# Twenty Year Impact of Pneumococcal Conjugate Vaccines (PCV) on the Burden of Invasive Pneumococcal Disease in US Children Less than 5 Years of Age Rotem Lapidot,<sup>1,2</sup> Ruth Chapman,<sup>3</sup> Kelly Sutton,<sup>3</sup> Desmond Dillon-Murphy,<sup>3,1</sup> Shreeya Patel,<sup>3</sup> Erica Chilson,<sup>4</sup> Vincenza Snow,<sup>4</sup> Raymond Farkouh,<sup>4</sup> Matt Wasserman,<sup>4</sup> Stephen Pelton<sup>1,2</sup>

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## BACKGROUND

- Before 2000 the highest rates of invasive pneumococcal disease (IPD) in the United States (US) population were observed in children younger than 2 years of age.<sup>1</sup>
- The reported incidence, at that time, of IPD in children aged <12 months and 12–23 months was estimated as 165 and 203 cases/100,000 population, respectively.<sup>1</sup>
- Streptococcus pneumoniae was the leading cause of bacterial meningitis in US children.<sup>1</sup>
- Prior to the introduction of PCVs in 2000, no pneumococcal vaccines were approved for use in children under age 2 as pneumococcal polysaccharide vaccines are poorly immunogenic in this age group.4
- Seven-valent pneumococcal conjugate vaccine (PCV7), containing serotypes (4, 6B, 9V, 14, 18C, 19F, and 23F) that caused >80% of IPD cases in North American children, overcame the problem of poor immunogenicity through conjugation with CRM197, a detoxified diphtheria toxin, and was introduced into the US infant immunization schedule in 2000.<sup>1</sup>
- In 2010, a 13-valent PCV (PCV13) (containing serotypes in PCV7 and 1, 3, 5, 6A, 7F, and 19A) was launched in the US, partly in response to increasing disease due to non-PCV7 serotypes.

### OBJECTIVE

• We computed IPD cases and related deaths averted over the past 20 years attributable to PCV7 and PCV13 use in US infants less than 5 years of age. We further computed cases and deaths averted by IPD syndrome: bacteremia, bacteremic pneumonia and pneumococcal meningitis.

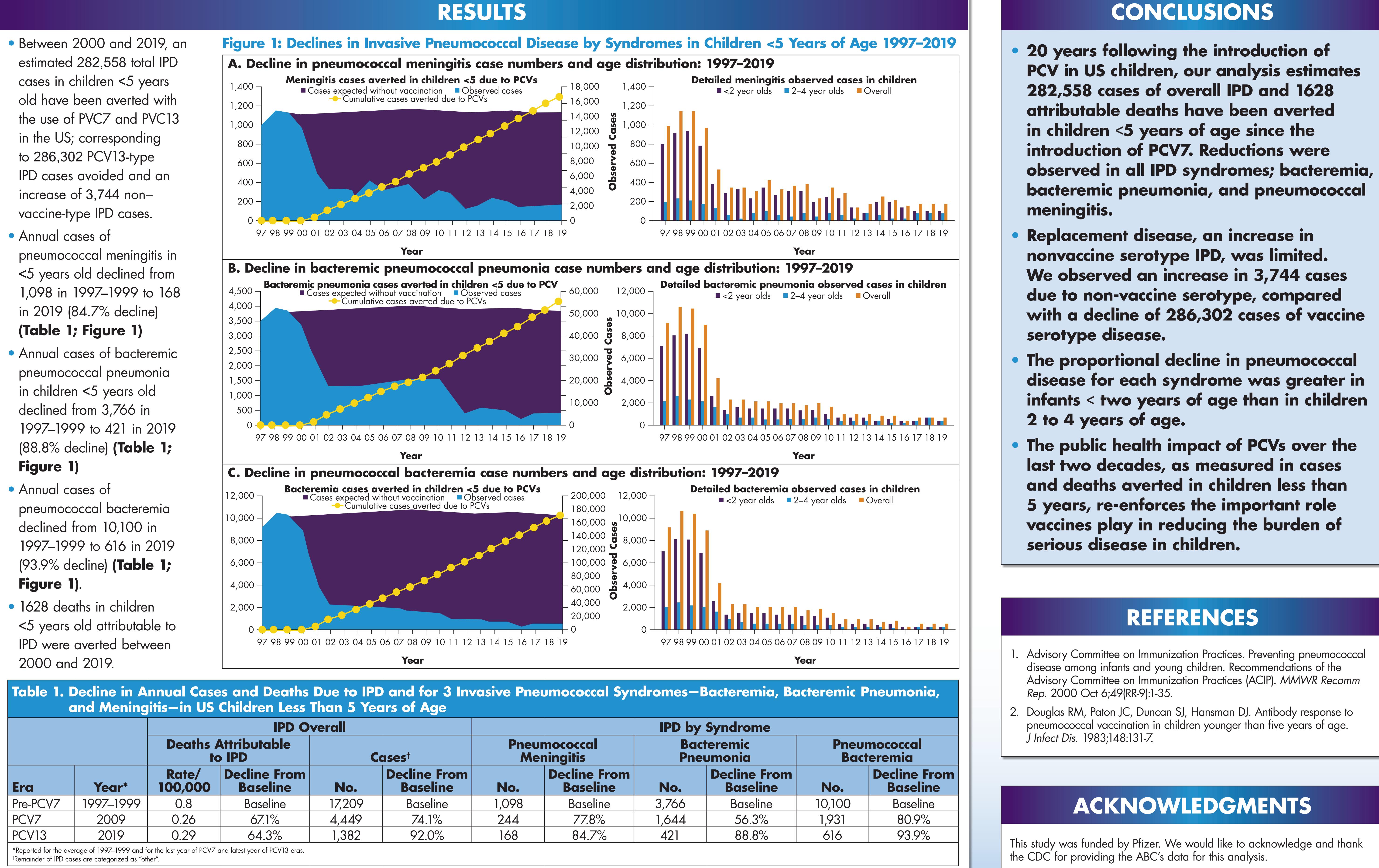
### METHODS

- Published and unpublished data from the Centers for Disease Control and Prevention (CDC) Active Bacterial Core (ABC) surveillance network were used to calculate the number of disease cases and deaths nationally over the 20-year period following the introduction of PCVs to determine the reduction in disease burden on children younger than age 5.
- Expected case numbers were calculated as the average incidence rate by age and year, times the population size in that year by age. Disease incidence was assumed to remain constant in the absence of PCVs.
- ABC's surveillance reports provided the overall IPD case numbers, rates, and specific syndromes in children <1 year, 1 year to <2, or 2–4 years of age. Due to unavailability of recent published data from ABC, rates in 2018 and 2019 were assumed to be the same as in 2017. These data were used to calculate the average incidence rates and distribution for three syndromes; bacteremia, bacteremic pneumonia, and meningitis during the three eras of PCV vaccination over the period 1997–2019. Expected PCV13-type and non–PCV13-type cases in the absence of vaccination were calculated by applying the average pre-vaccination distribution to the total expected number of IPD cases for subsequent years (2000–2019).
- Cases averted were calculated from ABC's published incidence for each IPD syndrome and population data for the pre-PCV, PCV7, and PCV13 eras compared to calculated expected cases.
- Changes in "all IPD" capture the impact on both vaccine- and non-vaccine serotypes over time and represent the "net impact" of vaccination; changes in "PCV13 IPD" represent only vaccine-type reduction in IPD without consideration of replacement.

- Between 2000 and 2019, an estimated 282,558 total IPD cases in children <5 years old have been averted with the use of PVC7 and PVC13 in the US; corresponding to 286,302 PCV13-type IPD cases avoided and an increase of 3,744 nonvaccine-type IPD cases.
- Annual cases of pneumococcal meningitis in <5 years old declined from 1,098 in 1997–1999 to 168 in 2019 (84.7% decline)

### (Table 1; Figure 1)

- Annual cases of bacteremic pneumococcal pneumonia in children <5 years old declined from 3,766 in 1997–1999 to 421 in 2019 (88.8% decline) (Table 1; Figure 1)
- Annual cases of pneumococcal bacteremia declined from 10,100 in 1997–1999 to 616 in 2019 (93.9% decline) (Table 1; Figure 1).
- 1628 deaths in children <5 years old attributable to IPD were averted between 2000 and 2019.



# and Meningitis—in US Children Less Than 5 Years of Age

		IPD Overall				IPD by Syndrome					
		Deaths Attributable to IPD		<b>Cases</b> <sup>†</sup>		Pneumococcal Meningitis		Bacteremic Pneumonia		Pneumoco Bacterer	
Era	Year*	Rate/ 100,000	Decline From Baseline	No.	Decline From Baseline	No.	Decline From Baseline	No.	Decline From Baseline	No.	Dec
Pre-PCV7	1997–1999	0.8	Baseline	17,209	Baseline	1,098	Baseline	3,766	Baseline	10,100	
PCV7	2009	0.26	67.1%	4,449	74.1%	244	77.8%	1,644	56.3%	1,931	
PCV13	2019	0.29	64.3%	1,382	92.0%	168	84.7%	421	88.8%	616	

\*Reported for the average of 1997–1999 and for the last year of PCV7 and latest year of PCV13 eras. <sup>†</sup>Remainder of IPD cases are categorized as "other".



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