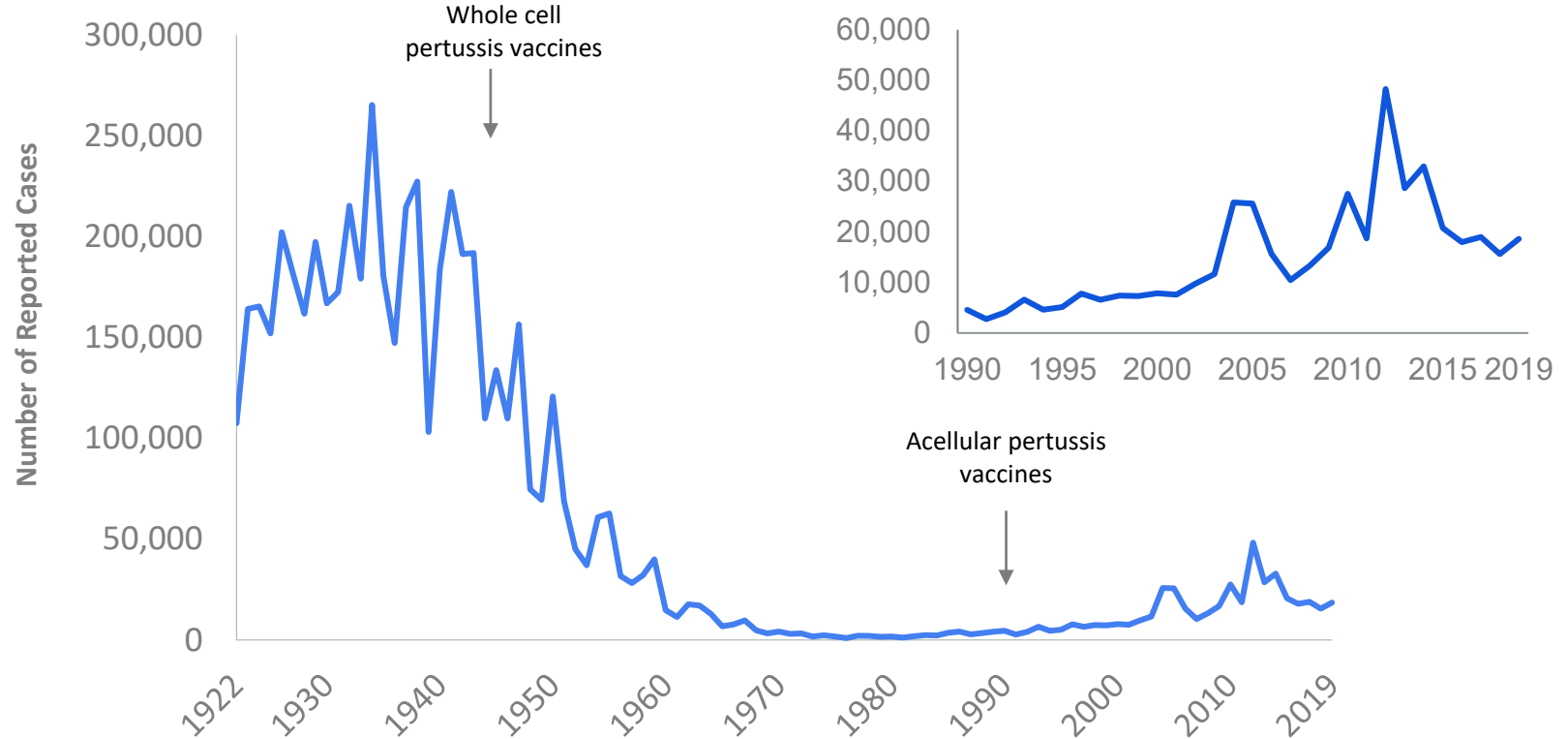


Maternal Tdap Coverage, United States, 2014-2023

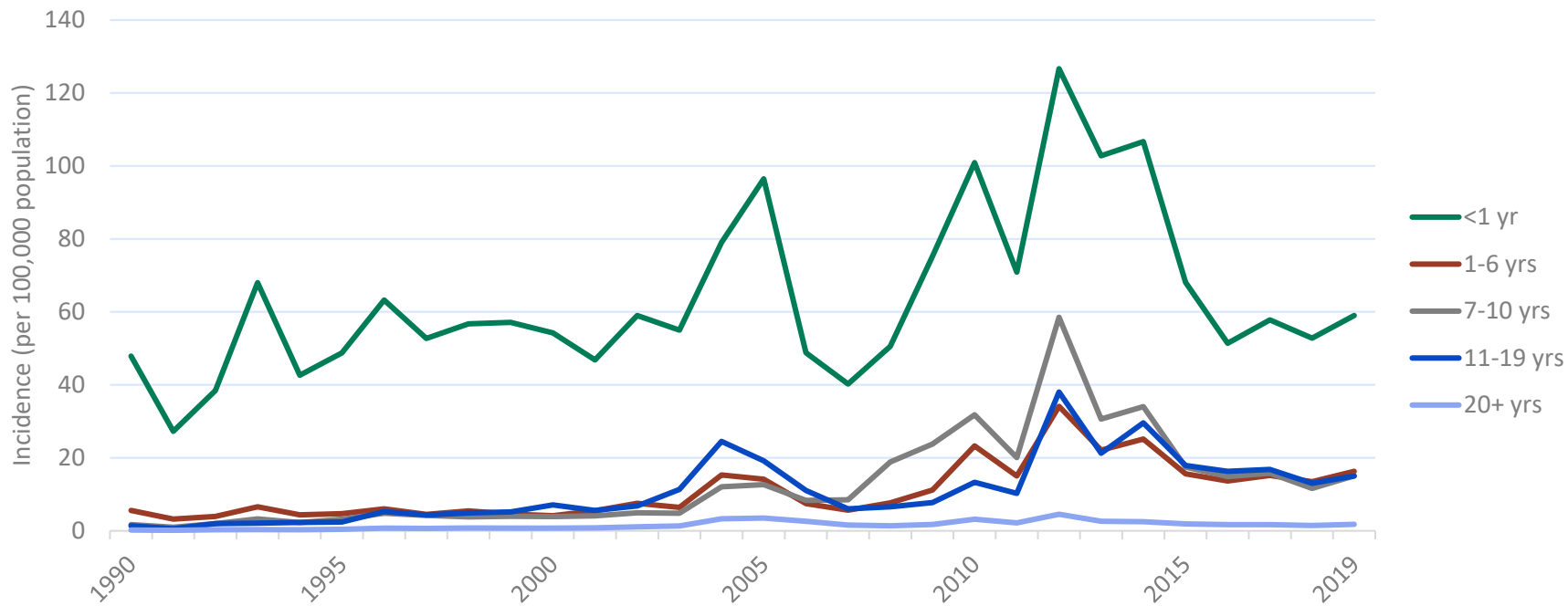


Historical trends in reported pertussis cases, United States

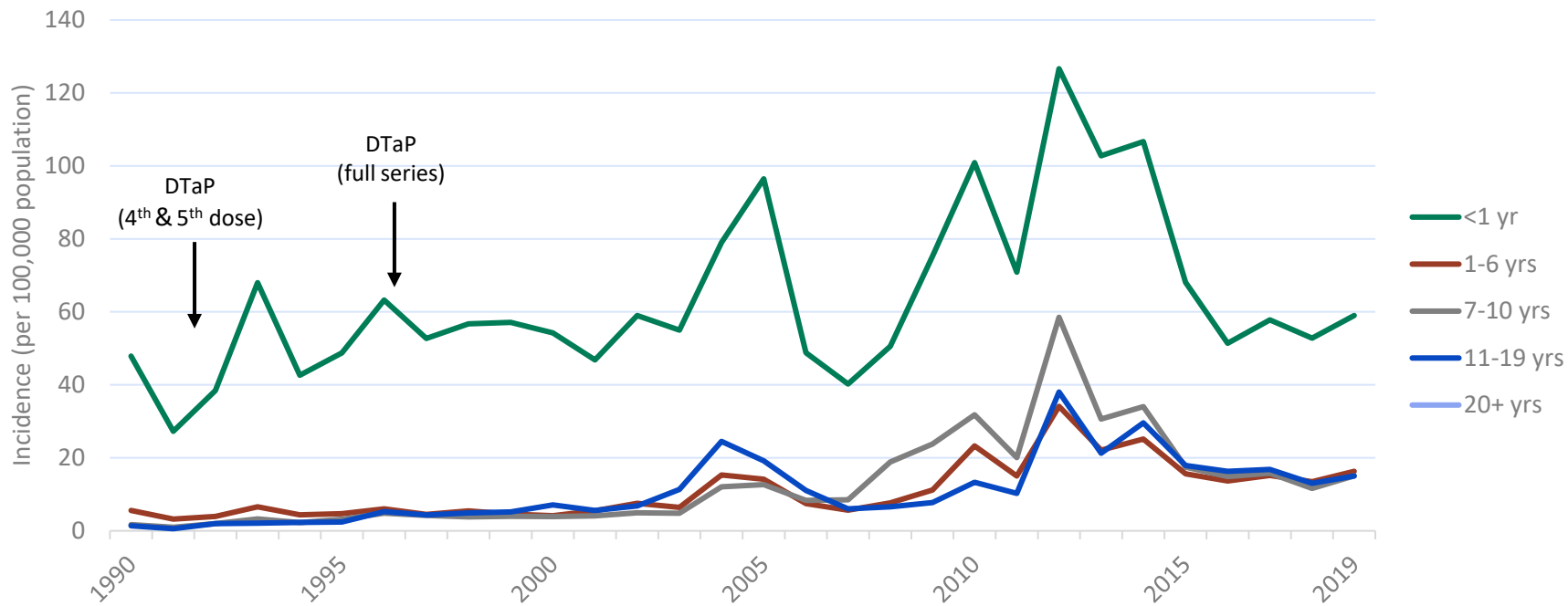
Reported Pertussis Cases, United States, 1922-2019



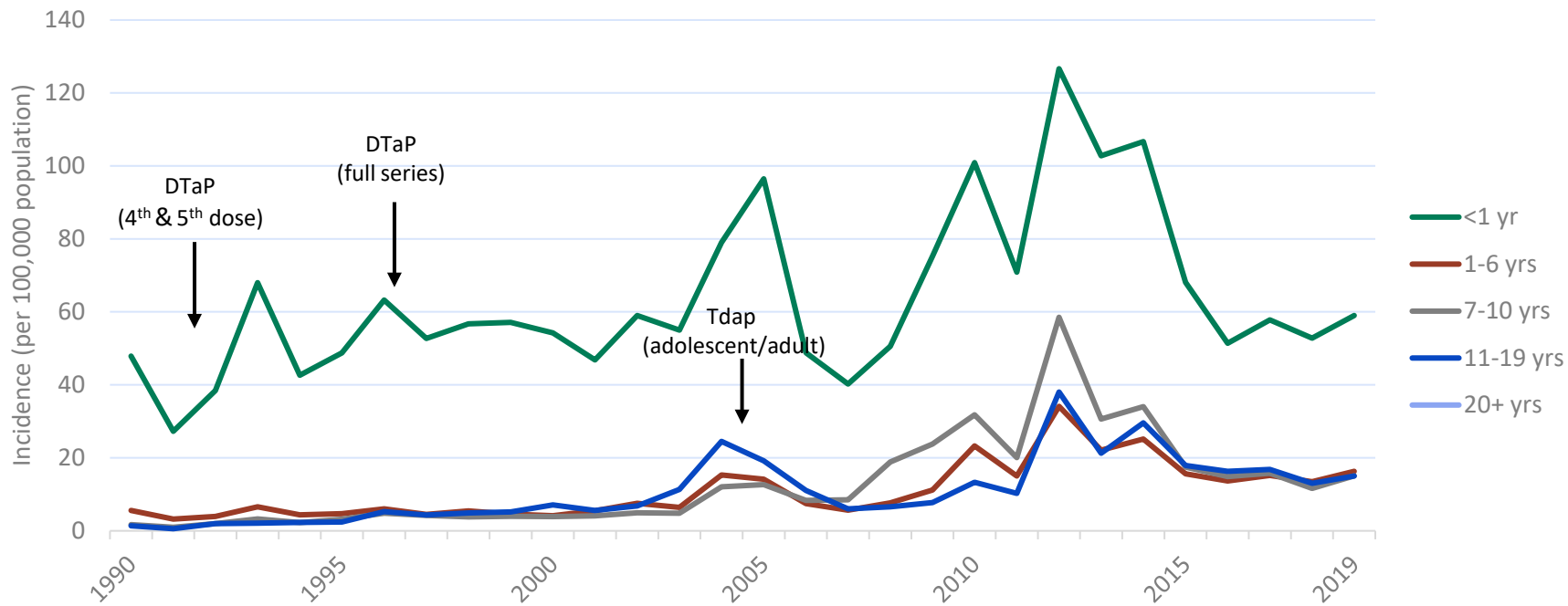
Pertussis Incidence by Age Group, United States, 1990-2019



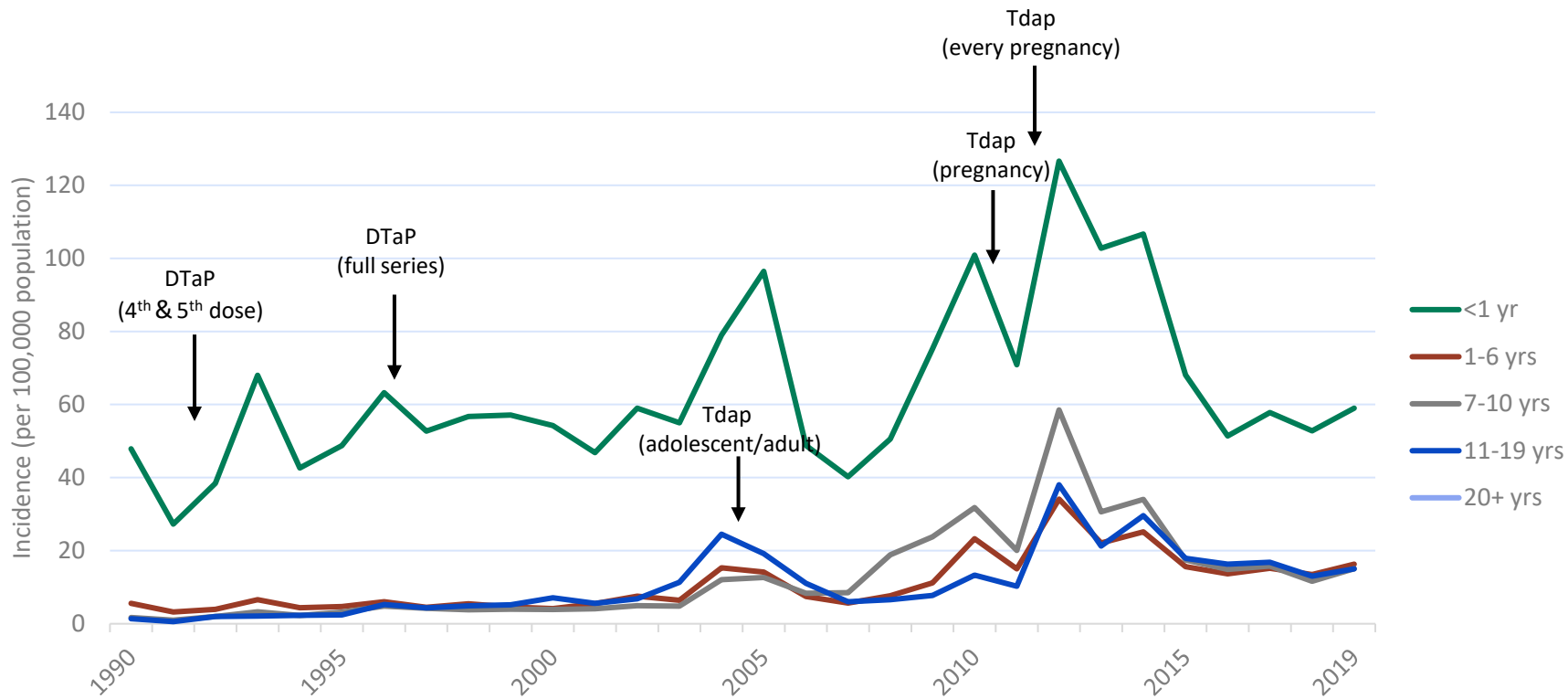
Pertussis Incidence by Age Group, United States, 1990-2019



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Possible Reasons for Pertussis Resurgence

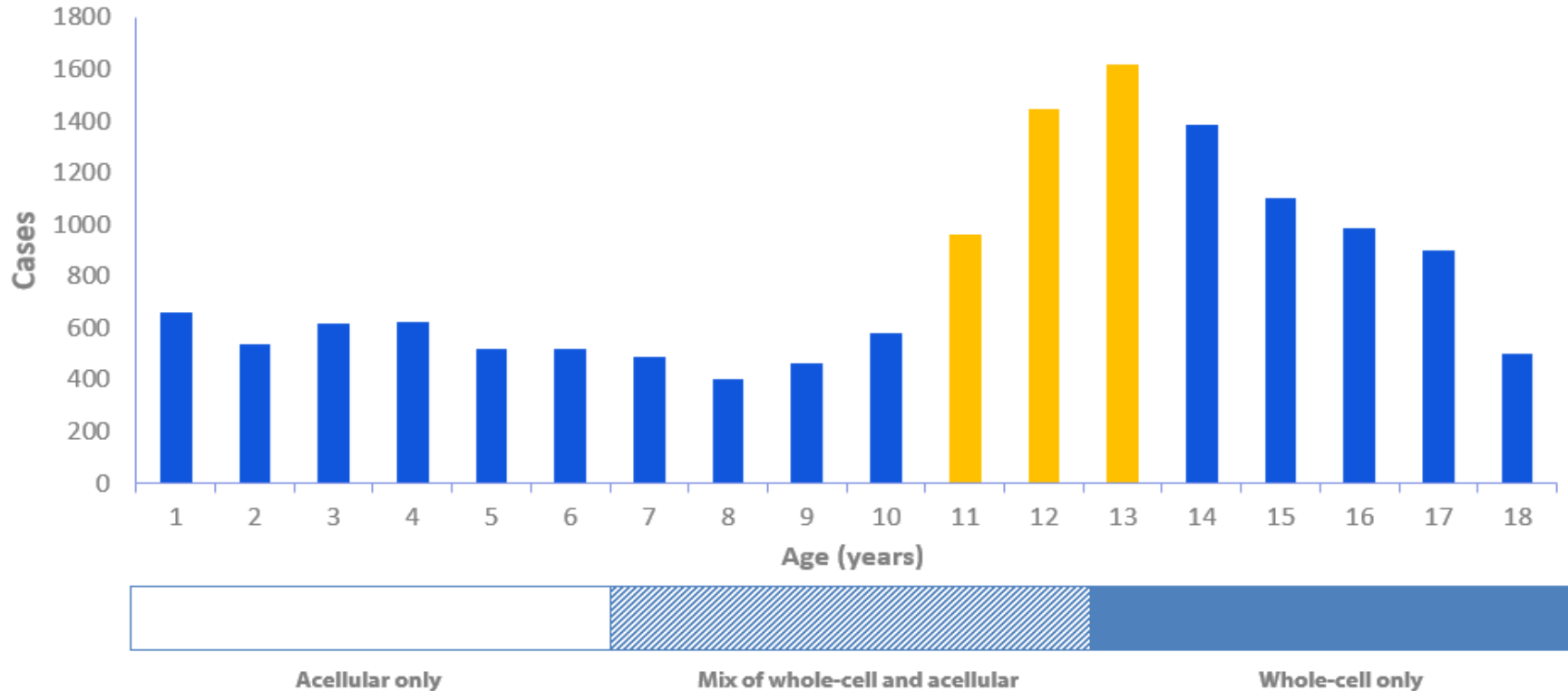
- Improved, more sensitive diagnostic tests
- Strain adaptation to vaccine pressure
- Increased awareness and testing

Possible Reasons for Pertussis Resurgence

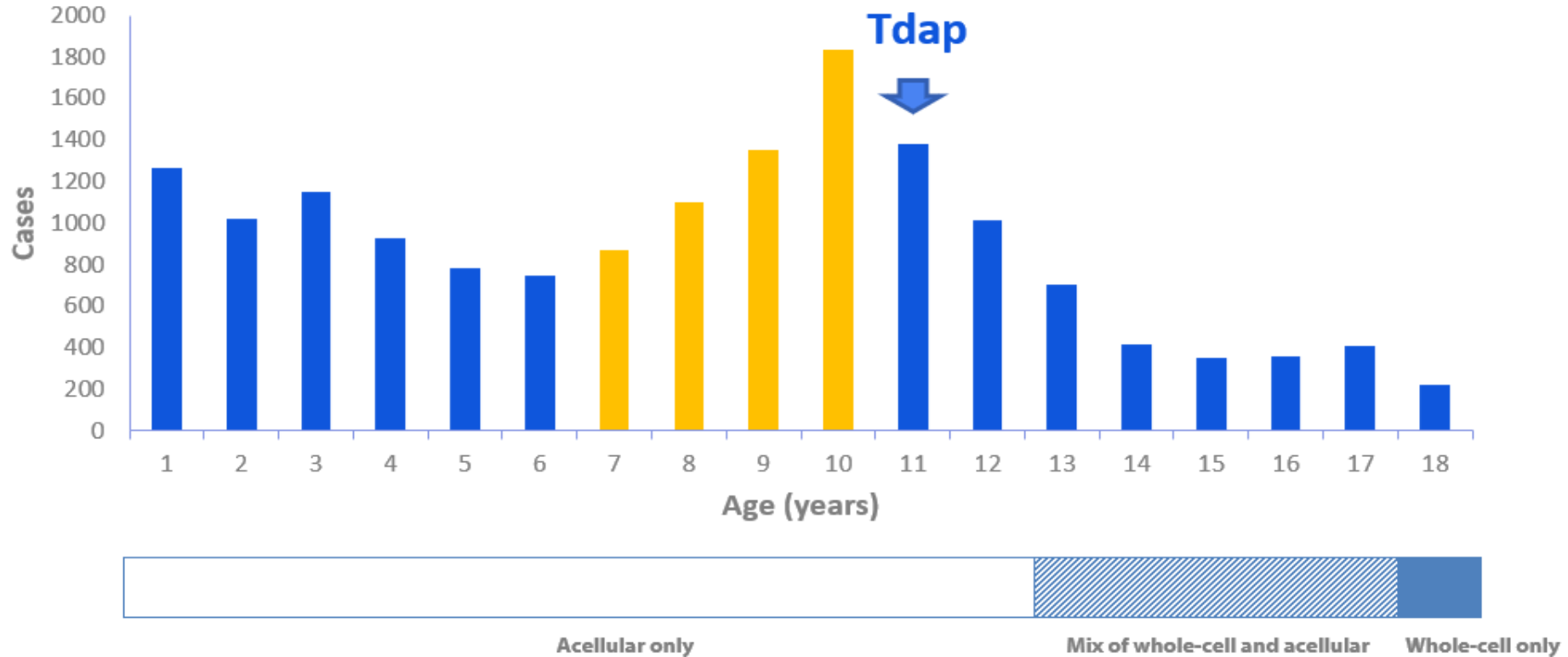
- Improved, more sensitive diagnostic tests
- Strain adaptation to vaccine pressure
- Increased awareness and testing
- **Flawed acellular vaccines**
 - Less protection against transmission
 - Faster waning of immunity

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

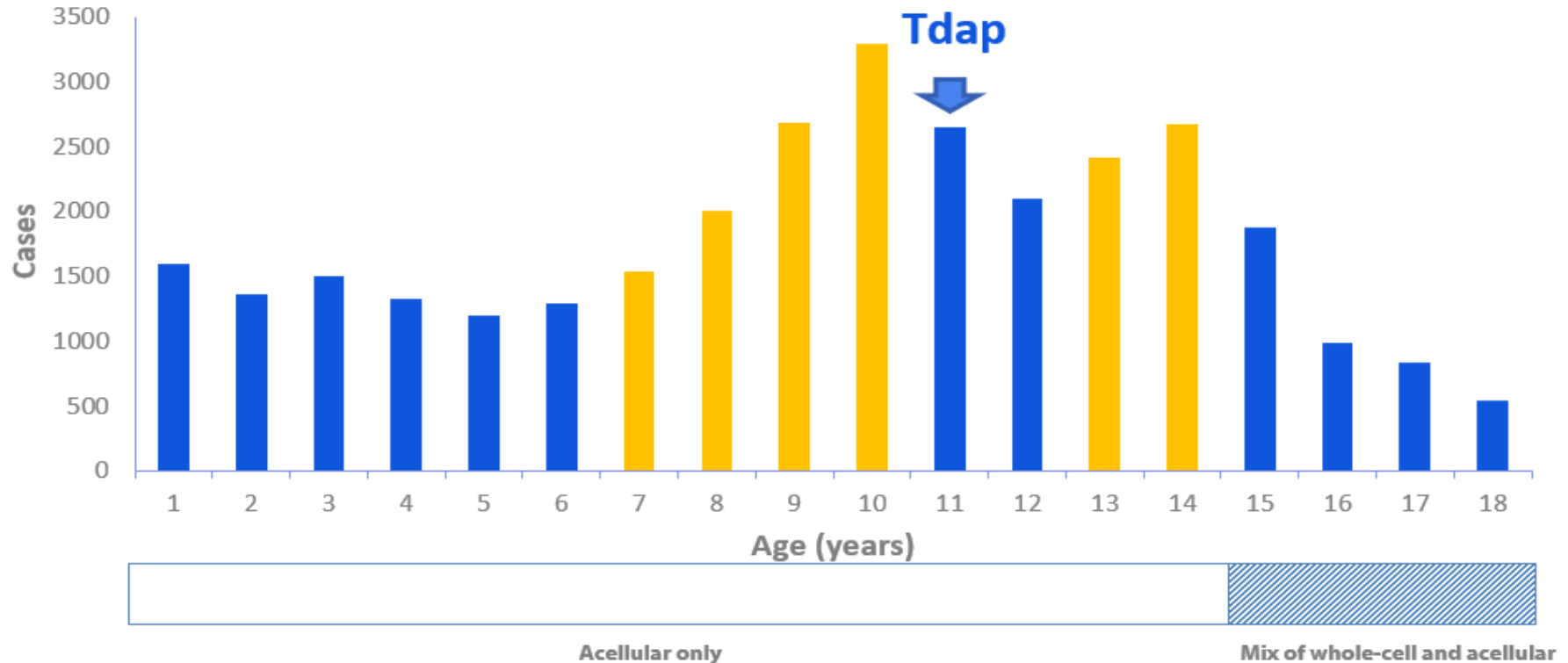
Reported Pertussis Cases by Age, United States 2004 (N=25,827)



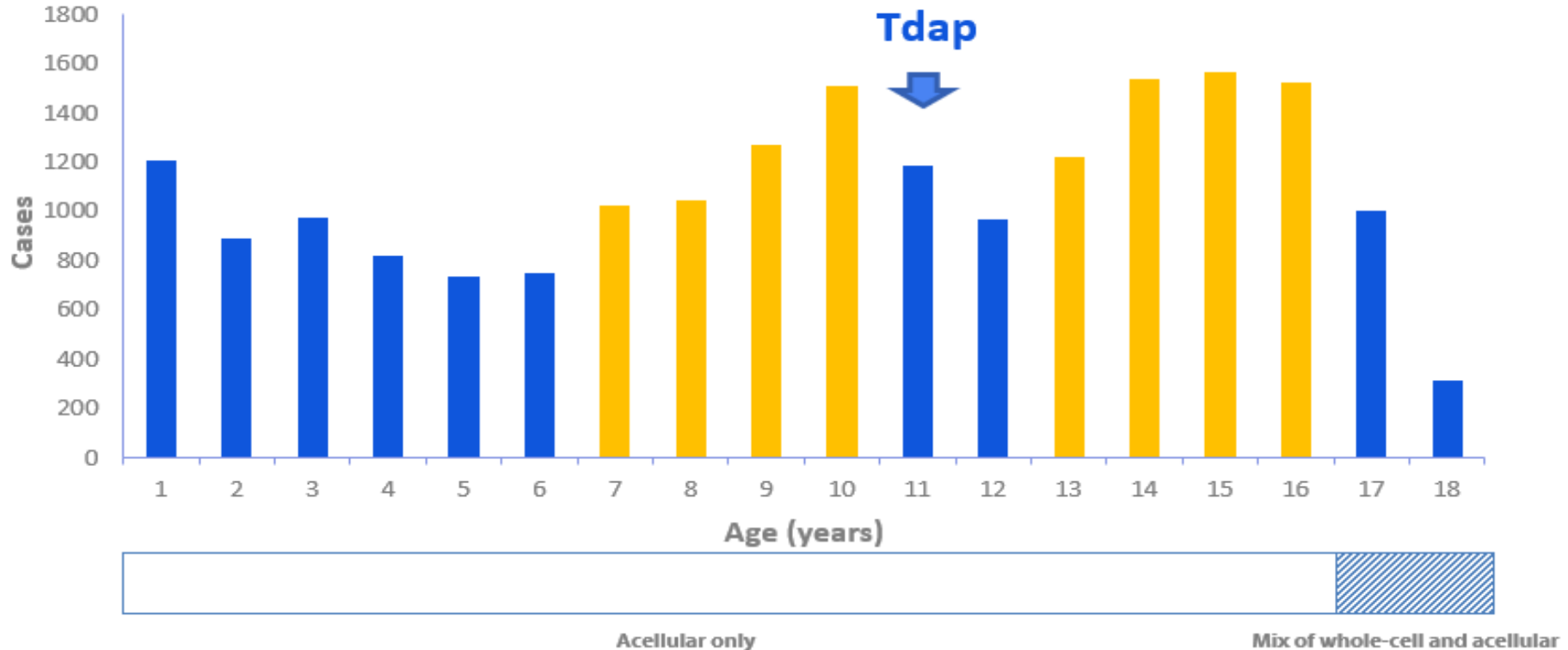
Reported Pertussis Cases by Age, United States 2010 (N=27,550)



Reported Pertussis Cases by Age, United States 2012 (N=48,277)



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



**Vaccine effectiveness studies evaluate
duration of protection**

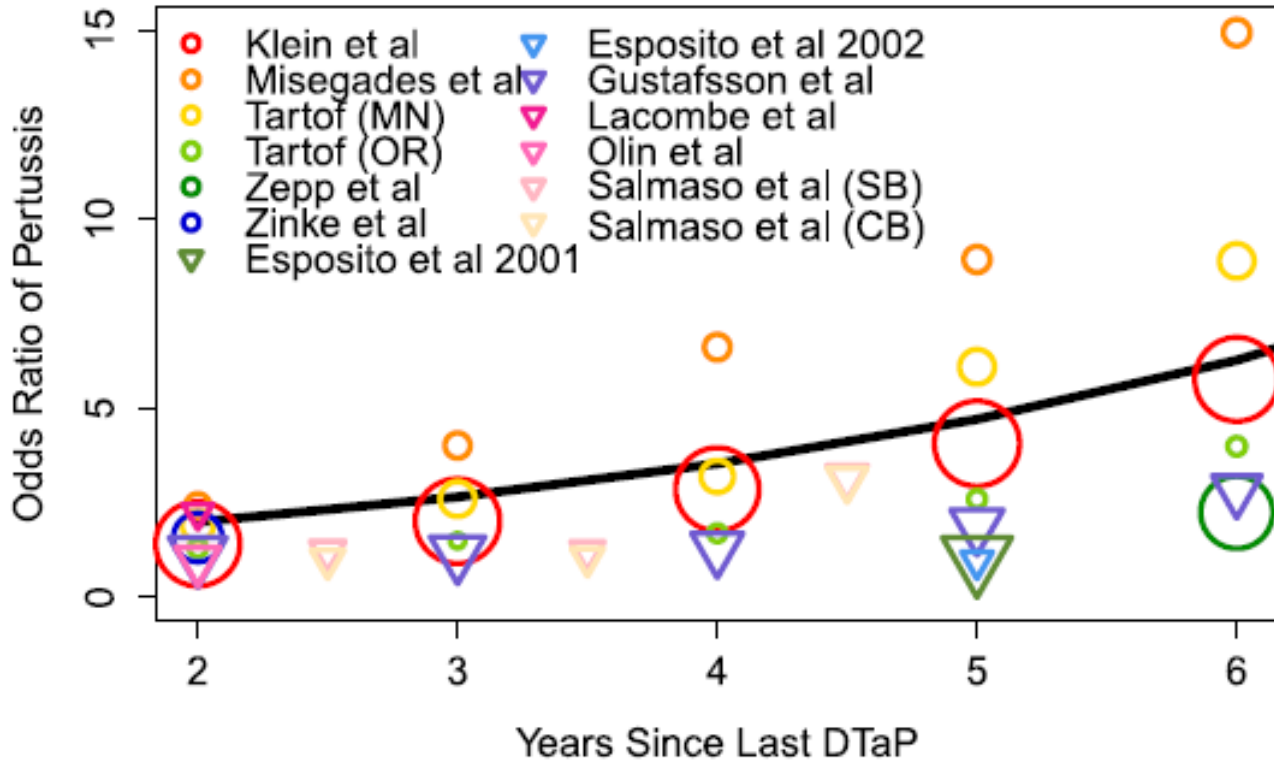
DTaP Vaccine Effectiveness (VE)– California, 2010

	Case (n)	Control (n)	VE, %	95% CI
Overall VE, all ages (4-10 years)				
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
Time since 5th dose				
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
Overall VE, all ages				
No Tdap dose	109	154	Ref	---
Tdap dose	342	1092	63.9	49.7 – 74.1

Tdap VE– Washington, 2012

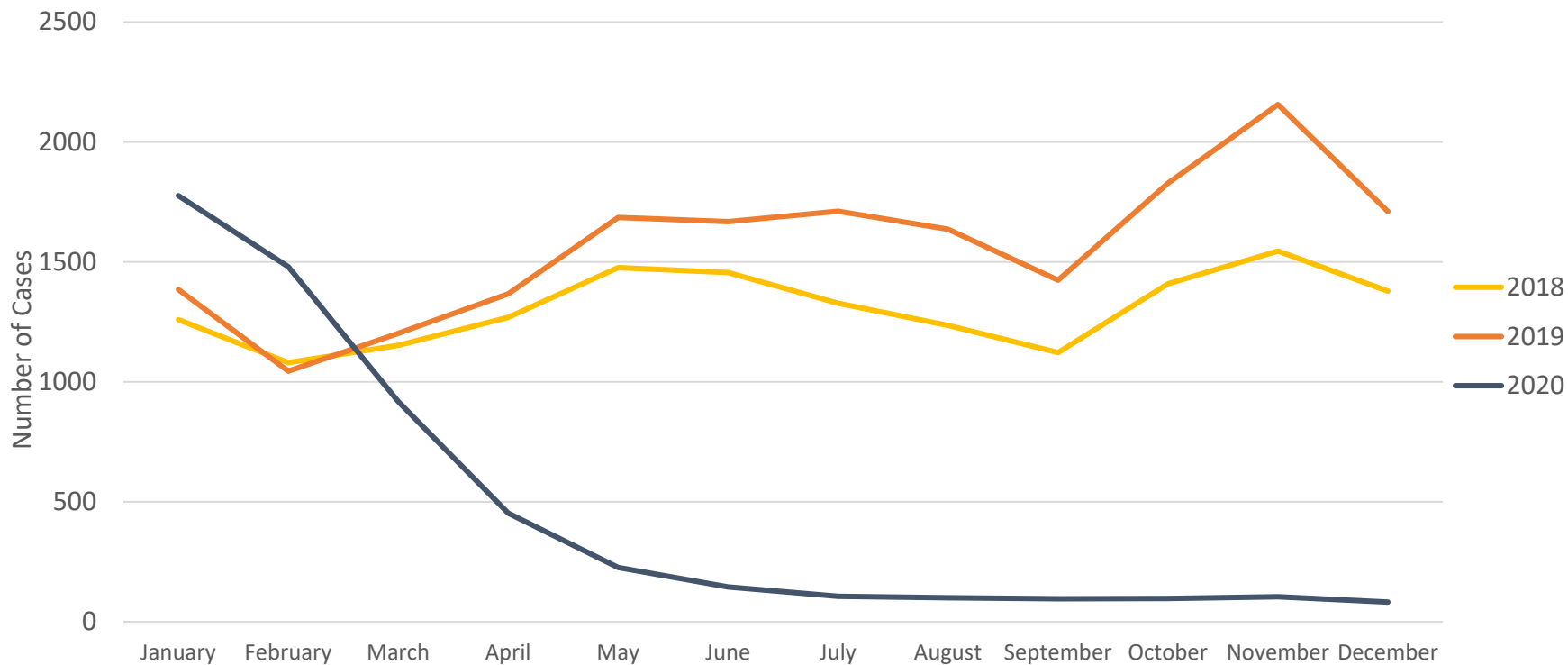
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Overall VE, all ages				
No Tdap dose	109	154	Ref	---
Tdap dose	342	1092	63.9	49.7 – 74.1
Time since Tdap				
No Tdap dose	109	154	Ref	---
< 1 year	69	332	73.1	60.3-81.8
1 - < 2 years	124	389	54.9	32.4-70.0
2 - < 4 years	148	371	34.2	-0.03-58.0

Tdap Duration of Protection

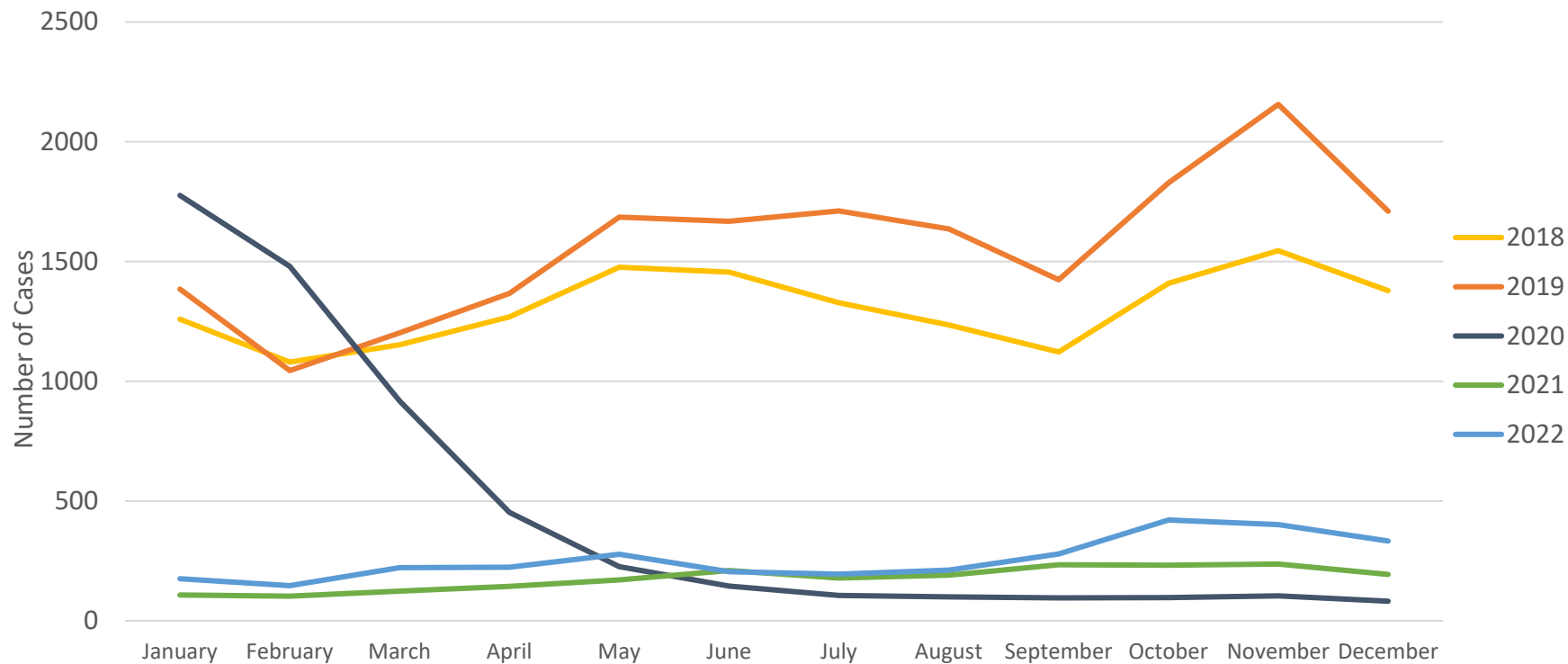
<i>Time since Tdap</i>	Koepke, 2014	Acosta, 2015	Klein, 2016	Breakwell, 2016	Briere, 2018
Vaccine effectiveness (%)					
<1 year	75	73	68	76	62
1- <2 years	68	54	56	63	
2- <4	34	32	25	56	21

Post-pandemic pertussis epidemiology

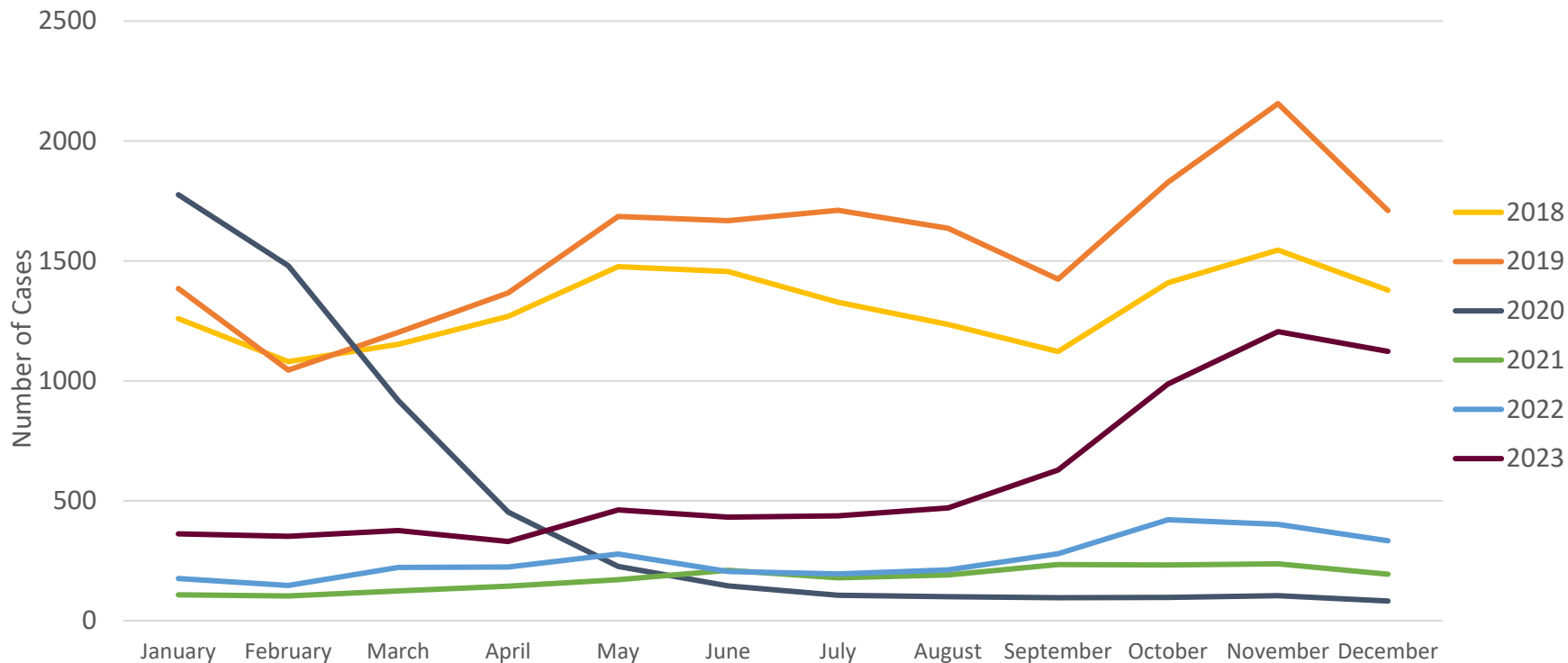
Reported Pertussis Cases, United States, 2018-2020



Reported Pertussis Cases, United States, 2018-2022

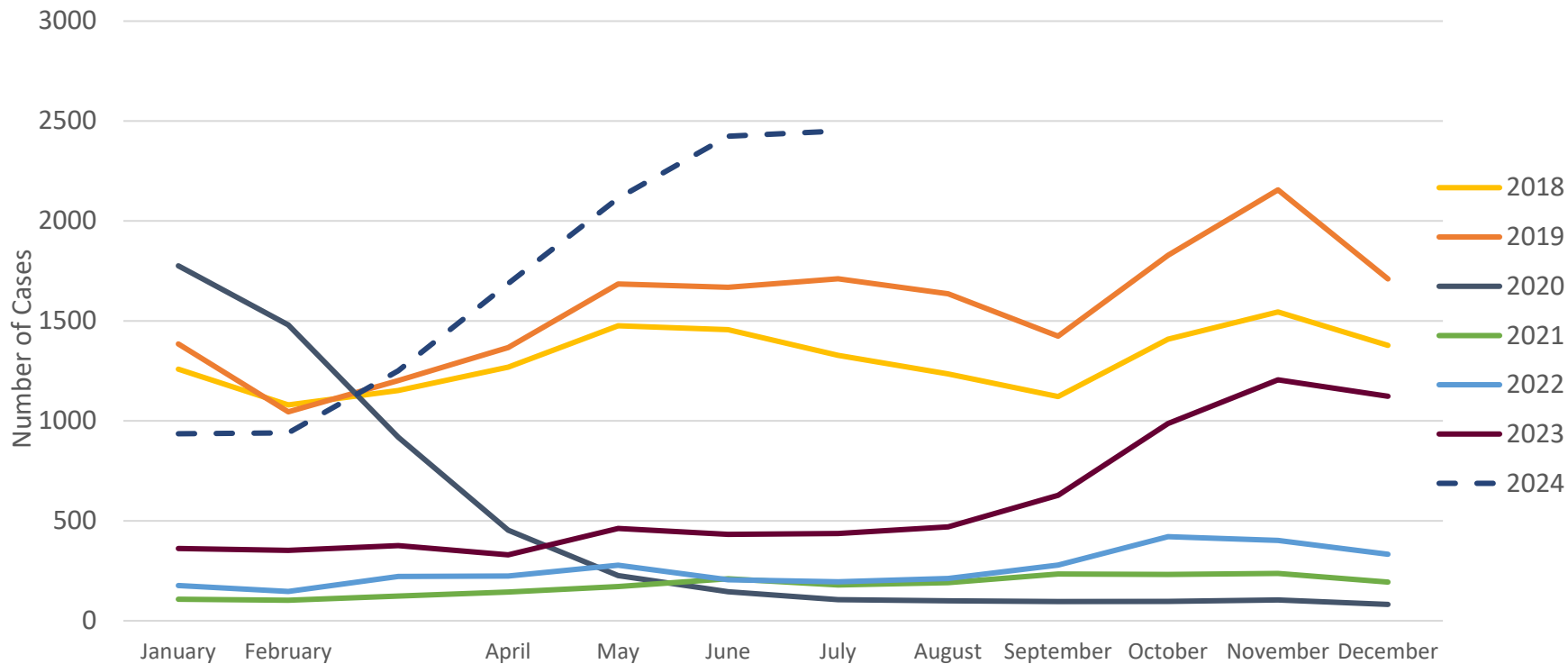


Reported Pertussis Cases, United States, 2018-2023*



*2023 and 2024 data are provisional
CDC, National Notifiable Diseases Surveillance System, Updated September 6th 2024

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

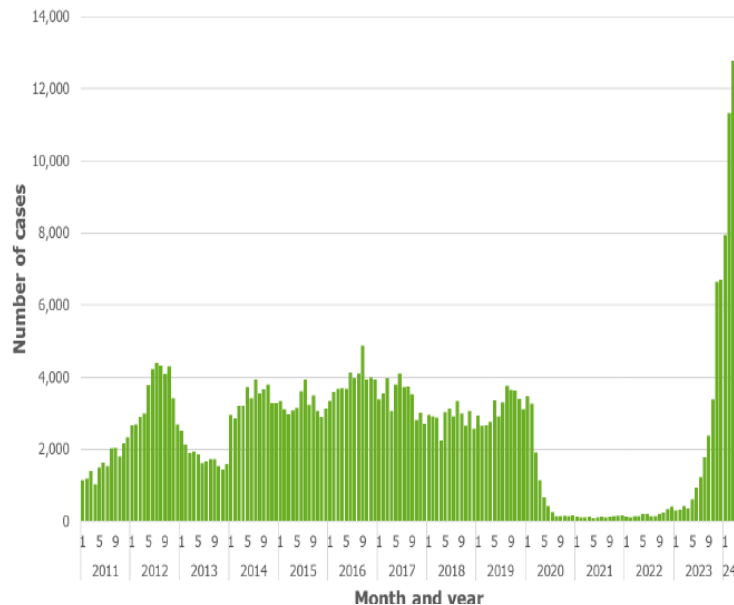


*2023 and 2024 data are provisional

SOURCE: CDC, National Notifiable Diseases Surveillance System, Updated September 6th 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 2024², EU/EEA³

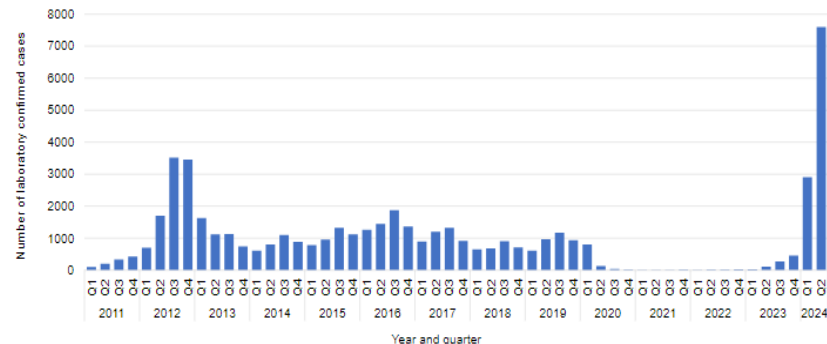


[Increase of pertussis cases in the EU/EEA \(europa.eu\)](https://europa.eu)

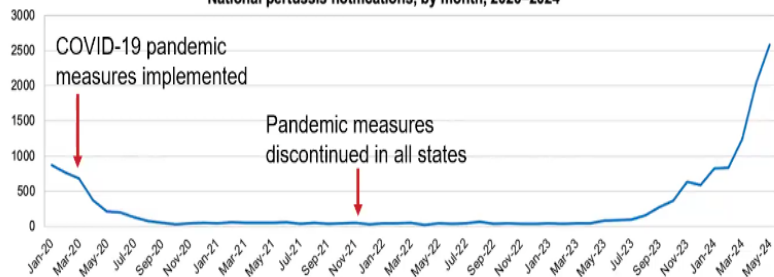
[Confirmed cases of pertussis in England by month - GOV.UK \(www.gov.uk\)](https://www.gov.uk)

Presentation at 14th International Bordetella Symposium

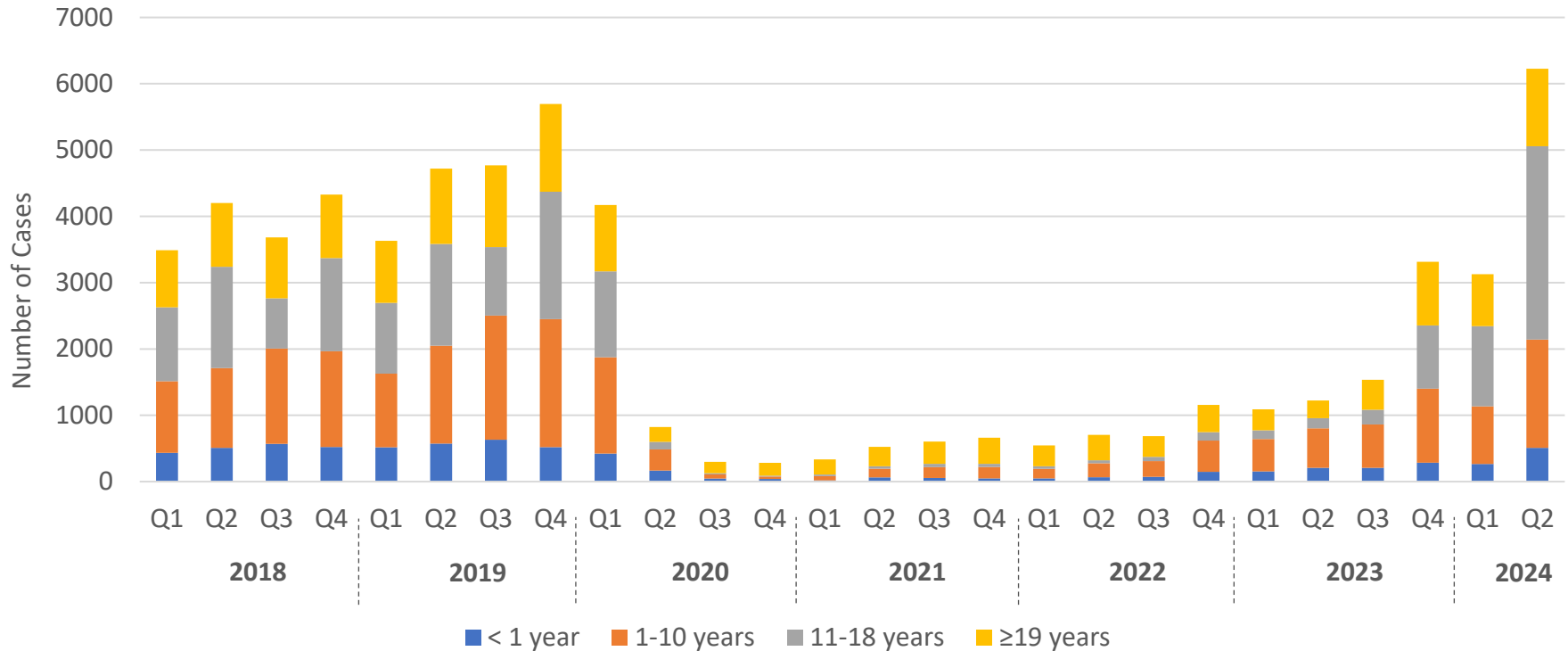
Figure 3. Laboratory confirmed cases of pertussis by quarter in England: 2011 to June 2024 (note 1)



National pertussis notifications, by month, 2020–2024



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 6th 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

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 The Mirror US on MSN · 3d


Schools across US seeing outbreaks of whooping cough as cases soar

 San Francisco Chronicle
<https://www.sfgchronicle.com>

Bay Area whooping cough outbreak reported in Lane County as Oregon case counts continue to spike

WEB Mar 27, 2024 · Whooping cough, also known as pertussis, the highly contagious illness has spread to at least 13 people in Lane County as Oregon case counts continue to spike the start of April. By Hope Kirwan. May 21, 2024.

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>


Whooping cough outbreak reported in Southern Michigan

WEB Oct 18, 2023 · Six cases of pertussis illness, also known as whooping cough, were reported in Southern Michigan.

 The Courier-Journal

Whooping cough outbreak in Kentucky

A highly contagious respiratory illness known as pertussis has been declared an outbreak by the Lexington-Fayette County Health Department.

 First Alert Safety Desk: Pertussis cases in South Dakota skyrocket

The South Dakota Department of Health tracks infectious disease dashboard shows

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

[f](#) [x](#) [e](#) [l](#)



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.



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
Division of Bacterial Diseases
National Center for Immunization and Respiratory Diseases
SHariri@cdc.gov

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the U. S. Centers for Disease Control and Prevention.