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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

* This placeholder textbox is for footnotes.

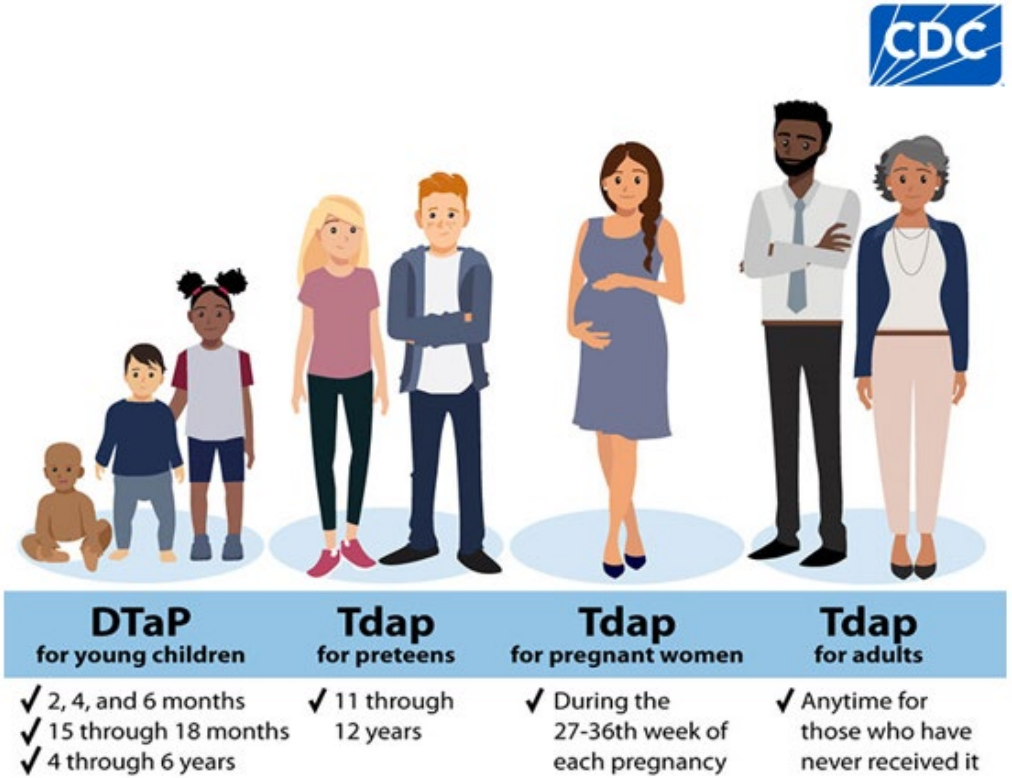
Pertussis Epidemiology

- **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

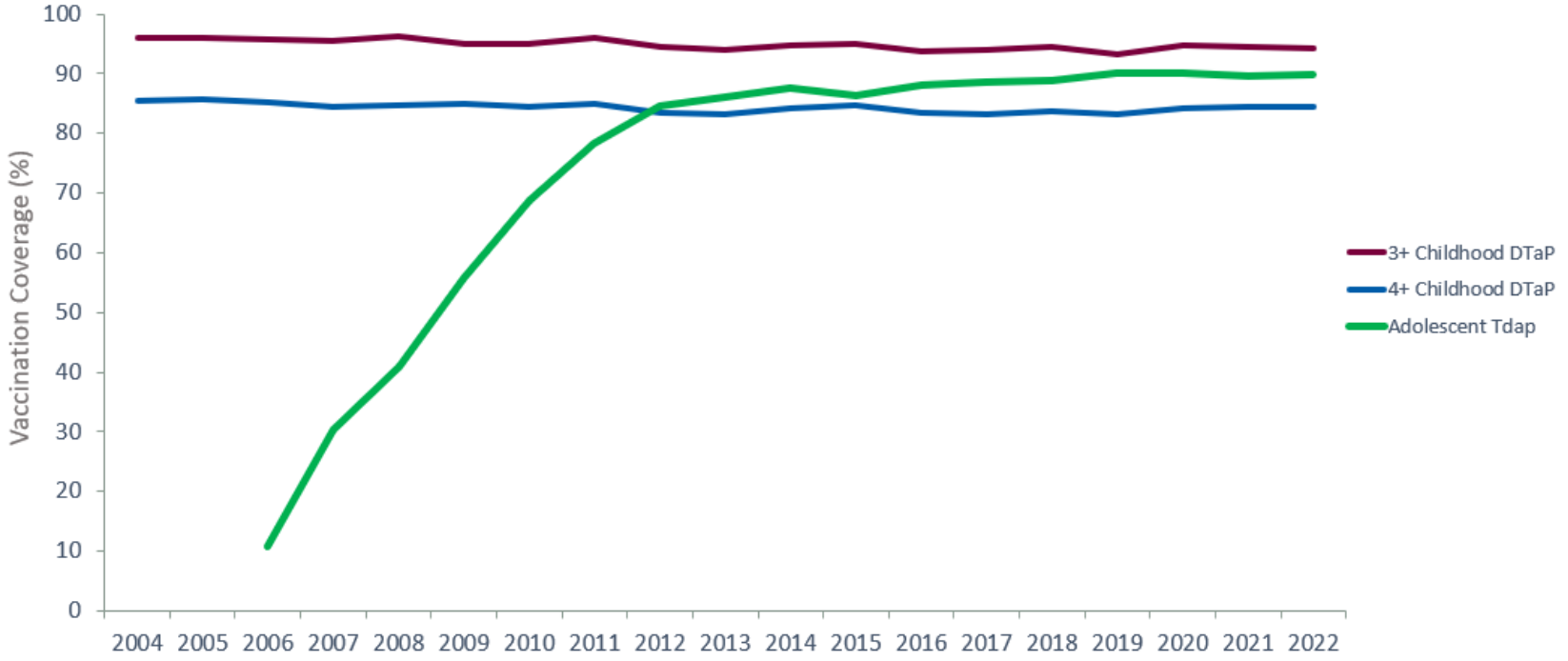
- **Whole cell vaccines (1940s)**
  - Safe and effective but reactogenic
  - Injection site reactions, fever, febrile seizures
  - Increased public concern and declines in vaccination
  - Led to global effort to develop vaccines with less adverse effects
- **Acellular vaccines (1990s)**
  - Recombinant 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



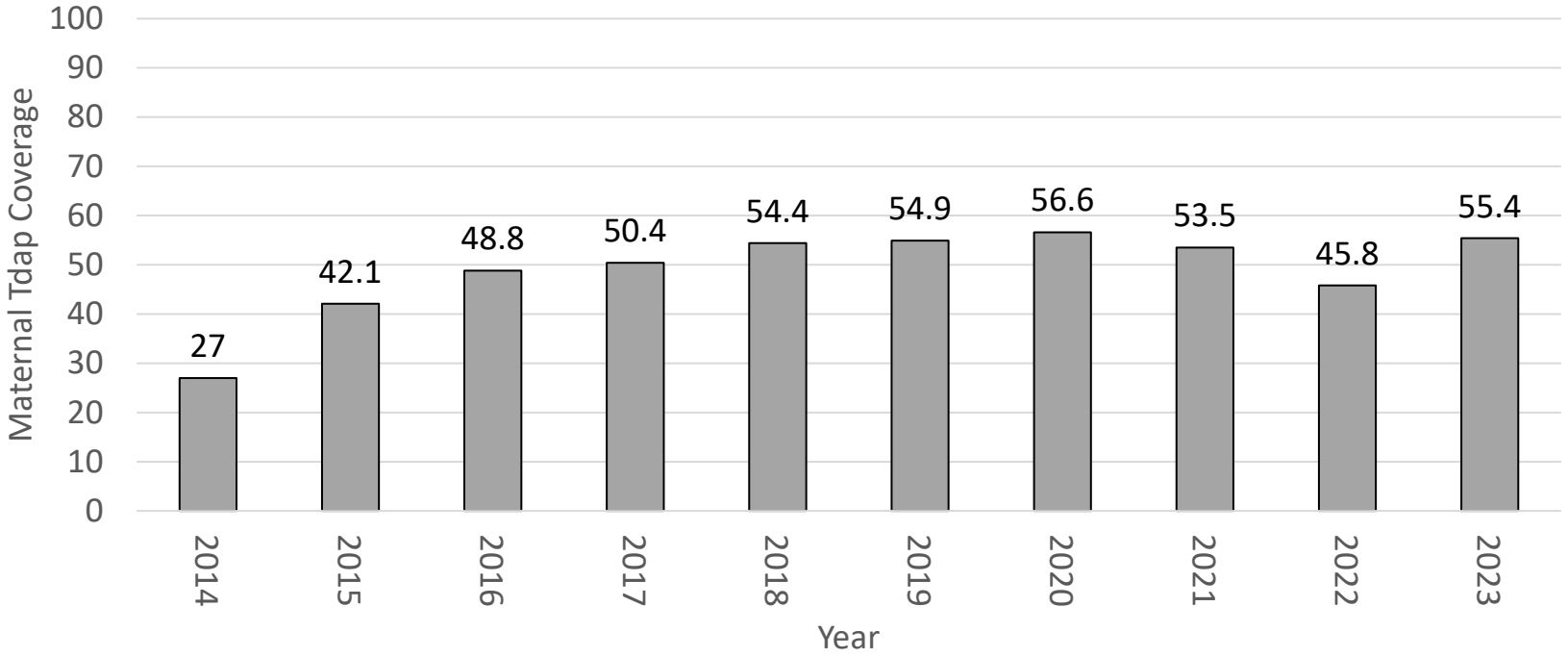
DTaP: diphtheria, tetanus, and acellular pertussis; Tdap: tetanus, diphtheria, acellular pertussis

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



CDC National Immunization Survey: DTaP among children aged 19 through 35 months, Tdap coverage among adolescents aged 13 through 17

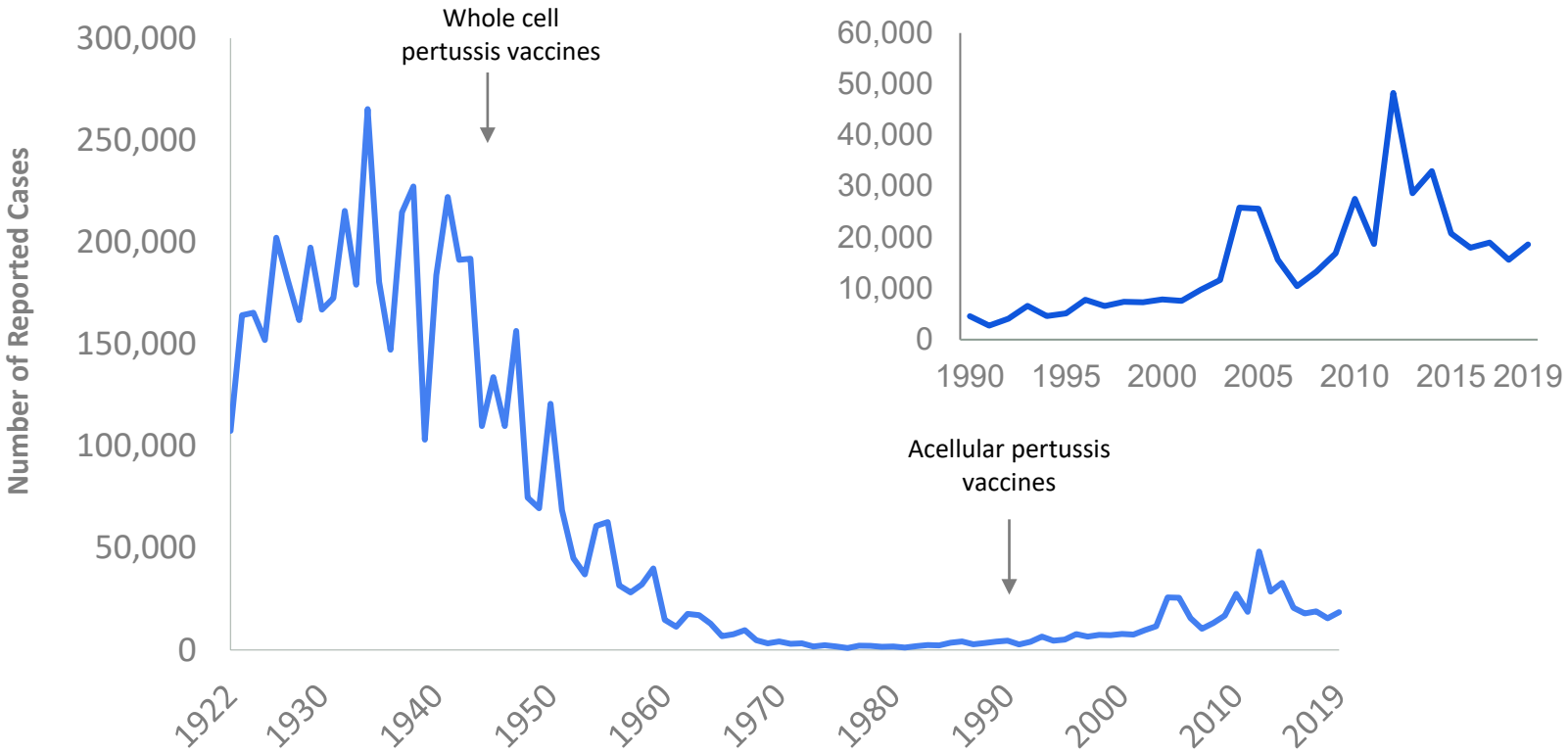
Maternal Tdap Coverage, United States, 2014-2023



CDC, Internet Panel Surveys

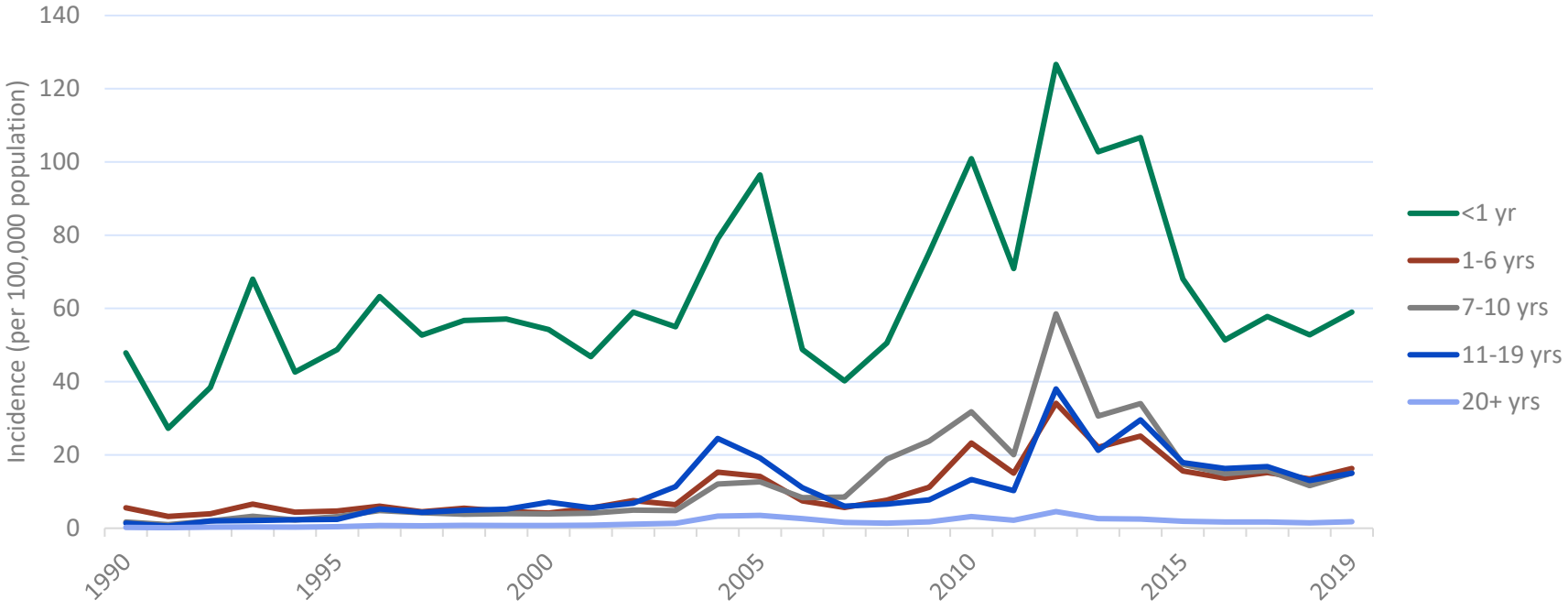
Historical trends in reported pertussis cases, United States

Reported Pertussis Cases, United States, 1922-2019



CDC, National Notifiable Diseases Surveillance System

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



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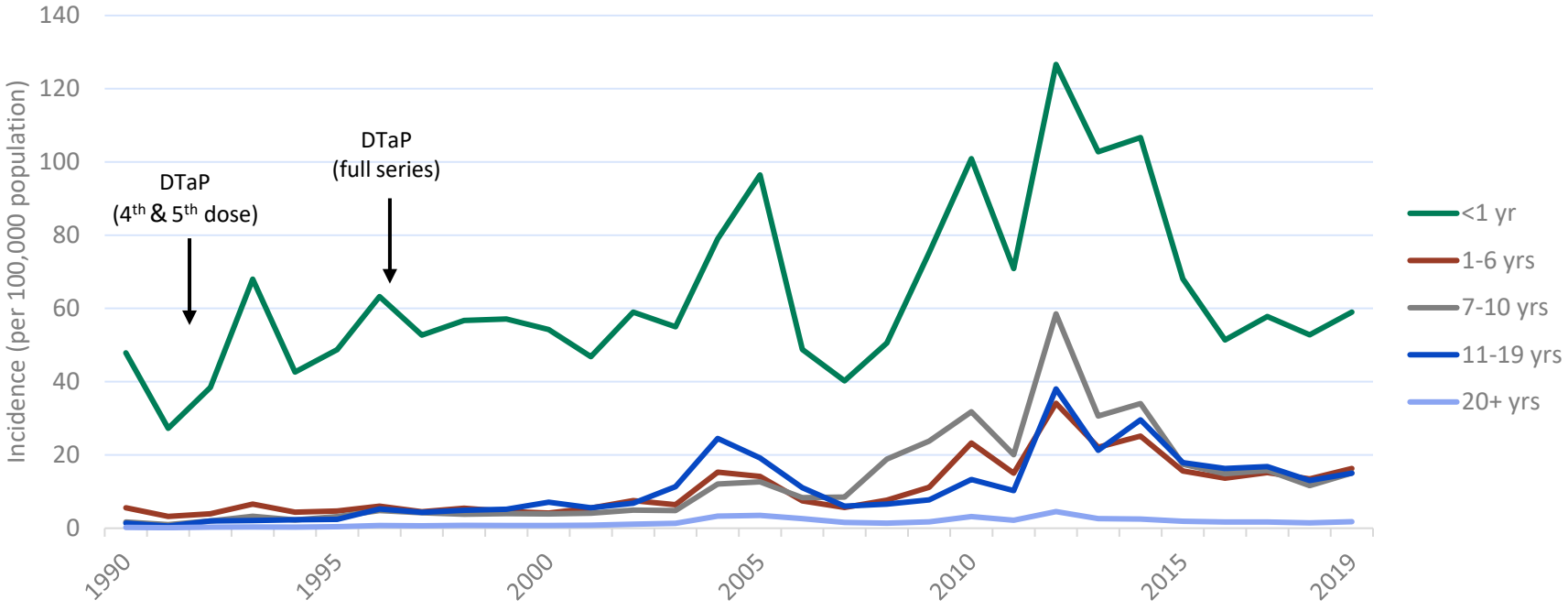
Pertussis Incidence by Age Group, United States, 1990-2019



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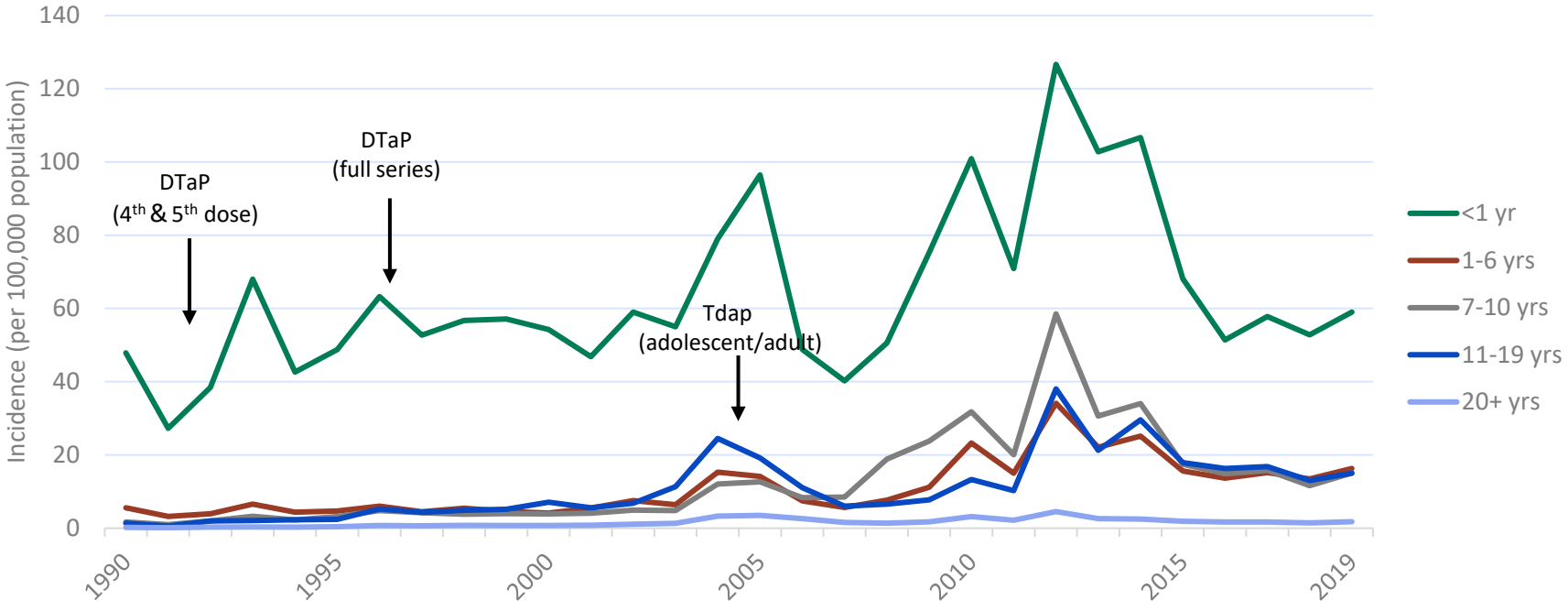
Pertussis Incidence by Age Group, United States, 1990-2019



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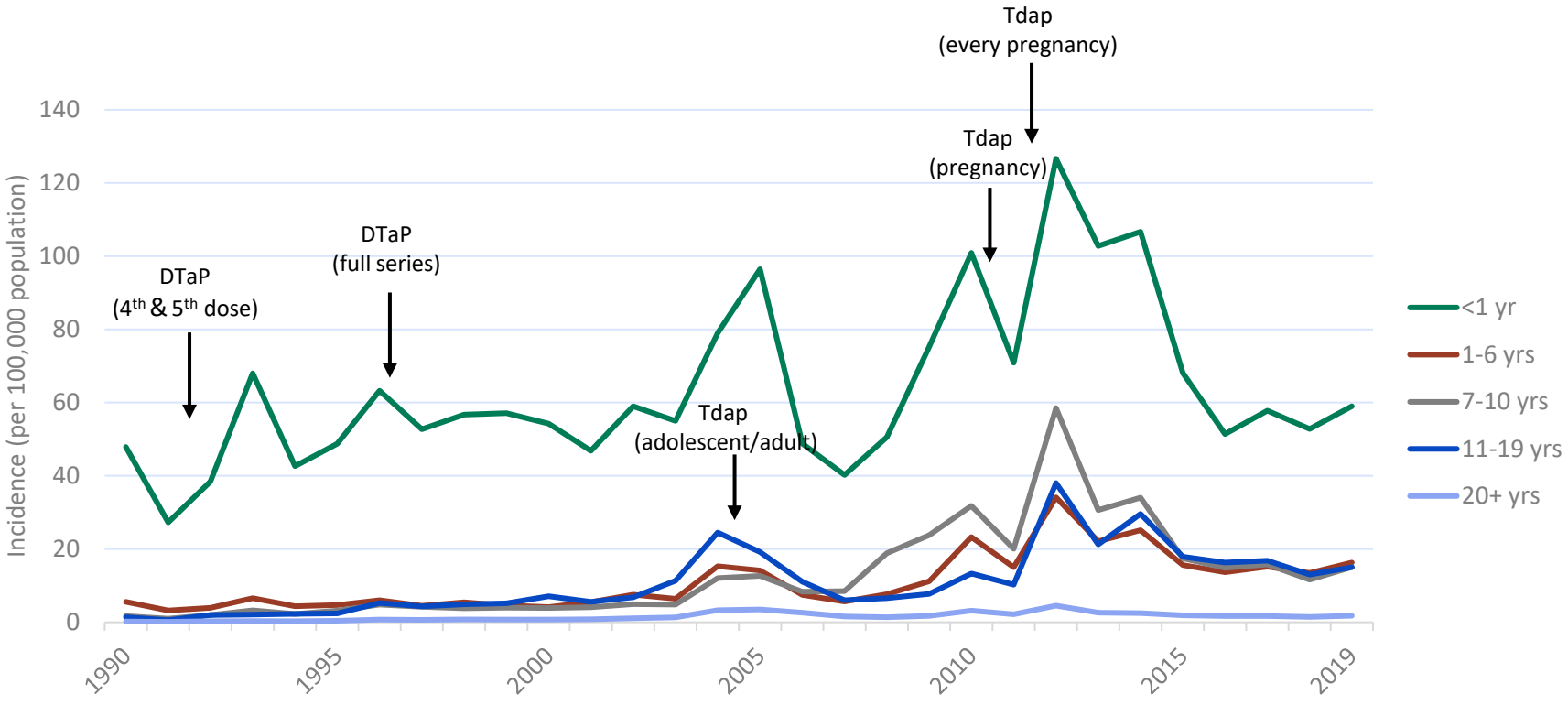
Pertussis Incidence by Age Group, United States, 1990-2019



CDC, National Notifiable Diseases Surveillance System

Possible Reasons for Pertussis Resurgence

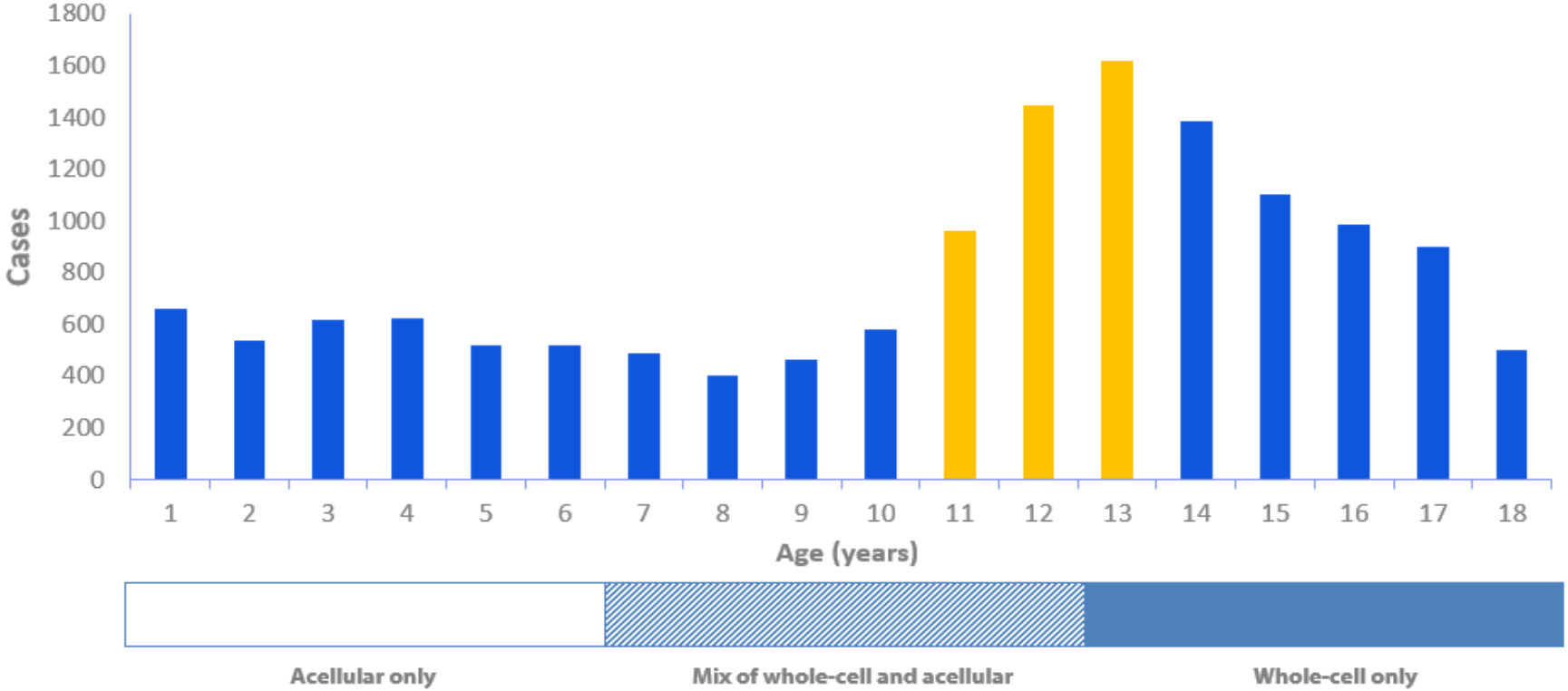
- Improved, more sensitive diagnostic tests
- Strain adaptation to vaccine pressure
- Increased awareness and testing

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

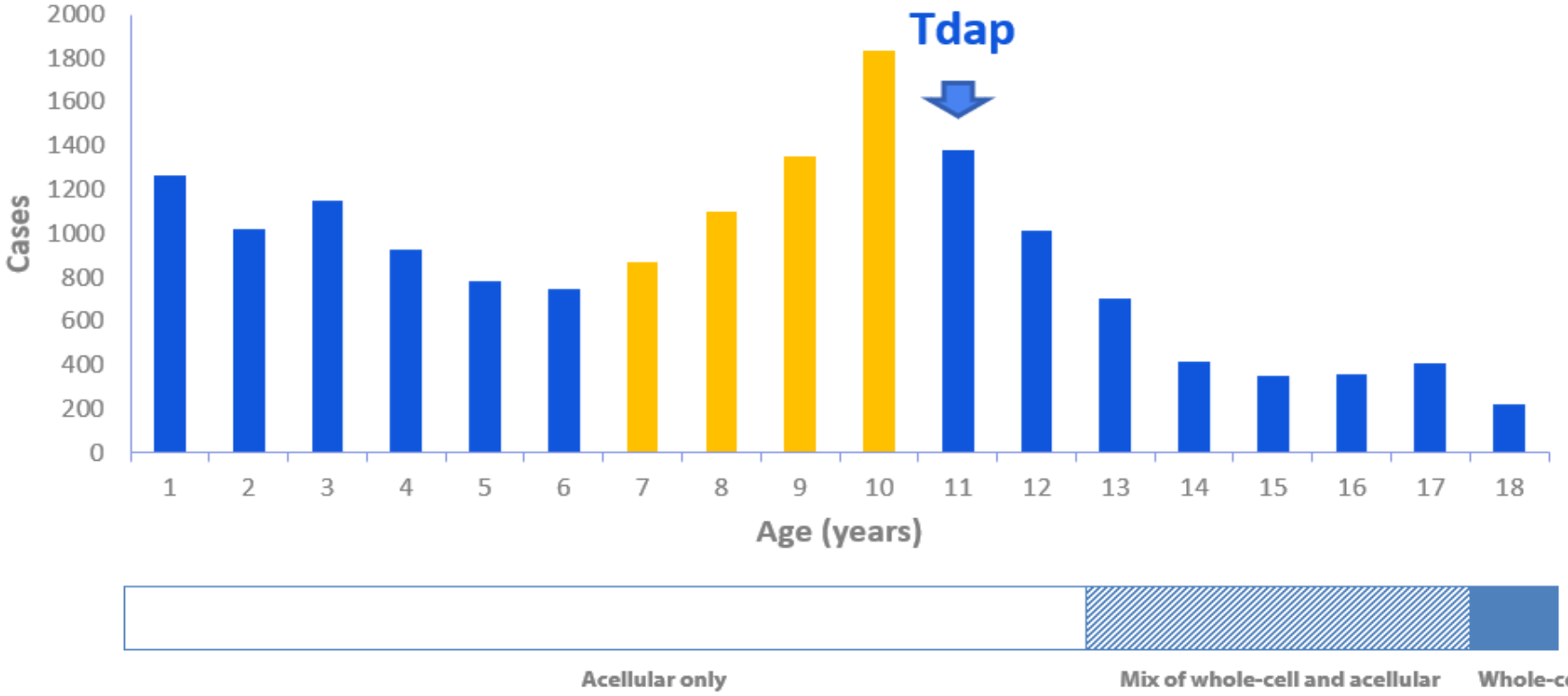
Age-related shifts during epidemic peak years in the United States

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



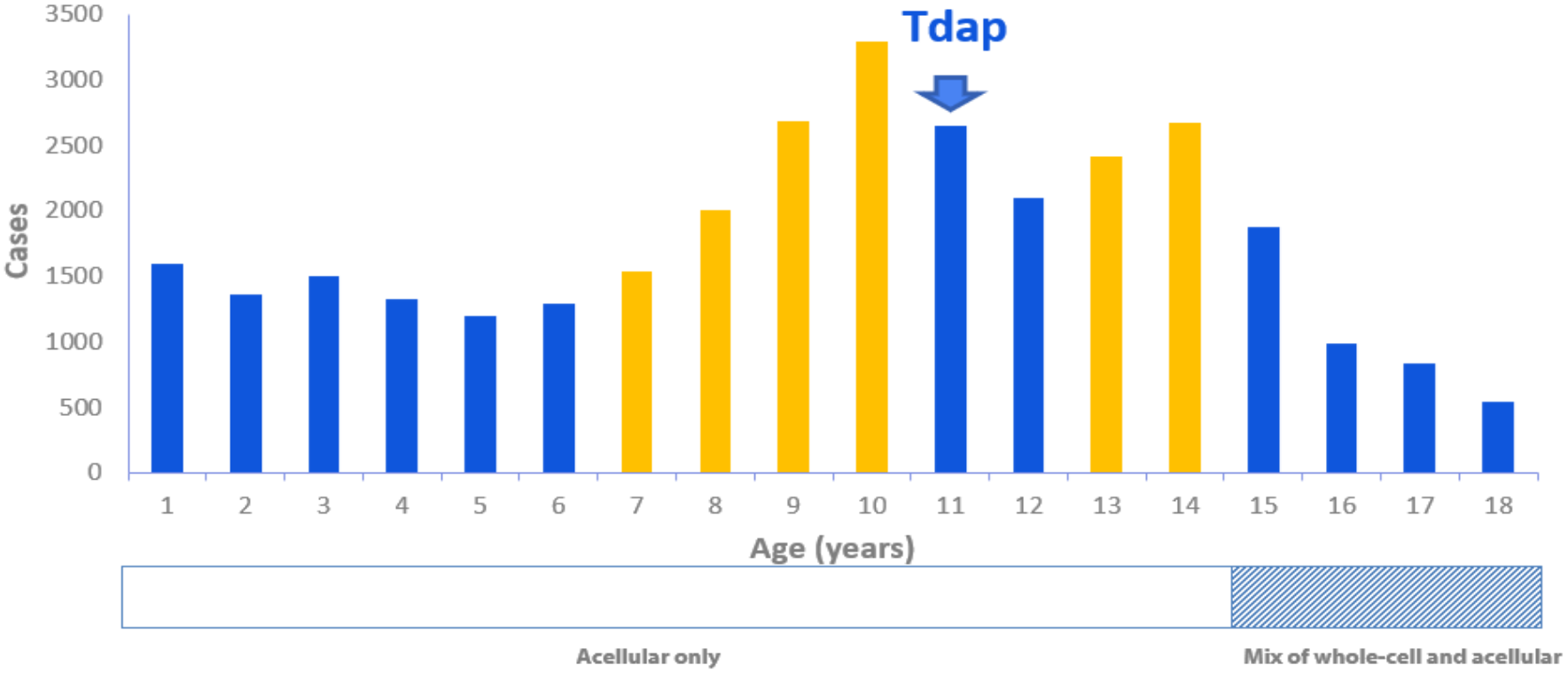
CDC, National Notifiable Diseases Surveillance System

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



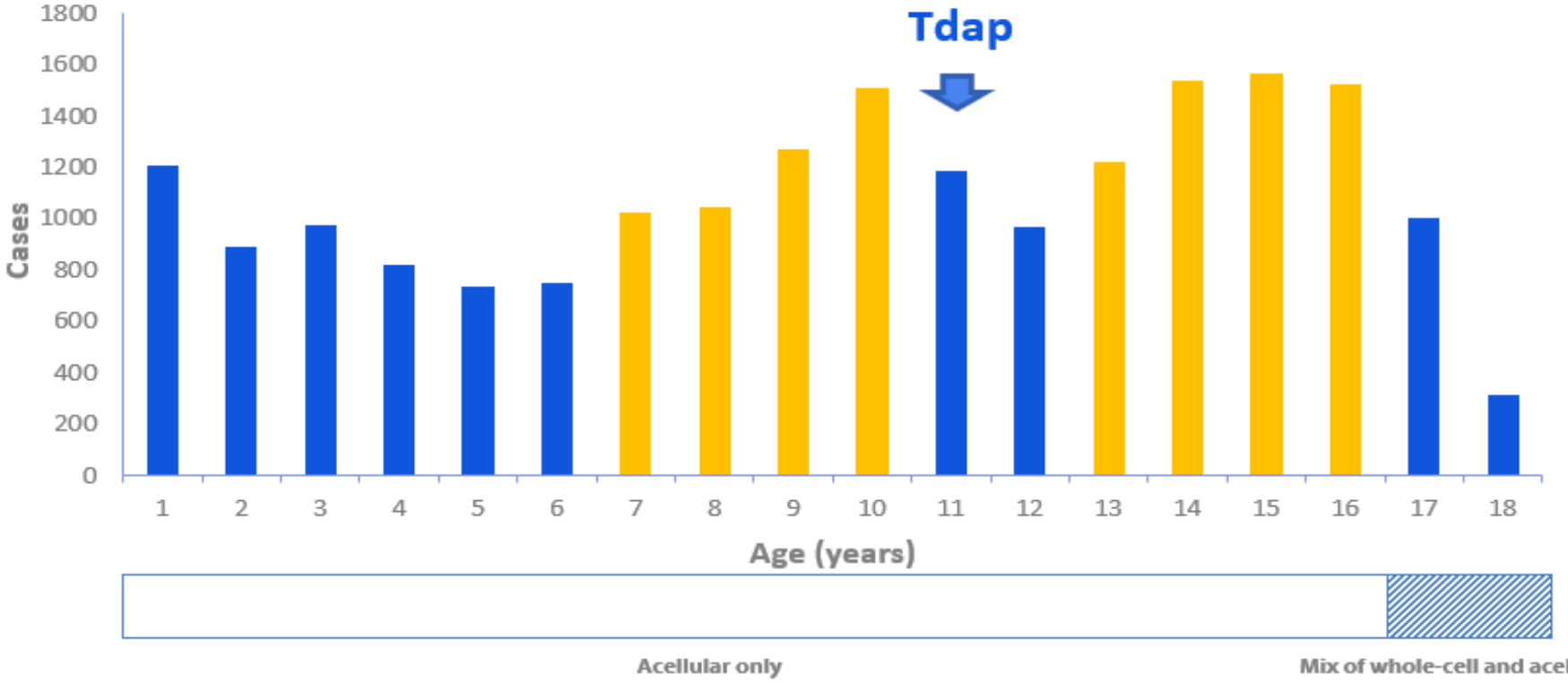
CDC, National Notifiable Diseases Surveillance System

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



CDC, National Notifiable Diseases Surveillance System

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



CDC, National Notifiable Diseases Surveillance System

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

Misegades et al. JAMA. 2012

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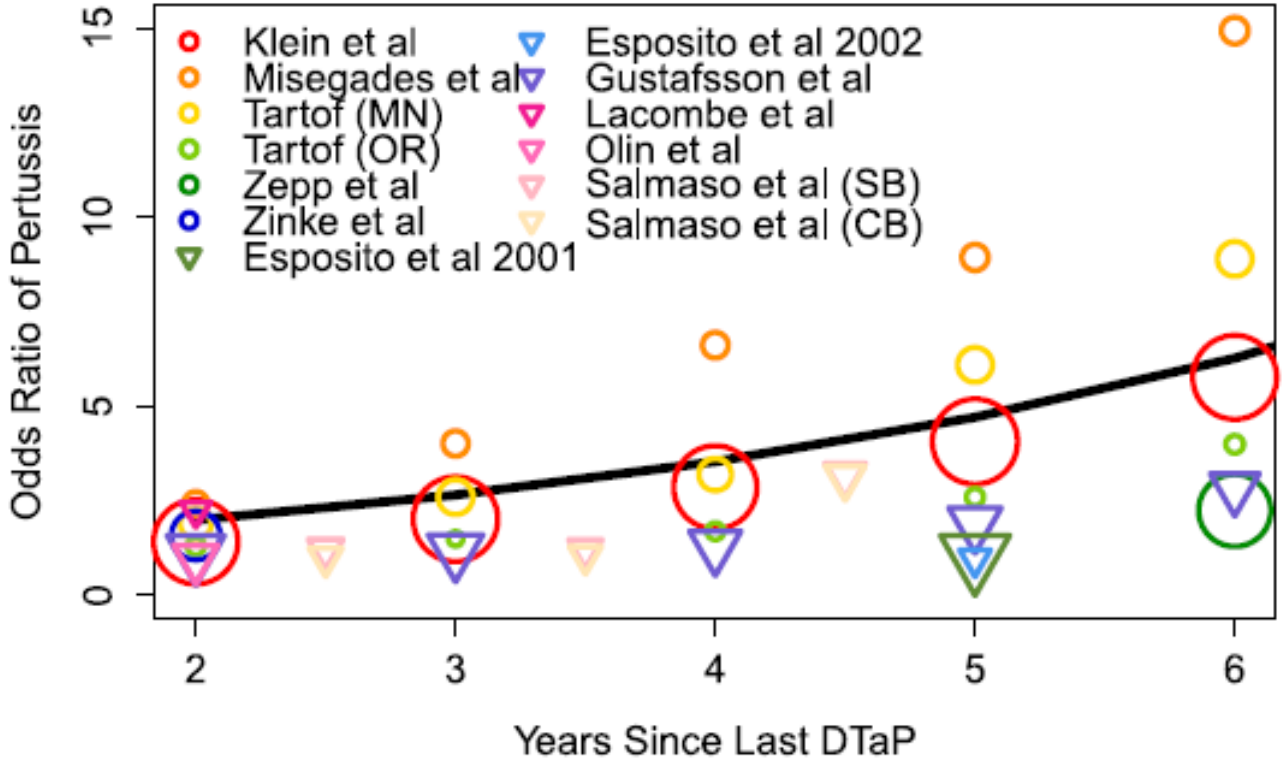
Overall VE, all ages (4-10 years)				
0 dose	53	19	Ref	--
5 doses	629	1,997	88.7	79.4 – 93.8
Time since 5th dose				
0 doses	53	19	Ref	--
< 12 months	19	354	98.1	96.1 – 99.1
12 – 23 months	51	391	95.3	91.2 – 97.5
24 – 35 months	79	366	92.3	86.6 – 95.5
36 – 47 months	108	304	87.3	76.2 – 93.2
48 – 59 months	141	294	82.8	68.7 – 90.6
60+ months	231	288	71.2	45.8 – 84.8

Misegades et al. JAMA. 2012

DTaP Duration of Protection



McGirr and Fisman. Pediatrics. 2015

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

Acosta et al. Pediatrics. 2015

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
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

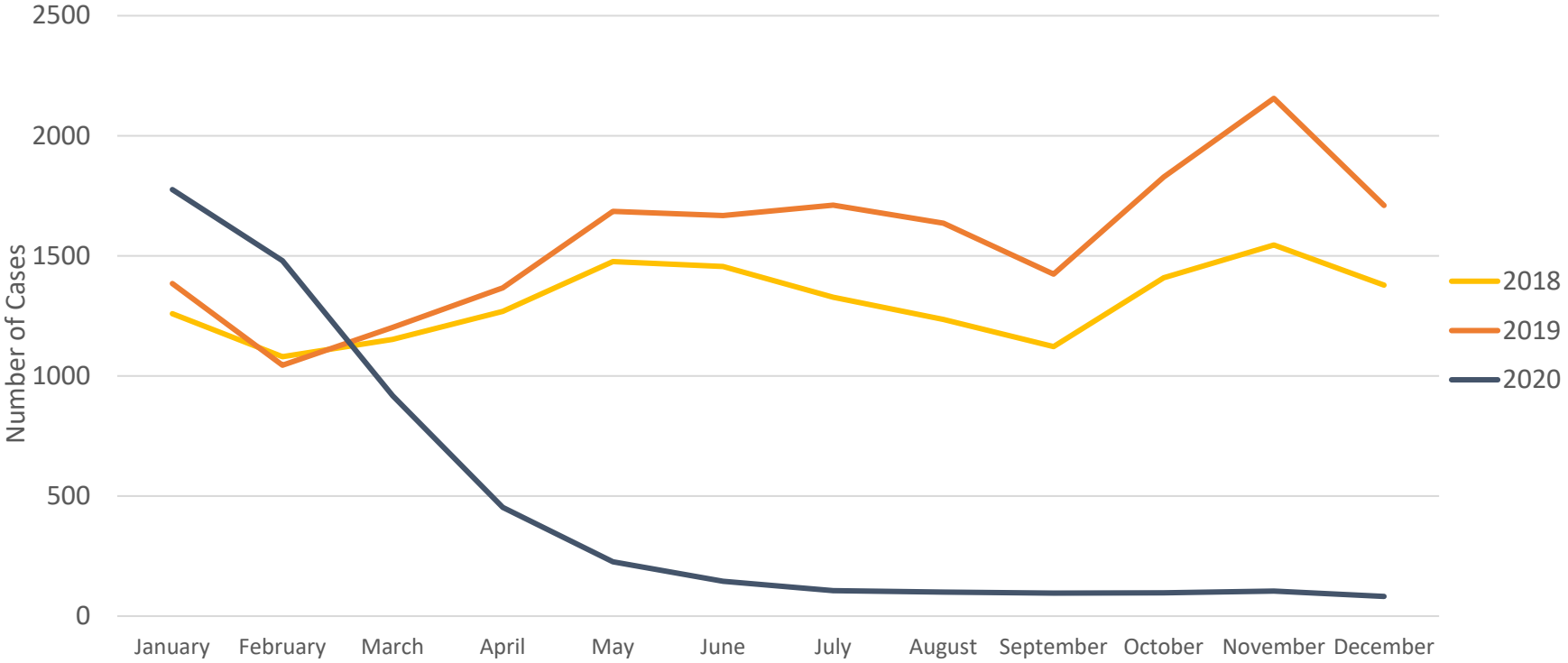
Acosta et al. Pediatrics. 2015

Tdap Duration of Protection

Time since Tdap	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

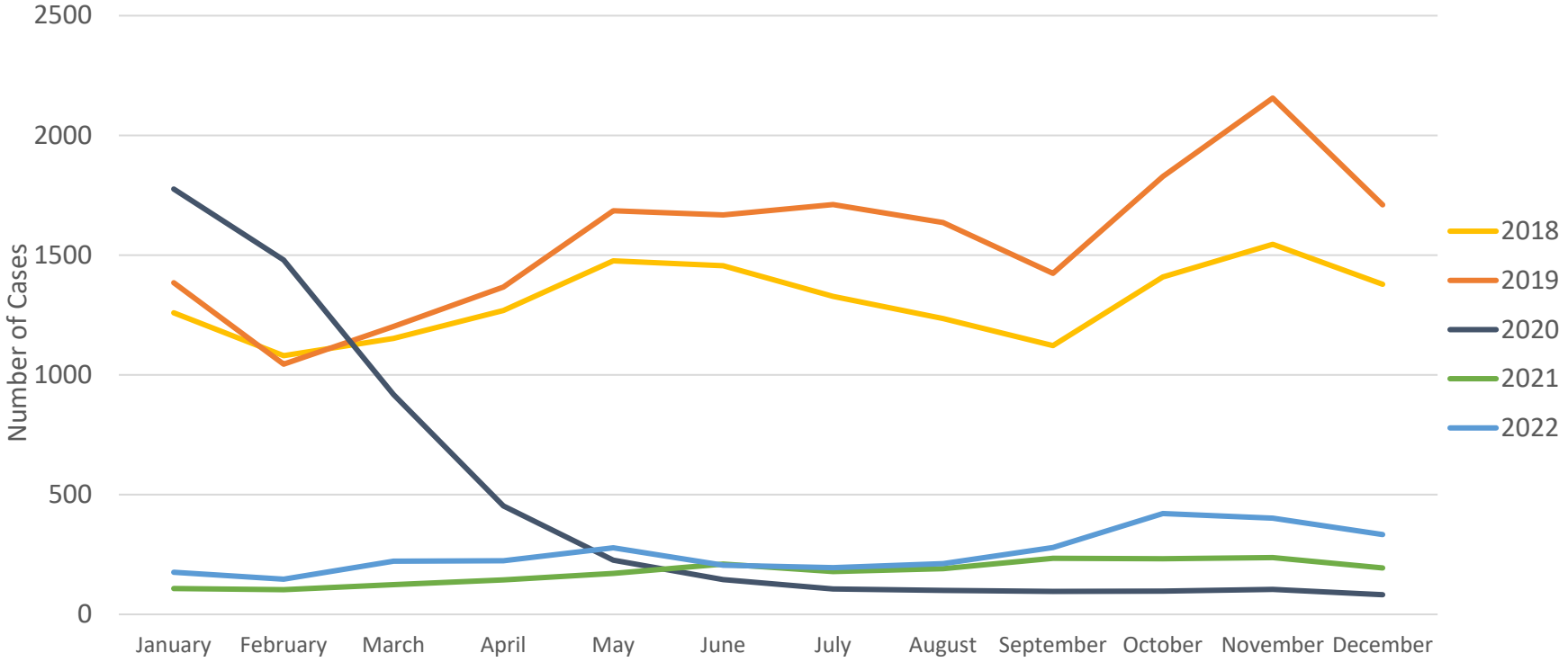
Post-pandemic pertussis epidemiology

Reported Pertussis Cases, United States, 2018-2020



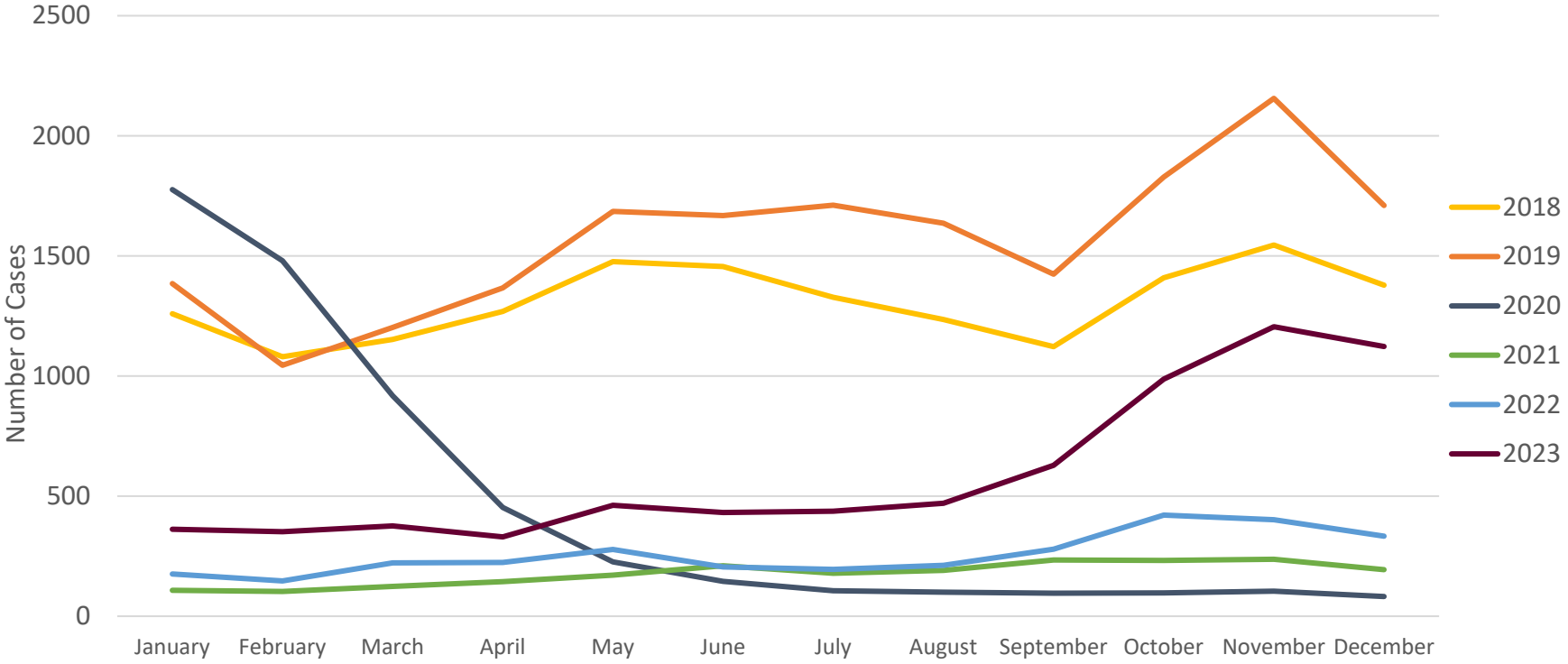
CDC, National Notifiable Diseases Surveillance System

Reported Pertussis Cases, United States, 2018-2022



CDC, National Notifiable Diseases Surveillance System

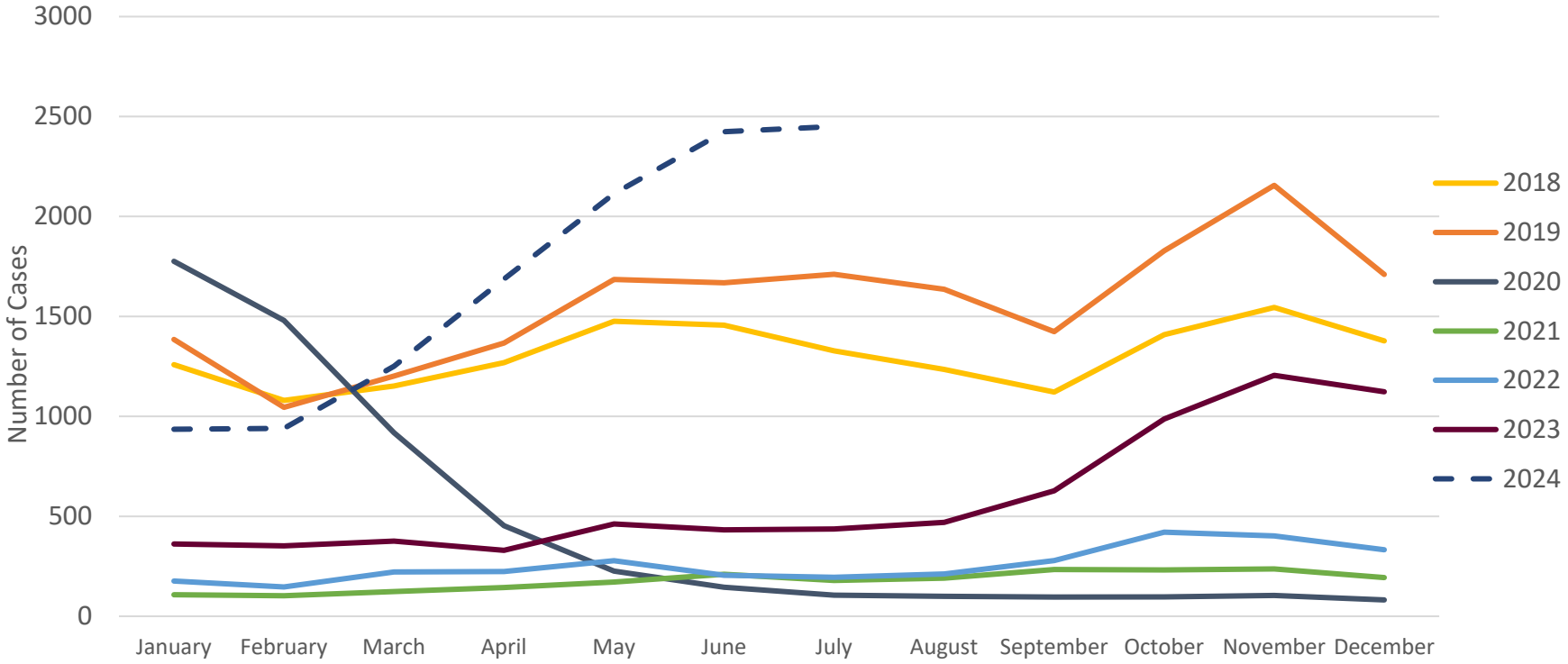
Reported Pertussis Cases, United States, 2018-2023*



*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 2024[2], EU/EEA[3]

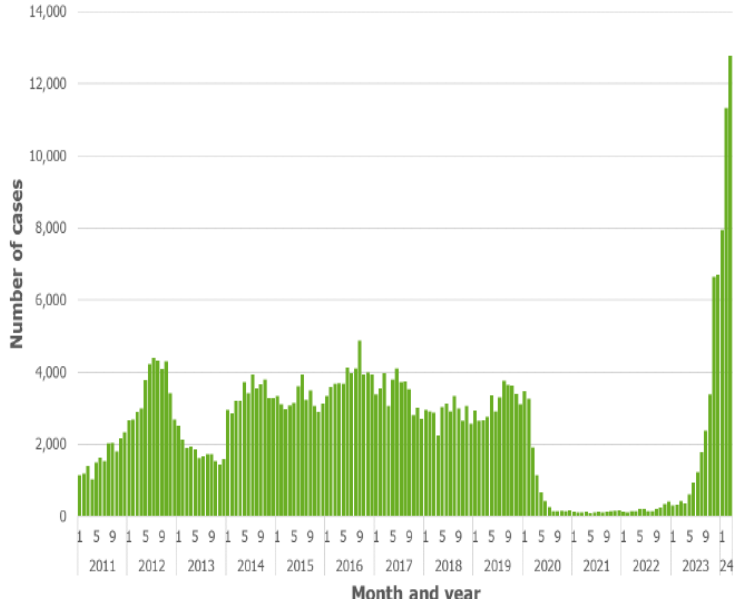
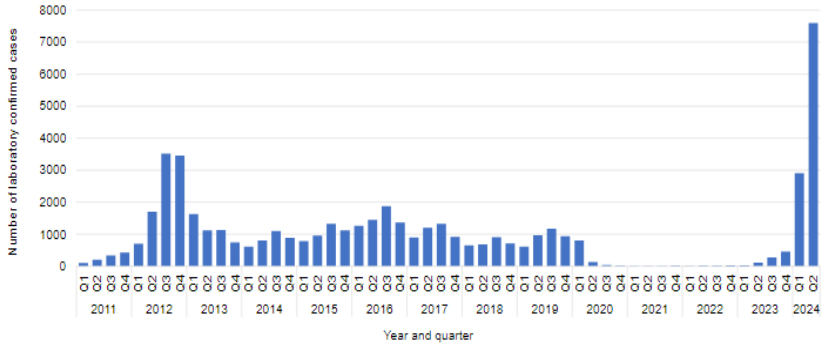
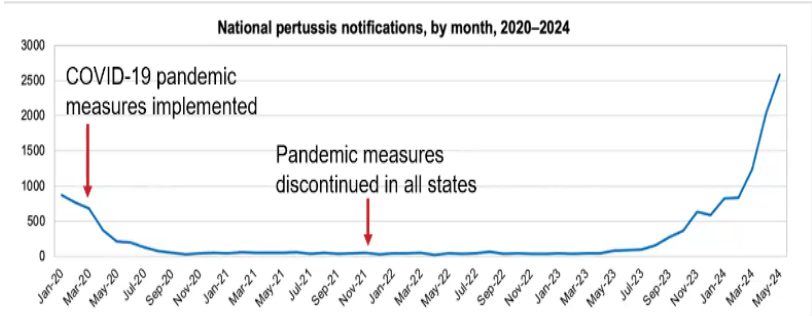


Figure 3. Laboratory confirmed cases of pertussis by quarter in England: 2011 to June 2024 (note 1)

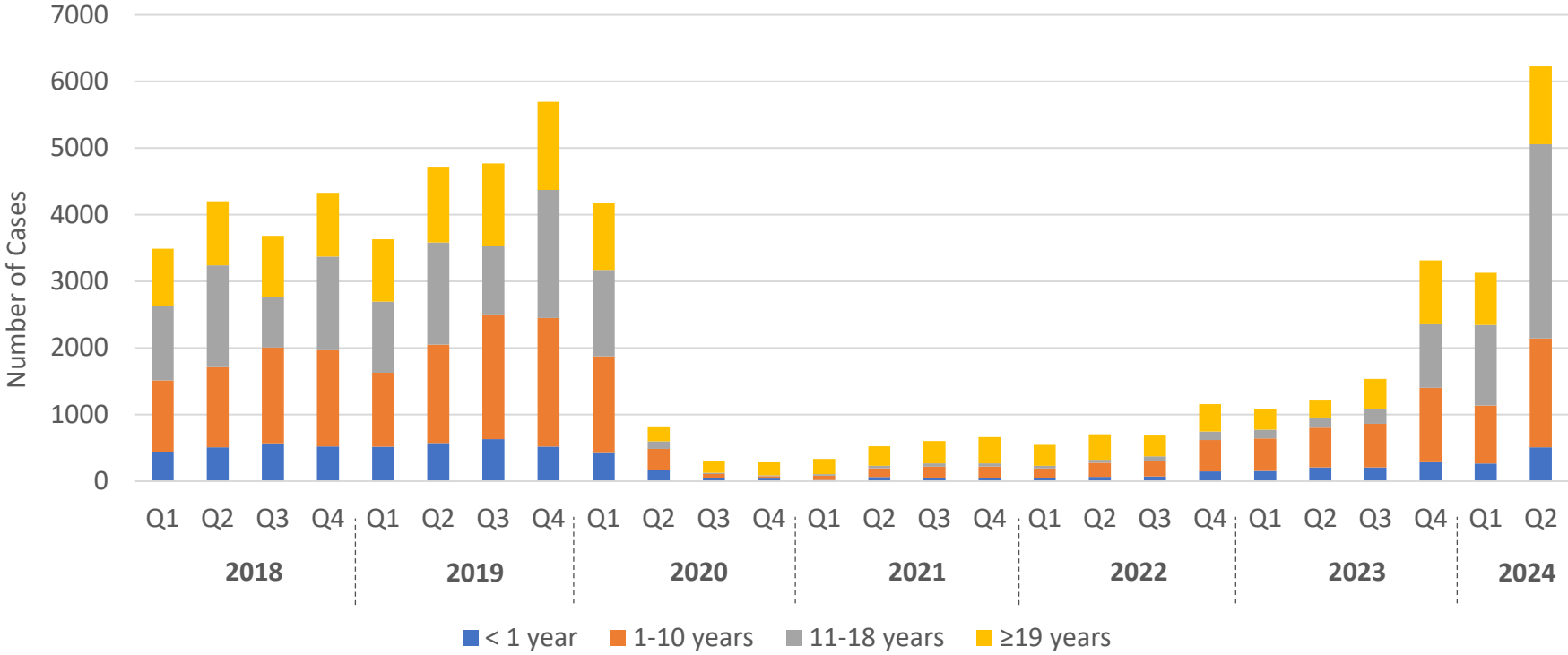




Increase of pertussis cases in the EU/EEA (europa.eu)

Confirmed cases of pertussis in England by month - GOV.UK (www.gov.uk)

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



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CDC, National Notifiable Diseases Surveillance System, Updated September 6th 2024

Outbreaks Reported Across the Country

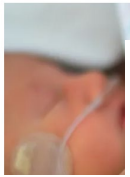
HEALTH

Whooping cough | Add Topic +

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

Emilee Coblentz
USA TODAY

Published 8:00 p.m. ET Jan. 3, 2024 | Updated 8:00 p.m. ET Jan. 3, 2024



Wausau-Rhinelander WSAW-TV + Follow

Marathon Co. health officials caution everyone amid ... in Athens

...gh outbreak reported in North Carolina

... (WSPA) – A whooping cough outbreak has been reported ... said 27 cases of whooping cough, known as ...

The Mirror US on MSN · 3d

Schools across US seeing outbreaks of whooping cough as cases soar

San Francisco ... https://www.sfchronicle...

Bay Area whooping cough ou...

WEB Mar 27, 2024 · Whooping cough, also known as ... ooping cough impacting Wisconsin

The highly contagious illness has spread to at least 13 p... the start of April. By Hope Kirwan. May 21, 2024.

The Register-Guard ·

Whooping cough o... ...red 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...

Whooping cough outbreak reported ...

WEB Oct 18, 2023 · Six cases of pertussis illness, also known as whooping cough, w... ...rthern Michigan -

The Courier-Journal

Whooping cough outbreak in Kentucky

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

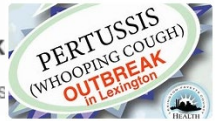
First Alert Safety Desk: Pertussis cases in South Dakota skyrock...

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



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

For more information, contact CDC
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