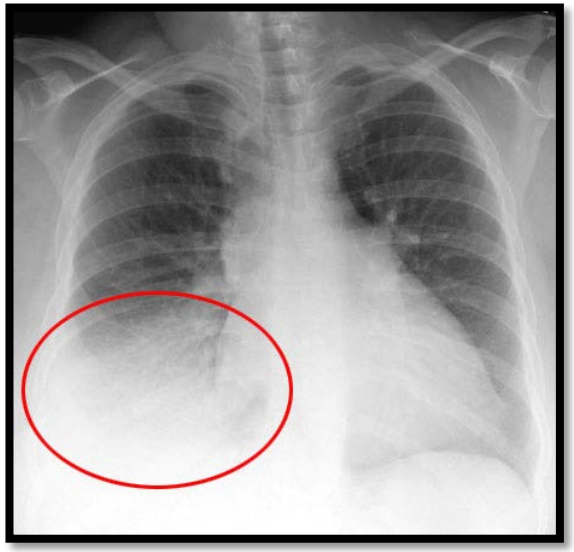
Effectiveness of PCV13 in Adults Hospitalized with Pneumonia Using Centers for Medicare & Medicaid Services Data, 2014-2017



Fernanda Lessa, MD, MPH
Michael (Trey) Spiller, PhD

Project Question

What is the direct effect of new adult PCV13 recommendation on pneumonia hospitalizations among adults ≥ 65 years of age?

METHODS

- **CMS Medicare Part A/B Data**
- **Study Cohort**
  - U.S. Medicare beneficiaries ≥ 65 years old enrolled in part A/B on September 1, 2014
  - After September 1, 2014, only beneficiaries who got part A/B coverage within 6 months of their 65th birthday were included
  - Cohort observed until December 31, 2017
  - Beneficiaries dropped from the cohort before the end of study if they:
    - died
    - moved out of the United States
    - dis-enrolled from part A/B
    - developed the outcome of interest
- **Pneumococcal vaccination categories**
  - PCV13 only, PPSV23 only, both vaccines (PCV13+PPSV23), no pneumococcal vaccine

High Risk Groups

- Four mutually exclusive groups based on underlying conditions

High Risk Group*	Conditions
High risk 1 (HR1) only	*Asplenia, CKD, generalized malignancy, HIV, hematologic malignancies, iatrogenic immunosuppression, immunodeficiencies, nephrotic syndrome, sickle cell anemia, solid organ transplant*
High risk 2 (HR2) only	*Alcoholism, chronic heart disease, chronic liver disease, chronic lung disease**, cigarette smoking, diabetes***
High risk 1 + 2 (Both)	At least one HR1 and one HR2 condition
Low risk	None of the conditions in HR1 or HR2

* Based on https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm
** prevalence of 42% among beneficiaries
Underlying conditions captured using inpatient (IP) and outpatient (OP) hospital facility claims for malignancies and IP+OP+ Physician/supplier part B (PB) for non-cancer conditions

Outcomes of Interest

- **Based on inpatient claims**
- **CAP: Community-Acquired Pneumonia (Griffin et al algorithm*)**
  - Primary diagnosis of pneumonia
  - Primary diagnosis of meningitis, septicemia, empyema, or acute respiratory failure with a pneumonia diagnosis in any secondary position
- **Non-HA CAP: Non-healthcare associated CAP**
  - CAP in a patient without admission to hospital or skilled nursing facility in the prior 30 days and without a prior healthcare-associated pneumonia hospitalization (*SUBSET OF CAP*)
- **Lobar Pneumonia**
  - Inpatient hospital claim with a diagnosis of lobar/pneumococcal pneumonia (ICD9:481/ICD10: J13/J181) in any discharge diagnosis position

* Griffin et al. NEJM. 2013 369:155-63

Statistical Approach

- Discrete time survival model
  - Instantaneous hazard ratio ≡ Incidence rate ratio
- Outcome: hospitalization with outcome of interest occurred in given month (yes/no)
- Generalized estimating equations (GEE) to adjust for correlations
- Incidence rate ratios and 95% confidence intervals
  - Vaccine effectiveness (VE) = (1-IRR)*100

Four Separate Models

- Stratified by influenza season and influenza vaccination status

➢ Influenza season (October-April)
  - Flu vaccinated person-months
  - Flu unvaccinated person-months

➢ Non-influenza season (May-September)
  - Flu vaccinated person-months
  - Flu unvaccinated person-months

Rationale:

a) Biological interaction between flu vaccine and outcome of interest
b) Pneumococcal and influenza vaccines are not independent observations
c) Flu vaccinated individuals ≠ flu unvaccinated individuals*

* Jackson ML Lancet. 2008

Model Adjustment Variables

- Age group (5-year bands)
- High risk condition category
- State
- Race
- Gender
- Hospital visits in prior year
- Outpatient non-ER visits in prior year
- Charlson comorbidity index
- Reason to enter CMS (Age, ESRD, Disabled, other)
- Month of year (e.g., January, February)
- Year
- Interactions: vaccine and age group, vaccine and risk group, age and risk group

Number of Hospitalizations Averted by PCV13

- Estimated the number of hospitalizations for each outcome in the absence of PCV13 based on model results
  - Observed/IRR

- Number of hospitalizations averted
  - Expected – Observed

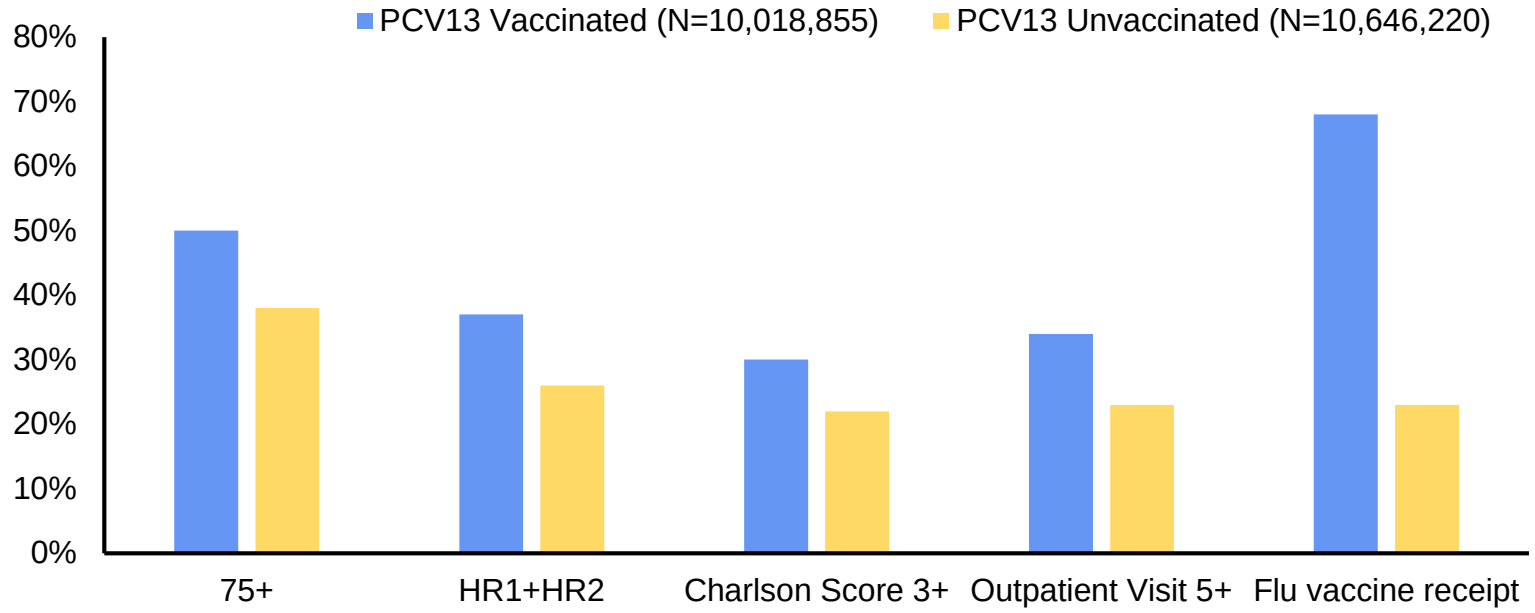
RESULTS

Patients Characteristics at Start and End of Cohort

Characteristics	Sept 2014 N=26,598,266 n (%)	Dec 2017 N=24,121,625 n (%)
65- 74	14,428,556 (54.2)	13,312,649 (55.2)
75-84	8,230,539 (30.9)	7,481,999 (31.0)
85+	3,939,171 (14.8)	3,326,997 (13.8)
Male	11,546,396 (43.4)	10,527,650 (43.6)
PCV13 use	210,567 (0.8)	10,018,855 (41.5)
High Risk 1	1,473,002 (5.5)	1,451,503 (6.0)
High Risk 2	9,967,701 (37.5)	8,521,792 (35.3)
Both HR1 and HR2	8,111,269 (30.5)	7,980,206 (33.1)
Low risk	7,046,294 (26.5)	6,168,124 (25.6)
Charlson score≥3	7,692,162 (28.9)	6,521,748 (27.0)
Outpatient visit ≥5	7,224,776 (27.2)	6,961,482 (28.9)

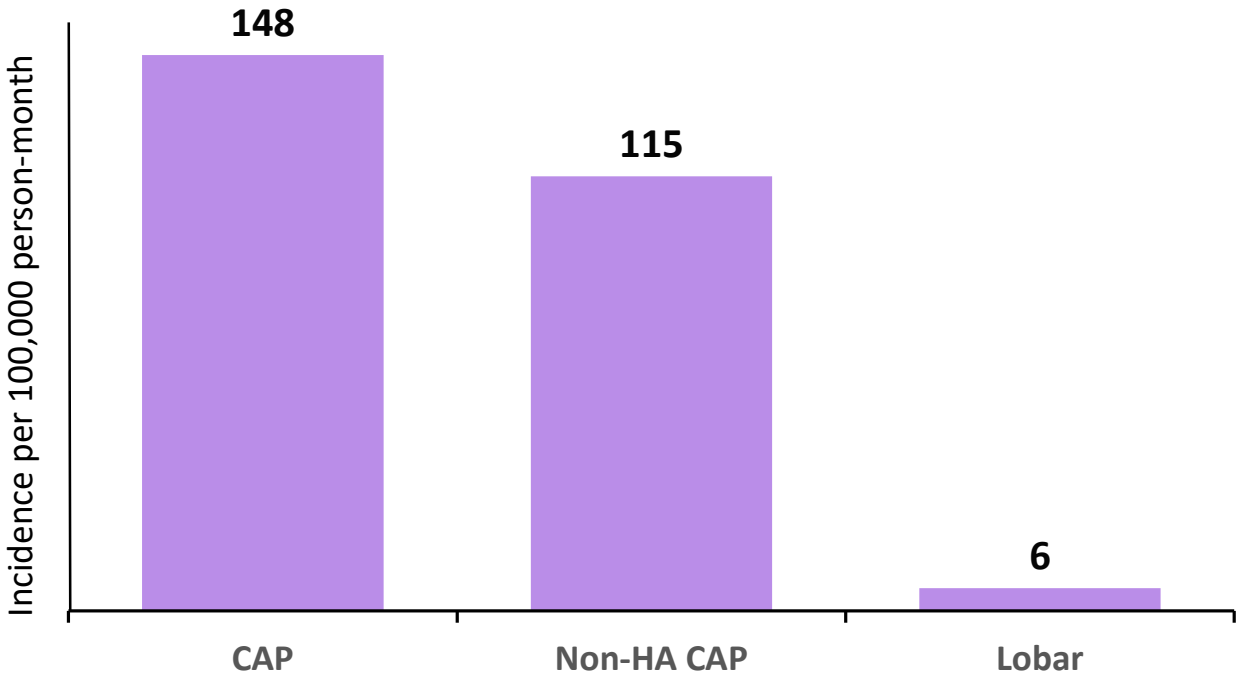
57.6% of 65+ US population

Are there differences in characteristics among PCV13 vaccinated seniors compared to unvaccinated*?

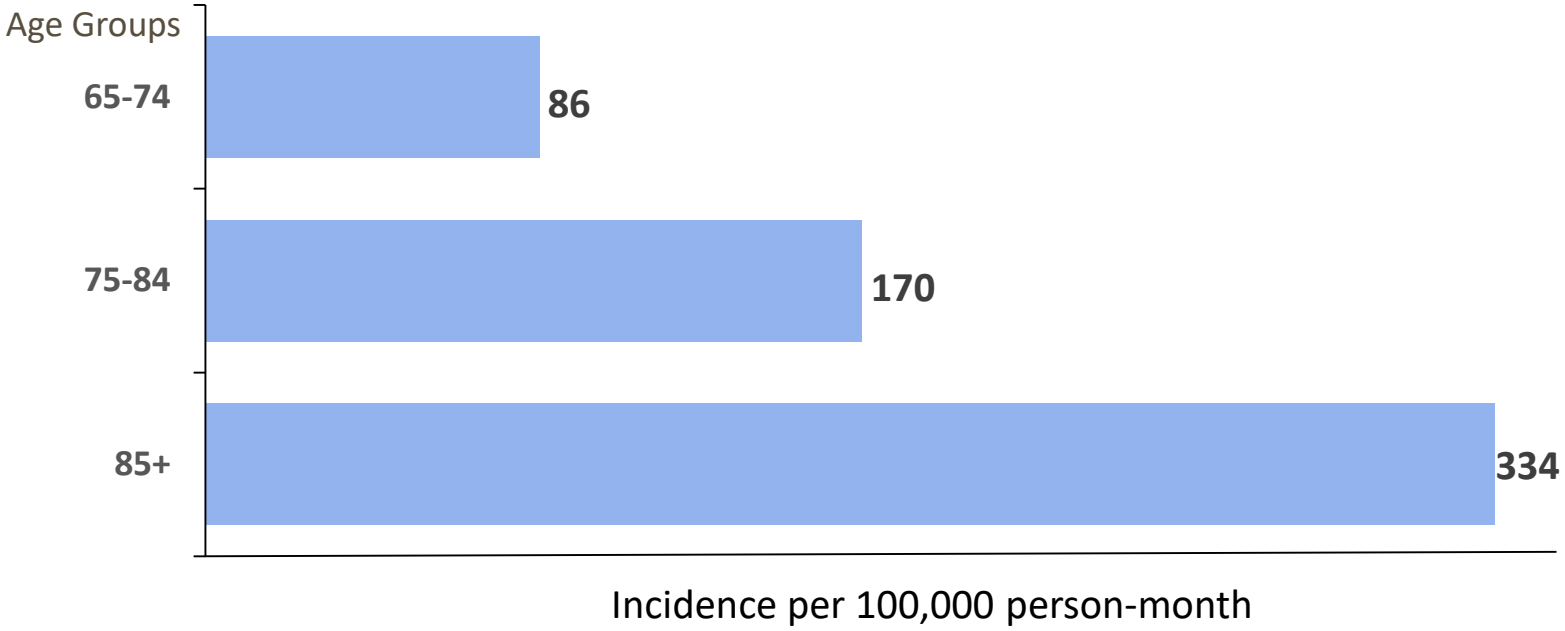


*Based on Dec 2017 data

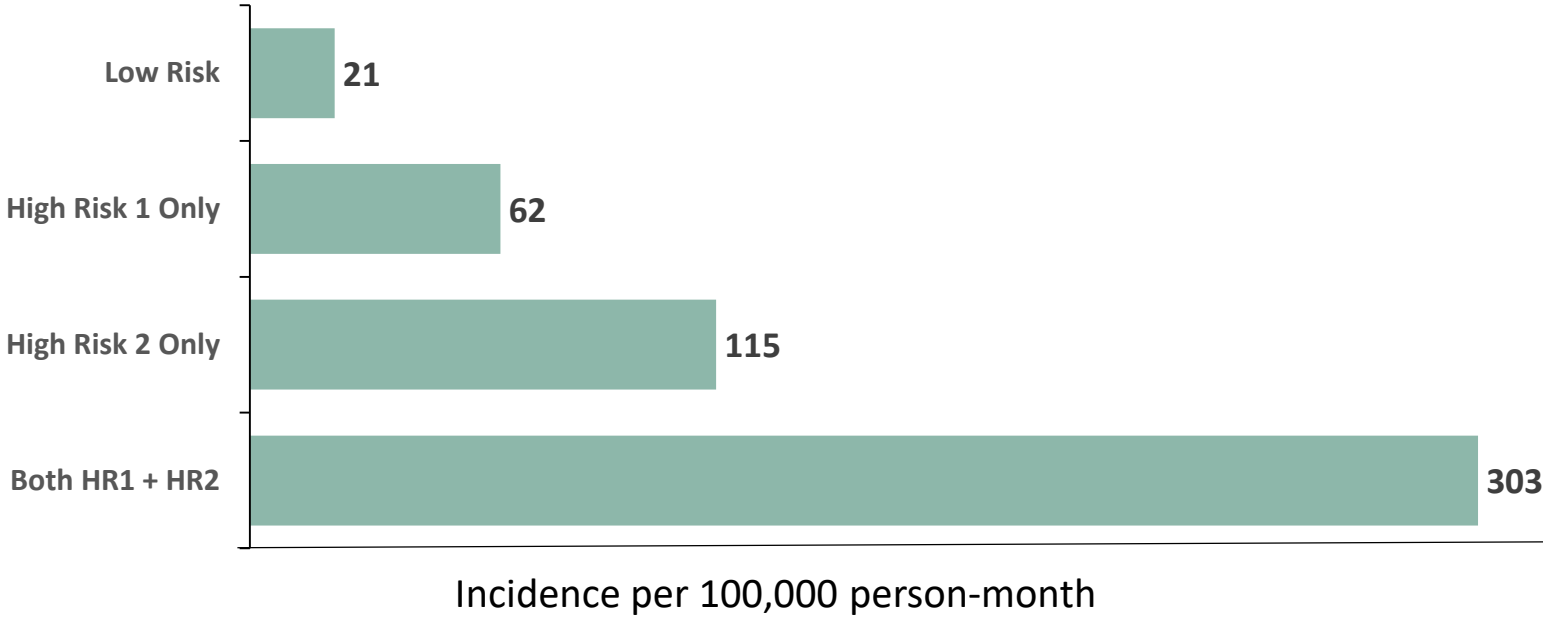
Incidence per 100,000 Beneficiary-Months by Outcome of Interest, Sept 2014-Dec 2017



CAP Incidence per 100,000 Beneficiary-Months by Age Group, 2014-2017



CAP Incidence per 100,000 Beneficiary-Months by Risk Group, 2014-2017



Model Results – PCV13 VE Estimates

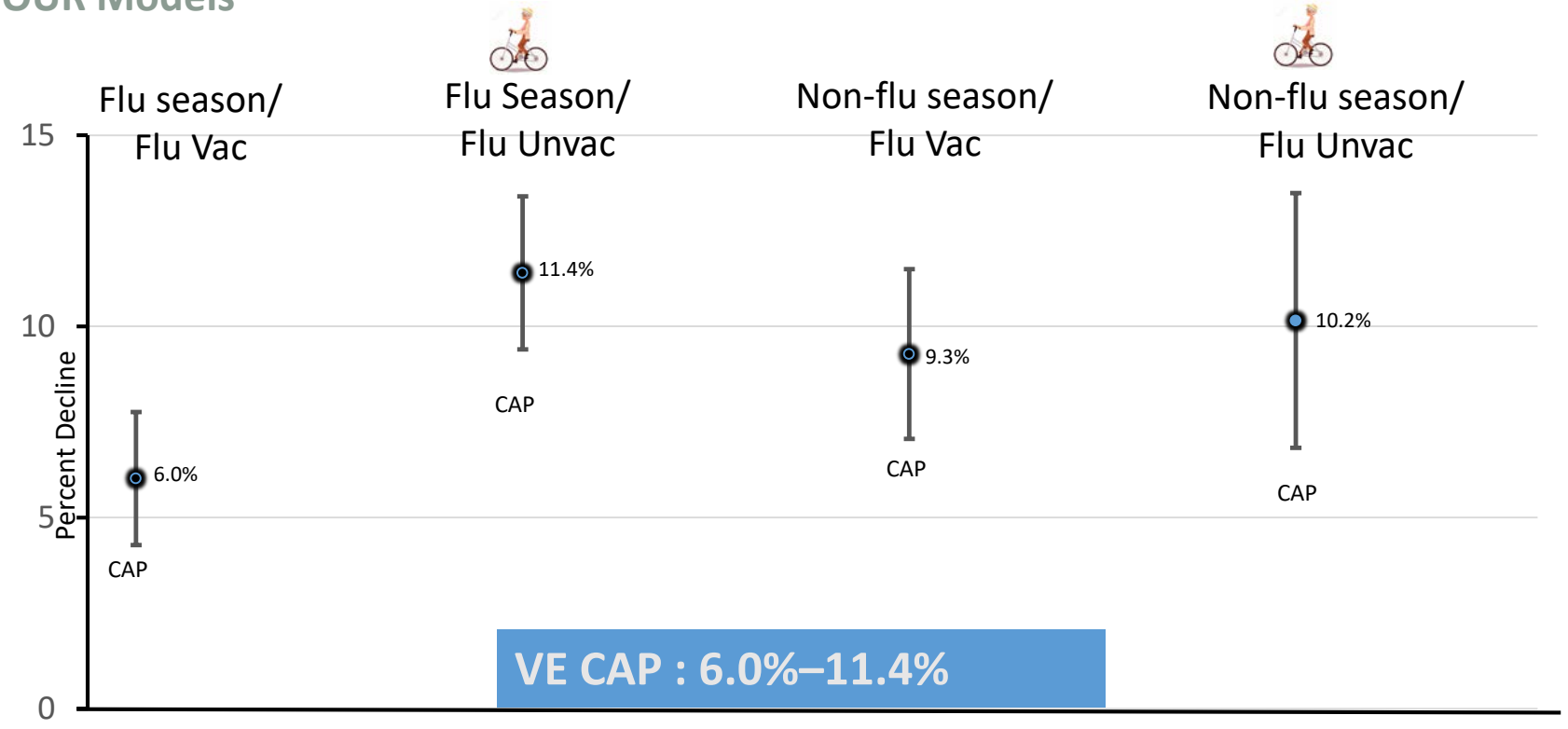
Characteristics of Beneficiaries in Each Model Across Entire Study Period (40 months)

	Flu season/ Flu Vac	Flu Season/ Flu Unvac	Non-flu season/ Flu Vac	Non-flu season/ Flu Unvac
Total person-months	234,757,324	366,014,989	189,023,134	182,313,686
% 65-74 years	48.3%	58.9%	47.8%	62.3%
% 75-84 years	34.9%	28.3%	35.2%	26.2%
% HR1+HR2	37.1%	28.3%	37.7%	26.0%
% Low Risk	19.2%	30.1%	18.6%	33.1%

Healthier elderly

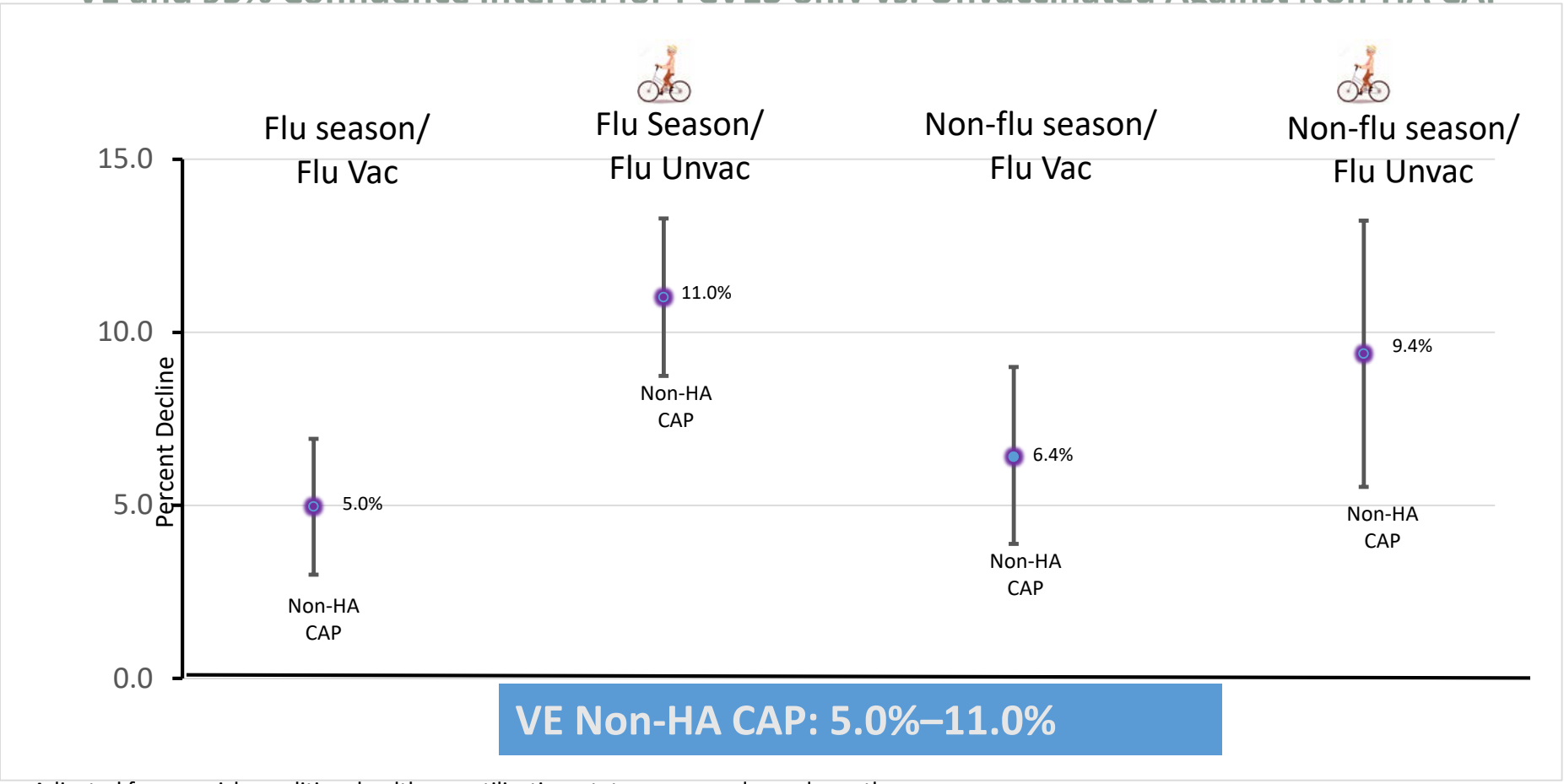
Healthier elderly

VE and 95% Confidence Interval for PCV13 only vs. Unvaccinated Against CAP Across the FOUR Models



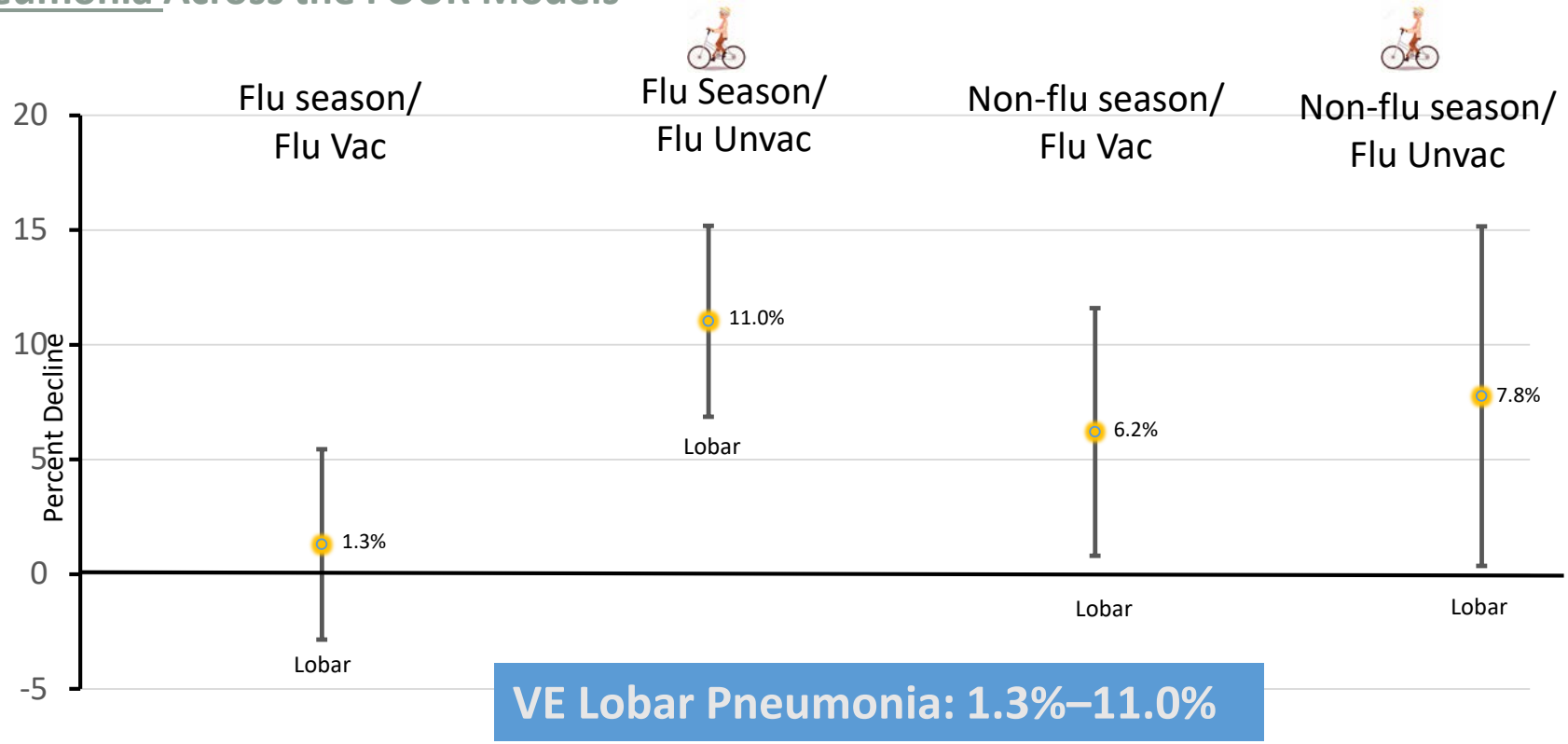
Adjusted for age, risk condition, healthcare utilization, state, race, gender and month

VE and 95% Confidence Interval for PCV13 only vs. Unvaccinated Against Non-HA CAP



Adjusted for age, risk condition, healthcare utilization, state, race, gender and month

VE and 95% Confidence Interval for PCV13 only vs. Unvaccinated Against LOBAR Pneumonia Across the FOUR Models



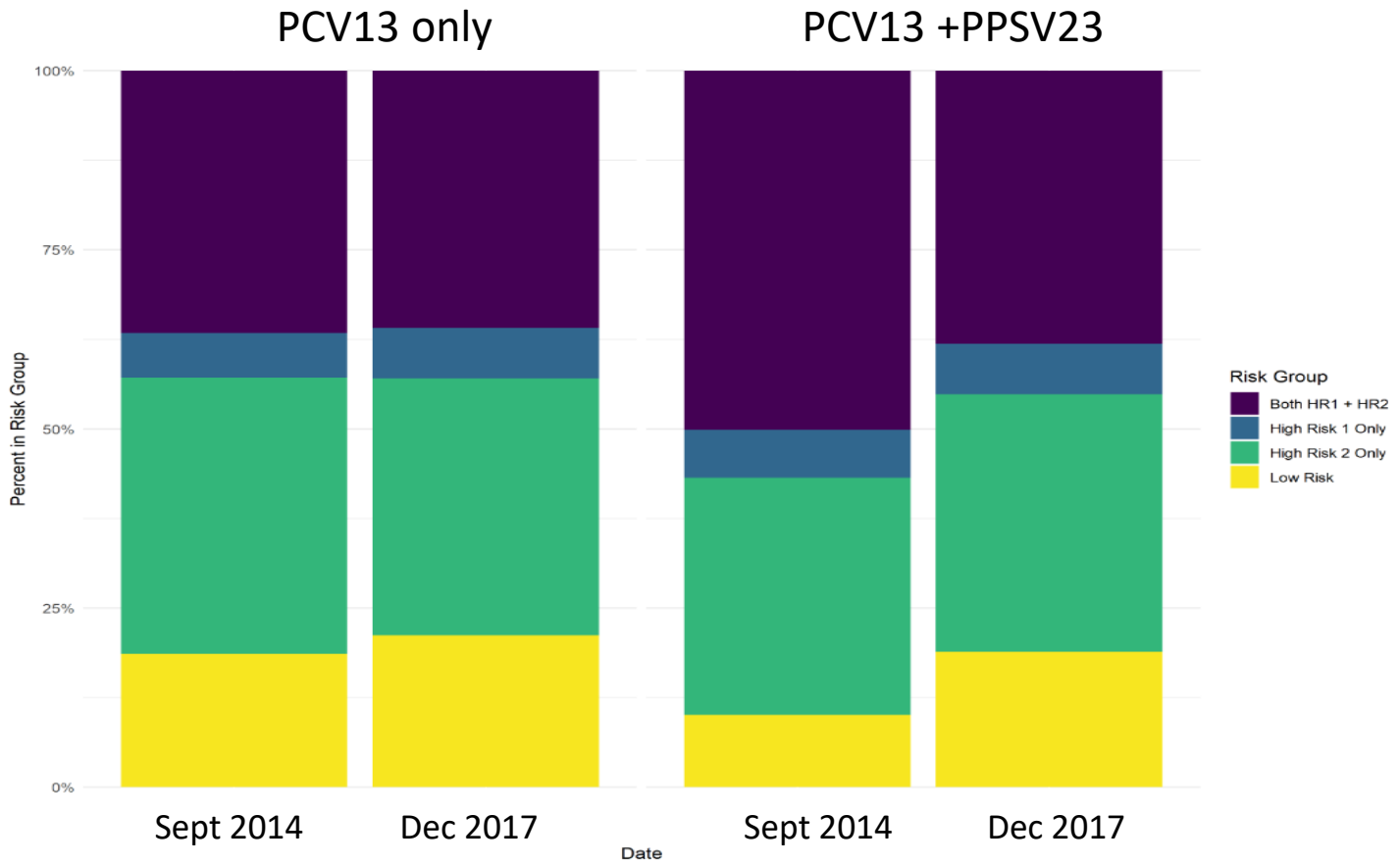
Adjusted for age, risk condition, healthcare utilization, state, race, gender and month

Hospitalizations Averted Due to PCV13 From September 2014 – December 2017 in the Study Cohort

Outcome	Episodes Averted during 40 Months of Study n (95% CI)
CAP	28,600 (21,000–36,600)
Non-HA CAP	18,700 (12,000–25,800)
Lobar	1,100 (190–1900)

18,700
(13,000-25,000)
from Jan-Dec2017

Changes in risk group distribution among PCV13 vaccinated individuals



Limitations

- Residual confounding
  - ICD codes fail to remove all confounding in pharmocoepidemiologic studies among seniors[1-3]
    - Lack of reliable ICD codes to measure functional status
    - Adjustment for chronic diseases and healthcare utilization can reduce biases but do not completely eliminate them
- Misclassification of vaccination status
  - Influenza vaccine: ~30% of individuals with documentation of flu vaccine based on HAIVEN* misclassified as unvaccinated in CMS
  - Pneumococcal vaccine: adequate capture of PCV13 status but ~30% of misclassification of PPSV23 status based on ABCs data

1. Jackson LA, Int J Epidemiol. 2006
2. Nelson JC, J Clin Epidemiol.2009
3. Jackson ML Pharmacoepidemiol Drug Saf. 2011

*US hospitalized Influenza Vaccine Effectiveness Network

Summary

- CAP incidence is highest among individuals >=85 years of age and those with HR1+HR2 conditions
- Individuals who got PCV13 were older, sicker and had more healthcare exposures
- Effectiveness of PCV13 observed against first episode of CAP, non-HA CAP and lobar pneumonia

Conclusion

- PCV13 VE for all-cause CAP: 6.0%–11.4%
  - Similar to *Gessner et al* (clinical trial)*: PCV13 VE of 8.1% (1.0%–14.6%) against all-cause CAP

- ~28,600 CAP hospitalizations averted within 40 months after implementation of new adult PCV13 recommendation
  - 18,700 (65%) prevented in 2017
    - Likely related to the characteristics of the individuals who are receiving the vaccine in more recent years
    - Represents 5.1% of all CAP hospitalizations in 2017 being prevented

*Gessner et al (Pfizer funded). Vaccine 2018

Acknowledgements

- **Acumen Team**
  - Zoe Wu
  - Rongrong Wang
  - Yoganand Chillarige
  - Shruti Parulekar
  - Yuchen Li
  - Liz Wartella
  - Thomas E. MaCurdy
  - Michael Wernecke
  - Robert Warnock
- **CMS**
  - Jeffrey Kelman
  - Steve Chu
- **CDC**
  - Trey Spiller
  - Tamara Pilishvili
  - Nong Shang
  - Cynthia Whitney
  - Almea Matanock
  - Brendan Flannery
  - Elif Alynak
- **Yale**
  - Dan Weinberger
- **Harvard**
  - Marc Lipsitch

THANK YOU!

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov