Pneumococcal vaccine effectiveness against invasive disease among adults 65 years or older

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Background

- **PCV13 efficacy against invasive pneumococcal disease (IPD) demonstrated in a large clinical trial (CAPITA)**
  - 75% efficacy (41, 91%) against PCV13-type IPD among adults 65 years or older
- **Effectiveness of PCV13 alone or PCV13 given in series with PPSV23 in the general population of US adults 65 years or older is not known**
- **Evaluation of the effectiveness is crucial to inform policy decisions**

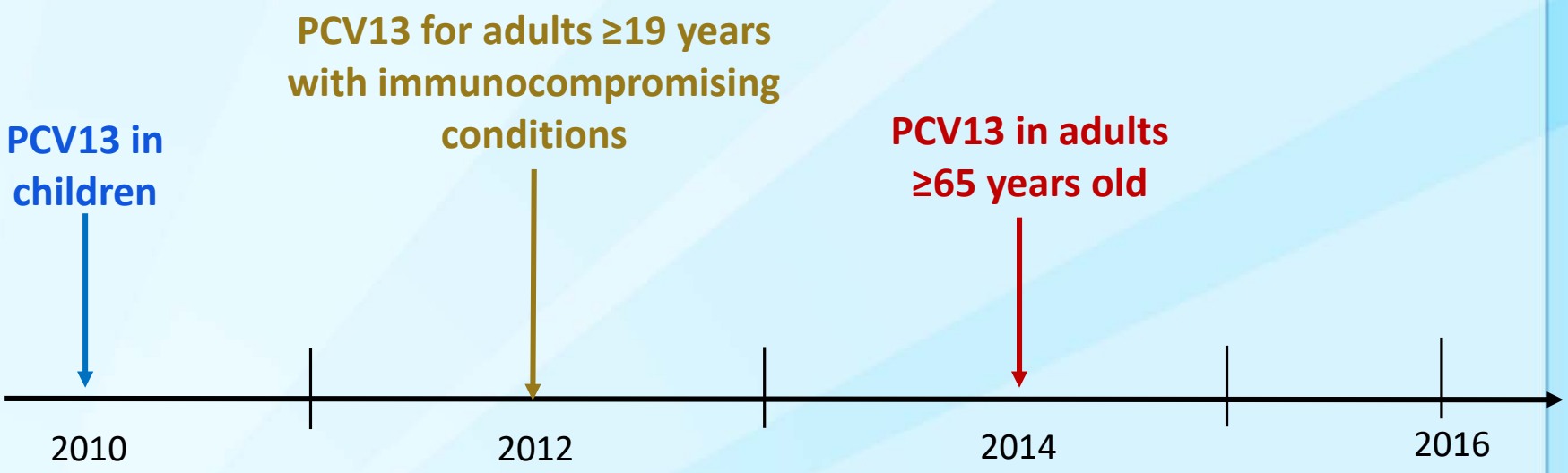
Objectives

- **Evaluate PCV13 effectiveness against PCV13-type IPD among adults ≥ 65 years old**

Study design

- **Two case-control evaluations conducted in parallel**
  - **Study 1:** Selecting population-based controls and vaccination history assessed through provider record review
  - **Study 2:** Selecting controls from Medicare part B beneficiaries and vaccination history through CMS data

PCV13 recommendations over time



Study 1: Methods

- Cases:
  - IPD among adults ≥65 years old identified through Active Bacterial Core surveillance
  - Pneumococcal isolate available for serotyping
- Controls:
  - Identified using the commercial database ReferenceUSAGov (InfoGroup)
  - 4 controls per case matched on age group and zip code

Study 1: Data Collection

- Phone interview for cases/controls:
  - Identify all the medical care encounters in the last 6 years, and their current and past medical care providers
  - Underlying conditions, previous hospitalizations, and household exposures to smoking
- Medical and vaccination history:
  - Contact all providers identified through case/control interview (including pharmacies and vaccine registries)
  - Obtain medical and vaccination history
  - Excluded vaccine doses received within 14 days of case culture date

Study 1: Data Analysis

- Underlying medical conditions:
  - **Chronic medical conditions:** diabetes; chronic heart, lung, or liver disease, alcoholism, cigarette smoking
  - **Immunocompromising conditions:** HIV, hematologic cancer, generalized malignancy, immunosuppressive therapy, sickle cell disease, asplenia
- Vaccine effectiveness estimation:
  - Conditional logistics regression, adjusted for presence of underlying conditions and race
  - VE = one minus odds ratio
  - VE against PCV13-type IPD (primary objective)

Study 1: Characteristics of cases and controls

	Cases N=267		Controls N=1,065	
Case Culture Dates	10/1/15 - to present			
Age, mean (SD)	74.8 (7.9)		74.6 (7.3)	
Race				
White	221	83%	956	90%
Black	25	9%	67	6%
Other	21	8%	42	4%
Sex				
Male	148	55%	601	56%
Female	119	45%	464	44%

Study 1: Characteristics of cases and controls

	Cases N=267		Controls N=1,065	
Case Culture Dates	10/1/15 - to present			
Chronic conditions	222	83%	640	60%
Immunocompromising conditions	159	60%	337	32%
Vaccination Status				
PCV13	60	23%	302	29%
PPSV23	58	22%	206	20%
Both	70	27%	260	25%
Unvaccinated	73	28%	287	27%

Study 1: Distribution of serotypes

	Enrolled Cases N=267		ABCs Cases N=2,226	
Case Culture Dates	10/1/15 - to present		10/1/15 - to present	
Serotype				
3	44	16%	282	13%
Other PCV13 (19A, 7F, 19F)	18	7%	146	7%
PPSV23-unique	94	35%	682	31%
06C	10	4%	73	3%
NVT	101	38%	681	31%
Missing Type			362	16%

Effectiveness by vaccine type and serotype group

	N case-control sets	PCV13 only		Any PCV13	
All IPD	267	**37%**	**(2, 60)**	24%	(-9, 47)
PCV13-type	62	**65%**	**(16, 86)**	**61%**	**(20, 81)**
PCV13-type + 06C	72	**65%**	**(19, 85)**	**54%**	**(12, 76)**
PPSV23-unique types	94	27%	(-48,64)	26%	(-34, 59)
All PPSV23 types	110	**44%**	**(4, 68)**	**40%**	**(6, 62)**
Non-Vaccine types	99	13%	(-90, 60)	-13%	(-121, 42)

Conditional logistic regression
Analyses adjusted for race and presence of underlying medical conditions

Study 2: Methods

- IPD Cases:
  - IPD among adults ≥65 years old identified through Active Bacterial Core surveillance
  - Pneumococcal isolate available for serotyping
  - Linking IPD cases to CMS Medicare part B data based on demographic, geographic, and clinical variables
- Controls:
  - Identified from CMS Medicare part B beneficiaries
  - Controls matched on age group, census tract, and length of enrollment in Medicare part B
  - All eligible controls within census tract of case included in the analyses
- Vaccinations and medical history:
  - Identified from CMS data
  - Excluded doses received within 14 days of case culture date

Study 2: Data Analysis

- Underlying medical conditions:
  - **Chronic medical conditions:** diabetes; chronic heart, lung, or liver disease, alcoholism, cigarette smoking
  - **Immunocompromising conditions:** HIV, hematologic cancer, generalized malignancy, immunosuppressive therapy, sickle cell disease, asplenia
- Vaccine effectiveness estimation:
  - Conditional logistics regression, adjusted for presence of underlying conditions and race
  - VE = one minus odds ratio
  - VE against PCV13-type IPD (primary objective)

Study 2: Characteristics of cases and controls

	Cases N=699		Controls N=10,152	
Case Culture Dates	1/1/15 – 12/31/16			
Age, mean (SD)	78.4 (8.4)		77.9 (8.3)	
Race				
White	587	84%	9,046	89%
Black	85	12%	715	7%
Other	27	4%	391	4%
Sex				
Male	328	47%	4,372	43%
Female	371	53%	5,780	57%

Study 2: Characteristics of cases and controls

	Cases N=699		Controls N=10,152	
Case Culture Dates	1/1/15 – 12/31/16			
Chronic conditions*	614	88%	5,876	58%
Immunocompromising conditions	376	54%	3,198	32%
Vaccination Status				
PCV13	95	14%	1,811	18%
PPSV23	152	22%	2,082	21%
Both	59	8%	790	8%
Unvaccinated	393	56%	5,469	54%

*Diabetes, heart disease, chronic lung disease, alcoholism, smoking

Study 2: Distribution of serotypes

	Enrolled Cases N=699		ABCs Cases N=2,246	
Case Culture Dates	1/1/15 – 12/31/16		1/1/15 – 12/31/16	
Serotype				
3	87	12%	294	13%
Other PCV13 (19A, 7F, 19F)	48	7%	148	7%
PPSV23-unique	215	31%	713	32%
06C	28	4%	87	4%
NVT	249	36%	812	36%
Missing Type	72	10%	279	12%

Effectiveness by vaccine type and serotype group

	N case-control sets	PCV13 only	
All IPD	699	**24%**	**(2, 41)**
PCV13-type	136	36%	(-18, 65)
PCV13-type + 06C	164	**47%**	**(4, 71)**
PPSV23-unique types	214	22%	(-22, 50)
All PPSV23-type	350	26%	(-5, 48)
Non-Vaccine types	247	13%	(-36, 44)

Conditional logistic regression
Analyses adjusted for race and presence of underlying medical conditions

Effectiveness of PCV13 comparing two studies

	ABCs (10/1/15 - to present)			CMS (1/1/2015-12/31/2016)		
	N sets	VE (95%CI)		N sets	VE (95%CI)	
All IPD	267	**37%**	**(2, 60)**	699	**24%**	**(2, 41)**
PCV13-type	62	**65%**	**(16, 86)**	136	36%	(-18, 65)
PCV13-type + 06C	72	**65%**	**(19, 85)**	164	**47%**	**(4, 71)**
PPSV23-unique types	94	27%	(-48,64)	214	22%	(-22, 50)
All PPSV23-type	110	**44%**	**(4, 68)**	350	26%	(-5, 48)
Non-Vaccine types	99	13%	(-90, 60)	247	13%	(-36, 44)

Conditional logistic regression

Analyses adjusted for race and presence of underlying medical conditions

Conclusions

- PCV13 was moderately effective in preventing IPD caused by PCV13-types
  - Study 1: 65% VE (16, 86%)
  - Study 2: 36% VE (-18, 65%)
- VE estimated similar when included type 6C IPD (evidence of cross protection)
- PCV13 not effective against PPSV23-unique and non-vaccine type IPD
- Estimates slightly lower compared to VE from clinical trial of 75% efficacy (95%CI 41, 91%)
- Unable to evaluate VE estimates for PPSV23 or for PCV13 and PPSV23 given in series

Next steps

- Enrollment continues through winter 2017-2018
- VE for PCV13 and PPSV23 given in series
- VE for PPSV23 against PPSV23-type IPD
- Age group-specific VE: 65-75 years vs. 75 years or older

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ABCs sites

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