

# Are We Underestimating the True Burden of Pertussis? A Comparison of PCR-Positive Cases Not Meeting Clinical Case Definition to Confirmed Cases in Washington State from 2007-2011

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## INTRODUCTION

The current pertussis case classification system may underestimate the true burden of disease. Cases testing positive for pertussis by PCR but not meeting clinical case definition cannot be classified as either confirmed or probable and are therefore not reported to the CDC. Many such individuals likely represent true pertussis infections with clinical illness but are misclassified and therefore missing from state and national surveillance data.

## OBJECTIVE

Compare 2007-2011 **PCR-positive suspect** cases with **confirmed** pertussis cases reported in Washington (WA) State to determine differences in:

- Demographics
- Symptoms
- Measures of severity, outcome & antibiotic treatment
- Vaccination status

## METHODS

### Pertussis Case Classification Methods

#### National Case Definition:

##### Confirmed

- Isolate Pertussis (*Bp*) + cough of any duration, **OR**
- Detect *Bp* DNA by PCR + clinical case definition, **OR** Link to lab-confirmed case + clinical case definition

##### Probable

- Meets clinical case definition **BUT**
- No *Bp* isolation or *Bp* DNA detected by PCR **AND** No link to a lab-confirmed case

Clinical case definition: Cough  $\geq$  2 weeks **AND** Cough paroxysms **OR** Inspiratory "whoop" **OR** Post-tussive emesis

Only confirmed and probable cases are reported to CDC.

#### Establishment of a "Suspect" Case Definition in WA for state and local use:

- Bp* PCR was implemented at WA State Public Health Laboratories in 1999 and was widely available at commercial labs by 2005. From 2005-2006 there were many PCR-positive cases who did not meet case definition.

##### Suspect Case Definition

- a person whose initial symptoms suggest pertussis **AND** subsequent testing is negative **OR** no testing done **OR** cough duration < 2 weeks or cough duration undetermined
- Bp* PCR-positive persons who do not meet clinical case definition
  - For case & contact management, persons should be treated as if they had pertussis

### Analysis

- Presence of clinical symptoms, treatment, outcomes, and vaccine receipt among PCR-positive suspect cases were compared to those among confirmed cases reported in WA with onsets from 2007-2011.
- Ascertainment of Vaccination Status. Vaccine dose dates entered in case report were used to calculate the number of doses received prior to onset. The variables for "Ever received pertussis-containing vaccine?" and/or "Number of doses received prior to illness onset" were used to determine if no vaccine doses had been received prior to onset.

Up-to-date for vaccine was defined as the minimum number of doses of pertussis-containing vaccine recommended for age by the Advisory Committee on Immunization Practices.

- Antibiotic Treatment Definitions. Early antibiotic treatment was defined as receipt of an appropriate antibiotic for pertussis which was received within one week of disease onset. Late antibiotic treatment was defined as 1) an appropriate antibiotic received greater than one week after onset **OR** 2) an inappropriate antibiotic received at any time.

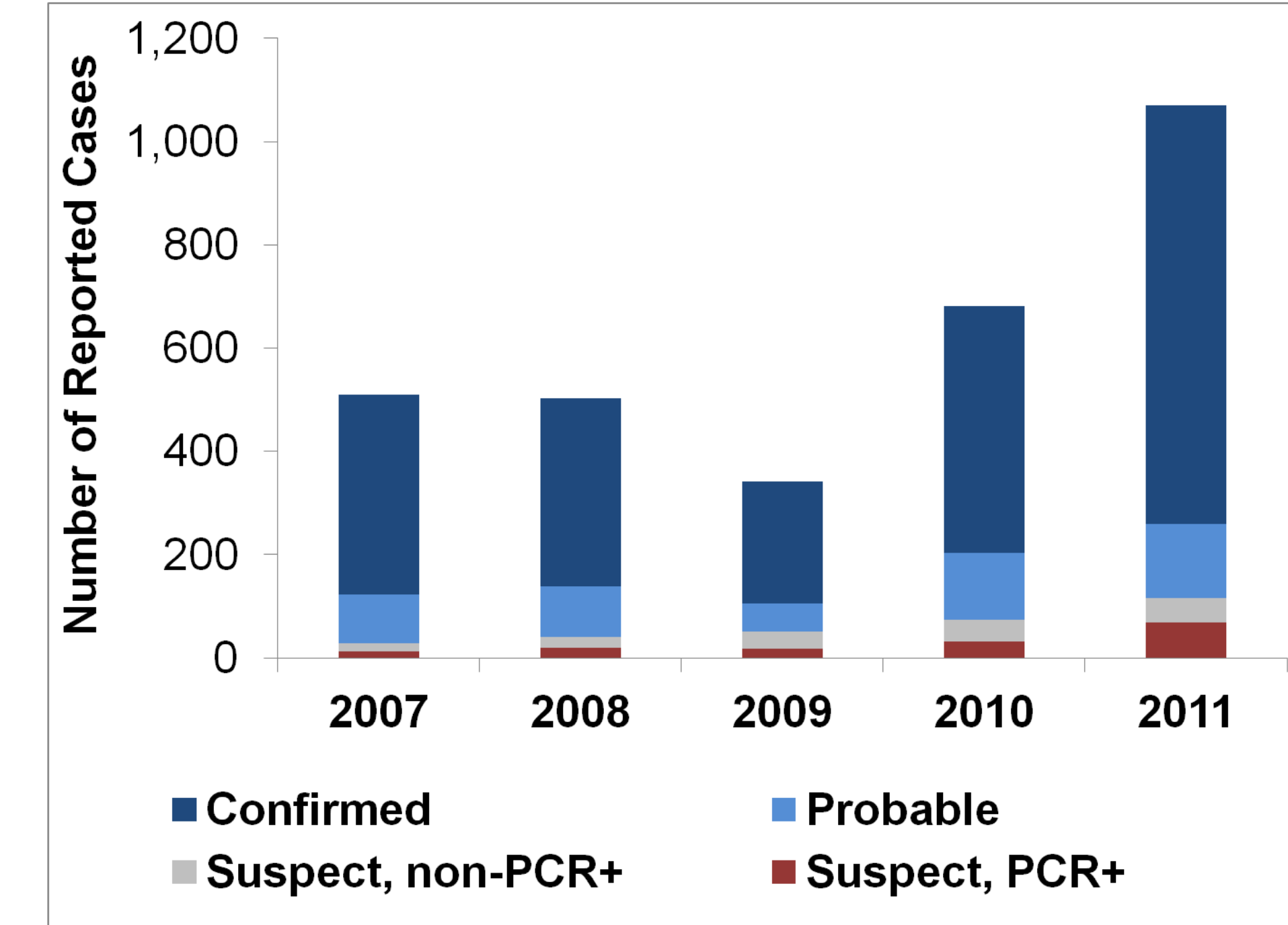
- $\chi^2$  test of independence (or Fisher's exact test) and t-test were performed in univariate analyses.

### Pertussis Cases in WA, 2007-2011

#### Total case reports

- Confirmed cases: 2,278 (73%)
- Probable cases: 519 (17%)
- Suspect cases: 309 (10%)
  - Among suspect cases, 150 (49%) *Bp* PCR-positive

#### Reported cases by onset year and classification



### Demographic Characteristics of Confirmed and PCR+ Suspect Cases, 2007-2011

	Confirmed n=2,278	PCR+ Suspect n=150
<b>Age group (years)</b>		
<1	16%	17%
1-4	16%	18%
5-9	17%	17%
10-17	28%	30%
18-44	15%	12%
45-64	7%	4%
$\geq$ 65	1%	2%
<b>Male</b>	47%	55%
<b>Residence (region)</b>		
Western WA	84%	83%
<b>Race*</b>		
White	87%	90%
Black	4%	4%
American Indian	2%	1%
Asian	2%	2%
Other	5%	3%
<b>Hispanic*</b>	19%	18%

\*Data completeness for race & ethnicity was not 100%. Percent completeness was slightly higher among confirmed versus PCR+ suspect cases: 61% and 62% versus 52% and 55%, respectively.

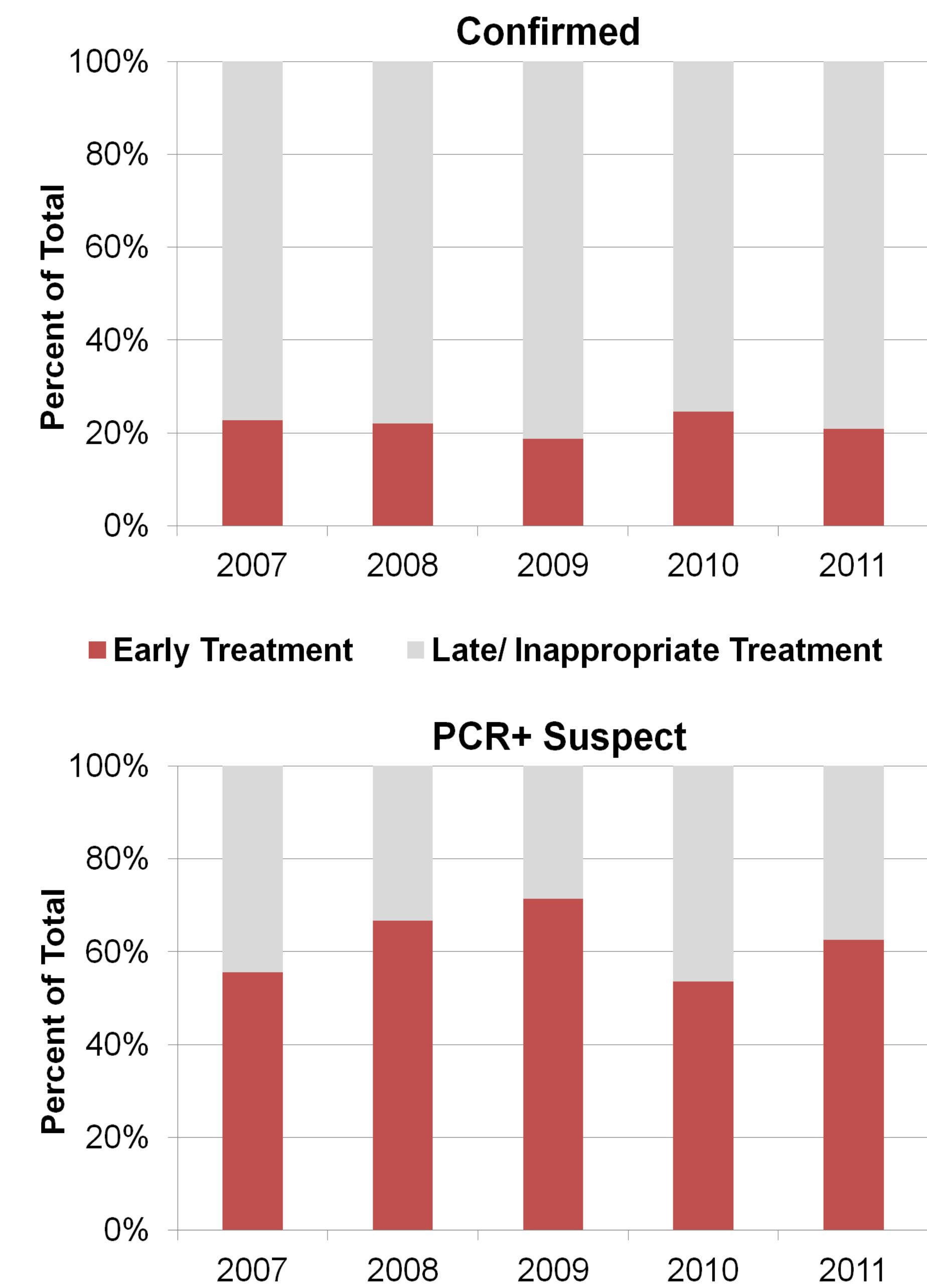
## RESULTS

### Comparison of Clinical Symptoms, Outcomes, Antibiotic Treatment and Vaccine Receipt, 2007-2011

	Confirmed	PCR+ Suspect	p-value
<b>Clinical Symptoms</b>			
Two-week cough*	99%	32%	p<0.0001
Paroxysmal cough	90%	38%	p<0.0001
Post-tussive emesis	54%	19%	p<0.0001
Whoop	36%	15%	p<0.0001
<b>Antibiotic Treatment</b>			
Receipt of appropriate antibiotic for pertussis	94%	98%	p<0.05
Onset to receipt of appropriate antibiotic (mean # days)	16	9	p<0.0001
Onset to <b>early</b> treatment with appropriate antibiotic	22%	62%	p<0.0001
<b>Syndrome/ Outcomes</b>			
Pneumonia	0.1%	0%	0.14
Encephalitis	5%	3%	0.94
ICU Admission	2%	2%	0.28
Hospitalized overnight	7%	7%	0.75
Case fatality	0.2%	0%	0.73
Chronic lung disease	8%	4%	0.06
<b>Vaccination Status</b>			
Up-to-date for age	57%	55%	0.55

\* Data completeness for 2-week cough was lower among PCR+ suspect cases compared to confirmed cases, 75% vs. 99%, respectively. Percent completeness for the remaining variables were similar among PCR-positive and confirmed cases and ranged from 88-100%.

### Antibiotic Treatment by Onset Year



## SUMMARY

- Of 309 suspect cases identified in Washington State from 2007-2011, 150 (49%) were associated with a positive pertussis PCR assay.
- PCR-positive suspect & confirmed cases differ markedly in symptoms, but are otherwise similar in age, gender, race and ethnicity, severity of illness, outcome, and up-to-date vaccine status.
- PCR-positive suspect cases were treated significantly earlier with an appropriate antibiotic than confirmed cases, which may have modified cough duration and presence of other case-defining symptoms.
- The current case definition may result in an underestimation of the true burden of pertussis. A new case definition could consider inclusion of PCR-positive cases as "probable cases" when 2-week cough, epidemiologic link, or association with an outbreak are not present.
- Next steps:
  - Evaluate pertussis PCR cycle threshold values by classification method from tests performed at Washington State Public Health Laboratories.
  - Continue to monitor trends in PCR-positive suspect case reports in Washington State.